



## Trial Management Group Meeting # 15

Held at 1:30 – 5:00pm, Wednesday 15<sup>th</sup> June 2005, [REDACTED]

### Draft Minutes

#### 1. Those present and apologies

[REDACTED]

#### Observers

[REDACTED]

#### Apologies

[REDACTED]

#### *Other abbreviations*

Principal Investigators	PI	Research nurse/assistant	RN, RA
Centre Leaders	CL	Data Manager	DM

#### 2. Congratulations and thanks

Congratulations from the TMG to [REDACTED] who is receiving an award today.

Thanks to everyone involved for the successful cover of GET in [REDACTED], which has involved everyone on the team, with special thanks to [REDACTED] and [REDACTED]

### 3. Agreement of agenda

- The agenda was agreed with Agenda for Change being added for discussion under second wave centres.
- The TMG agreed to reserve some business for TMG members alone.

### 4. Review of the TMG minutes #14

TMG #14 - Action 1 feedback (Assessment of differentiation of treatments):  
(thanks from [REDACTED] to [REDACTED] for putting all related action points together).

- 150 participants in each supplementary arm and all 600 participants receiving SSMC.
- Estimated £30 to listen and rate each recorded session. Therefore if independent raters listen to one recording per participant the cost would come to £13,500 not including SSMC sessions. With two raters this would be double. When including SSMC sessions as well this cost increases significantly.

**ACTION 1:** [REDACTED] and [REDACTED] -Therapy integrity scale for SSMC to be written.

**ACTION 2:** [REDACTED] to write a SOP on how the process of rating the tapes for therapeutic integrity and differentiation might be carried out. This will be considered further at the PI/treatment leaders' proposed meeting (see below).

- For Consort, need to sample a recording from every participant to be able to say how many received the therapy as described.
- Random sample of different therapy sessions might be preferable to picking the same session for every patient.
- Same-session tapes could be used and compared for assessing other predictors for recovery (i.e. emotional engagement).
- Need to be able to demonstrate to our potential critics that we can assure the quality of therapy on the trial. Other trials have been criticised when re-rating recordings and finding therapy quality not to be as good as thought.

**ACTION 3:** [REDACTED] to add the issue of rating treatment recordings to the agenda for the Treatment Leader/PI separate meeting to take place 9.30am on Thursday 21<sup>st</sup> July.

- ■ has identified people at King's who could listen and rate the tapes. They could not rate King's tapes however as they know the staff and therefore would not be independent.

**ACTION 4:** ■ to order equipment for video-conferencing and liaise with ■ to test this between Edinburgh and Bart's.

**ACTION 5:** All CLs to ensure that all honorary contracts have been obtained.

**ACTION 6:** ■ and ■ to ensure Health & Safety tests are completed on the steps as required under research Governance before the centres open to recruitment.

- Discussions ensued regarding the clinic logbooks and how this works at each centre.

**ACTION 7:** ■ to send a blank template DMEC report to the PIs so that they can see what types of information are contained in the report.

**ACTION 8:** ■ to request the logbooks every month.

- Discussion as to whether we need more actigraph watches for the trial. PIs report that three appear to be enough for each centre.

**ACTION 9:** ■ to order two more actiwatches.

**TMG #14, ACTION 23:** Still outstanding. ■ to submit protocol to Biomed Central (in due course).

**ACTION 10:** Equipose questionnaire – ■ to identify which ones are still missing and send a reminder.

**ACTION 11:** ■ to circulate the letter regarding campaign against PACE to all PACE staff so that they may use this if required.

## 5. Recruitment

### a) Screening

- We are picking up other illnesses through the screening process showing the usefulness of this process.
- Oxford criteria includes the main symptom being fatigue (or a synonym); pain secondary. Centres are finding that some participants emphasise pain more post-randomisation. This is not a problem in eligibility since this is judged at the baseline visit 1 assessment. The Oxford criteria relies on the observer deciding which is the primary problem at the first visit, although it may be worth clarifying this at visit 2 if there is a doubt.

