

The Biopsychosocial Approach to “CFS”: PACE, Music Therapy + CBT, and Other Crap

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“Conflicts-of-Interest” — My crowdfunded donations

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Big Question for All of This Research

*Open Label/Unblinded Trials

*Subjective Outcomes

Q: Can trials combining these two elements provide good data?

A: No

Big Questions About PACE

- Does a study in which participants had already met outcome thresholds for primary measures at baseline have a legitimate place in the domain called “science”?
- Is there a place in “science” for a study in which participants were simultaneously “disabled” and “recovered”?
- Why has a study containing this paradox been defended for so long by the U.K. (and Norwegian) academic and medical establishment?

IOM Report: 2015

- Institute of Medicine (now Academy of Medicine) and National Institutes of Health issue reports based on review of 1000s of studies.
- IOM declares that *“ME/CFS is a serious, chronic, complex, and multisystem disease that frequently and dramatically limits the activities of affected patients.”* Rejects idea that it is psychiatric disorder, or caused by deconditioning and false illness beliefs.
- Report refocuses away from “fatigue” and names “exertion intolerance” as cardinal symptom.

PACE Trial: “Definitive” study of CBT/GET

- Open label with subjective outcomes (all objective measures failed to show success, so they dismissed them as irrelevant)
- Use of bogus Oxford criteria conflating chronic fatigue and ME
- 641 participants
- Four trial arms: CBT, GET, APT, SMC
- Principal investigators: Dr. Peter White (QMUL), Dr. Michael Sharpe (Oxford), Dr. Trudie Chalder (KCL)
- Based on unproven theory that all symptoms due to deconditioning because of patients’ “dysfunctional cognitions” about their illness

PACE Trial

2011: First results in Lancet, 59-61 % "improved" with CBT/GET; "twice as many...back-to-normal"

Lancet commentary by Dutch: 30 percent met "strict criterion for recovery"

2013: Psychological Medicine: 22 % "recovered" with CBT/GET

October, 2015: Virology Blog publishes "Trial by Error" series

August, 2016: Tribunal orders QMUL to turn over raw trial data in scathing decision

March, 2018: BMC Psychology publishes full reanalysis of "improvement," "recovery" and long-term results

Conclusion: PACE outcome-switching changes null or placebo-induced results into decent ones. No long-term benefits from CBT/GET

Expert Responses to PACE

Professor Bruce Levin, Columbia: “The height of clinical trial amateurism”

Professor Jonathan Edwards, University College London: “It’s a mass of incomprehensibility to me.”

David Tuller, UC Berkeley: “A piece of crap.”

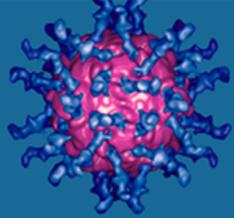
MP Monaghan: “One of the biggest medical scandals of the 21st century”

Sir Simon Wessely: “A thing of beauty”

Professor Esther Crawley, Bristol University: A “great, great” trial

My 15,000-word expose, plus follow-ups

Thanks to: Dr. Vincent Racaniello



virology blog
About viruses and viral disease

TRIAL BY ERROR: The Troubling Case of the PACE Chronic Fatigue Syndrome Study

21 OCTOBER 2015

By David Tuller, DrPH

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BY VINCENT RACANIELLO

Earth's virology Professor

Questions?

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Reasons for Concern

- *Bizarre outcome-switching

- *Lack of legitimate informed consent

- *Study design (open label/subjective outcomes) and use of Oxford criteria: Bad science but not clear that these warrant retraction

Outcome Switching in PACE

Primary outcome: Physical function on SF-36 (0-100)

Trial: Entry score required to demonstrate disability = 65 or less

Protocol: Score of 85 = “recovery” for physical function

Lancet: “normal range” for physical function = 60

Psychological Medicine: “recovery” for physical function = 60

13 % of 641 participants were already “within normal range”/“recovered” on physical function at entry

Why were they in the trial in the first place?

