

Research Article

Clinical research in Latin America: scientific production in high impact clinical research journals from 2000 to 2010

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ABSTRACT

Background: Scientific production has long been dominated by a few countries such as the United States, Europe and Japan. Historically Latin American countries have contributed marginally to the world's scientific production, however important changes are now taking place in the geography of scientific research.

Methods: In order to determine the current contribution of Latin America to global clinical research and whether the region has been participating in the growth of internationally collaborative research we reviewed the literature in 10 high-impact medical journals between 2000 and 2010. We manually searched original articles in 10 journals that have a strong focus on clinical research and had the highest impact factors in their fields during the study period. We identified a total of 1047 original articles published.

Results: Our results show that Latin America was a minor contributor of research published in high impact journals with only 4 (0.38%) of the articles citing a corresponding author affiliated with a Latin American institution. Furthermore, only 23 articles (2.2%) cited non-corresponding authors from Latin America in contrast to 358 articles (34.2%) in which all the authors were affiliated with US institutions.

Conclusions: Although these results show limited contribution from Latin America to the production of health and clinical research, it also shows that Latin America is represented in the most competitive journals given the relative lack of research infra-structure, training and challenges with language. Factors such as GDP and investment in research may play a significant role, but may not be the only contributing factors for this scenario.

Keywords: Clinical research, Publication, Impact factor, Latin America

INTRODUCTION

The production of scientific manuscripts has long been dominated by the United States, Europe and Japan, which have longstanding traditions and infrastructures that support research. Such infrastructures include greater funding opportunities and high-quality academic centers and research institutions.¹⁻³ Currently, important changes are taking place in the geography of scientific research. To start, in many "emerging" countries such as the so-called BRICs (Brazil, Russia, India and China), research

is now considered a critical component of their overall development strategy to create knowledge-based economies. For example, China and India made significant investments in higher education and research allowing their universities graduate millions of scientists and engineers. India launched an unmanned mission to the moon in 2008, while China recently announced plans for human lunar landings.⁴ China is also now the second largest producer of scientific publications after the US.⁵ While much of this research is published in Chinese-language journals³ and is not widely cited by other

researchers, the quality is improving and Chinese studies are increasingly being published in the world's leading journals.^{6,7}

The second major trend that is taking place in research is the rapid increase in international collaboration between 'developed' and developing countries.³ This is being driven by a number of global issues including climate change, the search for sustainable energy resources, and the need to improve health through affordable large-scale clinical trials.⁸ One example of this is the recent creation within the US National Cancer Institute (NCI) of its Center for Global Health⁹ and the launch of the United States-Latin America Cancer Research Network, which is a collaboration between the US National Cancer Institute and institutes in Argentina, Brazil, Chile, Mexico and Uruguay.¹⁰

Scientific research has often lagged in Latin America, but this is changing. The most obvious example is Brazil, a country whose economy is surging and is becoming a research powerhouse in number of fields, including bioenergy, plant biology and tropical medicine. Still, Latin America's current contribution to the total production of clinical research is not clear. Research efforts in Latin America have historically been directed towards neglected diseases such as malaria, leishmaniasis, and Chagas disease, with most of the research conducted in Mexico, Brazil, Chile and Argentina. Recent statistics on clinical research found that Latin America may have represented 2% of the total world production of clinical research with close to 0.3% published in 50 top biomedical journals (1995-2002).^{2,11} However, these data are more than 10 years old and the current situation in the region remains unclear.

In this study we reviewed the literature in 10 high-impact medical journals between 2000 and 2010, to determine the current contribution of Latin America to global clinical research and whether the region has been participating in the growth of internationally collaborative research.

METHODS

Manuscript search

We manually searched original articles published from 2000 through 2010 in 10 journals that have a strong focus on clinical research and had the highest impact factors in their fields during the study period (Thomson Reuters, Copyright 2011). Five are general medicine journals - New England Journal of Medicine (NEJM), The Lancet, Journal of the American Medical Association, (JAMA), Annals of Internal Medicine, BMJ - the other five are specialty journals: Circulation (cardiology), Gastroenterology, Clinical Infectious Disease, Brain (neurology), and American Journal of Psychiatry. We excluded any journals that began publishing after the study period began in 2000 (e.g., Lancet Neurology).

