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Augmenting Psychoeducation with a Mobile Intervention for Bipolar Disorder: A Randomized Controlled Trial

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Abstract

Background—Psychosocial interventions for bipolar disorder are frequently unavailable and resource intensive. Mobile technology may improve access to evidence-based interventions and may increase their efficacy. We evaluated the feasibility, acceptability and efficacy of an augmentative mobile ecological momentary intervention targeting self-management of mood symptoms.

Methods—This was a randomized single-blind controlled trial with 82 consumers diagnosed with bipolar disorder who completed a four-session psychoeducational intervention and were assigned to 10 weeks of either: 1) mobile device delivered interactive intervention linking patient-reported mood states with personalized self-management strategies, or 2) paper-and-pencil mood monitoring. Participants were assessed at baseline, 6 weeks (mid-point), 12 weeks (post-treatment), and 24 weeks (follow up) with clinician-rated depression and mania scales and self-reported functioning.

Results—Retention at 12 weeks was 93% and both conditions were associated with high satisfaction. Compared to the paper-and-pencil condition, participants in the augmented mobile intervention condition showed significantly greater reductions in depressive symptoms at 6 and 12 weeks (Cohen's *d* for both were *d*=0.48). However, these effects were not maintained at 24-week

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Contributors

CD: Led the concept formation, analysis, and interpretation of results as well as manuscript preparation

JC: Contributed to the intervention development, interpretation of results and manuscript preparation

VW: Contributed to the intervention development, interpretation of results and manuscript preparation

BM: Contributed to the statistical analytic strategy and interpretation of results

FY: Contributed to the technical development and manuscript preparation

WT: Contributed to organization of data collection, interpretation of results, and manuscript preparation

EG: Contributed to the intervention development, interpretation of results and manuscript preparation

follow up. Conditions did not differ significantly in the impact on manic symptoms or functional impairment.

Limitations—This was not a definitive trial and was not powered to detect moderators and mediators.

Conclusions—Automated mobile-phone intervention is feasible, acceptable, and may enhance the impact of brief psychoeducation on depressive symptoms in bipolar disorder. However, sustainment of gains from symptom self-management mobile interventions, once stopped, may be limited.

Keywords

Bipolar disorder; psychotherapy; technology; internet-based treatments; depression; ecological momentary assessment

INTRODUCTION

Mobile technology may extend the reach and impact of psychological interventions for people with bipolar disorder. The current availability of evidence-based psychological interventions for bipolar disorder is limited and likely worsening. For example, Olfson found a nearly 25% decline in psychotherapy participation and a significant reduction in the number of sessions attended among those who did participate in therapy among consumers with bipolar disorder between 1998 and 2007 according to a National Medical Expenditure survey.(Olfson and Marcus, 2010) The rate of this decline in therapy participation outpaced that in unipolar depression. While the causes of this decline in participation are likely multiply determined, it is clear that delivery innovations are needed to improve availability and engagement in brief treatments compatible with real-world constraints.

Mobile technology offers a particularly promising platform for delivery of interventions. For instance, the rate of penetration of mobile phones is greater than 91% in the United States and increasing yearly(Duggan, 2013). Extending work in ecological momentary assessment, where naturalistically assessed behaviors, symptoms, and related experiences are repeatedly sampled over time(Shiffman, 2006), automated ecological momentary interventions leverage real-time assessments to deliver interventions that map to symptoms and risk factors as they occur in the moment(Heron and Smyth, 2010). A number of mobile health-based assessments and interventions have been piloted in bipolar disorder(Bardram et al., 2013; Depp et al., 2010; Wenze et al., 2014), although there are no randomized controlled trials reported to date to our knowledge.

We have previously described an automated ecological momentary intervention for bipolar disorder called Personalized Real-Time Intervention for Stabilizing Mood (PRISM). Briefly, this mobile intervention builds upon established psychoeducational approaches for bipolar disorder focused on self-monitoring of mood states and on planning action steps to address both symptoms and early warning signs of illness(Bauer et al., 2009; Bauer and McBride, 2003; Depp et al., 2007). To increase palatability and adherence, these action steps are phrased by the participant to capitalize upon source memory and are formatted into implementation intentions(Gollwitzer, 1999; Gollwitzer and Schaal, 1998). Implementation

intentions are “if-then” statements that specify the circumstances (e.g., current state of illness), specific action/behaviors (e.g., coping strategies), and benefit of the action step (e.g., avoidance of negative outcomes). The result is an intervention that is highly personalized to both patient preferences and specific illness states or precursors, creating a framework for patients to “coach” themselves in critical moments. The inclusion of patient-developed statements into intervention content is consistent with broader literature on electronic interventions that indicate greater adherence and efficacy when compared to static and non-tailored intervention content (Chomutare et al., 2011; Schubart et al., 2011).

