

## Prospective registration and results disclosure of clinical trials in the Americas: a roadmap toward transparency

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### SYNOPSIS

*The objective of this article is to propose a roadmap toward transparency of clinical trials in the Americas by their prospective registration and results disclosure. This will broaden access to more complete and accurate data and facilitate evidence-informed decision-making and participation in research. Consequently, it should have a positive impact on people's health and should promote trust in health research. Existing initiatives were identified, registration of trials was analyzed following the World Health Organization (WHO) standards on trial registration, and a roadmap is proposed to address the gaps in advancing transparency. The analysis shows that, in spite of numerous regional and country initiatives, clinical trials taking place in non-English-speaking parts of the Americas are underregistered. A roadmap is proposed to enhance research governance and good research practice by improving the transparency of clinical trials. The proposed roadmap includes strategies for implementing WHO international standards for trial registration, for developing international standards of public disclosure of trial results, and for a potential role of the Pan American Health Organization.*

**Key words:** Clinical trials as topic; standards; Americas.

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“The right to search for truth implies also a duty; one must not conceal any part of what one has recognized to be true.” (1).

The objective of this article is to propose what the authors consider could be a roadmap toward transparency of clinical trial reporting in the Americas by trial registration and results disclosure. Trial registration is the listing of key elements of a trial protocol in a registry; results disclosure is inclusion of the results of the trial in an Internet-based repository. This article provides readers with background information about the World Health Organization (WHO) international standards for registration of clinical trials, their implementation in the Americas, and what the Pan American Health Organization (PAHO/WHO) and others are doing to advance its realization. The article also suggests possible future initiatives in this area.

Much emphasis is currently placed on the need to ensure that health care is informed by complete, accurate, and relevant research evidence. A key factor driving this demand is the interest in safe, effective, accessible, and affordable health care and the need to avoid unjustified variations in health care.

Clinical trials are considered a key source of evidence for informed health care decisions. They provide information that enables decision makers and health care providers to assess the efficacy and safety of health interventions, particularly those that involve pharmaceutical products and medical devices. However, clinical trials also raise ethical challenges, as they may expose participants to risks of interventions with unknown harms or administration of a placebo rather than a standard therapy.

Evidence-informed decisions require delivery of complete and unbiased trial results in a timely manner (2–4). But the medical and health policy literature illustrates that various types of trial reporting biases exist. These biases include lack of publication of entire trials, selective reporting of results from trials, and delayed reporting of trials with results unfavorable to the trial sponsor (5–16). Such deficiencies in trial reporting result in an overestimation of treatment effects and an underestimation of harms in the published literature, resulting in potentially serious consequences for patients and for health care systems.

The well-known 2004 case of the New York Attorney General against GlaxoSmithKline drew attention to the importance of ensuring that clinical trials are conducted in a transparent way and that all research results are available to the scientific community. In this case, the Attorney General prosecuted GlaxoSmithKline for allegedly using selective and biased results of clinical trials to promote off-label prescriptions of Paxil (17, 18). The company, according to the Attorney General's

statement, hid the fact that it had conducted several clinical trials on the safety and effectiveness of its antidepressant Paxil for the treatment of children and adolescents. It also selectively published only positive data, whereas the trial results were overall negative and raised safety issues. Alison Bass in her book *Side Effects* and an analysis of the literature document in detail the selective publication practices in this case (14, 18). At the time, the case highlighted the importance of trial transparency and generated a demand for better research publication practices.

In response to such selective reporting of trials, the International Council of Medical Journal Editors (ICMJE) issued a statement requiring the registration of clinical trials before beginning the recruitment of human subjects as a condition for publication of subsequent reports (19). Likewise, a broad range of stakeholders met during the Cochrane Colloquium in Ottawa, Canada, and developed the Ottawa Statement calling for transparency of clinical trials by registration of protocols and public disclosure of trial results (3, 20).

