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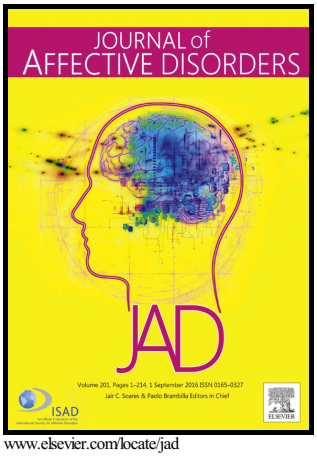

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Longitudinal Mood Monitoring in Bipolar Disorder: Course of Illness as Revealed Through a Short Messaging Service

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Abstract

Background

Online self-monitoring of mood can be used to investigate differences in course patterns across patient groups. This study explored the feasibility of remote symptom capture with True Colours, a self-rated online mood monitoring tool completed on a weekly basis.

Methods

Participants with bipolar disorder (N = 297) completed weekly depression and mania questionnaires over an average of 27.5 months (range 1 –81 months). Subgroups defined by sex, age, and bipolar I vs. II status were compared on time in various mood states, number of episodes, and week-to-week mood variability.

Results

Compliance with weekly questionnaires was generally high (median, 92% of weeks). Mood symptoms occurred for an average of 55.4% of weeks across the follow-up period. Females spent more time with hypomanic/manic and depressive symptoms and had more depressive episodes

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compared to males. Younger participants were found to experience more hypomanic/manic episodes and showed greater variability in mood symptoms than older participants. No significant differences in mood symptoms or variability were observed between bipolar I and II patients.

Limitations

This was a naturalistic study with a heterogeneous cohort, and did not include a control group. True Colours does not identify mood fluctuations that may occur in the days between weekly assessments.

Conclusions

Monitoring moods through an online tool is both feasible and informative regarding course of illness in patients with bipolar disorder. Interventions aiming to reduce mood variability and manic/hypomanic episodes in the early phases of bipolar disorder may enhance the long-term symptomatic course of the illness.

List of Abbreviations

BD, Bipolar Disorder; IQR, Interquartile Range; QIDS, Quick Inventory of Depression Symptomatology; ASRM, Altman Self-Rating Mania Scale

Keywords: Remote monitoring, patient reported outcomes, digital health technologies, mood instability, mania, depression

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BACKGROUND

Most modern treatment guidelines are oriented toward an episodic model of bipolar disorder (BD) in which the focus is on the treatment and prevention of acute episodes. The course of bipolar disorder, however, is highly heterogeneous. Although distinct episodes are clearly present in the majority of patients, many have significant inter-episode mood instability rather than euthymia

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(Henry et al., 2008; MacQueen et al., 2003). Mood instability – usually described as rapid and frequent movement away from the euthymic state - appears to lower the threshold for relapse into more severe mood episodes and has a chronic negative impact upon quality of life and functional ability (Bauer et al., 2009; Judd et al., 2000; Perlis et al., 2006). Mood instability is both a key feature of both bipolar 1 and bipolar 2 disorder (Judd and Akiskal, 2003; Judd et al., 2003; Judd et al., 2002) and a risk factor for developing BD (Howes et al., 2011).

Standard clinical assessments - such as the Life Chart methodology - are retrospective, with the inherent problem of recall bias (Denicoff et al., 1997). Further, course of illness data have usually been measured in small samples followed over short time periods (Denicoff et al., 2000). There is some evidence that paper-based daily mood monitoring can provide detailed mood variability data, but is practical only over short periods (Proudfoot et al., 2014). A reliable method of daily or weekly mood recording using remote monitoring may facilitate recognition of prodromal symptoms of new episodes. The increasing accessibility of portable and wearable technologies enables the tracking of both subjective and objective data related to mood and functioning (Faurholt-Jepsen et al., 2015a; Faurholt-Jepsen et al., 2015b). Such approaches have been found to be both acceptable and feasible in patients with serious mental illness (Naslund et al., 2015).

To date, only a few studies have described the use of such technology in BD, or reported mood data gathered by this method. Scharer et al (2002) reported a feasibility study in which they adapted the National Institute of Mental Health Prospective Life-Chart Form for use on a handheld computer (Scharer et al., 2002). Patients found this a preferable method to written forms and found it beneficial to be playing an active role in their treatment. Similarly, Bauer et al used a home computer based mood monitoring system in BD and reported a very low rate of missing data (Bauer et al., 2004). The only study to date to compare a clinician-rated mood scale to a self-reported computer scale in BD found high correlations between the two methods (Chinman et al., 2004). There are also numerous publically available smartphone/tablet applications for personal mood monitoring available. A systematic review of in 2015 suggested that whilst these are a potentially

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therapeutic tool, those available at present are not written along evidence-based lines and primarily do not use validated mood rating approaches (Nicholas et al., 2015).

