

The scenario of the studies on ragweed (*Ambrosia Sp.*) and related issues from its beginning to today: a useful tool for future goals in a one health approach

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Abstract. *Background and aim:* Airborne ragweed pollen is one of the agents of respiratory allergies in our changing environment. The monitoring of pollen is essential to manage pollen allergy and to improve its forecasting methods. Moreover, the control and fight against ragweed plants is important. Aim of this study is to understand the scenario of the studies on ragweed over time. *Methods:* We searched PubMed and Scopus for articles published until July 2022 reporting the words “ragweed”. Articles written in all languages were included. *Results:* Scopus was the database with the highest number of published papers. Among the papers on ragweed, the papers citing the word “allergy” were 59.4% in PubMed and 37.6% in Scopus. The subject areas more addressed were medicine, immunology, genetics/molecular biology, but agricultural/biological sciences too and, interestingly, other subjects like social sciences, art, humanistic, etc.. Among the top 40 institutions supporting research, 8 were European, 4 Asian, 1 Russian and 21 were American, the other 6 were pharmaceutical companies. *Conclusions:* This study shows a picture of the ragweed studies and some related subjects over time. A gap between the number of biomedical and not biomedical issues was evident. There is a need for greater involvement of institutions into support of knowledge and fight ragweed. The results will provide a useful tool to identify future goals in a global approach of ragweed related issues. (www.actabiomedica.it)

Key words: ragweed, research scenario, human health, environmental health, global approach

Background

Ragweed is an annual invasive weed belonging to the Asteraceae family, originating from the southern desert areas of North America, and moved to Europe and Asia, first, late 19th century and beginning 20th century, causing public health related problems in many countries due to its anemophilous, very allergenic pollen (1-4). International trade and the climate change are suspected to drive ragweed plant invasion (5-9).

In Europe, its most important areas of occurrence are the Pannonian Basin, mainly Hungary, Serbia,

Croatia and Slovakia, the Rhône Valley (France) and northern Italy (Lombardy) (10).

Ragweed seeds can persist for up to 40 years in the soil. Viability was estimated 85% after 20 years of burial, but recent shorter experiments spanning two to three years, the annual seed death rate was 7% and 12% (11), so an extended timescale is needed. Ragweed plants grow better in abandoned, and damaged, and disturbed soil by human activities and deforestation.

Ragweed pollen is transported over long distances (even thousand kilometers) and this phenomenon has been demonstrated in many European countries (12-16).

Six species of ragweed are present in Europe: *Ambrosia maritima* L. (Sea ragweed) with Euro-Mediterranean native habitat, *Ambrosia artemisiifolia* L. (Common ragweed), *Ambrosia tenuifolia* Sprengel, *Ambrosia coronopifolia* - *Ambrosia psilostachya* (Perennial ragweed) Torr. et Gray, *Ambrosia trifida* L. (Giant ragweed), and *Ambrosia confertiflora* DC (Burr ragweed).

Aerobiological and clinical studies from various countries have documented the importance of ragweed pollen as a powerful aeroallergen (17-18). Flowering and pollen spread of ragweed normally starts late of July until mid-September, in central Europe. Skin prick tests (SPT) for ragweed allergens are positive in over than 80% of allergic patients in Hungary, 30% in France, Austria and Czech Republic, 17% in Southern Switzerland (19-24). Ragweed pollen evokes allergic symptoms at low concentrations (even less than 10 pollen/m³); in comparison grass pollen evokes symptoms over 15 pollen/m³, and birch pollen over 30 pollen/m³ (25). Over 95% of ragweed allergic patients react to Amb a 1 with a positive skin prick test or showing increased Amb a 1 specific immunoglobulin. Amb a 11 is the second major allergen to which 66% of ragweed sensitized patients react. Amb a 3 and Amb a 7 are only described as minor allergens. Amb a 4 is homologue to the major mugwort allergen Art v 1. Amb a 6 (lipid transfer protein), Amb a 8 (prolin), Amb a 9 and Amb a 10 (calcium binding proteins) belong to the cross-reacting pan allergens, also present in mugwort (Art v 3, Art v 4 and Art v 5) (26).

The symptoms of ragweed allergy are mainly rhinitis, conjunctivitis, and asthma. Characteristics of ragweed allergy are the onset with asthma (26) and the onset in elderly people too. The overall evidence showed the effectiveness of sublingual immunotherapy for the treatment of allergic rhino-conjunctivitis with or without asthma, but optimal strategies for immunotherapy are still improving (27).

Due to cross-reactivity with allergens from ragweed foods like celery, aniseed, parsley, pepper, bell peppers, caraway, carrots, can induce oral allergy syndrome (28).

Although episodes of thunderstorm asthma (29) associated with ragweed pollen have not yet been described, some in vitro studies do not completely exclude this possibility in the occurrence of some concomitant situations (30,31).

It is epidemiologically and medically interesting how much time passes between exposure to new pollen, like ragweed, in a region and the appearance of measurable sensitization rates. This is about 10 to 15 years (32). Furthermore, it can be assumed that about 5 years pass between clinically silent sensitizations and the appearance of symptoms (22). This shows that the invasion of a region with ragweed does not immediately lead to health problems; instead, it takes some years. Knowing the existence of this time frame is important because it is essential not to underestimate the danger of ragweed expansion due to the current lack of diseased individuals in a new region.

Pollen monitoring is essential to the management of pollen allergy and to improve its forecasting methods (33-37). Real time pollen monitoring could improve allergy management.

In highly exposed countries, ragweed, and its pollen cause severe damage to the economy. In fact, outpatient, and hospital treatment for patients with allergic respiratory diseases caused by ragweed pollen, increasing crop losses due to the spread of ragweed habitats, tourist and nature conservation damage, seeds contaminated with ragweed seeds, etc. cause enormous economic damages (2, 38-39). In North America and parts of Europe, ragweed pollen is the main cause of allergic respiratory symptoms, causing an estimated financial burden for the health system of approximately 630 Euro per year per each person concerned (26) even estimating direct and indirect costs caused by common ragweed in the European Union by Euro 7.4 billion per year (38).

Considering ongoing global climate change, pollen concentrations are often increasing, pollen season is prolonging, habitats of allergenic taxa as well as those of ragweed are expanding northward in Europe, more and more people are exposed to ragweed pollen, the number of seasonal respiratory allergic diseases

is increasing globally, and global public health risk is increasing.

Chemical and biological fight against ragweed is also important, mainly if matched with a correct and continuous land management.

Recently, the beetle *Ophraella communa* (Coleoptera: *Chrysomelidae*), coming, like ragweed, from North America, known as eater of ragweed leaves, was successfully used in China as a biocontrol agent against ragweed (40). In the 2013, *Ophraella communa* was also detected in northern Italy and southern Switzerland (41-42). Since then, airborne pollen concentrations in these areas, where the beetle builds population outbreaks, has dropped by 80%. More recently, the beetle has spread eastwards and has now been found in Hungary, Slovenia, Croatia, Serbia, and Romania (43). Unfortunately, some plant tests conducted within the EU-COST action on sustainable management of *Ambrosia artemisiifolia* (44), including taxonomically related crop plants and other native and exotic species, assessed a potential risk by *Ophraella* for sunflowers intended for oil production, as ornament or as animal food and for closely related species. Recently, these results have been re-evaluated with apparently minor risks for sunflowers and related species (45). However, it remains to be understood how long *Ophraella* effects will keep the diffusion of ragweed pollen low considering that the number of areas where at first the concentration of the beetle was high are rapidly decreasing (Lombardy).

The control of ragweed is technically feasible and must be supported by the community: experiences in Germany and other countries show that legal regulations specific for ragweed are necessary for ragweed control (4, 46-49) to join health agricultural and environmental advantages.

From what has been described, there are many and different approaches to study issues related to plants and pollen spread of ragweed.

The aim of this study was to understand the changing over time of the appeal of the ragweed topic and its facets among the scientific community providing a picture of the evolution of the studies on ragweed and related issues.

Methods

We searched PubMed and Scopus for articles published until July 2022 reporting the word “ragweed”.

Articles written in all languages were included. Many issues involving ragweed were deepened cross-checking with i.e., “allergy”, “crop and seed”, “land management”, “*Ophraella*”, “pollen”, “prevention”, “spread”, “therapy and immunotherapy”.

The following variables were considered: the start of publishing, the type of document published, the type of journal, the nationalities of the authors, the public institutions supporting research, the institutions to which the authors belonged and of these those who provided the most numerous studies.

