original report

Scientific Productivity and Cancer-Related Mortality: A Case Study of a Positive Association in Colombia

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abstract

PURPOSE Cancer morbidity represents an increasing public health issue; this worldwide phenomenon also is true for emerging upper-middle-income countries, such as Colombia. The main purpose of this study was to uncover the relationship between scientific productivity and cancer-related mortality in our setting.

METHODS We conducted a temporal-trend ecologic study by means of bibliometric analysis from records of publications from SCOPUS database with Colombian institutional affiliations between 2000 and 2015. Productivity and overall mortality were estimated and compared using econometric modeling to identify potential correlations. Additional exploratory analyses per six most frequent cancer sites were performed.

RESULTS Of 2,645 publication records retrieved, 1,464 (55.3%) met selection criteria to be classified as Colombian scientific production (interobserver agreement, 92.96%; κ = 0.859; 95% CI, 0.800 to 0.918). Overall, 79.6% of the records corresponded to original or in-press articles; furthermore, almost half (49.7%) embodied descriptive study designs. Selected records reported a median of five authors and three different affiliations per publication; 66% had been cited at least once up to September 2017. The most-studied cancer-specific locations were cervix (16.1%), breast (11.5%), and stomach (9.8%), but nonspecific locations had the largest combined participation (23.4%). An increasing trend in scientific productivity was correlated to decreasing trend in overall cancer mortality, which was reported as an inverse proportional relationship in the linear regression modeling ($r = -0.958$; $P < .001$). Graphic analyses per cancer-specific sites revealed heterogeneous behaviors of this relationship.

CONCLUSION Colombian cancer-specific scientific productivity demonstrated a steady growth as opposed to a decreasing mortality trend in the recent years. The research output is predominantly descriptive with relatively low interinstitutional partnership and low impact in the international scientific community.

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INTRODUCTION

According to WHO estimates for the year 2011, cancer caused a greater number of deaths than coronary heart disease or stroke.[1,2] In the context of an aging population, unhealthy lifestyles, and socioeconomic transitions throughout the world, this phenomenon also implies an expected mortality increase from chronic noncommunicable diseases such as cancer, with an even greater burden in less-developed regions.[2,3] According to GLOBOCAN 2018, 18 million new occurrences of cancer and 9.6 million cancer-related deaths were predicted for both sexes and all age groups worldwide.[4] This analysis also revealed that, although the incidence of cancer in Latin America is lower than in other regions, such as Europe or North America, mortality in these three regions is much alike. In contrast to other regions, resource-limited settings, such as Latin American countries, are in great need of tailored public health interventions that provide optimal strategies for cancer burden control while they balance budgetary restrictions.[5] Affordable and equitable cancer prevention, diagnosis, and care policies are urgently required throughout the region. During past years, relevant actions have been undertaken by Latin American countries to improve cancer care; some examples are structural reforms in health care systems, new programs for marginalized populations, expansion of epidemiologic data through cancer registries and cancer plans, and implementation of policies to improve primary cancer prevention.[6] Although research capabilities in the region also have been strengthened, expert cancer commissions have urged parallel initiatives to increase research and evidence-based cancer care.

ASSOCIATED CONTENT

Appendix

Author affiliations and support information (if applicable) appear at the end of this article.

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CONTEXT

Key Objective

Is there a relationship between scientific productivity and cancer-related mortality in Colombia for the adult population?

Knowledge Generated

Cancer death rates decreased while trends in scientific productivity increased in this area. We found a linear relationship between two variables but heterogeneous behavior according to the cancer site per year. This association is interesting for public policy, but a causal relationship cannot be established, because cancer-related mortality is multifactorial. Mortality rates have shown constant decreasing trends for lung cancer, stomach cancer (women and men), and cervix uteri cancer. There was a sustained increase in mortality from breast cancer during all of the periods studied. Prostate cancer showed a slight increase in the period from 2011 to 2015.

Relevance

Beginning to focus our efforts on epidemiologic priorities and priorities in public health is our goal. It is important to start collaborative work not only at the local level but also at the regional level with different research groups.