Our group has demonstrated the feasibility of using a remote monitoring system ("True Colours") for the prospective collection of self-reported symptom ratings in bipolar disorder using text messaging, email, and internet-based technologies (Bopp et al., 2010; Miklowitz et al., 2012). Supporting the validity of this form of data collection, patient reported outcomes collected via True Colours have provided the basis for linking mood instability to biases in cognition in bipolar disorder. Longitudinal collection of self-report data via True Colours also formed the basis of evaluating a psychoeducational intervention for bipolar disorder (Bilderbeck et al., 2016). Thus, our motivation for developing this system has been manifold, including the potential for large volumes of curated data to provide insights into patterns of illness. In addition, access to one's own mood reports can help patients to understand and manage their illness more effectively, potentially improving clinical outcomes and reducing the need for high intensity professional input.

Here, we aimed to describe the range of mood phenotypes experienced by a new larger cohort of bipolar patients. More specifically, we aimed to examine the acceptability of the True Colours system, understand and quantify the course of mood symptoms experienced in BD, and examine course patterns using a mood variability score.

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METHODS

The OXTEXT-1 Cohort

OXTEXT-1 is a cohort study of participants (≥16 years of age) with a DSM-IV diagnosis of bipolar disorder type I, 2 or not-otherwise-specified (NOS) (APA, 2000). The diagnosis of cyclothymia was excluded. To qualify for inclusion, patients must also be in treatment with a psychiatrist and be willing to use SMS/internet to monitor their mood. Patients are recruited from Oxfordshire and surrounding counties through outpatient psychiatric clinics, inpatient wards, advertising in other

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local health services and general practitioners. All participants attend a 3hr screening and assessment session, during which they complete a clinical interview which is conducted by a member of the research team and audio-recorded for later confirmation of diagnosis by a research psychiatrist. All patients are provided with training for and are registered to use the True Colours remote monitoring system (see below). Whilst enrolled in the cohort individuals continue treatment as usual, consisting of contact with an outpatient psychiatrist, medications, psychological treatments and admission to hospital if necessary. OXTEXT-1 is not a treatment intervention: for information and risk monitoring purposes, treating psychiatrists receive the weekly data submitted by their patients and it is available to patients online.

Patients can be in any mood state at enrolment but must have capacity to give consent: those who are too unwell initially are contacted again once their mood stabilises. Written informed consent is obtained from all patients before registration in the cohort; ethical approval was granted by Oxfordshire REC 'A' (REC reference number 10/H0604/13). Recruitment into the cohort began in 2010 and is ongoing. Here, data were extracted and analysed from all participants (N=367) recruited between 8th July 2010 and 7th August 2013.

True Colours Prospective Mood Monitoring

The True Colours symptom monitoring system uses SMS texting and email to provide an inexpensive and practical means of submitting and reviewing self-reported symptom data for patients and clinicians. Participants are requested by a weekly SMS/email (at a time and day specified by the patient) to reply with responses to a depression scale (Quick Inventory of Depressive Symptomatology, a 16-item self-report version [QIDS-SR]) (Rush et al., 2003) and a mania scale (Altman Self-Rating Mania Scale [ASRM]) (Altman et al., 1997). Patients are given convenient mini versions of the scales and merely need to respond with a series of digits representing their question answers. One prompt is sent if a response is not received within 24 hours. True colours is an ongoing

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system with no set participation time. The True Colours system has been described in more detail elsewhere (Bopp et al., 2010).

Statistical Analysis

A macro within Microsoft Excel (Microsoft, 2010) was used to estimate the proportion of missing data and proportion of full days a patient had spent in each mood state. Missing data were defined as any 7-day period during which no data were received. Mood states were defined as per the validated questionnaire cut-offs: a mood episode was defined as being ASRM >5 for >1 consecutive week (Altman et al., 1997) (mania) and/or QIDS>10 (Rush et al., 2003) for >2 consecutive weeks (depression). Concurrent scores of ASRM >5 and QIDS >10 were seen as indicative of a mixed state.

