



### Kent referrals

King's have agreed that Kent referrals could be seen at King's. There is currently a 35 patient waiting list for the main King's service that need to be reviewed first.

### Actigraphy analysis

Actigraphy analysis is now part of the analysis strategy team action points.

### Subvention funding

**TMG#21 - ACTION 5:** Ongoing action for PIs and centre leaders to calculate actual NHS subvention spend versus money received (£3001 per participant randomised).

### Screening/CONSORT data

Logging database – This database contains data from the red and black book, consent logs and screen failure logs. A query list is being raised by [REDACTED] on this database to be distributed to centres for resolution before the DMEC report.

**TMG#22 - ACTION 14:** If complete CONSORT data can be obtained then a paper may be written in the future about screen negative patients. This action point will be ongoing for the remainder of the trial.

### GET self help guide

A self help guide for GET has been completed by the GET team therapists and [REDACTED] (Bart's research assistant) is currently reformatting and editing this. Once completed this will be sent to MREC for approval for the guide to be uploaded on to the PACE website. The need to maintain equipoise was discussed and all therapies guides much be equally accessible from website.

**ACTION 1:** [REDACTED] to send the GET self help guide to MREC once completed.

**ACTION 2:** [REDACTED] to ask permission from MREC for the list of approved self help guides to be added to the PACE trial website.

### Greetings cards

Patients have given feedback to say that they appreciate receiving birthday cards.

## **5. Extension bid approval and state of PACE trial finances**

The extension to the MRC portion of the PACE grant has been approved. Changes to recruitment targets and staff contracts need to be made as a consequence.

The MRC funding covers research staff and expenses only and will not cover an extension to therapists' contracts.

It was calculate that recruitment is now set to end at November 2008 with follow up continuing for a further 12 months. Data cleaning, 52 week discs and centre close down tasks such as archiving will need to be completed by the end of November 2009.

Subvention funds for therapists' salaries may have to stretch to cope with the extension to trial as it is possible no extra funding will be made available. Suggestions to achieve this were that new therapists are employed for two days a week and that Bart's therapists that leave are not replaced if there is another PACE therapist of the same discipline present at that centre.

It was also agreed that centres should be advised to push hard to recruit within the next 12 months as recruitment may get harder toward the end of trial time when some trial staff may leave.

**ACTION 3:** Final dates to be confirmed by PIs [REDACTED] and finance. Staff contracts will need to be reviewed. [REDACTED] to circulate final dates for end of recruitment end of treatment end of follow up and end of trial.

Some therapists contracts are coming up shortly for renewal and centre leaders and PIs need to review renewal of these once final dates are clear.

Patients requiring further therapy after 52 weeks will also need further treatment and centres may need to think creatively about how this might be managed as employing trial therapists long to cover for the last patients recruited this is unrealistic.

**ACTION 4:** Once renewed target recruitment rates are prepared all PIs and centre leaders should approach NHS organisations for extensions for NHS therapists.

## **6. TSC and DMEC impending meetings**

The DMEC meet 29th May 2007.

The next TSC meeting is 27<sup>th</sup> June 2007.

Both meetings are to be held at [REDACTED].

## **7. Recruitment (attached item #2)**

The decision was taken for parity across all centres for revised recruitment target figures.

Only centres that require an extra day of research time for smooth running should take up this option. This way trial funding may be extended further

toward the end of the study by using unused 'fourth day' salary funding to allow high recruiting centres to continue for longer.

## **8. Update from Analysis Strategy Group (ASG)**

In the meetings of 8/9 May 2007, the ASG discussed and agreed:

1. how missing data will be handled,
2. how to avoid multiplicity of testing
3. and definitions of adherence to treatment.

Adherence to treatment has been defined as attendance to 3/3 SSMC sessions and at least 8 out of 15 therapy sessions. Discussion at the TMG suggested that 10/15 sessions might be a better cut off as most participants seem to be having an average of 13 sessions.

The TMG recommended that the ASG consider 9 or 10 out of 15 received sessions or consider treatment as a continuous variable. Sessions 1-3 are assessment, sessions 4-12 are active treatment and the final three sessions are follow up and discussion.

**ACTION 5:** The Analysis Strategy Group to consider 10/15 sessions received as a minimum for adherence to treatment rather than 8/15 sessions.

