



RESEARCH PAPER

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A global bibliometric analysis of research productivity on vaccine hesitancy from 1974 to 2019

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ABSTRACT

Vaccine hesitancy is a phenomenon where individuals delay or refuse to take some or all vaccines. The objective of this study was to conduct a global bibliometric analysis of research productivity and identify country level indicators that could be associated with publications on vaccine hesitancy. We searched PubMed and Web of Science for publications from 1974 to 2019, and selected articles focused on behavioral and social aspects of vaccination. Data on country-level indicators were obtained from the World Bank. We used Spearman's correlation and zero-inflated negative-binomial regression models to ascertain the association between country level indicators and the number of publications. We identified 4314 articles, with 1099 eligible for inclusion. The United States of America (461 publications, 41.9%), Canada (84 publications, 7.6%) and the United Kingdom (68 publications, 6.2%) had the highest number of publications. Although various country indicators had significant correlations with vaccine hesitancy publications, only gross domestic product (GDP) and gross national income (GNI) per capita were independent positive predictors of the number of publications. When the number of publications were standardized by GDP, the Gambia, Somalia and Malawi ranked highest in decreasing order. The United States, Canada and United Kingdom ranked highest (in that order) when standardized by current health expenditure. Overall, high-income countries were more productive in vaccine hesitancy research than low-and-middle-income countries. There is a need for more investment in research on vaccine hesitancy in low-and-middle-income countries.

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Introduction

Vaccine hesitant individuals consist of a diverse group between vaccine acceptors and vaccine rejecters, who have varying degrees of doubts about vaccines.¹ The vaccine hesitant group may take or accept certain vaccines and deny some.² It is therefore imperative to communicate with vaccine hesitant individuals about the benefits of vaccination and address their concerns.³ Additionally, it is important to understand that vaccine hesitancy is multifaceted and therefore factors that contribute to hesitancy differ across populations, settings and vaccines.⁴ There are other factors that influence vaccine hesitancy including the confidence vaccine eligible individuals have in the providers. Another factor is complacency, i.e., not seeing the need to receive vaccines. Moreover, convenience, for example, access to and cost of vaccines may also play a role in driving vaccine hesitancy.^{3,5} Based on these factors, a model that explains the determinants of vaccine hesitancy, called the 3C model, was developed.⁶ This model has been used in different contexts, for various vaccines in order to assess the cause of vaccine hesitancy.⁷ Research publications have been identified as an important link between the generation of evidence and its use.⁸

Bibliometric methods have been used to provide quantitative analyses of written publications.⁹ Bibliometric analyses have

been conducted in different areas related to immunization research publications, some with a continental focus⁸ and others with a worldwide focus.¹⁰ However, we were not aware of a bibliometric analysis of vaccine hesitancy publications at the time of initiating this study. There was therefore a need to evaluate research productivity in the field of vaccine hesitancy. Conducting a bibliometric analysis on vaccine hesitancy would potentially contribute to establishing the factors that drive vaccine hesitancy in the world. In addition, this research will provide policy makers access to high-quality evidence concerning the factors that contribute to vaccine hesitancy research productivity. This study therefore aimed to conduct a worldwide bibliometric analysis of research productivity on vaccine hesitancy, provide insight into the growth of vaccine hesitancy research publications, and identify the country level factors that could be associated with vaccine hesitancy publications.

Materials and methods

Data sources

A search strategy was developed, and a comprehensive literature search performed in PubMed on the 10th of April 2019 and Web of Science on the 15th of April 2019, with no language

and date restrictions. The strategy comprised a broad list of keywords and related Medical Subject Headings (MeSH) terms. The keywords used in the search strategy included: vaccine, hesitancy, confidence, trust, convenience, complacency, refusal, acceptor, rejecter, delay, research and productivity (Table 1). Subsequently, titles and abstracts of the search output were screened by the lead author as per the inclusion and exclusion criteria. Articles related to vaccine hesitancy were considered eligible for inclusion and were defined as those which focused on public trust or distrust, refusal, acceptance, complacency, hesitancy, perceptions, concerns, confidence, attitudes and beliefs about vaccines and vaccination programmes. We excluded articles which were not about human vaccines or if publications were editorials, letters, commentaries and study protocols. We extracted data on country of first author and the year in which the paper was published. Country level indicators

We obtained data on different country level indicators from the World Bank on 11 March 2019.¹¹ These indicators included gross domestic product (GDP), adult total literacy, adult female literacy, adult male literacy, crude birth rate, crude death rate, current health expenditure, research and development (R&D) expenditure, gross national income (GNI) per capita, poverty head count rate and out-of-pocket expenditure (Table S1).