Why was this important fact NOT DISCLOSED in any of the published papers?

Other outcome switching:

- Multiple examples of this in PACE

- All had effect of weakening protocol measures

PACE Answers to Outcome-Switching

*We changed outcome measures before seeing the results, so they were pre-specified (DT: It was unblinded/subjective outcomes.)

*We decided our original measures were too stringent
(DT: Why bother writing a protocol?)

*It doesn't matter that people were "recovered" on key variables because we had other "recovery" measures as well.
(DT: A response from outer space)

*Reanalyzers "tweaked" our outcomes to make the results look worse
(DT: Reanalyzers "untweaked" what was "tweaked" without justification.)

PACE Trial did not obtain INFORMED consent

PACE Trial Protocol: Promise to adhere to Declaration of Helsinki

Declaration of Helsinki on Informed Consent:

*Researchers must tell prospective participants about “any possible conflicts of interests” and “institutional affiliations”

*PACE PIs have advised disability insurers that rehabilitative therapies like CBT/GET are indicated for ME/CFS claimants

*PACE PIs did not include promised disclosures in consent forms

PACE Answers to Lack of Informed Consent

- *We told the journals about our possible conflicts of interest
(DT: A non-response)
- *Insurance companies were not involved in the study
(DT: Another non-response)
- *Only three of 19 investigators did work for insurance companies
(DT: So...? Anyway, four of them had ties, not three)

Is PACE an example of research misconduct?

- Misrepresentation of data, for example suppression of relevant findings and/or data, or knowingly, recklessly or by gross negligence, presenting a flawed interpretation of data (MRC)
- Misrepresentation of interests, including failure to declare material interests either of the researcher or of the funders of the research (MRC)
- Falsification: Manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record (NIH)

Conclusions About PACE

*Reported PACE results cannot be taken at face value and proved that treatments in “definitive” trial didn’t work

*The data manipulations, lack of informed consent, and other issues could lead to the conclusion that this is research misconduct, according to standard definitions.

*PACE authors are the “anti-science” crowd, like climate-change deniers--not PACE patients.

*Best use of PACE—pedagogical tool

Norwegian Study: CBT and Music Therapy for Post-GF Fatigue

- Published in high-profile BMJ Paediatrics Open
- Research Question: Can CBT prevent chronic fatigue post-GF?
- Population: Adolescents with glandular fever
- Intervention: Half got CBT plus music therapy, half did not

Broken Peer Review System

Open peer review:

Reviewer #2: I haven't read "beyond the abstract"

In other words: Abstract was reviewed, but not the rest of the paper

THIS DID NOT BAR PUBLICATION IN BMJ PAEDIATRICS OPEN!!!!

HARD TO DESCRIBE HOW SHOCKING THIS IS—

Main Concern: Not a Feasibility Trial

Designed in protocol as a full-scale trial

Disappointing results

Re-purposed to be a “feasibility trial” —to ask for future funding

This could be considered research misconduct!!

Other Concerns:

***Post-hoc outcome:** PEM not in protocol, but added later and cited positively in conclusions

***Primary objective outcome**—average #steps/day

BOTH GROUPS WALKED—BUT INTERVENTION GROUP DID WORSE

Not mentioned in conclusion

***Recovery measure does not include primary outcome**

Resolution: Retract and Replace

- New Version as bad as the old one--just not referred to as a “feasibility” trial
- BMJ blames itself rather than authors for false information about trial
- PEM still included, main outcome still not mentioned in conclusions
- No mention of failure of peer review
- It is still CRAP, and findings still presented in misleading manner

Thanks To...

- Brilliant patients/advocates who first deconstructed and dissected the science—too many to name
- Vincent Racaniello for trusting in my reporting
- UC Berkeley for valuing academic freedom
- The Center for Global Public Health for supporting me
- Faculty colleagues at SPH and Berkeley who recognize nonsense