The Analysis Strategy Group had also discussed the issue of multiple ways in which the outcomes might be examined.

Quality control for differentiation of therapies is planned with an interim review of tapes of currently employed therapists to check for any therapeutic drift and for assurance of therapy content. The therapy integrity scale will be used to make this judgement.

## **9. Authorship of the PACE trial main papers (attached item #3)**

The issues as discussed again including a paper tabled by [REDACTED] and the following agreed:

- a) Authorship of all papers will be a combination of named authors with the qualifier of 'on behalf of the PACE trial team'. The authors named and the order of these will be determined by the contribution of individuals to writing them and in each case will be recommended by the writing group to the TMG for approval.
- b) The paper describing the design of the study will provide a reference for 'the PACE trial team' and will list all of the teams names affiliations and contribution to the trial as an appendix to the paper.
- c) There may be exceptions and some minor papers may not necessarily have to include 'on behalf of the PACE trial team' if,

for instance, it involves data from outside the PACE trial. This will be determined as in (a) above

Further agreements made regarding authorship were:

1. The TMG should have control over which papers are produced.
2. Within the constraints of the journal as many team members will be acknowledged as possible. PACE trial members should be able to include the main PACE papers on their personal publication list.
3. Named authors should resolve order of authorship at the time of producing the paper. This can be confirmed by TMGs and if necessary taken to the TSC in case of dispute.

**ACTION 6:** ■■■ to add the authorship recommendations to the TSC agenda for their consideration/approval.

#### **4. Bristol centre start-up**

This centre has now started recruiting and had randomised 3 participants at the time of this meeting.

#### **5. Update on screening data (RBB, Screen failures, Consent logs)**

■■■■■ will be generating a list of queries and discussing these with individual centre staff.

#### **6. Coeliac disease exclusions**

This discussion referred to the issue of whether patients being managed for coeliac disease should still be excluded from the trial. The same issue exists for patients with eating disorders.

The TMG agreed that in general, if the patient has a controlled condition they should not be excluded, but that coeliac disease is an exclusion already and the eligibility criteria should not be altered now. For this reason, coeliac remains an exclusion criteria.

#### **7. Specific centre issues**

Edinburgh – No major issues reported, although there are some minor issues with receiving completed follow up questionnaires and the role of telephone assessment was discussed.

■■■■■ is now competent to give back up APT at Edinburgh. ■■■■■ will be trained to GET once his CBT training is complete – which should be very soon.

The issued was raised of how to keep back up therapists competent. The suggestion was made that end of therapy treatment could be given by back up therapists and these tapes be used for ongoing competence.

**ACTION 9:** ■ to email all centres with the suggestion that end of therapy treatment could be given by back up therapists and these tapes be used for ongoing competence.

King's – Interviews take place for a new RA on 10 May 2007. SSMC difficulties have been noted at King's due to a lack of available doctors and a high turnover of staff. A new doctor has been SSMC trained for King's and will be with the service for at least six months. The APT therapist at King's is now able to stay in post.

Bart's – There are no major issues to report although two doctors are shortly leaving the service. An advert will be placed to replace one of these. One of the CBT therapists is leaving but will not be replaced as recruitment is not as high as anticipated. Referrals remain steady to this centre.

Oxford – No one from Oxford was available to speak at this meeting.

Royal Free – This centre does not yet have a data manager due to internal administrative staff reviews by the Royal Free Hospital Trust. ■ has provided some cover for this. The rate limiting factor to recruitment at this centre is doctor assessment and treatment time. As the unit is in debt due to delay to randomisation no extra doctor time can be purchased as yet. The unit has moved address; telephone numbers have changed but the postal address remains the same.

A participant at this centre had session 14 taken up with grief counselling. This was an APT session which the therapist foreshortened. The advice from ■ to ■ on this session was to count this as a non-session and re-book a session 14 as no APT was given. This may also apply to one or two other participants at this centre. For future cases it was advised that participants be referred back to the GP for other treatment or counselling and that treatment be kept within the protocol treatment window. The reason different advice to usual was given to the therapist on this occasion was because this had occurred at session 14 specifically.

This centre was monitored recently and has received an excellent report.

Bristol – There are no reported issues for Bristol at this time and there were no representatives from the centre at this meeting. All staff are trained and the site is recruiting. No data manager has been appointed as yet.