Statistical analyses

All data were analyzed using STATA, version15 (Stata Corp, College Station, Texas). Summary statistics were used to describe the number of vaccine hesitancy publications by country, and region using the World Bank country classification and time period. We also described the country-level indicators and ranked countries in terms of absolute number of publications as well as standardized by indicators. Spearman's correlation was used to determine the association between the number of publications (from 1974 to 2019) and 2015 country level indicators. We used 2015 because that was

Table 1. PubMed and web of science search strategies.

PubMed search query	Items found
Search terms	
#1 (Vaccination Refusal) OR (Vaccine refusal) OR (Anti Vaccination Movement) OR (Vaccine hesitant) OR (vaccination hesitant) OR (Vaccine hesitancy) OR (vaccination hesitancy) OR (immunization hesitancy) OR (immunization hesitant) OR (immunization refusal) OR (immunization hesitancy) OR (immunization hesitant) OR (immunization refusal)	1857
#2 "Pro-vaccination" OR "Vaccination acceptance" OR "vaccine acceptance" OR "Immunization acceptance" OR "Pro-vaccine" OR "Vaccine confidence" OR "Vaccination confidence"	738
#3 #1 OR #2	2391
Web of Science search query	
#1 (Vaccination Refusal) OR (Vaccine refusal) OR (Anti Vaccination Movement) OR (Vaccine hesitant) OR (vaccination hesitant) OR (Vaccine hesitancy) OR (vaccination hesitancy) OR (immunization hesitancy) OR (immunization hesitant) OR (immunization refusal) OR (immunization hesitancy) OR (immunization hesitant) OR (immunization refusal)	1428
#2 "Pro-vaccination" OR "Vaccination acceptance" OR "vaccine acceptance" OR "Immunization acceptance" OR "Pro-vaccine" OR "Vaccine confidence" OR "Vaccination confidence"	692
#3 #1 OR #2	1923

Table 2. Spearman correlations between indicators for different years.

	n	2015 vs 2010	n	2015 vs 2000
Adult female literacy	22	0.91	9	0.88
Adult male literacy	22	0.94	9	0.95
Adult total literacy	22	0.91	9	0.93
Crude birth rate	203	0.99	200	0.95
Crude death rate	204	0.96	200	0.81
Current health expenditure	185	0.89	181	0.73
GDP	200	0.99	192	0.98
GNI per capita	189	0.99	175	0.95
Out-of-pocket expenditure	184	0.93	177	0.84
Poverty head count	56	0.9	17	0.68
R&D expenditure	64	0.96	53	0.91

the most recent year with complete country level indicators. The country level indicators for 2015 were compared to the indicators for 2000 and 2010, using the Spearman correlation test (Table 2). We found high correlations (Table 2), suggesting that the 2015 indicators provide a suitable estimation of indicators from previous years. Predictors of publication output were assessed using univariable and multivariable zero-inflated negative-binomial (ZINB) models. Logistic regression was used to determine predictors of countries with no publication output to inform our ZINB model. Predictors for which most countries had information were also taken into consideration. Results were considered statistically significant when the *p* value was less than 0.05.

