

The 100 top-cited tuberculosis research studies

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SUMMARY

The examination of top-cited studies is a useful method for identify and monitoring outstanding scientific research. The objective of this study was to identify and analyse the characteristics of the top 100 cited research studies on tuberculosis (TB) based on the Web of Knowledge. Overall, the top 100 cited studies were cited between 366 and 4443 times, and were published between 1995 and 2010, with the largest number of publications in 2003 and in 1995. Four studies were attributed to a single author and 10 to two authors; the number of authors exceeded six in 50 studies. Nine authors had more than one study as the first author and 18 authors had more than one study as the correspond-

ing author. The United States contributed the largest number of studies, followed by the United Kingdom and France. The institutions with the largest number of articles were the *Institut National de la Santé et de la Recherche Médicale* in France and the University of California in the United States. The studies appeared in 35 journals, with 11 published in Science, followed by PNAS and NEJM. The majority of TB articles have been published in those medical journals with the highest impact factors, and are from the most industrialised countries.

KEY WORDS: tuberculosis; citation; top-cited studies

THE MOST WIDELY USED METHOD for evaluating the academic importance of a study in a specific area of knowledge is determining how many times the study has been cited by other researchers.¹ It is well known that the number of citations for a study might express the potential of the study for clinical practice, discussion, controversy or further research.² Citations analysis has become a useful method for assessing the quality, trend and future of some research fields.^{1,3,4} Although citations analyses from the Science Citation Index Expanded™ of the Web of Science™ (Thomson Reuters, Philadelphia, PA, USA) in recent years have enabled researchers to assess the importance of research in areas such as obstetrics and gynaecology, emergency medicine, urology and orthopedics,^{2,5–7} many new studies, such as research on tuberculosis (TB) studies, remain to be conducted.

TB is one of the most common causes of death due to an infectious disease,^{8–12} and is an important subject of medical research.^{13–15} Studies related to pathology, physiopathology, diagnosis, manifestations, treatment, prognosis, prevention, epidemiology and patient education are the most widely studied

issues in TB.^{16–20} To our knowledge, no citation analysis has been published in the field of TB.

The objective of the present study was to use the bibliometric resources of the Web of Science to identify the 100 most cited studies published on TB and to analyse their principal characteristics.²¹ This is, to our knowledge, the first bibliometric analysis of TB studies.

METHODS

Two independent reviewers (LMC and TYX) searched TB studies using the cited reference search tool of the Web of Knowledge in the Web of Science's core collection. A topic search with the terms 'tuberculo*' or 'tuberculosis' or 'TB' was conducted, and search results sorted by number of citations. The following inclusion criteria were used: 1) studies that reported mainly on TB disease or on *Mycobacterium tuberculosis*; and 2) studies that were articles, reviews, editorials or research letters. The exclusion criteria were as follows: 1) studies that mentioned the word 'tuberculosis' but did not deal with TB; and 2) abstracts, corrigenda/errata, correspondence. Any disagreements were resolved by discussion or decided by the third author (YQL).

Table 1 Authors with more than one study as first or corresponding authors included in the 100 top-cited studies

Author	Name	Studies <i>n</i>
Corresponding author	Behr, M A	2
	Casanova, J L	2
	Cooper, A M	2
	Dye, C	3
	Flynn, J L	3
	Franzblau, S G	2
	Friden, T R	2
	Hill, A V S	2
	Modlin, R L	4
	Musser, J M	2
	Nathan, C F	2
	Pai, M	2
	Rubin, E J	2
	Russell, D G	2
	Stover, C K	2
	Supply, P	2
	van Embden, J D	2
	Wayne, L G	2
	First author	Behr, M A
Dye, C		2
Flynn, J L		2
Friden, T R		2
Pai, M		2
Sasseti, C M		2
Stenger, S		2
Supply, P		2
Wayne, L G	2	

We identified the 100 top cited studies by number of citations on 10 January 2015. The following information was extracted for each study: number of citations, first author, corresponding author, number of authors, publication name, year, country of origin and number of pages. Country of origin was determined on the basis of the country of the first author.

RESULTS

Main characteristics of the included studies

The Appendix Table* shows the characteristics of the top 100 cited studies in TB research in descending order. The number of citations varied between 366 and 4443, with a total of 62 801. All of the first 11 studies exceeded 1000 citations each, and the first 46 had more than 500 citations each. It is possible to comment only on three of the most relevant articles here. The most cited study (4443 citations) was a research study about the complete genome sequence of *M. tuberculosis*, published in 1998 by Cole et al. in *Nature*.²² The second study (1881 citations), on TB associated with infliximab, was published in 2001 by Keane et al in *NEJM*.²³ The study reported that as active TB could develop soon after the initiation of treatment with infliximab, physicians could use the drug to screen patients for latent tuberculous

infection or TB disease. The third most cited study was a report published in *JAMA* in 1999 by Dye et al. on the global burden of TB.²⁴

Author distribution

Four articles were attributed to a single author and 10 to two authors; the number of authors exceeded six in 50 studies. Authors with more than one study as the first author or corresponding author have been listed in Table 1. Nine authors had more than one study as the first author, and 18 had more than one study as the corresponding author. The author with the largest number of studies as corresponding author was Modlin ($n = 4$).