We have previously reported initial preliminary data from an open-trial design that collected data from 15 outpatients with bipolar disorder who were followed for 2 weeks and participated in PRISM (Depp et al., 2010). After one psychoeducation session, participants in that trial were provided a mobile device used to prospectively monitor symptoms and early warning signs. The collected data were then connected through automated software to their pre-specified implementation intentions specific to a symptom state or early warning sign. This uncontrolled trial provided initial evidence of high retention and satisfaction with this approach, and significant pre-post reductions in depressive symptoms.

We report here on a 6 month randomized controlled trial of PRISM in which 104 outpatients with bipolar disorder I or II were enrolled in a 4-session individually-adapted psychoeducational program. They were randomized to either receive: a) 10 weeks of PRISM delivered by smart phone or b) 10 weeks of paper-and-pencil mood monitoring. Participants were assessed at baseline, 6 weeks (mid-point), 12 weeks (post-treatment), and 24 weeks follow up. The primary outcome of the study was the severity of depressive symptoms, as measured by the Montgomery Asberg Depression Rating Scale, based on our pilot findings that identified a significant change in depressive symptoms (Depp et al., 2010). Additionally, we assessed the following secondary outcomes: Manic symptom severity (Young Mania Rating Scale) and functional impairment (Illness Intrusiveness Scale). We also contrasted study conditions in terms of their satisfaction with the intervention. We hypothesized that participants assigned to PRISM would experience greater reductions in mood symptoms and functional impairment than participants assigned to the paper-and pencil condition, and they would be more satisfied with the intervention.

METHODS

Participants and Recruitment

Participants were outpatients diagnosed with either Bipolar Disorder I or II who were recruited from various sources including flyers and advertisements placed online and in community residential and drop-in settings, depression and bipolar disorder self-help support groups, and outpatient psychiatric clinics in the San Diego area. To be eligible, participants needed to be: 1) aged 18 and older, 2) outpatients and currently prescribed medications for bipolar disorder, 3) free of visual or manual dexterity disabilities that would preclude operation of a touch screen device. We excluded participants who: 1) met criteria for any substance use disorder in the prior 3 months, 2) were psychiatrically hospitalized in the prior month, or 3) scored in the severe range for either depressive symptoms (a score on the Montgomery Asberg Depression Rating Scale >32) or manic symptoms (a score on the

Young Mania Rating Scale >20). We excluded participants with more severe psychopathology because they would likely require more intensive interventions than those offered in this study, and we provided referrals for more intensive treatments.

Screening for the study was completed on an in-person basis and each individual's diagnostic status was primarily assessed with the MINI International Neuropsychiatric Interview for DSM-IV (Sheehan et al., 1998). Final diagnosis was attained by combining information from the MINI, chart reviews from treating providers, and confirmed in consensus meetings with the principal investigator. All participants provided written informed consent, and this study was approved by the UCSD Human Subjects Protections Program. Participants were compensated for time spent in assessments, but not treatment sessions. The study was registered in Clinicaltrials.gov (NCT01670123). We have previously reported preliminary data on the validity of the assessment data derived from the electronic assessments (Depp et al., 2012), but none of the outcome data have been reported elsewhere. Participants were compensated \$25 for each completed assessment (maximum = \$100), but not for therapy participation.

Measures

Demographics and Diagnosis—All participants were assessed at baseline for basic sociodemographic information as well as diagnosis and treatment history, along with current participation in treatment including medications.

