

RESEARCH PAPER



## The 100 top-cited studies on vaccine: a bibliometric analysis

Yonggang Zhang<sup>a,b</sup>, Liuliu Quan<sup>c</sup>, Bowen Xiao<sup>c</sup>, and Liang Du<sup>a,b</sup>

<sup>a</sup>Department of Periodical Press and National Clinical Research Center for Geriatrics, West China Hospital, Sichuan University, Chengdu, Sichuan, P. R. China; <sup>b</sup>Chinese Evidence-based Medicine Center, West China Hospital, Sichuan University, Chengdu, P.R. China; <sup>c</sup>West China School of Medicine, Sichuan University, Chengdu, P.R. China

### ABSTRACT

**Objective:** The objective of this study was to analyze the 100 most cited studies on vaccine.

**Methods:** A comprehensive search of studies on vaccine was performed in the Web of Science Core Collection without year or language restrictions. The 100 top-cited studies were retrieved after screening abstracts or full-texts. The outcomes of bibliometric analysis included citation time, citation density, journal name, impact factor, publication year, article type, category, open access, and country of origin.

**Results:** The citation times for the 100 top-cited studies ranged from 593 to 2406, with a median citation times of 834. The 100 top-cited studies were published in 32 journals, and the journal with the most studies was *New England Journal of Medicine* ( $n = 20$ ). They were published between 1969 and 2012, and 4 authors published at least 2 studies as the first author. The USA contributed the most studies ( $n = 70$ ), followed by Switzerland ( $n = 4$ ), England ( $n = 4$ ) and Finland ( $n = 4$ ). Eighty-one studies were published as Article, while 19 were Review. Eleven studies were about vaccine for therapeutic and 68 studies were about vaccine for prophylactic.

**Conclusions:** This is the first bibliometric analysis to provide a detailed list of the 100 most-cited studies on vaccine and helps to recognize the quality of the works, discoveries, and trends in the field.

### ARTICLE HISTORY

Received 18 March 2019

Revised 4 April 2019

Accepted 25 April 2019

### KEYWORDS

Vaccine; bibliometric analysis; citation analysis; top-cited; citation

### Introduction

The vaccine is a biological preparation that provides active acquired immunity to a particular disease.<sup>1–3</sup> The main types of vaccines include live-attenuated vaccine, inactivated vaccine, subunit, recombinant, polysaccharide, and conjugate vaccine and toxoid vaccine.<sup>4</sup> Vaccines help protect millions of healthy people,<sup>4–6</sup> they are considered as the most economical and effective preventive measure against the most deadly infectious diseases.<sup>2</sup> WHO reported that 116 million infants worldwide received three doses of diphtheria-tetanus-pertussis vaccine, and about 85% of the world's children received one dose of measles vaccine by their first birthday through routine health services in 2015.<sup>7</sup>

Studies for vaccine development have been conducted year by year,<sup>2,8–10</sup> although there has been marked progress in vaccine development, challenges still exist,<sup>8,11</sup> including economic, vaccination for new emerging infectious diseases, and so on. The achievement on vaccine was reflected by scientific studies,<sup>12</sup> particularly in the most cited studies.<sup>13,14</sup> Citation analysis is a type of bibliometric analysis in which evaluation and ranking of an article are done on the basis citation count.<sup>15</sup> Identification the milestones in a specific field can be done by analyzing the most cited study, especially by analyzing the 100 top-cited studies.<sup>13,14,16,17</sup> Assessment of the 100 top-cited studies had been conducted for various diseases including tuberculosis,<sup>18</sup> diabetes,<sup>14</sup> emergency medicine,<sup>19</sup> etc. However, there is no such study on the vaccine. Thus, we performed the current study to identify the 100 top-cited studies on vaccine.

### Results

#### Citation analysis

The 100 top-cited studies are listed in Table 1. They have been cumulatively cited 94,328 times. The median number of citations was 834, with a range of 593 to 2406. Only 3 studies were cited more than 2000 times, and a great number of studies ( $n = 32$ ) were cited between 1000 and 2000 times. The first top-cited study was “Vaccination with irradiated tumor-cells engineered to secrete murine granulocyte-macrophage-colony-stimulating factor stimulates potent, specific, and long-lasting antitumor immunity” published by Dranoff et al. in *Proceedings of The National Academy of Sciences of The United States of America* in 1993.<sup>20</sup> The second top-cited study was by Schenk et al. and received 2384 citations. The article explained the immunization with amyloid-beta attenuates Alzheimer disease-like pathology in the PDAPP mouse and was published in 1999 in *Nature*.<sup>21</sup> The third top-cited paper was published by Nestle et al. and it studied the vaccination of melanoma patients by using peptide- or tumor lysate-pulsed dendritic cells. It was published in *Nature Medicine*.<sup>22</sup>

#### Journal

The 100 top-cited studies were published in 32 journals (Table 2). The journal with the highest publication number was *New England Journal of Medicine* (NEJM) ( $n = 20$ ), followed by *The Lancet* ( $n = 11$ ). The *Science*, *Nature Medicine*, *Nature*, *Nature Reviews Immunology* each have at least five

Table 1. The 100 top-cited studies on vaccine.

