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Bibliometric analysis of pathogenic organisms

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ABSTRACT

Infectious diseases remain as an important public health threat to humans. Research into pathogens can be useful for planning an organized response to infectious diseases. Bibliometric analysis is an important method for scientific research and assessing capability. In this study, 100 pathogens of public health importance were selected, and the distributions of annual, national, institutional, and journal publications on Science Citation Index (SCI) journals were statistically analyzed. The United States of America ranked the first in terms of the number of relevant studies published. China attaches great importance to the prevention and control of infectious diseases, but still needs to improve in the following areas: for example, insufficient SCI reports on particular pathogens, institutions SCI reports on pathogens lower than world top pathogen research institutions, and lack of influential international pathogen-related journals. Scientific literature databases are important tools for science-of-science analysis. The findings of this study shed light on the hot spots and the ignored spots in pathogen researches, and thus would be useful for drawing a national and institutional research plan.

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1. Introduction

Living standards have continuously been improving on account of the rapid developments in science and technology. Although infectious diseases, in general, have become less common than other diseases such as cancer, cardiovascular disease, metabolic diseases, etc., the frequent genetic transformation of pathogens and the existence of antimicrobial-resistant pathogens are still issues that we have to face today.

During the last few decades, there have been significant advances in the treatment and prevention of infectious diseases, such as HIV, viral hepatitis, and tuberculosis. However, many new infectious diseases have emerged since the SARS epidemic in 2003, such as H5N1 and H7N9 avian influenza, Middle East Respiratory Syndrome, Ebolavirus disease, Zika virus disease, Chikungunya virus disease, and the current Coronavirus Disease 2019 (COVID-19). Consequently, human beings are constantly facing the threat of new and re-emerging infectious diseases [1]. In addition to naturally occurring infectious diseases, another danger posed by pathogens is their potential use as biological weapons or in bioterrorism. Large-scale research and development of biological weapons were once carried out in some countries [2]. In 2001, the anthrax mail attack in the United States resulted in significant public panic. Therefore, in recent years, both the United States and United Kingdom have released biosecurity or biodefense national strategies for responding to such threats [3].

Pathogens are defined as microorganisms and parasites that cause infectious and parasitic diseases. At present, there are still many infectious diseases that do not have effective treatments. The development of diagnostic test kits, drugs, vaccines and other countermeasures needs to be based on the full understanding of the biological characteristics and pathogenic mechanisms of these infectious diseases.

Bibliometric analysis is an important method of scientific research assessment. Science-of-science analysis in the field of biosafety and biosecurity can be called Science of Science of biosafety/biosecurity (SSBS). Based on the statistical data of published studies on pathogens, it is possible to gain overall understanding of the worldwide pictures, such as the number of studies on pathogens, the research capability of different countries, the key research institutions, the major journals reporting studies on pathogens, and other parameters of research capability. It is then possible to know the research status, dominant areas, and major gaps, which are important for making strategic plans for scientific research. In the present bibliometric analysis, 100 species of pathogens of public health importance were selected, and the related published literatures were retrieved and statistically analyzed. The findings shed light on the hot spots and ignored spots in pathogen research and can be useful for drawing a national and institutional research plan.

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2. Methods

An SCI literature search was performed in November 2018 by using Web of Science and the search scope of SCI-EXPANDED. We examined the titles and screened for article types. The names of pathogens, but not the names of the corresponding disease, were used for the search (Tables 1–3). Use of the title as the search target can avoid those non-essential studies, but in the same time some studies may have been missed, when compared with the search results using abstracts as the search target. The main purpose of the study is to compare the studies from different years, countries, institutions, and journals, under the same search conditions.

The selection of the 100 pathogens was based on their historical importance in infectious diseases or their potential impact on humans, in the case of newer pathogens. Several parasitic pathogens, such as those causing malaria and schistosomiasis, were also included. The pathogens were selected from the laboratory biosafety pathogen lists of the National Institutes of Health of the United States, the European Union, and China; the bioterrorism response pathogen lists of the Centers for Disease Control and Prevention of the United States, the European Union, and Russia; and select agent program pathogens listed by the United States [4]. Additionally, the World Health Organization’s list of key emerging pathogens for preparedness and response [5], the list of pathogens released by Law of the PRC on the Prevention and Treatment of Infectious Diseases [6], and the

Table 1
Query key words and comparison by the number of published pathogen studies between China and the United States (bacterial pathogens only).

