Contributors

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Registration of clinical trials first became a high level policy requirement when the health authorities of the Americas approved a Policy on Research for Health in 2009 (PAHO, CD49/10)[1]. In addition, interest from researchers, clinicians, scientists, and other medical professionals is growing in registration of observational studies[2]. There is also a growing realization that the gold standard of clinical research, the randomized clinical trial, is not the only good source of evidence. Although the majority of observational studies is unregistered, a weekly peer-reviewed medical journal, The BMJ, stresses that observational studies still are an important factor of medical research[3]. The BMJ strongly encourages all research studies such as observational studies that involve human subjects as research subjects to follow the World Health Assembly (WHA) and the World Medical Association's (WMA) Declaration of Helsinki.

The WHA approved a Strategy on Research for Health in 2010 (WHA 63.22) as a follow-up of the recommendations issued during the 2004 Mexico Ministerial Summit on Research for Health[4]. The Declaration of Helsinki by the WMA is an international widely respected statement of ethical principles for medical research that has called for registering research, transparency, and accountability on research[56]. The AllTrials.net campaign and leading publishers align with the mission of Helsinki Declaration. Therefore, registration of research has been considered a best practice and standard for research.

As the access to research knowledge and adherence with clinical trial registration improve, it is time to address the growing need to also register observational studies[7]. The research community has been urging for over a decade to implement registration of observational studies to reduce research waste or the impact of publication bias, improve transparency, and increase the value of research[8].

Scaling up the registration of observational research and studies is already happening, and can be done building on the existing infrastructure of research registries that deliver into the World Health Organization's International Clinical Trial Registry Platform (WHO's ICTRP). The WHO's ICTRP works as a meta-register that pulls information from a range of certified registries, also known as primary registries, and other data providers such as ClinicalTrials.gov[9]. Some of these data providers such as ClinicalTrials.gov, Brazilian Clinical Trials Registry (ReBec), and International Standard Randomized Controlled Trials Number (ISRCTN) are already including observational studies[10]. Registering research and clinical studies provides essential resources to improve access to information and to enhance the governance of research[11].

ClinicalTrials.gov is operated by the US National Library of Medicine of the National Institutes of Health (NIH), and it is one of the data providers that contain registered observational studies. By April 2016, an estimated 14,595 of 87,000 registered studies through ClinicalTrials.gov were listed as observational studies, including case-control, cross sectional, longitudinal, cohort, and ecological studies[12].

The benefits and rationale of registering observational studies in advance

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apply to those proposed for interventional studies[13]. Seven identified rationales for registration of clinical trials and observational studies are (1) respect for human subjects, (2) enabling evidence-informed health care, prevention, and policies, (3) mitigation of publication bias and detection of deviations, (4) clear documentation of pre-specified study design, (5) identification of knowledge gaps in research, (6) avoidance of duplication and research waste, and (7) public record and better governance of research for health. Can the promotion of registering observational studies become the next crucial step towards better research transparency in addressing publication bias and increasing public confidence in research?

Enhancing Transparency and New Possibilities

The research community encourages ensuring studies that involve human beings as research subjects have a protocol, and that the protocol is registered in a publicly accessible database[14]. The ethical and scientific justifications to register clinical trials that involve human subjects apply to observational studies. The identified purposes of registering studies would benefit the community at large, and more specifically also a variety of groups such as patients, clinicians, journal editors, funding agencies, stakeholders, institutional review boards (IRBs), ethicists, the research community, and the users of the medical literature (See Table 1). In addition, observational and interventional studies do the same job by enhancing transparency that will increase the research community's trust in research and also expand new possibilities to consider additional beneficial reviews.

When the recommendations and the required higher standards of research put forward by the WHO, WMA, [[and reflected in the Declaration of Helsinki,]] are not followed, publication bias and selective reporting impact on the reliability of health care and health policy decisions. Promoting registration of observational studies will ensure that all available evidence is used in systematic reviews. This will allow funding agencies, regulators, and researchers to improve research governance, to help identify research gaps, and to avoid unnecessary duplications. Researchers and potential participants will be able to engage in and collaborate with ongoing studies. This will provide significant benefits for several defined groups (see table 1).

Table 1: Trial Registry Purposes for Various Groups[15]

Registry Purpose	Group that benefits
Fulfill ethical obligations to participants and the research community	Patients, the general public, the research community
Provide information to potential participants and referring clinicians	Patients, clinicians
Reduce publication bias	Users of the medical literature; indirectly also general public, patients
Reduce outcome switching	Users of the medical literature (same)
Help editors and others understand the context of study results	Journal editors, users of the medical literature
Promote more efficient allocation of research funds	Funding agencies or stakeholders, research community
Help institutional review boards (IRBs) determine the appropriateness of a research study	IRBs, (ethicists)

How to register an observational study

The registration of research and a clinical study through the International Standard Randomized Controlled Trials Number (ISCRTN) has been described as an

example in a tutorial clip published by the Pan American Health Organization in 2016[16]. If you wish to register through other data provider such as ClinicalTrials.gov, you can use the similar guidance. Steps of registering clinical trials described below:[17]

1. Ensure you are the appropriate individual to register or submit a clinical study to ClinicalTrials.gov.
2. Make sure that your organization has an existing Protocol Registration and Results System (PRS) account before applying for one. If so, submit a PRS Administrator Contact Request Form. You will receive contact information for your organization's PRS Administrator, whom you can contact directly to request a user login.
3. In the event that your organization does not have a PRS account, you can identify an individual to serve as the PRS Administrator for your organization.
4. After creating the account, learn about submission requirements such as ethics review regulations, the protocol data element definitions, and applicable regulations of the national or regional health authority (or equivalent).
5. Login to PRS.
6. Enter the required and optional data elements.
7. Preview, inspect, and release the record, study, or trial.

How to Make Registration of Observational Studies Effective

There is a shared responsibility from different stakeholders (researchers, sponsors, publishers, and institutional review boards/ethics review committees) to scale up the registration of observational studies and to increase the value of research[18]. Increasing the number of registered observational studies will also raise awareness and knowledge among the research community. Potential participants and funding agencies could also benefit by: (1) avoiding potential duplications and publication bias, (2) enhancing recruitment of participants and health professionals, (3) promoting collaboration, and (4) encouraging more researchers to engage in registering studies that involve human or research subjects. In the near future, the research community will likely be confronted with a growing demand among journals and editors to register observational study protocols. Researchers should take the initiative to start registering these studies, because it is the appropriate thing to do.

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