ORIGINAL RESEARCH

Top 100 Most-Cited Papers in Herpes Zoster from 2000 to 2022: A Bibliometric Study

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Background: In recent years, the incidence of herpes zoster has risen steeply, the exact pathogenesis of the acute pain and the transformation into postherpetic neuralgia are still obscure, and the absence of effective management remains a major therapeutic challenge. The purpose of this study was to perform a qualitative and quantitative bibliometric analysis of the 100 most cited papers on herpes zoster.

Materials and methods: Related literature were retrieved from the Web of Science Core Collection. Excel and VOSviewer software were applied to quantitatively analyze, and construct the bibliometric network charts.

Results: The Top 100 most-cited papers published between 2000 and 2018 showed a fluctuating downward trend. The most studies were published in the year of 2000 (n = 12). The article entitled "A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults" from Oxman MN, was the most-cited publication. The United States was the most contributing country, followed by the United Kingdom, and Italy. Finland occupied the highest citations per publication (CPP). The University of Colorado topped the list of institutions with the most publications with 18 articles and also had the most citations (average citations: 281.78 per article). Myron J Levin from the University of Colorado School of Medicine is the most published and most cited researcher overall, whereas Duke University's John W Gnann tops the list in terms of average CPP.

Conclusion: In terms of the quantity of T100 articles, researchers, and organizations, the US is the predominant country. The most T100 papers were published in the special journal Clinical Infectious Diseases. The most academic focus remain the remedies for postherpetic neuralgia and vaccine development for individualized groups.

Keywords: herpes zoster, bibliometric study, top-cited, citation, VOSviewer

Introduction

Varicella zoster virus (VZV) belongs to the genus varicella virus of the family Herpesviridae and is transmitted in the population mainly through the respiratory tract.¹ It was first isolated in tissue culture in 1953.² Herpes zoster (HZ) is a cutaneous disease caused by reactivation of the VZV in the host.³ When immunity to VZV declines due to aging or immunosuppression, VZV reactivation occurs.⁴ The clinical presentation is typically a cluster of rashes and vesicles on a red base in a unilateral, dermatomal distribution, with intense neuralgia along the peripheral nerves near the skin lesion.⁴ Some patients may develop systemic symptoms such as nausea, fatigue and fever.³ The risk of HZ increases with age (>50 years).⁵ The classical risk factors also include immunosuppression, infections, and psychological stress.⁵ According to the Centers for Disease Control and Prevention (CDC), nearly one out of every three people in the United States will suffer from HZ during their lifetime.⁶ An estimated 19.4% of patients with HZ experienced postherpetic neuralgia (PHN), as observed in Chinese outpatients,⁷ which is one of the most common complications

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of HZ, with severe neuralgia in the affected dermatome after the rash recedes.⁸ The overall incidence of HZ has linearly increased over the past few decades, most likely due to an aging population and an increase in the number of immunocompromised people,⁹ which not only affects the quality of life of patients, but also poses a significant clinical and economic burden.^{10,11} Currently, the optimal treatment for immunocompetent patients with acute HZ usually consists of conventional antiviral drugs and analgesic therapy as well as topical treatment.¹² However, the effective therapy reliably relieved the pain of PHN is absent.⁴ Recently, VZV reactivation has been observed following the administration of various Corona Virus Disease 2019 (COVID-19) vaccinations, although the causality is not clear.¹³ Until now, the exact pathogenesis that how VZV causes acute pain and the mechanisms underlying the transition to PHN are far from explicit, so effective treatments remain a major therapeutic challenge.¹⁴

Highly cited papers are recognized as influential papers in the field of study and reflect research trends and scientific advancements in the field.¹⁵ In contrast to traditional literature reviews, bibliometrics is one of the key approaches to objectively measure the impact of scholarly publications by extracting measurements from knowledge in publications and then performing statistical analysis.¹⁶ This approach has now been applied to research in a variety of disciplines, such as dermatology,¹⁷ oncology,¹⁸ neurology.¹⁹ To our knowledge, no bibliometric analysis of highly cited publications has been conducted in the HZ field. In this study, we aimed to identify the 100 most cited HZ-related papers and analyze their bibliometric characteristics in order to identify research hotspots and future directions in this field for medical professionals and researchers.

Methods

Data Sources

We performed a literature search from the Web of Science Core Collection (WOSCC) on October 24th, 2022. Index selection is Science Citation Index Expanded (SCIE). Since the subject search and abstract search will retrieve a large number of non-relevant documents, the title search was chosen to ensure the validity of the search data source.²⁰ In this study, the search formula in the WoSCC database were as follows: TI = (Herpes Zoster) OR TI = (Shingles) OR TI = (Zoster) OR TI = (Postherpetic Neuralgia).

Inclusion Criteria

We included the research articles or reviews in the English language, which were published between January 1st, 2000 to October 24th, 2022, which contained the search term (herpes zoster) in the title and/or abstract. A total of 4655 articles were identified as eligible, including 4199 articles and 456 reviews. The literature search strategy and screening process of this study are shown in Figure 1.

