



[REDACTED]

[REDACTED]

#### 4. Previous minutes

##### Minor corrections

Page 6, 7 b) – For APT and GET there is four to six weekly telephone supervision. Whilst face to face supervision is less than for CBT, the overall quantity of supervision is the same, and consistent with the protocol.

For CBT, supervision is four to six weeks rather than every six weeks, in accordance with the protocol.

‘Peer supervision’ should be replaced with ‘peer support’.

Page 7, 7 e) – Clarification that the first trial screening in Oxford was in April and the first randomisation in May.

#### 5. Matters arising from TMG # 19 not on the agenda

##### a) SSMC

##### *King’s*

- [REDACTED] is now in a position to commit more of his time to PACE as a SSMC consultant now that the waiting list has been reduced at this centre.
- A Specialist Registrar has also been identified at King’s that can also be a PACE dedicated doctor.
- [REDACTED] will train these two doctors for SSMC.

**ACTION 1:** [REDACTED] and [REDACTED] to arrange a date for SSMC training at King’s

##### *Bart’s*

- Doctor population at Bart’s is stable apart from the rotational SpRs.

##### *Edinburgh*

- [REDACTED] will be monitoring the medical notes for SSMC at Edinburgh in the next few weeks.

##### *Oxford*

- [REDACTED] may still require SSMC training.

*Royal Free*

- [REDACTED] does not require training.
- b) Data Manager posts and training
- A new data manager, [REDACTED] has been appointed to Oxford and starts in August.
  - [REDACTED] has now left the Royal Free.
  - Training for new staff is currently being organised.
- c) MREC submission
- [REDACTED] will be making a submission in the next few days of a letter to advertise the trial to GPs.
- d) Supervision and training manuals
- The treatment leaders feel that it would not be possible to write a supervision and training manual but feel that what would be more useful would be guidance notes on the process of training and supervision to accompany the main trial manuals. The treatment leaders are happy in principle to work on a first draft for each therapy.

**ACTION 2: TLs with PI support to begin work on training and supervision guidance for all four treatments manuals.**

- e) Peer support meetings
- The feedback from TLs is that this is working effectively and that the therapists find it very useful and it useful for team building.
- f) DAR training and encryption
- This is ongoing and [REDACTED] is in discussion with the sponsor's Data Protection Officer on this. The concern remains that if CDs leave the original locked office without having been encrypted, this data may be vulnerable.
  - The TMG agreed that all recordings on CD being taken off site are encrypted unless they are sent by recorded post, subject to further advice from the DPO in the meantime.

**ACTION 3: [REDACTED] and [REDACTED] to trial putting WinZip on CD and listening to an encrypted recording.**

**ACTION 4: [REDACTED] and [REDACTED] to discuss Bart's DAR and encryption arrangements.**

- g) King's therapist recruitment
- Staff have been recruited for both GET and APT at King's and training of these staff will be arranged when they are in post.
- h) Actigraphy
- This will be discussed at a future meeting between [REDACTED] and [REDACTED].

**ACTION 5:** ■■■ and ■■■ to arrange a meeting to discuss actigraphy analysis.

**ACTION 6:** PIs and ■■■ to arrange a meeting to discuss the analysis strategy document. This meeting is proposed for late September/early October.

i) Publication of protocol

Protocol will be published as soon as the latest MREC submission is made but with an added caveat that this protocol may be subject to further amendments.

**ACTION 7:** ■■■ to re-send the abridged version of the protocol to ■■■.

## 6. Recruitment

A general discussion regarding recruitment was held specifically relating to the fact that the trial is currently under target and that it is unlikely that three centres will be able to double recruit in the last year of planned recruitment. Some measures to address this are already in place including recruiting from Sussex at Barts and King's increasing the target recruitment by a third.

Tabled document discussed.

It was thought that start up costs for new centres would come to £75k for the first year for each centre and £60k each year thereafter.

