Cumulative Dissertation

SMARTPHONE APPS: A TECHNICAL APPROACH FOR DEALING WITH BIPOLAR DISORDER?

Submitted by
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Statutory declaration

I hereby declare that this thesis is my own original work and that I have fully acknowledged by name all of those individuals and organisations that have contributed to the research for this thesis. Due acknowledgement has been made in the text to all other material used. Throughout this thesis and in all related publications I followed the "Guidelines of the Medical University of Graz on Good Scientific Practice".

Graz, 6.5.2024

Frederike Fellendorf eh

Disclosure

This cumulative dissertation summarises the following three publications.

All co-authors agree to the inclusion of their published data in the dissertation, and written consent has been obtained for this.

The second and third articles are open-access articles. All journals gave their written approval to distribute the articles in this thesis. Permission to reproduce tables/figures from own publications has been granted.

1. Fellendorf FT[1], Hamm C[1]*, Platzer M[1], Lenger M[1], Dalkner N[1], Bengesser SA[1], Birner A[1], Queissner R[1], Sattler M[2], Pilz R[1], Kapfhammer HP[1], Lackner HK[3], van Poppel M[2], Reininghaus E[1]. Notwendigkeit für Symptom-Monitoring und Frühwarnzeichenerkennung bipolarer Episoden durch eine App? – Ansichten von PatientInnen und Angehörigen zu e-health Bedarf [Symptom Monitoring and Detection of Early Warning Signs in Bipolar Episodes Via App - Views of Patients and Relatives on e-Health Need]. Fortschr Neurol Psychiatr. 2022 Jun;90(6):268-279. German. doi: 10.1055/a-1503-4986.

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Personal motivation

The recurrent course of bipolar disorder presents a significant burden for individuals affected, as well as their relatives, healthcare professionals and the broader healthcare system and economy. The overarching clinical objectives are extending symptom-free euthymic intervals, preventing further affective episodes and promoting well-being, autonomy, self-determination and functionality over the long term. The better the prophylaxis functions, the more illness episodes are prevented, leading to an improved overall illness course. This is particularly significant because severe episodes, especially severe mania, can damage the brain, cognition, and somatic factors. Therefore, investing in robust prophylactic measures mitigates immediate symptoms and safeguards long-term brain and somatic health and overall well-being. This is typically achieved through a multifaceted approach combining psychotropic medication, psychoeducation, and psychotherapy. Early recognition and intervention in the onset of illness episodes are crucial components of this strategy, with a key emphasis on identifying and responding to early warning signs.

From my personal perspective, it is remarkable how much people with bipolar disorder contribute to the course of the disease by accepting it, becoming experts through education, adhering to treatment plans developed collaboratively with healthcare professionals, living a healthy lifestyle with, among others, a structured sleep-wake rhythm, and implementing effective coping strategies in response to early warning signs. These signs can manifest as changes, particularly in sleep patterns and further in activity levels or social interactions.

The ubiquitous presence of smartphones offers a promising avenue for continuous monitoring and timely detection of deviations from baseline functioning. Traditionally, healthcare providers have relied on retrospective data provided by patients or their caregivers. Still, emerging technologies now offer the potential to collect more comprehensive and unbiased data in real-time. My motivation for delving into this innovative field through my thesis stems from a desire to empower individuals with bipolar disorder to integrate disease management into their daily lives.

Working with a start-up company has given me skills in collaborative work, negotiation, legal principles, and contract drafting. Independently planning and executing two studies for this thesis - a questionnaire survey and a medical device study - has equipped me with valuable experience in study design, protocol development, networking, regulatory compliance, patient recruitment, and adherence to good clinical practice guidelines. Furthermore, this endeavour has deepened my statistical skills and reinforced the scientific foundation of my clinical practice as a psychiatrist.

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Abbreviations

AGES	Agentur für Gesundheit und Ernährungssicherheit
App	application
BASG	Bundesamt für Sicherheit im Gesundheitswesen
BD	bipolar disorder
CANMAT	Canadian Network for Mood and Anxiety
CBT	cognitive behaviour therapy
COVID-19	coronavirus disease-19
DALY	disability-adjusted life-year
DSGVO	Datenschutz-Grundverordnung
e-health	electronic-health
EWS	early warning sign
GDPR	General Data Protection Regulation
GPS	global positioning system
HAMD	Hamilton Rating Scale for Depression
HC	healthy control
ICD	International Statistical Classification of Diseases and Related Health Problems
IPAQ	International Physical Activity Questionnaire
m-health	mobile-health
MONARCA	MONitoring, treAtment and pRediCtion of bipolAr Disorder Episodes
PSQI	Pittsburgh Sleeping Questionnaire
RCT	randomised control trial
SARS-CoV-2	severe acute respiratory syndrome coronavirus-2
TAU	treatment as usual
WHO	World Health Organisation
WIFI	wireless fidelity
YMRS	Young Mania Rating Scale

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Abstract in German

Hintergrund: Das frühzeitige Erkennen und Behandeln von Episoden der bipolaren Störung haben einen positiven Einfluss auf die einzelne Krankheitsphase sowie auf den gesamten Verlauf der Erkrankung. Betroffene erleben zu Beginn einer depressiven sowie (hypo) manischen Episode häufig Verhaltensveränderungen, insbesondere im Schlafverhalten. Diese Frühwarnzeichen sind individuell, jedoch bei einer Person meist wiederkehrend ähnlich und werden von den Betroffenen häufig zu spät erkannt. Ein kontinuierliches Monitoring dieser Frühwarnzeichen ist daher essentiell. Hierbei könnte eine technologische Unterstützung durch Smartphone-Apps, insbesondere in persönlichen oder gesellschaftlichen Krisenzeiten wie zum Beispiel während der COVID-19 Pandemie, hilfreich sein.

Ziele: Diese Arbeit untersuchte in drei klinischen Studien, ob Smartphone-Apps eine passende und valide Unterstützung im Frühwarnmanagement des Schlafverhaltens darstellen können. Daher wurde 1. der Wunsch von Betroffenen für solche Apps erhoben, 2. Veränderungen des Schlafverhaltens während der COVID-19 Pandemie untersucht und 3. die Validität der Schlafdaten und Akzeptanz des Produktes *UP!* evaluiert.

Methoden und Ergebnisse: 1. Eine Fragebogenerhebung ergab, dass Menschen mit bipolarer Erkrankung und deren Angehörigen ein Defizit in der rechtzeitigen und vollständigen Frühwarnzeichenerkennung haben und dass Befragte hierfür Apps als sinnvolle Unterstützung betrachten und diese nutzen würden. 2. Eine online Umfrage während des ersten Jahres der COVID-19 Pandemie fand, dass Menschen mit bipolarer Störung in dieser Krisenzeit eine schlechtere Schlafqualität, verlängerte Einschlafzeit und vermehrte Tagesmüdigkeit aufwiesen. 3. Die Software *UP!* mit dem Ziel automatischer Verhaltensmessungen, insbesondere des Schlafs, wurde mit medizinischer Beratung der Spezialambulanz für bipolare Störung von *meemo-tec OG* entwickelt. Eine Pilotstudie zeigte, dass die App im Vergleich zu einem Accelerometer und dem validierten Fragebogen ‚Pittsburgh Sleep Inventory' Einschlaf- und Aufstehzeiten valide misst. Des Weiteren waren die Nutzer*innen mit dem Appdesign zufrieden und hatten keine Bedenken bezüglich der Datensicherheit.

Diskussion: Durch kontinuierliches Monitoring von Verhaltensänderungen als Früherkennung können Betroffene entsprechend früh gegensteuern, wobei ihre Selbstwirksamkeit gestärkt ist. Smartphone-Apps sind weit verbreitet, überall und immer verfügbar und kostengünstig, sodass sie eine gute zusätzliche Behandlungsoption darstellen. Aufgrund der stetigen Entwicklung neuer Produkte, ist es wichtig die einzelnen Produkte gesammelt zu erfassen, sie hinsichtlich Validität, Effektivität, Effizienz und Nebenwirkung zu überprüfen, um schließlich auch mit Apps evidenzbasierte Leitlinien für Patienten*innen und Behandelnde zu schaffen.

Abstract in English

Background: Early detection and treatment of illness episodes of bipolar disorder is desirable as having a positive impact on both individual episodes and the overall course of illness. Frequently, individuals with bipolar disorder experience behavioural changes, particularly in sleep patterns, at the onset of depressive or (hypo)manic episodes. These early warning signs are individualised but often recurrently similar within a person and are frequently recognised too late by those affected. Continuous monitoring of these early warning signs is, therefore, essential. Technological support through smartphone apps, especially in times of personal or societal crisis, such as the COVID-19 pandemic, could be helpful.

Objectives: In three clinical trials, this thesis examined whether smartphone apps could provide suitable and valid support in early warning management of sleep behaviour. Hence, 1. the desire for such apps among affected individuals was assessed, 2. changes in sleep behaviour during the COVID-19 pandemic were investigated, and 3. the validity of sleep data and acceptance of the product *UP!* were evaluated.

Methods and Results: 1. A questionnaire survey of individuals with bipolar disorder and their relatives revealed a deficit in complete early warning sign detection and that those affected consider apps as meaningful support and would utilise them. 2. An online survey during the first year of the COVID-19 pandemic found that individuals with bipolar disorder exhibited poorer sleep quality, prolonged sleep onset latency, and increased daytime sleepiness during this crisis period. 3. The *UP!* software, aimed at automatic behavioural measurements, particularly of sleep, was developed with medical consultation from the outpatient clinic for bipolar disorder by *meemo-tec* OG. A pilot study demonstrated that the app validly measures sleep onset and wake times compared to an accelerometer and the validated questionnaire "Pittsburgh Sleep Inventory." Furthermore, users were satisfied with the app design and had no concerns regarding data security.

Discussion: By continuously monitoring behavioural changes for early detection, affected individuals can intervene early, thereby strengthening their self-efficacy. Smartphone apps are widely available, accessible anytime and anywhere, and cost-effective, making them a valuable additional treatment option. Due to the ongoing development of new products, it is essential to collectively assess individual products and evaluate them in terms of validity, effectiveness, efficiency, and side effects in order to create evidence-based guidelines for patients and healthcare providers.

1. Background

1.1. Bipolar Disorder

Bipolar disorder (BD) is a severe and lifelong mental disorder with recurrent episodes of depression and mania or hypomania, and, in some cases, mixed symptoms [1]. The criteria according to the International Statistical Classification of Diseases and Related Health Problems (ICD)-10 of the World Health Organisation (WHO) [2] are listed in Table 1. In addition to mood and energy levels, sleep is particularly affected. During severe illness episodes, psychotic symptoms may also arise. BD is characterised by at least one depressive and at least one manic (BD 1) or hypomanic (BD 2) episode or by the occurrence of two manic episodes in the whole lifespan [3]. The course differs between individuals, but generally, it is a chronic course with more than two episodes in a lifetime. However, there are also symptom-free episodes, the so-called euthymia.

Table 1. Criteria for depressive, manic, and hypomanic episodes according to the International Statistical Classification of Diseases and Related Health Problems

	Depressive Episode	**Manic episode**	**Hypomanic episode**
Duration	≥ 2 weeks	≥ 7 days (or hospitalization)	≥ 4 days
Main criteria	≥ 2: • depressed mood • loss of joy/ interest • energy reduction	severe elevated or irritable mood	elevated or irritable mood
Other criteria	≥ 2: • low self-confidence • ideas of guilt or worthlessness • concentration difficulties • sleep disturbances • appetite ↓or gain • psychomotor retardation or agitation • hopelessness to suicidal ideation	≥ 3 (or ≥ 4 if irritable mood) + severe dysfunction in professional/social functioning: • ↑ activity or restlessness • logorrhoea • new ideas, racing thoughts • loss of social inhibitions, inappropriate behaviour • ↓ need for sleep • excessive self-confidence, megalomania • ↑ libido • irresponsible, risky behaviour • over-familiarity, ↑confidentiality	≥ 3: + mild dysfunction in professional/social functioning: • ↑ activity or restlessness • talkativeness • concentrations difficulties • ↓ need for sleep • ↑ libido • reckless, irresponsible behaviour • over-familiarity, ↑confidentiality
Severity	Mild: 4-5 symptoms Moderate: 6-7 Severe: ≥ 8		

The lifetime prevalence of BD is approximately 5% [1]. The condition is prevalent worldwide and affects both sexes and all socioeconomic classes equally. BD is a significant challenge for those affected, their relatives, and the entire healthcare system. The disease ranks sixth among all medical illnesses in terms of disability-adjusted life-year (DALYs; [4]). BD impacts patients' daily lives due to illness symptoms, psychosocial issues [5], cognitive dysfunction [6], stigma, and the high prevalence of somatic and psychiatric comorbidities [7]. On a socioeconomic level, the costs for the healthcare system from high numbers of disabilities and hospitalisations are enormous [8].

BD is frequently misidentified or misdiagnosed due to lack of access (rural areas, insufficient number of physicians), lack of perception, lack of knowledge and awareness among those affected, and stigma [1]. Moreover, a misdiagnosis often delays the implementation of appropriate treatment strategies [9].

The aetiology of BD is multifactorial, with genetic, neurobiological processes and psychosocial factors playing a role (vulnerability-stress model; see figure 1). High heritability and biological, especially immunological underpinnings, contribute to varying risks of onset and relapses influenced by stressors and available resources. Chronic stressors such as childhood trauma, mobbing, inadequate support in school or work, and unfavourable relationships can lead to earlier onset. Maintaining factors for affective fluctuations or lack of remission can include unstable sleep-wake rhythms, personality characteristics, overwork, and psychotropic substance abuse. Acute crises or critical life events, such as interpersonal conflicts, health problems, job loss, and even the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic leading to coronavirus disease (COVID)-19 increase the risk of relapse. Therefore, it is important to strengthen resources and recognise and treat early signs of illness, particularly during these crises [10–14].

However, it has not yet been possible to explain why BD manifests differently in symptoms and the course of illness between individuals with BD.

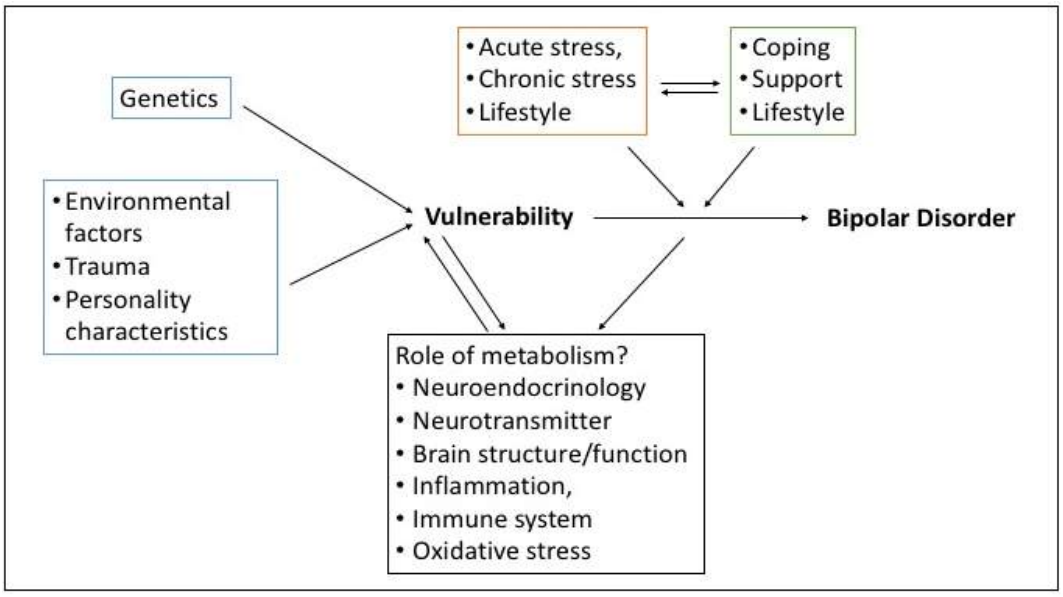

Figure 1. Vulnerability-Stress-Modell of Genesis of Bipolar Disorder

1.1.1. The course of episodes and illness

Untreated, the condition typically leads to recurring episodes, each with potentially severe social and psychological consequences and resulting in neurobiological damage. Moreover, over the long term, untreated illness increases the risk of irreversible cognitive impairments, somatic and psychiatric comorbidities, and suicide attempts [1,15].

Significant intra- and interindividual differences exist in the course and severity of each affective episode [1,16]. Thus far, diagnosis and treatment considerations have primarily relied on clinical phenomenology, whereas objective biomarkers have been the research focus but have not yet been used in clinical practice [17,18].

A higher number of both illness episodes is related to a lower level of global functioning, unhealthy lifestyle, impairment in workability, and poorer treatment response, resulting in an overall worsened course of illness [19].

Early access to appropriate treatment is associated with shorter and milder episodes and more extended remission periods [20,21]. Consequently, early detection and treatment can significantly reduce negative consequences such as social, psychological, and neurotoxic damage, with the latter being particularly significant in mania. Therefore, there must be a particular emphasis on continuous monitoring and education of those affected and their relatives to recognise illness symptoms early and employ appropriate coping strategies.

1.1.2. Early warning signs

Frequently, individuals with BD fail to recognise the beginning of a depressive and (hypo)manic episode in time to intervene effectively. Often, those affected by BD experience characteristic symptoms preceding a full affective episode, known as early warning signs (EWS) [22]. While not all illness episodes are accompanied by EWS, research has demonstrated that the presence of EWS increases the likelihood of depressive and manic episodes onset [23]. EWS can impact mood, thoughts, behaviour, circadian rhythm, body awareness, and social interaction. A literature review encompassing 1809 patients with BD identified various EWS preceding (hypo)manic episodes, including heightened talkativeness, increased activity and energy levels, goal-directed behaviour, racing thoughts, elevated self-esteem, heightened libido, and impulsive spending. Conversely, decreased interest and hypersomnia were identified as EWS preceding depressive episodes, though the study noted low specificity in these findings [24].

Although EWS might differ inter-individually, recurring EWS are often observed within the same person [25]. An investigation by Perich and colleagues found that detecting EWS of both polarities is more common than identifying only one, indicating that individuals who recognise EWS in one polarity often have better recognition of EWS in the second polarity as well. Furthermore, EWS recognition tends to be associated with younger age, a history of more depressive episodes, and fewer hospitalisations [26]. Some EWS may be quite specific, such as changes in perception of sounds and colours or a sudden inclination toward certain types of music [27]. Clinical observations suggest that EWS often manifest as alterations in physical activity and communication patterns, changes in smoking and eating habits, and disruptions in the sleep-wake cycle.

Treatment strategies incorporating EWS awareness and appropriate consideration have been shown to be more effective than relying solely on psychopharmacological interventions [27]. Consequently, relapse rates, hospitalisation, and overall functioning are affected positively [28]. Given that the trajectory of an episode can be significantly influenced during this early phase, a key focus in BD management is the timely detection of these EWS [1].

Sleep disturbances may serve as important EWS [29]. Whereas the need to sleep is reduced at the beginning of (hypo)manic episodes, depression can lead to problems in falling asleep, interrupted sleep patterns, excessive sleep, or insomnia. An unbalanced sleep-wake rhythm, in turn, can detrimentally impact the course of the acute illness episode [30].

Additionally, the individual extent of physical activity and its fluctuation could indicate an early stage of an illness episode. Increased activity often signals the onset of (hypo)manic symptoms, while reduced activity is an EWS of depressive episodes. By being aware of personal activity patterns, individuals may enhance their motivation for managing shifts. Engaging in regular moderate physical activity during the initial stages of depressive symptoms has been shown to impact the course of the episode positively and, furthermore, improve associated metabolic conditions positively. Probably, at the beginning of a (hypo)manic episode, a targeted moderate activity program can result in a better course of this episode. Conversely, disruptions in the sleep-wake cycle and activity patterns can complicate the course of the episode [31].

Changes in communication behaviours, such as personal conversations, phone calls, text messages, and social media activity, may also occur at the onset of a BD episode. However, it remains uncertain whether deliberately altering such behaviours can influence the course of the illness episode.

1.1.3. Treatment

The course of BD is favourably affected by a combination treatment approach comprising medication, psychotherapy, and psychoeducation, sometimes supported by electronic health (e-health) methods [32]. Moreover, the presence of a robust support system consisting of family, friends, healthcare professionals, and therapists plays a crucial role in influencing the progression of the illness [33]. During periods of euthymia, individuals may opt for low-threshold outpatient treatment, while moderate to severe episodes necessitate inpatient care [20]. Various psychiatric therapeutic options, including occupational therapy, sociotherapy, light therapy, electroconvulsive therapy, dietary modifications, or exercise, can be employed as needed.

In addition to striving for optimal quality of life, a primary objective is to minimise the frequency and severity of episodes by preventing or promptly recognising their onset before they escalate into significant episodes. Consequently, a key challenge in the multimodal treatment of BD lies in the continuous monitoring and detection of EWS, enabling individuals to remain attuned to their thoughts and feelings and react appropriately and adaptively to changes [34].

Patients and their relatives should undergo education to recognise their characteristic EWS and become acquainted with effective coping strategies [1]. In general, early interventions appear to yield more favourable outcomes for (hypo)manic episodes compared to depressive episodes [35]. Medication requirements are often substantially lower when administered during this pre-severe

symptomatic phase than during a full-blown episode. Consequently, identifying EWS holds the potential to prevent relapses, hospitalisations, and further morbidity.

Drug therapy modulates biological processes, especially certain neurotransmitter systems. Effective mood stabiliser treatment is essential in managing BD, as regular intake significantly diminishes both the frequency and severity of episodes. The gold standard is lithium [36]. Alternatively, specific anticonvulsants (valproic acid, lamotrigine, carbamazepine) or certain second-generation antipsychotics (quetiapine, olanzapine, asenapine, and aripiprazole) are used [32]. Antidepressants with a low risk of inducing mood switches are also prescribed during acute depressive episodes. However, many individuals with BD experience more frequent and protracted depressive episodes with only partial response to pharmacological therapy, underscoring the importance of personalised pharmacological approaches and exploration of other treatment modalities [37]. Increased dosages of lithium, valproic acid, and specific neuroleptics exhibit antimanic effects.

Psychotherapy aims to foster stable self-esteem, relaxation, improved well-being, enhanced quality of life, autonomy, a heightened awareness of EWS and illness symptomatology, reduced disease-specific symptoms, improved sleep hygiene, increased understanding of the illness, and relapse prevention. Life experiences, upbringing, socialisation, and psychosocial factors often play a pivotal role in shaping self-concepts and coping mechanisms, thus influencing the likelihood of developing a disease episode. Consequently, psychotherapy directly impacts the occurrence, frequency, and severity of subsequent illness episodes [20]. While no single psychotherapy approach has demonstrated superiority in effectiveness, cognitive behaviour therapy (CBT) [38], psychoeducative therapy [39], family-focused therapy [40], and interpersonal and social rhythm therapy [41] have all shown positive effects in relapse prevention.

The primary objective of psychoeducation is to provide comprehensive knowledge about the symptoms, course and progression, management, and treatment of the disease. According to the consensus-based German *S3*- and the *Canadian Network for Mood and Anxiety* (CANMAT) guidelines, psychoeducational therapy generally results in improved clinical outcomes, particularly through enhanced symptom monitoring and EWS detection [20,22,32,42]. Psychoeducation has been shown to impact the frequency and severity of illness episodes positively. Additionally, it enhances treatment adherence, reduces the reliance on psychotropic medications, and encourages healthy lifestyle choices by addressing sleep patterns, physical activity, and dietary habits [43]. Patients who receive psychoeducation demonstrate higher rates of scheduled

outpatient appointments, fewer emergency consultations, increased participation in self-funded psychotherapy, better medication compliance, and reduced hospitalisations [44].

In 2017, a study revealed that 81% of surveyed individuals with BD utilised the internet to educate themselves about the disorder. However, two-thirds of these patients did not discuss their findings, particularly regarding pharmacological issues, with their physicians [45]. This underscores the need for reliable online sources, including websites and app features, containing evidence-based, standardised psychoeducational content that physicians can recommend with confidence.

Participants in psychoeducation programs are educated on various aspects of BD, including symptomatology, aetiology, illness course, physical and mental health comorbidities, and available treatment modalities. They are also instructed on self-monitoring techniques to observe mood fluctuations, daily activities, life events, and sleep-wake cycles. This enables them to recognise connections between mood changes and their behaviour, medication adherence, social interactions, and sleep patterns. One key component is the identification of individual EWS [42].

Awareness of their EWS empowers patients to distinguish between common fluctuations and significant indicators of impending episodes. Consequently, this enables patients to address their health proactively. At times, consulting a healthcare professional may be necessary for a thorough assessment and, if warranted, medication adjustments. Furthermore, when deterioration occurs amidst psychosocial stressors, psychotherapeutic interventions can provide valuable support. In both situations, establishing a trusting relationship with the physician and therapist facilitates quicker access to assistance.

Clinical experiences showed, that in the initial stages, patients often can self-manage. For instance, moderate exercise can benefit when energy levels are high. If excessive alcohol consumption serves as a trigger for manic episodes, it may be prudent to steer clear of environments where alcohol is readily available and to eliminate all alcohol from the home environment. Similarly, employing learned relaxation techniques can aid in combating rumination and promoting better sleep. Setting specific time limits for Internet usage can be an effective tactic to address a surge in social media use. While various methods exist to mitigate the onset of episodes, it's crucial to tailor each approach to the individual's unique needs.

Involving family or close friends can also be helpful [46]. When they are informed about the illness and potential EWS, they can play a vital role in recognising and addressing them. Hence, it is

beneficial to develop concrete strategies for managing each EWS, ideally documented in written form as a contract with relatives.

To sum up, all of these measures require knowing and recognising EWS and learning effective counter-strategies. With well-established contingency plans, patients can reduce their reliance on physicians and therapists.

However, current methods for recording EWS and behaviours are primarily retrospective, relying on oral explorations, questionnaires, life charts, mood graphs, and behaviour diaries [47]. It was found that although well-educated patients acknowledge the importance and efficacy of monitoring, however, the daily completion of mood diaries can pose a burden [48]. Additionally, there's a tendency to recall positive events more accurately, and the interpretation of past events, emotions, and moods can be influenced by current mood [49].

Clinical research also requires valid, objective data on behavioural patterns collected daily over an extended period [50].

Thus, the existing approaches in clinical practice and long-term studies appear inadequate. In conclusion, there is a need for faster, more objective, individualised, and precise evaluation of behaviour patterns [51].

1.2. E-health

Numerous e-health products have been developed in recent years, driven by technological advancements. By 2023, approximately 5.4 billion people worldwide had internet access [52]. In 2021, 60% of the adult Austrian population reported using their internet access to research health-related issues [53]. The SARS-CoV-2 pandemic notably increased the adoption of digital health tools, as indicated by the Digital Health Index [53]. However, it was found that the population's acceptance is crucial for implementing e-health interventions [53].

E-health solutions offer accessibility to a wide range of users, are cost-effective and time-efficient, and empower individuals to take charge of their health [54,55]. Numerous e-health products have been developed, including those tailored to German-speaking regions, aimed at supporting health promotion and disease prevention through screening, monitoring, and therapy. Internet-enabled mobile phones (smartphones) serve as the primary form of digital communication for many people. Therefore, new avenues have emerged for disease research and treatment.

1.2.1. Applications for smartphones

One major domain of e-mental health is mobile health (m-health), a concept defined by the WHO as "…medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants, and other wireless devices" [55]. Applications (apps) designed for various devices, primarily smartphones, are key components of m-health. Notably, two-thirds of the Austrian population cannot envision life without a mobile phone [56]. Given their near-ubiquitous presence globally, mobile phones offer an excellent platform for continuous health data recording and collection [57].

There are three primary categories of apps: *Native apps* store data on the device and can be used offline. *Web apps* run in mobile device browsers and desktop operating systems with limited access to hardware. *Hybrid app*s combine features of both native and web apps [58–60].

At the beginning of 2021, 3.48 million apps could be found in the Android app store, and more than 2.22 million apps were found in the Apple app store [61]. Over 300,000 apps were available for download in the categories "Health & Fitness" and "Medicine" in 2017 [62]. Interestingly, while the number of health apps available for download has increased, actual downloads have not proportionately risen. According to the same Austrian report, around one-fifth of smartphone users utilise health-related apps, with younger individuals, higher education levels, and elevated social status correlating with greater usage. However, only about 30% of users continue to use health-related apps for 90 days or longer [62].

Given that many individuals carry their mobile phones with them at all times, utilising these devices for data collection offers an opportunity to gather both active and passive data continuously [63]. M-health enables symptom monitoring through user input of symptoms, emotions, or behaviours. Additionally, apps can assess and process data by various smartphone features such as wireless fidelity (WIFI), accelerometer, global positioning system (GPS), phone and text frequency, camera and speakers with speech recognition [64–66]. Consequently, behaviours like sleep patterns, physical activity, work and vacation times, as well as digital communication habits, including call and message frequency and app usage, can be objectively evaluated as individual patient health data [67]. Some apps can also interface with external sensors to measure physiological parameters such as heart rate, temperature, or blood pressure. Additionally, physiological conditions can be assessed through activity data calculations [68]. The app system can then

provide instant interpretation and statistical analysis of the collected data, ultimately enabling more personalised diagnostics and interventions.

1.2.2. Apps and behaviour tracking

Bennett and colleagues discovered that utilising smartphone-based accelerometer data enhanced the predictive capabilities of machine learning models for assessing the course of BD [69]. Furthermore, geolocation data, including visited locations, duration of stay, and travel distances, demonstrated a potential for continuous monitoring [70].

Sleep duration and interruptions can be measured using light sensors and smartphone activity-tracking features. An investigation by Ciman and Wac demonstrated that smartphone-based estimation of sleep duration is nearly as accurate as that of a smartwatch [71]. A review by Shin and colleagues presented that using smartphone-based interventions positively impacted sleep disorders and overall sleep quality in 14 out of 16 studies [72].

