

Cough as a Symptom and a Disease Entity: Scientometric Analysis and Density-Equalizing Calculations

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■ Abstract

Background: Cough is a prominent symptom of many allergic diseases and a major health burden but there is little information available on the current state of research in this area.

Objectives: To analyze long-term developments in cough research and recent trends.

Methods: We searched the Thomson Reuters Web of Science databases for cough-related items published between 1900 and 2007 and analyzed the results using scientometric methods and density-equalizing calculations.

Results: We found 12 960 cough-related publications from 132 countries for the period studied. The most productive country was the United States of America (USA), followed by the United Kingdom (UK), France, Japan, Canada, and Germany. These 12 960 published items were cited 165 868 times. The average number of citations per item increased from 1976 to 1992, with peaks in 1977, 1979, 1981, 1984, 1989 and 1992. Each of these years was followed by a decrease in citation numbers. Bilateral and multilateral cooperation analysis using the radar chart technique showed a progressive increase in international co-authorship starting at the beginning of the 1990s, with a leading role by the USA and the UK.

Conclusion: We detected a marked increase in cough-related research starting in the 1990s. While the majority of data originates from the US, other countries have taken a leading position in terms of research quality (number of citations per item).

Key words: Cough. Scientometry. Density-equalizing mapping.

■ Resumen

Antecedentes: La tos es un síntoma destacado en muchas patologías alérgicas y una carga sanitaria importante pero existe poca información disponible acerca del estado actual de la investigación en este área.

Objetivos: Analizar los desarrollos a largo plazo en la investigación de la tos y tendencias recientes.

Métodos: Buscamos en las bases de datos de Ciencia de Thomson Reuters Web, los artículos relacionados con la tos, publicados entre 1900 y 2007 y se analizó el resultado empleando métodos cientométricos y cálculos de densidad-equiparada.

Resultados: Encontramos 12 960 publicaciones relacionadas con la tos, procedentes de 132 países, para el período estudiado. El país más productivo fueron los Estados Unidos de América (EEUU), seguidos del Reino Unido (GB), Francia, Japón, Canadá y Alemania. Estos 12960 artículos publicados fueron citados 165 868 veces. La media de número de citas por artículo aumentó desde 1976 a 1992, con picos en 1977, 1979, 1981, 1984, 1989 y 1992. Cada uno de estos años fue seguido de una disminución en el número de citas. El análisis bilateral y multilateral de cooperación empleando la técnica de navegación por radar mostró un progresivo aumento en la co-autoría internacional comenzando en los principios de los noventa, con un papel de liderazgo por parte de EEUU y GB.

Conclusión: Detectamos un aumento marcado de las investigaciones relacionadas con la tos en los años noventa. Mientras que la mayoría de los datos fueron originados en los EEUU, otros países han adoptado posiciones prioritarias en términos de calidad de investigación (número de citaciones por artículo).

Palabras clave: Tos. Cienzometría. Trazado de densidades equiparadas

Introduction

Cough is a prominent symptom of many allergic disorders such as asthma [1,2], rhinitis [3], anaphylaxis [4], and drug allergies [5]. It is also common in the early years of life [6]. Together with lung disease and other symptoms such as tachycardia and dyspnea [5-8], cough is a major health burden in the area of respiratory medicine [9-11]. As a symptom, cough often accompanies other respiratory symptoms and may indicate the presence of serious disease such as bronchial carcinoma [12].

Although many experimental and clinical studies have focused on cough as a symptom, further insights are required in order to develop new diagnostic and therapeutic strategies [13]. This is particularly important in view of the major limitations associated with existing therapeutic options and the lack of novel developments in recent years [14-16]. Before novel treatment approaches can be established, however, it is necessary to analyze existing data. To the best of our knowledge, no in-depth scientometric analysis has ever been conducted of the current state of research in the field of cough. The aim of the present study was to analyze cough research using large-scale data analysis and bibliometric methods such as density-equalizing mapping.

Material and Methods

Data Source

Data were retrieved from the Web of Science databases developed by the Thomson Institute for Scientific Information [17,18].

Search Strategies

We searched the Web of Science databases using different Boolean operators in combination with the term cough. Because the present study was designed to assess the total number of publications on cough, we did not use the refine function to include only document types such as original articles, reviews, and abstracts or to exclude others such as letters, editorials, and news reports.

