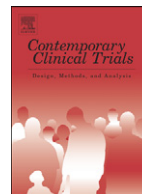


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Contemporary Clinical Trials

journal homepage: www.elsevier.com/locate/conclintrial

Feasibility and acceptability of web-based enhanced relapse prevention for bipolar disorder (ERPonline): Trial protocol



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ARTICLE INFO

Article history:

Received 14 October 2014

Received in revised form 9 January 2015

Accepted 10 January 2015

Available online 17 January 2015

Keywords:

Bipolar

Web-based

Trial

Online

Relapse prevention

Psychological intervention

ABSTRACT

Background: Relapse prevention interventions for Bipolar Disorder are effective but implementation in routine clinical services is poor. Web-based approaches offer a way to offer easily accessible access to evidence based interventions at low cost, and have been shown to be effective for other mood disorders.

Methods/design: This protocol describes the development and feasibility testing of the ERPonline web-based intervention using a single blind randomised controlled trial. Data will include the extent to which the site was used, detailed feedback from users about their experiences of the site, reported benefits and costs to mental health and wellbeing of users, and costs and savings to health services. We will gain an estimate of the likely effect size of ERPonline on a range of important outcomes including mood, functioning, quality of life and recovery. We will explore potential mechanisms of change, giving us a greater understanding of the underlying processes of change, and consequently how the site could be made more effective. We will be able to determine rates of recruitment and retention, and identify what factors could improve these rates. **Discussion:** The findings will be used to improve the site in accordance with user needs, and inform the design of a large scale evaluation of the clinical and cost effectiveness of ERPonline. They will further contribute to the growing evidence base for web-based interventions designed to support people with mental health problems.

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1. Introduction

Relapse prevention interventions for Bipolar Disorder (BD) involve supporting people to identify triggers and early warning signs (EWS) of relapse, and learn effective coping strategies to

manage mood [1]. Evidence shows that this kind of approach may reduce relapse rates, hospitalisations, and improve functioning and quality of life when offered alongside medication [2,3]. Consequently, this kind of approach is recommended as an adjunct to medication by international clinical guidelines.

Enhanced Relapse Prevention (ERP) [4] builds directly on the work of Perry et al. [2] but develops this approach by: (1) strengthening the coping strategies for depression (for which the Perry study showed no specific impact) in an attempt

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to increase effectiveness; (2) by allowing service users to involve a relative where appropriate; and (3) adapting the format to be delivered by frontline care staff in routine clinical services to aid implementation. However, many people with bipolar disorder do not have regular access to care staff able to offer this kind of intervention. To address this problem, we have developed a web-based version of the ERP intervention and here we outline a protocol to test the acceptability and feasibility of this approach.

Computer-based interventions, including web-based packages, are recommended to increase access to psychosocial interventions in mental health [5]. In treating depression and anxiety, computerised interventions have already been shown to be clinically and cost-effective, acceptable to service users, and highly accessed [6–10]. More research is needed to test the effectiveness of computer-based interventions for people with severe mood disorders including Bipolar Disorder.

To date, we have identified seven online interventions for Bipolar reported in the literature [11–17]. Whilst all support the internet as an acceptable mode of delivering treatment to this population, only 3 [11–13] have provided outcome data. *Beating Bipolar* was found to improve psychological quality of life, in post hoc analyses, but no other effects were found on overall quality of life, functioning, symptoms, or relapse [11]. *Living with Bipolar* [12] significantly improved quality of life, well-being and recovery compared to treatment as usual. In Australia, the *Online Bipolar Education Program* (BEP) [13] did not improve outcomes compared to an information control condition [18].

Taken together, these findings suggest a considerable amount of interest in the development of web-based interventions for BD, evidence that they are acceptable to service users and indications that this may be an effective way to increase access to evidence-based interventions. However, many questions regarding content, style of delivery, required support, and mechanism of action remain unanswered, suggesting a need for further research in this area.

1.1. Aims

The main aims of the study are to:

1. Assess the feasibility of (i) creating a web-based version of Enhanced Relapse Prevention for Bipolar Disorder and (ii) an RCT design using web-based and telephone data collection to evaluate effectiveness.
2. Determine the acceptability of ERPonline for people with BD via (i) amount of use of the ERPonline website (e.g. statistics per user, per module, per re-visit), (ii) number and type of adverse events associated with use of the site, and (iii) detailed feedback from participants about their experiences of this intervention which can be used to inform future developments. This will include feedback from those in the intervention arm who did not engage with ERPonline, where possible.
3. Determine the feasibility and acceptability of data collection via the internet and telephone as measured by rates of recruitment, retention, data completion, and direct feedback from participants including a feedback survey on taking part for the control arm, and qualitative interviews with those in

the intervention arm. This will include participants who dropped out of the study, where possible.

