

PB-PG-0609-16166 – NIHR Research for Patient Benefit Programme – Final report

Project title: Early identification and treatment of young people at high risk of recurrent mood disorders: a feasibility study

Authors: Professor Jan Scott - Newcastle University

Dr Paul McArdle - Northumberland, Tyne and Wear NHS Foundation Trust

Dr Thomas Meyer - University of Newcastle upon Tyne

Dr Aditya Sharma - Northumberland, Tyne and Wear NHS Foundation Trust

Dr Iain Macmillan - Northumberland, Tyne and Wear NHS Foundation Trust

Plain language summary

Despite 15-25 years being the peak age of onset for recurrent depression or bipolar disorders (BD), recognition of mood disorders (and differentiating them from transient distress) and/or the introduction of appropriate treatment are frequently delayed. This study examined ways to identify young people at high risk of repeated episodes of mood disorder and to work out whether they would get recurrent depression or BD. Also, we developed a therapy that could be offered to young people with 'emerging mood disorders' and we talked to those who are at 'above average' risk of getting these problems, to ask their views about future services or interventions. As well as working on our study, we collaborated with teams doing similar research in Australia, the USA, France, Norway and Germany. Interestingly, it appears that there are many common findings internationally. For example, even at a very early stage in the development of recurrent mood disorders, young people are already significantly impaired in their day to day functioning. Furthermore this problem is worsened if the young person tries to cope with their mood problems by using harmful amounts of alcohol or illicit drugs. We found that 20-30% of mood disorders developed into BD and this was most likely to occur in those with a family history of BD, with cyclothymia (a personality style characterised by fluctuating cycles of up and down moods), who had experienced depressions at an earlier age, and/or if they had recently experienced some milder symptoms of mania (that were similar to those seen in mania, but that did not add up to the full diagnosis). Young people who were at risk of BD because they had a parent with BD wanted both help to cope with the times when their parent was unwell, as well as help to learn how to cope better with any stress they experienced themselves. The young people were also clear that if they were 'at risk' of BD (but did not actually have BD), they were more likely to accept a psychological therapy rather than the medications used to treat those people who definitely have a BD diagnosis. We reviewed the types of therapies available for young people at risk of BD or with an emerging mood disorder and have adapted the approaches to include sleep hygiene, emotional coping, physical health and reduction of harmful use of drugs and alcohol. Overall, the study has delivered a screening tool for BD and a therapy acceptable to these young people.

Keywords

bipolar, at risk, early intervention, screening, mood disorders, CBT, identification, prospective

Summary of research findings

Study Aim 1: Retrospectively assess the number of and presentation of clinically diagnosed cases of mood disorders across a range of NHS settings over the preceding 2 years.

We were unable to answer the first goal exactly as initially planned (see next section for details), but we agreed with the RfPB manager on the following approach-

1. We would ask the NHS data managers to give 'ball park' figures on the prevalence of key symptoms related to bipolar disorders across 16-25 year olds. We would then try to construct clinical histories for a range of levels of symptoms e.g. individuals with single reports of depression, individuals with persistent recordings of depression, individuals identified as having depressive episodes, etc.
2. We would undertake a systematic review of the literature to address the original question we had posed.

With regard to item 1, we found that 70% of 16-25 year olds report depressive symptoms on at least one occasion, about 48% have persistent reports of depression and about 39% probably meet criteria for depression. Over one year, about 50% of these individuals were discharged, and about 30% dropped out of the services. Crude estimates suggested transition to BD was as frequent in those who were discharged as those who were in continuous treatment (we do not have enough data to know about dropouts). However, the reliability and validity of these data were insufficient to allow publication at this stage. Also, the data managers have not been able to give more detailed prior histories due to time issues and pressure of other work (please note we offered to pay for out of hours work, but this was deemed inappropriate, as the managers felt this work did fit within the terms of reference of department work. As such, it was listed as work to be done when time was available- but there have been many issues with the 'roll out' of RIO across the Trust and at the time of writing the work is incomplete. The data managers have stated they will still try to help to do this work and McCardle is liaising about the options).

With regard to item 2, the systematic review showed that alcohol and substance use may be associated with early onset of mood symptoms and the presence of subthreshold bipolar symptoms increases the risk of developing harmful substance use (i.e. the problems are bi-directional). This suggests screening in youth drug and alcohol services should be considered.

The review also showed that the best predictors of transition to BD in young people are: cyclothymia with a family history of BD and/or a prior history of one or more depressive episodes and evidence of subthreshold manic symptoms. (These findings are now confirmed by the data from the current study). Importantly, a childhood history of ADHD or of paediatric or juvenile BD was not a strong predictor of later BD in adolescence or early adulthood.

