Trial Management Group Meeting # 21

12th October 2006

[redacted]

1. Those present

[redacted]

Observers

[redacted]

2. Apologies

[redacted]

3. Announcements

- [redacted] starts as the GET treatment leader.
- The Royal Free will start eligibility assessments in two weeks time.
- [redacted] joins the [redacted] CTU as the new statistician assistant.
- Bristol Frenchay Hospital under [redacted], have LREC and R&D approval to start as the 7th PACE centre. The centre hopes to open to randomisation in March 2007.
- [redacted] remains the contact for [redacted] whilst [redacted] appointed.

4. Previous minutes of TMG # 20

TMG #20 – Action 6: Actigraphy analysis strategy development is ongoing.

5. Matters arising from TMG # 20 not on the agenda

ACTION 1: [redacted] to investigate taking referrals for PACE from the Kent CFS network.

a) Publication of protocol

This is going to be coordinated from Edinburgh as [redacted] discovered that submission from QMUL would cost over £800 as QMUL no longer has BioMed Central membership.

ACTION 2: [redacted] and [redacted] to coordinate the submission to BioMed Central of the abridged protocol.

b) SSMC alone arm

ACTION 3: [redacted] and [redacted] to organise further SSMC training.

c) Edinburgh ancillary study sponsorship

The issue of sponsorship for the Edinburgh ancillary study is being clarified by [redacted]

d) Training guides for manuals

Development of training manuals for the four PACE treatments are ongoing.

6. Recruitment (attached item #2)

The trial extension proforma, previously circulated was discussed and approved, with minor changes.

a) Reasons for non-recruitment and possible solutions

Barriers to recruitment:

- Delayed starts to all centres,
- Reduction in referrals due to less available monies in PCTs to refer CFS patients to secondary care services.

b) Strategic proposals to increase recruitment

i. Extend time of recruitment, without extra funding

ii. Extend time of recruitment with extra funding

iii. Add eighth centre

The TMG were happy on principle to extend the trial in the three ways suggested, with a caveat that there is concern about stretching the money across extra centres, specifically subvention costs.

There is no extra money to cover therapists NHS costs as this was calculated as payments per randomised participants not by numbers of staff. The original pot of money is to be stretched to cover other new centres, however this may create problems within NHS Trusts in the long run for centres that do not meet target recruitment. [redacted] is going to write a

letter of support on behalf of the TSC addressed to NHS R&D to ask for more money.

Potential 8th centres were discussed and the following suggestions made:

East Midlands

West Midlands

Southampton

Dorset

Belfast

ACTION 4: PIs to discuss in principle for MRC and TSC support to seek further funding from NHS R&D. [redacted] to contact [redacted] regarding a supportive letter to DH for more NHS money to cover therapist posts.

ACTION 5: Centre leaders to calculate actual NHS spending on trial versus money received (£3001 per participant recruited).

Other barriers to recruitment were discussed and the part-time posts of the RN/A was believed by all to be a rate limiting factor. Suggest that this resource should be shared amongst centres in the same way that therapists have been.

ACTION 6: [redacted] to speak to [redacted] to spend one day a week at the Royal Free Hospital and if required in the future, one day a week at King's to increase recruitment at these centres and support staff on [redacted].

ACTION 7: [redacted] and [redacted] to produce projected recruitment figures for PACE separately for all three recruitment increase strategy options.

When applying for an extension to grant, the MRC forms ask for the result status of the trial to date. The TMG are not happy about releasing this data as it would break the blindness of the trial.

ACTION 8: [redacted] and [redacted] will provide the MRC with the blinded DMEC report to the MRC board directly, through [redacted].

7. Second wave centres

a) Barts II

Recruitment is slow to the second Bart's centre. Marketing to local (London based) GPs, and the CFS network services in Sussex, Essex and

Hertfordshire is underway. Further to this permission is being sought to also advertise to GPs in these three counties.

ACTION 9: [redacted] to discuss with [redacted] [redacted] concerns regarding the allocation of participants to therapists between Barts I and Barts II. Originally this was to be done alternately but staff shortages and staff cover have made this impossible.

b) Oxford

The Oxford team were congratulated for being the only centre to be recruiting to target. [redacted] is obtaining an honorary contract to help cover maternity leave at this centre. There are still patients on a referral list for the RN and also on a waiting list to be assessed in clinic. Local links have been made with the OCMET PCT to ensure a continued flow of referrals.

c) Royal Free

Ethics approval and R&D has now been achieved. Randomisations to this centre are anticipated by the end of October. There are 14 patients banked for the trial. An estimated 28 banked patients were lost in the time waiting for ethics approval. It is anticipated that [redacted] (RN) may need an extra day a week at least for the first quarter to process the backlog and/or support from another RA.

d) Bristol

Logistics of the 7th centre (and 8th centre) were discussed, including travel, training days, supervision (specifically for the payment to therapy leads and travel costs to the trial of these journeys) and equipment purchasing.

