



Trial Management Group Meeting # 22
8th February 2007

Draft Minutes

1. Those present

[REDACTED]

Observers

[REDACTED]

2. Apologies

[REDACTED]

3. Announcements

Royal Free has started recruiting participants.

Bristol is expected to start recruitment in March.

[REDACTED] was congratulated on his appointment as Reader.

[REDACTED]
[REDACTED]
expected to attend next TSC and TMG meetings.

4. Matters arising from TMG # 21 not on the agenda

TMG #20 – ACTION 6: Actigraphy analysis strategy development is ongoing
[REDACTED] and [REDACTED].

TMG #21 - ACTION 1: [REDACTED] to investigate taking referrals for PACE from the Kent CFS network. (Ongoing)

SSMC training

██████████ has received SSMC training.

Two further SSMC sessions have taken place for Bart's doctors.

██████ doctor ██████████ is leaving shortly so has not received SSMC training.

Ongoing SSMC supervision and listening to tapes is advised for all centres.

Development of training manuals

Training manuals discussions are deferred to the next TMG as no treatment leaders were available this time.

ACTION 1: █████ to add treatment training manuals to TMG agenda #23.

Subvention money

TMG#21 - ACTION 5: Centre leaders to calculate actual NHS spending on trial versus money received (£3001 per participant recruited).

Action 5 not yet completed but to be reviewed when the bid response is received from the MRC. It was pointed out that subvention costs were based upon the highest staff costs at a senior grade. As many employed therapists are on a lower grade, and as there have been periods of vacancy, it is hoped that the subvention money will allow for some non-cost trial extension. It is, however, unclear as to the impact of Agenda for Change on these salaries.

Allocation of therapists between Bart's I and Bart's II participants

Bart's therapists are randomly allocated by therapist availability and patient choice of session time. I.e. the therapists supply the RN with two free new patient slots per week. At randomisation, the RN offers a choice of one of the four slots to the participant. Allocation is therefore not influenced by staff members.

52 week DAR CDs

No centres have yet supplied any 52 week CDs, although discussions with all centres suggest this task is underway.

ACTION 2: █████ to ask for update on 52 week discs from all centres.

ACTION 3: █████ to add 52 week discs to the next TMG agenda for review.

ACTION 4: █████ to remind all centres of the file naming protocol for DARs.

Blind assessment of therapy recordings

ACTION 5: █████ to confirm if someone has been identified to review the CDs for differentiation of therapies.

ACTION 6: Pls to review [REDACTED]'s advice on the process for making a judgement of a need for further treatment.

ACTION 7: [REDACTED] to circulate [REDACTED]'s advice on the process for making a judgement of a need for further treatment once reviewed by the Pls.

5. Extension bid (tabled item)

The extension bid was briefly discussed. It was agreed that no further action can be taken until the MRC response to the bid is received.

6. TSC summary report (attached item #2)

The TSC report was written at the request of [REDACTED] following the cancellation of the January TSC meeting. New sections in this report relate to adherence to treatment and the status of data entry and audit. It was reported that based upon 52 week data from therapists and SSMC doctors, adherence to therapy and SSMC overall appears to be good.

Substantial amounts of data audit have already taken place. This has focussed initially upon Bart's data as a means of testing the data management processes. It was reported that query rates were higher for earlier data, as would be expected, and that a drop off on query rates was noticed by the auditors. The next stage of data management will involve checking recently collected data as a means of testing that early data collection problems do not persist at any centre.

At this stage, data is not being collected on whether participants go on to receive further treatment. It is anticipated that this data would be recorded at the two year follow up data collection (perhaps on a newly created CSRI question).

It was suggested that future TSC reports might include number of forms expected versus number of forms collected. It was acknowledged that this report was more detailed on this occasion than might be expected and this was because there was no accompanying DMEC report or feedback.

ACTION 8: [REDACTED] and [REDACTED] to decide what level of data management detail will be needed for the DMEC and TSC summer reports and feed this back to [REDACTED] and [REDACTED].

The next TSC is June 27th 2007 from 1pm.

ACTION 9: [REDACTED] to contact [REDACTED] for dates for the next DMEC (a May date is anticipated). [REDACTED] *has done this.*

7. Recruitment (attached item #3)

Recruitment continues at a consistent rate and as of this meeting, 213 participants had been randomised.

The extension bid requests extra RN time (from 0.6 to 0.8). Geographical recruitment areas are being widened for every centre in a bid to increase recruitment.

8. Specific centre issues

Edinburgh

All therapists are now in post. The new CBT therapist [REDACTED] is almost competent to receive randomised therapists. Once competent, [REDACTED] will cross train to cover GET.

[REDACTED] completed [REDACTED], which has created a back log of screening at the centre. A bank research nurse is being trained by [REDACTED] to provide cover in [REDACTED] absence.

There is a four month waiting list on referrals at present.

