Clinical effectiveness and acceptability of structured group psychoeducation versus optimised unstructured group support for remitted bipolar disorder: a multi-centre pragmatic randomised controlled trial.

Richard Morriss, Fiona Lobban, Lisa Riste, Linda Davies, Fiona Holland, Rita Long, Georgia Lykomitrou, Sarah Peters, Christopher Roberts, Heather Robinson, Steven Jones and the NIHR PARADES Psychoeducation Study Group.

Department of Psychiatry and Applied Psychology, University of Nottingham, Nottingham, United Kingdom (Prof R Morriss MD, G Lykomitrou)

Spectrum Centre, University of Lancaster, Lancaster, United Kingdom (Prof F Lobban PhD, R Long, Prof S Jones PhD, H Robinson)

School of Psychological Sciences, University of Manchester, Manchester, United Kingdom (L Riste PhD, S Peters PhD)

Institute of Population Health, University of Manchester, Manchester, United Kingdom (Prof L Davies MSc, F Holland MSc, Prof C Roberts PhD).

Correspondence to:

Professor Richard Morriss, Institute of Mental Health, University of Nottingham, Triumph Road, Nottingham, NG7 2TU, United Kingdom. e-mail: richard.morriss@nottingham.ac.uk

Summary

Background Group psychoeducation is a low-cost National Institute for Health and Care Excellence-recommended treatment for bipolar disorder. However, the clinical effectiveness and acceptability of this intervention are unclear compared with unstructured peer support matched for delivery and aim of treatment, and for previous bipolar history.
We aimed to assess the clinical effectiveness and acceptability of structured group psychoeducation versus optimised unstructured peer support for patients with remitted bipolar disorder.
Methods We did this pragmatic, multicentre, parallel-group, observer-blind, randomised controlled superiority trial at eight community sites in two regions in England. Participants aged 18 years or older with bipolar disorder and no episode in the preceding 4 weeks were recruited via self-referral or secondary care referral. Participants were individually randomly assigned (1:1), via a computer-generated stochastic allocation sequence, to attend 21 2-h weekly sessions of either structured group psychoeducation or optimised unstructured peer support. Randomisation was minimised by number of previous episodes (one to seven, eight to 19, or ≥20) and stratified by clinical site. Outcome assessors were masked to group allocation. The primary outcome was time from randomisation to next bipolar
Episode with planned moderator analysis of number of previous bipolar episodes and qualitative interview of participant experience. We did analysis by intention to treat. This trial is registered with the International Standard Randomised Controlled Trial registry, number ISRCTN62761948.
Findings Between Sept 28, 2009, and Jan 9, 2012, we randomly assigned 304 participants to receive psychoeducation (n=153) or peer support (n=151); all (100%) participants had complete primary outcome data. Attendance at psychoeducation groups was higher than at peer-support groups (median 14 sessions [IQR three to 18] vs nine sessions [two to 17]; p=0·026). At 96 weeks, 89 (58%) participants in the psychoeducation group had experienced a next bipolar episode compared with 98 (65%) participants in the peer-support group; time to next bipolar episode did not differ between groups (hazard ratio [HR] 0·83, 95% CI 0·62–1·11; p=0·217). Planned moderator analysis showed that psychoeducation was most beneficial in participants with few (one to seven) previous bipolar episodes (χ^2; HR 0·28, 95% CI 0·12–0·68; p=0·034). Four (1%) participants (one in the psychoeducation group and three in the peer-support group) died during follow-up; these deaths were deemed unrelated to the study interventions or procedures.
Interpretation Structured group psychoeducation was no more clinically effective than similarly intensive unstructured peer support, but was more acceptable and improved outcome in participants with fewer previous bipolar episodes. Optimum provision of structured psychological interventions, such as group psychoeducation, early in the course of bipolar disorder might have important benefits on the course of illness, and merits further research.

Panel: Research in context.

Evidence before this study.

A meta-analysis published by Morriss et al (2007) of all randomised controlled trials (RCTs) of psychological treatment involving early warning signs in bipolar disorder, a core component of psychoeducation, identified only two RCTs of group psychoeducation versus group support from the same centre. These found that 38% and 60% allocated to group psychoeducation or group support experienced a bipolar episode in the subsequent 12 months. In 2015, a further meta-analysis by Bond and Anderson (2015) restricted to group psychoeducation versus treatment as usual or control psychological treatment identified 10 RCTs, but only five reported bipolar episodes at 12 or months follow up. Group psychoeducation was associated with fewer bipolar episodes at 12 months compared to controls (odds ratio 2.80, 95% confidence intervals 1.63 to 4.82) but effectiveness was uncertain once the two original RCTs were excluded. As well as selective reporting, RCTs were largely small, single centre, and did not control for the aim of treatment nor the natural history of bipolar disorder. An update of this meta-analysis was carried out from 1/8/13 to 31/7/16 using the same search terms as Bond and Anderson (2014). Two further RCTs of group psychoeducation were identified, each of which had a follow up of only 6 months and therefore provided no additional information to previous meta-analysis.

Added value of this study.

In a large multicentre RCT with two year follow up that controlled for the natural history of bipolar disorder and the delivery and aim of treatment, overall group psychoeducation was not found to be clinically effective on time to the next bipolar episode versus unstructured group support. However, there may be specific benefits of group psychoeducation, especially in people early in the course of bipolar disorder, on acceptability, time to next mania episode and interpersonal function. Both group psychoeducation and group support increase specific and individualised knowledge about bipolar disorder.

