



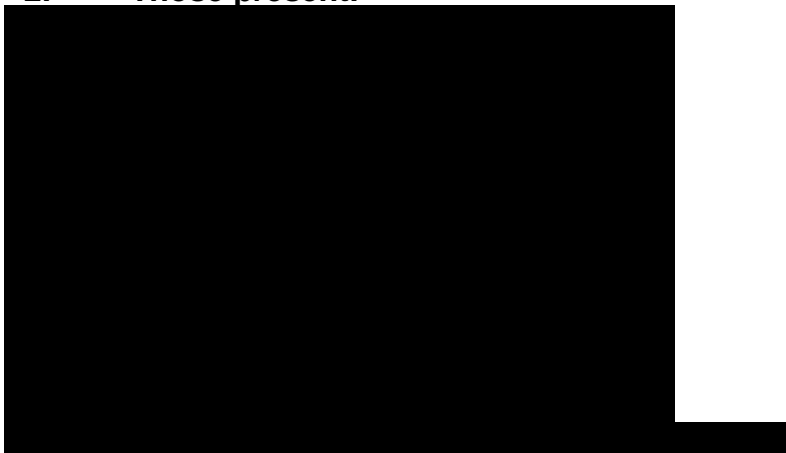
Trial Management Group Meeting # 13

Thursday 10th February 2005

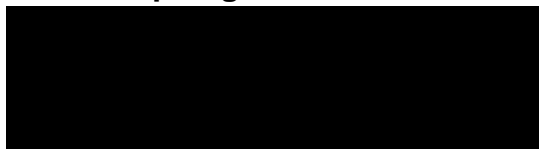
1. Welcome:

Introductions and welcome to all present

2. Those present:



3. Apologies:



4. Thanks for preparations for the trial

The PIs acknowledged the tremendous amount of work put into the trial preparations in the last few months by many people, both present and not present at the meeting. The PIs also thanked everyone for the extra work done by many people, which was usually unpaid and often done outside of office hours.

Action 1: Members of TMG agreed to pass on this thanks and acknowledgement from the PIs, and express thanks to members of their own teams.

5. Previous minutes:

Correction Action 32: substitute 'GET therapists' for 'therapists'.

6. Matters arising not on the agenda:

The TMG reviewed the action points from the last meeting. The following action points are still outstanding:

TMG 10 – A4: ■ is going to consider who, other than ■ could be an independent expert to rate the therapy tapes for differentiation.

TMG12 – A2: Videoconferencing system working in the University, but has yet to be tested with other sites. ■ to report back on this once tested.

TMG12- A3: ■ to let ■ know re Royal Free videoconferencing facilities. Other sites confirm have videoconferencing suites. ■ previously established that Bart's has no arrangements for videoconferencing.

TMG12-A5: ■ to send email to all those who have yet submitted their centre staff's CVs.

Action 2: ■ to put CVs of all trial staff on master file once received.

TMG12-A7: ■ to remind centre leaders (particularly at Bart's and Kings) to send therapists' CVs to Bart's to obtain Honorary NHS contracts. Copies of NHS contracts are required by staff outside of Bart's in order to be able to obtain honorary contracts for Bart's.

a) How to address possible destabilisation of the trial if a therapist is away long term:

Discussion pinpointed possibility of:

- Therapists being trained in one main therapy and a subsidiary therapy so as to be able to cover for colleagues (although there might be an issue of cost).
- Patients could be referred to another centre where the therapy is currently available. We would need to take care of patient documentation if referred to other centre.
- Reminder of contingency consent form (given ethical approval) for a centre running temporarily with three treatment arms.

Action 3: ■ to discuss what might be possible solution for local centres outside of London.

Action 4: ■ to consider multiple therapeutic experience, when recruiting.

Action 5: Therapy leaders to look at what might be possible when:

- advertising
- training current staff

TMG12-A8: Issue regarding actigraphy at 52 weeks, to be added on to a future agenda.

TMG12-A14: Banking patients has been happening. Bart's – have 3 (with one refusal) and Kings have 7- 8.

TMG12-A22: [REDACTED] to write SOP to clinic doctors on how to assess for delirium and dementia.

