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Editorial

The *Research Registry* – Answering the call to register every research study involving human participants

Imagine you're a patient signing a consent form for an operation and only knowing about the good outcomes and none of the risks. This is akin to what is happening in much of science today. Negative studies don't get published and positive studies sometimes get published twice [1]. Such publication bias is skewing the research base to the detriment of scientific progress. There is strong evidence that much research remains unpublished and this is especially true of those studies with inconvenient or negative findings [2].

1. Publication bias and selective reporting

In April 2014, we found out that the UK government had wasted £500m on stockpiling Tamiflu – a drug the Cochrane Collaboration determined had little or no impact on the complications of influenza infection such as pneumonia. This occurred because Roche, the pharmaceutical company behind it withheld crucial information on its clinical trials for half a decade [3]. We typically associate such publication bias and selective reporting with big pharmaceutical companies but there is increasing evidence that this is occurring in the academic community as well. In a cross-sectional analysis of 677 trials (excluding phase I studies) registered on ClinicalTrials.gov, just 46% of those that had completed by 2005 were published by 2007 [4]. In a more recent study, Jones et al. assessed 585 clinical trials that had recruited at least 500 participants and were prospectively registered on ClinicalTrials.gov and completed by January 2009. They found that, by November 2012, 29% of these trials remained unpublished [5]. Such evidence points to worrying rates of non-publication in both registered and large trials. This problem is likely to be magnified with smaller studies, especially unregistered ones.

2. The benefits of registering research

The benefits of research registries have been argued previously [6,7]. For the sake of brevity we have summarised these in the Table 1 below

3. Drive to increase registration.

Journal editors have been influential in raising awareness about these issues. In 2004, the International Committee of Medical Journal Editors (ICMJE) made registration of clinical trials a requirement for publication in their journals [8]. This led to a sharp increase in the number of trials being registered which did not occur when the US Federal Drug Administration (FDA) called for it in 2002 (see Fig. 1) [9]. In 2008, the Declaration of Helsinki (DoH) made registration of Clinical Trials mandatory and hence it became an ethical requirement in addition to a regulatory one.

4. Rise of observational research

Whilst the focus in the past has been on registering clinical trials, there has been tremendous growth in observational studies (case series, cohort, case-control, cross-sectional, etc), many of which are not registered. Whilst some trial registries do allow for the registration of observational studies, only a small fraction are actually registered. Nearly 80,000 observational studies were published in the period 1990–2000 across all fields, according to Thomson Reuters as reported in the Wall Street Journal [10]. In the following period, 2001–2011, this tripled to 263,557.

5. The Declaration of Helsinki 2013

Why is this important? In 2013, the DoH [11] changed to state:

> "Every research study involving human subjects must be registered in a publicly accessible database before recruitment of the first subject … …Negative and inconclusive as well as positive results must be published or otherwise made publicly available … . Reports of research not in accordance with the principles of this Declaration should not be accepted for publication."

This move away from clinical trials to "every research study" has important ramifications. Observational research must now be registered. As of 1 January 2015, ClinicalTrials.gov listed a total of 34,212 studies classified as observational [12]. Hence, they are registering less than 10% of observational studies. This is in part because the mandate and set-up of many of these registries was centred around randomised controlled trials and not a wide variety of research study designs. Lack of awareness is an issue too. Barriers include the practical difficulties of registering a study, with some requiring the researcher to determine who their institutional account manager is, poor usability and charging high fees to register a study are other issues.

Further evidence of the gap is provided in an article written by those working at ClinicalTrials.gov itself titled: *Registration of observational studies: Is it time?* Where they acknowledge a lack of focus and attention in this area [13]. This adds to several other recent calls to register protocols for observational research [14,15]. Indeed Chalmers et al. have written specifically on how to increase value and reduce waste when research priorities are set. One of their recommendations was that research funders and regulators should

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Table 1
Benefits of research registration.

Stakeholder	Benefit
Research and clinical community	❖ Reduce publication and reporting bias (not all studies performed are published – especially negative studies) ❖ Increase transparency ❖ Identify on-going studies in their field – the cutting edge and gaps ❖ Aids research quality – allows for open and early peer-review of study objectives and methods and their refinement ❖ Aids guideline development and evidence synthesis/systematic review ❖ global collaboration between researchers – more multicentre studies
Editors and peer-reviewers	❖ Compare study findings with registered study protocol ❖ Evidence-based medicine
Commissioners, funders and wider society	❖ Reduce unnecessary duplication saving funds
Institutions	❖ Increased collaboration – research that's more global, multicentre and more interdisciplinary
Patients and the public	❖ Can find out about research of interest to them (e.g. HIV treatments) ❖ Respect, dignity and ethics – people who enter studies expect a permanent record of it.