Oxford

No Oxford representatives were available at this TMG.

Oxford report that all is running smoothly and they are receiving referrals from OCCMET now.

[REDACTED] has agreed to cover APT for Bristol to cover the delay in recruitment and training of the therapist at this centre and to allow Bristol to start randomising in March.

Royal Free

This centre is now recruiting well.

At present, [REDACTED] is the only available doctor at this centre. [REDACTED] is carrying out two extra clinics a month for PACE specific work.

The data manager will be an internal re-deployment recruit. No news yet on when this might happen.

The Trust may ask the team to move office shortly.

Bart's

Two of the SSMC doctors are leaving the service.

[REDACTED] (CBT) needs to send another CD to [REDACTED] for competence rating.

Recruitment remains an issue for this centre. Bart's expect to start recruiting directly from Essex CFS service shortly.

ACTION 10: [REDACTED] to remind [REDACTED] to send [REDACTED] a further CD of sessions for competence rating.

Bristol

The centre is on course for opening to recruitment in March. All staff are employed with the exception of a data manager.

Therapists are all in training. GET and CBT therapists are expected to be competent by March; APT training will take longer but will be covered by [REDACTED] of Oxford as mentioned above. The RA is recruited to start in April but this post will be covered by a Research Psychologist in the meantime.

[REDACTED] and [REDACTED] are in the process of compiling all of the documentation and equipment for this centre to be sent in February. A site initiation visit has been scheduled for early March. [REDACTED] is coordinating centre set up until [REDACTED] the RA (occupational therapist by training) is in post. [REDACTED] has visited Oxford in order to develop an understanding of how to set up and coordinate the trial.

There may be a concern about therapy space at Bristol; this will be discussed at SCID training with [REDACTED] in Bristol on 19th February.

King's

[REDACTED] is back at work full-time. There may be a loss of APT therapist shortly and the SSMC dedicated doctor is also leaving.

9. Update from Analysis strategy group (morning meeting: [REDACTED]) including authorship of the PACE trial main papers (tabled item)

[REDACTED] spoke to the TMG about the discussions in the Analysis Strategy Group's morning meeting. A suggestion for the TMG for authorship of the trial papers was tabled at this meeting.

Summary

First protocol design paper to include the name of the entire PACE team in the appendix.

Consequent papers will list the writing committee by name, with the addition of "on behalf of the PACE team". All will be encouraged to be involved in further papers for the trial and to become a named author.

Some PACE associated papers (such as those relating to PhDs) may be subject to different authorship rules, if, for instance, they contain non-PACE data. In this instance, the ASG will advise the TMG of the recommended authorship for these papers.

ACTION 11: [REDACTED] to circulate the authorship recommendation document will be circulated to the entire TMG for discussion in Edinburgh.

10. Clarification of percentage checking of database data

A clarification was agreed that data is not being audited for non-randomised data. All agreed that this was acceptable. The TSC report sets out data management decisions on what constitutes 1% error rates.

11. Screening data (RBB, Screen failures, Consent logs) (tabled document)

[REDACTED] spoke to the report produced, based on the logging data compiled for the trial. A large number of queries have been raised on the data combined from

the (red and black) clinic screening book, screen failure logs and consent logs.

Whilst it was agreed that this represented a lot of work simply for the purposes of CONSORT, it was stated that this data did give useful information about how the clinics ran and where centres might be better supported. Particular points raised included:

- No single person at any centre is responsible for full patient pathway tracking
- The time from screening to randomisation can be very long. (Delay in obtaining blood results or medical assessments, or referral to RN?)
- There are duplicated patients in the screening book. (Local patient tracking issue?)
- There are missing patients from the screening clinic book. (A number of randomised patients could not be identified as having been seen in clinic)
- Potentially eligible and referred patients do not appear to be followed up (one such identified case has been re-approached and is being screened for the trial next week at Bart's). There are a significant number of such patients.

All data made available by the beginning of January was compiled in an Access database for each centre with a request to clean queries by mid-April and update the database from hereon. It is suggested that if RNs are able to spend one hour a week on this it may both help clean the data and allow a faster turn around within centres between screening and referral to the RN.

ACTION 12: RNs to review the logging database and report to CLs with a local timetable for completing and updating this.

ACTION 13: [REDACTED] to contact all doctors/centres to ask them to please state the diagnosis of the patient if Oxford criteria are not met.

It was reported that screening for PACE has resulted in a greater number of alternative diagnoses than CFS and the reasons for this were discussed.

ACTION 14: [REDACTED] to look at the potential for a paper on information on screen negative patients and the proportion of these with CFS diagnosis later changed.

12. Therapists' meetings

The TMG agreed that group supervisions may be held outside of London once a year, but the cheapest option should always be pursued. APT and GET are meeting in Edinburgh. CBT will only meet in London but more frequently than

the other therapy teams. The APT team have budgeted the Edinburgh trip to be similar to the cost of a London trip.