TMG12-A23: Physical examination guidance

[REDACTED] had circulated 'Guidance for Physical Examination of Potential Participants' and had revised it following feedback. The TMG noted that the Oxford criteria, which are the eligibility criteria, require a physical examination in order to meet criteria. Although this might be satisfactorily done by some GPs, this could not be assured across all centres. Such guidance might help those doctors not used to regular physical examinations, although concern was raised about how useful the guidance was. The preliminary consensus was that this was useful guidance for some doctors, so long as carried out by doctors overseen by a physician. Discussion was suspended to await [REDACTED] arrival at meeting.

Added Note after the meeting: As [REDACTED] was not in the end able to attend the meeting, the PIs have decided that the current guidance should be adopted, so long as inexperienced doctors are tutored in how to do an adequate physical examination by a practising physician, MRCP or FRCP.

Action 6: Centre leaders to ensure all screening doctors are competent, as suggested.

TMG12-A24: PIs to review the MRC ancillary guidelines. [REDACTED] to check MRC website to see if any such guidelines are available.

TMG12-A25: [REDACTED] to invite all Centre Leaders to consider submitting any other ancillary study proposals with a 2 month deadline.

TMG12-A27: [REDACTED] to meet with CDC researchers for genomic study on 6th March.

TMG12-A31: Importance of risk assessment under clinical governance to be carried out on steps bought. Patients can then be made aware of any risk identified.

Action 7: All centre leaders to write to R & D departments with MREC approved final protocol, which includes the use of the steps, as used in previous research. It is their responsibility to do a risk assessment.

TMG12-A32: [REDACTED] to check with [REDACTED] re back code numbers for HRM.

TMG12-A36: [REDACTED] to explain in protocol to be submitted for publication the percentages of efficacy on different treatments.

TMG12-A37: [REDACTED] to contact MRC and ask if and how power calculations are normally published on their website.

TMG12-A39: ■■■ to ask ■■■■■■■■■■ if the PI's can see copies of all correspondence sent to the MRC about PACE.

TMG12-A40: ■■■ to write an explanation of all the criteria for CFS/ME used for the trial in lay language, as this has been requested by ■■■■■■■■■■

7. Site Principal Investigator Agreement:

Action 8: ■■■■■■■■■■ to check out costs of getting the document checked by a lawyer, particularly regarding the issue of termination. Possible options through MRC lawyers, or free at Queen Mary's.

The Site Principal Investigator Agreement was approved with suggested amendments made during meeting, and pending legal opinion.

A discussion was held regarding how to deal with a centre which under-recruits or doesn't produce quality data:

The protocol stipulates that a centre is monitored carefully if greater than 1% errors detected in data submitted.

Several mechanisms are in place to detect failure in data:

- a) Several monitoring committees are in place including TMG
- b) Monitoring visits from trial manager could help rectify this.
- c) Monthly submission of data ensures regular monitoring
- d) Nurses will check data with patients to reduce any margin error.

Regarding under-recruitment, centre leaders are responsible to their Trusts, who do not receive payment for PACE therapists unless a centre recruits, so we already have an incentive to recruit adequately.

8. Update on MREC submissions:

Approval has now been given. Thanks were given to ■■■ for ■■■ work on securing this.

9. Therapy Competence:

Decision: Competence will be judged qualitatively using global judgement, informed by Therapy integrity scale scores.

10. SSMC competence:

Amendments noted to document 'Recruiting, screening and SSMC competencies', which was approved subject to these amendments.

A discussion was held about how to monitor the clinic log of all new patient attenders. Should this be on the basis of the referral letter mentioning CFS/ME or on the clinical diagnosis made in clinic. It was noted that the existing form contains an 'outcome' column that allows for non-CFS diagnoses to be recorded.

Action 9: Centre leaders to ensure that: ID clinics list all cases where the referral could plausibly have been for CFS/ME; CF clinics record all referrals seen.

11. Site Initiation Report:

Two suggested amendments were noted. The SOP was otherwise approved.

12. Database update:

Database is very nearly complete with only a few forms to go on. Randomisation can start. [REDACTED] is currently handing over to his replacement.