- The main reasons for exclusion at present are: SF-36 score too high, and not meeting Oxford.

b) Recruitment per centre

This is approximately equal across all three centres. 27 participants were recruited as of 15<sup>th</sup> June, which is 95 % of target.

**ACTION 12:** ■■■ to produce graphs of recruitment for future TMGs (both overall recruitment and per centre) against target recruitment.

- Approximately a third of new participants seen in CFS clinics are being referred for PACE.
- TMG would like to thank all recruiting staff for their successes in recruitment.

c) Any ongoing delays or issues

■■■ spoke about a ■■■ patient who wanted to come on to the trial to beat the waiting list but was threatening to drop out if ■■ didn't receive either GET or CBT. This was resolved with careful discussion with the patient as there were concerns that ■■ was not giving fully informed consent. Part of the discussion with the patient included reassurance that if ■■ received SSMC ■■ could still try other therapies on a self-help basis. ■■■ reported similar experiences and recommended regular role-play of the pros and cons of all of the therapies with the recruiters as useful ongoing training and peer support tool.

d) Randomisation errors

There has been one randomisation error identified at each centre. Each has resulted from the difficulty of differentiating between past and current depression, and confusion over use of the term 'depressive disorder' on the randomisation form (DSM-IV defines depressive disorder as being present if there is any history of a single major depressive disorder).

**ACTION 13:** ■■ to produce a new version of the randomisation form to clarify this and also add on the SF-36 and Chalder Fatigue scores.

e) SSMC

Discussion of the issue that ■■■ trial participants appear to be developing depression as a direct result of being randomised only to receive SSMC. These incidents are being monitored as they might become Serious Adverse Reactions (SARs).

Discussion as to what might be done to overcome this problem. Making self-help guides available to SSMC alone participants was suggested as a possible aid.

**ACTION 14:** PIs/CLs to circulate their lists of self-help guides to the other PIs/CLs (via ■■■ to make available to SSMC alone participants where required).

**ACTION 15:** ■ to investigate what graded exercise literature is available to add to this list.

**ACTION 16:** CLs to listen to SSMC recordings for supervision for doctors.

Discussion as to whether SSMC might vary between participants randomised to SSMC alone and those receiving an additional therapy. Inevitably there will be some variation since SSMC alone participants may choose a self-help approach, which would not be possible for those receiving supplementary therapy.

## **6. Cover for therapists in the event of absence and long term leave**

- ■■■■■ ■■■■■ has been recruited as the new GET therapist at ■■■■■
- ■ spoke to the current arrangement in Edinburgh whereby ■ is training ■ visiting Edinburgh once a month and carrying out joint sessions with participants by teleconference.
- A system of 'rolling competency' is being trialled for GET whereby a therapist can be developing competence on a session-by-session basis.
- Discussion that in the future we should aim to have a back-up for every therapist at every centre.
- TMG #14, Action 18 (to submit an amendment to MREC regarding contingency cover of therapy) is still outstanding because the TSC was not happy with all aspects of the contingency plan. This will be discussed at the TSC on 29 June 2005 and the MREC will be contacted after that time with a substantial amendment. A letter has been sent to the MREC with a copy of the supplementary consent form being used at Edinburgh with a notification that we will contact them with the full amendment after the TSC have met.
- Discussion as to when ■ can relinquish Edinburgh cover. ■ will be away for ■ weeks in August and ■ (■■■■■ therapist) away for ■ weeks from September. This situation will be monitored and looked at in more detail by the CLs. ■ could potentially cover one participant in this time.

### **Summary:**

#### New participants

- If a therapist is on leave for more than 4 weeks another therapist would need to cover any participants randomised in that period.
- The aim is that a participant should usually retain the same therapist throughout their therapy.
- The participant's holiday bookings should also be considered in this.

### Follow-up

- For therapist leave greater than 4 weeks, a second therapist will supply interim cover. The original therapist would take their participant back upon returning.

### Contingency plans

Discussion on the summary of the contingency plans that will be discussed with the TSC on 29 June 2005.

■ explained why from a statistical/trial analysis point of view, you would give GET if a CBT therapist was lost and vice versa. ■ would recommend that if an APT therapist was lost and no cover could be provided that randomisation was closed on that arm at that centre.

