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Trends, challenges and promotion of clinical and cardiovascular research in Latin America and the Caribbean ☆

Honorio Silva [a,*], Sandra J. Kleinstiver [b], Elif Sungar [c], Robert H. Rubin [d], Rafael Hernández-Hernández [e], Pablo Pulido [f], Herman Schargrodsky [g], Henry S. Fraser [h]

[a] *Science and Medical Professional Development, Pfizer Inc., New York, NY 10017, USA*
[b] *Katalyst Health Technology Assessments, London, ON, Canada N6G 5L7*
[c] *Inter American Foundation for Clinical Research, Cambridge, MA 02138, USA*
[d] *Center for Experimental Pharmacology and Therapeutics Harvard — MIT Division of Health Sciences and Technology, Boston, MA 02114, USA*
[e] *Clinical Pharmacology Unit and Hypertension Clinic, School of Medicine, Universidad Centroccidental, Barquisimeto, Venezuela*
[f] *Pan American Federation of Associations of Medical Schools, La Trinidad, Caracas, Venezuela*
[g] *Department of Cardiology, Buenos Aires Italian Hospital, Buenos Aires, Argentina*
[h] *Dean of the School of Clinical Medicine and Research, Tropical Medicine Research Institute, University of West Indies, Bridgetown, Barbados*

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Summary
Background: Cardiovascular disease (CVD) is a major cause of morbidity and mortality worldwide. It has been suggested that cardiovascular disease has not had a prominent place in the public health agenda in Latin America and the Caribbean. Recently there has been momentum toward formation of partnerships between public and private sectors to develop an improved capacity for CVD research. Notwithstanding these efforts, cardiovascular clinical research output in Latin America and the Caribbean has not kept pace with the need to overcome the burden of CVD.

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* Corresponding author. Tel.: +1 212 573 7270; fax: +1 212 499 3916.
E-mail addresses: silvah@pfizer.com (H. Silva), sandra.kleinstiver@katalyst.on.ca (S.J. Kleinstiver), elifsungar@yahoo.com (E. Sungar), rhrubin@partners.org (R.H. Rubin), rhernan@cantv.net (R. Hernández-Hernández), pablopulido1@cantv.net (P. Pulido), bubyscha@fibertel.com.ar (H. Schargrodsky), hfraser@sunbeach.net (H.S. Fraser).

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Methods: Bibliometric data for clinical medicine publications and cardiovascular specialties in the region were assessed from 2000 to 2005. Data were compared with previous bibliometric studies.
Results: Scientific output from Latin America and the Caribbean has not increased. In addition, our findings also suggest that Latin American and Caribbean investigators continue to prefer to publish in local and regional journals in languages other than English.
Conclusion: To overcome the expected economic impact of CVD and to diminish the burden of disease in the region it is necessary to raise the priority for funding of CVD research. With support from ethical research foundations, improved quality and quantity of clinical study data with allow for expedited transformation of the productivity of CVD research within Latin America and the Caribbean.

Introduction

Cardiovascular disease (CVD) is a major cause of morbidity and mortality worldwide. In 2001, CVD was the leading cause of death in Latin America and the Caribbean with 31% of all deaths attributed to CVD [1]. Global burden of disease studies conducted by the World Health Organization (WHO) indicate that the number of deaths due to cardiovascular disease in developing countries, will increase by more than 60% between 2000 and 2020 [2,3]. Developing countries include Latin America and the Caribbean where, between 1990 and 2020, ischemic heart disease alone is projected to increase by 120% for women and 137% for men in contrast to age related increases of only 30—60% in developed countries [4].

The burden of cardiovascular disease in developing countries is coincident with industrialization and urbanization as well as major lifestyle changes including a more sedentary lifestyle and poor dietary habits that have contributed to increasing rates of obesity, hypertension, diabetes and elevated lipids [5]. Regardless of its prevalence in Latin America and the Caribbean, it has been suggested that cardiovascular disease has not had a prominent place in the public health agenda [1]. There is some evidence that the situation may be changing, with national programs for chronic diseases being developed by Ministries of Health in some countries.

