

Cancer Research in Latin America, 2014-2019, and its Disease Burden

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ABSTRACT

There is little available information on cancer research overall in Latin American and Caribbean countries, and on its relationship with the disease burden from cancer, which is increasing as a proportion of the total. We identified cancer research papers in the Web of Science from 2014-19. Outputs of the region on anatomical cancer sites were compared with the relative disease burden from these cancers. Outputs of individual countries were compared with their wealth and their disease burden from cancer. Their usage and impact on other researchers were determined from U2, a new usage indicator, citation counts over three years (C0-2), and the impact factor of the journals in which they were published (JIF). In 2014-19, Brazil, Chile and Uruguay published twice the amounts expected from the Latin American trend-line, but much less than European countries, relative to their Gross Domestic Products (GDPs). Most countries under-researched cancer relative to its burden. Lung, pancreatic and oesophageal cancers were relatively neglected. Less populous countries' research was of high impact, principally due to international collaboration with larger nations. Latin American research funding was dominated by the public sector. Current research orientation and funding is insufficient to combat the growing cancer burden in Latin America. This reflects the lack of research funding overall, relative to the countries' GDPs. The paucity of private-non-profit support needs to be addressed with policies to encourage public donations, and the endowment of foundations. There is also a need to improve the infrastructure for clinical trials.

Keywords: Cancer research, Latin America, Citations, Funding, Journal impact factor, Disease burden.

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INTRODUCTION

The cancer burden in Latin America

As improvements in health are made world-wide, life expectancy has increased. Consequently, there are now many more old people and this trend is also observed in Latin America, many of whose countries are classified as upper-middle or lower-middle income nations according to the World Bank. Here, people are also tending to adopt the feeding and sedentary habits found in high-income countries, and also to suffer more exposure to environmental pollution. As a result, cancer has increased its share of the disease

burden.^[1,2] Infection-related cancers are also prominent in some Latin American countries.^[3]

The disease burden from cancer is normally measured in Disability-Adjusted Life Years (DALYs). These take account both of early death and of years lived with an often-painful disability. Tabulations by the World Health Organization (WHO) for 2000 and 2015^[4] show that in Latin America as a whole the burden from cancer rose from 8.2% to 10.2% of the total. This was an increase of 24% for the whole region, but the increase was twice as much (52%) in the low and lower-middle income countries (LMICs) of the region. It is therefore a major (and growing) health challenge in many Latin American countries, and thus requires a commensurate investment in research. In particular, prostate cancer imposes a relative burden 86% higher than in the rest of the world, and the cervical cancer burden is 37% higher. Conversely, lung cancer is relatively less burdensome in Latin America because cigarette smoking is less than the world average

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(385 *per caput, per year* compared with 1083, in 2016), and is likely to decrease further as tough tobacco laws are belatedly introduced in many countries. There are also geographical variations, with the Pacific-facing countries suffering more from gastric, oesophageal and gallbladder cancer.^[1]

Cancer research types and policies

Latin America is in particular need of health systems research in order to bring cancer control and treatment to the under-served parts of the region. Epidemiological research is necessary for the identification of geographically-specific cancer risk factors needed for the development of national cancer plans. Social science research helps with the design of interventions and programmes that are better adapted to the socio-cultural differences between populations. These are then more likely to be acceptable and feasible. Genomic research is needed to cater for the wide variation of the genotypes in the region, and their differences from those in other parts of the world. Cancer surgery is another area in which LMICs are lacking in research capability, and it is a major component of cancer treatment for adults.^[5] Furthermore, there is a need for independent ideas that are not part of the agenda of the pharmaceutical companies, but which can be translated to answer pressing clinical and scientific questions that affect sub-groups of the Latin American population.

However, efforts are under way to reduce environmental carcinogens, such as pesticides and aflatoxins in food processing,^[6] arsenic levels in drinking water,^[7] and other chemical pollutants in food and in the air. There are also coordinated efforts by the Pan American Health Organization (PAHO) to introduce Hepatitis B and Human Papillomavirus (HPV) vaccination, to implement the WHO framework convention on tobacco control, and to strengthen cervical cancer screening. However, there still remains a large disparity between the public and private sectors in healthcare, especially in cancer treatment.^[8]

LITERATURE REVIEW

There are a number of papers that treat of cancer research in Latin America, but most of them are concerned with a single country, or with a particular manifestation of cancer. In 2014, *Nature* published a brief overview of South American research^[9] which showed how dominant Brazil was, both in overall output of all research, and in its R&D expenditure (1.2% of GDP in 2011). A survey of Latin American medical oncologists examined the barriers to the development of clinical research,^[10] and this was also discussed at a workshop in Lima in 2015.^[11] Collaboration in clinical trials is an important component of cancer research in the region.^[12,13] More recently there have been studies on breast and cervical cancer in Latin America.^[14,15] In 2009, the US National Cancer Institute created a US-Latin America Cancer Research Network, and this has

been very beneficial.^[16,17] Two surveys of cancer research in Latin America have also appeared recently.^[18,19] As for cancer research in individual countries, Argentina's research covered in MedLine and the Latin American database, Lilacs, was surveyed in 2017.^[20] Brazil showed much more interest in cardiovascular research than in cancer in the last century;^[21] this reflected the much higher death rate from this disease. Only 9% of the health research budget was spent on cancer.^[22] Chile has provided a good snapshot of the current situation.^[8] Colombian cancer research was surveyed in 2006^[23] and again in 2015, 2016, 2017 and 2019.^[24-27] Mexican research on breast cancer,^[28] on cervical cancer,^[29] and in an ageing population^[30] has been described.

Objectives of this study

In this paper, we sought to analyse cancer research in all the 38 countries in the Latin American and Caribbean region. We identified cancer research papers published between 2014 and 2019 in the Web of Science (WoS, © Clarivate Analytics), and concentrated our analysis on the leading 16 countries,

Table 1: List of 16 leading countries in Latin America and the Caribbean (LAC), with their ISO2 country codes, and population and Gross Domestic Product in 2015.

