



Research report

A randomized head to head trial of MoodSwings.net.au: An internet based self-help program for bipolar disorder[☆]

Sue Lauder^{a,b,*}, Andrea Chester^c, David Castle^d, Seetal Dodd^{a,e}, Emma Gliddon^{a,e},
Lesley Berk^{a,f}, James Chamberlain^g, Britt Klein^{b,h,i}, Monica Gilbert^g, David W Austin^j,
Michael Berk^{a,e,f,k}

^a The University of Melbourne, Department of Psychiatry, Royal Melbourne Hospital, Level 1 North, Main Block, Victoria 3050, Australia

^b DVC-Research and Innovation Portfolio & School of Health Sciences, and the Collaborative Research Network Federation University, Ballarat, Victoria, Australia

^c RMIT University, Building 6, Level 5 Bowen Street, Melbourne 3000, Australia

^d The University of Melbourne, Department of Psychiatry, St Vincent's Hospital, P.O. Box, 2900, Fitzroy 3065, Australia

^e IMPACT Strategic Research Center, School of Medicine, Deakin University, Barwon Health, P.O. Box 291, Geelong 3220, Australia

^f Orygen Youth Health Research Center, 35 Poplar Road, Parkville 3052, Australia

^g Healthmaps Pty Ltd, PO Box 2501, Fitzroy, 3065 Melbourne, Australia

^h National Institute for Mental Health Research, The Australian National University, Building 63, Canberra 2000, Australia

ⁱ National eTherapy Center, Swinburne University of Technology, Hawthorn, Victoria, Australia

^j Deakin University, School of Psychology, Faculty of Health, Burwood Campus, 221 Burwood Highway, Burwood 3125, Victoria Australia

^k Florey Institute for Neuroscience and Mental Health, The University of Melbourne, Kenneth Myer Building, 30 Royal Parade, 3052 Parkville, Victoria, Australia

ARTICLE INFO

Article history:

Received 26 February 2014

Received in revised form

25 July 2014

Accepted 6 August 2014

Available online 22 September 2014

Keywords:

Bipolar disorder

Psychological

Internet

Online

CBT

Psychoeducation

ABSTRACT

Background: Adjunctive psychosocial interventions are efficacious in bipolar disorder, but their incorporation into routine management plans are often confounded by cost and access constraints. We report here a comparative evaluation of two online programs hosted on a single website (www.moodswings.net.au). A basic version, called MoodSwings (MS), contains psychoeducation material and asynchronous discussion boards; and a more interactive program, MoodSwings Plus (MS-Plus), combined the basic psychoeducation material and discussion boards with elements of Cognitive Behavioral Therapy. These programs were evaluated in a head-to-head study design.

Method: Participants with Bipolar I or II disorder ($n=156$) were randomized to receive either MoodSwings or MoodSwings-Plus. Outcomes included mood symptoms, the occurrence of relapse, functionality, Locus of Control, social support, quality of life and medication adherence.

Results: Participants in both groups showed baseline to endpoint reductions in mood symptoms and improvements in functionality, quality of life and medication adherence. The MoodSwings-Plus group showed a greater number of within-group changes on symptoms and functioning in depression and mania, quality of life and social support, across both poles of the illness. MoodSwings-Plus was superior to MoodSwings in improvement on symptoms of mania scores at 12 months ($p=0.02$) but not on the incidence of recurrence.

Limitations: The study did not have an attention control group and therefore could not demonstrate efficacy of the two active arms. There was notable (81%) attrition by 12 months from baseline.

Conclusion: This study suggests that both CBT and psychoeducation delivered online may have utility in the management of bipolar disorder. They are feasible, readily accepted, and associated with improvement.

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1. Background

In the treatment of bipolar disorder (BD), adjunctive psychosocial approaches (Lauder et al., 2010) have shown utility in terms of improvements in medication adherence (Colom et al., 2009); prevention and delay of relapse (Colom et al., 2003; Castle et al., 2010) and enhanced social and occupation functioning and

[☆]Clinical Trial Registration: Australian New Zealand Clinical Trials Registry (ANZCTR) Number 12607000118404.

* Correspondence to: Barwon Health, Department of Psychiatry, University of Melbourne, Swanston Center, PO Box 281, Geelong, Victoria 3220, Australia. Tel.: +61 3 5226 7450; fax: +61 3 5246 5165.

E-mail address: suela@barwonhealth.org.au (S. Lauder).

improved quality of life (Miklowitz, 2008). There is a strong evidence base for adjunctive psychosocial interventions in bipolar disorder (Reinares et al., 2014). Predominant approaches include Psychoeducation (PE); Cognitive Behavioral Therapy (CBT), Interpersonal Social Rhythm Therapy (IPSRT) and Family Focused Therapy (FFT). There are shared elements between these approaches, including education about the illness, collaborative relationships, plans to minimize relapse and development of a personal understanding of the illness including self monitoring (Lauder et al., 2010). How these approaches apply these elements, and the degree to which they do it is a differentiating factor (Reinares et al., 2014). Scott et al. (2007) meta-analysis of 9 RCT's with at least a 6 month follow up period noted that they reduced relapse by around 40% in a comparison with treatment as usual. Face-to-face psychosocial interventions are, however, limited in their reach and access. In contrast, web-based approaches offer potential advantages.

There are a small number of online studies that explore the benefits of online modality for psychosocial programs in bipolar disorder. These include Beating Bipolar (Smith et al., 2011), Recovery Road Bipolar (Barnes et al., 2007), Living with Bipolar (Todd et al., 2012), and Bipolar Education Program (BEP) (Proudfoot et al., 2012). Results for 2 of these trials have been published to date. On the quality of life, psychological subscale Smith et al. (2011) found a moderate effect size between treatment and control group, with findings bordering on statistical significance. This finding however, as noted by the authors, did not account for multiple comparisons. Proudfoot et al. (2012) compared a psychoeducation with and without peer supports with an attention control, for those newly (within past 12 months) diagnosed with bipolar disorder. While results failed to find significant between group differences, significant within group changes on perceived control, stigma, and symptoms of depression and anxiety were found. The results in this emerging work are encouraging, and the diversity of approaches between these studies provides much scope for future work.

