Trial Management Group Meeting #33

[redacted]

Wednesday 10th February 2010

Draft Minutes

1. **Welcome**

   All were welcomed to the last TMG for the PACE trial. Thanks were given for the hard work and contribution of all staff.

2. **Those present**

[redacted]

[redacted]

Observers

[redacted]

3. **Apologies**

[redacted]

4. **Agreement of agenda**

   The agenda was agreed by all although the order was amended slightly.

5. **Previous minutes of TMG #32**

   All accepted at this meeting.

6. **Ongoing actions from TMG #31**

TMG #32 ACTION 3: [redacted] to conduct final review of all clinician's monitoring reports

TMG #32 ACTION 8: The analysis strategy for the 2.5 year follow up study will be discussed at the next ASG meeting and should be decided before the main results are available.

TMG #32 ACTION 11: [redacted] to request no-cost extension from MRC (once planned uses of underspend agreed by TMG).

TMG #32 ACTION 12: [redacted] to collaborate to produce an excel file of all the AE and co-morbid data which could then be cleaned by [redacted].

TMG #32 ACTION 19: [redacted] to clarify with QMUL finance team whether maternity pay is covered by the MRC grant

The QMUL finance team have clarified that the PACE grant should not be used to cover maternity pay, this should be reclaimed from the appropriate government agency.

TMG #32 ACTION 13: TMG physician to volunteer to review all co-morbid condition and AEs along with [redacted]

[redacted] has kindly volunteered to assist with this task. The process of review of adverse events was discussed in detail and it was agreed that [redacted] and [redacted] would review all NSAEs and comorbid conditions blind to treatment group and patient identifiers. The coding categories implemented by the research nurses would be reclassified where appropriate including the addition of subcategories in the 'other' field as follows:

1. Social event
2. Major life event (as opposed to life stresses which would be coded under stress
3. Economic event

POST MEETING COMMENT: The coding categories agreed by [redacted] and [redacted] (and subjected to independent review) will be incorporated into the master datafile created by [redacted]. This data will not be amended on the study database, which will maintain the original Research Nurses'/Assistants' coding of events. The final database sign off sheet signed by the [redacted] and [redacted] should indicate that the adverse event data has been reclassified by the Investigators/independent assessors and therefore the masterfile differs from the study database. The main paper should report that all events were retrospectively reviewed and coded firstly by 2 trial investigators and subsequently by 3 independent assessors.

ACTION 1: [redacted] to remove unblinding information when reviewing NSAE data in order to ensure that [redacted] and [redacted] remain masked to treatment group. A search should be run for participant's surnames, centres and therapy or therapists' names.

ACTION 2: [redacted] and [redacted] to review non-serious adverse events prior to the independent assessment of adverse events on 11th March ([redacted] to coordinate)

7. Update from recent meetings

a) PACT, 1st December

Further to discussions at TMG# 32 the PACE Analysis Coordinating Team (PACT) has been set up to oversee the stage by stage completion of the main analysis. The first meeting has already taken place and the group is due to meet again on 19th February.

b) Analysis Strategy Group #15, 6th January

The Analysis Strategy group met in January to review the analysis strategy. The best strategy for the main comparison is still not clear, due to the complexities of four arms, 2 outcome measures and the issues of multiplicity and therapist clustering. Further discussion is also required on the policy for defining a clinical response to treatment. Another meeting is planned for 18th February, when it is hoped the strategy can be finalised and this will then require sign off by the TMG.

POST MEETING COMMENT: Since the TMG now only exists as a virtual committee it is suggested that the Analysis Strategy Group and TSC sign off the analysis strategy and it is circulated to the TMG for information only

c) WAPOC #7, 10th February

The TMG were updated on various trial timelines. It is anticipated the baseline data will be released to writing groups mid March. The main analysis is estimated to be complete by the end of August and a TSC/DMEC meeting will be planned for early September. The decision to publish the statistical analysis plan has been deferred, instead an audit trail will be kept of any changes to the document, so it is clear that decisions were made before the results were known.

ACTION 3: [redacted] to ask [redacted] if the TMG may attend the TSC/DMEC meeting as observers

8. Archiving arrangements

Centre Leaders provided feedback regarding their local archiving arrangements as follows:

Oxford: Records may be kept locally until the end of 2010 after which there will be a fee to store with R&D (who outsource this)

Royal Free: [redacted] has been working hard on trying to finalise arrangements with R&D.