Results

Figure 1 shows the number of papers published in Scopus and PubMed database; with 5 169 papers Scopus is the database with the highest number of published papers on ragweed starting from the year 1906. In PubMed ragweed appeared from the 1935 with a total of 3 529 papers.

In Scopus the subject areas most addressed with ragweed were medicine (3 511) and related subjects like immunology and microbiology (1 600), biochemistry, genetics, and molecular biology (549); however agricultural and biological sciences (1 048) too were subjects very addressed. Interestingly, many other kinds of subjects addressed ragweed like for example social sciences, humanistic, mathematics, economics, veterinary etc., (Figure 2).

Most part of the papers were original articles and reviews; in minor part conference papers, letters to editor, editorials or book chapters (Figure 3).

Among the top 10 Journals publishing papers about ragweed, 7 journals of medicine with a total of 1 404 published papers, 2 journals on weed with a total of 269 papers published and 1 journal on aerobiology with 78 papers published (Figure 4) were found.

Figure 5 shows the countries with at least 10 papers about ragweed. United States and Canada

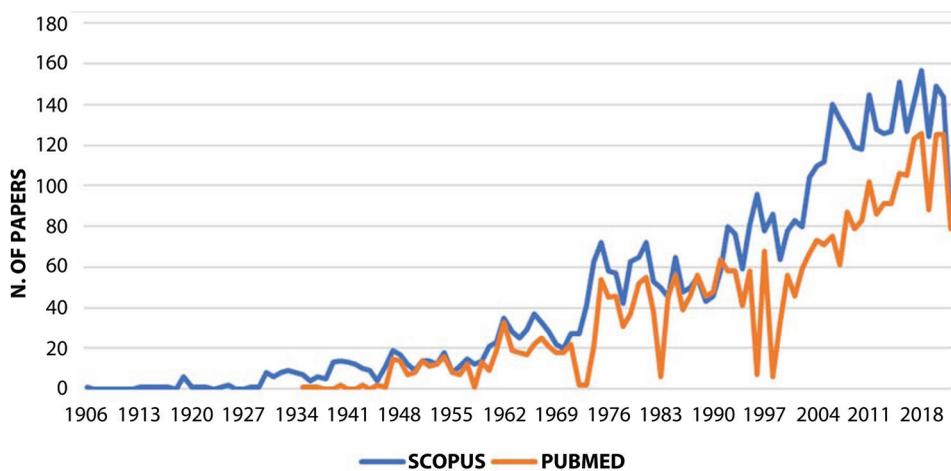


Figure 1. Number of papers published on ragweed in Scopus and PubMed databases.

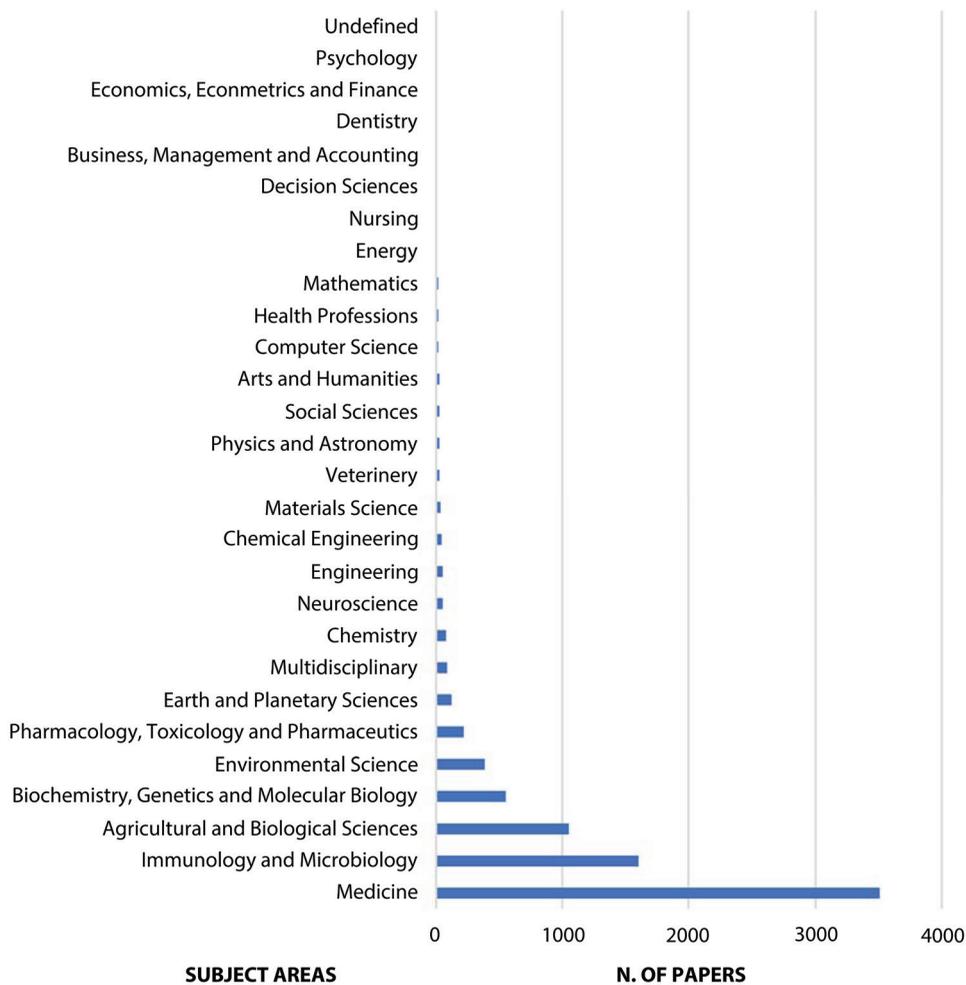


Figure 2. Subject areas addressed by ragweed studies.

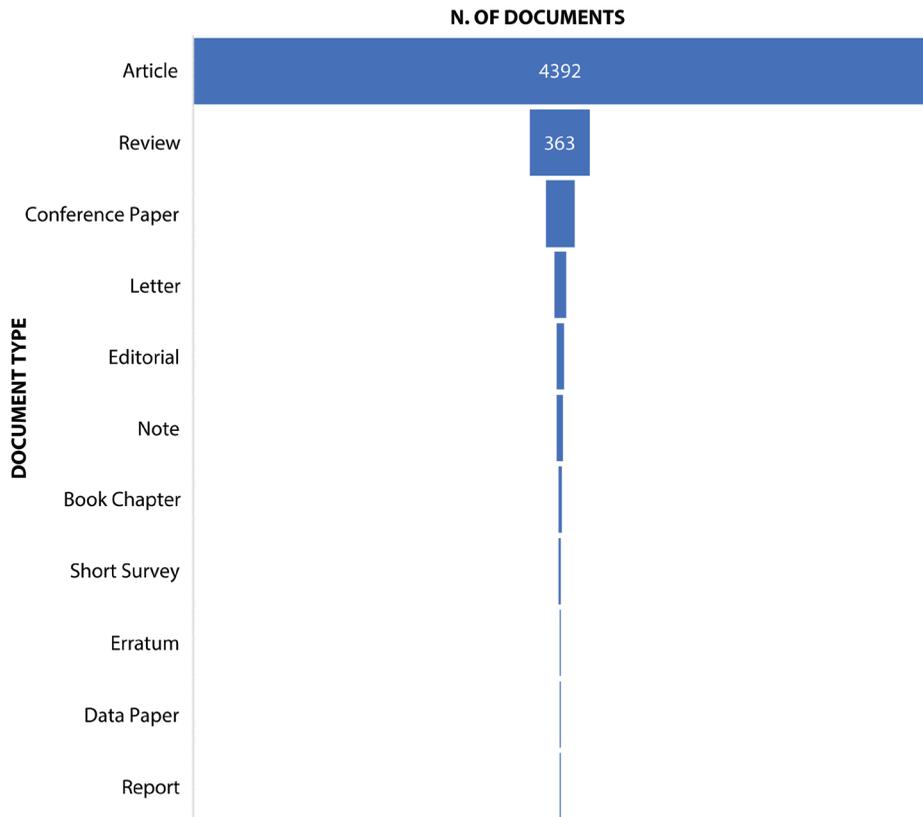


Figure 3. Type of documents published on ragweed.