A 12 week, clinician facilitated, face-to-face group based intervention for bipolar disorder that includes both psychoeducational and Cognitive Behavioral Therapy (CBT) based approaches was previously developed and evaluated by our group (MAPS: Castle et al., 2010; Lauder et al., 2012). We adapted the MAPS program to an online modality. This paper details the evaluation of two versions of this web based adaption, known as MoodSwings.

The MoodSwings online platform (<http://www.moodswings.net.au>) hosts two versions of the MoodSwings program. One is a text-based psychoeducation program that we refer to simply as MoodSwings (MS). The other version is identical to MS, but with the addition of online interactive Cognitive Behavioral Therapy (CBT) based tools. We refer to this version as MoodSwings-Plus (MS-Plus). The additional tools in MS-Plus provides an opportunity to operationalize some of the content, and include a mood monitoring tool, thought recording, and goal setting/regulation activity. There are no specific homework tasks and responses to the MS-Plus tools that were not monitored. It is estimated that each module would take 30–40 min to complete, with additional time for the MS-Plus activities. Both MS and MS-Plus include small-group discussion forums. A detailed description of the MoodSwings programs and the interactive tools can be found elsewhere (Lauder et al., 2012).

The comparison of two active treatment arms has advantages and limitations compared to other study designs. It has the advantage of study blinding and randomization, not achievable with study designs using waiting list or treatment-as-usual comparators. It also obviates the reduced expectancies of no-treatment control noted by Saks et al. (2002). In addition Kiluk et al. (2011) in their seminal paper on developing standards for online clinical

trials; were critical of the use of inactive control comparators, such as wait lists, which they note tend to result in exaggerated positive outcomes. The limitation in the use of an active comparator is the inability to determine efficacy of the program as an adjunctive bipolar treatment; however, this was not the aim of this study.

Our primary aims were to investigate the comparative efficacy of MS and MS-Plus in amelioration of mood symptomology and recurrence in people with bipolar disorder. The secondary aims were to establish the impact on functionality, Locus of Control, social support, medication adherence and quality of life.

It was hypothesized that, whilst both MS and MS-Plus would be associated with a reduction in mood symptoms, the effect would be significantly greater for the MS-Plus group. Further, we hypothesized that there would be improved levels of mood symptom severity, functionality, improved quality of life, reduced external chance-based Locus of Control, greater levels of social support and enhanced medication adherence, and reduction in the occurrence of mood episodes at the 3 months, 6 months and 12 months follow ups for the MS-Plus group relative to MS.

2. Methods

Persons aged 18–65 years with a diagnosis of bipolar disorder type I or II, confirmed using DSM-IV-TR (American Psychiatric Association, 2000) criteria via telephone clinical interview, were included. Participants needed access to an internet-enabled computer. The ability to register for the program successfully indicated a level of reading competence; in addition, potential participants were asked whether they had read and understood the plain language statement, and whether they had any queries about it. Exclusion criteria, evaluated via clinical interview, were the presence of any developmental disability or amnesic syndrome that might preclude full participation in the program. Consistent with other internet programs (Christensen et al., 2006) informed consent prior to study commencement was performed online.

Recruitment was through clinician referral, advertising and publicity via conferences and consumer and professional forums as well as online optimization strategies for the MoodSwings search term. Participants were randomly allocated to either MS or MS-Plus. The randomization was block simultaneous, with a block size of 12 (6MS, 6MS-Plus). The block design was utilized to accommodate small groups on asynchronous online group discussion boards. Allocation tables were pre-generated by the study statistician using the Stata random number generator with seeds from a PERL script random number generator. Allocation tables were concealed using encryption (TrueCrypt, www.truecrypt.org). Ethics approval was received from the Barwon Health Human and Research and Ethics Committee (Project number 06/108) and was conducted in accordance with the Helsinki Declaration as revised in 1989.

3. Outcome measures

Outcome measures were chosen to assess change in a wide variety of characteristics of bipolar illness. Measures had to be deliverable by an online format.

The Altman Self-Rating Mania Scale (Altman et al., 1997) is a 5 item scale on which manic symptoms for the previous week are rated from 0 to 4, with higher scores indicating greater symptom severity. At a cut-off score of ≥ 6 the scale has a sensitivity of 85% in being able to detect the presence of moderate manic symptoms and a specificity to identify mild or no symptoms of 87.3% (Altman et al., 2001).

The Montgomery-Asberg Depression Rating Scale Self-Assessment (Svanborg and Asberg, 1994), is a 9 item self-rated version of the

Montgomery Asberg Depression Rating Scale (Montgomery and Asberg, 1979). It has high concordance with the clinician rated MADRS ($r=0.83-0.93$) and has satisfactory internal consistency (Cronbach alpha 0.86) and construct validity. Higher scores indicate greater depressive symptomatology (Svanborg and Ekselius, 2003).

Relapse: relapse was assessed in two ways: firstly, via self-report questions at the conclusion of the 10 week intervention and at 3, 6 and 12 month boosters; and secondly, by a telephone-administered Structured Clinical Interview (SCID) (First et al., 2002) post-treatment and at 6 and 12 month follow up. The SCID assessor was appropriately trained and qualified and blinded to group allocation. Additional consent was necessary for the SCID interviews and was obtained from 30 participants.

Social support: the Medical Outcomes Study Social Support Survey (MOS-SSS) (Sherbourne and Stewart, 1991) is an 18-item scale specifically designed for people with chronic conditions. It encompasses 4 subscales targeting specific dimensions of perceived availability of social support. The MOS has reported acceptable reliability (alpha > 0.91) and construct validity (Sherbourne and Stewart, 1991).

Locus of Control: the Levenson's Internal, Powerful Others and Chance Locus of Control scale has three dimensions. "Internal control" measures the extent to which a person believes they have control over their own life. "Powerful others" and "chance" dimensions measure two different aspects of externality (Levenson, 1981). The scale has moderately high reliability and demonstrates convergent and discriminant validity with other scales (Levenson, 1981).

Medication adherence: the Medication Adherence Rating Scale (Thompson et al., 2000), is a 10-item scale which has acceptable reliability (Cronbach's alpha 0.75), test re-test reliability (0.72) and concordance with other measures of medication adherence (Thompson et al., 2000).

