Trial Management Group Meeting #29
4th December 2008, [redacted]

Draft Minutes

1. Welcome

[redacted] was welcomed to [redacted] first meeting as the [redacted]. [redacted] was welcomed as the new [redacted], and was thanked for taking the minutes at short notice.

2. Those present

[redacted]

[redacted]

3. Apologies

[redacted]

[redacted]

4. Agreement of agenda

An extra item was added under agenda item 13. 13b Training schedules and ethics approval for access to staff CVs.

5. Previous minutes of TMG #28

All accepted at this meeting. Thanks to [redacted] for all [redacted] work towards the participant newsletter.

6. Ongoing actions from TMG #28

TMG #28 ACTION 1: [redacted] to contact [redacted] to ensure that [redacted] agrees with the process for appointing independent assessors for adverse events as approved by [redacted]. (TMG #28)

7. Matters arising from TMG #28.

TMG #28 ACTION 5: [redacted] to create a project plan for the assessment of treatment recordings and [redacted] will contact the FINE nurses in order to update them on what is happening. (TMG #28)

This was discussed in great detail. The therapeutic alliance scales were discussed, with concerns raised over how it would be captured if the session monitored contained none of the therapy criteria encompassed by the therapy scales. [redacted] confirmed that this would be captured under the 'therapeutic alliance' scale. Therapist and patient factors would be recorded separately. It was accepted by all that the therapeutic alliance scale was vital, studying whether an aspect of the therapeutic alliance may predict outcome. ([redacted] speculated that the assessment of therapy recording would be approximately £50-60k. We have £20k budgeted for this.)

It was agreed that:

a) Two independent assessors to consider both categorical and dimensional judgements on adherence to therapy manuals and principles.
b) [redacted] to present at the next TMG on measurement and analysis of therapeutic alliance as a measure of outcome.
c) A sub sample should be assessed to viability, feasibility and experimental design.

ACTION 1: [redacted] to present at next TMG, with circulated paper beforehand
ACTION 2: [redacted] to circulate a recent paper in relation to this.

8. Final Recruitment

At the end of recruitment 641 patients had been recruited onto the trial. This was 41 patients over the target, with a record recruitment of 39 patients over the last month. The TMG congratulated all centres for this remarkable achievement.

ACTION 3: [redacted] to write to TSC, DMEC, MREC and individual funders to confirm the end of recruitment.

ACTION 4: Centre Leaders to forward this letter to their local R&D department to confirm the end of recruitment.

Allocation of funds

Since PACE has now been adopted by the UKCRN as a portfolio study, trial support funds to support PACE have been allocated to local NHS Trusts' R&D departments for use by PACE teams. [redacted] noted that some £25-30,000 are to be provided by the [redacted]. All centres should be able to access similar funds from their local trusts' R&D department. If these funds are not available, it may be that central UKCRN funds will be available.

If research staff are needed in the 12 months, Centre Leaders can apply to their local CRN to provide temporary staffing.

ACTION 5: Centre Leaders should urgently apply to their local R&D departments for trial support costs under the R&D tranche for the year. This has to be started to be spent by April 09.

9. Update from Analysis strategy group

Baseline papers

5 areas have been proposed as priority baseline papers.

I. Analysis strategy/rationale – [redacted]
II. Heterogeneity – [redacted]
III. Health economics – [redacted]
IV. Cognitive responses to belief/ psychological measures – [redacted]
V. Reliability/validity/modeling of disability – [redacted]

ACTION 6: [redacted] to ask [redacted] if they have any baseline papers they are interested in seeing as a priority.

ACTION 7: [redacted] to ask [redacted] whether [redacted] want to be involved with papers on heterogeneity and trial management.

ACTION 8: All to speak to local staff and raise items for potential baseline papers for the next TMG.

Writing Committee

A Writing and Publications Oversight Committee (WAPOC) will be constituted. The members are: [redacted]) . The function of the group will be to facilitate and supervise the process of writing and publishing PACE data. WAPOC will prioritise papers, agree the writing group for each paper and ensure the writing process is progressing.

It was agreed that WAPOC members should be offered authorship on all papers produced from the PACE trial data,

ACTION 9: [redacted] assisted by [redacted] to compile a database listing all proposed titles and writing groups. This will used monitor the progress of papers.