Ranking	Title	Journal	Citation times	Publication year	Mean citation per year	Country
1	Vaccination with irradiated tumor-cells engineered to secrete murine granulocyte-macrophage colony-stimulating factor stimulates potent, specific, and long-lasting antitumor immunity	P Natl Acad Sci USA	2406	1993	93	USA
2	Immunization with amyloid-beta attenuates Alzheimer disease-like pathology in the PDAPP mouse	Nature	2384	1999	119	USA
3	Vaccination of melanoma patients with peptide- or tumor lysate-pulsed dendritic cells	Nat Med	2343	1998	112	Germany
4	Cancer immunotherapy: moving beyond current vaccines	Nat Med	1891	2004	126	USA
5	Vaccination with ALVAC and AIDSVAX to Prevent HIV-1 Infection in Thailand	New Engl J Med	1769	2009	177	USA
6	Efficacy, safety and immunogenicity of heptavalent pneumococcal conjugate vaccine in children	Pediatr Infect Dis J	1591	2000	84	USA
7	Decline in invasive pneumococcal disease after the introduction of protein-polysaccharide conjugate vaccine	New Engl J Med	1551	2003	97	USA
8	Aromatic-dependent salmonella-typhimurium are non-virulent and effective as live vaccines	Nature	1497	1981	39	USA
9	Vaccination of patients with B-cell lymphoma using autologous antigen-pulsed dendritic cells	Nat Med	1484	1996	65	USA
10	Immunologic and therapeutic evaluation of a synthetic peptide vaccine for the treatment of patients with metastatic melanoma	Nat Med	1474	1998	70	USA
11	Efficacy of BCG vaccine in the prevention of tuberculosis – metaanalysis of the published literature	Jama-J Am Med Assoc	1326	1994	53	USA
12	A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults	New Engl J Med	1274	2005	91	USA
13	A beta peptide vaccination prevents memory loss in an animal model of Alzheimer's disease	Nature	1212	2000	64	USA
14	Universal hepatitis B vaccination in Taiwan and the incidence of hepatocellular carcinoma in children	New Engl J Med	1186	1997	54	China
15	Safety and efficacy of a pentavalent human-bovine (WC3) reassortant rotavirus vaccine	New Engl J Med	1181	2006	91	USA
16	Synthetic peptide vaccine design – synthesis and properties of a high-density multiple antigenic peptide system	P Natl Acad Sci USA	1179	1988	38	USA
17	A beta peptide immunization reduces behavioural impairment and plaques in a model of Alzheimer's disease	Nature	1151	2000	61	Canada
18	Safety and efficacy of an attenuated vaccine against severe rotavirus gastroenteritis	New Engl J Med	1151	2006	89	Chile
19	A controlled trial of a human papillomavirus type 16 vaccine	New Engl J Med	1151	2002	68	USA
20	Quadrivalent vaccine against human papillomavirus to prevent anogenital diseases	New Engl J Med	1132	2007	94	Australia
21	Respiratory syncytial virus disease in infants despite prior administration of antigenic inactivated vaccine	Am J Epidemiol	1132	1969	23	USA
22	Comparative genomics of BCG vaccines by whole-genome DNA microarray	Science	1123	1999	56	Canada
23	New use of BCG for recombinant vaccines	Nature	1102	1991	39	USA
24	Quadrivalent vaccine against human papillomavirus to prevent high-grade cervical lesions	New Engl J Med	1101	2007	92	USA
25	Broad and Potent Neutralizing Antibodies from an African Donor Reveal a New HIV-1 Vaccine Target	Science	1099	2009	110	USA
26	Sustained efficacy up to 4–5 years of a bivalent L1 virus-like particle vaccine against human papillomavirus types 16 and 18: follow-up from a randomised control trial	Lancet	1094	2006	84	USA
27	Efficacy of a bivalent L1 virus-like particle vaccine in prevention of infection with human papillomavirus types 16 and 18 in young women: a randomised controlled trial	Lancet	1092	2004	73	USA
28	Efficacy assessment of a cell-mediated immunity HIV-1 vaccine (the Step Study): a double-blind, randomised, placebo-controlled, test-of-concept trial	Lancet	1078	2008	98	USA
29	Prophylactic quadrivalent human papillomavirus (types 6, 11, 16, and 18) L1 virus-like particle vaccine in young women: a randomised double-blind placebo-controlled multicentre phase II efficacy trial	Lancet Oncol	1064	2005	76	Brazil
30	Eradication of established murine tumors using a novel cell-free vaccine: dendritic cell-derived exosomes	Nat Med	1044	1998	50	France
31	Efficacy of a pneumococcal conjugate vaccine against acute otitis media	New Engl J Med	1026	2001	57	Finland
32	DNA vaccines	Annu Rev Immunol	1020	1997	46	USA
33	Effector and memory T-cell differentiation: Implications for vaccine development	Nat Rev Immunol	1015	2002	60	USA
34	Hepatitis B vaccine: demonstration of efficacy in a controlled clinical trial in a high-risk population in the United States	New Engl J Med	1009	1980	26	USA
35	Neuropathology of human Alzheimer disease after immunization with amyloid-beta peptide: a case report	Nat Med	1001	2003	63	England
36	Replication-incompetent adenoviral vaccine vector elicits effective anti-immunodeficiency-virus immunity	Nature	988	2002	58	USA

(Continued)

Table 1. (Continued).

