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Bridget Phillipson MP
House of Commons
Westminster
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16th July 2018

Dear Bridget,

Many thanks for forwarding the letter of 14th June 2018 (PO-1133220) from Lord O'Shaughnessy, Parliamentary Under Secretary of State for Health (Lords) in response to my request for your support for Carol Monaghan MP's presentation in Parliament about the medical scandal of the PACE trial involving ME/CFS patients.

I should be grateful if you would kindly forward this reply to Lord O'Shaughnessy himself please and inform him that I require his response to the issues I raise herein.

Carol Monaghan MP has done a great service for the whole ME community, including not only patients and carers, but also sympathetic and informed clinicians.

Finally the truth is now emerging about the PACE study and hence I found Lord O'Shaughnessy's reply to be egregiously erroneous.

I feel sure that he did not write the letter himself, which I suspect was drafted by one of the many advocates of the PACE trial who are still trying to rescue something from the debacle of this now-infamous clinical trial.

Because the issue is of such immense national – and indeed international – public interest, I have addressed chronologically and in some detail the more glaring untruths contained in his letter.

By way of introduction, I bring to Lord O'Shaughnessy's attention relevant extracts about the PACE trial from a Submission on ME on 29th June 2018 to the Scottish Parliament by Professor Jonathan Edwards, Emeritus Professor of Medicine at University College, London (PE1690/F):

*"**Service Provision Problems. ….**A range of physical and psychological treatments including graded exercise therapy (and) cognitive behavioural therapy…based on theories of psychological perpetuation of the illness have been subjected to methodologically inadequate trials and have been introduced into mainstream healthcare based on uncritical interpretation of the results.*

*"**Specific Weakness in Clinical Trial Methodology.** No trial of a drug using the methods used in these trials would be acceptable for drug approval…If you are not able to obtain reliable evidence you cannot obtain unreliable evidence and treat it as reliable….Both CBT and GET are based on the idea that the patient is not just encouraged to, but instructed to, take responsibility for taking on a frame of mind in which they see themselves as likely to improve. That is to say that the treatment deliberately introduces subjective bias of exactly the sort that proper trial design is designed to avoid….The theory was that the persistence of disability in ME is due to unhelpful beliefs about inability to improve. What PACE seems to show is that it may be possible to change patients' beliefs…but crucially, the measure of disability did not change. This suggests that even if unhelpful thoughts were present, they were not the cause of the disability. Moreover, the long-term follow up data from PACE show no difference from controls even in reported well-being in the CBT and GET groups. It is now documented from trial committee minutes that detailed assessment of activity with actometers was abandoned because a previous study had already suggested no improvement would be seen – which would not have supported the preferred hypothesis.*

***"Failure of Communication.** It is reasonable to ask why these treatments have become routine practice despite the evidence base being valueless. These therapies have been promoted by a group of psychiatrists….but with other physicians largely unaware of what was going on until recently….The standard of assessment of evidence in psychological medicine appears to be well below other specialities. There is also a troubling hint that it is convenient…for patients to be shunted into standardised therapy protocols rather than given meaningful long term support. The patient community has been publicly vilified by the trial authors and colleagues but they have turned out to be right. They have identified a serious weakness in the quality of both science and peer review in psychological medicine.*

*"**Urgent Need to Address Legitimate Complaints.** The witnesses made two reasonable complaints. The first is that unproven treatments are being offered in place of meaningful care. The second is that these treatments cause distress and perhaps harm. CBT is demeaning because the patient works out that it presumes that their sense of being unwell is an illusion. Since very few people recover, it also offers false hope. GET makes no sense if the defining feature of ME is feeling ill after exertion….Patients report long-term deterioration after battling to achieve physical exercise goals…and the prima facie case is that they should be taken seriously. The appreciation in the last two or three years that CBT and GET have no sound evidence base leaves regional health services with difficult decisions….Specialist services are needed for an illness that very few doctors have practical knowledge of…It is likely that significant sums of money are being wasted on treatments that are distracting health care professionals from useful care and causing unnecessary distress. The situation needs urgent review".*

It is indisputable that there are serious problems with Lord O'Shaughnessy's DoH support for the PACE trial as set out in his letter.