| Order | Pathogens | Abbreviation | Group* | Disease | Query | Article Quantity | Country-wise distribution | United States | China |
|-------|------------|--------------|--------|---------|-------|------------------|--------------------------|---------------|-------|
| 1     | Bacillus anthracis | B. anthracis | A       | Andrax  | TI = “Bacillus anthracis” | 1,722 68 | 1 1,104 6 59 |               |       |
| 2     | Yersinia pestis   | F. pestis    | A       | Plague   | TI = “Yersinia pestis” | 1,216 59 | 1 715 2 137 |               |       |
| 3     | Clostridium botulinum | C. botulinum | A       | Botulism | TI = “Clostridium botulinum” | 794 56 | 1 238 12 13 |               |       |
| 4     | Francisella tularensis | F. tularensis | A       | Tularemia | TI = “Francisellatularensis” | 1,039 42 | 1 634 11 17 |               |       |
| 5     | Brucella spp.     | B.mallei     | A       | Brucellosis | TI = Brucella | 3,132 106 | 1 713 5 234 |               |       |
| 6     | Burkholderia mallei | B. mallei   | A       | Glanders | TI = “Burkholderia mallei” | 141 29 | 1 97 27 1 |               |       |
| 7     | Burkholderia pseudomallei | B. pseudomallei | C.perfringens | A         | Meliodosis | TI = “Burkholderiapseudomallei” | 1,041 54 | 2 285 11 31 |               |       |
| 8     | Clostridium perfringens | C.perfringens | A       | Gas gangrene | TI = “Clostridium perfringens” | 1,952 69 | 1 635 8 90 |               |       |
| 9     | Salmonella spp.   | Salmonella   | A       | Food poisoning | TI = Salmonella | 21,476 160 | 1 7,306 4 1,282 |               |       |
| 10    | Escherichia coli  | O157:H7      | A       | Enteric disease | TI = O157 AND TI=H7 | 4,261 93 | 1 2,226 3 329 |               |       |
| 11    | Shigella          | Shigella     | A       | Enteric disease | TI = Shigella | 2,283 115 | 1 692 3 253 |               |       |
| 12    | Staphylococcus    | Staphylococcus | A       | Skin infections | TI = Staphylococcus | 27,944 157 | 1 8,383 3 1,847 |               |       |
| 13    | Vibrio cholerae   | V. cholerae  | A       | Cholera   | TI = “Vibrio cholerae” | 3,151 102 | 1 1,361 5 156 |               |       |
| 14    | Helicobacter pylori | H. pylori    | B       | peptic ulcers | TI = “Helicobacter pylori” | 17,677 153 | 1 3,386 4 1,433 |               |       |
| 15    | Mycobacterium tuberculosis | M. tuberculosis | B       | Tuberculosis | TI = “Mycobacterium tuberculosis” | 13,511 155 | 1 4,634 4 1,220 |               |       |
| 16    | Mycobacterium leprae | M. leprae   | B       | Human leprosy | TI = “Mycobacterium leprae” | 632 66 | 1 212 13 14 |               |       |
| 17    | Haemophilus influenzae | H. influenzae | B       | Respiratory tract infections | TI = “Haemophilus influenzae” | 3,116 115 | 1 1,261 17 54 |               |       |
| 18    | Corynebacterium diphtheriae | C. diphtheriae | A       | Diphtheria | TI = “Corynebacterium diphtheriae” | 230 45 | 1 79 |               |       |
| 19    | Clostridium tetani | C. tetani   | B       | Tetanus   | TI = “Clostridium tetani” | 51 27 | 2 8 9 3 |               |       |
| 20    | Streptococcus pyogenes | S. pyogenes | B       | Tonsillitis | TI = “Streptococcus pyogenes” | 1,597 72 | 1 490 14 34 |               |       |
| 21    | Streptococcus pneumoniae | S. pneumoniae | B       | Respiratory disease | TI = “Streptococcus pneumoniae” OR TI = pneumococcus | 6,439 127 | 1 2,350 8 284 |               |       |
| 22    | Streptococcus suis | S. suis     | B       | meningitis, endocarditis, and arthritis in swine | TI = “Streptococcus suis” | 920 42 | 6 67 1 348 |               |       |
| 23    | Neisseria meningitidis | N. meningitidis | B       | Septicemia and meningitis | TI = “Neisseria meningitidis” OR TI = Meningococcus OR TI = Meningococci | 2,206 97 | 1 562 14 48 |               |       |
| 24    | Neisseria gonorrhoeae | N.gonorrhoeae | B       | Gonorrhea | TI = “Neisseria gonorrhoeae” OR TI = Gonococci OR TI = Gonococci | 2,029 109 | 1 887 8 88 |               |       |
| 25    | Bordetella pertussis | B. pertussis | B       | Whooping cough | TI = “Bordetella pertussis” | 1,205 63 | 1 345 16 29 |               |       |
| 26    | Legionella pneumophila | L.pneumophila | A       | Legionnaire’s disease | TI = “Legionella pneumophila” | 1,604 63 | 1 554 9 61 |               |       |
| 27    | Campylobacter jejuni | C. jejuni    | B       | Food poisoning | TI = “Campylobacter jejuni” | 2,958 127 | 1 850 9 113 |               |       |
| 28    | Borrelia burgdorferi | B. burgdorferi | B       | Lyme disease | TI = “Borrelia burgdorferi” OR TI = “Lyme disease spirochete” | 2,731 72 | 1 1,640 12 57 |               |       |
| 29    | Treponema pallidum | T. pallidum | B       | Pathogenic spirochete | TI = Treponema pallidum | 494 59 | 1 232 2 78 |               |       |
| 30    | Leptospira | Leptospira | B       | Leptospirosis | TI = Leptospira | 1,555 97 | 1 392 6 101 |               |       |
| 31    | Listeria monocytogenes | L. monocytogenes | B       | Meningitis and sepsis | TI = “Listeria monocytogenes” | 7,493 95 | 1 2,525 5 354 |               |       |

