BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2016-013615
Article Type:	Research
Date Submitted by the Author:	25-Jul-2016
Complete List of Authors:	Brueggmann, Doerthe; Keck School of Medicine of the University of Southern California, Ob/Gyn; Goethe-Universitat Frankfurt am Main, Institute of Occupational Medicine, Social Medicine and Environmental Medicine Köster , Corinna ; Goethe-Universitat Frankfurt am Main, Institute of Occupational Medicine, Social Medicine and Environmental Medicine Klingelhoefer, Doris; Goethe University, Institute of Occupational Medicine Bauer, Jan; Goethe-Universitat Frankfurt am Main, Institute of Occupational Medicine, Social Medicine and Environmental Medicine Ohlendorf, Daniela; Institute of Occupational Medicine, Social Medicine and Environmental Medicine, Goethe-University Frankfurt/Main, ; Bundschuh, Matthias; Goethe-Universitat Frankfurt am Main, Institute of Occupational Medicine, Social Medicine and Environmental Medicine Groneberg, David; Occupational, Social and Environmental Medicine, Medical Department of the Goethe-University Frankfurt am Main
Primary Subject Heading:	Infectious diseases
Secondary Subject Heading:	Global health, Paediatrics, Public health, Respiratory medicine
Keywords:	Respiratory Syncytial Virus, Scientometry, Publication, Gender, Economic benchmarks

Respiratory Syncytial Virus:

The architecture of the global research output and the gender distribution

Corresponding author: Dörthe Brüggmann – occup-med@uni-frankfurt.de, Institute of Occupational Medicine, Social Medicine and Environmental Medicine, Goethe-University, Theodor-Stern Kai 7, 60590 Frankfurt, Germany

Telephone: +49 (0) 69 6301 6650, Fax +49 (0) 69 6301 7053

Dörthe Brüggmann[1,2,*], Corinna Köster[2,*], Doris Klingelhöfer[2], Jan Bauer[2], Daniela Ohlendorf[2], Matthias Bundschuh[2], David A Groneberg[2]

[1] Department of Obstetrics and Gynecology, Keck School of Medicine of USC, Los Angeles, California, United States

[2] Institute for Occupational Medicine, Social Medicine and Environmental Medicine, Goethe University Frankfurt, Germany

* equal contribution

Word Count: 3882

Abstract

Objective: Worldwide, the respiratory syncytial virus (RSV) represents the predominant viral agent causing bronchiolitis and pneumonia in children. To conduct research and tackle existing healthcare disparities, RSV-related research activities around the globe need to be decoded. Hence, we aim to assess the associated country-specific scientific architecture in relation to socio-economic and gender parameters.

Design: retrospective, descriptive study

Setting: We employed the NewQIS platform to identify RSV-related articles published in the Web of Science from 1900 to 2013. Items were analyzed regarding quantitative and qualitative aspects; results were visualized by density equalizing mapping tools.

Results: We identified 4600 articles. The USA was leading in terms of overall publication and citation numbers. When output was related to economic benchmarks, Guinea-Bissau and The Gambia were leading the field. RSV research benefited from collaborative networks, primarily established between high-income countries. The gender analysis indicated that male scientists dominated in all countries except Brazil.

Conclusions: The majority of RSV-related research output originated from high-income countries. Developing nations were barely part of the research landscape or collaborative networks. Hence, research efforts of these nations have to be strengthened so apparent disparities can be minimized and the high mortality rates related to RSV can be tackled successfully.

Key words: Respiratory Syncytial Virus, Publication, Citation, Scientometry, Gender, Economic benchmarks

Strengths and Weaknesses

- This is the first concise depiction of the international RSV research landscape.
- The NewQIS platform combines scientometric methods and "density equalizing mapping projections" to evaluate the scientific output regarding quantitative and qualitative aspects, geographical and chronological developments, existing research networks and socio-economic benchmarks in a reliable and standardized way.
- Since the WoS has a preference for English journals, we have to acknowledge a language bias associated with our analysis.
- Citation based parameters were assessed, which we defined as "semi-qualitative" since these rather reflect the recognition of the research in the scientific community than truly measure quality.

INTRODUCTION

The human respiratory syncytial virus (RSV) is the worldwide predominant viral agent affecting the respiratory tract [1 2]. It is associated with 64 million infections that occur primarily in children under 5 years [3]. RSV belongs to the Paramyxoviridae family. It is a negative-sense, non-segmented, single-stranded RNA virus [4]. Mostly transmitted by droplets, RSV causes bronchiolitis, pneumonia, bronchitis and croup and is linked to recurrent wheezing and pediatric asthma [5 6]. There is no definitive treatment for RSV-related conditions. The efforts to develop effective and safe vaccines have remained unsuccessful to date. One prophylactic agent is commercially available, the neutralizing anti-RSV antibody Palivizumab. Its use is limited to preterm babies, chronic lung disease of prematurity or infants with congenital heart disease [7].

RSV-associated morbidity and mortality depends on many factors such as the geographic location, climate patterns, genetic susceptibility, socioeconomic factors and local virus strains [3]. The percentage of children having contracted RSV by their second year of life comes close to 100% [8 9]. In the United States of America (USA), over 2 million children aged 5 years and under need medical attention to treat their RSV infection every year [10]. On average, 0.3% of these children and 0.7% of infants younger than six months require hospitalization [10]. The general RSV mortality rate in this demographic varies between 0-33% [9]. Worldwide, up to 199 000 children die due to RSV infections, 99% of these deaths occur in in developing countries [3]. Hence, RSV represents a substantial burden for community health in these nations: According to WHO field studies in ten developing countries, RSV causes 70% of all acute respiratory-tract infections in children under 5 years of age [11]. Here, the virus is identified in about 15-40% of the hospitalized children with pneumonia or bronchiolitis

[12]. Further, the primary presentation of RSV infections and virus strains differ in industrialized versus developing nations: In the USA and continental Europe, the majority of children present with bronchiolitis linked to the viral subgroup A whereas in The Gambia, the same demographic suffers mainly from pneumonia associated with the B strain [13 14].

Although care of RSV patients has been improved considerably and extensive studies have been launched to estimate viral spread and disease burden in developing countries, tremendous challenges still remain. Considering the high prevalence, morbidity and mortality of RSV worldwide, we deduce that further research and the implementation of related public health measures are crucial for future successes. However, global research funds are limited and their allocation becomes challenging. In this context, the assessment of the scientific performance is a prerequisite for the reasonable distribution of monetary support and the planning of future research endeavors by scientists interested in the field. Hence, we employed scientometric tools with the goal to determine the RSV-related research output among the extensive amount of biomedical publications and to evaluate the scientific productivity of single countries in the framework of the global research landscape and in relation to socioeconomic and gender aspects. To guide individual scholarship and the publication of own research dedicated to the area, we also present the 15 most cited articles and the most proliferative journals in the field of RSV research.

METHODS

Methodical Platform

We used the New Quality and Quantity Indices in Science (NewQIS) platform to

assess RSV research. This tool combines scientometric methods and "density equalizing mapping projections" (DEMP) [15-18] to evaluate the scientific output regarding quantitative and qualitative aspects, geographical and chronological developments, existing research networks and socio-economic benchmarks in a reliable and standardized way.

Density-equalizing mapping

DEMP is a state-of-the-art technique to visualize benchmarking processes by anamorphic maps [15 19]. Based on the algorithm of Gastner and Newman, the size of each country was modified analogously to country-specific data on RSV research leading to a new geographic distribution of the global landscape [15].

Data collection

For data collection, the Web of Science (WoS) Core Collection database (Thomson Reuters) was employed. We used the following search term: Title=("RSV" OR "Respiratory Syncytial Virus" OR "RS Virus*") NOT Topic=(Rous Sarcoma). The Boolean operator NOT was used to exclude all publications concerning Rous Sarcoma (Virus). We acknowledge that not all eligible RSV publications were detected by the conducted "TITLE"-search. But this approach was preferred since a "TOPIC" search would include a significant amount of off-topic publications compromising the validity of our data collection. Further, our search was limited to the document type "article" to only cover original research studies. No additional platforms such as PubMed, Google Scholar or Scopus were employed to collect bibliometric data because the management, organization and the scope of data is slightly different among these databases, which affects triangulating, comparing and

integrating data related to RSV research in a meaningful way. Following our protocol, the time frame was restricted from 1900 to 2013; publications in 2014 were not included due to incomplete data acquisition at the time the study was performed.

Data analysis

RSV-related articles were analyzed regarding quantitative aspects such as the total number of publications, citation numbers, countries of origin, institutions, languages, document types, cited reference numbers, and publication date. As semi-qualitative variables, h-Indices, and the average citation number per item (citation rate, CR) were investigated. We defined them as “semi-qualitative”, because these performance indicators rather reflect the recognition of the research in the scientific community than truly measure quality. Regression analysis was used to investigate the chronological evolution of RSV research. We calculated the coefficient of determination (r^2) representing the slope of the growth in scientific output and citations.

Modified h-Index

The Hirsch-Index (h-Index) is a recognized semi-qualitative proxy measure to assess the impact of one author’s research output on the scientific community [20 21]. An h-index of 12 indicates that out of 12 published papers each has been cited at least 12 times. In this study, we applied this concept to the RSV-specific research productivity of single countries and calculated a “modified country-specific” h-Index.

Gender analysis

The proportionality of male and female researchers publishing on RSV was analyzed. Online name databases were utilized to identify the authors' genders [22]. If first names were not gender-specific or quoted as initials, a manual search (utilizing websites, corresponding addresses and social networks) was launched. We evaluated only countries, where more than 50% of authors were identified by gender and where a minimum of 60 gender-defined authors were working on RSV.

Cooperation analysis

We identified all RSV-associated publications that were issued based on international collaborative efforts. In brief, if at least two authors originating from different institutions or countries (as identified by the stated affiliations on the article) contributed to one article, this publication was defined as a collaborative work. Connecting vectors were used to visualize these co-operations; their width and shade of grey reflected the number of joint publications.

Journal analysis

The journals publishing on RSV were analyzed regarding quantitative and qualitative aspects, e.g. number of published RSV articles as well as citations these items received (CR).

Analysis of economic key figures

Two quotients were calculated to assess the scientific output of a specific country, (1) in relation to the number of citizens (Q1), and (2) in relation to its economic power (as

measured by the gross domestic product, GDP, Q2). We computed these in the following way:

1. Articles/population-index (Q1) = number of articles/population in millions
2. Articles/GDP-index (Q2) = number of articles/GDP in billions

All countries were classified into high-, upper-middle-, lower-middle- and low-income groups according to World Bank definitions [23].

RESULTS

Number of published items

We identified 4,600 articles on RSV published between 1900 and 2013; 57.5% of these were issued after 2000. After 1960, the number of articles increased significantly over time as indicated by r^2=0.9 (Fig. 1). Also, the number of authors per article grew from 3.8 in 1978 to 7.6 in 2013.

Analysis of research origin and citations

Although the publications originated from 92 countries, the majority of the articles were written in English (96.6 %) followed by French (1.4 %) and German (0.7%). More than 85% of the global research output was published by authors from high-income economies. The USA was the most productive nation (2,139 articles, a) followed by the United Kingdom (UK, a = 583), the Netherlands (a = 231), Canada (a = 217) and Germany (a = 196). Hence, the USA and UK dominated the cartogram, while major parts of Africa (with the exception of South Africa), Asia (with the exception of Japan, China, South Korea, and India) and Central America occupied only minor areas (Fig. 2A).

The country-specific citation numbers and modified h-Indices showed a global distribution similar to the number of publications: The US-American publications were cited most (83,000 citations, c), followed by articles from the UK (c = 19,240), the Netherlands (c = 5587), Canada (c = 5549) and Germany (c = 5319). Articles published by African, Asian and Middle American authors received hardly any citations.

The USA and the UK were the top ranked countries with a modified h-Index of 121 (USA) and 68 (UK) followed by the Netherlands (h-Index = 44), Germany (h-Index = 43) and Canada (h-Index = 40) (Fig. 2B).

Regarding the country specific citation rate (average number of citations per total number of publications for each country with more than 30 articles, CR), Sweden (CR = 40) dominated and was followed by the USA (CR = 38.8), Finland (CR = 34.9), the UK and Germany (CR = 27.13).

Analysis of citation performance

The absolute citation count of all identified RSV-related articles resembled the growing volume of published papers in the investigated timeframe. We documented a significant positive correlation between citation numbers and the time of publication (with r^2=0.72 for the timeframe from 1960 to 2008). The annual citation counts grew modestly from 1960 to 1994; after 1995, a rapid increase followed until 2004 whereas a steep decline was noticed after 2004. We identified visible peaks in citation activity for 1969, 1987, 2000, and 2004 (Fig. 3). Additionally, we compiled the 15 most cited

233 RSV articles, which constitute the publications that have sparked the most
234 documented interest in the field to date (Table 1).
235
236 Table 1. The 15 most cited articles in the area of RSV-related research are displayed
237 including their title, publication year, country of origin, citation count and journal.

Title	Publication Year	Country	Citations	Journal
Mortality associated with influenza and respiratory syncytial virus in the United States **Thompson WW et al.**	2003	United States	1520	JAMA
Pattern recognition receptors TLR4 and CD14 mediate response to respiratory syncytial virus **Kurt-Jones EA et al.**	2000	United States	856	Nat Immunol
Respiratory Syncytial Virus Disease In Infants Despite Prior Administration Of Antigenic Inactivated Vaccine **Kim HW et al.**	1969	United States	848	Am J Epidemiol
Respiratory syncytial virus in early life and risk of wheeze and allergy by age 13 years **Stein RT et al.**	1999	Brazil, United States	719	Lancet
Palivizumab, a humanized respiratory syncytial virus monoclonal antibody, reduces hospitalization from respiratory syncytial virus infection in high-risk infants **The Impact-RSV Study Group.**	1998	United States, Canada, UK	652	Pediatrics
An Epidemiologic Study Of Altered Clinical Reactivity To Respiratory Syncytial (Rs) Virus Infection In Children Previously Vaccinated With An Inactivated RS Virus Vaccine **Kapikian et al.**	1969	United States	552	Am J Epidemiol
Risk Of Primary Infection And Reinfection With Respiratory Syncytial Virus **Glezen et al.**	1986	United States	548	Am J Dis Child
Respiratory syncytial virus bronchiolitis in infancy is an important risk factor for asthma and allergy at age 7 **Sigurs N et al.**	2000	Sweden, Iceland	488	Am J Respir Crit Care Med
Wheezing, Asthma, And Pulmonary Dysfunction 10 Years After Infection With Respiratory Syncytial Virus In Infancy **Pullan CR and Hey EN**	1982	UK	449	Br Med J
Respiratory syncytial virus infection in elderly and high-risk adults **Falsey AR et al.**	2005	United States	430	NEJM
Prophylactic Administration Of Respiratory Syncytial Virus Immune Globulin To High-Risk Infants And Young-Children **Groothuis JR et al.**	1993	United States	427	NEJM
The Development Of Respiratory Syncytial Virus-Specific IgE And The Release Of Histamine In Nasopharyngeal Secretions After Infection **Welliver RC et al.**	1981	United States	425	NEJM

Respiratory-Syncytial-Virus Infections, Re-Infections And Immunity - Prospective, Longitudinal-Study In Young-Children **Henderson FW et al.**	1979	United States	418	NEJM
Generation of bovine respiratory syncytial virus (BRSV) from cDNA: BRSV NS2 is not essential for virus replication in tissue culture, and the human RSV leader region acts as a functional BRSV genome promoter **Buchholz UJ et al.**	1999	Germany	417	J Virol
Asthma and immunoglobulin-e antibodies after respiratory syncytial virus bronchiolitis - a prospective cohort study with matched controls **Sigurs N et al.**	1995	Sweden	416	Pediatrics

Relation to economic parameters

Relating the number of publications to the population of a country, high-income countries like Iceland (Q1 = 34.59), the Netherlands (Q1 = 13.90) and Denmark (Q1 = 12.25), issued a higher number of publications per million citizens compared to low- or lower-middle-income countries, e.g. Nigeria (Q1 = 0.03) and Indonesia (Q1 = 0.02) (Fig. 4A). We identified two exceptions: The low-income countries Guinea Bissau (Q1 = 6.30) and The Gambia (Q1 = 4.76) were represented among the 15 top ranked countries in this analysis.

When looking at the publication activity in relation to GDP, two low-income countries outperformed high-income nations (Fig. 4B): Guinea Bissau (Q2 = 11.776) and The Gambia (Q2 = 8.721) held leading positions, followed by Iceland (Q2 = 0.810), Kenya (Q2 = 0.516), and Croatia (Q2 = 0.319). Besides these two exceptions, other low- or lower-middle-income countries showed a weak performance (e.g. Philippines with Q2 = 0.004 or Indonesia with Q2 = 0.007). Also, the USA did not remain under the top 10 nations and was found at position 18 (Q2 = 0.132).

Gender analyses

71.3 % of authors were identified regarding their gender. While the majority of the senior authors were male (70.3 %), the relation between female (48.36 %) and male first authors (51.64 %) was almost balanced.

The country-specific gender analysis indicated that males represented the largest proportion of scientists in almost all evaluated countries (Fig. 5). Brazil was an exception. Here, males and females were almost equally represented, with a small over-representation of female scientists. By calculating the proportion of male to female scientists, we documented the lowest value (0.94) for Brazil, followed by Germany (1.1). Japan reached the highest score with 2.8 showing a clear dominance of male scientists.

International cooperation analysis

Since 1973, 614 joint articles were published on RSV accounting for 13.34% of all articles. The USA was the preferred partner for international collaborations on RSV: The most productive cooperation was established between the USA and the UK (67 joint works), followed by the USA and Canada (45 joint articles), and the USA and Germany (34 joint articles). The most fruitful cooperation not involving the USA existed between the UK and Spain (33 joint articles). The most productive cooperation between high- and lower-middle- or low-income economies was set up between Kenya and the UK (18 joint articles) followed by Guinea Bissau and Denmark (10 joint articles). Overall, co-operations with low-income or lower-middle-income countries were less popular (Fig. 6).

Journal analysis

We identified the most prolific journals in RSV research: The "Journal of Virology" was leading the field (334 articles, CR of 45.49), followed by “The Pediatric Infectious Disease Journal" (198 articles, CR = 24.66) and the "Journal of Infectious Diseases" (186 articles, CR 55.18) (Fig. 7). The highest citation rate was achieved by the "Proceedings of the National Academy of Sciences of the United States of America" (42 articles, CR = 81.43), followed by "Pediatrics" (66 articles, CR = 70.80), “Journal of Pediatrics” (65 articles, CR = 64.03), “American Journal of Respiratory Critical Care“ (47 articles, CR = 62.55), and „Journal of Infectious Diseases“ (186 articles, CR = 55.18).

DISCUSSION

In the WoS, we documented only 4,600 RSV-related articles since 1900. The first item on the disease in humans was published in 1957 [24]. This underscores that research on RSV is a relatively new field considering the virus was initially isolated in 1956 from laboratory primates [25]. The predominance of English in the majority of identified articles aligns not only with the fact that this language is the recognized “scientific lingua franca” but also reflects the abundant research output of English speaking countries such as USA, Canada and the UK found in our study.

The increasing number of RSV publications over time is typical for most biomedical research, e.g. on the John Cunningham Virus, influenza or breast cancer [26] [27]. Overall, the steady growth of article numbers can be explained by the rising interest in the field due to the increasing relevance of RSV in pneumonia and child mortality [8]. In the first few years after the detection of the virus, basic research was conducted -

aiming to characterize the virus, identify immunologic responses and develop vaccines [28-31] - and translated into a growing volume of articles on RSV. The continuous increase since the beginning of the 1990s may be attributed to the launch of modern communication systems based on new computer technologies like the World Wide Web, which made it easier to communicate, exchange ideas with other scientists and publicize articles in central databases.

The chronological development in publication quantity (Fig. 1) was resembled by the steady increase of related citations (Fig.3). Four prominent citation peaks in 1969, 1987, 2000 and 2004 coincided with milestone papers the field: In 1969, adverse effects of the formalin-inactivated RSV vaccine in children were reported [32]. Large epidemiologic studies investigated the risks of reinfection and the mortality associated with RSV in 1986 and 2003 [33 34]. The research on a prophylactic antibody licensed in 1999 and novel insights into immunologic responses involving pattern recognition receptors TLR4 and CD14 may be responsible for the peaking number of publications and citations in 2000 [35]. The citation decline after 2004 can be attributed to the short timespan articles had allotted to receive recognition within the scientific community and obtain the appropriate citation number reflecting their true impact [36]. Hence, we expect this trend to be reversed in the future.

The USA dominated RSV research in regards to overall publication quantity, citation numbers and h-index. This corresponds with a previous biomedical benchmarking study: Here, the USA was the most productive nation and authored 1,893,800 of 5,527,558 publications related to 22 organ systems from 1961 to 2007 [37]. The leading role of the USA might be linked to major financial resources this nation dedicates to research supporting manpower and an outstanding scientific

infrastructure. This is also illustrated by the majority of institutions working on RSV we identified in the USA, and the role of this nation as a preferred partner for national and international co-operations.