In particular, I seek his clarification about the diametric difference between his Department's support for the PACE trial as set out in his letter to you and his Department's stance as set out in Hansard.

Lord O'Shaughnessy will be aware that the two key arms of the PACE trial (CBT and GET) were predicated on the biopsychosocial model of ME/CFS (ie. that there is no underlying pathology) and which categorised it as a mental (behavioural/somatoform) disorder from which "recovery" is possible following cognitive restructuring and increasing aerobic exercise, whereas the Government's official policy is that ME/CFS is a neurological disorder from which recovery cannot be possible merely by changing a patient's (correct) perception that s/he is suffering from a biomedical disorder.

On 30th January 2006 the then Health Minister, Lord Warner, said on the record: *"There is only one World Health Organisation International Classification of Diseases code for chronic fatigue syndrome/myalgic encephalomyelitis, which is G93.3"* (HL3612), G93.3 being neurological disorders.

On 2nd June 2008 Lord O'Shaughnessy's predecessor, the Parliamentary Under Secretary of State, Department of Health (Lord Darzi of Denham) stated: *"My Lords, the Government accept the World Health Organisation's classification of CFS/ME as a neurological condition….My Lords, I have acknowledged that CFS/ME is a neurological condition"* (HLPQ: Health: Chronic Fatigue Syndrome/Myalgic Encephalomyelitis).

On 21st November 2011 Lord Freud, Minister for Welfare Reform, confirmed in a letter to the Countess of Mar that the Department for Work and Pensions does not consider ME/CFS to be a mental disorder. The letter was unequivocal: "*The Department of Health has indicated that they have 'always relied on the definition set out by the World Health Organisation in its International Classification of diseases (ICD) under ICD code G93.3, subheading other disorders of the brain'. The DWP is in agreement with this view. Therefore, for the avoidance of doubt, I can be clear that the Department does not classify CFS/ME as a mental health disorder".*

By supporting the now-proven fraudulent PACE trial results that categorise ME/CFS as a behavioural disorder, Lord O'Shaughnessy is contradicting his own Department's official policy.

The Department of Health and Social Care cannot pretend to be unaware that the PACE trial has now become a by-word for poor science in which data has been shamefully manipulated in an attempt (i) to achieve the pre-determined and promised outcome; (ii) to justify the cost of £5 million and (iii) to justify the extravagant claims made under the auspices of the Science Media Centre as part of its active campaign to discredit people with ME when the study was first reported in The Lancet in 2011. Lord O'Shaughnessy may be aware of the close link between the psychiatrists involved in the PACE trial and the industry-funded Science Media Centre, one of whose founder members (Professor Sir Simon Wessely) directed the PACE trial statisticians in his role of overseeing the Clinical Trials Unit. Lord O'Shaughnessy cannot be unaware that the SMC supports and publicly promotes in the media the PACE Investigators' disproven beliefs about the nature of ME despite the fact that the PACE Investigators are acting in contravention of DoH policy.

I now address specific inaccuracies in Lord O'Shaughnessy's letter:

1. *"The PACE trial…was funded by the MRC":* Lord O'Shaughnessy has been disingenuous when he implies that the PACE trial was funded by the MRC alone, the MRC being perceived by some less-informed individuals as demanding the highest scientific integrity (written evidence of the MRC's collusion in the numerous breaches of protocol and of the MRC's own code of practice is available if required). He will surely be aware that the PACE trial is the only clinical trial co-funded by the DWP; this is known to be because the Chief Principal Investigator promised a reduction in State benefit claims by people with ME/CFS once the pre-determined PACE trial results were published. Other co-funders included the Scottish Chief Scientist's Office and Lord O'Shaughnessy's own Department of Health.