Mood instability was calculated as a root mean square successive difference score (rmssd): the square-root of the number of mood changes per week, where one change is a one integer change in QIDS/ASRM score (Gershon, 2015; Jahng S, 2008). The square root function was used to allow a wide spread of variation values to be easily compared. For example, if the QIDS score was 4,5,7 on weeks 1,2,3, there would be 1 change between weeks 1 and 2, and 2 changes between weeks 2 and 3. Squaring and summing these change gives a total of 5 over 3 weeks or 2.5 changes per transition-point. Variability would thus be calculated as √2.5 =1.58 (Jahng et al., 2008). Evidence is starting to emerge of the relevance of rmssd scores to the treating clinician (Stange et al., 2016).

Most of the variables were positively skewed (i.e., more patients reported lower scores on the QIDS and ASRM than higher scores). Non-parametric analyses (i.e., Kruskal-Wallis one-way analysis of variance for age and diagnosis, and the Wilcoxon Rank Sum test for gender) were used to compare between groups (gender, age, diagnosis) using a significant alpha <0.05. Independent variables included age (<20 years, 21-40, 41-60, >60 years), gender and diagnosis (bipolar 1,2,NOS); dependent variables were time spent in mood state, mood episodes per year and mood variability score. Cohen's D was used to calculate effect sizes. SPSS.v.20 was used for all calculations (2011).

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RESULTS

Characteristics of the OXTEXT-1 cohort

Thirty-nine participants had withdrawn from OXTEXT-1 since enrolment, and six were lost to follow-up, leaving 297 active participants (91.7%). 66.9% of the cohort were female with a mean age of 41 years [SD ±13, range 16-76]. The baseline characteristics of the participants are shown in Table 1. Of these 297 participants, current medication data was only available for 265 (89%) due to procedural changes during the course of the trial.

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Table 1. Baseline Characteristics of OXTEXT-1 Cohort (N=297)

Characteristic	Percentage	Mean	SD	Range
Age, years		41	13.7	16-76
Female	66.7%			
Ethnicity				
White European	93.5%			
Mixed Black	1.55%			
Mixed Asian	0.31%			
Other	5.64%			
Educational Level				
Undergraduate degree or above	55.2%			
A-levels or equivalent (age 18)	23.6%			
GCSEs or equivalent (age 16)	16.1%			
DSM-IV Diagnosis				
Bipolar 1	62.6%			
Bipolar 2	33.3%			
Bipolar NOS	4.0%			
Age of onset of first depressive episode, years		21.3	9.7	4-57
Mean number of (self-reported) lifetime episodes of depression		22.8	27.5	1-100
Age of onset of first hypomanic/manic symptoms		26.0	11.5	3-72
Number of (self-reported) lifetime episodes of hypomania/mania		Mean: 17.2 Median: 6	22.8 4.4	1-100
Has ever had >=4 mood episodes in one year	64.7%			
Has ever experienced psychotic symptoms	48.5%			
Patient has ever attempted to take their own life	38.9%			
Proportion of lifetime patient reports having spent unwell since onset of mood disorder	36.5%			
0-49%	28%			
50-100%	35.5%			
Unknown				
Length of time using True Colours System (months)		27.6	22.5	1-81 [Median: 21 months]
Medication at entry into study*				
Lithium	32.8%			
Anticonvulsant	42.2%			
Antipsychotic	44.1%			
Antidepressant	37.0%			
Drug free	9.1%			

*Medication data shown as percentages of the 265 (89%) of study participants for whom this data was available.

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Compliance and acceptability of the True Colours System

Patients in the cohort used the system for an average of 27.5±22.5 months (range 1-81). The mean time between text messages and emails being received by the research team was 8.2 days; this approximates to one response to the text message or email prompt per week. 74% of responses were received by SMS. For the ASRM and QIDS, there was a median of 7.9% (interquartile range [IQR] 0-4.1) and 7.8% (IQR 0-2.7) of weeks with missing data. There was no significant difference in the amount of missing data between genders, diagnostic subtypes or when patients had submitted scores above validated cut-offs (compared to below) the previous week. Participants were equally likely to complete the ASRM and QIDS scales throughout the follow-up period.