The cluster of the USA, Western-European countries (e.g. UK or Germany) and Japan dominated the overall publication output and analyses of semi-qualitative benchmarks. This finding corresponds with other scientometric studies (e.g. on Influenza, Ebola, or Hepatitis B [26] [38]. Although Sweden and Finland published relatively low numbers of articles, they are characterized by the highest citation rates in our analysis indicating the outstanding quality and high recognition their articles receive in the scientific community. Further, it is striking that most African, Asian and Central American countries afflicted with a considerable RSV-related burden do not play a visible role in the field. Methodologically, we included only countries in the citation rate analysis that published more than 30 RSV articles aiming to generate a better the validity of the investigation by avoiding overestimation of few but frequently cited articles. Nevertheless, we want to stress that the absolute number of citations as well as the citation rate should be viewed critically due to self-citation, inaccurate citations or the Matthew effect [39] [40]. Hence, we also evaluated the modified h-index since it is less influenced by outstanding, frequently or rarely cited articles skewing the citation rate value [20] [21].

Our analysis of RSV research outputs changed in relation to economic capabilities (Fig. 4) and two developing, low-income nations, The Gambia and Guinea-Bissau, occupied the leading positions. This finding points towards the fact that both prioritize RSV research and might be connected to existing co-operations with a long standing shared history between collaborating nations and their focused support of RSV

scientific activities. For example, the United Kingdom's "Medical Research Council: The Gambia Unit" and the Danish "Bandim Health Project" encourage medical research in Guinea-Bissau and The Gambia [41 42]. Also, research in the field is promoted by single researchers with a strong dedication to conduct research in African sites: Here, Sir Brian Greenwood has spearheaded RSV-related research very successfully for decades while being faculty at the London School of Hygiene and Tropical Medicine as well as the Director of the Medical Research Council in The Gambia.

Collaborations are becoming increasingly important in the field of RSV research as indicated by existing tight-knit networks and the growing numbers of authors per article over time. We link this development to the globalization process, which connects scientists worldwide to exchange ideas, resources and knowledge facilitated by the growing availability of information technology. Further, it is noticeable that countries such as the USA or European nations play a more prominent role in international collaborations compared to low- and lower-middle-income countries. As exceptions, we could identify proliferative co-operations between the UK and Kenya as well as Denmark and Guinea-Bissau. The relation between Kenya and the UK might be based on their shared history and facilitated by implemented programs such as the *"KEMRI Welcome Trust Research Program"* between the Kenya Medical Research Institute and the University of Oxford [43]. Research activity on RSV in Guinea-Bissau is supported by the aforementioned Danish "Bandim Health Project", which was founded by the anthropologist Sir Peter Aaby in the 1970s. It gathers local epidemiological data on more than 200,000 individuals. Since its foundation, this group published more than 600 items on vaccines, maternal mortality and childhood infections such as RSV [41].

The evaluation of publication performance by gender is meaningful but should be evaluated critically: Although more than 70% of authors could be identified by gender, not all first names were included in our analysis since some were gender-neutral, not listed in name databases or displayed as initials. Therefore, the threshold of at least 60 publishing scientists and 50% gender definability was implemented to include only countries providing meaningful and valid data. We identified an overrepresentation of male authors in the majority of evaluated nations besides Brazil (Fig. 5). This result correlates with previous investigations on Yellow fever and Rotavirus infections [44] as well as with gender benchmarking studies (e. g. conducted by the "Konrad-Adenauer Foundation" or the "Organization for Women in Science for the Developing World" (OWSD)), which prove that Brazil pioneers in the support and participation of females in science [45 46].

Using the WoS to conduct this study is associated with an important strength but also with one weakness of the study: The WoS enabled us to assess not only quantitative but also semi-qualitative aspects of the scientific output related to RSV research. This is a unique feature allowing a multifaceted evaluation of the research productivity. On the other hand, the WoS displays a strong preference for English journals. Therefore, not all articles ever published on RSV could be analyzed here. However, we regard this bias as limited as the majority of high quality data is commonly published in international journals indexed by the WoS and therefore definitely included in our search.

Timing, intensity and clinical impact of RSV infections vary worldwide [3]. Hence, research is still needed to alleviate the burden related to RSV in high-risk

populations. Interventions should focus on data collection via established surveillance systems aiming to define local morbidity and mortality, assist disease modeling, and guide prophylactic measures and vaccine development [47]. In this context, our study revealed a striking discrepancy in scientific productivity and collaborative involvement between high- and low-income countries. Also, attention should be drawn to a further problem concerning low-income nations or countries whose researchers have a limited financial budget to pay for publication in renowned open access journals. This issue increases the apparent discrepancies regarding publication activities even further. To minimize this problem, a number of waiver programs already exists, i.e. for journals like PLOS, Biomed Central or BMJ OPEN [48-50], but these should be expanded more broadly. However, we can deduce from our findings, that developing nations - although experiencing the most significant consequences of RSV epidemics - cannot compete equally in the field of RSV research due to the lack of funding and infrastructure. Therefore, we want to underline the need – and almost ethical responsibility - to involve these nations in funding programs and successful international collaborations as seen for Guinea-Bissau, Kenya and The Gambia. We acknowledge that the establishment of these collaboration is challenging due to the lack of resources, manpower and funding opportunities, the political climate, cultural differences between the potential partners and a unrealistic assessment of the local research capacity and resources [51]. Nevertheless, tight-knit networks would be the key for developing countries to participate in the international exchange of data, resources and knowledge, and to facilitate their involvement in high quality research efforts despite an unequal starting point.

Conclusion

We evaluated the worldwide RSV-related research output and demonstrated large differences between industrialized and developing nations regarding most scientometric variables. These discrepancies partly diminished when country-specific scientific activities were related to economic key measures; here, the leading position of the USA in science was challenged by other nations. Hence, calculating these quotients is beneficial for the comparison of countries with unequal conditions and different scientific infrastructures. However, we can deduce from our study that research efforts of middle-income or low-income nations have to be strengthened, e.g. by the reduction of journal fees and inclusion in international collaborations, so apparent disparities can be minimized and higher mortality rates related to RSV in developing nations can be tackled successfully.

Acknowledgements:

We thank Cristian Scutaru for the development and provision of the NewQIS analyzing tools. We also thank Mario Schwarzer, MD for supporting the study and helpful discussions.

Source of Funding:

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors

Conflicts of Interest:

All authors state that they have no conflicts of interest to declare.

Data Sharing Statement:

Datasets of this study are available from the corresponding author upon request.

Authors' contributions:

DB, CK, DK, DAG, DO, JB and MB have made substantial contributions to the conception and design of the study, acquisition of the study data and have been involved in drafting and revising the manuscript. All authors have read and approved the final manuscript.

Figure Legends

Figure 1: Chronological development of the number of articles.

Figure 2: Density equalizing mapping projections (DEMP).

A) Number of publications B) Modified h-Index

Figure 3: Chronological development of annual citation numbers.

Figure 4: Density equalizing mapping projections (DEMP).

A) Articles/population-index (Q1)

B) Articles/GDP-index (Q2)

(Threshold ≥ 15 articles)

Figure 5: Country specific gender analysis of the authors publishing articles referring to RSV of countries.

(Threshold: > 50% definable genders, > 60 authors per country)

Figure 6: International cooperation (threshold ≥ 2 cooperations).

Numbers in brackets (number of publications/number of publications in cooperation

Figure 7: Most prolific journals in the field of RSV research in regards to overall publication numbers and the average citation rate.

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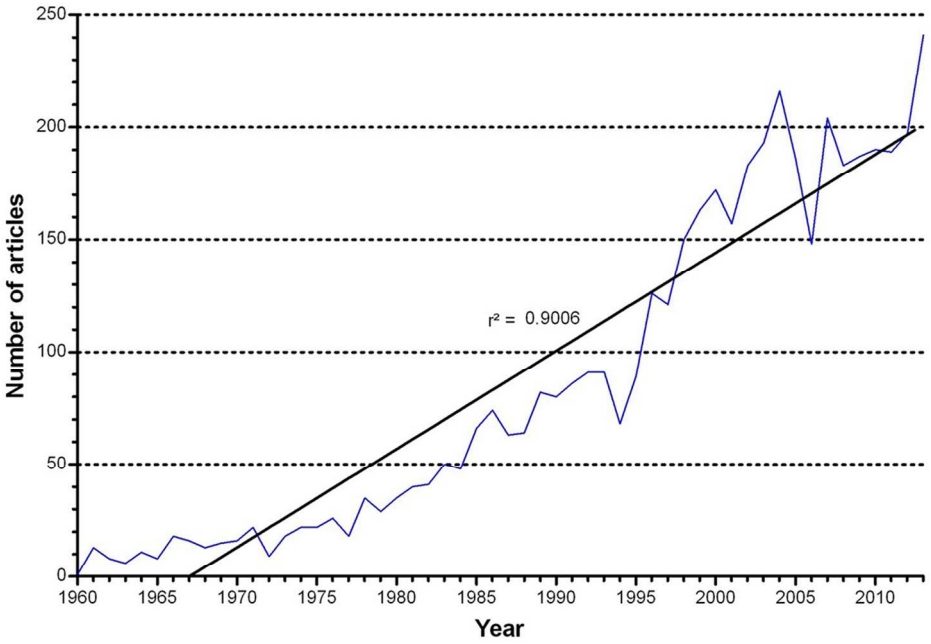

Figure 1: Chronological development of the number of articles.

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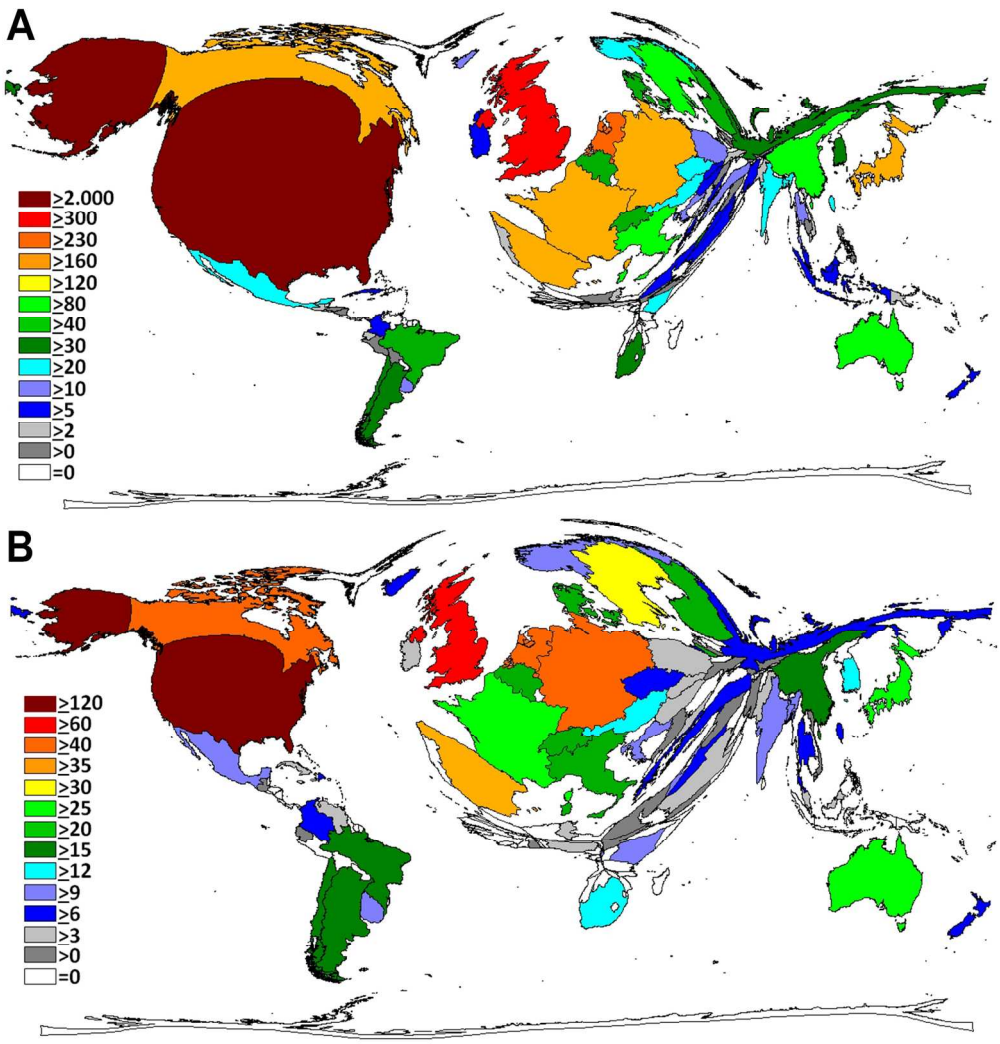

Figure 2: Density equalizing mapping projections (DEMP).
A) Number of publications
B) Modified h-Index

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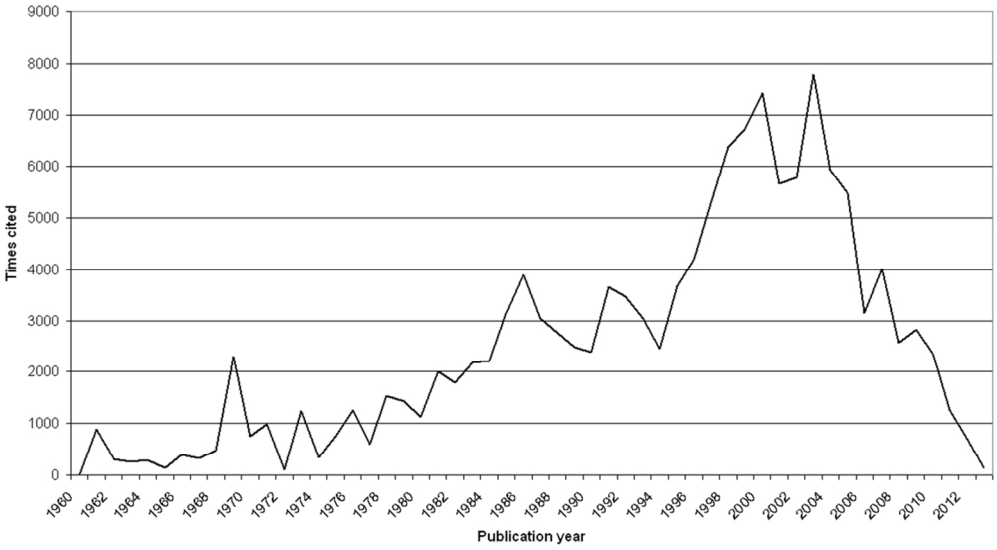

Figure 3: Chronological development of annual citation numbers.

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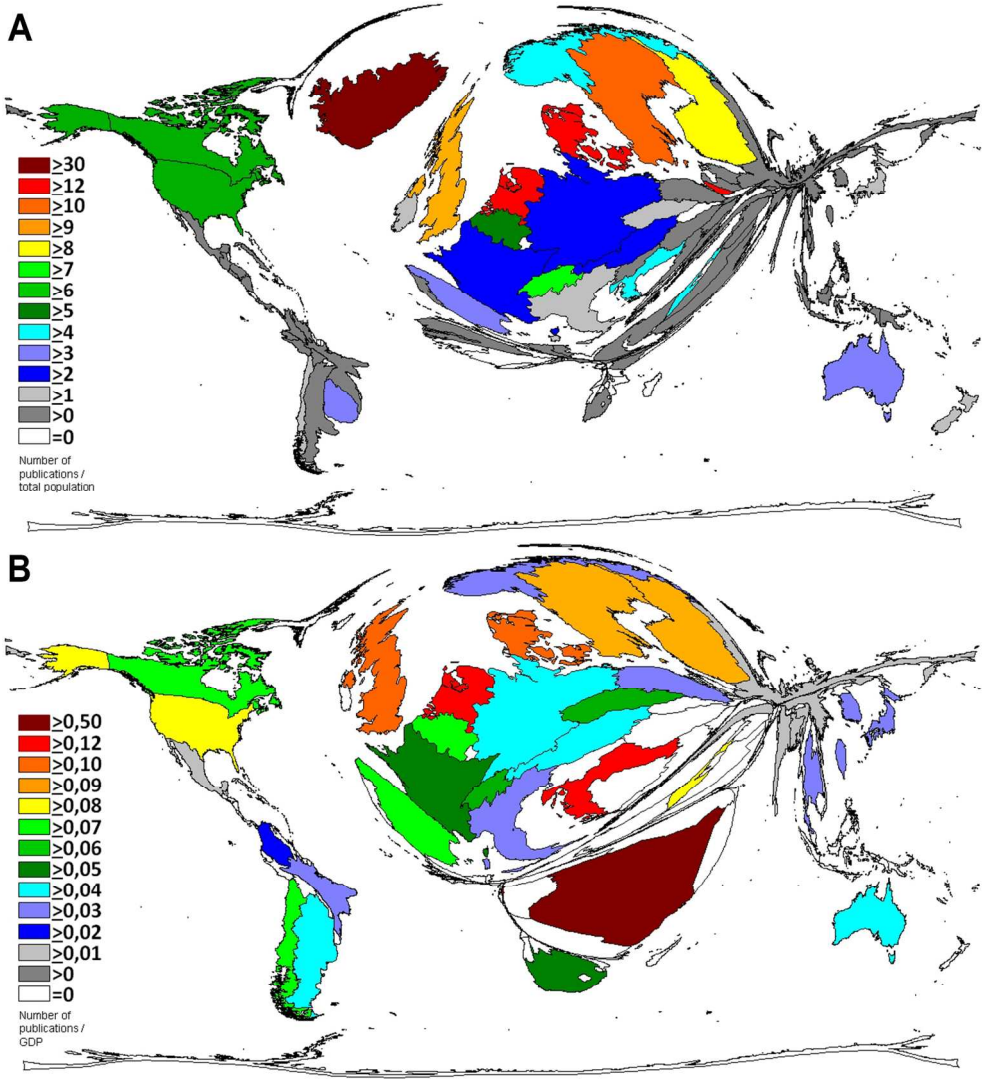

Figure 4: Density equalizing mapping projections (DEMP).
A) Articles/population-index (Q1)
B) Articles/GDP-index (Q2)
(Threshold > 15 articles)

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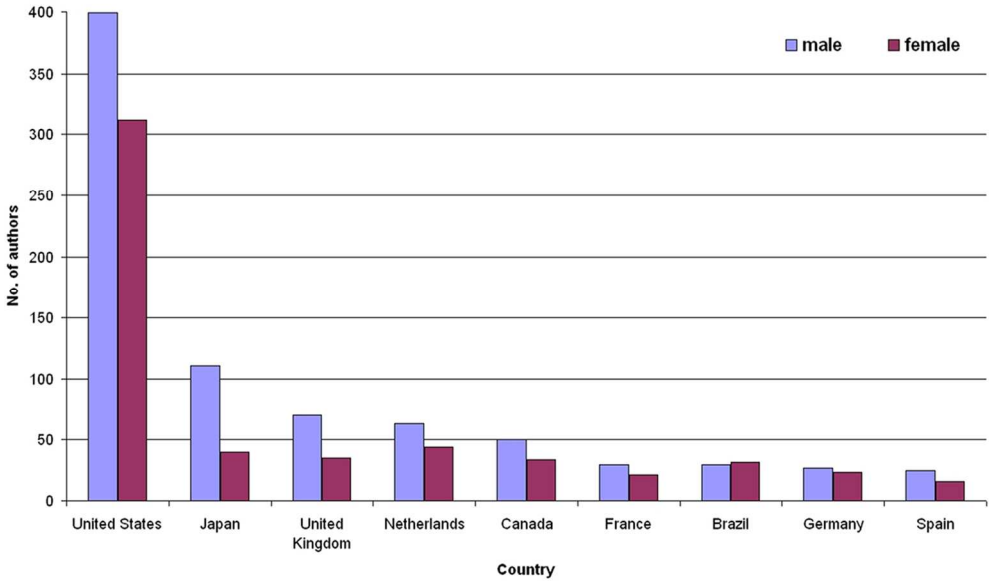

Figure 6: Country specific gender analysis of the authors publishing articles referring to RSV of countries. ‼ ┼ (Threshold: > 50% definable genders, > 60 authors per country)‼ ┼