Country distribution

The country of the corresponding author was used to analyse country contributions on TB (Table 2). Briefly, the top 100 cited studies were from 13 countries (Argentina, Belgium, Canada, Denmark, the United Kingdom, France, Germany, Japan, the Netherlands, South Africa, Spain, Switzerland and the United States) and one international organization (World Health Organization [WHO]). The country with the most top cited studies was the United States, with 58 studies, followed by the United Kingdom with 11 and France with 6. The country with the most citations was the United States, with 33 673 citations, followed by the United Kingdom, with 9498 citations. The countries with most citations on average were the United Kingdom, with 864, followed by Argentina, with 828.

Institutional distribution

To analyse contributions from institutions, those with at least two studies based on the first address of the corresponding author were examined (Table 3). Eighteen institutions with more than two studies were included. The institutions with the largest number of articles were the *Institut National de la Santé et de la Recherche Médicale* (INSERM) ($n = 6$) in Paris, France, and the University of California ($n = 6$) in the United States, followed by the University of Oxford, Oxford, UK ($n = 5$), the WHO, Geneva, Switzerland ($n = 5$), and Cornell University, Ithaca, NY, USA ($n = 5$).

Distribution by year of publication

The distribution by year of publication of the top 100 cited studies is shown in Table 4. The top-cited studies were published between 1995 and 2010. The years with the most studies were 2003 and 1995, with 11 studies each, followed by 1998 and 2001, with 10 each. The year with the most citations was 1998, with 9007 citations, followed by 2003, with 6858. The year with the most citations on average was 1998, with 901, followed by 2007, with 742.

* The Appendix is available in the online version of this article, at <http://www.ingentaconnect.com/content/iuatld/ijtd/2015/00000019/00000006/art00020>

Table 2 Country of origin of the 100 top-cited studies; based on country of first author

Country	Studies <i>n</i>	Total citations <i>N</i>	Average citations/article <i>n</i>	Studies in each ranking, <i>n</i>										
				1~10	11~20	21~30	31~40	41~50	51~60	61~70	71~80	81~90	91~100	
Argentina	1	828	828		1									
Belgium	1	674	674			1								
Canada	5	2 842	568		1		1	1				1		1
Denmark	2	800	400								1			1
France	7	3 370	481			1	1	1	2					2
Germany	1	421	421							1				
Japan	1	395	395									1		
Netherlands	4	2 916	729	1			1		1		1			
South Africa	1	372	372										1	
Spain	1	490	490					1						
Switzerland	2	1 377	689		1	1								
United Kingdom	11	9 498	864	1	2		1	1		1	2	1		2
United States	58	33 673	581	5	5	7	6	6	6	7	5	7		4
WHO	5	5 145	1 029	3						1			1	

WHO = World Health Organization.

Distribution by journal

The top 100 studies were published in 35 journals (Table 5). The journal with the largest number of articles cited was Science ($n=11$), followed by PNAS ($n=10$), the NEJM ($n=8$) and the Lancet ($n=8$). The journal with the most citations was Science, with 7107, followed by Nature, with 6388. The journal with the highest average number of citations per article was JAMA, with 1481 citations, followed by Nature, with 1352.

DISCUSSION

TB is historically the greatest killer worldwide due to an infectious agent.^{11,12,25} Although there has been considerable progress in anti-tuberculosis treatment,

8.6 million people were estimated to have TB and 1.3 million died from the disease in 2012. Although research on TB has increased each year, no bibliometric studies have been conducted on TB research. We performed the present study to determine the top 100 cited studies in TB research.

The 100 top-cited studies were cited 366–4443 times. Compared to citations in other medical fields, this occupies a middle position: in general surgery the number of citations for top-cited studies ranged from 278 to 1013,²⁶ compared to 781–26 578 for psychiatry.²⁷ The difference in the number of citations of the top 100 cited studies in each specialty reflects its research history and the number of researchers working in that field.²⁸ Studies with more than 100 citations are considered ‘classic’ studies that consti-

Table 3 Institutions with at least two studies based on the institution of the corresponding authors included in the 100 top-cited studies

Institution	Studies <i>n</i>	Country
Institut national de la Santé et de la Recherche médicale (INSERM), Paris, France	6	France
University of California	6	United States
University of Oxford, Oxford, UK	5	United Kingdom
World Health Organization, Geneva, Switzerland	5	—
Cornell University, Ithaca, NY, USA	5	United States
McGill University, Montreal, QC, Canada	4	Canada
Harvard University, Cambridge, MA, USA	4	United States
Netherlands National Institute for Public Health & The Environment, Bilthoven, The Netherlands	3	The Netherlands
University of Pittsburgh, Pittsburgh, PA, USA	3	United States
Colorado State University, Fort Collins, CO, USA	3	United States
Statens Serum Institute, Copenhagen, Denmark	2	Denmark
American Thoracic Society, New York, NY, USA/Infectious Diseases Society of America, Arlington, VA, USA	2	United States
Baylor College of Medicine, Houston, TX, USA	2	United States
Boston University, Boston, MA, USA	2	United States
United States Department of Veterans Affairs, Washington DC, USA	2	United States
GWL Hansen's Disease Center, Carville, LA, USA	2	United States
New York City Department of Health And Mental Hygiene, New York, NY, USA	2	United States
PathoGenesis Corporation, Seattle, WA, USA	2	United States

