Reducing relapse and suicide in bipolar disorder: practical clinical approaches to identifying risk, reducing harm and engaging service users in planning and delivery of care – the PARADES (Psychoeducation, Anxiety, Relapse, Advance Directive Evaluation and Suicidality) programme

Steven Jones,1* Lisa Riste,2 Christine Barrowclough,2 Peter Bartlett,3 Caroline Clements,4 Linda Davies,5 Fiona Holland,5 Nav Kapur,4,6 Fiona Lobban,1 Rita Long,1 Richard Morriss,7,8 Sarah Peters,2 Chris Roberts,5 Elizabeth Camacho,5 Lynsey Gregg2 and Dionysios Ntais5

1Spectrum Centre for Mental Health Research, Faculty of Health and Medicine, Lancaster University, Lancaster, UK
2School of Psychological Sciences, University of Manchester, Manchester, UK
3School of Law and Institute of Mental Health, University of Nottingham, Nottingham, UK
4Institute of Brain, Behaviour and Mental Health, University of Manchester, Manchester, UK
5Institute of Population Health, University of Manchester, Manchester, UK
6Manchester Mental Health & Social Care NHS Trust, Manchester, UK
7Institute of Mental Health, University of Nottingham, Nottingham, UK
8Nottinghamshire Healthcare NHS Foundation Trust, Nottingham, UK

*Corresponding author s.jones7@lancaster.ac.uk

Declared competing interests of authors: Richard Morriss received personal fees for chairing the National Institute for Health and Care Excellence Guideline Development Group for bipolar disorder from 2012 to 2014.

Disclaimer: This report contains transcripts of interviews conducted in the course of the research and contains language that may offend some readers.

Published September 2018
DOI: 10.3310/pgfar06060
Scientific summary

The PARADES programme
Programme Grants for Applied Research 2018; Vol. 6: No. 6
DOI: 10.3310/pgfar06060

NIHR Journals Library www.journalslibrary.nihr.ac.uk
Scientific summary

Background

Bipolar disorder (BD) is a potentially life-long condition characterised by recurrent episodes of mania and depression and by significant mood problems between mood episodes. This condition costs the English economy £5.2B annually, largely as a result of incomplete recovery after inadequate treatment. The importance of improving mental health recovery is emphasised in the UK government’s *No Health Without Mental Health* document (HM Government. *No Health Without Mental Health*. London: Department of Health; 2011) and, more recently, in NHS England’s call to action on parity of esteem for mental health. (NHS England. *A Call to Action: Achieving Parity of Esteem*. London: NHS England; 2014.)

Rationale and objectives

The programme contains a series of linked studies to help reduce harm and improve outcomes for people living with BD across five workstreams (WSs), as follows.

**Pragmatic randomised controlled trial of group psychoeducation versus group peer support in the maintenance of bipolar disorder**

The National Institute for Health and Care Excellence (NICE) guidelines for BD recommend structured psychological treatment delivered by experienced therapists. NICE’s recommendation may be facilitated by group psychoeducation (PEd) delivered by care co-ordinators without extensive training in psychological therapy. Pilot work prior to this programme on group PEd, delivered by a clinician and an expert patient, supported its feasibility. The objectives of this stream were to evaluate whether or not group PEd is feasible and sustainable across different NHS sites and to evaluate whether or not group PEd is clinically effective and cost-effective compared with group peer support (PS).

**Psychological treatment of anxiety in bipolar disorder**

Anxiety disorders respond to individual cognitive–behavioural therapy (CBT) group CBT and supported self-help. Despite the efficacy of such approaches, current approaches to BD do not include therapy for anxiety symptoms despite the high rates of comorbid anxiety disorders in those with BD. The objectives of this stream were to understand the impact of, and what psychological help is required for, anxiety in bipolar disorder (AIBD) and to develop and evaluate the feasibility of CBT-informed, time-limited therapy for people with anxiety and BD.

**Psychological treatment of comorbid alcohol use in bipolar disorder**

Alcohol and substance use disorders are amenable to treatment with motivational interviewing (MI) and CBT. Despite the high prevalence of such comorbid problems in BD (in particular cannabis and alcohol use disorders), and their association with worse clinical outcomes, there has been little progress in developing integrated psychological interventions. The objectives of this stream were to explore the reasons for and impacts of cannabis and alcohol use in BD, and to develop and evaluate the feasibility of MI-CBT for alcohol use in those with BD.

**Suicidal behaviour in bipolar disorder**

Despite the prevalence of self-harm and suicide in BD, and the Department of Health’s emphasis on reducing these problems, research in BD in this area has been limited. No studies have examined how risk factors combine, and few have investigated the role of clinical management in BD. The objectives of this stream were to understand the risk of suicide in BD in NHS service settings, to understand the demographic-, clinical- and management-related risk factors for suicidal behaviour and to understand how these risk factors link together in self-harm or suicide in BD.
Is the Mental Capacity Act 2005 changing clinical practice for patients with bipolar disorder?