Time Span

The initial time span analyzed was 1900 to 2007. The year 2008 was not included since the database entries for this period were not complete at the time of our analysis. For certain searches, we restricted the time span to periods in which at least 30 items were published to filter out mavericks.

Citation Numbers

Published items were analyzed using the citation report method as previously described [19]. In brief, we assessed the number of citations per year and the average number of citations per item, indicating the average number of citing articles for all the items in the set. This is the sum of the times cited divided by the number of results found.

Data Categorization

All the data files were examined for a range of aspects such as country of origin, publication date, name of institution, name of publishing journal, subject category, publishing authors, and most cited items. The results were transferred to Excel charts and visualized as diagrams.

Density-Equalizing Mapping

Density-equalizing mapping was used according to a recently described method [20]. In brief, contributing countries were resized according to a particular variable such as the number of published items or the average number of citations per item. For the resizing procedure, the area of each country was scaled in proportion to, for example, the total number of items it had published on cough. Specific calculations were based on Gastner and Newman's algorithm [20].

Results

Total Number of Published Items

The number of published items was used as an index of research productivity. During the period 1900 to 2007, 12 960 items containing the term cough in the title, abstract, or key words, were published and included in the Web of Science databases. The earliest studies were published in 1900 and there was a considerable peak in activity at the beginning of the 1990s (Figure 1). The maximum number of items (862) was found for the year 2007.

Total Number of Citations

Citation numbers were used as a quality indicator and citation analysis showed that the 12 960 items identified had been cited 165 868 times since 1900. Figure 1 shows a parallel increase in the number of citations and published items. The increase in citations observed at the beginning of the 1990s was greater than the increase in the number of published items. The year with the maximum number of citations (12 293) was 1997.

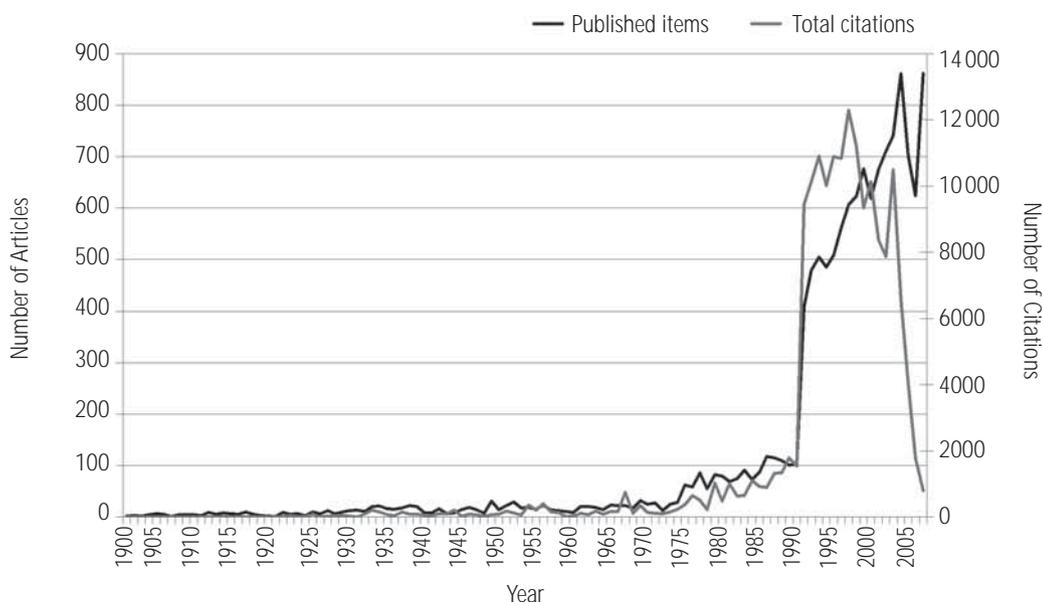


Figure 1. Number of cough-related items published in the Web of Science databases and corresponding citations between 1900 and 2007.