Table 4 Distribution by year of publication of the 100 top-cited studies

Year	Studies <i>n</i>	Total citations <i>n</i>	Average citations/article <i>n</i>
1995	11	6711	610
1996	6	2972	495
1997	8	5791	724
1998	10	9007	901
1999	9	5846	650
2000	7	3723	532
2001	10	6306	631
2002	5	2579	516
2003	11	6858	623
2004	7	3373	482
2005	1	674	674
2006	8	4404	551
2007	4	2968	742
2008	2	970	485
2010	1	619	619

tute historical reference points in the development of a specific area.²⁹ In the present study, the article that occupied position 100 in the rankings had 366 citations, suggesting that a large number of classic studies had not been analysed in the present study.

Our results show that most of the top 100 cited TB research studies were published between 1995 and 2010. Scientific studies are generally cited 1–2 years after publication, reaching a maximum citation rate 7–10 years after publication. An interval of 10–20 years is needed for maximum recognition of prominent articles in a field.^{28,29} This would explain why recent articles were cited rarely and why most of the studies included in our list were published in the 1990s.

It is also well known that the principal journals attract articles with a high citation rate,^{28,29} which in turn helps to maintain the impact factor of these journals; this accounts for the clustering of articles in a small number of journals, particularly those that frequently publish studies on TB. In the present study, 48 studies were published in journals with an impact factor of >20, including the Annual Review of Biochemistry, the Annual Review of Immunology, Cell, JAMA, The Lancet, Nature Immunology, Nature Medicine, Nature Reviews Immunology, Nature Reviews Molecular Cell Biology, the NEJM and Science. Our results confirm the close relation-

Table 5 Journals in which the 100 top-cited studies were published

Journal	Abbreviated name	Articles included in top 100 <i>n</i>	Total citations <i>n</i>	Average citations/article <i>n</i>	Impact factor (2013)
American Journal of Respiratory and Critical Care Medicine	Am J Respir Crit Care Med	4	2553	638	11.986
Annals of Internal Medicine	Ann Intern Med	2	1119	560	16.104
Annual Review of Biochemistry	Annu Rev Biochem	1	1047	1047	26.534
Annual Review of Immunology	Annu Rev Immunol	4	2455	614	41.392
Annual Review of Microbiology	Annu Rev Microbiol	1	388	388	13.018
Antimicrobial Agents and Chemotherapy	Antimicrob Agents Chemother	1	938	938	4.451
Archives of Internal Medicine	Arch Intern Med	1	1352	1352	13.246
Arthritis and Rheumatism	Arthritis Rheum	1	490	490	7.871
Biotechniques	Biotechniques	1	399	399	2.754
BMC Microbiology	BMC Microbiol	1	471	471	2.976
Cell	Cell	2	1212	606	33.116
Clinical Infectious Diseases	Clin Infect Dis	1	463	463	9.416
Clinical Microbiology Reviews	Clin Microbiol Rev	1	367	367	16.000
Immunity	Immunity	1	983	983	19.748
Infection and Immunity	Infect Immun	2	859	430	4.156
Journal of the American Medical Association	JAMA	2	2962	1481	30.387
Journal of Bacteriology	J Bacteriol	2	1028	514	2.688
Journal of Biological Chemistry	J Biol Chem	1	367	367	4.600
Journal of Clinical Microbiology	J Clin Microbiol	6	3572	595	4.232
Journal of Experimental Medicine	J Exp Med	6	3269	545	13.912
Journal of Immunology	J Immunol	2	942	471	5.362
Journal of Medicinal Chemistry	J Med Chem	1	387	387	5.480
Lancet	Lancet	8	3760	470	39.207
Lancet Infectious Diseases	Lancet Infect Dis	2	925	463	19.446
Microbiology (UK)	Microbiology	1	389	389	0.712
Molecular Microbiology	Mol Microbiol	3	2017	672	5.026
Nature	Nature	5	6388	1278	42.351
Nature Immunology	Nat Immunol	2	1353	677	24.973
Nature Medicine	Nature Med	3	1306	435	28.054
Nature Reviews Immunology	Nat Rev Immunol	1	421	421	33.836
Nature Reviews Molecular Cell Biology	Nat Rev Mol Cell Bio	1	372	372	36.458
New England Journal of Medicine	New Engl J Med	8	5454	682	54.420
Pediatrics	Pediatrics	1	366	366	5.297
Proceedings of The National Academy of Sciences of The United States of America	PNAS	10	5320	532	9.809
Science	Science	11	7107	646	31.477

ship between citations and impact, and that the most cited studies are often published in journals that top the impact factor list, which also helps maintain the high impact factor of these journals.

In line with other, similar studies, more than half of the publications originated from the United States, followed by the United Kingdom. Our results reflect the large number of TB researchers in the United States and the considerable scientific output in the United States, which dominates the field of TB publications.