By focusing on the development of clinical research programs, specifically in cardiovascular disease, there is potential for improved human health and knowledge gained from research to be utilized to lobby governments and policy makers. The goal would be cooperative programs and development of treatment and prevention interventions. Since the mid 1960's, prevention and intervention programs have shown promise at curtailing CVD in countries such as the United States, the United Kingdom, Australia and European nations. Studies in industrialized nations have shown that the decline in CVD was related to reduction in risk factors as well as progress in medical and surgical care including new non-invasive techniques and highly effective medications for treatment of hypertension and hypercholesterolemia [6]. The positive effects of action against CVD are apparent in nations where government agencies, medical leadership and professional organizations have increased public awareness of the major CVD risk factors [4]. We speculate that the investment in research and development in Latin America and the Caribbean has not improved thus translating into low productivity in cardiovascular research and an escalating burden of disease.

Cardiovascular clinical research in Latin America and the Caribbean has not kept pace with the burden of disease in the region. A limited number of epidemiologic studies have assessed the prevalence of chronic disease. However, these studies have been hampered by inconsistencies in risk factor definitions, sampling and assessment methods [7]. Research has demonstrated that much of this disease can be prevented if known risk factors are reduced [8]. Additional clinical research using consistent and comparable methods is required to draw more insight into the prevention and intervention measures for disease management with the resultant reduction in burden of disease. Accurate and reliable studies will provide the basis for policy and infrastructure development and justification for devotion of more resources to clinical research necessary to control CVD.

With recent support from organizations such as the Inter American Foundation for Clinical Research, the Latin American Society of Hypertension and the InterAmerican Heart Foundation, there has been momentum toward formation of partnerships with an improved capacity for cardiovascular research. These organizations not only provide support to the research community but most importantly might provide the advocacy required to lobby policy makers and governments. The Cardiovascular Risk Factors Multiple Evaluation in Latin America (CARMELA) study is an example of a cooperative research endeavor where the public and private sector, academia and professional societies worked together. The goal of the study was to evaluate the prevalence of CVD risk factors (arterial hypertension, diabetes, smoking, hypercholesterolemia) as well as other cardiovascular risk factors and socio-economic factors as correlated to carotid intima-media thickness and plaque in stratified multistage samples from the urban population in the region.

Notwithstanding these efforts, cardiovascular clinical research output specifically in Latin America and the Caribbean has not kept pace with the need to overcome the burden of CVD. There are limited data on relevant research across the region, and this study attempts to quantify CVD research with bibliometric methods.

Methods

Building upon our previous research [9], we investigated trends in cardiovascular research as a function of scientific publications generated in the region. The relationship between research and development funding and the scientific output of a region is related to the number of indexed scientific publications [10]. We assessed bibliometric data from 2000 to 2005 for clinical medicine and cardiovascular specialty publications as defined by medical subject headings. The National Library of Medicine and the National Institute of Health PubMed database (Bethesda, MD) and the Biblioteca Regional de Medicina or BIREME database (San Paulo, Brazil) were mined for publications indexed by country. The methodology for selection of the clinical medicine disciplines as well as the top 5 Latin American producers of scientific publications have been previously published [9]. PubMed indexes worldwide publications primarily in English including a limited number of peer-reviewed Spanish language journals. BIREME indexes medical and health science literature including Latin American and Caribbean Health Sciences (LILACS), Caribbean Health Sciences Literature (MEDCARIB) as well as MEDLINE (1996–2006). BIREME includes peer-reviewed local and regional journals published in English, Spanish, and Portuguese. We considered the most recent time frame (2000–2005) and compared the results to findings from 1999 to 2004 [9]. Economic indicators were obtained from the United Nations Educational Scientific and Cultural Organization (UNESCO) [11] and patent data were obtained from the World Intellectual Property Organization [12]. Data for Latin America and the Caribbean were compared to those from the United States, Germany and Japan. For the period, 1996–2006, the United States, followed by Germany and Japan were the top three countries in terms of scientific output [13].

Patent data are recognized as an indicator of research innovation and productivity, by country. Productivity in research and development conducted in health sciences and specifically, CVD research are included as a percentage of the total.

Results

When compared to the United States, Japan or Germany, expenditure on research and development as a percentage of gross domestic product (GDP) is comparatively low (Table 1) in Latin America and the Caribbean, falling short of these countries. The numbers of researchers per million population in the major research intensive countries of Latin America and the Caribbean are significantly less than for the world leaders. Interestingly, for Brazil, the gross expenditure on research and development (GERD) per researcher (US $, thousands) is approaching international standards and is comparable to the United States at $238 and $230, respectively. Economic indicators point toward a slight downward trend in research and development investment in Latin America and the Caribbean. In UNESCO's 2005 Science Report, it was noted that the GERD, as a measure of knowledge production, fell from 3.1% in 1997 to 2.6% in 2000 [11]. Patent filings per million dollar research and development expenditure as a measure of research productivity demonstrate that the output for Latin American countries is low compared to the above mentioned world leaders (Table 2).