Country	ISO2	Pop, m	GDP, \$bn	Country	ISO2	Pop, m	GDP, \$bn
Argentina	AR	43.4	585	Guatemala	GT	16.3	63.8
Brazil	BR	208	1804	Jamaica	JM	2.8	14.3
Chile	CL	17.9	241	Mexico	MX	127.0	1144
Colombia	CO	48.2	292	Panama	PA	3.9	52.1
Costa Rica	CR	4.8	54.1	Paraguay	PY	6.6	27.1
Cuba	CU	11.4	87.1	Peru	PE	31.4	189
Ecuador	EC	16.1	100	Uruguay	UY	3.4	53.4
Grenada	GD	0.1	0.98	Venezuela	VE	31.1	n.a.

Pop = population in millions; GDP = Gross Domestic Product, billions of US dollars.

listed in Table 1. Cancer research was defined very widely (by Lynne Davies of Cancer Research UK), as follows:

Cancer Research is intended to diminish cancer incidence and mortality and to improve survival and cures. It seeks to develop safe and effective methods to prevent, detect, diagnose, treat, manage, and ultimately, cure, human cancer. Primary research forms include basic, translational, clinical, and population research. They are aimed at the identification of the causative agents or underlying genetic or molecular defects producing cancer and at the development of these discoveries into prevention, diagnosis, and treatment, and the creation of effective and harmless surgical, radiation, and medical therapies.

We compared the countries' outputs with their wealth and disease burden, and we evaluated their influence using three

separate indicators. We also examined the types of research that they undertook, the anatomical cancer sites that they investigated, and their international collaboration and how this might be improved.

DATA AND METHODOLOGY

We applied a complex filter containing the names of 185 specialised cancer journals and 323 title words or phrases to the Web of Science for the six years 2014–19, and identified articles and reviews from the Science Citation Index – Extended, the Social Sciences Citation Index, and the Emerging Sciences Citation Index. The filter had previously been calibrated and had a precision, p , = 0.95 and a recall, r , = 0.98.^[31] The bibliographic details of all papers with an address in at least one of the 38 Latin American and Caribbean (LAC) countries listed below were downloaded, 500 at a time, and written to an Excel file.

ANTIGUA-BARBU OR ARGENTINA OR BAHAMAS
OR BARBADOS OR BELIZE OR BOLIVIA OR BRAZIL
OR CAYMAN-ISLANDS OR CHILE OR COLOMBIA
OR COSTA-RICA OR CUBA OR DOMINICA OR
DOMINICAN-REP OR ECUADOR OR EL-SALVADOR
OR GRENADA OR GUATEMALA OR GUYANA OR
HAITI OR HONDURAS OR JAMAICA OR MEXICO
OR NETH-ANTILLES OR NICARAGUA OR PANAMA
OR PARAGUAY OR PERU OR PUERTO-RICO OR
ST-LUCIA OR SINT-MAARTEN OR ST-VINCENT
OR SURINAME OR TRINID-TOBAGO OR TURKS-
CAICOS OR URUGUAY OR VENEZUELA OR W-IND-
ASSOC-ST

The addresses of the papers were parsed to show the fractional count of each country, both LAC ones and others. For example, a paper with one Brazilian, two Chilean and two United States addresses would be categorised as BR = 0.2; CL = 0.4; US = 0.4. A comparison was made with each country's output of biomedical research papers. This was based on a set of address terms, such as:

AGEING OR BAYER OR CARDIO* OR DAIICHI OR
EPIDEM* OR FARMAC* OR GLAXO* OR HLTH* OR
INSERM* OR JANSSEN OR KAROLINSKA* OR LILLY
OR MED OR NIH

In order to put the research outputs in context, they were compared with the countries' wealth, as expressed by their Gross Domestic Product (GDP). We also tabulated the percentages of GDP spent on all research, taken from World Bank for the latest year for which figures were available (<https://data.worldbank.org/indicator/GB.XPD.RSDV.GD.ZS>).

The three-year citation counts (C0–2) for papers from 2014–17 were also determined, matched to the papers, and written

to the file. We also added the “usage count” U2 (the number of times that the full text of the papers had been sought by WoS readers since 2013) and the journal impact factor (JIF) listed by Clarivate Analytics for most journals. The three values were each multiplied by the fractional counts of the 16 leading LAC countries on each paper in order to give a fairer impression of their contributions. These three indicators gave separate measures of the papers' likely impact on other researchers. However, because international papers tend to receive more citations than domestic ones, a better comparison of country research impact is given by the values for the leading countries' domestic papers, *i.e.*, those without any international collaboration.

The non-LAC countries were grouped in seven continental regions:

- EAP = East Asia and Pacific; 20 countries including Australia, China, Japan
- ECA = Eastern Europe and Central Asia; 26 countries including Poland, Russia
- EUR = Europe; 20 countries of pre-1996 European Union plus Cyprus, Iceland, Monaco, Norway and Switzerland
- MEN = Middle East and North Africa; 19 countries including the Maghreb
- NAM = North America; three countries: Bermuda, Canada, USA
- SAS = South Asia; five countries: Bangladesh, India, Nepal, Pakistan, Sri Lanka
- SSA = Sub-Saharan Africa; 22 countries

We analysed the extent to which the leading 16 countries collaborated with the seven regions. We also determined the percentages of their papers that included a foreign address, and the percentages of the foreign contributions to their output.