* A = Biodefense-associated pathogens (BDAPs), B = Health-threatening pathogens (HTPs).
| Order | Pathogens                        | Abbreviation | Group* | Disease                                | Query                                                                 | Article | United States Distribution | China Distribution |
|-------|----------------------------------|--------------|--------|----------------------------------------|----------------------------------------------------------------------|---------|----------------------------|-------------------|
| 1     | Variola virus                    | Variola      | A      | Smallpox                               | TI = "Smallpox virus" OR TI = "Variola virus"                         | 72      | 16                         | 1                 |
| 2     | Ebola virus                      | Ebola        | A      | Ebola virus disease                    | TI = "Ebola virus" OR TI = ebolavirus                                 | 1,641   | 97                         | 1                 |
| 3     | Marburg virus                    | Marburg      | A      | Marburg virus disease                  | TI = "Marburg virus" OR TI = marburgivirus                             | 211     | 30                         | 1                 |
| 4     | Lassa virus                      | Lassa        | A      | Lassa fever                            | TI = "Lassa virus"                                                    | 156     | 26                         | 1                 |
| 5     | Venezuelan equine encephalitis virus | VEE          | A      | Venezuelan encephalitis                | TI = "Venezuelan equine encephalitis virus"                           | 237     | 25                         | 1                 |
| 6     | Eastern equine encephalitis virus | EEE          | A      | Eastern equine encephalitis            | TI = "Eastern Equine Encephalitis virus"                              | 85      | 10                         | 1                 |
| 7     | Western equine encephalitis virus | WEE          | A      | Western equine encephalitis            | TI = "Western equine encephalitis virus"                              | 41      | 9                          | 1                 |
| 8     | Nipah virus                      | Nipah        | A      | Nipah virus infection                  | TI = "Nipah virus"                                                    | 307     | 27                         | 1                 |
| 9     | Hendra virus                     | Hendra       | A      | Hendra virus disease                   | TI = "Hendra virus"                                                   | 141     | 15                         | 2                 |
| 10    | Hantavirus                       | Hantavirus   | A      | Hantavirus hemorrhagic fever with renal syndrome (HFRS) | TI = "Hantavirus hemorrhagic fever with renal syndrome (HFRS)"          | 1,181   | 82                         | 1                 |
| 11    | Hantaan virus                    | Hantaan      | A      | Hantaan virus hemorrhagic fever         | TI = "Hantaan virus hemorrhagic fever"                                | 168     | 19                         | 2                 |
| 12    | Sin Nombre virus                 | SNV          | A      | Hantavirus pulmonary syndrome (HPS)    | TI = "Sin nombre virus"                                               | 84      | 7                          | 1                 |
| 13    | Crimean-Congo hemorrhagic fever virus | CCHFV      | A      | Crimean-Congo hemorrhagic fever         | TI = "Crimean Congo hemorrhagic fever virus"                           | 245     | 56                         | 1                 |
| 14    | Rift Valley fever virus          | RVFV         | A      | Rift Valley fever                      | TI = "Rift Valley fever virus"                                        | 390     | 58                         | 1                 |
| 15    | Junin virus                      | Junin        | A      | Argentine hemorrhagic fever            | TI = "Junin virus"                                                    | 102     | 14                         | 2                 |
| 16    | Yellow fever virus               | YFV          | A      | Yellow fever                           | TI = "Yellow fever virus"                                             | 259     | 43                         | 1                 |
| 17    | Dengue virus                     | Dengue       | B      | Dengue fever                           | TI = "Dengue virus"                                                   | 3,131   | 111                        | 1                 |
| 18    | Japanese encephalitis virus      | JEV          | A      | Japanese encephalitis                  | TI = "Japanese encephalitis virus"                                    | 932     | 44                         | 5                 |
| 19    | Tick-borne encephalitis virus    | TBEV         | A      | Tick-borne encephalitis                | TI = "Tick-borne encephalitis virus" OR TI = TBEV                     | 459     | 49                         | 8                 |
| 20    | West Nile virus                  | WNV          | A      | West Nile fever                        | TI = "West Nile virus"                                                | 2,802   | 104                        | 1                 |
| 21    | Zika virus                       | Zika         | B      | Zika fever                             | TI = "Zika virus"                                                     | 1,486   | 102                        | 1                 |
| 22    | Chikungunya virus                | Chikungunya  | B      | Chikungunya fever                      | TI = "Chikungunya virus" OR TI = "Chikungunya virus OR TI = TBEV"      | 849     | 90                         | 1                 |
| 23    | Severe fever with thrombocytopenia syndrome virus | SFTSV      | B      | Severe fever with thrombocytopenia syndrome | TI = "Severe fever with thrombocytopenia syndrome virus" OR TI = "SFTSV virus" | 113     | 14                         | 4                 |
| 24    | Influenza virus                  | Influenza    | A      | Influenza                              | TI = "Influenza virus"                                               | 6,869   | 116                        | 1                 |
| 25    | H5N1 influenza virus             | H5N1         | A      | Influenza                              | TI = H5N1 AND TI = "Influenza virus"                                  | 742     | 69                         | 1                 |
| 26    | H1N1 influenza virus             | H1N1         | A      | Influenza                              | TI = "H1N1 virus"                                                    | 635     | 60                         | 1                 |
| 27    | H7N9 influenza virus             | H7N9         | A      | Influenza                              | TI = H7N9 AND TI = "Influenza virus"                                  | 89      | 16                         | 2                 |
| 28    | Measles virus                    | Measles      | B      | Measles                                | TI = "Measles virus"                                                  | 1,317   | 84                         | 1                 |
| 29    | Rubella virus                    | Rubella      | B      | Rubella                                | TI = "Rubella virus"                                                  | 317     | 51                         | 1                 |
| 30    | Mumps virus                      | Mumps        | B      | Mumps                                  | TI = "Mumps virus"                                                    | 259     | 37                         | 1                 |
| 31    | Adenovirus                       | Adenovirus   | B      | upper respiratory tract infection       | TI = Adenovirus                                                       | 9,706   | 104                        | 1                 |
| 32    | Respiratory syncytial virus      | RSV          | B      | Upper respiratory tract infection       | TI = "Human respiratory syncytial virus" OR TI = HRSV                 | 428     | 63                         | 1                 |
| 33    | Severe acute respiratory syndrome coronavirus | SARS      | A      | Severe acute respiratory syndrome      | TI = "SARS Coronavirus OR TI = "Severe acute respiratory syndrome Coronavirus" OR TI = SARS-CoV | 1,394   | 50                         | 2                 |
| 34    | Middle East respiratory syndrome coronavirus | MERS      | A      | Middle-East respiratory syndrome        | TI = "Middle East Respiratory Syndrome Coronavirus OR TI = "MERS coronavirus" OR TI = MERS-CoV | 610     | 51                         | 1                 |
| 35    | Human immunodeficiency virus     | HIV          | B      | Acquired immunodeficiency syndrome (AIDS) | TI = "Human immunodeficiency virus"                                  | 17,846  | 147                        | 1                 |
| 36    | Human T-lymphotropic virus       | HTLV         | B      | T-cell leukemia                        | TI = "Human T-lymphotropic virus" OR TI = HTLV                        | 2,680   | 99                         | 2                 |
| 37    | Hepatitis A virus                | HAV          | B      | Hepatitis A                            | TI = "Hepatitis A virus"                                              | 1,088   | 81                         | 1                 |

(continued on next page)
The selected 100 pathogens were divided into two categories (50 each): biodefense-associated pathogens (BDAPs) and health-threatening pathogens (HTPs) (Table 1–3). HTPs mainly affect people’s health, while BDAPs, pathogens listed in some Chinese textbooks were also referred to [7–10]. The pathogenicity and epidemiologic potential of the pathogens were considered in the selection process.