#### Questionnaire completion

It had been noted by RNs that some patients seemed to misunderstand the scoring of the Chalder fatigue scale (what is usual for them – should use pre illness as stated at the top of the questionnaire not illness state). As this is a

primary outcome we must take action (a) to check errors due to this had not occurred and (b) to prevent this being a problem in future.

**ACTION 7:** [REDACTED] email all RA/Ns to remind them to always double check that the CFQ has been answered correctly. It was noted that all centres are believed to be checking this already.

**ACTION 8:** [REDACTED] to run a query on every centre to check all participants with a low CFQ score to ensure it is consistent with other data collected at follow up. This will be checked as part of the DMEC report.

## 8. Treatment training manuals

Rather than produce training manuals, the therapy leads propose producing guidelines for training.

A modular training package with competence pass points was recommended. This should include definition of competence and advice on suitable staff attributes and background.

Some form of guidance manuals for training is needed so that the trial could be repeated or training could be continued if a therapy leader left.

A paper could be generated on this process for tips for future trainers for complex therapies.

Items to consider for inclusion:

Model of supervision, case discussion, engagement, piloting, review of recorded sessions, numbers of days of training and supervision needed, qualifications of therapy leads.

**ACTION 10:** Therapy leads to provide [REDACTED] with dates for competence and rolling competence milestones for all therapists. Also of background/discipline of therapist, start date on PACE, number of years clinical experience and how much of that experience was in CFS. This needed so that there is a therapy start date per therapist to track learning curve affects of therapists on outcome.

**ACTION 11:** Therapy leaders to provide two sides of initial guidance notes on training therapists.

## 9. Therapists' meetings

No major issues except for discussions on contract extension.

APT – the team meet four times a year and have telephone supervision at six week intervals in between.

CBT – the team have monthly telephone supervision and face to face meeting every six-eight weeks.

GET – the team have telephone supervision once a month and meet face to face quarterly.

**ACTION 12:** Therapy leaders/█ to remind all therapists that the training logs must be kept up to date for supervision (face to face and telephone) and any other training. This forms part of the PACE trial documentation.

#### **10. Update on 52 week DAR discs**

This issue is ongoing. Not very many discs have been compiled as yet.

**ACTION 13:** █ to ask centres to add 52 week discs as a rolling local team meeting agenda item.

#### **11. Lancet and BioMed Central papers and approval**

The BioMed central paper is on the 'highly accessed' list.

The Lancet have agreed in principal to consider the PACE main paper for publication on a fast track review.

#### **12. Ancillary studies**

##### **d) 2 year follow up (item # 4 and 4a)**

**ACTION 14:** █ to be asked why 'occupational therapist' has not been included in the first question.

**ACTION 15:** █ to lead on approaching HTA for two year follow up funding.

**ACTION 16:** █ █ █ to add Oxford criteria to questionnaires asked.

It was estimated than a minimum of an hour per week would be needed to trace and interview participants by phone, more if participants are difficult to track.

**ACTION 17:** █ to lead on finalising the protocol for the two year follow up study.

**ACTION 18:** Centre staff to feedback to █ on how much additional time two year follow up would be estimated to take and whether there is capacity for this at present. (█ to circulate this question).

**e) [REDACTED] supervision study**

[REDACTED] is meeting with the RA next week to discuss progress.

**f) [REDACTED] study**

This will be a reflective paper on CBT.

**g) King's study**

The qualitative study is now under way.

**h) Edinburgh study**

No funding is secured as yet to conduct this. The MRC are being approached.

**i) SNP study**

It was reported that CDC are willing to fund the analysis but costs need to be met for cost of collecting, spinning and storing the blood samples. This was unlikely to be possible without funding. Further avenues of funding need to be explored.

**13. Adverse events**

Two doctors need to be identified to centrally review all adverse events.

**ACTION 19:** As medically qualified PIs [REDACTED] and [REDACTED] to discuss the issue of centrally classifying adverse events. This to be done on the basis of queries to be raised by [REDACTED].

[REDACTED] will be generating monthly adverse event lists for centre leaders / PIs to review locally. These should ideally be signed off as reviewed.

**14. Generation of questions for papers and ancillary studies**

**ACTION 20:** [REDACTED] to ask staff to state if they would be interested in writing papers or conducting ancillary analyses for PACE. Of these, background and research training should be ascertained. This should be a standing TMG item.