The papers were analysed by the anatomical cancer site with which they were concerned and the type or domain of research that they described. This analysis was based primarily on the papers' title words, and also on their journal name strings. For example, kidney cancer research was defined by these four title words: *kidney*, *neph*, *renal*, *Wilm* and three journal name strings: *KIDNEY*, *NEPHRO*, *RENAL*. The fractional count outputs from each country on each site, and in each domain, are listed in Tables 2 and 3. We also identified papers on clinical trials in a similar way. These are important for the development of new methods of diagnosis and treatment, and the subjects of these (*i.e.*, sites and treatments) were also analysed. The 16 leading LAC countries' relative commitment to research on each cancer site and of each type were compared with the average values for the whole region

Table 2. List of 21 cancer anatomical sites with trigraph codes

Site	Code	Site	Code	Site	Code
Bladder	BLA	Leukaemia	LEU	Oesophagus	OES
Cervix uteri	CER	Liver	LIV	Ovary	OVA
Brain & nervous system	CNS	Trachea, bronchus, lung	LUN	Pancreas	PAN
Colon and rectum	COL	Lymphomas, myeloma	LYM	Prostate	PRO
Gallbladder	GAL	Breast	MAM	Stomach	STO
Mouth and oropharynx	HEN	Melanoma, skin	MEL	Testicular	TES
Kidney	KID	Multiple myeloma	MYE	Uterus	UTE

Table 3: List of 12 research domains (or types), with tetragraph codes.

Domain	Code	Domain	Code	Domain	Code
Clinical trials	CLIN	Genetics	GENE	Quality of life	QUAL
Diagnosis	DIAG	Palliative care	PALL	Radiotherapy	RADI
Chemotherapy	DRUG	Pathology	PATH	Screening	SCRE
Epidemiology	EPID	Prognosis	PROG	Surgery	SURG

so as to show their specialisations, and which ones were significantly different from unity. These tables were intended to show how individual countries might benefit from more collaboration with another one that was relatively stronger in the subject area.

RESULTS

Papers, GDP and DALYs

There were 22,412 papers over the six years, 2014–19. [These included 138 “early access” papers published in 2020, but available online in 2019]. There was a jump from 2408 papers in 2014 to 3205 in 2015 (+33%) because of the accession to the WoS of the Emerging Sciences Citation Index, but after then output from the region increased at 6.3% per year. This is somewhat faster than the growth in world cancer research output in the same years (5.2%). It is noticeably faster than that in the NAM countries (2.7%) and the EUR ones (2.9%), but slower than in the EAP countries (8.4%), mainly because of the rapid growth in Chinese output.^[1] Figure 1 shows the outputs of the LAC countries plotted against their wealth. [Data from 26 countries have been used to generate the least-squares correlation line. Countries with either output or GDP < 10 units have been omitted.] The correlation is good, comparable with that found for European countries.^[32] Jamaica (JM), Brazil (BR), Chile (CL) and Uruguay (UY) all publish more than twice as much as the correlation line would suggest, but the Dominican Republic (DO), Guatemala (GT), and Panama (PA) less than half as much. The percentages of Latin American countries’ GDPs that was spent on all research are given in Table 4, with data for Portugal and

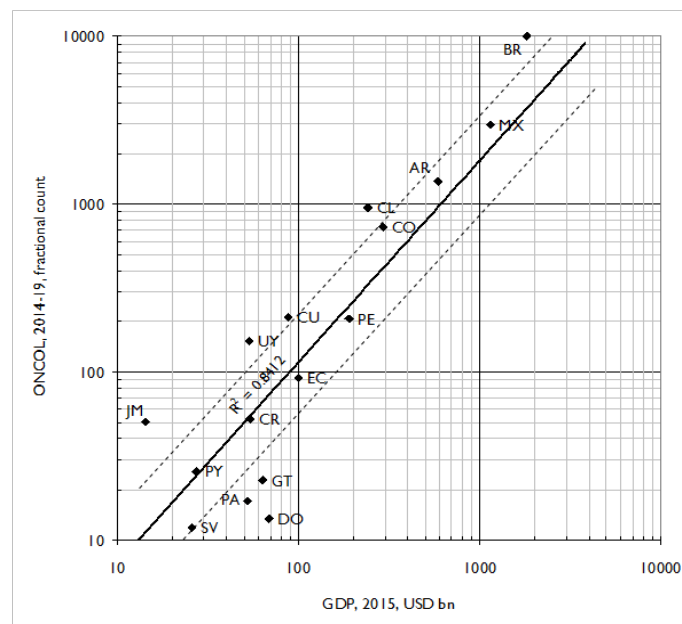


Figure 1: Plot of output of cancer research papers in the WoS from Latin American and Caribbean countries in 2014–19, fractional counts, against their Gross Domestic Product in 2015, billion US dollars. ISO2 codes as in Table 1; DO = Dominican Republic. Dashed lines show values twice and half those predicted by the least-squares correlation line.

Table 4: The expenditure on research by Latin American countries, and Portugal and Spain, as a percentage of Gross Domestic Product. The year is the latest for which the World Bank has data.

Country	ISO2	Year	Percent	Country	ISO2	Year	Percent
Portugal	PT	2018	1.37	Venezuela	VE	2014	0.34
Brazil	BR	2017	1.26	Mexico	MX	2018	0.31
Spain	ES	2018	1.24	St Lucia	LC	1999	0.31
Argentina	AR	2017	0.54	Colombia	CO	2018	0.24
Uruguay	UY	2017	0.48	El Salvador	SV	2017	0.18
Ecuador	EC	2014	0.44	Bolivia	BO	2009	0.16
Cuba	CU	2017	0.43	Panama	PA	2017	0.15
Costa Rica	CR	2017	0.42	Paraguay	PY	2017	0.15
Chile	CL	2017	0.36	Peru	PE	2018	0.13

Spain for comparison. These former colonial powers provide a fairer benchmark than research-intensive countries such as Germany or Israel. Brazil is the only country in the region that spends more than 1% of its GDP on research, according to World Bank data.

