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14 June 2016

Memorandum

To: Trialists

Fr: Curtis Meinert

Re: Data monitoring committees: Things I hate

Data monitoring committees go by a variety of names. The most common is Data and Safety Monitoring Committee (DSMB). Others are Data Monitoring Committee (DMC), Treatment Effects Monitoring Committee (TEMC), and Policy and Data Monitoring Board (PDMB).

The typical committee is comprised of three to seven voting members, not associated with any of the study centers or sponsor of the trial, and usually about an equal number of nonvoting members from the study. Voting members are vetted and appointed by the study sponsor or study investigators.

Typically, nonvoting members include at least two people from the study data center and the study chair or study vice chair, along with support analysis staff. The membership listing in study documents and publications should include nonvoting members (designated as nonvoting).

The primary function of the committee is to review data over the course of the trial in order to recommend whether the trial should continue unaltered, be altered, or stopped. The schedule of reviews may be calendar driven (e.g, every six months) or event driven (e.g., after specified enrollment goals are met or after specified number of events).

The committee may meet face-to-face or via conference phone or webinars.

Typically, each meeting concludes with a recommendation and vote by the committee as to whether the trial should continue unchanged, be stopped, or otherwise modified.

Now to things I hate.

Committees appointed by sponsors without input or vetting by study investigators

DSMCs serve both sponsors and investigators, hence, membership should be acceptable to both. This requires joint vetting, regardless of who does the appointing, with veto powers for both parties.

Monitoring plans handed to investigators

The "take it or leave it" approach of some sponsors dictating the monitoring approach and monitoring body without investigator input is arrogant and disrespectful of the responsibilities of investigators. Alas, we live with it because of the power of the purse.

Masked monitoring

Years ago I wrote a piece entitled "Masked monitoring in clinical trials - Blind stupidity?" (NEJM 1998; 338:1381-2). I thought it ill-advised then and still do. Why the practice continues is beyond me. My fundamental problem with it is that it reduces the competency of the monitoring process in order to create the trappings of contrived objectivity.

It is imperative in meeting the ethical requirement for doing trials that somebody has unfettered access to study data without masking. If it is not the investigators, than it has to be the DSMC.

Committees with some nonvoting members not at parity to other nonvoting members

The nonvoting members should be at parity to all other nonvoting members. A practice common in some NIH-sponsored trials is to allow the NIH project officer to sit in closed executive sessions while excluding other nonvoting members. If investigators are excluded out of a desire to insulate deliberation from interests possessed by investigators, then the same applies to NIH sponsors.

Committees that deliberate and vote in sessions closed to nonvoting members

Presences of nonvoting members ensure linkage of the monitoring process to study investigators. That assurance does not exist when deliberations and votes are taken behind closed doors.

Rules to indicate when to stop

Monitoring is not a "paint by the numbers" approach. The trouble with stopping rules is that it is difficult to construct rules that cover all eventualities. There may well be conditions encountered during the trial that make it prudent to continue beyond the stopping point dictated by the rule or to stop before the condition is encountered. No objection to stopping guidelines, but not so for stopping rules.

Committees that report only to sponsors

If DSMBs are appointed to serve both sponsors and investigators, they should report, simultaneously, to both. Arrangements in which the committee reports to the sponsor and the sponsor to the investigators has the potential of delaying reports to study investigators or of filtering what is reported.

Indifferent IRBs

When it comes to establishing the tenets for data monitoring the sponsor holds the strong hand because money speaks. You versus the sponsor, you lose. Your best partner in the battle are IRBs – if they are sensitive to issues outlined above. Alas, my experience has been that they will bury you in paper over protocol issues, but be largely passive on issues of monitoring.