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What's New in GCP? Investigator Group Calls for Longer Waiting Period for Data Sharing

A group of clinical investigators has developed a counter proposal to the International Committee of Medical Journal Editors (ICMJE) data-sharing plan.

In January, the ICMJE proposed that, as a condition of consideration for publication in their journals, researchers agree to share the deidentified individual patient data (IPD) that underlies the article's results no later than six months after publication.

In an Aug. 4 New England Journal of Medicine Perspective article, the International Consortium of Investigators for Fairness in Trial Data Sharing noted "investigators are partly motivated by opportunities to lead secondary publication," and "six months is insufficient for performing the extensive analyses needed to adequately comprehend the data and publish even a few articles."

The article noted investigators in developing countries "do not have the same level of infrastructure and support to conduct secondary analyses rapidly for additional papers. Further, many are not fluent in English and so need more time to prepare manuscripts of high quality. The ICMJE proposal to share data six months after publication puts investigators from developing countries at a substantial disadvantage."

The group said the ICMJE proposal "may lead some investigators to delay publishing their primary trial results to allow time to prepare several secondary manuscripts. Delay or failure to publish the primary results of trials is already a substantial problem. We believe the ICMJE's plan is likely to exacerbate this problem."

The group proposed study investigators be allowed exclusive use of the data for a minimum of two years after publication of the primary trial results and an additional six months for every year it took to complete the trial, with a maximum of five years before trial data are made available to those who were not involved in the trial.

"This approach would result in data release within 2.5 years for many small trials and within five years for many large ones. Such an approach would provide trial investigators a reasonable amount of time — consistent with their efforts — to explore the data they generated and would create an incentive to conduct RCTs and avoid delaying initial publication of their results," the group said.

Journals Should Do Independent Analyses

"One way to ensure confidence and trust in published trial data is for independent confirmatory analyses to be undertaken," the group added. "We believe that the best way to ensure that readers have confirmation of the validity of trial results is for journals to arrange for independent analyses." Without independent analysis, the journals "will not provide readers the assurance they may want regarding data confirmation when it is most important — at the time they are reading the original publication."

The group noted many investigators conducting investigator-initiated studies "spend substantial amounts of money they have generated from other activities to cross-subsidize trials that are not of interest to commercial sponsors. Investigators should be able to recoup some of their costs from charges to people who seek access to their data." In addition, a mechanism is needed to fund the data-preparation activities.

The group said the cost of preparing the data "should be borne by those who seek access to the data rather than by the primary trialists." In addition, "there should be provision for some degree of reimbursement for trialists for the resources they have invested in the trial, and the degree of reimbursement for resources invested in the trial should depend on the resources of the party or parties seeking access to the data (e.g., researchers vs. industry, investigators from high-income vs. low-income countries)."

The group noted that a "potential negative consequence of this proposal is that a novel analysis may not be undertaken if the individual wanting to access the data does not have the funds to obtain the data. It is for this reason that we have recommended that the degree of financial compensation should be influenced by resources of the party or parties seeking access to the data. If the analyses proposed are likely to lead to unique insights or important discoveries, we and several other groups conducting trials have generally co-opted the external person as a collaborator and either have conducted the analyses for free or at modest costs, as long as the resulting publication is jointly developed and authored."

The group said once data are released for public use, the deidentified data should be housed either in a reliable third-party data repository or at the trialists' center. "Whoever hosts the data will need to implement mechanisms to manage data requests in a timely and fair manner, avoid duplication of efforts, and ensure that such analyses are accurate and not conducted with the aim of inappropriately undermining the original findings."

The group recommended a review committee should evaluate all data requests and assess conflicts of interest. The committee would have representation of both the investigators involved in the trial and academic trialists who did not participate in it.

The group also laid out a process for accessing and publishing trial data.