Cancer research traditionally has been piloted in high-developed regions, such as Europe and North America; in contrast, Latin American countries have low participation in scientific conferences and publications in the field. Leading countries in the region, such as Brazil, recently have increased their scientific representation as well as their participation in worldwide research.[7,8] Although scientific productivity in the field is augmenting in smaller countries, these countries still lag and remain underrepresented on the global cancer research map.[9,10]

Colombia is an upper-middle-income country with nearly 50 million inhabitants (28th most populous country on Earth); it currently is experiencing particular demographic and epidemiologic transitions toward aging but also has had a continuously growing population during the past few years.[11-13] Since 1993, the Colombian Healthcare System (General Social Security Health System) has recognized health as a basic social right provided by social security insurance plans through nearly equal distribution of contributory (salaried workers, pensioners, and independent workers) and subsidized (individuals who cannot pay) regimens; there is also a third plan (approximately 5%) for workers from certain state institutions. Enrollment in the General Social Security Health System is mandatory and is administered through public or private health promotion agencies (known as EPS, from their acronym) and then provided by institutional health service providers (known as IPS, from their acronym), which may or may not be part of the EPS networks. Current system coverage reached up to 94.66% of the population in 2018, but timely and effective access to health care services restricts equitable health care among the population.[14] In this scenario, cancer burden implies a public health priority, because it represented the second greatest cause of death nationwide between 2007 and 2013 (17.1% of attributable mortality in the country). Recently, the estimated age-standardized rates for cancer incidence and mortality in Colombia were 178.8 and 79.2 person-years, respectively.[15] In parallel, the Colombian research system is designed and coordinated through a National Science, Technology, and Innovation System by the governmental administrative department—named Colciencias, established since 1968, and recently reorganized in 2009. Specific characterization of the research landscape related to cancer has been described fully elsewhere.[10]

Scientific productivity has been explored in relationship to economic and disease burden indicators for other populations and diseases, including cancer.[7,16-18] However, this analysis has not been performed specifically for cancer mortality in a single-country scenario. We therefore aimed to estimate the Colombian scientific productivity during 2000 to 2015 by means of bibliometric techniques and to assess its relationship to adult cancer mortality rates at all cancer sites. We performed additional descriptive analysis of the most important causes of death in the top six specific cancer sites in the same population.

METHODS

Study Design

An exploratory time-trend ecologic study according to the methodology described by Morgenstern[19] was conducted between the years 2000 and 2015 in two phases.

Phase 1: Estimation of Scientific Productivity in Cancer

A systematic literature search in SCOPUS (https://www.scopus.com/home.uri) was conducted in search of Colombian cancer publications. The search strategy is available in the Appendix. Two authors (D.B.-L. and A.M.A.-M.) searched and selected the records to be included independently on the basis of the following inclusion criteria: cancer-related research (including clinical trials regardless of phase, cancer diagnosis, risk factor evaluation, case reports, cohort studies, and more), applicability in humans or human models of adult population, and use of at least one Colombian institutional affiliation. Records that included patients younger than 15 years of age or without full-text availability were excluded. In case of discordance between the authors, a third independent author (A.R.-P.) decided upon the inclusion or exclusion of the record. Data were saved in a digital locked database for later analysis. Cohen's κ index for interobserver concordance was calculated.

Phase 2: Calculation of Mortality and Productivity Rates for Adult Population

A search on different repositories was conducted to estimate the following cancer-related indicators: (1) national annual sex-specific population distributions; (2) all-site sex-specific cancer mortality rates; (3) cancer-specific mortality rates by sex; and (4) cancer-specific productivity rates by site. Details for data extraction and calculation are provided in the Appendix.

Data Analysis and Statistical Considerations

The results were characterized by the determination of absolute and relative frequencies as well as measures of central tendency and dispersion according to each evaluated year. For the determination of associations between frequencies of continuous variables for each year evaluated, the distribution was evaluated graphically by a scatter plot. Furthermore, the relationship was established by calculating correlation coefficients. The relationship between variables was modeled with a linear regression to detect a direct or inversely proportional trend between the outcome and explanatory variables. The significance level was considered at an α of .05 for all tests. Finally, variable associations per each cancer-specific site were explored graphically by pairs of ordered data and were shown combined. All analyses were performed using Microsoft Excel 2010 (Microsoft; Redmond, WA).