Trial transparency was discussed in 2004 at the Mexico Global Forum and Ministerial Summit on Health Research (Mexico Summit), where it was recommended that WHO engage in trial registration and that all major stakeholders improve access to research findings (21).

The recommendations of the Mexico Summit prompted the creation of the International Clinical Trial Registry Platform (ICTRP) by WHO in 2005. ICTRP coordinated development of international standards for registration of clinical trials, which were launched in 2006. These standards urge the prospective registration of all clinical trials (followed by reporting of amendments to the protocol during trial implementation) in a publicly accessible registry that meets certain criteria (22). The minimum data set that needs to be registered is presented in Table 1. WHO adopted English as the working language of international trial registration and its ICTRP clinical trials search portal. WHO international standards were endorsed by ICMJE (23) and were also supported by the Ottawa Group (24).

As shown in Figure 1, a growing number of countries—including Argentina, Brazil, and the United States of America as well as the European Union—are requiring trial registration through legislation or through the establishment of procedural guidelines (25–29). The U.S. regulations specifically require registration of all phase 2–4 trials of pharmaceutical products and medical devices with ClinicalTrials.gov (25). Furthermore, major funding agencies and ethics review committees are increasingly requiring trial registration (30). Leading international groups such as the Ottawa Group (20) are further pressing for these requirements. Policy makers at the highest level have continued to stress the importance of trial registration, with a new call for trial registration being issued at the Bamako Ministerial Forum in 2008 (31).

**TABLE 1. World Health Organization trial registration data set<sup>a</sup>**

1.	Unique trial number
2.	Trial registration date
3.	Secondary identification
4.	Funding source(s)
5.	Primary sponsors
6.	Secondary sponsors
7.	Responsible contact person
8.	Research contact person
9.	Brief trial title
10.	Official scientific title
11.	Countries of recruitment
12.	Condition
13.	Interventions
14.	Inclusion/exclusion criteria
15.	Study type
16.	Anticipated start date
17.	Target sample size
18.	Recruitment status
19.	Primary outcome
20.	Key secondary outcomes

<sup>a</sup> This data set is often also called the minimum trial registration data set. The elaborated version of this list of data can be found on the World Health Organization website at: <http://www.who.int/ictrp/network/trds/en/index.html>.

In the Americas, trial registration was discussed at the meetings of PAHO/WHO (32), and the health authorities of the countries of the Americas approved the PAHO Policy on Research for Health. Furthermore, PAHO's Ethics Review Committee requires clinical trial registration as a prerequisite for ethics approval (33). This [web link](#) illustrates the growth of registration of new clinical trials in some countries of the Americas following these recommendations.

In 2010, the World Health Assembly approved the WHO Strategy on Research for Health. Both PAHO and WHO documents call for clinical trial registration in line with WHO international standards. The 7th revision of the Declaration of Helsinki in 2008 contributed to this process by clearly identifying trial registration and results disclosure as an ethical requirement for research involving humans (34, 35), as did the 2010 CONSORT guidelines for reporting of trials (36).

The historical development of trial registration and results disclosure initiatives is summarized in Figure 1. Key factors that enabled the development of a worldwide culture of trial transparency include the awareness of publication biases, opportunities provided by the development of the Internet, feasibility demonstrated by initial trial registries, WHO international standards, and the commitment of various stakeholders.

## RATIONALE SUPPORTING TRANSPARENCY OF CLINICAL TRIALS

Numerous overlapping ethical, scientific, clinical, and policy reasons can be invoked in support of registration, results reporting, and overall transparency of clinical research (15, 20, 32). Transparency

FIGURE 1. Timeline of trial registration and results disclosure initiatives at the international level and in the Americas