Data Collection and Statistical Analysis

The following information is extracted from the WoS database for each publication: author, institution, country, keywords, number of citations, year of publication. The impact factor (IF) of journals is defined through the Journal Citation Report (2021) (<u>https://JCR.Clarivate.com/</u>). Quantitative analysis of data was performed using Microsoft Excel and a co-linear network of countries, institutions, authors and keywords was plotted using VOSviewer (version 1.6.18). Different nodes in the network represent different terms, while the size of the nodes represents the frequency of occurrence, and the links between nodes indicate co-occurrence relationships. In addition, to eliminate the impact of the time of publication on article citations, we calculated the average citations per year (ACY) score of the article:

ACY=citation times/(2021-publication year+1).

Quality Control

Two investigators (NG and ML) independently performed the data retrieval and screening. Divergences were resolved by discussion or the arbitration of a third reviewer. Data retrieval and export were completed on the same day (October 24, 2022), preventing bias caused by database updates. Under the guidance of senior experts (ZL and YFG), the two researchers finally reached an agreement on the T100 papers. This study did not include any animals or experiments and therefore did not require ethics committee approval.



Figure I Flow chart of literature screening.

Results

We retrieved the 100 most frequently cited papers related to HZ and ranked them in descending order based on the citation count of the articles. Of the 100 papers, 88 were articles and 12 were reviews. A comprehensive list of 100 publications and article information is presented in Table 1. In terms of research type, the top 100 most cited papers (T100 papers) were divided into four categories: (1) Observational studies (OS), including epidemiological, randomized controlled trials (RCTs), case-control, and cohort studies; (2) Basic science research (BS), including pathology, experimental and animal studies; (3) clinical guidelines; (4) review articles, including meta-analyses and systematic reviews.

Year of Publication

The T100 papers were published between 2000–2018. Figure 2 illustrates the annual number of articles published during this 19-year period, and overall, the highly cited publications show a fluctuating downward trend. The highest number of T100 papers was published in the year 2000 (n = 12), followed by year 2004 (n = 9).

Citations

The T100 papers were cited a total of 6743 times, with citations ranging from 129 to 1646, with a median of 197, and we found seven papers cited more than 500 times. The most cited article was conducted by Oxman MN et al on HZ prevention, published in New England Journal of Medicine in 2005, and this article also has the highest ACY (Table 1). Figure 3 shows the total number of citations per year and the average number of citations per year. The year 2005 had the highest number of citations, with 2943, and the average number of citations per year has been increasing.

Contributions of Countries

A total of 25 countries contributed to the T100 papers, with the United States (US) being the leading contributor (n=72), followed by the United Kingdom (UK) (n=28), Canada (n=10) and Japan (n=7). The top 10 countries in terms of number of the T100 papers are shown in Figure 4A. In terms of the average citation rate of publications, Finland occupies the highest CPP, followed by Spain, Belgium and Japan. Figure 4B shows the regional distribution of publication volume,

Table I List of the Top 100 Most Cited Papers in Herps Zoster (2000-2022)

Rank	Article Title	Journal	IF	Year	тс	ACY
I	A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults	New England Journal of Medicine	176.08	2005	1646	111.39
2	Herpes zoster	New England Journal of	176.08	2002	838	95.33
3	Efficacy of an Adjuvanted Herpes Zoster Subunit Vaccine in	New England Journal of	176.08	2015	712	251.88
4	Pregabalin for the treatment of postherpetic neuralgia -	Neurology	11.80	2003	584	100.15
5	A randomized, placebo-controlled trial A population-based study of the incidence and complication rates	Mayo Clinic Proceedings	11.10	2007	557	125.44
6	of herpes zoster before zoster vaccine introduction Neurologic complications of the reactivation of varicella-zoster	New England Journal of	176.08	2000	541	86.96
7	virus. Efficacy of the Herpes Zoster Subunit Vaccine in Adults 70 Years	Medicine New England Journal of	176.08	2016	503	288.00
8	of Age or Older Recommendations for the management of herpes zoster	Clinical Infectious	21.00	2007	467	125.44
9	Gabapentin in postherpetic neuralgia: a randomised, double blind,	Pain	7.93	2001	461	90.95
10	Systematic review of incidence and complications of herpes	BMJ Open	3.01	2014	445	223.78
11	Risk of Herpes Zoster in Patients With Rheumatoid Arthritis Treated With Anti-TNF-alpha Agents	Jama-journal of the American Medical	157.34	2009	414	143.50
12	Epidemiology and impact on quality of life of postherpetic	Association Clinical Journal of Pain	3.42	2002	408	95.33
13	What does epidemiology tell us about risk factors for herpes	Lancet Infectious Diseases	71.42	2004	394	105.47
14	Opioids versus antidepressants in postherpetic neuralgia - A randomized, placebo-controlled trial	Neurology	11.80	2002	394	95.33
15	The incidence of herpes zoster in a United States administrative database	Journal of General Internal Medicine	6.47	2005	369	111.39
16	Varicella zoster virus vasculopathies: diverse clinical	Lancet Neurology	59.94	2009	340	143.50
17	The neurotropic herpes viruses: herpes simplex and varicella-	Lancet Neurology	59.94	2007	314	125.44
18	The varicella zoster virus vasculopathies - Clinical, CSF, imaging, and virologic features	Neurology	11.80	2008	309	133.87
19	Epidemiology of varicella zoster virus infection in Canada and the United Kingdom	Epidemiology and Infection	4.43	2001	303	90.95
20	Efficacy, Safety, and Tolerability of Herpes Zoster Vaccine in Persons Aged 50–59 Years	Clinical Infectious Diseases	21.00	2012	302	182.91
21	Recommendations of the Advisory Committee on Immunization Practices for Use of Herpes Zoster Vaccines	MMWR-morbidity and Mortality Weekly Report	35.30	2018	295	403.60
22	Postherpetic Neuralgia	New England Journal of Medicine	176.08	2014	276	223.78
23	Analgesic therapy in postherpetic neuralgia: A quantitative systematic review	PLoS Medicine	11.61	2005	272	111.39
24	Risk factors for postherpetic neuralgia in patients with herpes zoster	Neurology	11.80	2004	271	105.47
25	Dextromethorphan and memantine in painful diabetic neuropathy and postherpetic neuralgia - Efficacy and dose-response trials	Anesthesiology	8.99	2002	269	95.33

