Trial Management Group Meeting # 16

1:30 – 5:00pm, Wednesday 14th September 2005

[redacted]

1. Present

[redacted]

2. Apologies

[redacted]

3. Previous minutes TMG #15

Honorary Contracts

This process is still proving difficult at Barts.

ACTION 1: [redacted] to ensure [redacted] has an honorary contract for Barts cover.

Self help material

TMG #15 - ACTION 14 still outstanding: 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.

SSMC training and supervision

TMG #15 – ACTION 16 still outstanding: CLs to listen to SSMC recordings for supervision for doctors.

[redacted] will be visiting all centres to talk to CLs about SSMC training, listening to tapes and Quality Control. This is to be done in order to try to reduce doctor-specific and centre-specific effects and variation in treatment given.

TMG #15 – ACTION 26 ongoing: [redacted] to liaise with [redacted] to set a doctor's training day for Oxford staff in July.

A date is planned for October with [redacted] and [redacted] or [redacted] to visit Oxford.

It is also envisaged that a six-monthly teleconference and an annual training/dinner for SSMC doctors will be established.

Agenda for Change

TMG#15 – ACTION 25 ongoing: All CLs: Any successful job descriptions graded by a panel at 7 should be shared with the rest of the TMG.

Data collected on ineligible patients

TMG#15 – ACTION 29 not done: Discussion on what level of data that is collected on patients screened for the trial but not entered should be entered on to the database. It was concluded that we should enter all baseline data on eligible patients and minimal data on ineligible patients (descriptive data only to show generalisability of trial to patient population).

ACTION 2: [redacted] to write a SOP to define what data should and should not be entered of ineligible/refusal patients. For all eligible patients enter all available data on baselines 1 & 2.

Financial contracts

ACTION 3: [redacted] to chase up QMUL for King's copy of the financial agreement.

ACTION 4: [redacted] to ask [redacted] (QMUL) if [redacted] has circulated the centre leader agreements for signature and for copies of any received.

Recruitment of staff to second wave centres

ACTION 5: Any unfilled PACE posts to be reported to [redacted] so that [redacted] can advertise them at the National CFS Clinicians' Network meeting at Leeds.

Recordings of therapy sessions

TMG#15 – ACTION 32 outstanding: [redacted] and [redacted] to meet with [redacted] to discuss concerns about the qualitative ancillary study project proposal.

Publication of the PACE trial protocol

The aim is to prepare the protocol for an October submission to Biomed central alongside the FINE team. The particular journal has not yet been decided upon but is likely to be Medicine or Neuroscience.

ACTION 6: [redacted] to submit the protocol for publication to aim for October.

Discussion regarding sensitive areas of the protocol and how these should be handled. It was suggested that any sensitive areas be deleted and replaced by a referral to a general non-trial specific document. E.g. regarding the sensitive nature of the definition of an SAE it was proposed that the following might be written:

"SAEs will be defined in accordance with definitions in international guidelines for GCP for clinical trials."

Equipoise questionnaires

TMG#15 Action 10 outstanding: Equipoise questionnaire – [redacted] to identify which ones are still missing and chase those people.

ACTION 7: [redacted] to circulate equipoise questionnaires to newly appointed staff on an ongoing basis.

Letter regarding the campaign against PACE

TMG #15 - ACTION 11 outstanding: [redacted] to circulate the letter regarding campaign against PACE to all PACE staff so that they may use this if required.

ACTION 8: [redacted] to complete this action point on [redacted]s behalf (to circulate the letter regarding campaign against PACE to all PACE staff so that they may use this if required).

Randomisation form alterations

TMG #15 - ACTION 13 still outstanding: [redacted] to produce a new version of the Randomisation Form to change 'depressive disorder' to 'depressive illness'; to change 'SF36 less than 60' to 'SF36 less than 61'; and to create a box so the RN may write in scores of SF36 and CFQ.

ACTION 9: [redacted] to make the requested changes to the Randomisation Form and submit this to the MREC. MREC approval is required because this constitutes a change to a protocol document.

DMEC report for PIs

ACTION 10: [redacted] to re-send blank DMEC report to [redacted] and [redacted]

5. Participant recruitment

Recruitment rates and screening

Month	Month	Actual recruitment Barts 1	Cumulative recruitment Barts 1	Actual recruitment Edinburgh	Cumulative recruitment Edinburgh	Actual recruitment Kings	Cumulative recruitment Kings	Actual recruitment cumulative	Total Target Combined	Total target recruitment by centre
31 March 2005	1	3	3	0	0	0	0	3	7	2
30 April 2005	2	4	7	2	2	2	2	11	15	5
31 May 2005	3	0	7	6	8	4	6	21	22	7
30 June 2005	4	6	13	1	9	3	9	31	30	10
31 July 2005	5	0	13	1	10	1	10	33	38	13
31 August 2005	6	4	17	1	11	3	13	41	48	16

Edinburgh reported a summer dip in recruitment due to both PACE doctors being on holiday. There are only two/three screening doctors and so throughput of new patients will be slower than for other centres.

Proportion of patients screened and then entered is high at Edinburgh however.

