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Editorial

Sharing of Individual Participant Clinical Trial Data: It is Time to Abandon the "Look the Other Way" Attitude

Among the various best practices that have been implemented or recommended to increase clinical trial transparency, the one that could provide a particularly critical step forward is individual participant data (IPD) sharing. The benefits of de-identified IPD sharing are widely accepted, as it allows addressing issues concerning trial publication (e.g., nonpublication, selective reporting, lack of reproducibility), validation or correction of articles, and the conduct of IPD meta-analyses.

IPD sharing received a major boost with the release of the 2015 U.S. Institute of Medicine (IOM) recommendations,[1] which sought to make IPD sharing the expected 'norm' in the clinical trial enterprise. Aligned with this, ClinicalTrials.gov added in December-2015 two optional registration fields about this best practice: plan to share IPD and available IPD information. Influenced by a trend in favor of IPD sharing, in 2016 the International Committee of Medical Journal Editors (ICMJE) proposed that, for the publication of clinical trial results, there is an ethical obligation for authors to share de-identified IPD. Yet, in 2017 the ICMJE changed its mind and what was originally proposed as mandatory became a possibility: from July-2018 authors reporting trial results submitted to ICMJE member journals have to inform readers about IPD's availability plans – but they are free to deny such access.[2] This approach has been completely superseded by a recent US National Institutes of Health (NIH) policy: from January-2023 all NIH-funded trials should made IPD freely available to everyone at the time of publication of trial results – no embargo period will be allowed. This affects all trials funded in whole or in part by the NIH, regardless of the type of intervention assessed.[3] In addition, this approach will be expanded and made mandatory for all US federally funded trials (beyond NIH) no later than January-2026.[3] But, what is the current situation of IPD sharing? A review of the evidence of IPD sharing from three sources – general data from completed and published clinical trials, from US federally funded trials, and from commercial-sponsored trials –, would help to set the scene.

Soon after the IOM recommendations were issued, IPD sharing was almost non-existent. Thus, only 5 of approximately 4700 trials conducted in whole or in part in the US and completed in 2016, had links to IPD.[4] A few years later, evidence showed that according to an evaluation of 487 trials published in 2018–2020 in three ICMJE member journals (Journal of the American Medical Association, Lancet, and New England Journal of Medicine), only two of 334 IPD sets were actually available, while the rest had to be requested from authors, committees, repositories/archives or companies, or the access was unspecified; an embargo was set by 47% of all articles stating they were willing to share data.[5] Among 175 clinical trials published in 2021 in top-10 ophthalmology journals, 24% were willing to share IPD but only 3% shared IPD via an online repository.[6] Among 224 trials assessing therapies for COVID-19 that were posted as a preprint or published in 2020–2021, IPD sharing negative attitude ranged from 30% rejection at trial registration to 78% actual negative IPD accessibility.[7] To all these disappointing data, it should be added that there may be a remarkable time lag between the request and the response; furthermore, it could take one year after a sponsor's positive response.[8]

Most investigators reported that the primary reasons for not sharing IPD were to protect participant privacy (22%) and because of lack of research ethics committee approval of secondary use of IPD at the time the trial protocol was approved (19%).[9] However, these problems can be resolved if a research ethics committee approves the use of IPD for secondary research when adequate de-identification has been ensured – an approach often taken by, for example, many investigators willing to perform an IPD meta-analysis. Secondary use of fully anonymized IPD is exempt from approval by a research ethics committee in many jurisdictions.

The situation of US federally funded trials is also disappointing. Thus, IPD sharing is uncommon among NIH-funded trials. Among top-10 high-volume registrants of 25,551 trials in 2016–2017, only a median of 7% (range, 0–18%) of NIH-funded trials reported having IPD plans.[10] Among 213 NIH-funded pediatric trials, only 30 (14%) declared their data as available, and only in 7 (3%) the data was retrievable and downloadable for use.[11] A thorough analysis of the 154 trials conducted at two NIH institutes (National Heart, Lung, and Blood Institute, and National Cancer Institute) and completed in 2010–2013, found that only 16% shared data.[12] Finally, a study showed that among US federally funded trials, a predictive model exploring factors that influence the decision to support IPD sharing found that NIH-sponsored studies were the most likely to share their data and had the highest positive effect of any sponsor type. Conversely non-NIH US federal agencies had a negative effect, suggesting a lower probability of IPD sharing.[13]

Since 2012–2013, some pharmaceutical companies provide access to IPD. There are several websites hosting IPDs from commercial-sponsored trials. Vivli (https://vivli.org/), the largest repository, contains IPD belonging to more than 7300 trials from 31 pharmaceutical companies, and more than 20 non-commercial organizations (e.g., universities, charities, patients' organizations). Clinical Study Data Request (CSDR) (https://www.clinicalstudydatarequest.com/), the second largest repository, hosts data from more than 3000 trials from 9 companies. These figures are far from the more than 43,000 phase

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2–4 commercial-sponsored trials registered on ClinicalTrials.gov and completed since January-2013 and the many more hosted in other registers (e.g., European Union-Clinical Trials Register). Typically, IPD is provided after an independent committee has approved the proposals submitted by investigators. However, and for whatever reason, IPD is not always granted. Thus, from 1032 requests for IPD sharing to three repositories [(CSDR, Vivli, and Yale University Open Data Access Project (YODA) (https://yoda.yale.edu/)], only 614 (60%) led to actual data sharing.[14] It should be noted that IPD sharing from some commercial-sponsored trials could involve de-identified data from participants enrolled in many countries, something that is helping to spread the importance of IPD sharing across trialists from all the globe.

It is obvious that nowadays IPD sharing is the exception rather than the norm. The NIH policy on data sharing will likely impact the conduct of clinical trials – mainly in many low-and middle-income countries, but not so much in high-income countries.[3] However, it is to be expected that this US policy (and the one that will come into effect no later than in January-2026) will soon affect the way funders, trialists and journals approach IPD sharing. Spanish medical journals should urgently address data sharing (from both trials and from any type of scientific study) as most of them do not require (or even encourage) data sharing with third parties.[15] This is also applicable to the Spanish non-commercial most important clinical trials funder, the Instituto de Salud Carlos III. In fact, there are many Spanish investigators who have agreed to share IPD from both commercial and non-commercial sponsored trials hosted in repositories or published in international journals, so the generalization of IPD sharing in Spain should not be difficult to achieve.

At a global level, the attitude of all clinical trials stakeholders towards de-identified IPD sharing should change if we want to move towards a more transparent scenario regarding the availability of clinical trial data. This is something that, as the ICMJE recognized, is an ethical obligation to participants as they have put themselves at risk when consenting their participation into a clinical trial.[2]

Hopefully sooner rather than later, there will be a response from the ICMJE in a way that aligns its recommendations with the new US federal policies on IPD sharing. Yet, this would not be enough. The important thing is for journals to start requesting IPD sharing without restrictions at the time of publication of trial results. PLOS journals and The BMJ are leading this approach.[3] The sooner many other journals join this policy, the closer we will be to start foreseeing that IPD sharing could become the 'norm' proposed by the IOM almost a decade ago.[1] In the meantime, authors and readers are likely to consider the request to IPD sharing as an element of journal quality.

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Conflicts of Interest

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Declaration of Generative Artificial Intelligence in the Writing Process

No artificial intelligence tool has been used to prepare this manuscript.

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