Implications of all the available evidence.

Group psychoeducation is a cheap psychological intervention for bipolar disorder with a small number of specific clinical benefits, especially for people early in their illness course, if the focus of care is on improving self-management, improving interpersonal function and support, and preventing future mania relapse. However, it does not reduce overall bipolar relapse in people with long-established BD nor performance aspects of function.

Introduction.

Bipolar disorder (BD) is a common relapsing life-long mental health condition presenting in adolescence or early adulthood (1). The provision of information and emotional support is a National Institute for Health and Care Excellence (NICE) supported key recommendation and quality standard for all mental health service users (2). In the United Kingdom, such information and support is widely available to people with BD through unstructured peer run groups by both the NHS or the third sector e.g. over 130 national support groups through Bipolar UK (3) or across Europe through structured group psychoeducation in mental health services (4, 5).

In 2003, researchers from Barcelona published two randomised controls (RCTs) of 21 session structured manualised group psychoeducation for people with BD showing clinically important differences in time to all types of bipolar relapse at 12 and 24 months compared to attentional control

support groups (6, 7).). Group psychoeducation is a key NICE and CANMAT recommendation for BD and NICE development quality standard (1, 8). It is a cheap, efficient and easy to deliver easy- to-set- up option for mental health services because 10-18 participants can be treated at a time and therapists require supervision but not extensive training unlike many psychological treatments A recent meta-analysis of the effectiveness of psychoeducation on bipolar relapse noted that the original Barcelona trials (6. 7) seemed to be outliers (9). The evidence was reported as weak or very weak with few pre-registered large multicentre blinded RCTs conducted independently of the developers of the intervention (1, 9, 10). Few studies controlled for the natural history of BD e.g. people with 20 or more previous bipolar episodes relapse three times more frequently than those with only 1-7 previous bipolar episodes (11).

The aims of our current randomised controlled trial were to independently examine:

1. The clinical effectiveness of structured group psychoeducation (PEd) versus unstructured group support (PS) on time to the next bipolar episode, including the moderating effects of number previous bipolar episodes, plus secondary outcomes in groups matched for the duration, delivery and aim of treatment, and previous bipolar history.
2. The experience, acceptability and subjective value of both treatments based on systematic qualitative enquiry and attendance at group sessions.

Methods.

Study design.

This is a randomised, parallel group, interviewer blinded, superiority controlled trial with two year follow up of each participant. Recruitment occurred at eight sites by self-referral or secondary mental health care. The study was conducted in the community in two regions of England (the North West and East Midlands). At three sites recruitment occurred at two separate time periods so recruitment occurred in 11 waves (appendix, Figure 1a). Ethics approval was obtained from a national ethics committee in Nottingham. The study protocol was published (12 and the statistical analysis plan is available on line at https://dx.doi.org/10.6084/m9.figshare.3205738).

Participants.

The recruitment strategy was deliberately broad to ensure that the sample reflected a diversity of people with BD. Community mental health teams at NHS Trusts at each site were encouraged to invite potentially relevant participants. The study was also promoted at a primary care level, with local family doctors being asked to display posters about the trial, and through service user-run local BD groups, national BD publications and the general media, allowing people to self-refer. The target population was patients with bipolar 1 or 2 affective disorder at increased risk of further relapse (defined as having had an episode in the last 24 months), as preventing relapse is the key aim of the intervention.

Participants were included if they give written informed consent and:

- had a SCID-DSM-IV verified diagnosis of primary bipolar 1 or bipolar 2 disorder (13, 14),
- were at increased risk of relapse (at least one episode in the last 24 months),
- were aged 18 years or more

Participants were excluded if they had any of the following:

- presence of a manic, hypomanic, mixed affective or major depressive episode currently or within the previous four weeks,
- current suicide plans or high suicide intent,
- inability or unwillingness to give written informed consent to the study,
- inability to communicate in written and verbal English to a sufficient level to consent, complete the measures and take part in the groups.

Randomisation and masking.
Consecutive eligible patients were individually randomised by a clinical trials unit to either intervention, using a stochastic minimisation software. Randomisation was stratified by clinical site and minimised within site by number of previous bipolar episodes within three categories (1-7, 8-19, 20 or more previous bipolar episodes, determined by SCID-DSM-IV criteria for past mania, hypomania, mixed affective or major depression episodes). At each site, recruitment continued until there was a minimum of 20 and a maximum of 36 participants per wave (see appendix figure 1a). Research assistants (RAs) at each site enrolled participants. To ensure blindness of assessment the RAs sent participants details to the trial co-ordination team (trial administrator and trial co-ordinator) at a separate site who in turn passed the participant information to the clinical trials unit for randomisation. The clinical trials unit reported the randomisation allocation to the trial co-ordination team which directly informed each participant and the lead health professional running the treatment group the participant was allocated to.

Masking of randomisation allocation was achieved by blinding the RAs who recruited the participants at baseline and conducted follow ups by:

1. RAs were based separately from the trial co-ordinator and trial administrator and all treatment groups.
2. Treatment groups were run identically (over the same time period, frequency, duration of sessions, base, both groups received a manual, both led by the same health professional), to mask the day on which each group was run at each site,
3. All follow up data collected by self-complete questionnaire which could unblind the RA was returned in a sealed envelope to the RA carrying out the assessment and conveyed to the trial office for opening and subsequent data entry by another person.