Rank	Article Title	Journal	IF	Year	тс	ACY
26	Varicella-zoster virus-specific immune responses in elderly	Journal of Infectious	7.76	2008	266	133.87
	recipients of a herpes zoster vaccine	Diseases				
27	NGX-4010, a high-concentration capsaicin patch, for the	Lancet Neurology	59.94	2008	252	133.87
	treatment of postherpetic neuralgia: a randomised, double-blind					
	study					
28	Antidepressants and anticonvulsants for diabetic neuropathy and	Journal of Pain and	5.58	2000	249	86.96
	postherpetic neuralgia: A quantitative systematic review	Symptom Management				
29	Exposure to varicella boosts immunity to herpes-zoster:	Vaccine	4.96	2002	246	95.33
	implications for mass vaccination against chickenpox					
30	The impact of herpes zoster and post-herpetic neuralgia on	BMC Medicine	11.15	2010	243	154.62
	quality-of-life					
31	Practice parameter: Treatment of postherpetic neuralgia an	Neurology	11.80	2004	241	105.47
	evidence-based report of the Quality Standards Subcommittee of					
	the American Academy of Neurology					
32	Herpes zoster in older adults	Clinical Infectious	21.00	2001	240	90.95
		Diseases				
33	Varicella-zoster virus: Atypical presentations and unusual	Journal of Infectious	7.76	2002	239	95.33
	complications	Diseases				
34	Decline in Varicella-Zoster Virus (VZV)-specific cell-mediated	Journal of Infectious	7.76	2003	239	100.15
	immunity with increasing age and boosting with a high-dose VZV	Diseases				
	vaccine					
35	Herpes zoster ophthalmicus - Natural history, risk factors, clinical	Ophthalmology	14.28	2008	235	133.87
	presentation, and morbidity	,				
36	Herpes Zoster and Tofacitinib Therapy in Patients With	Arthritis &	15.48	2014	230	223.78
	Rheumatoid Arthritis	Rheumatology				
37	Varicella zoster virus infection	Nature Reviews Disease	65.04	2015	228	251.88
		Primers				
38	A cross-sectional cohort survey in 2100 patients with painful	Pain	7.93	2009	226	143.50
	diabetic neuropathy and postherpetic neuralgia: Differences in					
	demographic data and sensory symptoms					
39	Development of a measure of the burden of pain due to herpes	Journal of Pain	5.38	2004	225	105.47
	zoster and postherpetic neuralgia for prevention trials:					
	Adaptation of the brief pain inventory					
40	Molecular mechanisms of varicella zoster virus pathogenesis	Nature Reviews	78.30	2014	221	223.78
		Microbiology				
41	Herpes Zoster (Shingles) and Postherpetic Neuralgia	Mayo Clinic Proceedings	11.10	2009	218	143.50
42	Contacts with varicella or with children and protection against	Lancet	202.73	2002	211	95.33
	herpes zoster in adults: a case-control study					
43	Intrathecal methylprednisolone for intractable postherpetic	New England Journal of	176.08	2000	209	86.96
	neuralgia.	Medicine				
44	Epidemiology and cost of herpes zoster and post-herpetic	Epidemiology and	4.43	2009	208	143.50
	neuralgia in the United Kingdom	Infection				
45	Incidence of herpes zoster, before and after varicella-vaccination-	Journal of Infectious	7.76	2005	208	111.39
	associated decreases in the incidence of varicella, 1992–2002	Diseases				
46	Association Between Vaccination for Herpes Zoster and Risk of	Jama-journal of the	157.34	2012	206	182.91
	Herpes Zoster Infection Among Older Patients With Selected	American Medical				
	Immune-Mediated Diseases	Association				
47	Analysis of herpes zoster events among bortezomib-treated	Journal of Clinical	50.72	2008	206	133.87
	patients in the Phase III APEX study	Oncology				