**Note:** International: NY vs GSK: The case of New York Attorney General against GlaxoSmithKline (17, 18); ICMJE: International Council of Medical Journal Editors (ICMJE) statement on trial registration 2004 (19); OS I: Ottawa Statement part one (20, 24); Mexico Summit: Mexico Global Forum and Ministerial Summit on Health Research (21); WHO-ICTRP: World Health Organization/International Clinical Trials Registry Platform (22); ICMJE: International Council of Medical Journal Editors statement 2005 (49); OS II: Ottawa Statement part 2 (23); WHO Standards: WHO international standards for trial registration (22); OS III: Ottawa statement part 3, results disclosure (24); ICMJE: ICMJE statement 2007 (23); WHO Portal & Network: WHO search portal and registry network (30); CIHR-PROCTOR: Canadian Institutes of Health Research—Public Release of Clinical Trials Outcomes and Results 2008 (58, 59); DoH 2008: Declaration of Helsinki (34, 35).

Americas: CIHR-RCT: Canadian Institutes of Health Research trial registration policy 2004 (43); SciELO/LILACS: Scientific Electronic Library Online/LILACS database journals require trial registration 2006 (44); FDAAA: Food and Drug Administration Amendments Act 2007 (25); RELEM: Buenos Aires Declaration on Ethics and Clinical Trials 2008 (48); Brasil regulation: Brazil regulation on trial registration (27, 28); Argentina regulation: Argentina regulation on trial registration (29); PAHO Policy on Research: PAHO Policy on Research on Health 2009 (32).

enables the effective use of trial findings in policy and health care decision making and contributes to advancing science and innovation.

Academic freedom and the right to publish are key values in the scientific community and are essential for public trust. When members of the public and the scientific community can verify what trials have been undertaken and whether results have been published, public confidence in clinical trial evidence should arguably increase. Many controversies related to hiding and misrepresenting clinical trials data involve academic researchers (18, 37). Other controversies indicate that academic researchers participating in clinical trials can be prevented from publishing research results or be put under pressure not to do so (38, 39). It is expected that obligatory trial protocol registration and full reporting of results will help to prevent these practices and will give researchers a strong argument to resist such pressures (36, 40).

Other ethical and policy reasons relate to the interests and rights of research participants. When people agree to participate in research, they do so with the understanding that the new knowledge will benefit others and the greater good of humankind, and therefore they expect these results to be publicly available for future use. The research community owes it to research participants that relevant information, which may be of interest for their future health care or for the health care of their community, is made available for that purpose. This is a moral obligation to participants and is in line with core ethical principles for research (34).

Adequate trial registration can potentially reduce unnecessary duplicate and unethical research and facilitate enhanced governance and accountability of research.

## CLINICAL TRIAL REGISTRIES

Many different kinds of clinical trial registries exist in the public and private domains—for example, country- and region-specific registries and corporate (sponsor driven) registries. The amount and type of information in these registries differ; many have at least some information in English but may also have more details in the language of the country or the region.

Such a diversity of registries pointed to the need to establish basic principles and to develop international standards to guarantee unbiased and high-quality information and develop a standardized terminology and a common understanding of key concepts. It is expected, for example, that the use of identical key words would promote organization of the information and facilitate the retrieval of records.

WHO international standards and their implementation address this need. Clinical trial registries that follow WHO standards and feed into its ICTRP search portal are called WHO primary registries. As of December 2009, 10 WHO primary registries and Clinical Trials.gov meet the criteria of WHO standards and/or ICMJE (30). One or several registries are in each WHO region (Table 2). New registries continue to be developed. For example, the registry of the Republic of Korea

**TABLE 2. WHO primary registries and ClinicalTrials.gov by WHO region, language, area of coverage, and number of trials registered**

WHO region	WHO primary registries and ClinicalTrials.gov	Registry language besides English	Accepts trials from	No. of trials registered <sup>a</sup>
Africa	Pan African (PACTR)		Africa	12
Americas	ClinicalTrials.gov		International (U.S. based but accepts trials from any country)	80 975 <sup>b</sup>
Eastern Mediterranean	Iranian (IRCT)	Persian	Iran	172
Europe	ISRCTN Netherlands	Dutch	International Netherlands	8 066 1 964
	National (NTR) German (DRKS)	German	Germany or in German language	130
Southeast Asia	Chinese registry (ChiCTR)	Chinese	China	558
	Indian (CTRI)		India, intends to expand to the region	504
	Sri Lanka (SLCTR)		Sri Lanka	43
Western Pacific	Australia–New Zealand (ANZCTR)		International (accepts from any country but primarily Australia and New Zealand)	3 539
	Japanese network (3 registries)	Japanese	Japan	
	UMIN			2 596
	JapicCTI			331
	JMACCT CTR			33