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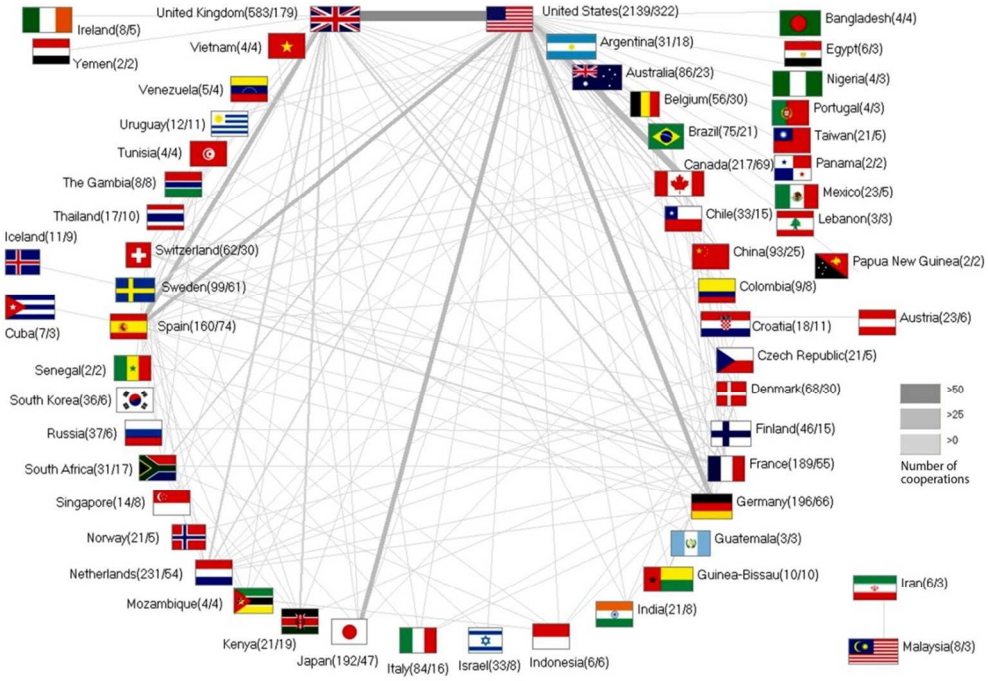

Figure 7: International cooperation (threshold > 2 cooperations). ‼ ┼ Numbers in brackets (number of publications/number of publications in cooperation)‼ ┼

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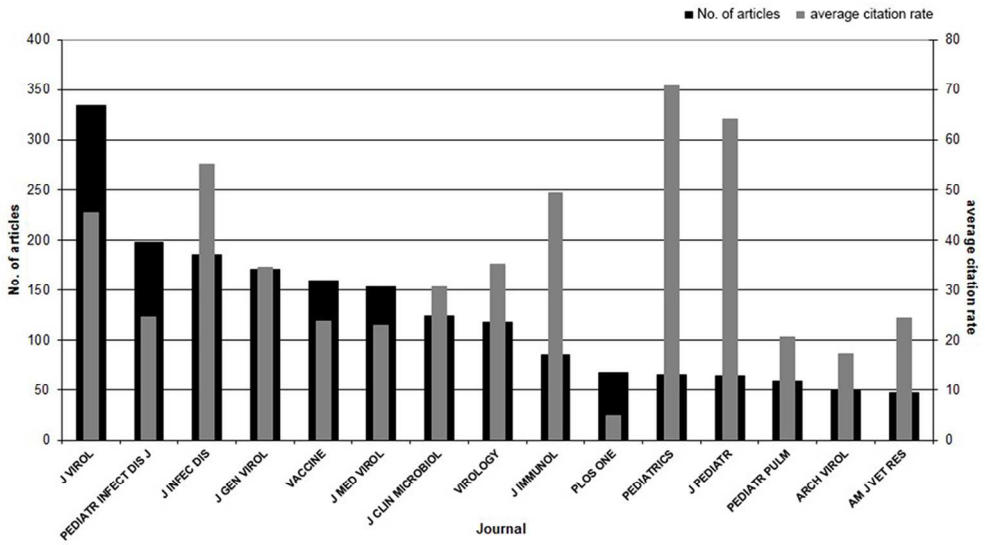

Figure 8: Most prolific journals in the field of RSV research in regards to overall publication numbers and the average citation rate.

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BMJ Open

Respiratory Syncytial Virus: A systematic scientometric analysis of the global publication output and the gender distribution of publishing authors

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2016-013615.R1
Article Type:	Research
Date Submitted by the Author:	18-Nov-2016
Complete List of Authors:	Brueggmann, Doerthe; Keck School of Medicine of the University of Southern California, Ob/Gyn; Goethe-Universitat Frankfurt am Main, Institute of Occupational Medicine, Social Medicine and Environmental Medicine Köster , Corinna ; Goethe-Universitat Frankfurt am Main, Institute of Occupational Medicine, Social Medicine and Environmental Medicine Klingelhoefer, Doris; Goethe University, Institute of Occupational Medicine Bauer, Jan; Goethe-Universitat Frankfurt am Main, Institute of Occupational Medicine, Social Medicine and Environmental Medicine Ohlendorf, Daniela; Institute of Occupational Medicine, Social Medicine and Environmental Medicine, Goethe-University Frankfurt/Main, ; Bundschuh, Matthias; Goethe-Universitat Frankfurt am Main, Institute of Occupational Medicine, Social Medicine and Environmental Medicine Groneberg, David; Occupational, Social and Environmental Medicine, Medical Department of the Goethe-University Frankfurt am Main
Primary Subject Heading:	Infectious diseases
Secondary Subject Heading:	Global health, Paediatrics, Public health, Respiratory medicine
Keywords:	Respiratory Syncytial Virus, Scientometry, Publication, Gender, Economic benchmarks

Respiratory Syncytial Virus: A systematic scientometric analysis of the global publication output and the gender distribution of publishing authors

Corresponding author: Dörthe Brüggmann – occup-med@uni-frankfurt.de, Institute of Occupational Medicine, Social Medicine and Environmental Medicine, Goethe-University, Theodor-Stern Kai 7, 60590 Frankfurt, Germany

Telephone: +49 (0) 69 6301 6650, Fax +49 (0) 69 6301 7053

Dörthe Brüggmann[1,2,*], Corinna Köster[2,*], Doris Klingelhöfer[2], Jan Bauer[2], Daniela Ohlendorf[2], Matthias Bundschuh[2], David A Groneberg[2]

[1] Department of Obstetrics and Gynecology, Keck School of Medicine of USC, Los Angeles, California, United States

[2] Institute for Occupational Medicine, Social Medicine and Environmental Medicine, Goethe University Frankfurt, Germany

* equal contribution

Word Count: 6,212

Abstract

Objective: Worldwide, the respiratory syncytial virus (RSV) represents the predominant viral agent causing bronchiolitis and pneumonia in children. To conduct research and tackle existing healthcare disparities, RSV-related research activities around the globe need to be described. Hence, we assessed the associated scientific output (represented by research articles) by geographical, chronological and socio-economic criteria and analyzed the authors publishing in the field by gender. Also, the 15 most cited articles and the most prolific journals were identified for RSV research.

Design: retrospective, descriptive study

Setting: The NewQIS platform was employed to identify RSV-related articles published in the Web of Science until 2013. We performed a numerical analysis of all articles, and examined citation-based aspects (e.g. citation rates); results were visualized by density equalizing mapping tools.

Results: We identified 4600 RSV-related articles. The USA led the field; US-American authors published 2,139 articles (46.5% % of all identified articles), which have been cited 83,000 times. When output was related to socio-economic benchmarks such as GDP or R&D expenditures, Guinea-Bissau, The Gambia and Chile were ranked in leading positions. 614 articles on RSV (13.34% of all articles) were attributed to scientific collaborations. These were primarily established between high-income countries. The gender analysis indicated that male scientists dominated in all countries except Brazil.

Conclusions: The majority of RSV-related research articles originated from high-income countries whereas developing nations showed only minimal publication productivity and were barely part of any collaborative networks. Hence, research

capacity in these nations should be increased in order to assist in addressing inequities in resource allocation and the clinical burden of RSV in these countries.

Key words: Respiratory Syncytial Virus, Publication, Citation, Scientometry, Gender, Economic benchmarks

Strengths and Weaknesses

- This is the first concise depiction of the worldwide scientific productivity related to RSV, which was assessed by geographical, chronological and socio-economic criteria.
- The NewQIS platform combines scientometric methods and "density equalizing mapping projections" to evaluate the scientific output regarding quantitative and qualitative aspects, geographical and chronological developments, existing research networks and socio-economic benchmarks in a reliable and standardized way.
- Since the WoS has a preference for English journals, we have to acknowledge a language bias associated with our analysis.
- Citation based parameters were assessed, which have limitations since these rather reflect the recognition of the research in the scientific community than truly measure quality.

INTRODUCTION

The human respiratory syncytial virus (RSV) is the predominant viral agent affecting the respiratory tract worldwide [1, 2]. It is associated with 64 million infections that occur primarily in children under 5 years [3]. RSV belongs to the Paramyxoviridae family and is a negative-sense, non-segmented, single-stranded RNA virus, which is mostly transmitted by droplets [4]. RSV causes bronchiolitis, pneumonia, bronchitis and croup. It is linked to recurrent wheezing and pediatric asthma [5, 6]. There is no definitive treatment for RSV-related conditions. Although the development of effective and safe vaccines has remained unsuccessful to date, the variety of candidate vaccines is constantly growing in the last years [7]. One prophylactic agent is commercially available, the neutralizing anti-RSV antibody Palivizumab. Its use is limited to preterm babies, chronic lung disease of prematurity and infants with congenital heart disease [8].

RSV-associated morbidity and mortality depends on many factors such as the geographic location, climate patterns, genetic susceptibility, socioeconomic factors and local virus strains [3]. The percentage of children having contracted RSV by their second year of life approaches 100% [9, 10]. In the United States of America (USA), over 2 million children aged 5 years and under need medical attention to treat their RSV infection every year [11]. On average, 0.3% of these children and 0.7% of infants younger than six months require hospitalization [11]. The general RSV mortality rate in this demographic varies between 0-33% [10]. Worldwide, up to 199 000 children die due to RSV infections. 99% of these deaths occur in in developing countries [3] hence, RSV represents a substantial burden for community health in these nations. According to WHO field studies in ten developing countries, RSV causes 70% of all

acute respiratory-tract infections in children under 5 years of age [12]. Here, the virus is identified in about 15-40% of the hospitalized children with pneumonia or bronchiolitis [13]. RSV epidemics occur during rainy seasons in tropical climates and during the winter months in temperate zones [4]. Both virus strains, RSV-A and -B, co-circulate during outbreaks in any given year. The A subtype is typically associated with more severe disease [14]. Distinct genotypes of both strains (identified by the genetic classification of their G protein) are predominant in any given year. This pattern is highly flexible, varies by region and may shift to other prominent genotypes the following year [15]. Epidemiological studies are dedicated to characterize the distribution of RSV strains and genotypes worldwide, often leading to the identification of new variants such as the RSV B genotype THB in Thailand [16].

Although care of RSV patients has been improved considerably and extensive studies have been launched to estimate viral spread and disease burden in developing countries, tremendous challenges still remain. In regards to the high prevalence, morbidity and mortality of RSV worldwide, we consider that further research and the implementation of related public health measures are crucial for future successes. However, global research funds are limited and their allocation becomes challenging. In this context, the assessment of the scientific performance is a prerequisite for the reasonable distribution of monetary support and the planning of future research endeavors by scientists interested in the field. Hence, we employed scientometric tools with the goals (1) to determine the RSV-related publication output among the extensive amount of biomedical publications and (2) to evaluate the scientific productivity of single countries in the framework of the global research landscape and in relation to socioeconomic and gender aspects. We also identified the 15 most cited landmark articles and the most prolific journals in the field of RSV

research.

METHODS

Methodical Platform

We used the New Quality and Quantity Indices in Science (NewQIS) platform to assess the worldwide RSV publication activity in a reliable and standardized way. This tool combines scientometric methods and "density equalizing mapping projections" (DEMP) [17-19] to evaluate the publication output regarding quantitative and qualitative aspects, geographical and chronological developments, existing research networks and socio-economic benchmarks.

Density-equalizing mapping

DEMP is a state-of-the-art technique to visualize benchmarking processes by anamorphic maps [17, 20]. Based on the algorithm of Gastner and Newman, the size of each country was modified analogously to country-specific data on RSV research leading to a new geographic distribution of the global landscape [17].

Data collection

For data collection, the Web of Science (WoS) Core Collection database (Thomson Reuters) was employed. The following search term was created: Title=("RSV" OR "Respiratory Syncytial Virus" OR "RS Virus*") NOT Topic=(Rous Sarcoma). The Boolean operator NOT was used to exclude all publications concerning the Rous Sarcoma (Virus). We limited our search to original research articles. Following our protocol, the time frame was restricted from 1900 to 2013; publications in 2014 were not regarded due to incomplete data acquisition at the time the study was performed.

Data analysis

RSV-related articles were analyzed regarding quantitative aspects such as the total number of publications, citation numbers, countries of article origin (defined as the 'country where the institution is located each author, who worked on publishing the article, is affiliated'), institutions, languages, cited reference numbers, and publication date. The number of authors publishing on RSV was only quantified for the years with 30 or more annual publications. Also, h-Indices, and the average citation number per item (citation rate, CR) were investigated. Regression analysis was used to investigate the chronological evolution of RSV research. We calculated the coefficient of determination (r^2) representing the slope of the growth in scientific output and citations.

Modified h-Index

The Hirsch-Index (h-Index) is a recognized semi-qualitative proxy measure to assess the impact of one author's research output on the scientific community [21, 22]. An h-index of 12 indicates that out of 12 published papers each has been cited at least 12 times. In this study, we applied this concept to the RSV-specific research productivity of single countries and calculated a "modified country-specific" h-Index.

Country-specific gender analysis

The proportionality of male and female researchers among authors publishing on RSV was analyzed. Online name databases were utilized to identify the authors' genders [23]. If first names were not gender-specific or quoted as initials, a manual search (utilizing websites, corresponding addresses and social networks) was launched. We only evaluated countries where a minimum of 60 authors were

affiliated and a minimum of 50% of authors were identified by gender to ensure a valid analysis. These thresholds were chosen arbitrarily based on previous studies.

Cooperation analysis

We identified all RSV-associated publications that were issued due to international collaborative efforts. The total count of collaborative items was related to the overall number of publications for each investigated country. In brief, if at least two authors originating from different institutions or countries (as identified by the affiliations in the article) contributed to one article, this publication was defined as a collaborative item. Publications with two or more authors affiliated to the same country were counted one time only towards the complete count of joint publications of this particular country. If an author had two affiliations, these were counted for every country mentioned in the affiliations. Connecting vectors visualized these co-operations; their width and shade of grey reflected the number of joint publications.

Journal analysis

The journals publishing on RSV were analyzed regarding quantitative and qualitative aspects, e.g. number of published RSV articles as well as citations these items received (CR).

Analysis of economic key figures

Two quotients were calculated to assess the scientific output of a specific country, (1) in relation to the number of inhabitants (Q1), and (2) in relation to its economic power (as measured by the gross domestic product, GDP, Q2). Data regarding the

population and GDP of investigated countries were obtained from 2012 from the CIA *World Factbook* [24]. We computed the quotients in the following way:

1. Articles/population-index (Q1) = number of articles/population in millions
2. Articles/GDP-index (Q2) = number of articles/GDP in billions

All countries were classified into high-, upper-middle-, lower-middle- and low-income groups according to World Bank definitions [25].

We compared the total number of RSV articles to the gross domestic expenditure on Research and Development (in % of GDP) as well as to the number of researchers (per billion inhabitants) affiliated to the investigated countries [26]. The analysis was limited to countries that published a minimum of 30 articles in the field of RSV.

RESULTS

Number of published items

We identified 4,600 articles on RSV published between 1900 and 2013; 2,645 (57.5%) of these were issued after 2000. 1960 and onwards, the number of articles increased significantly over time as indicated by r^2=0.9 (Fig. 1). 10,791 authors published in the field of RSV. The number of authors per article increased by 100% in the investigated timeframe. We identified a mean of 3.8 and a median of 3 authors in 1978, which was the first year with more than 30 annual publications. 10 years later, a mean of 4.59 and a median of 4 authors were found, followed by a mean of 5.05 and a median of 5 authors in 2000, a mean of 5.95 and a median of 5 authors in 2006 and a mean of 7.6 and a median of 6 authors in 2013

Analysis of research origin and citations

Although the publications originated from 92 of the 251 investigated countries and autonomous regions the majority of the articles were written in English (4444 articles, 96.6 % of all published RSV articles) followed by French (64 articles, 1.4 % of all articles) and German (32 articles, 0.7% of all articles). More than 85% of the global publication output was issued by authors from high-income economies. The USA was the most productive nation (2,139 articles, 46.5% of all published RSV articles) followed by the United Kingdom (UK, 583 articles, 12.7%), the Netherlands (231 articles, 5.0%), Canada (217 articles, 4.7%) and Germany (196 articles, 4.3%). Hence, the USA and UK dominated the cartogram, while major parts of Africa (with the exception of South Africa), Asia (with the exception of Japan, China, South Korea, and India) and Central America occupied only minor areas (Fig. 2A).

The country-specific citation numbers and modified h-Indices showed a global distribution similar to the number of publications. Articles with US-American affiliation of the authors were cited most (83,000 citations, c), followed by articles from the UK (c = 19,240), the Netherlands (c = 5587), Canada (c = 5549) and Germany (c = 5319). Articles published by African, Asian and Middle American authors received hardly any citations.

The USA and the UK were the top ranked countries with a modified h-Index of 121 (USA) and 68 (UK), followed by the Netherlands (h-Index = 44), Germany (h-Index = 43) and Canada (h-Index = 40) (Fig. 2B).

Regarding the country-specific citation rate (average number of citations per total number of publications for each country with more than 30 articles, CR), Sweden (CR = 40) dominated and was followed by the USA (CR = 38.8), Finland (CR = 34.9), the UK and Germany (CR = 27.13).

Analysis of citation performance

The absolute citation count of all identified RSV-related articles resembled the growing volume of published papers in the investigated timeframe. We documented a significant positive correlation between citation numbers and the time of publication (with r^2=0.72 for the timeframe from 1960 to 2008). The annual citation counts grew from 1960 to 1994 (e.g. from 19 annual citations in 1960 to 2448 annual citations in 1994); after 1995, a rapid increase followed until 2003 (e.g. 5274 annual citations in 1997 and 7790 annual citations in 2003) whereas a steep decline was noticed after 2006 (e.g. 3147 annual citations in 2006). We identified visible peaks in citation activity for 1969 (2294 annual citations), 1986 (3898 annual citations), 2000 (7411 annual citations), and 2003 (7790 annual citations) (Fig. 3). Additionally, we compiled the 15 most cited RSV articles, which constitute the publications that have sparked the most documented interest in the field to date (Table 1).

Table 1. The 15 most cited articles in the area of RSV-related research are displayed including their title, publication year, countries of article origin (defined as the countries where first, senior- and co-authors are affiliated), citation count and journal.

Title	Publication Year	Country of Article Origin	Citations	Journal
Mortality associated with influenza and respiratory syncytial virus in the United States **Thompson WW et al.**	2003	United States	1520	JAMA

Pattern recognition receptors TLR4 and CD14 mediate response to respiratory syncytial virus **Kurt-Jones EA et al.**	2000	United States	856	Nat Immunol
Respiratory Syncytial Virus Disease In Infants Despite Prior Administration Of Antigenic Inactivated Vaccine **Kim HW et al.**	1969	United States	848	Am J Epidemiol
Respiratory syncytial virus in early life and risk of wheeze and allergy by age 13 years **Stein RT et al.**	1999	Brazil, United States	719	Lancet
Palivizumab, a humanized respiratory syncytial virus monoclonal antibody, reduces hospitalization from respiratory syncytial virus infection in high-risk infants **The Impact-RSV Study Group.**	1998	United States, Canada, UK	652	Pediatrics
An Epidemiologic Study Of Altered Clinical Reactivity To Respiratory Syncytial (Rs) Virus Infection In Children Previously Vaccinated With An Inactivated RS Virus Vaccine **Kapikian et al.**	1969	United States	552	Am J Epidemiol
Risk Of Primary Infection And Reinfection With Respiratory Syncytial Virus **Glezen et al.**	1986	United States	548	Am J Dis Child
Respiratory syncytial virus bronchiolitis in infancy is an important risk factor for asthma and allergy at age 7 **Sigurs N et al.**	2000	Sweden, Iceland	488	Am J Respir Crit Care Med
Wheezing, Asthma, And Pulmonary Dysfunction 10 Years After Infection With Respiratory Syncytial Virus In Infancy **Pullan CR and Hey EN**	1982	UK	449	Br Med J
Respiratory syncytial virus infection in elderly and high-risk adults **Falsey AR et al.**	2005	United States	430	NEJM
Prophylactic Administration Of Respiratory Syncytial Virus Immune Globulin To High-Risk Infants And Young-Children **Groothuis JR et al.**	1993	United States	427	NEJM
The Development Of Respiratory Syncytial Virus-Specific IgE And The Release Of Histamine In Nasopharyngeal Secretions After Infection **Welliver RC et al.**	1981	United States	425	NEJM
Respiratory-Syncytial-Virus Infections, Re-Infections And Immunity - Prospective, Longitudinal-Study In Young-Children **Henderson FW et al.**	1979	United States	418	NEJM
Generation of bovine respiratory syncytial virus (BRSV) from cDNA: BRSV NS2 is not essential for virus replication in tissue culture, and the human RSV leader region acts as a functional BRSV genome promoter	1999	Germany	417	J Virol

Buchholz UJ et al.				
Asthma and immunoglobulin-e antibodies after respiratory syncytial virus bronchiolitis - a prospective cohort study with matched controls **Sigurs N et al.**	1995	Sweden	416	Pediatrics

264

265 **Relation to economic parameters**

266 Relating the number of publications to the population of a country, high-income
267 countries like Iceland (Q1 = 34.59), the Netherlands (Q1 = 13.90) and Denmark (Q1
268 = 12.25), issued a higher number of publications per million inhabitants compared to
269 low-or lower-middle-income countries, e.g. Nigeria (Q1 = 0.03) and Indonesia (Q1 =
270 0.02) (Fig. 4A). We identified two exceptions, which included the low-income
271 countries Guinea Bissau (Q1 = 6.30) and The Gambia (Q1 = 4.76). Both were
272 represented among the 15 top ranked countries in this analysis.