Symptomatic experience of the OXTEXT-1 cohort

The OXTEXT-1 cohort reported some level of mood symptoms for 55.4% of the period of follow up. Mild depression accounted for one-quarter of the time [QIDS 5-10: median 23.1% (IQR 10.5-38.9)], moderate depression for one-sixth [QIDS 11-15: 10.4% (2.8-21.9)] and severe depression and very severe depression for approximately 10% and 4%, respectively [QIDS 16-20: 2.6% (0-12.6), QIDS>20: 0.00% (0.0-0.34)]. The participants reported hypomanic/manic symptoms on an average of 7.5% weeks [ASRM>5, median 7.5% (IQR 0.89-24.0)]. Symptoms consistent with the diagnosis of a mixed state (ASRM>5 & QIDS>10) were infrequent (median % of spent in a mixed state 0.00% (0.00-3.46)). Overall, 52.5% of the cohort reported at least one week at an ASRM score> 10 and 87.5% at least one week at QIDS>10. The overall percentage of time spent with an ASRM>10 was 6.4%. The median number of hypomanic/manic episodes per year (i.e. at ASRM>5) was 1.78 [IQR 0.41-3.3] and depressive episodes 2.09 [0.41-4.89].

Effects of Gender and Age on Percentage of Time with Mood Symptoms

Females spent significantly more time with hypomanic or manic symptoms than men [ASRM>5: females median 8.23% (IQR 1.3-24.2) vs. males, 5.62% (IQR 0.63-22.6), Cohen's d effect size 0.32

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(95% CI 0.07-0.56), p=0.009] but there was no difference in the number of hypomanic/manic episodes between genders (Figure 2). Females experienced significantly more depressive episodes per year than males [2.16 (IQR 0.76-3.62) vs. 0.86 (IQR 0-2.53), ES 0.46 (0.24-0.70), p<0.001] and spent more days moderately depressed [females median 11.8% (IQR 4.1-23.8) v. males 7.10% (IQR 0.8-17.9), ES 0.14 (0.38-1.0), p<0.01]. Overall females spent more time depressed than men (Figure 2).

No significant difference in the amount of time spent manic, hypomanic or depressed was found between any age group. There was no significant difference in the severity of depression reported by different age groups. However, younger participants had significantly more manic/hypomanic episodes per year than older participants [age <20, mean = 6.47 (2.8-8.8) vs. ages 21-40 yrs, mean= 1.64 [0.55-3.8]; ES = 0.79 (0.2-1.38), p=0.001].

Comparison of Course Patterns in Patients with Bipolar I, Bipolar II, or Bipolar NOS Disorder

There was no difference in the amount of time spent depressed (QIDS>10) between those diagnosed with bipolar 1, 2 or NOS. There was no difference in the time spent with differing severity of depressive symptoms between the three diagnoses, or with hypomanic/manic symptoms. There was no significant difference in the number of mood episodes per year – at either pole – between diagnostic subgroups.

Mood Variability as Reflected by Root mean squared Successive Difference Scores

Overall the cohort experienced an average QIDS variability score of 1.55 [SD 0.54] and ASRM variability score of 1.21 [SD 0.7] (Table 2). The mean weekly score change for QIDS was 2.4 and 1.44 for ASRM, indicating an average 1-2 point scale change per week. Females reported a significantly greater change in weekly QIDS scores than males, but this was not the case for the ASRM [QIDS: mean 1.61 [SD 0.56] vs. 1.42 [0.51], ES 0.35 (0.1-0.55) p=0.001; ASRM: 1.24 [0.58] vs. 1.16 [0.59], ES 0.14 (-0.1- 0.38), p=0.323]. There was no difference in variability between diagnostic subgroups on

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either the QIDS or ASRM. Younger participants reported significantly more variability on both the QIDS and ASRM than older participants [QIDS: <20yrs 1.88 [SD 0.71] vs. >60yrs 1.31 [0.40], ES 1.12 (0.38-1.81), p<0.0001, ASRM: 1.67 [0.7] vs. 0.94 [0.46], ES 1.35 (0.59-2.06) p=0.001].

DISCUSSION

Systems such as True Colours may be of considerable clinical value, as doctors and patients may be able to collaborate in identifying episodes at their earliest, and intervene to prevent escalation. Mood monitoring is also fundamental to self-management approaches, enabling patients to gain insights into the ongoing relationship between behaviour (e.g. sleep patterns) and mood states. We aimed to describe the range of mood phenotypes reported by a cohort of bipolar patients using True Colours mood monitoring over a period of up to 81 months. Our findings are based on data drawn from a large, naturalistically recruited cohort with relatively little missing data, and which is comparable with others in terms of mean age, age of illness onset, proportions by gender and ethnicity (Joffe et al., 2004; Judd et al., 2002; Kupfer et al., 2002; Suppes et al., 2001), and level of education (Suppes et al., 2001). Our results suggest that mood symptoms are experienced by patients the majority of the time, and that age and gender, but not diagnostic subgroup, influence symptoms collected over an average period of 27.5 months.

