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Geography of clinical cancer research publications from 1995 to 1999

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Abstract

In this paper, we study the geography of publications in clinical cancer research from 1995 to 1999. A Medline search was performed to retrieve papers in clinical oncology reporting phase I, II and III studies published between 1995 and 1999. Only studies reporting antiblastic chemotherapy have been considered, either alone or in combination with other treatments. For each country, the total number of papers, the total Impact Factor (IF), and the mean IF were determined. Similar calculations were performed to compare the European Union versus North America. 3142 papers were identified. The United States ranks first by number of papers (37.7% share), followed by Italy (9.8%), the United Kingdom (8.5%) and Japan (6.9%). Investigators at European institutions published a higher number of papers compared with their North American colleagues (1362 versus 1288). Still the mean IF of North American papers is higher than the papers with a European address (3.54 versus 3.14). The majority of phase I studies were performed in North America, while most of phase III studies were performed in Europe. These results provide information on the geography of clinical cancer research worldwide, which may reflect the human and economic resources involved in this field.
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Keywords: Bibliometric analysis; Clinical cancer research; Clinical trials; Medline; Impact Factor; Countries; Journals

1. Introduction

In the scientific community, the productivity of a scientist is usually measured by its scientific output. Similarly, the productivity of a group, an institution, or, on a larger scale, of a country can be assessed. However, such evaluation may be difficult. Besides a quantitative criterion (i.e. number of publications), other parameters must be considered, namely the influence, significance and importance of the data reported, the publication type, and the journal prestige. The most popular indicator of quality for scientific articles is the Impact Factor (IF), created by Garfield and Sher in the 1960s [1]. However, the use of such an indicator is controversial. In fact, journal IFs are not representative of individual articles and depend on the research field [2]. Citation analysis provides a better assessment of quality, representing the relevance and usefulness of an individual article. Still, citation analysis requires a careful interpretation of the citation data by expert 'scientometrists' to identify common caveats [3]. Despite the limitations of scientific output analysis, promotions, grant decisions and hiring are mostly based upon the candidate's contribution to peer-reviewed publications, as evidenced by co-authorship [4]. 'Publish or perish' is still the rule.

Based on the analysis of overall scientific research output, a previous study addressed the scientific wealth of nations [5]. In the biomedical field, a similar evaluation has been performed recently [6].

Previous reports deal with cancer research outputs among several countries [7–9]. Still, these studies do not distinguish between basic and clinical cancer research and take into account publications in a limited number of journals and/or a limited time range.

In this study, we address the geography of clinical cancer research according to the clinical cancer research publications retrieved by a Medline search. In particular, chemotherapy trials (i.e. phase I, phase II and phase III studies) published during the years 1995–1999 have been considered.

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2. Patients and methods

2.1. Medline search and retrieved item evaluation

On 11 March 2001, a Medline search was performed using the National Library of Medicine's search service PubMed (http://www.ncbi.nlm.nih.gov) to retrieve research papers in clinical oncology. The retrieval was limited to papers published from 1 January 1995 to 31 December 1999. To identify phase I, phase II and phase III studies, the following search strings were used, respectively: 'cancer AND chemotherapy AND phase I [TITL] OR dose finding [TITL]'; 'cancer AND chemotherapy AND phase II [TITL]'; 'cancer AND chemotherapy AND phase III [TITL] OR randomised [TITL] OR randomized [TITL]'. Only studies reporting antiblastic chemotherapy in cancer patients have been considered, either alone or in combination with radiation therapy, surgery, immunotherapy, hormonal therapy, etc. Clinical trials dealing with supportive care as well as the prevention of emesis or the treatment of neutropenic fever in cancer patients undergoing chemotherapy were also included. Reviews, editorials, meeting abstracts and letters were excluded from this analysis, as well as articles which evaluate chemotherapeutic agents for the treatment of non-malignant diseases. Phase I/II trials were classified as phase I trials.

2.2. Countries

The country was assigned according to the address field in the Medline record. Although sometimes the affiliation in the address field may not reflect the actual major contribution to the study and various approaches have been proposed to address this issue, a comparison of different accounting methods suggests that the final result is not affected by the followed criterion [10]. China and Hong Kong have been considered as one country, and referred to as China.