### Table 2 (continued)

| Order | Pathogens | Abbreviation | Group* | Disease | Query | Article | Country-wise distribution United States China | China Quantity |
|-------|------------|--------------|--------|---------|--------|---------|-----------------------------------------------|----------------|
|       |            |              |        |         |        |         | Sort Quantity                                |                |
| 38    | Hepatitis B virus | HBV | B | Hepatitis B | TI = “Hepatitis B virus” | 10,712 | 147 | 2 | 2,017 | 1 | 3,099 |
| 39    | Hepatitis C virus | HCV | B | Hepatitis C | TI = “Hepatitis C virus” | 16,791 | 151 | 1 | 5,335 | 6 | 1,077 |
| 40    | Coxsackievirus | Coxsackievirus | B | Viral myocarditis | TI = Coxsackievirus OR | 1,489 | 61 | 1 | 409 | 2 | 376 |
| 41    | Rotavirus | Rotavirus | B | Severe diarrhea | TI = Rotavirus | 4,723 | 149 | 1 | 1,677 | 6 | 257 |
| 42    | Enterovirus 71 | ETV1 | B | Hand-foot-and-mouth disease | TI = “Enterovirus 71” OR ETV1 | 1,111 | 43 | 3 | 115 | 1 | 569 |
| 43    | Norwalk virus | Norwalk | B | Gastroenteritis | TI = Norwalk virus | 2,444 | 95 | 1 | 892 | 3 | 201 |
| 44    | Poliovirus | Poliovirus | B | Polio | TI = Poliovirus | 1,577 | 114 | 1 | 843 | 7 | 62 |
| 45    | Herpes simplex virus | HSV | B | Gingival stomatitis and neonatal infection, etc. | TI = “Herpes simplex virus” | 7,544 | 114 | 1 | 3,959 | 6 | 336 |
| 46    | Varicella-zoster virus | VZV | B | Varicella and herpes zoster | TI = “Varicella zoster virus” | 1,611 | 78 | 1 | 667 | 14 | 36 |
| 47    | Human cytomegalovirus | HCMV | B | Congenital malformation | TI = Cytomegalovirus | 10,832 | 113 | 1 | 4,170 | 7 | 492 |
| 48    | Epstein-Barr virus | EBV | B | Infectious mononucleosis | TI = “Epstein-Barr virus” | 7,497 | 107 | 1 | 2,295 | 3 | 746 |
| 49    | Monopox virus | Monopox | A | Monkeypox | TI = “Monkeypox virus” | 82 | 16 | 1 | 70 | 14 | 1 |
| 50    | Rabies virus | Rabies | B | Rabies | TI = “Rabies virus” | 1,129 | 92 | 1 | 321 | 2 | 179 |
| 51    | Human papillomavirus | HPV | B | Squamous epithelial proliferation of human skin and mucosa | TI = “Human papillomavirus” | 10,975 | 147 | 1 | 4,383 | 2 | 899 |
| 52    | Human parvovirus | B19 | B | Fetal severe anemia, abortion or death | TI = “Human Parvovirus B19” OR TI = “Erythrovirus B19” | 423 | 64 | 2 | 73 | 5 | 23 |
| 53    | Foot-and-mouth disease virus | FMDV | B | Foot-and-mouth disease | TI = “Foot-and-mouth disease virus” | 1,487 | 86 | 3 | 273 | 2 | 290 |
| 54    | African swine fever virus | ASFV | A | African swine fever | TI = “African swine fever virus” | 416 | 53 | 3 | 73 | 13 | 9 |
| 55    | Newcastle disease virus | NDV | A | Newcastle disease | TI = “Newcastle disease virus” | 1,317 | 96 | 1 | 371 | 2 | 324 |
| 56    | Vesicular stomatitis virus | VSV | B | Bubbles and erosion of the epithelium of the tongue, lip, oral mucosa | TI = “Vesicular Stomatitis AND VSV” | 932 | 46 | 1 | 640 | 3 | 58 |

* A = BDAPs; B = HTPs. 

### Table 3

Query key words and comparison by the number of published pathogen studies between China and the United States (Rickettsia, Mycoplasma, Chlamydia, fungi, and protozoa).

| Order | Pathogens | Abbreviation | Group* | Disease | Query | Article | Country-wise distribution United States China | China Quantity |
|-------|------------|--------------|--------|---------|--------|---------|-----------------------------------------------|----------------|
|       |            |              |        |         |        |         | Sort Quantity                                |                |
| 1     | Coxiella burnetii | C. burnetii | A | Q-fever | TI = “Coxiella burnetii” | 1,055 | 87 | 1 | 292 | 16 | 18 |
| 2     | Rickettsia prowazekii | R. prowazekii | A | Typhus | TI = “Rickettsia prowazekii” | 95 | 15 | 1 | 69 | 1 | 1 |
| 3     | Rickettsia rickettsii | R. rickettsii | A | Rocky Mountain Spotted Fever | TI = “Rickettsia rickettsii” | 132 | 15 | 1 | 78 | 3 | 6 |
| 4     | Orientia tsutsugamushi | O.tsutsugamushi | B | Scrub typhus | TI = “Orientia tsutsugamushi” OR TI = “Orientia tsutsugamushi” | 294 | 28 | 3 | 69 | 6 | 19 |
| 5     | Bartonella | Bartonella | B | Trench fever | TI = Bartonella | 1,504 | 94 | 1 | 706 | 12 | 35 |
| 6     | Mycoplasma pneumoniae | M. pneumoniae | B | Respiratory tract infections | TI = “Mycoplasma pneumoniae” | 1,289 | 63 | 1 | 287 | 2 | 188 |
| 7     | Chlamydia psittaci | C. psittaci | A | Psittacosis in birds | TI = “Chlamydia psittaci” OR TI = “Chlamydia psittaci” | 436 | 49 | 1 | 83 | 5 | 35 |
| 8     | Chlamydia pneumoniae | C. pneumoniae | B | Respiratory infections in people on the trachomatous trachoma | TI = “Chlamydia pneumoniae” OR TI = “Chlamydia pneumoniae” | 1,891 | 71 | 1 | 476 | 10 | 66 |
| 9     | Chlamydia trachomatis | C. trachomatis | B | Disease in either the eye or the urogenital tract | TI = “Chlamydia trachomatis” | 3,366 | 119 | 1 | 1,316 | 8 | 143 |
| 10    | Coccidioides immitis | C. immitis | A | Coccidioidomycosis | TI = “Coccidioides immitis” | 134 | 15 | 1 | 124 |
| 11    | Plasmodium spp. | Plasmodium | B | Human malaria | TI = Plasmodium OR TI = “malaria parasite” | 16,098 | 162 | 1 | 5,451 | 15 | 482 |
| 12    | Cryptosporidium | Cryptosporidium | A | Diarrhea | TI = Cryptosporidium | 3,862 | 114 | 1 | 1,602 | 3 | 259 |
| 13    | Schistosoma | Schistosoma | B | Schistosomiasis | TI = Schistosoma OR TI = “Blood flukes” | 704 | 78 | 1 | 292 | 3 | 58 |