The next comparison is between the percentages of LAC countries’ biomedical research outputs that are on cancer and the percentages of their total disease burden in DALYs attributable to malignant neoplasms. These data were taken from the tables published by the World Health Organization.^[1] This comparison is shown in Figure 2. Most countries are under-researching cancer, particularly Panama (PA), Uruguay (UY) and Cuba (CU). Although the comparison with GDP indicates countries’ capability to do cancer research, Figure

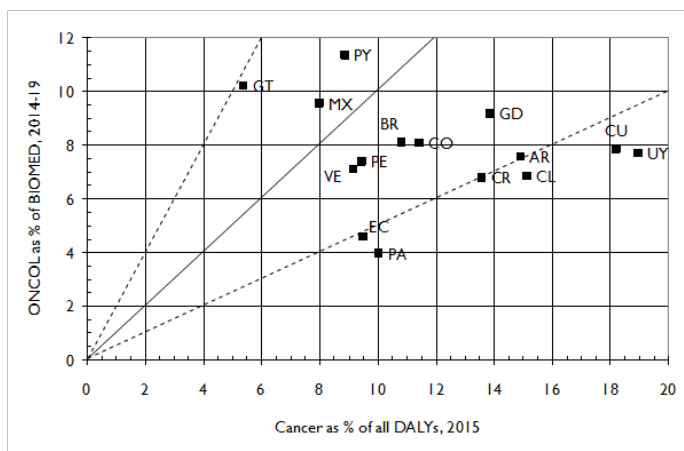


Figure 2: Comparison between cancer research as a percentage of all biomedical research for LAC countries, 2014-19, and the percentage of all DALYs in 2015 attributable to cancer. Note: data on DALYs not available for Grenada as it is not a Member State of the WHO. Dashed lines represent values twice and half those of equality. ISO2 codes are shown in Table 1. Integer counts.

2 shows whether their biomedical research portfolio is appropriately distributed to combat the challenge of cancer and the problems of the epidemiological transition.

Collaboration and impact

The 16 leading countries vary greatly in the extent to which they collaborate internationally. In Table 5, the countries are ranked by the percentage of their papers with a foreign co-author. Normally countries with small outputs need to seek partners abroad,^[33] and this is seen in the data in the table. This percentage is always lower than that of the contribution made by foreign countries. There is also a big variation in the countries and regions with which the individual LAC countries collaborate. This is shown in Figure 3. The countries are ordered by the extent to which they accept contributions from other LAC countries. This is clearly greatest for the small countries, such as Uruguay (UY), Guatemala (GT) and Cuba (CU). The chart shows that collaboration is mainly with EUR and NAM regions, and that NAM dominates in some

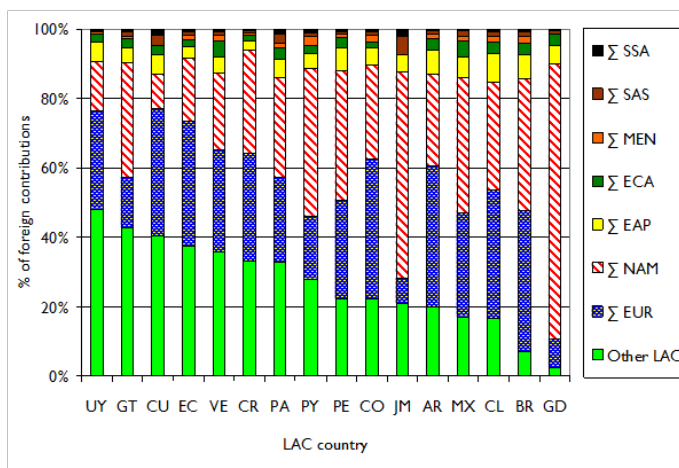


Figure 3: Chart of the different international partners' contributions to the foreign contributions to the cancer research papers of 16 leading LAC countries, 2014-19.

countries such as Jamaica (JM) and Grenada (GD), whereas EUR is much higher than NAM in Cuba for political reasons, and also in Ecuador (EC) and Uruguay.

The next results are the measures of impact on other researchers. They are different, but tend to be positively correlated. They are shown as three tables within Table 6 with the countries ranked separately in each. It is perhaps surprising that three small countries, Guatemala (GT), Panama (PA) and Paraguay (PY) show to advantage. This is because they all collaborate extensively internationally (Table 4) and so are benefiting from the probably superior research infrastructure and expertise of some of their partners. For example, of the 12 most-cited papers from Guatemala, eight have a US first author, and none of the other four have one from Guatemala itself. Of the 11 most-cited papers from Paraguay, four have a US first author, and the other seven first authors have a European affiliation.

Perhaps a fairer comparison of the countries' research impact is given in Table 7, which shows similar results for purely domestic papers. Data are given only for the 12 countries

Table 5: The percentages of the cancer research papers from 16 leading LAC countries in 2014-19 that have a foreign co-author (FOR %), and the percentages of fractional foreign contributions to the papers (INT'L %).

ISO2	INT	FRAC	FOR %	INT'L %	ISO2	INT	FRAC	FOR %	INT'L %
GT	92	22.7	75.3	97.8	CO	1263	729.3	42.3	60.8
GD	96	27.7	71.2	99.0	CL	1635	950.5	41.9	63.7
PY	81	25.5	68.5	92.6	VE	220	130.5	40.7	58.6
PA	53	17.1	67.8	86.8	JM	82	50.5	38.4	57.3
CR	152	52.6	65.4	80.9	AR	2109	1366.1	35.2	54.2
UY	338	153.1	54.7	75.1	CU	306	208.1	32.0	50.7
PE	433	207.1	52.2	69.5	MX	3898	2971.4	23.8	37.1
EC	183	92.5	49.5	68.3	BR	12887	10046.9	22.0	37.1

Countries ranked by the percentage of foreign co-authorship. INT = integer count of papers; FRAC = fractional count. ISO2 codes for countries in Table 1.

Table 6: Three measures of average impact of all cancer research papers from LAC countries, 2014-19, on other researchers: Journal Impact Factor (JIF), Usage count in WoS (U2), and count of citations in the three years beginning with publication year.