4. Estimate the likely effect size of the intervention on a range of outcomes, particularly noting any negative impacts.
5. Explore mechanisms of change on outcome measures to understand processes underlying the impact of the intervention.

For a large scale definitive trial to be feasible will require us to have produced an ERPonline website which functions as designed and which can be adapted to accommodate any key limitations identified in feedback from participants. We will have designed a strategy for the recruitment and retention of participants. We have chosen not to specify arbitrary criteria to decide if the rates achieved make a large scale trial feasible, because this depends on the level of precision required by funding bodies. However data from this trial will allow us to make reliable estimates of the rates of recruitment, rates of retention, level of use of the site, and effect size of the intervention across a number of outcome variables. This data will allow us to calculate sample sizes required for a large scale definitive trial of the clinical and cost effectiveness of ERPonline, across a range of precision estimates.

2. Methods

2.1. Design

A single blind RCT, with nested qualitative design, will compare individuals receiving access to the ERPonline website for 12 months alongside their usual treatment to a 'waitlist control' arm who will receive usual treatment only for the 12 months of the study but will then have access to the ERPonline website.

2.2. ERPonline intervention

The evidence-based Enhanced Relapse Prevention (ERP) manual, previously developed by members of our research team [4], has been adapted and translated into a free-to-access, web-based, self-management resource. ERPonline focuses on the acquisition of skills to prevent future relapse, which has already been shown to be effective when delivered face to face [19]. The adaptations for the web-based version of ERP were informed by a review of the relevant literature, and stated preferences of service users [20]. For example, ERPonline allows the user to access relevant sections, when required, based on individual needs (rather than in a staged sequential way) and will be available in an open and free-to-access format. The option to involve a supporter (a relative or health professional) has been retained as this was identified as beneficial in the delivery of face-to-face ERP by service users, Care Coordinators, and relatives [21].

In order to ensure that ERPonline is engaging and has high face validity, development of the site has featured an iterative cycle of clinical input, service user review of content and usability, and web-based prototyping. The Service User Reference Group (SURG) formed for this process will continue to inform the ERPonline trial including recruitment, retention, and dissemination of findings. Where possible, the site is

designed to comply with W3C web content accessibility guidelines [22].

ERPonline is not intended to replace current treatment where this is appropriate and available, but may increase choice and access by allowing individuals who do not currently have access to evidence-based psychological input to access helpful support.

The key modules in ERPonline are summarised in Table 1.

There is a logical order to the modules, though the participants are free to browse through them as they please. Each module includes an introductory video from a member of the research team outlining the aim of the module and the tasks within it. This information is also provided in the text which is deliberately arranged in short paragraphs providing only essential information with links to information dialog boxes which provide expanded information on key points. This allows the user to control the level of detail they receive. Case examples provided by the SURG are included to convey real lived experience illustrations of the problems identified and strategies to overcome them.

The introductory section includes information about what ERPonline is, who it is for, why someone might want to use ERPonline, how to involve a supporter, and how to use the site. The intervention section then includes the key modules outlined in Table 1, with a brief description of what is covered in each. In each module, the participants are asked to enter relevant personal information, which is collated in the final module to form a “Staying Well Plan”. This individualised plan includes (1) *key things to manage my stress*; (2) *things I can do to keep my social rhythms regular*; (3) *triggers for high moods and how to manage them*; (4) *triggers for low moods and how to manage them*; (5) *early warning signs and coping strategies for high mood*; and (6) *early warning signs and coping strategies for low mood*. The participants are encouraged to review this plan on a regular basis, especially following any relapses that do occur.

The final section provides additional support, including links to other statutory and non-statutory care providers, and access to technical support with the website. A user discussion forum was originally intended, but this proved too difficult to

manage within the resources available. Moreover, the participants in the trial of a web-based depression intervention, *Beating Bipolar* [23], reported that there was a tendency for the forum to be dominated by a few strong characters who would sometimes not listen to or accept other peoples’ point of view, causing distress among some individuals. Instead, ERPonline includes a Frequently Asked Questions (FAQ) function that is asynchronous, with questions submitted via an online form going straight to unblinded members of the multidisciplinary research team.

Throughout the site, users are encouraged to involve a supporter (close friend or relative) where they wish. The introductory section includes a rationale for why this might be helpful, and guides the participants to think through who they might like to invite to be their supporter. Highlighted advantages of involving a supporter include emotional and practical support, recognition of subtle changes in mood and behaviour, and facilitating implementation of coping strategies developed during ERPonline. Some of the potential disadvantages identified include not wanting to burden others with these tasks, sense of loss of autonomy, and not wanting to share personal details which may be relevant to understanding relapse. The ERPonline site emphasises that it is not necessary to involve a supporter.

