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View Point

Lack of transparency in clinical trials: a call for action

The purpose of any pharmacological and non-pharmacological medical interventions are maintenance of good health, retard the progression of pathological processes and rehabilitate patients with disability. Because any intervention have the risk of adverse effects, physicians have to weigh benefits against harms for deciding the best treatment for the patient condition, this decision is primarily supported by high quality evidence obtained from randomized clinical trials and meta-analysis of these studies. Failure to balance benefits with harms of therapeutic interventions could result in severe adverse drug reactions. Admissions to emergency rooms, increased hospitalization days, disability, loss of productivity, and preventable deaths are some characteristics of adverse drug reactions.

But is data from clinical trials sufficiently shared to support therapeutic decisions in daily clinical practice?

Approximately ten years ago the International Committee of Medical Journal Editors (ICMJE) published the statement for mandatory registration of clinical trials.[1] The original intention of clinical trials registration was to improve transparency in the design, methods, and reporting of clinical trials. Since the publication of this statement it has been demonstrated that such requirements are frequently ignored by medical journals around the world.[2]The Consolidated Standards for Reporting Clinical Trials (CONSORT) were published in 2001 with the intention to improve the quality of reporting clinical trials published in biomedical journals. A large number of interventional studies published in indexed medical journals do not comply with these guidelines.[2,3] Nowadays, these requirements are absent in a considerable number of peer-review medical journals around the world.The CONSORT were originally published for parallel group clinical trials with subsequent extensions added according to the clinical trial design (*i.e,* cluster trials, non-inferiority and equivalence trials, and pragmatic trials), intervention (*i.e.,* herbal medicinal interventions, non-pharmacological treatment interventions, and acupuncture), and data extension (*i.e,* patient-reported outcomes, harms, and abstracts).[4]

In Latin America only one out of five published clinical trials by Latin American and Caribbean journals reported a registration number. Author's information about CONSORT is provided by only 13% of medical journals.[2] The Latin-American Ongoing Clinical Trials Registry (LATINREC) is not operating despite the efforts of many persons involved in their creation and promotion.[5] The impact of unavailable clinical trials records is a major barrier in the process of data gathering for systematic reviews and meta-analysis. A recent cross-sectional study published in British Medical Journal found that 29% of registered phase III clinical trials, involving more than 500 patients, are still unpublished after more than five years of study completion.[6] Percentage of unpublished clinical trials in this study was higher among industry funded (32%) than other types of sponsors (18%). In addition, almost 8 out of 10 of the unpublished trials had no results available at clinicaltrials.gov.

According to ClinicalTrials.gov there are 712 studies registered for Colombia as a location for patient recruitment (Data search: December 5 2013). Most of these trials were designed to evaluate the safety and effectiveness of approved drugs in off-label conditions in postmarketing studies (phase IV) and to test investigational new drugs (clinical trials, phases one to three). The majority of ClinicalTrials.gov studies are multicentric phase III clinical trials, with patients are recruited in Colombian cities as well as other locations around the world. Only four out of ten studies are published after three years or more of the study completion date (Table 1). Moreover, some ClinicalTrials.gov registries are published more than one time, although several publications could be justified for some studies, the appearance of more than one publications for individual studies could lead to the perception of a greater quantity of scientific evidence for specific healthcare

Figure 1.

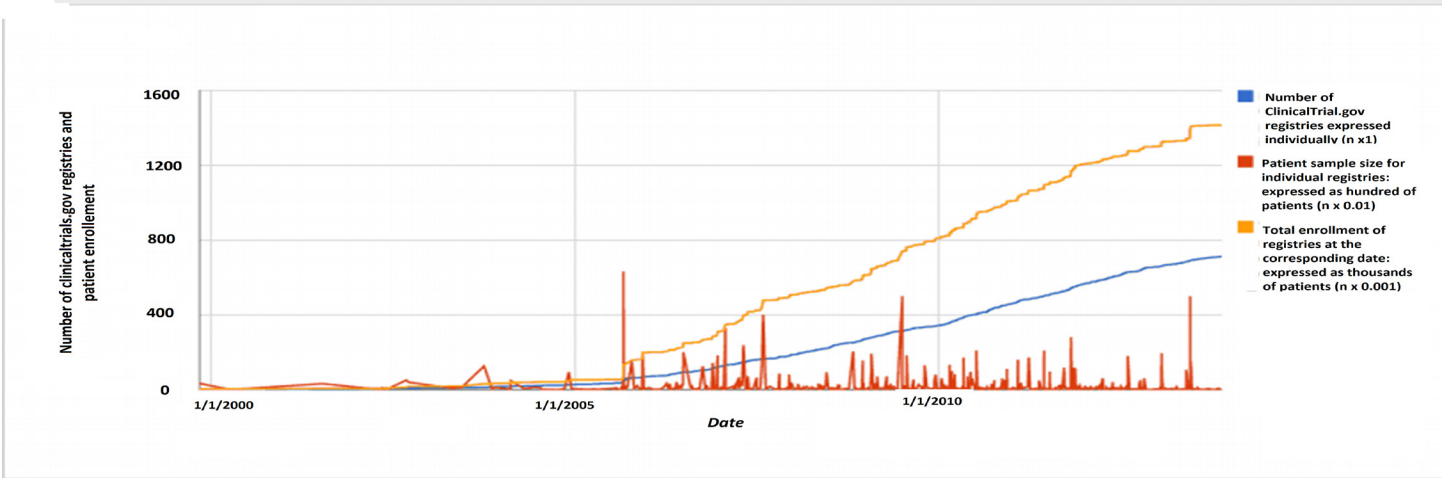

Table 1. Characteristics of clinicaltrials.gov records in which Colombian institutions are listed as locations for patient recruitment.