RESULTS

Record Selection

In total, 2,645 publications related to cancer research were retrieved by the original search strategy. The PRISMA flow diagram that details the selection process is presented in Figure 1. The interobserver agreement between evaluators for the articles that required discussion was estimated at 92.96% ($\kappa = 0.859$; 95% CI, 0.800 to 0.918). Finally, 1,464 included records (55.3%) were obtained for complete characterization and productivity estimation.

Descriptive Analysis

Publication characteristics are represented in Table 1. The predominant language was English in approximately 60% of the inspected literature, and the most common article type was original article (either published or in press). By content analysis, descriptive studies (observational and case reports) constituted approximately half of the records (49.7%). Intervention studies in preclinical and clinical phases were next (16.1%), followed by narrative reviews and book chapters (15.7%); the rest of the research designs constituted 10.2%. The group constituted as "others" added 4.5% and was represented mainly by models of biomedical and/or mathematical engineering applied to cancer research. With regard to primary cancer sites, the

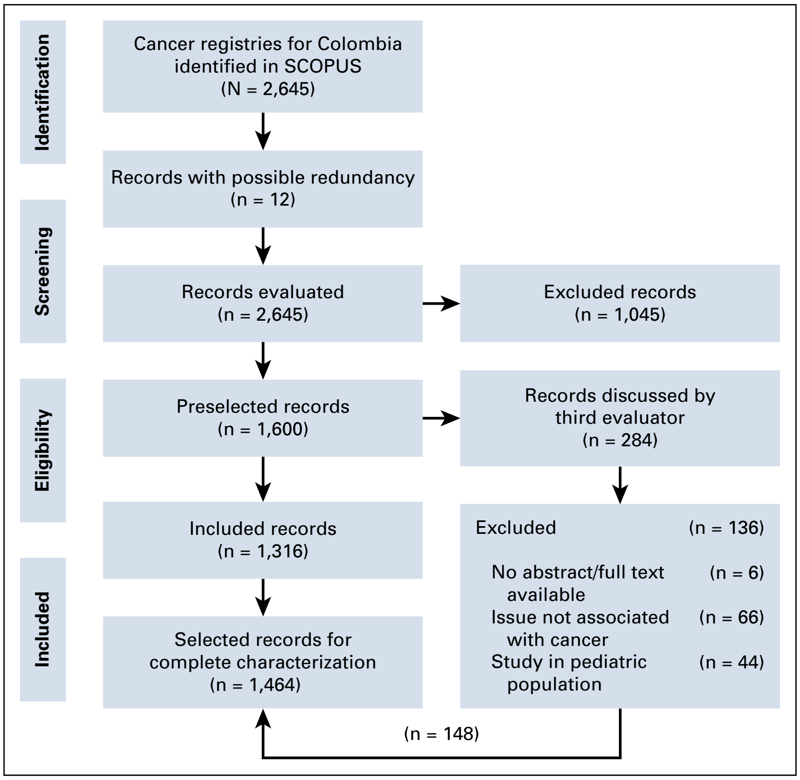

FIG 1. Prisma flow diagram for the systematic search: elaboration on the basis of data downloaded from SCOPUS, December 2016.

TABLE 1. Characteristics of Included Studies

Characteristic	No.	%
Included records for complete characterization	1,464	100
Bibliometric characterization		
Primary language of the text		
English	863	58.9
Spanish	416	28.4
Spanish and English	154	10.5
Not reported	13	0.9
Other language	11	0.8
English and another language other than Spanish	7	0.5
Document type		
All articles published and in press	1,166	79.6
Review research	128	8.7
Congress presentation	75	5.1
Letter	32	2.2
Note	20	1.4
Editorial	14	1.0
Not reported	13	0.9
Chapter book	9	0.6
Short survey	6	0.4
Errata	1	0.1
Some funding declared	67	4.6
Median of authors per record (IC range)	5 (3-8)	
Median of institutional affiliations per registry (IC range)	3 (2-5)	
Median of citations per record (IC range)	2 (0-11)	
Characterization of content		
Type of study		
Observational studies	488	33.3
Case reports	240	16.4
Narrative reviews and book chapters	230	15.7
Preclinical studies (in vitro or animal pharmacologic models)	136	9.3
Intervention studies	99	6.8
Other	66	4.5
Not reported	55	3.8
Systematic reviews and integrative studies	42	2.9
Diagnostic validity studies	32	2.2
Ecologic and epidemiologic studies	29	2.0
Qualitative research	28	1.9
Health technology assessment	14	1.0
Health systems and public health policies	5	0.3

