



17 December 2013

Memorandum

To: Trialists

Fr: Curtis Meinert

Re: The ICMJE registration requirement for trials

It is now almost 10 years since the International Committee of Journal Editors (ICMJE) announced 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. For trials that began enrollment prior to this date, the ICMJE member journals will require registration by September 13, 2005, before considering the trial for publication. (JAMA 2004; 292:1,363-1,364)

The statement did not specify where trials were to be registered but did specify that registry sites had to (1) be accessible to the public without charge, (2) be open to all prospective registrants, (3) be managed by a not-for-profit organization, (4) have mechanisms to ensure the validity of registration data, and (5) be electronically searchable.

ClinicalTrials.gov is the predominant registration site. It accounts for about 70% of all registrations on the WHO platform of sites meeting the above conditions.

So how is registration proceeding? Part of the problem in addressing the question is identifying studies subject to registration. The ICMJE requires registration for *Any research project that prospectively assigns human subjects to intervention and comparison groups to study the cause-and-effect relationship between a medical intervention and a health outcome. By "medical intervention" we mean any intervention used to modify a health outcome. This definition includes drugs, surgical procedures, devices, behavioral treatments, process-of-care changes, and the like. We update our 2004 editorial to state that a trial must have at least one prospectively assigned concurrent control or comparison group in order to trigger the requirement for registration. (http://www.icmje.org/update_may05.html)*

Clinical trial as a publication type in PubMed is

Work that is the report of a pre-planned clinical study of the safety, efficacy, or optimum dosage schedule of one or more diagnostic, therapeutic, or prophylactic drugs, devices, or techniques in humans selected according to predetermined criteria of eligibility and observed for predefined evidence of favorable and unfavorable effects.

The PubMed definition is broader than the ICMJE definition. Hence, not all publications indexed to the publication type [clinical trial] in PubMed are registration eligible under the

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ICMJE definition. To reconcile the difference we opted to focus on publications indexed in PubMed to the publication type [Randomized Controlled Trial] AND [Multicenter Study]. The AND requirement was used to focus on larger, high profile, trials almost certainly registration eligible.

There were 4,214 such publications identified August 2013 published in 2012. We downloaded the abstracts and then electronically and hand searched abstracts for registration numbers. Just over 27% of the abstracts contained registration numbers.

Of the eleven journals represented by signatories of the 2004 ICMJE statement, only five contained 2012 publications indexed to [randomized controlled trial] AND [multicenter study]; 240 papers. Of those papers all were registered except one; 202 (84%) were registered on ClinicalTrials.gov.

	No. papers	No. registered	Reg. in CT.gov
<i>Annals of Internal Med</i>	10	10	8
<i>Canadian Med Association J</i>	5	5	3
<i>J of the Am Med Association</i>	45	44	38
<i>Lancet</i>	72	72	52
<i>New Engl J of Med</i>	108	108	101
Total	240	239	202

The ICMJE recommends that registration numbers appear at the end of abstracts. Only three of the five journals followed their own recommendation. Registration numbers in the *Lancet* and the *Ann Int Med* were elsewhere in abstracts.

The ClinicalTrials.gov registration site provides a "first received" date (registration date) and enrollment start date. Of the 201 papers with dates provided, about one-third were registered after the start of enrollment; 29 six months or more after the date of registration.

The reality is that it is common for registration to occur after the start of enrollment. Files in ClinicalTrials.gov for interventional studies with 2012 registration dates (1,354 records as of 16 Aug 2013; limited to "randomized" AND "multicenter") yields 721 records of studies registered after the start of enrollment; 268 >120 days later.

There are numerous reasons for the lag, including the fact that registration is not foremost in the minds of trialists when struggling to get a trial started.

Fortunately, data indicates that signatories of the policy are not insistent on the requirement as a condition for publication. Given this fact, the ICMJE would do well to revise its policy to indicate flexibility on the date requirement.