2. *"The trial provided evidence that both cognitive behavioural therapy (CBT) and GET were moderately effective…and were better than adaptive pacing therapy or SMC alone in improving both symptoms and disability*": this has been supported by over 100 international experts as being untrue. From 2011 to 2016 there was a concerted attempt by all involved in the PACE trial to prevent the raw data from this publicly funded study being released (ie. by the Principal Investigators themselves, editors, publishers, funders and sponsors including the Department of Health, the Department for Work and Pensions, the Office of the Scottish Chief Scientist, the MRC and Queen Mary University of London). This is technically illegal since the Principal Investigators of such publicly funded research are required to make the obtained data available to bona fide interested scientists. As noted above by Professor Edwards, many of these scientists were repeatedly and publicly vilified and ridiculed by the PACE trial Investigators (and by their fellow

supporters of the psychosocial model who, like the PIs, work for and are involved with the medical insurance industry) as being "vexatious" in making their requests. Eventually after a FOIA request from a severely sick ME sufferer (which was resisted to the highest level of the tribunal), the data was finally released at a cost of £250,000 incurred by QMUL in its attempts not to release the actual data. Analysis of the data by a range of experts, patients and scientists (including world-renowned statisticians) showed that the originally published data had been grossly and deliberately manipulated in an attempt to justify the desired conclusions. This is scientific fraud and has no place in the scientific and medical literature. The study was doomed to fail because of basic flaws in its design (Goldin R. March 21st, 2016: http://www.stats.org/pace-research-sparked-patient-rebellion-challenged-medicine/). There were no objective measurements made to justify the claims of the work: only subjective and unblinded data was reported. Having registered and published the trial protocol, in contravention of accepted scientific norms, the Principal Investigators abandoned the trial's statistical analysis plan and changed the primary outcomes after the trial had finished and they did not publish their revised statistical analysis plan until after the primary results of the trial had been published in The Lancet. Importantly, the PI's new statistical analysis plan did not contain their new definition of "recovery", when in fact the new definition of "recovery" was markedly less stringent than the definition in the original protocol and was devised after the PIs had seen the trial data, to which they were unblinded. For the avoidance of doubt, I should be grateful if Lord O'Shaughnessy would be kind enough to ascertain the date of the meeting at which the PI's new definition of "recovery" was agreed. Crucially, it is important to note that the PI's new definition of "recovery" specified a physical function threshold lower than that required to enter the trial ie. a participant's physical function could deteriorate during the trial but the same participant would still meet the post-hoc definition of "recovery" so were classed and reported as "recovered". Indeed, 13% of participants met the new "recovery" threshold at the start of the trial. By any standards, this is indefensible. As noted by Professor Edwards, at long-term follow up there was no difference between the trial groups, so the favoured interventions of CBT and GET cannot be claimed to be even moderately effective as claimed by Lord O'Shaughnessy. Many clinicians and medical scientists have recognised that the PACE trial has invalidated the use of CBT and GET in ME (for example, Vink M. Journal of Neurology & Neurobiology 10 January 2017:3:1). The US National Institutes of Health, one of the world's foremost medical research centres, convened a Pathways to Prevention working group which in December 2014 published its draft Statement entitled "Advancing the Research on Myalgic Encephalomyelitis/Chronic Fatigue Syndrome". It is an important document, as it signifies a major change in attitude towards ME/CFS and casts further doubt on the claimed success of the PACE Trial. The NIH Statement is unambiguous that the Oxford criteria (used in the PACE trial) are flawed and lack reliability, thereby confounding the ability to interpret results drawn from studies which used them to select cohorts and noting that use of the Oxford criteria may impair progress and cause harm. The following quotations from the NIH are particularly significant:

- *"The Oxford criteria (published in the Journal of the Royal Society of Medicine in February 1991) are flawed and include people with other conditions, confounding the ability to interpret the science.*