Standard Clinical Ratings—The primary outcome measures for the study were the Montgomery Asberg Depression Rating Scale (MADRS) (Montgomery and Asberg, 1979) and the Young Manic Rating Scale (YMRS) (Young et al., 1978). The MADRS is a 10-item clinician-rated scale that is widely used in assessing the severity of bipolar depression. The total score was used in analyses. The YMRS is an 11-item clinician-rated scale that is the most commonly used scale for quantifying the severity of mania, again with total score used in the analyses. The MADRS and YMRS were interviewer-administered, and as part of our research protocols, raters are trained on reliability to a gold standard on these instruments by more senior raters.

We also assessed functional impairment associated with bipolar disorder as a secondary outcome with the self-rated Illness Intrusiveness Scale. The IIS is a 13-item self-report scale that assesses the degree of interference caused by an illness or its treatment as a general measure of the negative functional impact of chronic illness (Devins et al., 2001; Robb et al., 1997). The 13 items cover 13 different domains including health, diet, work, active and passive recreation, financial situation, relationship with spouse, sex life, family and other social relations, self-expression/self-improvement, religious expression, and community/civic involvement; scores range from 13 to 91.

Follow-Up Assessments—Participants were re-administered the MADRS, YMRS, and IIS scales at 6 weeks (mid-treatment), 12 weeks (post-treatment) and 24 weeks follow up. They were also assessed at these intervals for any changes to medications, other treatments, or other notable psychiatric changes during intervals between assessments.

Post-Intervention Feedback Questionnaire—At 12 weeks, we administered a two-part questionnaire, which was made anonymous so as to maximize frankness in responding. The first part of the questionnaire was applicable to both conditions, with 10-point satisfaction scales: 1) “In general how would you rate your satisfaction with the intervention?”, and 2) “How helpful was the intervention in learning to manage the symptoms of bipolar disorder?”. The second part of the questionnaire was only applicable to the PRISM condition and asked questions about the specific acceptability of mobile devices from that of Kimhy et al. (Kimhy et al., 2006) which focused on positive elements: 1) “A device like this could be helpful to me in the future”, 2) “I would use a device like this again”, rated on a 5-point scale from “Not at all likely” to “Very likely”. Additional questions were asked about negative elements “I had difficulty operating the device”, “I had difficulty understanding the questions”, and “The device interfered with my activities”, also rated on a 5-point scale from “Not at all” to “Very much”.

Randomization—Participants were randomized after completing baseline assessments to either the PRISM condition or the paper-and-pencil condition. Randomization was completed by an unaffiliated investigator who used a computerized random number generator. Raters were masked to study assignment. At the end of 12 weeks, participants turned in their mobile devices (93% of participants returned phones) or mood charts in a location that was kept separate from raters, so as to preserve the blind.

Four Session In-Person Intervention—After participants were assigned to a condition, all participants met with the project therapist for a standardized 4-session treatment that did not differ across conditions. The overarching aim of the four-session intervention is to identify an “Action Plan” which specifies adaptive responses to depressive and manic symptoms as well as early warning signs and triggers of illness exacerbations. The manual for this study was adapted from prior published works, in particular the Life Goals Program, the Overcoming Bipolar Disorder Workbook and Medication Adherence Skills Training Workbook (Bauer et al., 2009; Bauer and McBride, 2003; Depp et al., 2007). All participants regardless of condition were provided with a copy of the manual and their action plan, and the manual is available from the authors.

The contents of the four hour-long sessions were as follows: Session 1: General psychoeducation about bipolar disorder, its symptoms, and treatment along with the association between self-management of bipolar disorder and functional outcomes; Session 2: Identifying symptoms of depression, managing illness exacerbations and recognizing and responding to early warning signs for depression, Session 3: Identifying symptoms of mania, managing illness exacerbations, and recognizing and responding to early warning signs for mania, and Session 4: Developing implementation intentions keyed to levels of severity of depression and mania, as well as to early warning signs for symptoms (i.e., if-then statements linking context, symptom or early warning sign with adaptive response). In Session 4, participants also selected optional strategies from a list generated by an internet survey that solicited self-management strategies from over 1000 persons self-identified as having bipolar disorder (see our prior publication) (Depp et al., 2009).