	Industry		Other institutions*			
	Colombia	International	Colombia	International	US agencies**	Total
Total number of registries - n (%)	4 (0.6%)	596 (83.7%)	74 (10.4%)	25 (3.5%)	13 (2%)	712 (100%)
Closed studies before December 2010 - n (%)	0 (0%)	161 (27%)	29 (39.2%)	6 (20%)	7 (53.8%)	203 (28.5%)
Published	-----	72 (44.7%)	7 (24.1%)	3 (50%)	0 (0%)	82 (40.4%)
Unpublished	-----	89 (55.3%)	22 (75.9%)	3 (50%)	7 (100%)	121 (59.6%)
Study design						
Phase I or phase II clinical trial	0	111 (18.6%)	30 (40.5%)	6 (24%)	1 (7.7%)	148 (20.8%)
Phase III clinical trial	2 (50%)	386 (64.8%)	22 (29.7%)	14 (56%)	2 (15.4%)	426 (59.8%)
Phase IV or postmarketing study	0	67 (11.2%)	19 (25.7%)	1 (4%)	3 (23.1%)	90 (12.6%)
Observational studies	2 (50%)	32 (5.4%)	3 (4.1%)	4 (16%)	7 (53.8%)	48 (6.7%)
Number of papers per clinicaltrials.gov registries	0	1.9	1.1	1.3	0	1.3

Examples of postmarketing studies are pharmacological surveillance, new dosage forms, and research in special populations (e.g., pregnancy, children, and elders). The percentages depicted for 'closed studies before December 2010' and 'study design' were calculated from the total of registered studies by each type of sponsor. Closed studies before December 2010 includes records for 'active, not recruiting', 'completed', 'suspended', 'terminated', withdrawn' and 'enrolling only by invitation'. Percentages in the published and unpublished studies were estimated from the total number of studies completed before December 2010. The number of papers per clinicaltrials.gov registry was estimated dividing the total number of publications by the clinicaltrials.gov registries with available results in PubMed.

* Universities, hospitals, and governmental organizations.

** National Institute of Health, Center for Complementary and Alternative Medicine, United States Agency for International Development, and other US agencies.

interventions, in which results have been decided to be publicly shared in medical journals (Table 1). These ClinicalTrials.gov records have data of more than 1'400.000 patients, which have been recruited in Colombian cities, as well as other locations around the world for multicentric studies (Figure 1).

Administration of healthcare interventions is currently supported by a small number of clinical trials, preferentially published due to their positive results, and important data is hidden to physicians, patients, healthcare policy makers, and the general public.[7] A recent article analyzed the negative impact of the Trans-Pacific partnership on drug prices and data access.[8] Transparency of clinical trials, rights for open data, and strengthening of ethical committees should be appropriately discussed between the participating nations of this agreement.

An international campaign to restore invisible and abandoned trials is an initiative proposed by the Cochrane Collaboration, the British Medical Journal, PLOS publishers, Bad Science, the Centre for Evidence Based Medicine, The Dartmouth Institute for Public Policy & Health Practice, Sense About Science, and The James Lind Alliance. Several institutions around the world have signed the All Trials petition to restore abandoned and unpublished trials but only the Drug Information Center of the National University of Colombia (CIMUN) is included among Colombian institutions. Some Medical Journals are taking further actions to ensure clinical trials data access. For example, starting in January 2013 the British Medical Journal (BMJ) will no longer published any clinical trial in which authors do not compromise, upon reasonable request, to make relevant anonymized patient level data accessible. Information about these initiatives could be found in the following webpages:www.alltrials.net andwww.bmj.com/open-data.

Latin American Journals should consider the support of initiatives to restore abandoned and unpublished clinical trials, request the authors commitment to make anonymized patient level data available, and strengthen the requirements for clinical trial registration and appropriate guidelines (*i.e.,* CONSORT, STROBE, and PRISM).

The complete database for studies registered at ClinicalTrials.gov listing recruitment centers located in Colombia (December 05 2013) used for the Table and Figure presented in this letter is available in the following link: http://goo.gl/suzQ7m. Information about missed publications is appreciated considering that some data could have been released in medical journals not indexed in PubMed. The latest data for studies located in Colombia and other countries around the world is free for public consultation at the ClinicalTrials.gov webpage.

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