STUDY AIM 2: Prospectively examine the feasibility and acceptability of using self-rating tools to detect mood episodes and identify those at high risk of recurrences.

Although an initial plan for the use of screening instruments had been undertaken prior to the study, we noted that data increasingly suggested problems in the reliability of these tools in younger adults with emerging BD (rather than older adults with established mood problems). We therefore undertook a systematic review to identify appropriate screening instruments for adolescent onset mood disorders and assessed the validity of measures specifically used to screen for BD, risk factors for bipolarity, or a prior history of depressive, hypomanic or manic episodes. The systematic review identified only a small number (n=11) of studies that

adequately targeted the defined age group. The majority of instruments reviewed showed sub-optimal screening properties when applied to adolescents and young adults. We have published these findings and have collaborated with other groups in testing the best tools to use.

For our study, we were able to select established tools such as the HCL along with a combination of tools that examine personality traits or temperament (such as the General Behavioural Index; GBI), as these appear to perform better than those assessing discrete symptoms or episodes.

Our preliminary analyses of the study data suggest that the combination of screening measures with high sensitivity with ones that demonstrate high specificity should be included in a comprehensive assessment. If only one measure is to be selected, the GBI is the best available measure. However, the disadvantage is that it has about 73 items, and attempts to develop a briefer version are proving difficult. (We are now collaborating on an 'Item response' study to see if we can replicate findings for a 14-item version).

STUDY AIM 3: Assess symptoms, quality of life, service use and stability of diagnosis over one year.

We recruited 100 individuals to the study.

The overall transition rate was about 25% (being about 30-34% in secondary care cases). Many cases who developed BD and most of those who had a further depression had been discharged from the services and over 30% were re-referred via crisis services (suggesting inadequate understanding amongst clinicians of the risk factors for relapse or transition to BD).

Transition to BD occurred most often in those attending secondary care services who had a more severe depression and evidence of cyclothymia or subthreshold manic symptoms. Family history of BD was a good predictor of recurrent mood episodes, but did not predict specifically that the course of illness would be BD rather than unipolar. Lower rates of transition to BD were observed in primary care, but recurrent depression was common in these participants.

These preliminary findings have been presented at meetings on early intervention and at the RCPsych and the study investigators have been developing simple training packs to improve recognition of BD or risk factors for development of BD.

Detailed analysis of service use is currently ongoing (being delayed by the fact that there were changes in RAs and key personnel initially doing that analysis).

STUDY AIM 4: Explore the uptake, acceptability and outcomes of a CBT intervention specifically for individuals at high risk of recurrent mood disorder.

A subsample of 15 individuals were invited to participate in therapy sessions. IN this pilot study, 5 individuals dropped out, but the other 10 completed over 70% of the sessions offered. The sessions led to reduction in general stress and problems (daily hassles) as well as improvements in mood, sleep and levels of day-time activity.

Feedback from therapy participants identifies that this approach is probably an improvement over current therapies being offered to young people at risk of BD (as these tend to be derived from adult therapies for people with established BD).

Feedback from the young people helped identify that key targets for change should include both emotional (thought and mood regulation problems such as rumination) and physiological features (such as circadian-sleep changes e.g. delayed sleep phase). In

addition, many of the participants reported that they found the sessions on physical health (obesity etc) and substance use very helpful.

The findings have informed the development of a draft therapy manual and we are liaising with groups in the UK and abroad on a further project to formally test the therapy.

STUDY AIM 5: Develop young people panels to discuss their (and parental) views on acceptable service models".

As discussed with the RFPB manager, the original user representative was unable to undertake the work on the young people's panel as we had originally envisaged.

However, at a later date we were able to recruit a youth worker who held preliminary discussions with school representatives and with young people at risk of BD (but who had never received any mental health services and had no history of psychological problems). Following these discussions it was determined that rather than a 'panel', the youth worker would undertake individual interviews with individuals aged up to 25 years who had not themselves any mental health services and had no history of psychological problems, but who had a parent with BD. The aim was to determine what types of services and interventions they would like to have available and/or would be most likely to use.

These young people at risk of BD identified the following issues in regard to their need for services: (a) as they had a parent with BD (one of the key risk factors for developing BD), they would have liked more help to know how best to help that parent and advice on how they should cope during periods when their parent was unwell; (b) The young people were not certain if they wanted access to special services for those at risk but without symptoms- some thought it a good idea, others worried it may be stigmatising. Interestingly, the parents were keen for their offspring to receive 'monitoring' and have access to specific early intervention services and felt early input was more important than the potential for being stigmatized; (c) Some of the individuals interviewed were living independent lives, including cohabiting with a partner. However, these young adults were unclear on whether they thought there was a need for a 'genetic counselling' approach for those considering parenthood (to discuss possible inheritance of BD or recurrent unipolar disorder); (d) Preferences for interventions clearly favoured psychological rather than pharmacological interventions.