273

274 When looking at the publication activity in relation to GDP, two low-income countries
275 outperformed high-income nations (Fig. 4B). Guinea Bissau (Q2 = 11.776) and The
276 Gambia (Q2 = 8.721) again held leading positions, followed by Iceland (Q2 = 0.810),
277 Kenya (Q2 = 0.516), and Croatia (Q2 = 0.319). Besides these two exceptions, other
278 low- or lower-middle-income countries showed a weak performance (e.g. Philippines
279 with Q2 = 0.004 or Indonesia with Q2 = 0.007). Also, the USA did not remain under
280 the top 10 nations and was found at position 18 (Q2 = 0.132).

281

282 Chile, the Netherlands, South Africa, UK and Argentina were leading the analysis
283 when the total article count was related to the country-specific Research and
284 Development (R&D) expenditures (33.72, 13.32, 12.14, 11.46 and 9.56 articles per
285 billion GDP spent on R&D, respectively). The USA dropped to position 11 with 4.52
286 articles per billion GDP spent on R&D (Fig. 5A, Table 2A).

When we related the article count to the number of researchers (per billion inhabitants) as a proxy measure for the active research community working on RSV and the productivity of these researchers, the USA was leading the field (532.27 articles per researcher per billion inhabitants), followed by the UK, China, Chile and South Africa (137.10, 83.55, 77.10, and 76.60 articles per number of researchers per billion inhabitants) (Fig. 5B, Table 2B).

Table 2A. Total number of publications related to gross domestic expenditures on Research and Development in Billion USD of countries that have published more than 30 items on RSV.

Rank	Country	No. of articles	R&D expenditure in % GDP	GDP in billion USD	R&D Expenditure in billon USD	Articles/ billion USD of R&D Expenditure
1	Chile	33	0.38	258	0.98	33.72
2	Netherlands	231	1.97	879	17.34	13.32
3	South Africa	31	0.73	349	2.55	12.14
4	UK	583	1.70	2990	50.85	11.46
5	Argentina	31	0.61	529	3.24	9.56
6	Spain	160	1.23	1381	17.01	9.41
7	Canada	217	1.61	1783	28.73	7.55
8	Denmark	68	3.08	346	10.67	6.37
9	Sweden	99	3.16	571	18.05	5.49
10	Finland	46	3,17	272	8.63	5.33
11	USA	2139	2.73	17348	472.78	4.52

12	Belgium	56	2.46	531	13.09	4.28
13	Italy	84	1.29	2138	27.52	3.05
14	Switzerland	62	2.97	701	20.80	2.98
15	France	189	2.26	2829	63.82	2.96
16	Australia	86	2.20	1454	31.93	2.69
17	Israel	33	4.11	305	12.53	2.63
18	Brazil	75	1.24	2417	29.87	2.51
19	Germany	196	2.87	3868	110.96	1.77
20	Russia	37	1.19	2030	24.09	1.54
21	Japan	192	3.58	4596	164.73	1.17
22	South Korea	36	4.29	1411	60.55	0.59
23	China*	93	2.05	10351	211.79	0.44

Table 2B. Total number of publications related to articles per researcher (per billion inhabitants) of countries that have published more than 30 items on RSV.

Rank	**Country**	**Number of RSV articles**	**Number of researchers per billion inhabitants**	**Articles/researcher (per billion inhabitants)**
1	USA	2139	4.02	532.27
2	UK	583	4.25	137.10
3	China*	93	1.11	83.55
4	Chile	33	0.42	77.11
5	South Africa	31	0.40	76.60
6	Spain	160	2.64	60.55
7	Netherlands	231	4.48	51.58

8	Canada	217	4.52	48.02
9	France	189	4.20	44.99
10	Germany	196	4.38	44.74
11	Italy	84	2.01	41.86
12	Japan	192	5.39	35.65
13	Argentina	31	1.20	25.79
14	Sweden	99	6.87	14.41
15	Switzerland	62	4.48	13.83
16	Belgium	56	4.18	13.41
17	Russia	37	3.10	11.93
18	Denmark	68	7.20	9.45
19	Finland	46	7.00	6.58
20	South Korea	36	6.90	5.22
21	Israel	33	8.26	4.00

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305 **Country-specific gender analysis**

306 We identified the gender distribution among authors working on RSV in institutions
307 affiliated to 92 countries. Our analysis indicated a larger proportion of male scientists
308 in almost all evaluated countries (Fig. 6). Brazil was an exception. 95 authors with
309 affiliation to Brazilian institutions were identified as working on RSV. 62 of those were
310 identifiable by name and gender. Here, males and females were almost equally
311 represented (32 female authors, 51.6% of identifiable authors, 30 male authors,
312 48.4% of identifiable authors). By calculating the proportion of male to female

scientists, we documented the lowest ratio (0.94) for Brazil, followed by Germany (1.1). Japan had the highest score with 2.8.

International cooperation analysis

The first collaborative article on RSV was identified in 1973. It was published by researchers working in institutions located in Switzerland and the USA [27]. Since 1973, 614 joint articles were published on RSV accounting for 13.34% of all articles. The USA was the preferred partner for international collaborations on RSV. The most productive cooperation was established between the USA and the UK (67 joint works, 10.9% of collaborative articles), followed by the USA and Canada (45 joint articles, 7.3% of collaborative articles), and the USA and Germany (34 joint articles, 5.5% of collaborative articles).

The most fruitful cooperation not involving the USA existed between the UK and Spain (33 joint articles, 5.4% of collaborative articles). The most productive cooperation between high- and lower-middle- or low-income economies was set up between Kenya and the UK (18 joint articles, 2.9% of collaborative articles) followed by Guinea Bissau and Denmark (10 joint articles, 1.6% of collaborative articles). Overall, co-operations with low-income or lower-middle-income countries were less popular (Fig. 7).

Journal analysis

When we identified the most prolific journals in RSV research, the "Journal of Virology" led the field (334 articles, CR of 45.49), followed by “The Pediatric Infectious Disease Journal" (198 articles, CR = 24.66) and the "Journal of Infectious

Diseases" (186 articles, CR 55.18) (Fig. 8). The highest citation rate was achieved by the "Proceedings of the National Academy of Sciences of the United States of America" (42 articles, CR = 81.43), followed by "Pediatrics" (66 articles, CR = 70.80), “Journal of Pediatrics” (65 articles, CR = 64.03), “American Journal of Respiratory Critical Care“ (47 articles, CR = 62.55), and „Journal of Infectious Diseases“ (186 articles, CR = 55.18).

DISCUSSION

In the WoS, we documented only 4,600 RSV-related articles since 1900. The first item on the disease in humans was published in 1957 [28]. This emphasizes that research on RSV is a relatively new field considering the virus was initially isolated in 1956 from laboratory primates [29]. The predominance of English in the majority of identified articles aligns not only with the fact that this language is the recognized “scientific lingua franca” but also reflects the abundant research output of English speaking countries such as USA, Canada and the UK found in our study.

The increasing number of RSV publications over time is typical for most biomedical research, e.g. on the John Cunningham Virus, influenza or breast cancer [30, 31]. Overall, the steady growth of article numbers can be explained by the rising interest in the field due to the increasing relevance of RSV in pneumonia and child mortality [9]. In the first few years after the detection of the virus, basic research was conducted. These endeavors, which aimed to characterize the virus, identify immunologic responses and develop vaccines, translated into a growing volume of articles on RSV [32-35]. The continuous increase since the beginning of the 1990s may be attributed to the launch of a growing number of scientific journals providing a platform for

publishing. The development of modern communication systems based on new computer technologies like the World Wide Web made it easier to communicate, exchange ideas, and publicize articles in central databases. Also, it is noticeable that the increasing publication output since the 1960s was paralleled by a globally growing funding volume allocated to the R&D sector. In the USA alone, a total of 13,711 million US-Dollars (UDS) was allocated to R&D in 1960 as documented by the National Science Foundation. This amount increased to 26,271 million UDS in 1970 and 452,556 million USD in 2012 (https://www.nsf.gov/statistics/2015/nsf15315/).

The chronological development in publication quantity (Fig. 1) was resembled by the steady increase of related citations (Fig.3). Four prominent citation peaks in 1969, 1986, 2000 and 2003 coincided with milestone papers the field. In 1969, adverse effects of the formalin-inactivated RSV vaccine in children were reported [36]. Large epidemiologic studies investigated the risks of reinfection and the mortality associated with RSV in 1986 and 2003 [37, 38]. The research on a prophylactic antibody licensed in 1999 and novel insights into immunologic responses involving pattern recognition receptors TLR4 and CD14 may be responsible for the peaking number of publications and citations in 2000 [39]. The citation decline after 2006 can be attributed to the short timespan articles had allotted to receive recognition within the scientific community and obtain the appropriate citation number reflecting their true impact [40]. Hence, we expect this trend to be reversed in the future.

The USA dominated RSV research with regards to overall publication quantity, citation numbers and h-index. This corresponds with a previous biomedical benchmarking study. Here, the USA was the most productive nation and authored

1,893,800 of 5,527,558 publications related to 22 organ systems from 1961 to 2007 [41]. The leading role of the USA might be linked to major financial resources this nation dedicates to research. The US-American National Institutes of Health (NIH) are by far the biggest biomedical funder in the world (e.g. with a funding volume of 26.08 billion USD in 2013 compared to the biggest funding source in the EU, the European Commission, with a funding volume of 3.71 billion USD in 2013). Also, the Department of Defense constitutes another large US-American funding organization with a volume of 1.017 billion USD (2013), followed by private philanthropic institutions such as the Howard Hughes Medical Institute or the Bill & Melinda Gates Foundation with impressive funding volumes of 752.0 (2013) and 462.6 million USD (2011), respectively [42]. These funds can support manpower and an outstanding scientific infrastructure illustrated by the fact, that the majority of institutions working on RSV were identified in the USA, and that this nation is a preferred partner for national and international co-operations.

The cluster of the USA, Western-European countries (e.g. UK or Germany) and Japan dominated the overall publication output and analyses of citation-based benchmarks. This finding corresponds with other scientometric studies (e.g. on Influenza, Ebola, or Hepatitis B [30, 43]. Although Sweden and Finland published relatively low numbers of articles, they are characterized by the highest citation rates in our analysis indicating the outstanding quality and high recognition their articles received in the scientific community. Furthermore, it was striking that most African, Asian and Central American countries afflicted with a considerable RSV-related burden did not play a visible role in the field. Methodologically, we included only countries in the citation rate analysis that published more than 30 RSV articles aiming to generate a better the validity of the investigation by avoiding overestimation

of few but frequently cited articles. Nevertheless, we want to stress that the absolute number of citations as well as the citation rate should be viewed critically. These parameters can be affected by self-citation and inaccurate citations. Also, the Matthew effect might influence citation-based variables. Here, scientists prefer to cite articles issued by well-known researchers to papers by junior scientists leading to a disproportional increase of the related citation counts [44, 45]. Hence, we also evaluated the modified h-index since it is less influenced by outstanding, frequently or rarely cited articles skewing the citation rate value [21, 22]. Furthermore, all citation-based variables have limitations in assessing the quality of the identified articles because they rather reflect the recognition of the research in the scientific community than measure quality.

We identified an overrepresentation of male authors in the majority of evaluated nations. This corresponds to the study of Head et al. who documented the preferential funding of male researchers by UK institutions in the area of global infectious disease research. Between 1997-2010, funding agencies supported fewer studies of female PIs and awarded less monetary support to research supervised by women. Particularly for RSV, male researchers received 5-times more funding than female scientists, who spearheaded only half the funded studies compared to their male counterparts in the field [46]. In our gender analysis, Brazil was an exception with a majority of women authoring RSV research (Fig. 6). This result correlates with previous investigations on Yellow fever and Rotavirus infections [47] as well as with gender benchmarking studies (e. g. conducted by the “Konrad-Adenauer Foundation” or the “Organization for Women in Science for the Developing World” (OWSD)), which suggests that Brazil pioneers in the support and participation of females in science [48, 49].

Our analysis of RSV publication outputs changed in relation to economic capabilities (Fig. 4). Two developing, low-income nations, The Gambia and Guinea-Bissau, occupied the leading positions. This finding points towards the fact that both prioritize RSV research and might be connected to existing co-operations with a long standing shared history between collaborating nations and their focused support of RSV scientific activities. For example, the United Kingdom's "Medical Research Council The Gambia Unit" and the Danish "Bandim Health Project" encourage medical research in Guinea-Bissau and The Gambia [50, 51]. Also, research in the field is promoted by single researchers with a strong dedication to conduct research in African sites. Here, Sir Brian Greenwood has spearheaded RSV-related research very successfully for decades while being faculty at the London School of Hygiene and Tropical Medicine as well as the Director of the Medical Research Council in The Gambia [52, 53541355, 565758].

If the RSV article counts were related to R&D expenditures and number of researchers in specific countries, a different, more refined picture emerged compared to the assessments based on absolute publications numbers or related to socio-economic variables. Here, two Latin American countries gained importance, Chile and Argentina. It appears that these nations invest funding very efficiently in RSV research, with Chile ranked first position with 33.72 RSV articles per billion USD in R&D expenditures followed by Argentina in fifth position (9.56 articles per billion USD in R&D). Both nations' interest to fund RSV research might be linked to the fact that respiratory infections and RSV in particular impose a heavy burden on the local pediatric population. Respiratory infections constitute the second leading cause of death in Latin American children aged 5 years or under with RSV as the causative

agent in 70.0% of these infections.[3,459, 60]. In the temperate climate of Chile and Argentina, RSV causes predictable outbreaks during the summer months. A particular high RSV burden of up to 70% was reported in Chilean children aged 0-11 months with lower respiratory tract infection. This was substantially higher than in other Latin American countries (e.g.18.2 % Argentina and 44% in Brazil) [61]. Hence, RSV is constantly in the focus of the local health authorities, which routinely monitor and report the trends in RSV infections to better allocate resources for pediatric patients and limit related morbidity and mortality [6162].

Collaborations are becoming increasingly important in the field of RSV research as indicated by existing tight-knit networks and the growing numbers of authors per article over time. We link this development to the globalization process, which connects scientists worldwide to exchange ideas, resources and knowledge facilitated by the growing availability of information technology. Further, it is noticeable that countries such as the USA or European nations play a more prominent role in international collaborations compared to low- and lower-middle-income countries. As exceptions, we could identify productive co-operations between the UK and Kenya as well as Denmark and Guinea-Bissau. The relation between Kenya and the UK might be based on their shared history and facilitated by implemented programs such as the *"KEMRI Welcome Trust Research Program"* between the Kenya Medical Research Institute and the University of Oxford [63]. As revealed by Fitchett et al. [64], a substantial funding volume goes to infectious disease research in countries with colonial ties to the UK such as Kenya and The Gambia. From 1997 – 2010, these countries received 13.13 million £ (The Gambia) and 12.92 million £ (Kenya) of biomedical funding by UK based institutions. Research activity on RSV in Guinea-Bissau is also supported by the aforementioned Danish "Bandim

Health Project", which was founded by the anthropologist Sir Peter Aaby in the 1970s. It gathers local epidemiological data on more than 200,000 individuals. Since its foundation, this group has published more than 600 items on vaccines, maternal mortality and childhood infections such as RSV [50].

Timing, intensity and clinical impact of RSV infections vary worldwide [3]. Hence, research is still needed to alleviate the burden related to RSV in high-risk populations. Interventions should focus on data collection via established surveillance systems (e.g. aiming to define local morbidity and mortality, assist disease modeling, and guide prophylactic measures and vaccine development) [65]. In this context, our study revealed a striking discrepancy in scientific productivity and collaborative involvement between high- and low-income countries. Also, attention should be drawn to a further problem concerning low-income nations or countries whose researchers have a limited financial budget to pay for publication in renowned open access journals. This issue increases the apparent discrepancies regarding publication activities even further. To minimize this problem, a number of waiver programs currently exist, i.e. for journals like PLOS, Biomed Central or BMJ OPEN [66-68], but these should be expanded more broadly. However, we can deduce from our findings, that developing nations - although experiencing the most significant consequences of RSV epidemics - cannot compete equally in the field of RSV research due to the lack of funding and infrastructure. Therefore, we want to emphasize the need – an almost ethical responsibility - to involve these nations in funding programs and successful international collaborations as seen for Guinea-Bissau, Kenya and The Gambia. We acknowledge that the establishment of collaborations between high- and low-income nations is challenging due to the lack of resources, manpower and funding opportunities, the political climate, cultural

differences between the potential partners and a unrealistic assessment of the local research capacity and resources [69]. Also, existing collaborations and funding streams need to be viewed critically since they should rather reflect local disease burden, apparent healthcare disparities and scientific capability than being allocated based on a shared language or history between countries (e.g. guided by former colonial ties). Therefore, funding institutions should revise their policies appropriately [64]. Also, global investment surveillance systems need to be established such as the "Research Fairness Initiative" led by Cohred to guide and monitor sustainable, transparent and effective partnerships in research (, http://rfi.cohred.org/origin-of-the-rfi/). Nevertheless, tight-knit networks would be key for developing countries to participate in the international exchange of data, resources and knowledge, and to facilitate their involvement in high quality research efforts despite an unequal starting point.

Study Limitations

Our study has several limitations. Using the WoS to conduct this analysis is associated with an important strength but also with a weakness of the study. The WoS enabled us to assess not only quantitative but also qualitative aspects of the publication output related to RSV research. This is a unique feature allowing a multifaceted evaluation of the publication productivity. On the other hand, the WoS displays a strong preference for English journals. Therefore, not all articles ever published on RSV could be analyzed here. However, we regard this bias as limited as the majority of high quality data is commonly published in international journals indexed by the WoS and therefore definitely included in our search. Also, we acknowledge that not all eligible RSV publications were detected by the conducted "TITLE"-search. This approach was preferred to a "TOPIC" search, which identifies

the search term in the abstract and the keywords leading to a significant amount of off-topic publications compromising the validity of our data collection. We concentrated our study on original articles to focus on published “cutting edge research” in the field of RSV. We acknowledge that this strategy narrowed down the focus on the topic since other publication types such as commentaries, reviews, case reports, or meeting reports were not included. Further, we did not employ any additional platforms such as PubMed, Google Scholar or Scopus to collect bibliometric data because the management, organization and the scope of data is slightly different among these databases. This would affect triangulating, comparing and integrating data related to RSV research in a meaningful way.

We identified the first collaborative article on RSV in 1973, which would indicate that researchers from different countries did not work together on RSV before this point in time. This assumption is not necessarily true. In 1972, the WoS indexed author affiliations for the first time, which indicates that articles published in a joint effort before 1972 would not have been detected by our methodological approach. The evaluation of country-specific publication performance by gender is meaningful but should be evaluated critically. Not all first names were included in our analysis since some were gender-neutral, not listed in name databases or displayed as initials. Therefore, the threshold of at least 60 publishing scientists and 50% gender definability was implemented to include only countries providing meaningful and valid data. Further, we identified “Mortality associated with influenza and respiratory syncytial virus in the United States“ by Thompson et al. as the most cited journal article in the field of RSV. It received 1520 citations representing its outstanding recognition in the scientific community. The publication covers the topics RSV as well as Influenza, so the limitation has to be mentioned that our computed approach did

not differentiate if the article was cited in “influenza” or “RSV” papers. Employing a manual analysis, we found that 70,3% of citing articles can be attributed to influenza, only 15,8% to RSV, and 2.2% were covering both topics. Hence, the impact of this particular paper on the field of RSV must be considered as less than it initially appeared based on the citation count alone.

Conclusion

We evaluated the worldwide RSV-related research output and demonstrated large differences between high-, middle-income or low-income nations regarding most scientometric variables. These discrepancies partly diminished when country-specific scientific activities were related to economic key measures; here, the leading position of the USA in science was challenged by other nations. Hence, calculating these quotients is beneficial for the comparison of countries with unequal conditions and different scientific infrastructures. However, we can deduce from our study that research efforts of middle-income or low-income nations have to be strengthened, e.g. by the reduction of journal fees and inclusion in international collaborations, so apparent disparities can be minimized and higher mortality rates related to RSV in developing nations can be tackled successfully.