Exploratory Global Assessment Measures: based on the work of Zimmerman et al. (2006) we employed five Exploratory Global Assessment Measures. These single item ordinal scales rating questions from 0 to 4, with higher scores indicating more difficulties, were designed to explore key outcomes in a manner that is psychometrically sound, but without placing undue burden on participants. All use a time frame of 1 week.

Global measure of Severity of Depression (GSEVDEP): The GSEVDEP measures overall severity of depressive symptoms and is significantly correlated with clinician-rated Clinical Global Impressions scale for Severity of illness severity ($r = 0.64$, $p < 0.001$) (Zimmerman et al., 2006).

Global measure of Severity of Mania GSEVMANIA: This was developed from the GSEVDEP by the current researchers as an exploratory global measure of mania.

Global Measure of Psychosocial Functioning (GPF): Depression. The GPF measures the impact of depression on psychosocial functioning. It is significantly correlated with the clinician-rated Global Assessment of Functioning (GAF) across all areas of functioning, ($r = -0.41$, $p < 0.001$) (Zimmerman et al., 2006).

Global Measure of Psychosocial Functioning (GPF): Mania. This was developed from the GPF: depression scale by the current researchers as an exploratory measure of the impact of mania/hypomania on psychosocial functioning.

Global measure of Quality of Life (GQOL): the GQOL scale has significant correlations with specific quality of life domains of work, relationships, leisure and health (Zimmerman et al., 2006).

4. Procedure

Apart from relapse, all measures were administered at baseline, post-intervention (3 months) and at 6 and 12 month follow up. Questions regarding relapse and medication change were included

at the end of the core content modules and at 3, 6 and 12 months. To reduce questionnaire burden, baseline questionnaires were staggered across the first three modules. These staggered questionnaires were administered prior to any content related to the assessment. Measures were administered online with data automatically exported into a.csv file and converted to SPSS and Stata format.

4.1. Intervention

4.1.1. MoodSwings Program (MS)

MoodSwings was adapted for online delivery from the validated MAPS face to face group program for bipolar disorder (Castle et al., 2010). The MAPS program integrates effective coping strategies from existing psychosocial approaches in four areas: monitoring mood and activities (M); assessing prodromes (A); preventing relapse (P); and setting Specific, Measurable, Achievable, Realistic, Time-framed (SMART) goals (S); hence the acronym MAPS. The MAPS content provided the basis for the five online core psychoeducation modules (the active treatment component). In the same way the MAPS post-program booster sessions were used to structure the MS and MS-Plus booster sessions. The online core modules were spaced at 2-weekly intervals. The three booster modules were administered following the 3, 6 and 12 month assessments and were designed to encourage completion of the follow up assessments.

4.1.2. MoodSwings Plus Program (MS-Plus)

The MS-Plus program included the core MS psychoeducation modules, but with additional CBT-based interactive elements. These included tools to support mood and medication monitoring, development of a life chart, cognitive strategies such as thought monitoring, use of simple motivational interviewing techniques, self-reflection, problem solving, identification of personal triggers and a preventing relapse plan. Details of the program can be found in Lauder et al. (2012). Fig. 1 contains details of the components of the MoodSwings program.

4.1.3. Moderated discussion board

Both MS and MS-Plus arms included small group ($n=6$) moderated asynchronous discussion boards for participants to communicate and share experiences. The moderator was a registered psychologist and one of the researchers involved in the project (SL), who received automated email notification of participant posts and ensured they were not offensive or distressing, prior to posting on the discussion board. This is consistent with general discussion group etiquette and guidelines noted on the site. There was no formal moderator presence on the discussion boards; communication was between participants only. The randomization process allocated participants in block groups such that each group had its own discussion board of six people in the same study arm.

4.2. Statistical analyses

Primary analyses were undertaken by a statistician using mixed-model repeated measures (MMRM) (Mackinnon et al., 2008) using Stata 11.2 (StataCorp, 2009). For each outcome measure (apart from relapse), both within group change relative to baseline and between group difference in changes from baseline were examined. For all of the study outcomes apart from relapse, two analyses were undertaken for each measure: (i) a simplified model with pooled 3, 6 and 12 month data using a time variable coded as 0=baseline, 1=post baseline; and (ii) individual time point analysis. Analysis (i) looks at the average behavior over the

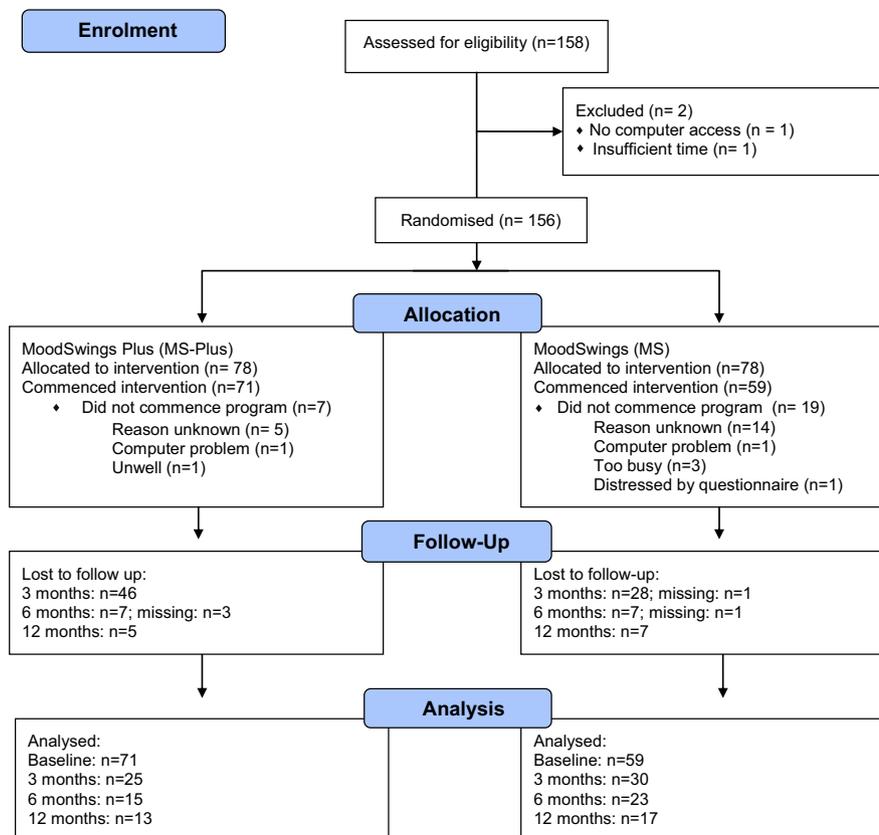


Fig. 1. Consort flowchart of study participants at each stage of the study.

follow-up period whereas analysis (ii) gives detailed results on individual time points.