ACTION 10: [redacted] will write a writing policy document

10. Data cleaning and checking

It was noted that the deadline for the cleaning and checking of all baseline data from all centres is March 09. Help with this has been offered by Bristol, King's and Oxford.

ACTION 11: [redacted] to prioritise the checking of baseline data from all centres.

ACTION 12: [redacted] to email all centre DMs to inform them of the urgency of this data process.

11. Budget issues

[redacted] enquired about expenditure and [redacted] reported that currently the trial in general was under budget when last examined in June, 2008.

ACTION 13: [redacted] to be asked to review forecast budget by March 2009.

ACTION 14: [redacted] to review subvention budget and send out final figures re: centre recruitment.

ACTION 15: [redacted] to ask MRC if any excess funds could be used to support the long term follow up study.

ACTION 16: The PIs to include reviewing notes for further therapy information as part of the costing for the full funding to run the follow up study.

12. Database update

There was nothing new to discuss on this point.

13. Centre reports

Monitoring visits

[redacted] has monitored all centres in 2008 with the exception of Oxford.

ACTION 17: All CLs to ensure that action is being taken in response to the monitoring visit reports.

ACTION 18: [redacted] and/or [redacted] to complete doctor's monitoring of King's.

ACTION 19: [redacted] to complete doctor's monitoring of Edinburgh.

Staff recruitment, retention and contracts

All present agreed that staff contract dates have been checked and date until January 2010.

Centre specific:
Kings: [redacted] is leaving as [redacted], recruitment interviews for replacement by Christmas.
[redacted] (CBT) is leaving in Feb 09, but will be covered by existing King's staff.
[redacted] on maternity leave ([redacted] covering from Barts).
Bristol: [redacted] has been recruited as DM.
[redacted] is to cover [redacted] leave.
Barts: The new trial manager [redacted] is to start 17/12/08.
[redacted] is covering 2 centres.

DAR encryption and transport

It was noted that currently the Royal Free in particular is prohibiting the movement of data. There is increasing pressure on all centres regarding movement of data and privacy/encryption of this data. The decision was made that level of encryption used should remain the same until further advice is given.

ACTION 20: [redacted] is in discussion with the MRC for advice on this issue.

14. Treatment leaders reports

Manual publication

The APT PACE patient and therapist manuals are to be published in their current state.

It was noted that the APT therapists are working on a user friendly 'how to' guide to APT. This may contain some group therapy work. It was discussed that this should be clearly separate from the PACE trial manual.

The GET self-help guide is with the copy editor and will released shortly for use outside of PACE.

The CBT PACE manuals will be posted onto the internet in its entirety. A user friendly guide to CBT has been proposed.

ACTION 21: No PACE manual or guide should be published until after the PACE trial main efficacy paper has been released.

ACTION 22: Treatment leaders will seek approval from WAPOC regarding publication of manuals and user friendly guides.

Therapy schedules

[redacted] has emailed all centres to check how centres are collecting and storing visit schedule data. Visit schedules from all centres except for Bart's are electronically recorded at 52 weeks. Edinburgh is slightly behind on this.

ACTION 23: [redacted] and [redacted] to establish a system to collate this data in a central role.

ACTION 24: All RN/As to ensure electronic visit schedules are completed by 26/01/09.

ACTION 25: All DMs should allocate the therapists at their centre a therapist identification number (TIN) and email these to [redacted] by 26/1/09.

ACTION 26: [redacted] to follow up DMs to ensure this deadline is met.

ACTION 27: [redacted] to submit a substantial amendment to ethics to consent therapists to use personal data for research and to use tapes for research review of therapeutic alliance and integrity.

ACTION 28: Homework compliance was discussed. [redacted] has emailed [redacted] with the database [redacted] has created for recording this. [redacted] will email this to the RN/As once the TINs have been created for them to complete.

It was agreed that any homework compliance data that has not been entered can be completed retrospectively. This should preferably be completed by the

patient's therapist, although if the therapist is no longer available the current therapist should complete this from the patient notes. Such data should be clearly identified as retrospectively collected data.