Results

A total of 5680 articles published between 1974 and 2019 was retrieved from PubMed and Web of Science databases. After removing duplicates, a total of 4314 records were left; and of those, 3215 were considered ineligible while 1099 were related to vaccine hesitancy and hence considered eligible for inclusion in this study (Figure 1). The data were stratified according to a country's number of vaccine hesitancy publications. The data show 217 countries with a total of 1099 publications over the 1974–2019 period (Figure 2, Table S2). The economic status of countries was classified according to GNI per capita, i.e., low-income (GNI per capita of \$1,035 or less), lower-middle income (GNI per capita between \$1,036 and \$4,045), upper-middle income (GNI per capita between \$4,046 and \$12,535), and high-income (GNI per capita of \$12,536 or more) countries. The number of publications were also classified according to seven regions derived from the World Bank,¹² namely, East Asia and the Pacific, Europe and Central Asia, Latin America and the Caribbean, Middle East and North Africa, North America, South Asia and sub-Saharan Africa (Figure 3, Table S2).

North America had the largest number of publications, followed by Europe and Central Asia, and East Asia and the Pacific (Figure 2, Table S3). Country ranking according to the number of publications were also indicated, with the United States of America (USA) having the highest number of vaccine hesitancy publications (461 publications, 41.9%), followed by Canada (84 publications, 7.6%) and United Kingdom (UK: 68 publications, 6.2%) (Table S4). Our results indicate some countries with between 20 and 30 publications, e.g., Australia (N = 28) and Italy (N = 28) while other countries like Malaysia, Nigeria, Pakistan, Sweden, South Africa and