Peer training was discussed as a method of relieving the burden on treatment leaders. There is already precedence for this with the second wave centres. For consistency to the trial it is important that all therapists receive some training from the treatment leaders and build up a relationship with this person, so realistically not many time savings are made by peer training.

ACTION 10: [redacted] to arrange for the trial database to accept the seventh centre at Bristol.

8. First wave centre issues

a) Edinburgh

The two CBT therapists appointed each withdrew their application following contract negotiations difficulties with NHS HR at Edinburgh. [redacted] has been covering CBT as well as doing APT for the trial. The rate limiting factor to recruitment at Edinburgh has been identified as a shortage of doctor's time. It is hoped that this may be resolved by adding another doctor's session per week for assessments and SSMC. Discussions regarding financing this from the trial are ongoing.

b) Kings

Two new therapists have been recruited and are being trained. The RA is in [redacted] at present and randomisations are set to increase again. Two main doctors are doing all of the recruitment and SSMC which is working better than doctors on rotation. Training for one of these doctors is scheduled for November.

9. Data on screened patients:

a) Level of detail in red and black book

ACTION 11: [redacted] and [redacted] to review the screening data to see how this can be simplified.

b) Consolidation of red and black book entries with screen failures (referred but not entered patients) and consent logs

ACTION 12: [redacted] to create a database of all logs on one form for each centre in lieu of [redacted] no longer having capacity to do this.

10. Analysis strategy

A review of the morning meeting was presented. The analysis strategy group plan to meet six times in the next 12 months to fully define this protocol.

ACTION 13: Any TMG members that would like a copy of draft version 0.1 of the Analysis Strategy Plan should contact [redacted]. All to subsequently contact [redacted] with any thoughts and questions they have regarding the proposed analysis strategy.

ACTION 14: [redacted] to add authorship options to the agenda for TMG #22 (Feb 2007).

11. Processing of File Notes

ACTION 15: PIs/CLs to locally review the use of File Notes to ensure that these are being completed for any protocol deviations, violations and losses of data (e.g. DAR recordings failing). PIs/CLs to ensure that copies of all File notes are being copied to participants research notes.

ACTION 16: [redacted] to add discussion of “use of File Notes” to local team suggested agenda.

ACTION 17: [redacted] to ask RN/As to ensure they send copies of File Notes in with CRFs and missing DAR File Notes electronically in with 52 week DAR discs.

12. Independent review of taped sessions

It is thought that it would be best if this is done in one go starting 9 months before the end of study. Raters would then only need to be trained once and all recordings can be assessed within one set time period.

ACTION 18: [redacted] to locally advertise for staff to review the CDs in a year's time.

ACTION 19: PIs/CLs to remind all staff about the collation of 52 weeks DAR discs and to name files according to the naming protocol laid out in the SOPs:

<Staff member initials (*3 if possible*)><PIN><Participant Initials><Date of session>

e.g.

<ABC01001XYZ05052005>

All staff are to ensure the correct data is given at the beginning of the recording. PIs/CLs to suggest that when the CGI is completed therapists also pass on the DAR recordings.

13.Post trial additional treatment

The guidelines on additional therapy after 52 weeks were reviewed. It was reiterated that the decision as to whether to offer a patient further treatment should not be made until after the 52 weeks research assessment. The decision for further therapy should not be made before 52 weeks as it may dilute the effect and judgement of the trial therapy.

Training needs for all staff were identified:

- All staff need to reinforce continuing to practise the therapy after the last session and the longer term benefits that might be expected and the importance of fully engaging with the therapy.
- All staff need to reinforce that patients offered additional therapy do not necessarily receive another 15 sessions of a different therapy but that they may be offered more sessions of the same or an alternative therapy if the patient's condition indicates a need.
- RN/As need to reinforce that no data they collect is fed back to either doctor or therapist and so they cannot discuss a need for further therapy and nothing the patient tells them will be fed back to doctors to help inform this decision.

ACTION 20: PIs/TLs/CLs/[redacted] to reinforce the RN/As and therapists that further therapy after the trial is not a certainty but will be judged on clinical indication after the end of the trials.

ACTION 21: All PIs and CLs at their next local centre meeting to reinforce to RN/As to explain to participants that they are there only to collect the research data and not to act as clinic nurses giving advice on CFS. RN/As should not write clinical letters to doctors about any ongoing health concerns but should instead ask the participant to raise any issues directly with the doctor. The only exception is in the case of a serious or severe adverse event or reaction.

