ITEM 1: Trial Management Group Meeting # 26

13th February 2008

[redacted]

Draft Minutes

1. Those present

[redacted]

2. Observers

[redacted]

3. Apologies

[redacted]

4. Previous minutes of TMG # 25 and matters arising

GET guide

The GET guide was sent to MREC in December. The guide co-authors have agreed that it may be used for clinical (non-PACE) purposes in PACE centres.

ACTION 1: [redacted] is revising the formatting of the GET guide and this will be distributed when complete. It cannot be used for PACE participants until ethics approval is received.

New doctor's CVs

ACTION 2: [redacted] to ask [redacted] and [redacted] for the new doctor's CV signed and dated. This CV to include GCP training experience.

ACTION 3: [redacted] to obtain CVs for current rotational doctors and send these to [redacted] copied to [redacted] for the local trial master file.

Follow on from PACE

ACTION 4: The PIs/TMG to consider a meeting the morning of the Edinburgh TMG to discuss potential trials after PACE.

Encryption

[redacted] has been unable to get [redacted] employer to get WinZip so far but this issue continues to be pursued.

ACTION 5: [redacted] to download WinZip software and use encryption as soon as possible.

5. Recruitment

The trial remained on target for recruitment at the end of January.

Where recruitment has slowed, some centres report that following the release of the NICE guidelines more patients are choosing which treatment they want rather than choosing to join the trial. Some clinics report seeing less CFS referrals to clinics.

King's have written to individual GPs in local districts to advertise the trial further.

ACTION 6: [redacted] to explore the possibility of referrals for consideration for the PACE trial from the Kent MDT.

6. Budget and contract extensions

[redacted]) presented an overview of the roles and functions of the Queen Mary costs and contracts team. The presentation discussed the need for the consortium to consider flexibility in the extension grants to allow all centres to continue recruiting and the project to finish within budget.

ACTION 7: [redacted] to ask [redacted] for a copy of the presentation given today for the meeting records.

ACTION 8: [redacted] to contact the Bristol centre and alert them to the fact that their invoicing is very slow.

Financial management queries

- It is noted that employers to PACE staff are concerned that extension contracts are in place soon to extend staff contracts.
- Grant shortfall can largely be explained by unexpected increases in salary costs. The National Pay Framework increased salary costs following regrading and the 46% overheads allowance on salaries has consequently increased this effect by a factor of 1.46. Inflation rates have also been greater than the MRC standard payments.
- There was discussion as to whether the subvention monies could be reallocated within individual Trusts. This is a local Trust decision and PIs/CLs should have local discussions about whether they can access these funds where the centre is in profit.

- The PIs have begun the process to ask for more subvention funds to cover the extra recruitment and treatment period.
- It was proposed that in order to ensure continued recruitment in all centres, those centres that are forecast to be under-spent will be expected to utilise funds from the current contracts to pay for staff at the beginning of the extension period. Extension funding will be allocated according to individual centres needs. The TMG agreed to this in principle, once agreement from the TSC Chairman was forthcoming.

ACTION 9: [redacted] to speak with [redacted] regarding allocation of extension contracts.

ACTION 10: [redacted] will write the extension contracts as agreed following approval from the TSC Chair.

[redacted] is available to speak with any PI, CL or finance officer that would like to discuss any PACE finance issues.

7. Analysis strategy for PACE

[redacted] gave a presentation about the Analysis Strategy that has been developed over the last 18 months. The slides and Analysis Strategy document were sent out with the documentation for this meeting.

The TMG thanked [redacted] and [redacted] for the enormous amounts of hard work put into the creation of this document and to congratulate them on their achievement in producing it.

There was discussion regarding the semantics of the terms 'active' (CBT and GET) and 'non-active' treatments (APT) and the controversy these terms may cause with patient groups and negative impact of morale it might have on APT therapists. It is proposed that from now on APT will be referred to as a 'new' treatment and the others as 'established'.

ACTION 11: [redacted] to alter this in the next version of the trial protocol and other associated documentation.

<u>Health Economics</u>

ACTION 12: The statisticians to supply data in due course to [redacted] to allow [redacted] to build models for the health economic analysis.

ACTION 13: The statisticians will provide data in due course with the agreement of the TMG for the production of other papers.

<u>Therapist effects</u>

[redacted] explained that in terms of therapist effect, there will be two analyses: treatment outcomes on the basis of the expected therapist versus actual therapists (and combinations) of therapists seen by each participant.

It was noted that ongoing supervision and training should take account of any issues of competence and treatment differentiation. Analysis is not expected to identify any great outliers in treatment competence between therapists.