Although the world's highest TB burdens are in low- and middle-income countries, most of the highly cited papers are from high-income countries. The authors tend to originate from high-income countries even though the actual research was conducted in low-income, high-burden countries, such as Gandhi et al.³⁰ and Bellamy et al.³¹ It is therefore necessary to strengthen TB research capacity in low- and middle-income countries, especially in BRICS (Brazil, Russia, India, China, South Africa) countries, which account for a substantial proportion of the global TB burden and are now making large investments in science and research.

There are several limitations of this study. First, it was based on the Web of Knowledge database alone; the Web of Science does not index all journals and we may have missed journals that figure in other databases such as Scopus and Google Scholar. Our results should therefore be used with caution. Second, as we only analysed the corresponding and first authors' contributions in our analysis, we may have missed important contributions from other authors; future studies should focus on this issue.

In conclusion, this is the first bibliometric assessment of TB literature. Interest in TB as a serious clinical problem continues to grow. Research published in high-impact journals and from industrialised countries is most likely to be cited in published TB research.

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- Dye C, Scheele S, Dolin P, Pathania V, Ravigione M C. Consensus statement. Global burden of tuberculosis: estimated incidence, prevalence, and mortality by country. WHO Global Surveillance and Monitoring Project. *JAMA* 1999; 282: 677–686.
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APPENDIX

Table A The 100 most cited articles in tuberculosis research

Ranking	Study	Citations <i>n</i>
1	Cole S T, Brosch R, Parkhill J, et al. Deciphering the biology of <i>Mycobacterium tuberculosis</i> from the complete genome sequence. <i>Nature</i> 1998; 393: 537–544.	4443
2	Keane J, Gershon S, Wise R P, et al. Tuberculosis associated with infliximab, a tumor necrosis factor alpha-neutralizing agent. <i>N Engl J Med</i> 2001; 345: 1098–1104.	1881
3	Dye C, Scheele S, Dolin P, Pathania V, Raviglione M C. Consensus statement. Global burden of tuberculosis: estimated incidence, prevalence, and mortality by country. WHO Global Surveillance and Monitoring Project. <i>JAMA</i> 1999; 282: 677–686.	1870
4	Kamerbeek J, Schouls L, Kolk A, et al. Simultaneous detection and strain differentiation of <i>Mycobacterium tuberculosis</i> for diagnosis and epidemiology. <i>J Clin Microbiol</i> 1997; 35: 907–914.	1452
5	Concato J, Shah N, Horwitz R I. Randomized, controlled trials, observational studies, and the hierarchy of research designs. <i>N Engl J Med</i> 2000; 342: 1887–1892.	1352
6	Liu P T, Stenger S, Li H, et al. Toll-like receptor triggering of a vitamin D-mediated human antimicrobial response. <i>Science</i> 2006; 311: 1770–1773.	1279
7	Flynn J L, Chan J. Immunology of tuberculosis. <i>Annu Rev Immunol</i> 2001; 19: 93–129.	1192
8	Raviglione M C, Snider D E, Jr., Kochi A. Global epidemiology of tuberculosis. Morbidity and mortality of a worldwide epidemic. <i>JAMA</i> 1995; 273: 220–226.	1092
9	Griffith D E, Aksamit T, Brown-Elliott B A, et al. An official ATS/IDSA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. <i>Am J Respir Crit Care Med</i> 2007; 175: 367–416.	1086
10	Sasseti C M, Boyd D H, Rubin E J. Genes required for mycobacterial growth defined by high density mutagenesis. <i>Mol Microbiol</i> 2003; 48: 77–84.	1072
11	Brennan P J, Nikaido H. The envelope of mycobacteria. <i>Ann Rev Biochem</i> 1995; 64: 29–63.	1047