Acknowledgements:

We thank Cristian Scutaru for the development and provision of the NewQIS analyzing tools. We also thank Mario Schwarzer, MD for supporting the study and helpful discussions as well as Jenny M. Jaque, MD for thoroughly editing our manuscript.

Source of Funding:

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors

Conflicts of Interest:

All authors state that they have no conflicts of interest to declare.

Data Sharing Statement:

Datasets of this study are available from the corresponding author upon request.

Authors' contributions:

DB, CK, DK, DAG, DO, JB and MB have made substantial contributions to the conception and design of the study, acquisition of the study data and have been involved in drafting and revising the manuscript. All authors have read and approved the final manuscript.

Figure Legends

Figure 1: Chronological development of the number of articles.

Figure 2: Density equalizing mapping projections (DEMP).

A) Number of publications B) Modified h-Index

Figure 3: Chronological development of annual citation numbers.

Figure 4: Density equalizing mapping projections (DEMP).

A) Articles/population-index (Q1)

B) Articles/GDP-index (Q2)

(Threshold ≥ 15 articles)

Figure 5: Density equalizing mapping projections (DEMP)

A) Articles/ R&D Expenditure in billion USD -index

B) Articles/ researcher (per billion inhabitants)-index

(Threshold ≥ 30 articles)

Figure 6: Country specific gender analysis of the authors publishing articles referring to RSV of countries.

(Threshold: > 50% definable genders, > 60 authors per country)

Figure 7: International cooperation (threshold ≥ 2 cooperations). Numbers in brackets (number of publications/number of publications in cooperation

Figure 8: Most prolific journals in the field of RSV research in regards to overall publication numbers and the average citation rate.

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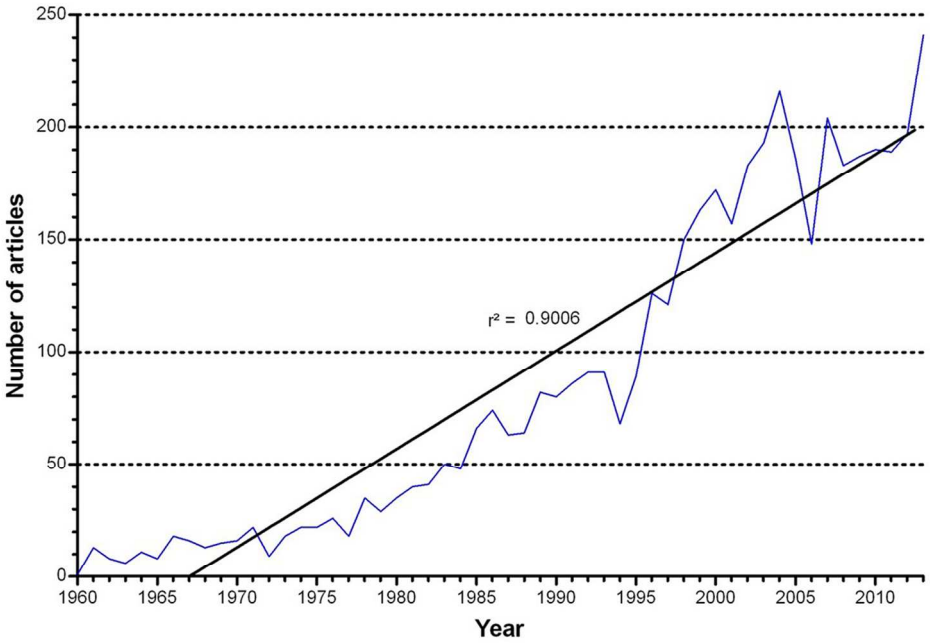

Figure 1: Chronological development of the number of articles.

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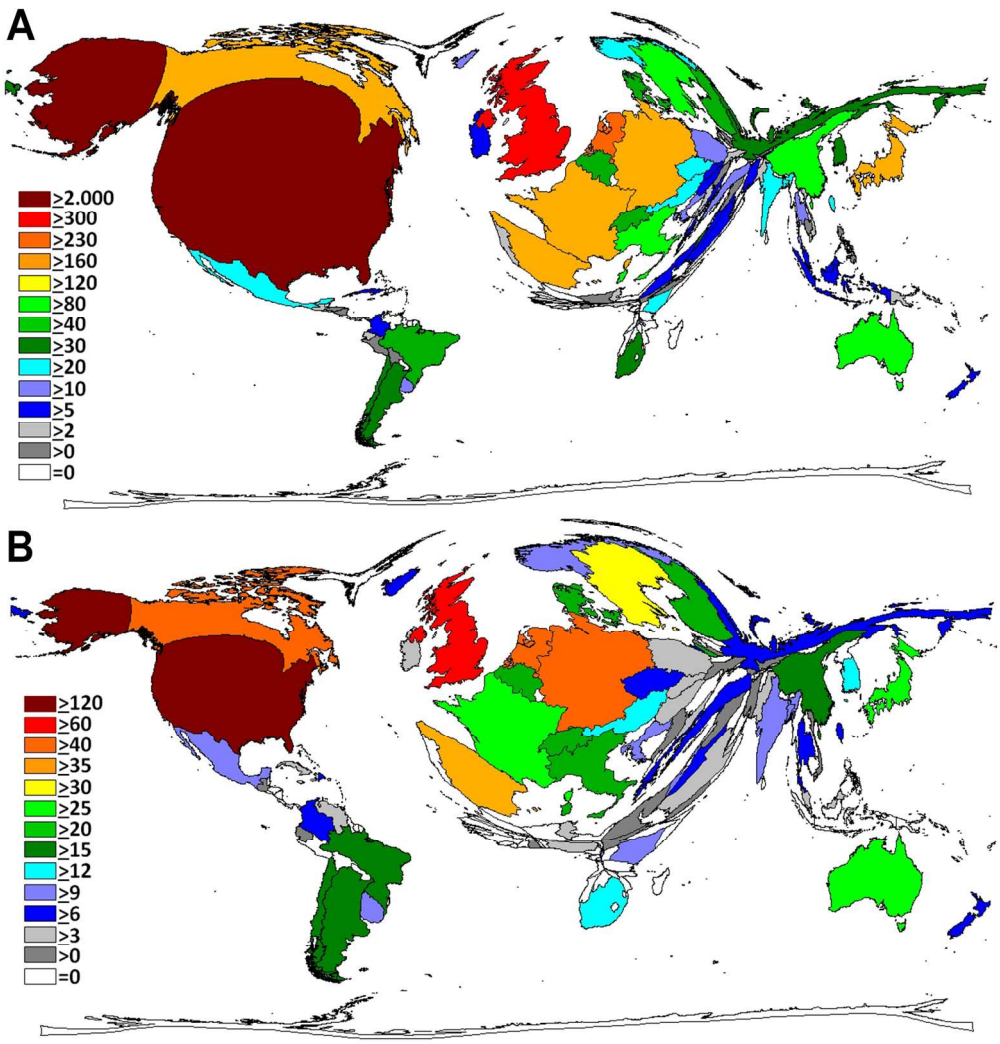

Figure 2: Density equalizing mapping projections (DEMP).
A) Number of publications
B) Modified h-Index

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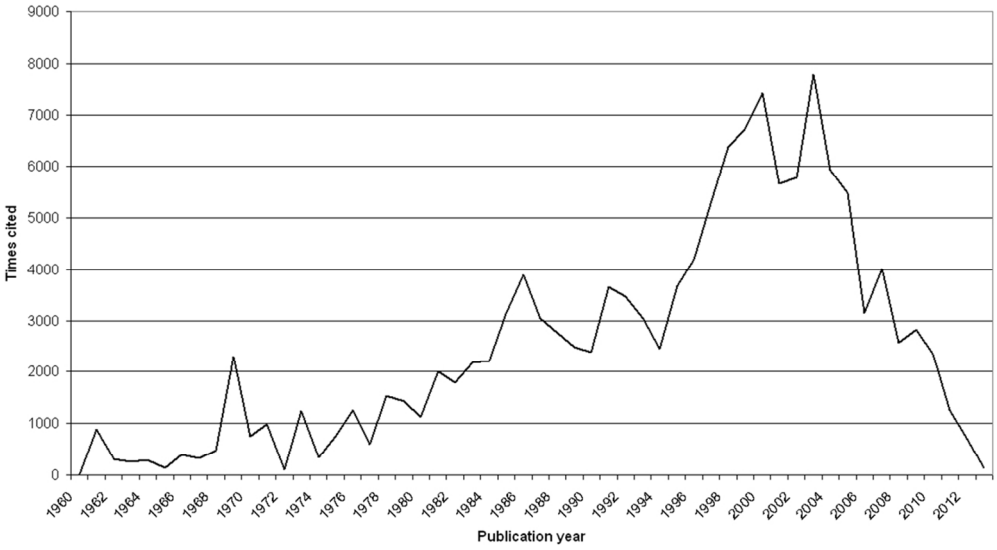

Figure 3: Chronological development of annual citation numbers.

109x61mm (300 x 300 DPI)

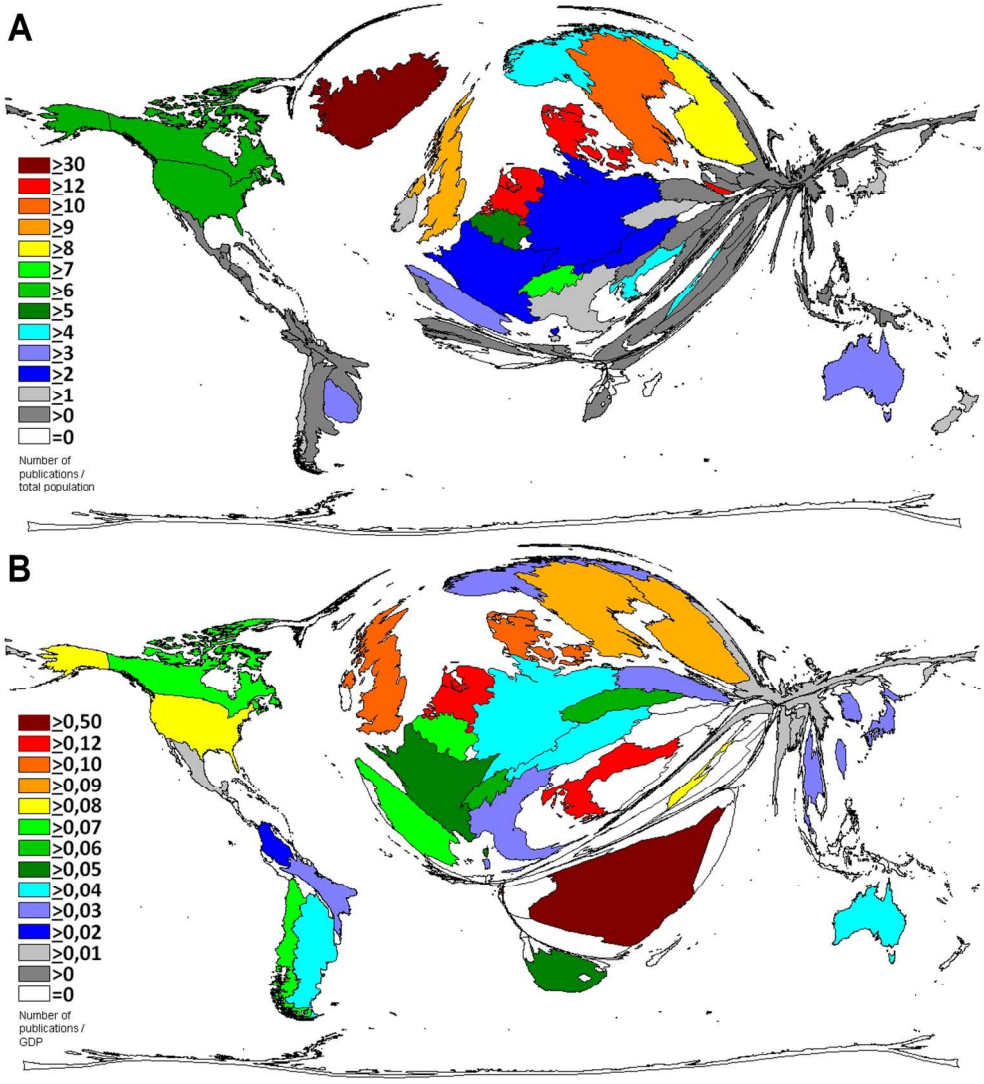

Figure 4: Density equalizing mapping projections (DEMP).
A) Articles/population-index (Q1)
B) Articles/GDP-index (Q2)
(Threshold > 15 articles)

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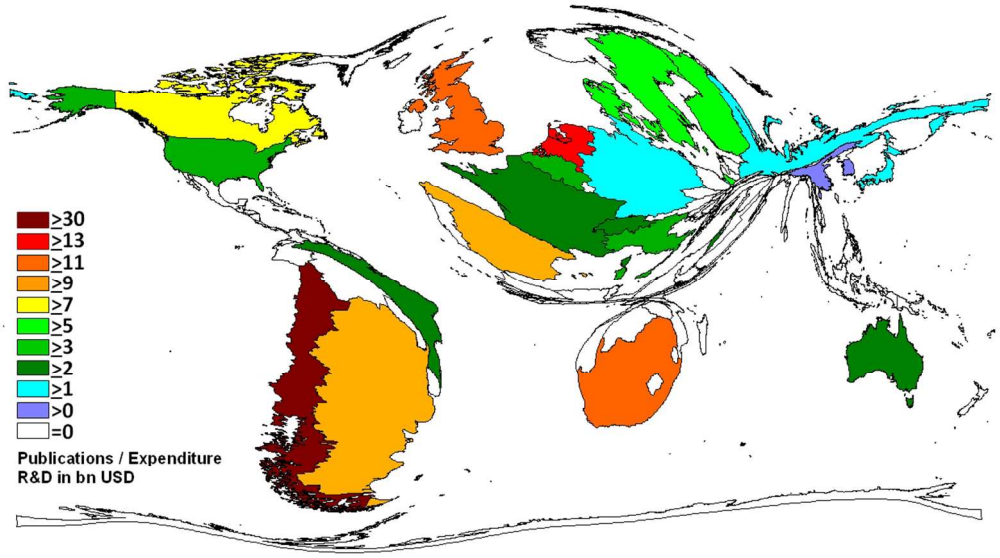

Figure 5A: Density equalizing mapping projections (DEMP). Articles/ R&D Expenditures in billion USD –index. (Threshold > 30 articles)

300x167mm (300 x 300 DPI)

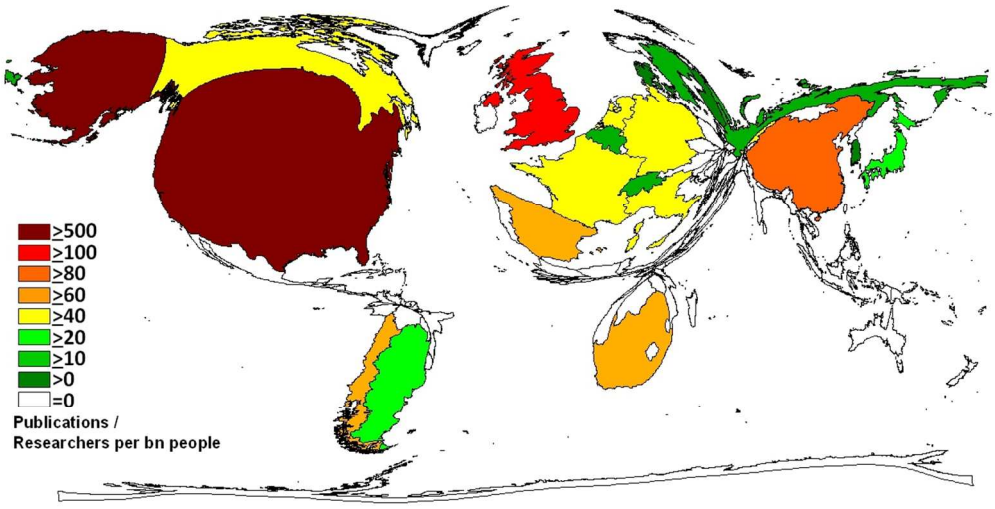

Figure 5B: Density equalizing mapping projections (DEMP). Articles/ researcher (per billion inhabitants)-index. (Threshold > 30 articles)

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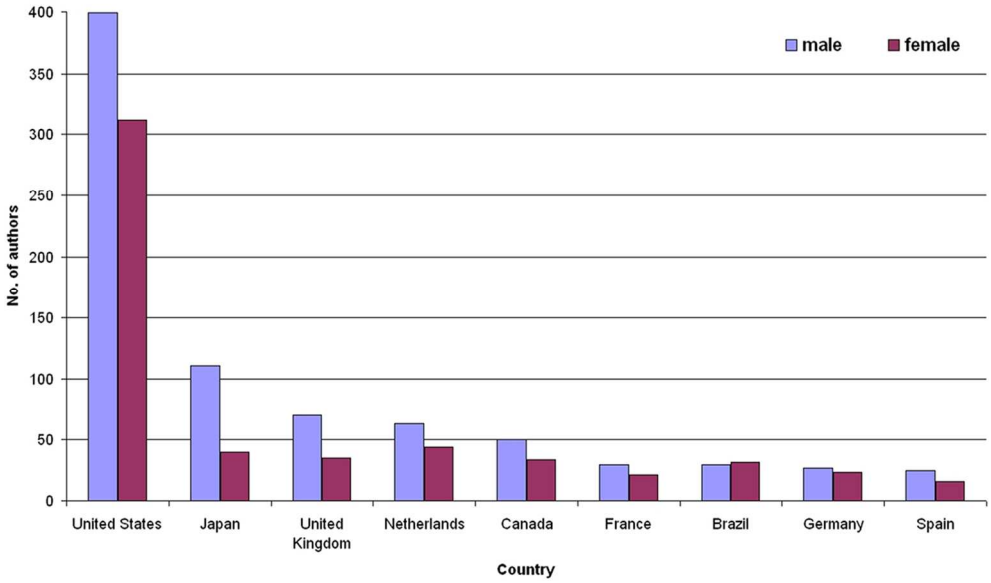

Figure 6: Country specific gender analysis of the authors publishing articles referring to RSV of countries. ‼ ┼ (Threshold: > 50% definable genders, > 60 authors per country)‼ ┼

109x65mm (300 x 300 DPI)

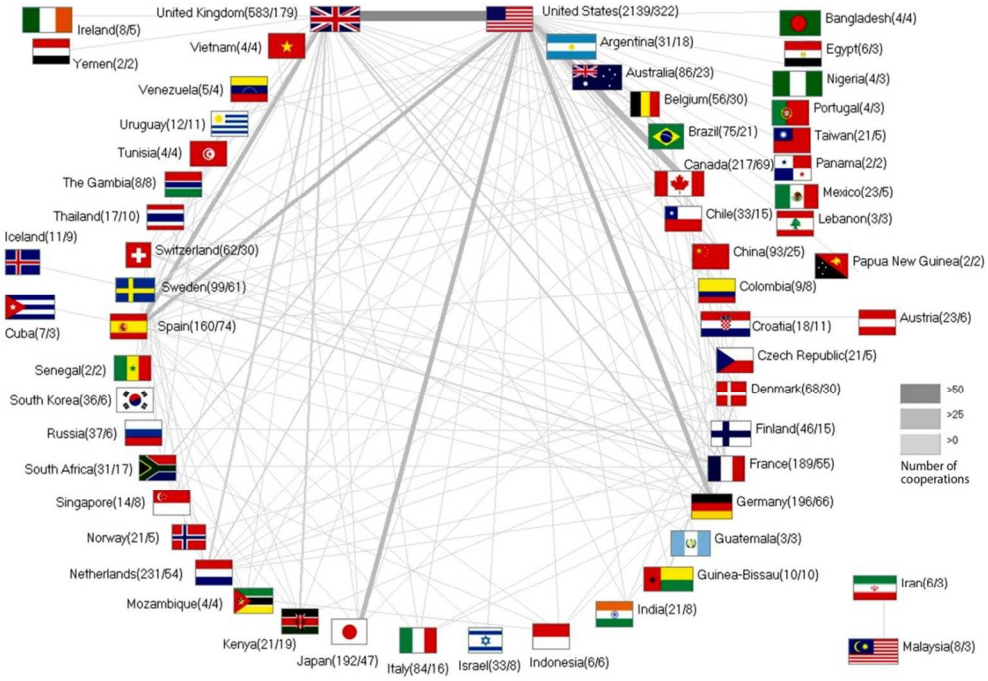

Figure 7: International cooperation (threshold > 2 cooperations). ‼ ┼ Numbers in brackets (number of publications/number of publications in cooperation)‼ ┼

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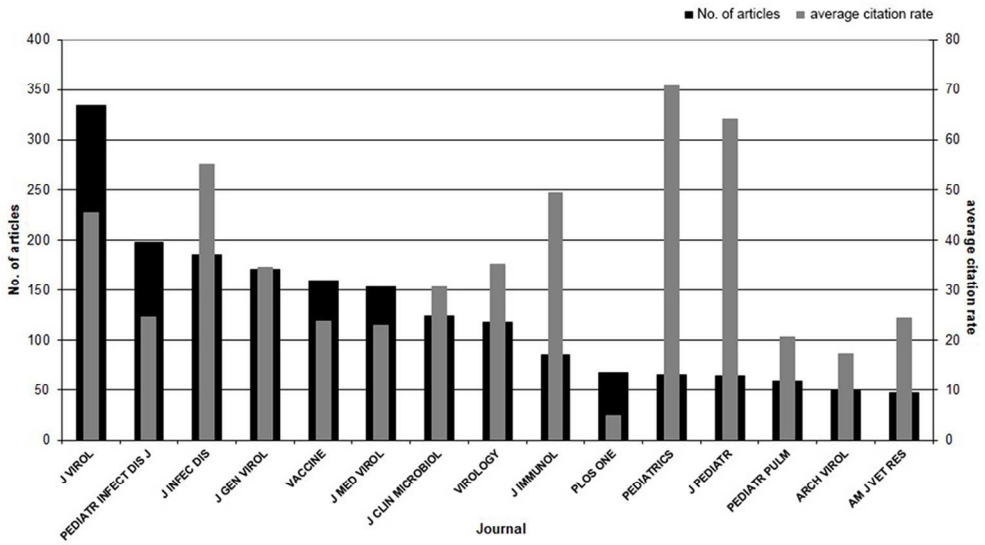

Figure 8: Most prolific journals in the field of RSV research in regards to overall publication numbers and the average citation rate.