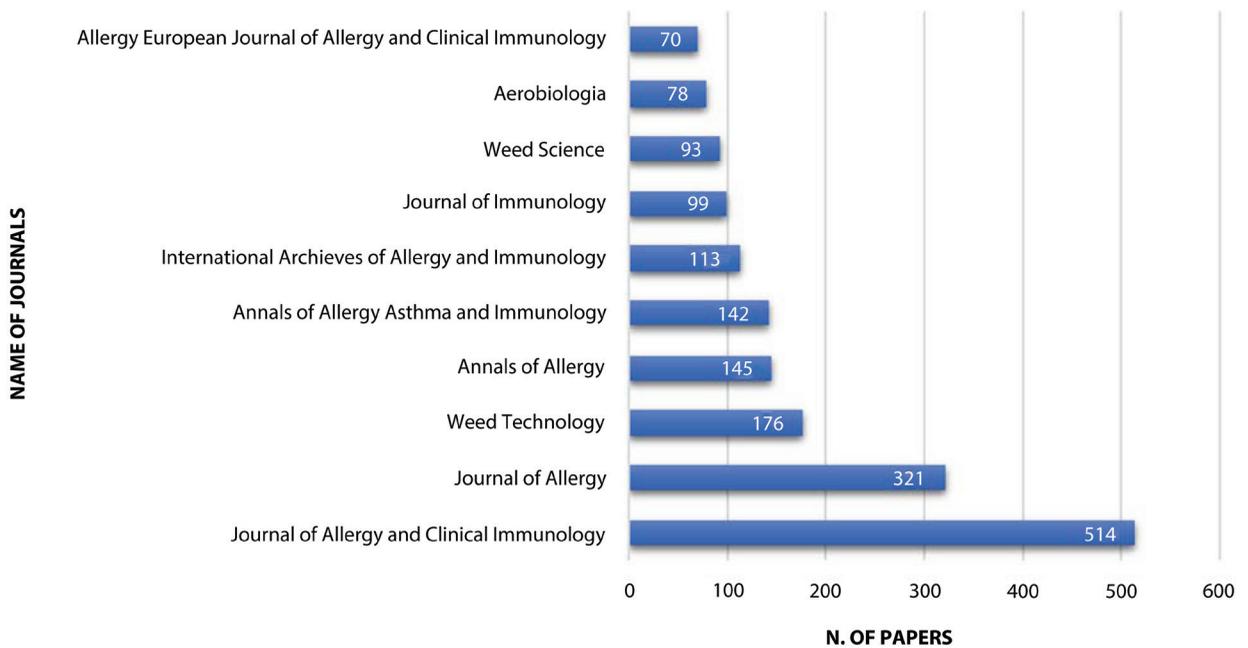


Figure 4. Top ten scientific journals publishing in ragweed articles.

United States	2650
Canada	528
Japan	228
France	216
Italy	209
Germany	193
United Kingdom	179
China	168
Hungary	159
Austria	142
Switzerland	112
South Korea	79
Spain	72
Australia	65
Poland	60
Serbia	53
Croatia	52
Russian Federation	50
Denmark	47
Sweden	40
Netherlands	36
India	30
Czech Republic	27
Mexico	27
Turkey	25
Belgium	23
Ukraine	21
Romania	20
Taiwan	20
Brazil	19
Slovenia	19
Argentina	18
Slovakia	16
Greece	14
Norway	14
Israel	13
Bularia	11
Finland	11
South Africa	11
Egypt	10
Lithuania	10

Figure 5. Number of papers by country (countries with at least 10 papers related to ragweed studies).

were at the top, Japan, France, Italy, and Germany were in the wake followed by United Kingdom, China, Hungary, Austria, and Switzerland.

Figure 6 shows the top 50 authors by number of published papers related to ragweed.

Among the Top 50 institution of research involved in ragweed studies, only eleven were European institutions (Figure 7). In the ranking, the first European institution is after six American institutions.

Table 1 shows the top 40 institutions and private companies supporting research on ragweed (2 168 papers - average 54.2 papers each): Six were pharmaceutical companies (104 papers - average 17.3). Among public institutions supporting research, 8 were European (192 papers - average 24.0), 4 were Asian (78 papers - average 19.5), 1 was Russian with 17 papers and 21 were American institutions (1 881 papers - average 89.6) (Table 1). No Italian, governmental, regional, or local institution appears in the list, as is the case for some institutions in other European countries (i.e., Hungary, Austria, Germany).

Regarding ragweed allergy the papers were 1 942, and the first appeared on Scopus in the 1928 (Figure 8). At the beginning of the 1970s and the 2000s there were two moments of sharp increase in the number of publications on this topic. The countries of scientists which published papers on this topic and among these in the top 10 there were United States, Canada, Italy, France, Germany, Austria, Japan, United Kingdom, Hungary, and Switzerland.

Land management appeared first in the 1967 and in the 1975, then until 2006 nothing more. In total, the papers were 27 with 41 authors involved (Figure 9a). The United States was the country from which most of the authors who have dealt with this topic come from, but some European and Asian countries appear in the list (Figure 9b).

The first paper about crop or seed and ragweed was published in the 1934, with a noticeable increase at the end of the 1990s, the papers were 494 (Figure 10a). The author countries with more than 10 papers were United States, Canada, Hungary, France, Italy, Switzerland, China, Austria, Germany, United Kingdom, Australia (Figure 10b).

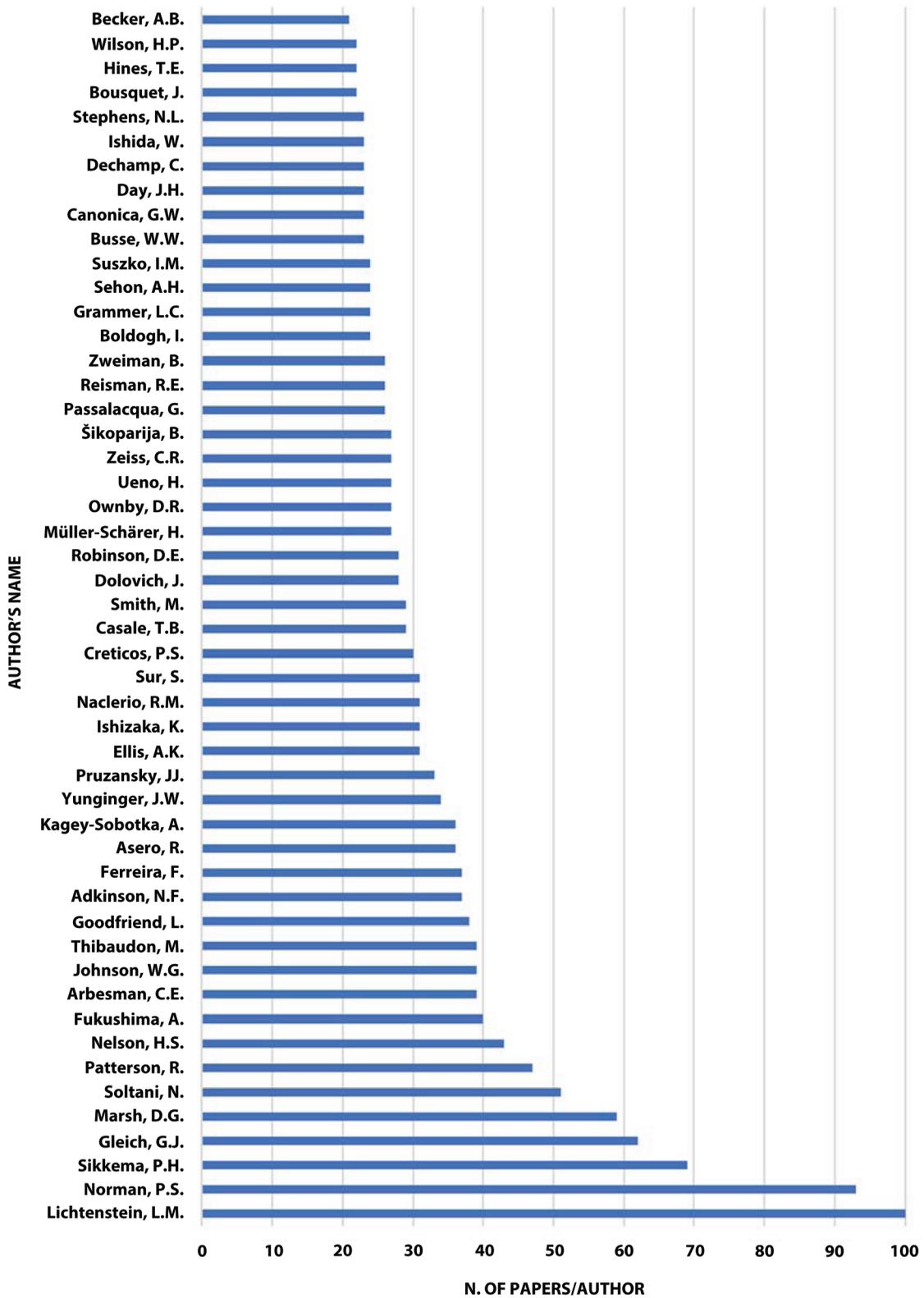


Figure 6. The top 50 authors by number of papers.