13. Printing of Manuals and CRFs

We have a budget of only £3,000 to print off the manuals and all the CRFs, with quotes greatly exceeding this sum. Various options discussed, including each team holding a copy of the participant manual and CRF masterfiles on CD, to print off when they need to.

Action 10: [REDACTED] to look at practicalities of options regarding CRF printing, and put forward proposal to [REDACTED] and [REDACTED] to decide on.

Decisions: The therapists' manuals will be bound at Bart's using monies from the PACE budget. The participants' manuals will be bound at local centres.

14. Definition of 'new' patients:

Two amendments were made to Draft 3 of the 'Operationalised definition of 'new patient' for the PACE trial'. The amended draft was accepted.

Decision: The trial will recruit using the adopted criteria for 3 months, and will be reviewed at the TSC and DMEC meetings.

15. Current randomisation of patients in second wave centres:

The suggestion was made to recruit patients from second wave centres into the trial as first wave participants before the second wave centres started. There would be a cost involved (eg. travel expenses).

Action 11: [REDACTED] and [REDACTED] to explore practical possibilities of cross-referral, particularly in London.

16. SCID:

Has been slimmed down to some 30 pages. Final touches to do, but is ready to try out.

17. CGI:

We will adopt the patient version, which uses the word "better" rather than the original "improved" for all CGI ratings.

18. CSRI as an interview or questionnaire:

A discussion was held regarding how to ensure patients don't feel pressured or their privacy intruded upon by the questions posed. Importance recognised

of nurses assuring patients of the confidentiality surrounding the information they give.

Action 12: CSRI will be given as a questionnaire to be filled in the presence of the RN/RA in order to clarify any questions, if required.

19. Mentoring of second wave centres:

Acknowledging the value of establishing mentoring arrangements across centres, it was decided:

Action 13: [redacted] to continue to mentor [redacted] at Royal Free, and also mentor [redacted] at Bart's.

Action 14: [redacted] to mentor [redacted] at Oxford.

20. Update on staff recruitment:

Oxford: Will be advertising for posts week 14th February.

Action 15: [redacted] to check with [redacted] and [redacted] re dates they may be free for interviewing.

Royal Free: Advertising for therapist in external bulletin as of February 14th.

Decision: Recruitment to be a standing point in the TMG agenda.

Action 16: [redacted] to include recruitment in next TMG agenda.

21. [redacted] meeting with RCPCH RCT group:

[redacted] recommended assisting this group, who would like a copy of the APT manual (will modify, and acknowledge authorship), and to see PACE protocol. The group is considering a two armed therapeutic approach – 'stairway' and APT.

Re appendix of advice to letter, all agreeable to TMG, except point 4 that needs checking.

Action 17: [redacted] to check re relevance of point 4 and inform [redacted]. Letter of advice regarding use of PACE materials was otherwise approved.

Decision: Agreement to share materials with RCPCH RCT group, accompanied by letter about use of PACE materials.

Action 18: [redacted] to write to [redacted] stating that the TMG would be open to further communication with the RCPCH RCT group, and to offer advice where appropriate.

Action 19: ■ to float the idea with ■■■■■, of developing trial on children/adolescents as extra stratum within PACE.

Action 20: ■ to email rest of TMG regarding potential for PACE for children and how to take this forward. This item to be added to next TMG agenda.

22. Future TMG Meetings:

A discussion was held regarding rotating the location of alternate future meetings (with ■■■■■ and ■■■■■ held in ■■■■■), which would also allow site visits. It was noted that the duration of meetings might now be reduced to 3 hours. When relevant specific topics might be addressed in more detail, which could be chaired by any PI.

Action 21: All to inform ■ if would like to host future meetings, and when.

23. Talk by ■■■■■ ■■■■■ of the MRC on the Freedom of Information Act (England and Scotland)

There was a most useful presentation by ■■■■■, with the most useful information being that we do not need to release information about the trial, as this is research in progress. The situation was slightly different in Scotland. ■■■■■ handed out 'Freedom of Information Briefing' to accompany ■■■■■ presentation.

Action 22: Each centre to identify Freedom of Information officer at each centre/Trust.

24. Date of TMG # 14:

Decision: Minutes of TMG meetings to include action points per person.

Action 23: To let ■ know if can't make the next TMG on the 20th April.