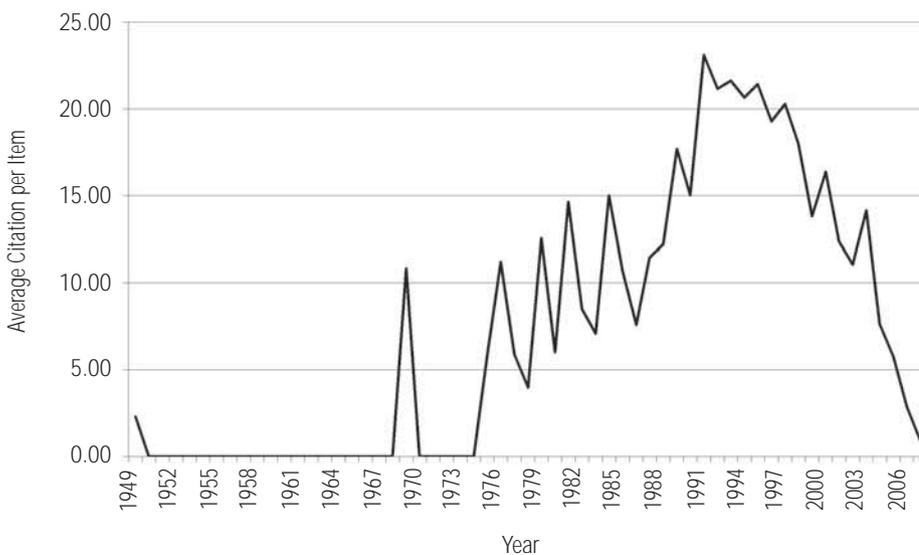


Figure 2. Average number of citations per cough-related item in the Web of Science databases between 1949 and 2007.

The average number of citations per item (Figure 2) increased from 1976 to 1992, with peaks in 1977 (11.21), 1979 (12.55), 1981 (14.62), 1984 (15.00), 1989 (17.68), and 1992 (23.09). In each of the years following these peaks, the number of citations per item decreased as follows: 1978, 5.88; 1980, 6.01; 1982, 8.49; 1985, 10.67; 1990, 15.03; and 1993, 21.15. This downward trend continued from 1993 onwards.

Average Number of Authors

The average number of authors per published item showed an increasing trend from the 1970s onward (Figure 3), rising from approximately 2 authors per article in the 1970s to a peak of 5.24 in 1997. The number of authors per article has remained relatively constant since 2003 (2003, 4.85; 2004, 4.89; 2005, 4.90; 2006, 4.91).

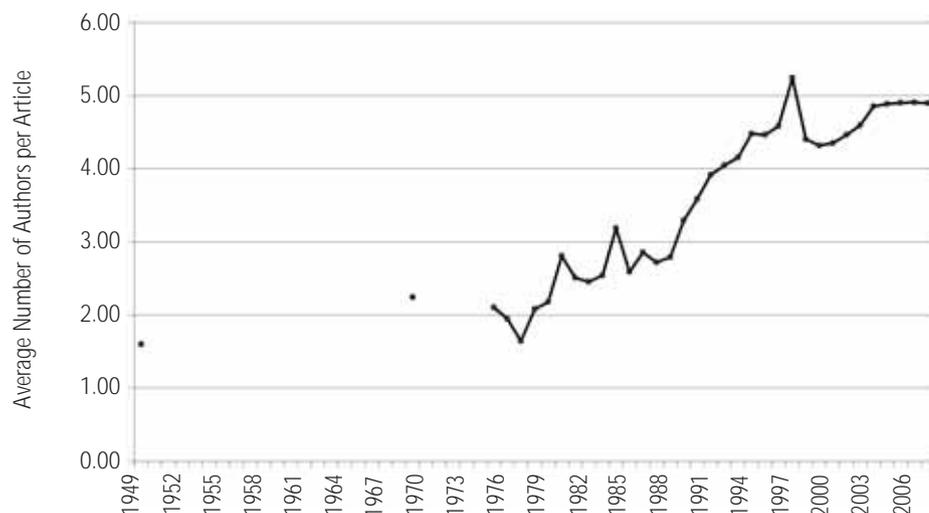


Figure 3. Average number of authors per cough-related item in the Web of Science databases between 1949 and 2007.

Country of Origin

The published items originated from 132 countries, with the United States (USA) (3522 items), the United Kingdom (UK) (1405), France (586), Japan (585), Canada (521), Germany (500), Italy (441), Australia (376), Sweden (306), the Netherlands (263), Spain (247), and Belgium (180) producing the most items. Density-equalizing mapping of this set of data shows that a relatively small number of countries were responsible for the majority of research efforts (Figure 4A).

Citation Parameters

Differences were found between research quality (average number of citations per item) and research quantity (total number of items published) when individual countries were analyzed. Argentina had the highest average citation rate (55.47/item), followed by Norway (29.48), Denmark (30.17), Sweden (24.92), Canada (22.49), and New Zealand (20.79). The USA and the UK, countries with a high production rate, had a citation rate per item of 18.21 and 17.99, respectively. The density-equalizing maps in Figure 4 show the differences between research quantity and research quality.