The intervention website uses Drupal, the PHP open source content management system, with custom Drupal modules built to deliver the interactive portions of the site. One of these custom modules handles the collection of web traffic data into the site database. This system sits on top of the MySQL open source database. Drupal is an intensely supported and developed project with security teams who work to ensure that security threats are dealt with proactively. The hardware on which the site runs is in a UK-based custom built data centre providing physical security, natural disaster protection, data redundancy and generator backed uninterruptible power supply.

The ERPonline intervention is being compared with treatment as usual (waitlist control group) to assess its feasibility, acceptability and potential impact on key outcomes. The trial is being conducted by a multidisciplinary team of academics,

Table 1

Key intervention modules in ERPonline.

| | | |
|--------------------|--|--|
| Getting started | How to use the site What is Bipolar? | Ways to navigate the site to get the best from the available modules Background information about what Bipolar Disorder is, theories about causes, common consequences, and an overview of available treatments |
| Key modules | Mood charting | How to use an online tool to monitor mood on a daily basis to help recognise normal mood fluctuation and pick up early signs of a mood episode |
| | Life charting | Complete a chart of past mood episodes, identifying potential triggers and coping strategies for future mood changes |
| | Identifying triggers | Detailed analysis of triggers of previous mood episodes, followed by a personalised plan of how to manage triggers |
| Specific moods | Early warning signs (EWS) – high mood Coping strategies – high mood | Detailed analysis of EWS of high mood to develop a relapse signature for (hypo)mania. Review of current strategies to manage high mood and introduction to new strategies that may be helpful |
| | Early warning signs (EWS) – low mood Coping strategies – low mood | Detailed analysis of EWS of high mood to develop a relapse signature for depression Review of current strategies to manage low mood and introduction to new strategies that may be helpful |
| Wrapping things up | Staying well strategies | Identifying and managing stress levels Understanding the importance of social rhythms and how to regulate these to manage mood How relationships with other people impact on mood |
| | Your staying well plan | An individualised summary of staying well strategies, early warning signs to look out for, and coping strategies to regulate mood |

clinicians, and service user researchers who have a diagnosis of bipolar disorder, based at Lancaster University, the University of Nottingham, and Cumbria Partnership NHS Foundation Trust in the North West of England. The trial is supported by an independent Steering Committee.

2.3. Sample size & participants

We aim to recruit 125 participants in total which, allowing for a conservative attrition rate of up to 35%, will provide a final sample of $n = 40$ per arm of the trial. The conservative estimate of attrition was based on a wide range of retention rates across previous trials of web-based interventions for BD, including 17% attrition for *Living With Bipolar* [24], 26% attrition for *Beating Bipolar* [25], and 46% attrition from randomisation for BEP [26]. This sample size is sufficient for the aims of the study including assessing feasibility of recruitment and retention strategies, and acceptability. Consistent with MRC complex interventions framework [27], this study is not powered to find a statistically significant difference on any one primary outcome. The trial will allow us to estimate the effect size of the impact of ERPonline on a range of outcome measures, but a large scale definitive trial, informed by the findings of this study, will be needed to test the clinical and cost effectiveness of ERPonline.

Inclusion criteria: (i) aged over 18 years of age; (ii) access to a telephone, computer and the internet; (iii) meet research diagnostic criteria for a diagnosis of bipolar disorder type 1 or 2; (iv) the ability to understand spoken and written English; and (v) have had at least 3 relapses in their lifetime, with 1 falling in the preceding 2 years. This is to ensure that we have a sample considered high risk for relapse, for who this kind of intervention is most appropriate.

Exclusion criteria: (i) in current episode (within previous 4 weeks) – this is because the intervention focuses on the identification and management of early warning signs of relapse and therefore is not intended for those currently in episode who would benefit from a different kind of approach; (ii) currently taking part in another intervention study (or follow-up period); and (iii) currently being treated under a section of the Mental Health Act or unable to give informed consent. Individuals who register an interest but who are either currently in episode and/or being treated under the Mental Health Act will be regularly contacted to reassess eligibility and invited to take part when they meet criteria. If this does not occur within the study period, they will be offered access to ERPonline at the end of the study.

2.4. Procedure

Progression through the study is outlined in Fig. 1.