Explanatory variables for all study outcome measures were treatment arm, time and time \times treatment arm. Both between group and within group effects could be assessed in each MMRM model by testing appropriate coefficients or combinations of coefficients. For the between group analyses, the coefficient of the time point \times treatment interaction was tested to examine the difference in change from baseline. For the within group analyses, the change from baseline was tested for the MS arm using the coefficient of the time point indicator; and for the MS-Plus arm using the coefficient of the time point indicator added to the treatment \times time point interaction. The within group analyses were relevant in this study because both arms were active. The analyses were available case i.e. all available data were used in the analyses, including data from participants who dropped out at one of the later time points.

The continuous mood scales (ASRM, MADRS) were analyzed using multilevel mixed effects linear regression using a MMRM model as detailed above. The continuous scale measures, MOS-SSS, Levenson Locus of Control and MARS were treated in the same way as the ASRM and MADRS scales noted above. Bipolar relapse data were analyzed using multilevel mixed effects logistic regression.

Ordinal data (GSEVDEP, GSEV MANIA, GPF Depression, GPF Mania, GQOL) were analyzed initially using ordinal logistic regression. Where the proportional odds assumption applied, generalized linear latent and mixed models were used. If the proportional odds assumption was not valid, then generalized ordinal logistic regression was used (Williams, 2006).

The results for the ordinal measures are reported using the odds ratio of being in a higher category, with higher categories indicating worse outcomes. In this analysis, an odds ratio less than 1.00 indicates a positive finding.

The continuous scales are reported as a between group difference in change from baseline and a within group change from baseline, using an effect size (d) relative to the standard deviation at baseline. A positive effect size is a positive finding. Two-tailed tests were used for all z -tests.

Relapse, which was coded as 0 (no relapse) or 1 (relapse) according to whether the participant had experienced a relapse in the previous time period, had no baseline reference point. Consequently, for relapse, the two arms were compared at the end of the core modules and at 3, 6 and 12 months, using multilevel mixed effects logistic regression to give odds ratios at each time point, where an odds ratio less than 1.00 indicates a positive result for MoodSwings-Plus.

5. Results

A total of 273 people registered their interest in participating in this trial. Of these, 158 agreed to be contacted by the researchers, and were screened by telephone: two were unsuitable, one due to lack of access to a computer, the other due to lack of time. The remaining 156 participants were randomized and received password protected secure access to their allocated program. Participants randomized to the MS group were not aware of the specifics regarding the extra program content available in the MS-Plus group, just that there were two versions of the program and one had more detail. All participants had access to the full MS-Plus program at the conclusion of the study. Participant flows are shown in Fig. 1. Both MS and MS-Plus contain five core modules as the active therapeutic content. A combined total of 48% of participants completed all five modules, which compares favorably to other online interventions (Eysenbach, 2005). A total of 86.2% of the participants completed at least two modules, and 75.4%

completed at least three modules. The follow-up and analysis numbers shown in Fig. 2 are based on the MADRS. Both intervention and follow-up assessments were administered via the website. The follow up phase was assessing changes over time, and did not involve active program elements. Failure to complete the online assessments implied loss to follow-up. With baseline spread over the first part of the intervention, different measures were affected differently by attrition.

5.1. Participants

Demographic and illness characteristics of participants are shown in Table 1; no statistically significant differences were observed between the two groups. Just over half the participants (52%; n= 67) had bipolar I disorder; the rest had bipolar II disorder. The majority (95%) were taking medication for bipolar disorder; the mean number of medications was 2.4 and only 21% were receiving monotherapy.

The significant pooled analysis results, examining the average change relative to baseline over data collected at 3, 6 and 12 months are reported in the text. All the individual time point between group comparison analyses as well as relevant means and

standard deviations are shown in Table 2. Table 3 reports the individual time point within group analyses.

5.2. Between group analyses (Table 2)

5.2.1. Relapse

There were no significant differences in the rate of occurrence of mania or depression between the two groups.

5.2.2. Symptomatic measures

A significant between group result for symptoms of mania scores on the ASRM was noted at 12 months, with lower scores for the MS-Plus group. The results for the ASRM are illustrated in Fig. 2, showing there was little change in the mean for the MR group, but scores for the MS-Plus group increased at 6 months (with no significant difference in change) and then decreased at the 12-month endpoint. We considered the possibility that the decrease at 12 months was due to selection bias, with the participants with higher scores at 6 months dropping out at 12 months. However, the three participants with ASRM scores 12 or higher at 6 months (two in MS-Plus and one in the MS arm), all remained in the study. All three were no longer manic at 12 months, with their ASRM scores equal to 1 or 0. In addition, investigating whether ASRM scores at the previous time point predicted dropout at the next time point using logistic regression gave null results. In particular, for ASRM at 6 months predicting dropout at 12 months gave the following odds ratios: for MS 0.97, (p=0.8, z= -0.24); and for MS-Plus, 1.06 (p=0.7, z=0.41). There were no between group differences on depressive symptoms as measured by the MADRS-S Fig. 3.

