South-south collaboration on HIV/AIDS prevention and treatment: when birds of a feather rarely flock together

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Abstract

South-south collaboration on health and development is a critical mechanism for social and economic progress, allowing sharing and replicating experiences to find a “southern solution” to meet specific needs. In this paper, bibliometric and social network analysis methods were used to assess the 10-year (2006-2016) scientific contribution of low- and middle-income countries (LMIC) to HIV/AIDS prevention and/or treatment, one of their shared health challenges. Four dimensions oriented the analysis: knowledge production, collaboration, research themes/types, and funding sources. We have shown a substantial increase in LMIC contribution, but a small expression of south-south collaboration, stressing the need for strategies to foster these partnerships. Research interests differed according to author income profile and funding source, suggesting a tendency of LMIC-based researchers and funders to embrace a “linear model” of innovation. It is expected that the evidence presented here can be used to strengthen a knowledge platform to inform future policy, planning and funding decisions, contributing to the development of enhanced collaboration and a common research agenda between LMICs.
**Introduction**

In less developed areas of the world, international cooperation on health and development is a critical mechanism for social and economic progress. It contributes to the provision of universal social basic standards, reduction of extreme inequalities and to engaging low- and middle-income countries (LMIC) as potential providers of international public goods (1). Although the traditional official development assistance (ODA) remains a unique and important driver of development cooperation, the global landscape has changed drastically in the last decades with an increasing participation of LMIC in collaborative learning models (2,3).

The World Health Organization (WHO), the Council on Health Research for Development (COHRED) and the Global Forum on Health Research have consistently emphasized that knowledge generated by health research should be utilized to improve health system performance and, ultimately, to promote health and health equity (4–6). Developing the capacity to effectively carry out health research is essential to strengthen health research systems at both national and global levels (7).

LMIC are usually vulnerable in international scientific cooperation, being frequently hindered of access to the results and health products of these collaborations (8). Cooperation in health research among LMIC allows sharing and replicating each other’s experiences in finding a “southern solution”, designed to meet their specific needs and circumstances and complement global solutions, contrasting with traditional cooperation with high-income countries (HIC) (9). South-South cooperation can facilitate access to strategic knowledge and specific technical skills. More advanced developing countries have addressed shared health problems through collaboration between biotech companies and research networks (10,11). Although LMIC research cooperation has been assessed
by mapping joint scientific publications (12–14), not much is known about the extent and characteristics of research collaborations in common health challenges.

Access to adequate HIV/AIDS prevention and treatment remains one of the shared health challenges among LMIC. The uneven geographical distribution of the disease has been related to social determinants of health and income inequality (15). According to UNAIDS, access to antiretroviral therapy ranged from as low as 16 to 55% in LMIC (16). The analysis of the LMIC collaboration on HIV/AIDS research can provide an indication of the scientific capacity and potential contribution to the Unites Nations sustainable development goal of ending the disease epidemics by the year 2030 (17).

This paper aims to assess the scientific contribution of LMIC to HIV/AIDS prevention and/or treatment, through the analysis of scientific publications. Four dimensions oriented the analysis: knowledge production, collaboration, research themes/types, and funding sources. The findings are expected to inform stakeholders on the progress and nature of collaboration towards achieving increased health research capacities in LMIC countries.

**Methods**

**Data collection**

Information on scientific publications on HIV/AIDS prevention and/or treatment for the period 2006–2015 were retrieved from the bibliometric database of the Centre for Science and Technology Studies (CWTS) of the Leiden University, which is an enhanced version of the Web of Science (WoS) database.

Queries were directed to the title, abstract and keywords of the publications. The search query used the terms (“HIV infection” OR HIV OR “hiv infect*” OR “human immunodeficiency virus” OR “human immunodeficiency virus” OR “human immuno-deficiency virus” OR “human immune-deficiency virus” OR “acquired
immunodeficiency syndrome” OR “acquired immunodeficiency syndrome” OR “acquired immuno-deficiency syndrome” OR “acquired immune-deficiency syndrome”) AND (prevent* OR vaccin* OR treat* OR cure OR curing OR therap*). The term “AIDS” was not included in the search query as it retrieved many non-related articles containing the word “aid”. In order to evaluate the collaboration pattern of developing countries, only articles involving at least one upper- or lower-middle, or low-income country (18) were retrieved (n=27,147). These represented 31.3% of the total HIV/AIDS prevention and/or treatment articles in the database.