Ranking	Title	Journal	Citation times	Publication year	Mean citation per year	Country
37	Immune-Correlates Analysis of an HIV-1 Vaccine Efficacy Trial	New Engl J Med	980	2012	140	USA
38	Vaccination with Mage-3A1 peptide-pulsed mature, monocyte-derived dendritic cells expands specific cytotoxic T cells and induces regression of some metastases in advanced stage IV melanoma	J Exp Med	963	1999	48	Germany
39	Protective effects of a live attenuated SIV vaccine with a deletion in the NEF gene	Science	941	1992	35	USA
40	Efficacy of human papillomavirus (HPV)-16/18 AS04-adjuvanted vaccine against cervical infection and precancer caused by oncogenic HPV types (PATRICIA): final analysis of a double-blind, randomised study in young women	Lancet	939	2009	94	Finland
41	Control of a mucosal challenge and prevention of AIDS by a multiprotein DNA/MVA vaccine	Science	938	2001	52	USA
42	DNA vaccines: Immunology, application, and optimization	Annu Rev Immunol	925	2000	49	USA
43	T-cell quality in memory and protection: implications for vaccine design	Nat Rev Immunol	920	2008	84	USA
44	DNA vaccines: protective immunizations by parenteral, mucosal, and gene-gun inoculations.	P Natl Acad Sci USA	913	1993	35	USA
45	Variation in protection by BCG: implications of and for heterologous immunity.	Lancet	874	1995	36	England
46	Multifunctional T(H)1 cells define a correlate of vaccine-mediated protection against <i>Leishmania major</i>	Nat Med	872	2007	73	USA
47	IL-23 and IL-17 in the establishment of protective pulmonary CD4(+) T cell responses after vaccination and during <i>Mycobacterium tuberculosis</i> challenge	Nat Immunol	849	2007	71	USA
48	Efficacy of a prophylactic adjuvanted bivalent L1 virus-like-particle vaccine against infection with human papillomavirus types 16 and 18 in young women: an interim analysis of a phase III double-blind, randomised controlled trial	Lancet	845	2007	70	Finland
49	Efficacy and effectiveness of influenza vaccines: a systematic review and meta-analysis	Lancet Infect Dis	835	2012	119	USA
50	Global burden of <i>Shigella</i> infections: implications for vaccine development and implementation of control strategies	B World Health Organ	834	1999	42	USA
51	Global distribution of rotavirus serotypes/genotypes and its implication for the development and implementation of an effective rotavirus vaccine	Rev Med Virol	833	2005	60	Brazil
52	Vaccine-induced escape mutant of hepatitis-B virus	Lancet	833	1990	29	England
53	Dendritic cells as therapeutic vaccines against cancer	Nat Rev Immunol	829	2005	59	USA
54	Identification of vaccine candidates against serogroup B meningococcus by whole-genome sequencing	Science	822	2000	43	Italy
55	Clinical effects of A beta immunization (AN1792) in patients with AD in an interrupted trial	Neurology	816	2005	58	USA
56	Sustained Reductions in Invasive Pneumococcal Disease in the Era of Conjugate Vaccine	J Infect Dis	795	2010	88	USA
57	Human immunodeficiency virus type 1 env clones from acute and early subtype B infections for standardized assessments of vaccine-elicited neutralizing antibodies	J Virol	785	2005	56	USA
58	The efficacy of influenza vaccine in elderly persons. A meta-analysis and review of the literature	Ann Intern Med	773	1995	32	USA
59	Control of viremia and prevention of clinical AIDS in rhesus monkeys by cytokine-augmented DNA vaccination	Science	761	2000	40	USA
60	Protection against foot-and-mouth-disease by immunization with a chemically synthesized peptide predicted from the viral nucleotide-sequence	Nature	753	1982	20	USA
61	The protective efficacy of polyvalent pneumococcal polysaccharide vaccine	New Engl J Med	750	1991	27	USA
62	Mucosal immunity and vaccines	Nat Med	749	2005	54	Sweden
63	Molecular analysis of genetic differences between <i>Mycobacterium bovis</i> BCG and virulent <i>M-bovis</i>	J Bacteriol	748	1996	33	USA
64	The mucosal immune-system – from fundamental-concepts to vaccine development	Vaccine	742	1992	27	USA
65	The efficacy and cost-effectiveness of vaccination against influenza among elderly persons living in the community	New Engl J Med	732	1994	29	USA
66	Enhancement of vaccine-mediated antitumor immunity in cancer patients after depletion of regulatory T cells	J Clin Invest	723	2005	52	USA
67	2008 estimate of worldwide rotavirus-associated mortality in children younger than 5 years before the introduction of universal rotavirus vaccination programmes: a systematic review and meta-analysis	Lancet Infect Dis	718	2012	103	USA
68	Treatment of established tumors with a novel vaccine that enhances major histocompatibility class II presentation of tumor antigen	Cancer Res	712	1996	31	USA
69	Against which human papillomavirus types shall we vaccinate and screen? The international perspective	Int J Cancer	703	2004	47	Spain
70	A trial of a 9-valent pneumococcal conjugate vaccine in children with and those without HIV infection	New Engl J Med	699	2003	44	USA
71	DNA-based immunization by <i>in vivo</i> transfection of dendritic cells	Nat Med	698	1996	30	USA

(Continued)

Table 1. (Continued).