To assess the quality of the papers, the IF was determined for each article, as reported in the corresponding year Institute for Scientific Information (ISI) Journal Citation Report [11]. For each country, the total number of published papers, the total IF, and the mean IF were determined. Similar calculations were performed to compare European Union with North American clinical cancer research. The current fifteen Member States of the European Union have been considered (Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Netherlands, Portugal, Spain, Sweden and the United Kingdom). The USA and Canada have been considered together, and referred to as North America.

In an attempt to normalise the scientific production among the considered countries regardless of the country population, the performance of the average individual investigator in a given country was determined by dividing the country total number of publications and total IF by the physician population of the respective country [12].

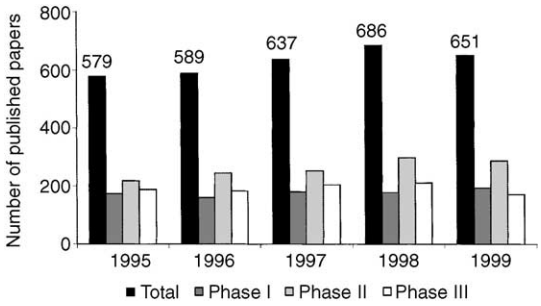

Fig. 1. Five-year trend of published papers in clinical cancer research (1995–1999). The number of phase, I, II and III studies is also shown.

2.3. Journals

The pattern of clinical cancer trial publications among medical/oncology journals has been assessed. Here, we report the medical journals which published at least 20 papers matching our inclusion criteria in the years 1995–1999, regardless the inclusion of the journal in the ISI report.

3. Results

3.1. General considerations

3247 articles were retrieved matching the search strings used. 105 out of these articles were excluded, according to the criteria reported in Methods section. Thus, 3142 papers were identified which report phase I, phase II or phase III clinical trials in oncology and have been published between 1995 and 1999 (Fig. 1). Phase II studies represent 41.4% of those identified, followed by phase III (30.5%) and phase I studies (28.1%).

3.2. Countries

Forty-six countries are represented. Among the retrieved items, 23 eligible papers do not report any address or affiliation. Here, we report the 25 countries which score at least ten records matching our criteria. These 25 countries account for 3057 eligible papers, corresponding to 97.3% of the eligible papers.

The United States ranks first by the number of papers, accounting for 37.7% of the world's papers. Italy is second (9.8%), followed by the UK (8.5%), and Japan (6.9%) (Table 1).

Considering the mean IF per paper, the rankings are different (Table 2): Canada is first, followed by the Netherlands, the UK and Australia. 233 papers from

Table 1
Top 25 countries ranked by number of papers published in 1995–1999

Country	Number of total papers 1995–1999	Share of papers 1995–1999	By year					By phase		
			1995	1996	1997	1998	1999	I	II	III
USA	1186	37.7	240	199	244	257	246	470	520	196
Italy	308	9.8	52	72	62	60	62	65	145	98
UK	267	8.5	58	52	61	63	33	72	71	124
Japan	217	6.9	34	39	40	44	60	43	95	79
France	197	6.3	36	51	33	37	40	45	84	68
Germany	164	5.2	22	33	36	41	32	47	69	48
Netherlands	120	3.8	20	25	24	27	24	37	47	36
Canada	102	3.2	21	24	12	25	20	32	37	33
Spain	68	2.2	12	11	12	17	16	6	33	29
Greece	57	1.8	4	13	12	15	13	3	32	22
Belgium	47	1.5	14	4	7	10	12	11	17	19
Denmark	39	1.2	9	8	8	7	7	3	13	23
Australia	37	1.2	7	4	11	6	9	14	11	12
China	32	1.0	4	9	6	11	2	3	11	18
Sweden	31	1.0	6	6	5	7	7	0	8	23
Switzerland	29	0.9	4	4	7	6	8	9	7	13
Austria	28	0.9	4	4	9	5	6	4	10	14
Finland	22	0.7	4	3	5	2	8	2	5	15
South Africa	21	0.7	7	5	0	5	4	2	9	10
Norway	19	0.6	3	3	6	7	0	2	9	8
Yugoslavia	18	0.6	1	2	5	3	7	0	9	9
Taiwan	14	0.4	0	1	7	4	2	1	12	1
Israel	13	0.4	1	1	2	3	6	4	5	4
Korea	11	0.3	1	1	2	4	3	2	6	3
Turkey	10	0.3	1	0	1	5	3	0	5	5
Total	3057	97.3	565	574	617	671	630	877	1270	910