ACTION 22: PIs and CLs to reinforce to the doctors that they should not be receiving feedback from the RN/As regarding participants progress or concerns, but that these must be fully explored in the SSMC session.

ACTION 23: [redacted] to write a script for therapists about what may be said to participants on further treatment.

ACTION 24: [redacted] to complete the guidelines for further treatment based upon feedback received.

ACTION 25: [redacted] to circulate an agenda list for all local team meetings based on the TMGs, identification of common local problems.

14. Feedback from TSC (attached item #4)

a) *Request that TMG further define 'adherence to treatment' taking in to account attendance and engagement. Definition to be sent to MREC after this meeting.*

This task has been deferred to the Analysis Strategy Group

b) *Request that the TMG consider the two year follow up study in more depth and prioritise what data from this would be of most use, and use these discussions to further develop this protocol*

Discussion covered elsewhere in the minutes.

15. SSMC arm including self help reading – check that this is not heterogeneous across centres

Discussion as to whether SSMC advice and guides are consistent across centres.

Not all centres have a library although all do have the reading list.

Concern expressed that there might be centre bias about treatments being advocated in the SSMC self-help group.

ACTION 26: [redacted] to add discussion of SSMC advice to the local centre team meeting suggested agenda. SSMC should be in equipoise and not push any one text or type of therapy over any other.

16. Archiving of notes – alert notices

Clinical trial notes to be clearly labelled or contain an alert for long term archiving. DH guidelines suggest 30 years storage for all clinical trial participant hospital/clinic notes.

ACTION 27: [redacted] to add "alerts to notes" to the local centre team meeting suggested agenda.

17. 52 week data recording discs

It was reported that no 52 week discs have yet been received at the PTCC from any centre. A number of issues were raised regarding the digital recordings:

- File naming protocols are not being adhered to making it difficult for some data managers to arrange these discs
- SOP for starting recordings with PIN, initials and date of visit are not always being adhered to and incorrect PINs are being used making it difficult for data managers to identify participants and session numbers
- Recordings are often difficult to hear due to background noise (including papers shuffling on desks and workmen outside the building). There is a background noise reduction setting on the DARs which staff are advised to use to reduce this problem

ACTION 28: [redacted] to add the DAR issues to local centre team meetings suggested agendas.

18.Work for treatment leaders

This was discussed under the issue of second/third wave centres. It is hoped that training for the replacement Edinburgh CBT therapist can be timed with the training for the Bristol staff.

19.Ancillary studies

a) 2 year follow up

Review of the measures in the two year follow up study was made by the group and it was decided that these could be reduced. CSRI could be reduced to key cost driver questions only, follow up should be by telephone (30 minute interview), EuroQol, SF-36 and CFQ, WSAQ, treatments received in the interim period should be included.

ACTION 29: All to provide feedback on the two year follow up study.

ACTION 30: [redacted] to provide statistical support data for the two year follow up study.

ACTION 31: [redacted] to add aims and objectives to the two year follow up protocol.

ACTION 32: [redacted] to provide the key cost driver questions for use in this study.

b) [redacted] supervision study

This study has been submitted to MREC.

c) [redacted] reflection on manual driven CBT study

The CBT group are now going to write a reflective paper but were not willing to run a research study across other treatment arms.

ACTION 33: [redacted] to contact [redacted] to let [redacted] know that the TMG would like the proposal for a wider study to be offered up to other therapists. [redacted] permission to be sought.

ACTION 34: Contingent upon Action point 29 - [redacted] to alert the whole PACE team that there is an opportunity for a study to be conducted on the experience of giving treatment to a manual across all the treatments.

ACTION 35: [redacted] to inform [redacted] and colleagues that the paper is supported and that this can be written but that publication may have to be deferred until after the main results and that the TSC will need to be consulted in advance of publication. This has to be offered first to an Open Access journal as it is related to an MRC sponsored study.

d) King's study

ACTION 36: [redacted] to send a copy of the proposal and LREC approval to the MREC for their information only.

e) Edinburgh study

Funding decision is awaited after which ethics approval will be sought.

20. Proposed dates and venues for TMG meetings in 2007:

a) Thursday February 8th 2007 [redacted]

b) Wednesday May 9th 2007 [redacted]

c) Thursday 20th September 2007

d) Wednesday 12th December 2007

Action Point Summary List

All

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PIs/CLs

ACTION 5: PIs and Centre leaders to calculate actual NHS spending on trial versus money received (£3001 per participant recruited).

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Treatment Leaders

ACTION 20: PIs/TLs/CLs[redacted] to reinforce the RN/As and therapists that further therapy after the trial is not a certainty but will be judged on clinical indication after the end of the trials.

[redacted]

TMG #20 – Action 6: Actigraphy analysis strategy development is ongoing.

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