For our analyses, we selected all the original research articles published in these journals during the randomly chosen sample month of July, excluding editorials, opinion articles, letters to the editor, reviews and education pieces. Two collaborators (GS, MH) independently searched the journals for original research articles published from July 2000 through July 2010. Any discrepancies were resolved by consensus, and two authors (EC, FF) were consulted if needed. We then extracted the data for our predefined outcomes of interest from each article: publication year, journal, title of the article, country of the corresponding author's institutional affiliation, specialty of the research, number of authors, and any information on the involvement of researchers from other countries in the study.

For the purposes of this study, we divided the world into six regions adapting the original geographical subdivisions: North America (US and Canada), Europe (Western and Eastern Europe), Asia (including Russia, India, and Middle Eastern countries), Africa, Australia (including New Zealand), and Latin America (Mexico, Central America, South America and the Caribbean countries).

Data synthesis and analysis

We quantified the number of publications per year, per journal, and the researchers in different countries involved in each study. We defined each study's specialty and country of origin using the information from the corresponding author's institutional affiliation, as this researcher is usually responsible for study design, data analysis, and writing the manuscript.¹²

In order to assess the collaboration of Latin American authors with scientists from other countries, we analyzed articles where authors from Latin America were included, but not as the corresponding author. We extracted the information of the country of affiliation from all authors in each article and used the articles that had authors from the US (to serve as a reference for Latin American authors alone) or in collaboration with authors from the US and countries from other regions. We then divided the total number of authors in each paper into tertiles of 1-5, 6-10, and ≥ 11 .

RESULTS

We identified a total of 1047 original research articles published in the 10 journals during the month of July in the years 2000 through 2010. Three articles were excluded because they did not contain information on the corresponding author's institutional affiliation (all were from the NEJM: one in 2005 and two in 2006). This left a final analytic sample of 1044 articles. The corresponding authors for nearly half the studies were affiliated with North American institutions (512 articles, 49.0%) followed by Europe (423 articles, 40.5%), Asia (69 articles, 6.6%), Australia (29 articles, 2.8%) Africa (7

articles, 0.7%) and Latin America (4 articles, 0.4%). The corresponding authors for nearly three-quarters of all the studies (73.5%) were from five countries: US (464 articles, 44.4%), UK (160 articles, 15.3%), France (49 articles, 4.7%), Canada (48 articles, 4.6%), and Germany (47 articles, 4.5%). The four Latin America studies (0.4%) were all from Brazil (Table 1).

Table 1: Number and percentage of publications per country.

Countries	Number of publications	Percent
USA	464	44.4
UK	160	15.3
France	49	4.69
Canada	48	4.60
Germany	47	4.50
Brazil	4	0.38

Three of the four Brazilian studies were published in the *Lancet* (one in 2001, two in 2007); the other was published in *Gastroenterology* (2004). The *Lancet* publications were in the field of infectious disease. One was a report of two cases of yellow fever and the adverse effects of a vaccine, which had 23 authors (2001); the other two were randomized clinical trials of antiviral

agents for HIV, with 14 and 13 authors respectively, and the same corresponding author for both (2007). The *Gastroenterology* paper had 9 authors and investigated how gene polymorphisms in *Helicobacter pylori* cagA strains decrease the risk of reflux esophagitis.

In more than a third of the articles (358 articles, 34.2%) all the authors were from the US; about half of these studies had between 6 and 10 authors (173, 16.5%). We found only one article in which all the authors were from Latin America (Brazil; *Gastroenterology* 2004). As for international collaboration, Latin Americans contributed to 23 articles (2.2%): 8 with US authors only (0.76%), and 15 (1.4%) with authors from various countries including the US (Table 2). Of these 23 articles, 7 appeared in *The Lancet* (30.4%) and 5 in the *Annals of Internal Medicine* (21.7%). These articles usually had 11 or more authors (62.5% of articles with US authors, and 73.3% with all other authors (Table 2). The authors were from Argentina, Brazil, Chile, Colombia, Mexico and the West Indies, with authors from the first three countries making the most frequent contributions. Most of the articles we analyzed did not include information on the specific contributions of each author, or their affiliations, which would have been useful in more precisely determining the roles of these Latin American authors.^{12,13}

Table 2: Number of publications according to journal and number of authors coming from US authors only, collaborations between US and LA and other countries and LA.