15. Ancillary studies

2.5 year follow up add-on study

Currently only a 50 % response has been achieved for the 2.5 year follow up. There was a long discussion over this issue, methods which could be used in order to aid collection and it was agreed that a minimum of a 70% response would be viable. The TMG noted that [redacted] regarded this as very important data and the meeting agreed that it was important to collect this data, although the collection of the main trial outcome data remained the priority. [redacted] expressed concern that whilst the data would be useful if it could be collected it would be of little value if the response rate was as low as at present. It was agreed to review whether and how to continue the study in the light of response rates achieved in 6 months time.

ACTION 29 [redacted] to communicate with [redacted] regarding current status of the 2.5 year follow up database.

ACTION 30: [redacted] to write to [redacted] to establish what needs to be done to the main database in order to incorporate the 2.5 year follow up data.

ACTION 31: [redacted] to check all RN/As are following the advice set out in TMG #28 meeting.

ACTION 32: [redacted] to ensure that all RN/As are cross referencing medical notes and 2.5 year CRF and recording any discrepancies.

ACTION 33: All RN/As should now focus on achieving a greater response, now that recruitment has finished.

It was proposed that a training day should be organised in January to cover methods and techniques for achieving a high level of follow up response.

ACTION 34: [redacted] to look at ways to improve data collection, including holding a training day. To seek advice from [redacted] regarding Gulf war veterans' data collection.

ACTION 35: The level of response and viability of the study will be re-evaluated at the summer 2009 TMG.

PACE/FINE genetic study

[redacted] had been to Bristol to further discuss the genetic proposals with [redacted] and [redacted]. It was confirmed that saliva sampling would provide a sufficient and stable DNA sample.

It was discussed that the study examining SNPs as a predictor of treatment response would have a limited power problem and therefore might not be viable. It was agreed in principle by the TMG that the SNP treatment predictors study should not be pursued further as a primary study, and that the genetic study should focus on a case control study.

This case controlled study would be a genome wide assay, comparing healthy controls to patients with CFS. 2000 cases' DNA samples and phenotypes would need to be collected. This would involve two separate but linked case control studies. One would examine the phenotype of chronic disabling fatigue, and the other would examine the more detailed phenotype of CFS, with heterogeneity. The PACE and FINE studies could provide up to a maximum of 937 cases with well described phenotypes.

It was also suggested that it may be possible at a later date to combine collection of DNA with the 2.5 year follow up data collection.

ACTION 36: [redacted] to submit this study for ethics approval as soon as possible so that DNA collection can commence in current participants in advance of exiting the trial and staff contracts ending.

Supervision study [redacted]

[redacted] reported that this has gone to press.

Psychiatric co morbidity study [redacted]

[redacted] reported that this is awaiting ethical approval.

16. Centre close-downs post PACE treatment and archiving

ACTION 37: [redacted] to write SOP for individual centre closedowns and both central and local archiving.

17. Actions carried across from the Analysis Strategy Group

ACTION 38: [redacted] to request that therapy leads send [redacted] their training schedules.

ACTION 39: [redacted] to find out whether PACE needs to seek permission to use information from CV's from ethics.

18. Dates for your 2009 diaries

Tuesday 10th March, 1pm lunch, 1.30pm: DMEC ([redacted])
Wednesday 11th March 1pm lunch, 1.30 – 4-30pm: TMG [redacted] welcome)
Wednesday 29th April, 11am (Analysis strategy) 1pm: TSC [redacted] – observers welcome)
Tuesday 23rd June, 1pm lunch, 1.30 – 4.30pm: TMG (volunteer site needed – observers welcome)
Wednesday 4th November, 1pm lunch, 1.30 - 4.30pm: TMG [redacted]– observers welcome)

ACTION POINT SUMMARY LIST

All

ACTION 8: All to speak to local staff and raise items for potential baseline papers for the next TMG.

ACTION 35: The level of response and viability of the study will be re-evaluated at the summer 2009 TMG.

PIs/CLs

ACTION 4: Centre Leaders to forward this letter to their local R&D department to confirm the end of recruitment.

ACTION 5: Centre Leaders should urgently apply to their local R&D departments for trial support costs under the R&D tranche for the year. This has to be started to be spent by April 09.

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Research Nurse/Assistants

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