- *"This is not a psychological disease in aetiology.*

- *"Existing treatment studies (CBT and GET)…(have) not translated to improvements in quality of life. Thus, they are not a primary treatment strategy.*

- *"The focus on exercise programmes has further stigmatised and discouraged research participation.*

- *"Current research has neglected many of the biological factors underlying ME/CFS onset and progression.*

- *"ME/CFS is a chronic, complex condition…with no cure…..Nothing has improved the lives of the patients.*

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

The Conclusions of the draft report reiterate key findings:

- *"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".*
  https://prevention.nih.gov/docs/programs/mecfs/ODP-MECFS-DraftReport.pdf

On 10th February 2015 The Institute of Medicine (now called The National Academy of Sciences) released a report entitled "Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness". The report considered 9,112 published papers on ME/CFS and concluded that it has serious, multi-system pathology and that it is not a behavioural disorder: *"It is clear from the evidence compiled by the committee that ME/CFS is a serious, chronic, complex, and multisystem disease that frequently and dramatically limits the activities of affected patients"* (http://www.cdc.gov/cfs/toolkit/archived.html). After publication of that report, the US Centres for Disease Control decided to archive its CFS Toolkit that recommended CBT and GET as interventions for ME/CFS because these interventions have been shown to be scientifically invalid. The US Agency for Health Research Quality ME/CFS Evidence Review (addendum July 2016) concluded that there was insufficient scientific evidence to support the use of CBT/GET on measurable outcomes like function, fatigue, quality of life, employment, and overall symptom improvement. CBT was also found to be inefficient or barely significant (https://www.ncbi.nlm.nih.gov/books/NBK379582/?report=reader). The PACE trial is now widely used to teach medical students how not to run a clinical trial because it provided no usable evidence as a result of serious methodological inadequacy; moreover, the objective data itself is reliable and it indicates that CBT and GET are no better than "usual medical care" which, for people with ME/CFS, is non-existent in the UK.

3. *"All the treatments were found to be safe":* Lord O'Shaughnessy is incorrect in stating that all the treatments used in the PACE trial were found to be safe and that any deterioration in patients' health was not due to the CBT or GET interventions. Although this claim was indeed made by the PACE Principal Investigators, it has now been demonstrated to be untrue. There are many reports from PACE participants of the extent to which they deteriorated whilst participating in the PACE trial. Before the PACE results were published, it had been shown beyond doubt that CBT was ineffective and GET was harmful to patients with ME/CFS as revealed in numerous patient surveys (some being professionally analysed) of over 5,000 patients. Well-documented cases of iatrogenic harm resulting from the psychiatrists' ideological imposition of GET are numerous. By dismissing symptoms as illusory, not only does this risk harming patients through misdiagnosis, but the "directive" CBT used in the PACE trial (as distinct from the more usual "supportive" CBT) effectively abandons sick people to their own devices, with the result that suicide rates in ME are known to be above average.

4. *"In 2013 a follow-up study, looking at recovery after one year, was published. This study supported the findings that CBT and GET were therapies most likely to lead to recovery":* this statement is wrong because the 2013 publication does not refer to a separate study, it simply reports a post-hoc analysis of the same PACE trial data and hence cannot be described as supportive since it is the same data.

5. "*Since 2011, PACE trial data has been shared with many independent scientists…including the internationally respected research organisation Cochrane, which independently validated the findings":* Lord O'Shaughnessy has been misinformed when he refers to the "*internationally respected research organisation Cochrane"* as having *"independently validated the findings*" of the PACE trial. The PACE trial was not *"independently validated"* by Cochrane because the PACE PIs themselves were authors of the claimed validation of their own work, the Cochrane review team having included Professor Peter White, the PACE Chief PI, as well as Professor Trudie Chalder, another of the PACE trial PIs, so they were in fact "validating" their own work and beliefs. Importantly, Professor Peter White has a proven financial interest, having personally funded the "Oxford" criteria used in the PACE trial. Furthermore, Professor White contributed financially to the production of the 2014 Cochrane with money from his own academic fund*. Professor James Coyne, Professor of Psychology at the University of Pennsylvania, holder of numerous Visiting Professorships, and author of over 400 papers who was recently designated as one of the 200 most eminent psychologists of the second half of the twentieth century, describes the Cochrane review in question as "untrustworthy" and states that it is complicit in endorsing the PACE investigators' misinterpretation of their findings.
   * http://cochranelibrary-wiley.com/doi/10.1002/14651858.CD011040/full