The TMG approved the analysis strategy.

ACTION 14: All to send any comments on the Analysis Strategy to [redacted] by 7th March.

ACTION 15: [redacted] will send finalised (subject to comments) the Analysis Strategy to DMEC and the TSC.

8. Update from Analysis Strategy group

The morning meeting was concerned with approval of the analysis strategy for the primary and secondary trial outcomes.

9. Authorship of the main trial paper

The issue of authorship on the main paper was revisited. It is proposed that as well as the analysis strategy group, centre leaders, treatment leaders and [redacted] should be included in the authorship. In other words, the main paper authorship should include everyone who has made a 'substantial intellectual contribution' to the development, operation and analysis of the PACE trial. The writing committee will write the main paper and other named authors would be asked to read it and agree content but would not be required to re-write any sections.

People can opt out of authorship at any time. The contracts supplied by journals ask authors to specify and sign to their individual contributions to the papers before publishing.

ACTION 16: [redacted] to ask the MRC whether there are any restrictions on journals that we can approach to publish the main paper bearing in mind the open access policy.

10. Writing committees for future publications

There was discussion regarding writing and authorship of PACE papers other than the primary outcome paper.

It was suggested that a subset of TMG members should convene to form a Publications Committee for overseeing the writing of papers other than those reporting the primary outcomes and health economics. An example would be a paper describing the baseline dataset. The Publications Committee would

not necessarily comprise the same people as the actual authors of these papers but would be responsible for monitoring progress of their production.

All subsequent papers would have the first named author as the principal writer and include other members of the writing committee that have been involved.

All trial related papers would be the listed named authors followed by 'on behalf of the PACE trial team'. There may be some modification of this for papers derived from PhDs.

11. Coding of non serious adverse events

[redacted] has located a simple guide from the University of Cincinnati for the coding of adverse events.

ACTION 17: [redacted] to circulate the adverse event severity guide to all research staff for use by research nurses/assistants.

ACTION 18: [redacted] to add the severity scale for adverse events to the SOP.

All Investigators retain the responsibility for checking severity on all adverse events.

12. Actigraphy and step test analysis

[redacted] and [redacted] have met and drawn up a policy for analysing these measures.

13. Ancillary studies

a) 2 year follow up

We are waiting for ethics approval on this study. The application appears to have been lost in the REC office location move.

b) [redacted] supervision study

This has been circulated for review and is in final editing phase.

c) King's study

[redacted] is currently writing this study up.

d) Edinburgh study

There is no further news on this currently.

e) SNP study

There is no further news on this currently.

14. Definition of drop-out

There was discussion as to whether someone who drops out of the trial after session 14 is a true drop-out. It was decided that for accurate recording, the drop-out should be recorded but they will also be analysed as having an adequate dose of treatment.

General reasons for drop out were reviewed by the TMG and no common themes could be identified.

15. Specific centre issues

King's

No issues to report.

Edinburgh

The centre is looking for a back up nurse. The local NHS trust is raising issue with regard to the subvention shortfall. There is no CFS service at Edinburgh, so in the long term there are no available posts for the therapists. This might also have implications for post-trial treatment.

ACTION 19: [redacted] to add to the May agenda the issues of therapist shortfall toward the end of the trial.

Bristol

No site representation at this meeting.

Oxford

A CBT therapist is being advertised for at this centre.

Bart's

Adverts are going out for an APT and a CBT therapist, and a trial administrator. We are waiting on feedback from finance as to when the data management vacancy may be advertised.

Royal Free

No site representation at this meeting.

16. Therapy/treatment arm issues

CBT

At present there is a shortage of CBT therapists on the trial.

APT

[redacted] will be competent for APT at the Royal Free by March.

GET

[redacted] is approaching competence rapidly for GET at Bart's and is also providing support at the Royal Free.

17. Reserve business

ACTION 20: [redacted] to talk to [redacted] and [redacted] about supplying temporary data management support to Bart's and data checking for the whole trial.

18. Confirmed dates and venues for TMG meetings in 2008:

a) Thursday 8th May 2008, [redacted]
b) Wednesday 17th September 2008, [redacted]
c) Thursday 4th December 2008, [redacted]

19. It was noted that the **DMEC** will meet at 1.15pm (lunch) followed by a 1.45pm start on Tuesday 4th March at [redacted].

20. It was noted that the **TSC** will meet at 1pm (lunch) followed by a 1.30pm start on Wednesday 9th April at [redacted]

pace

Summary of Action Points

All

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