**15. Any other business**

[REDACTED] will stand in as therapy lead cover for APT for July and August when [REDACTED] is away on [REDACTED].

**16. Proposed dates and venues for TMG meetings in 2007:**

**j) Thursday 20<sup>th</sup> September 2007**

**k) Tuesday 11<sup>th</sup> December 2007**

## Summary of Action Points

### PIs/CLs

**TMG#21 - ACTION 5:** Ongoing action for PIs and centre leaders to calculate actual NHS subvention spend versus money received (£3001 per participant randomised).

**TMG#22 - ACTION 14:** If complete CONSORT data can be obtained then a paper may be written in the future about screen negative patients. This action point will be ongoing for the remainder of the trial.

**ACTION 3:** Final dates to be confirmed by PIs [REDACTED] and finance. Staff contracts will need to be reviewed. [REDACTED] to circulate final dates for end of recruitment end of treatment end of follow up and end of trial.

**ACTION 4:** Once renewed target recruitment rates are prepared all PIs and centre leaders should approach NHS organisations for extensions for NHS therapists.

**ACTION 5:** The Analysis Strategy Group to consider 10/15 sessions received as a minimum for adherence to treatment rather than 8/15 sessions.

### Therapy Leaders

**ACTION 10:** Therapy leads to provide [REDACTED] with dates for competence and rolling competence milestones for all therapists. Also of background/discipline of therapist, start date on PACE, number of years clinical experience and how much of that experience was in CFS. This needed so that there is a therapy start date per therapist to track learning curve affects of therapists on outcome.

**ACTION 11:** Therapy leaders to provide two sides of initial guidance notes on training therapists.

**ACTION 12:** Therapy leaders/[REDACTED] to remind all therapists that the training logs must be kept up to date for supervision (face to face and telephone) and any other training. This forms part of the PACE trial documentation.

[REDACTED]  
**ACTION 15:** [REDACTED] to lead on approaching HTA for two year follow up funding.

**ACTION 16:** [REDACTED] [REDACTED] [REDACTED] to add Oxford criteria to questionnaires asked.

**ACTION 17:** [REDACTED] to lead on finalising the protocol for the two year follow up study.

**ACTION 19:** [REDACTED] and [REDACTED] to discuss the issue of centrally classifying adverse events. This to be done on the basis of queries to be raised by [REDACTED]

[REDACTED]  
**ACTION 19:** [REDACTED] and [REDACTED] to discuss the issue of centrally classifying adverse events. This to be done on the basis of queries to be raised by [REDACTED].

[REDACTED]  
**ACTION 14:** [REDACTED] to be asked why 'occupational therapist' has not been included in the first question.

[REDACTED]  
**ACTION 8:** [REDACTED] to run a query on every centre to check all participants with a low CFQ score to ensure it is consistent with other data collected at follow up. This will checked as part of the DMEC report.

[REDACTED]  
**ACTION 1:** [REDACTED] to send the GET self help guide to MREC once completed.

**ACTION 2:** [REDACTED] to ask permission from MREC for the list of approved self help guides to be added to the PACE trial website.

**ACTION 3:** Final dates to be confirmed by PIs [REDACTED] and finance. Staff contracts will need to be reviewed. [REDACTED] to circulate final dates for end of recruitment end of treatment end of follow up and end of trial.

**ACTION 6:** [REDACTED] to add the authorship recommendations to the TSC agenda for their consideration/approval.

**ACTION 7:** [REDACTED] to email all RA/Ns to remind them to always double check that the CFQ has been answered correctly. It was noted that all centres are believed to be checking this already.

**ACTION 9:** [REDACTED] to email all centres with the suggestion that end of therapy treatment could be given by back up therapists and these tapes be used for ongoing competence.

**ACTION 12:** Therapy leaders/[REDACTED] to remind all therapists that the training logs must be kept up to date for supervision (face to face and telephone) and any other training. This forms part of the PACE trial documentation.

**ACTION 13:** ■ to ask centres to add 52 week discs as a rolling local team meeting agenda item.

**ACTION 18:** Centre staff to feedback to ■ on how much additional time two year follow up would be estimated to take and whether there is capacity for this at present. ■ to circulate this question).