Physical activity monitoring relies on sensors such as accelerometers, step counters, GPS, and WIFI connectivity [68]. Wahle and colleagues showed correlations between social and physical behaviour measured with smartphone sensors and subjective data. Moreover, periodic movements and location tracking measured via GPS can be used to calculate the spatial extent of areas such as homes and workplaces. Discrepancies in these measurements could indicate psychomotor dysregulations evident in accelerometer data [73].

In their project, Naslund and colleagues [74] found that people with severe mental disorders expressed satisfaction using popular apps measuring physical activity like *FitBit, Zip, FuelBand* and *Nike Inc*. They found high feasibility rates ranging from 89% to 100%, along with similarly high levels of acceptability.

Specially designed microphones are capable of monitoring the pitch and volume of speech; however, the majority of systems lack the capability to analyse the actual content of spoken words [68]. Additionally, data such as the frequency and duration of telephone calls and the usage of communication platforms like messaging apps (e.g., WhatsApp) can be measured. GPS tracking can further be employed to analyse overall social activity patterns.

1.2.3. E-health and mental disorders

There has been an explosion of new e-health products offering free or paid access to mental health resources. Notably, meta-analyses give hints that app interventions can be beneficial in alleviating symptoms associated with depression, mania, and both positive and negative symptoms of schizophrenia. Particularly, products incorporating feedback, notifications, and data tracking features demonstrate even greater efficacy [75]. In mental disorders characterised by episodic courses such as BD, unipolar depressive disorder, and anxiety disorders, interventions can also yield beneficial outcomes on the chronic trajectory [67,76].

As early as 2015, a review found evidence from 29 publications supported the efficacy of internet-based psychological interventions [77]. The possibilities of e-health in psychiatry are far-reaching and various. Numerous diagnostic tools and freely accessible questionnaires are abundant on the internet, with some offering immediate computer-generated evaluations and feedback, while others require evaluation by a trained psychologist with feedback delivered online.

Furthermore, psychotherapies, particularly CBT, are increasingly available in internet-based formats, ranging from fully-automated programs to live video therapy sessions. Additionally, there are resources and guidelines for relaxation and physical activity exercises, some of which are supported by therapists and technicians in the background. Certain tools can monitor mood states and symptoms over extended periods.

Even if not scientifically proven, there are casuistically indications that e-health in general and apps in particular can be effective, feasible, and accepted by individuals with mental disorders. A recent literature review has identified that technologies such as mobile apps are gaining increasing importance in detecting prodromal relapses [78]. Increased engagement in self-management activities, such as regular physical activity and maintaining a balanced sleep-wake rhythm, has been associated with positive impacts on these behaviours [79], potentially reducing depressive symptoms [80]. Palmius and colleagues observed an association between geographic movements tracked via mobile phones and depressive symptoms in individuals with BD [81].

There is evidence that mobile phone-delivered interactive psychoeducation interventions are as effective as group interventions [82], and internet-based CBT can be as efficient as face-to-face therapy [83,84]. Additionally, Ben-Zeev and colleagues found that individuals with severe mental disorders were more likely to engage with and remain in smartphone-delivered therapy compared to clinical group interventions [83]. In contrast, some studies report inconsistent results, and there

remains limited understanding regarding specific indications and disorders [85]. Apolinario-Hagen and colleagues [86] found negative or ambivalent perceptions among the general population of internet-based psychotherapies in Germany. However, many respondents were unaware of existing tools and expressed a desire for improvements in the healthcare system.

1.3. E-health, m-health and bipolar disorder

Bauer and colleagues [87] demonstrated that individuals with BD often use the internet for self-education regarding their disease. Most e-health products designed especially for BD treatment provide psychoeducational content, yielding outcomes comparable to other psychoeducation methods [88–90]. Products can also facilitate symptom monitoring. For example, Bopp and colleagues used smartphones as digital diagnostic tools, with participants with BD reporting symptoms over a two-year period. Comparable ratings to standard symptomatology were observed [91]. A German and English version of the Personal Life-Chart App is deemed comparable to paper-based mood ratings and functional impairment assessments, thus offering a valid tool for recognising manic and depressive symptoms [92]. Furthermore, patients may accept online symptom monitoring more, as evidenced by Lieberman and colleagues' study comparing paper-pencil and online versions of the National Institute of Mental Health (NIMH) Life Chart Method-Self Rating. The online tool was utilised twice as often and yielded more complete data [93]. Such products serve purposes in self-observation, self-management, and research [50].

In a pilot study, Abdullah and colleagues demonstrated the validity of measuring data using an accelerometer, microphone, and location analyses to assess participants' social rhythms in seven patients with BD [64]. Tseng and colleagues identified correlations between self-reported mood, self-reported sleep, and GPS-tracked physical activity in 159 BD outpatients [94].

A not-published systematic search in 2019 conducted by the author of this thesis found 56 smartphone apps related to diagnostics or treatment for affective disorders in the Google Play Store and the IOS iTunes. These apps offered features such as mindfulness exercises, mood graphs, CBT approaches, and psychoeducation. However, descriptions of the products varied significantly, making comparisons challenging. The purposes were described as symptom relief (e.g. stress, depression and anxiety), general improved mental health status, relaxation and education about mental disorders.

Studies investigating individuals with mental disorders in general showed high acceptance and usage of the applications, with smartphone ownership ranging from 70 to 80% [95,96]. In 2014, 70% of 320 individuals with mental disorders expressed interest in using their smartphone for symptom monitoring [95]. In contrast, notably, a review found that only 0.5-28.6% of participants with depression or anxiety continued using unique apps after six weeks [97].

BD cohorts have generally demonstrated a positive attitude towards assistance tools and apps [98]. A recent survey of 919 individuals with BD revealed that 41.6% utilised apps related to mood and/or sleep, although only a small number reported access to apps developed explicitly for BD [99]. In a study of 89 individuals with BD, 40% used apps to manage some BD symptoms, and 79% of the participants reported desiring to use specific tools for BD [96].

1.3.1. Scientific research on mental m-health

Little scientific research has been done on the positive and negative effects of internet—and smartphone-based psychotherapeutic tools to date.

In 2015, Nicholas and colleagues reviewed Australian app stores focusing on apps for BD. They found very little information about privacy policy and sources and a significant lack of best-practice guidelines for users [57], which was confirmed by the authors' unpublished search in 2019. Only nine of the identified apps in the German language were supported by scientific research or federal authorities.

Similar results were found in the USA in 2020, where only one of the top 100 apps for BD had been evaluated for effectiveness, and 32 apps lacked a privacy policy [100]. As technology development is speedy and relatively easy from a technical point of view [63], the results of this investigation are presumably outdated. Even in 2016, it was reported that approximately 50% of apps related to depression, BD, and suicide changed within four months, with an app being removed from app stores every 2.9 days [101].

Moreover, most empirically evaluated products are not freely available [102], resulting in very few validated products for those affected. While individuals with mental illnesses use some products lacking medical evidence, others have casuistically shown to be beneficial to professionals but have not undergone clinical trials.

Despite the potential advantages of innovative products as add-on or self-contained therapies, the empirical basis thus far is insufficient. Given the pursuit of evidence-based medicine, the field of e-health remains a significant area for future research.

Furthermore, individuals are anticipated to increasingly inquire with their physicians about the use of and differences between apps. Ideally, doctors and therapists should be capable of assessing and classifying the medical quality of health-related apps, both non-medical devices and certified medical devices. However, this task is challenging due to the immense number of available apps.

A survey indicated that mental health care professionals are generally positive about integrating apps into mental health treatment. However, varying perspectives and usage in daily clinical practice result from differences in technology handling and knowledge of various m-health products [80]. Another study found that approximately half of healthcare professionals do not discuss and recommend apps to their patients with BD due to knowledge gaps about products and beliefs that patients are uninterested in BD-related apps [103].

Therefore, more research is needed on the desire for technological support in the form of apps, as well as on the validation, effectiveness, and efficiency of specific products.

1.4. Aims of the thesis and research questions

To date, the treatment of BD dramatically relies on patients' retrospective self-reporting. Continuous tracking of various behaviours, particularly sleep alterations via apps, could provide individuals with BD with valuable insights into their behaviour patterns [94]. This could lead to quicker and more individualised detection of changes in mood, symptoms, and behaviour, facilitating faster and more specific reactive interventions and thereby increasing individuals' self-efficacy [104]. Improvements in sleep, social, and activity patterns could also lead to better outcomes [105].

This thesis aims to investigate the potential of apps as an innovative, appropriate assistance approach in detecting changes in sleep behaviour for enhanced EWS management. Therefore, it assesses the demand for apps in the treatment of BD, specifically focusing on the perceived need for tracking sleep behaviour. Moreover, it investigates alterations in sleep patterns and the need for novel treatment modalities following a critical life event, using the COVID-19 pandemic as an illustrative example. Furthermore, it validates sleep data collected from patients with BD using the *UP!* product.

This thesis comprises three publications of three clinical trials, whereas methodologies and findings are elaborated upon within the manuscripts. The Ethics Committee of the Medical University of Graz, Austria, approved all studies (EK numbers: 28-260 ex 15/16; 29-290 ex 16/17; 25–335 ex 12/13) in accordance with the current revision of the Helsinki Declaration, the ICH Guideline for good clinical practice (GCP), and the current regulations.

1.4.1. Patients desire for app use regarding early warning sign recognition

Given the lack of conclusive evidence regarding the receptivity of individuals with BD and their relatives towards technological aids in managing the condition, a questionnaire study was undertaken. This study involved 51 individuals diagnosed with BD and 28 relatives of BD patients, focusing on their smartphone usage patterns. The participants with BD were either receiving inpatient or outpatient care at the specialised outpatient centre for BD within the Department of Psychiatry and Psychotherapeutic Medicine at the Medical University Graz.

The study pursued several objectives. Firstly, it aimed to determine whether the participants deemed the existing strategies for identifying EWS adequate. Secondly, the study investigated smartphone ownership among participants and their usage habits (e.g., ownership of paid apps, frequency of mobile phone usage, and whether digital response times varied with mood changes, categorised by depression/(hypo)mania as yes, shortened; yes, prolonged; or no). Thirdly, the study assessed participants' interest in and willingness to use an app designed to alert them to mood and activity changes, as well as an app specifically developed to support BD treatment.

1.4.2. Sleep following a critical life event

During the COVID-19 pandemic, as an example of a critical life event characterised by lockdowns and measures for social distancing, physical contact between patients and healthcare professionals had to be restricted. In such times, it would be beneficial to have alternative therapy options to face-to-face interactions. In an online survey conducted at two time points, initially in April 2020 during strict lockdown regulations and subsequently in May 2020 during a mild easing of restrictions, the well-being of individuals with BD and healthy controls (HC) without a mental disorder was assessed. Specifically, this publication focuses on measuring sleep quality with the *Pittsburgh Sleep Quality Index* (PSQI, [106]) and its influences during these times.

1.4.3. Development and sleeping times validation of the smartphone app UP!

The app *UP!* for Android smartphones was developed by the Styrian start-up company *meemo-tec* OG in collaboration with the medical expertise of the dedicated outpatient centre for BD, namely the writer of this thesis, and her supervisor, Eva Reininghaus. They contributed to generating ideas, overseeing graphic design elements, and ensuring clinical applicability. The apps' interface in the Google Play Store is shown in Figure 2. The ultimate purpose of the product is to monitor behaviour for early EWS detection and to prevent illness episodes. To achieve this, the app continuously gathers data on mood, movement, exercise, sleep patterns, and intensity of digital communication through sensor and localisation services (GPS, WIFI, etc.).

Figure 2. The interface of the app *UP!* as shown in the Google Play Store *(https://play.google.com/store/apps/details?id=com.meemo_tec.bip_app, October 2022)*

The study design of the six-month validation trial can be found in the publication [107]. Before evaluating a product's effectiveness and efficiency, the accuracy of the measurements must first be ensured. Therefore, the aims of this part of the thesis were: 1.) To evaluate the accuracy of the app's sleep data compared to data collected from an accelerometer (*Axivity 3* [108]) and the validated questionnaire PSQI. 2.) To assess user acceptance of the app.

The pilot validation trial included 22 individuals diagnosed with BD and 23 HC. Recruitment took place from 2017 to 2019 at the Department of Psychiatry and Psychotherapeutic Medicine of the Medical University of Graz. Participants used the app for six months and wore the accelerometer for one month. At four time points, current symptomatology and behaviour (e.g. sleep patterns) were assessed, along with feedback about the app. Furthermore, similar to trial I, the recognition of the beginning of the episode and EWS was surveyed.

2. Results

In the following, the results of the three included publications are summarised [107,109,110].

2.1. Patients desire for app use regarding early warning sign recognition

The results revealed that while patients with BD and their relatives felt adequately informed about the disease, a notable proportion expressed dissatisfaction with current treatment options: 13.7% (7/51) of patients and 35.7% (10/28) of relatives indicated they were not fully satisfied.

EWS indicating the onset of depressive episodes was recognised by 25.5% (13/51) of the patients. Conversely, indications of (hypo)manic episodes were identified by only 11.8% (6/51). However, a significant majority, comprising 88.2% (45/51) of patients and 85.7% (24/28) of relatives, consistently identified the same symptoms recurring at the onset of depression. Similarly, 70.6% (36/51) of patients and 67.9% (19/28) of relatives consistently recognised symptoms at the onset of (hypo)manic episodes, particularly noting changes in sleeping, sleep-wake rhythm, physical activity and communication behaviour.

Nevertheless, the overwhelming majority, comprising 84.3% (43/51) of patients and 89.3% (25/28) of relatives, acknowledged the potential usefulness of technical support and expressed keen interest in utilising a smartphone app for BD treatment.

2.2. Sleep during the COVID-19 pandemic

The online survey revealed that individuals with BD (n=20) experienced poorer sleep during the pandemic, both during the lockdown period and during the easing of restrictions, compared to HC. Particularly affected by poor sleep quality, sleep latency, and daytime sleepiness were those who

frequently sought information about the pandemic crisis and had significant fears about the virus, their own infection, or transmission to others.

2.3. Sleeping times validation of the smartphone app *UP!*

The study evaluating the smartphone app *UP!* found a high correlation in falling asleep times between the app paired with both the accelerometer and the PSQI, as well as high correlations in waking up times between the app and both the accelerometer and the PSQI. It was concluded that *UP!* can accurately measure changes in sleep durations. Additionally, the study did not identify strong concerns regarding data protection or continuous smartphone usage with *UP!*. Furthermore, patients viewed the measurement of changes in behaviour patterns as EWS using a smartphone positively.

3. Discussion

The findings of the publications indicate a demand from individuals with BD and their relatives for specific technological support in treatment, e.g. smartphone apps, particularly for a system that enhances the recognition and management of EWS. Sleep disturbances are among the most common EWS. No significant concerns regarding data protection or continuous smartphone usage were reported. Particularly during the COVID-19 pandemic, with social distancing measures, sleep disturbances were more prevalent in this vulnerable group, highlighting the potential benefits of adjunctive treatment through apps during such times to detect and manage phases of illness early on.

3.1. Early warning signs recognition as a target for apps

In summary, both the literature and the findings of our study indicate that EWS of bipolar episodes, which patients only partially recognise and not always in time, often manifest in changes in sleep-wake rhythm, physical activity, and communication behaviour. Although a relatively high proportion of patients recognise their repetitive individual EWS in psychoeducative settings after an episode or in euthymia, new possibilities are introduced to support this via apps or electronic devices. That could further increase the percentage of patients who recognise these EWS in good time and could therewith have a life-changing impact, especially for individual sufferers. The

enhancement in self-awareness contributes to the user's self-efficacy, a crucial determinant of self-esteem.

Importantly, patients rated their ability to recognise their own affective episodes higher than their relatives did. Both patients and relatives had the subjective feeling that they less frequently recognise the onset of (hypo)manic episodes compared to depressive episodes.

M-health products have the potential to capture individual behaviour patterns, especially deviations from typical patterns such as EWS. Smartphones could be used for EWS detection, which could be tailored to individual needs, enabling quicker and more accurate recognition. Studies have demonstrated that mentally healthy individuals who utilised an app displaying their typical low physical activity levels experienced increases in activity, life satisfaction, and sleep quality [79]. Similarly, Naslund and colleagues observed a high satisfaction rate among individuals with schizophrenia or affective disorders who were encouraged by mobile devices to engage in more physical activity [111].

3.1.1. Sleep disturbances as EWS

In line with other studies, our results show that individuals with BD stated that sleep is the most critical pattern to monitor with an app [80].

Importantly, sleep disturbances play a significant role in triggering illness episodes, and conversely, clinical symptoms in manic or depressive episodes can also manifest in and further impact disturbed sleep patterns. Therefore, addressing sleep disturbances is an essential aspect of the multifactorial therapy approach, not only during acute episodes but also during EWS periods. Regular sleep patterns serve as a preventive measure against the onset of depressive and (hypo)manic episodes and also impact various physiological processes such as cardiovascular activity, alertness, metabolism, and brain function [112]. Therefore, maintaining adequate and regular sleep, even during euthymic phases, is an important treatment goal. Similar to our assessed data, a study conducted in the Netherlands revealed that participants with BD reported increased insomnia after the COVID-19 outbreak, highlighting sleep disturbances as a reaction to critical life events. Insomnia was alongside insufficient treatment, loneliness, insufficient coping and alcohol consumption predictors for poor well-being and overall poor mental health [113].

However, mathematical and statistical models are crucial for distinguishing between apparently irregular circadian activity rhythms and critical disruptions. They allow for a more accurate assessment of individual patterns with continuous recording [114].

Similar to our findings, research has shown good agreement between automatically generated smartphone-based sleep duration and self-reported sleeping times with the PSQI [115]. Smartphone GPS data on circadian rhythms have been associated with changes in anxiety, serving as an EWS for depressive and BD episodes [116]. Another trial demonstrated changes in sleep-wake rhythms measured by actigraphy data as EWS could already be detected one month before affective episodes in seven out of eight patients, although these changes were not consistently in the expected direction [117].

Psychological interventions and behavioural modifications can significantly influence sleep duration and quality, which can be addressed through app-based recommendations and interventions. Sleep hygiene rules, including regular sleep schedules, avoiding daytime naps, minimising alcohol and nicotine consumption, and creating a conducive sleeping environment, pleasant atmosphere in the sleeping room, routines in the evening and morning, and optional relaxation exercises before bed, are recommended [118]. Additionally, reducing working hours, minimising appointments, and engaging in physical activity only during the daytime (avoiding exercise before bedtime) may be associated with improved sleep quality [119]. Furthermore, specific psychotherapeutic strategies such as hypnotherapy, mindfulness-based stress reduction, and CBT are effective for treating persistent sleep disturbances [120]. When necessary, short-term use of sleeping medication or sedating antidepressants can also be considered for managing remaining sleep disorders.

3.1.1.1. Sleeping times validation of the smartphone app UP!

This investigation found *UP!* a valid option for measuring falling asleep and wake-up times. Considering that events of changes during the night are only counted when present for some minutes, sleep disruptions might be underestimated, and total sleep duration is overestimated in this app and other accelerometers and apps [121]. However, while some inaccuracies may exist in measuring exact sleep times using accelerometers and apps, the primary focus in EWS detection is on changes in individual symptoms and behaviours rather than precise timing.

3.2. Apps acceptance and desire of the patients

According to this thesis' results, a meta-analysis by Miralles and colleagues published in 2020 indicated a growing interest in smartphone-based interventions for mental disorders [122], which is even higher since the COVID-19 pandemic [123].

Notably, in our study, only a small percentage of patients (13.7%) and relatives (35.7%) reported not being fully satisfied with the current treatment options. This may be influenced by the participants' extensive experience with multiple illness episodes and specialised professional treatment received at our dedicated BD unit, leading to a higher level of disorder knowledge compared to those without such specialised care. Relatives generally expressed lower satisfaction with current therapy compared to patients, potentially due to limited resources resulting in a wider range of professional information, treatment options, and psychoeducation available to patients.

Regarding dissatisfaction with treatment, patients cited reasons such as the desire for more knowledge and medical support, side effects of mood stabilisers, lack of trust in the therapeutic relationship, insufficiently treated depressive episodes, and too long intervals between appointments. Relatives cited reasons including lack of compliance from the affected individual, absence of mobile social psychiatric care, insufficient specialised psychotherapy for BD, and inadequate medication for minor fluctuations.

The survey's findings suggest that while not all desires and needs can be addressed through m-health, some can. Psychoeducation can be delivered via apps in a personalised manner to impart knowledge. While the frequency of in-person contacts may not be reduced, therapy can also be offered in between. Additionally, medication reminders and adherence tracking can be integrated into apps [124]. The results indicate the importance of providing access to m-health not only for patients but also for their relatives, particularly with psychoeducational content.

The results of the first survey revealed that individuals with BD utilise various treatment options, including psychopharmacological, psychoeducational, psychotherapeutic/psychological, and psychosocial interventions, as well as engagement in sports, nutrition management, and participation in scientific studies. Elements of these treatments could be partially integrated into a smartphone app. For instance, features such as medication reminders with connected alarm clocks and detailed descriptions of medication importance, effects, and side effects could be included. Additionally, the app could facilitate scheduling appointments with clinicians and therapists and remind users of other relevant dates. Changes in diet and appetite could be

assessed subjectively or analysed more comprehensively through the submission of photographs and input of quantities and ingredients.

In sum, both patients and their relatives expressed the utility of technological support in treating BD, particularly in the form of apps that could notify individuals about changes in mood and activity. The majority of participants indicated a willingness to use a specialised app designed for BD, with no significant concerns raised regarding feasibility, data protection, or continuous smartphone usage.

The findings of this thesis support other studies showing a positive attitude towards apps in BD treatment, particularly for measuring EWS. In Murnane and colleagues' study, a high number of individuals with BD emphasised the subjective importance of self-monitoring in various aspects such as mood, sleep, finances, exercise, and social interactions. Most participants reported positive experiences with technology-based monitoring [125]. One study, which involved using an app or a smartwatch to monitor steps and mood while maintaining regular communication with healthcare professionals, revealed that individuals appreciated sharing their daily life activities with physicians, and seeing their health data encouraged further progress [126]. Similarly, another study found increased awareness of EWS by reflecting on behaviours measured by the smartphone, particularly regarding sleep patterns [127]. A recent study reported that an app providing feedback about monitored behaviour resulted in greater adherence compared to an app without feedback [128]. In contrast, some patients with BD have expressed a preference for relaxation or time managing apps over those focusing too heavily on illness-associated deficits [129].

A survey of 47 individuals with BD found that adherence and satisfaction with a smartphone app were higher compared to a Fitbit fitness tracker, probably explained by the ubiquitous use of smartphones in society [130]. Likewise, in our study, participants expressed more annoyance with wearing the Axivity accelerometer than using the app.

Importantly, the survey conducted by van Til and colleagues highlighted the desire for regular, monthly personal appointments with clinicians in addition to using an app [130]. Notably, the interest in smartphone-based interventions and the personal need for technological approaches to treating mental disorders is not always leading to extended use [131]. It's possible that there are subgroups of individuals who would integrate m-health products into their treatment and prefer apps and/or accelerometers. Several factors, including age, gender, societal influences, peer

groups, general attitudes towards m-health, the course of BD, and various treatments such as psychopharmacology and psychotherapy, may influence the acceptance and effectiveness of smartphone-based interventions. Therefore, these factors should be considered in future trials.

In summary, surveyed individuals with BD reported, on the one hand, a desire for apps that facilitate self-management with EWS and trigger detection support, but on the other hand, an emphasis on the importance of easy usability, scientific quality, and data privacy. However, many available products for BD fail to address these requirements adequately [132] and there is currently no standardised assessment [133]. However, some studies have highlighted specific concerns among patients. For instance, concerns about the need for personalisation and fears of monitoring-induced paranoia have been raised [134]. A survey of 919 individuals with BD found concerns regarding data security, data sharing, and inter-app connectivity [135]. Adjustability, usability, trustworthiness and privacy guarantee were reported as the most important factors influencing BD patients' continuous use of m-health [136]. Furthermore, a study found a sporadic reporting of compliance in literature reviews of studies on these products, highlighting the need for clear definitions and systematic evaluation studies [137]. Additionally, individual and personalised discussions between professionals and potential users regarding products, potential effects, concerns, and follow-up consultations may be necessary.

3.2.1. Acceptance of UP!

Users of the *UP!* app expressed overall satisfaction with its features. The majority of individuals with BD rated the app positively, emphasising the usefulness of graphical feedback on their behaviours captured by the smartphone app. Participants highlighted continuous sleep monitoring, awareness of changes through a graphical presentation, and seamless integration into daily life as reasons for using the app as a supportive tool in BD treatment. Most users did not find the app annoying; however, a few cited reasons, such as constantly having the smartphone around or feeling pressured by mood demands. One participant expressed dissatisfaction with the measurement of movement via smartphone due to high battery consumption.

3.3. Further advantages of m-health

E-health products, including m-health solutions, offer diverse benefits that can significantly aid individuals affected by mental illness. These tools are widely integrated into today’s daily life,

providing easy access to those in need. Globally, a larger proportion of individuals with mental health disorders have access to the internet and mobile phones compared to appropriate mental health care services [138]. By using these resources, individuals can reduce their reliance on medical appointments, thereby enhancing their autonomy.

Employing the Internet and m-health for diagnostics and treatment can save time and consequently lead to cost reductions for the healthcare system. For instance, a smartphone-based intervention for BD was found to have lower monthly costs compared to traditional clinic-based treatment [139]. Similarly, studies have shown that e-therapy and m-therapy can effectively treat depression in a larger number of individuals compared to face-to-face therapy, potentially resulting in significant cost savings [140].

Furthermore, e-health presents opportunities to reduce outpatient waiting times and increase the accessibility of care. Research indicates that individuals undergoing regular video conferencing with experienced psychotherapists exhibit similar satisfaction levels to those attending in-person appointments [141]. Some even express a preference for anonymous psychotherapy via chat platforms over face-to-face therapy [142].

Apps can also bridge geographical distances, particularly benefiting regions with limited access to medical care [143]. Notably, some patient dissatisfaction with long treatment gaps and relatives' desire for more mobile psychosocial and specific psychotherapeutic options for BD were highlighted in this first survey.

In addition, utilising e-health products can help reduce the stigma surrounding mental illness. Individuals can anonymously educate themselves online before consulting professional help, thus overcoming psychological barriers associated with seeking treatment. In addition, self-help forums could help reduce an individual’s feeling of being alone with their illness.

Moreover, analysing accurate, objective, and continuous records of individuals' moods, patterns, and symptoms would be valuable to medical research [50]. Historically, in addition to physicians and therapists, researchers have depended on subjective and retrospective information. Integrating technological data with biological markers can achieve a more holistic and integrative approach to understanding BD [65,144,145].

3.3.1. EWS management via other behaviour tracking

Besides sleep patterns, smartphone-based tracking also allows monitoring of other behaviours that might be relevant as EWS, such as physical activity and digital communication.

Studies observed high agreement between smartphone-based self-reports and automatically measured data. However, these results did not align with the data obtained from the questionnaires over the last weeks, suggesting that activity behaviour may be variable and not accurately captured by one-time assessments [146]. Furthermore, decreases in physical activity measured with smartphone apps have been predictive of worsening depressive and manic symptoms over a 12-month period in BD individuals [147]. These findings highlight the potential utility of smartphone-based monitoring of physical activity in predicting mood symptoms in individuals with BD.

Furthermore, physical inactivity is a significant risk factor for various health conditions, while regular physical activity has proven benefits for both physical and mental health [148]. Studies have consistently shown a positive association between active mobility in everyday life and regular physical activity with mental well-being and prevention of depressive episodes [149,150]. However, individuals with BD often lead sedentary lifestyles [151] with only low physical activity compared to those without mental illness [152], which can exacerbate their health issues, including increased risk of obesity and metabolic and cardiovascular problems [153], associated with cognitive impairments [6,154], higher rates of hospitalisation [155], elevated mortality rates, and poorer prognoses for BD [156] with earlier mortality [148]. Conversely, regular physical activity has positively affected somatic health, including preventing and treating somatic comorbidities. Higher levels of physical activity in BD have been linked to improved cognitive function, at least in females [157], and impacts on the immune system [158]. To date, studies have investigated the anti-depressant and anxiolytic effects of regular physical activity, but the impact on manic symptoms remains unclear. It was discussed that exercise might, on the one hand, have a manic effect due to getting rid of too much energy. Still, on the other hand, it might induce or enhance mania due to physiological arousal [159]. Contributing factors to this inactive behaviour include psychopharmacological treatment [160], poor nutrition, inflammatory processes [161], drive disorders [162], social isolation and, especially in overweight people, low self-esteem [163,164].

Targeted physical activity interventions can positively impact mood states and overall mental well-being via increasing self-efficacy and -motivation, stress tolerance and decreasing negative

thinking [164] and daily life structuring [165], therefore potentially preventing illness episodes. However, the exact recommendations for the healthy extent of physical activity remain unclear and may vary depending on individual factors such as weight, occupation, and somatic and mental health status [164,166,167]. Overall, the WHO and the Austrian national associations recommend muscle-strengthening exercises at least twice a week and endurance training for 150 to 300 minutes with moderate intensity or 75 to 150 minutes per week with high intensity [168].

No general articles specifically addressing communication in BD during euthymia were found during this research. However, studies have shown that individuals with BD exhibit moderate verbal fluency impairments compared to HC, with variations depending on different mood states [169]. Furthermore, illness episodes are often characterised by speech abnormalities [170]. Oral fluency tends to be significantly restricted in depressed individuals with BD compared to euthymic patients [171]. However, it remains unclear whether this affects the desire of depressed individuals to communicate. Conversely, during manic episodes, individuals with BD typically experience an increased need and urge to communicate, often exhibiting enhanced speaking rates and volume.