Cooperation Analysis

Cooperation analysis was used to calculate bilateral and multilateral cooperation between international authors. International cooperation began to increase steadily at the beginning of the 1990s (Figure 5A) to reach a peak in 2007, with 142 articles featuring authors from different countries. Further analysis revealed that bilateral cooperation was the most common form of cooperation (981 articles), followed by trilateral cooperation (154 articles) and quadrilateral cooperation (42 articles) (Figure 5B). Co-authorship between the USA and the UK was the most common form of bilateral

cooperation but cooperation between the USA and Canada was also common (Figure 5C and Table 1).

Publishing Journals

The top-ranking journals in terms of the publication of cough-related items (Figure 6A) included both respiratory journals such as *Chest* (#1), the *American Journal of Respiratory and Critical Care Medicine* (#3), *Thorax* (#5), the *European Respiratory Journal* (#6) and general medicine journals such as the *British Medical Journal* (#2) and *Lancet* (#4) (Figure 6A). Journals in the fields of allergy, infectious disease, neurology, and gastroenterology were also among the top 25 journals in terms of publication of cough-related items. The highest average number of citations per item was observed in the *New England Journal of Medicine* (65.42 citations/item), followed by *Annals of Internal Medicine* (49.09), *Archives of Internal Medicine*, and the *American Journal of Respiratory and Critical Care Medicine* (35.77) (Figure 6B).

Discussion

Numerous revolutionary insights into pathogenetic and pathophysiologic mechanisms have created new challenges in the field of cough research in recent decades. Therapeutic approaches, however, are still largely limited. The present study provides the first large-scale scientometric analysis of cough literature. Because of the innovative nature of this study, we believe that the methodology employed needs to be discussed briefly. We based our analyses on data from the internationally established Thomson Reuters Web of Science databases [17,18] and the use of novel bibliometric tools linked to density-equalizing mapping [21]. In some searches, data points were limited (especially for periods before 1950)