Kings: Records will be archived locally for full archiving period

Edinburgh: Space locally to store records until main analysis complete and further access unlikely to be required. R&D (who outsource) will then store at a charge

Barts: Two options including a local archive which is free, but as the trial sponsor, the QMUL/Bart's R&D department have confirmed records must go to their central store. No cost has been identified for this but [redacted] is in further discussions with R&D to clarify arrangements

Bristol: TBC

ACTION 4: All Centre Leaders to confirm archiving arrangements and costs and inform [redacted] of final arrangements

ACTION 5: [redacted] to check with MRC if the project grant may be used to cover the cost of archiving or if this must be covered by the local institution as part of grant overheads.

ACTION 6: [redacted] to investigate if UKCRN can meet the costs of archiving for English centres

9. 2.5 year follow up study

[redacted] explained that Bristol had offered to take on the data collection and entry of the 2.5 year follow up study for any centre unable to do this locally, although it was agreed that continuing this locally would be preferable as this may improve return rates.

Centre Leaders provided feedback as follows:
Oxford: [redacted] to continue until the end of the year, but would like to continue locally until end of grant
Edinburgh: [redacted] is keen to see PACE through to the end and will do this [redacted].
Bristol: [redacted] keen to continue this role
Barts: Will continue locally
Royal Free: [redacted] to check with [redacted].
King's: [redacted] to continue until end of grant

It was agreed that if a local solution could not be found at any centre, this workload will be offered to Bristol.

The costing for a Research Nurse working 0.5 days per week on the 2.5 year follow up study for 15months (1st April 2010 – June 2011), is £6,222. This includes both data collection and entry (excluding overheads).

POST MEETING COMMENT: The figure including overheads is £11,206

10. Financial projections and proposals for use of underspend

ACTION 7: Centre Leaders to encourage local finance teams to send any outstanding invoices to QMUL so that the forecasts for the underspend can be made as accurately as possible. If figures held by QMUL do not match local predictions for underspend CLs to notify [redacted].

It was unclear whether QMUL had instructed all centres that they may bill up to 13th September not 31st March.

ACTION 8: [redacted] to ask [redacted] to forward appropriate confirmation to the finance departments of all sites (copied to Centre Leaders)

The possible uses for the underspend were reviewed and WAPOC's recommendations were given. The TMG agreed it was crucial to facilitate publication of the main paper and support for subsidiary studies. Support was therefore given to the following proposals:

1. 2.5 year follow up study
2. Extension of the Trial Manager contract by 1 year
3. Additional statistician support, to choose between extension of trial statistician, employing a second statistician, or both.
4. Additional Data Management support for 6 months

The contingency fund would be used to support the independent assessment of adverse events and review of therapy recordings to examine therapeutic differentiation.

ACTION 9: [redacted] to speak to QMUL finance department to look into the possibility of cross charging so that PACE funds may remain at local centres but be used to pay for staff at a different organisation

11. Summary therapist data for main paper

After a lengthy discussion it was decided that the following information should be reported in the main paper:

1. Average number of days training (to full competency)
2. Range of experience given as general description by Treatment Leaders

3. Professional healthcare qualification (collected from CVs)
4. Years of experience, non specific (Collected from CVs as years since qualified)

POST MEETING COMMENT: [redacted] to collect for each therapist whether they had or had not worked in a CFS/Chronic Pain service before being appointed to PACE.

ACTION 10: [redacted] to collate data on therapists to be presented in main paper

12. Ancillary studies

a) Genetics Study

[redacted] described the GENEME (GENE evaluation for ME) study which will seek associations between CFS/ME and the complete genome in 8,000 CFS/ME patients and 28,000 population controls. The pilot study for this project has received ethical approval and will commence at Bart's once R&D approval is received.

b) Qualitative study of therapy content

ACTION 11: [redacted] and/or [redacted] to speak to [redacted] for suggestions as to how to make use of the rich qualitative data available for PACE and inform further discussion between the three PIs. Further discussion between [redacted] and [redacted] about other uses of this data is planned.

13. Specific centre issues

No issues were raised

14. Therapy/treatment arm issues

No issues were raised

15. Any other business

Although this is the last physical meeting of the TMG, the committee will remain in the virtual setting for issues as and when they arise, including sign off of the analysis strategy.

[redacted] asked on behalf of [redacted] whether the manuals may be referenced. This was not possible before they have been published.

ACTION 12: WAPOC to discuss the release of the manuals prior to publication of the main results

ACTION POINT SUMMARY LIST

[redacted]

ACTION 2: [redacted] and [redacted] to review non-serious adverse events prior to the independent assessment of adverse events on 11th March [redacted] to coordinate)

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Analysis Strategy Group

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WAPOC:

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