Several publications have arisen from this work and the CI and some of the Co-PIs are now participating in multi-centre grant applications for further studies on our new model of CBT-R and whether it is possible to delay or reduce transitions to BD or recurrent unipolar disorders.

References published by the researchers on the issues discussed

Scott J, Meyer TD. Brief Research Report: A Pilot Study of Cognitive Behavioral Regulation Therapy (CBT-REG) for Young People at High Risk of Early Transition to Bipolar Disorders. *Front Psychiatry*. 2021 Jan 22;11:616829.

Tacchi MJ, Heggelund J, Scott J. Predictive validity of objective measures of physical fitness for the new onset of mental disorders in adolescents and young adults. *Early Interv Psychiatry*. 2019 Dec;13(6):1310-1318.

Davison J, Scott J. Should we intervene at stage 0? A qualitative study of attitudes of asymptomatic youth at increased risk of developing bipolar disorders and parents with established disease. *Early Interv Psychiatry*. 2018 Dec;12(6):1112-1119.

Scott J, Marwaha S, Ratheesh A, Macmillan I, Yung AR, Morriss R, Hickie IB, Bechdolf A. Bipolar At-Risk Criteria: An Examination of Which Clinical Features Have Optimal Utility for Identifying Youth at Risk of Early Transition From Depression to Bipolar Disorders. *Schizophr Bull*. 2017 Jul 1;43(4):737-744.

Scott, J., Grierson, A., Gehue, L. et al. Can consumer grade activity devices replace research grade actiwatches in youth mental health settings?. *Sleep Biol. Rhythms* 17, 223–232 (2019).

Geoffroy PA, Scott J. Prodrome or risk syndrome: what's in a name? *Int J Bipolar Disord*. 2017 Dec;5(1):7. Epub 2017 Apr 10.

Waugh MJ, Meyer TD, Youngstrom EA, Scott J. A review of self-rating instruments to identify young people at risk of bipolar spectrum disorders. *J Affect Disord*. 2014 May;160:113-21.

Meyer TD et al. The Hypomania Checklist (HCL) - systematic review of its properties to screen for bipolar disorders. *Compr Psychiatry*. 2014 Jul;55(5):1310-21.

Scott J et al. Functional impairment in adolescents and young adults with emerging mood disorders. *Br J Psychiatry*. 2014 Nov;205(5):362-8.

Douglas J, Scott J. A systematic review of gender-specific rates of unipolar and bipolar disorders in community studies of pre-pubertal children. *Bipolar Disord*. 2014 Feb;16(1):5-15.

Vallarino M.....Scott J. An evidence map of psychological interventions for the early stages of bipolar disorders. *Lancet Psychiatry*, 2015. 2, 548-554.

Loftus J, Etain B, Scott J. Offspring studies in bipolar disorders: What can we learn? In press. *Advances in Psychiatric Treatment*. 2016, 22, 176-185.

Patient and public involvement

We have had considerable interest from advocacy groups that specifically target young people eg Young Minds in UK. In addition, Professor Scott was invited to a youth mental health conference to give a plenary lecture to young people who were service users and to youth workers at the 'headspace' conference in Australia. The Bipolar Organisation (local newcastle branch) has been supportive and the national organization has agreed to distribute a follow-up questionnaire next year (regarding access to services and delays in diagnosis etc). Young people have been very helpful in informing our ideas about which

screening tools to use (they give feedback on eg readability/acceptability etc). The youth worker has been truly fantastic in working with schools and community groups to identify young people to be involved in interviews to discuss their ideas and beliefs about what is needed to support individuals who may be at risk of recurrent mood disorders at a very early stage (when there is not certainty that they will ever develop problems).

Data sharing statement

See link [<https://www.nihr.ac.uk/documents/nihr-position-on-the-sharing-of-research-data/12253>] for the NIHR position of the sharing of research data. The NIHR strongly supports the sharing of data in the most appropriate way, to help deliver research that maximises benefits to patients and the wider public, the health and care system and which contributes to economic growth in the UK. All requests for data should be directed to the award holder and managed by the award holder.

Disclaimer

This project is funded by the National Institute for Health Research (NIHR) under its Research for Patient Benefit (RfPB) Programme (Grant Reference Number PB-PG-0609-16166). The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

This final report has not been peer-reviewed. The report was examined by the Programme Director at the time of submission to assess completeness against the stated aims.

This project was carried out between January 2012 and July 2015.