(Continued in next column)

TABLE 1. Characteristics of Included Studies (Continued)

Characteristic	No.	%
Primary site(s) included		
Other site(s) localization	342	23.4
Unspecified site(s)/more than 10 simultaneous sites	238	16.3
Cervix uteri cancer	235	16.1
Breast cancer	168	11.5
Stomach cancer	143	9.8
Colorectum cancer	81	5.5

NOTE. This is our own elaboration that is based on data downloaded from SCOPUS, December 2016.

Abbreviations: IC, interquartile; %, relative frequency.

most frequently studied pathologies were cervix uteri, breast, stomach, colorectum, skin, prostate, and lung. Other primary sites were aggregated into a single category (23.4%); in the remaining 16.3%, no specific site was stated. Of note, half of the records reported five or fewer authors and three different institutional affiliations per record. Until search execution (September 2017), 970 records (66%) have been cited at least once according to SCOPUS database.

Relationship Between Cancer Productivity and Related Mortality

Table 2 lists age-adjusted cancer-related mortality rates for the Colombian adult population as well as estimated rates of scientific productivity. If mortality rates for all cancer sites for the past 2 years were not available in the reference database, then these were assumed according to the tendency of the previous years (Fig 2). The scatter plot exhibited an inverse proportional relationship between both variables (Spearman coefficient r = –0.958; $P < .001$); results for linear regression are shown in Figure 3. The model provided a good fit and a high explanatory level based on the variation in productivity (coefficient of determination R^2 = 0.911). Figure 4 shows the absolute mortality and scientific productivity rates for specific cancer sites evaluated, which allows graphic comparison between these variables.

DISCUSSION

For the period between 2000 and 2015, this study suggests an inverse relationship between scientific productivity and mortality related to specific cancer sites for the adult population in Colombia. Nevertheless, this association presented notable variations when analysis considered cancer-specific sites that encompass the top mortality rates for cancer in the country. On a global scale, the relationships between a country's scientific output and its cancer mortality rates seem inversely correlated. A recently published study conducted by Are et al,[18] which included a total of 142 nations, also identified an inverse correlation

TABLE 2. Cancer-Related Mortality by Site and Time Intervals

	Rate by Period			
Variable	**1999-2003**	**2004-2008**	**2009-2013**	**2013-2015**
Specific mortality by site(s)*				
Breast (women)	16.2	13.7	13.9	13.8
Cervix uteri	9.2	7.9	6.9	6.5
Prostate	18.6	17.5	16.7	17.4
Stomach (women)	10.7	9.8	8.1	8.2
Stomach (men)	19.9	18.2	15.2	14.4
Colorectum (women)	8.1	6.7	7.3	7.5
Colorectum (men)	7.6	8.2	9.5	10.2
Lung (women)	8.2	8.2	7.6	7.3
Lung (men)	18.8	16	14.3	14.4
Adult (> age 15 years) population projection†				
Women	14,124,114	15,504,992	16,970,105	17,549,122
Men	13,300,283	14,655,565	16,103,999	16,670,486
Total	27,424,397	30,160,556	33,074,104	34,219,608
Scientific productivity‡				
Breast (women)	0.004	0.013	0.049	0.068
Cervix uteri	0.013	0.045	0.061	0.059
Prostate	0.002	0.005	0.009	0.029
Stomach	0.006	0.013	0.018	0.018
Colorectum	0.001	0.004	0.013	0.015
Lung	0.001	0.005	0.006	0.008