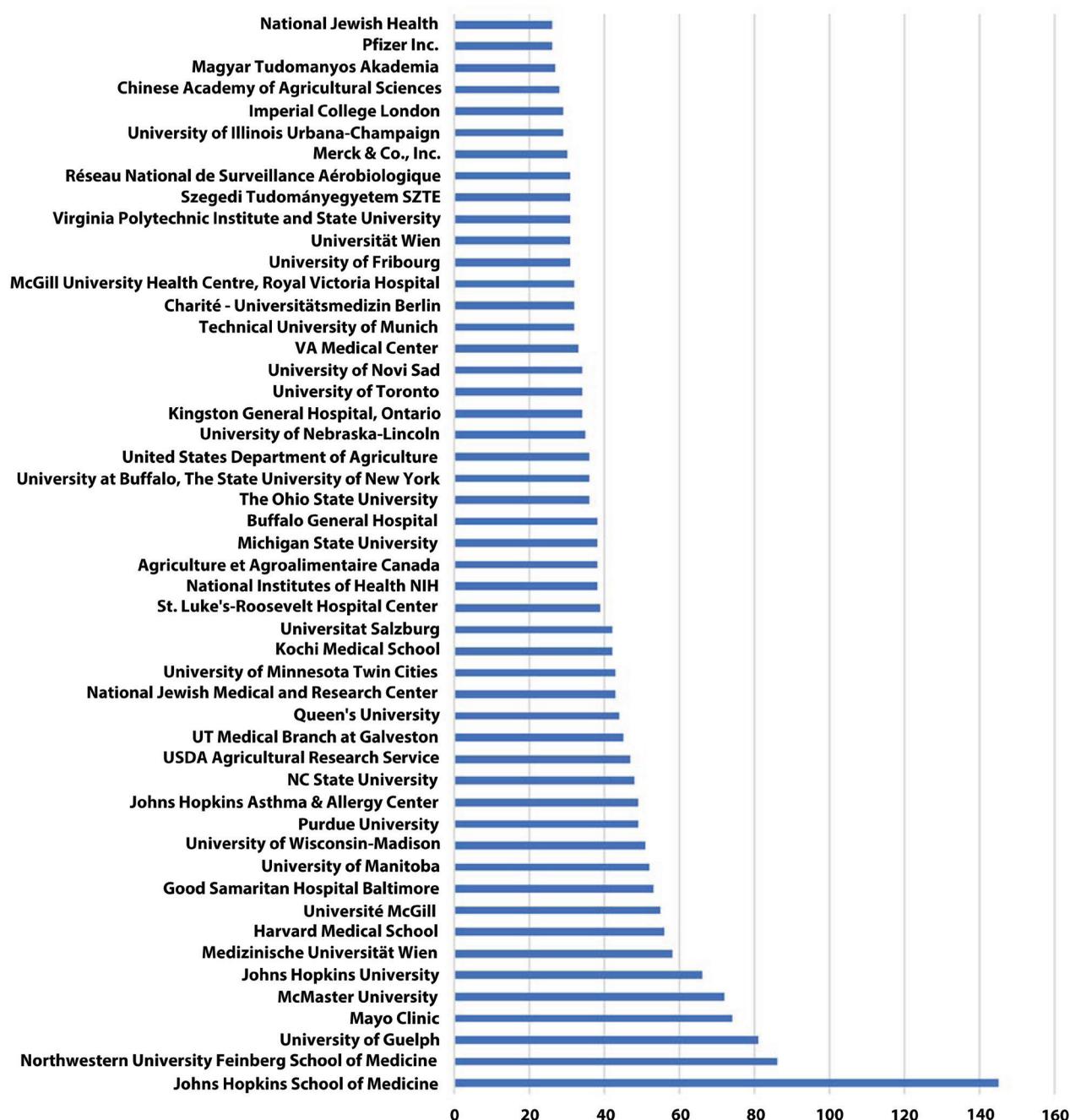


Figure 7. The top 50 institutions of research involved in ragweed issues.

The word “*Ophraella*” related to ragweed appeared for the first time in the 2002 with a total of 69 papers (Figure 11a). The authors by countries with more than 10 papers were 25 from China, 20 from Switzerland, 15 from Italy and Japan (Figure 11b).

Regarding therapy and immunotherapy of ragweed allergy the first paper appeared in the 1930, with a total of 1 075 documents, and as showed by the Figure 12 there were two increasing steps. The first at the beginning of the 1970s, and the second one at the beginning of the 2000s.

Table 1. The top 40 institutions and private companies supporting research on ragweed: private Companies and public Institutions which funded ragweed related studies and continent of belonging (Am, America; E, Europe; A, Asia; RU, Russia; P, Private Company).

Institutions and private Companies supporting research	N. of papers	Continent of Public Institutions - Private Company
National Institutes of Health	467	Am
National Institute of Allergy and Infectious Diseases	388	Am
U.S. Department of Health and Human Services	309	Am
National Heart, Lung, and Blood Institute	140	Am
European Commission	55	E
National Natural Science Foundation of China	54	A
National Institute of Environmental Health Sciences	53	Am
U.S. Public Health Service	51	Am
National Science Foundation	50	Am
Japan Society for the Promotion of Science	33	A
Ministry of Education, Culture, Sports, Science and Technology	29	A
U.S. Department of Agriculture	29	Am
Government of Canada	28	Am
Schweizerischer National fonds zur Förderung der Wissenschaftlichen Forschung	27	E
Austrian Science Fund	24	E
Medical Research Council Canada	23	Am
GlaxoSmithKline	22	P
Novartis	21	P
European Social Fund	20	E
Medical Research Council	20	Am
Merck	20	P
National Eye Institute	20	Am
Natural Sciences and Engineering Research Council of Canada	20	Am
European Cooperation in Science and Technology	19	E
U.S. Environmental Protection Agency	19	Am
Mayo Foundation for Medical Education and Research	18	Am
Seventh Framework Programme	18	E
Canadian Institutes of Health Research	17	Am
Ministarstvo Prosvete, Nauke i Tehnološkog Razvoja	17	RU
National Center for Research Resources	17	Am
National Institute of General Medical Sciences	16	Am
National Research Foundation of Korea	16	A
AstraZeneca	14	P
Genentech	14	P
National Cancer Institute	14	Am
National Institute of Food and Agriculture	14	Am
Deutsche Forschungsgemeinschaft	13	E
Ernest S Bazley Residuary Trust	13	Am
Hungarian Scientific Research Fund	13	E
Pfizer	13	P