There was a difference of opinion within the TMG about this. The discussion will be taken forward to the TSC for them to make a final decision.

The method by which participants are consented where a therapist is absent also needs to be carefully reviewed as part of this submission to MREC.

**ACTION 17:** ■ to include the details of the contingency plan in a Substantial Amendment to MREC once the TSC have made a final decision.

## **7. Social events combined with training**

Discussion held regarding whether we can do combined generic training in August for the new centres and tie this in with a trial social event for all staff. Further discussions to be held outside of this meeting (aim to hold this in the last two weeks of August).

**ACTION 18:** ■ and others to organise a weekday for this tied into the generic training.

## **8. Second wave centres**

### a) Staff recruitment

■ reported that there have been Trust management issues at Oxford regarding releasing the job adverts before any subvention monies are received. It is hoped these adverts will be released soon for interviewing in July.

A Bart's II physiotherapist has been found and will be appointed subject to references being satisfactory.

**ACTION 19:** Centre leaders to send job adverts to the therapy leaders.

**ACTION 20:** ■ will email second wave centre leaders again regarding the idea of a single mail shot listing the jobs at all the centres.

**ACTION 21:** ■ to send a copy of the OT advert to ■ and ■.

**ACTION 22:** ■ write a few lines for the CNCC network listing all of the PACE therapist posts available.

**ACTION 23:** ■ to send this to ■ and ■ (CFS network) for circulation to the physiotherapist, OT and CFS networks.

b) Therapist training (including timing and duration)

- It was discussed that three months may be the minimum training period required for the second wave therapists.
- Generic CFS training at the start thought by the TMG to be a good idea.
- Centres with experienced staff should use these to help train the second wave centres (if staff are agreeable).
- ■ and ■ have created a training logbook for GET, which defines what training needs to be delivered by the therapy leader and what can be taught by experienced peers from the first wave centres.
- It will be easier to formalise all training plans once all therapists are recruited.
- 'Rolling competence' for CBT would be harder to plan because there is no defined order to the sessions so a therapist would need to have experience of the whole programme before they could deliver any part of it.
- Peer supervision felt very useful by first wave therapists.
- Practice patients very important.
- Issue of opening up the training to all other therapists for cross-cover purposes.

Summary

- Thought the logbook process suggested by ■ and ■ will work best arranged on a modular basis. Therapists should come to as many of the sessions as they are able and their attendance against session competence should be logged per therapist.
- 'Rolling competence' will work better for GET than the other therapies.
- Generic training agreed for the end of August.
- Aim to open second wave centres to randomisation by the end of November.
- Aim for 3-5 practice patients for each new therapist.

c) Agenda for Change

- Early submissions of job descriptions for Agenda for Change are highlighting potential problems. For example, the [REDACTED] physiotherapist has been downgraded and might end up on a different (lower) pay scale from [REDACTED] peers [REDACTED] and at other centres. The trial will be affected if peer salaries are not equivalent, particularly if cross-covering therapists are on different scales. This also has implications for recruitment because ideal candidates may not match what is required for a grade 7 which will make it harder to employ them.
- The opportunity to register for a post-graduate certificate can help rate the job description on a higher scale.
- National Pay Framework will affect University employed RNs, RAs and DMs in a similar way.

**ACTION 24:** [REDACTED] to bring the issue of Agenda for Change and National Pay Framework to the TSC for their advice.

**ACTION 25:** All CLs: Any successful job descriptions graded by a panel at 7 should be shared with the rest of the TMG.

d) Doctor training

Only required for Oxford in the first instance as none of the Oxford team were able to attend the last SSMC training day. Second Bart's 2 centre doctor is currently being trained. King's centre doctors will need regular training because of high turn-over of training grades.

**ACTION 26:** [REDACTED] to liaise with [REDACTED] to set a doctor's training day for Oxford staff in July. [Or [REDACTED] if [REDACTED] cannot do this]

**ACTION 27:** [REDACTED] and PIs to ensure that doctors training is renewed annually.

e) Research staff training

This will be set once staff have been employed.

f) Site initiation visit

These will take place for the new centres once all training is complete.

g) TM monitoring visits

These will take place once a centre has recruited 10 participants, so will soon be happening in second wave centres.