Some m-health products and studies utilise audio data, such as pitch and volume of phone calls, to monitor symptoms in BD, although research data in this area is limited and inconclusive [172]. Studies have shown that individuals perceive emotional content similarly in both written and spoken communication [173]. Research revealed that currently depressed individuals with BD tend to engage in fewer phone calls and have more missed incoming calls compared to euthymic individuals. Conversely, currently, manic patients exhibit more outgoing calls but also more missed calls, which correlate with the severity of symptoms [174]. Similarly, it was found that depressive symptomatology was associated with decreased text messages, while manic symptoms were linked to increased text messages [147]. Moreover, decreased digital social activity, as evidenced by more missed calls but longer call durations, was demonstrated among individuals with BD compared to HC [146]. Furthermore, the same study group showed more incoming calls in automatically generated data of individuals with newly diagnosed BD than in HC. The number of outgoing calls correlated with the *Young Mania Rating Score* (YMRS) total score and activity and speech subscores [175]. These findings suggest that digital social activity could serve as a measurable criterion for current BD symptomatology and monitoring changes in symptomatology, including EWS of emerging episodes.

Concerning EWS management access to feedback on behaviour changes has the potential to facilitate early self-recognition of EWS, thereby enabling the implementation of timely and effective interventions. Various m-health products employ different methods to communicate rhythmic behaviour patterns to users, often utilising graphical overviews spanning recent days, weeks, and months. Figures 3 and 4 illustrate the visual feedback provided by *UP!,* encompassing parameters such as sleeping duration and times, working hours, physical activity duration and timing, digital communication patterns, and mood fluctuations.

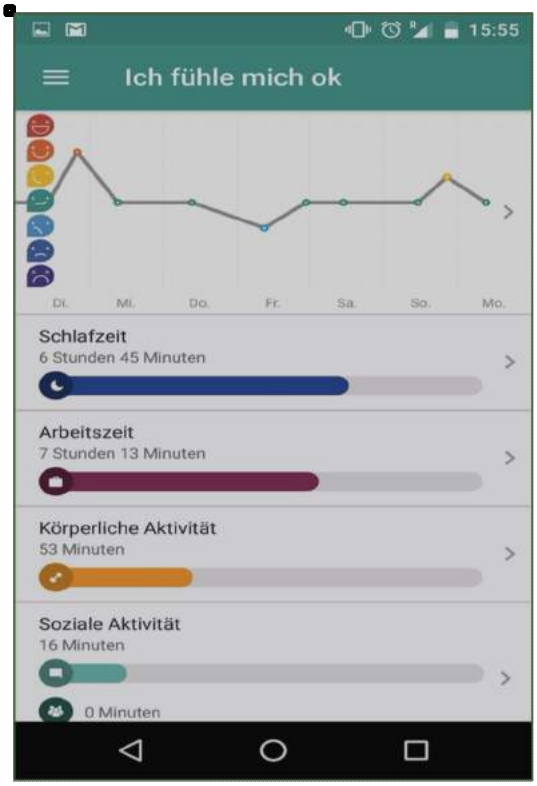

Figure 3. Daily graphical feedback of behaviour in *UP!*

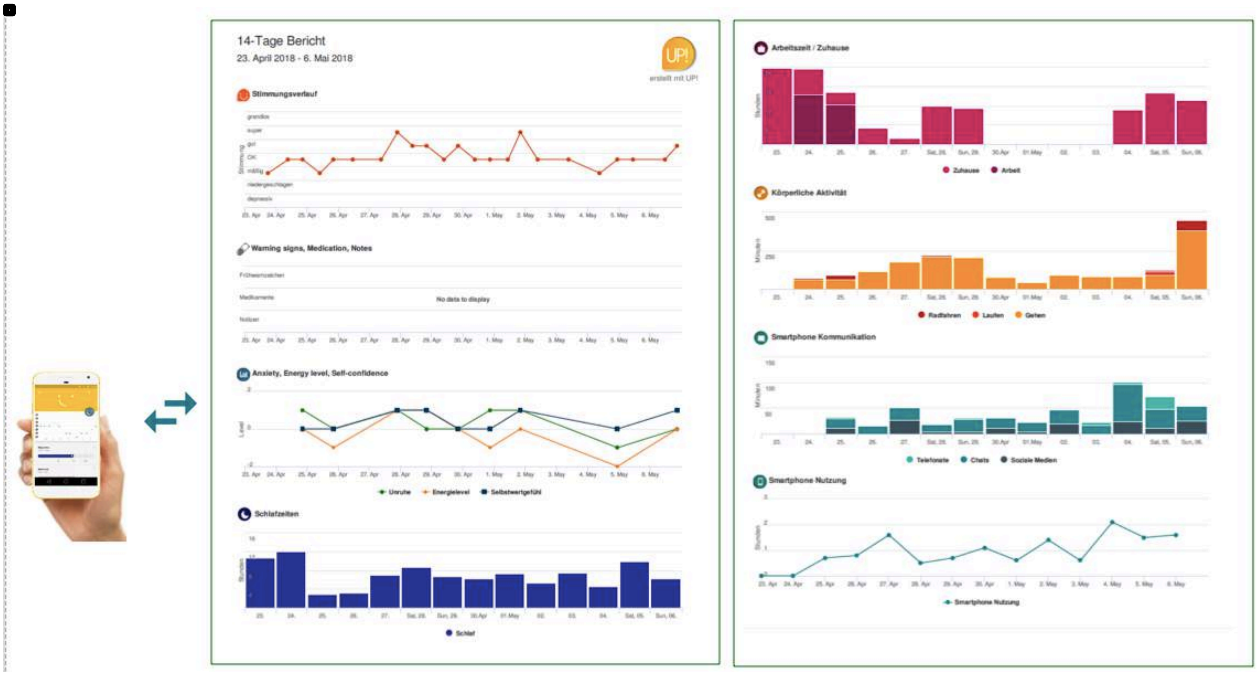

Figure 4. Graphical weekly report of *UP!*

The knowledge, visualisation, and realisation of behaviour patterns and alterations have the potential to positively influence the mindset of individuals with BD, promoting „healthy behaviours“ such as balanced sleep-wake rhythms, sufficient physical activity, conscious relaxation, planned activities, and positive social engagements. Moreover, many m-health products automatically calculate deviations and prompt users about other symptoms, allowing for personalised psychoeducation tailored to individual symptom complexes. Figure 5 depicts an example of *UP!* implementing this approach.

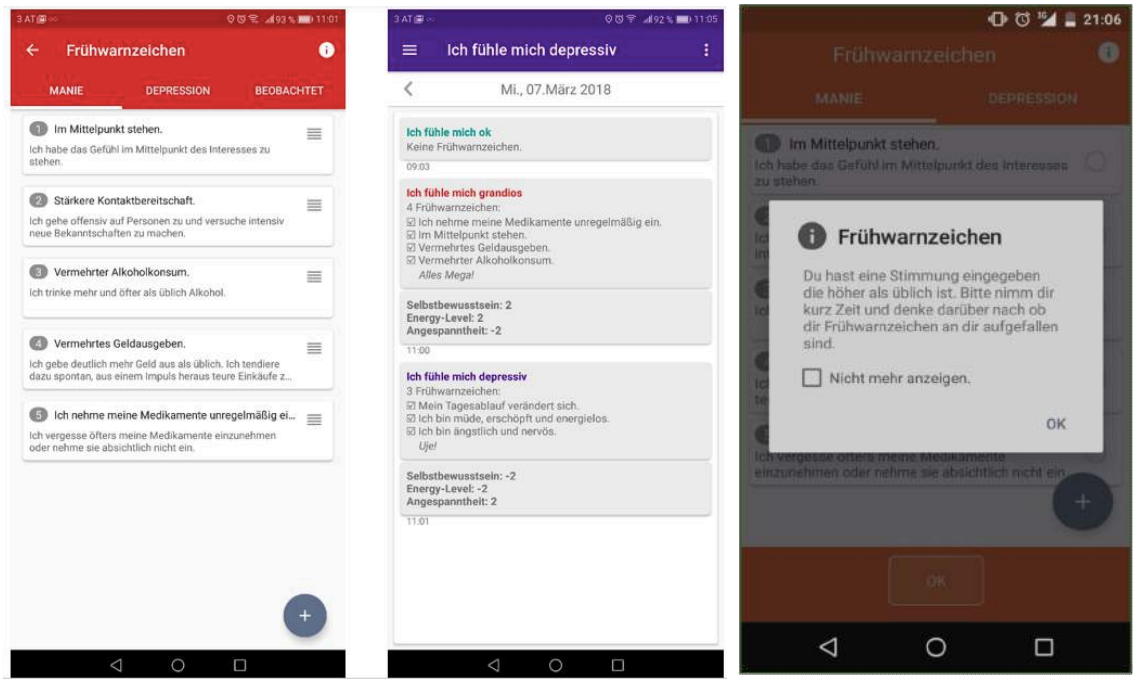

Figure 5. Selection and feedback of early warning signs in *UP!*

Thus, a realistic goal of m-health in the treatment of BD is to improve self-management and increase self-efficacy, which ultimately should prevent relapses, severe episodes, and hospital stays.

3.3.2. European Apps targeting early warning sign recognition

Several European research groups have developed or tested apps for BD management.

In Nottingham, UK, a wearable sensor system was designed to detect changes indicative of EWS. Although the number of participants was relatively small (four healthy participants and one individual with BD), the researchers could see activity patterns such as exercise (via the accelerometer), altered sleep (via bed and light sensors), increased social activity via number and

frequency of visited places (GPS) as well as via the number of calls and text messages (also keyboard control to analyse buttons presses), psychomotor agitation and retardation (via accelerometer and extra environmental motion sensor), and talkativeness (via microphones for pitch and speech). However, the individual with BD reported that the additional environmental sensors caused discomfort and that they sometimes forgot to charge the sensors [68].

Another product developed in the UK, the C.A.L.M app, targets mood tracking for young individuals with BD aged 16-25 years [176].

In Denmark, the MONARCA (MONitoring, treAtment and pRediCtion of bipolAr Disorder Episodes) trials by Faurholt-Jepsen and the study group evaluated smartphone-based mood monitoring. In the first study, the authors did not find a significant effect on depressive and manic symptoms of reporting daily self-monitoring and including a feedback loop over six months using a smartphone app [177]. The second study investigates the *Monsenso* system, which measures subjective and objective data about phone usage, social activity, physical activity and mobility [178]. In a nine-month randomised controlled trial (RCT), results showed no differences in depressive or manic symptomatology of the smartphone-based monitoring compared to treatment as usual (TAU). Conversely, quality of life was increased and perceived stress was lower in the intervention group. In a recent study, the group did not report an effect of smartphone-based monitoring on the rate and duration of hospital readmissions [179].

The German multicentre consortium *BipoLife* is investigating, among other targets, early episode detection using a smartphone app [180]. One study protocol is published on a project analysing an app that measures activity and communication. In an RCT over 18 months, one group automatically sends regular feedback about their behaviour to their clinician, and the other does not [181]. Initial findings suggest that alterations in sleep and daily activity patterns can predict upcoming episodes [182].

The Spanish group of Hidalgo-Mazzei and colleagues developed the *SIMPLe* app to monitor symptoms, identify relapses, and offer psychoeducation content [183]. Their first publication in 2015 about the feasibility and satisfaction of the app showed that 86% of the 51 participants were satisfied with the product, and 74% actively used it almost daily over three months [89]. A sample of 51 users showed that a three-month usage of *SIMPLe* led to a significant decrease in an assessment of biological rhythms disturbance only in the completers group compared to the non-completers group [184]. Furthermore, the group investigated cognitive parameters before and

after the app's usage for three months and found no impact; however, the sample size was small. The *SIMPLe* app does not have special cognitive training [185]. A recent paper showed that 173 of 390 people only used the real-life app for six months. The analyses found that age and illness duration were associated with the engagement and time of the app use [186].

Overall, these initiatives highlight the potential of smartphone apps in BD management, although challenges such as user engagement and sensor discomfort need to be addressed.

3.4. Further developments

Furthermore, preliminary data suggests that smartphone data may be useful in diagnostics, for example distinguishing between BD 1, BD 2 and a major depressive episode [187]. This indicates the potential of leveraging smartphone technology to aid in the differential diagnosis of these mood disorders. However, further research and validation studies are needed to confirm and refine these findings before smartphone-based diagnostic tools can be widely implemented in clinical practice.

However, research indicates that some m-health products did not fully exploit available technological capabilities [122]. Presumably, new products, including social media, conversational agents such as Siri or Alexa, and virtual reality, will complement existing products [63]. Additionally, wearables, such as smartwatches and fitness trackers, smart clothing, and ear-worn devices, will play a role in e-health [188]. In contrast, this fragmentation of different providers and devices assessing vast amounts of information for other databases constitutes a problem for Big Data analyses [189].

3.4.1. Target group for m-health

Possibly, not all individuals benefit equally from m-health interventions, and several factors influence their effectiveness. Beyond the technology itself, the success of using health apps depends on various factors, such as the general use of smartphones, skills with smartphones, application to health, sociodemographic factors such as age, education, and income, and societal and environmental influences [62].

Younger individuals tend to use smartphones more extensively and are generally more comfortable with them than older individuals who use them primarily for telephoning [190]. Similar findings were shown in a bipolar cohort [191]. In contrast, Garcìa-Estela and colleagues found

that individuals aged older than 45 years used the *SIMPLe app* longer than younger participants [186]. Interestingly, the M of the age in the BD group in our cohort was 43.68 years (min:25.37; max:60.01). We did not find any problems for middle-aged patients with BD dealing with their smartphones or having technical issues or difficulties participating in this study. This aligns with a survey from Fortuna and colleagues [192], which also found that middle-aged and older adults with mental disorders could participate in a smartphone intervention study without having any problems.

Some study groups found that individuals with mental disorders own and use smartphones less than the general population [193–195]. Presumably, there are also differences within the group of individuals with BD; for example, very creative individuals accept novel approaches more [196]. For the duration use of *SIMPLe,* some clinical characteristics such as illness duration, comorbid anxiety disorder and antipsychotic treatment were relevant [186].

3.4.1. Outlook of app buddy systems

Involving relatives and caregivers in the treatment process is also highly beneficial, as family dynamics and support can significantly impact the course of the illness, and outsiders are more aware of changes [197,198]. According to this literature, the results of the first study of this thesis revealed that individuals with BD do not always recognise EWS as quickly or accurately as close relatives. Of the surveyed patients with BD, 98.0% indicated that they have essential reference persons with whom they discuss their illness. Among these persons, 49.0% are perceived to have an influence on both depressive and (hypo)manic developments, while 19.6% are believed to impact only depressive episodes and 7.8% only (hypo)manic episodes. Additionally, 21.6% of patients stated that their reference persons have no effect. Furthermore, relatives reported that they can always influence the patient at the onset of an illness episode in 39.3% of cases.

Digital tools can facilitate this involvement by enabling caregivers to connect systems and give outsider input. Therefore, it may be beneficial for predefined individuals to have access to the data and potential changes. Discussing EWS during euthymic periods and allowing patients to specify countermeasures can facilitate the creation of digital emergency plans, allowing individuals and their relatives to quickly reach out to healthcare professionals in urgent situations, enhancing safety and supporting the creation of crisis plans.

3.4.2. Need during COVID-19 pandemic

Especially during the COVID-19 pandemic as a global health crisis, telehealth services have become crucial across all medical fields, with telepsychiatry seeing increased implementation and regulatory streamlining [123].

The COVID-19 pandemic had far-reaching impacts worldwide as well as on individuals' health and well-being due to emotional isolation, fears and somatic conditions [13]. People with severe mental disorders such as BD showed more mental symptoms of depression, anxiety, somatisation and stress compared to the general population [14]. The mental symptom severity was especially high during very strict regulations as individuals with BD suffered from more distress due to social distancing [199]. Additionally, the somatic health status was worse in patients with BD compared to mentally healthy people as they gained more weight, were less physically active and had a higher number and more severe courses of COVID-19 as well as other somatic disorders [200].

Importantly, individuals with BD face higher risks from severe infectious diseases like COVID-19 [201], with more severe disease courses, higher hospitalisation and mortality rates [202]. Reasons for these include somatically worse underlying health conditions in general, chronic inflammation, and limited healthcare access due to financial barriers, stigmatisation and discrediting. Moreover, during acute symptomatology, challenges such as cognitive and perceptual disturbances, drive disorders, and lack of insight may hinder individuals with BD from seeking appropriate help [203].

Additionally, the duration of symptom remission post-COVID-19 outbreak was longer compared to before [113]. Moreover, fewer individuals with BD and psychotic disorders sought treatment for their mental disorders post-outbreak, with a notable decline in treatment satisfaction and quality reported [113].

Given the heightened vulnerability of individuals with BD, it seems essential to strengthen mental health services in times of crisis, especially during social distancing. Hereby, e-health and m-health seem to be appropriate strategies.

3.1. Challenges of e-health

Misinterpreting EWS by untrained or underinformed patients or becoming overconfident in their recognition can lead to premature reactions or a decreased understanding of the biological components of mental illness [27,82]. Continuous monitoring may also contribute to stress, worries, rumination and overthinking, especially during depressive episodes [204].

While psychotherapy traditionally involves face-to-face communication, e-health must prioritise individual problems and topics to ensure efficacy. Some studies have suggested comparable efficacy between face-to-face therapy and e-psychotherapy [84,140]. However, innovations are often met with scepticism, and potential users should exercise caution with new, unproven forms of therapy.

Furthermore, for medical professionals, ensuring 24/7 accessibility in cases of immediate threats can be challenging [205].

Additionally, economic factors may hinder the sharing of Big Data for comprehensive behaviour monitoring across multiple devices and providers [189].

Moreover, the sheer number of new e-health products makes distinguishing between useful and less helpful tools difficult, hindering evidence-based practice in this field. It was shown that the use and, in particular, continuous use of health apps is higher when professionals recommend them as an add-on to other treatments [177,206]. However, to date, most people install apps through online searches [207], posing a challenge for professionals to stay informed about available products and recommendations.

In their critical review of smartphones in mental health, the team of Bauer and colleagues highlight several challenges that hinder the realisation of expected milestones in utilising smartphones for mental health treatment. These challenges include [208]:

- Diverse Usage Patterns: The unequal distribution of smartphones, along with preferences for wearables and social media consumption, results in varied usage patterns among individuals. This diversity complicates the standardisation and widespread adoption of mental health interventions via mobile technology.
- Lack of Regulations and Standards: There is a dearth of regulations governing the development and implementation of mental health apps. Issues such as medical device verification, measurement accuracy, and comparable efficacy standards must be addressed to ensure the quality and safety of these applications.
- Commercialisation and Privacy Concerns: Companies with financial interests are involved in developing mental health apps, raising concerns about privacy and data security. Digital data collection for commercial purposes may compromise user privacy and comfort, necessitating clear guidelines and safeguards.

- Rapid Technological Advancement: The rapid pace of technological advancement poses a challenge in keeping mental health apps relevant and up-to-date. The emergence of new technologies may render existing apps obsolete, highlighting the need for continuous innovation and adaptation in the field.

Addressing these challenges requires concerted efforts from researchers, developers, policymakers, and users to establish robust regulations, standards, and ethical guidelines for developing and using smartphone-based mental health interventions.

The authors, therefore, recommend for the future the following [208]:

- Diverse e- and m-health products for personal individual needs (respecting age, disabilities, lifestyle, budget, skills);
- Help to improve digital skills;
- A standardised evaluation of the efficacy of apps; using more than only smartphones for data collection;
- Extensive cohort studies involving patients and physicians; providing security information;
- Continuous support and training by physicians.

Likewise, Mathews and colleagues underscore the importance of establishing a clear framework for digital health tools. They demand that tools should be validated 1. technically in the form of measurement accuracy, 2. clinically providing illness-specific improvements, and 3. systematically giving an advantage in the users' daily lives and/or the work of health care professionals [209].

3.1.1. Need for scientific evaluation

A recent review by Eis and colleagues found a low rate of scientific work on apps and even fewer evaluations of efficacy in good study designs, indicating a lack of robust evidence regarding their efficacy [210]. The meta-analysis by Miralles and colleagues showed observational studies but still only a few RCTs [122].

Adams and colleagues discussed connecting the collection of psychosocial and biomedical data via smartphones, especially in the context of mental disorders. Still, they concluded that evidence for m-health tools is lacking [65]. Furthermore, using m-health of continuous data collections in longitudinal studies is suggested, but Rosa and colleagues warn of unvalidated products with little comparability [145].

In our unpublished trial data, we observed an improvement in *Hamilton Rating Scale for Depression* (HAMD) scores in the patient group from the beginning to the end of the six-month trial period (Z = -2.139; p = .032). However, there was no significant change in YMRS scores over the same period. It's important to note that while there was an improvement in HAMD scores, the value did not meet the criteria for depressive episodes, and further, the changes might be influenced by factors beyond the trial interventions. Therefore, it's difficult to draw conclusions about the app's impact on illness symptomatology based solely on these results.

Besides preventing new illness episodes, apps also impact the actual symptomatology. At least for depressive symptoms, a meta-analysis was conducted by Firth and colleagues in 2017, showing a positive effect with a moderate effect size of smartphone interventions compared to inactive controls and a small positive effect compared to active control groups [211]. Moreover, there are hints that smartphone interventions positively impact (hypo)manic symptoms as well [212]. Notably, it is still insufficiently investigated which interventions, e.g. monitoring of various parameters, psychoeducation, instructions of psychotherapy tools, patient-clinician contact chats, drug calendar, etc., are effective on depressive symptoms in particular.

Very few studies exist on the effects of using different products on illness symptomatology, relapses, quality of life, or cognitive functioning. However, adherence and continued use of m-health products might be worse than in-person interventions. Hidalgo-Mazzei found that of 201 participants with BD, only one-third completed a six-month psychoeducation program via an app. However, 62% of the completers were satisfied [213].

Some m-health products additionally use alert functions. In case of changes in, for example, sleeping times or mood over a predefined time slot, the system asks users about other symptoms or EWS. Current research is trying to develop algorithms for these alarm times. Presumably, the most promising approaches are self-learning systems using individual data based on machine-learning techniques [214]. The future aim would be to recognise EWS and further alarm individuals with BD on an individual and sufficient basis. However, up to date, a realistic objective for m-health in BD treatment is to improve self-management with feedback, psychoeducational and, in the case of EWS recognition, counteractive measures. In summary, this might improve the course of BD by preventing recurrences, relapses, severe episodes and hospital stays.

To conclude, with the development of Internet and smartphone-based products in the mental health sector, there is a growing need to assess their safety and effectiveness for their intended

users. Comparing similar products provides an opportunity to identify best practices and develop effective interventions collaboratively. Establishing gold standards through large-scale scientific studies is crucial for advancing the field of e-mental health. While m-health holds promise for new opportunities, it cannot yet be considered equivalent to evidence-based medicine and treatment. Although many new products are expected to be launched soon, it's unlikely that e-mental health will replace traditional medical and psychotherapeutic treatments. However, it should be considered a valuable supporting tool for clinician teams and clinical research. Nevertheless, clinical applications and outcomes must be thoroughly studied before making treatment decisions and recommendations.

A group of experts on smartphone-based mental health interventions recommends advancing the field by focusing on the following [63]: 1. Privacy and security; 2. Efficacy: effectiveness studies, particularly with active or placebo control groups; 3. Engagement: Studies on the reasons for usage; 4. Clinical integration: development of clinical services, including new digital interventions regarding feasibility, regulations and policies.

Moreover, there are indications that involving the target group early in the development and design process would be advantageous, suggesting that their inclusion would be beneficial [215].

Additionally, it is recommended that these products be classified as medical devices, and both app users and recommending professionals should be informed about potential risks [216].

3.1.2. Legal and ethical aspects

The European Union classifies e-health products as *Digital Therapeutics in order to prevent, manage or treat diseases as an add-on or stand-alone therapy*. However, specific European-wide regulations on digital therapeutics are currently lacking, although some countries have implemented national regulations [217].

Most m-health apps are developed by individuals or small start-up companies for commercial use, with only a few receiving support from research institutions or authorities. Consequently, developers must independently navigate issues such as clinical implementation, legal regulations, data protection, medical product registration, and financing.

Currently, few apps in Austria are covered financially by health insurance companies, highlighting the need for regulated solutions with easy access and cost coverage for digital medical devices in the future. Under medical device laws, apps undergo approval procedures to assess usage,

validity, and security. Those meeting safety standards receive a CE marking, with the manufacturer responsible for submitting the final decision and product classification.

However, most health-related apps available today are not classified as medical devices, leading to challenges in determining their validity and risk. There is a lack of uniform concepts for assessing the quality of health-related apps, resulting in unclear guidelines for their use. Various working groups in German-speaking countries are addressing this issue: evaluation of health apps with the CHARISMA study [58]; strategy papers such as “Mobile health recommendations from eHealth Suisse“ [59]; “Medical Apps Orientation Guide” for manufacturers from the German Federal Institute for Drugs and Medical Devices [60] and “Gesundheits-Apps. Grundlagenpapier unter besonderer Berücksichtigung des Aspekts Gesundheitskompetenz” in Austria [62]. However, Austria currently lacks an official m-health strategy, underscoring the need for further development and regulation in this field [62]

There is a general differentiation between studies that utilise a certified medical device for measurement or intervention and those that examine the medical device itself, which may still be undergoing the approval process. Clinical trials play a crucial role in providing insights into such devices’ applicability, clinical implementation, and effectiveness. While this information may not be a specific requirement for medical device approval, conducting these trials to share valuable insights with the scientific community and users is recommended.

Studies involving medical devices must be reported to the local ethics committee and relevant authorities, such as the *Agency for Health and Food Safety* (AGES) of the *Federal Office for Safety in Health Care* (BASG) in Austria. These studies must adhere to regular, official monitoring procedures to ensure compliance with GCP guidelines. Additionally, any serious adverse events occurring during the study must be reported to the AGES and the ethics committee.

Similar to any scientific study, participants must provide written consent to participate in the research and allow the use of their data. In the case of studies involving apps, participants must explicitly approve the installation and use of the required systems. All other aspects of study planning, procedure, data preparation, and storage follow standard protocols for clinical studies.

Table 2. presents the classification of healthcare apps as medical products according to the Austrian BASG [218] with some enhancements from Neumann and colleagues [219]. The classification of these products is determined by their intended purpose, with a fundamental distinction made between apps that collect health-related data and those with a clear medical goal

for diagnosing or treating an illness. Examples of the first ones are recording the number or speed of steps, calculating BMI, presenting healthy lifestyle tools, or collecting calories. The latter are classified as medical devices I, II or III and must be assessed as such by the Medical Devices Law [220] if the purpose is:

a) detection, prevention, monitoring, treatment or relief of diseases,

b) decision support, e.g. concerning therapeutic measures or

c) monitoring of a patient and collecting data if results influence diagnosis or therapy.

Table 2. Classification system of apps as medical products according to Austrian law (BASG)

Classification	Description
Ia	- only provide medical information
Ib	- data collection, storage, and graphic processing - as a basis for individualised reports of patterns and gradients
IIa	- delivering information leading to decision making concerning diagnostics or therapy - controlling physiological parameters
IIb	- app-based decisions with the potential for extensive health impact or surgery
III	- data processing as a replacement for health care providers - potential for irreversible extensive health worsening or death

Financing the systems is another challenge. At present, some programs are supported by care providers, while others have to be paid for by the patients themselves. Clear regulations are essential in this matter. The healthcare system should reward and financially support e-mental health, providing beneficial psychotherapy or educational measures.

Data protection is a critical concern, as governments, insurers, or companies for classification, discrimination, or targeted advertising could misuse personal health data [221]. However, this thesis did not find strong concerns of potential users with BD about the possible misuse of their data. There is a need for federal regulations concerning e-mental health products and data protection. With the overload of personal data on the internet, there is a high risk of abuse by service providers or other third parties [222].

Despite these concerns, many e-health products store data locally on mobile phones and never online. However, transferring data directly to clinicians presents technical, data protection and liability issues. Many individuals may not fully comprehend the extent of personal data they disclose through automated processes. While data encryption can provide some level of protection, the reality is that most data is stored indefinitely on the internet. Mental health information, including symptoms and behaviours, is of interest to various parties, such as therapists, like-minded individuals, insurance providers, and companies involved in targeted advertising. Individuals with mental illnesses, particularly those with chronic conditions, already face discrimination and disadvantages in areas such as health insurance. The potential for insurers to access data on treatment responses through electronic programs raises concerns about privacy and the potential for further discrimination. This situation highlights a conflict of interest, as there is a need for health insurance companies to support e-mental health initiatives financially, yet there are significant risks associated with the disclosure of personal data. Finding a balance between supporting e-mental health initiatives and protecting individuals' privacy is crucial in addressing this challenge [223].

The implementation of the new *European General Data Protection Regulation* (GDPR; *Datenschutz-Grundverordnung,* DSGVO) in May 2018 has some implications for m-health products that collect personal and health-related data. Under the GDPR, these products are legally subject to regulations governing the processing of personal data [62]:

- Increased user rights: Users now have enhanced rights regarding their personal data, including the right to information about how their data is processed, the right to rectify inaccuracies in their data, and the right to request the deletion of their data.
- Informed Consent: Users must provide explicit consent before their data is processed. This consent must be obtained through active and specific actions, such as ticking a box or clicking a button, indicating that the user understands and agrees to the purposes and methods of data processing.
- Transparency: App developers and data controllers are required to provide clear and understandable information about the app's purpose and how user data will be handled. This information must be presented to users in written form, ensuring that users are fully informed before consenting to data processing.

3.1. Limitations

The thesis has several limitations. One significant limitation is the rapidly evolving nature of technology and m-health. However, the overarching conclusion that more research is needed in this area remains valid despite potential shifts in product availability and functionality.

Another limitation is the small sample size in the trials, which hindered the ability to identify differences in the demand for m-health across various subgroups of individuals with BD 1 versus BD 2, different BD courses, age groups, gender, or socio-economic backgrounds (education, social network). Furthermore, EWS detection and acceptance of *UP!* were self-created variables with no reference parameters. This lack of subgroup analysis limits the generalizability of the findings and highlights the need for larger, more diverse samples in future research.