12	Flynn J L, Goldstein M M, Chan J, et al. Tumor necrosis factor-alpha is required in the protective immune response against <i>Mycobacterium tuberculosis</i> in mice. <i>Immunity</i> 1995; 2: 561–572.	983
13	Behr M A, Wilson M A, Gill W P, et al. Comparative genomics of BCG vaccines by whole-genome DNA microarray. <i>Science</i> 1999; 284: 1520–1523.	965
14	Shirakawa T, Enomoto T, Shimazu S, Hopkin J M. The inverse association between tuberculin responses and atopic disorder. <i>Science</i> 1997; 275: 77–79.	962
15	Collins L, Franzblau S G. Microplate alamar blue assay versus BACTEC 460 system for high-throughput screening of compounds against <i>Mycobacterium tuberculosis</i> and <i>Mycobacterium avium</i> . <i>Antimicrob Agents Chemother</i> 1997; 41: 1004–1009.	938
16	Gutierrez M G, Master S S, Singh S B, Taylor G A, Colombo M I, Deretic V. Autophagy is a defense mechanism inhibiting BCG and <i>Mycobacterium tuberculosis</i> survival in infected macrophages. <i>Cell</i> 2004; 119: 753–766.	828
17	Acosta-Rodriguez E V, Rivino L, Geginat J, et al. Surface phenotype and antigenic specificity of human interleukin 17-producing T-helper memory cells. <i>Nat Immunol</i> 2007; 8: 639–646.	758
18	Nathan C, Shiloh M U. Reactive oxygen and nitrogen intermediates in the relationship between mammalian hosts and microbial pathogens. <i>Proc Natl Acad Sci USA</i> 2000; 97: 8841–8848.	706
19	Dunlap N D, Bass J, Fujiwara P, et al. Diagnostic standards and classification of tuberculosis in adults and children. <i>Am J Respir Crit Care Med</i> 2000; 161(4 Pt 1): 1376–1395.	705
20	Fine P E. Variation in protection by BCG: implications of and for heterologous immunity. <i>Lancet</i> 1995; 346: 1339–1345.	692
21	McKinney J D, Honer zu Bentrup K, Munoz-Elias E J, et al. Persistence of <i>Mycobacterium tuberculosis</i> in macrophages and mice requires the glyoxylate shunt enzyme isocitrate lyase. <i>Nature</i> 2000; 406: 735–738.	683
22	Lu B, Rutledge B J, Gu L, et al. Abnormalities in monocyte recruitment and cytokine expression in monocyte chemoattractant protein 1-deficient mice. <i>J Exp Med</i> 1998; 187: 601–608.	677
23	Andries K, Verhasselt P, Guillemont J, et al. A diarylquinoline drug active on the ATP synthase of <i>Mycobacterium tuberculosis</i> . <i>Science</i> 2005; 307: 223–227.	674
24	Chang G, Spencer R H, Lee A T, Barclay M T, Rees D C. Structure of the Mscl homolog from <i>Mycobacterium tuberculosis</i> : a gated mechanosensitive ion channel. <i>Science</i> 1998; 282: 2220–2226.	672
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29	Boehme C C, Nabeta P, Hillemann D, et al. Rapid molecular detection of tuberculosis and rifampin resistance. <i>N Engl J Med</i> 2010; 363: 1005–1015.	619
30	Mahairas G G, Sabo P J, Hickey M J, Singh D C, Stover C K. Molecular analysis of genetic differences between <i>Mycobacterium bovis</i> BCG and virulent <i>M. bovis</i> . <i>J Bacteriol</i> 1996; 178: 1274–1282.	606
31	MacMicking J D, North R J, LaCourse R, Mudgett J S, Shah S K, Nathan C F. Identification of nitric oxide synthase as a protective locus against tuberculosis. <i>Proc Natl Acad Sci USA</i> 1997; 94: 5243–5248.	598
32	Geijtenbeek T B, Van Vliet S J, Koppel E A, et al. Mycobacteria target DC-SIGN to suppress dendritic cell function. <i>J Exp Med</i> 2003; 197: 7–17.	598
33	Khader S A, Bell G K, Pearl J E, et al. IL-23 and IL-17 in the establishment of protective pulmonary CD4+ T-cell responses after vaccination and during <i>Mycobacterium tuberculosis</i> challenge. <i>Nat Immunol</i> 2007; 8: 369–377.	595
34	Pai M, Zwerling A, Menzies D. Systematic review: T-cell-based assays for the diagnosis of latent tuberculosis infection: an update. <i>Ann Intern Med</i> 2008; 149: 177–184.	590