Ranking	Title	Journal	Citation times	Publication year	Mean citation per year	Country
72	An epidemiologic study of altered clinical reactivity to respiratory syncytial (RS) virus infection in children previously vaccinated with an inactivated RS virus vaccine	Am J Epidemiol	692	1969	14	USA
73	Combination immunotherapy of B16 melanoma using anti-cytotoxic T lymphocyte-associated antigen 4 (CTLA-4) and granulocyte/macrophage colony-stimulating factor (GM-CSF)-producing vaccines induces rejection of subcutaneous and metastatic tumors accompanied by autoimmune depigmentation	J Exp Med	681	1999	34	USA
74	Vaccine Adjuvants: Putting Innate Immunity to Work	Immunity	679	2010	75	USA
75	Allergen immunotherapy: Therapeutic vaccines for allergic diseases – A WHO position paper	J Allergy Clin Immunol	678	1998	32	Switzerland
76	Vaccination with cytotoxic T lymphocyte epitope-containing peptide protects against a tumor induced by human papillomavirus type 16-transformed cells	Eur J Immunol	670	1993	26	Netherlands
77	Nanoparticles as potential oral delivery systems of proteins and vaccines: A mechanistic approach	J Control Release	669	2006	51	Belgium
78	Risk of myocardial infarction and stroke after acute infection or vaccination	New Engl J Med	667	2004	44	England
79	Mucosal vaccines: the promise and the challenge	Nat Rev Immunol	657	2006	51	USA
80	The efficacy of live attenuated, cold-adapted, trivalent, intranasal influenzavirus vaccine in children	New Engl J Med	655	1998	31	USA
81	Immune and clinical responses in patients with metastatic melanoma to CD34(+) progenitor-derived dendritic cell vaccine	Cancer Res	645	2001	36	USA
82	Autoimmunity correlates with tumor regression in patients with metastatic melanoma treated with anti-cytotoxic T-lymphocyte antigen-4	J Clin Oncol	643	2005	46	USA
83	Effectiveness of maternal influenza immunization in mothers and infants	New Engl J Med	642	2008	58	USA
84	The adjuvant effect of interleukin-12 in a vaccine against <i>Leishmania major</i>	Science	635	1994	25	USA
85	Prevention of perinatally transmitted hepatitis B virus infections with hepatitis B immune globulin and hepatitis B vaccine	Lancet	633	1983	18	China
86	Effect of neonatal circumcision on pain response during subsequent routine vaccination	Lancet	628	1997	29	canada
87	A preliminary evaluation of a recombinant circumsporozoite protein vaccine against <i>Plasmodium falciparum</i> malaria	New Engl J Med	628	1997	29	USA
88	Intussusception among infants given an oral rotavirus vaccine.	New Engl J Med	624	2001	35	USA
89	Biologic activity of cytotoxic T lymphocyte-associated antigen 4 antibody blockade in previously vaccinated melanoma and ovarian carcinoma patients	P Natl Acad Sci USA	624	2003	39	USA
90	Immunization with a synthetic T-cell receptor V-region peptide protects against experimental autoimmune encephalomyelitis	Nature	621	1989	21	USA
91	Induction of antigen-specific cytotoxic T lymphocytes in humans by a malaria DNA vaccine	Science	620	1998	30	USA
92	Vaccine delivery: a matter of size, geometry, kinetics and molecular patterns	Nat Rev Immunol	619	2010	69	Switzerland
93	Efficacy of nine-valent pneumococcal conjugate vaccine against pneumonia and invasive pneumococcal disease in The Gambia: randomised, double-blind, placebo-controlled trial	Lancet	607	2005	43	Switzerland
94	Placebo-controlled phase 3 trial of a recombinant glycoprotein 120 vaccine to prevent HIV-1 infection	J Infect Dis	602	2005	43	USA
95	Antigenic similarities between brain components and bacteria causing meningitis. Implications for vaccine development and pathogenesis	Lancet	601	1983	17	Finland
96	Controlled vaccine release in the gut-associated lymphoid-tissues .1. Orally-administered biodegradable microspheres target the peyers patches	J Control Release	600	1990	21	USA
97	<i>In vivo</i> targeting of antigens to maturing dendritic cells via the DEC-205 receptor improves T cell vaccination	J Exp Med	599	2004	40	USA
98	Exploiting lymphatic transport and complement activation in nanoparticle vaccines	Nat Biotechnol	597	2007	50	Switzerland
99	<i>In vivo</i> priming of virus-specific cytotoxic T lymphocytes with synthetic lipopeptide vaccine	Nature	596	1989	20	Germany
100	The biology of interleukin-2 and interleukin-15: implications for cancer therapy and vaccine design	Nat Rev Immunol	593	2006	46	USA

highly cited studies; the remaining 27 journals contributed fewer than five studies each.

The IFs (impact factors) for the journals with the 100 top-cited studies ranged from 2.305 to 79.26 (median 13.251). We found 79 of the top 100 studies were published in journals with IFs more than 10. For the top 4 medical journals, expect for *BMJ*, the *NEJM*, *JAMA* and *Lancet* each had at least one published top-cited studies. For the “CNS” journals, *Nature*

and *Science* had at least one published top-cited studies, however, no top-cited study was published in *Cell*. There were 6 journals (*Journal of Virology*, *American Journal of Epidemiology*, *European Journal of Immunology*, *Vaccine*, *Journal of Bacteriology*, *Pediatric Infectious Disease Journal*) had lower IFs than 5 and contributed 1 or 2 studies each. We found there were no statistically significant correlations between the number of top-cited studies and journals’ IFs ( $P > .05$ ).