**9. Database, data cleaning and checking ([REDACTED])**



**ACTION 28:** ■■■ to circulate the current data cleaning and checking SOP to the TMG.

Discussion as to what data from failed patients should go on to the database. Suggestion that once a participant has given first consent any data they have given should go on to the database. Debate as to whether it is appropriate to put all of this data on to the database.

**ACTION 29:** ■■■ and ■■■ to write a SOP to put forward these issues.

a) Database

Database is ready to sign off with a three month period where we may request further changes to be written in.

Database manual has not yet been written.

**ACTION 30:** ■■■ to approach ■■■ to see if ■■■ would be happy to write a manual alongside ■■■

**10. TSC & DMEC meetings June 29<sup>th</sup> 2005**

a) Agendas

The TMG were happy with these.

**11. Centre leader/investigator & financial agreements**

TMG are satisfied with both the revised centre leader/investigator and financial agreements.

**ACTION 31:** ■■■ to ask QMUL to circulate the revised centre leader/investigator and financial agreements to all centres HEIs and Trusts. Once all centres have given agreement, all centre leaders and HEIs can sign these.

**12. Budget issues**

Once the agreements are all signed the budget will be put on every TMG agenda for monitoring. This cannot be done yet as we have not been able to pay centres without the agreements in place and therefore cannot accurately comment on the budget at present.

**13. Centre reports**

Nothing to report.

**14. Ancillary and add-on studies**

a) Kiddies' PACE trial (■■■)

\*remind ■■■ to send an electronic copy  
To be discussed at a future meeting.

b) ■■■■■■■■■■ qualitative ancillary study (circulated)

Some concerns about the sampling methodology were mentioned.

**ACTION 32:** ██████████ to meet with ██████ to discuss concerns about the qualitative ancillary study project proposal.

c) Two year follow up add-on study (circulated)

TMG gave support in principle for this project proposal. The following comments were made:

- Analyse in 2 ways, one by intention to treat and secondly by co-varying for other treatments received after the patient completed 52 weeks.
- Funding and resources. Could potentially be a four-year study starting two years after the first patient has completed. Could be started using the RNs and DMs for patients who reach two-year post-trial whilst the trial is still ongoing.
- Mailing questionnaires out requires chasing, this is an admin heavy task and should be funded accordingly.
- Increased postage costs should be built in.
- Consider some web-based follow-up – should consider collecting patient email addresses at this stage.

**15. Therapists and research staff as observers at future TMGs**

- TMG agree that this is a good idea but would like a brief reserved business section at the end for any HR sensitive issues.
- Local centre staff will be invited to meetings happening at their centre.

**ACTION 33:** Therapy leaders to let centre leaders know if they do not receive their monthly tapes from the therapists.

**16. Chaudhuri, Severens and Black studies (3 papers circulated)**

Brief discussion about these three papers, which were not immediately applicable to PACE. These papers have been sent to the TSC and DMEC.

**17. Diagnostic criteria used in the PACE trial (circulated)**

The TMG approved these criteria, with one minor revision.

**ACTION 34:** ██████ to send revised version of the Diagnostic criteria to ██████████ of MRC.

**18. Any other business**

PIs and Treatment leaders meeting date: 21<sup>st</sup> July 9:30am.

**ACTION 35:** ██████ to circulate the date of the therapy leader/PI meeting to all relevant parties.

**19. TMG #16:**

To be held on the afternoon of Wednesday 14<sup>th</sup> September, ██████████

**20.TMG #17**

To be held on the afternoon of Thursday 17<sup>th</sup> November at [REDACTED]

[REDACTED] 16.06.2005

## Summary of action points by person TMG #15

██████████

**ACTION 5:** All CLs to ensure that all honorary contracts have been obtained.

**ACTION 14:** PIs/CLs to circulate their lists of self-help guides to the other PIs/CLs (via █████) to make available to SSMC alone participants where required.