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Rank	Article Title	lournal	IF	Year	тс	ACY
48	The risk of herpes zoster in patients with rheumatoid arthritis in	Arthritis & Rheumatism-	5.18	2007	204	125.44
	the United States and the United Kingdom	arthritis Care &				
40		Research	4.42	2000	200	04.04
49	Modelling the impact of immunization on the epidemiology of	Epidemiology and	4.43	2000	200	86.96
50	varicella zoster virus	Infection	14.40	2010	100	15472
50	Advances in the understanding of the pathogenesis and	journal of Clinical	14.48	2010	199	154.62
F 1	epidemiology of nerpes zoster	Virology	14.94	2010	104	15472
51	The impact of herpes zoster and postnerpetic neuraigia on		16.86	2010	194	154.62
50	Veriable Zester Virus Sectific Internation Personance to Homes	Association journal	770	2009	101	142 50
52	Varicella-Zoster Virus-specific initialitie Responses to Herpes		1.70	2009	171	143.30
	Zoster Vascina	Diseuses				
53	Efficacy and tolerability of twice-daily pregabalin for treating pain	Current Medical	271	2006	190	118.00
55	and related sleep interference in postherpetic neuralgia: a 13-	Research and Obinion	2.71	2000	170	110.00
	week, randomized trial					
54	Long-term Persistence of Zoster Vaccine Efficacy	Clinical Infectious	21.00	2015	187	251.88
		Diseases				
55	Varicella-zoster virus infections of the nervous system - Clinical	Archives of Pathology &	5.69	2001	186	90.95
	and pathologic correlates	Laboratory Medicine				
56	Stress-induced subclinical reactivation of varicella zoster virus in	Journal of Medical	20.69	2004	185	105.47
	astronauts	Virology				
57	Highly potent and selective inhibition of varicella-zoster virus by	Journal of Medicinal	8.04	2000	182	86.96
	bicyclic furopyrimidine nucleosides bearing an aryl side chain	Chemistry				
58	Acute pain in herpes zoster and its impact on health-related	Clinical Infectious	21.00	2004	181	105.47
	quality of life	Diseases				
59	Pain, medication use, and health-related quality of life in older	Journal of Pain	5.38	2005	181	111.39
	persons with postherpetic neuralgia: Results from a population-					
	based survey					
60	Herpes Zoster Risk Factors in a National Cohort of Veterans	Clinical Infectious	21.00	2009	175	143.50
	with Rheumatoid Arthritis	Diseases				
61	A systematic review and meta-analysis of risk factors for	Pain	7.93	2016	175	288.00
	postherpetic neuralgia					
62	Varicella zoster virus infection: Clinical features, molecular	Neurologic Clinics	3.79	2008	175	133.87
	pathogenesis of disease, and latency					
63	Prevalence of postherpetic neuralgia after a first episode of	British Medical Journal	93.33	2000	173	86.96
	herpes zoster: prospective study with long term follow up					
64	Herpes zoster infection following solid organ transplantation:	American Journal of	9.37	2004	172	105.47
	Incidence, risk factors and outcomes in the current	Transplantation				
	immunosuppressive era					
65	The density of remaining nerve endings in human skin with and	Pain	7.93	2001	170	90.95
	without postherpetic neuralgia after shingles					
66	Frequencies of memory I cells specific for varicella-zoster virus,	Journal of Infectious	1.76	2000	16/	86.96
	herpes simplex virus, and cytomegalovirus by intracellular	Diseases				
17	detection of cytokine expression		5.71	2000		0/ 0/
6/	varicella zoster virus infections following allogeneic bone marrow	Biology of Blood and	5.61	2000	166	86.96
/ 0	transplantation: Frequency, risk factors, and clinical outcome	warrow transplantation	25.40	2007	144	110.00
00	Long-term acyclovir for prevention of varicella zoster virus	DOOD	23.48	2006	100	118.00
	usease alter anogeneic nematopoletic cell transplantation -					
	a randomized double-bind placebo-controlled study		1	1		

Rank	Article Title	Journal	IF	Year	тс	ACY
69	Similar herpes zoster incidence across Europe: results from	BMC Infectious Diseases	3.67	2013	160	201.30
70	Herpes zoster and postherpetic neuralgia: incidence and risk	Family Practice	2.29	2002	158	95.33
71	Varicella-zoster virus transfer to skin by T cells and modulation of viral replication by epidermal cell interferon-alpha	Journal of Experimental Medicine	17.58	2004	156	105.47
72	Herpes Zoster Vaccine in Older Adults and the Risk of Subsequent Herpes Zoster Disease	Jama-journal of the American Medical	157.34	2011	155	167.58
73	Characteristics of patients with herpes zoster on presentation to	Association Clinical Infectious	21.00	2001	152	90.95
74	Practitioners in France Herpes Zoster Incidence Among Insured Persons in the United States, 1993–2006: Evaluation of Impact of Varicella Vaccination	Diseases Clinical Infectious Diseases	21.00	2011	151	167.58
75	Herpes Zoster Vaccine Effectiveness against Incident Herpes Zoster and Post-herpetic Neuralgia in an Older US Population:	PLoS Medicine	11.61	2013	150	201.30
76	A Conort Study Antiviral therapy for herpes zoster - Randomized, controlled clinical trial of valacyclovir and famciclovir therapy in	Archives of Family Medicine	-	2000	150	86.96
77	Analysis of individual human trigeminal ganglia for latent herpes simplex virus type I and varicella-zoster virus nucleic acids using real-time PCR	Journal of Virology	6.55	2000	150	86.96
78	Update on Recommendations for Use of Herpes Zoster Vaccine	MMWR-morbidity and Mortality Weekly Report	35.30	2014	149	223.78
79	The epidemiology of herpes zoster and potential cost- effectiveness of vaccination in England and Wales	Vaccine	4.96	2001	147	90.95
80	Persistence of the Efficacy of Zoster Vaccine in the Shingles Prevention Study and the Short-Term Persistence Substudy	Clinical Infectious Diseases	21.00	2012	147	182.91
81	Association Between the Initiation of Anti-Tumor Necrosis Factor Therapy and the Risk of Herpes Zoster	Jama-journal of the American Medical Association	157.34	2013	146	201.30
82	Invasive group a streptococcal disease in children and association with varicella-zoster virus infection	Pediatrics	9.70	2000	146	86.96
83	Safety and Immunogenicity of an Adjuvanted Herpes Zoster Subunit Candidate Vaccine in HIV-Infected Adults: A Phase I/2a Randomized, Placebo-Controlled Study	Journal of Infectious Diseases	7.76	2015	145	251.88
84	The comparative sero-epidemiology of varicella zoster virus in 11 countries in the European region	Vaccine	4.96	2007	144	125.44
85	Diagnosis and assessment of pain associated with herpes zoster and postherpetic neuralgia	Journal of Pain	5.38	2008	141	133.87
86	Herpes Zoster and Tofacitinib: Clinical Outcomes and the Risk of Concomitant Therapy	Arthritis & Rheumatology	15.48	2017	141	336.17
87	Herpes zoster guideline of the German Dermatology Society (DDG)	Journal of Clinical Virology	14.48	2003	139	100.15
88	Incidence and risk factors for herpes zoster among patients with inflammatory bowel disease	Clinical Gastroenterology and Hepatology	13.58	2006	138	118.00
89	The incidence of varicella and herpes zoster in Massachusetts as measured by the Behavioral Risk Factor Surveillance System (BRFSS) during a period of increasing varicella vaccine coverage, 1998–2003	BMC Public Health	4.14	2005	138	111.39

