



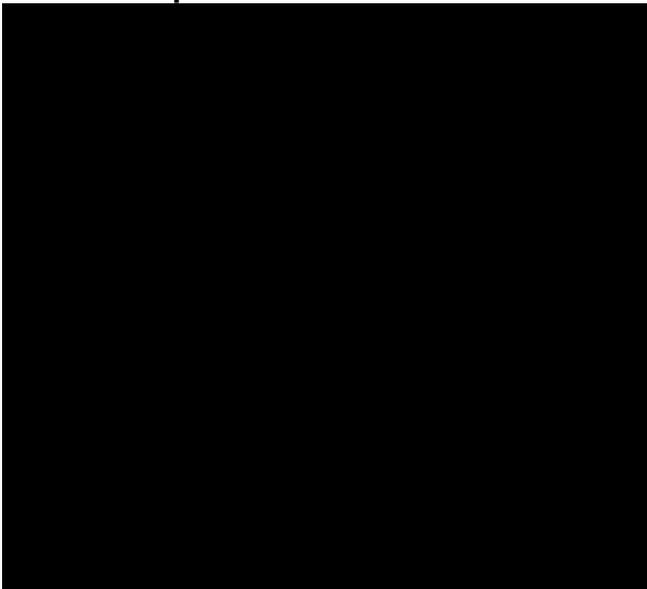
## **Trial Management Group Meeting # 14**

Thursday 28<sup>th</sup> April 2005. [REDACTED]

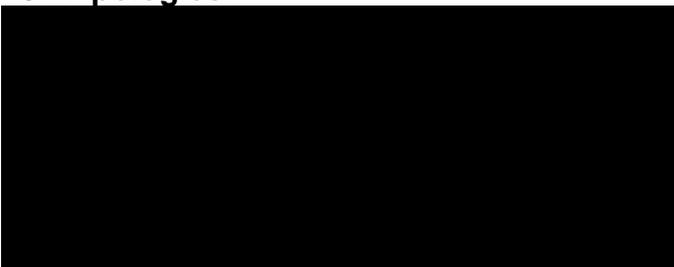
### **1. Welcome:**

Introductions and welcome to all present

### **2. Those present:**



### **3. Apologies:**



### **4. Agreement of agenda**

The agenda was agreed.

### **Previous minutes of TMG # 13**

The previous action points were discussed.

### **5. Assessment of differentiation of trial treatments**

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

This was discussed and the following agreed:

**ACTION 1:** ■ to:

- i) Identify how many recordings per participant should be reviewed by a blind assessor, and write this up as a SOP
- ii) Calculate the time required to complete the task of listening to the tapes and work out a reasonable hourly rate for doing this.
- iii) Identify people at the IoP/King's that might be available and willing to be a blind assessor and report back to next meeting.

## **6. Video and desktop conferencing**

**TMG12, A2:** ■ to report back on JANET videoconferencing once tested.

The option of using videoconferencing had been explored by the Edinburgh team and they reported that it was a good system. The costs involved are: £90 software; £50 webcam; free use of network using JANET (universities only). It was agreed that this method might be a suitable and cost effective medium to utilise for small meetings; although the security would need to be checked.

**ACTION 2:** ■ to test desk top conferencing between Edinburgh and London before next TMG and report back.

**TMG12, A3:** All centres to report back to ■ relating to arrangements for videoconferencing.

■ reported that teleconferencing is available at the Royal free but is very costly.

## **7. CVs and honorary contracts**

**TMG13, A2:** ■ to put CVs of all trial staff on master file once received.

Some CVs are still outstanding. The process for obtaining an honorary contract is very complex and cannot be set up centrally as it requires each staff member to fill out a number of forms about themselves to be signed off by their centre leader or PI. It was reported that the Trial Manager and Data Managers might not need honorary contracts for some Trusts as there is no patient contact, but this depends on local Trust regulations.

**ACTION 3:** ■ to write to Centre Leaders to remind them to find out local requirements for setting up honorary contracts.

**TMG12, A5; TMG 14, A3-A5:** Each centre leader to ask for CVs for all trial staff. Therapy leaders to look at what might be possible when advertising and training current staff.

Not all of the posts for the second wave centres have been advertised and there was further discussion as to whether the remits for the posts could be extended beyond just Physiotherapy and Occupational Therapy.