**ACTION 16:** CLs to listen to SSMC recordings for supervision for doctors.

**ACTION 18:** █████ and others to organise a weekday for this tied into the generic training.

**ACTION 24:** █████ to bring the issue of Agenda for Change and National Pay Framework to the TSC for their advice.

**ACTION 25:** All CLs: Any successful job descriptions graded by a panel at 7 should be shared with the rest of the TMG.

**ACTION 26:** █████ to liaise with █████ to set a doctor's training day for Oxford staff in July. [Or █████ if █████ cannot do this]

**ACTION 27:** █████ and PIs to ensure that doctors training is renewed annually.

**ACTION 29:** █████ and █████ to write a SOP to put forward these issues.

**ACTION 31:** █████ to ask QMUL to circulate the revised centre leader/investigator and financial agreements to all centres HEIs and Trusts. Once all centres have given agreement, all centre leaders and HEIs can sign these.

██████████

**ACTION 5:** All CLs to ensure that all honorary contracts have been obtained.

**ACTION 6:** █████ and █████ to ensure Health & Safety tests are completed on the steps as required under research Governance before the centres open to recruitment.

**ACTION 14:** PIs/CLs to circulate their lists of self-help guides to the other PIs/CLs (via █████) to make available to SSMC alone participants where required.

**ACTION 16:** CLs to listen to SSMC recordings for supervision for doctors.

**ACTION 19:** Centre leaders to send job adverts to the therapy leaders.

**ACTION 25:** All CLs: Any successful job descriptions graded by a panel at 7 should be shared with the rest of the TMG.

██████████

**ACTION 15:** █████ to investigate what graded exercise literature is available to add to this list.

**ACTION 32:** Therapy leaders to let centre leaders know if they do not receive their monthly tapes from the therapists.

██████████

**ACTION 1:** █████ and █████ -Therapy integrity scale for SSMC to be written.

**ACTION 20:** █████ will email second wave centre leaders again regarding the idea of a single mail shot listing the jobs at all the centres.

**ACTION 32:** Therapy leaders to let centre leaders know if they do not receive their monthly tapes from the therapists.

\_\_\_\_\_

**ACTION 1:** \_\_\_\_\_ and \_\_\_\_\_ -Therapy integrity scale for SSMC to be written.

**ACTION 2:** \_\_\_\_\_ to write a SOP on how the process of rating the tapes for therapeutic integrity might be carried out. This will be considered at a future TMG.

**ACTION 5:** All CLs to ensure that all honorary contracts have been obtained.

**ACTION 14:** PIs/CLs to circulate their lists of self-help guides to the other PIs/CLs (via \_\_\_\_\_) to make available to SSMC alone participants where required.

**ACTION 16:** CLs to listen to SSMC recordings for supervision for doctors.

**ACTION 22:** \_\_\_\_\_ to write a few lines for the CNCC network listing all of the PACE therapist posts available.

**ACTION 23:** \_\_\_\_\_ to send this to \_\_\_\_\_ and \_\_\_\_\_ for circulation to the physiotherapist, OT and CFS networks.

**ACTION 25:** All CLs: Any successful job descriptions graded by a panel at 7 should be shared with the rest of the TMG.

**ACTION 27:** \_\_\_\_\_ and PIs to ensure that doctors training is renewed annually.

**ACTION 30:** \_\_\_\_\_ to approach \_\_\_\_\_ to see if \_\_\_\_\_ would be happy to write a manual alongside \_\_\_\_\_

**ACTION 32:** \_\_\_\_\_ and \_\_\_\_\_ to meet with \_\_\_\_\_ to discuss concerns about the qualitative ancillary study project proposal.

\_\_\_\_\_

**ACTION 29:** \_\_\_\_\_ and \_\_\_\_\_ to write a SOP to put forward these issues.

\_\_\_\_\_

**ACTION 32:** Therapy leaders to let centre leaders know if they do not receive their monthly tapes from the therapists.

\_\_\_\_\_

**ACTION 3:** \_\_\_\_\_ to add the issue of rating treatment recordings for the Treatment Leader/PI separate meeting to take place later in the summer.