NOTE. This is our own elaboration that is based on data downloaded from SCOPUS, December 2016.
*Standardized rate per 100,000 person-years.
†Departamento Administrativo Nacional de Estadística (DANE) projections for Colombia.
‡Crude rate per 10,000 person-years.

between cancer-based scientific productivity and cancer-related mortality. It is also worth mentioning that this effect was present after data from the United States, as the main contributor of scientific publications, were excluded. Around the globe, the same phenomenon is observed in the Americas, Europe, and Asia but not in Africa.[18] This relationship has been explored slightly in some Latin American countries, and results identified highly heterogeneous associations between research productivity and mortality in cancer.[10,17,20-24] Furthermore, in some cases, discordance between the relative weight for specific cancer-site research and mortality is observed. In this study, we identified a similar finding between research productivity and mortality by cancer site. Analysis on cancer-specific locations is needed to fully understand the observed correlations. The results of this study highlight the importance of close linkage among research on health priorities, evidenced-based policy making, and cooperation strategies. Such efforts would contribute greatly to common, previously described public health issues in developing regions, such as Latin America.[25]

Overall, it would be extremely difficult to assume any causal relationship from this study. A more cautious approach is to consider scientific productivity and its effect on cancer mortality as a result of the sum of socioeconomic and cultural factors (eg, public health interventions, health care system structure and dynamics, quality epidemiologic surveillance, and translational capabilities from academics into community, among others). First, any form of health-related research output requires reliable, rigorous data collection and follow-up procedures to allow precise estimation of attribution to cancer mortality. Aspects such as loss to follow-up or underrepresentation or misrepresentation of cancer statistics could significantly alter results in terms of mortality, which makes cancer registries key information sources for decision making.[26] Colombia is a remarkable example, with a city-based approach of long-running high-quality epidemiologic data on the basis of centralized death records (eg, the Registro Poblacional de Cáncer de Cali) that has provided useful data for decision making by encouraging specific public health strategies in the region and worldwide.[27,28] However, these local data may not be representative on a national level, which makes

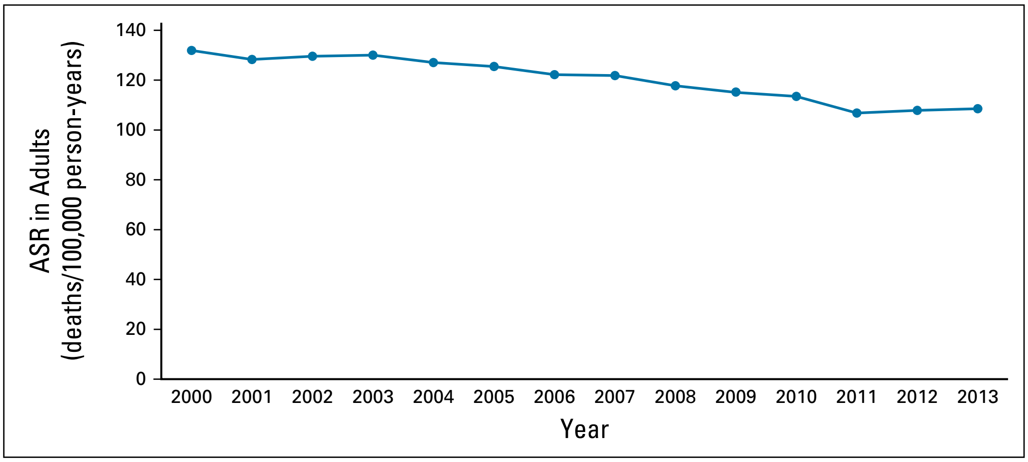

FIG 2. Cancer related mortality: elaboration on the basis of data downloaded from the annual mortality rates reported by GLOBOCAN for Colombia. ASR, age-standardized rates.

nationwide cancer data registries an imperative need.[27] Recent efforts to expand cancer registries in different Colombian cities have been conducted, and implementation of an electronic national information system for cancer surveillance is underway.[29]

