

Malcolm Hooper PhD, B Pharm., MRIC, C Chem.
Emeritus Professor of Medicinal Chemistry
University of Sunderland, UK

2, Nursery Close
Sunderland
SR3 1PA
United Kingdom

Phone +44 (0)191-528-5536
mobile 07957-634935
Email hoopersecundus@talktalk.net

Dr Richard Horton
Editor-in-Chief
The Lancet
125 London Wall
LONDON
EC2Y 5AS

April 15, 2016

Dear Dr Horton,

I write to call again for the retraction of the PACE study paper by White PD et al. (Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial. *Lancet* 2011;377:823-836).

Although not within your personal remit, subsequent papers flowing from it and purporting to validate the initial findings of the PACE study also need to be retracted, namely:

- White PD, Goldsmith K, Johnson AL, Chalder T, Sharpe M (2013) Recovery from chronic fatigue syndrome after treatments given in the PACE trial. *Psychol Med* 43: 2227-2235.
- Chalder T, Goldsmith KA, White PD, Sharpe M, Pickles AR (2015) Rehabilitative therapies for chronic fatigue syndrome: a secondary mediation analysis of the PACE trial. *Lancet Psychiatry* 2: 141–152.
- Sharpe M, Goldsmith KA, Johnson AL, Chalder T, Walker J, et al. (2015) Rehabilitative treatments for chronic fatigue syndrome: long-term follow-up from the PACE trial. *Lancet Psychiatry* 2: 1067-1074.

- Chalder T, Goldsmith KA, White PD, Sharpe M, Pickles AR (2015) Supplement to: Rehabilitative therapies for chronic fatigue syndrome: a secondary mediation analysis of the PACE trial. *Lancet Psychiatry* 2: 141-152.
- McCrone P, Sharpe M, Chalder T, Knapp M, Johnson AL, et al. (2012) Adaptive pacing, cognitive behaviour therapy, graded exercise, and specialist medical care for chronic fatigue syndrome: a cost-effectiveness analysis. *PLoS One* 7: e40808

On 28th March 2011 I sent your Executive Editor, Dr Stuart Spencer (your fast track editor who was responsible for publishing the selective PACE results) a closely reasoned paper pointing out numerous failings and flaws in the PACE paper which, on 18th April 2011 on Australian radio, you publically and contemptuously dismissed as a “diatribe”.

However, since then, other people have systematically and comprehensively dismantled the PACE trial, including the following:

Tuller D (2015) TRIAL BY ERROR: The Troubling Case of the PACE Chronic Fatigue Syndrome Study. <http://www.virology.ws/2015/10/21/trial-by-error-i/>

Tuller D (2015) TRIAL BY ERROR: The Troubling Case of the PACE Chronic Fatigue Syndrome Study (second installment). <http://www.virology.ws/2015/10/22/trial-by-error-ii/>

Tuller D (2015) TRIAL BY ERROR: The Troubling Case of the PACE Chronic Fatigue (final installment) <http://www.virology.ws/2015/10/23/trial-by-error-iii/>

Tuller (2016) <http://www.virology.ws/2016/02/01/trial-by-error-continued-a-few-words-about-harassment/>

Goldin R. PACE: The research that sparked a patient rebellion and challenged medicine. www.stats.org/pace-research-sparked-patient-rebellion-challenged-medicine

The final *coup de grace* is the paper by Dr Mark Vink (The PACE Trial Invalidates the Use of Cognitive Behavioral and Graded Exercise Therapy in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: A Review. *J Neurol Neurobiol* 2(3): doi <http://dx.doi.org/10.16966/2379-7150.124>).

The arguments presented in this paper vitiate the PACE study published results and make clear that the claims that CBT and GET are in any way effective in treating ME/CFS are not supported by the data.

Others have also comprehensively dismantled the foundations upon which the PACE study was predicated, but I draw your attention to just two:

(1) The Institute of Medicine (IOM) of the National Academies was asked by the Health and Human Services (HHS), the Centres for Disease Control (CDC), the National Institutes of Health (NIH), the Food and Drug Administration (FDA) and the Agency for Healthcare Research and Quality (AHRQ) to convene an expert committee to examine the evidence base for ME/CFS. The committee was charged with developing evidence-based clinical diagnostic criteria for use by clinicians. Their report "Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness" was published on 10th February 2015 and stated that *"ME/CFS is a serious, chronic, complex, multisystem disease that frequently and dramatically limits the activities of affected patients. In its most severe form, this disease can consume the lives of those whom it afflicts"* <https://iom.nationalacademies.org/Reports/2015/ME-CFS.aspx> After publication of the IOM committee report, the CDC decided to archive its "CFS Toolkit" which had recommended the cognitive behavioural and exercise interventions so strenuously promoted by the UK psychiatric lobby.