From 2000 to 2005 compared to 1999–2004, we noted a slight increase in the number of cardiovascular and diabetes publications indexed in both the PubMed and BIREME databases (no significant

Table 1 Economic indicators

	Population (millions)	Researchers/million population	Research expenditure as % of GDP	GERD per researcher (US $, thousands)
Latin America and Caribbean	530.0	261	0.6	156.5
Argentina	38.4	720	0.4	61.5
Brazil	183.9	344	1.0	238.0
Mexico	105.7	268	0.4	159.7
Chile	16.1	444	0.6	No data
Venezuela	26.3	176*	0.3	No data
USA	295.4	4605	2.8	230.0
Japan	127.9	5287	3.1	164.5
Germany	82.6	3216	2.5	211.4

2004 UNESCO [11], *2006 [17]. GDP = gross domestic product, GERD = gross expenditure on research and development, data from 2002.

difference) (Table 3). For the major clinical medicine disciplines examined in both PubMed and BIREME, publications by investigators from Brazil, Mexico and Chile lead the region in scientific output (Table 4). All countries published more papers in BIREME than in PubMed. Our findings suggest that Latin American investigators continue to prefer to publish in local and regional journals in Spanish and Portuguese. Notably, in BIREME, Venezuela contributed the second largest number of cardiovascular research papers; 6.1% compared to 9.6% for Brazil, 4.6% for Mexico, 3.6% for Chile and 3.0% for Argentina. On the other hand, the contributions from Caribbean countries were limited with publications from Barbados, Jamaica, Trinidad and Tobago (major Caribbean English speaking countries) and Cuba, the Dominican Republic and Puerto Rico (major Caribbean Spanish speaking

Table 2 Patent data for resident patent filings, 2004 World Intellectual Property Organization [12]

Patents by country 2004	Filings per million population	Filings per $Billion GDP	Filings per $Million R&D expenditures
Argentina	28.41	2.32	0.56
Brazil	21.16	2.81	0.29
Chile	14.88	1.49	0.25
Mexico	5.44	0.60	0.14
Venezuela	No data available		
USA	645.44	17.70	0.68
Japan	2883.56	107.26	3.41
Germany	587.13	22.57	0.90

Table 3 Comparison of six most frequently indexed clinical medicine disciplines in Latin America (Brazil, Mexico, Chile, Argentina and Venezuela) in PubMed and BIREME

	Clinical medicine disciplines			
	PubMed		BIREME	
	1999–2004	2000–2005	1999–2004	2000–2005
% of total	*N* = 2025	*N* = 2294	*N* = 2921	*N* = 3459
Diabetes	24.6%	30.8%	29.5%	31.8%
Gastroenterology	23.8%	1.9%	12.5%	5.6%
Pulmonary disease	21.9%	29.3%	21.7%	13.0%
Cardiovascular	19.8%	25.8%	23.0%	26.9%
Infectious disease	5.2%	6.0%	7.6%	17.2%
Psychiatry	4.6%	6.3%	5.5%	5.6%

Table 4 Percent of publication data by clinical medicine specialty and by country in PubMed (P) and BIREME (B) for the time period 2000–2005 (Total publications in PubMed *n* = 2294; BIREME *n* = 3459)

	Brazil		Mexico		Chile		Argentina		Venezuela	
	P% *N* = 1017	B% *N* = 1323	P% *N* = 767	B% *N* = 815	P% *N* = 241	B% *N* = 427	P% *N* = 205	B% *N* = 327	P% *N* = 64	B% *N* = 567
Cardiovascular	13.4	9.6	6.4	4.6	2.7	3.6	2.0	3.0	1.2	6.1
Diabetes	10.9	10.8	14.4	11.4	3.2	4.2	1.7	2.1	0.5	3.3
Pulmonary disease	12.7	5.6	9.1	3.0	3.1	1.5	3.6	1.9	0.8	1.0
Gastroenterology	0.7	0.6	0.9	0.3	0.1	0.1	0.2	0.1	0.1	4.4
Infectious disease	3.3	8.7	1.2	3.6	0.8	2.0	0.5	1.9	0.2	0.9
Psychiatry	3.3	2.9	1.4	0.7	0.6	0.9	1.0	0.5	0.1	0.7
% of Total	44.3	38.2	33.4	23.6	10.5	12.3	9.0	9.5	2.9	16.4

countries), indexed in PubMed and BIREME being less than those in Latin America (Table 5).