Unblindings were recorded and if they occurred, all subsequent follow up assessments were conducted by another RA who was masked to treatment allocation. At baseline, before attending either group, participants were asked whether they had a preference for PEd, PS or no preference; all participants indicated they were prepared to attend either group.

Intervention procedures.
In both the PEd and PS groups, participants were told when they consented to the study and at the first and subsequent sessions that the purpose of this intervention was to share experiences to help manage BD using: i) the information given by the group facilitators, ii) their own experience, and iii) the collective experience of the group. The groups differed only in the structure, nature of delivery within the sessions, choice of content and type of content. The PEd group followed a curriculum developed in Spain (8, 9) (appendix, Table A1) but contextualised to English current practice by the research team and a panel of service users recruited for the purpose. The PS group set their own agenda and chose the content of their own programme (appendix, Table A2).

Both PEd and PS groups were run by three facilitators, comprising two health professionals (usually one experienced and one trainee facilitator) and a service user-facilitator with a diagnosis of BD. The facilitators were trained for the purpose and supervised by a psychiatrist (RM) or clinical psychologist (FL or SJ) experienced in delivering psychological treatment for BD. However, none of the research team had devised PEd or PS nor gained from favouring either intervention allowing a completely independent trial. Service user facilitators were also offered additional peer support. Both programmes comprised 21 sessions, delivered once per week for two hours, spread over a maximum of 26 weeks (6, 7). The group sessions comprised a closed group starting with a minimum of 10 and a maximum of 18 participants to capture a variety of service user experience about the topics of every session. The sessions were held at the same community based site away from hospital e.g. day centre for both PE and PS contemporaneously on different afternoons of the week. A manual was produced for both PEd (15 adapted by authors) and PS on the aims and conduct of each group (available from authors). Participants in PEd were encouraged to share their staying well plan with their health professionals e.g. community psychiatric nurse, psychiatrist, general practitioner; and other people who were personally important to them. They were discouraged from sharing any information about the content of the group with other service users with BD until their follow up was complete. In both trial arms participants received the trial group therapies in addition to their usual treatment, usually medication. They were discouraged from attending any other course of group, family or individual psychological treatment for BD at the same time as attending the groups in the study. Otherwise treatment as usual was unconstrained and recorded by interview and from case notes.

The PEd group was run as a collaborative workshop with a brief taught introduction of the topic for the session, and the rest of the work taking the form of active interaction using the collective experience of the participants (6, 7). Embedded in the PEd programme is the acquisition of specific skills by each individual, including life charting, recognition of early warning signs, problem solving and other forms of coping, sleep hygiene and care planning, as well as general skills of actively participating and working collaboratively in groups. They were encouraged and supported to develop a plan that fitted their personalised goals for recovery and have two elements: (i) those actions they take every day to stay well, e.g. taking medication and keeping a regular early morning routine; and (ii) those actions they would take if they started to become unwell with mania or depression.

In the PS group, participants collectively decided upon an agenda for discussion at each session. The three facilitators were present to facilitate discussion, encourage participation, prevent unhelpful group behaviour such as bullying or scapegoating, prevent factual misinformation, and if directly asked to, clear up factual uncertainty. Compared to group support delivered routinely by Bipolar UK, PS was optimised by being closed to new participants so that they got to know each other well and facilitation by both a peer service user and two health professionals allowing the delivery of expert information from health professionals if participants requested it.

Treatment fidelity.

Treatment fidelity was maintained by training and supervision, written record of the content and delivery of the sessions completed by therapists and supervisors, and qualitative interviews with participants. Audiotaping and videotaping of sessions were not employed because some participants reported that they would find such recording intrusive and unacceptable.

Outcomes.

The primary outcome measure was time to next bipolar episode (12, 14) recorded by RAs at each site. This was based on the SCID-LIFE (14, 16), carried out every 16 weeks for 96 weeks. We calculated

time from randomisation to the first week of recurrence of an episode of mania, hypomania, a mixed episode, or major depression that lasted two consecutive weeks, satisfying DSM-IV criteria. When a follow up interview was not conducted, a bipolar episode was recorded when there was: (i) a description of symptoms of a manic or depression type episode, in primary or secondary care mental health records, with symptoms of sufficient duration to meet episode criteria (12, 17) and (ii) there was a change of medication, care setting (inpatient or crisis team) or urgency of being reviewed because of these symptoms.

Secondary outcome measures (12) were:

- time to next mania-type episode (mania, hypomania or mixed affective episode) and time to next depressive episode (14, 17);
- assessment of mean weekly symptoms of mania type symptoms and depression symptoms using the LIFE (14, 17);
- assessment of function using the Social Adjustment Scale (SAS) (18) and SOFAS (19);
- observer and self-rated measures of mood: 17 item Hamilton-GRID (HDRS) (20), Bech-Raphaelson Mania Scale (MAS) (21), Hospital Anxiety and Depression Scale (HAD) (22);
- self-rated overall mental and physical health (SF-12 mental and physical component scores) (23)

At each assessment, suicide, neglect and risk were recorded in addition to other assessments. We recorded the type and amount of medication rather than medication adherence as a secondary outcome in our protocol (12). A nested qualitative study was conducted to explore the experiences of group participants and reasons for drop out from group treatment. A maximum variance sample (number of treatment sessions attended, sex, age, number of previous bipolar episodes, geographical location of group) of participants received a single semi-structured digitally recorded interview on completion of group treatment at that site.

