



Why ME patients are critical of the PACE trial

What is the PACE trial and why does it matter?

The PACE trial is a £5 million study that promotes the view that ME/CFS patients can recover if they gradually increase their physical activity. It is based on a psychogenic theory that the debility of the disease is due to patient's "fear of activity" and subsequent deconditioning, despite extensive evidence to the contrary. This view negatively affects how ME/CFS patients are viewed by society and cared for in medical practice.

What are the flaws in the PACE trial?

A recent investigation by *The New York Times* journalist David Tuller reported major flaws in the study's methodology. A letter authored by several prominent British and American researchers in fields as diverse as statistics, epidemiology, psychology, microbiology and genetics has called on *The Lancet* to conduct an independent review.

Key criticisms include: changing the definition of "recovery" after the study was already underway; the failure to report objective measures included in the original trial design in favor of reporting subjective outcome measures; a newsletter distributed to patients in the middle of the experiment touting the benefits of some of the treatment therapies and critiquing drug therapies; and failure to disclose conflicts of interest.

Yet when patients join these scientists in critiquing the PACE trial, they are criticised for expressing their views. Here are a few common myths about ME patients and an explanation of what we are really fighting for:

MYTH: The controversy is fueled by a vocal minority of "vociferous" ME militants on the internet

Patients connect with each other on the internet because many are housebound and bedbound. Over 10,000 patients have signed a petition calling for an independent review of two studies: <http://my.meaction.net/petitions/pace-trial-needs-review-now> It has been translated into six languages.

MYTH: ME sufferers oppose GET because they are afraid of exercise

Many ME sufferers oppose GET because exercise makes them worse. The purpose of GET is to reverse the effects of deconditioning. A large body of scientific literature has found evidence

of neurological, immunological, and energy production impairment. Findings include alterations in cytokines, vascular signalling, and inflammation.

The cardinal feature of ME is Post-Exertional Malaise (PEM), which is the worsening of all symptoms (neurological, cognitive, orthostatic) following physical or mental exertion. PEM has been confirmed in studies using two-day exercise tests. These studies compared sedentary controls to ME sufferers, and found an increased debility and degradation in maximum aerobic capacity (VO₂Max) on the second day for ME but not the controls, proving the primary pathology is unrelated to deconditioning.

In a recent survey by the ME Association in the UK, 74% of people indicated that they felt worse as a result of GET treatment.

MYTH: ME sufferers oppose CBT because they are afraid of the stigma of mental illness

ME patients want effective treatments, no matter their origin, and would gladly accept psychological treatment if ME were a psychological illness. ME patients are also open to psychological support; standard CBT is used in a wide range of life-altering illnesses (e.g., cancer and MS) to help patients cope. But PACE-style-CBT is different. Instead of helping patients cope with an organic disease, it claims it can cure patients by convincing them that they do not have an organic disease and that they are just deconditioned; therefore, exercise will cure them.

Why these myths cause harm

1. ME/CFS is grossly under-researched, making it imperative that misleading claims of recovery are not substitutes for real science and social intervention.□□
2. ME/CFS patients need treatment regardless of the branch of medicine providing the solutions. However, these treatments should be based on solid scientific processes that are repeatable and objectively measurable. The processes must utilize consistent patient selection criteria, which has been inconsistent across many studies due to the lack of global consensus.
3. It is rational and logical to petition for research which could treat the underlying cause and symptoms of ME/CFS and go beyond mere coping mechanisms provided within the psychogenic model of treatment. It is rational and logical to petition for a cure.
4. Despite its significant flaws and patient reports of harms, the PACE trial has informed medical guidelines around the world.

Top researchers who have reviewed the study conclude it is fraught with indefensible methodological problems

From David Tuller's *Virology* article:

Dr. Bruce Levin, Columbia University: "To let participants know that interventions have been selected by a government committee 'based on the best available evidence' strikes me as the height of clinical trial amateurism. I have never seen a trial design where eligibility requirements for a disease alone would qualify some patients for having had a successful treatment... I find it nearly inconceivable that a trial's data monitoring committee would have approved such a protocol problem if they were aware of it."

Dr. Ronald Davis, Stanford University: "I'm shocked that the Lancet published it...The PACE study has so many flaws and there are so many questions you'd want to ask about it that I don't understand how it got through any kind of peer review."

Dr. Arthur Reingold, University of California, Berkeley: "Under the circumstances, an independent review of the trial conducted by experts not involved in the design or conduct of the study would seem to be very much in order."

Dr. Jonathan Edwards, University College London: "It's a mass of un-interpretability to me...All the issues with the trial are extremely worrying, making interpretation of the clinical significance of the findings more or less impossible. There is no 'stigma of mental illness'. But there is an implication that there is no real illness beyond an irrational belief of being ill, for which there is no justification."

References:

- Background and news coverage of the PACE trial: <http://www.meaction.net/background-to-the-petition/>
- The most comprehensive examination of PACE, by David Tuller DrPH, was published October 22, 2015: <http://www.virology.ws/2015/10/22/trial-by-error-i/>
- Open letter to Richard Horton, editor of *The Lancet*: <http://www.virology.ws/2015/11/13/an-open-letter-to-dr-richard-horton-and-the-lancet/>
- ME Association's treatment survey: <http://www.meassociation.org.uk/2015/05/23959/>

NIH and top US Scientists take a different direction

- <http://www.nih.gov/news-events/news-releases/nih-takes-action-bolster-research-myalgi-c-encephalomyelitis/chronic-fatigue-syndrome>
- <http://phoenixrising.me/archives/26602>
- <http://www.cortjohnson.org/blog/2015/08/23/lipkin-nih-grants-chronic-fatigue-syndrome-2015/>

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