Rank	Article Title	Journal	IF	Year	тс	ACY
90	Global identification of three major genotypes of Varicella-Zoster virus: Longitudinal clustering and strategies for genotyping	Journal of Virology	6.55	2004	137	105.47
91	Increased Risk of Stroke After a Herpes Zoster Attack	Stroke	10.17	2009	136	143.50
92	Development and validation of a gamma interferon ELISPOT assay for quantitation of cellular immune responses to varicella-zoster	Clinical and Diagnostic Laboratory Immunology	-	2001	136	90.95
93	virus Quantification of risk factors for herpes zoster: population based case-control study	BMJ-British Medical Iournal	93.33	2014	135	223.78
94	Brain activity for spontaneous pain of postherpetic neuralgia and its modulation by lidocaine patch therapy	Pain	7.93	2007	135	125.44
95	Disseminated varicella infection due to the vaccine strain of varicella-zoster virus, in a patient with a novel deficiency in natural killer T cells	Journal of Infectious Diseases	7.76	2003	134	100.15
96	The PINE study of epidural steroids and local anaesthetics to prevent postherpetic neuralgia: a randomised controlled trial	Lancet	202.73	2006	133	118.00
97	EMA401, an orally administered highly selective angiotensin II type 2 receptor antagonist, as a novel treatment for postherpetic neuralgia: a randomised, double-blind, placebo-controlled Phase 2 clinical trial	Lancet	202.73	2014	132	223.78
98	Varicella-zoster virus gene expression in latently infected and explanted human ganglia	Journal of Virology	6.55	2000	131	86.96
99	Incidence of herpes zoster, 1997–2002	Epidemiology and Infection	4.43	2005	129	111.39
100	Epidemiology and economic burden of herpes zoster and post- herpetic neuralgia in Italy: A retrospective, population-based study	BMC Infectious Diseases	3.67	2010	129	154.62

with North America publishing the most articles (n=83), followed by Europe (n=78). We constructed a collaborative network between countries through VOSviewer (Figure 4C). The US has the highest total link strength (TLS=260) and has established collaborative relationships with 20 countries, with the strongest collaborative linkages being the UK, Canada, Japan and Germany.

In addition, we also find that: (1) the participation of less economically developed countries such as West Asia, North Africa and South America is low, and there are obvious regional differences in research in this field; (2) in recent years, countries such as Australia, Sweden, Mexico and Brazil have positively engaged in international research cooperation and become a new force in research in the field of HZ.

Contributions of Institutions

A total of 279 institutions contributed to the T100 papers, of which 209 (74.91%) published only one paper. The top 10 institutions in terms of number of the T100 papers published all had at least six papers (Table 2). The University of Colorado topped the list with 18 articles, totaling 5072 citations, followed by Duke University (n=10) and Harvard University (n=10), both with more than 1800 citations. In its collaborative network, the University of Colorado collaborates with 94 different institutions. Of these, it collaborates most closely with the University of California, San Diego, Duke University, Harvard University, and the University of Tampere (Figure 5).



Figure 2 Annual number of the published publications in herpes zoster research.







Figure 4 The distribution of countries in herpes zoster research. (A) The distribution of countries in HZ research. (B) Worldwide distribution of the top 100 most-cited papers in herps zoster. (C) Map of cooperation network between countries or regions.

Rank	Institution	ТР	тс	СРР
1	University of Colorado	18	5072	281.78
2	Duke University	10	2378	237.80
3	Harvard University		1885	188.50
4	The University of Alabama at Birmingham	9	2477	275.22
5	University of California San Diego	9	2067	229.67
6	University of Rochester	9	2271	252.33
7	Merck Research Laboratories	7	1763	251.86
8	Centers for Disease Control and Prevention	6	980	163.33
9	University of Bristol	6	1501	250.17
10	University of Pennsylvania	6	1040	173.33

 Table 2 Top 10 Institutions in the Top 100 Most-Cited Publications

Abbreviations: TP, total publications; TC, total citations; CPP, number of citations per publication.