This was a study of predictors of mood cycling within patients with bipolar disorder. Therefore, we did not include a comparison group of healthy individuals to evaluate how frequently mood episodes or changes occur in the general population. However, a new study has been published that followed bipolar and healthy control individuals using the True Colours system for up to 52 weeks (Tsanas et al., 2016). The study reported that patients with BD and patients with borderline personality disorder both consistently reported higher levels of mania, depression, and anxiety than healthy controls. Thus, True Colours ratings of moods are unlikely to reflect the day-to-day variability in mood states that it common in the general population.

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We found very high rate of compliance (92%) with the True Colours system; comparable to those reported by similar technologies (Bauer et al., 2004). True Colours was designed to be flexible, convenient & personalised: patients can choose the frequency and timing of prompts, send in extra information and access their graphs on any internet-enabled device. The high rate of compliance suggests these qualities are attractive to patients, perhaps more so than a system requiring access to a conventional computer or that must be completed at a set time each week. 74% of participants returned responses by SMS, with the remainder by e-mail (10%) or a mixture of the two methods, suggesting that having a choice of communication methods is likely to enhance patient experience and compliance.

Whereas patients reported mood symptoms between 50-60% of the time, symptoms meeting diagnostic criteria for an episode only occurred about twice per year for each illness pole (an average of 4 recurrences per patient). This pattern suggests that patients experience ongoing subsyndromal symptoms a large proportion of the time. These findings are consistent with the view of BD as a condition of chronic mood instability with episodic exacerbations rather than an episodic disorder with return to baseline in between episodes. This study also confirms previous findings that depressive symptoms occur for longer intervals than hypomanic or manic symptoms; here we found a ratio of 9 weeks:1 week (Bopp et al., 2010; Joffe et al., 2004; Judd et al., 2002; Kupka et al., 2007; Post et al., 2003). This ratio is much higher than that found by life-chart methodology publications, possibly due to our use of a more sensitive measure of depression, our use of self-report rather than clinician-reported symptoms, and/or the use of prospective monitoring rather than techniques dependent on retrospective recall (Judd and Akiskal, 2003). As discussed further below, the Altman self-rating scale may not capture subthreshold variations in hypomania to the degree observed with Life Chart methodology. It is unclear whether depression is inherently more prominent in BD than mania, given that patients have a tendency to under-report mania (Youngstrom, 2015) and that mood stabilizing medications and second generation antipsychotics are more effective for controlling manic than depressive symptoms.

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Several other publications using life chart or computer-based mood monitoring systems have collected data similar to ours; these are summarised in Table 3. Most studies find no significant difference in the mood states over time of patients with bipolar I or 2 disorders. We also observed no difference in variability of depressive or manic mood symptoms between the diagnostic subgroups. Together, these data suggest that the long-term course of bipolar I and II disorder are more similar than different, although effective treatments for the two subtypes may differ.

We observed that females reported more weeks with depression and hypomanic/manic symptoms than males. In some previous reports females with BD were observed to spend more time with depressive symptoms compared to male patients (Kupfer et al., 2002; Nivoli et al., 2011; Taylor and Abrams, 1981) although this pattern has not been consistent (Diflorio and Jones, 2010). Female participants also reported a significantly higher variability in depressive scores. As discussed by other investigators, differences between females and males in mood symptoms may have a variety of causes, including differences in reporting thresholds, the tendency to ruminate when depressed, hormonal changes that vary with age, and patterns of alcohol abuse (Frye et al., 2003; Picinelli and Wilkinson, 2000)

To the best of our knowledge, ours is the first report linking age with self-reported mood stability. We observed that younger patients experienced more episodes of mania or hypomania and more mood variability compared to their older counterparts, in concordance with previous reports suggesting that younger patients experience more severe manic episodes than older patients and show greater illness severity (Broadhead and Jacoby, 1990; Depp and Jeste, 2004). Frequent mood variability in the early phases of BD, even if the variability is subsyndromal, may signal the need for more aggressive pharmacological or psychosocial interventions to prevent a more recurrent course of illness.

Study Limitations

The cohort, recruited primarily from Oxfordshire and the surrounding counties, is almost entirely British and Caucasian, and has a higher than average level of education. Within the

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inclusions criteria, it is a clinically heterogeneous sample. The True Colours system excludes patients who do not feel able to use email/SMS as a method of communication or do not have access to the internet. However, only one patient referred to the OXTEXT study did not consent due to communication difficulties. One patient used an adapted system where they telephoned in the mood scores weekly.