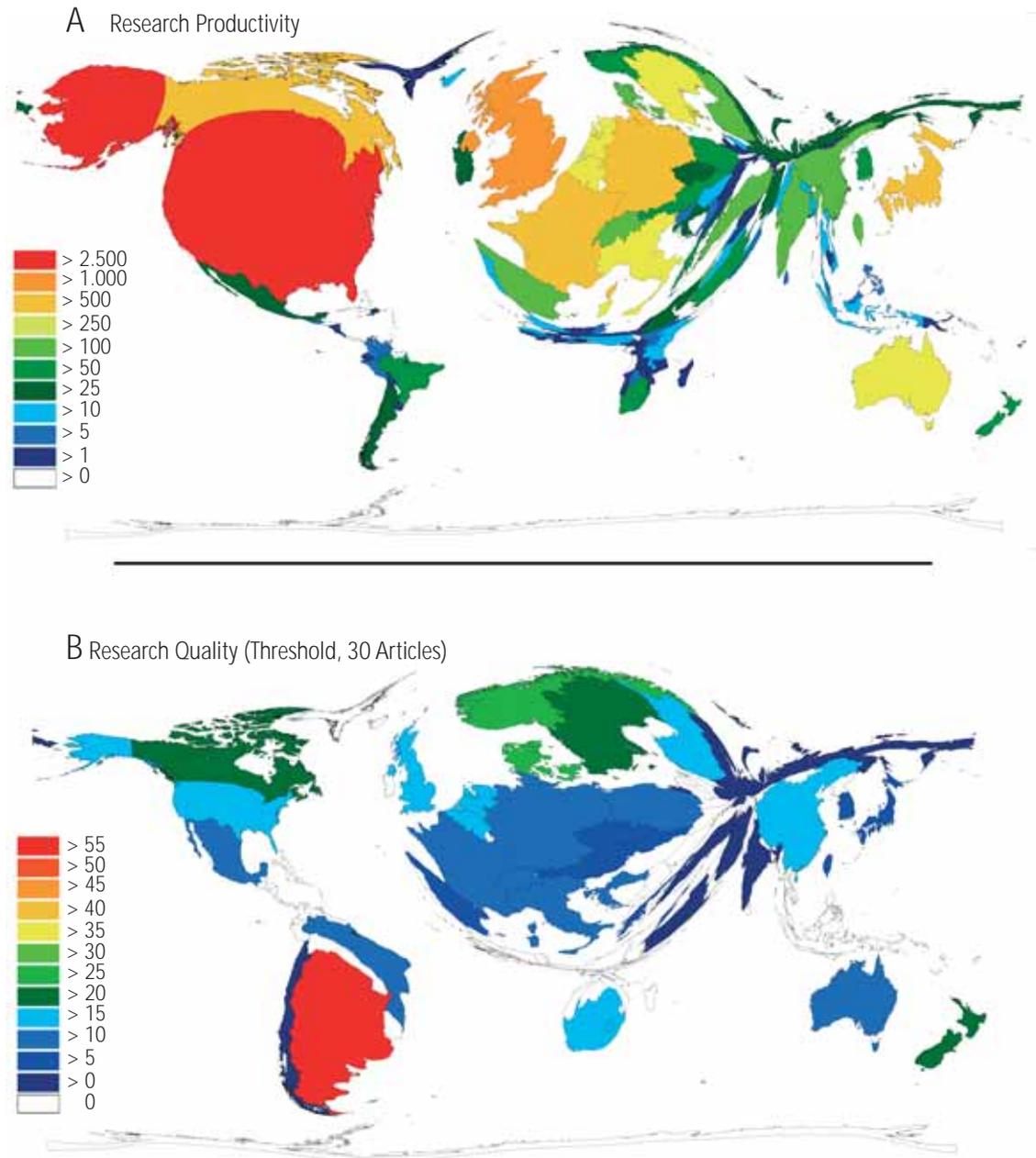


Figure 4. Density-equalizing calculations. A, map illustrating the number of cough-related publications by country. The size of each country has been scaled in proportion to the total number of publications. A color-coded system shows the publication numbers. B, map showing the average number of citations per item per country. The size of each country has been scaled in proportion to the average number of citations per item. A color-coded system shows the average number of citations per item.