Journal Impact Factor				U2 usage count				Citations in 3 years			
ISO	N	Total	Mean	ISO	N	Total	Mean	ISO	N	Total	Mean
GT	16.5	75.1	4.54	PA	17.1	157	9.22	GT	12.3	117	9.50
PE	93.8	383	4.08	CL	950	7405	7.79	PY	15.7	137	8.76
PY	18.9	71.2	3.76	AR	1366	10098	7.39	EC	44.4	270	6.09
CR	35.2	124	3.52	MX	2971	21154	7.12	CR	30.1	165	5.50
UY	99.5	333	3.35	BR	10047	71460	7.11	CL	566	3106	5.49
AR	1192	3684	3.09	UY	153	1035	6.76	AR	875	4678	5.35
EC	51.6	152	2.95	EC	92.5	523	5.66	PA	10.6	51.7	4.88
CU	106.7	306	2.87	PY	25.5	140	5.49	GD	17.4	84.7	4.87
CL	805	2251	2.80	VE	131	658	5.04	BR	6193	29965	4.84
PA	14.2	39.3	2.77	CO	729	3548	4.86	PE	118	526	4.47
BR	8530	22739	2.67	CR	52.6	238	4.52	MX	1788	7764	4.34
MX	2468	6391	2.59	GT	22.7	101	4.46	CO	405	1449	3.58
CO	444	1145	2.58	CU	208	875	4.20	UY	96.3	344	3.57
GD	19.1	49.1	2.57	PE	207	747	3.61	CU	125	328	2.62
VE	57.9	132	2.28	JM	50.5	158	3.13	VE	91.6	235	2.57
JM	38.8	73.2	1.88	GD	27.7	85	3.08	JM	39.0	92.1	2.36

ISO codes in Table 1, fractional counts. N = number of papers with this parameter

Table 7: Three measures of average impact of domestic-only cancer research papers from LAC countries, 2014-19, with at least 10 papers, on other researchers: Journal Impact Factor (JIF), Usage count in WoS (U2), and count of citations in the three years beginning with publication year.

Journal Impact Factor				U2 usage count				Citations in 3 years			
ISO	N	Total	Mean	ISO	N	Total	Mean	ISO	N	Total	Mean
UY	41	129	3.15	AR	966	6425	6.65	EC	28	151	5.39
CU	58	157	2.71	CL	594	3899	6.56	AR	613	2713	4.43
AR	828	2198	2.65	BR	8103	53142	6.56	BR	5027	19959	3.97
EC	24	59.3	2.47	MX	2451	15884	6.48	MX	1488	5692	3.83
CR	15	37	2.47	VE	91	375	4.12	CL	360	1301	3.61
MX	2000	4819	2.41	UY	84	330	3.93	UY	46	114.0	2.48
BR	6770	16159	2.39	CO	495	1660	3.35	VE	67	143	2.13
CL	487	1061	2.18	EC	58	184	3.17	JM	28	58	2.07
PE	34	69	2.02	JM	35	103	2.94	CR	15	29	1.93
VE	29	56	1.91	CU	151	362	2.40	CU	91	159	1.75
CO	244	440	1.80	CR	29	63	2.17	CO	270	414	1.53
JM	26	33	1.27	PE	132	255	1.93	PE	76	86.0	1.13

ISO codes in Table 1

with at least ten domestic papers. If equal weight is given to the rankings in the three individual tables, then Argentina emerges clearly as the country with the best performance, followed by Brazil, Ecuador and Uruguay equally, Mexico and then Chile.

Anatomical sites and research domains

Figure 4 examines the relative commitment to research on the different cancer anatomical sites for the LAC region as a

function of their relative disease burden. This shows a rather familiar pattern, with breast cancer (MAM) relatively over-researched (but only by 47%), and lung cancer (LUN) under-researched by 69%. However, some less burdensome cancers are also relatively neglected, such as gallbladder (GAL) and oesophageal (OES) cancers, which are under-researched by 82%, and pancreatic (PAN) cancer by 78%.

Table 8 shows the relative commitment of the 16 leading LAC countries to research on the ten main cancer anatomical sites.

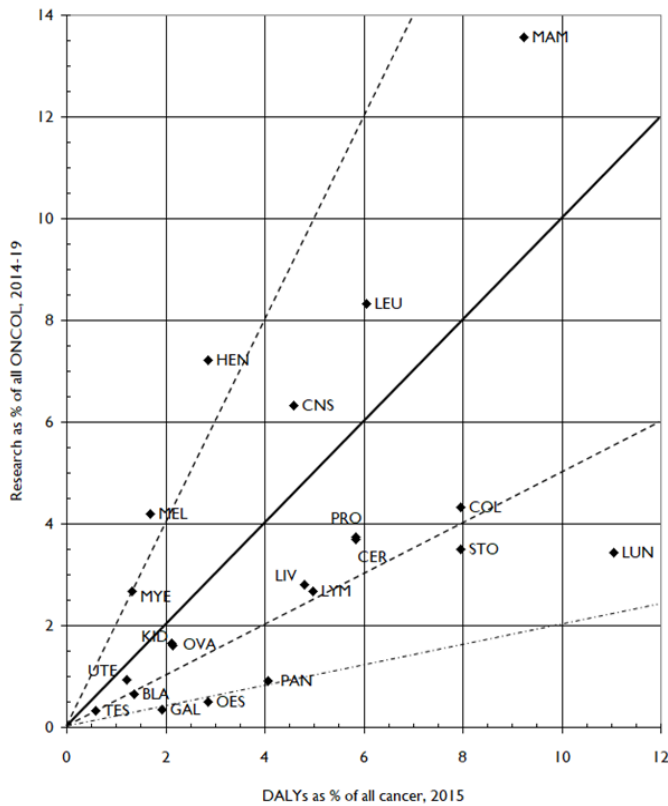


Figure 4: Relative commitment to research on different cancer anatomical sites (for codes, see Table 2) compared to the relative disease burden in 2015 for the LAC countries as a group. Solid diagonal line represents equivalence; dashed lines represent research outputs twice or half the equivalent disease burden; chain dotted line shows outputs one-fifth the equivalent disease burden.

