National Patient Safety Agency

National Research Ethics Service

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Dear Ms Chapman

Assessing the feasibility and acceptability of comparing the Lightning Process with specialist medical care for Chronic Fatigue Syndrome (CFS/ME) - pilot Randomised Controlled Trial

This study, exploring how best we might treat children with Myalgic Enchephalitis or Chronic Fatigue Syndrome under the guidance of Dr Esther Crawley, Senior Lecturer/Consultant, Child and Adolescent Health sponsored by Bristol university and with the active participation of the association of Young People with ME (AYME) was reviewed on 8 July 2010 by the South West Research Ethics Committee (REC) as part of standard research regulation and ultimately received a favourable opinion on 8 September 2010.

Subsequently the National Research Ethics Service (NRES) received a number of emails and letters about this study and, despite being satisfied with the ethical review, felt it fair to give consideration to the issues raised.

It was clear that the application had received a considered and extensive review of the ethical issues of the project prior to the issue of the favourable opinion. This met all required procedures and processes, however, in view of the weight of correspondence received, much of which raised very similar issues, NRES asked the REC to consider the application, taking into account the issues that had been raised in the subsequent correspondence. Dr Hugh Davies, NRES Ethics Advisor provided a summary to the REC on the issues which had been raised and the opportunity was offered to Dr Crawley and the research sponsor to respond to the issues raised.

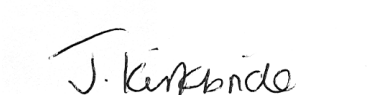
In December 2010, the South West REC met again to consider the application and associated documentation. Dr Davies and Mrs Kirkbride attended the meeting to provide advice and support to the REC in relation to ethical matters and operational processes. Dr Crawley was also invited to attend the meeting and was accompanied by sponsor representative Professor David Gunnell. The Chief Executive of the Association of Young People with ME (AYME) had been due to attend to offer support but as a result of illness was unable to do so and sent in a letter of support. The REC considered all the information available to it and discussed the application and agreed a number of questions which they then put to Dr Crawley. After this interview and further consideration the REC agreed that they would uphold their initial decision to grant a favourable opinion to the research with one minor change to the patient information documentation and one suggestion for the future should the research progress beyond a feasibility study.

Given the uncertainties of treatment of this condition and the need to resolve these, in line with professional guidance and duties, the REC felt this project would be a valuable start.

A copy of the minutes of the meeting are attached and provide full detail of the discussions and agreements reached.

I would like to thank you for your time in raising with NRES your concerns about the study. NRES believes that the initial application received a thorough review and an extensive reconsideration of the application at the December meeting and that it has fulfilled all its duties in the ethical review of the application.

Yours sincerely



JOAN KIRKBRIDE
Head of Operations, England

Encs Minute of the application discussion

Extract of Minutes from South West 2 REC meeting held on 2 December 2010.

5.1	**10/H0206/32**	**Assessing the feasibility and acceptability of comparing the Lightning Process? with specialist medical care for Chronic Fatigue Syndrome or Myalgic Encephalopathy (CFS/ME) - pilot Randomized Controlled Trial.**
	Chief Investigator:	Dr Esther Crawley
	Type of review:	Other
	Sponsor:	Royal National Hospital for Rheumatic Diseases NHS Foundation Trust

Joan Kirkbride, NRES Head of Operations advised that the REC had previously given this study a favourable opinion to this study. Following this, NRES had dealt with a number of requests under the Freedom of Information Act from people and organisations who had raised a number of objections about the study. In view of this correspondence NRES asked the REC to debate these representations. Her attendance and that of Dr Hugh Davies, NRES Ethics Advisor at today's meeting was to provide the REC with any guidance they may require in relation to process and ethical considerations.

To facilitate this review, Dr Davies, had put together a paper which included a collection of representations made on this study. The points raised by the representations were distilled into 15 issues that the Committee discussed in turn.

Permission had been sought from people who had sent correspondence to NRES to forward this information to Dr Crawley. Dr Crawley had provided a detailed response, which included letters from Mary-Jane Willows, CEO of Association for Young people with ME (AYME) and Colin Barton, Chairmen of the Sussex and Kent ME/CFS Society which the REC had available for consideration.