Patients with BD, especially those requiring inpatient treatment, often lose mental capacity in acute episodes. The Mental Capacity Act 2005 (MCA) (Department of Constitutional Affairs. Mental Capacity Act 2005. London: Department of Constitutional Affairs, HMSO; 2005) could be used to design care plans that help individuals with BD to ensure that they receive the treatment they want and avoid treatments they find unhelpful in acute episodes. There are also concerns about capacity assessment in BD, and ethical and practical issues about its implementation in a condition in which severe harm can arise but capacity loss may be brief. The objectives of this stream were to determine whether or not people living with BD are making use of the MCA, to determine whether or not the MCA promotes joint care planning in the event of capacity being lost and to examine the barriers and drivers at service user (SU) and staff levels to use of the MCA in general.

Methods

Pragmatic randomised controlled trial of group psychoeducation versus group peer support in the maintenance of bipolar disorder

A single-blind randomised controlled trial (RCT) compared the clinical effectiveness and cost-effectiveness of 21 weekly bipolar group PEd sessions delivered by two health professionals and a SU facilitator, plus treatment as usual (TAU), with group PS sessions delivered in the same way.

The trial was in two centres in England (East Midlands and North West). Patients were individually randomised to one of the two interventions with stratification by clinical site and minimisation in terms of their number of previous episodes.

The primary outcome measure was time to next bipolar episode using 16-weekly the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders longitudinal interval follow-up evaluation interviews.

A Cox proportional hazards model was fitted to the primary outcome measure. Longitudinal statistical models were fitted across follow-up time points to the secondary outcome scale data. Qualitative interviews were used to investigate the experiences of the group. A cost-effectiveness analysis was used to compare the relative costs and outcomes of the bipolar group PEd intervention with those of the bipolar PS control group.

Psychological treatment of anxiety in bipolar disorder

Phase 1
Semistructured interviews were carried out with individuals with BD and experience of anxiety symptoms to understand how they experienced anxiety and discover their preferred type of psychological treatment.

Phase 2
Focus groups were run to inform the development and delivery of the therapy to be trialled in phase 3.

Phase 3
A single-blind RCT was conducted to determine the feasibility and acceptability of the AIBD intervention compared with TAU. We also conducted a preliminary analysis of anxiety and mood outcomes.

Psychological treatment of comorbid alcohol use in bipolar disorder

Phase 1
Q-Sort methodology was used to explore experiences and consequences of substance use in those with BD.
Phase 2
Focus group meetings were held to inform the planned intervention.

Phase 3
A single-blind RCT was conducted to determine the feasibility and acceptability of the integrated intervention compared with TAU. We also conducted a preliminary analysis of alcohol and mood.

**Suicidal behaviour in bipolar disorder**

Phase 1
Phase 1 used data from a large national case series of individuals with BD who died by suicide to explore the overall characteristics of suicide in BD.

Phase 2
Phase 2 used a smaller case-control data set of current and recent inpatients to systematically compare the characteristics identified in phase 1.

Phase 3
Phase 3 used a cohort design to explore the characteristics of people with BD who self-harm.

Phase 4
Phase 4 used qualitative methods to further explore factors found to be important in the previous studies, how these and other factors are experienced on an individual level, and the role of Mental Health Services (MHS) in the prevention of suicidal behaviour in those with BD.

Is the Mental Capacity Act 2005 changing clinical practice for patients with bipolar disorder?
This WS included a:

1. national postal survey of psychiatrists in England and Wales, which covered experiences of receiving and applying MCA training
2. national postal survey of SUs with BD recruited through a SU organisation (Bipolar UK, previously Manic Depression Fellowship – the BiPolar Organisation) to explore the application of the MCA and related advance directives from a patient perspective
3. qualitative study of SUs and psychiatrists to examine, in greater detail, the issues faced by participants in advance planning.

**Key findings**

*Pragmatic randomised controlled trial of group psychoeducation versus group peer support in the maintenance of bipolar disorder*

Psychoeducation and PS are feasible to deliver in routine NHS care across inner-city, urban and rural clinical sites across two regions of England. Overall, the PEd and PS groups did not differ in terms of the primary outcome variable, namely time to the next bipolar relapse. However, there was evidence of a large effect favouring PEd over PS in delaying time to relapse (hazard ratio 0.28, 95% confidence interval 0.12 to 0.68) in the 13% (39/304) of participants with fewer than eight previous bipolar episodes.