Countries with a similar level of commitment to the LAC average are shown with a ratio of unity. Some of the cells are tinted so to draw attention to the countries with a noticeably different relative commitment. However, most differences are not statistically significant and different typefaces are used to show this.

Among the larger countries scientifically, Mexico (MX) has a statistically high relative commitment to four anatomical sites, and a low one to four others. It particularly favours work on cervical cancer, as does Colombia (CO). One of the most striking results is the very high concentration of Chile (CL) on gallbladder cancer research (GAL, more than 11 times the LAC average). Breast cancer, which in most countries is the one most researched, is here relatively favoured only by Mexico. Jamaica (JM) is notable for its high output on prostate cancer.

Table 9 shows similar ratios for different research domains, including clinical trials (CLIN). These are important for the region, but in most countries are under-researched, except in Costa Rica (CR). Out of a total of 555 clinical trials papers, 41% concerned drug treatments, 12% prognosis, and 9% each surgery and radiotherapy. As for the anatomical sites, 20% concerned breast cancer, 10% lung cancer and 9% leukaemia and other haematological cancers. These clinical trials papers were extremely international: 264 (48%) involved the USA, more than twice the percentage for all the LAC papers (21%).

Table 8: The commitment of 16 leading LAC countries, relative to the LAC group as a whole, to research on cancer on different anatomical sites. For country ISO codes, see Table 1. For site trigraph codes, see Table 2.

	CER	CNS	COL	GAL	HEN	LEU	LUN	MAM	MEL	PRO	STO	Total
BR	0.88	1.04	1.01	0.24	1.41	0.79	0.70	0.95	1.16	0.89	0.96	10047
MX	1.88	1.07	0.87	0.23	0.37	1.28	1.36	1.30	0.63	0.61	1.09	2970
AR	0.39	0.93	1.13	0.97	0.71	1.39	1.13	1.07	1.13	0.80	0.65	1366
CL	0.65	0.72	0.83	11.2	0.63	0.87	0.91	0.77	1.11	1.65	1.97	950
CO	1.60	0.96	0.76	0.02	0.77	1.24	1.17	0.85	0.94	1.26	1.33	729
CU	1.03	0.64	0.80	1.40	0.69	0.41	2.67	1.01	0.51	0.64	0.23	208
PE	1.34	0.47	0.75	1.48	0.55	1.71	1.10	1.23	0.47	0.90	2.18	207
UY	1.19	0.48	1.87	0.00	0.87	1.84	0.96	0.84	1.17	0.95	0.10	153
VE	1.33	0.57	0.86	0.00	0.20	0.64	0.88	0.96	0.59	0.95	1.20	131
EC	1.49	0.80	1.21	0.45	0.63	0.92	0.88	0.88	0.31	0.86	2.07	92.5
CR	1.79	1.22	0.63	0.00	0.79	0.42	2.66	0.52	0.60	0.51	4.39	52.6
JM	0.71	0.39	1.75	0.00	1.01	0.79	0.00	0.68	0.47	6.28	0.28	50.5
GD	1.54	1.84	2.70	0.00	0.60	1.03	0.35	0.64	1.32	2.69	3.31	27.7
PY	1.55	0.36	0.54	0.00	0.01	0.95	0.76	0.27	1.25	0.39	0.28	25.5
GT	2.71	0.00	0.08	0.00	3.42	2.86	0.00	0.10	0.43	0.10	0.74	22.7
PA	3.16	0.72	0.21	0.00	0.00	0.38	0.86	1.06	1.00	0.22	1.80	17.1
	830	1419	970	77	1618	1896	768	3040	939	836	785	22412

Bold type indicates that $p < 0.5\%$; normal type indicates $p < 5\%$, and *small italics* indicates that $p > 5\%$ and that the result is not statistically significant. The calculations are based on the Poisson distribution with one degree of freedom. Values that differ by a factor of two or more are tinted green (higher) or pink (lower). Those that differ by a factor of $\sqrt{2}$ or more are tinted pale green (higher) or pale yellow (lower).

Table 9: The commitment of 16 leading LAC countries, relative to the LAC group as a whole, to different types or domains of cancer research. For country ISO codes, see Table 1. For domain tetragraph codes, see Table 3.

Ratio	CLIN	DIAG	DRUG	EPID	GENE	PALL	PATH	PROG	QUAL	RADI	SCRE	SURG
BR	0.70	1.02	1.01	0.82	1.03	1.26	1.14	0.96	1.21	1.11	1.04	1.14
MX	0.52	1.00	0.88	1.16	1.11	0.65	0.84	0.93	0.81	0.66	0.82	0.72
AR	0.48	0.59	1.14	0.80	0.91	0.29	0.52	0.81	0.53	0.63	0.54	0.82
CL	0.50	0.80	0.71	0.89	0.78	0.88	0.73	0.88	0.90	1.08	1.26	1.03
CO	0.49	1.16	0.72	1.06	0.78	1.45	0.74	1.04	1.29	1.13	1.03	1.15
CU	1.00	1.13	0.91	0.89	0.40	1.22	0.31	0.48	0.58	0.58	1.03	0.49
PE	0.37	2.13	0.68	0.95	0.67	0.93	1.08	1.16	0.80	0.82	1.47	1.05
UY	0.95	0.73	0.87	1.66	0.74	0.74	0.66	0.83	0.18	0.84	0.62	1.07
VE	0.02	1.31	0.68	0.74	1.11	0.92	1.22	0.75	1.22	0.63	0.19	0.75
EC	0.58	1.48	0.52	2.61	0.77	0.11	1.12	0.80	0.83	0.42	0.73	1.16
CR	3.56	1.62	0.97	1.31	0.59	1.88	0.60	0.99	3.43	0.22	1.89	0.74
JM	0.20	0.09	0.35	1.54	0.35	0.00	0.60	0.81	2.31	0.00	5.24	1.72
GD	0.18	1.05	0.84	2.10	0.16	0.81	0.27	1.82	0.90	0.38	2.17	1.45
PY	0.11	1.09	0.12	3.09	0.78	0.00	5.02	1.63	0.50	0.41	0.66	2.18
GT	0.07	1.61	0.13	0.77	0.72	0.64	4.36	0.62	0.00	0.39	2.41	2.06
PA	1.03	1.70	0.42	0.94	0.57	0.00	0.00	1.83	0.00	0.46	0.21	1.55