Individuals requesting data should:

- Provide evidence that at least one of the individuals requesting data has conducted and published data from a clinical trial;
- Demonstrate that the requesting parties have the appropriate biostatistical capabilities to conduct the proposed analyses;
- Submit a thorough statistical analysis plan;
- Provide evidence of an institutional review board approval for the proposed analyses;
- Establish a timeline to submit a manuscript for publication, based on the analyses;
- Propose a mechanism to collaborate with some of the trial investigators who generated the original trial data or another means to appropriately provide credit to these investigators; and
- Sign a data usage agreement.

The review committee evaluating data requests should:

- Review and provide feedback within eight weeks of receiving a request;
- Inform individuals requesting data of the strengths and weaknesses of the trial data that are requested;
- Encourage collaboration between groups if more than one group requests to conduct similar analyses around the same time;
- Establish a reasonable modified timeline for publication submission, if a group approved to undertake analyses does not submit a paper from this work within the originally established timeline, prior to allowing other investigators access to the data for the same or a similar analysis;
- Provide a data usage agreement to the individuals fulfilling the requirements to obtain data; and

- Ensure the analyses are accurate and any publication is fair and balanced.

In addition, an ICMJE ombudsman would investigate and facilitate resolution of any complaints related to sharing clinical trial data.

The group's article was endorsed by 282 investigators in 33 countries.

Warren Supports ICMJE Proposal

In a separate *Perspective* article, Sen. Elizabeth Warren, D-Mass., supported the ICMJE proposal, saying it "would be a significant step forward in improving the transparency of clinical trials for consumers and the academic medical community."

"Linking data sharing with publication can also help address the patchwork landscape of current regulations related to the sharing of clinical trial data," she added. "Because regulatory agencies have different protocols and requirements for sharing data related to the drugs and devices they approve, access to data about a clinical trial often hinges on which agency handles a regulatory submission rather than on the value of these data to consumers and researchers. By requiring data sharing as a condition of publication, journals can help synchronize and expand existing data-sharing practices."

Although the ICMJE proposal "will not automatically harmonize existing regulations, it could nonetheless create a baseline expectation that data will be shared and prepare researchers to comply with other mandates," Warren said. "Requiring researchers to file a data-sharing plan for patient-level data when they initially register a trial could increase pressure on trial sponsors to post results in a timely fashion, regardless of the type of trial, the country of origin of the research, and whether or not the research is being performed to support approval of a new medical product."

Warren said the costs associated with preparing data for sharing "can and should be built into the grants, cooperative agreements, and contracts that researchers negotiate with trial sponsors; in other words, expenses associated with administering data-sharing protocols must be treated as a standard, necessary aspect of the costs of carrying out a clinical trial. And, over the long run, data sharing may help reduce costs by allowing researchers to avoid duplicating trials or to answer questions without undertaking a separate data collection effort."

Widespread data sharing also can "help to address concerns about conflicts of interest that may arise when clinical trials are funded by industry sponsors that stand to profit from favorable research results. By making trial results available for independent scrutiny by outside reviewers, data sharing makes it less likely that trial sponsors can buy the analysis and results they want. Expanding opportunities for scrutiny through data transparency raises the bar for integrity in analysis and interpretation of results, helping to improve the reproducibility and rigor of our clinical trial system," Warren said.

In a third *Perspective* article, Harlan Krumholz with Yale University and Joanne Waldstreicher with Johnson & Johnson said, "The ICMJE proposal has the potential to spur the transformation of the research culture so that data sharing becomes the norm. Indeed, if properly implemented, the proposal could promote a culture that maximizes the contributions of patients who volunteer to participate in clinical trials."

The two added the "growing interest in data sharing will not translate into progress without the development of supportive infrastructure and policies that enable data to be shared effectively and responsibly… The next steps in data sharing will involve leveraging the progress and experience to date to develop consensus standards for implementation, with attention to affordable ways of sharing data sets responsibly and giving credit to the researchers who generated them."

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