**Table 2.** Journals of the 100 top-cited studies on vaccine.

Journal	Total citation times	Number of studies	Average citation times per study	Impact factor (2017)*
<i>American Journal of Epidemiology</i>	1824	2	912	4.322
<i>Annals of Internal Medicine</i>	773	1	773	19.384
<i>Annual Review of Immunology</i>	1945	2	973	22.714
<i>Bulletin of The World Health Organization</i>	834	1	834	6.361
<i>Cancer Research</i>	1357	2	679	9.13
<i>European Journal of Immunology</i>	670	1	670	4.248
<i>Immunity</i>	679	1	679	19.734
<i>International Journal of Cancer</i>	703	1	703	7.36
<i>Jama-Journal of The American Medical Association</i>	1326	1	1326	47.661
<i>Journal of Allergy and Clinical Immunology</i>	678	1	678	13.258
<i>Journal of Bacteriology</i>	748	1	748	3.219
<i>Journal of Clinical Investigation</i>	723	1	723	13.251
<i>Journal of Clinical Oncology</i>	643	1	643	26.36
<i>Journal of Controlled Release</i>	1269	2	635	7.877
<i>Journal of Experimental Medicine</i>	2243	3	748	10.79
<i>Journal of Infectious Diseases</i>	1397	2	699	5.186
<i>Journal of Virology</i>	785	1	785	4.368
<i>Lancet</i>	9224	11	839	53.254
<i>Lancet Infectious Diseases</i>	1553	2	777	25.148
<i>Lancet Oncology</i>	1064	1	1064	36.421
<i>Nature</i>	10304	9	1145	41.577
<i>Nature Biotechnology</i>	597	1	597	35.724
<i>Nature Immunology</i>	849	1	849	21.809
<i>Nature Medicine</i>	11556	9	1284	32.621
<i>Nature Reviews Immunology</i>	4633	6	772	41.982
<i>Neurology</i>	816	1	816	8.055
<i>New England Journal of Medicine</i>	19908	20	995	79.26
<i>Pediatric Infectious Disease Journal</i>	1591	1	1591	2.305
<i>Proceedings of The National Academy of Sciences of The United States of America</i>	5122	4	1281	9.504
<i>Reviews In Medical Virology</i>	833	1	833	5.034
<i>Science</i>	6939	8	867	41.058
<i>Vaccine</i>	742	1	742	3.285

\* Impact factors were from the journal citation report of 2017.

### Language and year

All 100 top-cited studies were published in the English language. They were published from 1969 to 2012 (Table 3); most of the studies were published in the 1990s and 2000s. We found that the highest number of studies was published in 2005.

### Country

As shown in Table 4, a total of 16 countries produced 100 top-cited studies. The USA was the most productive country with 70 studies, followed by Switzerland, England, and Finland with 4 studies. Moreover, the United States had the highest total citation times (citation time: 67,581), Germany had the highest mean citation times per study (citation time: 1301).

### First author and contact author

Table 5 lists the authors published more than one study as first authors and contact authors. For the first author, only 4 authors published more than one study as the first author, and they all published only two studies each. For contact

**Table 3.** Years of the 100 top-cited studies on vaccine.

Year	Number of studies	Total citation times	Average citation times
2012	3	2533	844
2010	3	2093	698
2009	3	3807	1269
2008	3	2640	880
2007	6	5396	899
2006	6	5345	891
2005	11	8925	811
2004	5	4952	990
2003	4	3875	969
2002	3	3154	1051
2001	4	3233	808
2000	6	6462	1077
1999	5	5985	1197
1998	6	6814	1136
1997	4	3462	866
1996	4	3642	911
1995	2	1647	824
1994	3	2693	898
1993	3	3989	1330
1992	2	1683	842
1991	2	1852	926
1990	2	1433	717
1989	2	1217	609
1988	1	1179	1179
1983	2	1234	617
1982	1	753	753
1981	1	1497	1497
1980	1	1009	1009
1969	2	1824	912

**Table 4.** Countries of the 100 top-cited studies on vaccine.

Country	Number of study	Total citation times	Average citation times
USA	70	67581	965
Switzerland	4	2501	625
Finland	4	3411	853
England	4	3375	844
Canada	3	2902	967
Netherlands	1	670	670
Germany	3	3902	1301
China	2	1819	910
Brazil	2	1897	949
Sweden	1	749	749
Spain	1	703	703
Italy	1	822	822
France	1	1044	1044
Chile	1	1151	1151
Belgium	1	669	669
Australia	1	1132	1132

**Table 5.** Authors with at least two studies as first author or contact author in the 100 top-cited studies on vaccine\*.

Authorship	Name	Number of studies
Contact author	Rosenberg, SA	3
	Harper, DM	2
	Koutsky, LA	2
	Robinson, HL	2
	Seder, RA	2
	Stover, CK	2
First author	Banchereau, J	2
	Harper, DM	2
	Rosenberg, SA	2
	Villa, LL	2

\*If more than 1 author contributed as contact author for 1 study, the first contact author was used for data analysis.

authors, Rosenberg SA, Harper DM, Koutsky LA, Robinson HL, Seder RA, Stover CK were the most productive contact authors who published at least two studies.