13. Missed therapy sessions

All are agreed that missed therapy sessions are handled as per protocol, and that sessions can only be replaced within a +/- 5 day window.

ACTION 15: ■ to send an email to treatment leaders to reinforce to all therapists the protocol for DNAs when the participant falls outside of the visit window.

ACTION 16: ■ to add the issue of missed therapy sessions to the next TMG agenda so that it can be discussed again when therapy leads are present.

ACTION 17: ■ and ■ to discuss the data being collected by therapists that is not presently being collated in any database. This to include homework compliance and visit schedule forms.

ACTION 18: If data is available, ■ will examine the issue for the next DMEC of therapists giving sessions outside of protocol windows.

14. Lancet and BioMed Central papers and approval

The Lancet editorial team replied saying that they were pleased to receive the protocol and would be interested in publishing the main paper via fast track review in the future.

BioMed Central Neurology has requested minor editorial changes to the protocol for publication. These have been submitted and publication is anticipated shortly.

15. Ancillary studies

a. 2 year follow up

ACTION 19: ■ will circulate a final version of the protocol for two year follow up, for discussion and agreement by the TMG. Replies will be collated before the next TMG to allow an MREC submission and approval before the first participant reaches two years.

ACTION 20: Once approved by the TMG by email, ■ to submit the two year follow up protocol to MREC as a Substantial Amendment.

ACTION 21: ■ to ask ■ to redesign the CSRI for the two year follow up study. (Identification of key cost drivers only). This to include additional therapy received after 52 weeks.

ACTION 22: ■ to source alternative funding in case DWP reject funding the two year follow up study or limit offered money to £50k.

b. [REDACTED] supervision study

11/18 questionnaires have been received so far.

Reminders have been sent out to non-responders.

c. [REDACTED] study on the experience of delivering manualised therapy

[REDACTED] and [REDACTED] are considering using pilot patient data rather than PACE trial data.

d. King's study on the experience of taking part in a trial

A researcher has been appointed to conduct this research. The paper will need to be approved by TMG and TSC before any publication.

ACTION 23: [REDACTED] to email [REDACTED] and [REDACTED] about concerns of malevolent misinterpretation and the need for the TMG and TSC to review and approve any papers before publication.

e. Edinburgh study on therapeutic recordings

ESRC liked the study but have not funded it. Further funding opportunities will be investigated.

ACTION 24: [REDACTED] to follow up ethics status for the Edinburgh study on therapy recordings.

f. SNP study

The CDC are willing to put \$200-400,000 for analysis of the data. Further money needs to be secured for collection of samples. Budget issues will be discussed at a meeting in Washington on March 21st 2007.

16. Audio books for CFS – supporting SSMC alone

Some centres are reporting that participants are not always able to make use of the SSMC self help reading list if their fatigue is such that prolonged periods of reading are made impossible. Bristol report that they have created their own recordings for some literature in the past. As far as is known, no formal recordings exist for any of the books on the reading list.

ACTION 25: [REDACTED] to find out if talking books for CFS exist (RNIB).

17. Self help guides for GET

The GET team have produced a draft pamphlet. Once completed and approved this can be added to the self help reading list.

18. Sending of cards and newsletters after 52 weeks

Newsletters should be sent to everyone even after they have left the trial. Trial results will be distributed to participants via this method.

Birthday cards should be sent up to two years.

Season's Greetings cards (at Christmas) should be sent up to two years.

Cards should be signed off "from the PACE team".

ACTION 26: ■ to inform all RN/As of the decisions regarding sending cards and newsletters.

19. Any other business

Treatment schedules

ACTION 27: ■ to ask all centres how data gathering on visit schedules is progressing.

Recording of AE information on the database

As noted in the past by ■, recording of AEs (especially non-serious) on the database requires a coding system. At present long event descriptions are written where a one word diagnosis (or symptom or sign where no confirmed diagnosis) is preferable.

At present, ■ is raising queries on these AEs requesting simplified diagnoses be entered.

In addition, some unblinding is taking place where long descriptions are entered (e.g. pt DNA'd three CBT sessions).

ACTION 28: ■ to produce a document of all recorded AEs in the database.

ACTION 29: ■ to provide codings of AEs up to the last DMEC.

ACTION 30: ■ to ask ■ if ■ would be willing to re-code AEs and help ■ raise queries to centres on the basis of these.

20. Proposed dates and venues for TMG meetings in 2007:

ACTION 31: ■ to ask ■ if ■ would be willing and able to host the TMG in ■ in December.

- a. 12pm to 4pm Wednesday May 9th 2007 (■■■■■) –
(Analysis Strategy Meeting 8th and 9th May)
- b. 1pm to 5pm Thursday 20th September 2007 ■■■■■
- c. Wednesday 12th December 2007

ACTION POINTS

CLs

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