Major Contributing Authors

A total of 507 authors were involved in T100 papers in the field of HZ, and there were 10 authors who contributed more than five highly cited publications (Table 3). Myron J Levin from University of Colorado Medical School and Kenneth E Schmader from Duke University were the top contributors with 11 articles. The most cited author was Myron J Levin (n=2974), and the article by John W Gnann Jr had the highest average number of citations (n=376.80).

Figure 6 shows the author collaboration network, with Myron J Levin having the highest TLS (TLS=170), having successively collaborated with 100 authors. Among them, the closest collaboration is with Michael N Oxman, Kenneth E Schmader and Ivan S F Chan, who have co-authored seven research articles and formed a relatively stable collaborative team.

Distribution of Journals

The T100 papers were published in 49 journals, of which 31 journals published only one T100 article. Table 4 shows the top 10 journals that published the most T100 articles. All journals belong to Q1 or Q2 according to the JCR categories. The journal with the highest IF was Lancet at 202.73. Clinical Infectious Diseases published the most articles (n=9), followed by Journal of Infectious Diseases (n=8) and New England Journal of Medicine (n=7). New England Journal of Medicine was the most frequently cited journal (n=4469), followed by Clinical Infectious Diseases (n=1898) and Neurology (n=1685).



Figure 5 Co-authorship overlay visualization map of institutions.

Rank	Author	ТР	тс	СРР	Institution	Country
I	Myron J Levin	11	2974	270.36	University of Colorado Medical School	US
2	Kenneth E Schmader	11	2608	237.09	Duke University	US
3	Donald H Gilden	8	2010	251.25	University of Colorado Health Sciences Center	US
4	Michael N Oxman	8	1826	228.25	University of California, San Diego	US
5	Randall J Cohrs	7	1829	261.29	University of Colorado Denver School of Medicine	US
6	Robert W Johnson	7	1731	247.29	Sanofi Pasteur MSD	France
7	Ivan S F Chan	7	1497	213.86	University of Bristol	UK
8	Robert H Dworkin	6	1661	276.83	University of Rochester School of Medicine and Dentistry	US
9	John W Gnann	5	1884	376.80	Duke University	US
10	Anne A Gershon	5	1279	255.80	Columbia University College of Physicians and Surgeons	US

Table 3 Top 10 Authors in the Top 100 Most-Cited Publications

Abbreviations: TP, total publications; TC, total citations; CPP, number of citations per publication; US, United States; UK, United Kingdom.

Co-Occurrence Analysis of Keywords

Keywords are high-level summaries and condensations of topics in an article.²¹ High-frequency keywords represent popular topics in a research field.²² A total of 448 keywords were included in this study, of which 326 keywords were studied at a frequency of one. In addition to the search terms, the most frequently studied keywords were postherpetic neuralgia (n=34), epidemiology (n=28), pain (n=27), and vaccine (n=24) (Table 5). The keyword co-occurrence network was created using VOSviewer (Figure 7), and the size of each node in the figure represents the research frequency of a keyword. According to the color of the nodes, the keywords can be divided into four clusters, which are as follows: Cluster 1 (red): drug therapy, including acyclovir, amitriptyline, gabapentin and other nine keywords; Cluster 2 (green): Immunoprophylaxis, including vaccine, immune-responses, immunogenicity and other nine keywords; Cluster 3 (blue): including diagnosis, DNA, epidemiology and other six keywords; Cluster 4 (yellow): Complications, including postherpetic neuralgia, infection, neuropathic pain and other five keywords.

Discussion

Basic Information Analysis

In this study, we identified the 100 most influential papers correlated to HZ from 2000 to 2022. The 100 papers were also assessed for specific characteristics, including year of publication, number of citations, country of origin, institution,



Figure 6 Co-authorship overlay visualization map of authors.

Journal	ТР	JCR	IF	тс	СРР
Clinical Infectious Diseases	9	QI	21.00	1898	210.89
Journal of Infectious Diseases	8	QI	7.76	1507	188.38
New England Journal of Medicine	7	QI	176.08	4469	638.43
Neurology	5	QI	11.80	1685	337.00
Pain	5	QI	7.93	1090	218.00
Epidemiology and Infection	4	Q2	4.43	798	199.50
Jama - journal of the American Medical Association	4	QI	157.34	886	221.50
Journal of Pain	3	QI	5.38	515	171.67
The Lancet	3	QI	202.73	455	151.67
Lancet Neurology	3	QI	59.94	860	286.67
Mayo Clinic Proceedings	3	QI	11.10	849	283.00
Vaccines	3	Q2	4.96	528	176.00

Table 4 Top 10 Journals in the Top 100 Most-Cited Publications

Abbreviations: TP, total publications; IF, impact factor; TC, total citations; CPP, number of citations per publication.