**Co-authorship analysis**

Data was imported into the data/text mining software VantagePoint (Search Technology Inc.) to generate co-occurrence matrixes based on the authors’ country of professional affiliation. Affiliations originating from England, Scotland, Northern Ireland and Wales were collectively reviewed as the UK (United Kingdom). These matrixes were imported into the Gephi software (19) to build and visualize co-authorship network graphs.

In the networks, nodes represent countries and two or more countries were connected if their members shared the authorship of one or more publications. Publications co-authored by at least one LMIC along with one or more HIC author were considered representation of North-South research collaborations. Publications co-authored exclusively by two or more LMIC researchers were used as a proxy for LMIC South-South research collaboration.

**Thematic mapping and clustering**

A combined approach of mapping and clustering research topics was used to provide an overview of the research themes contained in the full set of retrieved publications. Bibliometric maps were constructed using the VOS (visualization of similarities)
mapping technique available on the VOSviewer software (20). The software estimates their “similarity” (affinity) using the “association strength” measure, proposed by Van Eck and Waltman (21), based on the number of co-occurrences of terms in the title or abstract of the same publication, The larger the number of publications in which two terms co-occur, the stronger the terms are considered to be related to each other. Therefore, terms that often co-occur in the same publications are positioned close to each other in a term map while weakly related terms (low co-occurrence) are positioned further away from each other in the map. Each term is represented by a circle, where its diameter and label size indicate the number of publications that have the corresponding term in their title or abstract. To identify clusters of related terms, the software uses a weighted and parameterized variant of modularity-based clustering (22). A cluster can be understood as a theme in which one or more research terms can be identified.

**Classification of research types**

LMIC collaborative articles (n=451) were individually reviewed and classified according to the type of research. The review of titles and abstracts allowed the identification of seven major categories, as follows: i) Social sciences research: articles that explores beliefs, attitudes and behavioral perspectives, including interpersonal relations, sexual behavior, risk perceptions, knowledge of the disease; ii) Product development & new technologies: discovery, development and testing of new drugs, vaccines and biopharmaceuticals; testing and evaluation of markers and technologies for detection, diagnosis, prediction, prognosis and monitoring in clinical, community or applied settings including medical devices and diagnostic kits; iii) Health systems research: examination of healthcare practices, health service delivery and the structure of healthcare systems (access, barriers and quality); iv) Health policy and strategies: research targeted to the study of processes used in the implementation of initiatives (policies, programmes, or
individual practices) as well as the contextual factors that affect these processes; v) Clinical research: clinical and laboratory-based studies conducted in human subjects, including evaluation of treatment regimens intended for human use; vi) Basic science research: laboratory-based research; studies of genes and gene products, molecular, cellular and physiological structures and functions, biological pathways and processes including immune function, bioinformatics, development and characterization of mathematical models; vii) Epidemiology research: studies of disease surveillance and distribution that track incidence, prevalence, morbidity, co-morbidity and mortality including ongoing monitoring of large scale cohorts, social determinants of health, factors relating to physical environment associated with the cause, risk or development of disease. The categorization was initially done by one of the authors (PCA) and them crossed-checked with 2 other co-authors (BPFF, FZ). Discordant classifications were reviewed together and a final classification agreed by consensus. For this analysis, articles on diseases known to be associated to HIV that were not carried out on HIV-infected patients were excluded (n=88).

Funding sources

Funding information was obtained from the funding acknowledgments in the retrieved publications. Although this information was only available in the database from mid-2008, the scale and detail of the funding can be important data to probe questions related to research funding sponsorship (23). The VantagePoint software was used to clean, and harmonize funder’s names to minimize ambiguity. Harmonisation was done using the highest organization level of a funder.
The sampling process is shown in Figure 1.

Figure 1: Sampling and selection of papers.
Results

Knowledge production: contribution of LMIC have sustainably increased

The contribution of LMIC on HIV/AIDS prevention and/or treatment, estimated based on the indexing of publications solely or in collaboration with other countries (n=27,147), has sustainably increased in the study period (Figure 2).

![Figure 2: WoS indexing rate of scientific publications on HIV/AIDS prevention and/or treatment involving authors from LMIC and HIC (2006-2015). The indexing rate was estimated by the number of indexed papers in each year, relative to the number of HIV/AIDS prevention and/or treatment papers indexed in the database in 2006. Indexing of papers involving at least one LMIC-based scientist have tripled in the past ten years while articles involving only HIC-based researchers maintained a constant rate. The number of papers of the top ten most productive LMIC is shown on Table 1.](image-url)
Table 1: Top ten most productive LMIC according to leading authors’ country of professional affiliation (2006-2015).