Therapist Characteristics—The same therapist delivered the four-session psychoeducational intervention regardless of random assigned condition. The content and manual was also identical. The therapist was a master's trained family therapist and was trained by the lead author in the manual in a one day training session. Subsequent supervision was performed using direct observation, review of audiotapes, and review of cases performed by the lead author. Due to the highly structured nature of the educational protocol and identical content of the interventions across conditions, we did not collect routine measures of therapist fidelity. Eighty-two participants completed all four sessions of the intervention. There were five patients who did not complete all four sessions in the PRISM condition and three patients with less than four sessions completed in the paper-and-pencil condition; there was no statistical difference between conditions in the number who completed all four sessions (Chi-square (1)=0.5, $p=0.500$).

PRISM Condition

Technical Aspects—Participants assigned to PRISM were provided with an internet-enabled smart phone (Samsung Fascinate) at the end of Session 2 that was used to deliver subsequent interactive elements. We did not allow participants to use their own devices so as to reduce the possibility of a loss of confidentiality. We developed a mobile enabled web-based program to deliver personalized questionnaires capable of delivering pre-programmed interactive algorithm-based responses based on symptoms or early warning signs reported. The web-based system was capable of independently scheduling and initiating interactive content for each participant, based on branching algorithms that were pre-defined. At each survey epoch, users received an invitation to complete a “survey” at a randomly scheduled time within two 3-4-hour blocks in the mornings and evenings. This was accomplished by using an SMS gateway that generated timed text messages that automatically opened the web browser on the device. Participants could select the earliest and latest times they wish to be alerted, so as not to interfere with their typical sleep/wake cycle. Responses were recorded by use of a touch screen interface with categorical or Likert-type responses. Once prompted to respond, participants had 15 minutes to complete the survey, after which they received a reminder prompt if no response was provided. All of the data obtained were stored on the server and not on the device; thus, partial responses were stored. A separate program provided on-demand graphical feedback about any of the mood items expandable from the past week to the past month.

At the conclusion of Session 2, participants were trained in an individualized session lasting approximately 30 minutes as to how operate the device, the meaning of all questions and response choices, and procedures for carrying the device and responding to alarms. Participants also received a written manual describing the operation of the device.

PRISM Assessments and Intervention—At each survey epoch (twice per day for 10 weeks), participants answered four questions: What are you doing? (Activity, 7 options such as “Working”), Where are you? (7 options, such as “At home”), and Who are you with? (5 options, such as “Alone”). Subsequently, respondents answered 6 questions about mood state, which were rated on a 7-point Likert scale from “Not at all” to “Extremely”. Next, participants rated their current mood state on a 9-point bipolar anchored scale. A value of 1

represented “most ever depressed”, a 2: “severely depressed”, a 3: “moderately depressed”, and 4: “mildly depressed”. A value of 5 represented “euthymic or even mood”. Values for mania were transposed from depression with 9 being “most ever manic”. The scaling was identical for phone and paper-and-pencil conditions. Written descriptors of each of the anchors were provided in an accompanying manual.

Depending upon their rating on the 9-point mood scale, participants were presented with a random selection of one of the implementation intentions that they had developed in Session 4. They were subsequently asked about their intention to “try this” on a 3 point scale (“I will not try this”, “I may try this”, “I will definitely try this” after the Morning survey). They were also asked if they wanted to see a different coping strategy drawn at random from a list. On the Evening Survey, participants were first asked if they had tried the strategy that was recommended earlier in the day and whether it was helpful, again on a 3 point scale (not at all, somewhat, very helpful). The subsequent questions were identical to the Morning Survey, with the addition of a question about the presence of Early Warning Signs/Triggers that were encountered that day. This was presented in “check box” fashion, so that participants could select whether any of the Warning Signs/Triggers had occurred that day and were subsequently presented with a predefined selected implementation intention that was mapped on to that Warning Sign/Trigger. Finally, participants had an option to view a randomly selected coping strategy generated from the list of general coping strategies culled from a prior survey of community-dwelling patients with bipolar disorder described above.

Paper and Pencil Condition—At the end of Session 2, participants assigned to the paper and pencil condition were provided with a binder containing mood charts for the subsequent ten weeks. The layout of the paper-and-pencil mood chart was adapted from the NIMH mood chart (Denicoff et al., 2000), and was completed once per day. Participants were told to complete the paper-and-pencil mood charts every day, although they were not told to complete it at any particular time of day. Participants received a paper copy of the implementation intentions they had developed to parallel that of the PRISM condition.