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BMJ Open

Respiratory Syncytial Virus: A systematic scientometric analysis of the global publication output and the gender distribution of publishing authors

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2016-013615.R2
Article Type:	Research
Date Submitted by the Author:	01-Mar-2017
Complete List of Authors:	Brueggmann, Doerthe; Keck School of Medicine of the University of Southern California, Ob/Gyn; Goethe-Universitat Frankfurt am Main, Institute of Occupational Medicine, Social Medicine and Environmental Medicine Köster , Corinna ; Goethe-Universitat Frankfurt am Main, Institute of Occupational Medicine, Social Medicine and Environmental Medicine Klingelhoefer, Doris; Goethe University, Institute of Occupational Medicine Bauer, Jan; Goethe-Universitat Frankfurt am Main, Institute of Occupational Medicine, Social Medicine and Environmental Medicine Ohlendorf, Daniela; Institute of Occupational Medicine, Social Medicine and Environmental Medicine, Goethe-University Frankfurt/Main, ; Bundschuh, Matthias; Goethe-Universitat Frankfurt am Main, Institute of Occupational Medicine, Social Medicine and Environmental Medicine Groneberg, David; Occupational, Social and Environmental Medicine, Medical Department of the Goethe-University Frankfurt am Main
Primary Subject Heading:	Infectious diseases
Secondary Subject Heading:	Global health, Paediatrics, Public health, Respiratory medicine
Keywords:	Respiratory Syncytial Virus, Scientometry, Publication, Gender, Economic benchmarks

Respiratory Syncytial Virus: A systematic scientometric analysis of the global publication output and the gender distribution of publishing authors

Corresponding author: Dörthe Brüggmann – occup-med@uni-frankfurt.de, Institute of Occupational Medicine, Social Medicine and Environmental Medicine, Goethe-University, Theodor-Stern Kai 7, 60590 Frankfurt, Germany

Telephone: +49 (0) 69 6301 6650, Fax +49 (0) 69 6301 7053

Dörthe Brüggmann[1,2,*], Corinna Köster[2,*], Doris Klingelhöfer[2], Jan Bauer[2], Daniela Ohlendorf[2], Matthias Bundschuh[2], David A Groneberg[2]

[1] Department of Obstetrics and Gynecology, Keck School of Medicine of USC, Los Angeles, California, United States

[2] Institute for Occupational Medicine, Social Medicine and Environmental Medicine, Goethe University Frankfurt, Germany

* equal contribution

Word Count: 6,212

Abstract

Objective: Worldwide, the respiratory syncytial virus (RSV) represents the predominant viral agent causing bronchiolitis and pneumonia in children. To conduct research and tackle existing healthcare disparities, RSV-related research activities around the globe need to be described. Hence, we assessed the associated scientific output (represented by research articles) by geographical, chronological and socio-economic criteria and analyzed the authors publishing in the field by gender. Also, the 15 most cited articles and the most prolific journals were identified for RSV research.

Design: retrospective, descriptive study

Setting: The NewQIS platform was employed to identify RSV-related articles published in the Web of Science until 2013. We performed a numerical analysis of all articles, and examined citation-based aspects (e.g. citation rates); results were visualized by density equalizing mapping tools.

Results: We identified 4600 RSV-related articles. The USA led the field; US-American authors published 2,139 articles (46.5% % of all identified articles), which have been cited 83,000 times. When output was related to socio-economic benchmarks such as GDP or R&D expenditures, Guinea-Bissau, The Gambia and Chile were ranked in leading positions. 614 articles on RSV (13.34% of all articles) were attributed to scientific collaborations. These were primarily established between high-income countries. The gender analysis indicated that male scientists dominated in all countries except Brazil.

Conclusions: The majority of RSV-related research articles originated from high-income countries whereas developing nations showed only minimal publication productivity and were barely part of any collaborative networks. Hence, research

capacity in these nations should be increased in order to assist in addressing inequities in resource allocation and the clinical burden of RSV in these countries.

Key words: Respiratory Syncytial Virus, Publication, Citation, Scientometry, Gender, Economic benchmarks

Strengths and Weaknesses

- This is the first concise depiction of the worldwide scientific productivity related to RSV, which was assessed by geographical, chronological and socio-economic criteria.
- The NewQIS platform combines scientometric methods and "density equalizing mapping projections" to evaluate the scientific output regarding quantitative and qualitative aspects, geographical and chronological developments, existing research networks and socio-economic benchmarks in a reliable and standardized way.
- Since the WoS has a preference for English journals, we have to acknowledge a language bias associated with our analysis.
- Citation based parameters were assessed, which have limitations since these rather reflect the recognition of the research in the scientific community than truly measure quality.

INTRODUCTION

The human respiratory syncytial virus (RSV) is the predominant viral agent affecting the respiratory tract worldwide [1, 2]. It is associated with 64 million infections that occur primarily in children under 5 years [3]. RSV belongs to the Paramyxoviridae family and is a negative-sense, non-segmented, single-stranded RNA virus, which is mostly transmitted by droplets [4]. RSV causes bronchiolitis, pneumonia, bronchitis and croup. It is linked to recurrent wheezing and pediatric asthma [5, 6]. There is no definitive treatment for RSV-related conditions. Although the development of effective and safe vaccines has remained unsuccessful to date, the variety of candidate vaccines is constantly growing in the last years [7]. One prophylactic agent is commercially available, the neutralizing anti-RSV antibody Palivizumab. Its use is limited to preterm babies, chronic lung disease of prematurity and infants with congenital heart disease [8].

RSV-associated morbidity and mortality depends on many factors such as the geographic location, climate patterns, genetic susceptibility, socioeconomic factors and local virus strains [3]. The percentage of children having contracted RSV by their second year of life approaches 100 % [9, 10]. In the United States of America (USA), over 2 million children aged 5 years and under need medical attention to treat their RSV infection every year [11]. On average, 0.3% of these children and 0.7 % of infants younger than six months require hospitalization [11]. The general RSV mortality rate in this demographic varies between 0-33% [10]. Worldwide, up to 199 000 children die due to RSV infections. 99% of these deaths occur in in developing countries [3] hence, RSV represents a substantial burden for community health in these nations. According to WHO field studies in ten developing countries, RSV causes 70 % of all

acute respiratory-tract infections in children under 5 years of age [12]. Here, the virus is identified in about 15-40 % of the hospitalized children with pneumonia or bronchiolitis [13]. RSV epidemics occur during rainy seasons in tropical climates and during the winter months in temperate zones [4]. Both virus strains, RSV-A and -B, co-circulate during outbreaks in any given year. The A subtype is typically associated with more severe disease [14]. Distinct genotypes of both strains (identified by the genetic classification of their G protein) are predominant in any given year. This pattern is highly flexible, varies by region and may shift to other prominent genotypes the following year [15]. Epidemiological studies are dedicated to characterize the distribution of RSV strains and genotypes worldwide, often leading to the identification of new variants such as the RSV B genotype THB in Thailand [16].

Although care of RSV patients has been improved considerably and extensive studies have been launched to estimate viral spread and disease burden in developing countries, tremendous challenges still remain. In regards to the high prevalence, morbidity and mortality of RSV worldwide, we consider that further research and the implementation of related public health measures are crucial for future successes. However, global research funds are limited and their allocation becomes challenging. In this context, the assessment of the scientific performance is a prerequisite for the reasonable distribution of monetary support and the planning of future research endeavors by scientists interested in the field. Hence, we employed scientometric tools with the goals (1) to determine the RSV-related publication output among the extensive amount of biomedical publications and (2) to evaluate the scientific productivity of single countries in the framework of the global research landscape and in relation to socioeconomic and gender aspects. We also identified the 15 most cited landmark articles and the most prolific journals in the field of RSV

research.

METHODS

Methodical Platform

We used the New Quality and Quantity Indices in Science (NewQIS) platform to assess the worldwide RSV publication activity in a reliable and standardized way. This tool combines scientometric methods and "density equalizing mapping projections" (DEMP) [17-19] to evaluate the publication output regarding quantitative and qualitative aspects, geographical and chronological developments, existing research networks and socio-economic benchmarks.

Density-equalizing mapping

DEMP is a state-of-the-art technique to visualize benchmarking processes by anamorphic maps [17, 20]. Based on the algorithm of Gastner and Newman, the size of each country was modified analogously to country-specific data on RSV research leading to a new geographic distribution of the global landscape [17].

Data collection

For data collection, the Web of Science (WoS) Core Collection database (Thomson Reuters) was employed. The following search term was created: Title=("RSV" OR "Respiratory Syncytial Virus" OR "RS Virus*") NOT Topic=(Rous Sarcoma). The Boolean operator NOT was used to exclude all publications concerning the Rous Sarcoma (Virus). We limited our search to original research articles. Following our protocol, the time frame was restricted from 1900 to 2013; publications in 2014 were not regarded due to incomplete data acquisition at the time the study was performed.

Data analysis

RSV-related articles were analyzed regarding quantitative aspects such as the total number of publications, citation numbers, countries of article origin (defined as the 'country where the institution is located each author, who worked on publishing the article, is affiliated'), institutions, languages, cited reference numbers, and publication date. The number of authors publishing on RSV was only quantified for the years with 30 or more annual publications. Also, h-Indices, and the average citation number per item (citation rate, CR) were investigated. Regression analysis was used to investigate the chronological evolution of RSV research. We calculated the coefficient of determination (r^2) representing the slope of the growth in scientific output and citations.

Modified h-Index

The Hirsch-Index (h-Index) is a recognized semi-qualitative proxy measure to assess the impact of one author's research output on the scientific community [21, 22]. An h-index of 12 indicates that out of 12 published papers each has been cited at least 12 times. In this study, we applied this concept to the RSV-specific research productivity of single countries and calculated a "modified country-specific" h-Index.

Country-specific gender analysis

The proportionality of male and female researchers among authors publishing on RSV was analyzed. Online name databases were utilized to identify the authors' genders [23]. If first names were not gender-specific or quoted as initials, a manual search (utilizing websites, corresponding addresses and social networks) was launched. We only evaluated countries where a minimum of 60 authors were

affiliated and a minimum of 50 % of authors were identified by gender to ensure a valid analysis. These thresholds were chosen arbitrarily based on previous studies.

Cooperation analysis

We identified all RSV-associated publications that were issued due to international collaborative efforts. The total count of collaborative items was related to the overall number of publications for each investigated country. In brief, if at least two authors originating from different institutions or countries (as identified by the affiliations in the article) contributed to one article, this publication was defined as a collaborative item. Publications with two or more authors affiliated to the same country were counted one time only towards the complete count of joint publications of this particular country. If an author had two affiliations, these were counted for every country mentioned in the affiliations. Connecting vectors visualized these co-operations; their width and shade of grey reflected the number of joint publications.

Journal analysis

The journals publishing on RSV were analyzed regarding quantitative and qualitative aspects, e.g. number of published RSV articles as well as citations these items received (CR).

Analysis of economic key figures

Two quotients were calculated to assess the scientific output of a specific country, (1) in relation to the number of inhabitants (Q1), and (2) in relation to its economic power (as measured by the gross domestic product, GDP, Q2). Data regarding the

population and GDP of investigated countries were obtained from 2012 from the CIA *World Factbook* [24]. We computed the quotients in the following way:

1. Articles/population-index (Q1) = number of articles/population in millions
2. Articles/GDP-index (Q2) = number of articles/GDP in billions

All countries were classified into high-, upper-middle-, lower-middle- and low-income groups according to World Bank definitions [25].

We compared the total number of RSV articles to the gross domestic expenditure on Research and Development (in % of GDP) as well as to the number of researchers (per billion inhabitants) affiliated to the investigated countries [26]. The analysis was limited to countries that published a minimum of 30 articles in the field of RSV.

RESULTS

Number of published items

We identified 4,600 articles on RSV published between 1900 and 2013; 2,645 (57.5%) of these were issued after 2000. 1960 and onwards, the number of articles increased significantly over time as indicated by r^2=0.9 (Fig. 1). 10,791 authors published in the field of RSV. The number of authors per article increased by 100% in the investigated timeframe. We identified a mean of 3.8 and a median of 3 authors in 1978, which was the first year with more than 30 annual publications. 10 years later, a mean of 4.59 and a median of 4 authors were found, followed by a mean of 5.05 and a median of 5 authors in 2000, a mean of 5.95 and a median of 5 authors in 2006 and a mean of 7.6 and a median of 6 authors in 2013

Analysis of research origin and citations

Although the publications originated from 92 of the 251 investigated countries and autonomous regions the majority of the articles were written in English (4444 articles, 96.6 % of all published RSV articles) followed by French (64 articles, 1.4 % of all articles) and German (32 articles, 0.7 % of all articles). More than 85% of the global publication output was issued by authors from high-income economies. The USA was the most productive nation (2,139 articles, 46.5 % of all published RSV articles) followed by the United Kingdom (UK, 583 articles, 12.7 %), the Netherlands (231 articles, 5.0 %), Canada (217 articles, 4.7 %) and Germany (196 articles, 4.3 %). Hence, the USA and UK dominated the cartogram, while major parts of Africa (with the exception of South Africa), Asia (with the exception of Japan, China, South Korea, and India) and Central America occupied only minor areas (Fig. 2A).

The country-specific citation numbers and modified h-Indices showed a global distribution similar to the number of publications. Articles with US-American affiliation of the authors were cited most (83,000 citations, c), followed by articles from the UK (c = 19,240), the Netherlands (c = 5587), Canada (c = 5549) and Germany (c = 5319). Articles published by African, Asian and Middle American authors received hardly any citations.

The USA and the UK were the top ranked countries with a modified h-Index of 121 (USA) and 68 (UK), followed by the Netherlands (h-Index = 44), Germany (h-Index = 43) and Canada (h-Index = 40) (Fig. 2B).

Regarding the country-specific citation rate (average number of citations per total number of publications for each country with more than 30 articles, CR), Sweden (CR = 40) dominated and was followed by the USA (CR = 38.8), Finland (CR = 34.9), the UK and Germany (CR = 27.13).

Analysis of citation performance

The absolute citation count of all identified RSV-related articles resembled the growing volume of published papers in the investigated timeframe. We documented a significant positive correlation between citation numbers and the time of publication (with r^2=0.72 for the timeframe from 1960 to 2008). The annual citation counts grew from 1960 to 1994 (e.g. from 19 annual citations in 1960 to 2448 annual citations in 1994); after 1995, a rapid increase followed until 2003 (e.g. 5274 annual citations in 1997 and 7790 annual citations in 2003) whereas a steep decline was noticed after 2006 (e.g. 3147 annual citations in 2006). We identified visible peaks in citation activity for 1969 (2294 annual citations), 1986 (3898 annual citations), 2000 (7411 annual citations), and 2003 (7790 annual citations) (Fig. 3). Additionally, we compiled the 15 most cited RSV articles, which constitute the publications that have sparked the most documented interest in the field to date (Table 1).

Table 1. The 15 most cited articles in the area of RSV-related research are displayed including their title, publication year, countries of article origin (defined as the countries where first, senior- and co-authors are affiliated), citation count and journal.

Title	Publication Year	Country of Article Origin	Citations	Journal
Mortality associated with influenza and respiratory syncytial virus in the United States **Thompson WW et al.**	2003	United States	1520	JAMA

Pattern recognition receptors TLR4 and CD14 mediate response to respiratory syncytial virus **Kurt-Jones EA et al.**	2000	United States	856	Nat Immunol
Respiratory Syncytial Virus Disease In Infants Despite Prior Administration Of Antigenic Inactivated Vaccine **Kim HW et al.**	1969	United States	848	Am J Epidemiol
Respiratory syncytial virus in early life and risk of wheeze and allergy by age 13 years **Stein RT et al.**	1999	Brazil, United States	719	Lancet
Palivizumab, a humanized respiratory syncytial virus monoclonal antibody, reduces hospitalization from respiratory syncytial virus infection in high-risk infants **The Impact-RSV Study Group.**	1998	United States, Canada, UK	652	Pediatrics
An Epidemiologic Study Of Altered Clinical Reactivity To Respiratory Syncytial (Rs) Virus Infection In Children Previously Vaccinated With An Inactivated RS Virus Vaccine **Kapikian et al.**	1969	United States	552	Am J Epidemiol
Risk Of Primary Infection And Reinfection With Respiratory Syncytial Virus **Glezen et al.**	1986	United States	548	Am J Dis Child
Respiratory syncytial virus bronchiolitis in infancy is an important risk factor for asthma and allergy at age 7 **Sigurs N et al.**	2000	Sweden, Iceland	488	Am J Respir Crit Care Med
Wheezing, Asthma, And Pulmonary Dysfunction 10 Years After Infection With Respiratory Syncytial Virus In Infancy **Pullan CR and Hey EN**	1982	UK	449	Br Med J
Respiratory syncytial virus infection in elderly and high-risk adults **Falsey AR et al.**	2005	United States	430	NEJM
Prophylactic Administration Of Respiratory Syncytial Virus Immune Globulin To High-Risk Infants And Young-Children **Groothuis JR et al.**	1993	United States	427	NEJM
The Development Of Respiratory Syncytial Virus-Specific IgE And The Release Of Histamine In Nasopharyngeal Secretions After Infection **Welliver RC et al.**	1981	United States	425	NEJM
Respiratory-Syncytial-Virus Infections, Re-Infections And Immunity - Prospective, Longitudinal-Study In Young-Children **Henderson FW et al.**	1979	United States	418	NEJM
Generation of bovine respiratory syncytial virus (BRSV) from cDNA: BRSV NS2 is not essential for virus replication in tissue culture, and the human RSV leader region acts as a functional BRSV genome promoter	1999	Germany	417	J Virol

Buchholz UJ et al.				
Asthma and immunoglobulin-e antibodies after respiratory syncytial virus bronchiolitis - a prospective cohort study with matched controls **Sigurs N et al.**	1995	Sweden	416	Pediatrics

263

264 **Relation to economic parameters**

265 Relating the number of publications to the population of a country, high-income
266 countries like Iceland (Q1 = 34.59), the Netherlands (Q1 = 13.90) and Denmark (Q1
267 = 12.25), issued a higher number of publications per million inhabitants compared to
268 low-or lower-middle-income countries, e.g. Nigeria (Q1 = 0.03) and Indonesia (Q1 =
269 0.02) (Fig. 4A). We identified two exceptions, which included the low-income
270 countries Guinea Bissau (Q1 = 6.30) and The Gambia (Q1 = 4.76). Both were
271 represented among the 15 top ranked countries in this analysis.

272

273 When looking at the publication activity in relation to GDP, two low-income countries
274 outperformed high-income nations (Fig. 4B). Guinea Bissau (Q2 = 11.776) and The
275 Gambia (Q2 = 8.721) again held leading positions, followed by Iceland (Q2 = 0.810),
276 Kenya (Q2 = 0.516), and Croatia (Q2 = 0.319). Besides these two exceptions, other
277 low- or lower-middle-income countries showed a weak performance (e.g. Philippines
278 with Q2 = 0.004 or Indonesia with Q2 = 0.007). Also, the USA did not remain under
279 the top 10 nations and was found at position 18 (Q2 = 0.132).