**ACTION 4: Centre leaders to consider widening the disciplines necessary for each therapy (e.g. exercise or sports physiologist for GET, nurse for APT).**

## **8. Actigraphy**

**TMG12, A8:** [REDACTED] to ensure actigraphy at 52 weeks is added on to a future agenda.

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 if desired.

**ACTION 5:** [REDACTED] to add actigraphy at 52 weeks to the September TMG agenda for discussion.

## **9. Assessment for delirium and dementia**

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

This has now been circulated and it was agreed at this TMG that the MMSE would be a suitable test for use by assessing doctors.

## **10. Referrals to PACE from second wave centres to first wave centres**

**ACTION 6:** [REDACTED] to instigate email discussion with [REDACTED] and [REDACTED] to decide whether referrals could be accepted from the second wave centres to the first wave centres. [N.B. There was a query over the practicalities of doing this without skewing the sample to be discussed further with [REDACTED] outside of the meeting].

## **11. Medical assessment SOP**

**TMG12, A23:** [REDACTED] to review the SOP for medical examinations and to look into writing a more operational version of this.

Discussed the PACE specific Physical Examination guidelines and these were agreed.

## **12. Equipment for new centres**

Second wave centres were advised to find out about Health and Safety requirements of their institutions with specific reference to the steps. It was advised that this be done as soon as possible to avoid delays later to the start of the trial.

**ACTION 7:** ██████ to send the remaining two sets of steps to the new centres as soon as possible.

**ACTION 8:** ██████ to ensure health and safety checks are made on the steps as soon as possible after they are received. Further advice on this available from ██████.

## **13. Screening Log (red and black clinic books)**

**TMG13, A9:** 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.

The details will be gathered from each centre for the consort diagram to be presented to DMEC.

**ACTION 9:** All centres to ensure that the screening book is up to date.

## **14. PACE children add-on study**

**TMG13, A20:** ██████ 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.

**ACTION 10:** ██████ to start designing an add-on to PACE to run a RCT on children in communication with others (GOS etc.), and bring to a future TMG for discussion.

## **15. Centre leader/investigator agreements**

The Centre Leader Investigator Agreement is not yet ready. There is one outstanding paragraph which has been re-written by QMUL finance and which will hopefully be approved in one week.

**16. Cover for therapists in the event of absence and long term leave.**  
**Draft SOP was circulated with the agenda to this meeting.**

## **Discussion:**

The following issues were discussed in light of the resignation of the GET therapist at ██████

a) *Should the GET arm be closed at ██████ ?*

It was decided that every effort would be made to keep randomisation open to all four arms of the trial at ██████. The possibility of increasing in percentage the numbers randomised to GET at other centres if one arm is

disabled was discussed. It was stated that suspension of a treatment arm in one centre could statistically affect trial results because it may create a centre effect with patients only volunteering because they know GET (the most controversial therapy) is not available; different randomization schemes should be explored.

*b) Could GET be jeopardised within the whole trial?*

This could happen if another GET therapist were to resign, but the loss of one therapist only was not likely to cause this problem.

*c) Can anyone located in [REDACTED] cover GET?*

No local physiotherapist is available to cover GET.

*d) Can a different [REDACTED] PACE therapist cover GET?*

[REDACTED] [REDACTED] has volunteered to supply cross cover however [REDACTED] will first need to be trained to the GET manual and assessed for competence. The manual has been written assuming prior knowledge of physiotherapy and so [REDACTED] will need to act as a physiotherapy assistant and receive supervision from a qualified physiotherapist. A discussion was held as to whether some of this supervision could take place with therapy sessions held as a tele/video conference between [REDACTED] and the participant.

*e) What should happen to the participant currently randomised to receive GET treatment at [REDACTED]?*

The current GET patient at [REDACTED] can receive the majority of sessions delivered by telephone by the 01 Barts GET therapist. [REDACTED] agreed by telephone to cover two or three [REDACTED] patients provided her London work load allowed this and would be prepared to travel to [REDACTED] once a month.

In the meantime, recruitment of a replacement therapist should take place as quickly as possible to replace the therapist, and a newly recruited therapist should receive their training at the same time as the therapists to the second wave centres.

*f) How essential is it that the participant receive their therapy face-to-face?*

Four sessions out of 15 have been identified as being required as face-to-face sessions. The remainder could be delivered by telephone although concern was expressed that this might be a sub-optimal method of treatment delivery.