Table 2
Top 25 countries ranked by mean IF

Country	Total IF	Mean IF	Papers without IF (%)
Canada	403.107	3.95	2.0
Netherlands	451.521	3.76	1.7
UK	1000.583	3.75	5.2
Australia	136.909	3.70	2.7
USA	4162.636	3.51	4.1
Finland	74.074	3.37	4.5
Israel	43.486	3.35	0.0
France	646.255	3.28	14.2
Austria	90.484	3.23	0.0
Yugoslavia	57.296	3.18	0.0
Sweden	97.646	3.15	0.0
Belgium	141.881	3.02	10.6
Germany	483.255	2.95	4.3
Italy	846.634	2.75	2.9
Greece	151.673	2.66	1.8
Denmark	101.679	2.61	0.0
South Africa	54.516	2.60	0.0
Spain	168.709	2.48	8.8
Switzerland	71.207	2.46	3.4
Taiwan	28.635	2.05	0.0
Norway	37.633	1.98	10.5
Korea	19.897	1.81	27.3
Turkey	15.080	1.51	10.0
Japan	319.561	1.47	39.6
China	43.573	1.36	46.9

IF, Impact Factor.

the 25 countries considered have been published in journals without an IF (7.6%).

The productivity of the European Union versus North America has also been evaluated (Fig. 2). Despite a higher number of papers from investigators at European institutions compared with North America (1362 versus 1288), the mean IF of North American papers is higher than the papers with a European address (3.54 versus 3.14). It is noteworthy that 56.7% of the world's phase I trials were conducted at North American institutions compared with 33.4% at European institutions. Conversely, 55.1% of phase III trials were performed in Europe compared with 23.9% at US and Canadian institutions.

Ranking the countries by mean number of publications per physician population, the Netherlands is in the number one spot (3.05 papers/1000 physicians) followed by the United Kingdom (2.78), Denmark (2.55) and the USA (1.55). In terms of mean IF per physician population, the top rankings are similar (Table 3).

3.3. Journals

Overall, clinical cancer trials have been published from 1995 to 1999 in 224 journals. The top journals ranked by number of papers are reported in Table 4.

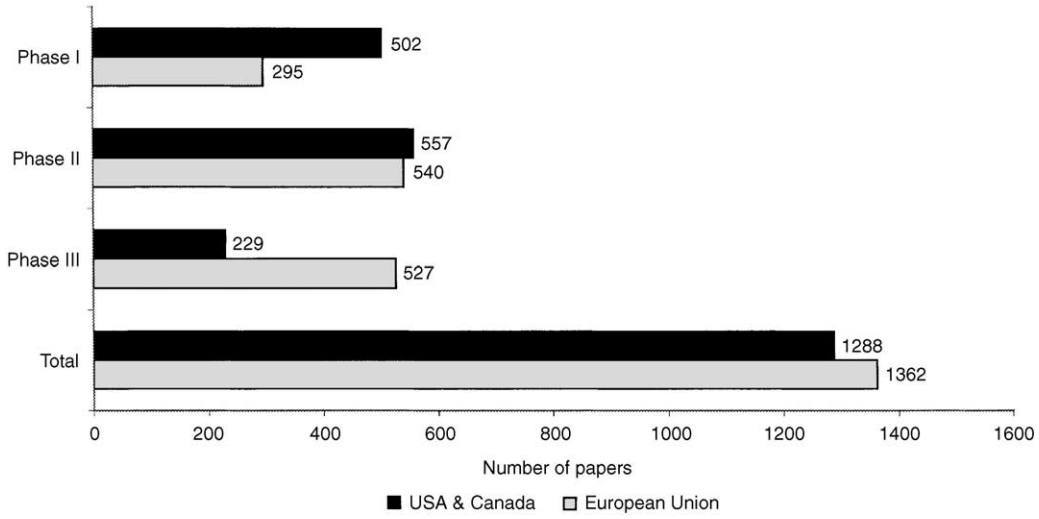

Fig. 2. European Union versus North America: quantitative comparison of paper production in clinical cancer research in the years 1995–1999.

