PE1690/PP
Professor Brian Hughes submission of 1 November 2019

I wish to present some comments on the statements made in "PE1690/LL NHS Lothian submission of 23 August 2019". These comments are not exhaustive. They focus on methodological points relating to the PACE Trial.

My perspective is that of an academic psychologist of twenty years' experience, who specialises in critiquing research on health psychology. I am not professionally connected to the PACE Trial authors or to their wide network of collaborators and colleagues. Nor have I professional contact with the NHS. I am unaware of any conflict of interest that I need to declare. My input is derived from the perspective of academic peer-review and critique.

In my view the PACE Trial is a case study in how studies of behavioural health and health psychology face many methodological challenges, some of them seemingly incorrigible.
In my view, it is in few people's interest to deny these challenges, especially given that they have been identified widely by others. As such, I was somewhat surprised at the tone and content of the NHS Lothian document. In the remainder of this statement, I provide some comments on points made in the NHS Lothian submission.

"ALLEGATIONS ABOUT THE TRIAL"
"The trial finding that CBT and GET are superior to APT and standard medical care is false because it used patient rated outcomes"

COMMENTS:

(a) The document states that "*patient-rated outcomes are the most important to patient*."

No context or evidence is provided for this assertion. It is entirely disputable whether patient-rated outcomes are "most important," especially in physically ill populations.

(b) On the problem of bias, the document then states that "*this is a problem for all trials of therapies of which the patient must be aware…*"

That is correct. Note that no rebuttal is provided for this point. The fact that a problem affects "all" such trials does not make it any less of a problem. The consequences of the problem – namely, unreliable findings – remain problematic. There is no pardon on the grounds of unavoidability.

(c) The document then states that "However, in PACE whilst CBT and GET were found to be more effective than ABT which had similar therapist contact time and similar if not better credibility with patients…[making] bias…a very unlikely explanation"

This subjective phrasing shows how the document authors appear committed to a partisan interpretation of the PACE findings. A better

phrasing would be "*it is claimed that* CBT and GET were found to be more effective…" The PACE dataset has been re-analysed according to the original PACE protocol, and it is clear that so-called "recovery" rates in PACE are extremely low and non-significantly different from spontaneous recovery over time [1,2].

"The investigators changed the trial outcomes to make CBT and GET look better"

COMMENTS:

(a) The document states that "the trialists used the originally registered primary outcomes to report the trial findings". The document *then* states that "The precise way the outcomes were used in the analysis was changed from the initial protocol…"

This seems like wordplay. The fact that "the precise way" was "changed from the initial protocol" is exactly the problem – the investigators quite clearly changed the outcomes, and those changes quite clearly had the effect of making CBT and GET "look better". This is demonstrable when the published analyses are compared with analyses conducted according to the original statistical protocol. Such analyses show how the CBT and GET look better when the "changed" analyses are used. When the "not changed" analyses are used CBT and GET look worse [1,2].

(b) The document states that "Other ways of analysing the relative effects of the treatment produce similar findings"

This also seems like wordplay. Yes, some "other" ways of analysing the effects produce similar findings. However, other "other" ways produce findings that are quite different, and indeed damning to the PACE Trial. This is the whole point. The issue here is not whether "some" way can be found to analyse the data to produce flattering findings. The issue is whether an "objective" way of doing so has the desired effect. The study's own original analysis protocol can surely be said to be "objective". This protocol produces null findings.

A key additional point here is as follows. The only positive effects for PACE relate to self-report measures, which as noted are subject to self-report bias. Objective measures, such as activity trackers, physical endurance tests, disability payments, or return-to-work rates, show that CBT and GET had no discernible positive effect in the PACE Trial.

The phrasing of statements of this type to refer to "other" analyses amounts to obfuscation and is highly misleading.

"The proportion of patients regarded as recovered was inflated and no better with CBT and GET than with the other treatments"

COMMENTS:

(a) The document states that "the definition of recovery, especially with limited data (as in a trial), is contentious."

Correct. However, for the purpose of their study, the PACE Trial authors provide a working definition of recovery. It is this definition of recovery, analysed using the PACE authors' own original protocol, that produces null findings [1,2].

"The trial was fraudulent or in some way influenced by the DWP or the insurance industry"
COMMENT: This type of point is not related to methodology and the rebuttals offered in the document do not relate to the flaws identified with the PACE Trial, and therefore it is beyond my expertise to comment.

"The PACE authors refused to share or hid the trial data"
COMMENT: Again, this point is not related to methodology. I would note, however, that the legal proceedings relating to this episode are a matter of public record.

"The PACE Trial is universally regarded as flawed and consequently discredited"
COMMENT: This point is argumentative. Nobody seriously claims that the PACE Trial is "universally regarded" as flawed. If that were true, there would be no controversy. However, it is a matter of recorded that the PACE Trial is "regarded as flawed" by very many informed and authoritative individuals. The controversy is widely discussed in peer-reviewed academic literature.

"HAVE SIMILAR FINDINGS BEEN MADE BY OTHERS?"

(a) The document states: "The PACE trial results have been replicated many times."

COMMENT: This statement is highly misleading. The PACE Trial itself stands alone and has never been replicated in its current form.
A number of related studies by the same research group have been published, all with the same inherent research design flaws. None are replications of PACE.

Further, virtually no *independent* replication of this type of work exists; virtually all existing research emanates from the same group of researchers and their colleagues, all of which is based on the same research approach. All the findings have the same flawed nature: none of the studies yield objective (i.e. non self-report) data to support claims that the proposed interventions are effective.

Finally, the body of work here is by any standards very small. It is wholly misleading to claim that the PACE Trial has somehow been augmented by a large body of corroborating research.

"*CONCLUSIONS"*

(a) In the conclusions, the document refers to "*activist groups (not patients in general)*".

COMMENT: This point does not relate to methodology, but I would point out that it appears deeply dismissive to refer to "activist groups" in this manner.

As noted above, the controversies here are widely discussed in the academic and scientific literature. I have no doubt that such discussion is propelled by conscientious concern about the adverse consequences of the flaws identified in PACE. As researchers, we hold ethical obligations to address such controversies wherever they arise.

In conclusion, I encourage the authors of the NHS Lothian document to engage in serious collaborative debate in a spirit of open inquiry. I encourage them to recognise conscientious criticism where it is presented. It is in nobody's interest to entrench views in such a way as to deny the legitimacy of critique, or to mislead non-specialists into believing that no true controversy exists.

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References:

1. Wilshire, C., Kindlon, T., Matthees, A., & McGrath, S. (2017). Can patients with chronic fatigue syndrome really recover after graded exercise or cognitive behavioural therapy? A critical commentary and preliminary re-analysis of the PACE trial. *Fatigue: Biomedicine, Health & Behavior*, *5*(1), 43-56. DOI: 10.1080/21641846.2017.1259724.
2. Wilshire, C.E., & Kindlon, T. (2019). Response: Sharpe, Goldsmith and Chalder fail to restore confidence in the PACE trial findings. *BMC Psychology*, 7(19). DOI:10.1186/s40359-019-0296-x.