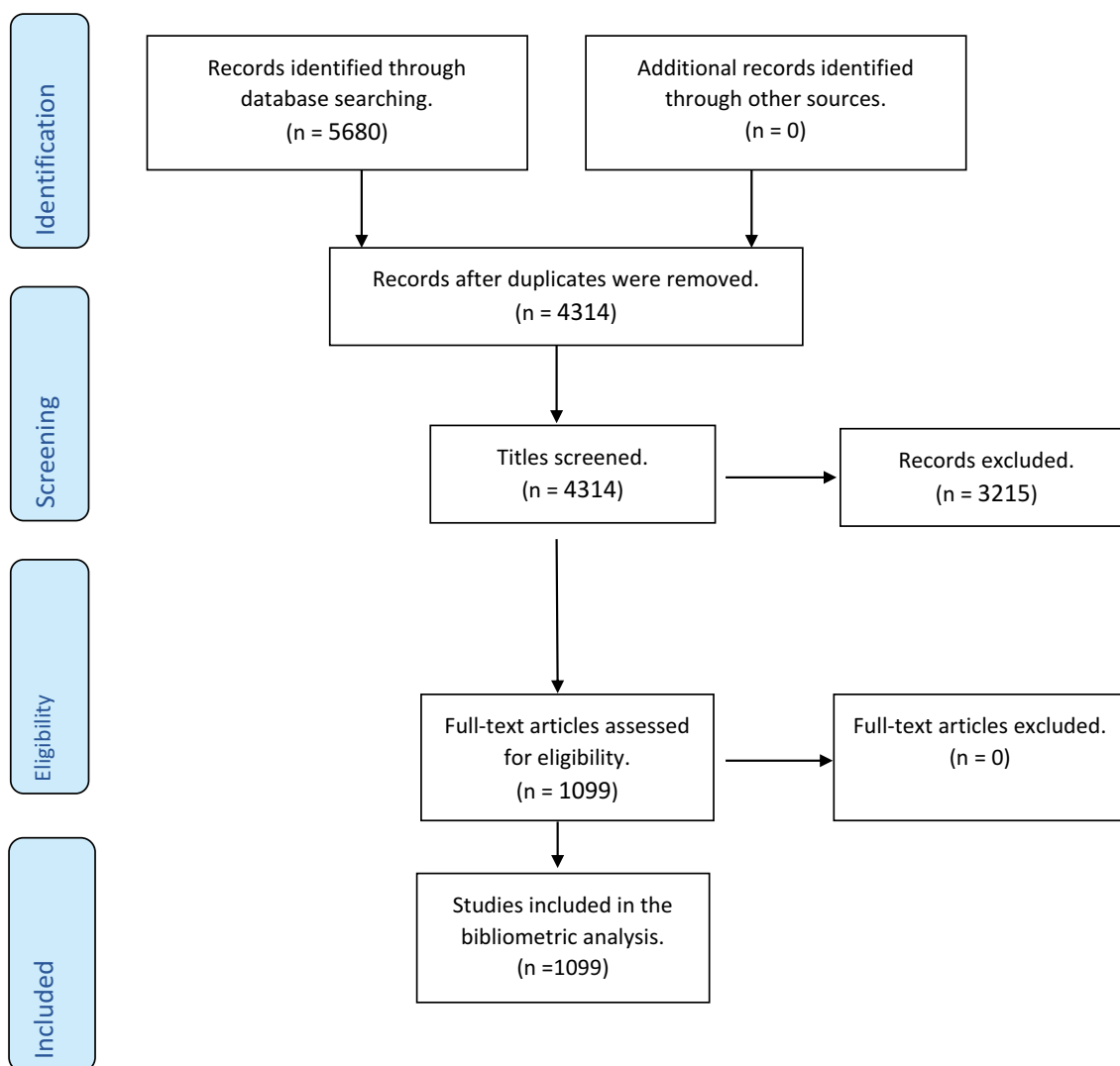


Figure 1. Study selection process for the bibliometric analysis.

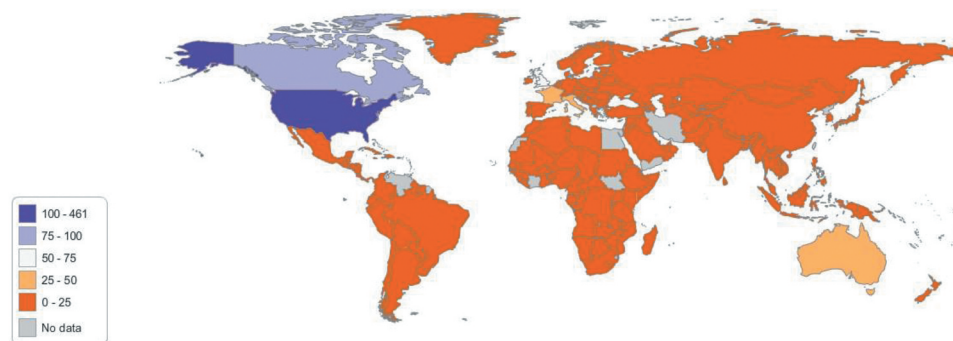


Figure 2. Geographic distribution of publications in vaccine hesitancy from 1974 to 2019. The map was created using StatPlanet version 2.2. The map is color coded where countries with the purple color had the highest publications while those with the orange color had the lowest publications. Countries with no color indicate that there were no publications available.

Thailand had 10 publications or less. When we standardized the countries' number of vaccine hesitancy publications by GDP, our results showed that the Gambia followed by Somalia and Malawi ranked highest (Table S5a). The USA followed by Canada and the UK ranked highest when standardized by current health expenditure (Table S5b).

There was a strong positive and statistically significant correlation between countries' number of vaccine hesitancy publications and crude death rate (p value = .016), GDP (p value = .001), GNI per capita (p value = .002) and R&D expenditure (p value = .001). Furthermore, a strong and negative correlation was observed between countries'