This ranking is obviously affected by the frequency of publication and the number of articles published in each issue.

4. Discussion

To address the geography of clinical cancer research, we performed a quantitative and qualitative assessment of the scientific output in this field, based on the results of a Medline search. Such analysis is difficult and may be biased for several reasons. The search strings used may not retrieve the numerous trials which evaluate treatments apart from traditional chemotherapy (i.e. hormonal therapy, new biological agents), and trials evaluating surgery and/or radiotherapy protocols. Several trials were excluded because search words such as 'phase', 'dose finding', or 'randomized'/'randomised' were missing in the paper title. In addition, the Medline database is biased in favour of English-language journals. Thus, our analysis may penalise countries which have a tradition of publishing in their own language journals. It may also be proposed that citations would have been a more accurate quality indicator. However, IF analysis provides an indirect estimate of the citations gained and can be used as a surrogate for large, aggregated sets of papers [13]. Further objections may be raised with regard to the attribution of the international studies, such as large phase III trials, to the country of the corresponding author. Still, the corresponding authorship usually reflects the major contribution of that author to the study.

Despite these limitations, our results do allow several considerations to be made. First, the top eight countries in clinical cancer research include seven of the group of eight countries (the US, Italy, the UK, Japan, France, Germany, Canada); the eighth is Russia, at 28th (datum not shown). In terms of quality, as determined by the IF analysis, the picture is different. Canada, the Netherlands, the UK, Australia, and the USA occupy the top spots, while Japan, Spain, Italy and Germany appear much lower in the rankings. Such differences may be partially explained by the language bias: four out of the top five countries are English-speaking. It is also interesting that, in spite of its fourth rank in terms of published

Table 3
Performance by physician population over the 1995–1999 period

Country	Physicians (*n*)	Papers/1000 physicians (*n*)	IF/1000 physicians
Netherlands	39,352	3.05	11.47
UK	96,184	2.78	10.40
Denmark	15,283	2.55	6.65
USA	764,538	1.55	5.44
Canada	70,020	1.46	5.76
Finland	15,410	1.43	4.81
Greece	41,552	1.37	3.65
Switzerland	23,576	1.23	3.02
Belgium	40,057	1.17	3.54
Austria	24,583	1.14	3.68
Sweden	27,601	1.12	3.54
France	177,809	1.11	3.63
Norway	18,250	1.04	2.06
Italy	317,824	0.97	2.66
South Africa	22,158	0.95	2.46
Japan	243,975	0.89	1.31
Australia	44,448	0.83	3.08
Germany	287,466	0.57	1.68
Israel	23,038	0.56	1.89
Spain	168,023	0.40	1.00
Korea	62,754	0.18	0.32
Turkey	78,020	0.13	0.19
China	2,041,233	0.02	0.02
Taiwan	MD	MD	MD
Yugoslavia	MD	MD	MD

IF, Impact Factor; MD, missing data.

Table 4
Top medical journals ranked by published clinical cancer trials in the years 1995–1999