* A = BDAPs; B = HTPs.
which are characterized by rapid and widespread infection, have a serious impact on social stability. We retrieved the relevant literature on the pathogens published from 1995 to retrieval time in 2018. For the annual analysis, we retrieved the literatures published from 1995 to 2017, and used all the literatures for the country-, institution-, and journal-wise analysis based on Web of Science online statistics. The Web of Science literature statistics does not distinguish the first author from the other authors for country-wise and institution-wise analysis, so the cumulative number of studies for each country or institution may higher than the total number of studies.

3. Results

3.1. Annual number of publications

In this study, a total of 309,624 articles were retrieved. Of these, 295,866 were published in the period 1995–2017, and the highest number of articles (n = 16,658) was published in the year 2006. Based on the trends in the published literatures, three stages were identified: from 1995 to 2002, the increase in the number of published articles was not very remarkable; during 2002 to 2011, the increase was rapid; and during 2011–2017, the increase tended to slow down (Fig. 1).

We noted that the number of studies for some pathogens showed (1) continuous growth, such as *Mycobacterium tuberculosis*, Dengue virus, Hepatitis B virus, Norwalk virus, and *Plasmodium* spp.; (2) a rapid increase followed by a gradual decrease, such as *Bacillus anthracis*, *Yersinia pestis*, Ebola virus, H5N1 Influenza virus, H1N1 Influenza virus, H7N9 Influenza virus, SARS coronavirus, and *Chlamydia pneumoniae* (Fig. 2); and (3) a generally decreasing trend. For example, there were 1109 reports on human immunodeficiency virus in 1995, but the number decreased to 471 in 2017.

In addition to the above three trends, the reports on other pathogens showed (4) a plateau followed by an increase, such as Zika virus; (5) an increase followed by a plateau, such as *Escherichia coli* O157:H7; (6) a decrease followed by an increase, such as *Vibrio cholerae*; (7) a consistent plateau, such as Epstein-Barr virus; (8) a plateau followed by a decrease,
such as measles virus; (9) a decrease followed by a plateau, such as poliovirus; and (10) an irregular pattern, mainly for pathogens with a small number of reports (Table 4, Supplementary Table 1).

In the case of some pathogens, particularly BDAPs, the literature showed a decrease followed by a rapid increase. For example, after the outbreak of SARS, many studies were focused on vaccine researches and productions [11–13], which were discontinued thereafter. Had the research been continued, the world would have been better prepared for the current COVID-19 pandemic.

### Table 4

| Order | Trend                  | Pathogens                                                                 |
|-------|------------------------|---------------------------------------------------------------------------|
| A     | Sustained growth       | Brucella; B. pseudomallei; Salmonella; M. tuberculosis; L. monocytogenes; Hendra; Dengue; SFTSV; HBV; HCV; Norwalk; Rabies; M. pneumoniae; Plasmodium |
| B     | Plateau followed by increase | S. suis; N. gonorrhoeae; Leptospira; Marburg; Lassa; CCHFV; RVFV; YFV; JEV; TBEV; Zika; Chikungunya; RSV; Coxsackievirus; Rotavirus; EV71; HPV; FMDV; ASFV; NDV; C. burnetii; O. tsutsugamushi; C. trachomatis |
| C     | Increase followed by plateau | F. tularensis; B. mallei; O157:H7; Staphylococcus; S. pneumoniae; L. pneumophila; C. jejuni; WNV; MERS; Cryptosporidium |
| D     | Increase followed by decrease | B. anthracis; Y. pestis; H. pylori; Ebola; Influenza; H5N1; H1N1; H7N9; SARS; Bartonella; C. pneumonia |
| E     | Decrease followed by increase | V. cholerae; T. pallidum |
| F     | Plateau                 | C. botulinum; Shigella; M. leprae; H. influenzae; C. diphtheriae; C. tetani; N. meningitidis; B. pertussis; B. burgdorferi; Variola; EEE; WEE; Hantavirus; Rubella; Adenovirus; HAV; VZV; HCMV; EBV; B19; VSV; Schistosoma |
| G     | Plateau followed by decrease | Measles; Mumps virus; C. immitis |
| H     | Decrease followed by steady | HTLV; Poliovirus |
| I     | Continued reduction     | HIV; HSV |
| J     | Irregular               | C. perfringens; S. pyogenes; VEE; Nipah; Hantaa; SNV; Junin; Monkeypox; R. prowazekii; R. rickettsii; C. psittaci |

3.2. Country and region distributions of pathogen studies

The pathogens with the highest number of published studies were *Staphylococcus* (27,944), *Salmonella* (21,476), human immunodeficiency virus (17,846), *Helicobacter pylori* (17,677), and Hepatitis C virus (16,791). The most common pathogens across countries were *Plasmodium* (162), *Salmonella* (160), *Staphylococcus* (157), *Mycobacterium tuberculosis* (155), and *Helicobacter pylori* (153) (Tables 1–3, Fig. 3).