Journal	USA			USA/LA			Other/LA		
	1 to 5	6 to 10	≥11	1 to 5	6 to 10	≥11	1 to 5	6 to 10	≥11
NEJM	9	17	13	0	1	1	0	0	1
Lancet	1	4	2	0	0	1	0	1	5
JAMA	18	35	12	0	1	0	0	1	1
Annals of IM	15	12	7	1	0	1	0	1	2
BMJ	9	1	2	0	0	0	0	0	0
Circulation	7	20	6	0	0	1	0	1	1
Gastroenterology	10	15	4	0	0	0	0	0	0
Brain	6	9	1	0	0	1	0	0	1
Clinical Infectious Disease	23	23	9	0	0	0	0	0	0
AJP	24	37	7	0	0	0	0	0	0
Total collaborations (381)	122	173	63	1	2	5	0	4	11

We also found that US authors collaborated much more frequently with authors from regions other than Latin America (193 vs. 8 studies). European authors contributed more with authors from other regions than Latin America (126 vs. 3 studies), but US authors collaborated with Latin American authors at nearly twice as often as Europeans (4.7% vs. 2.4%).

DISCUSSION

The In this study, Latin America was a minor contributor of research published in high impact-factor general

medicine and specialty journals, with only 4 (0.38%) of the articles published in the months of July from 2000 through 2010 citing a corresponding author affiliated with a Latin American institution. Furthermore, only 23 articles (2.2%) cited non-corresponding authors from Latin America, in contrast to 358 articles (34.2%) in which all the authors were affiliated with US institutions.

Our results support other reports of Latin America's limited contribution to the production of health and clinical research. A 2009 *Lancet* editorial¹¹ claimed that Latin America contributed 2% or less to the world's

production of health research, though it did not indicate how these numbers were calculated. A study of the contributions by the world's regions to 50 top biomedical journals between 1995-2002 found that Latin American accounted for only 0.3% of the articles,² while an earlier study that evaluated Latin American researchers' contributions to the field of nephrology in the 1980s and 1990s found that less than 1% of the peer-reviewed publications in the Institute of Scientific Information and Medline databases were from the region.¹⁴

At the same time our results also indicate that Latin Americans were co-authors on nearly six times the number of papers whose contributing authors were from outside the region than the number of publications on which they were themselves the contributing author [23 (2.2%) vs. 4 (0.38%)]. This is in line with international trends in which collaborative and outsourced research are growing tremendously.³

It is important to put these findings into context. While the numbers are very small, we looked at studies from 10 clinical journals with the highest impact factors in their fields. They include some of the most pre-eminent journals published/in existence, and their rejection rates are correspondingly high. Our findings are broadly similar to those of the earlier Soteriades et al study,² but that study investigated the contributions of the world's regions to the top 50 biomedical journals. Our focus was much focused in terms of both the specialties and number of journals we looked at. It therefore seems likely that a larger percentage of articles from Latin America might be getting published in lower impact factor journals.

Although our findings may indicate a relative increase in the representation of Latin America in journals of high impact factor in the past decade, it is important to underscore the heterogeneity of our findings in terms of countries contributing to this pool of articles published in major journals. Indeed the four studies that originated in Latin America were all from Brazil. The countries in Latin America exhibit great diversity in terms of resources and infrastructure that support research, including income per capita, Gross Domestic Product (GDP), health research budgets, academic centers dedicated to research, and private investment in health research. Brazil, Argentina, and Chile were the most important contributors in this study and they also have some of the highest GDPs in Latin America. In 2010, Brazil's GDP was the world's seventh largest-larger than Italy's and smaller than the United Kingdom's. Brazil currently invests about 1.2% of its GDP in research, which is twice the average in the region. It doubled its per capita research spending (from 0.7% to 1.2%) between 1996 and 2008, and has announced plans to increase research spending to 2.5% of GDP by 2022,^{3,15-17} which is close to what the US currently spends on research. In the meantime, Brazil's share of the world's scientific papers rose 63% from 1.7-2.7%, between 2002 and

2008.^{16,17} Collaboration is also increasing: 30% of Brazilian scientific papers have foreign co-authors.¹⁷

But factors other than GDP also play a role in research production. Venezuela has a relatively high GDP, but it was not represented in any of the articles we searched. Colombia's scientific output was lower than other leading countries in the region during the period 1987-1996,¹⁸ when the state was under serious threats both from drug cartels and internal armed conflict. Political stability has been reestablished, and it would be interesting to see whether this has affected research output. We can see an article by Pellegrini, et al., where the production of scientific articles in six of the leading Latin American countries in health research at the time (Argentina, Brazil, Chile, Cuba, Mexico, and Venezuela) was characterized between 1973-1992 and they found a 117% increase between the first and last five-year periods within the study period.¹⁹ There is a notable difference in capabilities to perform high quality scientific research amongst Latin American countries; in this scenario, collaborative efforts within and outside of Latin American countries prove to be helpful to improve research capacity and increase relative contribution of Latin America to clinical research production.