At King's a larger portion of patients opt for CBT over the trial. King's also has a higher portion of referral with mis-diagnoses or previous treatment.

The TMG clarified that if patients have had one of the trial treatments for CFS in a secondary care fatigue clinic they are ineligible. Broadly *the patients could still be eligible if they have had CBT/GET for any other problem, or have had CBT/GET in the community for CFS. This should be judged on a case-by-case basis.*

ACTION 11: [redacted] to include the clarification of 'previous treatment for CFS' in a SOP.

King's has a high number of patients excluded on SF36 scores. This may be an issue of explaining the questionnaire carefully to the patient to ensure that they are describing a typical day.

Further training on the clinic screening (Red and Black) book is needed.

ACTION 12: [redacted] to create a list of issues with the R&B book to pass to PIs.

ACTION 13: PIs to ensure [redacted] recommendations for the R&B screening book are implemented by all doctors at their centres.

ACTION 14: [redacted] to create a screening/referral form for doctors.

6. Medical screening

It was reiterated that care should be taken when screening patients especially where there are any anomalous blood results. It has been proposed that, when there is any significant doubt about medical screening, [redacted] or [redacted] would be available to discuss and advise on such patients.

At the Royal Free blood forms are sent out with the appointment letter and bloods results are available before the patient sees the doctor. This resolves two issues:

i) all bloods are in before the first screening appointment
ii) there is time to investigate alternative diagnoses where results are ambiguous

ACTION 15: If there is a doubt about a possible medical exclusion, [redacted] will be on hand in an advisory role (or [redacted] if [redacted] unavailable) to discuss these ambiguities within 24 hours.

ACTION 16: [redacted] to ensure that in the SOP's it is stated that both doctor and research nurse/assistant should check the notes for eligibility prior to baseline.

ACTION 17: [redacted] to write a SOP to clarify that we must ensure that the patient is not in any other trials and that no other involved healthcare professional has an objection to the patient going into the trial.

ACTION 18: Recommendation to all PIs, CLs and screening doctors to send out blood forms and instructions to have blood test two weeks before the clinic appointment.

On this matter, the TMG reiterated ITT – Intention to treat. Once a participant is randomised they are analysed.

Research nurse baseline issues
SCID – Algorithm still not right, this needs revision.

ACTION 19: [redacted] to revise the SCID to follow a logical order.

Step test – a participant at Edinburgh reported an AE as a result of the step test. Reported physical set back from doing the test and emotional set back at not feeling they had done very well. In conclusion the participant acknowledged that they had pushed themselves too hard (possibly in response to wanting to do well for the RN).

Discussion held regarding instructions to the step test to try to avoid a repeat of this in the future.

ACTION 20: [redacted] to review the SOP for step test instructions to ensure that it includes an explanation to the patient that they may feel a little stiff or tired afterwards, that the test should be carried out at a pace that suits the patient. Explain that the patient might feel worse but that it won't do any harm.

7. Second wave centres
a) Staff recruitment update
CBT
Barts II will be interviewing next Thursday for the CBT therapist.
Oxford have recruited a CBT therapist.
Interviews for the CBT therapist are scheduled for 24th October for the *Royal Free.*

APT
Barts II have advertised three times at a part time senior 1 post and had no response to adverts. A fourth advert will go out as a full time senior 2 post or more junior.
Oxford have recruited an APT therapist.
Royal Free have recruited an APT therapist.

GET
Barts II had recruited a GET therapist but unfortunately [redacted]. A potential candidate for this post has been identified.
Oxford are interviewing on the 23rd September and have six candidates short listed.
Royal Free have recruited a GET therapist.

Research staff
Barts II – a full time RN to cover both Barts centres has now started.
Oxford – Hopefully soon to advertise.
Royal Free are re-advertising for an RN and have DM interviews set up.

b) Therapist training
The fact that not all centres have been able to recruit therapists at the same time has had an implication for training and discussions were held regarding the best ways of getting around this.

It was reported that the GET training log is working really well in helping to make training more efficient, reduce days training and facilitate more peer training.

Some peer training and sitting in with sessions planned for CBT.

Generic PACE and CFS training is to be offered to second-wave centres staff once all are employed. This could be either centrally or at their local centre.

It was reiterated that some therapists will need 3 to 4 months of training patient experience before they can be assessed for competence, although this depends on the applicability of the training log approach. The start date for opening the second wave centres is likely to be affected as a result of this. It was noted that if a centre has two therapists trained then the third therapy could potentially be covered by a trained PACE therapist from a first wave centre whilst recruitment/training of the third therapist takes place.

ACTION 21: Treatment leaders to discuss the issue of cross cover for the second wave centres with relevant therapists and centre leaders.

c) Doctor training

Discussion regarding assurance of quality and equipoise between doctors delivering SSMC. The following was discussed in relation to this.

i) A doctor's pack has been produced at King's for new doctors joining the department to help assure same practice between different doctors.
ii) A national dinner for doctors is proposed.
iii) A six-monthly teleconference with doctors is planned, but was thought to be less practical than a face to face meeting.
iv) Centre leaders should listen to two tapes per doctor. This workload should be carried across the trial so that centres with many doctors are not penalised by a heavy workload listening to tapes.