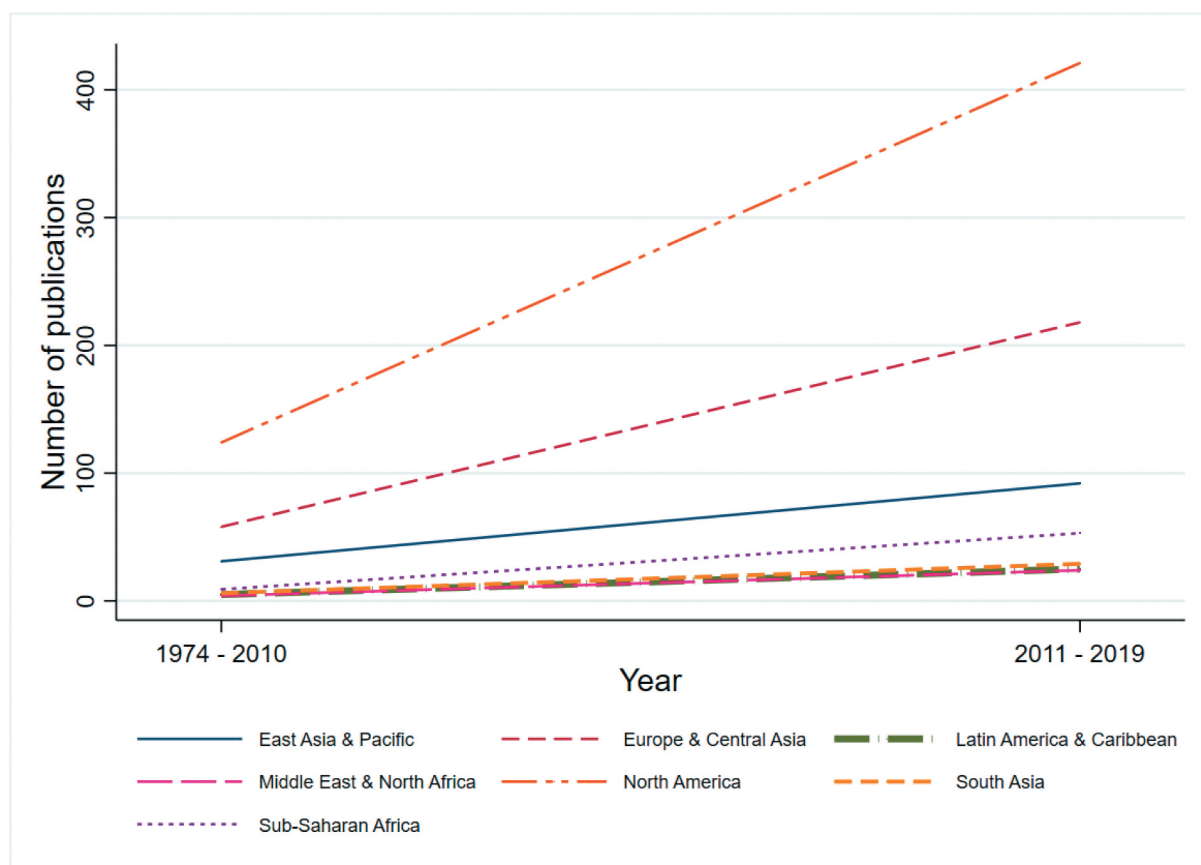


Figure 3. The number of publications in the seven World Bank regions of the world, namely, East Asia and the Pacific, Europe and Central Asia, Latin America and the Caribbean, Middle East and North Africa, North America, South Asia, and sub-Saharan Africa.

number of vaccine hesitancy publications and crude birth rate (p value = .03). No significant association was seen between countries' number of vaccine hesitancy publications and other indicators, such as adult female literacy, adult male literacy, adult total literacy, current health expenditure, out-of-pocket expenditure and poverty head count (Table 3). Table 4 presents the regression results. In the univariable model, crude birth rate (incidence rate ratio [IRR] 0.92, 95% confidence interval [CI] 0.89 to 0.94), current health expenditure (IRR 1.31, 95% CI 1.22 to 1.40), GDP (IRR 1, 95% CI 1 to 1), GNI per capita (IRR 1, 95% CI 1 to 1), out-of-pocket-expenditure (IRR 0.96, 95% CI 0.95 to 0.98), poverty head count (IRR 0.97, 95% CI 0.94 to 1.00) and R&D expenditure (IRR 2.78, 95% CI 1.86 to 4.16) had a statistically significant association with number of vaccine hesitancy publications. In the multivariable model, only GDP and GNI per capita were significantly associated with countries' number of vaccine hesitancy publications (Table 4).

Discussion

In this investigation, we evaluated vaccine hesitancy research productivity from 1974 to 2019 and determined if that was correlated with country level indicators in different settings

Table 3. Correlation of publications between 1974 and 2019 with country level indicators (2015).

