

**Minutes of The MRC Pace Trial Management Group
Meeting No. 4
Friday 23rd January 2004**

1. Present

██
██

2. Welcome to:

██ (centre co-leader from
██)
██ at ██████████, who will be
training and supervising the physiotherapists in graded exercise therapy

3. Apologies

██

4. Agenda Agreed

The majority of the meeting was spent finalising the protocol.

5. Previous Minutes

Minutes were agreed. ██████████ confirmed that Edinburgh were going ahead with LREC approval.

6. Matters Arising not on the Agenda

██ sent ██████████ trial management group (TMG) minutes to ██████████
██ We also have received their trial protocol.

7. Trial Steering Committee (TSC): Final Membership and Date of 1st Meeting

The MRC have confirmed approval of the membership. ██████████
██ who is the director of the Clinical Trials Unit at the MRC, has
agreed to chair the TSC. ██████████ has vast experience of clinical trials and was
██ suggestion. The other members will include ██████████
██ and ██████████
the PIs, and the trial co-ordinator. Observers will include ██████████

██
██
██
██

The date of the TSC needs to be organised. The TSC will meet after the final protocol changes have been approved by the TMG. The first meeting will be to approve the protocol, agree the membership of the DMEC. The manuals will be approved separately since they will be piloted in the first few months of the study.

The possibility of having a joint TSC and Data Monitoring and Ethics Committee (DMEC) meeting to approve the protocol was discussed. This might occur approximately 6 weeks prior to randomisation starting.

Action 1

██████████ will write letters to be written to ██████████ and ██████████ acknowledging the change in their membership of the TSC.

Action 2

It was agreed that it would be useful to have the same person in Manchester and London on the TMGs. The three PI's have been invited to attend Manchester's TMG. We agreed it would be helpful to have a reciprocal arrangement. ██████████ agreed to write to ██████████.

Action 3

██████████ to speak to ██████████ at the MRC to ascertain whether joint meeting of TSC and DMEC is necessary. It was agreed that after the start of the trial the TSC and DMEC would be held on separate occasions. Realistically it looks as though the first meeting of the TSC could occur after Easter; mid to late April. ██████████ to organise the first meeting in liaison with ██████████.

8. The MRC have approved the members of the DMEC, although this needs confirmation by the TSC. These are ██████████ ██████████ at the Royal Free and UCL, ██████████ who is also ██████████ and ██████████ who is ██████████ ██████████

9. The final award letter has still not been received from the MRC. Draft costings have only just been received by the MRC from QM finance. We agreed that the £1.9 million could be used flexibly, and there are established parameters under which this may be done.

10. Salaries

Costings did allow for incremental points. However, clarification is needed regarding costs of inflation. ██████████ agreed to give ██████████ costings of the CTU over the next five years.

Action

██████████ to liase with ██████████ a regarding the CTU costs.

11. Timing of start of Grant

Trial is due to start 15th March 2004. Therapists should start first. Advertisements need to go out as soon as possible with a view to starting employment in the beginning of May. From 1st May we will need three physio's, three OT's two CBT therapists and one Trial Co-ordinator. Edinburgh will need one research nurse and one data clerk. Barts and Kings will need the latter by June 2004. The trial is due to start recruiting on 1st October 2004.

Action

██████████ and ██████████ to advertise therapy posts as soon as possible, and other posts soon after.

12. Research staff Job Descriptions

Job descriptions were briefly discussed and approved in principle.

13. Job Descriptions and Person Specs of Therapists

These were discussed.

Action

██████████ to talk to ██████████ and ██████████ about specifications for physiotherapists.

14. Recruitment Interviews

It was agreed that there should be as much flexibility as possible with regards to part and full-time posts and the possibility of recruiting across centres, such as having a joint post between Bart's and King's.

15. Video conferencing for future meetings briefly discussed.

Action

Centre leaders to find out specific costs.

16. NHS Service Support Costs (SSCs)

Action

██████████ to liaise with ██████████ over confirming SSCs

18. Possible effects of new Department of Health funded CNCCs and LMDTs to be discussed at the next meeting.

19. With regards to prior consideration of publication eg. submitting protocol to Lancet.

We agreed to defer discussion until future meeting.