280

281 Chile, the Netherlands, South Africa, UK and Argentina were leading the analysis
282 when the total article count was related to the country-specific Research and
283 Development (R&D) expenditures (33.72, 13.32, 12.14, 11.46 and 9.56 articles per
284 billion GDP spent on R&D, respectively). The USA dropped to position 11 with 4.52
285 articles per billion GDP spent on R&D (Fig. 5A, Table 2A).

When we related the article count to the number of researchers (per billion inhabitants) as a proxy measure for the active research community working on RSV and the productivity of these researchers, the USA was leading the field (532.27 articles per researcher per billion inhabitants), followed by the UK, China, Chile and South Africa (137.10, 83.55, 77.10, and 76.60 articles per number of researchers per billion inhabitants) (Fig. 5B, Table 2B).

Table 2A. Total number of publications related to gross domestic expenditures on Research and Development in Billion USD of countries that have published more than 30 items on RSV.

Rank	Country	No. of articles	R&D expenditure in % GDP	GDP in billion USD	R&D Expenditure in billon USD	Articles/ billion USD of R&D Expenditure
1	Chile	33	0.38	258	0.98	33.72
2	Netherlands	231	1.97	879	17.34	13.32
3	South Africa	31	0.73	349	2.55	12.14
4	UK	583	1.70	2990	50.85	11.46
5	Argentina	31	0.61	529	3.24	9.56
6	Spain	160	1.23	1381	17.01	9.41
7	Canada	217	1.61	1783	28.73	7.55
8	Denmark	68	3.08	346	10.67	6.37
9	Sweden	99	3.16	571	18.05	5.49
10	Finland	46	3,17	272	8.63	5.33
11	USA	2139	2.73	17348	472.78	4.52

12	Belgium	56	2.46	531	13.09	4.28
13	Italy	84	1.29	2138	27.52	3.05
14	Switzerland	62	2.97	701	20.80	2.98
15	France	189	2.26	2829	63.82	2.96
16	Australia	86	2.20	1454	31.93	2.69
17	Israel	33	4.11	305	12.53	2.63
18	Brazil	75	1.24	2417	29.87	2.51
19	Germany	196	2.87	3868	110.96	1.77
20	Russia	37	1.19	2030	24.09	1.54
21	Japan	192	3.58	4596	164.73	1.17
22	South Korea	36	4.29	1411	60.55	0.59
23	China*	93	2.05	10351	211.79	0.44

Table 2B. Total number of publications related to articles per researcher (per billion inhabitants) of countries that have published more than 30 items on RSV.

Rank	**Country**	**Number of RSV articles**	**Number of researchers per billion inhabitants**	**Articles/researcher (per billion inhabitants)**
1	USA	2139	4.02	532.27
2	UK	583	4.25	137.10
3	China*	93	1.11	83.55
4	Chile	33	0.42	77.11
5	South Africa	31	0.40	76.60
6	Spain	160	2.64	60.55
7	Netherlands	231	4.48	51.58

8	Canada	217	4.52	48.02
9	France	189	4.20	44.99
10	Germany	196	4.38	44.74
11	Italy	84	2.01	41.86
12	Japan	192	5.39	35.65
13	Argentina	31	1.20	25.79
14	Sweden	99	6.87	14.41
15	Switzerland	62	4.48	13.83
16	Belgium	56	4.18	13.41
17	Russia	37	3.10	11.93
18	Denmark	68	7.20	9.45
19	Finland	46	7.00	6.58
20	South Korea	36	6.90	5.22
21	Israel	33	8.26	4.00

Country-specific gender analysis

We identified the gender distribution among authors working on RSV in institutions affiliated to 92 countries. Our analysis indicated a larger proportion of male scientists in almost all evaluated countries (Fig. 6). Brazil was an exception. 95 authors with affiliation to Brazilian institutions were identified as working on RSV. 62 of those were identifiable by name and gender. Here, males and females were almost equally represented (32 female authors, 51.6% of identifiable authors, 30 male authors, 48.4 % of identifiable authors). By calculating the proportion of male to female scientists (m/f ratio), we documented the lowest ratio (m/f ratio = 0.94) for Brazil,

followed by Germany (m/f ratio = 1.1). Japan had the highest score with m/f ratio = 2.8.

International cooperation analysis

The first collaborative article on RSV was identified in 1973. It was published by researchers working in institutions located in Switzerland and the USA [27]. Since 1973, 614 joint articles were published on RSV accounting for 13.34% of all articles. The USA was the preferred partner for international collaborations on RSV. The most productive cooperation was established between the USA and the UK (67 joint works, 10.9 % of collaborative articles), followed by the USA and Canada (45 joint articles, 7.3 % of collaborative articles), and the USA and Germany (34 joint articles, 5.5 % of collaborative articles).

The most fruitful cooperation not involving the USA existed between the UK and Spain (33 joint articles, 5.4 % of collaborative articles). The most productive cooperation between high- and lower-middle- or low-income economies was set up between Kenya and the UK (18 joint articles, 2.9 % of collaborative articles) followed by Guinea Bissau and Denmark (10 joint articles, 1.6 % of collaborative articles). Overall, co-operations with low-income or lower-middle-income countries were less popular (Fig. 7).

Journal analysis

When we identified the most prolific journals in RSV research, the "Journal of Virology" led the field (334 articles, CR of 45.49), followed by “The Pediatric Infectious Disease Journal" (198 articles, CR = 24.66) and the "Journal of Infectious

Diseases" (186 articles, CR 55.18) (Fig. 8). The highest citation rate was achieved by the "Proceedings of the National Academy of Sciences of the United States of America" (42 articles, CR = 81.43), followed by "Pediatrics" (66 articles, CR = 70.80), “Journal of Pediatrics” (65 articles, CR = 64.03), “American Journal of Respiratory Critical Care“ (47 articles, CR = 62.55), and „Journal of Infectious Diseases“ (186 articles, CR = 55.18).

DISCUSSION

In the WoS, we documented only 4,600 RSV-related articles since 1900. The first item on the disease in humans was published in 1957 [28]. This emphasizes that research on RSV is a relatively new field considering the virus was initially isolated in 1956 from laboratory primates [29]. The predominance of English in the majority of identified articles aligns not only with the fact that this language is the recognized “scientific lingua franca” but also reflects the abundant research output of English speaking countries such as USA, Canada and the UK found in our study.

The increasing number of RSV publications over time is typical for most biomedical research, e.g. on the John Cunningham Virus, influenza or breast cancer [30, 31]. Overall, the steady growth of article numbers can be explained by the rising interest in the field due to the increasing relevance of RSV in pneumonia and child mortality [9]. In the first few years after the detection of the virus, basic research was conducted. These endeavors, which aimed to characterize the virus, identify immunologic responses and develop vaccines, translated into a growing volume of articles on RSV [32-35]. The continuous increase since the beginning of the 1990s may be attributed to the launch of a growing number of scientific journals providing a platform for

publishing. The development of modern communication systems based on new computer technologies like the World Wide Web made it easier to communicate, exchange ideas, and publicize articles in central databases. Also, it is noticeable that the increasing publication output since the 1960s was paralleled by a globally growing funding volume allocated to the R&D sector. In the USA alone, a total of 13,711 million US-Dollars (UDS) was allocated to R&D in 1960 as documented by the National Science Foundation. This amount increased to 26,271 million UDS in 1970 and 452,556 million USD in 2012 (https://www.nsf.gov/statistics/2015/nsf15315/).

The chronological development in publication quantity (Fig. 1) was resembled by the steady increase of related citations (Fig. 3). Four prominent citation peaks in 1969, 1986, 2000 and 2003 coincided with milestone papers the field. In 1969, adverse effects of the formalin-inactivated RSV vaccine in children were reported [36]. Large epidemiologic studies investigated the risks of reinfection and the mortality associated with RSV in 1986 and 2003 [37, 38]. The research on a prophylactic antibody licensed in 1999 and novel insights into immunologic responses involving pattern recognition receptors TLR4 and CD14 may be responsible for the peaking number of publications and citations in 2000 [39]. The citation decline after 2006 can be attributed to the short timespan articles had allotted to receive recognition within the scientific community and obtain the appropriate citation number reflecting their true impact [40]. Hence, we expect this trend to be reversed in the future.

The USA dominated RSV research with regards to overall publication quantity, citation numbers and h-index. This corresponds with a previous biomedical benchmarking study. Here, the USA was the most productive nation and authored

1,893,800 of 5,527,558 publications related to 22 organ systems from 1961 to 2007 [41]. The leading role of the USA might be linked to major financial resources this nation dedicates to research. The US-American National Institutes of Health (NIH) are by far the biggest biomedical funder in the world (e.g. with a funding volume of 26.08 billion USD in 2013 compared to the biggest funding source in the EU, the European Commission, with a funding volume of 3.71 billion USD in 2013). Also, the Department of Defense constitutes another large US-American funding organization with a volume of 1.017 billion USD (2013), followed by private philanthropic institutions such as the Howard Hughes Medical Institute or the Bill & Melinda Gates Foundation with impressive funding volumes of 752.0 (2013) and 462.6 million USD (2011), respectively [42]. These funds can support manpower and an outstanding scientific infrastructure illustrated by the fact, that the majority of institutions working on RSV were identified in the USA, and that this nation is a preferred partner for national and international co-operations.

The cluster of the USA, Western-European countries (e.g. UK or Germany) and Japan dominated the overall publication output and analyses of citation-based benchmarks. This finding corresponds with other scientometric studies (e.g. on Influenza, Ebola, or Hepatitis B [30, 43]. Although Sweden and Finland published relatively low numbers of articles, they are characterized by the highest citation rates in our analysis indicating the outstanding quality and high recognition their articles received in the scientific community. Furthermore, it was striking that most African, Asian and Central American countries afflicted with a considerable RSV-related burden did not play a visible role in the field. Methodologically, we included only countries in the citation rate analysis that published more than 30 RSV articles aiming to generate a better the validity of the investigation by avoiding overestimation

of few but frequently cited articles. Nevertheless, we want to stress that the absolute number of citations as well as the citation rate should be viewed critically. These parameters can be affected by self-citation and inaccurate citations. Also, the Matthew effect might influence citation-based variables. Here, scientists prefer to cite articles issued by well-known researchers to papers by junior scientists leading to a disproportional increase of the related citation counts [44, 45]. Hence, we also evaluated the modified h-index since it is less influenced by outstanding, frequently or rarely cited articles skewing the citation rate value [21, 22]. Furthermore, all citation-based variables have limitations in assessing the quality of the identified articles because they rather reflect the recognition of the research in the scientific community than measure quality.

We identified an overrepresentation of male authors in the majority of evaluated nations. This corresponds to the study of Head et al. who documented the preferential funding of male researchers by UK institutions in the area of global infectious disease research. Between 1997-2010, funding agencies supported fewer studies of female PIs and awarded less monetary support to research supervised by women. Particularly for RSV, male researchers received 5-times more funding than female scientists, who spearheaded only half the funded studies compared to their male counterparts in the field [46]. In our gender analysis, Brazil was an exception with a majority of women authoring RSV research (Fig. 6). This result correlates with previous investigations on Yellow fever and Rotavirus infections [47] as well as with gender benchmarking studies (e. g. conducted by the “Konrad-Adenauer Foundation” or the “Organization for Women in Science for the Developing World” (OWSD)), which suggests that Brazil pioneers in the support and participation of females in science [48, 49].

Our analysis of RSV publication outputs changed in relation to economic capabilities (Fig. 4). Two developing, low-income nations, The Gambia and Guinea-Bissau, occupied the leading positions. This finding points towards the fact that both prioritize RSV research and might be connected to existing co-operations with a long standing shared history between collaborating nations and their focused support of RSV scientific activities. For example, the United Kingdom's "Medical Research Council The Gambia Unit" and the Danish "Bandim Health Project" encourage medical research in Guinea-Bissau and The Gambia [50, 51]. Also, research in the field is promoted by single researchers with a strong dedication to conduct research in African sites. Here, Sir Brian Greenwood has spearheaded RSV-related research very successfully for decades while being faculty at the London School of Hygiene and Tropical Medicine as well as the Director of the Medical Research Council in The Gambia [52, 53541355, 565758].

If the RSV article counts were related to R&D expenditures and number of researchers in specific countries, a different, more refined picture emerged compared to the assessments based on absolute publications numbers or related to socio-economic variables. Here, two Latin American countries gained importance, Chile and Argentina. It appears that these nations invest funding very efficiently in RSV research, with Chile ranked first position with 33.72 RSV articles per billion USD in R&D expenditures followed by Argentina in fifth position (9.56 articles per billion USD in R&D). Both nations' interest to fund RSV research might be linked to the fact that respiratory infections and RSV in particular impose a heavy burden on the local pediatric population. Respiratory infections constitute the second leading cause of death in Latin American children aged 5 years or under with RSV as the causative

agent in 70.0% of these infections.[3,459, 60]. In the temperate climate of Chile and Argentina, RSV causes predictable outbreaks during the summer months. A particular high RSV burden of up to 70% was reported in Chilean children aged 0-11 months with lower respiratory tract infection. This was substantially higher than in other Latin American countries (e.g.18.2 % Argentina and 44% in Brazil) [61]. Hence, RSV is constantly in the focus of the local health authorities, which routinely monitor and report the trends in RSV infections to better allocate resources for pediatric patients and limit related morbidity and mortality [6162].

Collaborations are becoming increasingly important in the field of RSV research as indicated by existing tight-knit networks and the growing numbers of authors per article over time. We link this development to the globalization process, which connects scientists worldwide to exchange ideas, resources and knowledge facilitated by the growing availability of information technology. Further, it is noticeable that countries such as the USA or European nations play a more prominent role in international collaborations compared to low- and lower-middle-income countries. As exceptions, we could identify productive co-operations between the UK and Kenya as well as Denmark and Guinea-Bissau. The relation between Kenya and the UK might be based on their shared history and facilitated by implemented programs such as the *"KEMRI Welcome Trust Research Program"* between the Kenya Medical Research Institute and the University of Oxford [63]. As revealed by Fitchett et al. [64], a substantial funding volume goes to infectious disease research in countries with colonial ties to the UK such as Kenya and The Gambia. From 1997 – 2010, these countries received 13.13 million £ (The Gambia) and 12.92 million £ (Kenya) of biomedical funding by UK based institutions. Research activity on RSV in Guinea-Bissau is also supported by the aforementioned Danish "Bandim

Health Project", which was founded by the anthropologist Sir Peter Aaby in the 1970s. It gathers local epidemiological data on more than 200,000 individuals. Since its foundation, this group has published more than 600 items on vaccines, maternal mortality and childhood infections such as RSV [50].

Timing, intensity and clinical impact of RSV infections vary worldwide [3]. Hence, research is still needed to alleviate the burden related to RSV in high-risk populations. Interventions should focus on data collection via established surveillance systems (e.g. aiming to define local morbidity and mortality, assist disease modeling, and guide prophylactic measures and vaccine development) [65]. In this context, our study revealed a striking discrepancy in scientific productivity and collaborative involvement between high- and low-income countries. Also, attention should be drawn to a further problem concerning low-income nations or countries whose researchers have a limited financial budget to pay for publication in renowned open access journals. This issue increases the apparent discrepancies regarding publication activities even further. To minimize this problem, a number of waiver programs currently exist, i.e. for journals like PLOS, Biomed Central or BMJ OPEN [66-68], but these should be expanded more broadly. However, we can deduce from our findings, that developing nations - although experiencing the most significant consequences of RSV epidemics - cannot compete equally in the field of RSV research due to the lack of funding and infrastructure. Therefore, we want to emphasize the need – an almost ethical responsibility - to involve these nations in funding programs and successful international collaborations as seen for Guinea-Bissau, Kenya and The Gambia. We acknowledge that the establishment of collaborations between high- and low-income nations is challenging due to the lack of resources, manpower and funding opportunities, the political climate, cultural

differences between the potential partners and a unrealistic assessment of the local research capacity and resources [69]. Also, existing collaborations and funding streams need to be viewed critically since they should rather reflect local disease burden, apparent healthcare disparities and scientific capability than being allocated based on a shared language or history between countries (e.g. guided by former colonial ties). Therefore, funding institutions should revise their policies appropriately [64]. Also, global investment surveillance systems need to be established such as the "Research Fairness Initiative" led by Cohred to guide and monitor sustainable, transparent and effective partnerships in research (, http://rfi.cohred.org/origin-of-the-rfi/). Nevertheless, tight-knit networks would be key for developing countries to participate in the international exchange of data, resources and knowledge, and to facilitate their involvement in high quality research efforts despite an unequal starting point.

Study Limitations

Our study has several limitations. Using the WoS to conduct this analysis is associated with an important strength but also with a weakness of the study. The WoS enabled us to assess not only quantitative but also qualitative aspects of the publication output related to RSV research. This is a unique feature allowing a multifaceted evaluation of the publication productivity. On the other hand, the WoS displays a strong preference for English journals. Therefore, not all articles ever published on RSV could be analyzed here. However, we regard this bias as limited as the majority of high quality data is commonly published in international journals indexed by the WoS and therefore definitely included in our search. Also, we acknowledge that not all eligible RSV publications were detected by the conducted "TITLE"-search. This approach was preferred to a "TOPIC" search, which identifies

the search term in the abstract and the keywords leading to a significant amount of off-topic publications compromising the validity of our data collection. We concentrated our study on original articles to focus on published “cutting edge research” in the field of RSV. We acknowledge that this strategy narrowed down the focus on the topic since other publication types such as commentaries, reviews, case reports, or meeting reports were not included. Further, we did not employ any additional platforms such as PubMed, Google Scholar or Scopus to collect bibliometric data because the management, organization and the scope of data is slightly different among these databases. This would affect triangulating, comparing and integrating data related to RSV research in a meaningful way.

We identified the first collaborative article on RSV in 1973, which would indicate that researchers from different countries did not work together on RSV before this point in time. This assumption is not necessarily true. In 1972, the WoS indexed author affiliations for the first time, which indicates that articles published in a joint effort before 1972 would not have been detected by our methodological approach. The evaluation of country-specific publication performance by gender is meaningful but should be evaluated critically. Not all first names were included in our analysis since some were gender-neutral, not listed in name databases or displayed as initials. Therefore, the threshold of at least 60 publishing scientists and 50% gender definability was implemented to include only countries providing meaningful and valid data. Further, we identified “Mortality associated with influenza and respiratory syncytial virus in the United States“ by Thompson et al. as the most cited journal article in the field of RSV. It received 1520 citations representing its outstanding recognition in the scientific community. The publication covers the topics RSV as well as Influenza, so the limitation has to be mentioned that our computed approach did

not differentiate if the article was cited in “influenza” or “RSV” papers. Employing a manual analysis, we found that 70,3 % of citing articles can be attributed to influenza, only 15,8 % to RSV, and 2.2 % were covering both topics. Hence, the impact of this particular paper on the field of RSV must be considered as less than it initially appeared based on the citation count alone.

Conclusion

We evaluated the worldwide RSV-related research output and demonstrated large differences between high-, middle-income or low-income nations regarding most scientometric variables. These discrepancies partly diminished when country-specific scientific activities were related to economic key measures; here, the leading position of the USA in science was challenged by other nations. Hence, calculating these quotients is beneficial for the comparison of countries with unequal conditions and different scientific infrastructures. However, we can deduce from our study that research efforts of middle-income or low-income nations have to be strengthened, e.g. by the reduction of journal fees and inclusion in international collaborations, so apparent disparities can be minimized and higher mortality rates related to RSV in developing nations can be tackled successfully.

Acknowledgements:

We thank Cristian Scutaru for the development and provision of the NewQIS analyzing tools. We also thank Mario Schwarzer, MD for supporting the study and helpful discussions as well as Jenny M. Jaque, MD for thoroughly editing our manuscript.

Source of Funding:

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors

Conflicts of Interest:

All authors state that they have no conflicts of interest to declare.

Data Sharing Statement:

Datasets of this study are available from the corresponding author upon request.

Authors' contributions:

DB, CK, DK, DAG, DO, JB and MB have made substantial contributions to the conception and design of the study, acquisition of the study data and have been involved in drafting and revising the manuscript. All authors have read and approved the final manuscript.

Figure Legends

Figure 1: Chronological development of the number of articles.

Figure 2: Density equalizing mapping projections (DEMP).

A) Number of publications B) Modified h-Index

Figure 3: Chronological development of annual citation numbers.

Figure 4: Density equalizing mapping projections (DEMP).

A) Articles/population-index (Q1)

B) Articles/GDP-index (Q2)

(Threshold ≥ 15 articles)

Figure 5: Density equalizing mapping projections (DEMP)

A) Articles/ R&D Expenditure in billion USD -index

B) Articles/ researcher (per billion inhabitants)-index

(Threshold ≥ 30 articles)

Figure 6: Country specific gender analysis of the authors publishing articles referring to RSV of countries.

(Threshold: > 50% definable genders, > 60 authors per country)

Figure 7: International cooperation (threshold ≥ 2 cooperations).

Numbers in brackets (number of publications/number of publications in cooperation

Figure 8: Most prolific journals in the field of RSV research in regards to overall publication numbers and the average citation rate.

