

Responses to PACE questions tabled by the Countess of Mar in the House of Lords

22nd May 2012

On 7th May 2012 Professor Malcolm Hooper provided The Countess of Mar with a list of questions about the PACE Trial (“Questions submitted by Professor Malcolm Hooper to The Countess of Mar re: the PACE Trial for the attention of the Minister of State for Universities and Science, the Rt Hon David Willetts MP, who is responsible for the Medical Research Council”).

The Countess of Mar kindly agreed to re-word and table the questions in the House of Lords.

Baroness Wilcox, who is the Parliamentary Under-Secretary for Business, Innovation and Skills, responded to the questions on the 22nd May:

Question 1

Countess of Mar - *whether a publicly-funded trial has to be registered in the ISRCTN (International Randomised Controlled Trial Number) Register; whether this is a condition for publication in reputable journals; and, if so, whether they consider that the PACE (Pacing, graded Activity and Cognitive behaviour therapy: a randomised Evaluation) trial registration ISRCTN54285094 is complete and includes records of all changes in procedure from the point of registration onwards*
HL43

Baroness Wilcox - There is a requirement for publicly funded clinical trials to be registered and there are a number of different registers.

The PACE study was funded by a Medical Research Council (MRC) grant to Queen Mary, University of London. The Department of Health for England, the Chief Scientist Office in Scotland and the Department for Work and Pensions co-funded the trial; their contributions were paid via the MRC grant.

The MRC has been a strong supporter of trials registration for many years and provided financial support to help set up the ISRCTN scheme. The MRC was also involved in helping to refine the scheme and in promoting its widespread adoption in the UK.

The MRC requires that all MRC-funded clinical trials comply with the CONSORT Statement, which is an evidence-based, minimum set of recommendations for reporting Randomised Controlled Trials. CONSORT, which stands for Consolidated Standards of Reporting Trials, offers a standard way for authors to prepare reports of trial findings, facilitating their complete and transparent reporting, and aiding their critical appraisal and interpretation. CONSORT includes guidance on ISRCTN registration.

The results of the trial were reported in *The Lancet*, which also follows the CONSORT guidelines. The PACE trial report would have had to meet this standard as a prerequisite for publication.

The MRC is not responsible for assuring the quality of data in the ISRCTN. The Government cannot comment on the completeness of the data.

Question 2

Countess of Mar - *When and why the PACE (Pacing, graded Activity and Cognitive behaviour therapy: a randomised Evaluation) trial sponsor was changed from the Medical Research Council Clinical Trials Unit to the Medical Research Council and then to the Queen Mary University of London; and why these changes are not recorded in the ISRCTN (International Randomised Controlled Trial Number) Register. HL44*

Baroness Wilcox - The PACE study was funded by a Medical Research Council (MRC) grant to Queen Mary, University of London, the Principal Investigator was Professor P White at QMUL, co-investigators were Professor T Chalder, King's College London and Professor M Sharpe, University of Edinburgh. The Department of Health for England, the Chief Scientist Office in Scotland and the Department for Work and Pensions co-funded the trial; their contributions were paid via the MRC grant.

Queen Mary, University of London, has been identified as the formal Sponsor of the PACE trial throughout the duration of the study. The MRC would normally only be identified as the formal Sponsor of a clinical trial where the principal investigator was an MRC employee or where an MRC unit designed and managed the trial.

Questions 3 and 4

Countess of Mar - *why the “normal range” for both PACE (Pacing, graded Activity and Cognitive behaviour therapy: a randomised Evaluation) trial primary outcome measures (fatigue and physical function) were re-defined so that it was possible for a participant to deteriorate on both measures during the course of the trial yet still fall within the Chief Principal Investigator’s “normal range”; and what impact they consider this re-definition to have had on the validity of the trial. HL46*

Countess of Mar - *why the recovery statistics and other outcomes as defined in the published Protocol of the PACE (Pacing, graded Activity and Cognitive behaviour therapy: a randomised Evaluation) trial have not been published HL45*

Baroness Wilcox - The PACE study was funded by a Medical Research Council (MRC) grant to Queen Mary, University of London. The Department of Health for England, the Chief Scientist Office in Scotland and the Department for Work and Pensions co-funded the trial; their contributions were paid via the MRC grant.

As for all MRC-funded studies, it is the responsibility of the investigators and the relevant journals, guided by peer reviewers, to determine how findings are published and when. The investigators’ first paper on the outcomes of the PACE study was published in *The Lancet* in March 2011, this includes descriptions of normal ranges and how they calculated. The MRC understands that further publications are planned, one of which will address the issue of recovery.

Question 5

Countess of Mar - *what is the position of the Medical Research Council as co-funder of the PACE (Pacing, graded Activity and Cognitive behaviour therapy: a randomised Evaluation) trial regarding the subsequent reliance by the National Institute for Health and Clinical Excellence and the Department for Work and Pensions on the outcome as reported in the Lancet. HL47*

Baroness Wilcox - The Medical Research Council (MRC) is an independent research funding body which receives its grant in aid from the Department for Business, Innovation and Skills. The selection of projects for funding is determined through peer review.

The decision to fund the PACE trial, a randomised controlled trial of Cognitive Behavioural Therapy (CBT), graded exercise, adaptive pacing and usual medical care for the chronic fatigue syndrome, was based on MRC’s usual rigorous peer review process for clinical trials. The study aimed to evaluate treatments that were already in use, and for which there was insufficiently strong evidence

to support their effectiveness. The MRC strongly supported this research and the publication of the findings.

The MRC strongly supports the publication of the findings of all MRC funded research to advance medical research worldwide and to inform new therapies and treatments. The investigators' first paper on the finding of the PACE study, was published in *The Lancet*; Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial, P White et al, *The Lancet*, Volume 377, Issue 9768, Pages 823 - 836, 5 March 2011.

The MRC does not have a position on how the outcome of MRC-funded studies are interpreted and used by regulators or policy makers although, as above, it supports prompt publication of its research findings so they are widely available to all potential users and to support evidence-based treatment of patients.

Question 6

Countess of Mar - *which disease or condition was being studied in the PACE (Pacing, graded Activity and Cognitive behaviour therapy: a randomised Evaluation) trial that was co-funded by the Medical Research Council, the Department of Health, the Department for Work and Pensions and the Scottish Chief Scientist's Office, in the light of the statement made by the Chief Principal Investigator, Professor Peter White, that the PACE trial did not purport to be studying myalgic encephalomyelitis*
HL69

Baroness Wilcox - The PACE study was funded by a Medical Research Council (MRC) grant to Queen Mary, University of London, the Principal Investigator was Professor P White at QMUL, co-investigators were Professor T Chalder, King's College London and Professor M Sharpe, University of Edinburgh. The Department of Health for England, the Chief Scientist Office in Scotland and the Department for Work and Pensions co-funded the trial; their contributions were paid via the MRC grant.

The criteria for the PACE study were published in the trial protocol and are also addressed in the main findings published in *The Lancet*.

