Joint meeting of the Trial Steering Committee and Data Monitoring and ethics committee (TMG invited as observers)

Friday 10th September 2010

[redacted]

Draft Minutes

1. **Those present:**

DMEC:

[redacted]

TSC Independent Members

[redacted]

TSC Non-voting members

[redacted]

TMG Observers

[redacted]

Changes to TSC members since the last meeting:

[redacted] has replaced [redacted] at the [redacted] and was welcomed to the TSC.

2. Apologies

DMEC

[redacted]

TSC

[redacted]

TMG

[redacted]

3. Previous minutes of TSC # 8 (document #1)

All agreed the minutes were an accurate reflection of the previous meeting with a minor correction to [redacted] title.

4. Ongoing actions from TSC #8

TSC #8 ACTION 16: [redacted] to speak to [redacted] regarding the Science Media Centre.

5. Matters arising not on the agenda

A complaint has been received by the MRC regarding the PACE trial. The Corporate Advisory Group is reviewing the dossier submitted to determine the nature of the complaint, and continues to do so.

6. No cost extension

An extension has been awarded to use the remaining trial underspend on achieving the PACE objectives until 13th May 2011. [redacted] was thanked for [redacted] support with this application to the MRC.

7. The background to the PACE trial and context of its results

[redacted] summarised the aim of the afternoon's meeting to present the preliminary results to the TSC, DMEC and TMG and receive feedback. All committee members were thanked for their involvement in PACE and in particular the trial funders:

- Medical Research Council (MRC)
- Chief Scientist's Office (CSO) - Scotland
- Department of Health (DH)
- Department of Work and Pensions (DWP)

In addition all local centre staff were praised for their hard work which has resulted in high quality data and well delivered treatments.

The context of the original PACE trial application was revisited. Back in 2002, both cognitive behavioural therapy (CBT) and graded Exercise Therapy (GET) had been shown to be effective in a series of small trials and reviews were cautiously supportive of the treatments. The scientific evidence appeared to be contrary to the views of the charities set up to support patients whose general enthusiasm for APT was not based on such evidence. Concern had also been raised by the charities about the potential harm of GET. This lack of consensus set the scene for the development of the PACE trial.

8. Presentation of statistical analysis for main paper

[redacted] presented an overview of the statistical analysis strategy for the trial. The changes made to the analysis since the original protocol was drafted were highlighted and it was noted that the analysis plan was agreed by the TSC and signed off before analysis commenced.

ACTION 1: [redacted] to ensure that the review and sign off of the analysis strategy by the TSC is well documented

9. Presentation of preliminary main results

All were reminded that information presented at the meeting remains confidential until the main paper is published. [redacted] will notify all committee members when publication occurs and thanked all those that contributed to the analysis he presented.

10. Therapy differentiation and integrity

[redacted] summarised the review conducted using the audio recordings of therapy sessions to assess the treatment integrity. A random sample of recordings (two per therapist) were reviewed by two raters (blind

to treatment) to establish whether treatment was delivered as per protocol. Session 10 was chosen as differences between therapies were considered more likely. Two items per therapy were used to assess the extent to which aspects of therapy had occurred and each item was rated on a 7 point Likert scale. Overall therapeutic alliance was assessed by 1 item using a 7 point scale.

The outcome of the review was presented and the Treatment Leaders were praised for their excellent job in keeping the treatments on track. This process was aided by the very detailed treatment manuals and a dedicated team of therapists who were also thanked for their contribution.

11. Interpretation of preliminary main results

[redacted] summarised the main trial findings and asked the TSC to consider:

a) What they considered to be the most interesting findings

b) What were the limitations of the research

c) What the thrust of the main paper should be

12. Discussion of preliminary main results by TSC and DMEC

The TSC and DMEC praised the trial team for the low dropout and high follow up rates which are indicative of a very well conducted trial. The rigour with which the trial has been conducted gives confidence in the results. [redacted] on behalf of the MRC commented on the excellent oversight of the trial by the TSC and DMEC and was very pleased to see a robust outcome.

[redacted]

All those in a care providing role were asked to consider how the PACE trial results would affect how they treat patients. This is a potential way for results to leak if colleagues/participants become aware of a change in their clinical practice.

ACTION 2: All to bear in mind the implication of learning the outcome of the PACE trial and to discuss any concerns with the PIs.

NB: A detailed record of the points discussed was made, but will not be circulated for reasons of confidentiality.