5.3. Within group analysis (Table 3)

Significant reductions in level of mood symptoms were found for the within group analyses for both depression scores on the MADRS-S and mania scores on the ASRM. On the MADRS-S there was a significant within-group effect for both MoodSwings Plus and MS at six months. Based on the pooled analyses, the MADRS-S showed a significant (p=0.03) reduction in scores for MS (z= -2.17, effect size 0.37, 95% CI 0.04 to 0.70). These within group results reflect improvement in both arms relative to baseline and are therefore consistent with the null result for the between group results on the MADRS-S which are based on the

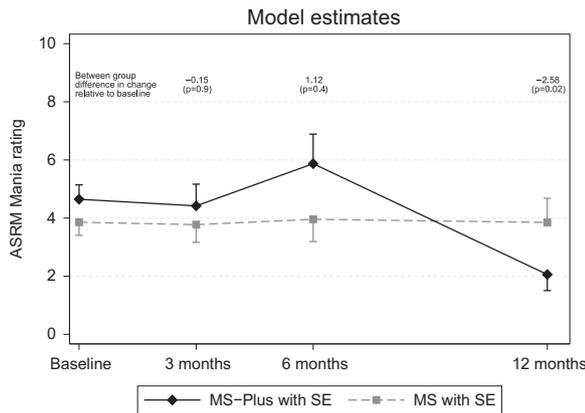


Fig. 2. Model estimates of the mean profile for mania (ASRM), with error bars showing the standard error (SE) of each estimate. For clarity, the error bars are unidirectional. The between group difference in change relative to baseline, used to determine significance, is tabulated above the line plots. The difference in change relative to baseline is significant at 12 months, with the MS-Plus arm showing greater improvement (reduction) in mania scores.

Table 1 Baseline demographic and self reported clinical characteristics of Bipolar Disorder Patients Randomly Assigned to MoodSwings-Plus or MoodSwings.

Variable	MoodSwings-Plus (N= 71)		MoodSwings (N=59)		Comparison: Fisher's exact test P
	N	%	N	%	
Female	52	73	45	76	0.8
Australian	45	63	37	63	1.0
Rural area	19	27	13	22	0.5
Bachelor degree or higher	42	59	38	64	0.6
Married/defacto relationship	41	58	29	49	0.5
Living with family/friends	54	76	43	73	0.7
Work/study	46	65	40	68	0.9
Bipolar I	35	49	32	54	0.6
Bipolar II	36	51	27	46	
Not receiving pharmacological treatment	3	4	3	5	1.0
Previous psychological counseling	44	62	45	76	0.1
Age (years)	Mean 39.87	SD 11.26	Mean 41.35	SD 9.85	t-test: t ₁₂₆ =0.78, p=0.4
	Median	IQR	Median	IQR	Mann-Whitney
Number of episodes in last 5 years	8	4–15.75	5	3–8	z= -1.96, p=0.05

Table 2
Between-Group Analysis on Self-Report Ratings at 3, 6 and 12 months for Bipolar Disorder Patients Randomly Assigned to MoodSwings-Plus or MoodSwings Condition.

	Score										
	Patients Assigned to MoodSwings-Plus			Patients Assigned to MoodSwings			Between group comparison				
	n	Mean	SD	n	Mean	SD	z	p	d	OR	95% CI (d or OR)
Relapse (0=no relapse, 1=relapse in previous period)											
End of core modules (10 weeks)	27	0.33	0.48	33	0.36	0.49	-0.13	0.9		0.90	0.21 to 3.91
3 month	24	0.25	0.44	29	0.31	0.47	-0.55	0.6		0.63	0.12 to 3.23
6 month	16	0.38	0.50	24	0.21	0.41	0.86	0.4		2.29	0.35 to 15.04
12 month	12	0.33	0.49	17	0.12	0.33	1.22	0.2		4.44	0.41 to 48.48
Montgomery Asberg Depression Rating Scale – Self Assessment											
Baseline	71	9.62	4.83	59	9.91	5.59					
3 month	25	8.58	4.87	30	8.38	5.86	0.71	0.5	-0.18		-0.66 to 0.31
6 month	15	7.03	5.48	23	8.22	5.50	-0.72	0.5	0.18		-0.31 to 0.66
12 month	13	8.00	5.75	17	7.00	6.54	0.40	0.7	-0.15		-0.87 to 0.57
Altman Self-Rating Mania Scale											
Baseline	71	4.65	4.19	58	3.84	3.46					
3 month	25	4.20	3.86	30	3.87	3.32	-0.13	0.9	0.04		-0.52 to 0.60
6 month	15	6.00	4.16	23	4.13	3.65	0.83	0.4	-0.29		-0.97 to 0.39
12 month	13	1.77	1.92	17	4.0	3.59	-2.27	0.02*	0.66		0.09 to 1.24
Medical Outcomes Study Social Support Survey Instrument											
Baseline	59	59.14	16.86	53	56.42	15.00					
3 month	25	62.28	18.95	30	54.20	17.37	0.82	0.4	0.20		-0.28 to 0.68
6 month	15	65.61	19.48	23	57.44	18.17	1.27	0.2	0.37		-0.20 to 0.93
12 month	13	58.80	16.81	17	61.02	17.11	-0.34	0.7	-0.09		-0.63 to 0.44
Medication Adherence Rating Scale											
Baseline	48	6.79	2.06	50	6.36	2.78					
3 month	25	7.28	2.13	30	7.10	2.28	-1.15	0.3	-0.21		-0.58 to 0.15
6 month	14	7.93	1.54	22	6.82	2.54	0.09	> 0.9	0.02		-0.41 to 0.44
12 month	13	8.15	1.52	17	7.53	2.10	0.04	> 0.9	0.01		-0.44 to 0.45
Locus of Control Chance Subscale											
Baseline	65	21.05	10.09	55	19.15	10.64					
3 month	24	18.75	9.77	28	18.14	11.71	0.22	0.8	-0.04		-0.39 to 0.31
6 month	15	18.00	7.08	23	18.74	10.73	0.26	0.8	-0.06		-0.52 to 0.40
12 month	13	20.77	7.68	17	19.12	9.16	-0.02	> 0.9	0.00		-0.38 to 0.39
Global Measure of Quality of Life											
Baseline	59	1.97	0.87	53	1.92	0.96					
3 month	25	1.52	0.92	30	1.60	0.89	-0.13	0.9		0.91	0.21 to 3.96
6 month	15	1.33	0.98	23	1.65	0.93	-0.68	0.5		0.55	0.10 to 3.09
12 month	13	1.92	0.86	17	1.41	1.06	1.67	0.09		5.30	0.75 to 37.44
Global Measure of Psychosocial Functioning Depression											
Baseline	59	1.75	1.28	53	1.72	1.29					
3 month	25	1.20	1.12	30	1.30	1.12	-0.53	0.6		0.70	0.19 to 2.63
6 month	15	0.67	0.98	23	1.17	1.27	-1.72	0.09		0.22	0.04 to 1.23
12 month	13	1.15	1.46	17	1.06	1.14	-0.49	0.6		0.64	0.10 to 3.91
Global Measure of Psychosocial Functioning Mania/Hypomania											
Baseline	59	0.86	1.01	53	1.02	1.17					
3 month	25	0.32	0.69	30	0.67	0.76	-1.69	0.09		0.26	0.05 to 1.24
6 month	15	0.67	0.90	23	0.91	1.04	-0.61	0.5		0.59	0.11 to 3.14
12 month	13	0.54	0.88	17	0.29	0.59	0.54	0.6		1.73	0.23 to 13.01
Global Measure of Severity of Depression											
Baseline	71	1.99	1.10	59	1.90	1.17					
3 month	25	1.56	1.16	30	1.60	1.07	-1.00	0.3		0.49	0.12 to 1.99
6 month	15	0.87	1.06	23	1.35	1.23	-1.18	0.2		0.36	0.07 to 1.96
12 month	13	1.54	1.45	17	1.35	1.32	0.42	0.7		1.50	0.23 to 9.72
Global Measure of Severity of Mania/Hypomania											
Baseline	71	1.03	1.04	59	1.22	1.07					
3 month	25	0.92	0.95	30	1.00	0.95	0.56	0.6		1.34	0.48 to 3.74
6 month	15	1.40	0.99	23	1.35	1.07	1.25	0.2		2.26	0.63 to 8.11
12 month	13	0.69	0.85	17	0.53	0.87	1.10	0.3		2.48	0.49 to 12.60