**Note:** PACTR: Pan African Clinical Trials Registry, IRCT: Iranian Registry of Clinical Trials, ISRCTN: International Standard Randomised Controlled Trial Number, NTR: National Trial Register, DRKS: German Clinical Trials Register, ChiCTR: Chinese Clinical Trials Register, CTRI: Clinical Trials Registry–India, SLCTR: Sri Lanka Clinical Trials Register, ANZCTR: Australian and New Zealand Clinical Trials Registry, UMIN: University Hospital Medical Information Network, JapicCTI: Japan Pharmaceutical Information Center–Clinical Trials Information, JMACCT CTR: Japan Medical Association Center for Clinical Trials Clinical Trial Registry.

<sup>a</sup> Data from registries' websites as of 5 November 2009. Numbers from PACTR and JAPIC CTI are estimates.

<sup>b</sup> Breakdown by regions of the Americas is presented in Figure 1.

joined the WHO primary registries network in 2010 and the Cuban Public Registry of Clinical Trials in 2011.

Two specific issues are worth pointing out with respect to these registries. First, although ClinicalTrials.gov provides data to the WHO search portal, it is not a primary registry in the WHO registry network. ClinicalTrials.gov, which was established by U.S. federal law and is operated by the U.S. Government, must comply with the Food and Drug Administration Amendments Act (FDAAA) and other applicable U.S. laws. Thus, it cannot commit to WHO (or any other) standards and procedures that may diverge from U.S. federal requirements now or in the future (Deborah Zarin, personal communication, October 2010). Second, for historical reasons, and in the context of WHO standards, which allow only one primary registry per country, the Japanese network of three registries is considered by WHO as one national registry.

These registries supply minimum data sets to the WHO/ICTRP portal in English, while some offer the possibility of registering trials in languages of their country or region as follows: Chinese, German, Dutch, Persian, and Japanese (Table 2). Some of these reg-

istries post links to publications; ClinicalTrials.gov also developed fields to capture the results of registered clinical trials as required by the FDAAA of 2007. The results are cross-referenced to the protocol fields (25).

At the end of 2010, none of these registries offered the opportunity to register a trial in United Nations/WHO official languages other than English and Chinese. For example, no primary registry was accepting data in Spanish, Portuguese, or French—all official languages in the Americas.<sup>5</sup> At the time, ClinicalTrials.gov was the only registry in the Americas providing data to the WHO/ICTRP search portal and it captured trial data in English only.

## CLINICAL TRIALS AND THEIR REGISTRATION IN THE AMERICAS

According to the WHO/ICTRP search portal, in October 2009 there were about 90 000 registered trials worldwide and approximately 48 000 (53.3%) were re-

<sup>5</sup> There is now a primary registry in Cuba, which may have data in Spanish.

cruiting participants in the Americas. Most of these trials were registered at ClinicalTrials.gov, and some were registered in the International Standard Randomised Controlled Trial Number registry or the Australian and New Zealand Clinical Trials Registry. At that time, ClinicalTrials.gov contained about 55 000 trials recruiting in the Americas: about 6 500 in Canada, 44 000 in the United States, and 5 000 in other countries of the Americas (Figure 2). It is important to emphasize that these numbers are approximate. Some trials may end up being counted more than once because multiple registrations were done—that is, the same trial might be registered in more than one primary registry and in ClinicalTrials.gov, as discussed in the evaluation section.