Though collaboration has been facilitated through easier methods of communication between distant areas, new challenges come with this globalization phenomenon. For instance, issues such as ethical and regulatory oversight, the generalization of results to other populations and quality of the scientific work to assure the overall validity need to be carefully considered.¹

One important aspect is the research agenda of Latin America that is different than other countries. For instance, health problems related to the environment, accidents, violence, infectious diseases, nutrition and alcoholism have a greater significance than in other regions such as in Europe or other developed nations.²⁰ Although cardiovascular diseases, diabetes and cancer are also priorities, those other conditions need also to be included in the research agenda. In an interesting article from Perel et al., authors report Randomized Clinical Trials (RCTs) conducted in Latin America that were published in five leading medical journals (same journals as in our study) and compared them with the burden of disease in the region. The authors found no correlation between these two.²¹ There is good data that supports these findings.^{22,23} In fact international medical journals might be less interested in studies investigating local conditions. It is important thus to recognize this gap in scientific information in order to address it properly and direct efforts to diseases that have an important local impact.

There are significant hurdles that Latin American researchers encounter namely funding, language and training. Countries within Latin American are Non-English speaking; thus creating additional obstacles for

scientists to write high quality manuscripts and publish them in English language medical journals. In a study by Man. et al., the Netherlands, Switzerland, and Sweden, countries who are particularly proficient in English had the highest rate of publication in the five highest ranked general medical journals, while Asian countries had generally the lowest rates of publication. Research economical investment and English proficiency seem to be strongly associated with publication rate in the highest ranked general medical journals.²⁴

Another important factor that may explain the lack of representativeness of Latin America in scientific publications is the lack of proper training in clinical research methodology. In Latin America, training in clinical research methodology is limited in the medical school curriculum and doctors are not familiar with the use of different tools to perform clinical investigation.²⁵⁻²⁸ Ideally the training of future researchers should have a direct involvement in the practical aspects of clinical research and globalization.²⁹ They should be under the supervision of faculty members who are accomplished investigators and learn how to review published data, research design, data collection, data analysis and research ethics.³⁰

Although we systematically searched for manuscripts published in journals of high impact factor during a 10-year period and selected 1044 manuscripts, some limitations need to be discussed. First, we selected only journals of high impact factor. It is likely that lower impact factor journals might publish a larger percentage of articles from Latin America; however, it is also important to learn the contribution of Latin America countries to manuscripts published in the leading medical journals. Although it is also important to consider that impact factor does not measure the quality of a given study³¹ or is representative of the rate of citations of a specific article,³² it is certainly more competitive to publish in high impact factor journals as they usually accept a smaller percentage of submitted manuscripts. Second, the relative contribution of authors to published papers is not disclosed in most manuscripts; therefore it is difficult to characterize the relative contribution of Latin American authors when collaborating with other authors in the publications of high-impact factor.

Our work can confirm that Latin America still has a relatively low representation in health research publications in high impact medical journals. Though there are many challenges for Latin America to increase research capacity such as increase in funding, lack of proper training, language issues, there are also many opportunities in Latin America for clinical research. For instance, research can be conducted in a much more cost effective fashion, clinical research centers are increasing in size and quality and medical professionals are becoming more interested in research in the last few years. Appropriate research training in this scenario is critical to increase research capacity. In addition

collaborative efforts across countries of Latin America such as the Council on Health Research for Development (COHRED), and the Pan-American Health Organization (PAHO) are supporting the strengthening of health research systems in the region. Finally journal editors are also responsible to ensure representative of research published in their journals. In fact, in our study we observed that The Lancet published 7 (30.4%) of our 23 articles with Latin American authors. In their study of the globalization of clinical research, Falagas et al found that the proportion of articles that originated from the country in which a medical journal is based ranged from 71.7% to 95.1%. The Lancet was the most diverse journal regarding the origin of publications, a diversity that reflects its commitment to covering health and research from around the world.³³

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