Trial Management Group Meeting # 12

Friday 10th December 2004

1. Welcome
Introductions and welcome to all present

2. Those present

[redacted]

3. Apologies

[redacted]

4. Previous minutes
The minutes of the last meeting were accepted.

5. Matters arising not on the agenda
The TMG reviewed the action points from the last meeting. The following action points are still outstanding:

a) SL&M R&D
[redacted] has now contacted SL&M R&D for a copy of the sponsorship and indemnity letter and is awaiting a response.

b) Therapeutic competence and differentiation

[redacted] is leading on the SOP for analysis of therapists' competence from the tapes – a meeting is scheduled.

TMG10 – A2: [redacted] leading meeting to discuss analysis of therapists' competence from tapes before TMG in February. This will include an agreed minimum score on the therapy competence scale.

TMG10 – A3: [redacted] to write SOP for tape analysis and incorporate individual assessment early on for differentiation between therapies – agenda item for February.

TMG10 – A4: [redacted] is going to consider who, other than [redacted], could be an independent expert to rate the therapy tapes for differentiation.

ACTION 1: All treatment leaders to rate a few tapes for the first few patients to monitor early competence. Tapes should be rated throughout the trial and not just at the end - in order to ensure that competence is maintained.

c) Videoconferencing

[redacted] spoke about JANET desktop videoconferencing which is free to all users and currently being trialled at Edinburgh.

ACTION 2: [redacted] to report back on JANET videoconferencing once tested.

ACTION 3: All centres to report back to [redacted] relating to arrangements for videoconferencing.

d) Local team meetings

These are working well. Discussion held as to who should view the minutes to these.

ACTION 4: All centre leaders to ask local data managers to set up distribution lists for local centre team meeting minutes. These should include all local staff at each centre. The Data Manager will forward other centres' minutes to their own team.

It was suggested that the minutes and other documentation could be added to the website in the future.

e) CVs

ACTION 5: Each centre leader to ask for CV's for all trial staff.

ACTION 6: These CVs should mention their employment on the PACE trial and their role in the trial, and should have a 'wet ink' signature of the staff member. Copies to be forwarded to [redacted]. This is necessary for ethical purposes (good clinical practice).

ACTION 7: Centre leaders (in Oxford and London) should send each other copies of all therapists' CVs and then use them to obtain Honorary NHS contracts in order to allow therapists from one centre to treat participants from another.

f) Actigraphy

The issue of using actigraphy as an outcome measure was raised. It was noted that the Dutch study by Bleijenberg and colleagues reported that actigraphy was not a good outcome measure since the majority of patients are reasonably active and there is no change in this in spite of improvement in fatigue. However, pervasively passive people at baseline may do worse on CBT and perhaps better on GET.

A final decision on using this as an outcome has been postponed until we see how much of a measurement load actigraphy is, and it was agreed that this may be changed later next year if desired.

ACTION 8: [redacted] to ensure this item (regarding actigraphy at 52 weeks) is added on to a future agenda.

ACTION 9: [redacted] to circulate Prins and other related papers on actigraphy.

g) Patient process

The patient process handout (explaining the patient's pathway through the trial) was not included in all manuals. This can be explained to the participant verbally if required, or given to the participant if requested, since we will have ethical approval for this.

h) Request from children's services for advice regarding pacing ([redacted]

This group seem uncertain as to aims and definitions of their research. They will visit Edinburgh in January to discuss pacing with [redacted]. To be decided: if manual to be issued in what form should this be released?

ACTION 10: [redacted] to advise the TMG on possible release of APT manual to this group.

i) Freedom of information act

Freedom of information – new regulations will state that any requests for any information must be responded to within 20 working days. Discussion as to how this may affect PACE ensued.

Issues

- Non-PACE staff have been using material from the manuals to save them re-creating handouts already available within the department with PACE.
- Query whether the manuals be made freely available?
- For the non-copyrighted material, this may adversely affect recruitment; or may lead to inexperienced people practising the therapies and blaming PACE if the patient comes to harm (bad use of manuals could

happen anyway). Pacing is an experimental therapy and we have no definite data that this will work well.
- There are copyright issues associated with distributing anything from the CBT participants' manual as [redacted] book will be published [redacted].

Decisions
- If copies of trial documentation are requested, a copy may be given with distribution restrictions and conditions and with instructions to acknowledge the authors of the manuals and the PACE TMG in all published work.
- Caveat that PACE team is not responsible if the therapy doesn't work or causes harm.
- Instructions that these are not self-help guides and that the therapists manuals must only be used after several months close training and supervision with an expert, and that the participant manuals are only effective as extra material to therapy sessions.
- PACE centres – therapists can use copies freely.

ACTION 11: [redacted] to design and issue a standard letter/form for the issuing of any PACE materials to non-PACE persons.

ACTION 12: [redacted] to seek advice from MRC regarding the dissemination of PACE Material outside of the trial.