Second, socioeconomic issues are possible confounders for late diagnosis and advanced-stage disease presentation. These are partially related to accessibility barriers for quality diagnostic services and affordable treatments; limited technologic availability; and geographic, environmental, cultural, and ethnic particularities.[5,30] Recently, Colombia has experienced a large growth in the number of oncology services, which opens the possibility for timely, quality health care diagnosis and treatment provision. Unfortunately, remote areas are a less promising setting, because the lack of interconnectivity and uninterrupted care remain as critical issues that requires attention to affect the disease burden in these specific regions.[31,32]

Third, research and taskforce resources are unmet challenges. Research investment in Colombia traditionally has been low: 0.27% of the GDP was allocated to research, science and technology in 2016. In addition, the approval of research projects is performed in an isolated and decentralized manner, which makes it difficult to consolidate capacities.[33] Moreover, the country is in urgent need of an economic investment program to orient research resources and efforts on priority public health issues. When the type of scientific production and its quality are analyzed, the majority of articles included in this study were observational studies, case reports, and reviews. This indicates that there is substantial room for improvement on the design of research

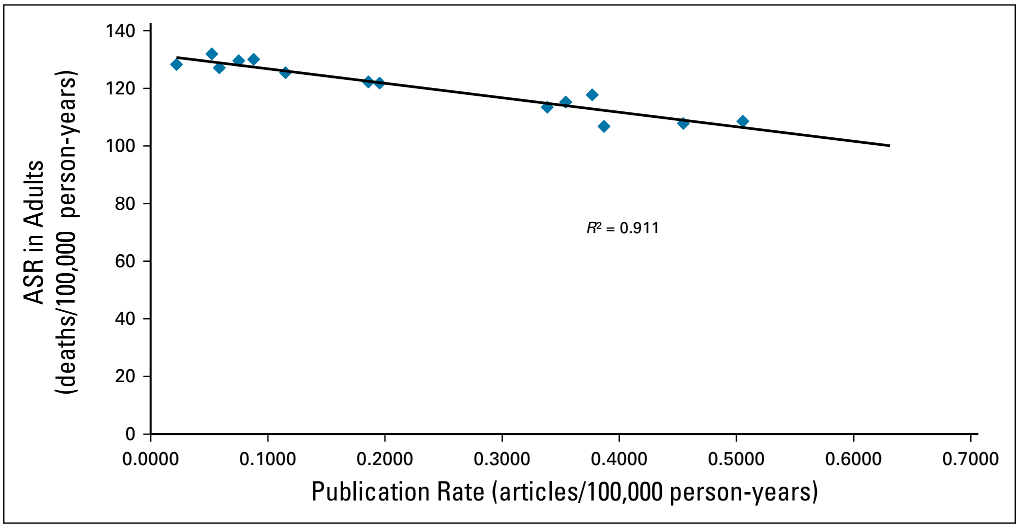

FIG 3. Correlation graph for yearly publication rate and cancer related mortality: elaboration on the basis of data downloaded from SCOPUS and the population register of Cali, December 2016. ASR, age-standardized rates.