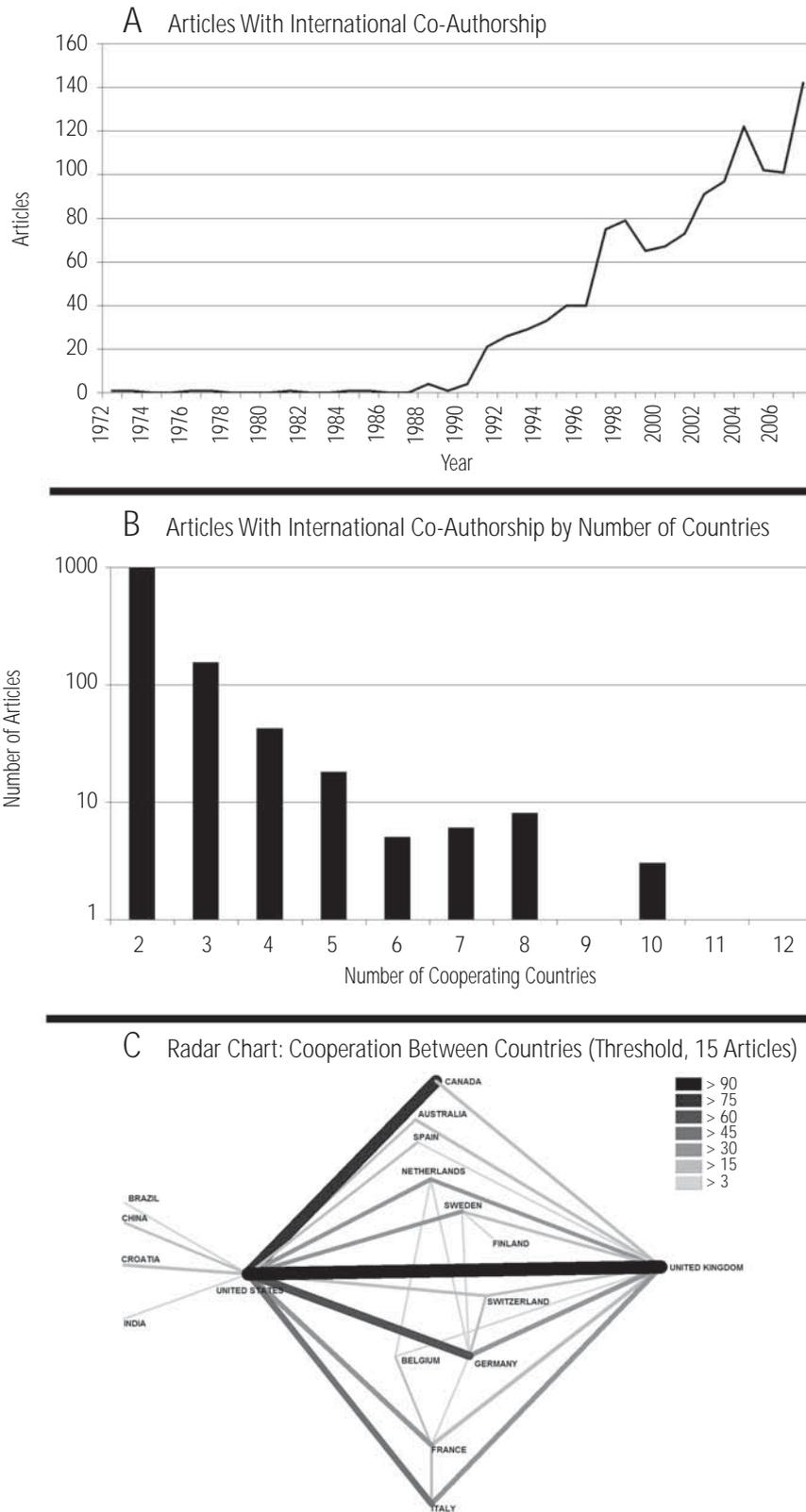


Figure 5. A, B, C, Bilateral and multilateral cooperation in the field of cough research. A, number of articles with international co-authorship between 1972 and 2007 in the Web of Science database. B, number of articles in relation to number of collaborating countries. C, radar chart of cooperation density. A grayscale coded system shows the number of cooperations between countries.

Table. Top 20 Bilateral Cooperations

Rank	Country	Country	No. of Cooperations
1	United Kingdom	United States	100
2	Canada	United States	91
3	Germany	United States	64
4	Italy	United States	48
5	France	United States	39
5	Italy	United Kingdom	39
6	Germany	United Kingdom	37
7	Netherlands	United States	35
8	Netherlands	United Kingdom	34
8	Sweden	United States	34
9	France	United Kingdom	31
10	Australia	United Kingdom	29
11	Canada	United Kingdom	26
11	Sweden	United Kingdom	26
11	Switzerland	United States	26
12	Croatia	United States	24
13	Germany	Switzerland	22
14	Australia	United States	21
14	China	United States	21
14	France	Italy	21
14	Spain	United States	21
14	Switzerland	United Kingdom	21
15	Belgium	France	19
16	Germany	Netherlands	17
17	Belgium	Netherlands	16
17	Belgium	United Kingdom	16
17	Finland	Sweden	16
17	France	Germany	16
17	Spain	United Kingdom	16
18	Brazil	United States	15
18	Brazil	United States	15
18	Germany	Sweden	15
18	India	United States	15
19	Australia	Canada	14
19	Canada	France	14
19	Canada	Germany	14
19	Italy	Spain	14
19	Mexico	United States	14
19	Norway	Sweden	14
20	Finland	United States	13
20	Germany	Italy	13
20	Italy	Netherlands	13
20	Netherlands	Sweden	13
20	South Korea	United States	13

due to the fact that a threshold of 30 items was established to prevent mavericks.

The interest in cough grew progressively over the time period analyzed, with a marked upturn at the beginning of the 1990s. This increase, however, was attributable not only to intensification in research efforts in the area but also to an extension of database inclusion criteria. Similar increases have been reported in other fields [19].

Research groups from the USA were the most productive in the area of cough research, with a total of 3522 published items between 1900 and 2007. They were followed by the

UK (1405), France (586), Japan (585), Canada (521), and Germany (500). This ranking is similar to that reported for asthma animal model research, where the USA, Japan and the UK were found to be the most productive of the 52 countries responsible for the 3489 entries detected [19]. As illustrated by density-equalizing mapping, the tendency in both fields is for a relatively small number of countries to contribute to the majority of research.

Argentina ranked first in terms of research quality with an average of 55.47 citations per published item, followed by Norway, Denmark, Sweden, and Canada. The USA, which was most productive country, had a rate of 18.21 citations per published item. Similar tendencies have been reported in other scientometric studies [19,20]. Nonetheless, closer analysis of the cited items with contributions by Argentinean authors revealed that the majority of citations corresponded to 2 multilateral multicenter studies on cardiovascular drugs [22,23] in which cough was discussed as an adverse reaction rather than as a disease entity. Furthermore, none of the Argentinean scientists listed were leading or senior authors [22,23].