The countries/regions with the largest number of published studies on pathogens included the United States of America, China, Japan, England, Germany, France, Canada, Italy, Spain, and India. The United States of America led the highest number of publications on most of the pathogens (82 of the 100 pathogens selected), and also had the second highest number of publications on the following pathogens: Hepatitis B virus, Human T-lymphotropic virus, severe acute respiratory syndrome coronavirus, *Burkholderia pseudomallei*, Human parvovirus B19, Hendra virus, Hanta Virus, Junin virus, H7N9 Influenza virus, and *Clostridium tetani*. It had the third and after highest number of publications on the following pathogens: Foot-and-mouth disease virus, Enterovirus 71, African swine fever virus, *Oriental tutsugamushi*, severe fever with thrombocytopenia syndrome virus, Japanese encephalitis virus, *Streptococcus suis*, and tick-borne encephalitis virus.

China had the highest number of published studies on the following pathogens: Hepatitis B virus, Enterovirus 71, severe acute respiratory syndrome coronavirus, *Streptococcus suis*, Japanese encephalitis virus, Hanta virus, severe fever with thrombocytopenia syndrome virus, and H7N9 Influenza virus. It had also the second highest number of publications on the following pathogens: Adenovirus, Influenza virus, human papillomavirus, Coxsackievirus, Newcastle disease virus, foot-and-mouth disease virus, H5N1 Influenza virus, *Mycoplasma pneumoniae*, rabies virus, H1N1 Influenza virus, *Yersinia pestis*, hepatitis A virus, *Treponema pallidum*, and Eastern equine encephalitis virus. In addition, it had the third highest number of publications on the following pathogens: *Staphylococcus*, Epstein-Barr virus, *Escherichia coli O157:H7*, *Cryptosporidium*, *Shigella*, Norwalk virus, *Zika* virus, Middle East respiratory syndrome coronavirus, vesicular stomatitis virus, *Schistosoma*, and *Rickettsia rickettsii*.

Japan had the highest number of studies on human T-lymphotropic virus and human parvovirus B19, while England had the highest number of studies.

![Fig. 3. Number of published studies and country/region distribution for each type of pathogen.](image-url)
on foot-and-mouth disease virus. Further, France had the highest number of studies on *Clostridium tetani*, while Spain had the highest number of studies on African swine fever virus. For Australia, it was Hendra virus; for Korea, *Orientalia tsutsugamushi*; for Russia, tick-borne encephalitis virus; for Thailand, *Burkholderia pseudomallei*; and for Argentina, Junin virus (Table 5).

The number of studies exploring various pathogens in the selected 15 countries and regions is shown in Supplementary Table 2. The countries have been selected mainly based on the total number of published studies.

### 3.3. Top-ranked institutes on published pathogen studies

With regard to the distribution of studies across institutions, the following institutions had the highest number of publications: Pasteur Institute (4,688), Harvard University (4,330), Unites States National Institute of Allergy and Infectious Diseases (NIAID) (3,808), Johns Hopkins University (3,188), University of Washington (3,140), University of Oxford (2,753), University of California San Francisco (2,658), Emory University (2,314), University of Maryland (2,220), and University of Tokyo (2,178). Furthermore, some institutions had the highest number of studies for specific pathogens, such as: Baylor College of Medicine on *Helicobacter pylori*; Harvard University on human immunodeficiency virus; Chinese Academy of Sciences on severe acute respiratory syndrome coronavirus (Table 6).

The number of studies exploring various pathogens by the selected 20 institutions is shown in Supplementary Table 3. The list also included some universities and institutions in China, such as Fudan University and the Chinese Academy of Medical Sciences, University Center for Disease Control and Prevention, and Peking University. “CIR DIS CONTROL PREVENT” ranked the first for its number of published studies. However, as “CIR DIS CONTROL PREVENT” represents the Centers for Disease Control and Prevention of the United States, its published number of studies may come from more than one institution, therefore, it was not selected. The next institution was Pasteur Institute, but studies on influenza virus, severe acute respiratory syndrome coronavirus, and *Francisella tularensis* were relatively rare. Harvard University was listed next to Pasteur Institute, but studies on Japanese encephalitis virus, influenza virus, Middle East respiratory syndrome coronavirus, and foot-and-mouth disease virus were relatively rare. The Chinese Academy of Sciences had a relatively high number of studies on *Yersinia pestis*, *Escherichia coli* O157:H7, Zika virus, Influenza virus, and severe acute respiratory syndrome coronavirus, and the University of Hong Kong also had a relatively high number of studies on *Burkholderia pseudomallei*, *Helicobacter pylori*, influenza virus, severe acute respiratory syndrome coronavirus, and hepatitis B virus. Some universities and institutions in China, such as Fudan University and the Chinese Academy of Medical Sciences, had a small number of studies on BDAPs, such as *Bacillus anthracis* and *Francisella tularensis*, in comparison with some universities and institutions in the United States, such as the Centers for Disease Control and Prevention of the United States, its published number of studies may come from more than one institution, therefore, it was not selected. The next institution was Pasteur Institute, but studies on influenza virus, severe acute respiratory syndrome coronavirus, and *Francisella tularensis* were relatively rare. Harvard University was listed next to Pasteur Institute, but studies on Japanese encephalitis virus, influenza virus, Middle East respiratory syndrome coronavirus, and foot-and-mouth disease virus were relatively rare. The Chinese Academy of Sciences had a relatively high number of studies on *Yersinia pestis*, *Escherichia coli* O157:H7, Zika virus, Influenza virus, and severe acute respiratory syndrome coronavirus, and the University of Hong Kong also had a relatively high number of studies on *Burkholderia pseudomallei*, *Helicobacter pylori*, influenza virus, severe acute respiratory syndrome coronavirus, and hepatitis B virus. Some universities and institutions in China, such as Fudan University and the Chinese Academy of Medical Sciences, had a small number of studies on BDAPs, such as *Bacillus anthracis* and *Francisella tularensis*, in comparison with some universities and institutions in the United States, such as