**ACTION 4:** \_\_\_\_\_ to order equipment for video-conferencing and liaise with \_\_\_\_\_ to test this between Edinburgh and Bart's.

**ACTION 8:** \_\_\_\_\_ to request the logbooks every month.

**ACTION 9:** \_\_\_\_\_ to order two more activatches.

**TMG #14, ACTION 23:** Still outstanding. \_\_\_\_\_ to submit protocol to Biomed Central (in due course).

**ACTION 10:** Equipose questionnaire – \_\_\_\_\_ to identify which ones are still missing and chase those people.

**ACTION 11:** \_\_\_\_\_ to circulate the letter regarding campaign against PACE to all PACE staff so that they may use this if required.

**ACTION 13:** \_\_\_\_\_ to produce a new version of the randomisation form to clarify this and also add on the SF-36 and Chalder Fatigue scores.

**ACTION 17:** [redacted] to include the details of the contingency plan in a Substantial Amendment to MREC once the TSC have made a final decision.

**ACTION 35:** [redacted] to circulate the date of the therapy leader/PI meeting to all relevant parties.

[redacted] [redacted]

**ACTION 5:** All CLs to ensure that all honorary contracts have been obtained.

**ACTION 14:** PIs/CLs to circulate their lists of self-help guides to the other PIs/CLs (via [redacted]) to make available to SSMC alone participants where required.

**ACTION 16:** CLs to listen to SSMC recordings for supervision for doctors.

**ACTION 25:** All CLs: Any successful job descriptions graded by a panel at 7 should be shared with the rest of the TMG.

**ACTION 26:** [redacted] to liaise with [redacted] to set a doctor's training day for Oxford staff in July. [Or [redacted] if [redacted] cannot do this]

**ACTION 27:** [redacted] and PIs to ensure that doctors training is renewed annually.

**ACTION 32:** [redacted] and [redacted] to meet with [redacted] to discuss concerns about the qualitative ancillary study project proposal.

**ACTION 34:** [redacted] to send revised version of the Diagnostic criteria to [redacted] of MRC.

[redacted] [redacted]

**ACTION 1:** [redacted] and [redacted] -Therapy integrity scale for SSMC to be written.

**ACTION 5:** All CLs to ensure that all honorary contracts have been obtained.

**ACTION 6:** [redacted] and [redacted] to ensure Health & Safety tests are completed on the steps as required under research Governance before the centres open to recruitment.

**ACTION 14:** PIs/CLs to circulate their lists of self-help guides to the other PIs/CLs (via [redacted]) to make available to SSMC alone participants where required.

**ACTION 16:** CLs to listen to SSMC recordings for supervision for doctors.

**ACTION 19:** Centre leaders to send job adverts to the therapy leaders.

**ACTION 25:** All CLs: Any successful job descriptions graded by a panel at 7 should be shared with the rest of the TMG.

**ACTION 27:** [redacted] and PIs to ensure that doctors training is renewed annually.

[redacted] [redacted]

**ACTION 5:** All CLs to ensure that all honorary contracts have been obtained.

**ACTION 14:** PIs/CLs to circulate their lists of self-help guides to the other PIs/CLs (via [redacted]) to make available to SSMC alone participants where required.

**ACTION 16:** CLs to listen to SSMC recordings for supervision for doctors.

**ACTION 19:** Centre leaders to send job adverts to the therapy leaders.

**ACTION 21:** [redacted] to send a copy of the OT advert to [redacted] and [redacted].

**ACTION 25:** All CLs: Any successful job descriptions graded by a panel at 7 should be shared with the rest of the TMG.

██████████\_██████████  
**ACTION 4:** ██████████ to order equipment for video-conferencing and liaise with ██████████ to test this between Edinburgh and Bart's.

██████████\_██████████  
**ACTION 7:** ██████████ to send a blank template DMEC report to the PIs so that they can see what types of information are contained in the report.

**ACTION 12:** ██████████ to produce graphs of recruitment for future TMGs (both overall recruitment and per centre) against target recruitment.

**ACTION 28:** ██████████ to circulate the current data cleaning and checking SOP to the TMG.