<table>
<thead>
<tr>
<th>Rank</th>
<th>Country</th>
<th>Number of publications</th>
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<tbody>
<tr>
<td>1</td>
<td>South Africa</td>
<td>3,714</td>
</tr>
<tr>
<td>2</td>
<td>China</td>
<td>2,846</td>
</tr>
<tr>
<td>3</td>
<td>Brazil</td>
<td>2,310</td>
</tr>
<tr>
<td>4</td>
<td>India</td>
<td>1,869</td>
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<tr>
<td>5</td>
<td>Thailand</td>
<td>825</td>
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<tr>
<td>6</td>
<td>Uganda</td>
<td>674</td>
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<tr>
<td>7</td>
<td>Nigeria</td>
<td>503</td>
</tr>
<tr>
<td>8</td>
<td>Kenya</td>
<td>373</td>
</tr>
<tr>
<td>9</td>
<td>Mexico</td>
<td>338</td>
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<tr>
<td>10</td>
<td>Argentina</td>
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**Collaboration: partnerships between LMIC are lower than expected**

Of the 27,147 publications analyzed, 16,973 (62.5%) were published in co-authorship with international researchers; 451 (3%) involving exclusively LMIC researchers and 16,522 (97%) involving collaboration between LMIC authors with at least one HIC. General display of the authorship relations between countries is shown in Figure 3.

LMIC authors were the leading authors in 37.6% of the publications among articles involving HIC. Leading authors from South Africa accounted for 1,751 (10.5%) publications, China for 876 (5.3%) and Uganda for 529 (3.2%), as the most frequent leaders in collaborations. USA-based authors led most publications in collaboration with LMIC (n=5,693 or 34.5%). South Africa and UK-based authors collaborated frequently in the study period, with 1,483 collaborative papers. USA- and Chinese-based authors also collaborated very often with 1,248 papers in co-authorship.
Among LMIC collaborative articles, South African authors accounted for 26.8% (n=113) of all first-authored papers, followed by India (7.1%), Nigeria (6.4%) and Brazil (5.7%). South Africa, India and Brazil-based authors were the ones that most collaborated with other LMIC researchers. South Africa and Nigeria were the two LMIC that mostly collaborated in the period (32 papers).
Figure 3: Map of HIC and LMIC-based researchers’ collaborations on HIV/AIDS prevention and/or treatment research. Country links were mapped based on authors’ affiliations. Each node represents one country and two countries were considered connected if their researchers shared the authorship of a paper. Only relationships between first author and their co-authors are shown. Links are color-coded according to the continent of the leading author.
Research themes/types: different interests according to income profile

The thematic map of all publications on HIV/AIDS prevention and/or treatment involving LMIC is shown in Figure 4. The 5,982 terms identified in titles and abstracts of all publications were grouped by the VOSviewer software in eight major clusters (depicted in different colors). Research themes majorly present in each cluster were identified by interpreting their most frequent terms in light of HIV research (Figure 4A). Starting from the bottom (green cluster) and moving clockwise: i) HIV diagnosis, opportunistic infections and HIV-associated diseases (sensitivity, specificity, T cell count, pneumonia, tuberculosis); ii) Virology and molecular biology (activity, expression, protein, mechanism, interaction); iii) Immunology and vaccinology (vaccine, T cell, antibody, antigen, immune response, vaccination); iv) Drug resistance and virus mutations (mutation, resistance, assay, strain); v) Drug therapy and vertical transmission (efavirenz, nevirapine, concentration, protease inhibitor, breastfeeding); vi) Hepatitis co-infection (HCV, HBV, HBsAg); vii) Human behavior and healthcare (man, sex, service, partner, condom use, stigma); viii) Other sexually transmitted diseases (HPV, cervical cancer, gonorrhea).

The overall thematic mapping was used as a base to overlay publications authored in collaboration with HIC (Figure 4B) and those exclusively authored by LMIC (Figure 4C), as single or multi-country collaborations. These maps were color-coded according to the frequency of occurrence of a term relative to the whole dataset. Blue represents a low occurrence (rarely present), green an average occurrence, and red a high occurrence (frequently present).