### Publication type, open access, and Web of Science categories

For the type of the 100 top-cited studies, as shown in Table 6, 81 studies in the form of “Article” and 19 studies in the form of “Review” were cited 78,651 and 15,677 times, respectively. The studies in the form of “Article” had higher average citation times per study with 971 times than “Review” with 825 times. A total of 14 Web of Science research categories were identified. Medicine, General & Internal was the most popular category, with 33 studies, followed by Multidisciplinary Sciences with 21 studies and Immunology with 18 studies. The studies in the Medicine, General & Internal category were with the highest total citation times, however, Biochemistry & Molecular Biology had the highest mean citation times per study. As for the research category, 11 studies were about therapeutic vaccines, 68 studies were about prophylactic vaccines, and 21 studies cannot be divided into the therapeutic or prophylactic vaccine.

### Discussion

The study is the first bibliometric study summarizing several features of the most influential studies on vaccine. Understanding the characteristics of highly cited studies on vaccine may be worthwhile for several reasons. First, the findings of the present study could aid young researchers to keep themselves abreast of classic knowledge.<sup>17</sup> Second, trends identified by the current analysis may be of interest to clinicians in their clinical practice.<sup>17</sup> The studies cover important advancements on vaccine. Finally, the findings of the present

analysis may help journal editors, reviewers, and funders in critically evaluating manuscripts and funding applications.<sup>17</sup>

In our study, 100 top-cited studies were cited from 593 to 2406 times. The journal with the most studies was *NEJM* ( $n = 20$ ). The studies were published between 1969 and 2012, and 4 authors published at least two studies as the first author. The USA produced the most studies ( $n = 70$ ), followed by Switzerland ( $n = 4$ ), England ( $n = 4$ ) and Finland ( $n = 4$ ). Eighty-one studies were in the form of “Article” and 19 studies in the form of “Review”. Medicine, General & Internal was the most popular category.

The present bibliometric analysis found that the 100 top-cited studies were published in 32 journals. Nearly, four in the fifth of the studies were published in high impact factor journals. It should be noted that almost one-third of the 100 top-cited studies were published in 3 of top 4 medical journals, including *JAMA*, *Lancet*, and *NEJM*, while no study was published in *BMJ*. This phenomenon indicated that most researchers focused on not only the impact factor but also the influence in their research field when choosing journals to publish their studies.<sup>17,23</sup> Of course, several other factors might influence the selection process of target journal,<sup>13,17,24</sup> including difficulty to be accepted, time from submission to acceptance, charges and so on. This is entirely different from some other fields, only a few numbers of studies were published in the four famous journals.<sup>16,17,24</sup> Why most of the top-cited vaccine studies are published in highly IF journals, the reasons might be that vaccine researches covers all aspects of medicine,<sup>2,9</sup> which were quickly accepted by general medical journals. Besides, the most important vaccine researches should be published in the most famous medical journals, so that it can help the most populations.

In our study, original studies had higher mean citation times per study when compared with reviews. This finding indicated that vaccine researchers paid more attention to the new findings in this topic.<sup>17</sup> Besides, our bibliometric analysis proved that Medicine, General & Internal was the most popular category. The vaccine in clinical practice was indeed the most important,<sup>2,24,25</sup> which should raise more researchers’ concern. All the included studies were published in English. One of the main reasons for this is that English is the most common language of influential articles in the field of vaccine research.<sup>26</sup>

The USA ranked first with 70 studies, which was more than the other countries. This finding was in accordance with other previous studies.<sup>19,27</sup> The USA had the highest total citation times. Besides, most productive authors were from the USA. Overall, all this information supported that the USA made the most significant contribution to the developments of research on the vaccine. Our study found that some developing country such as China, Brazil and Chile were selected in rankings, which was entirely different from some other fields, such as infection in orthopedics.<sup>19,27</sup> It should be noted that the two studies from China were not from China mainland, where has the most populations worldwide. Besides, no study was from India, which has the second largest population worldwide. Therefore, developing countries should try their best to improve the quality of vaccine articles in future.<sup>26,27</sup>

There are several limitations in this study. First, we selected the Web of Science Core Collection based on previous

**Table 6.** Type of study and categories in the 100 top-cited studies on vaccine.

Variable	Number of studies	Total citation times	Average citation times per study
Type of study			
Article	81	78651	971
Review	19	15677	825
Web of Science categories*			
Allergy	1	678	678
Biochemistry & Molecular Biology	9	11556	1284
Biotechnology & Applied Microbiology	1	597	597
Chemistry, Multidisciplinary	2	1269	635
Clinical Neurology	1	816	816
Immunology	18	14749	819
Infectious Diseases	2	1553	777
Medicine, General & Internal	33	31231	946
Medicine, Research & Experimental	1	723	723
Microbiology	1	748	748
Multidisciplinary Sciences	21	22365	1065
Oncology	5	3767	753
Public, Environmental & Occupational Health	3	2658	886
Virology	2	1618	809
Research categories			
Therapeutic	11	8621	784
Prophylactic	68	61410	903
Other	21	24297	1157

\*Web of Science categories were identified from web of science, if one article was listed in more than 1 category, the first category was used for data analysis.

researches. Web of Science Core Collection does not include all vaccine articles; there is a probability of true top-cited articles that may be available in other databases such as Scopus and Google Scholar; therefore, the results of our study might not be comprehensive.<sup>18,28</sup> Second, this was a cross-sectional study design with a single time point. The rankings identified may change if the study is replicated in the future.<sup>26</sup> Third, despite the methods described above, we could not guarantee that all retrieved articles accurately focused on this topic, which was an inherent weakness of all bibliometric analyses.<sup>23</sup> Despite limitations, we believed this study could contribute to obtaining vital developments of vaccines and providing new insights into innovation in this field.

