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14 March 2019

**Memorandum**

To: Trialists

Fr: Curtis Meinert

Re: Data and safety monitoring boards: The downside

The NIH decreed:
*It is the policy of the NIH that each Institute and Center (IC) should have a system for the appropriate oversight and monitoring of the conduct of clinical trials to ensure the safety of participants and the validity and integrity of the data for all NIH-sponsored clinical trials. The establishment of the data safety monitoring boards (DSMBs) is required for multi-site clinical trials involving interventions that entail potential risk to the participants* (10 June 1998)

The concept of bodies independent of investigative groups to monitor and advise existed long before the NIH decree.

The concept is expressed in the Greenberg Report (named after the chair) produced for the National Heart Institute (1967; published in Controlled Clinical Trials 1988; 137-148)
*The data should be subjected to frequent analysis, including sequential analysis when possible, to assure constant awareness of current status . . . A Policy Board or Advisory Committee of senior scientists, experts in the field of the study but not data-contribution participants in it, is almost essential for a large complex cooperative project. Such a group can review the overall plan, make recommendations on any possible change, adjudicate controversies that may develop, and advise the National Heart Institute on such matters as the addition of new participants or the dropping of nonproductive units.*

In 1979 the NIH Clinical Trials Committee (chaired by Robert Gorden) recommended that:
*Every clinical trial should have provision for data and safety monitoring. Provision should be approved by IRB.*

*A multicenter trial should have an independent treatment effects monitoring committee. Monitoring committee should include clinicians with expertise in disease under study, biostatisticians, and scientists from other pertinent disciplines. Physicians in the study engaged in patient care should be excluded from membership.*

So how many multicenter trials have data monitoring committees? To address that question we turned to the ClinicalTrials.gov dataset (because it has a data field “Has Data Monitoring Committee”; answered “Yes”, “No”, or “Not stated”).

**Completed multicenter trials (2005-2015) registered in ClinicalTrials.gov, by funding source**

| | | U.S. gov't-funded | | Other-funded | |
|---|---|---|---|---|---|
| DMC? | Total | Gov't-funded | % | Other-funded | % |
| Yes | 11,096 | 2,918 | 46.18% | 8,178 | 19.89% |
| No | 23,404 | 1,728 | 27.35% | 21,676 | 52.71% |
| Not stated | 12,941 | 1,673 | 26.48% | 11,268 | 27.40% |
| | **47,441** | **6,319** | **100.00%** | **41,122** | **100.00%** |

Trials were counted as "U.S. gov't-funded" if they had any U.S. government funding even if other funding sources were also listed. The category "Other-funded" was used when there was no U.S. government funding. Almost 50% of government-funded trials had DMCs compared to just 20% of other-funded trials. The percentages for "not stated" were about the same for the two types of funding.

Largely, DSMCs are constructed to have watertight separations from clinic personnel. That means that people who generate data and responsible for writing up results are in the dark until the trial is stopped or finished. (Technically, there is nothing stopping investigators from seeing results by treatment group as the trial proceeds, but the prevailing norm is against the practice because of concerns of introducing treatment-related bias in the results, even if treatments are masked.)

The end result is a numbing effect on the intellectual climate in research groups. Basically, after writing the protocol, investigators are reduced to twiddling their thumbs without any knowledge of the results they are generating until the trial is stopped or finished. And then hurry up and analyze and publish results without having seen them. Makes no sense.

Part of the joy in research is being able to see and know results before anyone else in the world. Now that joy in trials is reserved to people not involved in the trials.

I am reminded of Mark 8:36
*For what shall it profit a man, if he shall gain the whole world, and lose his own soul?*