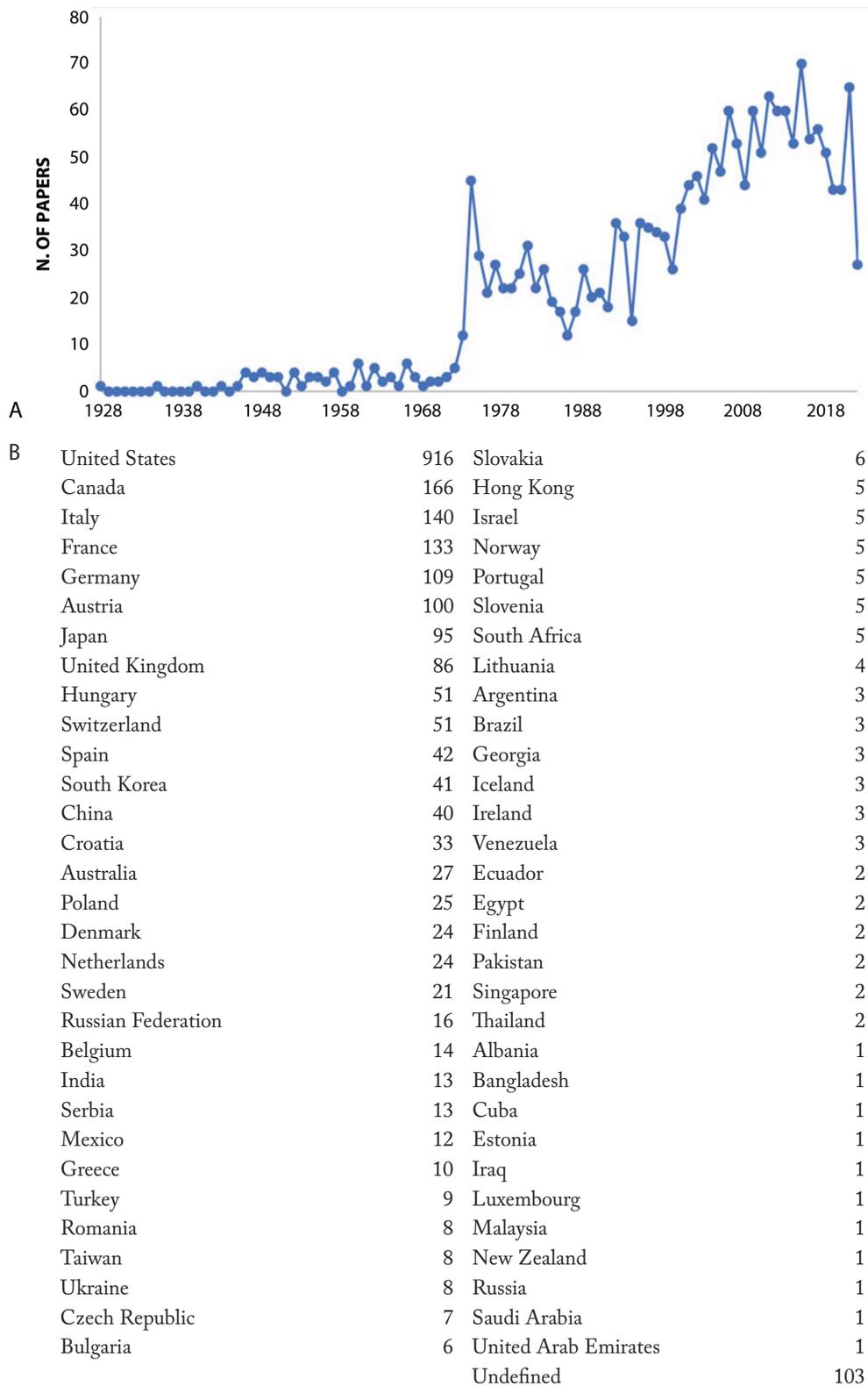


Figure 8. Allergy and ragweed: numbers of papers/year (a) and countries of the authors ranked by number of papers (b).

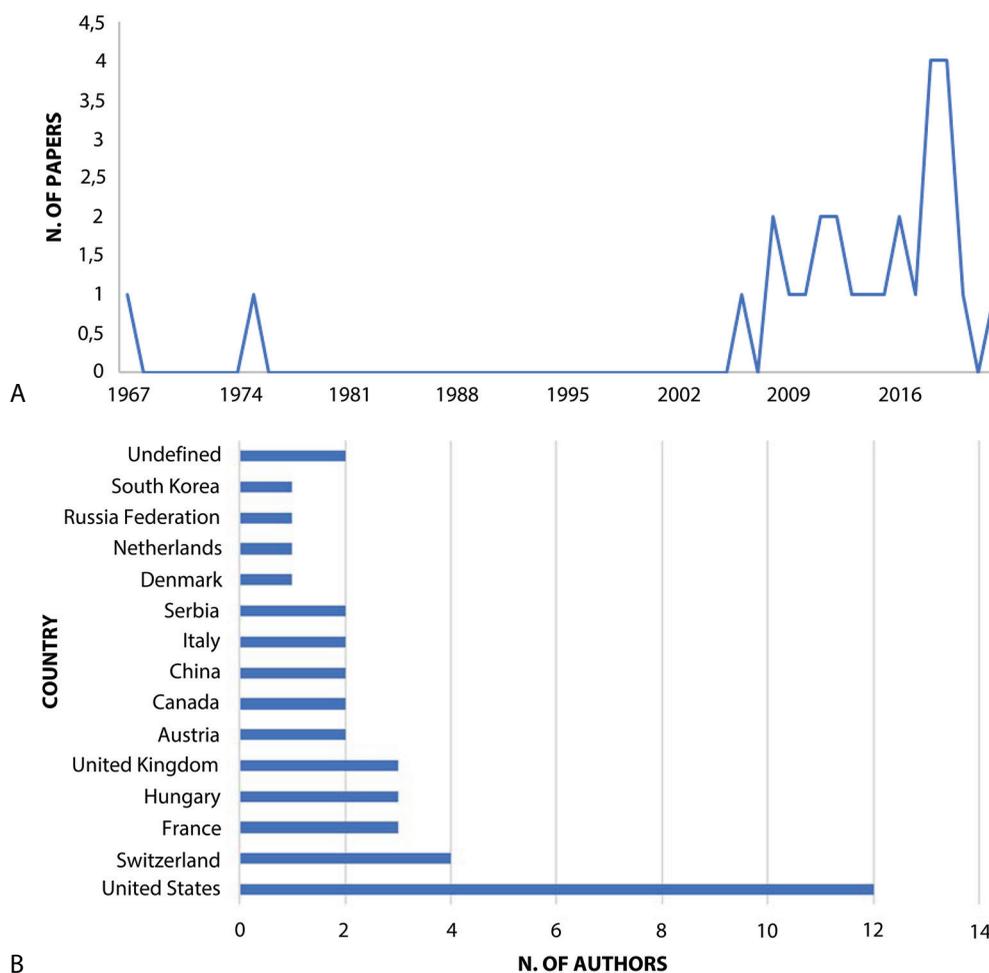


Figure 9. Number of papers on ragweed and land management (a) and countries of the authors ranked by number of papers (b).

The total of 131 articles citing the word “prevention” about ragweed were found, starting from the 1949 with increases at the beginning of the 1980s, and the 2000s (Figure 13a shows). Figure 13b shows the countries of the authors.

Studies on pollen and ragweed starting from the 1914 were 2 892. They show two important increases of the trend, mainly at the mid of the 1970s, and the 2000s (Figure 14a). Figure 14b shows the number of papers by country and Figure 14c their countries.

Regarding the spread of ragweed plants or pollen, the first article appeared in the mid-40s, but only from the mid-2000s the continuous increase of interest in this issue was observed (Figure 15a). One hundred seventy-five articles on the subject were found. The top

ten research centres involved in this subject are only from Europe (Figure 14b).

Conclusions

This study shows a picture of the evolution of studies on “ragweed” and some important related issues over time.

We searched only the word “ragweed” because “ambrosia” could be confused with “ambrosia beetles” (not the beetle *Ophraella*), subfamilies of coleoptera feeding fungi of “ambrosia” (polymorphic asexual anamorphs from the genera *Ambrosiella*, *Raffaelea*, *Ambrosiozyma*, and *Dryadomyces*, occasionally *Fusarium*) (50) or

