Improved mental health among LABILE study participants: a qualitative exploration

Abstract

Results of the LABILE trial showed no difference between people with borderline personality disorder who were prescribed lamotrigine, and those on placebo. However, most study participants experienced sustained improvement in their mental health during the trial.

We conducted a thematic analysis of qualitative data from interviews with 47 LABILE study participants to identify factors that may have contributed to this improvement. We identified three main themes: initial reasons and expectations regarding trial participation, patients’ experiences of the trial, and areas of change.

Reasons for participating in the trial included a search for consistent and stable professional care as well as altruistic motives. Improvements in symptoms over the course of the trial were explained by several factors including consistency provided by the research team, salience of the social context, and the availability of alternative support networks.

Whilst participants appreciated the autonomy provided by the voluntary nature of the trial, they felt that improvements stemmed from the ‘structure’ brought about by their actively engaging in the study.
This study highlights the importance of clear, and transparent communication when treating people with borderline personality disorder. Mental health professionals should ensure that services for people with borderline personality disorder are consistent and structured.
Introduction

Borderline personality disorder (BPD) is a serious and debilitating mental health condition; around 10% of patients seen in outpatient mental health settings are diagnosed with BPD (1). The problems experienced by people with this condition are pervasive, and include impulsivity, affective instability, chronic fears of abandonment and unstable interpersonal relationships (2). Levels of substance misuse, acts of deliberate self-harm and suicide are also high among this group (3).

Whilst there is no licenced medication for treating people with borderline personality disorder, psychotropic medications including mood stabilisers are widely prescribed. Up to 90% of patients are taking psychotropic medication and about two thirds are on long-term use of antipsychotics (4, 5).

The LABILE (Lamotrigine And Borderline personality disorder: Investigating Long-term Effects) trial was set up to explore the clinical and cost effectiveness of lamotrigine compared to placebo (6). Lamotrigine is an anticonvulsant licenced and used for treatment of bipolar disorder (7). Previous small scale studies have suggested some benefits including reduced impulsivity and affective instability compared to placebo when used in people with borderline personality disorder (8, 9).
The LABILE study was a large scale two-arm, parallel group, double-blind randomised controlled trial of lamotrigine versus placebo for adults with borderline personality disorder. A total of 276 patients were allocated to either an active treatment group in which they were prescribed up to 200mg of lamotrigine per day (400mg if also taking combined oral contraceptives), or to a placebo group. The study’s outcome measures assessed over a 12-month period, focused on core symptoms of borderline personality disorder as well as depression, social functioning and health-related quality of life. The findings of this trial showed that core symptoms of borderline personality disorder improved over the first three months, irrespective of whether participants were taking the active trial medication or placebo. There was no statistically significant difference between the two arms of the trial. This improvement was maintained throughout the course of the trial (10).

The findings of the LABILE study raise questions about what could have contributed to the improved mental health of most study participants, and whether aspects of the trial that were valued by study participants could be adopted in normal clinical practice outside of the context of the trial.
Objectives
To examine what aspects of participation in the LABILE trial may have contributed to the improvement in symptoms of borderline personality disorder among those who took part in the LABILE study.

Methods
This was a qualitative study that was conducted in parallel with a multicentre phase III trial of lamotrigine versus placebo for people with borderline personality disorder. The qualitative component was planned in the early stages of the recruitment phase of the trial. We aimed to develop a better understanding of the experiences of study participants in order to generate data that could support future trials of pharmacological interventions for people with borderline personality disorder.

Study sample
Participants in the LABILE trial, were aged 18 or over and were in contact with secondary care mental health services in England. To be eligible to take part in the LABILE trial, potential participants had to meet criteria for borderline personality disorder according to the DSM-IV criteria (10-12),
and were excluded if they met criteria for bipolar affective disorder or psychotic disorder.

For this qualitative study, we selected participants from all three of the main study centres in the LABILE trial. We selected a diverse sample of study participants, using purposive sampling strategy, accounting for gender, age and ethnicity. We aimed to include up to 45 participants, up to 15 from each of the three study sites to ensure representation across different parts of the country.

Interviews were conducted at some point between the participants’ six-month and 12-month follow-up appointments. We chose to conduct interviews at this time because we judged that participants would be familiar with study procedures by then, but also able to recall their experiences of the process of recruitment and their motivation for taking part in the study.

All LABILE trial participants who took part in this qualitative study as well as the researcher obtaining the data were blind to the trial allocation status at the time of the interview.
Study procedures

We obtained approval for this study from the London Central Research Ethics Committee (Ref: 12/LO/1514) and from the Research and Development departments of the participating NHS Trusts prior to the start of data collection.