2.5. Recruitment

Referrals are sought from participating NHS Trusts in the UK, with support from the Mental Health Research Network, a publicly funded national workforce to aid the recruitment of participants to nationally funded research studies. The participants from across the UK will also be able to self-refer, and will be recruited via newsletters sent to existing service user networks (e.g., voluntary sector websites, mental health web

forums), social media (e.g. Twitter and Facebook), and in posters displayed in public areas (e.g., libraries, community centres), in NHS services, and in the offices of voluntary sector organisations. Recruitment materials ask potential participants to visit the study website (www.erponline.co.uk) where they can access information about the study, contact details of the research team, an eligibility checklist, and can register their interest in taking part. To facilitate recruitment, registration will be available during the setup phase of the study for 2 months before the trial starts. Registered individuals will be sent regular email updates to encourage continued interest. Once the trial starts, eligible participants will be sent a link via email to an online consent form. Consent is taken online but requires the participants to indicate that they have read and understood the online Participant Information Sheet. They are encouraged to print out the PIS, discuss the content with friends and family, and contact the research team by telephone or email with any queries. Following online consent they are contacted by telephone to arrange a convenient time to complete the first screening interview to confirm diagnosis and assess relapse history. Verbal consent is reassessed at this point.

2.6. Screening, assessments, randomisation and blinding

The Structured Clinical Interview for the DSM-IV (SCID) [28] will be used to confirm a diagnosis of bipolar disorder and assess the number of previous mood episodes. This will be administered via telephone by a trained researcher. Good reliability between telephone and face-to-face interviews has been found for diagnosing a variety of affective disorders [29,30]. All SCID interviews are followed by a telephone call within 48 hours to inform the participant whether or not they are eligible for the study, and to check for any adverse consequences from the telephone SCID. People who are not eligible are directed to information about other relevant research opportunities. Those who are not eligible only because they are currently in a mood episode, will be monitored on a regular basis so they can come into the trial at the appropriate time. Those who are eligible for the study will then complete the baseline assessment measures (listed below). Interviewer rated measures are conducted by trained researchers over the telephone. Self-report measures are completed online via a link sent by email.

After baseline assessment, random allocation to the intervention or waitlist control arm will be conducted by an independent unit based at the Christie NHS Foundation Trust, Manchester. The 1:1 individual randomisation between the two arms is minimised on the number of previous episodes banded as (<8, 8–20, 20+), and includes a random element. Allocation of each participant is given to the trial manager by telephone. The participants are informed by telephone or email. The trial manager will also inform the Care Coordinator and/or GP that the participant is taking part in the study and which arm they have been randomised to. Minimisation was chosen in preference to stratification because of the small sample size and a random element was included to minimise predictability of allocation. The researchers carrying out the follow-up assessments will remain blind to the study arm of all the participants throughout the trial period. To maximise blindness, blind researchers are housed in a separate office and