6. *"NICE clinical guidelines represent best practice. They are based on the available evidence":* as Lord O'Shaughnessy confirms in his letter, after years of prevarication, NICE is now committed to a complete rewriting of the 2007 Guideline CG53. For the avoidance of doubt and contrary to Lord O'Shaughnessy's assertion, the 2007 Guideline was not based on the available evidence: despite many requests to consider it, NICE intentionally disregarded many thousands of published papers and intentionally excluded from the Guideline Development Group experienced clinicians who were involved on a daily basis with ME/CFS patients and who knew it to be a biomedical disorder. This was known to be due to the existence of the then-Government's three-pronged strategy about ME/CFS. The PACE trial was but one arm of this three-pronged strategy and thus needs to be viewed in context. The results were a foregone conclusion in favour of CBT/GET because of the "integrated plan" of the New Labour Government to roll out CBT and GET across the nation for those with ME/CFS (Department of Health, 2004, Statement of Information released via the Welsh Assembly Disclosure Log 2296). The other two prongs of the three-armed strategy were to be the NICE Clinical Guideline 53 published in August 2007 and the national "Fatigue" Clinics that cost taxpayers £8.5 million to deliver interventions shown to be ineffective in ME/CFS (CBT) and to have made at least 50% of those who have undertaken it significantly worse (GET).

7. *"NICE also makes it clear that…those with CFS/ME have the right to refuse or withdraw from any component of their care plan":* what Lord O'Shaughnessy fails to mention is that if people with ME/CFS do withdraw from or refuse NICE-recommended interventions of CBT and GET, their State benefits are often withdrawn.

8. "*The Department of Health and Social Care funds research through the National Institute for Health Research (NIHR). The NIHR…is speaking with the UK CFS/ME Research Collaborative (CMRC)…about how best we can support a joined-up approach to high-quality research into this complex disorder*": Is Lord O'Shaughnessy and his DoH aware that the CMRC started life as the CFS/ME Clinical & Research Network Collaborative (CCRNC), whose CEO was Dr (now Professor)

Esther Crawley who was so instrumental in the 2007 NICE Guideline Development Group and whose Collaborative's charter stated that its objective was "*To champion evidence-based approaches to the treatment of CFS/ME, such as those provided in the (2007) NICE Guideline*"? Does he know that the CCRNC became the British Association for CFS/ME (known as BACME), again led by Dr Esther Crawley and which, via the MRC CFS/ME expert group (2008-2011) has now morphed into the CMRC? Many patients have expressed a continued distrust of the CMRC despite the change in its Governance, Professor Crawley having resigned as CEO. That Professor Stephen Holgate remains at the CMRC is an issue for many patients who do not trust him because of his previous roles at the MRC and his very close association with Professor Crawley. He is not considered to be a 'safe pair of hands'. Indeed, many patients believe that the changes at the CMRC were a forced 'cabinet reshuffle' as a result of the bad publicity around Esther Crawley's behaviour on various public platforms and because of their failed funding bids for the MEGA project. Patients and scientists alike are confused about why the CMRC was deemed necessary at all, given that a worldwide collaboration already exists founded by the charity Invest in ME, whose annual London Colloquia and Conferences are attended by leading academics and clinicians. Of particular concern is that membership of the CMRC includes Action for ME (AfME), who are almost universally distrusted by knowledgeable patients as being "part of the problem, not the solution" and many informed patients will not engage with any organisation where Action for ME has a seat at the table. An example of this concern is that Action for ME has announced that Professor Cathie Sudlow, now the holder of a personal chair in neurology at Edinburgh, is a conference speaker at the 2018 CMRC conference. When he was the holder of a personal Chair in psychology at Edinburgh, Professor Michael Sharpe (one of the PACE trial PIs) worked on the Scottish Neurological Symptoms Study and his collaborators included (then Dr) Cathie Sudlow. Professor Sharpe leaked a computer file containing 70 patients' names and addresses which he sent to a member of the public and it contained confidential information and personal statements made by patients to a number of high-profile clinicians involved in the Scottish Neurological Symptoms Study, including Dr Cathie Sudlow. Examples of the leaked confidential information about the study participants made by those clinicians include the following comments: *"putting it on"; "mad"; "imagining symptoms"; "examination was a waste of time".* The study from which the confidential data was leaked was looking at the prevalence of medically unexplained symptoms (MUS) in new patients attending Scottish Neurology clinics, particularly at *"illness-related beliefs and behaviours"*, a category in which the study investigators included patients with ME/CFS.