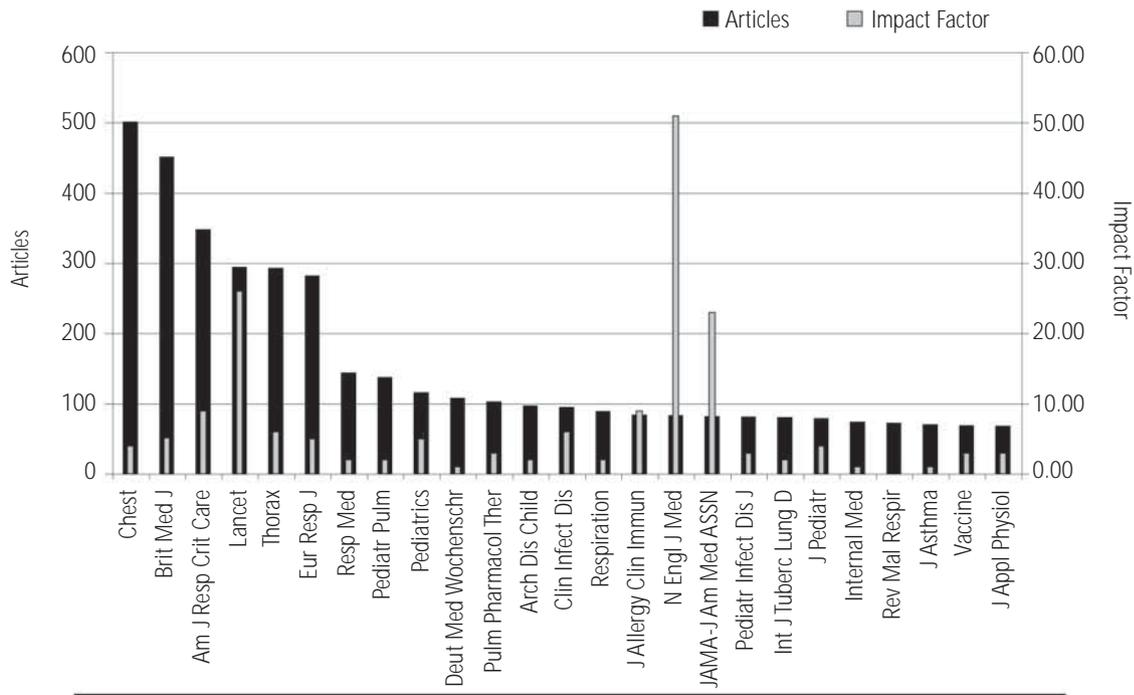
The cause of chronic cough in over 90% of non-smoking patients with a normal chest radiograph is asthma, heartburn, or postnasal drip [24]. Together with lung cancer, thus, these conditions should rank high among the research priorities in the field of cough. However, as we found in the case of Argentina, the majority of cited publications report cough as an adverse reaction of cardiovascular medications such as angiotensin-converting enzyme inhibitors. This means that analyses such as ours, in which cough is considered both a disease entity and an adverse reaction, should not be used as a basis for international funding allocation. In such cases, more focused scientometric approaches are required.

As already mentioned, contributions to the field of cough research were high by both respiratory journals such as *Chest* and the *American Journal of Respiratory and Critical Care Medicine* and general medicine journals such as *Lancet* and the *British Medical Journal*. One limitation of our study is related to the fact that novel open access journals are not included in the Web of Science databases. The journal *Cough*, for example, published 35 cough-related articles between 2005 and 2008. We thus believe that citation tracking and analysis should be made available for open access journals for scientometric analyses.

It is interesting to note that the 2 general medicine journals that contributed most to cough research were British. A detailed analysis of the reasons for this special focus revealed that cough as both a disease entity and a symptom holds special interest for prominent UK research centers such as the National Heart and Lung Institute.