*g) How soon can [REDACTED] take over the care of GET participants?*

[REDACTED] will need training and assessment of competence first. The first wave therapists received six months training to reach this but were also engaged in piloting and revising the therapies, so future training may not take as long. Discussions were held regarding the fact that the therapist's level of experience may not necessarily be indicative of efficacy of treatment; the less experienced therapist can often be more efficient. It was considered whether a cross-cover therapist would have enough previous experience in order to

bypass the full 6-month training and whether with training from the other therapists [REDACTED] might reach competence in a shorter time period.

*h) The SOP for Therapist Absence was explained in some depth.*

*i) What else needs to be considered/completed?*

- Permission needs to be sought from the MREC, TSC and DMEC and the participant already enrolled. Explicit consent is needed from future participants to accept these contingency arrangements.
- Consistency for patient important; problems with patients discussing treatment and deciding sub-standard treatment/sub-optimal situation
- Finances for additional training and travel to be considered.
- Additional workload to Barts GET therapist to be monitored.
- [REDACTED] to begin training with other current GET physiotherapists [REDACTED] at [REDACTED] and [REDACTED] at [REDACTED]) with [REDACTED] being classed as a physiotherapy assistant.
- Web-cam Internet supervision to be considered
- Cover across all centres and all treatment arms to be developed to cover therapy for any future resignations/prolonged absences of trial staff

**Plan:**

**ACTION 11:** [REDACTED] to arrange Honorary Contract for [REDACTED] to cover GET at [REDACTED]

**ACTION 12:** [REDACTED] to obtain R&D approval for temporary cover arrangements

**ACTION 13:** [REDACTED] to contact the current GET participant and re-consent them to continue in the trial under this contingency arrangement.

**ACTION 14:** [REDACTED] to supply a copy of this consent to [REDACTED] to send to MREC.

**ACTION 15:** [REDACTED] to recruit a new therapist as soon as possible (long term plan)

**ACTION 16:** [REDACTED] to take over treatment of the GET participant at [REDACTED] and future GET therapists according to [REDACTED] availability/workload

**ACTION 17:** [REDACTED] to begin training for GET cross-cover by:

- sit in and observe [REDACTED] for 4 weeks until [REDACTED] leaves
- attend supervision with a physiotherapist at [REDACTED]
- shadow [REDACTED] in [REDACTED] treatment of the current GET patient
- receive training in GET from [REDACTED] and [REDACTED] for GET training

**ACTION 18:** [REDACTED] to seek MREC, TSC and DMEC approval for:

- [REDACTED] to treat the both the current and future [REDACTED] GET participants until [REDACTED] is trained or another therapist in post and competent
- Eligibility criteria to be widened for recruitment for this post – i.e. specialist nurses, exercise physiologists etc.
- Cross-cover from a PACE therapist of a different discipline to be written in to each of the manuals
- Alteration to the PIS to reflect the fact that the treatments will be given by a trained therapists without defining their core discipline
- Alter consent forms to reflect a modified delivery of therapy where cover is long distance (more by telephone; less face-to-face)

**ACTION 19: [REDACTED] to ask [REDACTED] if:**

- [REDACTED] would be prepared to cover [REDACTED]s participants if required
- [REDACTED] would be prepared to help train [REDACTED]

**17. Blood results and recruitment**

Discussion regarding obtaining blood results before Baseline 2 visit - before randomisation and the difficulties experienced. The question was asked whether a participant could be randomised and their blood tests checked as soon as possible after and risk exclusion later.

It was agreed that the current SOP guidelines should stand: blood test results should be known before randomization and individual cases will be monitored at centres

12 participants are awaiting baseline assessment but have not yet been seen due to blood test delays at Kings.

**18. Recruitment targets and achievements**

11 participants have been randomized to date; had the trial opened as planned in January the target number of patients to recruit by now would be 28. Based upon a start date of March 1<sup>st</sup>, the target is 13 participants randomised by then of April. The progress on recruitment will be rechecked at next TMG.

It is hoped that the DMEC and TSC will not be concerned by the delay to start up at their June meetings, but they are likely to expect at least 80% recruitment target met.

The Edinburgh team reported that a lack of equipment – specifically actiwatches – is slowing down randomisation; therefore, more actiwatches are required. It was debated whether participants could be randomised without completing the actiwatch assessment to ensure randomisation is not slowed by a lack of available equipment but it was agreed that Edinburgh would receive another actiwatch next week and 2 more would be purchased.