Instruments that measure subthreshold levels of hypomanic or manic symptomatology, for example, the Internal State Scale (Bauer et al., 2000), may prove more sensitive in assaying manic symptoms than the ASRM. Additionally, collecting data from family members may increase the sensitivity of all self-report instruments, especially among patients with significantly elevated mood. Whilst the QIDS is anchored to the DSM-IV, neither it nor the ASRM are validated as diagnostic tools, so they should be used as indices of the severity of current symptoms rather than syndromal onset or offset.

One limitation of the True Colours system is that the individual's mood states are treated as static between weekly measurements. Indeed, some participants may have had exacerbations of manic or hypomanic symptoms in the days between weekly ratings. More frequent monitoring could provide important clinical information on daily or intra-daily mood fluctuations that might be used to distinguish patients who, for example, would meet the course specifier criteria for rapid cycling or who might be diagnosed with a comorbid borderline personality disorder (Tsanas et al., 2016). However, there is no evidence that daily rather than weekly monitoring improves validity, and it is possible that daily monitoring would result in poorer compliance. In future research, we intend to investigate variations in latency between a patient receiving a prompt and returning mood data.

This study was also limited by the lack of measures of stressful life events, which may have predated or occurred in tandem with changes in mood. The study was not designed to answer questions about the relationship between stress and mood cycling in bipolar disorder. We see this as a fruitful area for exploration, with the proviso that life events reported by patients on a mood

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tracking device may not accurately reflect the specifics of these events or how they were affected by his/her behaviour.

This study did not include a comparison sample of healthy volunteers who made weekly mood ratings. Thus, we are unable to conclude that the observed mood fluctuations reflect the diagnosis of bipolar disorder or normal variations in mood that can be detected when individuals provide self-ratings over a 2-year interval. Additionally, future studies with psychiatric comparison groups (e.g., patients with personality disorders) may help clarify whether there are patterns of mood fluctuation that are truly "signatures" of bipolar disorder.

Finally, concurrent psychopharmacological information for our cohort was only available for 89% of participants and at the point of enrolment. An analysis of the time-lagged relationships between changes in specific medications or dosing plans and mood variations was not possible at this stage.

Conclusions

Our results suggest that mood symptoms are experienced by patients the majority of the time, and that classically defined episodes of depression and mania are superimposed upon subsyndromal mood symptoms, including pervasive mood instability. Age and gender, but not diagnostic subgroup, influenced our longitudinal symptom data, with females reporting more depressive episodes and more time hypomanic/manic than males, and younger patients experiencing greater mood variability than older patients. Longitudinal mood monitoring using electronic data collection methods are increasingly likely to contribute to our understanding of the course of bipolar disorder and its response to various treatments or self-management strategies.

Accepted manuscript

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Consent for Publication

Not applicable

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Competing Interests

GMG reports grants and personal fees from Servier, personal fees from Teva, personal fees from Otsuka, personal fees from Takeda, grants and personal fees from Lundbeck, personal fees from Ei Lilly, personal fees from Merck, personal fees from GlaxoSmithKline, personal fees from Astra Zeneca, and grants from P1vital during the conduct of the study. DJM reports grants from American Foundation for Suicide Prevention and National Institute of Mental Health; and book royalties from Guilford Press and John Wiley and Sons, outside the submitted work. ACB has received salaries from P1vital. All other authors declare no conflicts of interest.

Accepted manuscript

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Author's Contributions

RM downloaded data, designed and performed analyses and results interpretation and drafted the manuscript. ACB assisted with reference research and helped to draft the manuscript. DJM, GMG, JFG initiated the OXTEXT project, helped design the methodology, helped to interpret findings and provided guidance with the manuscript. CH performed the variability design and analysis. JFG is guarantor.

Accepted manuscript

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Table 2. Mood Variability

	Variability Score[a]mean [SD]				
Measure	**WHOLE COHORT (n=297)**				**p-value**
QIDS	1.55 [0.54]				N/A
ASRM	1.21 [0.7]				N/A
	FEMALE (n=198)	**MALE (n=99)**			
QIDS	1.61 [0.56]	1.42 [0.51]			**0.003**[b]
ASRM	1.24 [0.58]	1.16 [0.59]			0.323[b]
	BIPOLAR 1 (n=187)	**BIPOLAR 2 (n=98)**	**BIPOLAR NOS (n=12)**		
QIDS	1.55 [0.49]	1.57 [0.64]	1.38 [0.59]		0.954[c]
ASRM	1.19 [0.55]	1.27 [0.64]	1.01 [0.5]		0.461[c]
	Age <20	**Age 21-40**	**Age 41-60**	**Age >60**	
QIDS	1.88 [0.71]	1.68 [0.62]	1.42 [0.4]	1.31 [0.40]	**0.0001**[c]
ASRM	1.67 [0.7]	1.31 [0.66]	1.12 [0.44]	0.94 [0.46]	**0.001**[c]

[b]Wilcoxon Rank Sum Test [c]Kruskall-Wallis Test

[a] Variability =√(changes per week) where 1 change is equal to a one integer change in score on QIDS/ASRM between weekly questionnaire replies.