Rank	Keyword	ТР	Rank	Keyword	ТР
I	Herpes-zoster	34	11	Neuropathic pain	14
2	Postherpetic neuralgia	34	12	Therapy	12
3	Epidemiology	28	13	Clinical-trials	10
4	Pain	27	14	Immune-responses	9
5	Infection	24	15	Quality-of-life	9
6	vaccine	24	16	Varicella-zoster	9
7	Age	21	17	Safety	8
8	Varicella	20	18	Amitriptyline	7
9	Acyclovir	18	19	Efficacy	7
10	Double-blind	17	20	Gabapentin	6

Table 5 Top 20 Keywords in the Top 100 Most-Cited Publications

Abbreviation: TP, total publications.

journal, author, and subject. The earliest cited researches in the highly cited literature were published in 2000. The mostcited publication was Michael N Oxman's 2005 article titled "A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults", which marked the introduction of a vaccine for shingles, offering new hope for the prevention of this afflicting disease.²³ The top 10 institutions in terms of the number of published T100 papers are all from the US and the UK. The institution with the highest number of publications (n=18) and the highest citation frequency (average citations: 281.78 citations per article) is the University of Colorado. The Clinical Infectious Diseases has published the most highly cited articles. Among the authors who published T100 papers, Myron J Levin from the University of Colorado is the most published and most cited researcher overall, followed by Kenneth E Schmader from Duke University, whereas Duke University's John W Gnann Jr tops the list in terms of average citations per article. Myron J Levin is engaged in investigating an effective, low side-effect HZ vaccine for people of different age groups^{24,25} and health backgrounds.²⁶ In addition, as principal investigator of the PROVENT trial, he is involved in the development of the Evusheld long-acting antibody combination for pre-exposure prophylaxis of COVID-19, which has received emergency authorization in the US.²⁷ John W Gnann Jr from Duke University, who has contributed to the efficacy and safety study of the HZ vaccine.²⁸ Myron J Levin, Michael N Oxman, and Kenneth E Schmader, established a relatively stable cooperative group. The academic community mainly studied the impact of HZ on patients' quality of life²⁹ and the corresponding social burden,^{30,31} and also participated in the publication of high-quality recommendations for the management of HZ.³² The academic group's co-published research mainly focused from 2007 to 2015.



Figure 7 Map of keyword clustering in herpes zoster research.

Research Hotspots and Fronts

Based on the analysis of co-cited references, high-frequency keywords, keyword clusters and keyword burst, we believe that the research hotspots in the HZ field are mainly focused on: (1) Drug Therapy; (2) Immunoprophylaxis; (3) Complications. In this study, the top four keywords were counted according to the frequency of research in each hotspot and displayed in Table 6. Acyclovir, vaccine, and PHN were the most important research items in each research hotspot.

Drug Therapy

Prompt administration of antiviral drugs within 72 hours of the onset of the rash can reduce viral replication, shorten the duration of symptoms, and prevent complications.³³ Studies have shown that the main antiviral drugs currently used in clinical practice for HZ are valacyclovir and famciclovir, while the frequency of acyclovir use is gradually decreasing.³⁴ Acyclovir was first mentioned in 1974 by Nick Oliver³⁵ and then its antiviral properties were first discovered by Peter Collins and John Bauer of Wellcome Laboratories in Beckenham, the UK.³⁶ The anti-herpetic activity of acyclovir is achieved by inhibition of herpes-specific replicative DNA polymorphases.³⁷ Acyclovir has been shown to be significantly more effective against herpes simplex virus types 1 and 2 than against varicella virus.³⁸ The duration of maximum drug

Research Hotspots	Keyword	Frequency	Total Frequency
Drug Therapy	Acyclovir	18	35
	Amitriptyline	7	
	Gabapentin	6	
	Topical capsaicin	4	
Immunoprophylaxis	Vaccine	24	40
	Immune-responses	9	
	Immunogenicity	4	
	Immunization	3	
Complications	Postherpetic neuralgia	34	75
	Infection	24	
	Neuropathic pain	14	
	Central-nervous-system	3	

Table 6 The Top Four Keywords in Three Research Hotspots

concentration for intravenous acyclovir and initial oral doses is approximately one hour and two hours, respectively.³⁹ Compared with placebo, oral administration of aciclovir within 47 hours after the onset of the disease reduced the average time to the last day of new lesion formation by 0.5 days, 1.8 days, and 2.2 days.⁴⁰ In some studies, Famciclovir has been shown to be superior to aciclovir in reducing shingles-related pain.⁴¹ Timely initiation of treatment with high-dose acyclovir, valacyclovir, or famciclovir may limit the severity, duration, and complications of the disease outbreak.⁴²