TMG agreed that all proposals should be recommended to the TSC:

1. Recruit two more centres (Bath & Bristol to act as a double centre with shared staff and Birmingham to start as a separate centre). These would require more mentoring by senior members of the TMG.
2. Increase time to end of recruitment by a minimum of eight months
3. Increase funding to current centres to increase recruitment targets, as possible, at already existing centres
4. Include in funding requests for more TL monies
5. Include in funding new equipment and start up costs including the fact that equipment has increased in cost since the initial grant
6. Subventions monies should also request cover for maternity leave
7. Include in funding, finances for statistician
8. Apply for R&D approvals and LREC SSA approvals now for one new centre, in advance of any monies being secured
9. Estimated end of randomisation in July 2008, whole trial would end in 2010.

**ACTION 8:** PIs to present the proposed recruitment solutions to the TSC at their next meeting.

## 7. Second wave centres

a) Barts II

GET therapist has been recruited to Barts II.

██████████ is now competent to give APT.  
A GET therapist is to start soon.

- b) Oxford  
Oxford are doing well and are recruiting just over target at present.  
All staff have now been recruited.  
██████████ is now covering a 0.4 post in ██████████ outside of PACE.
- c) Royal Free  
LREC approval still not achieved.

## 8. First wave centre issues

- a) **Monitoring (see circulated report summary)**  
Thanks to ██████████ and ██████ for their efforts monitoring the first wave centres.

- i. Gap between baseline 2 and randomisation

**ACTION 9:** ██████ to submit an amendment to MREC to increase allowance of time between baseline 1 and baseline 2 and the gap between baseline 2 and randomisation. A one month allowance from baseline 1 to randomisation and a repeat of the primary outcome questionnaires if this is breached.

**ACTION 10:** ██████ to inform all RN/As to try and get all blood results before baseline 1 and watch and report process on the success of this.

- ii. ESR and C-reactive protein  
TMG confirmed that both of these blood results are required.
    - iii. Individual centres  
PIs and RN/As are leading to address any issues identified.

**ACTION 11:** ██████ to email ██████ and ██████ with staff start dates of new therapists.

**ACTION 12:** ██████ to lead with checking for SAEs at King's centre.

## 9. Screening Log for referred but non-randomised patients

The issue of patients in gap between R&B book and baseline 1.

**ACTION 13:** All centres to ensure that any RN/RA screening decisions with a referred patient must be recorded in the screen failure log (even if by telephone) and if the patient is not brought to baseline 1 they must be recorded on the Screen Failure Log. ██████ to reinforce this SOP to RN/As by email.

## 10. Post trial additional treatment

The TMG clarified that post-trial treatment does not need to be given according to manual or protocol. Furthermore, TMG clarified that the

participant cannot simply receive extra therapy on request, and any decision must be made in consultation with both the SSMC doctor and therapist, if one is involved. This is a clinical decision according to necessity. Reinforcement that patients may need longer to consolidate their improvements from trial treatment before any further referral.

**ACTION 14: TLs to inform therapists that a participant may have more of the same therapy after 52 weeks.**

**ACTION 15: PIs and TLs to reinforce to SSMC doctors that a discussion should be held between the SSMC doctor and the original PACE therapist before a further therapy is offered.**

**ACTION 16: ■■■ and ■■■ to write guidance on criteria for needing further therapy after 52 weeks.**

#### 11. Feedback from DMEC

DMEC were impressed with all of the work carried out for PACE so far. DMEC have also come to a decision on what constitutes serious deterioration.

**ACTION 17: ■■■ to write a proposal regarding changing adverse outcome according to DMEC recommendations. If all agree, ■■■ to submit MREC amendment to protocol to alter adverse outcomes being compared to baseline.**

#### 12. Ancillary studies

- a) ■■■ ancillary study
  - Preparation for this is ongoing. This study will be submitted as a substantial amendment to the main trial.
- b) Edinburgh ancillary study
  - This will be submitted as a separate study for sponsorship purposes, but to the West Midlands MREC, which has approved the main PACE trial.
- c) Genomics ancillary study
  - There has been no further progress on this so far.
- d) Two year follow up study  
Two year follow up study is still in production.
- e) ■■■ ancillary study on utility of manualised therapy

#### *Summary of comments*

1. TMG supported this study in principle

#### *2. Qualitative or quantitative but not both*

It was noted that using both qualitative interview and quantitative questionnaire might be excessive and might contaminate each other. A qualitative study would need to be completed by just one person

(interviews and transcriptions). ■■■ has a preference for a qualitative study. The quantitative questions were designed to add support to the results but it was agreed this could be dropped.