Bold type indicates that $p < 0.5\%$; normal type indicates $p < 5\%$, and *small italics* indicates that $p > 5\%$ and that the result is not statistically significant. The calculations are based on the Poisson distribution with one degree of freedom. Values that differ by a factor of two or more are tinted green (higher) or pink (lower). Those that differ by a factor of $\sqrt{2}$ or more are tinted pale green (higher) or pale yellow (lower).

The most popular research domain overall was genetics (GENE) with 17% of the total output. This was followed by prognosis (PROG) with 11% and drug treatment with 10%. Surgery (SURG) accounted for 8%, but radiotherapy (RADI) for only 3.2%. There was little research on screening or palliative care (only 2% on each). In Peru, collaboration between cancer researchers and workers on artificial intelligence at the Pontificia Universidad Católica del Perú led to the development of automated analysis of medical images. Most of the departures from unity in Table 8, except for Brazil, are too small to be discussed even though the results may achieve statistical significance.

DISCUSSION

Because of continued political instability and skepticism over their scientific capabilities, many Latin American countries have few or highly fluctuating long term research policies, which ultimately affects cancer research and treatment. There are budgetary delays, and sometimes massive reductions, which make sustainable planning and implementation difficult, except in the state of São Paulo in Brazil. This is the background to our study.

The first two Figures compare the individual countries' outputs to their wealth, and to the amount of their disease burden attributable to cancer. The intention is to show whether the volume of cancer research is appropriate in view of these two comparators. Although Figure 1 shows that there

is a good correlation between cancer research and wealth for these Latin American and Caribbean countries, the volume of research is far below that produced by European countries with similar levels of wealth. Thus, for the four leading LAC countries (Brazil, Mexico, Argentina, Chile) the mean ratio of papers in 2014–19 to GDP in US \$ billions is 5.2. However, for four similarly wealthy European countries (in descending order: Italy, Spain, Poland and Finland) the corresponding ratio is 20.3, almost *four times as high*. This differential parallels the much lower share of GDP that is spent on all research in Latin America compared with Europe. Latin America largely depends economically on primary goods and services with scarce development of manufacturing and technology, and so regards medical research, and expenditure on research in general (Table 4), as a much lower priority than it is in Europe. If this is to be rectified, then research needs to be much higher on the governmental agenda, and scientists and medical personnel must be more active in making the case for it. There is good evidence that medical research in a country enables its clinicians to incorporate appropriate advances made elsewhere into the diagnosis and treatment of their patients,^[34,35] subject of course to local exigencies. It can also attract intellectually able people to work in the healthcare system, and provide jobs for the large numbers of well-trained students who might otherwise go abroad.

Health intelligence is one of the areas of research highly in demand in LMICs. More than 80% of the world population was not covered by a population-based cancer registry in

2012.^[36] Fundamental epidemiological information is lost wherever there is no adequate registry of diagnosis and treatment, resulting in an underserved and non-reported health care system. An example of improvements was when the patient advocacy groups and academics in Chile successfully petitioned the government to introduce a national cancer law that not only guaranteed better health coverage, but also developed a national cancer registry and stipulated the requirement for both basic and clinical investigation.^[37]

Better health also enhances economic productivity. One avenue for this promotion of research is the mass media. Stories about new discoveries in medicine can be stimulated through contacts between researchers and journalists, and mentions of successes funded by state and other agencies can be helpful. Although there are few medical research charities collecting from the public in Latin America (the Fundação do Câncer in Rio de Janeiro is a conspicuous exception), there are endowed foundations in several countries, particularly Argentina. Publicity for their activities may stimulate other rich individuals and companies to create them, and persuade politicians to provide fiscal stimuli.

Figure 2 compares the leading countries' relative commitment to cancer research within their biomedical research portfolio, and shows a great variation. It is based on integer counts, but small countries which collaborate extensively with others in cancer are also likely to do so in other medical subject areas. The five richest countries, measured by GDP *per caput*, are Uruguay, Argentina, Chile, Panama and Costa Rica, and all of them are relatively neglecting cancer within biomedical research, most by a factor of two or more. Their ageing populations will suffer increasingly from cancer rather than the infectious, perinatal and nutritional diseases that form the first group of diseases on the WHO classification, and so a re-ordering of medical research priorities is needed.

Tables 6 and 7 show three indicators of research impact and usage. Because of the big variation in country size in Latin America, and the countries with small populations favouring international collaboration, the data for all papers from each country in Table 6 do not give a true impression of the effectiveness of the work of the more populous countries, which is much better seen in Table 7. Argentina scores highly on all three indicators, and this accords with one of the findings in the *Nature* survey of South American science,^[9] namely that this country has much the highest proportion of researchers per 1000 workers. It is also the only Latin American country to have won three Nobel prizes for science.

We have also examined the distribution of cancer research by site for individual countries, because the allocation of research is done mainly at the national level. [In the less populous countries, where the large majority of their cancer research

papers are international, the distribution of their papers by anatomical site may reflect rather more the disease burden pattern of their main collaborators and sources of financial support]. There are some notable differences, seen in Table 8, and many of them reflect national cancer burdens.