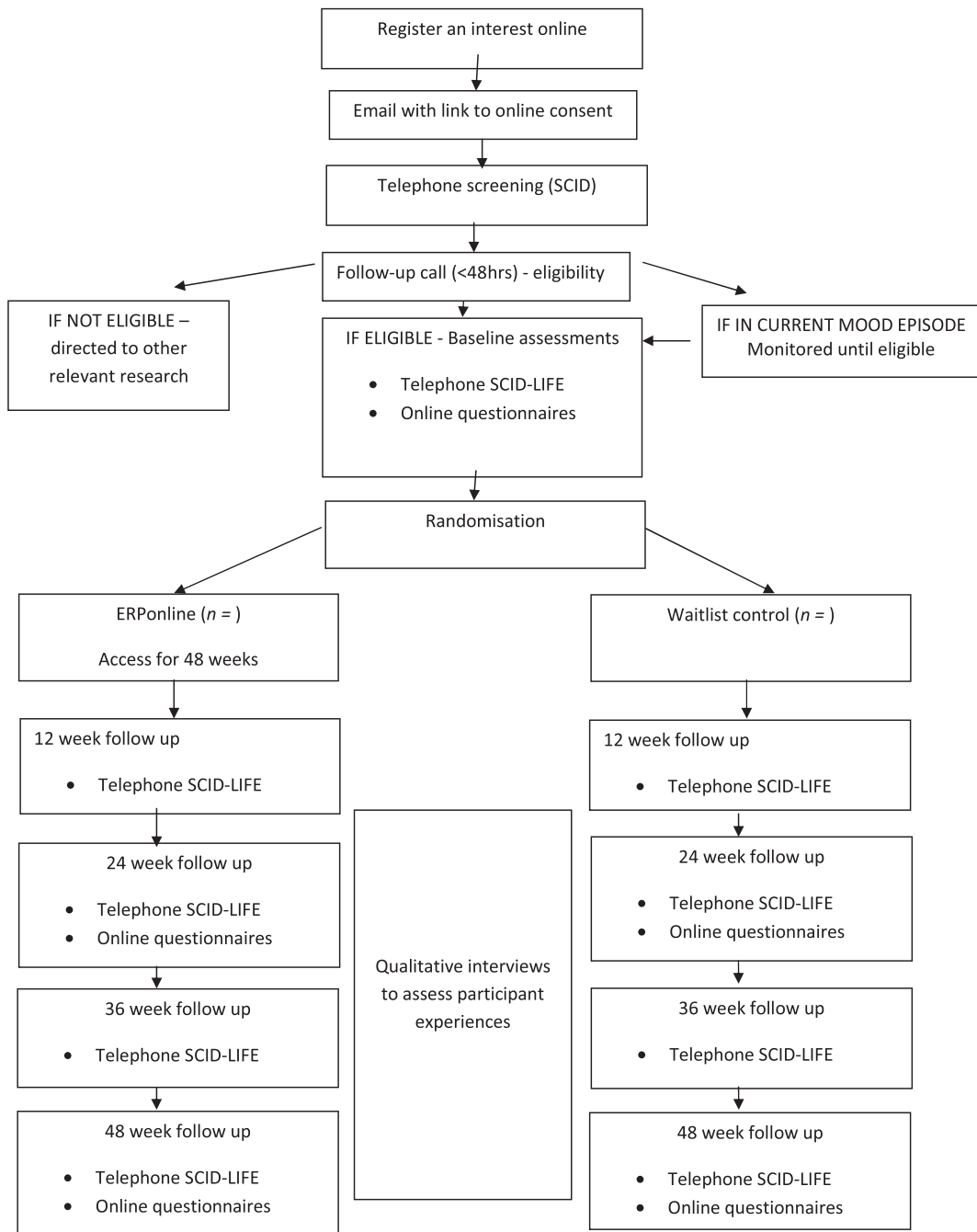


Fig. 1. E-consort for ERPonline.

have no access to electronic study databases containing randomisation information. Prior to all follow-up assessments, participants will be reminded by the trial manager not to disclose which arm of the trial they were allocated to or provide any information that may indicate this. This is reiterated by the interviewer at the start of all follow-up interviews. Any instances of un-blinding will be recorded and reasons noted.

Following randomisation, the participants in the ERPonline arm will be provided with a username and password (which

they can reset for personal preference) via email to access the intervention website. The participants can then access ERPonline as often as they would like from a location of their choice for 12 months. Reminder emails encouraging participants to visit the site will be sent every 4–8 weeks during the trial. The research team can be contacted with queries via the FAQ link or Technical Support link. These links will not involve any contact with the researcher responsible for blind follow-up assessments.

Assessments are carried out at 0 (baseline), 12, 24, 36 and 48 weeks post-randomisation. At 0, 24 and 48 week assessments, interviewer rated measures are conducted by telephone, and online self-report measures are also completed. At 12 and 36 week assessments, only interviewer rated assessments by telephone are carried out. To encourage retention during the follow-up period, participants will be contacted by telephone and/or email to confirm the scheduled date and time date for each follow-up interview and to answer any queries that they may have 2 weeks prior to the date their next interview is due. In acknowledgement of their contribution to the study, the participants also receive £10 in vouchers at each assessment point.

2.7. Measures

2.7.1. Baseline and outcome measures

2.7.1.1. Interviewer-rated outcome measures (administered at baseline, 12, 24, 36 and 48 weeks)

Structured Clinical Interview for DSM-IV Longitudinal Interval Follow-up Examination (SCID-LIFE) [31]. The SCID-LIFE will be delivered via telephone to generate weekly scores of mania and depression on a 1–6 severity scale. The SCID-LIFE includes items from the SCID as well as the Hamilton Depression Rating Scale (HDRS) [32] and Mania Rating Scale (MRS) [33]. The SCID-LIFE is reliable for use in BD [34]. Scores of 5/6 indicate the presence of symptoms and impact on functioning that corresponds to criteria for major mood episode as defined by the DSM-IV. Weekly scores will be used to examine the number of weeks out of episode (4 or less on SCID LIFE), number of weeks without impairment (2 or less on SCID LIFE) and time to first episode of depression and mania.

Personal & Social Performance Scale (PSP) [35]. The PSP is an interview schedule to assess functioning in the domains of socially useful activities, personal and social relationships, self-care, and disturbing and aggressive behaviours. It has been used previously to assess outcome in response to treatment for BD [36].

Multidimensional Scale of Independent Functioning (MSIF) [37]. The MSIF will assess functioning in terms of role responsibility, presence and level of support, and performance quality in relation to work, education, and living. The MSIF is a valid and reliable indicator of functioning and has been used as an outcome measure in relation to treatment for BD [38].

2.7.1.2. Self-report outcome measures (baseline, 24 and 48 weeks)

Work & Social Adjustment Scale (WSAS) [39]. WSAS is a brief 5-item measure of functioning in the domains of work, home management, social leisure, private leisure, and relationships. It has been extensively used in longitudinal research on BD [40,41], including trials of web-based therapy [42]. This will be used to estimate self-reported impact of ERPonline on functioning.