(2) The National Institutes of Health (NIH) convened a "Pathways to Prevention" (P2P) working group which on 16th July 2015 published its Report "Advancing the Research on Myalgic Encephalomyelitis/Chronic Fatigue Syndrome". The Report is clear:

"Strong evidence indicates immunologic and inflammatory pathologies, neurotransmitter signalling disruption, micorobiome perturbation, and metabolic or mitochondrial abnormalities in ME/CFS that are potentially important for defining and treating ME/CFS" (page 3).

"Both society and the medical profession have contributed to ME/CFS patients feeling disrespected and rejected. They are often treated with skepticism, uncertainty, and apprehension and labeled as deconditioned or having a primary psychological disorder" (page 4).

"Although psychological repercussions (e.g., depression) may accompany ME/CFS, it is not a primary psychological disease in etiology" (page 5).

"fMRI and imaging technologies should be further studied as diagnostic tools and as methods to better understand the neurologic dysfunction of ME/CFS" (page 10).

"An integrated, systems-level approach should be followed to understand how immunologic, neurologic, and metagenomic factors may contribute to ME/CFS. Immunologic mechanisms of ME/CFS and pathway associated with disease progression must be defined and characterized (e.g., defining cytokine profiles involved in pathogenesis; studying inflammation; and comprehending the basis for natural killer cell dysfunction observed in many ME/CFS patients)" (page 12).

"Many clinicians do not fully understand ME/CFS" (page 14).

"Specifically, continuing to use the Oxford definition may impair progress and cause harm. Thus, for needed progress to occur we recommend that the Oxford definition be retired" (page 16).

<https://prevention.nih.gov/programs-events/pathways-to-prevention/workshops/me-cfs/workshop-resources#finalreport>

No-one can dispute that the PACE trial Principal Investigators used the Oxford criteria or that the PIs continue to believe that ME/CFS is a primary behavioural disorder from which recovery is possible with the use of CBT and GET.

Finally, of utmost importance is the call for the anonymised data from the original PACE trial to be made available to eminent scientists and clinicians (who are supported by Nobel Laureates, several members of the National Academy of Sciences, biochemists, biophysicists, geneticists, immunologists, neuroscientists, experts in public health and infectious disease and epidemiologists) who wish to carefully re-evaluate it and check the validity of the PACE conclusions.

The obduracy of authors, editors, publishers, and institutions to collectively resist these requests, in defiance of the highest standards of scientific enquiry and the agreed rules of publishing, raises the obvious question: what do the PIs have to fear by the release of the anonymised data?

The integrity of science and publishing of scientific papers depends upon access to experimental data so that others may examine it and challenge any conclusions drawn from it, especially when these form the basis of public policy that affects the well-being of many sick people.

Given that you are on record as calling for transparency of clinical research data, why do you make special pleading in the case of the PACE trial data?

Immeasurable damage has been done to the health and well-being of people with ME/CFS by the ideological and doctrinaire application of CBT/GET as a purported treatment for this complex chronic neurological illness, most recently exposed in the Report by George Faulkner from The Centre for Welfare Reform (“In the Expectation of Recovery” <http://www.centreforwelfarereform.org/news/misleading-mability-cuts/00270.html>).

In light of the abundant evidence which has discredited the PACE trial, this situation cannot continue and proper regard must be given to the vast number of papers that identify biomedical features of ME/CFS and the possible effective treatments that might follow.

It is to be regretted that The Lancet, once regarded as an eminent medical journal, has aligned itself with these obstructions to the progress of medical understanding and continues to resist calls for retraction of the paper and/or release of the anonymised data for others to study.

It is within your purview to change this and restore the reputation of the journal and

medical science in the UK and internationally.

Yours sincerely

A handwritten signature in black ink that reads "Malcolm Hooper". The signature is written in a cursive style. The name "Hooper" is underlined with a single horizontal line.

Malcolm Hooper