The SF-12 was added to the measures outlined in the protocol to measure physical health with the approval of the study Trial Steering Committee. The economic analysis, medication adherence and theoretical psychological measures of process will be separately reported.

Sample size.

Based on the first two RCTs of group psychoeducation versus group support with at least 12 month follow up (6,7), a differential treatment effect of 0.22 was estimated (60% recurrence in the control group, 38% in the psycho-education group at 12-months follow-up). As the study involved a group administered intervention, we adjusted the sample size for the clustering effect assuming a mean group size of 18 at randomisation, with an intra-cluster correlation (ICC) for group therapy of 0.05. Based on these assumptions a study with 360 participants (10 groups per arm) has power greater than 80% assuming 15% loss to follow-up. During the conduct of the RCT, the average group size was observed to be 14. With the agreement of the independent trial data monitoring committee, the numbers of groups per arm was increased and sample size was adjusted as a smaller group size reduces the effect of clustering. Assuming a mean groups size of 14, a trial with 308 participants (11 groups per arm) has 82% power.

Statistical and qualitative data analysis.

All analyses are intention to treat subject to the availability of data with a two sided type 1 error rate set at five per cent. Kaplan Meier curves and median time for first relapse are presented as summary statistics. A Cox model with robust standard errors to account for the therapy group effect was

planned for the primary analysis. However, there was no clustering effect by therapy group for time to next bipolar episode, time to next mania episode or time to next depression episode so the standard Cox model results are presented. The proportional hazards assumption was checked by using log-log plots by arm alone and with additional covariates in the model. The treatment effect (PEd compared with PS) was adjusted for gender, number of previous bipolar episodes, and recruitment wave. We examined two pre-specified treatment moderators for the primary outcome: number of previous episodes (1-7, 8-19, >20 episodes minimised in the randomisation as part of the design) and participant treatment preference at baseline.

For continuous longitudinal data, the main statistical analysis used to compare the two interventions was a linear random effects model (LME) incorporating time as a continuous variable. Random effects were included to account for between-patient variation in the intercept and the gradient of the patient-specific lines. In addition, the models that also included random effects for wave and arm (nested within wave), to take account of therapy group clustering effects, were fitted. Fixed covariates were included to model systematic differences due to treatment, assessment time point and participant characteristics. Time since randomisation was calculated in months and was centred by subtracting the overall (grand) mean of assessment times for each outcome measure. In order that that all subjects with outcome data could be included in the LME analyses missing baseline response values were imputed using simple (deterministic) imputation (24). We estimated a time-treatment interaction (i.e., difference in slopes) and a main effect. More detail of the analysis can be found in appendix (Table A3) and Statistical Analysis Plan on line. All analyses were carried out using STATA Release 13.

Qualitative interviews were analysed using thematic analysis (31) taking an inductive and emergent approach based on participant's experiences of the groups. Coding was performed by a multidisciplinary panel (health and clinical psychology, psychiatry, service user) and subsequent interviews sought evidence to refute emerging themes. Themes were continuously compared against the data using a constant comparative approach. Interviews were conducted until themes were saturated.

Role of the funding source.
The funder of the study had no role in study design, data collection, data analysis, data interpretation or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results.
Between Sept 28, 2009, and Jan 9, 2012, we randomly assigned 304 participants to receive structured group psychoeducation (n=153) or optimised unstructured peer support (n=151; figure 1). When asked about treatment preference before randomisation, all participants indicated that they were prepared to attend either group; however, there was a slight preference for psychoeducation over peer support if participants were given a choice rather than randomisation (table 1). Data for all bipolar, mania, and depression relapses were completed with primary care and secondary care records. Ten unmaskings were reported (n=3 during psychoeducation and n=7 during peer support) whereby the participant divulged their group allocation to their research assistant; subsequent follow-up was done by a different assistant masked to allocation. Six raters made 292 inter-rater reliability assessments of 17 (6%) participants across all baseline and follow-up timepoints. The intracluster correlation was 0·71 (95% CI 0·64–0·85) for depression scores and 0·57 (0·40–0·83) for mania scores, showing a high level of inter-rater reliability for depression symptoms and a moderate level of agreement for mania symptoms, with no evidence of changes in inter-rater reliability over time. Therapist and

supervision records and qualitative interviews confirmed that psychoeducation sessions followed the manual and were therapist led, whereas peer-support sessions followed topics decided by the participants and were peer led.

Baseline characteristics were similar between groups (table 1). More than half the participants had 20 or more previous bipolar episodes and most were taking mood stabilising medication and either antipsychotic drugs or antidepressants (table 1). Participants scored below the clinical threshold for significant depression, mania, or anxiety symptoms, and showed mild to moderate impairment in social adjustment at baseline (appendix pp 4–6). Demographic and clinical characteristics did not differ significantly between participants who self-referred or were referred by secondary care, nor between participants from different sites.

Table 2 shows attendance at treatment groups. Overall, attendance at psychoeducation groups was greater than at peer-support groups (median 14 sessions [IQR three to 18] vs nine sessions [two to 17]; Mann–Whitney test Z score 2·23; p=0·026). By 96 weeks, 89 (58%) participants in the psychoeducation group had experienced a next bipolar episode versus 98 (65%) participants in the peer-support group (figure 2).