Additionally, the thesis acknowledges technical challenges encountered during the third trial, including missing data from the app and accelerometer and difficulties comparing sleep interruptions between different measurement devices. These technical issues may have affected the accuracy and reliability of the data collected, thus influencing the study outcomes. However, the approximate sleep duration seems more relevant considering EWS recognition than the exact amount of very short sleep interruptions.

The validation of other data from *UP!,* such as physical activity, is still pending. Additionally, mood and behaviour during all measurement time points of the six-month study have only been analysed descriptively so far. It would be interesting for further analysis to consider how illness phases and life circumstances such as work, infections, or vacations affect these factors. However, the study duration of six months may not have been sufficient to capture meaningful outcomes, such as relapse rates and episode course, under regular use of the apps. Longer observation periods and larger sample sizes are needed to fully investigate the efficacy of m-health apps, including specific interventions like *UP!*, in managing BD over time.

Despite these limitations, the thesis provides valuable insights into the potential benefits and challenges of m-health interventions for individuals with BD. It underscores the importance of continued research and development in this field to optimise the effectiveness and usability of these digital tools in supporting BD treatment and management.

4. Conclusion

Individuals with BD and clinicians would benefit from additional treatment options to better manage the condition, as in the past, physicians, therapists, and researchers have had to rely on subjective, retrospective information. Monitoring via smartphone apps holds promise for enhancing BD treatment in several ways. Individuals with BD have positively evaluated EWS management through smartphone apps. Detecting EWS, which often manifests as changes in behaviour such as sleep, physical activity, and digital communication patterns, is crucial for preventing acute episodes and strengthening self-management. The structured presentation of behaviour via graphical representations during clinical appointments can provide clinicians with objective data, enhancing treatment planning and monitoring. Furthermore, structured, objective, continuous, and individualised data collected through validated smartphone apps have the potential to contribute to BD treatment and research significantly.

However, the majority of these apps lack scientific evaluation, highlighting the urgent need for research, validation, and evaluation in the m-health sector. Moreover, physicians and psychotherapists require education about these apps to discuss their advantages and limitations with patients effectively.

This work showed that *UP!* presents a product that sufficiently measures changes in sleep duration. However, further investigation is needed to validate the efficacy of this app in preventing illness episodes and assess its ability to quantify various EWS beyond sleep duration accurately.

In conclusion, while it is unlikely that m-mental health products will entirely replace traditional medical and therapeutic approaches, they offer a promising adjunctive approach. Alongside clinical therapy, these products can support research efforts by providing objective data for analysis. Moving forward, it is imperative to prioritise developing, validating, and evaluating m-health products to ensure their effectiveness in managing BD and improving patient outcomes.

5. Bibliography

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6. Appendix

6.1. Publications

6.2. Congress contributions

Notwendigkeit für Symptom-Monitoring und Frühwarnzeichenerkennung bipolarer Episoden durch eine App? – Ansichten von PatientInnen und Angehörigen zu e-health Bedarf

Symptom Monitoring and Detection of Early Warning Signs in Bipolar Episodes Via App – Views of Patients and Relatives on e-Health Need

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ZUSAMMENFASSUNG

Hintergrund Der Beginn und Frühwarnzeichen von Krankheitsepisoden der bipolaren Störung werden von Betroffenen häufig erst spät erkannt. Je früher eine Krankheitsepisode behandelt wird, desto prognostisch günstiger ist der Verlauf. Die Symptomüberwachung per Smartphone-Applikation (App) könnte eine innovative Möglichkeit darstellen, um Frühwarnzeichen zu erkennen und schneller mit den richtigen Strategien darauf zu reagieren. Das Ziel dieser Studie war es zu evaluieren, ob PatientInnen mit bipolarer Erkrankung und deren Angehörige eine technische Unterstützung durch eine App als sinnvoll und praktikabel in der Früherkennung sowie in der Behandlung erachten.

Methoden In der vorliegenden Studie wurden 51 PatientInnen mit bipolarer Störung und 28 Angehörige befragt. Es wurde ermittelt, ob die ProbandInnen Frühwarnzeichen in Form von Verhaltensänderungen derzeit subjektiv ausreichend und rechtzeitig wahrnehmen können. Zudem wurde erhoben, ob die StudienprobandInnen ein Smartphone als Behandlungsunterstützung nutzen würden.

Ergebnisse Obwohl sich 94,1 % der befragten PatientInnen und 78.6 % der Angehörigen gut über die Erkrankung informiert fühlten, waren 13,7 % beziehungsweise 35,7 % mit den derzeitigen Behandlungsmöglichkeiten nicht zufrieden. Frühwarnzeichen jeder depressiven Entwicklung wurden von 25,5 % der PatientInnen wahrgenommen (Angehörige 10,7 %). Jede (hypo) manische Entwicklung wurde lediglich von 11,8 % der PatientInnen wahrgenommen (Angehörige 7,1 %). 88,2 % der Patien-

tInnen und 85,7 % ihrer Angehörigen bemerkten zu Beginn einer Depression und 70,6 % beziehungsweise 67,9 % zu Beginn einer (hypo)manischen Episode wiederkehrend dieselben Symptome (insbesondere Veränderungen der körperlichen Aktivität, des Kommunikationsverhaltens und des Schlaf-Wach-Rhythmus). 84,3 % der PatientInnen und 89,3 % der Angehörigen gaben an, dass sie eine technische Unterstützung, welche auf Veränderungen in Stimmungs- und Aktivitätslage aufmerksam macht, als sinnvoll erachten und dass sie eine Smartphone-App für die Behandlung nutzen würden.

Diskussion Die derzeitigen Möglichkeiten zur Wahrnehmung von Frühwarnzeichen einer depressiven oder (hypo)manischen Episode bei bipolarer Störung sind klinisch unzureichend. Bei Betroffenen und Angehörigen besteht der Wunsch nach innovativen, technischen Unterstützungen. Die rechtzeitige Früherkennung von Krankheitssymptomen, die sich oft in Veränderungen von Verhaltens- oder Aktivitätsmustern äußert, ist für den Verlauf essentiell. Apps könnten hierbei durch objektive, kontinuierliche und individuelle Datenerhebung in der Zukunft für die klinische Behandlung und die Forschung genutzt werden.

ABSTRACT

Background The onset and early warning signs of episodes of bipolar disorder are often realized late by those affected. The earlier an incipient episode is treated, the more prognostically favorable the course will be. Symptom monitoring via smartphone application (app) could be an innovative way to recognize and react to early warning signs more swiftly. The aim of this study was to find out whether patients and their relatives consider technical support through an app to be useful and practical in the early warning sign detection and treatment.

Methods In the present study, 51 patients with bipolar disorder and 28 relatives were interviewed. We gathered information on whether participants were able to perceive early warning signs in form of behavioral changes sufficiently and in a timely fashion and also whether they would use an app as treatment support tool.

Results Although 94.1 % of the surveyed patients and 78.6 % of their relatives felt that they were well informed about the disease, 13.7 % and 35.7 %, respectively were not fully satisfied with the current treatment options. Early warning signs of every depressive development were noticed by 25.5 % of the patients (relatives 10.7 %). Every (hypo)manic development was only noticed by 11.8 % of the patients (relatives 7.1 %); 88.2 % of the patients and 85.7 % of the relatives noticed the same symptoms recurrently at the beginning of a depression and 70.6 % and 67.9 %, respectively, at the beginning of a (hypo) manic episode (in particular changes in physical activity, communication behavior and the sleep-wake rhythm). 84.3 % of the patients and 89.3 % of the relatives stated that they considered technical support that draws attention to mood and activity changes as useful and that they would use such an app for the treatment.

Discussion The current options for perceiving early warning signs of a depressive or (hypo)manic episode in bipolar disorder are clinically inadequate. Those affected and their relatives desire innovative, technical support. Early detection of symptoms, which often manifest themselves in changes in behavior or activity patterns, is essentiell for managing the course of bipolar disorder. In the future, smartphone apps could be used for clinical treatment and research through objective, continuous and

Hintergrund

Bipolare affektive Erkrankung

Die bipolare affektive Störung ist eine chronische psychische Störung, die durch wiederkehrende krankhafte Veränderungen in der Stimmungslage und im Energieniveau (depressive und manische beziehungsweise hypomanische Episoden, sowie gemischte Episoden) charakterisiert ist. Zudem leiden PatientInnen oftmals an Schlaf-, Konzentrations-, Denk- und Appetitstörungen, sowie an vermindertem beziehungsweise erhöhtem Selbstwertgefühl. Die Erkrankung stellt für die Betroffenen, deren Angehörigen und das gesamte Gesundheitssystem eine große Herausforderung dar. Sozioökonomisch gesehen sind die Kosten für das Gesundheitssystem durch eine hohe Anzahl von Krankenhausaufenthalten und körperlichen sowie psychiatrischen Komorbiditäten enorm [1]. Das Auftreten von Komorbiditäten und häufig beobachteten kognitiven Defiziten erhöht das Risiko einer Arbeitsunfähigkeit und kann die vorzeitige Sterblichkeit massiv erhöhen [2]. Verlauf und Schweregrad der einzelnen affektiven Episoden sind jedoch bei PatientInnen sehr unterschiedlich [3, 4]. Eine größere Anzahl von depressiven oder (hypo)manischen Episoden ist mit einer höheren Wahrscheinlichkeit verbunden, dass ein Individuum nicht zu seinem prämorbiden Funktionsniveau zurückkehrt [5]. Jede einzelne Episode, sowohl depressive als auch (hypo) manische, führt zu einem Rückgang der Leistungs- und kognitiven Funktionsfähigkeit, was wiederum einen insgesamt schlechteren Krankheitsverlauf zur Folge hat [6].

Mittlerweile weiß man, dass es sich positiv auf den Verlauf einer einzelnen affektiven Episode auswirkt, wenn diese möglichst früh erkannt und durch eine Kombination aus bewusster Verhaltensänderung, Psychopharmaka und Psychotherapie behandelt wird [7]. In vielen Fällen erkennen Personen mit einer bipolaren Störung den Beginn einer Episode zu spät, um angemessen entgegensteuern zu können. Es zeigt sich jedoch häufig ein wiederkehrendes Bild mit für eine Person typischen Frühwarnzeichen [8]. Nach den S3 Leitlinien führt die psychoedukative Therapie im Allgemeinen sowie im Besonderen über Symptom-Monitoring und das Erkennen von Frühwarnzeichen zu einem besseren klinischen Outcome [9]. Frühwarnzeichen können sich in unterschiedlichen Bereichen bemerkbar machen. Sie sind jedoch häufig bei einer Person wiederkehrend [10]. Studien sowie die klinische Erfahrung führt uns zu der Annahme, dass Frühwarnzeichen sich häufig in einer Veränderung des körperlichen Aktivitätenverhaltens, des Schlaf-Wach-Rhythmus und des

Kommunikationsverhaltens manifestieren [11, 12]. Das individuelle Ausmaß der körperlichen Aktivität sowie die Veränderung dieser Aktivität können auf eine depressive oder (hypo)manische Episode im Frühstadium hindeuten. Eine erhöhte körperliche Aktivität spielt eine wichtige Rolle als Frühwarnzeichen (hypo)manischer Phasen und eine verringerte Aktivität als Frühwarnzeichen depressiver Phasen. Darüber hinaus können Schlafstörungen (Einschlafstörungen, Durchschlafstörungen, zu viel Schlaf oder Schlaflosigkeit) als Warnsignal für depressive sowie (hypo)manische Episoden interpretiert werden [13]. Störungen des Schlaf-Wach-Rhythmus und des Aktivitätsniveaus können wiederum den Verlauf einer Episode erschweren [14]. Ein besonderer Schwerpunkt in der Behandlung der bipolaren Störung liegt daher in der kontinuierlichen Überwachung und Aufklärung der Betroffenen und ihrer Angehörigen über Verlauf und mögliche Frühwarnzeichen, damit sie ebendiese frühzeitig erkennen und entsprechende Bewältigungsstrategien anwenden können [11].

Eine Herausforderung im multimodalen Therapiekonzept der bipolaren Erkrankung besteht darin, dass PatientInnen bestmöglich dabei unterstützt werden, diese abnormen Verhaltensmuster und -änderungen rechtzeitig wahrzunehmen [4]. In der Regel werden die Symptome und Verhaltensweisen retrospektiv durch mündliche Explorationen, Fragebögen oder Stimmungstagebücher erkannt und erfasst. Hierbei spielt die subjektive Bewertung der schildernden Personen eine große Rolle und kann zu Missinterpretationen führen. Zudem werden aktuellere Ereignisse deutlicher wahrgenommen als vergangene. Dies führt dazu, dass aktuelle Krankheitssymptomatik wie Depressivität, Pessimismus, Sorgen und Ängste aber auch Getriebenheit und Euphorie die Erhebung von Symptomen und Verhalten in der Vergangenheit deutlich beeinflussen. Daher wäre es wünschenswert, Verhaltensmuster schneller, objektiver, individueller und genauer bewerten zu können [15]. Auch in der klinischen Forschung ist es erforderlich, valide, objektive Daten zu Verhaltensmustern zu sammeln und Daten über einen längeren Zeitraum zu überwachen. Daher scheinen die gegenwärtigen Möglichkeiten für das klinische Arbeiten sowie für Langzeitstudien nicht ausreichend zu sein.

E-health

In den letzten Jahren gab es insbesondere in den industrialisierten Ländern einen großen technologischen Fortschritt. Im Jahr 2016 hatten mehr als 51,5 % aller Haushalte weltweit und rund 84 % in Europa Zugang zum Internet [16]. Nach Angaben des Statistischen Bundesamtes hatten 2018 in Deutschland rund 52 Millionen der über Zehnjährigen ein internetfähiges Mobiltelefon, auch Smartphone genannt. In Österreich nutzten 65,7 (über 65 Jahre) bis 98,1 Prozent (16 bis 24 Jahre) ein eigenes Smartphone für einen Internetzugang [17, 18]. Diese Gegebenheit eröffnet neue Möglichkeiten sowohl in der Diagnostik, als auch in der Behandlung und in der Erforschung von Krankheiten. Produkte aus dem Bereich der „electronic-health“ (e-health) sind für viele Personen leicht zugänglich, kostengünstig, zeiteffizient und stärken die Autonomie [19]. Ein wichtiges Gebiet der e-health ist die Technologie von Applikationen (Apps) für Smartphones (mobile-health: m-health; WHO, [20]). Da viele Menschen ihr Mobiltelefon fast immer bei sich haben, bietet die Datenerfassung per Telefon die Möglichkeit einer kontinuierlichen Aufzeichnung.

E-health und bipolare Störung

[21] konnten zeigen, dass Menschen mit einer bipolaren Störung häufig das Internet nutzen, um sich über ihre Krankheit zu informieren. Eine Untersuchung von [22] zeigte, dass Personen mit einer bipolaren Störung eine positive Einstellung für technologische Unterstützungen und Apps im Allgemeinen haben. Eine weitere Studie fand heraus, dass die PatientInnengruppe Tools für Selbstmanagement, Schlafmanagement, Frühwarnzeichen und auslösender Trigger mit guter wissenschaftlicher Qualität und Datensicherheit wünschen [23]. ■■[24]■■ fanden in einer kleinen Stichprobe heraus, dass bipolare Menschen eine App einem Fitnessband vorziehen würden und zudem regelmäßige ärztliche Kontrolltermine wünschen. Zahlreiche e-health-Produkte wurden entwickelt, um unterstützend in den Bereichen Screening, Monitoring und letztlich in der Therapie selbst wirksam zu sein. Die meisten Produkte zur Behandlung einer bipolaren Störung bieten psychoedukative Inhalte mit unterschiedlichen Ergebnissen in Bezug auf die Wirksamkeit [25]. [26] zeigten in einem Review zwar, dass viele Produkte keine ausreichende Wirksamkeit, Selbstwirksamkeitsmöglichkeiten oder Datenschutzangaben aufweisen können, diskutierten jedoch auch, dass die Erfassung von Daten eine gute Monitoringmöglichkeit bietet und daher die Entwicklung und Validierung einzelner m-health Produkte verbessert werden sollte. Eine weitere der e-health zugrundeliegende Möglichkeit ergibt sich aus der individuellen Eingabe von Symptomen, emotionalen Zuständen oder Verhaltensweisen. NutzerInnen können sich diese dadurch besser bewusstmachen und im Nachhinein Verläufe ihrer Einträge nochmals betrachten. Selbst das bloße Wissen über positive und negative Verhaltensmuster kann zu Veränderungen führen und so das Selbstmanagement verbessern. Zudem können mit der Hilfe von Apps Bewegung, körperlicher Aktivität, Schlaf, Arbeits- und Urlaubszeiten, Telefonanrufe, Sprechgeschwindigkeiten und digitale Chatzeiten aufgezeichnet und verarbeitet werden [27–29]. Dafür werden WIFI, Global Positioning System (GPS), Beschleunigungs- und Lichtsensoren genutzt. Die meisten Daten werden von objektiven Sensoren gesammelt, welche kontinuierlich messen. Das App-System kann Daten sofort interpretieren und statistisch auswerten. Dies kann wiederum zu personalisierten Verhaltensweisen, Zuständen und letztendlich Diagnosen führen und in weiterführenden Schritten unterstützend in die Behandlung einfließen.

Wir gehen davon aus, dass eine App, mit der Verhaltensmuster sowie Verhaltensänderungen zuverlässig gemessen werden können, ein wertvolles Hilfsmittel in der Behandlung der bipolaren Störung sein könnte. Unzureichend belegt ist jedoch bislang, ob Betroffene und deren Angehörige eine solche Möglichkeit begrüßen und nutzen würden. In der vorliegenden Studie wurden PatientInnen mit einer bipolaren Störung und Angehörige hinsichtlich ihrer Smartphone-Nutzung befragt. Es wurde erstens erhoben, ob die derzeitigen bekannten Strategien zur Erkennung von Frühwarnzeichen als ausreichend empfunden werden. Zweitens wurde untersucht, ob PatientInnen Bezugspersonen in ihrem Umfeld haben, mit denen sie über die Erkrankung sprechen und ob diese einen Einfluss auf einen Episodenverlauf haben. Drittens, wurde analysiert, ob bei den Befragten der Wunsch nach einer technischen Unterstützung durch eine Smartphone App in der Detektion von Frühwarnzeichen und in weiterer Folge als Behandlungsunterstützung bestehen würde.

Methoden

Durchführung

Die vorliegende Studie wurde an der Universitätsklinik für Psychiatrie und Psychotherapeutische Medizin der Medizinischen Universität Graz durchgeführt. Es wurden 51 PatientInnen mit einer bipolaren Störung und 28 Angehörige von Menschen mit einer bipolaren Störung hinsichtlich ihrer Smartphone-Nutzung befragt und untersucht. Die Diagnose einer bipolaren Störung wurde mit dem Strukturierten Klinischen Interview für DSMIV (SKID; Wittchen et al., [30]) gestellt. Die PatientInnen waren zum Untersuchungszeitpunkt entweder in stationärer oder ambulanter Behandlung der Spezialambulanz für bipolare Störungen. Die Angehörigen wurden über die Spezialambulanz im Rahmen der Angehörigenarbeit über die Studie informiert. Sie waren somit teilweise Verwandte beziehungsweise PartnerInnen der in die Studie eingeschlossenen PatientInnen und teilweise unabhängige Angehörige. Alle TeilnehmerInnen waren volljährig und gaben zuvor ihr schriftliches Einverständnis. Die Studie wurde von der Ethikkommission der Medizinischen Universität Graz, Österreich (EK-Nummer: 28–260 ex 15/16) in Übereinstimmung mit der aktuellen Revision der Deklaration von Helsinki, der ICH-Richtlinie für good clinical practice und den aktuellen Vorschriften genehmigt.

Inventar

Für diese Studie wurde ein Selbstbeurteilungs-Fragebogen entwickelt, der demographische Informationen zur Person sowie krankheitsspezifische Daten zu Diagnosezeitpunkt, Phasenanzahl, aktueller Behandlung sowie Aufklärungsmodalitäten über die Erkrankung ermittelt. Zudem wurde erhoben, ob PatientInnen beziehungsweise ihre Angehörige am Beginn von Episoden immer dieselben Veränderungen bemerken. Die wichtigsten Items sind in ▶ **Tab. 1** angeführt. Des Weiteren wurde erhoben, ob die StudienprobandInnen ein Smartphone besitzen und wie sie dieses nutzen („Besitzen Sie (kostenpflichtige) Apps?“, „Wie oft schauen Sie auf Ihr Handy?“, „Verändert sich Ihre digitale Antwortdauer bei Stimmungsveränderungen?: Antwort für Depression/(Hypomanie): Ja, verkürzt; Ja, verlängert; Nein“). Zudem wurden sowohl PatientInnen als auch Angehörige befragt, ob ihrer Meinung nach, Angehörige einen Einfluss auf den Verlauf der einzelnen Episoden und Symptome haben. Des Weiteren wurde ermittelt, ob die TeilnehmerInnen sich eine App wünschen, die auf Veränderungen in der Stimmungs- und Aktivitätslage aufmerksam machen würde und ob sie eine App, die speziell als Behandlungsunterstützung für die Bipolare Störung entwickelt wird, nutzen würden.

Ergebnisse

Demographische sowie krankheitsspezifische Daten zum Diagnosezeitpunkt und Phasenanzahl der PatientInnen mit einer bipolaren Störung und Angaben der Angehörigen über die Betroffenen sind ▶ **Tab. 2** zu entnehmen. Die Aufklärungsmodalitäten sowie die derzeitigen Behandlungen sind in ■▶ **Abb. 1**■ angeführt. PatientInnen fühlten sich im Vergleich zu Angehörigen zu einem größeren Anteil „ausreichend“ über die Erkrankung aufgeklärt. Zudem schätzten Angehörige das Wissen der Betroffenen über die Erkrankung schlechter ein als die Betroffenen selbst. In mehr als der Hälfte der Fälle erfolgte die Aufklärung über die Erkrankung hauptsächlich über einen Arzt/eine Ärztin. Die Aufklärung dauert bei PatientInnen durchschnittlich 122,75 (± 207,73) Minuten und bei Angehörigen 113,33 (± 93,34). Die PatientInnen waren zum Untersuchungszeitpunkt nahezu alle in psychopharmakologischer Behandlung und zu einem großen Teil auch in psychotherapeutischer Behandlung. Als weitere Behandlungsmaßnahmen wurden „Sport“, „Ernährung“, „Teilnahme an Studien“ und „mobil-psychiatrische Betreuung“ angeführt. Die Zufriedenheit mit der aktuellen Behandlung war bei den Angehörigen deutlich niedriger als bei den PatientInnen. Als Gründe für eine Therapieunzufriedenheit wurden jeweils in 2,0 % der PatientInnen „der Wunsch nach mehr Wissen und ärztlicher Begleitung“, „Nebenwirkungen der Phasenprophylaxe“, „unzureichendes Vertrauen in die therapeutische Beziehung“, „weiterhin unzureichend behandelte depressive Episoden“ und „zu große Kontrollabstände“ genannt. Angehörige gaben als Gründe für eine Therapieunzufriedenheit in 7,2 % „fehlende Compliance des Betroffenen“ und in jeweils 3,6 % „fehlende mobile sozialpsychiatrische Betreuung“, „fehlende spezielle Psychotherapie für die bipolare Störung“ und „unzureichende Medikation für geringe Schwankungen“ an.

In ■▶ **Abb. 2**■ sind Angaben zur Früherkennung depressiver und (hypo)manischer Episoden dargestellt. Hier zeigt sich, dass sowohl PatientInnen als auch Angehörige ihrer Einschätzung nach in mehr als der Hälfte der Episoden den Beginn einer depressiven Entwicklung immer oder meistens wahrnahmen. PatientInnen schätzten ihre Fähigkeit zur Erkennung eigener affektiver Episoden im Vergleich zur Meinung der Angehörigen hierüber höher ein. Es zeigten sich Großteils dieselben wiederkehrenden Symptome zu Beginn von depressiven Episoden bei den einzelnen Betroffenen, wobei vor allem weniger Bewegung in der Freizeit, körperliche Ermüdbarkeit, erhöhtes Schlafbedürfnis, weniger Lust FreundInnen zu treffen und weniger telefonieren angegeben wurde. Zudem berichteten PatientInnen in 4,0 % über „ungesunde Ernährung“ zu Beginn von depressiven Episoden und in je 2,0 % über „Schuldgefühle“ und „Vernachlässigung hygienischer Maßnahmen“. Angehörige berichteten in je 3,6 % zu bemerken, dass Betroffene zu Beginn „wenig auf das Äußere wertlegen“ sowie „die Fernsehgewohnheiten ändern“.

Den Beginn von (hypo)manischen Episoden erkennen sowohl PatientInnen als auch Angehörige deutlich weniger häufig im Vergleich zu einer depressiven Episode. Es sind jedoch ähnliche Anzeichen zu Episodenbeginn zu einem großen Teil für die Befragten erkennbar, wie vermehrte Bewegung in der Freizeit, generell gesteigerte körperliche Aktivität, Entwickeln neuer Ideen und Pläne, geringeres Schlafbedürfnis, vermehrtes Bedürfnis nach Treffen mit FreundInnen sowie vermehrtes Telefonieren. Zu Beginn von (hypo) manen Episoden gaben PatientInnen zu jeweils 2,0 % an, dass sie „vermehrt Alkohol trinken“, „gesteigerte Freizeitausgaben“ haben, „mehr reden“ und „generell risikobereiter“ seien. Angehörige gaben an, dass sie bei ihren kranken Angehörigen in jeweils 3,6 % „Reizbarkeit“, „gesteigertes sexuelles Bedürfnis“ und „vermehrtes Aufsuchen von Gasthäusern“ wahrnehmen würden.

PatientInnen mit einer bipolaren Störung gaben zu 98,0 % an, dass sie wichtige Bezugspersonen haben, mit denen Sie über ihre Erkrankung sprechen. In 41,2 % sei dies die Mutter, in 15,7 % der Vater, in 29,4 % Geschwister, in 15,7 % sonstige Verwandte, in

▶ **Tab. 1** Items des Fragebogens zu Aufklärungsmodalitäten und Früherkennung bipolarer Krankheitsphasen

Fühlen Sie sich ausreichend über die Bipolare Erkrankung aufgeklärt?
Bzw zusätzlich für Angehörige: Denken Sie Ihr/e Angehörige/r ist ausreichend über die Erkrankung aufgeklärt?
A: JA/ NEIN
Wer hat Sie hauptsächlich über die Bipolare Erkrankung aufgeklärt? (1 Antwort)
A: Arzt/Ärztin; PsychotherapeutIn; Psychoedukationsgruppe; Selbsthilfegruppe/ Betroffene; Selbstständig; Anderes und zwar:
Informieren Sie sich eigenständig über die Bipolare Störung?
A: JA/ NEIN
Wenn ja, welche Quellen nutzen Sie?
A: Vorwiegend Bücher; Vorwiegend Internet; Anderes
Sind Sie mit der derzeitigen Therapie zufrieden?
Bzw: Sind Sie mit der derzeitigen Therapie Ihre/s Angehörigen zufrieden?
A: JA/ NEIN; wenn nicht, was fehlt Ihnen?
Erkennen Sie selbst, wenn eine depressive Phase beginnt?
Bzw zusätzlich für Angehörige: Denken Sie, Ihr/e Angehörige/r erkennt, wenn eine depressive Phase beginnt?
A: Ja immer; Ja meistens; In etwa der Hälfte der Phasen; Nein, aber Angehörige machen mich darauf aufmerksam; Nein
Bemerken Sie am Beginn einer depressiven Phase immer wieder die gleichen Anzeichen?
A: JA/ NEIN
Wenn ja, welche der folgenden treten in mehr als der Hälfte der Phasen auf? (Mehrfachantworten möglich)
A: Weniger Bewegung in Freizeit; Weniger Bewegung/ Aktivität im Beruf; Körperliche Ermüdbarkeit; Grübeln/Sorgen; Weniger Spaziergänge; Weniger Energie den gewohnten Alltag zu erledigen; Weniger Interesse an gewohntem Alltag; Erhöhtes Schlafbedürfnis; Geringeres Schlafbedürfnis; Einschlafstörungen; Gehäuftes Aufwachen; Weniger Lust auf Treffen mit Freunden/Bekannten; Weniger Telefonieren; Weniger Textnachrichten via Mobiltelefon versenden; Vermehrte Internet Nutzung; Verminderte Internet Nutzung; Andere und zwar
Erkennen Sie selbst, wenn eine manische Phase beginnt?
Bzw zusätzlich für Angehörige: Denken Sie, Ihr/e Angehörige/r erkennt, wenn eine manische Phase beginnt?
A: Ja immer; Ja meistens; In etwa der Hälfte der Phasen; Nein, aber Angehörige machen mich darauf aufmerksam; Nein
Bemerken Sie am Beginn einer manischen Phase immer wieder die gleichen Anzeichen?
A: JA/ NEIN
Wenn ja, welche der folgenden treten in mehr als der Hälfte der Phasen auf? (Mehrfachantworten möglich)
A: Vermehrt Bewegung in Freizeit; Vermehrt Bewegung/ Aktivität im Beruf; Innerliche Unruhe; Gesteigerte körperliche Aktivität; Neue Ideen/Pläne für den gewohnten Alltag; Erhöhtes Schlafbedürfnis; Geringeres Schlafbedürfnis; Einschlafstörungen; Gehäuftes Aufwachen; Vermehrtes Bedürfnis Freunde/ Bekannte zu treffen; Vermehrtes Telefonieren; Vermehrt Textnachrichten über das Mobiltelefon versenden; Vermehrte Internet Nutzung; Verminderte Internet Nutzung; Andere und zwar:
Fänden Sie eine technische Unterstützung in der Therapie der Bipolaren Störung sinnvoll?
A: JA/ NEIN
Würden Sie es begrüßen, wenn Sie durch eine App darauf aufmerksam gemacht werden, dass ihre Stimmungs- und Aktivitätslage sich verändert hat?
Bzw: Denken Sie, Ihr/e Angehörige/r würde davon profitieren, wenn sie/er durch eine App darauf aufmerksam gemacht wird, dass ihre/seine Stimmungs- und Aktivitätslage sich verändert hat?
A: JA/ NEIN
Würden Sie eine speziell für die Bipolare Störung entwickelte App nutzen?
A: JA/ NEIN

56,9 % der/die PartnerIn, in 49,0 % FreundInnen, in 5,9 % KollegInnen und in 2,0 % Internetbekanntschaften. Die befragten PatientInnen berichteten, dass diese Bezugspersonen in 49,0 % sowohl bei depressiven als auch (hypo)manischen Entwicklungen einen Einfluss auf den Verlauf und die Betroffenen nehmen; 19,6 % gehen von einer Einflussnahme nur auf depressive und 7,8 % nur auf (hypo) manische Entwicklungen aus und 21,6 % gaben an, dass Bezugspersonen keinen Einfluss nehmen. Angehörige berichteten zu 71,4 %, dass die Betroffenen mit ihnen über die bipolare Erkrankung sprechen. Sie gaben an, dass sie zu, 39,3 % immer Einfluss auf den/die PatientIn zu Beginn einer Krankheitsphase haben, zu 17,9 % nur Einfluss auf depressive und zu 7,1 % nur Einfluss auf (hypo)manische Entwicklungen und zu 32,1 % überhaupt keinen Einfluss nehmen können.