1. The study is misnamed and should be seen as more than a pilot study.
The Committee felt that 96 participants may be quite a lot to recruit for a feasibility study and queried if a 30% drop out rate was expected. In discussion with the researchers the REC were happy with the title of the study
2. Purpose
The Committee reviewed what data was available comparing the effectiveness of different treatments. This data seems to indicate that the Lightning Process is as effective/ ineffective as many other current treatments and that more research is needed to resolve these uncertainties for the benefit of ME patients.

3. The Lightning Process (LP) is subject to trading standard and Advertising Standards Authority (ASA) enquiries
Complaints that Mr Parker made unsubstantiated claims of effectiveness have been upheld by the ASA and this is in line with data from the ME society indicating it is effective (or ineffective) or harmful as other therapies. It was noted that the judgement of the ASA was made after the submission of the application to the ethics committee . And corrective action had been taken
4 Mr Parker is shortly to attend court for making false claims about his product
The Committee noted the correspondence submitted by Dr Crawley from Mr Parker and the refutation of this. The Committee considered this but had no further comments to make on this point

5 Conflict of interest
The REC considered this and felt they were similar to much other research and that they were adequately handled in the application

6. Mr Parker has a history of past failed businesses
The Committee noted the correspondence submitted by Dr Crawley from Mr Parker refuting this. The Committee considered this.

7. Mr Parker has used the study to increase sales
No evidence has been provided that Mr Parker has specifically used this study to increase sales. It was noted that the adjudication by the Advertising Standards Authority (ASA) had stated that "The ad [16 June 2010 Internet sponsored search] must not appear again in its current form. We [the ASA] told Withinspiration to ensure they held substantiation before making similar efficacy claims for the lightning process" and that all Lightning Practitioners had been advised of this. The protocol and application clearly state that practitioners had been informed that they must make NO therapeutic claims on the basis of this study.

8. The complainants claim it is not appropriate to research children before work has been conducted in an adult population that can give consent
It was felt that respondents had selectively quoted from guidance about the acceptability to undertake research on children. The Committee accepted the researcher's view that t CFS/ME is different in children and adults and therefore results from research on adults cannot be extrapolated to children.

9. Risk
The Committee noted that the intervention was in addition to standard care. The ME association survey data seemed to suggest it is as effective, ineffective or harmful as many other current treatments. Evidence of the risk provided to NRES was anecdotal and of low evidential value, reinforcing the need for such a trial as this one.

The Committee felt that there may be a slight risk of a child being worse after therapy (but equally a chance of improvement) and considered that they could withdraw at any time from the study if they wanted to. Supervision of the process was in place

10. Service user involvement
The Committee were reassured by the fact that AYME had been consulted during the planning of this study.

11. The role of the External Advisory group
The Committee considered that AYME has been consulted during the planning of this study.

12. The claims that the LP is coercive and bullying
The Committee considered this but were satisfied by the processes and precautions in place in the study..

13. Concern about the "primary endpoint"
The Committee clarified that this is only a feasibility study and that the primary endpoint is to see if it a full study is possible. The Committee also suggested that the secondary endpoint could be altered to assess the return to the education that children were in prior to their treatment rather than attendance at school.

14. A lack of generalisability
The Committee considered that the researchers accepted that they would not be able to generalise from this to children who had severe ME that kept them at home. It would still provide data on other children with this condition.

15. Participant Information

The Committee was unsure if the ME groups have enough information in the PIS to join. The Committee felt that the PIS should include statistics on the risks of getting worse, whether there was no change, or whether the treatment was helpful.

The Committee debated whether, in order to address a possible perceived lack of training of those that might be conducting the Lightning therapy that a practitioner who is subject to a professional code of conduct could be used to deliver the therapy. This was also considered in discussion with the researcher.

The Committee also wanted to know if the research has begun recruitment.

Dr Esther Crawley and Professor Gunnell were invited to join the meeting and were asked by the Vice-Chair to clarify the following issues:

Q1: Is there anything you would like to say regarding your study?

Dr Crawley said that this research had the full support of children and families, indeed the impetus for starting it came from children and families and had the support of AYME. They started recruiting in September and this is well up to schedule. Dr Crawley said that it was a feasibility study and the Committee were content with this.