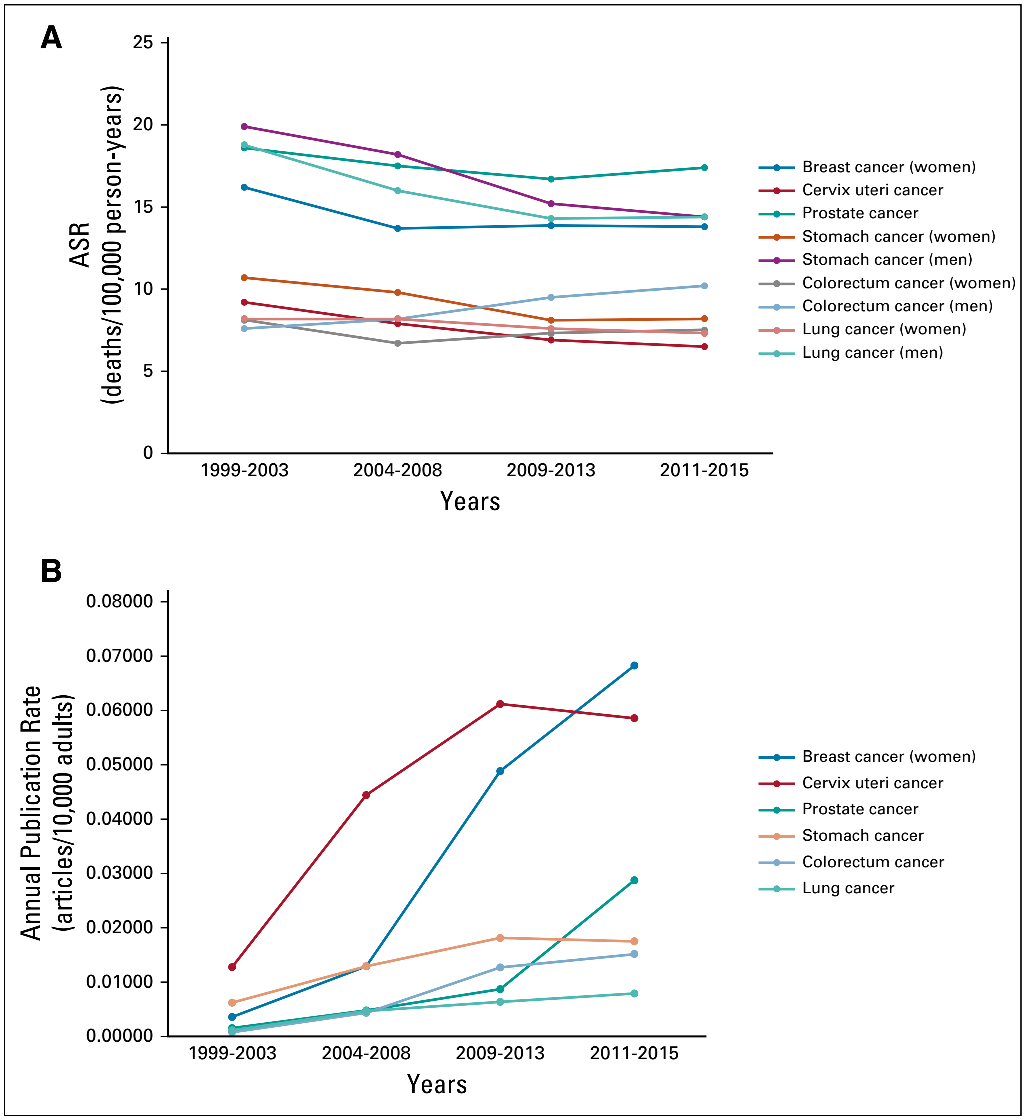

FIG 4. (A) Site-specific mortality and (B) scientific productivity by main sites: elaboration on the basis of data downloaded from SCOPUS, December 2016. Sex-specific cancer sites are shown separately. ASR, age standardized rates.

strategies to increase both quantity and quality of publications. Several proposed strategies include universal training of authors, establishment of standardized operating procedures, encouragement of publication of negative results, and strengthened research oversight.[34] Recent characterizations have revealed increasing trends in the number of investigators and research groups dedicated to cancer in the country[10] and in author networking in centralized groups of high-productivity authors; these changes indicate that cooperation is a key factor in publication competence growth.[35] This study found a low median number of coauthors per records—as seen in other developing countries, where average coauthorship in cancer publications was estimated as between two and five authors.[36]This lack of collaboration could be addressed through the conformation of strong academic and scientific alliances and with associations that comprise national and regional networks. The recent governmental efforts to promote English literacy in Colombia should result in an easier articulation in global research networks. Although results from this program have not yet been dramatically effective, the number of English-speaking graduates has increased in the recent years.[37]