When collaborating among themselves or publishing as single country-based authors, LMIC tend to have greater interest in diagnosis, opportunistic infections and other HIV-associated diseases (fungal diseases, tuberculosis etc.) and in basic biomedical research,
with emphasis on virology and molecular biology. When partnering with a HIC, research interest shifts to social sciences-oriented research including human behavior and healthcare, as well as drug therapy and vertical transmission. Articles with LMIC authors’ leadership did not expressively change this pattern.
Figure 4: Thematic map of HIV prevention and/or treatment articles authored by low- and middle-income scientists. The map shows 5,982 terms obtained from titles and abstracts of publications on HIV prevention and/or treatment involving at least one LMIC-based author. The closer two terms are positioned to each other, the stronger their relation. Each term is represented by a circle and its diameter and label size is proportional to the number of publications that have the corresponding term in their title or abstract. A) Colors indicate clusters of terms that have co-
occurred more frequently in the dataset. **B and C)** Colors indicate the occurrence of a term in publications co-authored by HIC and LMIC-based scientists (B) or in publications involving LMIC authors only (C) relative to the whole dataset. Blue represents a low occurrence, green an average occurrence, and red a high occurrence.

As collaboration between LMIC authors accounted for a small number of articles (n=451), they were reviewed individually and classified according to the type of research (Figure 5). From this review, articles focused on HIV-associated diseases that did not involve HIV-infected patients were excluded (n=88). The universe of analysis comprised 363 papers, involving 79 LMIC.

![Figure 5: Types of research (%) of articles published in collaboration exclusively between LMIC-based authors.](image)

Social sciences research accounted for 25.3%, clinical research represented 16.5% of publications, followed by health systems research (14.3%), basic science research and
epidemiology research, (11.8% each), and health policy and strategies (10.7%). A smaller proportion (9.4%) of articles were related to product development.

**Funding source: LMIC-based funders tend to promote basic science research**

Priorities of funding agencies may have important influence on research topics addressed by scientists (24). An overview of the funding landscape for LMIC researcher’s collaboration was produced retrieving information on funding acknowledgements in the articles. This approach has the potential to establish a direct link between funding inputs and research outputs on a larger scale, without the need to gain direct access to data via individual funders or researchers (25).

The analysis revealed that 44% (160 of 363 publications) of publications co-authored by LMIC disclosed at least one funder. The Brazilian National Council for Scientific and Technological Development (CNPq) was the most frequent funder acknowledged (n=16), followed by the National Research Foundation (NRF) of South Africa (n=13) and the Medical Research Council of South Africa (n=12). LMIC-based funders tend to support basic science research whereas international/HIC-based funders seem to cover predominantly social science-oriented research, focused on beliefs, behavior and attitudes related to HIV prevention and/or treatment (Figure 6).
**Figure 6: Funders of LMIC collaboration according to the type of research.** Funding information was retrieved from acknowledgements of scientific publications involving exclusively two or more LMIC-based authors. Bubble sizes are proportional to the number of papers funded of each type.

**Discussion**

Over the past two decades, a major development in health research has been the promotion of collaborative partnerships involving researchers from LMIC. The current review documented a substantial increase in LMIC contribution to HIV/AIDS prevention and treatment research, particularly from South African, Chinese, and Brazilian researchers. This is a significant finding considering that several studies have shown that future savings in healthcare resources can occur if LMIC countries invest in HIV/AIDS prevention (26–28).

The analysis showed that LMIC researchers have collaborated in approximately 62% of all HIV prevention and treatment papers published, mostly with HIC partners. The cumulative effect of global scientific collaboration has been the formation of a core group
of collaborating countries that usually excludes developing countries (29), limiting their capacity to efficiently absorb and implement scientific knowledge. An enquiry with HIC researchers about the nature of the research contributions made by their LMIC co-authors revealed that the collection of location-specific data, as well as the contextualization of the findings obtained, were their main research inputs (13). LMIC-based scientists were the leading authors in only 37% of papers with HIC collaborators. Lack of guidance with respect to authorship order in general and power differentials due to access to research funds could potentially lead to insufficient recognition of LMIC researchers. (30).

However, specifically for HIV research on prevention and treatment, a recent study by (31) found a substantial absolute increase in LMIC first and last authorships in cohort studies or randomized trials based in LMICs, reflecting a possible expansion of HIV research capacities in these countries.