Table A (continued)

Ranking	Study	Citations <i>n</i>
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36	Pablos-Mendez A, Raviglione M C, Laszlo A, et al. Global surveillance for anti-tuberculosis drug resistance, 1994–1997. World Health Organization/International Union against Tuberculosis and Lung Disease Working Group on Anti-Tuberculosis Drug Resistance Surveillance. <i>N Engl J Med</i> 1998; 338: 1641–1649.	581
37	Betts J C, Lukey P T, Robb L C, McAdam R A, Duncan K. Evaluation of a nutrient starvation model of <i>Mycobacterium tuberculosis</i> persistence by gene and protein expression profiling. <i>Mol Microbiol</i> 2002; 43: 717–731.	576
38	Means T K, Wang S, Lien E, Yoshimura A, Golenbock D T, Fenton M J. Human toll-like receptors mediate cellular activation by <i>Mycobacterium tuberculosis</i> . <i>J Immunol</i> 1999; 163: 3920–3927.	572
39	Jouanguy E, Altare F, Lamhamedi S, et al. Interferon-gamma-receptor deficiency in an infant with fatal bacille Calmette-Guérin infection. <i>N Engl J Med</i> 1996; 335: 1956–1961.	549
40	Pai M, Riley L W, Colford J M, Jr. Interferon-gamma assays in the immunodiagnosis of tuberculosis: a systematic review. <i>Lancet Infect Dis</i> 2004; 4: 761–776.	533
41	Menzies D, Pai M, Comstock G. Meta-analysis: new tests for the diagnosis of latent tuberculosis infection: areas of uncertainty and recommendations for research. <i>Ann Intern Med</i> 2007; 146: 340–354.	529
42	Sassetti C M, Rubin E J. Genetic requirements for mycobacterial survival during infection. <i>Proc Natl Acad Sci USA</i> 2003; 100: 12989–12994.	519
43	Casanova J L, Abel L. Genetic dissection of immunity to mycobacteria: the human model. <i>Annu Rev Immunol</i> 2002; 20: 581–620.	516
44	Huygen K, Content J, Denis O, et al. Immunogenicity and protective efficacy of a tuberculosis DNA vaccine. <i>Nat Med</i> 1996; 2: 893–898.	515
45	Underhill D M, Ozinsky A, Smith K D, Aderem A. Toll-like receptor-2 mediates mycobacteria-induced proinflammatory signaling in macrophages. <i>Proc Natl Acad Sci USA</i> 1999; 96: 14459–14463.	512
46	Bellamy R, Ruwende C, Corrah T, McAdam K P, Whittle H C, Hill A V. Variations in the NRAM1 gene and susceptibility to tuberculosis in West Africans. <i>N Engl J Med</i> 1998; 338: 640–644.	503
47	Frieden T R, Fujiwara P I, Washko R M, Hamburg M A. Tuberculosis in New York City—turning the tide. <i>N Engl J Med</i> 1995; 333: 229–233.	498
47	Frieden T R, Sterling T R, Munsiff S S, Watt C J, Dye C. Tuberculosis. <i>Lancet</i> 2003; 362: 887–899.	498
49	Wayne L G, Hayes L G. An in vitro model for sequential study of shutdown of <i>Mycobacterium tuberculosis</i> through two stages of non-replicating persistence. <i>Infect Immun</i> 1996; 64: 2062–2069.	491
50	Gomez-Reino J J, Carmona L, Valverde V R, Mola E M, Montero M D, BIOBADASER Group. Treatment of rheumatoid arthritis with tumor necrosis factor inhibitors may predispose to significant increase in tuberculosis risk: a multicenter active surveillance report. <i>Arthritis Rheum</i> 2003; 48: 2122–2127.	490
51	Clemens D L, Horwitz M A. Characterization of the <i>Mycobacterium tuberculosis</i> phagosome and evidence that phagosomal maturation is inhibited. <i>J Exp Med</i> 1995; 181: 257–270.	471
51	Brudey K, Driscoll J R, Rigouts L, et al. <i>Mycobacterium tuberculosis</i> complex genetic diversity: mining the fourth international spoligotyping database (SpolDB4) for classification, population genetics and epidemiology. <i>BMC Microbiol</i> 2006; 6: 23.	471
53	Supply P, Allix C, Lesjean S, et al. Proposal for standardization of optimized mycobacterial interspersed repetitive unit-variable tandem repeat typing of <i>Mycobacterium tuberculosis</i> . <i>J Clin Microbiol</i> 2006; 44: 4498–4510.	470
54	Wallis R S, Broder M S, Wong J Y, Hanson M E, Beenhouwer D O. Granulomatous infectious diseases associated with tumor necrosis factor antagonists. <i>Clin Infect Dis</i> 2004; 38: 1261–1265.	463
55	van Soolingen D, Qian L, de Haas P E, et al. Predominance of a single genotype of <i>Mycobacterium tuberculosis</i> in countries of east Asia. <i>J Clin Microbiol</i> 1995; 33: 3234–3238.	460
55	Stover C K, Warrener P, VanDevanter D R, et al. A small-molecule nitroimidazopyran drug candidate for the treatment of tuberculosis. <i>Nature</i> 2000; 405: 962–966.	460
57	Garnier T, Eiglmeier K, Camus J C, et al. The complete genome sequence of <i>Mycobacterium bovis</i> . <i>Proc Natl Acad Sci USA</i> 2003; 100: 7877–7882.	457
58	Espinal M A, Laszlo A, Simonsen L, et al. Global trends in resistance to anti-tuberculosis drugs. World Health Organization-International Union Against Tuberculosis and Lung Disease Working Group on Anti-Tuberculosis Drug Resistance Surveillance. <i>N Engl J Med</i> 2001; 344: 1294–1303.	451
59	Cooper A M, Magram J, Ferrante J, Orme I M. Interleukin 12 (IL-12) is crucial to the development of protective immunity in mice intravenously infected with <i>Mycobacterium tuberculosis</i> . <i>J Exp Med</i> 1997; 186: 39–45.	438
60	Voskuil M I, Schnappinger D, Visconti K C, et al. Inhibition of respiration by nitric oxide induces a <i>Mycobacterium tuberculosis</i> dormancy program. <i>J Exp Med</i> 2003; 198: 705–713.	437
61	Andersen P, Munk M E, Pollock J M, Doherty T M. Specific immune-based diagnosis of tuberculosis. <i>Lancet</i> 2000; 356: 1099–1104.	432
62	Singh S B, Davis A S, Taylor G A, Deretic V. Human IRGM induces autophagy to eliminate intracellular mycobacteria. <i>Science</i> 2006; 313: 1438–1441.	427
63	Thoma-Uszynski S, Stenger S, Takeuchi O, et al. Induction of direct antimicrobial activity through mammalian toll-like receptors. <i>Science</i> 2001; 291: 1544–1547.	426
64	Nau G J, Richmond J F, Schlesinger A, Jennings E G, Lander E S, Young R A. Human macrophage activation programs induced by bacterial pathogens. <i>Proc Natl Acad Sci USA</i> 2002; 99: 1503–1508.	425
65	Tascon R E, Colston M J, Ragno S, Stavropoulos E, Gregory D, Lowrie D B. Vaccination against tuberculosis by DNA injection. <i>Nat Med</i> 1996; 2: 888–892.	424
66	Sherman D R, Voskuil M, Schnappinger D, Liao R, Harrell M I, Schoolnik G K. Regulation of the <i>Mycobacterium tuberculosis</i> hypoxic response gene encoding alpha-crystallin. <i>Proc Natl Acad Sci USA</i> 2001; 98: 7534–7539.	422
66	Fleischmann R D, Alland D, Eisen J A, et al. Whole-genome comparison of <i>Mycobacterium tuberculosis</i> clinical and laboratory strains. <i>J Bacteriol</i> 2002; 184: 5479–5490.	422
68	Kaufmann S H. How can immunology contribute to the control of tuberculosis? <i>Nat Rev Immunol</i> 2001; 1: 20–30.	421