**ACTION 20:** ■ to send ■ an actiwatch for the Edinburgh centre. Equipment to be reviewed in 2-3 months time and discussion held as to what more can be afforded.

The TMG agreed that second wave centres could recruit to first wave centres now, so long as the clinic log books were kept of all patients considered (see Action 6).

No other teething issues were reported to be affecting randomisation.

### **19. TSC/DMEC meeting June 29<sup>th</sup>**

Log books were reported as being up-to-date

**ACTION 21:** ■ to ask for faxed copies to be sent to the coordinating centre in the last week of May.

### **20. Second wave centres**

#### **Staff recruitment**

**TMG13, A15:** ■ to check with ■ and ■ re dates they may be free for interviewing.

■ aims to run interviews in Oxford from the second week in June.

■ will contact people for their availability for attending for interview soon.

The second Bart's centre has interviews scheduled for June 2<sup>nd</sup>.

All second wave centres are scheduled to start recruiting on 15<sup>th</sup> September; however delays to staff recruitment mean that this is now unlikely to happen before the end of the year.

**ACTION 22:** Second wave centre leaders to send their job adverts to the therapy leaders for wider dispersal to (free) discipline specific recruitment websites.

### **21. Database update**

It was reported that the database is not ready yet as there are still many amendments required, however an enormous amount of work has gone into this in the last few weeks and progress is being made rapidly. It is hoped that it will be live in the next few weeks.

### **22. SOPs**

Ongoing, a list of SOPs in development were circulated to the TMG

### **23. FINE trial meeting**

A summary of the most relevant points for PACE was distributed at this meeting:

- Medical care – some patients have expressed a preference for this because it requires less time commitment amidst too many other life stressors
- Supervision – it was noted that FINE are audio taping all supervision sessions
- Noted that honorary contracts only last for a year
- All staff completed a quiz detailing their treatment expectations. These are being retained in sealed envelopes not to be opened until the end of the study.
- Decision that we would consider a joint submission of the PACE and FINE protocols to Biomed Central

**ACTION 23:** [REDACTED] to prepare protocol for publication in Biomed Central as a joint submission with the FINE protocol

**ACTION 24:** [REDACTED] to request a copy of the FINE trial equipoise questionnaire for staff and distribute a similar document to the PACE team.

#### **24. Public Relations**

TMG approved the draft letter, already approved by the MRC, to be sent by those staff who wish it to their regulatory bodies, subject to the approval of the TSC.

**ACTION 25:** [REDACTED] to send the letter regarding the campaign against PACE and FINE to the TSC for their approval for use.

*Note added after the meeting:* On checking the previous minutes, the TSC have already agreed this in principle. Although [REDACTED] will send this letter on to the TSC, staff can start to adapt and use this now.

#### **25. Ancillary Studies**

It was noted that both the provisionally approved ancillary studies were either submitted for funding or about to be.

**Action 26:** [REDACTED] to submit [REDACTED] proposed study to the next TMG for consideration.

#### **26. Date of the next meeting**

June 15<sup>th</sup> at [REDACTED]

September 14<sup>th</sup> at [REDACTED]



**Action 26:** [REDACTED] to submit [REDACTED] proposed study to the next TMG for consideration.

[REDACTED]  
**TMG13, A2:** [REDACTED] to put CVs of all trial staff on master file once received.

**ACTION 3:** [REDACTED] to write to Centre Leaders to remind them to find out local requirements for setting up honorary contracts.

**ACTION 7:** [REDACTED] to send the remaining two sets of steps to the new centres as soon as possible.

**ACTION 5:** [REDACTED] to add actigraphy at 52 weeks to the September TMG agenda for discussion.

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[REDACTED]

**ACTION 8:** [REDACTED] and [REDACTED] to ensure health and safety checks are made on the steps as soon as possible after they are received. Further advice on this available from [REDACTED].

[REDACTED] \_\_\_\_\_ [REDACTED]  
**ACTION 2:** [REDACTED] [REDACTED] [REDACTED] to test desk top conferencing between Edinburgh and London before next TMG and report back.

**ACTION 11:** [REDACTED] to arrange Honorary Contract for [REDACTED] to cover GET at Edinburgh.

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