South-South collaboration is often underrepresented in the scientific literature, usually discussed within the context of HIC-LMIC relationships (32). Our results show that cooperation with other LMIC is uncommon and accounted for only 3% of all papers in collaboration. It is more likely that a LMIC does not engage in international collaboration than cooperate with other LMIC, as suggested by the high number of single-LMIC papers (n=10,174). Such small expression of collaboration with other LMIC scientists can be explained by the lack of research infrastructure in these countries, inadequate human and financial resources (33), weaknesses in manuscript preparation and limited access to scientific literature (34). Additional reasons that could influence the limited number of LMIC co-authorships are editorial bias against articles by LMIC authors, as suggested by (35); linguistic barriers that may affect communication of results (36); and author-pays models of open access publications (37,38). As a strategy to mitigate these effects in LMICs, models offering author mentoring schemes along the lines of AuthorAID (39),
combined with differential publication fees and open access platforms whilst maintaining scientific rigor are likely to play a significant role in addressing these issues.

Knowledge maps based on publication data can offer information about research trends and explore the knowledge structure of different research fields (40,41). The review of publication themes showed that research focus on HIV prevention and treatment research differed according to the income profile of the countries involved. While LMIC-HIC collaborations were more focused on human behavior, healthcare, drug therapy and vertical transmission, LMIC authors alone were more interested in diagnosis, opportunistic infections and basic biomedical research. However, when collaborating with other LMIC researchers, the research focus shifts from the “hard sciences” to the social issues related to HIV prevention and treatment, similar to collaboration with HIC.

With the growing academic field of global health, research on human behavior and healthcare provide HIC scholars with opportunities to engage in field work in high burden LMICs, to expose themselves to new cultures, epidemiological settings, and possibly develop expertise to address existing and emerging challenges in HIV healthcare (42,43). LMICs interest in diagnosis strategies can be explained by the imperative need of identifying the HIV status as an optimal strategy to reduce HIV-associated morbidity and mortality in these countries (44). Opportunistic infections such as tuberculosis are also particularly important in LMICs as they have a substantial contribution on the early mortality of HIV-infected patients (45,46).

Social science approaches are especially important in HIV prevention and treatment, as they are central to understand acceptability, adoption and sustained use of new products/technologies (47). Engaging with the local social and political contexts of populations and communities at risk is key to understand the needs and processes for shaping health systems. It’s surprising that single-country LMIC papers are targeted to a
more biomedical-oriented research, since it is usually more expensive and highly dependent on infrastructure and specialized human resources. Indeed, recent studies have shown that LMIC research areas are dominated by biomedical and natural science fields (48,49). This could be a consequence that most LMICs S&T institutions were inspired by what is known as the “linear model”, assuming that good-quality basic research could produce, eventually, applied research that would increase the society welfare (49). A more socially-oriented focus would align prevention and treatment strategies with country development objectives, such as education, law reform, gender equality, poverty reduction, community systems, employer practices and health systems/infra-structure (47).

The fact that collaboration between LMIC-based authors emphasizes socially-oriented research indicates a common concern that could be nurtured by local funding agencies. Yet, in south-south collaboration, LMIC-based funders tend to support basic science research instead, probably as a consequence of the above-mentioned “linear model”. As effectiveness of new products/technologies is shown to be dependent not only on the efficacy of the technology or tool, but also on a range of social, cultural and political factors, funding more integrated approaches, combining social science with biomedical research could be an important way of tackling the HIV/AIDS pandemic that disproportionately affect these countries (50).

We recognize that co-authorship does not necessarily denote research collaboration, meaning that there is a difference between co-producing knowledge and co-reporting knowledge. In other words, not all instances of research collaboration will lead to a jointly authored paper, and not all co-authored papers imply that the authors listed have worked together. One must therefore accept a certain level of uncertainty when relying on co-authorship analyses (51). Also, although WoS covers more than 12,000 scientific journals
and has been widely used in the study of LMIC collaboration (14,48,52) it is possible that some national, regional or specialized journals were not included in the reviewed database.

The present study is not a comprehensive review of all LMIC collaboration experiences in health research, but an initial exploration of the approach and theme. Different types of cooperation are known, involving multiple stakeholders, governmental agencies, science and technology organizations, non-governmental organizations and the private sector. It is expected that the methods presented here can be used to assess shared intellectual contributions between countries, in order to strengthen a knowledge platform to inform future policy, planning and funding decisions, contributing to the development of enhanced collaboration and a common research agenda between LMICs.

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