Q2: You stated that the study has started recruiting,

Dr Crawley stated there has been a high recruitment rate so far. Participants have not started receiving treatment yet**.**

Q3: Please explain your recruitment figures and what dropout rate are you expecting?

Dr Crawley replied that 96 participants may seem high for a feasibility study this number is smaller than that for some other feasibility studies and reflects both the expectation of up to 50% dropout in one of the arms and a moderate treatment effect (participant numbers reflect the need to ensure there is sufficient data to reliably estimate sample size requirements for the full trial) .Therefore they need high numbers to keep the numbers up to judge across the arms and see why people are dropping out.

Q4: Are there differences in the way children and adults are treated?

Dr Crawley replied that the treatment approaches are very different in the two groups. There are lots of points of difference but given the outcome is so different between adults and children, adult services tended to focus on symptom management whilst paediatric services aimed for recovery. In addition, paediatric services involved families and dealt with education not work. She added that children are already receiving this treatment and that we need to evaluate it to see if it works.

Q5: The practitioner of the lightning therapy has no other allied professional qualifications. The Committee suggested that it might be beneficial to the research if the practitioner had external qualifications other than in Lightning therapy and was covered by a code of conduct?

Dr Crawley replied there is a geographical limitation to who can be chosen and that she has worked before with the Bath practitioner who is good. In addition, the children will remain under her care. Prof Gunnell pointed out that children will continue to be under the specialist service in both arms. As the Chief Investigator for the study Dr Crawley

accepted responsibility for the activities of the research team and pointed out that in this feasibility study, all Lightning intervention sessions will be recorded and some observed.

The Committee requested that the fact that the practitioner is not clinically qualified be added to the PIS.

The Committee suggested that consideration should be given to using "clinically qualified" Lightning Practitioners should the feasibility study proceed to a full study in the future.

Q6: The risk balance of the study is not included in the PIS.

Dr Crawley and Professor Gunnell replied that they would be happy to add this to the PIS. They added that according to the figures in the Parliamentary Inquiry into NHS Service provision for ME/CFS, Lightning therapy fares better than the standard NHS therapies of Graded Exercise Therapy (GET) and Cognitive Behavioural Therapy (CBT). It was noted that this information related to treatment in adults. Data for children was not available. They also added that when patients get better they also don't tend to take part in surveys.

The Committee asked for these figures to be added to the PIS and to reference them so they are available but to note that they are relative to adults.

Q7: The Committee discussed the secondary endpoint regarding returning to school and suggested that it could be altered to assess the return to the education that they were in prior to their treatment rather than attendance at school.

Dr Crawley replied that recruitment and retention is the primary endpoint of the study as it is a feasibility study. She added that the inventory used to measure school attendance also measures home tuition. Those children that are house bound are excluded from the study as they have to be able to get to the clinic.

Dr Esther Crawley and Professor Gunnell left the meeting.

The committee felt that given current treatment uncertainty research was vital in this area and the proposal is a standard way to assess this. Currently survey data were limited and it was unwise to base health policy on individual case reports. It is vital to see if the lightening process is or is not helpful as children are already receiving this therapy.

The committee voted unanimously to confirm the favourable opinion of the application with the following additional conditions:

1. PIS for Teenagers and PIS for Parents: Please add the fact that the Lightning Practitioner is not clinically (medically) qualified (trained).

2. PIS for Teenagers and PIS for Parents: Please include the following text in the 'Are there any disadvantages to taking part' section:

"Teenagers with CFS/ME can get worse with any intervention offered. There is no data in teenagers, see tables 1 and 2 for data in adults."

3. PIS for Teenagers and PIS for Parents: Add the figures for GET, CBT and the LP from the Parliamentary Inquiry into NHS Service provision for ME/CFS include Data

taken from Action for ME (AfME) and Association of Young people with ME (AYME) joint report “M.E. 2008: What progress” and reference it.

4. PIS for Teenagers and PIS for Parents: Add the figures for GET, CBT and the LP from the 2008 MEA survey and reference this.

The Committee suggested that for the future Dr Crawley might consider using Lightening Practitioners who were additionally clinically qualified.

Decision

The Committee restated the favourable opinion of the application.

The Committee nominated Tom Lucas to be the point of contact should further clarification be sought from the applicant.