The median time from baseline to next bipolar episode was 67 weeks (95% CI 37–91) in the psychoeducation group versus 48 weeks (31–66) in the peer-support group. There was no evidence of an intervention effect after adjustment for prespecified covariates in a Cox proportional hazards model (hazard ratio [HR] 0·83, 95% CI 0·62–1·11; p=0·217; figure 2). Planned moderator analysis based on an interaction between treatment group and number of previous bipolar episodes showed that psychoeducation delayed time to next bipolar episode compared with peer support in participants with one to seven previous episodes (χ^2 6·80; HR 0·28, 95% CI 0.12 to 0.68; p=0·034; appendix p 13). There was no difference between groups for participants with eight to 19 previous bipolar episodes (HR 0·86, 95% CI 0·50–1·49) or 20 or more episodes (1·01, 0·70–1·46). Participant treatment preference before randomisation had no moderating effect on time to next bipolar episode (χ^2 1·95; p=0·38).

The proportion of participants with a next mania-type episode was lower in the psychoeducation group (25% [n=39]) than in the peer-support group (35% [n=53]). In both treatment groups, insufficient numbers of participants relapsed to report the median time to relapse with 95% CIs. The 25th percentile of the time to episode was longer in the psychoeducation group (90 weeks) than in the peer-support group (53 weeks), but the upper 95% CI could not be defined. After adjustment for prespecified covariates in a Cox proportional hazards model, there was weak evidence that time to mania-type episode was longer in participants in the psychoeducation group than in those in the peer-support group (figure 3). The difference between groups in time to mania episode appeared at around session 15 when early warning signs of mania were being discussed during psychoeducation.

The proportion of participants with a depressive episode was 52% (n=80) in the psychoeducation group compared with 54% (n=82) in the peer-support group. Again, insufficient participants relapsed to report the median time to relapse with 95% CI. The 25th percentile for time from baseline to next depressive episode was 22 weeks (95% CI 15–29) in the psychoeducation group and 19 weeks (15–28) in the peer-support group. Time to next depressive episode did not differ significantly between groups (figure 4).

There were no significant intervention effects on symptoms or self-rated mental or physical health outcomes (appendix pp 6, 7). Participants undergoing psychoeducation had faster improvement in the SAS interpersonal domain than did those undergoing peer support (difference in gradient –0·017, 95% CI –0·030 to –0·004; p=0·012; appendix p 8). There was no treatment by time interaction for the remaining SOFAS and SAS (overall, friction, and dependency) functional outcomes (appendix p 7). There were no clinically important differences in medication use between groups (data not shown).

Two themes emerged from qualitative study of the value of both groups: "increased knowledge", in general about bipolar disorder and specifically applied to the participant as an individual, and "people like me" tackling isolation and stigma and sharing similar experiences of having bipolar disorder (appendix pp 9–11). Some participants attributed dropping out of treatment to the lack of structure of the peer-support groups (appendix p 10).

Four (1%) participants (one undergoing psychoeducation and three undergoing peer support) died during follow-up; three from natural causes and one from open verdict. The independent trial steering and data monitoring and ethics committees deemed these deaths unrelated to the interventions or procedures in the trial.

Discussion.

The primary clinical results indicate that there was no significant difference on the primary clinical outcome of group psychoeducation (PEd) for BD versus group support (PS) given adjunctively to medication on time to first bipolar episode after randomisation. Both groups provided general information about BD tailored to the participant, and provided emotional support beyond general written information (1, 2). However there was evidence of some important benefits of PEd over PS and none for PS over PEd. There may be a substantial delay in time to the next bipolar episode in people with seven or fewer previous bipolar episodes, while time to mania was delayed and interpersonal function improved faster for all participants. Attendance at PEd groups was better than at PS groups and the lack of structure was seen as a reason for dropping out of PS.

The strengths of the study are its large size, multicentre design, independence of the research team, pre-registration, allocation concealment, complete follow up on the primary outcome over two years, careful matching of therapists and duration of treatment, minimisation of patients across treatment arms for the natural history of the condition, few unblindings, training and supervision to ensure fidelity to treatment, and full reporting of clinical outcomes identified by NICE as being relevant to patients and clinicians (1). Broad eligibility criteria and 22 groups at eight centres increased its generalisability but, compared to the Barcelona RCTs (6,7), only four weeks of euthymia were required compared to 6 months, there was more comorbidity and less experienced therapists were used, all of which may have reduced the effect size of PEd.

Limitations of the study are the low rate of completion of self-rated symptomatic and functional outcomes, moderate reliability of the assessment of mania symptoms, no formal rating of blinding, and the lack of recording of treatment sessions to absolutely ensure fidelity to treatment. We do not report overall time spent in relapse but it will be separately reported in an economic analysis. A limitation of the trial design is that there is no treatment-as-usual control group with minimal information giving, although such practice is not supported by NICE (1, 2). Given that the PS group included some approaches that may be components of effective psychological treatments for BD such as problem solving (1, 26), PS may have been more effective than treatment as usual.