Immunoprophylaxis

In addition to innate immunity, acquired immunity, represented by T-cell-mediated immunity (CMI), plays a decisive role in the host's defense against VZV infection.^{43,44} One study found that HZ is more severe in immunocompromised patients and has a higher risk of serious complications.⁴⁵ For example, HZ has become a common complication of HIV infection.⁴⁶ Due to the limited efficacy of pharmacological interventions, immunoprophylaxis is now the preferred option to address VZV infection.⁴⁷ As of 2018, approximately 24.1% of the US population \geq 50 years of age was expected to have been vaccinated against HZ.⁴⁸ Currently, only two HZ vaccines are available⁴⁹ and the live-attenuated zoster vaccine (ZVL, Zostavax, Merck Sharp & Dohme Corp) is one of them. It is similar in composition to the vaccine used to prevent primary VZV infection, but is more potent.⁵⁰ The ZVL vaccine is recommended by The Advisory Committee on Immunization Practices for immunization of people aged 60 years and older.⁵¹ One study found that the efficacy of ZVL exhibited the following characteristics: (i) A decrease with age,²³ for example, 64% in subjects aged 60-69 years and only 18% in subjects \geq 80 years;⁵² (ii) The effectiveness rate decreases with the duration of vaccination, and will decrease from 68% to 32% at eight years after vaccination.⁵³ It is also noted at the time of vaccination that since ZVL is a live vaccine, it is contraindicated for immunocompromised individuals.²⁵ Another vaccine is recombinant zoster vaccine (RZV) (Shingrix; GlaxoSmithKline, Brentford, the UK), approved for marketing in October 2017,⁵⁴ a double-dose subunit vaccine containing recombinant somatic glycoprotein E and AS01B adjuvant.⁵⁵ The Advisory Committee on Immunization recommended setting the lower age limit for RZV vaccination at 50 years.⁵⁶ Meanwhile, immunocompromised patients are an important target population for RZV,²⁵ showing good safety and efficacy.⁴⁷ In addition, immune serum globulin is used clinically for prophylaxis in immunocompromised populations and in high-risk groups exposed to VZV.⁵⁷ In 1969, Varicella zoster immunoglobulin (VZIG) was first extracted in humans from patients recovering from VZV infection.⁵⁸ In 2012, Varicella zoster immune globulin (VARIZIG, Saol Therapeutics, Roswell, GA, the US) was approved for marketing to replace VZIG, which had been in clinical use for more than 20 years.⁵⁹ Derived from human plasma containing high levels of anti-VZV antibodies, VARIZIG is recommended for use within 96 hours of VZV exposure for passive immunization.⁶⁰

Complications

PHN is a chronic neuropathic pain syndrome⁶¹ and is also the most common complication of HZ.⁶² Approximately 5.8% of patients with HZ will develop PHN.⁶³ It is now generally accepted that the diagnosis of PHN needs to be met by pain in the skin area lasting more than three months after the lesions of HZ have subsided.⁶⁴ More than 30% of patients have had pain for more than one year.⁶⁵ The site of disease is concentrated in the chest and abdomen.⁶⁶ The nature of the pain is pins and needles, burning or electric shock-like.⁶⁷ In some patients, the pain is uncontrollable and leads to depression, fatigue and sleep disturbances.⁶⁸ There is no agreement on the time requirement for diagnosis, for example, 30 days after the onset of HZ,⁶⁹ pain lasting one month after the onset of rash,⁷⁰ and pain lasting 90 days after the onset of blistering.²³ Risk factors for the development of PHN include advanced age, female sex, and severe immunosuppression.⁷¹ The pathogenesis of PHN is still unclear⁷² and may be related to acute nerve injury, local ischemia, and neurotrophic disorders.⁷³ Prevention of PHN, timely and effective pain control, and improvement of the patient's quality of life have become the focus of PHN interventions.^{74,75} In recent decades, the standard treatment regimen for PHN has included the use of opioids, antiepileptics, and the addition of tricyclic antidepressants when necessary.^{64,76} However, the above therapeutic effects remain controversial.⁷⁷ For example, the efficacy of oral gabapentin for moderate to severe PHN was only 14-17% higher than that of the placebo group⁷⁸ and there is a risk of adverse effects such as thirst, dizziness, and drowsiness.^{79,80} In addition, interventional therapy represented by spinal radiofrequency therapy as an emerging therapy to intervene in PHN⁸¹ has the advantages of less trauma, significant efficacy, and high safety.⁸² Since the National Institutes of Health (NIH) consensus conference in 1998,⁸³ acupuncture has been widely used in Europe and the United States and other countries for the management of chronic pain.⁶³ Systematic reviews have shown that acupuncture reduces pain intensity, relieves anxiety, and improves quality of life in patients with PHN, and its efficacy is superior to that of drug controls.⁸⁴

Our study also has several limitations. First, some recent prominent papers may have been excluded due to the lack of time to obtain as many citations as the T100 articles; second, the citation analysis was influenced by many factors, such as self-citations. We did not remove the number of citations that were influenced by other factors.

Conclusion

In terms of the quantity of T100 articles, researchers, and organizations, the US is the predominant country. From 2000 to 2022, the most T100 papers were published in the special journal Clinical Infectious Diseases. The most academic focus remain the remedies for postherpetic neuralgia and vaccine development for individualized groups.

Abbreviations

ACY, average citations per year; CDC, Centers for Disease Control and Prevention; CMI, T-cell-mediated immunity; CPP, number of citations per publication; HZ, herps zoster; IF, impact factor; NIH, National Institutes of Health; PHN, postherpetic neuralgia; RCTs, randomized controlled trials; RZV, recombinant zoster vaccine; SCIE, Science Citation Index Expanded; T100 papers, top 100 most-cited papers; TC,

total citations; TLS, total link strength; TP, total publications; UK, United Kingdom; US, United States; VARIZIG, varicella zoster immune globulin; VZIG, varicella zoster immunoglobulin; VZV, varicella-zoster virus; WOSCC, web of science core collection; ZVL, live-attenuated zoster vaccine.

Data Sharing Statement

Data is available upon reasonable request.

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Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests.

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