We developed a draft topic guide and shared it with the trial management group, which included members of the research team from all three recruiting centres as well as researchers and service user representatives. Researchers in each study centre used the topic guide flexibly in digitally recorded semi-structured interviews to elicit information regarding: 1) the participants’ expectations before the trial and their life circumstances at the time of their participation; 2) their reflections about the LABILE trial and the study medication; and 3) any areas of change they had observed since the start of the trial. These interviews were then transcribed, and verbatim transcripts were used to analyse the data. We used thematic analysis approach to analyse data from the transcripts; as noted by Braun and Clarke, ‘rigorous thematic approach can produce an insightful analysis that answers particular research questions’ (13).

Two independent researchers coded the first six transcripts and discussed their codings to develop initial categories. This involved an initial stage of detailed sentence-by-
sentence coding to ensure that we missed no potentially important information and to devise a coding frame. We then applied the coding frame to the rest of the data so that it could be further improved through an iterative analysis process. In the next stage we identified the recurring themes; and grouped them together. This yielded the final three themes and the related sub-themes presented in the results section. We continued the analysis until the point of theoretical saturation was reached.

**Results**

We interviewed a total of 47 study participants from the three main study centres in the LABILE trial. The study sample comprised 32 women and 15 men, including seven participants from personality disorder specialist services, and the age range was between 25 and 60 years old. In terms of trial allocation status, 26 participants were from the active arm of the trial, and the remaining 21 from the control arm. Interviews were conducted face to face by researchers and clinical studies officers (CSO’s) at each study site. The duration of interviews varied between 45 and 90 minutes.

To ensure anonymity, the participant identifiers accompanying direct quotes will be restricted to the age, gender and
allocation status of each trial participant, e.g. M45P1 indicates that the participant is male, 45 years old, part of the placebo group and recorded as participant 1 of 47.

We identified three main themes: 1) Initial reasons and expectations regarding trial participation, 2) Participants’ experience of the trial, and 3) Areas of change. The main themes to emerge from the data were further divided into relevant sub-themes and are presented in Table 1.

Table 1: themes and sub-themes

<table>
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Initial reasons and expectations regarding trial participation

The first theme focuses on the reasons participants indicated for choosing to take part in the trial, and any specific outcomes they expected to achieve by participating. The sub-themes in this category reflect the participants’ motivation to take part in the LABILE trial: desperation; search for gaining stability; and altruism. The subthemes in this category are interwoven, in that most participants expressed their frustration with lack of available medication for borderline personality disorder and subsequent feelings of helplessness and desperation for taking any opportunity to try new medications/interventions. Some participants explicitly mentioned that they took part in the trial hoping to ‘gain stability’ and/or improvement in their specific symptoms.

Desperation

The most commonly reported reason for taking part in the trial was ‘desperation’, due to lack of currently available treatments which left participants feeling helpless:

“I’d always kind of held this personal frustration that the diagnosis I had, that there was no medication for it...” – F31P6
“I was more than happy to [take part] because there is nothing that...there aren’t any medications for borderline personality disorder and after 10 years of having been diagnosed with it and not coping... there was a chance that this medication could work” – F30L7

**To gain stability**

Participants hoped to achieve some level of stability both in terms of their clinical symptoms as well as continuity of care with a mental health team. Reasons given for taking part were associated with the positive expectations about the treatment that was being tested in the trial. Initial participant attitudes towards the trial medication ranged from pragmatic expectations about the impact on specific symptoms, to higher hopes associated with wanting a “quick fix”.

“I expected it to help me. I thought my anger issues and self-harming would be helped.” – F32P30

“I was seeing the psychiatrist when I first heard about the trial, I wanted some medication, I wanted something, you know as much as I was kind of willing to, put in the work of the therapy and that kind of intervention I think I will go through times where I just think God, I just want something that might make me feel better without
having to like make an effort or have to engage in it – F31P6

“It would mean that I’d have a bit of stability with mental health services for a year.” – M45L16

Altruism

Most of the participants indicated that they also had altruistic motivations, by commenting that they felt that they wanted to help researchers find an effective medication that could be used to treat other people with this condition. However, such altruistic reasons were generally secondary to other reasons; for example, the idea that the trial would bring more stability to their lives.

“I know it sounds a bit la-di-da but it’s kind of that trying to contribute to making things better for other people too…” F28P1

“. . . it’ll probably make me sound like a real martyr, but I think in the long run, you know the fact that people are in so much difficulty and there is nothing you can really do about it . . . If there’s something like, you can find out, whether it does relieve a pressure off of those people; then it’s worth doing” F24L6
**Participants’ experience of the trial**

Overall, people who participated in the LABILE trial, held a positive view regarding trial participation. Most participants appreciated the ‘caring’ attitude of the research team, organisation of the trial, and that participants were kept well-informed about the trial structure. This theme explores the comments and criticisms made by the participants when asked about their experience of the LABILE trial. It is split into three sub-themes, which focus on two key aspects of the trial, the assessment interviews and the organisation / process of the trial as well as the overall experience with the trial (autonomy, structure, and support).