ACTION 13: [redacted] to invite MRC to talk to the TMG about the Freedom of Information regulations.

j) Banking patients for the trial

Edinburgh have already started to bank patients for the trial.

ACTION 14: [redacted] to start banking patients at their centres now.

ACTION 15: Centre leaders to ensure that Research Nurses sit in on therapy and medical assessment sessions before the start of the trial.

k) Stationery

ACTION 16: [redacted] to confirm design for trial stationery (removal of all addresses, addition of funders' names).

l) Randomisation and database training

[redacted] would like one day of training supported by site visits. Training suggested for the week beginning 10/01/2004.

ACTION 17: [redacted] to decide dates for randomisation and database training. Randomisation training should be completed in early January and before Data Manager training.

m) Unsolicited mail

Most staff have not received any, although [redacted] and [redacted] have and the MRC has received a lot of correspondence.

Reminder than any such mail should be forwarded to [redacted].

Freedom of information act may have a bearing on the handling of this mail.

n) Future TMG meetings

ACTION 18: [redacted] to distribute meeting locations and secure a room for the April meeting. Please note all meetings will take place in [redacted]

6. Update on the MREC submissions

[redacted] described the two recent MREC submissions. Earliest possible date for randomisation is Jan 17th (once MREC have responded). However, actual start date is likely to be later as CRFs cannot be printed up until approved by MREC.

Before the trial may start, in addition to the MREC approval to the protocol, manuals and all amendments, each centre must have the following in place:

a) R&D approval – final approval is granted once the correspondence from MREC has been forwarded to your R&D department along with a copy of the most up to date protocol.
b) Confirmation of local sponsorship as part of above
c) LREC approval which should now have been obtained by all the first wave centres, [redacted] is awaiting confirmation from King's. MREC do not appear to know about this centre.

7. Update on training of therapists

a) In Edinburgh [redacted] reported that the usefulness of sitting in on therapists' sessions.

TMG11 – A29: [redacted] to give additional support to that given by the treatment leaders on generic skills of engaging patients and more general CFS/ME training, by sitting in on sessions to review skills and from that give further supervision and support to build up confidence.

TMG11 – A32: Treatment leaders have not yet had time to swap audiotapes – they will undertake this in the near future.

ACTION 19: Competence to be checked as specified in SOP (see above) required by two raters for each therapist. If the raters are not confident in a therapist's competence, the tape should be passed on to another PACE treatment leader for assessment.

Equipment problems – most centres have had a lot of difficulty locating tape machines, and those that they have found have turned out either to be broken or to record too poor a quality to assess.

The digital audiorecording equipment has been tested by Edinburgh, and a decision is to be made at this meeting regarding what equipment should be ordered (see below). It was noted that this was likely to cost more than the allocated budget. The committee were informed that digital recording equipment should be delivered one day after the order placed.

ACTION 20: [redacted] to order digital recording equipment next week.

ACTION 21: [redacted] to write SOP by end December regarding assessment of competence.

b) Timelines for assessments of competency

Nothing to report – training sessions are ongoing.
[redacted] – Previous concerns in hand and improving.
SSMC training was on 29th Nov – nothing to report

8. Update on training of research staff

a) SCID training

SCID first training day to take place in [redacted] December. This will involve an introduction to the subject, and role-playing, staff to watch selected excerpts of the tapes in advance of this. The SCID will need further sessions - to be decided later. London training will probably be managed by [redacted]

Competence and concordance issues – SCID to be taped at each baseline assessment. Somatoform disorders questions are no longer to be included.

b) Doctors training

Cognitive assessment will be carried out by the clinic doctors to exclude delirium and dementia.

ACTION 22: [redacted] to write SOP for the clinic doctors on how to assess for delirium and dementia.

It was agreed that a SOP is needed on physical examinations for the clinic doctors. A form of this already exists in the protocol appendix.

ACTION 23: [redacted] to review the SOP for medical examinations and to look into writing a more operational version of this.

9. Ancillary studies – chaired by [redacted]

A suggestion was made that detailed decisions about ancillary studies be postponed until the trial is up and running. It was noted that the process of the TMG and TSC approving a study, and this being sent forward for ethical approval may take up to a year. It was noted that all project proposals should undergo independent review. Initial discussion was held about the proposed ancillary studies:

a) Genomics study (Barts)

There was mixed support for this study, with some enthusiastic, and others concerned that a blood test at all four assessments may be intrusive to the participants. A view was expressed that some patients would be more interested in PACE if they knew there was a biological arm to the trial. There may be ethical issues involved in mapping phenotypes. Separate ethical approval would be required.

b) Edinburgh study

No objection in principle to this study, though it was noted that a separate consent form would be required even though the original one states that tapes would be used for research purposes. The MREC would expect us to give out new information and details of how the recordings would be used.

ACTION 24: PIs to review the MRC ancillary guidelines. [redacted] to check MRC website to see if any such guidelines are available.