### Table 5

| Countries/regions | Top-ranked |
|-------------------|------------|
| United States     | Except: HBV, HTLV, SARS, *B. pseudomallei*, B19, Hantaan, Junin, H7N9, C. tetani, Hendra (Rank 2); FMDV, EV71, ASV, O. tsutsugamushi (Rank 3); SFTSV; JEV; S. suis; TBEV (Rank after 3) |
| China             | S. suis; Hantaan; JEV; SFTSV; H7N9; SARS; HBV; EV71 |
| Japan             | HTLV; B19 |
| England           | FMDV |
| France            | C. tetani |
| Spain             | ASPV |
| Australia         | Hendra |
| Russia            | TBEV |
| South Korea       | O. tsutsugamushi |
| Thailand          | *B. pseudomallei* |
| Argentina         | Junin |

### Table 6

| Countries/regions | Institutes | Pathogens |
|-------------------|------------|-----------|
| United States     | ARS        | O157:H7   |
|                   | Bayor Coll Med | *H. pylori* |
|                   | Colorado State Univ | *M. leprae* |
|                   | Ctr Dis Control | S. pneumonia; Variola; EEE; Nipah; CCHFV; Prevent |
|                   | Univ        | WNV; Influenza; Rotavirus; Norwalk; Poliovirus; Monkeypox; Bartonella; Cryptosporidium |
| Georgia State Univ | Rabellia |
| Harvard Univ      | Staphylococcus; HBV; HSV |
| Mayo Clin         | Measles |
| NCi               | HPV |
| NIAID             | Ebola; *C. trachomatis* |
| Northwestern Univ | L. pneumophila |
| Univ              | HCMV |
| Oregon Hlth Sci   | Thomas Jefferson | Rabies |
| Univ              | Univ Arizona | C. immitis |
|                   | Univ Colorado | VZV |
|                   | Univ Georgia | *M. pneumoniae* |
|                   | Univ Kentucky | Y. pestis |
|                   | Univ New Mexico | SVV |
|                   | Univ Pittsburgh | C. perfringens |
|                   | Univ S Alabama | R. prowazekii |
|                   | Univ Texas | Adenovirus; Zika |
|                   | Univ Washington | T. pallidum |
|                   | US FDA | Mumps |
|                   | USA (US Army) | B. antracis; B. mallei; VEE |
|                   | USDA ARS | Salmonella |
|                   | Yale Univ | B. burgdorferi; VSV |
|                   | Chinese Acad Agr Sci | FMDV; NDV |
|                   | Chinese Acad Sci | SARS |
|                   | Chung Shan Med Univ | B19 |
|                   | Fourth Mill Med Univ | Hantaan |
|                   | Fudan Univ | HBV |
|                   | Univ Hong Kong | H1N1; H7N9; MERS |
|                   | Chang Gung Univ | EV71 |
|                   | (Taiwan of China) | JEV |
|                   | Narl Def Med Ctr | (Taiwan of China) |
| Japan             | Hokkaido Univ | HSN1 |
|                   | Kagoshima Univ | HTLV |
|                   | Narl Inst Infect Dis | SFTSV |
|                   | Univ Birmingham | EBV |
|                   | Univ Oxford | H. influenzae; N. meningitidis |
|                   | Univ York | Schizosacme |
| Germany           | Bernhard Nocht | Lassa |
|                   | Inst Trop Med | Marburg |
|                   | Univ Marburg | Marburg |
|                   | INRA | Brucella |
|                   | INSERM | HCV |
|                   | Inst Pasteur | Shigella; *M. tuberculosis*; C. tetani; B. pertussis; L. monocytogenes; RVFV; YFV; Chikungunya |
| Canada            | Def Res Dev | WEE |
|                   | Canada Suffolk | |
|                   | Narl Res Council | C. jejuni |
|                   | Canada | |
|                   | Univ British Columbia | Coxsackievirus |
|                   | Univ Montreal | S. suis |
| Spain             | Inst Salud Carlos III | RSV |
|                   | Univ Autonoma Madrid | ASFV |
|                   | Univ Barcelona |HAV |
|                   | Narl Inst Cholera | |
|                   | Ester Dis | |
| India             | Natl Inst Cholera | V. cholerae |
| Australia         | CSIRO | |
| Sweden            | Lund Univ | S. pyogenes |

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**Table 5**

Top ranked Countries/regions by number of published studies on various pathogens.

**Table 6**

Institutions with the highest number of published studies on select pathogens.
Table 6 (continued)

| Countries/regions | Institutes | Pathogens |
|-------------------|------------|-----------|
| Brazil            | Univ Estado Río De Janeiro | C. diphtheriae |
| Argentina         | Univ Buenos Aires | Junin |
| South Korea       | Seoul Natl Univ | O. sutsugamushi |
| Thailand          | Mahidol Univ | B. pseudomallei; Dengue; Plasmodium |

Table 7

| Journals | Impact Factor (2018) | Pathogens |
|----------|----------------------|-----------|
| Emerg Infect Dis | 7.2 | Hantavirus; SNV; MERS |
| J Virol | 4.3 | Ebola; Marburg; Lassa; VEE; VEE; Nipah; Hendra; Hantaan; CCHFV; RVFV; Junin; YFV; Dengue; JEV; TBEV; SFTSV; Influenza; H5N1; H1N1; H7N9; Measles; Rubella; Mumps; Adenovirus; RV; SARS; HIV; HBV; HCV; Coxsackievirus; Norwalk; Poliovirus; HSV; VZV; HCMV; EBV; Monkeypox; Rabies; HPV; FMDV; ASFV; NDV; VSV |
| PLoS Negl Trop Dis | 4.5 | Leptospirosis; Chikungunya |
| Antimicrob Agents Chemother | 4.7 | Staphylococcus; S. pneumoniae |
| Helicobacter | 3.4 | H. pylori |
| J Clin Microbiol | 5.0 | M. tuberculosis; C. diphtheriae; T. pallidum; Variola; Bartonella; M. pneumoniae |
| AppI Environ Microbiol | 4.1 | C. botalicum; C. jejuni |
| Infect Immun | 3.2 | Y. pestis; F. tularensis; Brucella; B. mallei; B. pseudomallei; Shigella; H. influenzae; S. pyogenes; N. meningitidis; B. pertussis; L. pneumophila; B. burgdorferi; C. burnetii; R. rickettsii; C. pneumoniae; C. immitis |
| J Bacteriol | 3.2 | B. anthracis; V. cholerae; R. prowazekii |
| PLoS One | 2.8 | EV71 |
| Am J Trop Med Hyg | 2.3 | C. tetani; EEE; O. sutsugamushi |
| Infectious Diseases | 1.9 | WNV |
| J Med Virol | 2.0 | B19 |
| Sex Transm Dis | 2.3 | N. gonorrhoeae; C. trachomatis |
| AIDS Res Hum Retroviruses | 1.8 | HTLV |
| J Food Prot | 1.6 | Salmonella; O157:H7; L.monocytogenes |
| Vaccine | 4.8 | Rotavirus |
| Sci Rep | 4.0 | Zika |
| Malar J | 2.8 | Plasmodium |
| Anaerobe | 2.7 | C. perfringens |
| Parasitology | 2.5 | Schistosoma |
| Lepr Rev | 0.5 | M. leprae |
| Netherlands | Vet Microbiol | 2.8 | S. suis; C. psittaci |
| Vet Parasitol | 2.0 | Cryptosporidium |