There was a 35% probability of PEd being cost-effective, compared with PS, if decision-makers are willing to pay £30,000 to gain 1 quality-adjusted life-year.
Psychological treatment of anxiety in bipolar disorder

Phase 1
Participants highlighted the importance of a flexible integrated psychological approach to anxiety problems in the context of BD.

Phase 2
Focus groups indicated the importance of enhancing behavioural and cognitive self-management in flexible and collaborative sessions with high-quality support materials.

Phase 3
The AIBD intervention is feasible and is acceptable to, and valued by, participants, although the clinical outcomes were not significantly different from those of TAU.

Psychological treatment of comorbid alcohol use in bipolar disorder

Phase 1
There were indications that the reasons for substance use, and the after-effects of such use, differed between cannabis and alcohol users, with more negative effects in the latter group.

Phase 2
Focus groups highlighted the importance of therapy being non-judgemental, collaborative and normalising. Flexibility, setting and timing for sessions and very clear information on confidentiality were emphasised as enhancing engagement.

Phase 3
Motivational interviewing-CBT was feasible and was acceptable to and valued by participants. Clinical outcomes did not differ significantly between the trial arms.

Suicidal behaviour in bipolar disorder

Phase 1
Ten per cent of psychiatric patients who died by suicide had a primary diagnosis of BD. This group were more likely than those with schizophrenia or depression to be female, be aged > 45 years and have had a diagnosis for > 5 years.

Phase 2
Higher rates of depression, previous self-harm, adverse life events and comorbid alcohol and/or personality disorders were reported in individuals with BD who died by suicide than in those who did not.

Phase 3
A comparison of participants with BD who self-harmed with those who did not showed that the former group included more women in late middle age, higher levels of contact with MHS and a higher incidence of sleep disturbance and unemployment/long-term sickness.

Phase 4
Qualitative interviews with SUs with BD who had self-harmed and with the relatives of SUs who had died by suicide indicated that both groups prioritised fast access to good-quality mental health care.

Is the Mental Capacity Act 2005 changing clinical practice for patients with bipolar disorder?
Around 50% of psychiatrists surveyed indicated that they would not discuss advance directives to refuse treatment and the majority felt that the MCA had not increased advance planning in BD. SUs regard
advance planning as important but the MCA has only rarely been used. Both groups indicated that lack of support for advance planning was a factor, even for those individuals who were aware of the possibility of doing this.

Conclusions

The findings from the Psychoeducation, Anxiety, Relapse, Advance Directive Evaluation and Suicidality programme have a number of important implications for both clinical practice and further research in BD.

Clinical practice implications

1. If NHS trusts are looking to implement either group PEd or PS, then group PEd appears more acceptable, and there are some clinical benefits, especially for people early in the course of their BD. There is a demand for improved psychological therapy for people with BD with anxiety and/or alcohol comorbidities, which needs to be delivered with due recognition of the bipolar experiences people have. However, it may be less cost-effective to implement group PEd than PS in the NHS. The extent to which either intervention could be cost-effective will depend, in part, on the initial set-up and implementation costs.
2. The risk of suicide and self-harm is high compared with the general population, and illness/treatment factors are important.
3. Implementation of the MCA and use of advance planning in BD is poor and requires improved information sharing with SUs.

Research implications

1. Further research is required to evaluate individual versus group PEd early in the course of BD delivered in person and/or through the internet or video conferencing.
2. Definitive trials of integrated approaches to comorbid anxiety and alcohol use are suggested by the present research, although with alterations to the current interventions required.
3. The persistence over time and age of suicide and self-harm risk in BD highlights the importance of developing interventions to reduce this risk. An exploration of optimal mechanisms to improve their implementation and support by psychiatrists is warranted.

Trial registration

The trial entitled ‘Group psychoeducation versus group support using expert patients and clinical staff in the management of bipolar disorder’ is registered as the International Standard Randomised Controlled Trial Number (ISRCTN)62761948.

The trial entitled ‘Evaluating the feasibility and acceptability of a time limited anxiety in bipolar disorder’ is registered as ISRCTN84288072.

The trial entitled ‘Integrated psychological therapy for people with bipolar disorder (BD) and co-morbid alcohol use: a feasibility randomised trial’ is registered as ISRCTN14774583.

Funding

Funding for this study was provided by the Programme Grants for Applied Research programme of the National Institute for Health Research.
Programme Grants for Applied Research

ISSN 2050-4322 (Print)
ISSN 2050-4330 (Online)

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) (www.publicationethics.org/).

Editorial contact: journals.library@nihr.ac.uk

The full PGfAR archive is freely available to view online at www.journalslibrary.nihr.ac.uk/pgfar. Print-on-demand copies can be purchased from the report pages of the NIHR Journals Library website: www.journalslibrary.nihr.ac.uk

Criteria for inclusion in the Programme Grants for Applied Research journal
Reports are published in Programme Grants for Applied Research (PGfAR) if (1) they have resulted from work for the PGfAR programme, and (2) they are of a sufficiently high scientific quality as assessed by the reviewers and editors.