The results confirm a recent meta-analysis of RCTs on psychoeducation (9) that concluded the first RCTs of group psychoeducation versus group support (6,7) may be outliers in showing a much greater treatment effect versus control treatment than subsequent RCTs When methodological issues from previous RCTs are addressed there is less evidence of clinical superiority of structured group psychoeducation versus unstructured group support. In a planned analysis, the current RCT demonstrated that in people with few previous bipolar episodes , PEd may have been more effective than PS against time to next depression episode and time to next bipolar episode, confirming findings from two post-hoc analysis of RCTs (17, 26) and two RCTs for psychological treatment confined to early onset BD (28, 29) . Previous RCTs of group psychoeducation versus group support may have shown a greater effect size on time to the next bipolar episode than the current study because more participants were recruited in the early course of their illness (6, 26). PEd may be more effective if early warning sign interventions are delivered earlier in the course because half the participants had dropped out by week 14 when these effective techniques (30, 31) were discussed and differences in time to mania relapse between the two groups start to emerge.

Group psychoeducation provides both general and tailored information and support from both health professional and service user perspectives at a relatively cheap price so it is an approach that may have merit in clinical practice, but not to the exclusion of other approaches that may deliver the same quality of information and support alongside medication (1). However, the optimised group support provided in this study is unavailable routinely in the United Kingdom in the precise form delivered in this RCT. Furthermore the effects of PEd on mania and interpersonal function may provide additional benefits to service users in work and family life, and to clinical services through reduced in-patient and crisis team involvement (1,31).

Although meta-analysis of previous RCTs suggests that group psychoeducation may increase time to relapse compared to treatment as usual, these RCTs were of low or very low quality so there remains some doubt requiring further research. Our results and the results of other recent psychological interventions (17, 27-29 suggest that the optimal provision of structured psychological interventions such as PEd early in the course of BD may have important benefits on the course of illness, and merits further research.

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Roles of the authors
All authors designed, interpreted data, wrote and approved the final version of the paper. RM, FL, LD, SP, CR and SJ obtained funding for the study. RM led the study in the East Midlands and FL for the North West site. LR was the trial co-ordinator. RL was the service user lead for the study, SP the qualitative analysis lead, CR led and supervised the statistical analysis. GL and HR led the data collection for the study. FH conducted the statistical analysis. RM, FL and SJ supervised the

interventions, and also supervised the data collection with LR and SP. RM led the writing of this manuscript.

Conflict of Interest.
None of the authors report any financial or personal conflict of interest.

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Figure 1. Flowchart of participants into the study from all sites and waves combined in group psychoeducation (PEd) and group support (PS) for bipolar disorder.

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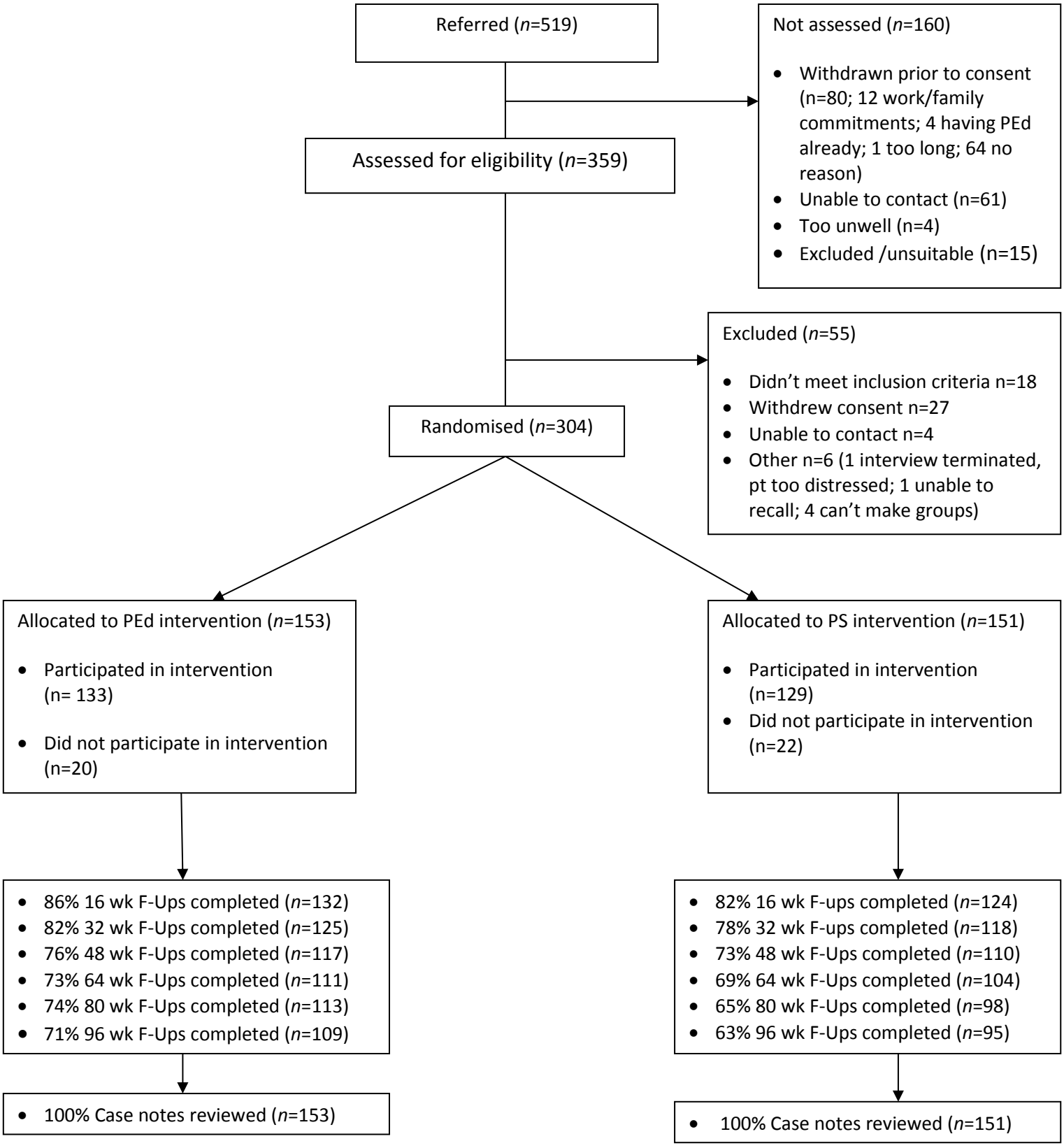

