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Letter to the Editor, Re

John C Newman, MD, PhD and **Michael A Steinman, MD**

Division of Geriatrics; San Francisco VA Medical Center and University of California, San Francisco; San Francisco, CA USA

Behavioral complications of dementia can be highly distressing, and new interventions to treat this condition are needed. However, several aspects of the recent paper by Cummings et al caused us concern[1].

First, the increase in falls associated with use of dextromethorphan-quinidine (8.6%, vs 3.9% for placebo) is substantial and belies the conclusion stated in the abstract that the drug is "generally well tolerated." Although the finding of excess falls may be due to chance or an imbalance in baseline characteristics between the intervention and control groups, this effect should be presumed real until proven otherwise. This interpretation is supported by previous randomized trials of dextromethorphan-quinidine for pseudobulbar affect, in which rates of dizziness were consistently and markedly higher in the active treatment group, although data on falls are conflicting[2–4]. The history of antipsychotic use for treatment of behavioral problems of dementia, in which substantial increases in mortality were only discovered after the drugs were widely used for years, cautions us to temper enthusiasm for new drugs until their adverse effects are well-understood.

Second, we have concerns about the patenting and use of proprietary study designs in research, such as the "Trimentum™" methodology (a form of crossover study design) used here. Regardless of the merits of the methodology, the study cannot be replicated as performed without license from the patent holders. This gives the patent holders a veto over the replication of this particular study and indeed over any validation of the methodology in general. Patented study designs violate the long-cherished principle that scientific findings must be able to be readily reproduced by an independent party. Moreover, allegations of patent infringement, whether reasonable or not, are bludgeons that could be used to halt competing research. How different must a study design be to avoid allegations of infringement? In practice, this is decided by the patent holders through threat of litigation, as such cases are rarely contested to trial. The effect on research into improved study design is sadly predictable[5]. If a patented methodology becomes widespread in a field, patent holders can selectively threaten action against studies they disapprove of, while licensing on favorable terms to sympathetic investigators. If there is any place in medical research for patented study designs, it must include universal, default, open-access licensing to academic

Corresponding author contact information: Mail: 4150 Clement Street, 181G, San Francisco, CA 94121, newman@ucsf.edu, Phone: 415-502-5134.

Cummings JL, Lyketsos CG, Peskind ER, et al. Effect of Dextromethorphan-Quinidine on Agitation in Patients With Alzheimer Disease Dementia: A Randomized Clinical Trial. *JAMA*. 2015;314(12):1242–1254.

or federally-funded researchers to permit free replication of scientific results and the free development of improved methodologies without fear of legal reprisal.

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