In conclusion, the present analysis is the first reported attempt to recognize 100 top-cited studies in the field of vaccine. The observations of the present study reflect the exciting potential and the increasing role of vaccine in basic research and clinical practice. It also provides a reference of what may be considered as the most influential papers in vaccine and serves as an indication of what comprises a 'highly citable' manuscript for both researchers, clinicians, and healthcare providers. It also helps funding agencies to assess the whole significant research areas in the field to direct future research trends.

## Materials and methods

The study was a retrospective bibliometric analysis, and there was no need for institutional review board approval.

### Search method and strategy

We performed a search on January 10, 2019 using the Web of Science Core Collection database hosted by Clarivate Analytics as the previous studies.<sup>18</sup> The Web of Knowledge Core Collection is a multidisciplinary database with searchable author abstracts covering the journal literature of the sciences.<sup>27</sup> It fully indexes the major journals more than 170 subject categories, providing access to current information and retrospective data from 1945 forward.<sup>24</sup> Based on a pilot search, the author found that some top-cited studies mentioning the word immunization in the abstract are not related to the vaccine, and these studies should be excluded. Thus, the search was performed by two steps: first, we search the following words: vaccine or vaccination; second, we search the following words: immunization. The identified publications were sorted in descending order of citation times. Only studies concerning the vaccines were included.

### Data extraction

The 100 top-cited vaccine studies were identified by citation times. They were sorted in descending order of citation times. The following data were extracted, including the author, affiliation, country, journal, language, Web of Science category, publication year, number of citations, number of pages, and status of open access, the publication type. The country of affiliation was identified by using the country of the contact author. If the contact author had more than one affiliations

from different countries, the country of the first affiliation was extracted. If one study was categorized into more than one categories, the first category was extracted.<sup>18</sup> The majority of vaccines are prophylactic for infectious diseases, a smaller number are therapeutic, typically for cancer and autoimmune disease, so the studies were divided into therapeutic study and prophylactic study, if the study could not be divided into the two types of studies, it was divided into the other group.

### Data analysis

Data analysis was performed using SPSS 17.0 software. The following outcomes were analyzed: citation times, year, country, author, journal, language, publication type, open access and Web of Science categories and research categories.

### Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

### Ethics committee approval

This is a bibliometric analysis, so ethics approval is not applicable.

## References

- Poland GA, Kennedy RB, Ovsyannikova IG, Palacios R, Ho PL, Kalil J. Development of vaccines against Zika virus. *Lancet Infect Dis.* 2018;18:e211–e9. doi:10.1016/S1473-3099(18)30063-X.
- Hotez PJ, Bottazzi ME, Strych U. New vaccines for the world's poorest people. *Annu Rev Med.* 2016;67:405–17. doi:10.1146/annurev-med-051214-024241.
- Haber P, Amin M, Ng C, Weintraub E, McNeil MM. Reports of lower respiratory tract infection following dose 1 of RotaTeq and Rotarix vaccines to the vaccine adverse event reporting system (VAERS), 2008–2016. *Hum Vaccin Immunother.* 2018;1–5. doi:10.1080/21645515.2018.1491509.
- Demicheli V, Jefferson T, Di Pietrantonj C, Ferroni E, Thorning S, Thomas RE, Rivetti A. Vaccines for preventing influenza in the elderly. *Cochrane Database Syst Rev.* 2018;2:CD004876.
- Jefferson T, Rivetti A, Di Pietrantonj C, Demicheli V. Vaccines for preventing influenza in healthy children. *Cochrane Database Syst Rev.* 2018;2:CD004879.
- Hu Y, Chen Y, Liang H, Wang Y. Routine vaccination coverage of children aged 1–7 years in Zhejiang province, China. *Hum Vaccin Immunother.* 2018;14:2876–83. doi:10.1080/21645515.2018.1486156.
- Casey RM, Dumolard L, Danovaro-Holliday MC, Gacic-Dobo M, Diallo MS, Hampton LM, Wallace AS. Global routine vaccination coverage, 2015. *MMWR Morb Mortal Wkly Rep.* 2016;65:1270–73. doi:10.15585/mmwr.mm6545a5.
- Zanotto PMA, Leite LCC. The challenges imposed by dengue, zika, and chikungunya to Brazil. *Front Immunol.* 2018;9:1964. doi:10.3389/fimmu.2018.01964.
- Rauch S, Jasny E, Schmidt KE, Petsch B. New vaccine technologies to combat outbreak situations. *Front Immunol.* 2018;9:1963. doi:10.3389/fimmu.2018.01963.
- Song JY, Lim JH, Lim S, Yong Z, Seo HS. Progress toward a group B streptococcal vaccine. *Hum Vaccin Immunother.* 2018;1–13. doi:10.1080/21645515.2018.1493326.
- Mao QY, Wang Y, Bian L, Xu M, Liang Z. EV71 vaccine, a new tool to control outbreaks of hand, foot and mouth disease (HFMD). *Expert Rev Vaccines.* 2016;15:599–606. doi:10.1586/14760584.2016.1138862.
- Daley EM, Vamos CA, Zimet GD, Rosberger Z, Thompson EL, Merrell L. The feminization of HPV: reversing gender biases in