Language barriers and translations of records are probably significant obstacles to registration of trials that occur in a large part of the Americas. This most likely resulted in an underrepresentation of clinical trials conducted in Latin America and the Caribbean.

### REGIONAL AND COUNTRY INITIATIVES RELATED TO TRIAL REGISTRATION IN THE AMERICAS

Countries of the Americas have begun to address trial registration in different ways: some started developing national clinical trial registries, while others focused on regulation and legislation requiring trial registration in available registries in compliance with WHO registration standards. Some have even taken initiatives related to the public disclosure of trial results. The United States and Argentina have developed regulations for trial registration (25, 29). Some countries opted to encourage voluntary registration (27, 28). Overall, most countries have yet to develop regulations related to trial registration that would en-

sure compliance with WHO international trial registration requirements (41, 42).

There is support for trial registration at other levels, including public funders and editors. For example, the Canadian Institutes of Health Research has been requiring registration of the randomized controlled trials it funds since 2004 (43). In 2010, the trial registration was included in the revised *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans, TCPS-2*, and it now requires registration and results disclosure of all trials funded by the [Canadian Institutes of Health Research](#) or two other federal funding agencies (30). Editors of scientific journals in the Americas joined the ICMJE initiative. In 2006, journals participating in the Scientific Electronic Library Online (SciELO) network agreed on requiring trial registration in line with ICMJE requirements (44).

There are also numerous initiatives related to the creation of national trial registries, with various degrees of compliance with international standards. ClinicalTrials.gov, launched in 2000, has expanded over the years to meet the national and WHO/ICMJE requirements and now enables registration of all trials, including phase 1 as well as observational studies (45).

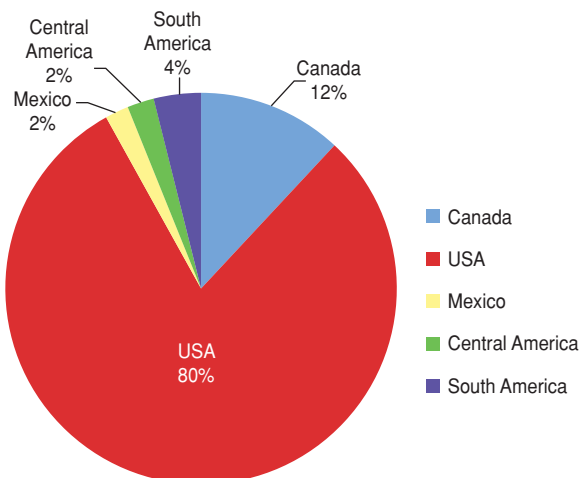
Other examples of registries in the region include: LatinRec, based in Bogota, Colombia (46); the [Peruvian registry](#); the [Cuban registry](#); the [Brazilian registry](#) (27, 28); and the [Argentinean registry](#) (27–29). In 2010, none of these registries in the region met the criteria of WHO international standards.

Although countries are able to retrieve information about registered trials from the WHO search portal, local needs and policy may require data beyond the 20 items of the minimum WHO data set. Hence, some countries might decide to establish their own national registries. These country-specific registries are susceptible to duplication and compatibility problems. Furthermore, a proliferation of registries can result in confusion and access difficulties because of information overload.

### POTENTIAL ROADMAP TOWARD TRANSPARENCY OF CLINICAL TRIALS

We propose a roadmap for implementation of clinical trial registration in the Americas, taking into consideration the needs and realities of the member states and the global context in which registration and clinical research take place (32, 47). This roadmap is based on the premise that implementation of existing international standards for clinical trial registration is a priority and recognizes the significant challenges that implementation will face in different regulatory, economic, financial, political, and organizational contexts. The roadmap also proposes some initiatives under the assumption that PAHO/WHO will continue leading the development of international standards and good research practices for public disclosure of trial results and their implementation. The roadmap is summarized in Table 3.