**Assessment interviews**

The assessment interviews were generally well-received among the trial participants. Some believed that the thorough nature of assessments was helpful to understand their condition better. Some went as far as attributing the improvements in their symptoms to the assessment sessions and the time researchers spent listening to them.

“I don’t think it’s the pills or anything, it’s me personally coming here [for the assessments], getting to talk to you, you listen - you made me feel good” – M41L45
However, some participants stated that some of the assessment questions were ‘too intrusive’, and others criticised the length of the interviews:

“There was a lot of questions, I mean there was A LOT of questions” – F40P47

Process and organisation of the trial

The general process of the trial was discussed at length by some participants. Some mentioned factors that made it difficult for them to continue their participation in the trial. One of the main criticisms of the trial focused on difficulties participants had when collecting the study medication. Furthermore, some explained how factors such as the size of the trial tablets, had a negative impact on their willingness to continue with the trial:

“Why do they make the tablets so big? When I first saw them I thought I’d never manage!” – F53P21

Autonomy, Structure, and Support

Despite the criticisms, a common remark regarding the general experience with the trial was that it provided the stability and support that many participants were hoping to gain:

“You’ve been in constant contact, you’re always available, and if you’re not available somebody has been available.” – F36P39
Most participants also referred to the voluntary nature of the trial and ‘sense of autonomy’ with regards to their taking part in the LABILE trial.

When asked directly, most participants agreed that they would recommend participation in a drug trial to friends and family:

“I would recommend it straight away because, I’ve benefited so much from it.” – M48P10

**Areas of change**

This theme explores the aspects of the participants’ mental health that improved over the course of the LABILE trial, and any possible reasons for the observed / perceived changes. The sub-themes explore the salience of each participant’s social context, and the availability or lack of alternative support networks.

**Increased confidence to ask for help**

A commonly reported outcome of the trial was one of increased confidence and self-esteem; participants stated that they felt more secure and content with themselves than they did before the trial. The increased confidence would also translate into feeling more able to ask for help from healthcare professionals. Another key finding was that some participants
had observed a reduction in their anxiety or other symptoms that previously affected their social lives:

“I seem to be more able to push past the anxiety and panic about contacting the friends that I haven’t talked to for a month.” – M45L16

**Salience of social context**

The individual circumstances that the study participants were coping with before taking part in the trial varied greatly. Some, reported that they were struggling to deal with serious circumstances at the time, such as domestic abuse or serious financial difficulties.

Some participants were explicit in that the progress they made during the trial was not due to the trial medication; instead, they believed it was attributable to their own life decisions.

“Whether I’m on it or not, I think I’d have still made the progress that I’ve made because of the life choices I made.” – F30L35

This participant elaborated further, indicating that her stressful marriage was the primary cause of her mental distress and mood instability:
“I felt trapped in a marriage so the fact that I made that decision (to separate) probably had more of an impact on me becoming more stable than the medication.” – F30L35

Availability of alternative support networks

It became apparent that several trial participants sought comfort and reassurance from others as a key aspect of their efforts to improve their mental health. For example, some participants openly expressed satisfaction about their ability to confide in a close friend or their psychiatrist, while others lamented the fact that they felt entirely alone:

“It could probably be not the pills they need, they need more... maybe they need someone to talk to... if I cannot talk to my partner or my kids, maybe there could be someone they could trust.” – M41L45
Discussion

In this qualitative study, we explored the experience of participants in a large scale randomised trial of lamotrigine versus placebo among people with borderline personality disorder. The participant experience of the LABILE trial was largely positive, although there were some critical and constructive comments regarding the trial structure, and ways it could have been improved.

Most participants mentioned ‘desperation’ as one of their motives for taking part in the LABILE trial, in the hope that trial medication might make a difference. Previous research has repeatedly highlighted the lack of good quality evidence for the effectiveness of pharmacological treatment for BPD (14, 15). However, the rate of prescription is disproportionately high, despite the side-effect profile of the prescribed medication (14), and the poor rate of physical health checks among people with personality disorder (16).

Many patients participated in the trial to gain stability, and this was often reflected in their attitudes towards the trial and the expectations they held about possible outcomes. They thought that ‘stability’ was achieved through regular contact with the research team for the duration of the study. This was
complemented by the clarity with which important information about the trial structure was conveyed.