Quality Of Life in Bipolar Disorder Scale (QoLBD) [43]. The QoLBD was developed specifically to assess quality of life in BD within several areas including physical, sleep, mood, leisure,

spirituality, and identity. A rating scale from 1 = 'strongly disagree' to 5 = 'strongly agree' is used to describe to what extent the participants have experienced a range of items over the past week (e.g., 'Kept a routine in my sleep-wake cycle'). Questions relating to work (including voluntary) and education are only answered if applicable. This will be used to estimate impact of ERPonline on quality of life and has been shown to be sensitive to change in previous studies of interventions for BD [24].

Bipolar Recovery Questionnaire (BRQ) [44]. The BRQ consists of 36 items developed specifically to measure personal recovery in BD (e.g., 'I am able to engage in a range of activities that are valuable to wider society'). The participants mark to what extent each statement describes their mental health and recovery over the past week on a visual analogue scale anchored 'Strongly disagree' and 'Strongly agree'. The BRQ has been shown to be sensitive to change in previous studies evaluating interventions for BD [12,45].

Current Treatment Questionnaire. This measure was developed by the research team for this study, and will record treatment actually received by participants (other than ERPonline). This will allow a definition of current treatment to which ERPonline will be compared, and to explore current accessibility to evidence-based psychological interventions.

EQ5D5L [46]. This is a widely used brief self-report measure with 5 scales (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) each rated on 5 levels (no problem, slight, moderate, severe, extreme). There is good evidence that this measure reflects the impact of a wide range of physical and mental health problems including anxiety and depression [47]. The measure has been used in previous trials of interventions for people with bipolar disorder [48]. However, pilot use of the measure in this study would further assess the feasibility of using the measure online, with a population recruited via a wider range of methods than previous trials including online forums and media, and would allow us to test whether it is sensitive to change in this format.

Client Socio-Demographic and Service Receipt Inventory – European version (CSRI; [49]). CSRI will collect data to allow calculation of the direct costs and savings of offering and supporting ERPonline in the intervention arm, and indirect costs/savings in both arms. Indirect costs will include health and social care contacts, medications prescribed, and time off work. The feasibility of collecting this data in self-report form will be assessed. The participants will be asked to identify any other substantial changes that are not captured by the pro-forma.

2.7.1.3. Self-report process measures (baseline, 24 and 48 weeks)

Early warning signs checklists for relapse (EWS depression and EWS mania; [50]). These are 32-item and 31-item checklists assessing the frequency of monitoring of EWS and then timing of common early warning signs in relation to onset of depression and mania, respectively. Initially respondents are asked to indicate how frequently they monitor EWS and to spontaneously generate the signs they monitor. They then

complete a checklist in which each item is marked as to whether it is absent altogether, an early sign, a late sign, or comes during full relapse. The full measure is used at baseline but only the item assessing frequency of monitoring is included in the follow-up assessments to assess the impact of ERPonline on monitoring impact, whilst reducing the participant burden of measures.

Brief Illness Perception Questionnaire (BIPQ; [51]). This measures 11 beliefs about mood swings (e.g., ‘Do you think you are to blame for your mood swings?’) on a Likert scale from 0 to 10 where 0 indicates an absence of that belief and 10 indicates a strong conviction in that belief. The BIPQ is associated with time to relapse and depression in BD [51] and will be used to explore the mechanism of change in this study.

Medication Adherence Rating Scale [52]. This measure has 10 yes/no items relating to behaviours and attitudes towards medication over a week long period (e.g., ‘Are you careless at times about taking your medication?’). This scale will be used to determine the impact of medication adherence as a mechanism of change in this study.

2.7.1.4. ERPonline feedback

A brief questionnaire was developed to obtain written feedback about the ERP intervention from all users at 24 and 48 week follow-up. This is a combination of free text boxes, rating scales, and multiple choice questions, asking for general feedback on ERPonline (e.g. how satisfactory they found it, what was/was not useful), questions about relevance and helpfulness of specific modules, and practical issues about internet use and access. Qualitative interviews will be used to explore peoples' experiences of participating in the trial and using ERP-online. A sample ($n = \text{approx } 20$) will be purposively selected from the treatment group to ensure appropriate gender and age distribution and different patterns of website use. The sample will be invited to take part in topic guided telephone interviews lasting 45–60 min. Topics will include: perceptions of impact/outcome of the intervention, factors shaping usage of the resource, attitude towards the online format, and experience of participating in research. Interviews will be digitally recorded and transcribed. People in the waitlist control group will be invited to provide feedback on their experience of taking part in the study using an open-ended online-survey.

2.8. Dropout from the study

The participants who wish to cease participation in the project will be invited to complete a form stating their reason for dropping out, or to provide information so that a member of the research team can complete this on their behalf. Understanding the reasons for dropout is essential information both to guide the design of future definitive trials with a view to minimising dropout, and to enable the analysis protocol to handle incomplete follow-up data appropriately. Depending on the participant preference, this form will either be completed with the participant by a researcher over the telephone, or the participant can opt to complete an online self-report questionnaire. The participants will be asked at this point whether they still consent to

be contacted about taking part in a qualitative interview, which will further explore reasons for dropout.