Action points per person:

ALL:

- **Action 1:** To express thanks to members of their teams for their work in the preparations for the trial
- **Action 5:** Therapy leaders to look at what might be possible when advertising and training current staff to reduce risks destabilisation of the trial if a therapist is away long term.
- **Action 6:** Centre leaders to ensure all screening doctors are competent, as suggested.
- **TMG12-A24:** PIs to review the MRC ancillary guidelines.
- **Action 7:** All centre leaders to write to R & D departments to inform them of the use of the steps, as used in previous research.
- **Action 9:** Centre leaders to ensure that: ID clinics list all cases where the referral could plausibly have been for CFS/ME; CF clinics record all referrals seen.
- **Action 11:** [REDACTED] and [REDACTED] to explore practical possibilities of cross-referral, particularly in London.
- **Action 21:** To inform [REDACTED] if would like to host future TMG meetings, and when.
- **Action 23:** To let [REDACTED] know if can't make the next TMG on the 20th April.
- **Action 22:** Each centre to identify Freedom of Information officer at each centre/Trust. To ensure risk assessment carried out on steps.

[REDACTED]

- **Action 3:** Re how to address possible destabilisation of the trial if a therapist is away long term - to discuss with [REDACTED] what might be possible solutions for local centres outside of London
- **Action 4:** To consider multiple therapeutic experience, when recruiting
- **Action 15:** To check with [REDACTED] and [REDACTED] re dates they may be free for interviewing staff in Oxford recruitment.

[REDACTED]

- **Action 17:** With [REDACTED] to check relevance of point 4 of appendix of advice (regarding use of PACE materials outside of the PACE trial).

[REDACTED]

- **TMG 10 A4:** To consider who, other than [REDACTED], could be an independent expert to rate the therapy tapes for differentiation
- **Action 13:** To continue to mentor [REDACTED] at Royal Free, and also mentor [REDACTED] at Bart's.
- **Action 20:** To email rest of TMG regarding potential for PACE for children and how to take this forward.

[REDACTED]

- **TMG12 –A5:** To send email to all those who have yet to submit the CVs of the staff of their centre
- **Action 2:** To put CVs of all trial staff on master file once received.
- **TMG12-A7:** To remind centre leaders (particularly at Bart's and Kings) to send therapists' CVs to Bart's to obtain Honorary NHS contracts.
- To write on behalf of [REDACTED] to two ancillary study proposers re developing protocols and seeking external funding.
- **TM12-A32:** To check with [REDACTED] re back code numbers for HRM
- **Action 8:** With [REDACTED] to check out costs of getting the 'Site Principal Investigator Agreement' document checked by a lawyer, particularly regarding the issue of termination
- **Action 10:** To look at practicalities of options, and put forward proposal to [REDACTED] and [REDACTED] to decide on.
- **Action 16:** To include recruitment in next TMG agendas

[REDACTED]

- **TMG12–A3:** To let [REDACTED] know re videoconferencing arrangements at Royal Free.

[REDACTED]

- **TMG12-A2:** To report back next meeting on JANET videoconferencing once tested between University and other sites.
- **Action 3:** Re how to address possible destabilisation of the trial if a therapist is away long term - to discuss with [REDACTED] what might be possible solutions for local centres outside of London.
- **TMG12-A40:** 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].
- **Action 14:** [REDACTED] to mentor [REDACTED] at Oxford
- **Action 17:** With [REDACTED] to check relevance of point 4 of appendix of advice (regarding use of PACE materials outside of the PACE trial).
- **Action 18:** To write to [REDACTED] stating that the TMG would be open to further communication with the RCPCH RCT group, and to offer advice where appropriate.
- **Action 19:** [REDACTED] to float the idea with [REDACTED], of developing trial on kids/adolescents as extra stratum within PACE.

[REDACTED]

- **TMG12-A24:** To check MRC website to see if any ancillary guidelines are available.

[REDACTED]

- **TMG12-A22:** To write SOP to clinic doctors on how to assess for delirium and dementia.
- **TMG12-A25:** To invite all Centre Leaders to consider submitting any other ancillary study proposals with a 2 month deadline.
- **TMG12-A27:** To meet with CDC researchers for genomic study on 6th March.
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