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Table 3. Comparison of symptomatic course of bipolar disorder in different publications

Reference	Percentage of time spent in mood State (%)				
	Diagnosis	**Euthymia**	**Depression**	**Hypomania or mania**	**Differences found between diagnostic groups**
This study	Whole cohort	40.1	35.0	7.5	No significant differences between bipolar 1 & 2
	Bipolar 1	41.5	36.5	6.9	
	Bipolar 2	41.2	36.4	7.9	
Faurholt-Jepsen et al, 2015 (Faurholt-Jepsen et al., 2015b)	Bipolar 1	74.0	18.0	5.5	Bipolar 2 spent more time depressed than bipolar 1.
	Bipolar 2	51.0	45.1	2.7	
Bopp et al,2010(Bopp et al., 2010)	Bipolar 1,2, NOS	36.5	47.7	7.0	Bipolar 1 spent more time depressed than bipolar 2
Kupta et al, 2007(Kupka et al., 2007)	Bipolar 1	47.7	36.2	12.5	No significant differences between bipolar 1 & 2
	Bipolar 2	50.2	36.9	10.0	
Joffe et al,2004(Joffe et al., 2004)	Bipolar 1 & 2	53.1	40.9	6.0	No significant differences between bipolar 1 & 2
Post et al, 2003(Post et al., 2003)	Bipolar 1 & 2	52.6	33.2	10.8	No significant differences between bipolar 1 & 2
		Subsyndromal symptoms	**Mild mood* symptoms**	**Syndromal mood* symptoms**	**includes depression and mania*
Judd et al, 2002(Judd et al., 2002)	Bipolar 1	14.8	20.2	12.3	No significant differences between bipolar 1 & 2
Judd et al, 2003(Judd et al., 2003)	Bipolar 2	15.7	25.2	13.0	

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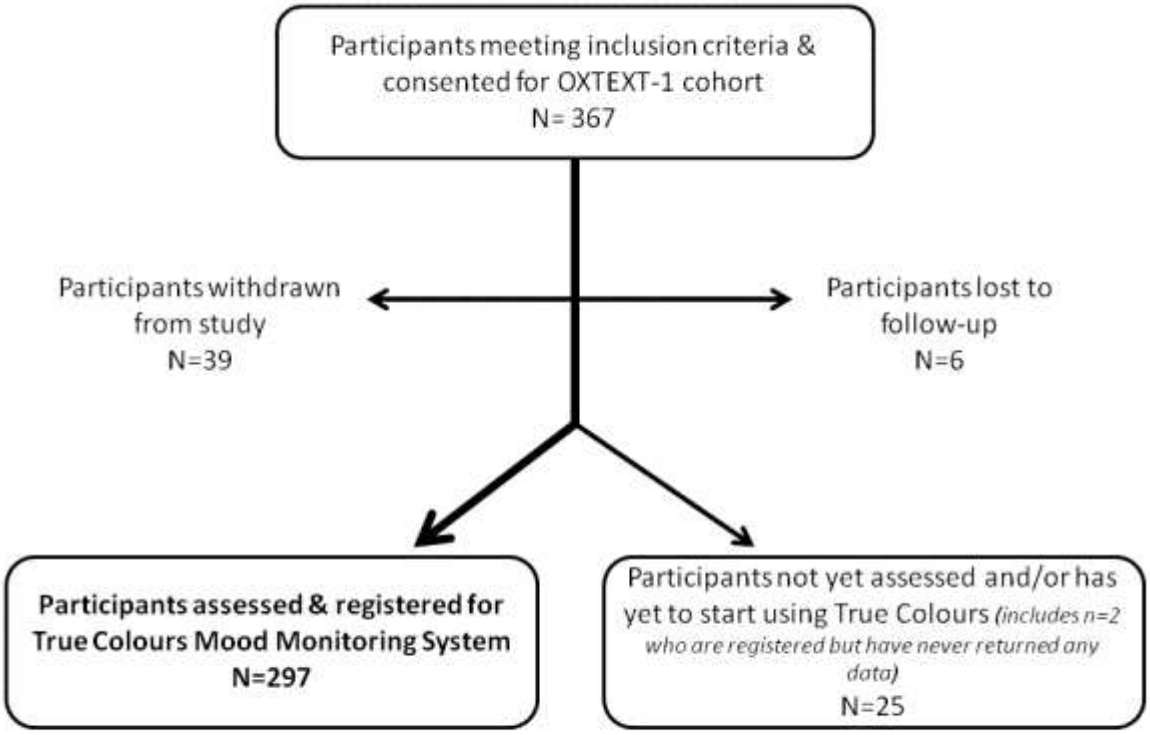
Highlights