Participants were informed that investigators would be able to monitor compliance remotely (phone condition) or would collect the completed paper-and-mood charts at the end of the study. Therefore, compliance was encouraged; however lapses in compliance did not result in withdrawal from the study. Notably, participants were only asked to participate in surveys on the device or with paper-and-pencil mood charts and did not perform both. The indicator of compliance in both the PRISM and paper-and-pencil conditions was the number of days completing a phone survey (at least one of two sent) or an entry into a mood chart divided by the number of possible entries.

Statistical Analyses—Data were analyzed from all participants who completed the baseline assessment, randomized, and who completed all four of the in-person sessions. Values were checked for normality and for meeting the assumptions of parametric analyses. We addressed the association of PRISM compliance with demographic and baseline MADRS, YMRS and IIS scores with Pearson correlations. Outcome analyses were longitudinal mixed effects models with restricted maximum likelihood estimation, using the following parameters: Treatment, time, and treatment-by-time were fixed effects and

subjects was a random effect. The treatment-by-time effect was the primary effect of interest with planned contrasts assessing change from baseline to 6, 12, and 24 weeks across conditions. These analyses were conducted with the primary outcome of MADRS Total Score, and secondary outcomes of YMRS and IIS Total Scores. These were intention-to-treat analyses as we included data from persons who did not appear for follow up assessments (i.e., drop outs). However, given that the focal point of the study was the effect of extending the 4 session individual therapy, we only included participants if they completed the four sessions. We calculated effect sizes (Cohen's *d*) at 6 weeks, 12 weeks, and 24 weeks following guidance from Feingold (2009) (Feingold, 2009) on estimation of effect sizes in growth curve modeling, with the estimate for condition-by-time interaction at each planned contrast divided by the baseline standard deviation. Patient satisfaction scores, assessed once at Week 12, were contrasted between conditions by way of non-parametric tests for two group samples due to non-normality of distributions. Finally, we examined Pearson correlations between compliance in the PRISM condition and treatment response. Analyses were conducted with SPSS Version 21. The alpha level was set to 0.05, two-tailed.

RESULTS

Recruitment and Sample Characteristics

A total of 195 persons participated in the consent, initial diagnostic, and eligibility screen for the study (see Consort diagram). Of these persons, a total of 37 (19%) were found to be ineligible due to not having bipolar disorder or failing other eligibility criteria and 54 (28%) screened participants did not complete the baseline assessment due to lack of interest in the study or inability to be re-contacted. Of the 104 who were randomized to the study, 82 attended all four sessions of the intervention (79%). A total of 14 participants did not attend a single session of the intervention (13% of total randomized). Eight (8%) (five in the PRISM condition and three in the paper-and-pencil condition) participated in less than four sessions and were not included in the analyses. Of those who completed the psychoeducation intervention, three (7%) of the PRISM and five (12%) of the paper-pencil condition participants did not complete the 12-week assessment (but were included in the intent to treat analyses). There were no differences in attrition between the study conditions. Comparing those who were randomized but not included in analyses with those who were retained, drop-outs were more likely to be younger (mean age = 41.6 (sd=12.5) vs. 47.5 (sd=12.8), $t=4.5$, $p=0.034$) and had more severe manic symptoms on the YMRS (mean YMRS score 9.5 (sd=6.9) vs. 6.1 (sd=5.5), $t=7.0$, $p=0.009$). There were no other differences in demographic, diagnostic/symptom severity, or functional impairment variables between those analyzed and excluded from analyses. As seen in Table 1, the sample was, on average, middle aged, educated beyond a high school level, and residing independently in the community. The sample was largely comprised of patients with Bipolar I (vs. II) who were experiencing near to, but slightly below, threshold level of symptoms on the YMRS and MADRS. The relatively low level of symptoms at baseline was likely due to the outpatient sampling scheme and the upper cut-offs for severity of illness at baseline. The great majority of the sample was prescribed a mood stabilizer, with a substantial proportion prescribed anti-depressants and/or antipsychotic medications.

