

[www.margaretwilliams.me](http://www.margaretwilliams.me)

## **Proposed MEGA study of ME/CFS**

**Professor Malcolm Hooper and Margaret Williams**

24th October 2016

There is an urgent need for high quality biomedical research into ME/CFS that is untainted by the influence of members of the biopsychosocial school who believe that the disease is perpetuated by dysfunctional beliefs and behaviour.

The proposed MEGA study (ME/CFS Epidemiology & Genomics Alliance) has the potential to provide a deeper understanding of the biology of ME/CFS by investigating the distinctive genetics, epigenetics, proteomics and metabolomics of people with ME/CFS, but the involvement of Professor Peter White, Chief Principal Investigator of the PACE trial, and Dr Esther Crawley is deeply troubling.

We believe their approach to research does not comply with essential tenets of the scientific process such as the primacy of objective over subjective measures, the requirement to adhere to pre-specified outcome measures and the need not to exaggerate results.

Before the re-analysis of the PACE raw data, Esther Crawley co-authored a paper which claimed up to 40% recovery in the PACE trial participants (BMC Health Services Research 2011, 11:217 doi:10.1186/1472-6963-11-217).

It is also of concern that Dr Crawley is involved in a paediatric study of the psycho-behavioural Lightning Process which is widely considered to be pseudoscience; furthermore, despite the obvious failure of the PACE trial, she has embarked on a study of graded exercise in children.

Hence their influence in the design and execution of MEGA could undermine the integrity of the whole study.

Pragmatic concerns relate to the size and feasibility of the endeavour which seeks to recruit 12,000 people with the disease. The PACE trial had to assess 3,158 individuals

to find 641 who met the broadest definition of "chronic fatigue" (the Oxford criteria) and who were willing to participate in the study. If the same ratio applies in MEGA, then about 60,000 people will have to be assessed to find the 12,000 said to be necessary to tease apart the presumed subgroups that fall within such a broadly defined cohort.

Furthermore, such a large study group severely limits the range and quality of testing that can be applied to each individual due to budgetary constraints. Even with funding of £10 million, the most that could be spent on each participant would be around £800, and most likely far less due to administrative costs.

Would a better understanding of the disease not emerge from more in-depth investigations of a smaller but better characterised cohort?

Professor Holgate's stated belief that "CFS" could be as many as fifteen separate conditions may well be true, but this traps us in a circularity: if you believe that "CFS" is no more than broadly defined chronic fatigue and design your study on this basis, then of necessity you will capture people with many different underlying conditions (which would fulfil the psychiatrists' current infatuation with MUPS or medically unexplained physical symptoms).

Hence we are concerned about the use of what Dr Crawley refers to as the "NHS criteria", which can only be the criteria set out in the NICE Guideline CG53 with which she was closely involved and which are non-specific and have not been operationalised and moreover have been superseded by internationally accepted criteria.

A final issue is the central role of AfME as the supposed voice of patients, given their enthusiastic collaboration with the PACE trial and their failure to unequivocally condemn its many failings.

Professor Malcolm Hooper  
Margaret Williams

24<sup>th</sup> October 2016