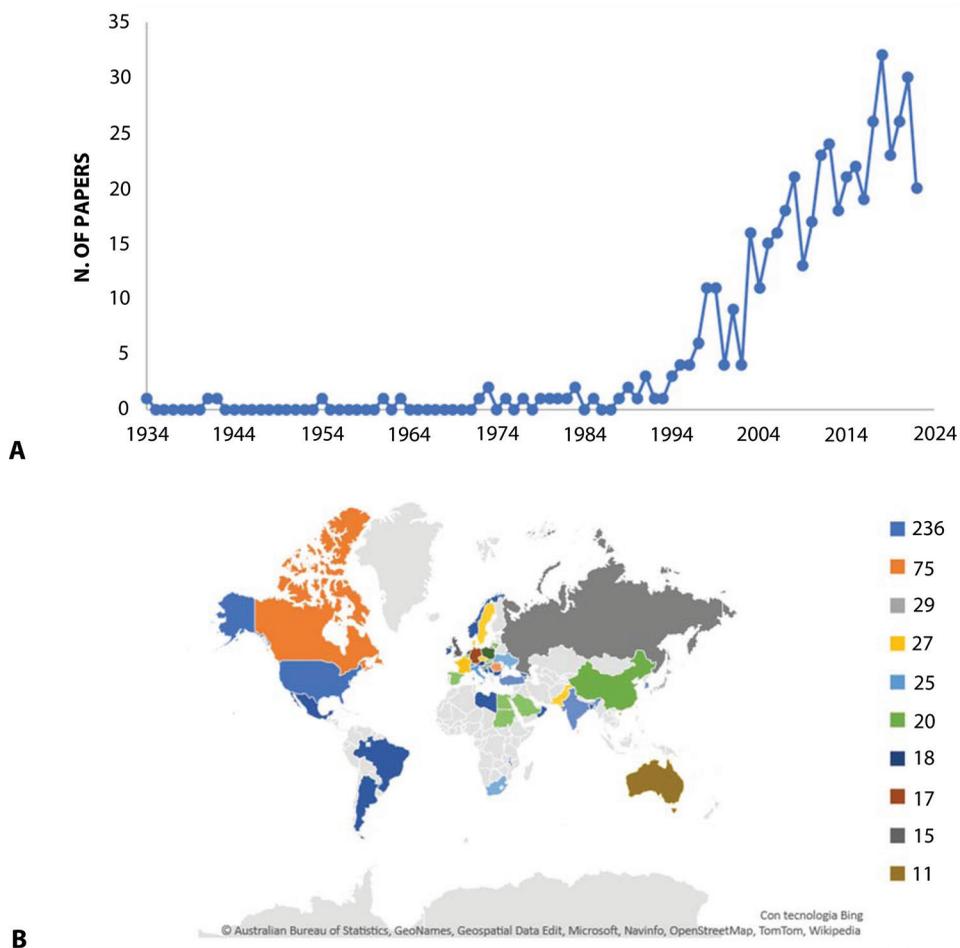


Figure 10. Number of papers by year on ragweed and crop or seed (a) and number of scientists by country (b).

Chenopodium ambrosioides, an herbaceous plant belonging to the genus *Chenopodium*.

Given that PubMed is naturally almost exclusively dedicated to biomedical research, we believe that Scopus best represents the whole research scenario. For this we have analysed the data of this database.

Most of the papers had authors of North American origin, as expected considering that the phenomenon of ragweed originated in that geographical area. However, Europeans were involved in all topics; authors from some countries were more involved in some issues while authors from other countries were involved in other research areas. The studies about prevention, in the territories, and *Ophraella* have mostly involved

authors from Asian countries, but also Europeans were very active in this issue too.

A large gap is evident between the interest in biomedical issues and the other issues which, on the other hand, could be addressed more precisely in support of biomedical ones. This gap should somehow be bridged in the interest of all the actors involved, and primarily public Institutions and citizens.

Outside the North American continent, there is also a clear need for greater involvement of national and local institutions (in Europe and, especially, in Italy) in support of knowledge and the fight against ragweed. It shown that there are researchers working in this topic without any public funding support.

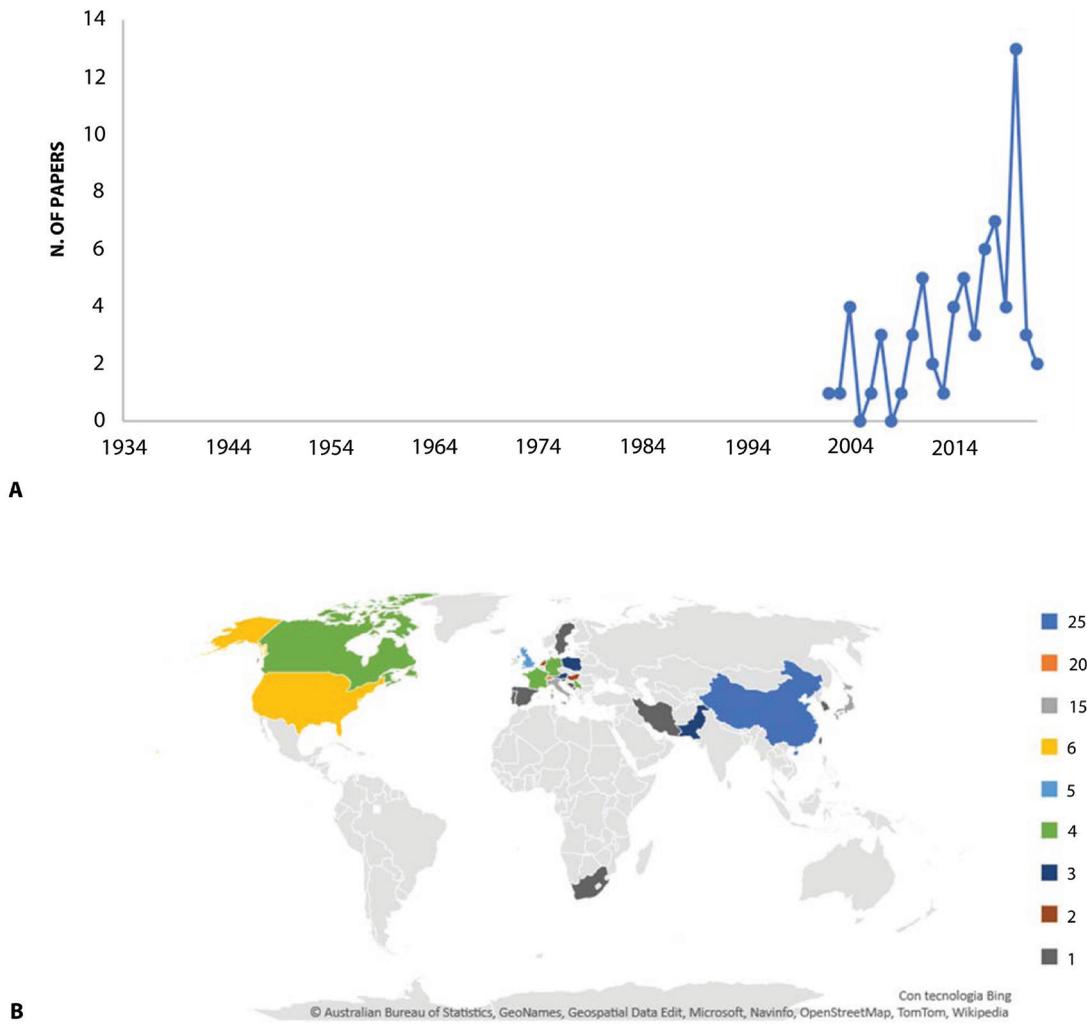


Figure 11. Trend of *Ophraella* studies and the countries of scientists.

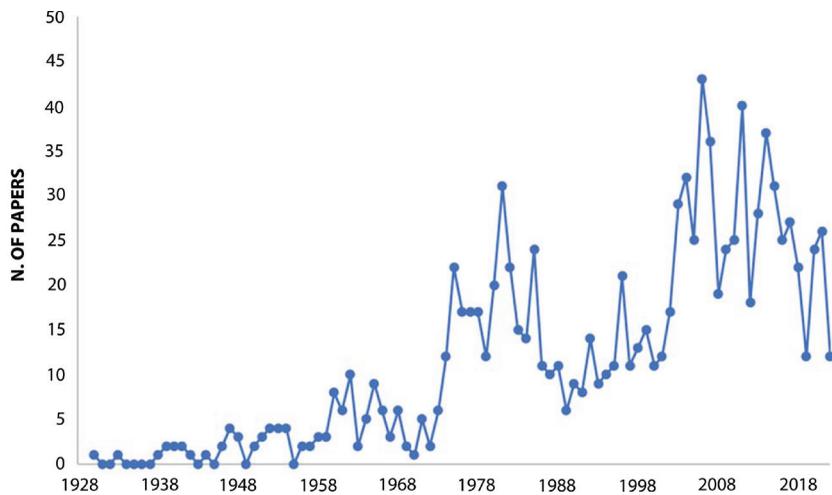


Figure 12. Trend of therapy and immunotherapy papers related to ragweed.