FIGURE 2. Trials registered with ClinicalTrials.gov in the Americas, November 2009 (N = 54 667)



### Implementation of WHO international standards for prospective registration of trial protocols at the global level, with emphasis on the Americas

Implementation of international standards will require simultaneous work on national regulations and other forms of support for trial registration by various constituencies, including national regulatory agencies, research ethics committees, consumers and patient representatives, the pharmaceutical industry, guideline developers, publishers and editors, research funders, academia, and other stakeholders (e.g., the science and technology sector, research and professional associations). We believe PAHO/WHO can be a suitable convener by keeping its lead in the field, supporting the uptake of international standards, facilitating technical cooperation, promoting collaboration and harmonization, monitoring and assessing progress, and supporting the development of regulatory and legislative frameworks. Important steps have been outlined in the Declaration of Helsinki (34, 35), the Ottawa statement (3, 20, 24), the Buenos Aires Declaration on Ethics and Clinical Trials (48), the requirements of the ICMJE and other journal editors (19, 23, 44, 49), trial reporting guidelines in the EQUATOR Network (50) [e.g., the CONSORT 2010 Statement (36)], policy documents (31–33), and numerous educational initiatives promoting trial registration and results reporting as conditions for research ethics approval (summarized in Figure 1).

We also think PAHO/WHO is well placed to promote the creation of a regional WHO primary registry that would facilitate access to clinical trial regis-

tration in the Americas. Such a registry would offer a range of benefits: a broader representation of clinical trials in the Americas, equitable service to researchers, consistency in translations, focus on compliance, and efficiencies and cost-effective use of resources.

Many countries would find it a sound option to use the shared regional primary registry. Although such a registry would not be country based and controlled, trials could be listed by the country where the trial is implemented. This would enable participating countries to reach a better understanding of the resources invested in research, the available expertise, and the research taking place within their boundaries. The opportunity to register trials in the languages of the region is expected to stimulate registration. Moreover, such a multilingual registry could further enable collaboration with other countries where these languages are spoken.

A common software platform (CSP) could be created (ideally under the lead of, or in coordination with, PAHO/WHO) in an open source format that reduces duplication and allows adaptation so that countries might share such a CSP that feeds the essential 20 variables to the WHO/ICTRP search portal and at the same time allows local adaptations (e.g., different interface, capturing additional data) (47).

In 2009, PAHO/WHO signed a cooperation agreement with the Council for Health Research for Development to jointly collect, organize, and present data on national health research systems in the Americas through specially designed [platform](#). This allows for capturing essential data and knowledge about de-

**TABLE 3. Roadmap toward transparency of clinical trials and authors' view on a potential role of PAHO/WHO**

1. Implementation of (WHO) international standards for prospective registration of trial (protocols) at the global level, with special emphasis on the Americas
  - a. Set up a registry for the Americas that would enable entries in languages of the region
  - b. Develop or enhance national regulations with compliance mechanisms (sanctions)
  - c. Promote uptake of trial registration as preconditions of ethics review
  - d. Ensure support and buy-in by ethics organizations, journals, professional associations, academia, and industry
  - e. Promote international compliance with international standards
2. Evaluation of trial registration practice and of (WHO) international standards
  - a. Evaluation of trial registration practice
    - a.1. Contributions of various stakeholders
    - a.2. Evaluation of registries that meet WHO and ICMJE criteria
      - a.2.1. Number of registries
      - a.2.2. How they comply with international standards (fields)
      - a.2.3. Quality of data in registries
      - a.2.4. Timing of registration: late versus prospective registration
      - a.2.5. Evaluate specific items added by registries beside the (WHO) international standards data set
  - b. Evaluation of (WHO) international standards
    - b.1. Revisit standards
    - b.2. Analyze registry items from the perspective of
      - b.2.1. The evidence that needs to be achieved
      - b.2.2. Results reporting
      - b.2.3. Outcome reporting bias and publication bias
3. Development of international standards for public disclosure of trial results and findings
  - a. Engage in a dialogue with WHO headquarters and other regions
  - b. Collaborate in development of international standards
  - c. Promote regulatory initiatives and compliance mechanisms on national and international levels
  - d. Promote results disclosure commitment as preconditions of ethics review
  - e. Ensure support and buy-in by ethics organizations, journals, professional associations, academia, and industry

**Note:** PAHO/WHO: Pan American Health Organization/World Health Organization, ICMJE: International Council of Medical Journal Editors.

velopments of clinical trial registration and legislation. The agreement has also led to the development of [training modules](#) and the identification of key partners in countries that maintain the platform site promoting local ownership (51, 52).