- Online self-monitoring of mood can be used to investigate mood patterns in a cohort.
- Bipolar patients experience subsyndromal mood symptoms the majority of the time.
- No significant differences in mood variables were observed between bipolar I and II patients.
- Younger patients experience more variability in mood than older patients.
- Long-term outcomes may be improved by interventions to reduce mood variability.



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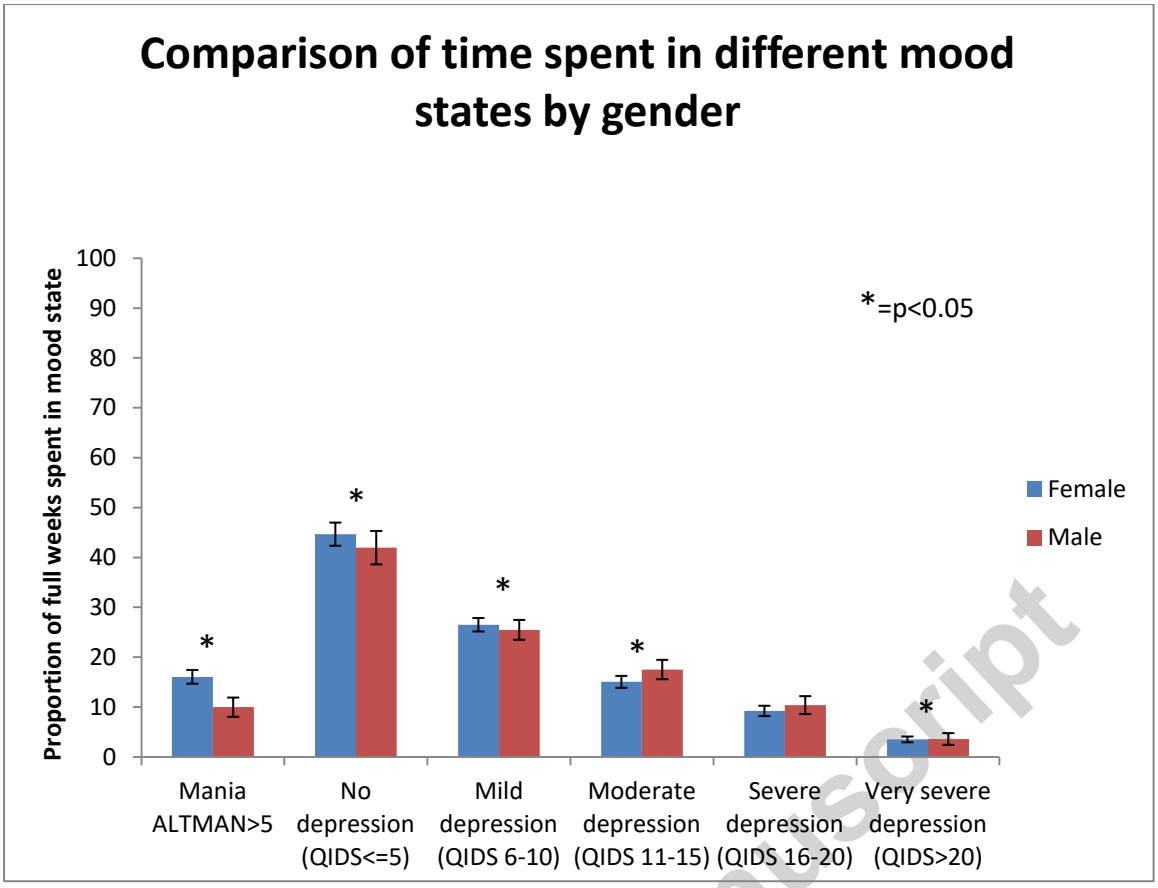

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