For cardiovascular research specialties, we found very little change in the overall distribution of research focus from 1984 to 2004 compared to the most recent six year period (Table 6). We also found that when identified by more detailed subject headings i.e. cardiovascular and hypertension, PubMed indexed a greater number of cardiovascular publications with 705 papers indexed versus

Table 5 Percent of publication data by clinical medicine specialty and by country for Caribbean countries (3 major English speaking and 3 major Spanish speaking), 2000–2005

%	Jamaica		Trinidad		Barbados		Puerto Rico		Cuba		Dom. Republic	
	P	B	P	B	P	B	P	B	P	B	P	B
n	99	132	70	85	53	48	143	141	102	90	17	19
Cardiovascular	9.3	2.7	4.5	3.9	3.7	1.0	8.9	5.6	9.5	1.0	0.2	0
Diabetes	8.5	15.9	6.4	9.7	4.8	9.7	10.7	12.4	4.8	1.2	1.0	1.2
Pulmonary disease	1.7	1.4	3.1	1.4	2.1	0.6	7.2	2.9	3.5	2.5	1.2	0.4
Gastroentero.	0	0	0	0	0	0	0.4	0.6	1.0	1.4	0	0
Infectious disease	0.6	4.5	0.2	1.0	0	0.8	0.4	4.5	1.0	3.9	0.6	1.9
Psychiatry	0.4	1.2	0.2	0.6	0.4	0.8	1.9	1.4	1.2	1.9	0.4	0.2
% of Total	20.5	25.6	14.5	16.5	11.0	9.3	29.5	27.3	21.0	17.5	3.5	3.7

Total publications in PubMed (P) *n* = 484; BIREME (B) *n* = 515. Gastroentero = gastroenterology, Dom. Republic = Dominican Republic.

Table 6 Publication data indexed by PubMed and BIREME; comparison of cardiovascular specialty as a percentage of total Latin American cardiovascular publications

	PubMed		BIREME	
	1984–2004	2000–2005	1984–2004	2000–2005
Cardiovascular Specialties	*N* = 2964	*N* = 705	*N* = 1208	*N* = 638
Hypertension	22.1%	19.3%	26.0%	30.6%
Epidemiology	40.0%	42.6%	23.4%	23.2%
Coronary disease	13.9%	4.7%	11.5%	15.5%
Chagas disease	5.5%	4.4%	23.5%	13.9%
Stroke	4.2%	5.7%	4.2%	6.7%
Pharmacology	9.6%	17.9%	2.6%	5.0%
Heart failure	4.3%	4.8%	5.5%	3.8%
Peripheral vascular disease	0.5%	0.7%	0.6%	1.3%

Note: For BIREME,1984–2004, 2.7% of cardiovascular publications were classified as other.

591 papers when searched by cardiovascular only. Comparison of the two overlapping six year periods (1999–2004 and 2000–2005) did show a 20% and 23% increase, respectively in diabetes and cardiovascular related papers in PubMed (Table 3). BIREME data demonstrated a more modest increase in both of these subject areas and a marked increase in publications relating to infectious disease. For Latin American countries sampled, only Brazil had more than 10% of its total publications relating to cardiovascular disease (Table 4). Interestingly, from 2000 to 2005, publications relating to pharmacology research increased two-fold in both PubMed and BIREME (Table 6).