Program Participation

In the PRISM Condition, mean compliance was 65% (sd=24%, range 12% to 97%). The association between the number of days on study and compliance was not significant ($r=-0.122, p=0.448$), indicating that adherence was stable over time (i.e., minimal fatigue effects). There were also no significant correlations between PRISM compliance and age ($r=.174, p=0.278$) or education ($r=-0.101, p=0.528$). Similarly, there were no significant associations between PRISM adherence and baseline MADRS Score ($r=0.058, p=0.717$), YMRS Score ($r=-0.121, p=0.451$), or IIS score ($r=0.076, p=0.636$). We note that we collected paper-and-pencil mood charts from those in the paper-and-pencil condition from all but 5 participants (in a preliminary subsample rate of completion of paper-and-pencil chart data among those who returned them was 83% (Depp et al., 2012)).

Treatment Outcomes

Inspection of the pattern of change in both conditions (see Table 2) indicated decline in depressive symptoms over the 12 weeks of the active phase of PRISM and little change in the paper-and-pencil condition; however, after treatment ended, the two groups converged. The mixed-effect model (see Table 2) showed that, despite random assignment, the PRISM condition had significantly higher MADRS scores ($F(1, 80) = 4.5, p=0.036$) at baseline, but there was no effect of visit. Of primary interest, the omnibus visit-by-condition interaction was significant ($F(3,164) = 2.6, p=0.049$). Planned contrasts for the visit-by-condition interaction during active phase of treatment were each significant: 6 weeks (estimate = 3.6, S.E.=1.7, $t(223)=-2.2, p=0.031$) and 12 weeks (estimate = 3.6, S.E.=1.8, $t(181)=-2.0, p=0.042$). However, the contrast at the 24 weeks follow up assessment was not significant (estimate = 0.3, S.E.=1.8, $t(179)=-0.2, p=0.858$). Cohen's d effect sizes were as follows: 6 weeks (mid-treatment): $d=0.47$, 12 weeks (post-treatment): $d=0.47$, and 24 weeks (follow up), $d=0.02$. There were no significant omnibus time, condition, or condition by time effects on the YMRS or the IIS, with small to negligible effect sizes for each of the contrasts as seen in Table 2.

Due to the group difference in depressive symptom severity, we performed an additional sensitivity analysis in the group of subjects who scored 10 or higher on the MADRS [$n=29$; an established criterion for clinically significant depressive symptoms (Hawley et al., 2002)]. In a mixed effect models indicated no group effect ($F(1,30)=1.9, p=0.169$) but a significant effect for time ($F(1,30)=6.7, p=0.001$) and group $\times$ time ($F(3,64) 2.9, p=0.038$). Finally, there were no significant correlations between change in depressive symptoms and PRISM Compliance (change 0 to 6 weeks: $r=-0.022, p=0.893$; change 0 to 12 weeks: $r=-0.164, p=0.324$; change 0 to 24 weeks; $r=0.203, p=0.223$). There was a significant association between PRISM Compliance and change in YMRS Scores at 12 weeks with greater compliance associated with reduction in YMRS Score ($r=-0.453, p=0.004$) but not at 6 ($r=-0.058, p=0.727$) or 24 weeks ($r=-0.011, p=0.946$).

Satisfaction with the Intervention

In general, participants rated both of the conditions very positively in anonymous self-report feedback questionnaires. None of the comparisons between conditions reached statistical significance. On a 10-point scale (0: very unsatisfied to 10: very satisfied) there was a

median rating of 10 in the PRISM condition and 9 in the paper and pencil condition. Moreover, the median rating in the PRISM condition was 9 and the median rating in the paper-and-pencil condition was 8. In the PRISM condition, the additional ratings about the device were also largely positive, responding to “I would use this device again in the future” and “A device like this could help me” with a median rating of Very Likely (on a 5 point scale from very unlikely to very likely). In terms of adverse effects, participants’ median ratings were “A Little Bit” to the question of “I had difficulty operating the device” and “Not at All” to the question of “The device interfered with my activities” and “I had difficulty interpreting the device”.