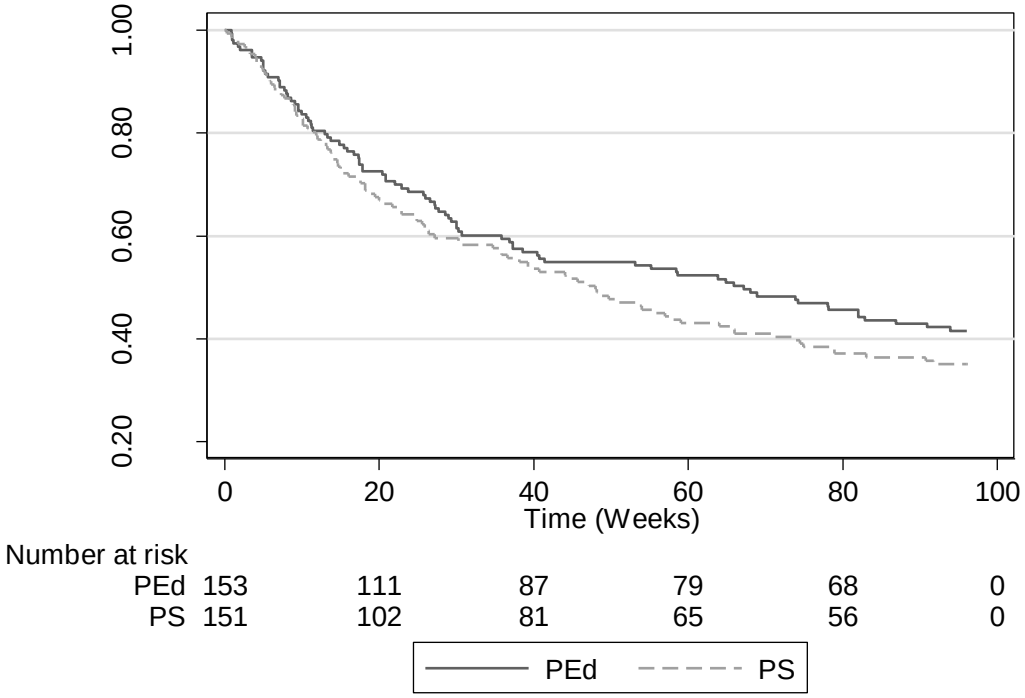

Figure 2. Kaplan-Meier estimates of time to first depression or mania-type bipolar episode in group psychoeducation (PEd) and group peer support (PS).

Figure 3. Kaplan-Meier estimates of time to first mania-type bipolar episode in group psychoeducation (PEd) and group support (PS)

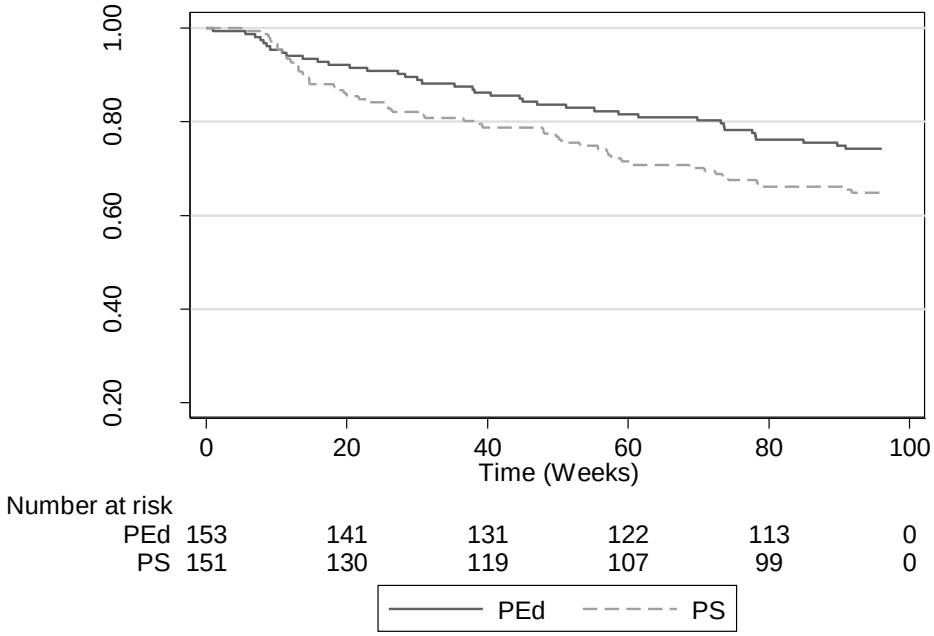

Figure 4 Kaplan-Meier estimates of time to first bipolar depression episode in group psychoeducation (PEd) and group support (PS).

