

A priori registration of global health research – necessity or absurdity?

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An ongoing trend has sparked debates about the need to prospectively register all health research.^{1–3} Research registration involves obtaining a unique identification number, and registering the protocol of a study and any subsequent amendments, at recognised registries.⁴ Proponents of a priori registration argue that it improves transparency by tying researchers to an analysis plan, promotes efficiency in knowledge production by minimising unnecessary duplication and increases the availability and reliability of evidence for decision-making by ensuring that researchers publish their results, even when negative.^{3,4} However, others have argued that registration is unnecessary for some research and may even be counterproductive. But what is the implication of this debate for global health research?

A priori registration gained widespread legitimacy in 2004, after journal editors under the platform of the *International Committee of Medical Journal Editors (ICMJE)* made registration a requirement for publication of clinical trials in journals.⁵ Within 5 years of the ICMJE policy on research registration, there was an approximately fivefold increase in the number of registered studies on ClinicalTrials.gov.⁶ Registration of clinical trials is now an ethical as well as a legal requirement in some jurisdictions like the USA.³ The World Medical Association's Declaration of Helsinki expanded the scope of a priori research registration in 2013 by recommending that every study involving human subjects must be registered in a publicly accessible database before enlisting the first subject.⁷

The call for a priori registration of other study types has been associated with a growing trend in the establishment and expansion of research registries; some with unique and overlapping methodological or intervention scopes.^{3,8} Registries now exist for various other purposes such as vertical interventions, data registration, systematic reviews and other study designs.^{8,9} Although ClinicalTrials.Gov

was initially established to register clinical trials, it has since expanded to include observational studies.¹⁰ Journals have also been encouraged to make a priori registration a condition for publishing systematic reviews and other forms of evidence synthesis.^{11,12} Yet, most studies go unregistered.^{3,10} There is currently no consensus that a priori registration of studies other than clinical trials is necessary and desirable.^{13,14}

The same concerns that made registering clinical trials a necessity—that is, selective reporting of positive results and suppression of negative results—have found resonance in global health, especially in studies funded by foreign actors, for example, philanthropists and bilateral or multilateral agencies in low-income and middle-income countries.^{15,16} These concerns apply to local actors too. In many instances, the funders, designers, promoters and implementers of policies or projects play a dual role in evaluating the same policies or projects. This situation has raised concerns about independence, integrity and transparency. It is well known that to avoid reputational damage donors, policy-makers and governments have a strong incentive to conceal undesirable outcomes of their policies and projects.^{15,16}

But global health is methodologically neutral. Approaches to solving global health problems may draw on clinical trials, but often more on other study designs—from epidemiology, the social sciences, health systems research, implementation science and from evidence syntheses and other forms of knowledge. Even when human subjects are involved, studies vary in the extent to which they are 'clinical'. In current practice, while journals mandate the registration of a 'clinical' trial protocol of a social intervention to improve the use of vaccines, the same journals may not demand the registration of an anthropological study of the same social intervention involving the same human subjects, and with the same goal. It is more complicated when

studies are interdisciplinary, as is ideally the case in global health.¹⁷

Clinical trials are typically conducted to determine the efficacy of interventions in ideal environments. In such trials, which are often 'biomedical', risk to human subjects can be significant. Thus, there is much emphasis on avoiding unnecessary duplications;¹⁰ and on the need for open scrutiny such as through a priori registration. In contrast, global health research seeks to close equity gaps in real-world systems.¹⁸ Other methods are more often employed. Clinical trials in global health are typically pragmatic, thus allowing for contextual nuances. Results are often contextual. So, it is not unusual to see the same or similar studies repeated in different locations, or at different times—just as it is for evidence syntheses on complex interventions, processes and phenomena with so many moving parts that little is discrete or predictable a priori.¹⁹

A priori registration can be burdensome, demanding, costly or even asphyxiate beneficial learning and data exploration.¹⁴ It may also constrain the initiation of sensitive research in which potentially negative finding may be politically stifled by interested parties,^{15 16} if a priori registration reveals such potential concerns to 'conflicted parties' ahead of the study. Concerns related to political interests and influences are critical considerations in global health research.²⁰ Thus, a priori registration may lead to inefficiencies and even create ethical challenges of its own, while not necessarily preventing ethically or methodologically questionable research.^{21 22} And while registration may promote the publication of negative findings, it is limited as a strategy for preventing the cherry picking or hyping of positive findings.¹³

Nonetheless, a priori registration is feasible. Global health journals can agree to only publish registered evaluations. It worked to promote the registration of clinical trials. But there is also the issue of power imbalance and contextual misinterpretation given the biomedical bias and high-income country location of go-to research registries and global health journals.²³ However, this may be the only enforceable strategy in global health. First, donors, funders, policy-makers or governments may lack the incentives to enforce rules that are designed to monitor and limit their excesses. Second, there are often contractual obligations in donor-funded or government-funded projects,¹⁵ which, even if a study is registered, may determine which analyses are registered or which results can be published or disclosed to a third party.

Looking ahead, perhaps for some studies, requirements for local ethics approval would address some of the concerns raised by advocates of a priori registration. But such research governance structures are weak in many settings.²⁴ And ethics requirements will need to be strengthened to address a broader range of potential issues at the start of a study, but also through its life cycle, including how findings are used and disseminated.²⁵ Other strategies may involve asking government departments and donor agencies who commission research and

evaluations to develop strong accountability measures between their operational departments and their research or evaluation departments.¹⁵ Or that they only issue tenders for or commission evaluation of their own programmes, or even have a third party do so.²⁶

A more holistic discussion on open registration, open data, open peer reviews, preprints, open access and the uses of knowledge may result in more effective strategies to address scientific and ethical concerns in global health research. To be effective and adopted, transparent research initiatives in global health must be contextually adapted. And given the multiplicity of spaces and ways in which knowledge is produced and used,²⁵ perhaps more relevant will be geographically decentralised (eg, national and subnational level) registries. This may help to mitigate concerns around power imbalance that compound ethical debates in global health. Even then, it is worth reflecting on broadly and openly whether a priori registration is a right solution. We welcome such a holistic discussion in *BMJ Global Health*.

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