Last, public health policies and interventions have been undertaken as population measures for cancer control—by sites and by specific risk factor–disease dynamics— have been identified in the Americas. It is estimated that up to 26% of cancer deaths in the American continent are attributable to lifestyle and environmental exposures, such as tobacco, and this rate is higher than the worldwide rate (22%). Meanwhile, incident cancer cases attributable to infections agents are higher in Latin America than worldwide (17% and 16.1%, respectively).[38,39] In Colombia, public policy efforts have been implemented during the past decade through specific laws and regulations for tobacco control, human papillomavirus vaccination in young women of reproductive age, alcohol, diet, physical activity, radiation, and expositional occupational risk control on a population level.[32] Furthermore, screening recommendations have been included in national clinical practice guidelines issued by the Health Ministry for breast, cervical, prostate, and colorectal cancer in the adult population. Some of these strategies may have contributed to the observed decrease in mortality rates for the most aggressive anatomic sites, such as the breast, cervix, lung, and prostate; these also are paralleled with increasing scientific productivity trends, as seen in this study. All of these factors are a reflection of the recent governmental focus on high-burden cancer sites. However, real-world, real-time cancer data that demonstrates the impact attributable to public health policies and strategies are still lacking throughout the country.

This study also has some limitations. Population-based registries do not encompass the whole population and could miss several occurrences. Conversely, the inclusion of four official registries in the International Agency for Research on Cancer by 2013 could correct for under- or over-diagnosis of the Registro Poblacional de Cáncer de Cali for the previous years and therefore introduce bias in the cancer-related mortality rates.[27] Because of author barriers, many research records may remain as gray literature. Because the majority of articles published are written in English, non-proficient speakers would have a greater challenge in the diffusion of their results.[40]

In conclusion, many factors related to social and economic development seem associated with increased scientific productivity, which results in decreased mortality rates in cancer. This is the first study, to our knowledge, that examines a time-trend relationship. These findings should be validated in larger studies that examine this phenomenon in other cultures, populations, nations, and continents.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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APPENDIX

Bibliometric Search Strategy

The systematic search was performed with the use of the following bibliometric filters by means of cancer-related MeSH or EMTREE keywords.

((TITLE-ABS-KEY(Cancer*) OR TITLE-ABS-KEY(Carcin*) OR TITLE-ABS-KEY(Oncolog*) OR TITLE-ABS-KEY(Tumor*) OR TITLE-ABS-KEY(Neoplas*) OR TITLE-ABS-KEY(Incidentaloma) OR TITLE-ABS-KEY(Antineoplastic) OR TITLE-ABS-KEY(Antitumor) OR TITLE-ABS-KEY(Chemothera*) OR TITLE-ABS-KEY(Quimioterap*) OR TITLE-ABS-KEY(radioterap*) OR TITLE-ABS-KEY(radiotherap*) OR TITLE-ABS-KEY(Anticancer*) OR TITLE-ABS-KEY(Anticarcin*) OR TITLE-ABS-KEY(Germinoma) OR TITLE-ABS-KEY(Precancer) OR TITLE-ABS-KEY(Metastasis)) AND PUBYEAR > 1999 AND PUBYEAR < 2016) AND AFFILCOUNTRY(Colombia)

Cancer Rate Indicators: Data Extraction and Calculation

National annual sex-specific distributions for adult population. The official annual sex-specific distributions for the population age 15 years or older in Colombia from 2000 to 2015 were extracted from the governmental agency responsible for national statistics—named Departamento Administrativo Nacional de Estadística (DANE; accessible at www.dane.gov.co/index.php/estadisticas-por-tema/demografia-y-poblacion/proyecciones-de-poblacion).

All-site sex-specific cancer mortality rates for adult population. Standardized all-site cancer-related mortality rates were obtained for the population age 15 years or older on the basis of WHO/GLOBOCAN mortality database rates between 2000 and 2015 (accessible at www-dep.iarc.fr/WHOdb/WHOdb.htm). These rates then were weighted according to previous adult population sex distributions to obtain sex-standardized rates for all cancer sites.

Cancer-specific rates by sex for adult population. Rates for specific cancer sites were retrieved from a reference Colombian cancer registry (Registro Poblacional de Cáncer de Cali, or RPCC, accessible at rpcc.univalle.edu.co/es/Mortalidad/Estadisticas/index.php) for both sexes per 5-year period according to availability.

Annual cancer-specific productivity rates. Finally, we calculated productivity rates per all sites and each cancer site by considering total number of records that met selection criteria (per year or 5-year period, respectively) and dividing it by the number of estimated adult population. Specific cancer sites considered were breast, cervix uteri, colorectum, lung, prostate, and stomach.