13. Presentation of preliminary health economic results

[redacted] presented the objectives and preliminary outcomes of the health economic analysis.

14. Discussion of preliminary Health Economic results by TSC and DMEC

[redacted] was thanked for [redacted] hard work on the complex health economics analysis. The TSC felt that there was more work to do and specific actions will be recorded separately.

It was suggested that a comparison with the FINE trial would be very interesting although this data has not yet been analysed.

ACTION 3: [redacted] was asked to liaise with colleagues to complete health economics analysis for the FINE trial as soon as possible and contact [redacted] to assist with a comparative analysis

15. Authors and acknowledgements for main paper

A list of the planned authors and acknowledgements for the main paper was circulated. The TSC, DMEC and TMG were asked if they were happy to be acknowledged by name in the main paper.

ACTION 4: Any committee member wishing to opt out of acknowledgement in the main paper to please contact [redacted] to circulate this message to all not present)

16. Publication strategy:

a. Preliminary plans for public dissemination of main results

The intended publication strategy was discussed. The Lancet is the first choice for publishing the paper and they have already agreed to fast track the submission. The aim is to submit by the end of October. All the relevant press offices (sponsor, funders, [redacted] and MRC) should be notified at the point of submission (or when the likely submission date is known). It will be important to work with the press offices so that an explanatory press statement is ready ahead of time. The sponsor's press office should take the lead in drafting the press release and accompanying frequently asked questions. The MRC's press office, The Lancet (if accepted) and [redacted] will work closely with the team at Queen Mary

University of London and it will be important for all press offices to present the same message, working from a single set of FAQs.

[redacted] will need to brief his colleagues at [redacted] regarding the results and will require permission from [redacted] as [redacted] to do so.

A participant newsletter should be drafted ready to distribute at the time of publication.

ACTION 5: Writing and publication oversight committee (WAPOC) to plan a timetable of when the results will be disclosed and to whom (with confidentiality agreements in place)

ACTION 6: [redacted] to complete draft of main paper ready for submission by end of October

ACTION 7: [redacted] to clarify with MREC whether ethical approval is required for a participant newsletter after trial end and to take a lead in producing this.

It was agreed that this would be the last formal meeting of the TSC but that the committee would have a useful role in reviewing the final report before publication and commenting on issues around access to data.

The MRC would like to see a copy of the manuscript when submitted along with the accompanying FAQs. All communication including results should be password protected with a caveat that this is not to be passed on.

ACTION 8: [redacted] to contact all press offices to identify any precedence for handling a press statement (e.g. Department of Health may require 30 days notice) and to liaise appropriately with all communication teams at the time of submission

b. Release of manuals on PACE website

A further request has been made for access to the trial treatment manuals and in the spirit of scientific openness the PIs felt the manuals should be made available on the PACE trial website with a statement regarding their use in place. The TSC were happy with the draft statement circulated but did not support release at this time, and favoured release at the time of

publication of the main paper. It was suggested the PIs may wish to rethink their decision.

ACTION 9: PIs to revisit decision to publish manuals in light of TSC's comments

c. Policy for third party access to data

The intention to publically release PACE data to legitimate researchers in line with the MRC policy on data sharing was discussed. It was agreed the first priority is to release the results of the trial into the public domain. The trial team could then consider releasing part or all of the dataset to external third parties however it was noted that coming to a dataset cold with no access to the trial team for clarifications would be difficult. There could be more potential for harm than good if the data was analysed incorrectly or misinterpreted. There would also be a cost associated with data extraction and manipulation to create a format suitable for distribution.

[redacted] emphasised the aim of the MRC to maximise the use of public money whilst maintaining high quality outputs. It was suggested that in response to enquiries about data sharing, the team should emphasise that the trial has been registered with ISRCTN, the protocol has been published, the treatment manuals will be publically available on the trial website and the results are due to be published in a peer reviewed journal. Access to raw data can be available by request to the PIs but only after receipt of a robust, fully funded and ethically approved proposal written by bona fide scientists. The TSC were happy with the draft statement circulated.

17. Update for information only

An update on publications and presentations from the trial was circulated prior to the meeting and the TSC were pleased to see more papers are in the planning and publication stage.

The long-term follow-up study also appeared to be proceeding well with current return rates of 75%. The importance of this data for the health economic outcomes was noted.

18. Any other business

The procedure for obtaining feedback from the TSC and DMEC was discussed. Documents should be circulated with a deadline to respond and no response by that time will be taken as approval.