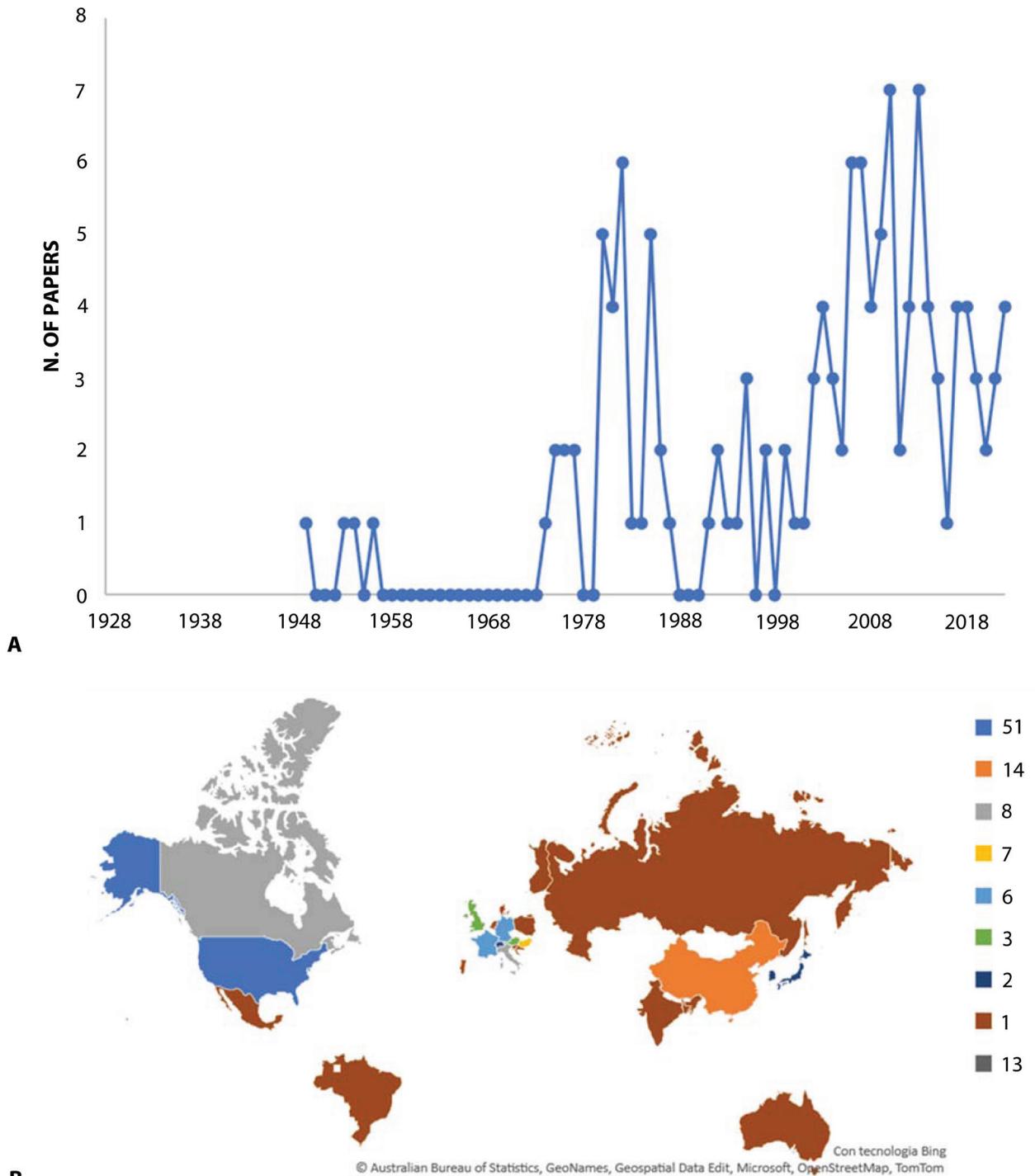


Figure 13. Number of papers written using the word “prevention” regarding ragweed (a) and countries of the authors (b) highlighting the number of papers by country.

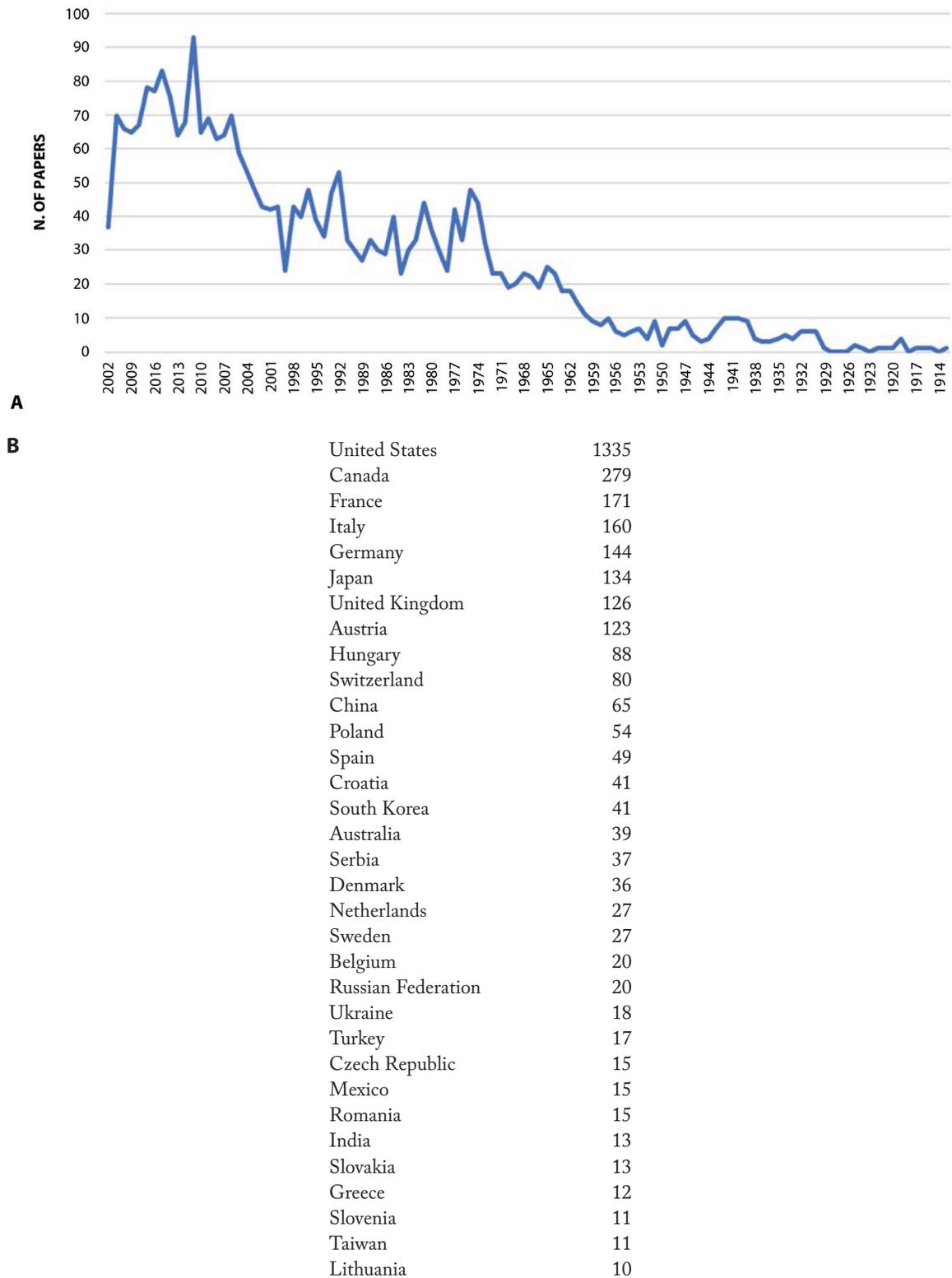
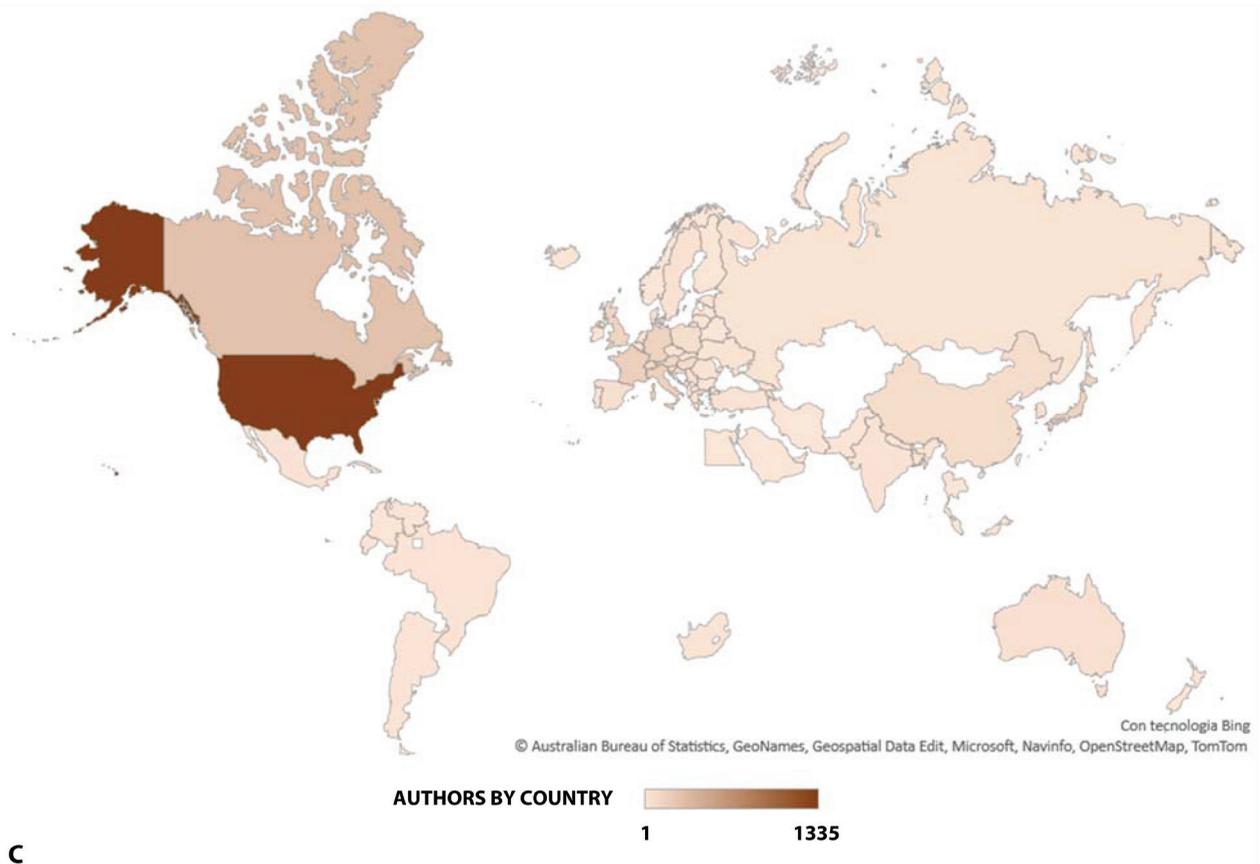