University of Maryland or National Institute of Allergy and Infectious Diseases (NIAID) (Supplementary Table 3).

3.4. Journal distribution of the published studies

With regard to the total number of studies on various pathogens, the following journals had published the highest number of studies: Journal of Virology (14,586), Journal of Clinical Microbiology (7,273), Infection and Immunity (6,885), Journal of Infectious Diseases (5,643), and Vaccine (4,151) (Supplementary Table 4). Some journals had the highest number of studies on some particular pathogens: For example, Emerging Infectious Disease had the highest number of studies on Ebola virus, Infection and Immunity had the highest number of studies on Junin virus, and Vaccine had the highest number of studies on Rotavirus (Table 7).

The number of studies exploring various pathogens for the selected 20 journals is shown in Supplementary Table 4. The journals were selected mainly based on their impact factor and the total number of pathogens studies published. Infection and Immunity and Molecular Microbiology had the highest number of publications on bacterial pathogens; Vaccine had publications on almost all kinds of pathogens; PNAS mainly had reports on viruses; and Emerging Infectious Diseases had more virus-related literature. Some top journals published a number of related studies on particular pathogens: pathogen studies published on Science rank first and second are Plasmodium spp. and Salmonella spp., Nature are Plasmodium spp. and influenza virus; Cell are Plasmodium spp. and Zika virus; New England Journal of Medicine are human immunodeficiency virus and human cytomegalovirus; Lancet are Helicobacter pylori and Hepatitis C virus. (Supplementary Table 4).

4. Discussion

4.1. Characteristics of the retrieved studies

From the quantitative analysis of studies on the selected pathogens, the following characteristics were evidenced:

1. The number of studies is closely related to disease epidemics. Some pathogens, such as SARS coronavirus, H1N1 influenza virus, and Ebola virus, have resulted in a rapid increase in the number of studies published after the disease outbreaks. However, once the epidemic has been controlled, the number of studies declined.

2. The number of studies was closely related to disease distribution. The number of studies related to pathogens tended to be related to the geographical distribution of the corresponding diseases. For example, the literatures on H7N9 avian influenza is predominante in China, while the most relevant literatures on Burkholderia pseudomallei is in Thailand. In studies assessing Junin virus, it was Argentina which published the most studies.

3. Core research institutions play significant roles on pathogen studies. Such as the Pasteur Institute in France, Harvard University, the National Institute of Allergy and Infectious Diseases in the United States, and the Chinese Academy of Sciences.

4.2. Research studies on pathogens in China

China attaches great importance to the prevention and control of infectious diseases; thus has made significant progress in relevant research and biosafety management since the SARS outbreak in 2002–2003 [14].
Although the great advance and progress have been made, improvement in the following areas are still needed:

1. Pathogens studied are unbalanced. Relatively large number of published studies is on health-threatening pathogens, such as hepatitis B virus and Japanese encephalitis, while relatively small number of published studies is on biodefense-associated pathogens such as Bacillus anthracis and Ebola virus, specifically at the university level.

2. Institutions SCI reports on pathogens lower than world top pathogen research institutions. In the field of pathogen research, national institutions such as the Chinese Academy of Sciences, Chinese Academy of Medical Sciences, and Chinese Center for Disease Control and Prevention play an important role. However, in comparison with the world’s top pathogen research institutions such as the Pasteur Institute in France and the National Institute of Allergy and Infectious Diseases in the United States of America, there are still some gap on pathogen research SCI reports.

3. The level of Chinese pathogen-related journals needs to be enhanced. It can be seen from the data that the pathogen-related SCI journal are mainly from the United States and Europe. Although the total number of Chinese SCI reports on pathogens is the second largest in the world, there are still not many influential international journals in China in this field.

4.3. Pathogen research is closely related to biosafety and biosecurity

Pathogen research can protect human health, but it can also create potential biosafety and biosecurity issues that threaten human health.

1. The level of research on pathogens is an important index for the ability of the level of research on pathogens is an important index for the ability to deal with infectious diseases. Pathogen research is based on handling infectious diseases, emerging infections, and control of new biological threats. In addition, it is also an important aspect of national biodefense capacity. By strengthening investment in science and technology, China’s ability to prevent and control infectious diseases has increased significantly [15]. Consequently, the number of related SCI reports has grown significantly [16], although there is still gap between China and the United States [17].

2. Pathogen research can result in biosafety and biosecurity risks. With the rapid development of life sciences and biotechnology, biosafety and biosecurity issues are receiving increasing attention [18–21]. Pathogen-related research may lead to an increased likelihood of pathogen laboratory errors, and there is also the possibility of deliberate use by humans [22].

3. Towards reducing the biosafety and biosecurity risk, it is necessary to ameliorate the supervision and support for pathogenic research, including improvement on biosafety management monitoring and risk assessment systems [23]. Furthermore, researches on molecular biocontainment and other methods should also be strengthened [24–25].

Conflict of interest statement

The authors declare that there are no conflicts of interest.

Supplementary data

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