- US human papillomavirus vaccine policy. *Am J Public Health*. 2016;106:983–84. doi:10.2105/AJPH.2016.303084.
13. Kolkailah AA, Fugar S, Vondee N, Hirji SA, Okoh AK, Ayoub A, Al-Ogaili A, Rios LHP, Kumar SK, Camacho MT, et al. Bibliometric analysis of the top 100 most cited articles in the first 50 years of heart transplantation. *Am J Cardiol*. 2019;123:175–86. doi:10.1016/j.amjcard.2018.09.010.
  14. Zhao X, Guo L, Lin Y, Wang H, Gu C, Zhao L, Tong X. The top 100 most cited scientific reports focused on diabetes research. *Acta Diabetol*. 2016;53:13–26. doi:10.1007/s00592-015-0813-1.
  15. Shen J, Li Y, Clarke M, Du L, Wang L, Zhong D. Visualization of evidence-based medicine domain knowledge: production and citation of Cochrane systematic reviews. *J Evid Based Med*. 2013;6:34–42. doi:10.1111/jebm.12022.
  16. Berlinberg A, Bilal J, Riaz IB, Kurtzman DJB. The 100 top-cited publications in psoriatic arthritis: a bibliometric analysis. *Int J Dermatol*. 2018. doi:10.1111/ijd.14261.
  17. Gondivkar SM, Sarode SC, Gadabail AR, Gondivkar RS, Choudhary N, Patil S. Citation classics in cone beam computed tomography: the 100 top-cited articles. *Int J Dent*. 2018;2018:9423281. doi:10.1155/2018/9423281.
  18. Zhang Y, Huang J, Du L. The top-cited systematic reviews/meta-analyses in tuberculosis research: A PRISMA-compliant systematic literature review and bibliometric analysis. *Medicine (Baltimore)*. 2017;96:e4822. doi:10.1097/MD.0000000000004822.
  19. Shuaib W, Acevedo JN, Khan MS, Santiago LJ, Gaeta TJ. The top 100 cited articles published in emergency medicine journals. *Am J Emerg Med*. 2015;33:1066–71. doi:10.1016/j.ajem.2015.04.047.
  20. Dranoff G, Jaffee E, Lazenby A, Golumbek P, Levitsky H, Brose K, Jackson V, Hamada H, Pardoll D, Mulligan RC. Vaccination with irradiated tumor cells engineered to secrete murine granulocyte-macrophage colony-stimulating factor stimulates potent, specific, and long-lasting anti-tumor immunity. *Proc Natl Acad Sci U S A*. 1993;90:3539–43. doi:10.1073/pnas.90.8.3539.
  21. Schenk D, Barbour R, Dunn W, Gordon G, Grajeda H, Guido T, Hu K, Huang J, Johnson-Wood K, Khan K, et al. Immunization with amyloid-beta attenuates Alzheimer-disease-like pathology in the PDAPP mouse. *Nature*. 1999;400:173–77. doi:10.1038/22124.
  22. Nestle FO, Aljagic S, Gilliet M, Sun Y, Grabbe S, Dummer R, Burg G, Schadendorf D. Vaccination of melanoma patients with peptide- or tumor lysate-pulsed dendritic cells. *Nat Med*. 1998;4:328–32.
  23. Bullock N, Ellul T, Bennett A, Steggall M, Brown G. The 100 most influential manuscripts in andrology: a bibliometric analysis. *Basic Clin Androl*. 2018;28:15. doi:10.1186/s12610-018-0076-0.
  24. Yoon DY, Yun EJ, Ku YJ, Baek S, Lim KJ, Seo YL, Yie M. Citation classics in radiology journals: the 100 top-cited articles, 1945–2012. *AJR Am J Roentgenol*. 2013;201:471–81. doi:10.2214/AJR.12.10489.
  25. Zhu B, Dockrell HM, Ottenhoff THM, Evans TG, Zhang Y. Tuberculosis vaccines: opportunities and challenges. *Respirology*. 2018;23:359–68. doi:10.1111/resp.13245.
  26. Wu Y, Zhao Y, Lin L, Lu Z, Guo Z, Li X, Chen R, Ma H. Fifty top-cited spine articles from mainland China: A citation analysis. *J Int Med Res*. 2018;46:773–84. doi:10.1177/0300060517713804.
  27. Jiang Y, Hu R, Zhu G. Top 100 cited articles on infection in orthopaedics: A bibliometric analysis. *Medicine (Baltimore)*. 2019;98:e14067. doi:10.1097/MD.00000000000014067.
  28. Chen W, Yu J, Tao H, Cai Y, Li Y, Sun X. Motherwort injection for preventing postpartum hemorrhage in pregnant women with cesarean section: A systematic review and meta-analysis. *J Evid Based Med*. 2018;11:252–60. doi:10.1111/jebm.2018.11.issue-4.