*3. Needs to be carried out across all four treatment arms*

The TMG thought that it might be a better use of time and resources to carry this out as one study and also that for good qualitative research practice one person would need to conduct all interviews. In addition, it was felt important that a study to tease out similarities and differences between the treatments be carried out. This would not prejudice whether one combined paper or three separate therapy specific papers were produced.

*4. Need to identify MSc students or similar to do the data collection*

■■■ agreed that this was a good idea and had already been discussed and agreed with the other researchers who wish to be involved in this.

5. All therapists should be interviewed including those who have left the trial

6. The two questions relating to supervision should be removed as these duplicate the supervision study

7. Advice was given that interviews should be completed in random order not CBT, then GET then APT etc.,

8. There are specific design issues to be addressed but it was recognised that this protocol is in early stage development and ■■■ stated that further work needed to be done on this.

9. All staff offered support as needed.

**ACTION 18: All people with comments on the proposal to email their comments to ■■■.**

**13. PACE annual team day**

Positive feedback received from all attendees.

**14. Any other business**

York have published guides to the Stairway to Health for CFS available through [www.winslow-cat.com](http://www.winslow-cat.com).

**15. Dates and venues for next meeting**

Thursday October 12<sup>th</sup> at the ■■■■.

**16. Dates and venues for TMG meetings in 2007:**

- i. Thursday February 8<sup>th</sup> 2007
- ii. Wednesday May 9<sup>th</sup> 2007 ■■■■
- iii. Thursday 20<sup>th</sup> September 2007
- iv. Wednesday 12<sup>th</sup> December 2007

## Summary of Action Points

### All

ACTION 18: All people with comments on the ancillary proposal to email their comments to [REDACTED].

ACTION 13: All centres to ensure that any RN/RA screening decisions with a referred patient must be recorded in the screen failure log (even if by telephone) and if the patient is not brought to baseline 1 they must be recorded on the Screen Failure Log. [REDACTED] to reinforce this SOP to RN/As by email.

### PIs

ACTION 6: PIs and [REDACTED] to arrange a meeting to discuss the analysis strategy document. This meeting is proposed for late September/early October.

ACTION 8: PIs to present the proposed recruitment solutions to the TSC at their next meeting.

### Treatment Leaders ([REDACTED] and [REDACTED])

ACTION 2: TLs with PI support to begin work on training and supervision guidance for all four treatments manuals.

ACTION 14: TLs to inform therapists that a participant may have more of the same therapy after 52 weeks.

ACTION 15: PIs and TLs to reinforce to SSMC doctors that a discussion should be held between the SSMC doctor and the original PACE therapist before a further therapy is offered.

[REDACTED]  
ACTION 16: [REDACTED] and [REDACTED] to write guidance on criteria for needing further therapy after 52 weeks.

[REDACTED]  
ACTION 11: [REDACTED] to email [REDACTED] and [REDACTED] with staff start dates of new therapists.

ACTION 12: [REDACTED] to lead with checking for SAEs at King's centre.

ACTION 16: [REDACTED] and [REDACTED] to write guidance on criteria for needing further therapy after 52 weeks.

[REDACTED]  
ACTION 7: [REDACTED] to re-send the abridged version of the protocol to [REDACTED].

ACTION 9: [REDACTED] to submit an amendment to MREC to increase allowance of time between baseline 1 and baseline 2 and the gap between baseline 2 and randomisation. A one month allowance from baseline 1 to randomisation and a repeat of the primary outcome questionnaires if this is breached.

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[REDACTED]  
ACTION 1: [REDACTED] and [REDACTED] to arrange a date for SSMC training at King's

ACTION 4: [REDACTED] and [REDACTED] to discuss Bart's DAR and encryption arrangements.

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