The most conspicuous example is the emphasis on research and high burden from gallbladder cancer in Chile (7.2% of all cancer DALYs in 2015, compared with 1.9% in all LAC countries). Until 2009, it was the malignancy with the highest female mortality. Another example is the high relative concentration of Cuba (CU) on lung cancer (LUN) research which reflects its burden of 22% of all cancer. Another striking result is the high relative concentration of Jamaica (JM) on prostate cancer. This probably reflects its Afro-Caribbean population who are more susceptible to this cancer^[38] than whites and Asians, and its high prostate cancer burden, 15.6% of all cancer DALYs compared with 5.8% for the LAC region, and 3.1% for the world. The other Caribbean island states, especially Barbados, also suffer greatly from prostate cancer. Brazil's highest relative research concentration is on head and neck cancer, and it also suffers the most from this cancer manifestation among all the Latin American countries (4.5% of its total cancer DALY burden). Costa Rica has a high relative commitment to stomach cancer research (STO), again reflecting its burden from that cancer (14.7% of all cancer DALYs compared with 8.0% for both the LAC region and the world). It is also highly prevalent in Central America, and in the Pacific-facing states of South America. [Curiously, it is also a major source of cancer burden in the western Pacific countries of China, Japan and South Korea].

However, as many Latin American academics undertook post-graduate training in other continents, their research interests on their return home may reflect the cancer specialisms of their country of training rather than those of their country of residence. These observations highlight the necessity for individual Latin American countries to perform more cancer research and determine the underlying causes of their specific national mortality. More work is also needed throughout Latin America on screening and diagnosis, and on end-of-life care which is neglected almost everywhere. However, the prime need is for the national funding bodies, who are the main sources of research support, to develop mechanisms that enable them to change their priorities in favour of the ones of greatest need for enhancement. There is also very little work in the four largest countries in terms of research output (Brazil, Mexico, Argentina, Chile) on clinical trials, which are needed to develop new and improved methods of treatment that are appropriate for the countries in the region. Latin America is seen by the pharmaceutical industry as a potentially attractive area for clinical trials. This is because European and North American patients who are enrolled in trials of new drug

Table 10: Numbers of Latin American and Caribbean cancer papers (N) published in journals from those countries and in Portugal and Spain, 2014-19.

ISO2	N	Jnls	ISO2	N	Jnls	ISO2	N	Jnls	ISO2	N	Jnls
Total	4024	309	CL	291	21	VE	74	17	CR	10	6
BR	2236	118	CO	166	20	PE	61	6	PT	10	3
MX	432	22	AR	155	22	UY	42	3	EC	8	3
ES	419	57	CU	88	8	JM	25	1	PY	7	2

ISO2 codes in Table 1; ES = Spain, PT = Portugal.

treatments have often already been extensively treated with other drugs. However, the shortage of highly-qualified people and the lack of a good regulatory infrastructure in the region make this difficult. For example, patient records are often paper-based rather than electronic, and the ethical approval process is slow, bureaucratic, and in need of standardisation. The transfer of drugs and clinical samples across national borders for research purposes is difficult because of customs duties and delays. Latin American clinicians are often not very research-minded, and hospitals are not well equipped with specialised pharmacy and nursing staff to conduct clinical trials. Government support for trials infrastructure would enhance research capacities and public-private collaborations, and improve access to new and alternative clinical protocols for cancer patients. Therefore, regulatory agencies should seek a proper balance between public and private interests in the development of clinical research.

The study has some limitations. The main one is that it was confined to papers in the WoS, most of them (92%) in English. There are many papers published in regional and Iberian journals, mainly in Portuguese and Spanish, which may more effectively convey research results to local medical personnel, even if not to the international scientific community. However, since 2015 when the Emerging Science Citation Index was formed, the WoS has covered many more journals from outwith North America and Western Europe. Table 10 shows that almost 18% of the papers in our database were published in over 300 regional or Iberian journals. Compared with the papers published in journals from other countries, they had much lower JIF values (0.85 compared with 4.03), U2 values (3.2 compared with 9.1), and C0-2 values (1.39 compared with 9.68). So, the addition of more papers in regional journals would likely have depressed these values even further.

CONCLUSION

This is the first comprehensive bibliometric study of cancer research in Latin America. Cancer is an increasing problem in all countries of the region, but the response in the form of research is seriously under-funded. This is part of a more general lack of support for all research in the region relative to the countries' GDP. As a result, not enough is known about

the causes of the cancer burden, which are often specific to one country, or a small group of them. This knowledge is needed for the development of better measures of management and control of the disease. There also need to be mechanisms that allow funding bodies to tailor their research support to the cancer sites, and research types, that are most in need of more attention. Most funding comes from national funding agencies, except in Brazil where state-level agencies, especially in São Paulo, make a large contribution. There is little private-non-profit support except from some endowed foundations in Argentina. The conduct of clinical trials is hampered by a shortage of human resources and a lack of a good regulatory infrastructure in the region. There also needs to be more co-ordination between the public and private sectors in health-care in order to maximize the benefit from existing resources.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

C0-2: Three-year citation count; **DALY:** Disability-Adjusted Life Year; **EAP:** East Asia and Pacific countries; **ECA:** Eastern Europe and Central Asia countries; **EUR:** Western European countries; **GDP:** Gross Domestic Product; **HPV:** Human Papillomavirus; **ISO:** International Standards Organization; **JIF:** Journal Impact Factor; **LAC:** Latin America and the Caribbean; **LMIC:** Lower-Middle Income Country; **MEN:** Middle East and North Africa countries; **NAM:** North America countries; **PAHO:** Pan-American Health Organization; **R&D:** Research and Development; **SAS:** South Asia countries; **SSA:** Sub-Saharan Africa countries; **U2:** Usage of the paper since 2013; **UK:** United Kingdom of Great Britain and Northern Ireland; **WHO:** World Health Organization; **WoS:** Web of Science.

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