The marked increase in the number of cough-related studies from the 1990s onwards should have been paralleled by the emergence of novel diagnostic and therapeutic approaches. This has not been the case, however and there is still a need for evidence-based medicine strategies for the efficient treatment of cough as a symptom. Several studies that have addressed ion channels such as TRPV1 and their relevance might lead to novel therapeutic targets [25-27]. In the pathogenesis of chronic cough, research has concentrated on supposedly established concepts. Although there is evidence that eosinophilic

A



B

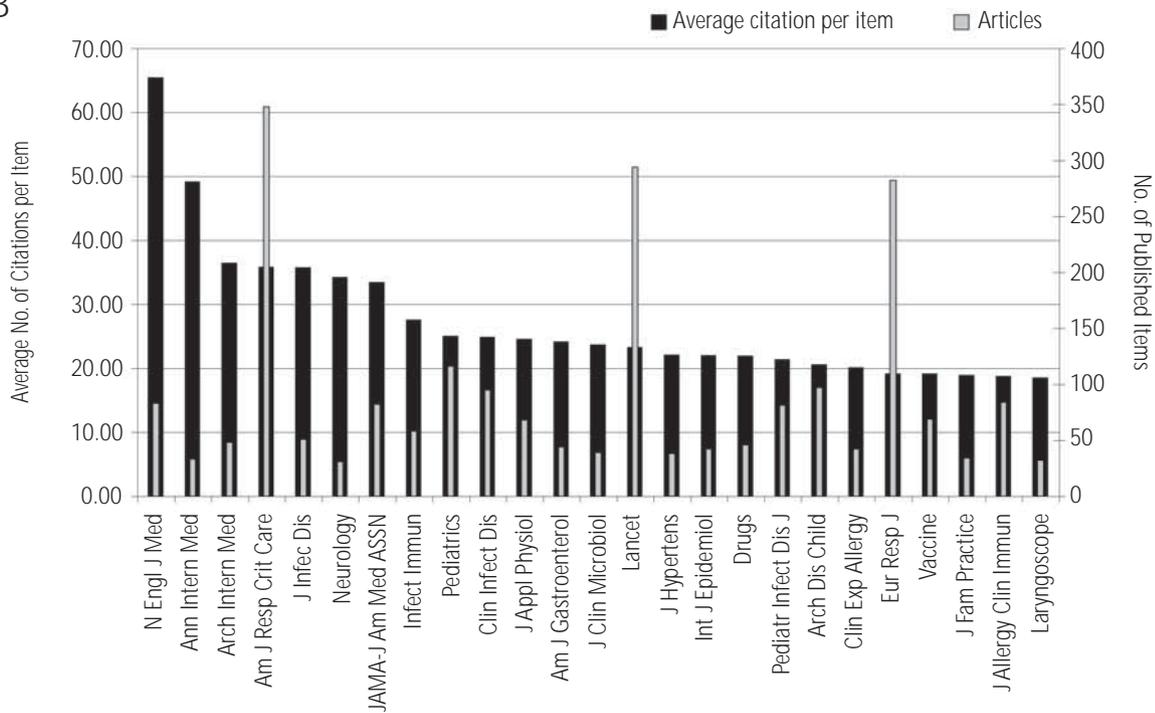


Figure 6. Ranking of journals that publish cough-related articles in terms of quantity and quality. A, top 25 journals in terms of number of articles. B, top 25 journals in terms of citations per item.

bronchitis is the underlying cause of chronic cough in 10% to 15% of patients referred for specialist evaluation [28,29], just 0.1% of all cough-related research work has focused on this association. A more detailed analysis of yearly research output shows that there has been no tendency for further research in this area since the association between eosinophilic bronchitis and cough was first described by Gibson et al [30] 18 years ago. Following an initial increase, the number of published papers has oscillated between 8 and 18 a year.

In the field of allergic asthma, the focus of pharmacologic research has primarily focused on approaches targeting single immune mechanisms. Most new immunomodulatory drug classes for asthma, however, have failed to reach clinical practice [31], thus raising the question of whether global research efforts to identify novel single immune targets might be too reductionistic. In this respect, the current rate of introduction of novel compounds to the pharmaceutical market is lower than at any time in the past 50 years [31] even though the overall number of new discoveries in the field of underlying immune mechanisms has continued to increase. The search for new cough-targeting compounds, in contrast, has focused on both immune mechanisms and neuromediating substances [27,32-34] and such an approach might lead to more promising future targets.

In conclusion, the present study provides the first detailed scientometric analysis of the role and impact of cough research in the field of biomedicine. Our studies show that there has been a marked increase in research productivity since the 1990s and on the basis of our citation analysis results, it can be assumed that the interest in the results of cough studies is also on the rise. While the majority of data originate from the USA, other countries have taken a leading position in citation per item rankings.

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