Table A (continued)

Ranking	Study	Citations <i>n</i>
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70	Cox J S, Chen B, McNeil M, Jacobs W R, Jr. Complex lipid determines tissue-specific replication of <i>Mycobacterium tuberculosis</i> in mice. <i>Nature</i> 1999; 402: 79–83.	414
71	Kremer K, van Soolingen D, Frothingham R, et al. Comparison of methods based on different molecular epidemiological markers for typing of <i>Mycobacterium tuberculosis</i> complex strains: interlaboratory study of discriminatory power and reproducibility. <i>J Clin Microbiol</i> 1999; 37: 2607–2618.	406
72	Dheda K, Huggett J F, Bustin S A, Johnson M A, Rook G, Zumla A. Validation of housekeeping genes for normalizing RNA expression in real-time PCR. <i>Biotechniques</i> 2004; 37: 112–114, 116, 118–119.	399
73	Ewer K, Deeks J, Alvarez L, et al. Comparison of T-cell-based assay with tuberculin skin test for diagnosis of <i>Mycobacterium tuberculosis</i> infection in a school tuberculosis outbreak. <i>Lancet</i> . 2003; 361: 1168–1173.	395
73	Mori T, Sakatani M, Yamagishi F, et al. Specific detection of tuberculosis infection: an interferon-gamma-based assay using new antigens. <i>Am J Respir Crit Care Med</i> . 2004; 170: 59–64.	395
75	Gardam M A, Keystone E C, Menzies R, et al. Anti-tumour necrosis factor agents and tuberculosis risk: mechanisms of action and clinical management. <i>Lancet Infect Dis</i> 2003; 3: 148–155.	392
76	Frothingham R, Meeker-O'Connell W A. Genetic diversity in the <i>Mycobacterium tuberculosis</i> complex based on variable numbers of tandem DNA repeats. <i>Microbiology</i> 1998; 144 (Pt 5): 1189–1196.	389
77	Reed M B, Domenech P, Manca C, et al. A glycolipid of hypervirulent tuberculosis strains that inhibits the innate immune response. <i>Nature</i> 2004; 431: 84–87.	388
77	Wayne L G, Sohaskey C D. Non-replicating persistence of mycobacterium tuberculosis. <i>Annu Rev Microbiol</i> 2001; 55: 139–163.	388
79	Brickner S J, Hutchinson D K, Barbachyn M R, et al. Synthesis and antibacterial activity of U-100592 and U-100766, two oxazolidinone antibacterial agents for the potential treatment of multidrug-resistant gram-positive bacterial infections. <i>J Med Chem</i> 1996; 39: 673–679.	387
80	Campbell E A, Korzheva N, Mustaev A, et al. Structural mechanism for rifampicin inhibition of bacterial rna polymerase. <i>Cell</i> 2001; 104: 901–912.	384
81	Gagneux S, DeRiemer K, Van T, et al. Variable host-pathogen compatibility in <i>Mycobacterium tuberculosis</i> . <i>Proc Natl Acad Sci USA</i> 2006; 103: 2869–2873.	380
81	Dye C. Global epidemiology of tuberculosis. <i>Lancet</i> 2006; 367: 938–940.	380
81	Serbina N V, Jia T, Hohl T M, Pamer E G. Monocyte-mediated defense against microbial pathogens. <i>Annu Rev Immunol</i> 2008; 26: 421–452.	380
84	Rozwarski D A, Grant G A, Barton D H, Jacobs W R, Jr, Sacchettini J C. Modification of the NADH of the isoniazid target (<i>inhA</i>) from <i>Mycobacterium tuberculosis</i> . <i>Science</i> 1998; 279: 98–102.	377
85	Russell D G. <i>Mycobacterium tuberculosis</i> : here today, and here tomorrow. <i>Nat Rev Mol Cell Biol</i> 2001; 2: 569–577.	372
85	van Rie A, Warren R, Richardson M, et al. Exogenous reinfection as a cause of recurrent tuberculosis after curative treatment. <i>N Engl J Med</i> 1999; 341: 1174–1179.	372
85	Belisle J T, Vissa V D, Sievert T, Takayama K, Brennan P J, Besra G S. Role of the major antigen of <i>Mycobacterium tuberculosis</i> in cell wall biogenesis. <i>Science</i> 1997; 276: 1420–1422.	372
88	Stenger S, Mazzaccaro R J, Uyemura K, et al. Differential effects of cytolytic T-cell subsets on intracellular infection. <i>Science</i> 1997; 276: 1684–1687.	370
88	Lockhart E, Green A M, Flynn J L. IL-17 production is dominated by gamma delta T-cells rather than CD4 T cells during <i>Mycobacterium tuberculosis</i> infection. <i>J Immunol</i> 2006; 177: 4662–4669.	370
88	Wilkinson R J, Llewelyn M, Toossi Z, et al. Influence of vitamin D deficiency and vitamin D receptor polymorphisms on tuberculosis among Gujarati Asians in west London: a case-control study. <i>Lancet</i> 2000; 355: 618–621.	370
91	Supply P, Lesjean S, Savine E, Kremer K, van Soolingen D, Locht C. Automated high-throughput genotyping for study of global epidemiology of <i>Mycobacterium tuberculosis</i> based on mycobacterial interspersed repetitive units. <i>J Clin Microbiol</i> 2001; 39: 3563–3571.	369
91	Camacho L R, Ensergueix D, Perez E, Gicquel B, Guilhot C. Identification of a virulence gene cluster of <i>Mycobacterium tuberculosis</i> by signature-tagged transposon mutagenesis. <i>Mol Microbiol</i> 1999; 34: 257–267.	369
93	Sorensen A L, Nagai S, Houen G, Andersen P, Andersen A B. Purification and characterization of a low-molecular-mass T-cell antigen secreted by <i>Mycobacterium tuberculosis</i> . <i>Infect Immun</i> 1995; 63: 1710–1717.	368
94	Whalen C, Horsburgh C R, Hom D, Lahart C, Simberkoff M, Ellner J. Accelerated course of human immunodeficiency virus infection after tuberculosis. <i>Am J Respir Crit Care Med</i> 1995; 151: 129–135.	367
94	Musser J M. Antimicrobial agent resistance in mycobacteria: molecular genetic insights. <i>Clin Microbiol Rev</i> 1995; 8: 496–514.	367
94	Faure E, Equils O, Sieling P A, et al. Bacterial lipopolysaccharide activates NF-kappa B through toll-like receptor 4 (TLR-4) in cultured human dermal endothelial cells: differential expression of TLR-4 and TLR-2 in endothelial cells. <i>J Biol Chem</i> 2000; 275: 11058–11063.	367
94	McShane H, Pathan A A, Sander C R, et al. Recombinant modified vaccinia virus Ankara expressing antigen 85A boosts BCG-primed and naturally acquired antimycobacterial immunity in humans. <i>Nat Med</i> 2004; 10: 1240–1244.	367
94	Hill A V. The immunogenetics of human infectious diseases. <i>Ann Rev Immunol</i> 1998; 16: 593–617.	367
99	Colditz G A, Berkey C S, Mosteller F, et al. The efficacy of bacillus Calmette-Guerin vaccination of newborns and infants in the prevention of tuberculosis: meta-analyses of the published literature. <i>Pediatrics</i> 1995; 96(1 Pt 1): 29–35.	366
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RESUME