Despite the intransigent insistence by those who are involved in the medical insurance industry that ME/CFS is a behavioural disorder and despite their continued dismissal and ignoring of the ever-increasing scientific evidence that their beliefs about the nature of ME/CFS are unsustainable (permanent health insurance excludes mental disorders from payment if the insured person is unable to work and there is a significant amount of written evidence that PHI companies are determined to avoid pay-outs for ME/CFS), there can no longer be any credible doubt that the biopsychosocial (BPS) model which is the foundation of the CBT/GET paradigm for ME is now comprehensively discredited.

US research has provided a range of possible biomarkers of organic disease (see https://www.nature.com/articles/s41598-018-28477-9). ME/CFS is a complex, chronic multisystem illness (CMI) for which at least three immunological biomarkers have existed for some time. The problem in the UK is that NICE specifically proscribes testing for those biomarkers, thereby halting the progress of medical science and denying medical care and support to patients with ME.

By using terms of ignorance such as MUS (medically unexplained symptoms) and abusive language that castigates ME/CFS as mass hysteria or as a behavioural disorder, the BPS model so favoured by certain psychiatrists has been used to belittle and denigrate not only ME/CFS but also patients with environmental illnesses such as organophosphate poisoning (seen in farmers and shepherds), Gulf War

Syndrome (seen in veterans of the first Gulf War 1990-1991), Aerotoxic Syndrome (seen in cabin crews and some passengers), the Camelford water poisoning (in which initially seven people died but at least 20 people later died from drinking contaminated water, 25,000 people suffered serious health effects and 40,000 animals were affected: The Ecologist 1999:20:6:228-233; Sue Reid, Daily Mail, 14th December 2007) and chronic Lyme disease. We now know that all these disorders have chronic and multisystem correlates which can be understood and – given adequately funded appropriate research -- eventually treated.

The attempt to group together such CMIs and apply the BPS theory to them has become a cornerstone of contemporary medicine. It is attractive to Government Departments because it offers interaction with patients that relies on relatively inexpensive talking "therapy", not on necessary targeted investigations and treatments.

Unless the Parliamentary Under Secretary of State Lord O'Shaughnessy and his DoH cease to support the PACE trial's alleged "success" and recognises it for the scientific fraud it has been shown to be, patients with the devastating disorder ME/CFS will continue to be abused by UK Departments of State.

In the interests of patient safety and also to ensure that no further public money is spent on ineffective interventions, I look forward to Lord O'Shaughnessy's prompt response and to his assurance that he and his Department will desist from supporting "research" that is so methodologically flawed that it cannot be relied upon to guide public policy.

With many thanks for your own help.

Yours sincerely

Malcolm Hooper