2.9. Dealing with risk

There are several potential risks which need to be addressed in this study.

It is possible that researchers are made aware of risk to the participants or others, at any point during the study. At initial consent the participants will be required to provide contact details for their Care Coordinator and/or GP. It will be made clear that although information collected during the study will remain confidential, if there are any risk issues then information will be shared with existing care teams. If an urgent risk is identified, the researcher will attempt to ensure the immediate safety of the participant and other individuals by informing the care team/GP/emergency services as appropriate.

Conducting the SCID-LIFE interview over the telephone is a relatively new and potentially efficient way to collect data. However, the impact of this on participants is not yet fully understood. Following each telephone interview, all participants will be offered a ‘support call’ 24–48 hours later to assess any adverse impact of the assessment process. A log will be kept of any reported impacts. Supervision is provided to the researchers by a qualified Clinical Psychologist.

The intervention site invites users to submit queries to a multidisciplinary team of clinicians, academics, and service users. The team replies directly to the individual submitting the question and the question and answer can then be considered for the Frequently Asked Questions page. However, it is made clear that the research team cannot respond to individual urgent clinical need, which should be directed to existing care teams. The intervention website also includes a list of national organisations that can be contacted for further information and support including Mind, ReThink, Bipolar UK, the NHS and Samaritans.

2.10. Analysis

A key focus of this trial is on issues of feasibility and acceptability, therefore much of the outcome data will be descriptive statistics summarising rates of recruitment, demographics of recruited sample, pattern and frequency of website use, retention to follow-up assessments, and qualitative feedback from participants about their experiences of the intervention.

Quantitative outcome data will be examined to inform the selection of measures sensitive to change, and to identify potential positive and negative impacts that should be further tested in a large scale definitive trial. This study is not powered to test for a statistically significant impact. As such, we neither specify a primary outcome, nor set a level of statistical significance for interpreting analyses.

To assess the impact of ERPonline on each of the repeated outcome measures we will analyse the data using linear mixed models, which allow for correlation between repeated measures from the same participant. We will compare the results from unadjusted analyses, which include the treatment effect as the only covariate, and analyses that adjust for baseline variables. These analyses will inform the details of any future trial design by providing estimates of likely effect sizes, variability of outcome within treatment groups and any substantial main effects of baseline variables and/or their

interactions with the treatment effects; the last of these would suggest that a stratified design will be more efficient than a simple randomisation. Incomplete records from patients who drop out of the study will be retained. The analyses will use maximum likelihood estimation for all model parameters. This ensures validity under the assumption that dropouts are missing at random in the sense of Rubin (1976)[53]. The implied estimand for any effect is then the effect that would be experienced in the absence of dropout. To analyse time to first relapse we will use a competing risks Cox proportional hazards regression model with subject-level frailty and stratified by type of relapse (depressive or hypomanic/manic/mixed episodes). We will explore potential mechanisms of change by analysing the ability of process measures to predict change in outcome measures over time, using multivariate hierarchically structured linear models. Process measures include beliefs about mood swings, frequency of early signs monitoring, and medication adherence. Finally, direct and indirect costs in both arms of the trial will be described, along with an assessment of the suitability of the measures for a large trial.

All analyses will use the R open-source computing environment. R code will be lodged in an open-access repository to ensure reproducibility of results.

Qualitative data from the feedback survey will be summarised into key themes. Transcripts from the in-depth interviews will be analysed thematically, which involves coding of data, identification of thematic headings, and then extraction of data. Patterns and connections across the themes will be explored. The analysis will be validated by cross-checking of independent coding and transcript extraction by another member of the research team. The analysis team will include a service user and as the analysis progresses a consult with the Service User Reference Group will be used to check the team's interpretations and ensure that this perspective is brought to the analysis.

3. Discussion

Consistent with the MRC framework for development of complex interventions [27], this study aims to develop and test the feasibility and acceptability of the ERPonline intervention. Specifically, we will determine to what extent the site was used, receive detailed feedback from users about their experiences of the site, and identify any reported benefits and costs to their mental health and wellbeing. This information will be used to improve the site in accordance with user needs. We will gain an estimate of the likely effect size of ERPonline on a range of important outcomes, and explore potential mechanisms of change, giving us a greater understanding of the underlying processes of change, and consequently how the site could be made more effective. We will be able to determine rates of recruitment and retention, and identify what factors could improve these rates. All of these data are required to inform further development of the intervention, and the design of a large scale definitive evaluation of clinical and cost effectiveness. At this stage, it is not possible to state exactly how the large scale definitive trial will differ from the current study as the findings from this study are needed to inform the design. For example, any barriers to using the intervention, recruitment and retention of participants,

telephone assessment, and completion of the online measures, could lead to substantial modifications to the design of the subsequent definitive trial. However, the following differences are likely: (1) a modified intervention in light of feedback; (2) a larger sample to power a clinical and cost effectiveness analysis, informed by estimates of effect sizes from the data collected in this study; and (3) an analysis of cost effectiveness using the online version of the CSRI developed in this study.