* $p < 0.05$.

difference in change relative to baseline. On the ASRM, a significant within-group effect at 12 months for MS-Plus was observed.

5.3.1. Social support, medication adherence and quality of life

5.3.1.1. Between Group Analyses (Table 2): No significant between-group differences were found for the secondary outcomes social support, medication adherence and quality of life.

5.3.1.2. Within-group analyses (Table 3). Social support: a significant improvement in the MS-Plus group was found at six months for the total score on the MOS-SSS scale. In addition, the emotional support subscale improved significantly within the MS-Plus group at six months ($p=0.02$, $z=2.29$, effect size 0.49, 95% CI 0.07 to 0.91). Similar changes were not seen in the MS group.

Table 3

Within-group analysis improvement on primary and secondary outcomes relative to baseline on Clinical Self-Report Ratings at 3, 6 and 12 months for Bipolar Disorder Patients Randomly Assigned to MoodSwings-Plus or MoodSwings condition.

	MoodSwings Plus					MoodSwings				
	z	p	d	OR	95% CI	z	p	d	OR	95% CI
Montgomery Asberg Depression Rating Scale – Self Assessment										
3 month	-0.81	0.4	0.15		-0.21 to 0.50	-1.95	0.05	0.32		0.00 to 0.65
6 month	-2.80	0.005**	0.51		0.15 to 0.87	-2.00	0.045*	0.33		0.01 to 0.66
12 month	-1.72	0.09	0.36		-0.05 to 0.77	-1.68	0.09	0.51		-0.09 to 1.10
Altman Self-Rating Mania Scale										
3 month	-0.29	0.8	0.06		-0.35 to 0.46	-0.11	> 0.9	0.02		-0.37 to 0.41
6 month	1.13	0.3	-0.31		-0.86 to 0.23	0.12	> 0.9	-0.03		-0.45 to 0.40
12 month	-3.96	< 0.001***	0.67		0.34 to 1.00	-0.01	> 0.9	0.00		-0.47 to 0.47
Medical Outcomes Study Social Support Survey Instrument										
3 month	0.45	0.7	0.08		-0.25 to 0.41	-0.70	0.5	-0.12		-0.47 to 0.22
6 month	2.14	0.03*	0.44		0.04 to 0.85	0.39	0.7	0.08		-0.31 to 0.47
12 month	0.51	0.6	0.10		-0.28 to 0.48	1.01	0.3	0.19		-0.18 to 0.56
Medication Adherence Rating Scale										
3 month	0.95	0.3	0.13		-0.13 to 0.39	2.66	0.008**	0.34		0.09 to 0.59
6 month	1.84	0.07	0.30		-0.02 to 0.61	1.87	0.06	0.28		-0.01 to 0.57
12 month	2.37	0.02*	0.43		0.07 to 0.78	2.97	0.003*	0.42		0.14 to 0.69
Locus of Control Chance Subscale										
3 month	-0.79	0.4	0.09		-0.14 to 0.33	-0.95	0.3	0.13		-0.14 to 0.41
6 month	-1.01	0.3	0.15		-0.14 to 0.44	-1.11	0.3	0.21		-0.16 to 0.59
12 month	-0.44	0.7	0.07		-0.24 to 0.39	-0.59	0.6	0.07		-0.16 to 0.29
Global Measure of Quality of Life										
3 month	-2.03	0.04*		0.33	0.11 to 0.96	-1.92	0.06		0.36	0.13 to 1.02
6 month	-1.98	0.048*		0.26	0.07 to 0.99	-1.27	0.2		0.48	0.15 to 1.49
12 month	-0.58	0.6		0.68	0.18 to 2.51	-2.73	0.006**		0.13	0.03 to 0.56
Global Measure of Psychosocial Functioning Depression										
3 month	-1.73	0.08		0.43	0.16 to 1.12	-1.07	0.3		0.61	0.24 to 1.51
6 month	-3.41	< 0.001***		0.09	0.02 to 0.36	-1.73	0.08		0.40	0.14 to 1.13
12 month	-2.00	0.046**		0.23	0.05 to 0.97	-1.77	0.08		0.36	0.12 to 1.12
Global Measure of Psychosocial Functioning Mania/Hypomania										
3 month	-2.99	0.003**		0.15	0.04 to 0.52	-1.16	0.2		0.56	0.22 to 1.48
6 month	-1.16	0.2		0.46	0.13 to 1.70	-0.46	0.6		0.78	0.27 to 2.24
12 month	-1.96	0.050*		0.23	0.05 to 1.00	-2.70	0.007**		0.13	0.03 to 0.57
Global Measure of Severity of Depression										
3 month	-1.73	0.08		0.40	0.14 to 1.13	-0.40	0.7		0.82	0.32 to 2.14
6 month	-2.83	0.005**		0.15	0.04 to 0.56	-1.65	0.10		0.41	0.14 to 1.18
12 month	-0.71	0.5		0.60	0.15 to 2.45	-1.43	0.15		0.40	0.12 to 1.40
Global Measure of Severity of Mania/Hypomania										
3 month	-0.30	0.8		0.89	0.42 to 1.89	-1.13	0.3		0.67	0.33 to 1.35
6 month	1.68	0.09		2.43	0.86 to 6.85	0.20	0.8		1.08	0.51 to 2.29
12 month	-0.83	0.4		0.59	0.17 to 2.05	-2.72	0.007**		0.24	0.08 to 0.67

* $p < 0.05$.
 ** $p < 0.01$.
 *** $p < 0.001$.