In ▶ **Tab. 3** ist dargestellt, ob die Befragten ein Smartphone besitzen, wie oft sie dieses auf Nachrichten überprüfen und ob sie darauf Apps verwenden. Betroffene gaben an, dass sich subjektiv die Antwortlatenz auf Nachrichten im Rahmen von depressiven Episoden zu einem großen Teil verlängert und bei etwa der Hälfte der Fälle im Rahmen von (hypo)manischen Episoden deutlich verkürzt.

▶ **Tab. 2** Demographische und klinische Merkmale von PatientInnen mit einer bipolaren Störung beziehungsweise Angaben von Angehörigen über die Erkrankung der Betroffenen.

	Bipolare PatientInnen (n = 51)	Angehörige (n = 28)	Angehörigenaussagen über Betroffene
Alter (Jahre)	43,47 (± 13,08)	49,79 (± 12,89)	43,57 (± 13,54)
Geschlecht (männlich)	39,2 %	32,1 %	
Betroffener Angehöriger			
Vater/Mutter			7,2 %
Sohn/Tochter			32,2 %
PartnerIn			57,1 %
Diagnosezeitpunkt (Alter)	34,66 (± 13,81)		34,42 (11,29)
Anzahl der Depressionen	6,49 (5,59)		5,05 (5,05)
Anzahl der (Hypo)manien	3,40 (3,89)		3,83 (4,54)
Derzeitige Behandlung			
Stationär	25,5 %		7,1 %
Ambulant, mindestens alle 6 Monate	43,1 %		60,7 %
Ambulant, unregelmäßig	25,5 %		25,0 %
Keine Angabe	5,9 %		7,1 %

Sowohl PatientInnen als auch Angehörige stuften eine technische Unterstützung in der Therapie der bipolaren Erkrankung als sinnvoll ein und würden es begrüßen, wenn die Betroffenen durch eine App auf Veränderungen in der Stimmung- und Aktivitätslage aufmerksam gemacht werden würden. Sie gaben zu einem sehr großen Teil an, dass sie eine speziell für die bipolare Störung entwickelte App nutzen würden (▶ **Tab. 3**).

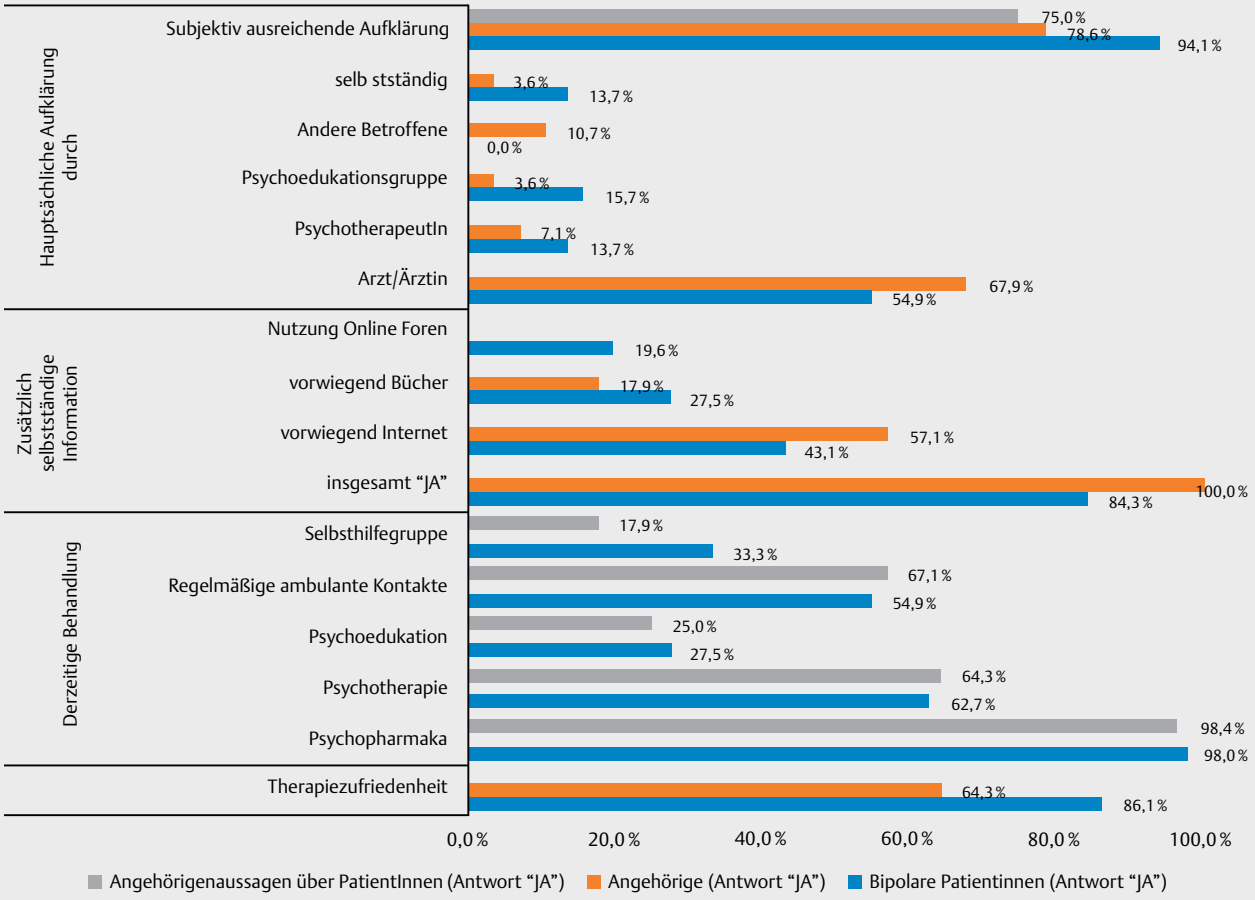
Diskussion

Das Ziel dieser Studie war es zu erheben, ob PatientInnen mit bipolarer Störung und deren Angehörige eine technische Unterstützung durch eine Smartphone-App als sinnvoll und praktikabel in der Früherkennung von Symptomen und in der Behandlung der Erkrankung erachten.

Die Ergebnisse dieser Fragebogenstudie zeigen, dass sich PatientInnen mit einer bipolaren Erkrankung und deren Angehörige subjektiv gut über die Erkrankung informiert und aufgeklärt fühlen, aber dass sie dennoch in 13,7 % beziehungsweise 35,7 % nicht mit den derzeitigen Behandlungsmöglichkeiten zufrieden sind. Zudem muss darauf hingewiesen werden, dass die TeilnehmerInnen dieser Studie zu einem Großteil einerseits bereits mehrere Krankheitsepisoden erlebt haben und andererseits zum Untersuchungszeitpunkt an der Spezialambulanz für bipolare Erkrankungen spezifische professionelle Therapie erhalten hatten und somit möglicherweise bereits eher zu Experten ihrer Erkrankung geworden sind als andere Menschen mit einer bipolaren Erkrankung ohne ein solches Therapieangebot. Generell waren Angehörige mit der aktuellen Behandlung weniger zufrieden als PatientInnen. Dies könnte damit zusammenhängen, dass es bisher aufgrund limitierter Ressourcen ein deutlich größeres Angebot für professionelle Aufklärung, Behandlung und vor allem Psychoedukation für Betroffene selbst gibt. Dennoch gaben auch 84,3 % der PatientInnen und 89,3 % der Angehörigen dieser Kohorte an, dass sie eine technische Unterstützung als sinnvoll erachten und dass sie eine Smartphone App für die Behandlung der bipolaren Erkrankung nutzen würden.

Auch wenn BehandlerInnen evidenzbasiert psychopharmakologische und psychotherapeutische Therapien anwenden, gibt es derzeit dennoch häufig schwere Verläufe einer bipolaren Erkrankung. Folgend besteht aus BehandlerInnensicht die Notwendigkeit der Erforschung innovativer Behandlungsstrategien. Je häufiger schwere affektive Episoden durchlebt werden, desto mehr biologische sowie soziopsychologische Folgeschäden entstehen [4]. Je früher also erste Anzeichen beziehungsweise der Beginn einer Krankheitsepisode erkannt werden, desto besser ist die Prognose für den Verlauf der einzelnen Episode und somit der lebenslangen Erkrankung [8]. Psychotherapeutische sowie selbstwirksame Maßnahmen, die zur Regulierung des Schlafverhaltens, sowie des Bewegungsverhaltens und einer Ausgeglichenheit sozialer Unternehmungen eingesetzt werden, könnten frühzeitig der Entwicklung einer krankheitswertigen Symptomatik entgegenwirken [31]. Daraus ergibt sich, dass der Fokus in der Behandlung der bipolaren Erkrankung noch mehr auf der Erkennung von Frühwarnzeichen liegen sollte.

Laut dieser Untersuchung werden Frühwarnzeichen jeder depressiven Episode von 25,5 % und die manische Entwicklung sogar nur von 11,8 % der PatientInnen erkannt. Angehörige gaben an, in 10,7 % der Fälle Frühwarnzeichen einer depressiven und in 7,1 % der Fälle, jene einer manischen Entwicklung wahrzunehmen. Die Angehörigen hatten jedoch das subjektive Gefühl die betroffene Person nur wenig beeinflussen zu können. 88,2 % der PatientInnen und 85,7 % ihrer Angehörigen bemerken zu Beginn einer Depression wiederkehrende Symptome, insbesondere einen Energieverlust. Frühwarnzeichen manischer Episoden werden von 70,6 % der Pa-

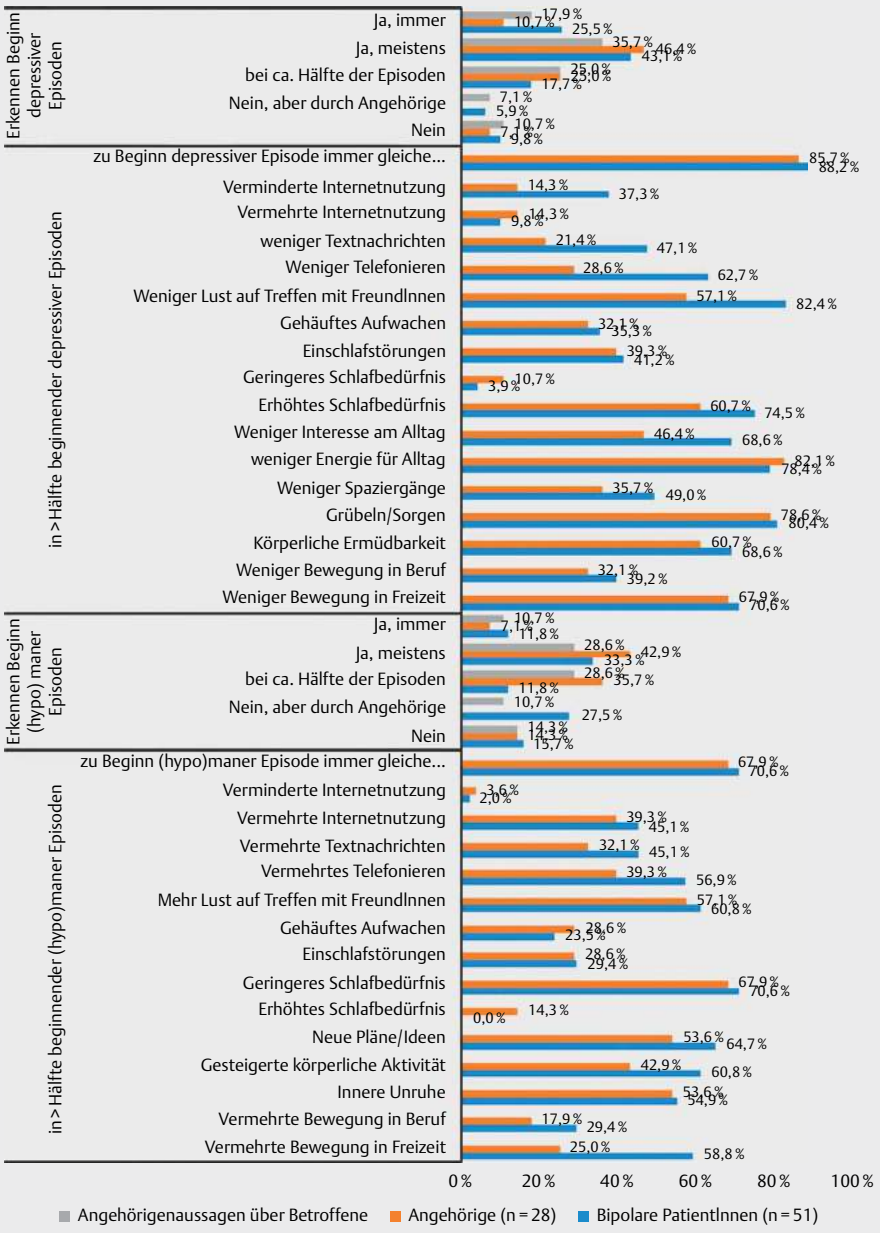


▶ **Abb. 1** Aufklärungsmodalitäten und therapierelevante Variablen von PatientInnen mit einer bipolaren Störung beziehungsweise Angaben von Angehörigen über die Erkrankung der Betroffenen.

tientInnen und 67,9 % ihrer Angehörigen wahrgenommen, insbesondere Ruhelosigkeit und reduziertes Schlafbedürfnis. Zusammenfassend lässt sich also anführen, dass Frühwarnzeichen von bipolaren Krankheitsepisoden, welche von PatientInnen nur teilweise erkannt werden, sich häufig in Veränderungen der körperlichen Aktivität, des Kommunikationsverhaltens und des Schlaf-Wach-Rhythmus äußern. Auch wenn der Anteil der PatientInnen, die ihre individuellen Frühwarnzeichen gut erkennen, relativ hoch erscheint, könnte das Hinzukommen von neuen Möglichkeiten diesen Prozentsatz noch erhöhen und vor allem für einzelne Betroffene lebensverändernd sein.

M-health Produkte könnten in der Erfassung individueller Verhaltensmuster und insbesondere Abweichungen von den individuell üblichen Mustern hilfreich sein. Das Ziel soll dabei sein, Frühwarnzeichen anhand objektiver, kontinuierlicher und individueller Daten zu detektieren und anschließend individuelles Feedback zur Selbstwirksamkeitssteigerung der Betroffenen zu geben. Veränderungen in der Stimmungslage, in den Symptomen und im Verhalten könnten schneller und individueller erkannt werden. Die gemessenen Verhaltensmuster werden je nach Produkt unterschiedlich an die NutzerInnen rückgemeldet. So entsteht beispielweise eine graphische Übersicht über Arbeitszeit, körperliche Aktivität, Schlafrhythmus, digitale Kommunikation und Stimmungslage. Es gibt Hinweise in der Literatur, dass Verhaltensweisen wie beispielweise die Reduktion der Sitzdauer [32] sowie eine Ernährungsumstellung [33] durch visuell ansprechende Apps bei psychisch gesunden Menschen, verändert werden können. In einer bipolaren Kohorte war das digitale Erfassen sozialer Rhythmik vergleichbar mit der validierten Paper-Pencil Ausführung und wirkte sich nach einer Nutzung am Mobiltelephon zudem positiv auf eine Veränderung aus [34]. Daraus sowie aus der klinischen Erfahrung lässt sich ableiten, dass alleine schon die Visualisierung und Kenntnis über Verhaltensweisen, -muster, und -veränderungen das Potenzial ergibt, die Denkweise der Betroffenen zu verändern und zu „gesundem Verhalten" wie beispielsweise einen ausgeglichenen Wach-Schlaf-Rhythmus oder ausreichend Aktivität und Bewegung zu verstärken. Hierbei sollte die Erfassung häufiger Verhalten und Frühwarnzeichen in m-health Lösungen immer inkludiert sein, jedoch auch die Möglichkeit für eine Eingabe individueller Frühwarnzeichen wie in dieser Studie erhobene „Ernährung" „Schuldgefühle", „Veränderung hygienischer Maßnahmen/ auf das Äußere wertlegen" „Fernsehgewohnheiten", „Alkohol trinken", Freizeitausgaben", „sexuelles Bedürfnis".

Durch eine Erhöhung der Selbstmanagementaktivitäten könnten depressive Symptome reduziert werden [35]. ■■[36] ■■fan-



▶ **Abb. 2** Angaben zur Früherkennung depressiver und (hypo)manischer Episoden.

den in einer Studie einen Zusammenhang zwischen GPS Daten, die durch eine App gemessen wurden, und depressiven Symptomen in einer Kohorte von Personen mit einer bipolaren Störung. Zudem berechnen viele Produkte im Hintergrund Abweichungen und fragen die NutzerInnen bezüglich weiterer Symptomanzeichen. So kann eine maßgeschneiderte Psychoedukation hinsichtlich einzelner Symptomkomplexe erfolgen. Ein realistisches Ziel von m-health in der Behandlung der bipolaren Störung ist somit die Verbesserung des Selbstmanagements und die Steigerung der Selbstwirksamkeit, wodurch letztlich Rezidive, Rückfälle, schwere Episodenverläufe und Krankenhausaufenthalte besser verhindert werden sollen. Aus den Ergebnissen dieser Befragung geht hervor, dass Menschen mit bipolarer Erkrankung psychopharmakologische, psychoedukative, psychotherapeutisch/psychologische, mobilpsychiatrische sowie Sport, Ernährung als auch Teilnahme an Studienprojekten als Behandlungsoptionen in Anspruch nehmen. Aspekte aus diesen Bereichen könnten teilweise in eine App aufgenommen werden. So könnten beispielsweise Wecker mit Medikamentennamen und Dosierungen zu vorher definierten Einnahmezeitpunkten läuten sowie Medikamentenänderungen in die Graphiken mit Stimmungs- und Verhaltensmonitoring dargestellt werden. Zudem könnte eine Vernetzung zu einer verständlichen Beschreibung der einzelnen Medikamente mit Wirkweise und Nebenwirkungen hergestellt werde. Ebenso Termine bei BehandlerInnen sowie einschlä-

▶ **Tab. 3** Smartphone-Nutzung sowie Wunsch nach technologischer Unterstützung von PatientInnen mit bipolarer Störung sowie deren Angehörigen.

	Bipolare PatientInnen (n = 51) (Antwort JA)	Angehörige (n = 28) (Antwort JA)	Angehörigenaussagen über Betroffene (Antwort JA)
SmartphonebesitzerIn	82,4 %	82,1 %	
Appnutzung auf Smartphone	68,6 %	71,4 %	
Facebook	47,1 %	32,1 %	
Whatsapp	62,7 %	71,4 %	
Kommunikation (zB Skype, Viber)	23,5 %	21,4 %	
Bewegungsverhalten (zB Runtastic)	13,7 %	10,7 %	
Schlafverhalten	3,9 %	14,3 %	
Andere	15,7 %	17,9 %	
Nutzung kostenpflichtiger Apps	9,8 %	17,9 %	
Handycheck nach Neuigkeiten			
Nur bei Klingeln	17,6 %	14,3 %	
1–2 mal täglich	11,8 %	7,1 %	
3–4 mal täglich	25,5 %	35,7 %	
Nahezu stündlich	19,6 %	28,6 %	
Mehrmals in der Stunde	21,6 %	10,7 %	
Nahezu sofortiges Antworten auf Nachrichten	58,8 %	53,6 %	57,1 %
Veränderung der Antwortdauer in depressiven Phasen			
nein	9,8 %		25,0 %
ja, verlängert	78,4 %		50,0 %
ja, verkürzt	9,8 %		14,3 %
Veränderung der Antwortdauer in (hypo)manischen Phasen			
nein	37,3 %		32,1 %
ja, verlängert	7,8 %		28,6 %
ja, verkürzt	52,9 %		25,0 %
Subjektive Sinnhaftigkeit technischer Unter-stützung in Behandlung der bipolaren Störung	84,3 %	89,3 %	
Subjektive Sinnhaftigkeit einer App, die auf Änderungen von Stimmungs- und Aktivitätslage aufmerksam macht	78,4 %	85,7 %	
Bereitschaft zur Nutzung einer App für bipolare Störungen	84,3 %	89,3 %	

gige Themen ebendort könnten festgehalten werden. Die Ernährung könnte entweder nur als kleiner Bereich in Form von Appetitveränderungen subjektiv erfragt werden oder komplex mit fotographischer und schriftlicher Eingabe von Mengen und Inhaltsstoffen. Ob dies in der Sicht von PatientInnen in der Früherkennung affektiver Episoden sinnvoll ist und der Nutzen dem Aufwand überlegen ist, müsste in weiteren Befragungen untersucht werden.

Zudem ergab diese Untersuchung, dass die meisten PatientInnen mit einer bipolaren Störung wichtige Bezugspersonen haben, mit denen Sie über ihre Erkrankung sprechen, wobei diese zu einem kleineren Anteil Einfluss auf Krankheitsepisoden nehmen können. Es ist sinnvoll während euthymen Phasen Krisenpläne mit konkreten Handlungsplänen bei speziellen Frühwarnzeichen zu erstellen. Bisher sind auch diese Krisenpläne in Papierform und meist im Verlauf nicht angepasst. Daher wäre es eine Möglichkeit solche Krisenpläne zu digitalisieren und flexibel zu gestalten. Zudem gibt es Überlegungen extra Apps für nahe Angehörige zu entwickeln, die mit der App des Betroffenen vernetzt sind (nur mit dezidierter Zustimmung aller Beteiligten). So könnten Außenansichten wie Veränderungen in der Sprechweise, Reizbarkeit oder Meldefrequenz von Angehörigen in das System eingegeben werden und in die Analysen miteinbezogen werden um noch mehr Daten zur Berechnung von Krankheitsepisodenfrühstadien zu generieren. Da die Einsicht für den Beginn von Krankheitsepisoden von PatientInnen manchmal wenig vorhanden ist, wäre eine solche Außeneinschätzung sinnvoll. Eine technologische Analyse könnte für die zwischenmenschliche Beziehung von Vorteil sein. Es könnte sein, dass mhealth Produkte als Zusatz- oder Einzeltherapie einen Vorteil gegenüber der derzeitigen Therapie bringen können [37], auch wenn derzeit aufgrund der Heterogenität der Produkte und fehlenden

Goldstandards keine generellen Empfehlungen für das Monitoring bipolarer PatientInnen ausgesprochen werden kann [38]. In der Vergangenheit waren ÄrztInnen und TherapeutInnen auf subjektive, retrospektive Informationen angewiesen. Nun könnten Personen mit einer bipolaren Störung objektive Daten über ihre Symptome und Verhaltensweisen zu den ärztlichen Terminen mitbringen, was wiederum zur weiteren Verbesserung des Verständnisses des individuellen Krankheitsverlaufs und der Behandlung der Erkrankung verwendet werden könnte. Zudem stellt es ein Gewinn für die medizinische Forschung dar, wenn Einzelpersonen objektive und kontinuierliche Aufzeichnungen über ihre Symptome liefern würden [29, 39].

Unsere Studie zeigte, dass ein sehr großer Anteil der Befragten ein Smartphone besitzt und den Wunsch nach einer technischen Unterstützung in der Behandlung der bipolaren Erkrankung hat. Weiterführend berichteten die meisten Befragten, dass sie eine Smartphone App für die Behandlung der bipolaren Erkrankung nutzen würden. Auch eine Studiengruppe in den USA untersuchte 320 Menschen mit einer psychischen Störung und stellte fest, dass 62.5 % ein Smartphone hatten und davon 70.6 % das Interesse haben dieses zur Symptomüberwachung zu nutzen [40]. Eine kürzlich durchgeführte Umfrage ergab, dass auch im Gesundheitsbereich tätige Personen eine positive Einstellung zur Verwendung von Apps in der klinischen Praxis haben. Das technologische Wissen sowie die Produkte und damit der Einsatz im täglichen klinischen Arbeiten waren jedoch sehr unterschiedlich [35]. Es gibt im deutschsprachigen Raum bereits einige m-health Produkte speziell für die Behandlung der bipolaren Erkrankung. Bisher wurden einige Studienprotokolle für klinische Validierungs- und Bewertungsstudien veröffentlicht, jedoch sind endgültige Ergebnisse und Wirksamkeitsbewertungen noch wenig beschrieben [41–44]. Zudem wird derzeit an der Medizinischen Universität Graz eine Validierungsstudie einer App durchgeführt (NCT03275714). Ziel der derzeit laufenden Studien ist es, zu erforschen, ob die Untersuchungsprodukte valide sind und ob aufgezeichnete Verhaltensmusteränderungen mit Veränderungen in der Stimmungslage und weiteren Krankheitssymptomen einhergehen. Darüber hinaus soll analysiert werden, ob mithilfe der App eine Früherkennung von manischen oder depressiven Episoden verbessert werden kann. Ein weiteres Ziel ist die Evaluierung der Akzeptanz der NutzerInnen. Insgesamt wird so wissenschaftlich überprüft, ob eine Smartphone-App ein valides Assistenzsystem für ein selbstbestimmtes Leben für Menschen mit einer bipolaren Erkrankung darstellen kann. Generell sind keine direkten Schäden durch die Nutzung einer App zu erwarten. Der Datenschutz sollte selbstverständlich stets umfassend beachtet werden. Bei vielen Produkten werden sämtliche Daten lokal im Mobiltelefon gespeichert und niemals online gestellt. In anschließenden Sitzungen mit Behandelnden, die mit dem Produkt vertraut sind, können die Daten gemeinsam gesichtet werden beziehungsweise an einen lokalen Computer übertragen werden.

E-health-Produkte im Allgemeinen und m-health-Produkte im Besonderen könnten zudem in weiteren Gebieten auf vielfältige Weise nützlich sein. Smartphones sind im heutigen Alltag weit verbreitet und ermöglichen einen einfachen Zugang zu den Produkten. Eine Studie zeigte, dass Personen mit psychischen Erkrankungen, die regelmäßig per Videokonferenz von erfahrenen PsychotherapeutInnen behandelt wurden, nicht weniger zufrieden waren als Personen, die einen persönlichen medizinischen Termin hatten [45]. In einer Studie von [46] wurde gezeigt, dass fast doppelt so viele Menschen mit Depressionen mit e- und m-health Therapie behandelt werden können im Vergleich zu Face-to-Face-Therapien. Dadurch ist es möglich lange ambulante Wartezeiten auf Termine zu minimieren. Besonders während der aktuellen Pandemie mit Empfehlungen der Kontaktminimierung, Einschränkungen des Bewegungsumkreises und erhöhtem Ansteckungsrisiko in Krankenhäusern und Arztpraxen sind telemedizinische Behandlungen und m-health Lösungen attraktiv. Des Weiteren können durch den Einsatz von Apps auch große Entfernungen überwunden werden. Dies würde sich positiv auf Regionen auswirken, in denen eine medizinische Versorgung nicht ohne weiteres möglich ist. Auch in dieser Untersuchung waren PatientInnen unter anderem aufgrund zu großer Kontrollabstände und Angehörige aufgrund fehlender mobiler sozialpsychiatrischer Betreuung und fehlender spezieller Psychotherapie für die bipolare Störung mit der derzeitigen Behandlung unzufrieden. Diese Bereiche könnte eine Smartphone-App positiv beeinflussen. Durch die Zeitersparnis und Nutzung vorhandener Strukturen ist es möglich, kostengünstigere Diagnosen und Therapien durchzuführen, wodurch die Kosten für das gesamte Gesundheitssystem gesenkt werden. Des Weiteren könnte das Stigma um psychische Erkrankungen verringert werden. Betroffene können sich anonym im Internet informieren, bevor sie die Hürde überwinden und sich an eine/n Professionierte/n wenden. Darüber hinaus können Selbsthilfeforen möglicherweise dazu beitragen, das Gefühl einer Person, mit ihrer Krankheit allein zu sein, zu verringern.

Auch wenn es unwahrscheinlich ist, dass e-health Produkte medizinische und therapeutische Behandlungen vollständig ersetzen, können sie in der Zukunft eine zusätzliche Behandlungsstrategie darstellen und sollten daher von Behandlungsteams und WissenschaftlerInnen vermehrt evaluiert werden. Aktuell sind nur wenige Produkte wissenschaftlich validiert. Daher ist eine der Herausforderungen der Zukunft, mehr Validierungsstudien durchzuführen und bestmögliche Produkte für die AnwenderInnen zu finden.

