21 March 2017

PERSONAL & IN CONFIDENCE

Sasha Nimmo
ME Australia
nimmosasha@gmail.com

Dear Ms Nimmo

The Vice Chancellor has passed your letter regarding a UNSW trial on to me and asked that I respond to you.

The trial you refer to in the correspondence to Professor Jacobs (UN1111-1180-1073), is entitled “A randomised controlled trial investigating the efficacy of online continuing education for health professionals to improve the management of chronic fatigue syndrome (CFS)” on the Australian and New Zealand Clinical Trial Register (ANZTR; Trial No. ACTRN12616000296437). The trial has funding support from the Mason Foundation (MAS201540) “A randomised controlled trial of online continuing education for health professionals to improve the management of CFS” CI-A Dr Sophie Li, CI-B Dr Ben Barry, CI-C Dr Carolina Sandler, and CI-D Professor Andrew Lloyd. The project has Human Research Ethics Committee approval (No. HC16419).

The research study relates to management of the medical condition referred to internationally as chronic fatigue syndrome (CFS), and in the UK as myalgic encephalomyelitis (ME). As you well know, this is a difficult, and often controversial, clinical syndrome featuring disabling subjective fatigue often accompanied by muscle and joint pain, headaches, neurocognitive difficulties, disturbed sleep, and sometimes disturbed mood. The diagnosis is made after careful exclusion of alternative medical and psychiatric explanations for the fatigue state. The controversy typically relates to the validity of the illness as a separable diagnostic entity, and also whether the illness has a purely ‘psychological’ basis. I do not propose getting into those arguments here.

This condition has been the subject of research over many years by Professor Lloyd, who is an infectious diseases physician / laboratory scientist and NHMRC Practitioner Research Fellow. This research interest arose from the Dubbo Infection Outcomes Study (DIOS) which he led for over a decade, funded by NHMRC and the Centers for Disease Control, USA. In DIOS, acute infections due to Epstein-Barr virus (EBV; glandular fever), Ross River virus (RRV), or Q fever (Coxiella burnetii) were each found to trigger a case rate of CFS lasting six
months or longer of approximately 10%. 2 Subjects meeting diagnostic criteria for CFS and matched (control) subjects with uncomplicated recovery were recruited into multiple intensive research studies examining possible mechanisms underlying the prolonged illness course. DIOS is now internationally-recognised to be a unique and highly informative research program, as this post-infective fatigue syndrome (PIFS), is a unique model of the onset and evolution of the potentially more heterogeneous condition, CFS. The broad goal of this aspect of Professor Lloyd's research is to gain a better understanding of disease mechanisms to guide development of effective treatment.

With regard to treatment, over many decades and more than 100 randomised controlled trials, no curative therapy for CFS has been identified. Hence, clinical management of patients remains a major challenge. However, there is clear Level One evidence for both cognitive-behavioural therapy (CBT) and graded exercise therapy (GET), both from the Cochrane Collaboration and from a recent NIH expert workshop4-6. On the basis of this evidence, Professor Lloyd led establishment of the Fatigue Clinic at UNSW, which is an integrated multi-disciplinary CBT/GET program with exercise physiologists and clinical psychologists providing clinical services within an academic framework to facilitate research to optimize the intervention. The integrated CBT / GET intervention has been shown to be effective,7 and has been improved with the addition of a cognitive remediation component.8 The Fatigue Clinic now has a six-month waiting list. The Fatigue Clinic research program has been regularly awarded research funding: from the Mason Foundation, including to develop a clinician's manual and training materials to allow the program to be implemented widely across the country; and from Cancer Australia to develop and evaluate a comparable CBT/GET program for post-cancer fatigue (PCF).

Since listing the trial on the Register, the study investigators and the UNSW HREC have been receiving correspondence from critics requesting the trial not go ahead. This response essentially reflects resentment against the notion that CFS may have 'psychological' causes. Many of the issues raised in the correspondence to the Vice-Chancellor were actually addressed in the application to the HREC as complaints were received prior to the study being approved by the HREC and then subsequently opened for enrolment. This study will likely complete enrolment of the planned 128 clinicians by mid-2017. It is important to emphasise that this trial is not an evaluation of the effectiveness of the CBT/GET intervention, but a trial of education for health care practitioners on how to conduct the CBT/GET intervention for patients with CFS.

In relation to the specific issues you raise in your correspondence:

1. **The proposed trial is based on poor science and is likely to cause harm to patients:**

As described above, the scientific evidence base for CBT and GET for patients with CFS, both individually and combined is very strong. The concern of harm from GET is not supported by the systematic reviews which state "no evidence suggests that exercise therapy may worsen outcomes". In this context it can be reasonably argued...
that one of the key goals of the current online education study is to ensure that clinicians are appropriately trained before seeking to apply GET protocols for patients with CFS – specifically to safeguard against any notional risk of harm.

2. **We ask the NHMRC to redirect funding from trials using GET and CBT to promising biomedical research:**

NHMRC is not funding this trial. It is funded by the Mason Foundation (as specified on ANZCTR). Professor Lloyd receives Fellowship support from NHMRC with a research plan, which predominantly relates to his main research focus on hepatitis C, but includes some studies on CFS – hence there is limited indirect NHMRC support for the trial.

3. **This proposed study is based on the PACE trial’s evidence:**

The PACE trial was a multi-centre study conducted across the UK and published in Lancet 20119. The study compared adaptive pacing, CBT, GET, and standard medical care for CFS in 641 patients. It concluded that CBT and GET moderately improved outcomes but adaptive pacing therapy did not. After the publication there has been considerable controversy about the findings played out both in the general media and in scientific publications (reviewed in 10) culminating in a freedom of information release of much of the trial data and re-analysis – suggesting modest benefits only. The PACE investigators have published analyses refuting all of these concerns. 11-15.

As outlined above, the integrated CBT/GET intervention implemented in the Fatigue Clinic at UNSW (which forms the basis of the online educational content for the current study), has Level One evidence – this is regardless of the controversies about the PACE trial.

4. **...funding should go towards biomedical research which is uncovering important new findings... there is important evidence on genetic and immune markers for the condition...**

Professor Lloyd's research program has contributed substantially to the international literature on the pathophysiology of CFS with a total of 60 peer reviewed original articles, and 15 review articles or editorials. These include numerous studies in relation to altered immunity and genetic risk. His approach combining pathophysiological research and treatment research underpins his NHMRC Practitioner Fellowship as it seeks to improve the care of patients with CFS, both locally and across the country, as well as to elucidate the pathophysiology and thence guide new and improved treatments.

5. **... consider strengthening the ethics review:**

As outlined above, the study has been subject to rigorous scientific and ethical review.
Based on the evidence I have outlined above, I am not prepared to require that the study be suspended or abandoned. It is in fact nearly complete in any case. This Trial and its protocol has been through a rigorous approval process both at the level of its main scientific funding body and through the Human Research Ethics Committee processes of UNSW and we are satisfied that it should continue to completion and the findings should be published.

I realise this is not the response you are seeking, but I can only reiterate that UNSW Medicine maintains the most rigorous scientific and ethical review and monitoring systems and I do not accept that there is any reason to accede to your request.

Yours sincerely

Professor Rodney Phillips
Dean, UNSW Medicine

References
9. White PD, Goldsmith KA, Johnson AL, et al. Comparison of adaptive pacing therapy,