Journal	Total papers	Phase I	Phase II	Phase III	Impact Factor				
	n	*n* (%)	*n* (%)	*n* (%)	1995	1996	1997	1998	1999
J Clin Oncol	498	150 (30.1)	161 (32.3)	187 (37.6)	6.922	7.811	7.878	8.228	7.963
Ann Oncol	186	51 (27.4)	85 (45.7)	50 (26.9)	2.256	2.736	2.548	2.867	3.195
Cancer	178	36 (20.2)	87 (48.9)	55 (30.9)	2.864	3.296	3.296	3.660	3.632
Eur J Cancer	160	31 (19.4)	70 (43.7)	59 (36.9)	2.095	2.017	2.407	2.743	2.537
Sem Oncol	160	88 (55.0)	53 (33.1)	19 (11.9)	1.608	1.872	2.325	2.252	2.986
Am J Clin Oncol	157	32 (20.4)	107 (68.1)	18 (11.5)	0.754	0.921	0.769	0.867	0.956
Br J Cancer	134	32 (23.9)	62 (46.3)	40 (29.8)	3.449	3.666	2.938	3.036	3.282
Clin Cancer Res	128	99 (77.3)	26 (20.3)	3 (2.3)	0	3.162	3.419	2.941	3.442
Invest New Drugs	106	42 (39.6)	64 (60.4)	0 (0.0)	0.495	0.703	0.543	1.837	1.890
Cancer Chem Pharmacol	102	56 (54.9)	41 (40.2)	5 (4.9)	1.598	1.261	1.224	1.740	1.689
Gynecol Oncol	77	16 (20.8)	48 (62.3)	13 (16.9)	1.374	1.552	1.542	1.636	1.860
Gan To Kagaku Ryoho	70	10 (14.3)	35 (50.0)	25 (35.7)	0	0	0	0	0
Anticancer Drugs	68	28 (41.2)	32 (47.0)	8 (11.8)	1.418	1.397	0.985	1.320	1.594
Lung Cancer	58	11 (19.0)	32 (55.2)	15 (25.9)	0.000	0.638	1.065	1.902	1.913
Blood	55	10 (18.2)	6 (10.9)	39 (70.9)	8.569	9.745	9.507	8.372	8.782
Int J Rad Oncol	50	18 (36.0)	17 (34.0)	15 (30.0)	2.484	2.367	2.636	2.589	2.996
Oncology	46	8 (17.4)	28 (60.9)	10 (21.7)	1.857	2.097	2.141	2.858	2.684
Bone Marrow Transpl	32	12 (37.5)	4 (12.5)	16 (50.0)	2.041	2.771	2.184	2.111	2.277
Anticancer Res	30	7 (23.3)	16 (53.3)	7 (23.3)	0.926	1.049	1.045	1.236	1.375
Leukemia	30	9 (30.0)	11 (36.7)	10 (33.3)	2.350	2.945	3.227	3.163	3.562
Breast Cancer Res Tr	28	3 (10.7)	15 (53.6)	10 (35.7)	2.879	3.121	2.430	2.287	2.889
Cancer Invest	26	5 (19.2)	21 (80.8)	0 (0.0)	1.282	1.655	1.570	1.697	1.514
J Neuro-Oncol	26	2 (7.7)	21 (80.8)	3 (11.5)	0.777	1.111	1.232	1.641	1.655
J Urol	23	2 (8.7)	5 (21.7)	16 (69.6)	2.792	2.668	2.719	2.685	2.486
Lancet	22	0 (0.0)	0 (0.0)	22 (100)	17.490	17.948	16.135	11.793	10.197
Tumori	22	2 (9.1)	14 (63.6)	6 (27.3)	0.360	0.446	0.408	0.595	0.569
Jpn J Clin Oncol	21	7 (33.3)	8 (38.1)	6 (28.6)	0.462	0.472	0.359	0.728	0.728
Leuk Lymphoma	21	7 (33.3)	9 (42.9)	5 (23.8)	0.790	1.134	1.046	1.099	1.140

papers, Japan drops to 24th. The observation that Japanese output includes around 40% of papers being published in Japanese-language journals that have no IF, which lowers the mean IF, may explain such a low placement for this country.

Second, phase II studies represent the majority of clinical cancer trials. This may partially be explained by the higher feasibility of these trials compared with phase I and III trials. In fact, phase II studies do not require either the availability of a new drug or the collaboration of many sites. In addition, whereas phase I trials for each treatment are performed once and do not need to be performed separately for each tumour type, phase II trials must be performed separately in the different cancer types. Furthermore, phase I trials were mostly performed at US institutions, while the majority of phase III studies reported a European address. Based on these data, it is likely that the vast majority of phase I trials in clinical oncology are conducted in the same country where the preclinical testing had been performed. In fact, the USA is currently the richest reservoir of new drugs: approximately half of the 'world class' medicines developed from 1975 to 1994 originated in the US [14].

Finally, the observation that clinical cancer trials have been published in more than 200 journals reflects the wide audience and multidisciplinarity of this field. As expected, prestigious journals which cover general interest topics and comprise a large and heterogeneous audience (i.e. *The Lancet, JAMA, The New England Journal of Medicine*) exclusively published phase III trials (data not shown).

In conclusion, we should emphasise that this data is provided by three clinical oncologists who are not experts in scientometrics. Nevertheless, the geography of clinical cancer research derived from our bibliometric analysis may reflect the human and economic resources involved in this field worldwide.

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