15th March 2018

Complaints against Professor Carmine Pariente concerning his statement as ‘spokesperson’ for the College of 21st February 2018, in relation to Cipriani et al ‘Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis’, Lancet ‘Online First’, 21st February 2018

Professor Pariente’s statement, according to the Science Media Centre:

‘This meta-analysis finally puts to bed the controversy on antidepressants, clearly showing that these drugs do work in lifting mood and helping most people with depression. Importantly, the paper analyses unpublished data held by pharmaceutical companies, and shows that the funding of studies by these companies does not influence the result, thus confirming that the clinical usefulness of these drugs is not affected by pharma-sponsored spin. Of course, these type of studies cannot look at individual differences, so cannot inform us about the specific personal characteristics that make an individual more likely to respond in general, or to respond to one medication rather than another one. Indeed, we still need to understand why some antidepressants work better than others, even within classes of drugs that supposedly have the same pharmacological actions. Also, this paper does not help us understand how best to help patients who have treatment-resistant depression and cannot improve on any of the 21 antidepressants tested here. Nevertheless, for the millions

1 http://www.sciencemediacentre.org/expert-reaction-to-largest-review-of-antidepressants/
2 http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(17)32802-7/fulltext
of individuals with depression who are taking antidepressants at present, or will need to take antidepressants in the future, it confirms that these drugs are safe and effective.’

I submit the following complaints:

‘finally puts to bed the controversy on antidepressants’

1. Most aspects of psychotropic medication are controversial and it is irresponsible to suggest, on the day of an ‘Online First’ pre-publication, that a single study comprehensively deals with those around antidepressants. In any case, Cipriani et al only claim to address eight-week effectiveness, ‘acceptability’, and publication bias, so this statement is misleading as well.

‘Importantly, the paper analyses unpublished data held by pharmaceutical companies, and shows that the funding of studies by these companies does not influence the result, thus confirming that the clinical usefulness of these drugs is not affected by pharma-sponsored spin.’

2. Cipriani et al’s implicit claim is that the prospect of funnel plots dissuaded these pharmaceutical companies from selectively handing over their ‘unpublished’ trials. They rely on no other method. But such funnel plots are useless: the Cochrane Handbook for Systematic Reviews of Interventions, which Cipriani et al claim to have followed, clearly states that ‘Publication bias need not lead to asymmetry in funnel plots.’

I am writing to the Lancet about this serious error in Cipriani et al’s paper. It took me about twenty minutes to identify it, and I published my observation as a British Medical Journal ‘Rapid Response’ on 27th February. It appears that the College’s

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3 ‘Funnel plots’, Section 10.4.1, http://handbook-5.1.cochrane.org/
4 http://www.bmj.com/content/360/bmj.k847/rr-3
‘Academic Psychiatrist of the Year’ may not have bothered to read the paper properly before commenting on it to the public.

However, if Professor Pariante is of the opinion that Cochrane is wrong, and funnel plots are to be so relied on, he should make clear that it is a personal opinion, and give reasons for it. He undermines the work of many members of the College, including the immediate past President, done within the Cochrane Collaboration.

3. In dismissing the notion of ‘pharma-sponsored spin’ Professor Pariante trivialises the extent of wrongdoing, including criminal behaviour, by pharmaceutical companies over the last decades, in promoting and marketing their products. In the United States alone, where it seems likely that many of the studies used by Cipriani et al took place, and where many such companies are based, the Justice department has obtained convictions against dozens of them, in relation to over fifty products. Professor Pariante has a history of such behaviour (see question 2, below).

4. In fact, Cipriani et al themselves state that ‘the field of antidepressant trials in the past has been prone to publication bias’. The Cochrane Collaboration supports the AllTrials campaign, with its central principle that the only way to reduce such bias is to reject all trials that have not been independently registered in advance, and to penalise organisations which register but do not publish. Professor Pariante must be aware of this issue but his statement evades it.

‘for the millions of individuals with depression who are taking antidepressants at present, or will need to take antidepressants in the future, it confirms that these drugs are safe and effective’

5. It is irresponsible to endorse overmedication, and Professor Pariante’s statement is in conflict with the current College view that ‘mild depression’ should not be treated

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6 [http://www.alltrials.net/find-out-more/about-alltrials/](http://www.alltrials.net/find-out-more/about-alltrials/)
with antidepressants. The overwhelming majority of the ‘millions of individuals ...taking antidepressants’ in the United Kingdom have a mild disorder, and will not have seen a psychiatrist. As President, Professor Susan Bailey disowned responsibility for such prescribing by GPs, while clearly stating it was undesirable.

6. ‘will need to take antidepressants in the future’ is ambiguous: it could be taken to mean that Cipriani et al makes claims about treatment beyond eight weeks.

7. It simply false to state that Cipriani et al significantly addresses drug safety. Their claims are in regard to ‘acceptability’.

8. Professor Parriante fails to mention a central fact, untouched by Cipriani et al’s claims, about response to antidepressants: the very substantial component attributable to placebo response. Therefore his statement that ‘these drugs do work’ and his further comments about how they ‘work’ are misleadingly biased towards drug treatment, even if the issue of publication bias is excluded.

I ask that the College publishes, and promotes, the appropriate retractions and clarifications of Professor Parriante’s statement, which has been widely quoted and will have significantly damaged the College’s reputation.

The above complaints may not be exhaustive in regard to how the College should respond to published research of this kind, in particular they do not address the validity of the ‘network meta-analysis’ of efficacy in Cipriani et al.

In view of the seriousness of the above complaints, and also the disturbing allegation (now part of a complaint) that the College document ‘Coming Off Antidepressants’ was silently removed from the College website, I ask the following questions:

7 http://www.rcpsych.ac.uk/healthadvice/treatmentswellbeing/antidepressants/antidepressantskeyfacts.aspx
1. Was Professor Pariante’s statement seen by Professor Wendy Burn (President), Professor David Baldwin (Chair of the Psychopharmacology Committee), or any other College officer(s), before release?

2. Is the President aware that in 2013 Professor Pariante promoted the work of disgraced Professor Charles Nemeroff, who lied to his employer Emory University concerning payments from GSK (a company punished in 2012 with a 3 billion dollar fine for criminal and civil wrongdoing),

3. Given that at least one other media statement on 21st February claimed Cipriani et al ‘puts to bed’ concerns about antidepressants, was Professor Pariante provided with material by Cipriani et al, or any third party, other than the Lancet paper (which does not contain that phrase)? If so, I ask that the College provide that material to ordinary members, and name the source(s), as it would have been received by Professor Pariante while acting on the College’s behalf.

4. Will the President provide a list of all College ‘spokespersons’, with full disclosure of interests, and keep it updated on the College website, for members and the public?

5. Will the President ask the College’s PR/media professionals to provide an online version of statements by its ‘spokespersons’ to the media and other bodies, on the College website, for members and the public?

(signed & dated) Dr Neil MacFarlane MRCPsych 15th March 2018

10 Letter to Professor Pariante, 3rd June 2013. www.madinamerica.com/wp-content/uploads/2013/06/Nemeroff-letter.pdf My thanks to Derek Summerfield for drawing my attention to this episode and for commenting on previous drafts of this complaint.