PAHO/WHO has proposed and supported the development of an open source platform to be used as the backbone for national registries (27, 51). This should increase compatibility and enhance consistency in the submission of data to WHO's search portal yet allow for flexibility and adaptation to local needs. The country-specific registries based on this open source platform can include customized interfaces in different languages and custom features and fields. Furthermore, it would be useful to explore options to develop and offer access to a regional primary registry that would allow registration in languages of the region (e.g., Spanish, Portuguese, French), and this could perhaps be done under the auspices of PAHO/WHO. This would allow countries to focus on compliance, especially if they are not developing a national or primary registry. It could also enhance efficiencies and consistency in translation and data management.

### Evaluation of trial registration practice and revision of international standards

The field of trial registration has been rapidly evolving, and both registry staff and registrants are faced with a steep learning curve. New registries are being created, while existing ones are expanding and adapting to WHO international standards. International standards for trial registration were launched by WHO in 2006 (22) with the idea that potential revisions would be implemented as needed. As the field develops, it is expected that the public will soon be able to systematically follow trials from registration to publication and implementation of research results.

Evaluation and monitoring of progress are essential in assisting member states and taking corrective action when needed. Indicators for monitoring and evaluation may include compliance with international standards, such as the timeliness of registration, the quality of data provided, how well these data address the needs of different stakeholders, incorporation of unpublished clinical trials in systematic reviews, and the impact on bias.

With the launch of WHO international standards and the events and consensus building that led to the PAHO and WHO policy documents on research for health, considerable progress was achieved toward establishing a global trial registration culture. Implementation of international standards for trial registration remains a challenge but one that increasingly seems within reach: the number of registered trials has grown significantly since 2004 (42). Although there is plenty of room for improvement, data are flowing in and increasing awareness. A recent study noted that by 2007 a third of the clinical trials published in high-ranked journals had been registered and that in-

creased registration was associated with higher quality in results reporting (53).

Data also show that prospective registration—that is, before recruitment of the first trial participant as opposed to registering clinical trials after the enrollment of participants—is progressing. The Australian and New Zealand Clinical Trial Registry reports that about 41% of the 2 618 trials registered between 2006 and 2009 were registered prospectively, while the remainder were registered with a median delay of 146 days (54).

Some studies indicate that there is a need to improve the completeness and quality of data entries and to fulfill requirements of WHO standards (55–57). For example, a recent study highlighted differences in data quality among registries and suggested that the structure of the registry fields may be associated with this difference (55). Increasingly, researchers find the completeness and quality of data in registries so disturbing that they argue for the publication of the full protocol (13, 45, 57). Some primary registries have developed additional fields to capture more data than is required by the WHO international standards. The analysis and monitoring of these additional data will likely influence the evolution of international standards.

Some trials are registered twice in the same registry, while some are registered simultaneously in several registries (42). Registries and the WHO/ICTRP search portal are developing deduplication strategies, including posting on the registry website the identification number issued by other registries, to facilitate cross-referencing. It is important to note that duplicate registration in more than one registry is sometimes justified. For example, many jurisdictions require registration of trials in a specific, usually country-based, registry (e.g., FDAAA and ClinicalTrials.gov). In the case of multicountry studies, this practice often leads to unavoidable duplicate registration. Overall, duplicate registration is not an issue if it is clearly indicated in each registry, and it is certainly a minor inconvenience compared with not registering a trial at all.