Discussion

Latin America and the Caribbean face many challenges in the promotion of cardiovascular disease research. Scientific output from Latin America and the Caribbean has not improved over the previously assessed 6 year time period and this slow pace of development is a concern when compared to the expected growth of CVD burden. Large scale epidemiologic studies and specific clinical research are necessary to gain knowledge about regional challenges of CVD and to understand factors that contribute to an increase in associated risks. Foremost is the need for development of a culture of research with the infrastructure and expertise in the conduct of clinical and epidemiological studies and, importantly, sponsoring institutions for funding of these studies. International agencies that support health research in developing countries tend to focus on infectious diseases (i.e. the Gates Foundation and HIV/AIDS research) [5]. An effort to balance priorities and funding by raising awareness of the burden of CVD, diabetes and obesity in these developing countries is required [5]. It should be noted that in developed countries, critical public sector investment in research is complimented by private sector funding and research is viewed as an investment in knowledge transfer that translates into economic, social and political power. In Latin America and the Caribbean, investment in research has traditionally been viewed as an expense not an attribute and has been funded predominantly from the public sector [9]. Therefore, it is necessary to raise the priority of funding for chronic disease research, such as prevention and intervention in CVD, at the time when governments as well as national and international funding agencies are being lobbied.

In a bibliometric study of global production of CVD research, it was reported that developed world countries contribute 85.5% of the total number of articles published but that the annual rate of increase in production is declining in these countries [14]. Additionally, from 1995 to 2002, the number of CVD research articles increased slightly in Latin America (and other developing countries). In contrast to these findings we noted that the rate of publication by cardiovascular specialties, in PubMed, declined from 1984–2004 to 2000–2005. However in BIREME, there was an increase in the annual rate of CVD research, again pointing to the bias to publish in local and regional journals. To address the issue of publication in languages other than English, it is necessary to consider two interventions: (1) creation of a climate that encourages publication and (2) creation of incentives to conduct research and publish in the English language to enhance the reach of this research. The noted increase in the number of cardiovascular publications related to pharmacology may be an indicator of the capabilities of Latin American investigators and the interest of pharmaceutical companies to invest in clinical research in the region.

One of the limitations of the study methodology was the difference in yield from each database dependant upon the detail of search criteria utilized. The search criteria, ''cardiovascular disease'' did not identify all related specialty publications. Additionally, for the Caribbean there was a very modest yield for cardiovascular disease publications that did not necessarily capture all of the papers identified in an earlier, more qualitative study of health research in the Caribbean Commonwealth [15].

In spite of increasing research investment, as evident by the GERD in Brazil, the region's productivity must be leveraged. There is urgent need for large-scale epidemiologic and clinical studies to provide answers to the challenges faced in tackling the epidemic of CVD in individual regions. As concluded by Leeder and colleagues, CVD unlike communicable diseases, has yet to be recognized as a problem in the developing world. Combating CVD requires research, trial interventions and changes to health systems, assessment of alternative prevention and treatment regimes, health education initiatives as well as consultations with governments, professionals and private industry to change individual, social, legislative and commercial behavior. A CVD control program would provide the critically important research base for development of interventions and changes to the health system. [4] In order to overcome the identified risk factors it is necessary to develop intervention projects that demonstrate the value of intervention.

Proper education in clinical research is also necessary. We recognize that the ultimate purpose of medical education is to improve the health of the population and certainly new priorities must be defined to meet population needs. Clinical research has been neglected in the teaching and practical core curricula of Latin American medical schools and postgraduate programs. Aligned efforts to include education in clinical research in the medical curriculum of undergraduate and graduate programs are needed to develop skills and competencies in clinical research for new medical graduates in the region [16].

We speculate that professional societies such as the InterAmerican Heart Foundation and the Inter American Foundation for Clinical Research are catalysts for promotion of cooperative research programs that will involve both public and private sectors. Studies such as CARMELA are examples of the collaboration between academia, government and industry to cooperatively achieve the promotion of CVD research in the region. The uniqueness of CARMELA is that the study synergistically combined the efforts of international foundations, scientific societies, and the private sector to support a research initiative that is a major public health problem. These efforts aim to benefit the Latin American population. Government now need to utilize knowledge gained to minimize risk factors for cardiovascular disease through appropriate interventions. Cardiovascular diseases greatly exceed in numbers those affected by HIV/AIDS, and the successful model of a National HIV/AIDS Commission may provide an effective approach for a truly national response to the chronic disease epidemic.

The benefits of improved cardiovascular research, promotion of systemic interventions, further development of collaborations and the potential for resultant economic impact are necessary to effectively lower the burden of disease in the region. Support from research foundations with a mandate to promote and enhance development of ethical clinical research through education programs, policy interventions, monitoring and evaluation through on-going surveillance is required for success. The resultant improved quality of clinical study data will allow for the expedited transformation of the productivity of cardiovascular disease research within Latin America and the Caribbean.

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