Limitationen

Aufgrund der kleinen Stichprobe war es nicht möglich Unterschiede zwischen PatientInnen mit bipolar I versus II Störung, verschiedenen Krankheitsverläufen (Anzahl der depressiven und (hypo)manischen Episoden, Länge der euthymen Episoden), Altersgruppen, Geschlechtern oder sozioökonomische Hintergründen (Bildungshintergrund, soziales Netzwerk) zu analysieren. Zudem wurde das bisherige Wissen über die bipolare Erkrankung nicht objektiv erfassen. Zukünftige Untersuchungen sollten diese potentiell wichtigen Aspekte berücksichtigen um Apps spezifisch auf die Bedürfnisse der NutzerInnen entwickeln und anpassen zu können. Des Weiteren könnte einige der gestellten Fragen mit binären Antwortmöglichkeiten weitere Wünsche oder Anmerkungen der PatientInnen unbeachtet lassen.

Konklusion

Die derzeitigen konventionellen Behandlungsmöglichkeiten in der bipolaren Störung sind aus BehandlerInnen- und Betroffenensicht unzureichend. Aus Sicht einiger PatientInnen und deren Angehörigen besteht der Wunsch nach innovativen, technischen Unter-

stützungen. Die Früherkennung von Krankheitsepisoden, die sich oft in veränderten von Verhaltensweisen (körperliche Aktivität, Schlaf-Wach-Rhythmus, digitale Kommunikation) äußert, ist für den Krankheitsverlauf essentiell. Hier könnten validierte Smartphone-Apps durch objektive, kontinuierliche und individuelle Datenerhebung in der Zukunft für die klinische Behandlung und die Forschung einen wesentlichen Beitrag leisten. Um evidenzbasiert arbeiten zu können, ist zukünftig jedenfalls die Entwicklung, Validierung und Wirksamkeitsbeurteilung spezifischer Produkte notwendig.

Interessenkonflikt

Die Autorinnen/Autoren geben an, dass kein Interessenkonflikt besteht.■ korrekt?■

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ORIGINAL RESEARCH

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COVID-19-related fears and information frequency predict sleep behavior in bipolar disorder

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Abstract

Introduction: The coronavirus disease (COVID-19) pandemic and consequent restrictions including social distancing had a great impact on everyday life. To date, little is known about how the restrictions affected sleep, which is commonly disturbed in bipolar disorder (BD). The aim of this study was to elucidate sleep patterns during the pandemic in Austrian BD individuals.

Methods: An online survey assessed sleep with the Pittsburgh Sleep Quality Index (PSQI) and COVID-19-associated attitudes, fears, and emotional distress of 20 BD individuals and 19 controls (HC) during the pandemic. The survey was conducted in April 2020, when very strict regulations were declared, and repeated in May, when they were loosened.

Results: Individuals with BD reported overall poor sleep according to PSQI sum at both time points. Subjective sleep quality, sleep latency, daytime sleepiness, and PSQI sum were worse in individuals with BD than in HC. Individuals with BD informed themselves more frequently about pandemic-related topics. Higher information frequency and more COVID-19 fears (about the virus, own infection, contracting others) correlated with worse PSQI values. Regression models found in BD group that higher information frequency as well as higher COVID-19 fears in April predicted worse sleep characteristics in May, in particular subjective sleep quality, sleep duration, sleep efficiency, and daytime sleepiness.

Conclusion: As sufficient sleep duration and quality are essential for well-being and particularly important for vulnerable BD individuals, it is important that information about the pandemic is gathered to a reasonable extent and mental health professionals include COVID-19-related fears when currently treating BD.

KEYWORDS

bipolar disorder, COVID-19 pandemic, Pittsburgh Sleep Quality Index, sleep

1 | INTRODUCTION

An unbalanced sleep–wake rhythm can complicate the course of illness episodes of bipolar disorder (BD) and can trigger relapse. Sixty-nine percent of individuals with BD suffer from sleep disturbances (Laskemoen et al., 2019). Beside manic and depressive episodes, sleep disturbances can also occur in euthymia and are associated with lower global and cognitive functioning (Laskemoen et al., 2019, 2020). Clinical symptoms of BD, such as sleep disorders, are affected by circadian rhythms, but disturbed sleep–wake rhythms can also influence or trigger illness episodes (Lewis et al., 2017). In turn, both depressive and manic episodes can lead to sleep disturbances in the early stages. Different levels of vulnerability for BD are assumed to exist due to biological processes such as genetics, unstable biological rhythms (Bengesser et al., 2018), inflammatory processes (Goldstein et al., 2009), imbalance of central neurotransmitters, and psychosocial influences such as life events, personality, and family environment. Additional chronic or current psychosocial stressors such as trauma, separations, job loss, and abuse of psychotropic substances, but also unstable sleep–wake rhythms, may provoke an exacerbation of (symptoms of) the disorder. The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic, which causes the novel coronavirus disease (COVID-19), and its consequences including social distancing and self-isolation, might be severe triggers for the development of BD illness episodes. There are preliminary studies that show elevated psychosocial distress and lifestyle changes during the pandemic in BD subgroups (Van Rheenen et al., 2020).

To contain the spread of the pandemic, governments across the world have passed new laws and restrictions. Like many other countries, Austria imposed a lockdown, enforced social distancing as well as home office wherever possible. From March 15th 2020 until the end of April, the lockdown included all nonessential shops, restaurants, universities, schools, nurseries, and gyms. Additionally, public events or meetings with people from different households were not allowed. Everybody except key workers had to work from home. It was compulsory to wear face masks in supermarkets and to keep a distance of at least one meter. In case of transgressions, fines had to be paid. On the first of May, the restrictions were loosened. Gatherings of up to ten people were allowed, and nonessential shops, hairdressers, and leisure venues reopened. By the end of May, restaurants, schools, and nurseries opened again and events with up to 100 people were allowed.

Very recent studies, highlighting the effects of the pandemic in 2020, found that the pandemic itself, but also the statutory restrictions, has been shown to be associated with multiple psychosocial symptoms. This extraordinary situation correlates with feelings of uncertainty, general low well-being, stress, depression, somatization, anxiety, sleep disturbances, changes in alcohol and nicotine intake, and fear of infection (Pérez-Fuentes et al., 2020; Stanton et al., 2020). Social distancing and quarantine can result in confusion, anger, frustration, and boredom, being misinformed as well as financial problems (Brooks et al., 2020). These factors may lead to behavioral and lifestyle changes, in lifestyle, for example, the disruption of the sleep–wake rhythm. However, the manifestation of symptoms depends on previous mental (Vindegaard & Benros, 2020) and somatic diseases, personality structure, resilience, and individual coping mechanisms (Pfefferbaum & North, 2020). Due to these reasons, the COVID-19 pandemic directly and indirectly leads to exceptional challenges for mental health services (Fatke et al., 2020).

To date, very little is known about sleep during such an extraordinary situation as the COVID-19 pandemic. It is discussed that uncertainty, worries about one's own and others' health and the situation, changes in daily routines, omission of sports and hobbies, working from home, home-schooling, financial problems, and other pandemic-related stressors have a negative impact on sleep (Altena et al., 2020; Morin et al., 2020). Sleep is essential for the human organism. Sufficiently long and good sleep is necessary for recovery, cell growth, synaptogenesis, and cognitive function (Frank & Heller, 2018). An individual's required sleep time is commonly between 7 and 9 hr. However, duration or quality of sleep is often and easily disturbed. Insomnia with problems falling asleep, staying asleep, and early morning awakening and hypersomnia are possible disorders that occur in isolation or in the context of various mental illnesses (Saletu-Zyhlarz et al., 2013). In general, sleep is influenced by daylight, light from electronic devices, particularly in the evening, melatonin metabolism, daily routines, physical activity, alcohol and diet as well as stress. In addition, poor sleep quality was associated with increasing age, female sex, migration background, unemployment, physical inactivity, somatic health problems, mental illness, and again stress (Azevedo Barros et al., 2019). Social isolation and loneliness are related to poor sleep too, presumably mediated by depression and stress (Wakefield et al., 2020). There are contradicting findings about the impact of social interactions on sleep quality. Some research indicated that social interactions and social support are related to better sleep quality (Kent de Grey et al., 2018); however, a Chinese study group found that fewer social contacts during the pandemic improved sleep quality by reducing anxiety and stress (Xiao et al., 2020). Moreover, time spent occupying oneself with pandemic-related topics might be relevant for feelings, lifestyle, and sleep. On the other hand, good sleep can have a preventive effect against psychosocial consequences. It was shown that people living in Wuhan, who had better sleep quality and less early awakenings in times of the severe pandemic, had an decreased risk of developing post-traumatic stress symptoms (Liu et al., 2020). Assessing sleep disturbances as critical pathophysiological elements in BD could help to gain a deeper understanding of the psychological consequences on the course of BD due to the COVID-19 crisis.

To date, no trial has investigated sleep quality and sleep patterns during the COVID-19 pandemic in the especially vulnerable group of individuals with BD. Therefore, the present study aimed to determine whether (a) sleep was different in individuals with BD compared to mentally healthy people during COVID-19 restrictions, (b) sleep patterns changed in individuals with BD when transitioning from strict distancing regulations to loosened regulations, (c) sleep is related to how frequently individuals access information about COVID-19-related topics, and (d) sleep is associated with COVID-19-related fears and attitudes.

2 | METHODS

2.1 | Procedure and participants

The survey was conducted at the Medical University of Graz, Department of Psychiatry and Psychotherapeutic Medicine as a part of the ongoing multicenter BIPLONG study. The BIPLONG study aims to explore the relationship between BD and obesity, metabolism, lifestyle, and cognitive function in a longitudinal setting. Individuals with BD—diagnosed with the Structured Clinical Interview for DSM-IV (SCID-I)—as well as individuals without a mental disease (healthy controls, HC) are invited to participate in the study for up to thirteen visits every 6 months in the dedicated outpatient center for BD of the Medical University Graz. Individuals with BD were either former inpatients or outpatients of the dedicated outpatient center for BD. HC were recruited from the general population via written invitations and word of mouth (circle of acquaintances, medical students, clinical personnel staff). HC were screened for psychiatric diseases with a short screening questionnaire based on the SCID. From 9 April to 28 April 2020 (t1), at the time of the complete lockdown, an additional online survey was sent out to study participants using the software LimeSurvey (www.limesurvey.org; Limesurvey GmbH). The same survey was rerun from 5 May to 4 June 2020 (t2), when the restrictions were loosened. The study has been approved by the local ethics committee (Medical University of Graz, Austria; EK-number: 25–335 ex 12/13) in compliance with the current revision of the Declaration of Helsinki, ICH guideline for Good Clinical Practice and current regulations.

The current investigation included 20 individuals with BD (10 females, 10 males) as well as 19 HC (14 females, 5 males) who completed the survey at both time points. Individuals with BD were outpatients of the special unit for BD, and like HC, had to be of legal age and had given written informed consent prior to their participation in this study. The participation of the online survey was voluntary and pseudo-anonymously used the participant code of the former study participation.

2.2 | Materials

The *Pittsburgh Sleep Quality Index* (PSQI) by Bysse et al. (1989) is a self-rated questionnaire, which assesses sleep quality and disturbances over a 1-month time interval. The questionnaire consists of 19 items, which generate seven components: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime sleepiness. Each component scores from 0 ("no difficulty") to 3 ("severe difficulty"). A total PSQI score (range 0–21) of more than 5 reaches a diagnostic sensitivity of 89.6% and specificity of 86.5% (*kappa* = 0.75; $p \leq .001$) in distinguishing good and poor sleepers (Bysse et al., 1989), whereas higher scores indicate worse sleep quality. Despite the prevalence of sleep complaints among psychiatric patients, few questionnaires have been specifically designed to measure sleep quality in clinical populations. The PSQI was evaluated over an 18-month period in a mentally healthy cohort, as well as in individuals with depression and in individuals with sleep disorders. Acceptable measures of internal homogeneity, consistency (test–retest reliability), and validity were obtained.

The *Beck Depression Inventory-II* (BDI-II), German version by Kühner et al. (2007), is a self-rated questionnaire with 21 items, which assesses depressive symptomatology. The total score ranges from 0 to 63 points, whereas a score of 18 points or more indicates clinical depression. There is an internal consistency with Cronbach's $\alpha \geq 0.84$ and a reliability of $r \geq 0.75$.

The *Altman Self-Rating Mania Scale* (ASRM) by Altman et al. (1997) is a 5-item scale for assessing mood, self-confidence, sleep disturbances, speech, and activity level over a 1-week period. Each question can be rated with 0 to 4 points, and a total score above 5 correlates with manic symptoms.

The self-constructed COVID-19 questionnaire in German collected data about sociodemographic variables, living situation, activities, hobbies, and use of medication. Moreover, it inquired about COVID-19-related attitudes, lifestyle, and fears as well as trust in regulations and emotional distress due to physical and social distancing over the last week. Inter alia, to assess *information frequency* participants were asked to rate how often they inform themselves about the pandemic and associated topics on a 6-point scale (1 = "less than once a week," 2 = "1–3 times per week," 3 = "3–6 times per week," 4 = "1–3 times per day," 5 = "4–6 times per day," and 6 = "more than 6 times a day"). *COVID-19 fears* were assessed by a mean index of "*How strongly do you rate your concerns and fears about the coronavirus?*", *"How strongly do you rate your fear of contracting the coronavirus?" and "How strongly do you rate your fear of infecting others with the coronavirus?"*. Each question could be answered with 0 ("no fear") to 10 ("very strong fear"). The sum was calculated and divided by three. *Emotional distress* was surveyed by five items with a 6-point rating scale from 0 ("not at all") to 5 ("very strong"). The items included the questions "*Social distancing makes me feel lonely/bored/frustrated/hopeless/anxious."* The index was calculated by the sum of the questions divided by five.

2.3 | Statistical analyses

All analyses were performed with the IBM Statistical Package for Social Sciences (SPSS), version 25.0. Chi-square test (nominal data), *t* tests (metric data), and Mann–Whitney U tests (ordinal data) were conducted to test for differences between the BD and HC group in descriptive variables. Multivariate covariance analyses (MANCOVAs) were used to calculate the differences between the BD and HC group in the PSQI components at t1 and t2, whereas age and sex were used as covariates due to their known clinical impact and statistical group differences. Paired-sample *t* tests or Wilcoxon tests were used to analyze differences between the two time points. Partial correlations with age and sex as covariates were performed to identify associations of the PSQI components with COVID-19 fears and emotional distress variables. As the information frequency

TABLE 1 Sociodemographic characteristics and differences in mood symptomatology as well as COVID-19-related attitudes and fears of individuals with BD and HC

	BD ($n = 20$)	HC ($n = 19$)	Statistics	p value
Sex	50% male	26.3% male	$x^2 = 2.309$	.129
Age in years (M, *SD*)	49.35 (±15.55)	33.05 (±9.66)	$t_{37} = 3.906$	**<.000****
Diagnosis	60.0% BD I 40.0% BD II	–		
t1				
Professional activity			$x^2 = 19.988$	**.003****
Working as before	0%	26.3%		
Working in home office	25.0%	52.6%		
Invalidity pension	50.0%	0%		
On demand/reduced hours	10.0%	5.3%		
Jobless due to pandemic	5.0%	0%		
Jobless as before pandemic	5.0%	0%		
In education	5.0%	15.8%		
BDI-II	15.45 (±10.74)	2.95 (±2.50)	$t_{21.164} = 5.062$	**<.000****
ASRM	0.95 (±2.28)	0.53 (±1.22)	$t_{37} = 0.718$	.472
Information frequency†	4.55 (±0.89) MR: 23.55	3.79 (±0.86) MR: 16.26	$U = 119.000$	**.047***
COVID-19 fears‡	4.45 (±2.69)	3.58 (±2.00)	$t_{37} = 1.121$	.269
Emotional distress§	1.56 (±1.16)	0.76 (±0.51)	$t_{26.372} = 2.819$	**.009****
t2				
BDI-II	12.20 (±11.69)	2.21 (±2.10)	$t_{20.285} = 3.759$	**.001****
ASRM	1.5 (±2.19)	0.16 (±0.37)	$t_{20.170} = 2.701$	**.014***
Information frequency†	3.60 (±1.19) MR: 21.90	3.16 (±1.02) MR: 18.00	$U = 152.000$	.296
COVID-19 fears‡	3.98 (±2.39)	3.16 (±1.85)	$t_{37} = 1.204$	.236
Emotional distress§	1.13 (±1.05)	0.73 (±0.61)	$t_{37} = 1.460$	.153

Abbreviations: ASRM, Altman Self-Rating Mania Scale; BD, bipolar disorder; BDI, Beck Depression Inventory; COPD, chronic obstructive lung disorder; HC, healthy controls; MR, mean rank; PSQI, Pittsburgh Sleeping Quality Index.

†1 = less than once a week, 2 = 1–3 times per week, 3 = 3–6 times per week, 4 = 1–3 times per day, 5 = 4–6 times per day, 6 = more than 6 times a day.

‡*"How strongly do you rate your concerns and fears about the coronavirus?", "How strongly do you rate your fear of contracting the coronavirus?" and "How strongly do you rate your fear of infecting others with the coronavirus?"* Mean of 3 0- to 10-point scales.

§*"Social distancing makes me feel lonely/ bored/ frustrated/ hopeless/ anxious"* Mean of 5 0- to 5-point scales.

*$p < .05$; **$p < .01$.

Bonferroni correction for multiple comparisons for the PSQI components (0.05/7 tests): bold values indicate $p < .0071$ and are considered significant.

is an ordinal variable, Spearman correlations were used for this item. Correlation analyses were calculated separately for the BD and HC group. The items of t1 correlating significantly with items concerning sleep of t2 as well as age and sex were used in regression models to analyze the variance of prediction of the sleep components. Error probabilities below 0.05 were accepted due to the clinical nature of the study. Bonferroni corrections were adjusted in correlation and regression analyses for the seven PSQI components (0.05/7 tests = 0.0071).

3 | RESULTS

Table 1 displays the sociodemographic characteristics and differences in current mood as well as COVID-19-associated fears and attitudes in April and May 2020. Individuals with BD were significantly older, had a higher body mass index, and were less often in an employment relationship compared to HC. No participant was tested positive for SARS-CoV-2, lived together with a person tested positive or was in quarantine until survey participation. Individuals with

BD scored significantly higher in the BDI-II, informed themselves more frequently and had more COVID-19-related emotional distress than HC at t1. At t2, there were significant differences between the groups in BDI-II and ASRM. The means of BDI-II, information frequency, COVID-19 fears, and emotional distress decreased in both groups from April to May, whereas the ASRM score increased in the BD group. Importantly, only the information frequency change was statistically significant (BD group: $Z = 3.226$, $p = .001$; HC group: $Z = -2.585$, $p = .010$). All values of BDI-II and ASRM were in the nonpathological range (see Table 1).

3.1 | Sleep differences between BD and HC during strict and loosened restrictions

A MANCOVA with age and sex as covariates showed significant group differences between the BD and the HC group in the sleep components and the sum of the PSQI at t1 (see Figure 1; $F_{7,29} = 3.270$, $p = .011$, $\eta^2 = 0.441$). Patients with BD scored higher in all components which correspond to worse sleep. Significant differences were found in subjective sleep quality ($F_{1,35} = 5.569$, $p = .024$, $\eta^2 = 0.137$), sleep latency ($F_{1,35} = 4.305$, $p = .045$, $\eta^2 = 0.110$), daytime sleepiness ($F_{1,35} = 8.195$, $p = .007$, $\eta^2 = 0.190$), the PSQI sum ($F_{1,35} = 7.041$, $p = .012$, $\eta^2 = 0.167$), and a tendency in sleep disorders ($F_{1,35} = 3.009$, $p = .092$, $\eta^2 = 0.079$).

At t2, the scores of the BD group were still higher, but there was no significant difference to HC anymore ($F_{9,27} = 1.517$, $p = .192$, $\eta^2 = 0.336$). Individuals with BD scored 6 or above in PSQI sum at both times, which indicates a poor sleep. Standard deviations were higher at t1 than at t2.

3.2 | Changes in sleep from April (strict -) to May (loosened restrictions)

The means in Figure 1 show an improvement in all sleep components from t1 to t2 in the BD group and almost all items in HC, but these changes were not statistically significant in paired *t* test analyses.

3.3 | Correlations of sleep and information frequency as well as COVID-19 fears

Within the BD group, in April (t1) the PSQI sum correlated significantly with information frequency ($r = 0.603$, $p = .005$) and COVID-19 fears ($r = 0.490$, $p = .039$), but not with emotional distress ($r = 0.301$, $p = .225$). Apart from sleep duration significantly correlating with information frequency ($r = 0.593$, $p = .006$), no significant correlation between information frequency as well as COVID-19 fears and the PSQI components was found after Bonferroni correction.

There were found large significant correlations in May (t2) between the PSQI sum score and information frequency ($r = 0.541$, $p = .014$), COVID-19 fears ($r = 0.536$, $p = .022$), and emotional distress ($r = 0.593$, $p = .009$) in the BD group. There were multiple relations between PSQI components and COVID-19-related attitudes, but after Bonferroni correction, only the correlation between daytime sleepiness and COVID-19 fears remained significant ($r = 0.640$, $p = .004$).

Within the HC group, we found only a few significant correlations. Analyses showed that lower information frequency was associated with more sleep disturbances at t1 ($r = -0.597$, $p = .007$). Moreover, the higher COVID-19 fear scores were at t2, the worse the sleep efficiency was ($r = 0.737$, $p = .001$).

Furthermore, in the BD group, there were significant correlations of PSQI sum at t2 and information frequency at t1 ($r = 0.712$, $p = <0.001$) as well as COVID-19 fears at t1 ($r = 0.561$, $p = .015$) and some sleep components after Bonferroni correction (subjective sleep quality and information frequency: $r = 0.609$, $p = .004$; subjective sleep quality and COVID-19 fears: $r = 0.644$, $p = .004$; daytime sleepiness and COVID-19 fears: $r = 0.616$, $p = .006$). Therefore, these variables were used for regression analyses.

3.4 | Regression models of information frequency and COVID-19 fears at t1 and sleep at t2

Tables 2 and 3 show the results of the linear regression models. Age and sex were also used as variables but did not explain any variance.

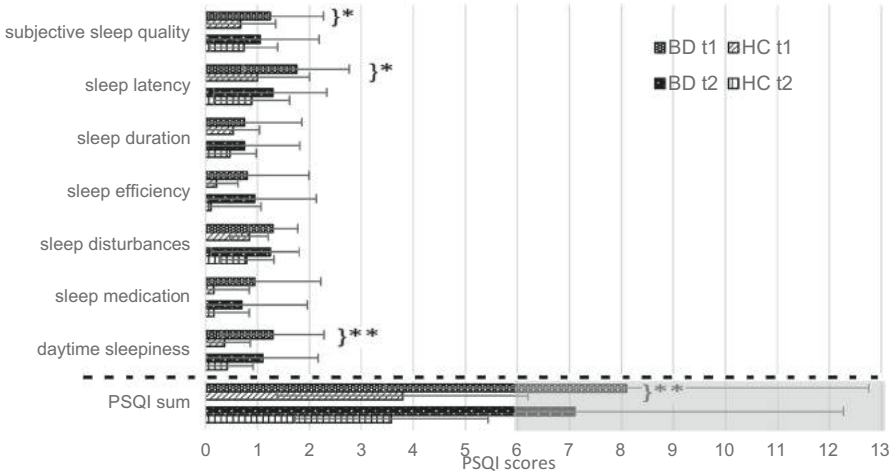

FIGURE 1 PSQI components at t1 and t2 in BD and HC. BD, bipolar disorder; HC, healthy controls; PSQI, Pittsburgh Sleeping Quality Index; gray underlaid = poor sleep in total; $^*p < .05$; and $^{**}p < .01$

TABLE 2 Results from linear regression with information frequency about COVID-19 from April 2020 as predictor of PSQI components in May 2020 in patients with BD adjusted for age and sex

	Model		Unstandardized coefficients		Standardized coefficients		
	R^2	$F_{3,19}$	*B*	*SE*	ß	*t*	*p* value
PSQI sum	0.533	6.081	4.211	1.030	0.721	4.086	**.001****
Subjective sleep quality	0.504	5.421	0.945	0.235	0.732	4.024	**.001****
Sleep latency	0.217	1.477	0.505	0.266	0.434	1.901	.075
Sleep duration	0.601	8.019	0.797	0.197	0.661	4.050	**.001****
Sleep efficiency	0.407	3.662	0.883	0.267	0.657	3.307	**.004****
Sleep disturbances	0.293	2.214	0.190	0.135	0.306	1.412	.177
Sleep medication	0.171	1.104	0.180	0.334	0.127	0.540	.597
Daytime sleepiness	0.339	2.740	0.711	0.253	0.589	2.806	.013*

Note: Bonferroni correction for multiple comparisons for the PSQI components: threshold of significance: $p < .0071$ (0.05/7 tests) are marked in bold letters.

Abbreviations: BD, bipolar disorder; PSQI, Pittsburgh Sleeping Quality Index.

*$p < .05$; **$p < .01$.

TABLE 3 Results from linear regression with COVID-19 fears from April 2020 as predictor of PSQI components in May 2020 in patients with BD adjusted for age and sex

	Model		Unstandardized coefficients		Standardized coefficients		
	R^2	$F_{3/19}$	*B*	*SE*	ß	*t*	*p* value
PSQI sum	0.252	6.073	0.968	0.393	0.502	2.464	**.024***
Subjective sleep quality	0.416	3.792	0.280	0.083	0.657	3.364	**.004****
Sleep latency	0.157	0.996	0.134	0.090	0.350	1.493	.155
Sleep duration	0.401	3.564	0.186	0.079	0.468	2.365	.031*
Sleep efficiency	0.173	1.114	0.187	0.103	0.423	1.818	.088
Sleep disturbances	0.589	2.838	0.079	0.042	0.385	1.866	.081
Sleep medication	0.162	1.032	−0.037	0.110	−0.078	−0.334	.743
Daytime sleepiness	0.388	3.388	0.249	0.080	0.625	3.128	**.006****

Note: Bonferroni correction for multiple comparisons for the PSQI components: threshold of significance: $p < .0071$ (0.05/7 tests) are marked in bold letters.

Abbreviations: BD, bipolar disorder; PSQI, Pittsburgh Sleeping Quality Index.

*$p < .05$; **$p < .01$.

Information frequency explained a significant proportion of variance in PSQI sum, subjective sleep quality, sleep duration, and sleep efficiency. COVID-19 fears at t1 predicted the PSQI sum score as well as subjective sleep quality and daytime sleepiness at t2 with a high variance.

4 | DISCUSSION

The present study investigated sleep characteristics in individuals with BD in comparison with HC during the COVID-19 pandemic in Austria. The results show overall poor sleep in the group with BD and worse sleep scores compared to HC. Individuals with BD informed themselves more frequently about the pandemic and had more emotional distress related to the social distancing in April when restrictions were very strict. In May, when legal regulations were loosened, the significant differences between the groups regarding information frequency, emotional distress, and sleep disappeared. At both points in time, BD individuals' sleep was worse, the more they informed themselves about the virus. Moreover COVID-19-related fears—including fears about the virus generally, contracting it themselves or infection of loved ones correlated with poor sleep. High information frequency and more COVID-19-related fears in April predicted sleep in May, in particular subjective sleep quality, sleep duration, sleep efficiency, and daytime sleepiness.

Individuals with BD reported worse sleeping habits than HC during the pandemic, in particular during very rigorous restrictions. This was independent of age and sex. Especially impairments in subjective sleep quality and sleep latency, daytime sleepiness, and sleep disorders were observed. This confirms findings from nonpandemic times. However, when regulations were less strict, the difference between the groups was not statistically significant anymore. As median PSQI scores showed, individuals with BD slept poorly at both

points in time, whereas healthy controls reported good sleep in both April and May. This could be a consequence of depressive symptomatology found in BD, generally impaired sleep quality in BD even in euthymia or a warning symptom. As poor sleep leads to a decrease of functioning, concentration problems, stress, dissatisfaction, and an overall decreased quality of life, it is a serious problem for this vulnerable group (Slyepchenko et al., 2019). Among other biological mechanisms, the suprachiasmatic nucleus of the hypothalamus and the paraventricular nucleus of the thalamus control the sleep–wake rhythm. Studies have found altered morphologies in patients with BD (Manaye et al., 2005). Moreover, the clock genes play an essential role in BD as well as in the sleep–wake rhythm (Bengesser et al., 2018). The circadian clock affects a variety of physiological processes such as cardiovascular activity, sleep and alertness, metabolism, and brain function (Lyall et al., 2018).

The aim of the treatment of BD is the prevention of severe illness episodes as well as supporting a good psychosocial functioning and quality of life. The psychosocial consequences of BD could be decreased well-being, stigma, cognitive dysfunction, loss of work, conflicts and disturbances in families, financial problems and suicide attempts. As sleep disturbances can trigger illness episodes and situations like the pandemic—as shown by this investigation—can negatively influence sleep, the treatment of these is one essential part of the multifactorial therapy concept. Direct interventions can impact sleep. For example, relaxation exercises in the evening support falling asleep. It is recommended to adhere to sleep hygiene like: regular sleeping times, regularity during the day, no sleep at daytimes, no heavy meals in the late evening, restricted alcohol consumption, and pleasant atmosphere in the sleeping room. Also, physical activity in daylight, in particular not in the late evening, positively influences sleep (Hartescu et al., 2015). Psychotherapeutic interventions such as cognitive behavioral therapy (CBT) and hypnotherapy have been shown to be beneficial for sleep disturbances (Friedrich et al., 2018). A special development for CBT-insomnia (CBT-I) was evaluated as more effective than psychoeducation only in BD (Harvey et al., 2015). In addition, the mindfulness-based approach to the treatment of insomnia (MBT-I) is based on interventions aiming to increase emotion regulation and to reduce stress and proved to be efficient to treat sleeping disorders as well (Ong & Sholtes, 2010). If this is not sufficient, the use of short-term sleeping medication or medium-term sedating antidepressive drugs is recommended to treat sleep disturbances. Moreover, the intestinal-brain axis is related to sleep via various mechanisms such as intestinal permeability, immune system activation, inflammation, energy harvest, and bacterial diversity (Wagner-Skacel et al., 2020). Consequently, diet impacts sleep as well (St-Onge et al., 2016).

