



## Sharing of clinical trial data and research integrity

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Imagine that you went to see your family physician with an ailment, and she/he prescribed some medication. After taking it, you developed a nasty reaction, were hospitalized and learned only there and then (if ever) that you should not have been prescribed this particular medication given your other conditions, age or sex. How could that happen? Well, chances are your doctor did not have access to all the information about the medicines prescribed. Oops! Or imagine that you are a researcher who spent a few years preparing a study to test a promising new medicine. You then started the clinical trial, and your study participants experienced no effects or serious side-effects. Only then did you learn (if ever) that this particular intervention had proven to be unsuccessful or even harmful in several unreported or currently ongoing studies that you were unaware of. Thus, you wasted several years on a useless or potentially harmful study.

Clinical trials\* are indispensable in the development of most new and improved medical interventions (1). Integrity in clinical trials seems to be difficult to achieve due to numerous barriers, including the culture of non-sharing of research data. I argue that full transparency of clinical trial data is an essential prerequisite to achieving research integrity, and is equally important as factors such as the initial idea, a high quality research plan and protocol, and the ethically sound conduct of research.

In the health field, we (cl)aim to make evidence-informed decisions. This would be phenomenal provided we had reliable evidence; evidence based on all knowledge available at a given moment in time. However, we don't. Evidence gained by systematic review, meta-analysis of aggregate data and pooled analysis of raw data of clinical trials is considered to be the most reliable evidence we can devise for health care decision-making, including for the development of new diagnostics and therapies.

Research is continuously getting more powerful largely due to new technologies and related know-how. It benefits from the ever-increasing possibilities offered by digital and cloud-based software technologies, including electronic data management and record keeping that should have enabled faster knowledge creation, and a higher level of efficiency

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\*Clinical trials (also known as interventional studies) are performed on human participants, which can be either healthy volunteers or individuals that suffer from a disease or condition for which diagnostic procedures or therapies are being developed. The intervention, for example, could be that a candidate for a new drug is given to study participants and its effects are measured and compared to the existing medication or to the placebo if there is no existing medication.

and integrity of research. Alas, this has been true only to a degree: clinical trial research is burdened with various biases that arise from the non-sharing of research data (1). Research, especially health research, seems to be a hostage to the existing, more or less unchanged fear of sharing data, and of the “it’s mine” and “no data sharing until there is clear and unambiguous proof that no harm will result (especially to me)” culture viewpoint (2). In short, research paradigm changes lag behind the advancements of technology.

Numerous benefits are anticipated from increasing the sharing of clinical research data: it accelerates the development of new knowledge and innovation, enhances translational research, informs decision-making and helps ensure the efficiency and integrity of research. Specific benefits include avoiding unnecessary and redundant research and thus decreasing the burden on research participants. On the other hand, there is increased awareness of the harm caused by the non-sharing or partial sharing of such data.

I want to believe that researchers aim to perform meaningful and efficient research, which is ethically and economically sound and contributes to the common good. Thus I expect that any given researcher would take advantage of existing tools to develop, conduct, and report high quality and efficient trials. These tools include systematic reviews to capture the existing knowledge, SPIRIT guidelines (3) for protocol development, ethics approvals guaranteeing the respect of study participants’ wellbeing, and CONSORT guidelines (4) for the publication of summaries of findings.

WHO International standards define trial registration, and its International Clinical Trials Registry Platform links to the basic protocol information hosted by a network of WHO trial registries. One of these registries, Clinicaltrials.gov, also accepts results in aggregate data format. Supported by journal editors (5, 6), funders, the Ottawa group, All Trials initiative and others, and enforced by national legislations, trial registration is gradually becoming an integral part of the clinical trial process.

The next step is to complement trial registration with results disclosure, publication of findings and public disclosure of all data, including raw data; i.e. individual participant data (IPD). However, although there are repositories that host clinical trial data, the methodology for preparation of data for public release and reuse is still under development and no standards exist. Researchers need to know what the analysable data set consists of and where to deposit it, which calls for the development of methodology and standards to guide data preparation for public release and re-analysis. Such datasets would include anonymized IPD, metadata, dictionary (descriptors) and more; presented in a structured format, which should follow certain standards across repositories.

Initiatives aimed at opening clinical trial data have been taking place in many parts of the world in various forms (7, 8). The strength of this movement is that it brings together people from various fields, including data managers, scientists and knowledge users.

The abundance of research and the benefits that researchers seek from it have led to increased concerns for research integrity and responsible research. There are numerous scientific, practical, legal and ethical issues that prevent the achievement of fully responsible and efficient research. Physician clinical trialists are also bound by the Hippocratic Oath and its “do no harm” principle, as well as the promise that “the health of my patient will be my first consideration...” The Declaration of Helsinki (9) is increasingly calling for trial registration and sharing of results, as is the World Health Organization. Offices of research integrity have been formed, and the World Conference on Research Integrity produces statements aiming at increasing the integrity in research. An issue of particular concern is that of data sharing. Public disclosure of data would not only facilitate the verification of published information and increase the speed of knowledge creation, but it would also contribute to the prevention of other research integrity issues such as plagiarism and fraud.

Interest in broader sharing of research data is increasing and many initiatives are underway. In the clinical trial field, notable recent efforts include the US Institute of Medicine (IOM) recommendations on sharing clinical trial data (10), the European Clinical Trial Regulations (11) as well as policies of the European Medicine Agency (EMA) (12) that will enable access to clinical trial reports as of January 2015. Many, including the Ottawa Group and its IMPACT Initiative, are looking for methods and standards for the public disclosure of trial data and related repositories.

The field is so complex that it would merit structured monitoring of the impact of changes in data sharing on clinical trials in order to connect dots and indicate trends. The recently started IMPACT Observatory (natural experiment) aims to do just that.

Overall understanding of the advantages of open data and open science is increasing. New technological opportunities are enabling the analysis of big data sets with new algorithms. This does not only serve the purpose of verifying whether a report is biased, but the reanalysis of several trials can lead to more findings. The clinical trial field is not isolated in this evolution of research; it could learn a lot from other areas as many are more advanced. However, there is insufficient communication of experience with data sharing among scientific fields, which again might be due to its novelty and dynamics.

The opening of oncology clinical trials data is particularly important as it would contribute to the desperately

needed increase in knowledge and innovation, which is essential to in the fight against cancer. One example of data sharing initiatives in oncology is the CEO Roundtable on Cancer and its Project DataSphere (PDS) as it aims to bring together private, public and not-for-profit organizations to fight cancer. In 2014, following several years of preparation, the CEO launched the DataSphere platform of oncology with the goal of gradually making oncology data available for further research, to “share, integrate and analyse” and thus speed up the development of new therapies.

The vast majority of clinical research data is still not open but rather is of limited access, including semi-open data sharing, sharing within certain groups, sharing pre-competitive data only, and sharing for research purposes only, upon request or by agreement.

The opening of clinical trial data would enhance the efficiency and responsibility of research, and contribute to strengthening or even regaining people’s trust in research and medicine. It has been emphasized over and over again that we have to do whatever it takes to overcome the remaining barriers in opening clinical trial data as we primarily owe it to trial participants. After all, they are the ones who take a risk by participating in the clinical trials that enable data gathering to begin with.

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