20. Publication of final protocol by Bio Med Central health services ejournal. There was support and opposition to this proposal.

We agreed to defer decision until later as to whether this would be a good idea.

21. PACE Logo

This was circulated. [REDACTED] was given feed back from various members of the team.

Action:

[REDACTED] will circulate the draft final version, taking into account views expressed.

22. The Draft Final Protocol

This was minuted in detail by [REDACTED], and will be circulated separately from the minutes. There were some important discussion points that were not resolved at the meeting. These included the exclusion of somatisation disorder, the definition of SUSMC, and action required for an adverse event. Various action points arose from discussion of the protocol.

a) Somatisation disorder

There was much discussion about whether to stick to excluding somatisation disorder (SD) and how to measure it. Some held that SD was a meaningless concept that is as hard to define as CFS itself. Others maintained that SD represented a developmental personality disorder and that the PACE trial was not designed to test the management of patients with such a disorder.

Action:

[REDACTED] and [REDACTED] to discuss further and bring back to the TMG.

b) SUSMC

There was a significant discussion as to whether we should limit what a clinic doctor can either do or say. On the one hand, the view was expressed that it would be unethical to limit what such a doctor can do to help his/her patient. On the other hand it was thought that it would be confusing for a trial participant if the doctor and therapist gave different advice. Most discussion centred around how the doctor should act when the participant was randomised to SUSMC alone.

We agreed that the only prescriptions excluded where those putative treatments for CFS itself, e.g. immune treatments such as Immunovir, “metabolic” treatments such as NADH.

We agreed that patient advice and information sheets given out by the doctor needed to be consistent both with the trial equipoise and across all four arms.

Action 1

[REDACTED] agreed to revise the SUSMC protocol and circulate a revised version.

Action 2:

██████████ agreed to draft a hand-out for all patients attending SUSMC.

c) Additional therapy

We agreed to offer additional therapy, different to that received during the trial, to participants at the end of their trial participation, if agreed as necessary by both participant and clinician.

d) Adverse events

We discussed how to define a severe adverse event, an adverse event, and actions necessary to deal with both.

Action 1

██████████ agreed to draft a list of all relevant serious adverse events and less serious adverse.

Action 2

██████████ agreed to write a procedure regarding what to do about adverse events. For example what to advise GP writing in the medical notes, plan of action, follow up appointments liaison etc.

e) New revised international criteria

The new international CDC criteria (Reeves W et al, 2003) were discussed.

Action

██████████ to check the revised international (CDC) criteria, to ensure that we are measuring everything we need to measure, and will send everyone the actual paper.

f) Therapy adherence

Some discussion regarding treatment adherence took place, in other words the degree to which patients had complied with their homework.

Action

██████████ agreed to devise a Visual Analogue Scale to measure concordance with homework on a sessional basis.

23. Standard operating procedures (SOPs)

We agreed that we needed various standard operating procedures (SOPs) for the trial.

We agreed that a responsibility SOP should be drawn up for each centre leader. This would include a description of how patients are consented.

We agreed that an SOP would be required for the randomisation procedure.

We agreed that a data entry SOP was required. This would include entry, transmission, checking, back-up and encoding.

We agreed we needed an SOP for a trial log book in which everything related to the trial participants was recorded.

We agreed that we do not need a web site for the randomisation to take place, but phone/email number to contact the clinical trials unit (CTU) so that randomisation could occur in office hours.

We agreed that it is the centre leaders responsibility to ensure that patients were told about which group they are allocated to.

Action 1

Relevant SOPs would be drawn up by the Trial Coordinator, once appointed.

Action 2

██████ *agreed to complete the case report form (CRF), which will consist of all of the questionnaires and demographic information.*

Action 3

██████ *will ask ████████ to give advice on the contra-indications of graded exercise therapy, and thus the trial.*

24. Outcomes

Discussion of outcomes was deferred to a future meeting.

Action

██████ *and ██████ to discuss this further before the next meeting.*

23. Next meeting

Next meeting on February 20th between 2pm and 5pm in the ████████

██████ The main focus of discussion will be the therapy manuals, information sheet for patients, training programme for therapists, and final comments and revisions of protocol, if time allows.

██████████
END