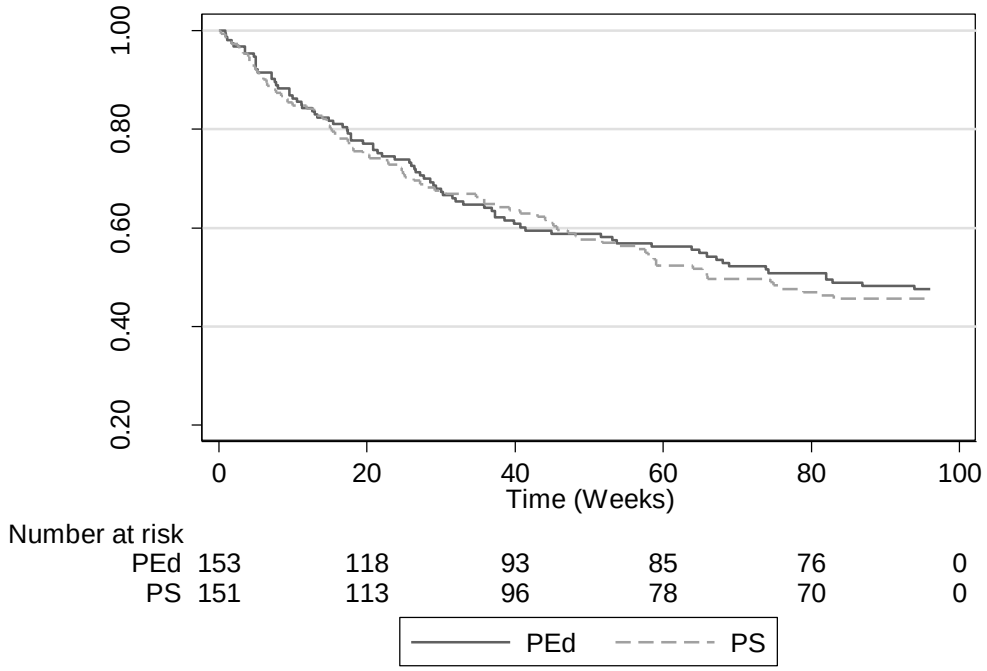

Table 1. Baseline characteristics in psychoeducation (PEd) and peer support (PS) groups.

Characteristic	**PEd, *n* = 153** ***n* (%)**	**PS, *n* = 151** ***n* (%),**
Mean age (SD)	44.2 (11.1)	46.5 (11.4)
Gender, female	92 (60.1)	85 (56.3)
No. previous bipolar episodes		
1-7	21 (13.7)	18 (11.9)
8-19	50 (32.7)	45 (29.8)
20+	82 (53.6)	88 (58.3)
Bipolar 1	114 (74.5)	129 (85.4)
Marital status		
Married/living as married	63 (41.2)	46 (30.5)
Never married	46 (30.1)	53 (35.1)
Divorced/separated/widowed	44 (28.7)	52 (34.4)
With children, one or more	90 (58.8)	93 (61.6)
Employment		
In full-time/part-time work	45 (29)	37 (24)
Unemployed/sickness/retired	108 (71)	114 (76)
Ethnicity: White British	140 (91.5)	138 (91.4)
Region		
North West	86 (56.2)	86 (56.9)
East Midlands	67 (43.8)	65 (43.1)
Group preference		
Prefer PEd	55 (35.9)	54 (35.8)
No preference	66 (43.1)	57 (37.7)
Prefer PS	29 (19.0)	35 (23.2)
Missing	3 (2.0)	5 (3.3)
Psychosis, lifetime	97 (63.3)	114 (75.5)
Any anxiety disorder		
Lifetime	87 (56.9)	75 (49.7)
Past month	68 (44.4)	57 (37.7)
Any alcohol abuse/dependence		
Lifetime	56 (36.6)	61 (40.3)
Past month	4 (2.6)	12 (7.9)
Any drug abuse/dependence		
Lifetime	10 (6.5)	21 (13.9)
Past month	2 (1.3)	2 (1.3)
Borderline/antisocial personality disorder	12 (7.8)	13 (9)

Baseline Medication		
Mood stabiliser	108 (70.5)	118 (78.1)
Antipsychotic drugs	83 (54.2)	84 (55.6)
Antidepressant drugs	71 (46.4)	71 (47.0)
Hypnotic/anti-anxiety	21 (13.7)	19 (12.6)
Baseline medication equivalences (mg/d)		
Chlorpromazine	188.2	182.8
Imipramine	83.6	80.4
Diazepam	2.25	2.43

Table 2**.** Number of sessions attended at PEd (*n* = 153) and PS (*n* = 151) groups

	Psychoeducation (*n* = 153)			**Peer support (*n* = 151)**		
Sessions attended	**No.**	**% each category**	**Cumulative %**	**No.**	**% each category**	**Cumulative %**
0	20	13.1	-	22	14.6	-
1-5	25	16.3	86.9	41	27.2	85.4
6-10	12	7.8	70.6	17	11.3	58.2
11-15	29	19.0	62.8	25	16.6	46.9
16-21	67	43.8	43.8	46	30.5	30.5