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Memorandum

To: Trialists

Fr: Curtis Meinert

Re: Editors: ICMJE help please

As trialists we are threatened with hefty fines if we fail to register our trials before we start enrollment and are told by editors that they will not publish our results if we fail to register. We have done what has been asked of us. Now, it is editors who have to do their part to make registration work.

The push for registration emerged in the 1980s from concerns that published results are subject to publication bias and that assessments of treatments may not be reliable when based on published results alone.

This concern led the NIH, via the NLM, to establish ClinicalTrials.gov (opened in 2000) for registration of trials.

The International Committee of Medical Journal Editors (ICMJE) elevated registration to a new level with the requirement that *member journals will require, as a condition of consideration for publication, registration in a public trials registry. Trials must register at or before the onset of patient enrollment. This policy applies to any clinical trial starting enrollment after July 1, 2005.* (JAMA 2004; 292: 1363-4)

The edict also required ICMJE journals to publish registration numbers as the last entry in abstracts accompanying publications of trials.

An important step forward in registration was the decision of the NLM to index ClinicalTrials.gov registration numbers reported in publications (started with 2005 publications); subsequently extended to include registration numbers from virtually all recognized registries.

The indexing of registrations in ClinicalTrials.gov enables operators of the website to troll for publications indexed as having NCT registration numbers and adding those citations to registrations, thereby reducing dependence on registrants for updating publication listings.

The rationale for the edict was that it purported to address the problem of “selective reporting” by not publishing trials not registered before the start of enrollment, but it is hard to understand how not publishing is a solution to that problem, especially since editors do not follow their own rules. Fifteen of the 259 publications appearing in journals represented by editors signing the edict, published in 2015, indexed in PubMed as being randomized controlled trials, and

with NCT numbers published, were registered a year or more after the start of enrollment without notice or explanation to readers.

In truth, only a fraction of papers include registration numbers as evident from the table below. The ICMJE website lists over 3,100 journals ascribing to ICMJE policy, yet just over one-third of 2015 publications indexed in NLM as being randomized controlled trials have registration numbers reported. Either one has to assume that most trials are not registered or (more likely) that they are registered but that editors do not publish registration numbers.

2010-2015 publications indexed as [randomized controlled trial] and numbers registered

Year	No. pubs	Counts by registration site			Total no. registered*	%	
		NCT	ANZCTR	Other sites		NCT	Total
2010	20,519	2,628	549	557	3,734	12.8	18.2
2011	23,153	3,395	646	658	4,699	14.7	20.3
2012	25,015	3,936	622	652	5,210	15.7	20.8
2013	27,231	4,692	802	820	6,314	17.2	23.2
2014	27,436	5,272	1,072	1,338	7,682	19.2	28.0
2015	25,135	5,662	1,185	1,593	8,440	22.5	33.6

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* Total includes 38 registration databases indexed by NLM

If I could have my way, the ICMJE would revise its *JAMA 2004; 292: 1363-4* edict to read:
henceforth member journals will require authors of randomized controlled trials to indicate if the trial being reported was registered and if registered, when relative to the start of enrollment. The information requested should be supplied as the last entry in the abstract accompanying the manuscript.

Note that the revision is limited to randomized controlled trials in contrast to the 2004 edict pertaining to “any clinical trial”. Randomized controlled trials are clearly registration eligible, whereas the line of demarcation between non-randomized trials and observational studies (not registration eligible) is ill-defined making it difficult to know whether registration is required. There is no such uncertainty regarding randomized controlled trials meaning that the discordance between journal editors and NLM indexers in how those trials are classified is likely to be low.

The advantages of the change would be several.

First, the change eliminates the notion that “selective reporting” can be prevented by editors not publishing. Publication, by definition, is a selective process that is the product of authors and editors. It remains so regardless of the blocks editors place on what they are willing to publish.

Second, the revision eliminates the guess work when a trial is published without a registration number. Is it because the trial was not registered or is it because editors did not publish the number?

Providing information on when registration took place relative to start of enrollment gives readers information relevant in determining how much they should discount the results reported because of the possibility of “selective reporting”.

Third, the change would provide information on the registration behavior of trialists. As it is now, we have no way of knowing the non-registration rate for registration eligible trials. With the change proposed we would get a peek at that behavior at least for published trials.

A side benefit of the change might well be to render editors more willing to comply with publishing registration information because it removes the stigma associated now with publishing trials that are not registered or registered late. Editors with the 2004 edict in place may be more comfortable simply not knowing about registration than knowing they have results from a trial that was not registered or that was registered late and hence not in compliance with the 2004 ICMJE edict.