Programme Grants for Applied Research programme
The Programme Grants for Applied Research (PGfAR) programme, part of the National Institute for Health Research (NIHR), was set up in 2006 to produce independent research findings that will have practical application for the benefit of patients and the NHS in the relatively near future. The Programme is managed by the NIHR Central Commissioning Facility (CCF) with strategic input from the Programme Director.

The programme is a national response mode funding scheme that aims to provide evidence to improve health outcomes in England through promotion of health, prevention of ill health, and optimal disease management (including safety and quality), with particular emphasis on conditions causing significant disease burden.

For more information about the PGfAR programme please visit the website: http://www.nihr.ac.uk/funding/programme-grants-for-applied-research.htm

This report
The research reported in this issue of the journal was funded by PGfAR as project number RP-PG-0407-10389. The contractual start date was in October 2008. The final report began editorial review in January 2016 and was accepted for publication in November 2016. As the funder, the PGfAR programme agreed the research questions and study designs in advance with the investigators. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The PGfAR editors and production house have tried to ensure the accuracy of the authors’ report and would like to thank the reviewers for their constructive comments on the final report document. However, they do not accept liability for damages or losses arising from material published in this report.

This report presents independent research funded by the National Institute for Health Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, CCF, NETSCC, PGfAR or the Department of Health and Social Care. If there are verbatim quotations included in this publication the views and opinions expressed by the interviewees are those of the interviewees and do not necessarily reflect those of the authors, those of the NHS, the NIHR, NETSCC, the PGfAR programme or the Department of Health and Social Care.

© Queen’s Printer and Controller of HMSO 2018. This work was produced by Jones et al. under the terms of a commissioning contract issued by the Secretary of State for Health and Social Care. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Published by the NIHR Journals Library (www.journalslibrary.nihr.ac.uk), produced by Prepress Projects Ltd, Perth, Scotland (www.prepress-projects.co.uk).
**NIHR Journals Library Editor-in-Chief**

**Professor Tom Walley**  Director, NIHR Evaluation, Trials and Studies and Director of the EME Programme, UK

**NIHR Journals Library Editors**

**Professor Ken Stein**  Chair of HTA and EME Editorial Board and Professor of Public Health, University of Exeter Medical School, UK

**Professor Andrée Le May**  Chair of NIHR Journals Library Editorial Group (HS&DR, PGfAR, PHR journals)

**Dr Martin Ashton-Key**  Consultant in Public Health Medicine/Consultant Advisor, NETSCC, UK

**Professor Matthias Beck**  Professor of Management, Cork University Business School, Department of Management and Marketing, University College Cork, Ireland

**Dr Tessa Crilly**  Director, Crystal Blue Consulting Ltd, UK

**Dr Eugenia Cronin**  Senior Scientific Advisor, Wessex Institute, UK

**Dr Peter Davidson**  Director of the NIHR Dissemination Centre, University of Southampton, UK

**Ms Tara Lamont**  Scientific Advisor, NETSCC, UK

**Dr Catriona McDaid**  Senior Research Fellow, York Trials Unit, Department of Health Sciences, University of York, UK

**Professor William McGuire**  Professor of Child Health, Hull York Medical School, University of York, UK

**Professor Geoffrey Meads**  Professor of Wellbeing Research, University of Winchester, UK

**Professor John Norrie**  Chair in Medical Statistics, University of Edinburgh, UK

**Professor John Powell**  Consultant Clinical Adviser, National Institute for Health and Care Excellence (NICE), UK

**Professor James Raftery**  Professor of Health Technology Assessment, Wessex Institute, Faculty of Medicine, University of Southampton, UK

**Dr Rob Riemsma**  Reviews Manager, Kleijnen Systematic Reviews Ltd, UK

**Professor Helen Roberts**  Professor of Child Health Research, UCL Great Ormond Street Institute of Child Health, UK

**Professor Jonathan Ross**  Professor of Sexual Health and HIV, University Hospital Birmingham, UK

**Professor Helen Snooks**  Professor of Health Services Research, Institute of Life Science, College of Medicine, Swansea University, UK

**Professor Jim Thornton**  Professor of Obstetrics and Gynaecology, Faculty of Medicine and Health Sciences, University of Nottingham, UK

**Professor Martin Underwood**  Director, Warwick Clinical Trials Unit, Warwick Medical School, University of Warwick, UK

Please visit the website for a list of editors: www.journalslibrary.nihr.ac.uk/about/editors

**Editorial contact:** journals.library@nihr.ac.uk