	Spearman's rho	p-value
Adult female literacy	-0.1637	.326
Adult male literacy	-0.1105	.509
Adult total literacy	-0.1612	.334
Crude birth rate	-0.1521	.030
Crude death rate	0.1681	.016
Current health expenditure	0.1027	.162
GDP	0.6512	<.001
GNI per capita	0.2276	.002
Out-of-pocket expenditure	-0.0898	.341
Poverty head count	-0.2094	.087
R&D expenditure	0.4966	<.001

and regions categorized by the World Bank. During the 1974 to 2019 period, vaccine hesitancy research productivity increased in all the regions, although the increase in low-and-middle-income regions was insignificant. This study shows that three high-income countries (two countries from North America, that is, the USA and Canada, and one country in Europe and Central Asia, i.e., the UK) produced most of the world's research around vaccine hesitancy. It is interesting to note that when countries were standardized by current health expenditure, the same pattern was observed where the USA, Canada and the UK were the most productive countries.

Table 4. Univariable and multivariable zero-inflated negative-binomial regression models.*

Variable	Univariable			Multivariable (n = 182)	
	n	IRR (95% CI) ^a	p-value	IRR (95% CI) ^a	p-value
Adult total literacy	37	1.03 (1.01–1.05)	.007		
Crude birth rate	185	0.92 (0.89–0.94)	<.001		
Crude death rate	185	1.15 (0.92–1.43)	.217		
Current health expenditure	182	1.31 (1.22–1.40)	<.001	0.92 (0.82–1.03)	.142
GDP	191	1 (1–1)	<.001	1 (1–1)	.002
GNI per capita	191	1 (1–1)	<.001	1 (1–1)	<.001
Out-of-pocket expenditure	180	0.96 (0.95–0.98)	<.001		
Poverty head count	68	0.97 (0.94–1.00)	.033		
R&D expenditure	83	2.78 (1.86–4.16)	<.001		

*Using GDP and GNI (2015) as predictors for the zero-inflation.

^aIncidence-rate ratio (IRR) presented with the 95% confidence interval (CI).

However, when the countries were adjusted by GDP, three low-income countries (the Gambia, followed by Somalia and Malawi) ranked the highest in vaccine hesitancy research productivity.

Bibliometric analysis is an active area of research and has been used to statistically evaluate published scientific articles from numerous geographical areas and scientific fields.^{13–24} In our study, the settings with high research productivity around vaccine hesitancy are high-income countries. In concordance with previous investigations, this study has shown that the more developed a country's economy is, the higher its research productivity.^{13–19} This might be because rich countries are more likely to provide funding to develop research infrastructure and fund research activities.

While high-income countries had a significant number of vaccine hesitancy publications in the period between 1974 and 2019, the contribution of low-and-middle-income countries to vaccine hesitancy research productivity was minimal. The study shows that regions with predominantly low-income and middle-income countries (i.e., Latin America and the Caribbean, Middle East and North Africa, South Asia and sub-Saharan Africa) are behind in the number of vaccine hesitancy research publications. Previously conducted bibliometric studies reported similar results in different fields, where low-and-middle-income countries had lower research productivity relative to high income-settings.^{13–20} One of the studies reported that Western Europe led the world regarding the scientific production of research papers in parasitology from 1995 to 2003.¹⁵ Another study, by Falagas et al., reported that North America and Western Europe produced three-quarters of publications in virology between 1995 and 2003, with North America exceeding Western Europe in the number of published articles.¹⁶ The study by Cimmino et al. reported that Europe plays an important role in otolaryngology research and publications.¹⁷ In addition, a recent bibliometric study found that North America produced most of the top 50 publications on the management of pelvic trauma.¹⁹ Another recent study showed that most of the 100 top-cited publications on vaccines originated from North America and Western Europe.¹⁴ Similar findings were reported from an assessment of global vaccine hesitancy literature from 1990 to 2019.¹³