### Development of international standards of public disclosure of trial results and findings

As important as prospective registration of trial elements is, it does not by itself correct the problem of selective reporting bias (41, 57). Trial registration must be complemented by mandatory reporting of the results of registered trials to ensure that the public has transparent and complete evidence for making informed health-related decisions. It has been recognized that public disclosure of trial results is necessary because not all trial outcomes may be reported in peer-reviewed journals. It goes beyond publication in peer-reviewed journals and complements it (58–60). Consequently, WHO international standards for trial registration need to be complemented by international standards for results disclosure.

Considering initiatives including the Ottawa statement (20) and PROCTOR (58, 59) and calls and declarations about open access in the [Budapest, Berlin](#), and

Salvador declarations on open access (61); the 2008 revision of the Declaration of Helsinki (34, 35); plus local and regional regulatory developments, PAHO/WHO is in an advantageous position to advance the development of international standards for results disclosure and contribute to their development. PAHO/WHO can broker discussions and deliberative dialogues among stakeholders on implementation of such standards and their monitoring and evaluation, promoting transparency and compliance, coherence, and coordination. It can also facilitate discussion about further national and international initiatives, linking them to other efforts such as those aimed at improving knowledge translation for development of health policy.

## Conclusion

The final goal of clinical research transparency is to improve people's health and trust in research. Prospective trial registration and public disclosure of results will advance these efforts by providing access to more complete and accurate data and thus will facilitate evidence-informed decision making. While trial registration advanced significantly in a relatively short time, having developed international standards, numerous registries, and the WHO search portal, the results disclosure merits more international coordination starting with development of international standards and creation of repositories.

Prospective trial registration has gained tremendous support and momentum. During the past 4 years several high-quality registries have been developed and WHO has implemented a search portal (ICTRP) that allows for retrieving information about registered clinical trials according to different criteria. In a short time, a wealth of information that otherwise would have been missed or retrieved with great delay and effort has been accrued and is available to inform secondary research (e.g., systematic reviews and syntheses of the evidence) and provide access to more reliable data about clinical trials. Given PAHO/WHO's leadership in setting norms and standards and convening countries to join efforts working for the greater good, the organization may be well placed to play an important role in supporting its member states in implementing trial registration, promoting adherence, and engaging stakeholders. In accordance with the objectives of its policy on research for health and the WHO strategy on research for health, PAHO can advance good research practices by engaging in the

development and implementation of complementary standards for public disclosure of trial results.

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## SINOPSIS

### Registro prospectivo y comunicación de los resultados de los ensayos clínicos en la Región de las Américas

*El objetivo de este artículo es proponer una hoja de ruta que fomente la transparencia de los ensayos clínicos en la Región de las Américas mediante el registro prospectivo de los ensayos y la comunicación de sus resultados. Esto brindará un acceso más amplio a datos más completos y exactos, y facilitará la toma de decisiones fundamentada en datos probatorios y la participación en las investigaciones clínicas. En consecuencia, debería tener una repercusión positiva en la salud de la población y promover la confianza en la investigación médica. Después de identificar las iniciativas existentes y analizar los registros de ensayos clínicos según las normas de la Organización Mundial de la Salud (OMS) para el registro de ensayos, se propone una hoja de ruta para salvar las brechas y promover la transparencia. El análisis demuestra que, a pesar de las numerosas iniciativas regionales y de los distintos países, hay un subregistro de los ensayos clínicos que tienen lugar en zonas no anglohablantes de la Región de las Américas. Se propone una hoja de ruta para mejorar la gobernanza en la investigación y las buenas prácticas clínicas mediante una mayor transparencia en los ensayos clínicos. La hoja de ruta propuesta incluye estrategias para ejecutar las normas internacionales de la OMS sobre el registro de los ensayos clínicos, formular normas internacionales de comunicación pública de los resultados de los ensayos, y una función potencial de la Organización Panamericana de la Salud.*

**Palabras clave:** Ensayos clínicos como asunto; normas; Américas.

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