Even if not statistically significant, an improvement from April to May of all sleep components in both groups was obvious regarding the means. The values of the different PSQI parameters varied a little bit more at t1, particularly in the BD group. The reason for this might be that some individuals with BD had more difficulties adjusting to this extraordinary situation in April. Then, an adaption of the situation and a reduction of the initially complete uncertainty might have improved sleep problems of this particular group and approximate to the individuals, who slept better the whole time. Moreover, since the loosened restrictions people were allowed to live a less restricted and little more normalized life. Furthermore, it is conceivable that fewer working hours, fewer appointments, and more time for physical activity in daylight might have had a positive effect on sleep (Altena et al., 2020). Then again, having more time might correlate with gathering more information resulting in rumination and worse sleep. Contrary Some people were able to adhere to a sleep–wake rhythm which corresponds more to their endogenous morning or evening type while working from home, which supports good sleep (Wheaton et al., 2016). Moreover, our results show that COVID-19-related fears and information frequency also have a considerable impact on sleep a month later.

The information frequency in the beginning of the pandemic was quite high, as the mean of informing oneself was higher than once a day. In the second month, the frequency decreased. A study in China showed that people who spent more time focusing on information about COVID-19 had a higher prevalence for generalized anxiety disorder (Huang & Zhao, 2020). Individuals with BD informed themselves even more than HC, which could be explained by a different lifestyle. In particular, in April the uncertainty about the virus, the disease and the association with somatic and mental comorbidities was immense. Physical contact with others in order to validate one's feelings and opinion was not possible. Furthermore, it was unclear whether patients with mental disorders could get their usual psychosocial treatment including regular appointments in the outpatient setting due to social distancing regulations. Presumably, the biggest burden was not knowing how the future will unfold. Obtaining informing about infection rates, case of deaths and legal regulations might have increased individuals' feeling of certainty and control. However, our results also show that higher information frequency was related to worse sleep in the bipolar cohort during strict and loosened restrictions. As the information frequency decreased over time and with it subjective sleep quality, sleep duration, and sleep efficiency improved, the hope remains that sleep disturbances will be getting better in follow-up investigations in this vulnerable group of BD. Potentially, the mentally healthy people in our cohort could cope more effectively with the flood of information. In our cohort significant more HC had to work in April and therefore had a structured day. Consequently, individuals with BD had more time for informing themselves and think about pandemic-related topics. Possibly, the permanent engagement with COVID-19-related topics resulted in rumination and, subsequently, poor sleep, especially for the BD group. The WHO officially recommends to minimize watching, reading or listening to news about COVID-19 to once or twice a day. Everybody should aim to be informed just enough to be able to act responsibly (World Health Organization, 2020). The same was advised for individuals with BD (Siqueira et al., 2020).

Individuals with BD as well as HC had concerns and fears about the virus, their own health and infection of loved ones to a moderate extent. The emotional distress due to social distancing was

rather low in our study in both groups. The findings show associations of COVID-19-related fears with poor sleep in April and May. Moreover, fears in the early stages predict subjective sleep quality and daytime sleepiness in the follow-up. We therefore recommend to include acknowledging COVID-19-related fears in psychotherapy of BD, addressing not only psychosocial symptoms such as mood, but also sleep. However, our results indicate that fears of the virus in general have a bigger impact on sleep than social distancing measured with the emotional distress variable. The task force of the European CBT Academy recommends applying common sleep hygiene during the pandemic. Moreover, they advise using the opportunity of following the endogenous sleeping type and adapted CBT methods if possible in home office (Altena et al., 2020). Stefana et al. (2020) stated that the pandemic could also be an opportunity for new therapeutic ways, such as mindfulness trainings, sleep hygiene, psychoeducation or even pharmaceutical prescription, and psychotherapy can be offered online or via telephone. Social media interaction grew in times of restrictions, but presumably this is not equally valuable as face-to-face contact (Altena et al., 2020). In sum, our results make a considerable contribution when developing future treatment approaches for BD during pandemics or crises. Further studies should investigate the impact of online communication on sleeping disorders associated with loneliness and depression.

4.1 | Limitations

There are several limitations of this study. Due to the online design, no objective rating of current psychopathological symptoms was assessed. Furthermore, COVID-19-related fears and emotional distress were self-conducted variables with no reference value. Additionally, the sample size is rather small, but therefore we had complete data of almost as many patients as HC over two points of measurement. Due to the clinical design, the groups differed in age, which was adjusted in the statistical analyses. Finally, we do not have pre-COVID-19 baseline measures of mood and sleep quality in our participants.

5 | CONCLUSIONS

Austrian individuals with BD reported sleeping more poorly than HC during the COVID-19 pandemic in April 2020. Individuals' sleep in May 2020—in particular worse subjective sleep quality, sleep duration, sleep efficiency, and daytime sleepiness—could be predicted by higher information frequency, increased fears of the virus generally, and either oneself or others getting infected. Good sleep is essential for functioning and well-being, especially for the vulnerable BD group. Therefore, it is important that information about the pandemic is gathered to a reasonable extent and mental health professionals include COVID-19-related fears when currently treating bipolar individuals.

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Monitoring Sleep Changes via a Smartphone App in Bipolar Disorder: Practical Issues and Validation of a Potential Diagnostic Tool

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Background: Sleep disturbances are common early warning signs of an episode of bipolar disorder, and early recognition can favorably impact the illness course. Symptom monitoring via a smartphone app is an inexpensive and feasible method to detect an early indication of changes such as sleep. The study aims were (1) to assess the acceptance of apps and (2) to validate sleeping times measured by the smartphone app *UP!*.

Methods: *UP!* was used by 22 individuals with bipolar disorder and 23 controls. Participants recorded their time of falling asleep and waking-up using *UP!* for 3 weeks. Results were compared to a validated accelerometer and the Pittsburgh Sleep Quality Index. Additionally, participants were interviewed regarding early warning signs and their feedback for apps as monitoring tools in bipolar disorder (NCT03275714).

Results: With *UP!*, our study did not find strong reservations concerning data protection or continual smartphone usage. Correlation analysis demonstrates *UP!* to be a valid tool for measuring falling asleep and waking-up times.

Discussion: Individuals with bipolar disorder assessed the measurement of sleep disturbances as an early warning sign with a smartphone as positive. The detection of early signs could change an individual's behavior and strengthen self-management. The study showed that *UP!* can be used to measure changes in sleep durations accurately. Further investigation of smartphone apps' impact to measure other early signs could significantly contribute to clinical treatment and research in the future through objective, continuous, and individual data collection.

Keywords: Mobile-health, bipolar disorder, smartphone app, symptom monitoring, sleep, early warning sign

INTRODUCTION

Bipolar disorder (BD), a severe and lifelong mental disorder, is often misdiagnosed due to failure to identify characteristic symptoms, which leads in many cases to delayed adequate treatment strategies (1, 2). A higher number of depressive or manic episodes is associated with a lower level of functioning (3), unhealthy lifestyle, impaired cognitive function, and reduced ability to

work, leading to an overall worsened course of the illness (4). Studies show early treatment with a combination of psychopharmaceuticals and psychotherapy can favorably affect the course of BD (5) and that early access to treatment is associated with shorter and milder episodes as well as longer remission (6). However, each affective episode's course and severity can vary a lot intra- and inter-individually (1, 7), and early symptoms can appear non-related to the disorder (8).

Early warning signs (EWS) are symptoms that typically occur before an affective episode (9). EWS can be observed in different modalities, including mood, thoughts, and behavior and differ inter-individually; however, individuals' unique combination of EWS is often recurring (10). Interventions taking EWS into account result in a longer time to recurrence, lower probability of hospitalization, positive impact of overall functioning (11), and are more effective than mood-stabilizing medication alone (12). One of the most common EWS is the change in sleeping patterns (13). Sleep disturbances in BD (insomnia with problems in falling asleep, sleeping interruptions, or hypersomnia) are diagnostic criteria and highly prevalent in manic and depressive episodes. Additionally, they also occur in euthymia and are associated with lower global and cognitive functioning (14), stress, dissatisfaction, and an overall decreased quality of life (15). Disturbances of the sleep-wake rhythm, in turn, can complicate the course of the episode and trigger relapse (16, 17).

Therefore, supporting patients by monitoring and noticing changes in behavior patterns early (1) is a challenge in BD's multimodal treatment (1). Usually, symptoms and behaviors are identified and recorded retrospectively through verbal explorations, questionnaires, or mood diaries. A faster and more objective, individual, and precise behavioral pattern evaluation is highly needed (18).

Mobile phones, usually available, could be an excellent opportunity for continuous recording and data collection (19). Mobile-health (m-health) is accessible for everyone, inexpensive, time-efficient, and strengthens autonomy (20, 21). One major field of m-mental health is the technology of applications (apps) for smartphones. The development of numerous m-health products provides support in screening, monitoring, and therapy in BD. Previous investigations have shown that individuals with BD have a positive attitude toward assistance tools and apps in general (22). Most of the products for BD treatment provide psychoeducational content with diverse outcomes regarding efficacy (23). Another possibility from m-health is symptom monitoring via the input of symptoms, emotional condition, or behavior.

Moreover, apps can record and process behaviors by using wireless fidelity (WIFI), accelerometer, a global positioning system (GPS), light sensors, phone and text frequency, as well as speech recognition (24–26). Objective data about exercise, physical activity, sleep, work and vacation time, and digital communication can be gathered. However, Nicholas et al. (19) found a lack of sleep monitoring with only 51% of the available monitoring apps for affective disorders measuring sleep. There is a need to validate the accuracy of measurement, the acceptance of individuals with BD, and its effectiveness as up-to-date scientific data is rare.

The aim of this study was (1) to assess the acceptance of a smartphone application (app) for individuals with BD and healthy controls (HC) and (2) to validate sleeping times within *UP!* using both a validated accelerometer and the Pittsburgh Sleep Quality Index.

METHODS

Setting and Participants

This trial included 22 individuals with BD and 23 HC. The Department of Psychiatry and Psychotherapeutic Medicine of the Medical University of Graz conducted recruitment. Individuals with BD were either inpatients or outpatients of the dedicated outpatient center for BD. According to the Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV, the diagnosis of BD was made with a structured clinical interview [SCID; (27)]. HC were recruited from the general population via written invitations and word of mouth (circle of acquaintances, medical students, clinical personnel staff). HC were screened for psychiatric diseases with a short screening questionnaire based on the SCID. Participants had to be of legal age, own an Android smartphone, and have given prior written informed consent. The trial was approved by the ethics committee of the Medical University Graz, Austria (EK-number: 29–290 ex 16/17) in compliance with the current revision of the Declaration of Helsinki, ICH guideline for GCP, and current regulations. The trial is registered at ClinicalTrials.gov as NCT03275714.

Procedure

Participants used the app *UP!* for 6 months after instructed to use their smartphone as usual. After 1 month, participants attended a scheduled visit to collect clinical data through an interview and standardized questionnaires (see **Figure 1**). For the first month, participants additionally wore a validated accelerometer (Axivity) on their wrist, which collected data 24 h a day for 3 weeks (due to battery and storage capacity). The study used the first month's collected data to compare the app *UP!* and the Axivity accelerometer. The first month's data collection resulted in 322 nights (of 24 participants) where both app and Axivity accelerometer measured the same nights. Demographic parameters and information about illness duration, number of episodes, and regular smartphone use were also collected. Additionally, mood symptoms from the last 2 weeks were evaluated with self-rating inventories *Becks Depression Scale* (28), *Manie-Selbstbeurteilungs-Skala* (29), and external rating scales *Hamilton Depression Scale* (30), *Young Mania Rating Scale* (31). Subjective sleep patterns were assessed by *Pittsburgh Sleep Quality Index* [*PSQI*, (32)]. Furthermore, the study participants completed a self-constructed questionnaire about observed EWS and feedback about the app.

Material

The Android Smartphone software solution *UP!* was developed by *meemo-tec OG* with the medical consult of the dedicated outpatient center for BD, Graz, Austria. Automatic data collection includes sleep, physical activity, and social profiles. The sleeping behavior of the user is recorded using the phone's

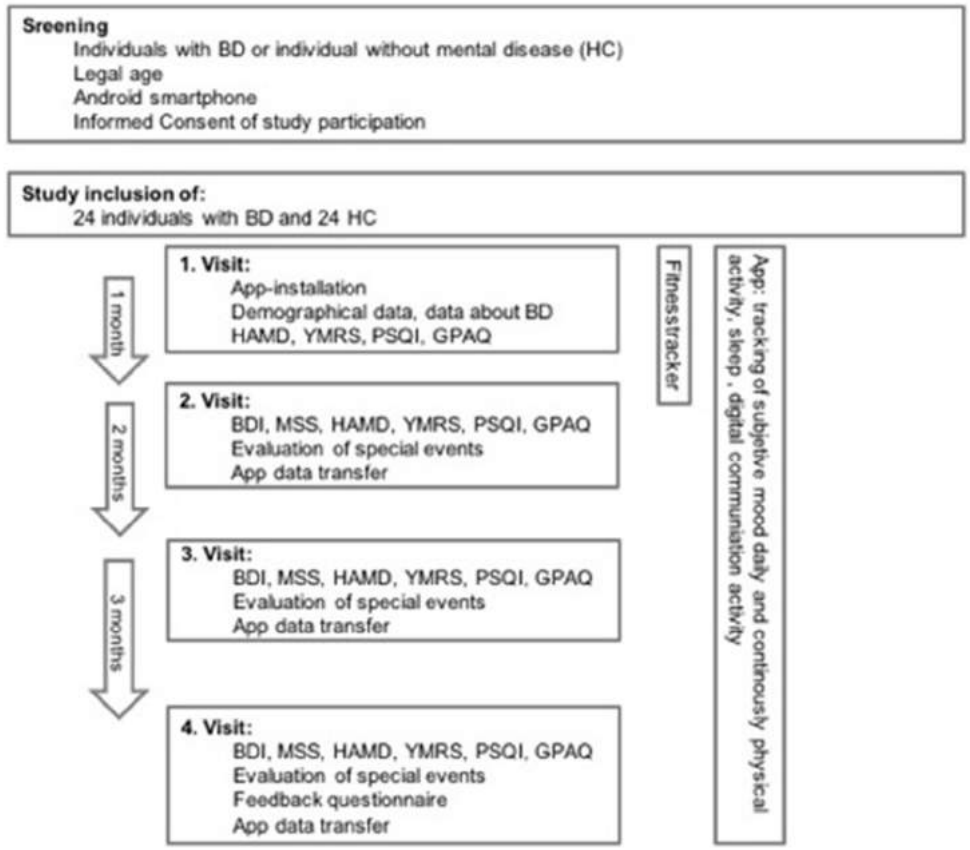

FIGURE 1 | Procedure of the study.

accelerometer and light sensors. As a result, real sleeping events are distinguishable from simple inactivity. The app determines the time of falling asleep and waking up and time slept during the day. Moreover, users were asked to rate their mood with seven smiley-emoticon options once daily in the evening. Data were extracted and converted by meemo-tec software. Timestamps were used to record minutes of sleep disruption activity via timestamps of falling asleep and waking up for single nights.

The accelerometer *Axivity3* [*AX3, Axivity, Newcastle upon Tyne, UK*, (33)] is a triaxial accelerometer worn on the wrist of the non-dominant hand. This waterproof device consists of a flash-based memory, a real-time quartz watch that was not visible for users, and a temperature sensor. The tracker was validated in assessing physical activity behaviors as well as sleep periods in adults (34). In our study, the acceleration was recorded at 50 Hz. The devices were programmed to start measuring 1 week after the first visit due to the maximum storage capacity of 3 weeks using 50 Hz (based on data from pilot tests). Raw data were extracted using GENEActiv PC software version 3.2. Signal processing was performed in R (version 3.5.1; http://cran.r-project.org) using package GGIR (version 1.6–7). A description of the analysis and applied algorithms can be found elsewhere (35). Briefly, the vector magnitude (expressed in mg) using the Euclidean norm minus 1 g (ENMO) was calculated for each 5-s epoch. The non-wear periods were defined by windows of 60 min. The sleeping duration was estimated using the Change in Z-Angle algorithm (34).

The *PSQI* by Buysse et al. (32) is a self-rated questionnaire, which assesses sleep quality and disturbances over a 1-month time interval. The questionnaire consists of 19 items, which generate seven components: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime sleepiness. Each component scores from 0 ("no difficulty") to 3 ("severe difficulty"). A total PSQI score (range 0–21) of more than 5 distinguishes good and poor sleepers, whereas higher scores indicate worse sleep quality.

The *self-constructed questionnaire* in the German language contained, among others, questions about EWS as "Do you recognize when a depressive episode begins?," "Do you notice the same signs again and again at the beginning of a depressive/(hypo)manic episode?," "If yes, which of the following occur in more than half of the episodes? (Multiple answers possible)." Furthermore, questions about app use were: "What apps do you use on your smartphone?," "Do you think a technical support in the treatment of BD is meaningful?," "How often do

you check your smartphone?," and "Does your response time in texting change in depressive/(hypo)manic episodes?." Moreover, questions about study participation included: "Did you find the app annoying?," "Have you been concerned about the protection of your personal data?," "Can the app be integrated into everyday life?," "Does the measurement of sleep/movement/working time via smartphone make sense in BD treatment?," "Do you desire graphical feedback of behavior measured by the app,?" and "Would you use this app as a support tool in BD treatment?-reasons for yes/no."

Statistical Analyses

All analyses were performed with the IBM Statistical Package for Social Sciences (SPSS), version 26.0. Unpaired *t*-tests (metric data), Mann–Whitney *U*-tests (ordinal data; metric data not normally distributed), and chi-square tests were conducted to test for differences between the BD and HC group in descriptive variables and acceptance. Wilcoxon tests investigated the difference of mood inventory scores between the start and the end of the trial. Due to technical issues in the clinical trial setting, there were only sleeping times of 24 participants (12 with BD, 12 HC) available within the app. Pearson correlation coefficients were calculated to compare and validate falling asleep and waking-up times for the three measurement methods: the app with accelerometer and app with PSQI. For the correlations between the app and the accelerometer, all nights were included when the app and accelerometer data were coincidently available ($n = 322$). As the PSQI only measures a mean of the last 4 weeks, for the analyses between app and PSQI, means of the app data were built first and then correlated ($n = 24$). Error probabilities of $p < 0.05$ were accepted. Bonferroni corrections were adjusted in correlation analyses for the four sleeping time tests (0.05/4 tests = 0.0125).

RESULTS

Sociodemographic and illness-specific data regarding the number of episodes and current treatment of the participants can be observed in **Table 1**. Individuals with BD differed significantly in age to HC, while the proportion of females and males did not differ between the groups. There were significant differences in HAMD and YMRS scores between individuals with BD at the beginning of the study and after 1 month; still, all values did not correspond to clinically relevant depressive nor manic symptomatology (**Table 1**). In the patient group, the HAMD improved significantly from the start of the trial to the end after 6 months ($Z = -2.139$; $p = 0.032$). There was no significant difference in YMRS.

Table 2 demonstrates how often participants checked their smartphone for messages and whether they used apps on it. Participants with BD and HC did not differ in most of the apps used on the smartphone. Only communication apps were used more by HC. Individuals with BD stated that the response latency to messages lengthened considerably during the onset of depressive episodes. Two-thirds of individuals with BD stated that the response latency decreased significantly during the onset of (hypo)manic episodes.

Table 3 depicts the times of falling asleep and waking up measured using the PSQI, the app *UP!*, and the Axivity accelerometer. There were no differences between individuals

TABLE 1 | Sociodemographic and illness specific data of individuals with BD and HC.

	Individuals with BD ($n = 22$)	HC ($n = 23$)	Value	*p*
Sex	54.5% male	43.5% male	$X^2(1) = 0.018$	0.894
	45.5% female	56.5% female		
Age	43.36 (±10.89)	35.00 (±11.39)	$U = 148.50$	**0.018***
Diagnosis of BD (age)	32.32 (±13.41)	–		
Number of depressive episodes	6.82 (±4.64)	–		
Number of (hypo)manic episodes	4.23 (±3.52)	–		
Current treatment		–		
- Psychopharmaceuticals	86.4%			
- Psychotherapy	54.5%			
- Psychoeducation	18.2%			
- Self-help group	27.3%			
- Other (e.g., acupuncture, painting, exercise)	27.3%			
Mood inventories:				
- HAMD t1	6.18 (±5.89)	0.26 (±0.45)	$U = 49.50$	**<0.001****
- YMRS t1	3.23 (±4.89)	0.04 (±0.21)	$U = 109.50$	**<0.001****
- HAMD t2	4.82 (±5.78)	0.96 (±1.11)	$U = 104.50$	**0.001****
- YMRS t2	2.27 (±3.09)	0.00 (±0)	$U = 126.50$	**<0.001****
- HAMD t3	3.50 (±3.85)	1.60 (±2.77)	$U = 79.50$	**0.044***
- YMRS t4	1.06 (±2.10)	0.00 (±0)	$U = 90.00$	0.108

*BD, bipolar disorder; HC, healthy controls; HAMD, Hamilton Depression Scale; YMRS, Young Manie Rating Scale; t1, start; t2, 1 month after start; t2, 6 months after start; *p < 0.05; **p < 0.01. Significant results are presented in bold.*

TABLE 2 | Smartphone usage of individuals with BD and HC.

	Individuals with BD ($n = 22$)	HC ($n = 23$)	Value	p
App usage on smartphone	100%	100%		
- Facebook	54.5%	43.5%	$X^2(1) = 0.55$	0.458
- Whatsapp	95.5%	91.3%	$X^2(1) = 0.31$	0.577
- Other communication (e.g., Skype, Viber)	18.2%	52.2%	$X^2(1) = 5.67$	**0.017***
- Physical activity (e.g., Runtastic)	13.6%	26.1%	$X^2(1) = 1.09$	0.297
- Sleep	0%	8.7%	$X^2(1) = 2.00$	0.157
- Others	36.4%	39.1%	$X^2(1) = 16.99$	0.386
Smartphone check during week			$X^2(4) = 4.46$	0.348
- Only when ringing	18.2%	4.3%		
- 1–2 times a day	0%	4.3%		
- 3–4 times a day	31.8%	26.1%		
- Almost every hour	36.4%	34.8%		
- Several times an hour	13.6%	30.4%		
Smartphone check during weekend			$X^2(2) = 4.10$	0.353
Only when ringing	18.2%	4.3%		
- 1–2 times a day	0%	8.7%		
- 3–4 times a day	36.4%	30.4%		
- Almost every hour	31.8%	34.8%		
- Several times an hour	13.6%	21.7%		
Almost instant reply to messages	50%			
Change in response time in depressed mood				
- No	16.7%			
- Yes, extended	75.0%			
- Yes, shortened	8.3%			
Change in response time in euphoric mood				
- No	33.3%			
- Yes, extended	8.3%			
- Yes, shortened	58.3%			

*BD, bipolar disorder; HC, healthy controls; *$p < 0.05$. Significant results are presented in bold.*

with BD and HC in falling asleep and waking-up times during testing. Additionally, no difference in sleeping times variblities were found between the groups [app falling asleep: $M_{Pat} = 1{:}19$, $M_{HC} = 1{:}16$, $T_{(25)} = 0.230$, $p = 0.820$; app waking-up: $M_{Pat} = 1{:}11$, $M_{HC} = 1{:}13$, $T_{(25)} = -0.255$, $p = 0.801$; accelerometer falling asleep: $M_{Pat} = 1{:}13$, $M_{HC} = 1{:}13$, $T_{(39)} = 0.022$, $p = 0.983$; accelerometer waking-up: $M_{Pat} = 1{:}08$, $M_{HC} = 1{:}04$, $T_{(39)} = 0.431$, $p = 0.669$].

For correlations between the app and accelerometer, all coincident data nights were analyzed using the whole group of individuals included in the study. As PSQI sleeping times are parameters for the last 4 weeks, the mean values of the app's data were used. The significant correlation between the app's and the accelerometer falling asleep times correspond to a high validity ($n_{\text{nights}} = 322$; $r = 0.77$, $p < 0.001$). There was a high correlation between the app and the PSQI in falling asleep times ($n_{\text{participants}} = 24$, $r = 0.64$, $p = 0.001$). There were also significant high correlations for the waking-up time of the app and the accelerometer ($n_{\text{nights}} = 322$; $r = 0.59$, $p < 0.001$), as well as between the app and the PSQI ($n_{\text{participants}} = 24$, $r = 0.53$, $p = 0.007$). All correlations survived Bonferroni corrections (0.05/4 tests = 0.0125).

Individuals with BD positively evaluated the app *UP!* for measuring sleep, physical activity, and working duration (see **Table 4**). Moreover, participants reported they found a graphical feedback of their behavior measured by an app to be helpful. Most of the interviewed individuals stated that they would use an app as a support tool in BD treatment, mainly because of continual sleep observance, awareness for changes due to graphical presentation/feedback, and easy integration into everyday life. Most individuals with BD did not perceive the app *UP!* as "annoying." For three BD individuals who reported annoyance, this was due to wearing the Axivity accelerometer (which was only done for the study as the app would be used as a standalone post-study). No participant was annoyed by having the smartphone around all the time. One individual with BD reported being annoyed by other things such as "active GPS" and "high battery need."

DISCUSSION

This study aimed to determine whether individuals with BD consider technical support through a smartphone app to be useful and practical in the early detection of symptoms during BD

TABLE 3 | Sleeping times measured with PSQI, *UP!* app, and Axivity accelerometer in individuals with BD and HC.

	Individuals with BD (M ± SD)	HC (M ± SD)	Value	*p*
PSQI ($n_{BD} = 22$, $n_{HC} = 23$)				
- Time falling asleep	22:45 (±1:45)	22:41 (±0:41)	$U = 243.50$	0.827
- Time waking up	6:52 (±1:12)	6:46 (±0:43)	$U = 247.50$	0.900
- Sleeping duration (hours)	7.18 (±1.78)	6.92 (±1.21)	$U = 204.00$	0.260
- Duration falling asleep (min)	24.75 (±26.69)	18.57(±11.97)	$U = 247.50$	0.900
- Subjective sleep quality	0.95 (±0.72)	0.91(± 0.60)	$U = 246.00$	0.858
- Sleep disturbances	1.00 (±0.54)	1.04(±0.37)	$T(43) = -0.32$	0.751
- Sum score	6.95 (±4.38)	5.26(±2.83)	$U = 195.00$	0.185
App ($n_{BD} = 12$, $n_{HC} = 15$)				
- Time falling asleep	23:03 (±1:00)	23:06 (± 0:51)	$U = 807.50$	0.903
- Time waking up	7:31 (±0:51)	7:09 (0:46)	$T(25) = 1.16$	0.257
Tracker ($n_{BD} = 21$, $n_{HC} = 20$)				
- Time falling asleep	23:35 (±1:25)	23:33 (±1:11)	$T(39) = 0.08$	0.934
- Time waking up	7:15 (±0:51)	7:20 (±0:59)	$T(39) = -0.28$	0.778

BD, bipolar disorder; HC, healthy controls; PSQI, Pittsburgh Sleep Quality Index; M, mean (of sleeping times); SD, standard deviation.

TABLE 4 | Desire for an app in BD treatment.

	Individuals with BD ($n = 18$)	HC ($n = 15$)	Value	*p*
Did you find the app annoying?				
- No	81.8%	47.8%	$X^2(3) = 6.07$	0.103
- Rare, <1/week	4.5%	17.4%		
- Sometimes, 1–2/week	13.6%	30.4%		
- Often, almost daily	0%	4.3%		
Have you been concerned about the protection of your personal data? (Yes)	13.6%	21.7%	$X^2(1) = 0.51$	0.477
Can the app be integrated into everyday life? (Yes)	90.9%	100%		
Does the measurement of movement via smartphone make sense in BD treatment? (Yes)	100%	93.3%	$X^2(1) = 1.24$	0.266
Does the measurement of sleep via smartphone make sense in BD treatment? (Yes)	100%	100%		
Does the measurement of working duration via smartphone make sense in BD treatment? (Yes)	88.9%	93.3%	$X^2(1) = 0.20$	0.658
Desire for graphical feedback (Yes)	100%	86.7%	$X^2(1) = 2.56$	0.110
Would you use this app as a support tool in BD treatment? (Yes)				
Reasons for use	83.3%	100%	$X^2(1) = 2.75$	0.097
- Too little everyday overview with current treatment	33.3%	37.5%	$X^2(1) = 0.68$	0.409
- Continual sleep observance	60.0%	40.%	$X^2(1) = 0.60$	0.439
- Continual movement observance	20.0%	20.0%	$X^2(1) = 0.00$	>0.999
- Continual mood observance	46.7%	46.7%	$X^2(1) = 0.00$	>0.999
- Awareness for changes due to graphical presentation/feedback	73.3%	80.0%	$X^2(1) = 0.19$	0.666
- Easily integrable into everyday life	73.3%	73.3%	$X^2(1) = 0.00$	>0.999

BD, bipolar disorder; HC, healthy controls.

treatment. Individuals with BD assessed the monitoring of EWS with a smartphone as positive. Our investigation did not register strong reservations concerning data protection or continual smartphone usage. Moreover, correlations demonstrate that the app *UP!* is a valid tool for measuring falling asleep and waking-up times.