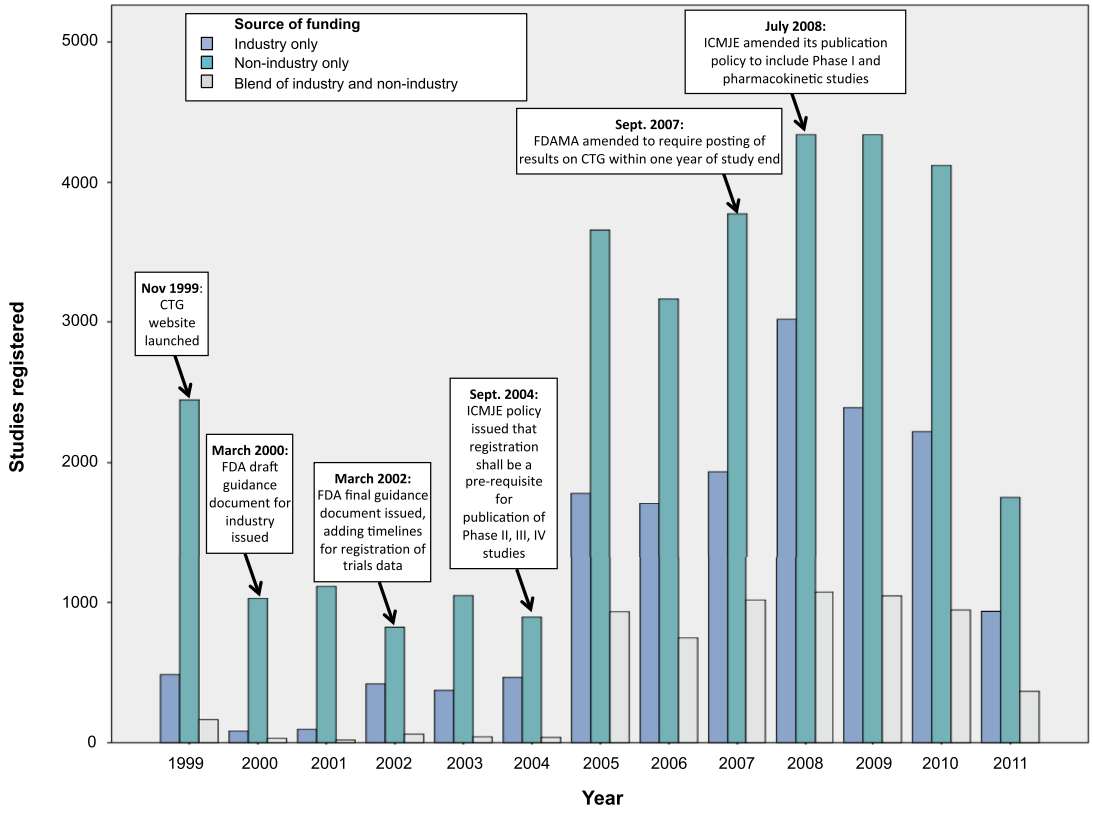

Fig. 1. Studies registered on Clinicaltrials.gov, by year and funding source (taken from Gill, 2012[9]).

strengthen and develop sources of information about research that is in progress, ensure that they are used by researchers, insist on the publication of protocols at study inception, and encourage collaboration to reduce waste [16].

7. Introducing the Research Registry for health research

For over a decade now as Editors at the International Journal of Surgery (IJS) as well as editorial and reviewer roles in many other journals (including its sister Journal Annals of Medicine and Surgery), the vast majority of research studies which come across "our desk", are not registered in a publicly accessible database. This practice has continued despite the change in the DoH in 2013. As academics, clinicians, scientists and as a scholarly community, we have a duty to help find the solution to this problem.

The *Research Registry* (www.researchregistry.com) is a 'one-stop shop' for registering all types of research studies as well as systematic reviews and meta-analyses. The data we collect is based on the WHO data set [17] and includes some additional items. Our aim is to adapt this resource to the needs of the users. The Research Registry will not only register research prospectively (as is best practice), but also retrospectively. This is because if a study is not prospectively registered, subsequently performed and then rejected by a journal and not published, no record of it will exist. We wish to address this by allowing retrospective registration for all those studies not prospectively registered prior to recruitment of the first participant and which have not yet been published in a journal.

The *Research Registry* will record negative studies and ones where the outcome may be suboptimal. It will thus provide a comprehensive scientific and historical record. It is open access, searchable, simple to use and free to register. It was launched quietly on 1st February 2015 and since then all research studies involving human participants being submitted to the IJS or our sister publication Annals of Medicine and Surgery must be registered first (over 50 registered already at the time of writing). We have also recently been endorsed by the IDEAL Collaboration, an initiative to improve the quality of surgical research. Its Chair Professor Peter McCulloch commented: "*We welcome this initiative which allows registration of studies and protocols at every stage of the innovation lifecycle.*"

The ResearchRegistry.com is work in progress and will evolve with time to meet the needs of the community. We call on readers, authors, reviewers, editors and the scholarly community at large to encourage use of this service for the benefit of us all and future generations.

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