L'examen des études les plus citées est une méthode utile pour identifier et suivre les recherches scientifiques les plus intéressantes. L'objectif de cette étude était d'identifier et d'analyser les caractéristiques des 100 études de recherche relatives à la tuberculose les plus citées basées sur le Web of Knowledge. Dans l'ensemble, les 100 études les plus citées ont été citées entre 366 et 4443 fois et ont été publiées entre 1995 et 2010, la plus grande partie ayant été publiée en 2003 et 1995. Quatre études ont été attribuées à un seul auteur et 10 articles à deux auteurs, tandis que le nombre d'auteurs dépassait six dans 50 études. Neuf auteurs étaient l'auteur

principal dans plus d'une étude et 18 auteurs étaient l'auteur correspondant dans plus d'une étude. Les États-Unis arrivaient en tête du nombre d'études, suivis par le Royaume Uni et la France. Les institutions à l'origine du plus grand nombre d'articles étaient l'Institut national de la Santé et de la Recherche médicale en France et les campus de l'Université de Californie aux États-Unis. Les études sont apparues dans 35 revues, dont 11 publiées dans Science, suivie par le PNAS et le NEJM. En résumé, la majorité a été publiée dans les revues médicales ayant le plus d'impact et à partir des pays les plus industrialisés.

RESUMEN

El análisis de los estudios más citados constituye un método útil de reconocer y verificar las investigaciones científicas destacadas. El objetivo del presente estudio fue reconocer y analizar las características de los 100 estudios más citados de investigación en tuberculosis, con base en el servicio Web of Knowledge. En general, los 100 estudios aparecían citados de 366 a 4443 veces, habían sido publicados entre 1995 y el 2010 y en su mayoría entre 1995 y el 2003. Cuatro estudios se atribuían a un solo autor, 10 artículos a dos autores y el número de autores era superior a seis en 50 estudios. Nueve autores aparecían en más de un estudio como

autor principal y 18 eran el autor de contacto en más de un estudio. La mayoría de los estudios provenía de los Estados Unidos y luego del Reino Unido y Francia. Las instituciones con el mayor número de artículos citados fueron el *Institut national de la Santé et de la Recherche médicale* de Francia y el sistema de la Universidad de California en los Estados Unidos. Los estudios se publicaron en 35 revistas, 11 de ellos en Science y luego en los PNAS y el NEJM. En conclusión, la mayoría de los artículos se publicaron en las revistas médicas de mayor impacto y procedían de los países más industrializados.