Participants received an assessment at baseline, 12, 24 and 52 weeks which took about 90 minutes. Trial medication was provided to participants every two weeks during the titration period. Once the maintenance dose was reached, further trial medication was issued either four-weekly or fortnightly, depending on assessment of risk of intentional overdose. Prior to issuing any new supply of trial medication, researchers contacted the participants to enquire about any adverse events and establish if there had been breaks in taking the trial medication. Many participants in the trial, received their study medication either by post or in person by the research staff. This meant that participants had more frequent contact with staff than is usual in normal clinical practice.

The key aspects of the trial that were appreciated by participants included the way in which they felt generally well-informed about the process of the trial, the frequency of interview sessions, and the approachability and friendliness of the research staff. The latter reflects the conclusions of previous research (17, 18) regarding the importance of positive relationships between patients with borderline personality disorder and healthcare professionals in eliciting long-term recovery.
Our findings about the value of ‘structure’ are corroborated by previous reports highlighting the value of structured treatment and care for people with borderline personality disorder (19, 20).

The positive expectations of most patients who took part in the trial are important when considering reasons why many subsequently experienced improvements in their mental health. Several studies that have examined the placebo effect (21-23) have reported that positive outcomes are more likely when people have positive expectations beforehand.

However, the placebo effect is a phenomenon that is still far from fully understood. It is generally considered to be a physiological response evoked by the mindset of the individual, although there is no universally agreed definition for the term (22). It has been estimated that as many as 90% of medical conditions can be at least partially influenced by the placebo effect, and neurobiological research over the past few decades has shed some light on the underlying mechanisms behind it (24). Distinct areas of the brain associated with anxiety, pain, and reward have been implicated (23), but current knowledge of the mechanisms through which the placebo effect manifests itself is still at a relatively rudimentary stage in research literature.
Most participants in the LABILE trial experienced some improvement in their mental health, and this was usually attributed to the trial medication, the availability of external support, or to changes in their life circumstances. The availability of alternative support networks and coping strategies varied considerably among participants. It became clear that such support networks were central to many participants in helping them cope better at times of crisis. This further validates conclusions made in previous literature (25, 26).

Several study participants identified changes in their social environment, as the cause of improvements in their mental health rather than to study medication. This observation emphasises the importance of social as well as psychological interventions in treatment planning for people with borderline personality disorder. Nidotherapy provides a more systematic approach to the assessment and modification of a patient’s social and physical environment. Our findings on the significance of social context and support networks to improve mental health, provide further support for the role of nidotherapy in the treatment of people with personality disorder (27).
**Strengths and limitations**

To the best of our knowledge, this is the first study which has examined the experience of people with borderline personality disorder who took part in a randomised controlled trial of a pharmacological treatment.

The LABILE trial is the largest ever trial of the effectiveness of using a mood-stabiliser for treatment of borderline personality disorder. This provided the opportunity for applying a purposive sampling strategy to ensure diversity.

However, our study has some limitations which might impact on the generalisability of our findings. Whilst we made every possible attempt to interview a diverse sample, some of those we approached to take part in an interview declined to do so. It is possible that the views and experience of those who refused to participate differ from those we interviewed. We were unable to interview a group of participants who dropped out. Their views about the trial and their reasons for dropping out would have provided valuable information.
However, we interviewed some participants who stopped taking trial medication but carried on with the assessments.

The qualitative data we collected does not provide a strong basis for drawing conclusions about what may or may not have contributed to the improved mental health that many of the participants in the LABILE trial experienced. While aspects of the trial process, placebo effect and changes in the social environment of some participants may have contributed to this, it is possible that regression to the mean, and factors that were not explored in this study also had an effect (28).

Implications for clinical practice and future research

The results of this study highlight the importance of structure and clarity in planning and delivering treatment for people with borderline personality disorder. Our findings support national guidelines which emphasise the importance of having an explicit plan for treatment which is shared with the service user and for working with people in a non-judgmental, consistent and reliable manner (20). While specialist teams for treating people with personality disorder are generally designed to deliver a clear and structured service (29), most people with borderline personality disorder are treated by community mental health teams (CMHT). Given the multiple competing demands made on staff working in CMHTs and the broad range of mental disorders that staff working in these settings
have to deliver, it is particularly important that staff working in general mental health services receive the support and training they need in order to deliver consistent care in keeping with recommended practice (20).

The links that many study participants made between improved mental health and changes in the social environment highlight the importance of supporting people with borderline personality disorder to develop their social networks and solve housing, work and other social problems (30). Future research should examine the process and outcomes of psychosocial interventions which deliver these aspects of care such as structured clinical management and nidotherapy.

**Conclusion**

Based on the findings of our study we suggest that clinicians actively involve patients with borderline personality disorder in working out the best treatment and crisis management plan. Consistency, transparency, and structured clinical management need to be embedded in mental health services.
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References


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