ACTION 22: [redacted] to send an electronic version of the doctor's pack to [redacted] for integration into the doctor's SOP.

ACTION 23: [redacted] to write to all centre leaders to remind them to listen to a minimum of two tapes per SSMC doctor to provide feedback and ensure quality control.

ACTION 24: [redacted] and PIs to plan national meeting and dinner for SSMC doctors.

d) Research staff training
RNs & DMs – There is a plan for group training followed by mentoring between peers.

Discussion held regarding incentives that might be put in place for participant recruitment for the staff:

- Newsletters.
- Christmas party for staff.
- Christmas cards for all staff and all past staff.
- Frequent verbal feedback.

ACTION 25: PIs to consider a Christmas party for all staff.

ACTION 26: PIs to encourage all staff to write contributions for the newsletter.

e) Target dates and process for starting recruitment
As and when staff recruited and competent and the Site Initiation Visit completed.

It is envisaged all centres should be recruiting no later than January 2006.

8. Database update
Database final version has been released; we are waiting for sign off before beginning entering live data.

TMG give permission for DMs to begin entering starting database but DMs need to be trained to data queries first.

ACTION 27: PIs to consider who might deliver training to the DMs and when.

ACTION 28: [redacted] to discuss and agree arrangements for accepting the database and practical arrangements for the future use thereof.

9. CD recordings and central storage
Discussion regarding storage of sound recordings. A SOP is in the process of being completed which will include instructions for cataloguing sessions.

ACTION 29: Centre leaders to identify someone at each centre to take responsibility for encrypting and burning CDs and storing to secure network drives and maintain logs of every recording (PIN, date of recording, date of file, therapist/doctor and length of recording).

ACTION 30: [redacted] to re-circulate logs for recordings to everyone who has a sound recorder.

ACTION 31: [redacted] to train each designated person to the procedure for storing and back up of sound recordings.

10. TSC & DMEC meetings
a) TMG to develop an operational definition of serious deterioration. This definition should be sent to the DMEC & TSC.

TMG would recommend that those items already listed in the protocol should be enough to measure deterioration i.e. CGI and SF-36 changes in scores, drop outs and a substantial percentage of deterioration or drop out.

Discussion was held as to what proportion of participants would meet this definition of deterioration would constitute a reason to review or close an arm of the trial. It was determined that this should be 20% of those receiving the treatment, when the number of participants in that treatment group is at least 30 people. The suggestion would be to review the content of the treatment, monitor the arm carefully, before considering stopping recruitment into that arm.

ACTION 32: [redacted] to contact [redacted] with the TMGs suggested measures for an operational definition of serious deterioration, and to suggest the threshold for review of an arm.

b) TMG/PIs to consider how best to measure life participation.

WSAS is the measure of life participation.

ACTION 33: [redacted] to inform [redacted] that the WSAS is the measure on PACE used for life participation.

c) PI's/TMG to address how participant attendance might be recorded on a session by session basis and the format of the report for DMEC.

Participant attendance is already being recorded at discharge. It would constitute a greater paperwork trial to staff but theoretically a chart could be created for each doctor, therapist and nurse to record attendance for every patient.

ACTION 34: [redacted] to clarify exactly what DMEC wanted regarding participant attendance.

ACTION 35: [redacted] to design a form for attendance recording to circulate to all staff if required.

11. PR issues

A cautionary note was issued regarding the release of any information and the experience cited of one TMG member having patient data revealed to an outside agency via an embedded chart in a PowerPoint presentation that was released.

ACTION 36: All to add the following to the end of all PACE email or to include in signatures:-

The information contained in this message is confidential and is intended for the addressee only. If you have received this message in error or there are any problems please notify the originator immediately. The unauthorised use, disclosure, copying or alteration of this message is strictly forbidden. This mail and any attachments have been scanned for viruses prior to leaving St Elsewhere's NHS Trust/University network. St Elsewhere's NHS Trust will not be liable for direct, special, indirect or consequential damages arising from alteration of the contents of this message by a third party or as a result of any virus being passed on.

12. Length of agenda

A number of issues of the agenda could not be discussed at this meeting due to a time shortage. It was discussed that more meetings should take place separately for the TMG and the TMG meetings could mostly be used to review trial status and 'rubber stamp' any decisions made in smaller working party groups.

The first two such additional meetings proposed is to tackle the issues of recording the actigraphy data and training the data management teams in query raising, recording and resolution.

13. Date of next meeting
17th November 2005, [redacted].

14. 2006 programme for TMG meetings
Venues to be announced.
8th February 2006
26th April 2006
12th July 2006
11th October 2006

[redacted] 26/09/2005

Summary of Action Points

All PIs/CLs
TMG #15 - ACTION 14 still outstanding: 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.

TMG #15 – ACTION 16 still outstanding: CLs to listen to SSMC recordings for supervision for doctors.

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Treatment Leaders
ACTION 21: Treatment leaders to discuss the issue of cross cover for the second wave centres with relevant therapists and centre leaders.

[redacted]
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ACTION 19: [redacted] to revise the SCID to follow a logical order.

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