The earlier EWS of both depressive and (hypo)manic episodes are recognized, the better the prognosis for the course of the individual episode and thus the influence on lifelong illness (9). Psychotherapeutic and self-effective interventions used to regulate sleep behavior, physical activity, and a balance in social activities could counteract the development of disease-related symptoms at an early stage (36). Consequently, the detection of EWS should be a focus in the treatment of BD. Using smartphones, EWS, presenting in mood, symptoms, and behavior changes such as sleep disturbances, may be detected more quickly and better tailored to the individual. Access to the detection of these changes could lead to early self-recognition of EWS and the users' faster reactions and, therefore, increase self-efficacy. It seems likely that innovative products could bring

advantage as an add-on or self-contained therapy. Although there was an improvement in HAMD in individuals with BD, the small values do not represent depressive symptomology. Moreover, many other factors influenced mood besides the inventions of the trial. In sum, with these results, a conclusion on the impact of the app alone on illness symptomatology cannot be drawn.

Individuals with BD stated that sleep is the most critical pattern to monitor with an app (37). We hypothesized in this study that smartphone apps could reliably measure sleep patterns and changes in these patterns equivalent to EWS. Our results showed *UP!* to be a valid option for that. The aim should be to detect EWS based on objective, continuous, and individual data. Kolla et al. (38) stated that accelerometers and apps underestimate sleep disruptions and overestimate total sleep times compared with polysomnography. However, EWS detection's target is the change of individual behavior rather than registering the accurate falling asleep and waking-up time. The recorded behavior patterns are presented to the users in different ways, depending on the product. For example, the advanced version of *UP!* offers a graphic overview of sleeping times, working hours, physical activity, smartphone usage time, and mood. Just the visualization and knowledge of behaviors, patterns, and changes can change the mindset of those affected and reinforce "healthy behavior" such as a balanced sleep-wake rhythm or sufficient movement. By increasing self-management activities, depressive symptoms can be reduced (39). Moreover, the daily use of apps can strengthen the introspective abilities. However, the efficacy is dependent on regular use of the monitoring apps, also in euthymia.

In addition, many products alert users when pathological parameters, such as no or very little sleep or a very bad mood, are measured. The system then automatically asks users about other symptoms from a list of general or individual EWS. A few first trials were conducted to develop learning systems based on machine learning techniques (40). This development aims to recognize EWS and notifying patients on a very individual basis. Presently, a realistic goal of apps in BD treatment is to improve self-management, which should ultimately prevent recurrences, relapses, severe episodes, and hospital stays.

The results support the finding of a larger trial showing that a substantial proportion of individuals with BD appreciate an app that measures EWS in particular sleep and would use it in BD treatment. In 2014, a study group in the USA also examined 320 people with a mental disorder and found that 62.5% had a smartphone, and 70.6% of those were interested in using it to monitor symptoms (41). A survey of 89 individuals with BD showed that 40% already used apps for managing illness symptoms, and 79% of the others would like to use specific tools (42). Participants reported wanting self-management tools, sleep-management, EWS, and triggers, emphasizing easy usage, scientific quality, and data privacy. However, the same study group found in a review that a large part of the available apps for BD do not meet these needs (43). A recent survey of 47 individuals with BD found that more were adherent to a smartphone app than a Fitbit fitness tracker (37). Similarly, participants in this study rated the wearing of the Axivity accelerometer as more annoying than using an app. Moreover, Van Til et al. (37) surveyed that individuals with BD would like to have monthly personal talk with their clinician in case of using an app. However, presumably subgroups of individuals with BD prefer apps and/or accelerometers. Factors such as age, sex, mobile phone use, and psychopharmacological and psychotherapic treatment should be considered in more extensive trials.

In general, no direct negative impact is to be expected from using an app. Apps should always comply with data protection regulations. Participants in this study did not have any concerns about the misuse of their personal data. Most of the available apps store the data locally on the smartphone. Directly sending data to clinicians would result in data protection problems and lead to potential liability issues. There is also evidence of adverse effects of EWS interventions. While individuals with BD might become over-confident with self-management strategies and stop their needed medication (12), recognizing EWS of depression might lead to rumination and worsening depressive symptomatology (44).

Monitoring via an app could bring additional advantages to treat BD. First, links for psychoeducational tools could be implemented within apps. Bauer et al. (45) showed that individuals with BD often use the Internet to inform themselves about their disease. It seems very likely that individuals with BD would appreciate and use direct links via smartphones. Second, it would be an asset for clinicians if individuals with BD could provide a structured data format of their symptoms at their physicians' appointments. In the past, physicians, therapists, and researchers have had to rely on subjective, retrospective information. A recent survey stated that health care professionals' attitudes toward using apps in clinical practice are quite positive. However, the knowledge of technology and products and consequently the use in their daily clinical practice differed a lot (39). Third, assessing valid, objective data on behavioral patterns and monitoring them over a longer time is necessary for clinical research (25, 46) and could be used to further understand and treat BD.

Even though it is unlikely and not desirable that m-mental health products will replace medical and therapeutic treatments, treatment teams, and scientists have to evaluate the extent to which m-mental health could be a useful support tool in BD. One major challenge in the near future is to validate products' effectiveness on symptom reduction, well-being, and hospitalization rate. There are already many m-health products tailored for BD available. So far, a few study protocols for clinical validation and evaluation studies have been published, but final results and efficacy assessments are still insufficient (47–50). Therefore, further aims of studies may be to test whether apps are valid and whether recorded changes in behavior are associated with mood changes and other symptoms of the disease.

Limitations

There are several limitations of this study. Noticing EWS and acceptance of the app were self-conducted variables with no reference value. Furthermore, the sample size is relatively small. Due to technical problems in the clinical setting, the app did not measure all participants' sleeping data. Additionally, it was not possible to compare sleep interruptions as the *UP!* and Axivity accelerometer did not comparably analyze this data.

However, sleep duration seems to be more relevant as EWS than interruptions. As the study duration was only 6 months, the frequency of affective episodes is relatively small. Further studies to investigate the impact of using apps on sleep, behavior, and illness symptomatology are therefore necessary.

CONCLUSION

Individuals with BD as well as clinicians would benefit from additional options in BD treatment. Individuals with BD assessed the measurement of sleep as an early warning sign with a smartphone as positive. Detecting early signs is essential for improving the course of the disease and could change individuals' behavior and strengthen self-management. Thus, in the future, validated smartphone apps can significantly contribute to clinical treatment and research through objective, continuous, and individual data collection. The study showed that *UP!* can be used to measure changes in sleep durations accurately. The validity for measuring other early signs needs to be investigated further. Even if it is unlikely that m-health products will completely replace medical and therapeutic treatments, they can represent an additional treatment strategy. The development, validation, and evaluation of specific products' effectiveness will be necessary for the future.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Medical University Graz. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

FF has designed the study, written the first and last draft, and was responsible for the study conception, coordination, and publication of data. CH and RP were involved in study coordination and data collection. ND and MPl were involved in the conception of the study and writing. In addition, MPl supervised and guided us through the whole process of publication. MS and MPo were involved in study conception and technical support of data of the accelerometer. SB, ML, AB, RQ, AT-B, MR, and AM were responsible for proofreading and revising the manuscript. ER supervised the whole study procedure and revised for important intellectual content. All authors contributed to the article and approved the submitted version.

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BiP-APP: a technical approach for dealing with Bipolar Disorder

Frederike T. Fellendorf[a], Eva Z. Reininghaus[a], Helmut K. Lackner[b]

Background

Bipolar disorder (BD) is a severe psychiatric disease with episodes of depression and (hypo)mania. These recurrent mood changes have serious consequences on the patients' and their relatives' lives, as well as on the health care system. BD is furthermore associated with increased medical comorbidities such as obesity, cardiovascular diseases, diabetes, cognitive dysfunction, leading to a higher mortality rate ([1,2]). Until now the best outcome of BD was obtained by a combination of medication, regular appointments with the attending doctor, psychotherapy and psychoeducation ([3,4]).

The therapy of BD is challenging as there are no biological markers that could give information at what time a new episode is reaching. Diagnosis and therapy relies on clinical symptoms realized by patients, relatives and professionals.

Nevertheless, a high number, frequency and severity of the episodes are associated with a negative course of disease and equally negative outcome.

Depressive as well as (hypo)manic episodes do not occur without previous warning-symptoms. If people with BD are aware of this warning-symptoms they can react accurately and seek help in time, which might prevent the onset of a manic or depressive episode. To identify and realize this warning-symptoms in time, the patient has to learn a lot about and to deal with his own illness and has to constantly check his behavior and possible warning-symptoms.

Rerferences:
[1] Fagiolini et al., 2005
[2] Leboyer et al., 2012
[3] DGBS&DGPPN, 2014
[4] Bauer, 2013

Purpose/ Hypotheses

This project, which will be part of a dissertation, will investigate whether people with BD would profit from a technical support in their treatment.

We suggest that patients would like to have an additional possibility to deal with their disease. The hypothesis of the study is that an app for the smartphone can help to recognize incipient symptoms of depression and (hypo)manic episodes and can help to sensitize patients to their individual course of disease through the use of psychoeducation tools. By identifying the beginning of an episode as soon as possible the treatment could be adapted earlier and the illness course could be influenced positively.

Methods

As a first step the smartphone-behavior, as use in general and use of apps in people with BD will be evaluated in in- and outpatients with BD from the Department of Psychiatry of the Medical University of Graz. Furthermore, individual sensed warning symptoms of the onset of (hypo)manic and depressive episodes should be identified by a conducted questionnaire.

This interrogation will help to develop an app for smartphones in cooperation with a startup company. This BiP-App will be able to detect changes in personal behavior by measuring exact sleeping- and activity times, the frequency of telephoning as well as texting, locating environment and mood states. If the system identifies an aberration a problem-based psychoeducation video will be played.

Studyprotocoll

In the last month the questionnaire was established to find out about smart-phone using and self realized warning symptoms. This form will be filled out in the next month by patients with BD and by relatives of patients with BD.

After an elaborately literature research the Austrian Medical Devices Act and the current use of technical support in a medical context should be described.

Moreover the dissertation will evaluate the test phase of the developed BiP-App on healthy controls as well as on patients with BD by conducting a study which compares clinical findings with BiP-App data.

We target that the app will be integrated in the outpatient setting with individuals with BD. Furthermore, the relatives of the patients should be involved by giving input of changes in the patients behavior to the BiP-App system.

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Medizinische Universität Graz

BiP-APP: A technical approach for treating Bipolar Disorder? – Patients and relatives perspectives

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Background

Bipolar disorder (BD) is a severe psychiatric disease with episodes of depression and (hypo)mania. These episodes are often recognized late by those who are affected, even though they are preceded by warning-symptoms. Early detection may facilitate better course of illness and treatment. Up to now the social surroundings and medicals appointments provide limited observation options regarding the early warning symptoms.
Another fact is, that nowadays smartphones are widespread used by the population and therefore might be a supporting tool in the treatment of medical conditions.

Methods

In this preliminary study we aimed to assess smartphone use, observed warning-symptoms and the potential demand for an application for smartphones in a cohort with BD as well as in a cohort of relatives of patients with BD. Therefore 50 individuals with BD (30 females, 20 males) and 27 relatives (18 females, 9 males) completed a self-conducted questionnaire in German language (41 questions) at the Department of Psychiatry and Psychotherapeutic Medicine, Medical University of Graz.

Results

The results show that 94.0% of the patients and 84.0% are subjectively well informed about the BD. But still 14.0 % of the patients and 33.3% are not satisfied with the current treatment and treatment options.

Table 1.: Number of depressive/manic episodes of the patients with BD and current treatment reported by patients and relatives

	BD-group	Relatives
Age	43.06 (12.87)	49.15 (12.67)
Number of depressions	6.49 (5.59)	5.05 (5.05)
Number of (hypo)manias	3.40 (3.89)	3.83 (4.54)
Current treatment		
Psychopharmacy	98.0%	96.3%
Psychotherapy	62.0%	63.0%
Psychoeducation	26.0%	22.2%
Regular outpatient controls	54.0%	55.6%
Patients' support group	34.0%	18.5%

Patients observe the beginning of a depressive episode in 26.0% as well as manic symptoms in 12.0% subjectively. Relatives note depressive as well as maniac symptoms in 7.4% but have low influence on the affected person, according to their own feeling.

It is known that early symptoms of depressive and manic symptoms vary only slightly between different patients. In our cohort, the awareness of these so called warning symptoms of depression are noticed by 88.0% of patients and 85.2% of relatives. Warning-symptoms of manic episodes are noticed by 70.0% of patients and 72.0% of their relatives. Nevertheless, in clinical practice the awareness of early symptoms is often realized to late.

Table 2.: Subjectively observed warning-symptoms

DEPRESSION	BD-group	Relatives
Less movement in leisure time	71.4	72.0
Less movement in professional time	40.8	36.0
Rumination, Worries	81.6	84.0
Physical fatigue	69.4	68.0
Less walks	49.0	36.0
Less energy in daily routine	79.6	88.0
Less interest in daily routine	69.4	48.0
Increased need to sleep	75.5	64.0
Less need to sleep	4.1	12.0
Difficulties to fall asleep	42.9	44.0
Increased awakening	36.7	36.0
Less interest for meeting friends	83.7	60.0
Less phoning	63.3	28.0
Less texting	46.9	24.0
Increased internet usage	10.2	16.0
Less internet usage	36.7	12.0

(HYPO)MANIA	BD-group	Relatives
Increased movement in leisure time	65.9	27.3
Increased movement in professional time	34.1	21.7
Inner restlessness	63.6	65.2
Increased physical activity	68.2	47.8
New ideas/plans	75.0	65.2
Increased need to sleep	0.0	0.0
Less need to sleep	81.8	82.6
Difficulties to fall asleep	34.1	34.8
Increased awakening	27.3	34.8
More need to meeting friends	68.2	65.2
Increased phoning	65.9	43.5
Increased texting	50.0	34.8
Increased internet usage	50.0	43.5
Less internet usage	2.3	4.3

Overall, 84.0% of patients and 96.0% of their relatives indicate that they desire a smartphone-based support system in the BD treatment.

Conclusion

Warning-symptoms of BD episodes often manifest in changes in physical activity, communication behaviour and sleep-wake rhythm, which are only partly recognized by patients. Therefore, we developed the BiP-App to record individual behaviour patterns. The BiP-App is currently being evaluated and aims at detecting warning-symptoms of BD episodes on the basis of objective, continuous and individual data.

BiP-APP: Eine technische Unterstützung in der Behandlung der bipolar affektiven Erkrankung?
- Ansichten von PatientInnen und Angehörigen

F.T. Fellendorf[1], M. Platzer[1], C. Hamm[1], R. Pilz[1], N. Dalkner[1], S. Bengesser[1], R. Gruber[3], M. Weiss[3], C. Pendl[3], H. Lackner[2], E.Z. Reininghaus[1]

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HINTERGRUND

PatientInnen mit einer **Bipolar affektiven Störung** (BD) erkennen den Beginn von Depressionen und (Hypo)Manien oft erst spät, obwohl **Warnsymptome** vorausgehen.

Bisher bieten das soziale Umfeld und regelmäßige psychiatrische Kontrollen nur eingeschränkte Symptom-Beobachtungsmöglichkeiten. Die weit verbreitete Verwendung von Smartphones könnte hierbei ein unterstützendes Werkzeug sein.

METHODEN

In der vorliegenden Studie der Universitätsklinik für Psychiatrie und Psychotherapeutische Medizin der Medizinischen Universität wurden **50 PatientInnen mit BD und 27 Angehörige** hinsichtlich ihrer Smartphone-Nutzung befragt und untersucht, ob die derzeitige **Erkennung von Frühwarnsymptomen** als ausreichend empfunden wird und ob eine Nachfrage einer technischen Unterstützung durch eine Applikation (kurz: App) in der Detektion von Frühwarnzeichen bestehen würde.

ERGEBNISSE

94% der befragten PatientInnen und 84% der Angehörigen fühlen sich gut über die Erkrankung informiert. Dennoch sind **14% der PatientInnen und 33,3% der Angehörigen nicht mit den derzeitigen Behandlungsmöglichkeiten zufrieden.**

Laut Angabe der PatientInnen werden Frühwarnzeichen jeder **depressiven Episode von 26%** und die **manische Entwicklung sogar nur von 12%** der PatientInnen erkannt. Angehörige gaben an in 7,4% Frühwarnzeichen einer depressiven als auch manischen Entwicklung wahrzunehmen, hatten jedoch das subjektive Gefühl die betroffene Person nur wenig beeinflussen zu können.

88% der PatientInnen und 85,2% ihrer Angehörigen bemerken zu **Beginn einer Depression** wiederkehrende Symptome, insbesondere einen Energieverlust. Frühwarnsymptome **manischer Episoden** werden von **70% der PatientInnen und 72% ihrer Angehörigen** wahrgenommen, insbesondere Ruhelosigkeit und reduziertes Schlafbedürfnis.

84% der Patienten und 96% ihrer Angehörigen geben an, dass sie in der BD-Behandlung ein Smartphone basierendes Unterstützungssystem wünschen.

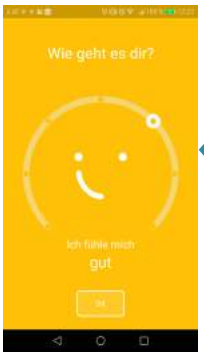
Subjektiv erkannte Frühwarnsymptome

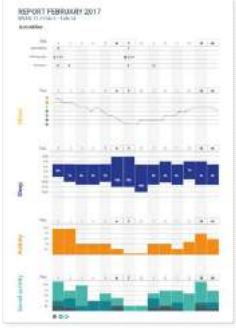
Frühwarnzeichen der DEPRESSION	Pat	Angehörige
Weniger Bewegung in der Freizeit	71,4%	72%
Weniger Bewegung im Berufsleben	40,8%	36%
Grübeln, Sorgen	81,6%	84%
Körperliche Ermüdung	69,4%	68%
Weniger Spaziergänge	49%	36%
Weniger Energie im Alltag	79,6%	88%
Weniger Interesse am Alltag	69,4%	48%
Erhöhtes Schlafbedürfnis	75,5%	64%
Vermindertes Schlafbedürfnis	4,1%	12%
Einschlafstörungen	42,9%	44%
Durchschlafstörungen	36,7%	36%
Weniger Interesse FreundInnen zu treffen	83,7%	60%
Weniger Telefonieren	63,3%	28%
Weniger Versenden digitaler Nachrichten	46,9%	24%
Erhöhte Internetnutzung	10,2%	16%
Verminderte Internetnutzung	36,7%	12%

Frühwarnzeichen der (HYPO)MANIE	Pat	Angehörige
Vermehrte Bewegung in der Freizeit	65,9%	27,3%
Vermehrte Bewegung im Berufsleben	34,1%	21,7%
Innere Unruhe	63,6%	65,2%
Vermehrte körperliche Aktivität	68,2%	47,8%
Neue Ideen/Pläne	75%	65,2%
Erhöhtes Schlafbedürfnis	0%	0%
Vermindertes Schlafbedürfnis	81,8%	82,6%
Einschlafstörungen	34,1%	34,8%
Durchschlafstörungen	27,3%	34,8%
Erhöhtes Interesse FreundInnen zu treffen	68,2%	65,2%
Vermehrtes Telefonieren	65,9%	43,5%
Vermehrtes Versenden digitaler Nachrichten	50%	34,8%
Erhöhte Internetnutzung	50%	43,5%
Verminderte Internetnutzung	2,3%	4,3%

AUSBLICK

Frühwarnsymptome von BD-Episoden, welche von PatientInnen nur teilweise erkannt werden, äußern sich häufig in **Veränderungen der körperlichen Aktivität, des Kommunikationverhaltens und des Schlaf-Wach-Rhythmus**. Deshalb entwickelten wir in Kooperation mit *meemo-tec OG* eine App, die zum Ziel hat, individuelle Verhaltensmuster zu erfassen. Die **BiP-App** wird derzeit evaluiert und zielt darauf ab, Frühwarnsymptome anhand objektiver, kontinuier-licher und individueller Daten zu detektieren und anschließend individuelles **Feedback zur Selbstwirksamkeits-steigerung** der Betroffenen zu geben.





Frühwarnsymptome beginnender bipolarer Episoden und Vorteile sowie Wunsch einer unterstützenden Smartphone-App in der Behandlung der bipolaren Erkrankung: *Ansichten von PatientInnen und Angehörigen*

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ERGEBNISSE

	PatientInnen	Angehörige
Anzahl der Depressionen	6,49 (5,59)	5,05 (5,05)
Anzahl der (Hypo)manien	3,40 (3,89)	3,83 (4,54)
Aktuelle Behandlung		
Psychopharmaka	98%	96,3%
Psychotherapie	62%	63%
Psychoedukation	26%	22,2%
Ambulante Kontrollen	54%	55,6%
Selbsthilfegruppe	34%	18,5%

94% der befragten PatientInnen und 84% der Angehörigen fühlen sich gut über die Erkrankung informiert. Dennoch sind **14% der PatientInnen und 33,3% der Angehörigen nicht mit den derzeitigen Behandlungsmöglichkeiten zufrieden.**

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Weniger Spaziergänge	49%	36%
Weniger Energie im Alltag	79,6%	88%
Weniger Interesse am Alltag	69,4%	48%
Erhöhtes Schlafbedürfnis	75,5%	64%
Vermindertes Schlafbedürfnis	4,1%	12%
Einschlafstörungen	42,9%	44%
Durchschlafstörungen	36,7%	36%
Weniger Interesse FreundInnen zu treffen	83,7%	60%
Weniger Telefonieren	63,3%	28%
Weniger Versenden digitaler Nachrichten	46,9%	24%
Erhöhte Internetnutzung	10,2%	16%
Verminderte Internetnutzung	36,7%	12%

Frühwarnzeichen der (HYPO)MANIE	Pat	Angehörige
Vermehrte Bewegung in der Freizeit	65,9%	27,3%
Vermehrte Bewegung im Berufsleben	34,1%	21,7%
Innere Unruhe	63,6%	65,2%
Vermehrte körperliche Aktivität	68,2%	47,8%
Neue Ideen/Pläne	75%	65,2%
Erhöhtes Schlafbedürfnis	0%	0%
Vermindertes Schlafbedürfnis	81,8%	82,6%
Einschlafstörungen	34,1%	34,8%
Durchschlaf-störungen	27,3%	34,8%
Erhöhtes Interesse FreundInnen zu treffen	68,2%	65,2%
Vermehrtes Telefonieren	65,9%	43,5%
Vermehrtes Versenden digitaler Nachrichten	50%	34,8%
Erhöhte Internetnutzung	50%	43,5%
Verminderte Internetnutzung	2,3%	4,3%

84% der Patienten und 96% ihrer Angehörigen geben an, dass sie in der BD-Behandlung ein Smartphone basierendes Unterstützungssystem wünschen.

AUSBLICK

Frühwarnsymptome von BD-Episoden, welche von PatientInnen nur teilweise erkannt werden, äußern sich häufig in **Veränderungen der körperlichen Aktivität, des Kommunikationverhaltens und des Schlaf-Wach-Rhythmus**. Deshalb entwickelten wir in Kooperation mit *meemo-tec OG* eine App, die zum Ziel hat, individuelle Verhaltensmuster zu erfassen. Die **BiP-App** wird derzeit evaluiert und zielt darauf ab, Frühwarnsymptome anhand objektiver, kontinuierlicher und individueller Daten zu detektieren und anschließend individuelles **Feedback zur Selbstwirksamkeitssteigerung** der Betroffenen zu geben.

Sleep-wake rhythm in Bipolar Disorder measured by a smartphone app

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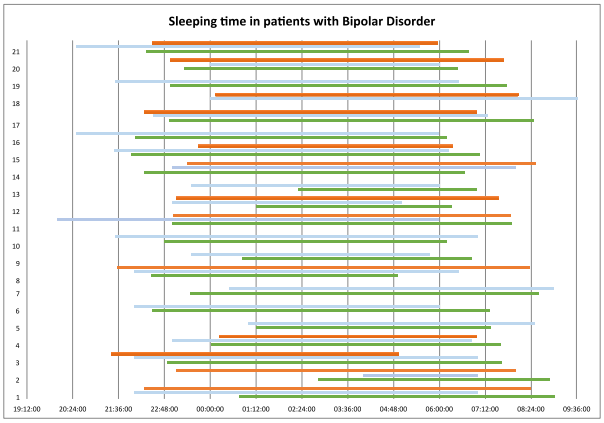
OBJECTIVE

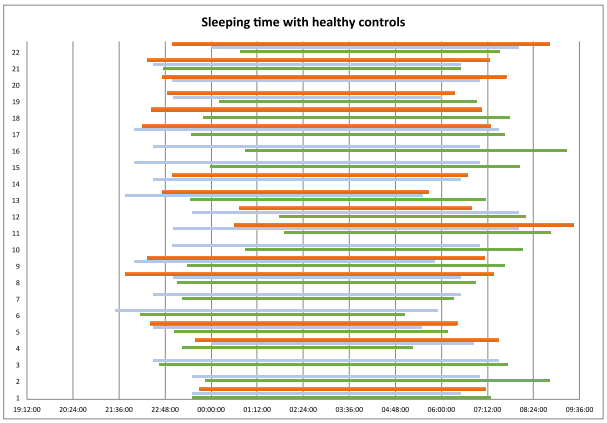
Bipolar disorder (BD) is characterized by mood fluctuations, which are often recognized late by those who are affected. Symptom monitoring via smartphone seems to be an inexpensive and feasible method to detect these fluctuations earlier. The **UP! app** for Android smartphones was developed in Graz, Austria to collect subjective mood daily and objective continuous data about sleep duration, movement, exercise and intensity of digital communication via GPS and sensors (NCT03275714).

METHODS

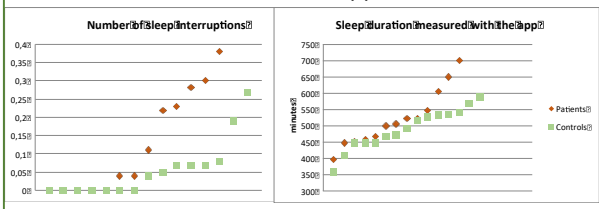
One aim amongst others of our trial is to assess the app's sleeping data validity in comparison to a validated questionnaire (PSQI) and a fitness tracker. Patients with BD (n=22) and healthy controls (n=23) used the app for one month and wared a fitness tracker at their wrist. Moreover they completed the PSQI, which assesses the sleeping of the last month. A second aim is to determine whether changes in the sleep-wake rhythm, measured with the app, can predict mood symptoms and furthermore early warning symptoms.

RESULTS





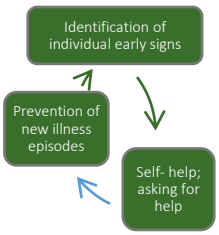
ANOVAs with repeated measurement showed differences in the sleeping time $F_{1,23}$= 726.084, p < .05) as well as in the wake time ($F_{1,23}$= 2451.438, p < .05) between the tracker, PSQI and app.



There was no difference found in the sleeping time measured by the app between patients with BD and HC ($F_{1,28}$= 1.222, p < .05). Moreover there is no difference in the number of sleeping interruptions ($F_{1,28}$= 2.549, p > .05). Regression analyses showed that the sleeping duration measured with the app can not predict the HAMD or YMRS score (r^2 = .079, $F_{1,12}$= .950, p > .05).

CONCLUSION

The exact sleeping time cannot be evaluated by the app. There should be more studies with more participants as well as more detailed analyses. But the changes in sleep patterns are a common warning sign in the early episode. Therefore tools which measure continuous data are necessary. Showing patients their patterns could increase their self-efficacy behavior.



Digitale Therapeutika für die bipolar affektive Störung
- Online-Psychoedukation und Smartphone-App

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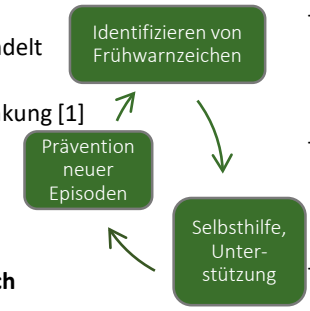
HINTERGRUND

- Bipolare Erkrankung verläuft **individuell** sehr unterschiedlich.
- Je früher eine Episode erkannt wird, desto besser kann sie behandelt werden und weniger schwer verläuft sie.
- **Psychoedukation** macht Betroffene zu Expert*innen ihrer Erkrankung [1]
- Frühwarnzeichen am Beginn einzelner Episoden äußern sich häufig in einer Veränderung des Aktivitätsverhaltens und Schlaf-Wach-Rhythmus.
- Internetzugang und Smartphones sind weit verbreitet
- 84% der Patient*innen und 96% ihrer Angehörigen **wünschen sich technologische Unterstützung** in der Krankheitsbehandlung [2]



PROBLEME

- Betroffene erkennen Beginn einer Episode häufig zu spät, um Ausbruch adäquat entgegenwirken zu können.
- Bisher nur eingeschränkte Symptom-Beobachtungsmöglichkeiten (Stimmungstagebuch, Checklisten).
- Anfahrtswege, Arbeitszeit, Gruppengrößen, Pandemie

PSYCHOEDUKATION ONLINE

BIPOLAR-ACADEMY

SMARTPHONE-APP

- **Objektive** Messung von **körperlicher Aktivität, Schlafdauer** [3] **und –unterbrechungen, digitalem Kommunikationsverhalten** (Sprachnachrichten-häufigkeit, Telefonierdauer, Social media)
- Erfragen von **Stimmungslage**, Energielevel, Medikamenteneinnahme, besonderen Ereignissen
- Abfrage häufiger sowie individuell erstellter **Frühwarnzeichen**
- Möglichkeit zum individuellen graphischen **Feedback** über Verhaltensmuster

→ **Detektion von krankhaften Episoden durch Verhaltensmusteränderungen**

→ **Psychoedukative Empfehlungen „maßgeschneidert“**

→ **Symptombewusstsein und Selbstwirksamkeit steigern**

AUSBLICK

- Erweiterung der App für **Freunde und Familie**
- Digitaler **Krisenplan**
- Verhalten bei ärztlichen/therapeutischen **Kontrollterminen** aufzeigen
- **Langzeitforschung** mit individuellen, kontinuierlichen Daten

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https://bipolar-academy.com/