ACTION 25: [redacted] to invite all Centre Leaders to consider submitting any other ancillary study proposals with a deadline of the April TMG.

ACTION 26: Letters to go from [redacted] to the two ancillary study proposers stating that the TMG are happy for them to produce more developed protocols and to seek external funding. The final protocols will be subject to PACE TMG and TSC approval.

ACTION 27: Additionally, [redacted] to inform researchers for genomic study to do the same but advise them that there are reservations about the blood tests, and to ask whether buccal swabs may be offered to participants as an alternative.

10. Recruitment of staff for second wave centres

a) Oxford

[redacted] requested a visit to Oxford to get things moving and help prepare for the launch of the trial there.

ACTION 28: [redacted] to visit Oxford in the New Year. [redacted] to agree date by email.

b) Mentoring

The TMG agreed that mentoring from existing centres should be made available to help new centres.

c) Timing of start for second wave centres

As noted at a previous TMG meeting, MRC to release research money from 14 Jun 2005; which is when research staff should be employed from. Therapists' adverts should go out in January, in order to recruit early spring, in order to start employment in March, so that they will be able to complete 6 months of training before opening these centres for recruitment in September 2005.

Double of recruitment rate in three centres to commence mid-2006.

Recruitment panel: therapy leads, and the trial manager should be contacted to sit on interview panels if the centres feel this would be helpful.

11. Piloting of CRF

To be started asap. NCR packs will be produced after the MREC has approved the CRFs.

ACTION 29: [redacted] to email CRF's to each research nurse and data manager.

ACTION 30: CRF's to be piloted by each centre's research staff.

12. Equipment

a) Equipment ordering

[redacted] reported that some equipment is still to be ordered – there are some problems with costs and locating correct items.

b) Steps

The steps cannot be bought but will have to be made. No cost in grant to cover this. There is a width and height restrictions for the steps (20hx30dx40w so for entire two-step unit 40x60x40cm). We agreed that these should all be made at the same time for consistency.

ACTION 31: [redacted] to arrange ordering of steps equipment.

c) Digital equipment

The budgetary restrictions were noted.
Options discussed: Olympus DM10 or DM20 are the preferred machines. Broadcast at top quality on DM10 has 4 hrs; DM20 has 8 hrs; £30 difference in price.
TMG agreed 41 machines to be ordered. Agreed to order DM20 and have high quality – not worth risk of loss of data.

It was noted that if the Edinburgh ancillary study goes ahead, funding from this might allow us to recoup some of the additional costs of these machines.

d) Heart rate monitors

[redacted] has created a standardised system for listing and tracking code numbers on the HRMs.

ACTION 32: [redacted] to email therapists at other centres to send back code numbers for HRM.

13. Database update

[redacted] - Manual to be written; [redacted] has almost finished database.

ACTION 33: [redacted] to collaborate with [redacted] and [redacted] to write manual for database in January.

Training date to be set.

ACTION 34: [redacted] to email [redacted] with list of Data Managers contact details.

14. Centre reports

It was pointed out that Barts centre meeting minutes #1 - item 10 should be corrected (i.e. either the DMEC or TSC can make the decision to stop a trial and this does not need funders' approval).

ACTION 35: [redacted] to alter item 10 on the Bart's meeting minutes as per [redacted] suggestion.

15. Unsolicited mail and MRC request for publication of protocol

The MRC have received 30-40 letters of complaint about the PACE trial. It was explained that this is a result of a concerted campaign by the MEA and others.

[redacted] will be meeting with [redacted] and anyone else who wants to may also attend.

It was suggested that the protocol be submitted for publication in a BioMed Central electronic journal. The MRC were agreeable to this. This gives open access for anyone to view. There were concerns about how estimates for improvement with each treatment might be interpreted by a lay reader. It was agreed that sections of the protocol would be re-written and edited for a lay audience before publication.

The MRC would like to print the name of the DMEC members on their website. [redacted] has written to the DMEC to ask for permission to have their names printed. Some positive feedback has been received so far.

ACTION 36: [redacted] to explain in published protocol percentages of efficacy on different treatments.

ACTION 37: [redacted] to contact MRC and ask if and how power calculations are normally published on their website.

ACTION 38: [redacted] to circulate the MEA article and response to the TMG.

ACTION 39: [redacted] to ask [redacted] if the PI's can see copies of all correspondence sent to the MRC about PACE.

ACTION 40: [redacted] to write an explanation of all the criteria for CFS/ME used for the trial in lay language as this has been requested by [redacted]

16. Any other business

a) Expenses for therapists

Continued problems encountered by some therapists in claiming expenses were noted. This had arisen due to either contractual issues with the institution or misunderstanding in the claims process. These issues have now been resolved.

b) Accommodation and travel policy

The Guidance for Accommodation and Travel was agreed by the TMG.

ACTION 41: [redacted] to circulate to all staff.

17. Date and time of TMG #13 is 1 – 5pm 10th February 2005