
Publishing Patient Level Data

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Just like doctors who look at clinical practice guidelines from specialty societies in taking care of their patients, our Journal looks at directions provided by the International Committee of Medical Journal Editors (ICMJE) in determining its publication practices. Recently, the ICMJE, as a condition of consideration for publication of a clinical trial report in member journals, proposes to require authors to share with others the de-identified individual-patient data underlying the results of their clinical study (including tables, figures, and appendices or supplementary material) no later than six months after publication. De-identification involves preventing patient identity from being linked to the clinical data.

At first glance, this can only be good, right? After all, in this era of evidence based medicine, getting more information particularly about clinical trial results that can substantially influence or even change standards of patient care stands to benefit patients and even doctors who treat them. In a previous editorial⁷ I had written about ownership of scientific information impacting our ability to not only see more evidence which can guide us in the management of our patients but also even help us in deciding which diagnostic tests, devices and drugs products are actually better. If “owners” of scientific information are not willing to share this through publication,⁹ how can the medical community at large be able to use it?

But even before this, the ICMJE already requires the prospective registration of all clinical trials (actually first introduced earlier by the US FDA; see in www.clinicaltrials.gov) prior to enrolment of the first clinical trial participant as a precondition for subsequent publication of the results in ICMJE journals. After the study, results are likewise reported. Among other reasons, this is thought to provide transparency of the clinical trial data out there: be it positive or negative. The assumption is that by knowing what clinical trials are being done out there, doctors would be able to see even the studies with negative results – i.e., studies which show no efficacy advantage or an inferior safety profile of a new drug or test, allowing for a more balanced view. From an ethical perspective, the medical community also needs to be made aware of the outcomes no matter what in order to justify the risks that patients take to participate in such studies, allowing themselves to be exposed to drugs of uncertain safety and efficacy, so that others may benefit from the information generated from such studies. It has been estimated that 85% of research resources are wasted^{4,9} and what we see is a distorted view (usually leaning to showing a positive benefit of what is commonly a new drug or test being introduced in the market).

The sharing of patient level data goes one step further. More than requiring that results to be shared de-identified individual patient data (IPD) also need to be provided by authors if this proposal pushes through. Although discussions are being done as to how exactly these data will be shared,¹ the question of whether such patient level data should be shared in the first place needs to be addressed. To be fair, ICMJE does give readers the opportunity to respond and comment on this proposal in their website (www.icmje.org) up to April 18, 2016. Also, authors and study sponsors are given up to one year later before the requirements are enforced in order to address the various ethical, legal, and resource issues this requirement might create.

Those who support the initiative cite certain benefits from sharing IPD. The most commonly mentioned one is that the ability to reanalyze previous studies by disinterested groups can hope to validate the results initially published. For example, a re-analysis of IPD from a previous study which was reported to have positive results,² found that paroxetine and imipramine were no better than placebo for the treatment of depression in adolescents.³ The label for paroxetine has since been revised to remove its indication for adolescent depression. It is also hoped that sharing (rather than “owning”) the information could help foster more collaboration and thus, could potentially increase the knowledge generated.⁵

But it may not be all good.⁶ Others have expressed the view that data in the wrong hands and those who are not able to use it properly may also end up distorting it according to their own agenda. It has also been mentioned that those who have invested time, effort and money in the original study would end up losing their investments if the data can just as easily be provided to someone else who have not put in similar time, effort and money. This can serve as a disincentive for anyone in the future wanting to get truly original data. Warnings about “data pirates” have also been aired.⁸

There have certainly been much previous debate arising with the clamor to have more access to clinical trial data. These have been during instances when the true safety profile of a drug has not been clearly defined to the full confidence of potential prescribers. Past events over the last decade and a half have shown how this

can be more sensational rather than truly a scientific exercise. Citing the more infamous examples, starting in 2000, there was rofecoxib (Vioxx) followed by rosiglitazone (Avandia) in 2007 and most recently, ticagrelor (Brilinta) in 2013. Rofecoxib ended up being withdrawn in 2004. Rosiglitazone is no longer available in many countries outside of the US – where the US FDA removed the black box warning for rosiglitazone in 2013. Ticagrelor continues to be available worldwide.

Therefore, even though it seems easy to conclude that sharing data can only be good, in the end, the outcome may not necessarily be always positive for patients and their doctors. As doctors, we would never knowingly prescribe a drug that would put patients at peril; but we would not also like to deprive them of potential therapies especially for diseases that remain problematic. Finding the right balance – and science – that will allow us to do this is key. That is why perhaps very closely linked to the success or failure of this initiative is defining HOW the data is going to be shared and more importantly being able to make sure that the “rules” are followed by everyone. ICMJE and other groups continue to discuss and debate how sharing of IPD can be properly addressed. As doctors who will see this unravel, we should maintain our vigilance and continue to be updated.

References

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