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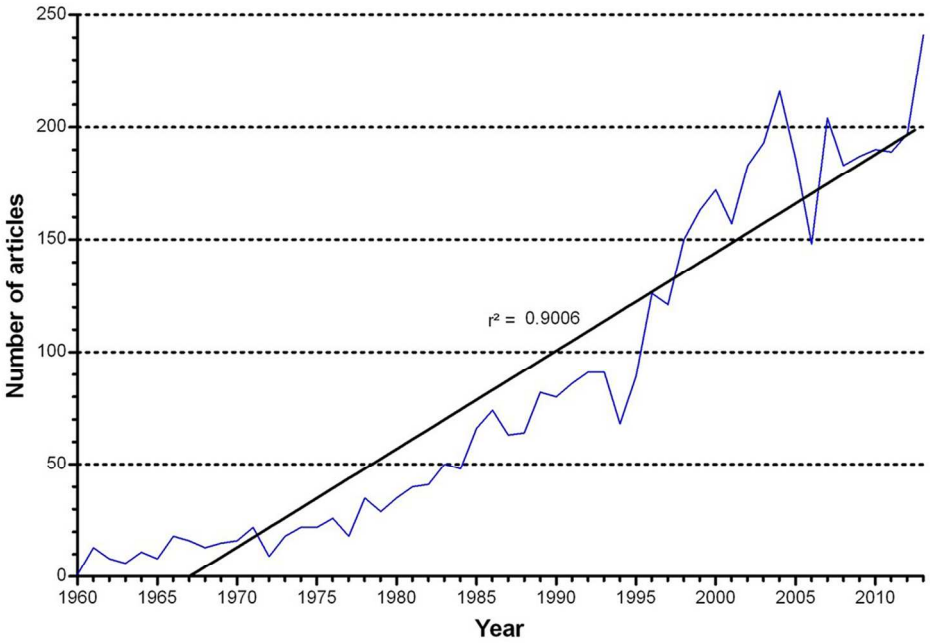

Figure 1: Chronological development of the number of articles.

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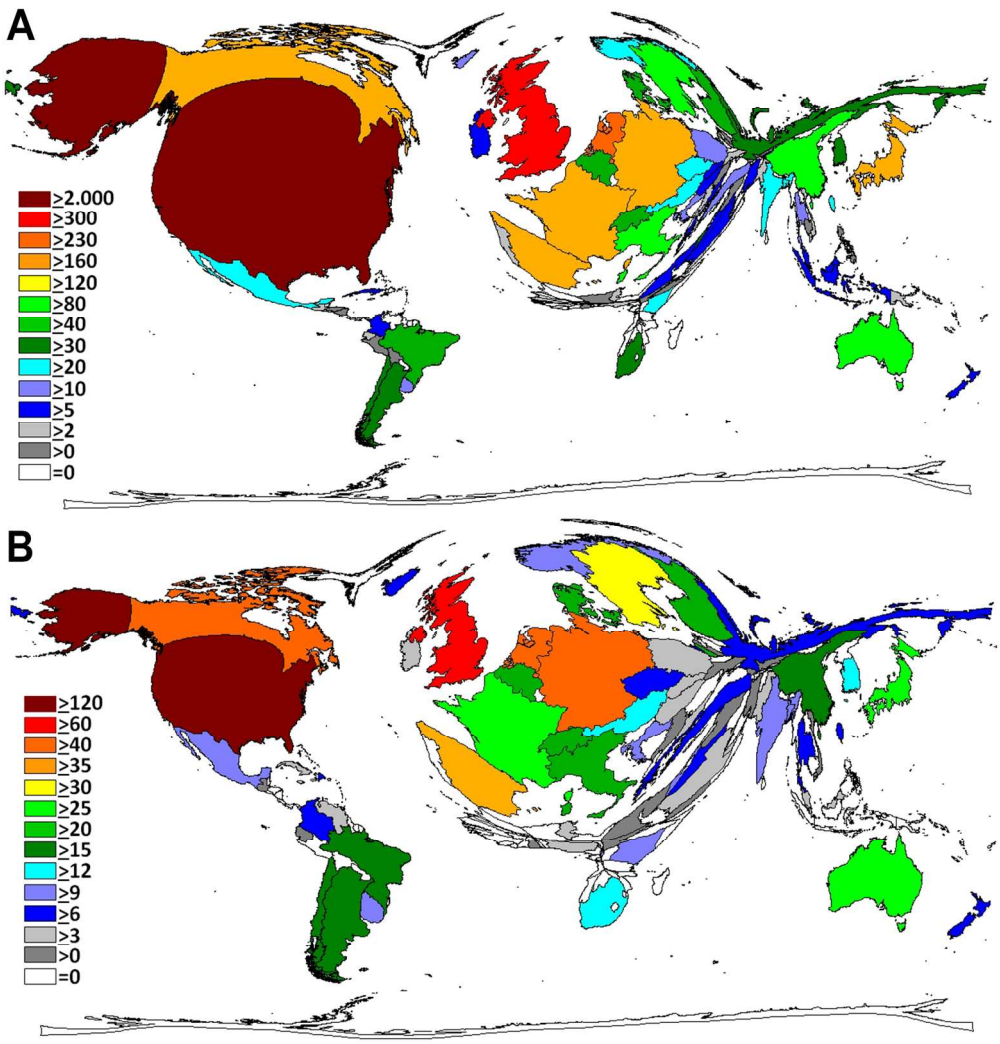

Figure 2: Density equalizing mapping projections (DEMP).
A) Number of publications
B) Modified h-Index

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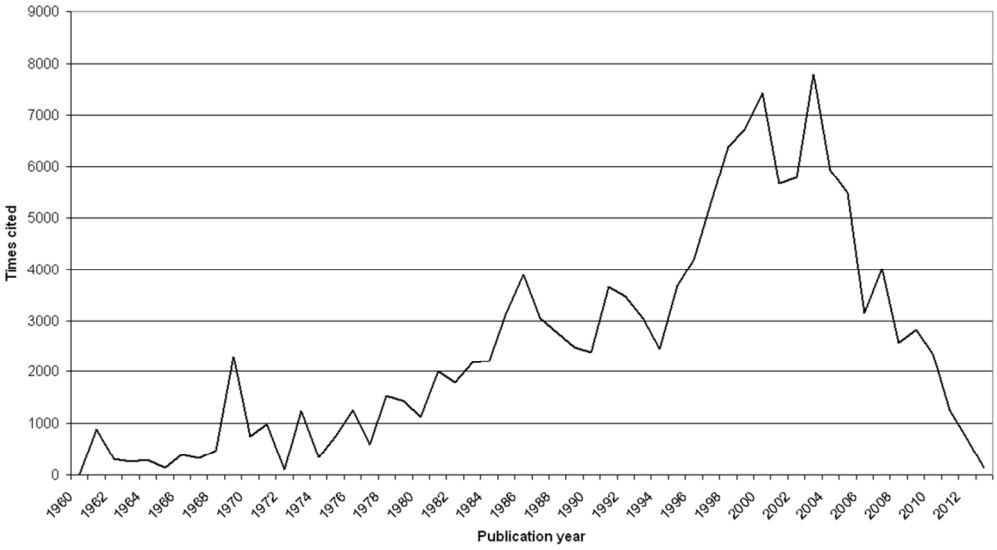

Figure 3: Chronological development of annual citation numbers.

109x61mm (300 x 300 DPI)

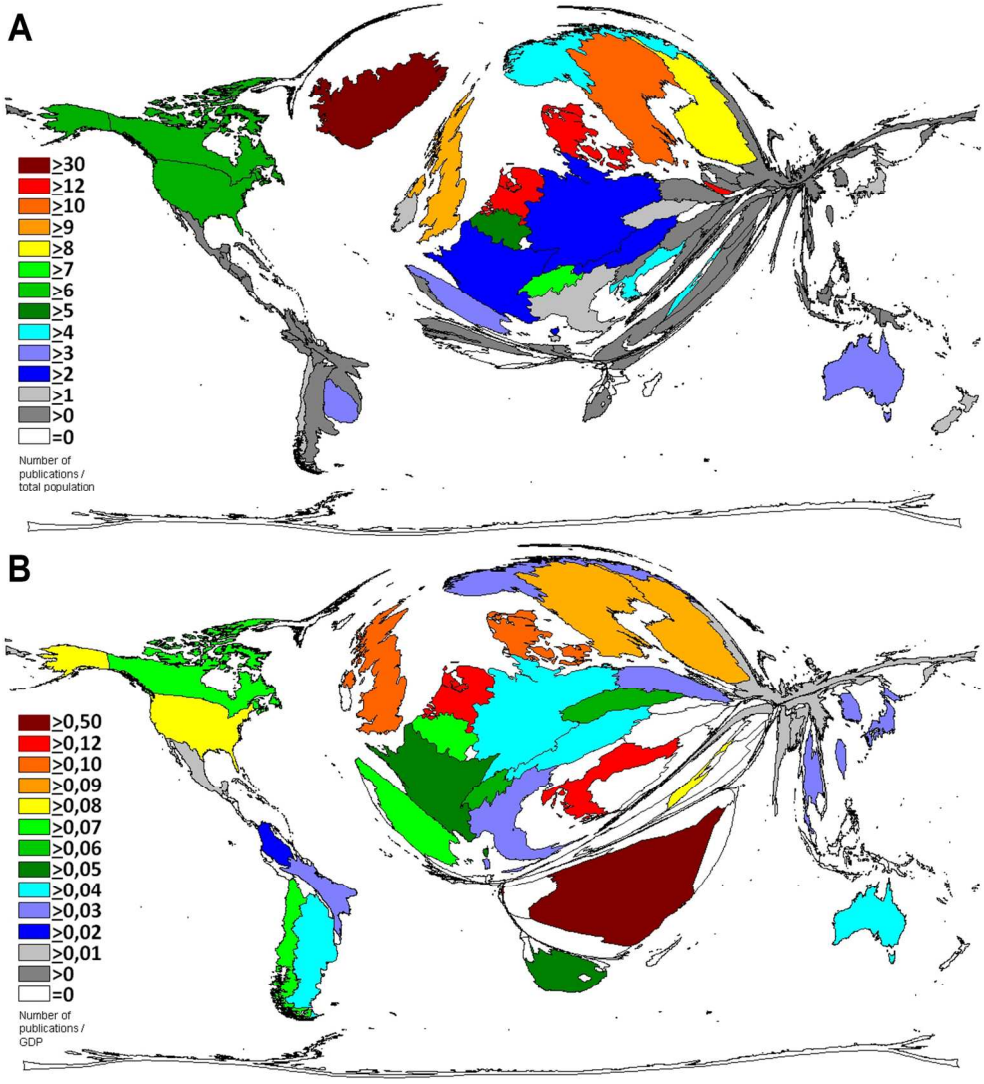

Figure 4: Density equalizing mapping projections (DEMP).
A) Articles/population-index (Q1)
B) Articles/GDP-index (Q2)
(Threshold > 15 articles)

203x220mm (300 x 300 DPI)

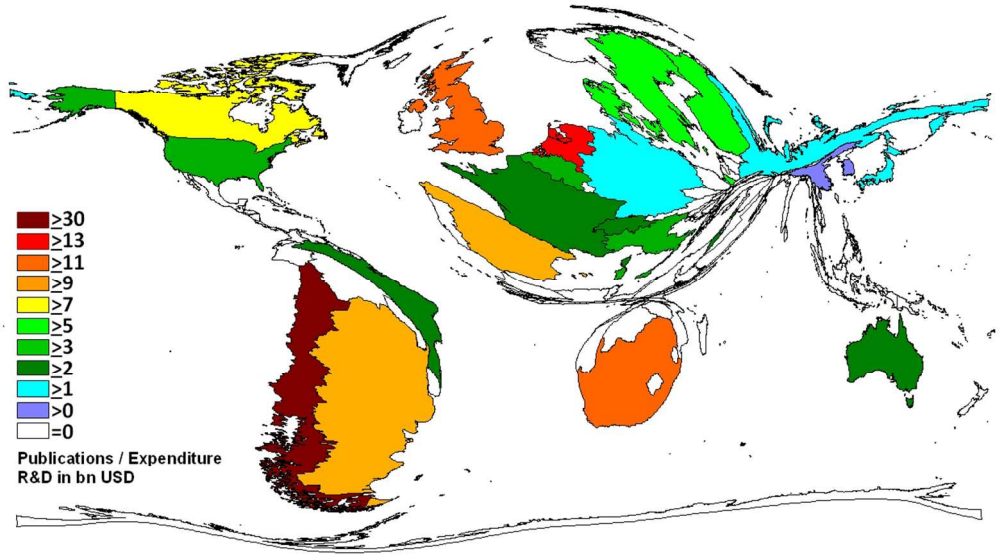

Figure 5A: Density equalizing mapping projections (DEMP). Articles/ R&D Expenditures in billion USD –index. (Threshold > 30 articles)

300x167mm (300 x 300 DPI)

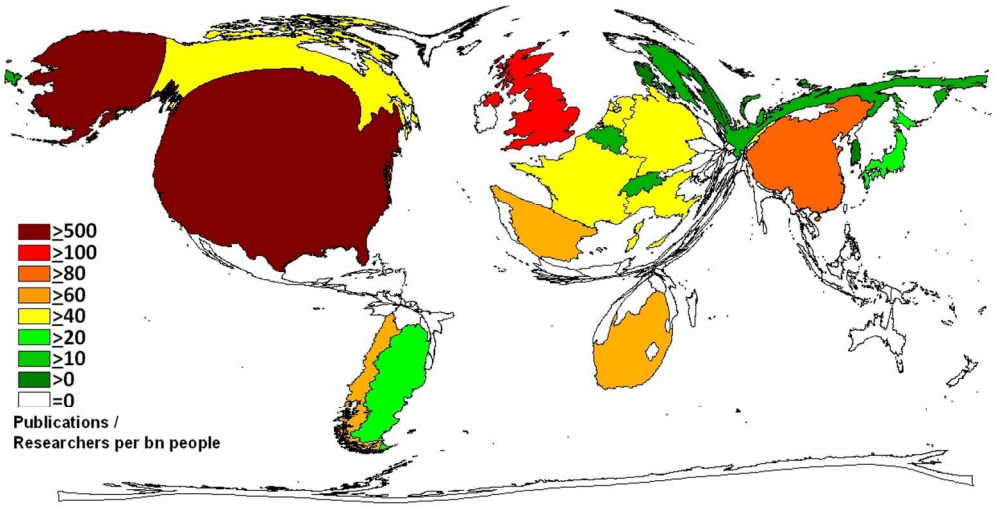

Figure 5B: Density equalizing mapping projections (DEMP). Articles/ researcher (per billion inhabitants)-index. (Threshold > 30 articles)

439x223mm (72 x 72 DPI)

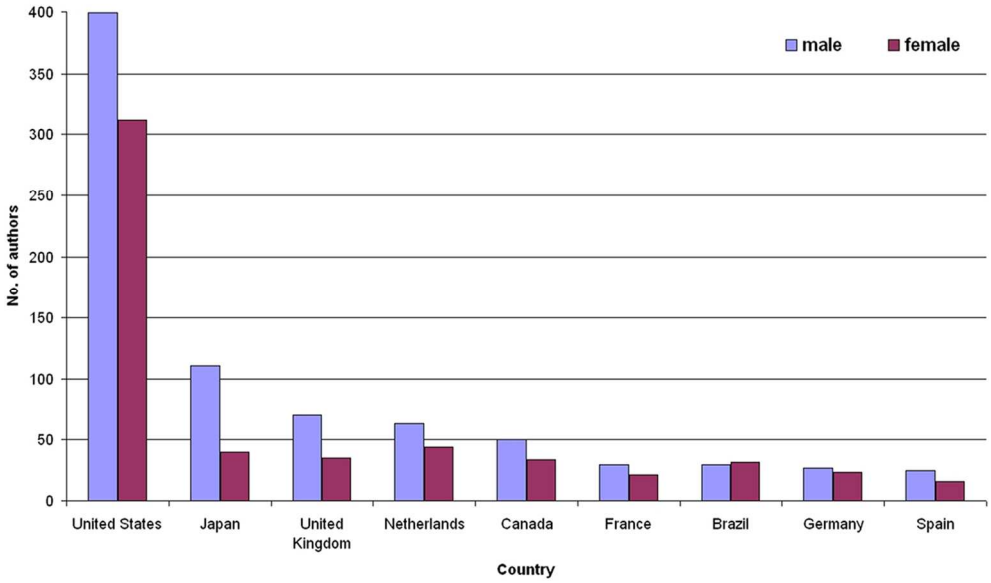

Figure 6: Country specific gender analysis of the authors publishing articles referring to RSV of countries. ‼ ┼ (Threshold: > 50% definable genders, > 60 authors per country)‼ ┼

109x65mm (300 x 300 DPI)

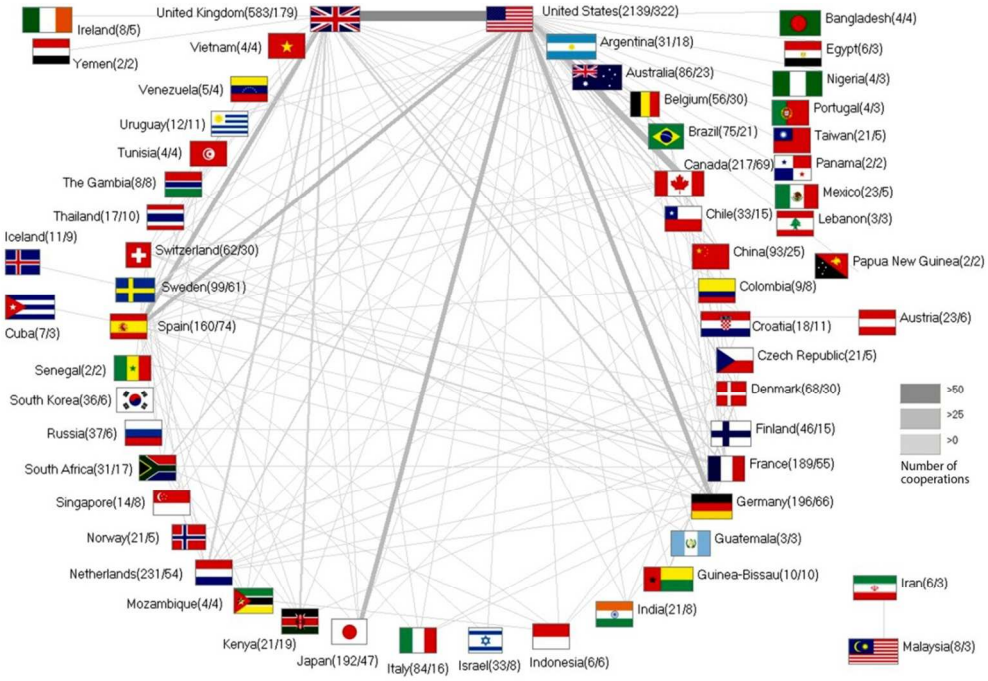

Figure 7: International cooperation (threshold > 2 cooperations). ‼ ┼ Numbers in brackets (number of publications/number of publications in cooperation)‼ ┼

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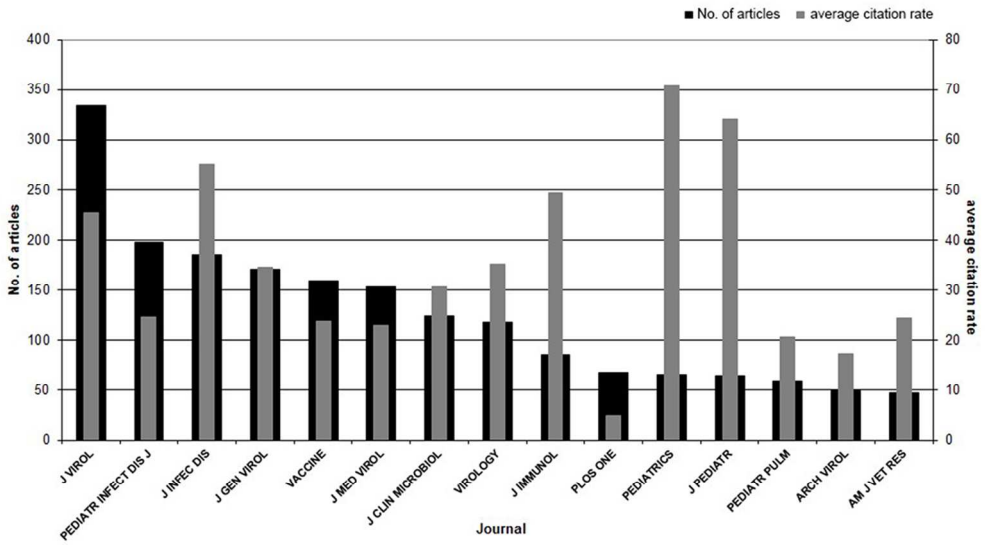

Figure 8: Most prolific journals in the field of RSV research in regards to overall publication numbers and the average citation rate.

109x65mm (300 x 300 DPI)