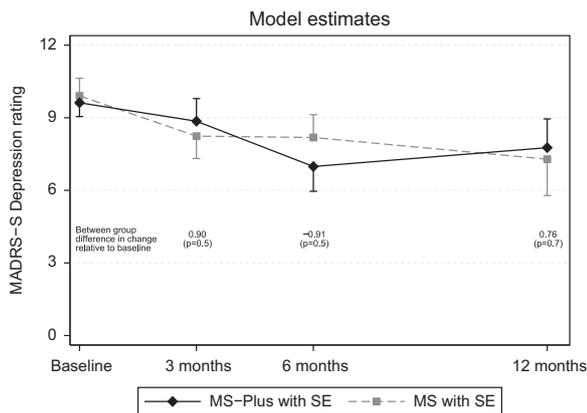


Fig. 3. Model estimates of the mean profile for depression (MADRS-S), with error bars showing the standard error (SE) of each estimate. For clarity, the error bars are unidirectional. The between group difference in change relative to baseline, used to determine significance, is tabulated below the line plots. While the between group differences are not significant, the within group improvement relative to baseline is significant for both MS at 6 months ($p=0.045$, change -1.72) and for MS-Plus at 6 months ($p=0.005$, change -2.64).

Medication adherence: there were significant improvements on medication adherence for the MS group at 3 months. A significant improvement for both MS-Plus and MS was observed at 12 months. For the pooled analyses there were significant improvements for the MS group ($p=0.001$, $z=3.21$, effect size 0.34, 95% CI 0.13 to 0.54) and a significant improvement ($p=0.046$) in the MS-Plus group ($z=1.99$, effect size 0.23, 95% CI 0.00 to 0.47).

Quality of life: there was a significant within-group improvement in QOL for both MS-Plus and MS, notably at three months and six months for the MS-Plus group and at 12 months for the MS group. There was also a trend to significance for the MS group at 3 months. The pooled analyses showed significant within group improvements for both MS-Plus ($p=0.02$, $z=-2.42$, odds ratio 0.37, 95% CI 0.17 to 0.83) and MS ($p=0.01$, $z=-2.44$, odds ratio 0.39, 95% CI 0.19 to 0.83).

5.3.1.3. Exploratory Global Assessment Measures. Functionality: significantly improved levels of functionality on the GPF depression scale were found for the MS-Plus group at 6 months and 12 months. For the pooled analyses there was a significant

positive within-group result for the MS-Plus group ($p=0.003$, $z=-2.99$, odds ratio 0.29, 95% CI 0.13 to 0.65) and for MS ($p=0.03$, $z=-2.19$, odds ratio 0.44, 95% CI 0.21 to 0.92). The odds ratios show that the MS-Plus group had greater improvement although the difference between the two groups was not significant.

On the GSEV depression item there was significant improvement within the MS-Plus arm at 6 months but a non-significant change for the MS arm. In the pooled analyses a significant positive within-group result for MS-Plus was observed ($p=0.01$, $z=-2.47$, odds ratio 0.34, 95% CI 0.14 to 0.80). For GPF Mania, the pooled analysis gave a significant within group improvement in the MS-Plus participants ($p=0.007$, $z=-2.71$, odds ratio 0.28, 95% CI 0.11 to 0.71), but not for the MS group. The between group difference in change from baseline for the ASRM-S mania scale at 12 months showed significantly greater improvement for MS-Plus, but on the GSEV Mania there was a significant within group improvement for MS at 12 months, and a non significant change for MS-Plus at 12 months. The results of the exploratory single item measure GSEV Mania were inconsistent with the ASRM-S results both at single time points and in the pooled analysis. Correlation analysis of these 2 scales was low at 0.50 and suggests the GSEV Mania lacked construct validity.

6. Discussion

This study compared two online interventions for bipolar disorder, one containing basic psychoeducation and asynchronous discussion boards and the other having these same elements with the addition of interactive CBT based tools. The components of both MS and MS-Plus contained the common shared elements found in face-to-face programs noted earlier. The primary hypothesis, that the MS-Plus group would show greater reductions in relapse rates to both depression and mania was not supported by these data. The hypothesis that the MS-Plus group would show more reduction in mood symptomatology and severity of illness episode in comparison to the MS group, was partially supported by this study. On the ASRM scale, MS-Plus showed superiority over MS, with separation between the two groups at 12 months. While both groups showed improvements in medication adherence, the improvement in elevated mood for the MS-Plus condition suggests these improvements are not fully explained by enhanced medication adherence. Given the provenance of CBT in the treatment of depression (Lam et al., 2003), it is noteworthy that no separation between the groups on the MADRS-S, a primary outcome measure, was found. Within-group analyses showed a significant reduction in depressive symptom for both MS-Plus and MS groups at 6 months. Pooled results on the MADRS-S were also significant for the MS group. Reductions in symptom severity (GSEV Depression) were found for the MS-Plus group on pooled data analysis, and at the 6 months time point. This suggests that participants may benefit from both interventions, as both were 'active', although placebo effects cannot be excluded due to the lack of an attentional control group. More within group changes were, however, noted in the MS-Plus group on symptomatology measures (both for depressed and elevated mood), quality of life and social support. The lack of validity in the GSEV (mania) is perhaps not surprising, given it asks directly about the severity of impact of elevated mood symptoms. Self assessment of such impact is likely to be distorted when mood is elevated.