DISCUSSION

This is the first randomized controlled trial, to our knowledge, that has augmented brief psychoeducation via a mobile telephone technology targeting mood symptoms in bipolar disorder. Retention was similar to that in other randomized trials of brief psychoeducational interventions for bipolar disorder (Eker and Harkin, 2012; Parikh et al., 2012), and the satisfaction feedback from participants was quite positive in regard to the perceived utility of the mobile device in managing symptoms. Expanding upon to our previous uncontrolled pilot study of PRISM, we found a significant effect on depressive symptom severity, with greater improvement in the brief psychoeducation + PRISM condition compared to those assigned to the brief psychoeducation + pencil-and-paper monitoring condition. The medium effect size found for reduction in depressive symptoms during PRISM treatment is impressive given the relatively strong active control condition and the previously limited effect of brief psychoeducational programs on bipolar depression (Bauer et al., 2006; Simon et al., 2005) when compared to intensive psychotherapies (Miklowitz et al., 2007; Parikh, 2008). No significant impact was found for the secondary outcomes of manic symptom severity and self-reported functional impairment. Although the conditions were not balanced at baseline in depressive symptom severity, sensitivity analyses among those above criterion for clinically significant depressive symptoms at baseline revealed significant condition-by-time effects in favor of the PRISM condition with no significant effect of condition. The study provides evidence that the mobile PRISM intervention was highly feasible, acceptable, and could improve efficacy of brief psychoeducational interventions for depressive symptoms in bipolar disorder.

Our findings add to the growing literature on the promise of mobile health interventions for mental health problems, including several uncontrolled trials in bipolar disorder (Bardram et al., 2013; Depp et al., 2010; Wenzel et al., 2014), schizophrenia (Ben-Zeev et al., 2014; Granholm et al., 2012), and other mental health problems (Mohr et al., 2013). It was notable that depressive symptoms improved during the active phase of PRISM treatment (baseline to 12 weeks) but these benefits were lost during the follow up period (12 weeks to 24 weeks). We speculate that once participants in the PRISM condition returned the mobile phones at week 12 and stopped receiving prompts, the behaviors surrounding monitoring, awareness of symptoms, and implementation of positive coping waned. Conversely, it is possible that participants assigned to the paper-and-pencil condition continued to participate in mood charting on their own, despite not having been instructed to or provided materials with which to do so. If this is the case, mobile interventions designed similarly to PRISM may be

effective in prompting positive coping behavior but not necessarily in inculcating self-initiated symptom recognition and use of coping strategies. This would mean that either this type of mobile intervention should be designed for indefinite use (e.g., as electronic medication reminders are designed) or should more specifically target intervening variables that may create more sustainable changes (e.g., as interventions that target beliefs about medications are designed to do). In either case, optimal design features for mobile health intervention in time-limited versus perpetual interventions for bipolar disorder should be investigated (Morrison et al., 2012), particularly those that promote long-term engagement and sustainability of effects.

There are a number of additional limitations to the study that deserve mention. The level of symptom severity of the participants was on average in the mild range, and participants with a greater severity of symptoms who are more appropriate for more intensive treatments were excluded. As such, there was a truncated range of possible symptom reduction. The sample was comprised of outpatients who were mostly college educated and residing independently, and all were prescribed medications. As such, the generalizability to patients who are inpatients or more severely psychiatrically symptomatic is unknown. There was a greater severity of manic symptoms among patients who dropped out of the study; however, this was not specific to the PRISM condition. This was a small clinical trial that lacked statistical power to detect small effects such as seen on the Young Mania Rating Scale, nor the capacity to examine moderators and mediators of change in symptoms. It would be important to examine factors such as comfort and proficiency with mobile devices and neurocognitive impairment as possible moderators, and change in adaptive self-management behaviors and illness beliefs as mediators. It would also be useful to determine the impact and necessity of personalizing intervention content by the individual, which is common element of effective E-health interventions (Morrison et al., 2012) but does create additional time and effort beyond more static intervention content. In the PRISM intervention, we prompted self-management behaviors and asked patients at a later time about the effectiveness of these strategies, but we were not able to independently ascertain whether these behaviors were actually enacted. There are a variety of passive data collection approaches that utilize embedded sensors in smart phones (e.g., GPS, measures of vocal prosody) that could both aid in the recognition of symptoms and detection of behaviors consistent with prompted self-management activities (Burns et al., 2011; Mohr et al., 2013).