There are several studies completed or underway to develop and evaluate web-based interventions for Bipolar Disorder. All differ in the content of the intervention, mode of delivery and support, and design of evaluation. This study has several key strengths. Firstly, the content of the intervention is based on existing interventions which have already been shown to be effective when delivered in face to face therapy. When offered in routine clinical care as a structured face to face intervention, a pilot trial suggested that ERP may increase time to next mood episode, and improve functioning [19]. The adaptation of the content and design of the online version of ERP is an iterative process involving a multidisciplinary team and extensive service user involvement. Secondly, this protocol describes a rigorously controlled trial in which diagnosis of Bipolar Disorder is confirmed using the SCID interview, an independent trial unit will conduct the randomisation, all outcome assessments are blind rated or self-report, and there is detailed data collected to define current treatment in both study arms. Thirdly, the broad recruitment strategy offers the approach to a wide range of people who meet the criteria for Bipolar Disorder, including those who may not choose to access routine mental health services.

This study protocol also highlights some limitations of the design. Firstly, the intervention focuses on preventing relapse. We recognise that for some individuals, this may not be their most valued goal, and that a more recovery-focussed approach, such as that described by Jones and colleagues [36], may be more flexible and able to meet the range of individual goals. However, the evidence-base for this approach is only just beginning to emerge [45], and there are challenges in conceiving how this can be adapted to an online environment. Secondly, this design fails to answer important questions about the role of support in online interventions. Due to resources available, we are unable to offer either peer or clinical support alongside the website. Users are encouraged to engage supporters from existing social networks where appropriate, and are given the chance to post questions on our Frequently Asked Questions page. This has the advantage that if effective, the site offers a more efficient way to deliver support that is more likely to be adopted in routine clinical services. However, previous research in this broad area suggests that self-management interventions are likely to be more effective when they are supported [54,55], that this may be because of greater adherence and use of the site [14], and that peer and therapist support are both potential options [56]. However, evidence is mixed with some studies finding no significant benefit of support [57], suggesting that more research is needed into the role of support in this area. Finally, this study does not have an active treatment control arm so it will not be possible to estimate the impact on outcome relative to a different kind of website.

ERPonline has the potential to offer an easy to access, freely available online resource that can provide an evidence-based

approach to reduce relapse in people diagnosed with Bipolar Disorder. This protocol describes the development of the intervention and the acceptability and feasibility of evaluating it using a RCT design, providing essential information to inform a large definitive clinical and cost effectiveness evaluation.

3.1. Ethics and research governance approval

We have full ethical approval from the Lancaster NHS Research Ethics Committee and Lancaster University Research Ethics Committee. We have R&D approvals from the following NHS Foundation Trusts: Cumbria Partnership, Lancashire Care, Greater Manchester West, Cheshire & Wirral, Derbyshire Healthcare, and Lincolnshire Partnership. In addition, we have approval from Manchester Mental Health & Social Care NHS Trust and Nottinghamshire Healthcare NHS Trust.

4. Trial registration

Title of trial: A web-based Enhanced Relapse Prevention (ERP-online) intervention for bipolar disorder.

Trial Identifier: ISRCTN56908625.

Date of ISRCTN assignment: 26/03/2013.

Link to record in ISRCTN Register: <http://www.controlled-trials.com/ISRCTN56908625>.

Competing interests

This study both develops and tests the ERPonline intervention and therefore is not an independent evaluation.

Authors' contributions

FL is the Principal Investigator of the trial and led the design of the web-based intervention and trial design. AD is a co-investigator and trial manager, responsible for ethical and R&D approvals and managing the process of randomisation and data management. RP has developed and maintains the ERPonline site. SJ, RM and DD are all co-investigators and contributed clinical expertise to the design of the intervention. SM and MG have taken a lead on the qualitative aspects of the study design. PD provides statistical expertise. BH will oversee collection and analysis of health economics data. DK and AS lead on recruitment and retention, and all assessments, RL is a service user researcher who chairs the Service User reference Group.

Acknowledgements

This paper presents independent research commissioned by the National Institutes of Health Research (NIHR) under its Research for Patient Benefit (RfPB) Programme (Grant Reference Number PB-PG-0211-10001). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

The authors would like to thank all members of the Service User Reference Group and Spectrum Centre Advisory Panel.

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