Greater statistical power may have detected additional separation between the two groups and the current findings are quietly encouraging that the addition of the CBT based interactive tools in the MS-Plus group does provide some further improvements on outcomes. A larger sample size may have been able to detect

additional between-group differences, and the study was under-powered particularly with regards to relapse.

Interpretation of any study is contingent on the methodological characteristics. In this regard, a recent paper by Kiluk et al. (2011) suggested 14 quality criteria for internet studies, and reported that only 3 out of 75 published studies of psychiatric disorders met at least 13 of these criteria. Our study met 10 of the stated quality standards; having a balanced randomization procedure, blind outcome assessments, appropriate statistical analysis, standard diagnostic criteria and specified inclusion and exclusion criteria, basis on a validated manualised face-to-face therapy, objective measures of adherence, equivalence of exposure across conditions and credible measures. The criterion not met was replication in an independent study sample, follow-up assessment on > 80% of the ITT sample and substantive power. For both groups of the study, the non-usage attrition rate, a noted issue in online programs, (Eysenbach, 2005) was comparable to similar self-guided programs (Meyer et al., 2009). Predictors of dropout and issues around attrition warrant more detailed consideration, which is beyond the scope of this current paper. The use of the online discussion board to encourage retention also warrants investigation.

The inclusion and exclusion criteria in our study were broad and represented a 'real-world' sample. Medical or psychiatric comorbidities, or previous treatments including previous CBT were not exclusion criteria. Mediators and moderators of this study are important elements and will be explored in subsequent analyses.

7. Limitations

The limitations of this study include the lack of an attention control which could determine the effectiveness of online interventions in the management of bipolar disorder. Consequently, the study compared two very similar internet interventions and found little significant difference between them. A further limitation was that this study attempted to assess MoodSwings in as naturalistic a setting as possible, imposing very few exclusion criteria. Bipolar disorder is a pleomorphic disorder associated with many co-morbidities, which were not controlled for. The spacing of the baseline measures was a limitation; however all groups were treated the same, and this would tend to underestimate the change relative to the start of the intervention. The dropout limits the generalizability of the results, but the MMRM statistical method used is a practical method that has good theoretical properties for handling missing data (Rabe-Hesketh and Skrondal, 2012).

8. Conclusion

In summary, this study found that both versions of our online intervention were associated with improvements in symptoms and functionality for people with bipolar disorder. The MS-Plus program, which included an interactive CBT component, was superior to the MS program on mania scores at 12-months relative to baseline. This suggests that online interventions may have potential for the adjunctive management of bipolar disorder. Interestingly, the principal area of difference between the full MS-Plus program compared to the MS group was in symptoms of mania scores. This is concordant with face-to-face CBT data (Lam et al., 2003) reported in the parent MAPS study (Castle et al., 2010). Further refinement and development of online interventions for bipolar disorder in general, and the MoodSwings programs in particular, are warranted and on-going.

Role of funding source

MoodSwings was supported by Beyondblue, the Victorian Center of Excellence in Depression and Related Disorders. This funded the project design, development implementation and analysis. Assistance was also received by Eli Lilly for the statistical analysis.

Conflict of interest

Sue Lauder has received research support from Beyondblue and conference support from Sanofi Aventis.

Andrea Chester has received Funding from the Office of Learning and Teaching. David J Castle has received Grant Monies Received From: Eli Lilly, Janssen Cilag, Roche, Allergan, Bristol-Myers Squibb, Pfizer, Lundbeck, Astra Zeneca, Hospira; Travel Support and Honoraria for Talks and Consultancy from Eli Lilly, Bristol-Myers Squibb, Astra Zeneca, Lundbeck, Janssen Cilag, Pfizer, Organon, Sanofi-Aventis, Wyeth, Hospira and has been an Advisory Board Member for Lexapro: Lundbeck (current), Zyprexa (Relprev): Eli Lilly (current), Abilify: Bristol-Myers Squibb (not current), Seroquel: Astra Zeneca (current), Desvenlafaxine: Wyeth/Pfizer (current), Bipolar Advisory: Janssen-Cilag (current), Varenicline: Pfizer (current), Asenapine: Lundbeck (current) and Serdolect: Lundbeck (current).

Seatal Dodd has received Grant/Research Support from the Stanley Medical Research Institute, NHMRC, Beyondblue, ARHRF, Simons Foundation, Geelong Medical Research Foundation, Eli Lilly, Glaxo SmithKline, Organon, Mayne Pharma and Servier, speaker's fees from Eli Lilly and conference travel support from Servier.

Emma Gliddon has received a PhD scholarship from Australian Rotary Health and the Ian Parker Bipolar Fund.

Lesley Berk has received a PhD scholarship from NHMRC

James Chamberlain and Monica Gilbert have received grant research support from Eli Lilly, Janssen Cilag, Beyondblue and MBF.

James Chamberlain received grant support from Janssen Cilag, MBF, Beyondblue and Eli Lilly.

Britt Klein has nothing to declare.

Monica Gilbert received grant support from Janssen Cilag, MBF and Beyondblue.

David Austin has received grant/research support from the NHMRC, ARC, Beyondblue, rotary Health Research Fund, CIHR Broad Foundation and Wyeth.

Michael Berk has received Grant/Research Support from the NIH, NHMRC, Cooperative Research Center, Simons Autism Foundation, Cancer Council of Victoria, Stanley Medical Research Foundation, MBF, Beyondblue, Geelong Medical Research Foundation, Bristol Myers Squibb, Eli Lilly, Glaxo SmithKline, Organon, Novartis, Mayne Pharma and Servier, has been a speaker for Astra Zeneca, Bristol Myers Squibb, Eli Lilly, Glaxo SmithKline, Janssen Cilag, Lundbeck, Merck, Pfizer, Sanofi Synthelabo, Servier, Solvay and Wyeth, and served as a consultant to Astra Zeneca, Bristol Myers Squibb, Eli Lilly, Glaxo SmithKline, Janssen Cilag, Lundbeck and Servier.

Acknowledgments

MB is supported by a NHMRC Senior Principal Research Fellowship 1059660. The authors also acknowledge the earlier contributions of Professor Greg Murray and Professor Leon Piterman AM.

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