Finally, PRISM represents one of many possible technological applications for extending or augmenting the reach and impact of psychosocial interventions for bipolar disorder. Future directions for mobile technology could be to integrate the information garnered from PRISM and other mobile interventions with clinical care management, the electronic medical record, and patient social networks, which may further facilitate timely action when emergent symptoms or early warning signs are present. Such integration of mobile health approaches with mental health services would require substantial consideration of privacy, risk management, and provider capacity and workflow. Beyond personalization at the outset of interventions, it may be possible to further tailor and shape interventions by online analyses of streams data garnered within patients over time, such as personalized approaches to identify and prevent behavioral emergencies such as emergent suicidal ideation (Thompson et al., 2014). Our findings indicate that evaluating such innovations with randomized

controlled trials that specifically assess sustainability will be critical in evaluating treatment effects.

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CONSORT Diagram

Fig. 1.

Table 1

Baseline Characteristics (n=82)

	Entire Sample	PRISM Condition		Paper-and-Pencil Condition	
		Mean (SD) or %	Mean (SD) or %	Mean (SD) or %	Mean (SD) or %
Age		47.5 (12.8)	46.9(11.8)	48.1 (12.9)	
Sex (% female)		58.5%	53.7%	63.4%	
Ethnicity					
White	69.5%	78.0%		61.1%	
African-American	8.5%	9.8%		7.3%	
Asian	2.4%	2.4%		2.4%	
Latino/Hispanic	14.6%	4.9%		24.4%	
More than one ethnicity	4.9%	4.9%		4.9%	
Education (Years)	14.6 (2.4)	14.9(2.1)		14.3 (2.6)	
Marital Status (% Married)	9.8%	14.6%		4.9%	
Living Situation					
Independent living, in community	88.7%	90.2%		85.3%	
Residential facility	6.4%	4.9%		9.8%	
Homeless	4.9%	4.9%		4.9%	
Bipolar I (vs II)	87.8%	87.8%		87.8%	
Age of First Onset of Mood Symptoms	21.1 (11.0)	21.9 (10.4)		20.4 (11.6)	
Self-Reported Medications Prescribed					
Mood stabilizer	78.0%	75.0%		83%	
Antipsychotic	49.8%	46.3%		51.2%	
Anti-depressant	57.3%	56.1%		58.5%	

Note: The groups did not differ significantly on any characteristic.

Table 2

Outcomes Across the Study Period by Condition

	Baseline (n=82) M (sd)	6 weeks (midpoint) (n=79) M (sd)	12 weeks (post) (n=75) M (sd)	24 weeks (follow up) (n=73) M (sd)	Omnibus Significance Tests for Fixed Effects ¹	Cohen's d for contrasts
MADRS						
Phone	11.7 (9.0)	9.7 (6.8)	8.7 (6.9)	10.0 (8.3)	Condition: F(1,81)=4.5, p=0.036 Time: F(3,164)=1.2, p=0.301 Time × Cond: F(3,164)=2.7, p=0.049	Baseline to 6 weeks: 0.49 Baseline to 12 weeks: 0.49 Baseline to 24 weeks: 0.02
Paper-and-Pencil	7.1 (5.4)	8.8 (7.7)	7.5 (7.5)	5.6 (5.8)		
YMRS						
Phone	7.4 (6.0)	6.3 (4.9)	5.7 (5.8)	6.0 (5.3)	Condition: F(1,81)=2.5, p=0.114 Time: F(3,164)=1.1, p=0.342 Time × Cond: F(3,164)=1.3, p=0.262	Baseline to 6 weeks: 0.31 Baseline to 12 weeks: 0.33 Baseline to 24 weeks: -0.09
Paper-Pencil	4.8 (4.7)	5.8 (5.1)	5.0 (4.2)	4.2(4.1)		
IIS						
Phone	54.2 (20.6)	52.3 (21.6)	48.3 (21.8)	51.3 (23.2)	Condition: F(1,81)=1.5, p=0.229 Time: F(3,164)=1.7, p=0.180 Time × Cond: F(3,164)=0.4, p=0.757	Baseline to 6 weeks: 0.15 Baseline to 12 weeks: 0.18 Baseline to 24 weeks: 0.17
Paper-Pencil	46.4 (20.4)	48.0 (21.8)	43.7 (19.6)	46.7 (21.9)		

Abbreviations: MADRS: Montgomery Asberg Depression Rating Scale; YMRS: Young Mania Rating Scale; IIS: Illness Intrusiveness Scale

¹Mixed model analysis with subjects entered as a random effect