Figure 14. Number of papers written using the word pollen and ragweed (a); countries with authors who had published almost 10 papers (b) and countries of the authors (c).

(continued)



C

Figure 14. (continued)

From the analysis of the results, it can be underlined how the trend behaviour of the studies on “pollen”, “allergy”, “therapy and immunotherapy” and “prevention” are similar. Vice versa, the papers showing the words “spread”, “land management”, “crop and seed”, “*Ophraella*” were less numerous and showed a trend behaviour which was different from that referring to the words “pollen”, “prevention”, “allergy”, “therapy and immunotherapy”. In addition, a decrease of papers dealing with these issues corresponding with the appearance in Europe of *Ophraella*, starting from the mid-2010s is evident. Among the institutions to which researchers on therapy and immunotherapy belong, the most numerous are American; the first European in the rank is the University of Salzburg, sixth position (however the European institutions are numerous in this list). No Asian institutions appear in this rank.

It seems that the two different “scientific communities” biomedical and not biomedical have been

moving without any apparent link or synergy. It seems that biomedical studies are detached from ecological and environmental studies and vice versa.

This suggests that the role of the IRS (International Ragweed Society), a scientific society, founded in the 2009, aimed at knowledge concerning ragweed (*Ambrosia* L.) and its development; to facilitate collaboration, research, education, information, technical development, practical applications and laws concerning ragweed and its direct and indirect impacts, as well as fight against that plant; to create a platform for the people, associations, societies and institutions with an interest in ragweed; to encourage collaboration with other areas related to environmental and health issues, should be better understood by all researchers involved in the topic. IRS should become the crossroads to optimize efforts, disseminate knowledge, share experiences, raise awareness among stakeholders, attract funding and activate local, national, and supranational institutions for coordinated action to study and fight ragweed.

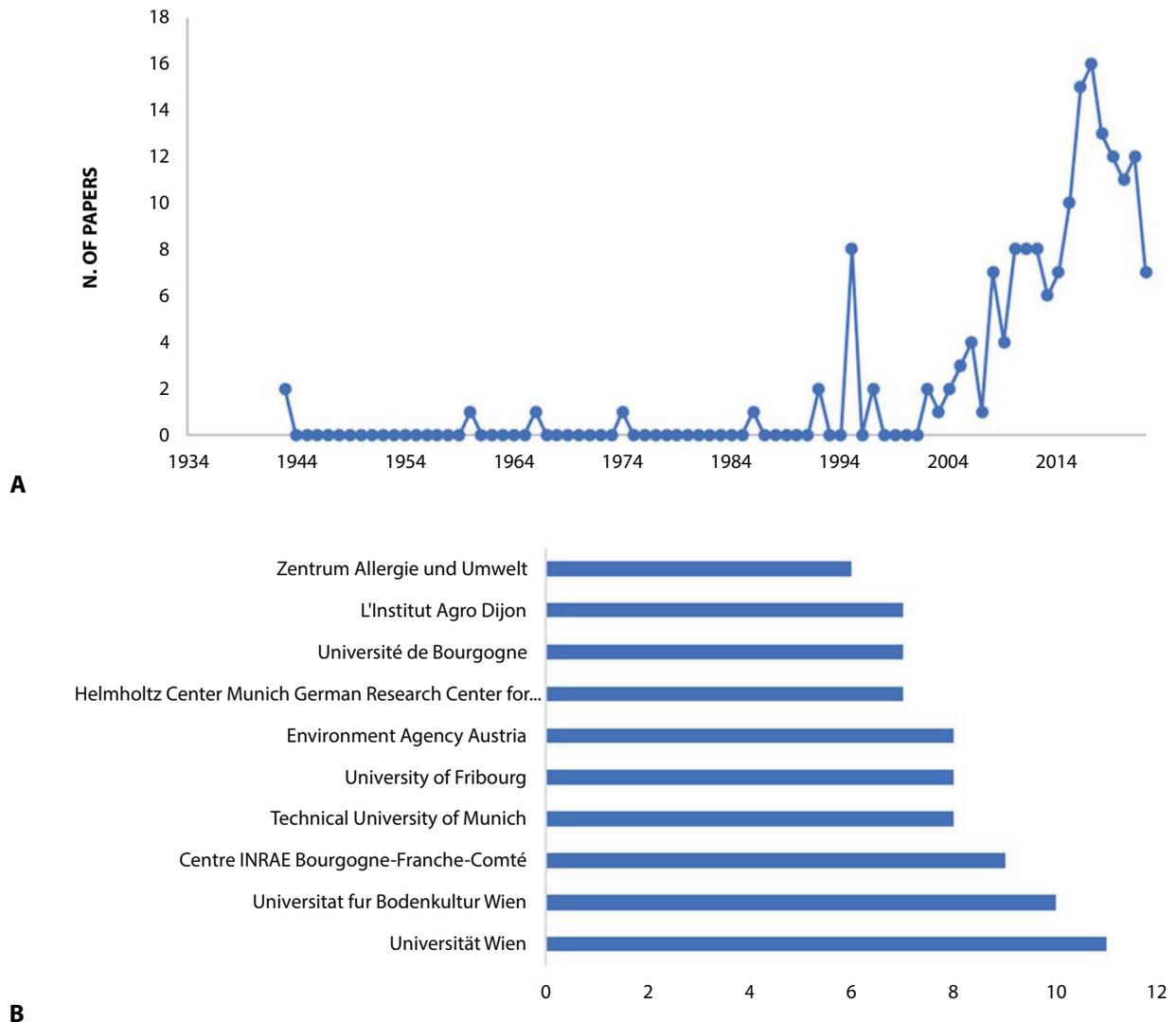


Figure 15. Number of papers reporting using the word “spread” about ragweed (a) and Institutions of research of the authors (b).

We think that analysis of the results of our study will provide a useful tool to identify the evolution of interest in ragweed research and to provide awareness to start the flywheel towards future goals in a “One Health” approach.

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Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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