Within low-and-middle-income regions, countries at not at the same level of productivity.^{20,21,23,24} For example, while Africa's contribution to the global research output is minimal,²⁴ research

productivity on the continent is highly skewed.^{8,20,21} Uthman reported that three sub-Saharan African countries (South Africa, Nigeria and Uganda) produce more than half of the peer-reviewed publications on HIV.²⁰ The author found that the better economic ranking of a country the higher the quantity of its research productivity; a finding which has been confirmed by others.^{8,24} These data imply that there may be poor health research funding support and poor research infrastructure in under-productive countries, which may be possible contributors to low productivity in vaccine hesitancy research. Based on the present and previous findings, it is evident that there is a need to invest in research infrastructure in low-and-middle-income countries. These include countries not only in African but also those in the Middle East, Latin America and the Caribbean, and South Asia. The vaccine hesitancy publication output in each region could also experience healthy growth with definition of a coordinated, strong and up-to-date strategic plan for research on the topic in the region.²⁴

Based on our analyses, GDP and GNI per capita are the main factors associated with vaccine hesitancy research productivity. In consonance with this present investigation, other studies also reported that GDP, GNP per capita and R&D expenditure were significantly associated with research productivity in other scientific fields.^{21–23} These results suggest that low-and-middle-income countries from all the different regions should focus on strengthening or improving research capacity and infrastructure to enhance research outputs. Increasing capacity will enable researchers to conduct research that assesses whether vaccine hesitancy is a problem in their respective countries, and research on tailored interventions to address it. This is especially important in the current context of the global rollout of vaccination against coronavirus disease 2019, amidst increasing vaccine hesitancy.²⁵

Limitations of the study

This investigation has some limitations including the fact that we did not search all databases and therefore may have missed some publications around vaccine hesitancy. In addition, the databases where the articles were sourced were limited to the English language and therefore this may have contributed to the risk of selection bias. We would like to highlight that the titles and abstracts of the search outputs were screened by one author (AJ). Similarly, eligible studies for this investigation

were selected by AJ and hence there may be possible human error during this process. Other limitations include the possible incorrect citation of the authors' countries of origins where the addresses listed in the research articles were used to identify this. Moreover, we only used the number of publications as a standard of research productivity and acknowledge that other factors including impact factor, citation index and conference presentations may also be used as a measure.²²

Conclusions

This paper evaluated vaccine hesitancy research productivity from the 1974 to the 2019 period. The findings of the study indicate that countries in high-income regions, viz., North America (USA and Canada) and Europe and Central Asia (UK) produced the highest number of vaccine hesitancy publications compared to low-and-middle-income regions, e.g., Sub-Saharan Africa. The data from this investigation also prove that country level indicators, such as the GDP and GNI per capita are the main determinants of productivity in vaccine hesitancy research. This bibliometric analysis will lead the development and implementation of suitable multi-component interventions to strengthen research capacity in Sub-Saharan Africa and enhance vaccine hesitancy research productivity. Our results show that there is a relationship between research advancement and the countries' economies, i.e., wealthy and poor countries differ in their research output around vaccine hesitancy research. Countries with higher relative productivity had the highest economic growth compared to those with low research productivity. It is important to understand the role that economic growth and stability play as a determinant of a country's research and development, which affects research productivity. This shows that a country's economy is effective in achieving a higher research productivity. The difficulties encountered in producing knowledge in low- and middle-income countries give the government a role in promoting research and development to improve productivity. Research institutions in low- and middle-income countries, particularly in Africa, face serious challenges in terms of research funding as they do not receive enough funds from their governments.

Therefore, governments from low- and middle-income countries must increase funding for research, as this will potentially increase human capital and build capacity to carry out research which will in turn contribute to socioeconomic development. Furthermore, activities to strengthen capacity in research are based on an individual (e.g., the knowledge, skills, attitudes and competencies of early career researchers) and organizational level (e.g., based on support structures including finance and management). Early career researchers also play pivotal roles in the creation of new knowledge. Therefore, a detailed more understanding of the challenges faced by these young researchers and investing in the factors influencing their research productivity is also important.

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Author contributions

CSW conceived the manuscript. EP designed the search strategies. YB conducted all the statistical analyses. AJ wrote the first draft. CJI, YB, EP and CSW made a significant intellectual contribution to the manuscript and approved the final version.

Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

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