Epidemiological features of and changes in incidence of infectious diseases in China in the first decade after the SARS outbreak: an observational trend study

Shigui Yang, Jie Wu, Cheng Ding, Yuanxia Cui, Yuqing Zhou, Yiping Li, Min Deng, Chencheng Wang, Kaijin Xu, Jingjing Ren, Bing Ruan, Lanjuan Li

Lancet Infect Dis 2017; 17: 716–25

Published Online April 12, 2017 http://dx.doi.org/10.1016/S1473-3099(17)30227-X

This online publication has been corrected. The corrected version first appeared at thelancet.com on April 19, 2017

See Comment page 675

State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, China (S Yang PhD, J Wu PhD, C Ding MS, Y Cui MS, Y Zhou MS, M Deng PhD, C Wang MS, K Xu PhD, J Ren PhD, Prof B Ruan PhD, Prof L Li PhD); **and Zhejiang Institute of Medical-care Information Technology, Hangzhou, China** (Y Li MS)

Correspondence to: Prof Lanjuan Li, State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou 310003, China **ljli@zju.edu.cn**

See Online for podcast

Summary

Background The model of infectious disease prevention and control changed significantly in China after the outbreak in 2003 of severe acute respiratory syndrome (SARS), but trends and epidemiological features of infectious diseases are rarely studied. In this study, we aimed to assess specific incidence and mortality trends of 45 notifiable infectious diseases from 2004 to 2013 in China and to investigate the overall effectiveness of current prevention and control strategies.

Methods Incidence and mortality data for 45 notifiable infectious diseases were extracted from a WChinese public health science data centre from 2004 to 2013, which covers 31 provinces in mainland China. We estimated the annual percentage change in incidence of each infectious disease using joinpoint regression.

Findings Between January, 2004, and December, 2013, 54 984 661 cases of 45 infectious diseases were reported (average yearly incidence 417·98 per 100 000). The infectious diseases with the highest yearly incidence were hand, foot, and mouth disease (114·48 per 100 000), hepatitis B (81·57 per 100 000), and tuberculosis (80·33 per 100 000). 132 681 deaths were reported among the 54 984 661 cases (average yearly mortality 1·01 deaths per 100 000; average case fatality 2·4 per 1000). Overall yearly incidence of infectious disease was higher among males than females and was highest among children younger than 10 years. Overall yearly mortality was higher among males than females older than 20 years and highest among individuals older than 80 years. Average yearly incidence rose from 300·54 per 100 000 in 2004 to 483·63 per 100 000 in 2013 (annual percentage change 5·9%); hydatid disease (echinococcosis), hepatitis C, and syphilis showed the fastest growth. The overall increasing trend changed after 2009, and the annual percentage change in incidence of infectious disease in 2009–13 (2·3%) was significantly lower than in 2004–08 (6·2%).

Interpretation Although the overall incidence of infectious diseases was increasing from 2004, the rate levelled off after 2009. Effective prevention and control strategies are needed for diseases with the highest incidence—including hand, foot, and mouth disease, hepatitis B, and tuberculosis—and those with the fastest rates of increase (including hydatid disease, hepatitis C, and syphilis).

Funding Chinese Ministry of Science and Technology, National Natural Science Foundation (China).

Introduction

Several decades ago, the health burden of infectious diseases was believed to be becoming insignificant, because basic sanitation, proper nutrition, drugs, and vaccines had caused a steady decline in overall incidence and mortality.[1] However, the threat of serious infectious diseases to human and animal health persisted,[2] with infectious diseases remaining a leading source of human morbidity and mortality.[3] Of 57 million deaths per year reported worldwide, 14·9 million were attributed to infectious diseases, representing more than 25% of all deaths.[4] In the global human population, 335 infectious diseases emerged between 1940 and 2004.[5]

In China, the yearly incidence of 18 consistently reported infectious diseases decreased rapidly from 1970 to 2007, with rates falling from more than 4000 per 100 000 people to less than 250 per 100 000.[3] However, these reported data also indicated that the incidence of infectious diseases rose after 2004,[3] and several outbreaks of emerging and re-emerging infectious diseases (eg, severe acute respiratory syndrome [SARS],[6] avian influenza A H5N1,[7] pandemic H1N1 influenza,[8] poliomyelitis,[9] and avian influenza A H7N9)[10] have been reported in the 21st century. The SARS tragedy in 2003 greatly afflicted China and revealed the shortcomings of China's infectious disease prevention system, propelling the Chinese Government to accelerate reforms.[11] The model of infectious diseases prevention and control in China was changed significantly from non-collaborative prevention and control to joint, multisectorial, integrated prevention and control strategies.[12] Moreover, to comprehensively improve infectious disease prevention and control, major special national science and technology projects on prevention and control were started in China at the end of 2008.[13]

Understanding the epidemiological distribution of infectious diseases is the most important task for controlling infectious diseases.[5] However, the specific geographic patterns and temporal trends of major infectious diseases in the post-SARS era have been researched rarely. In this study, we aimed to assess

Research in context

Evidence before this study

We searched PubMed on Dec 20, 2016, with the terms "infectious disease" AND "trend" AND ("tuberculosis" AND "hepatitis B" AND "hand, foot and mouth disease") for articles published in English. Our search did not identify any reports of trends and epidemiological features of infectious diseases in China in the period after the severe acute respiratory syndrome (SARS) outbreak in 2003. We retrieved one report from 2013 of morbidity and mortality characteristics of infectious diseases in China, and we found another report of emergence and control of infectious diseases in China before 2004, including data for 18 infectious diseases. However, the model of infectious disease prevention and control has changed significantly since 2003, when the great tragedy of the SARS outbreak revealed the shortcomings of China's infectious disease prevention system and propelled the Chinese Government to accelerate reforms. Based on literature searches in PubMed after the 2003 SARS outbreak, no complete, systematic, long-term, and comprehensive description of infectious disease characteristics and trends has been made available.

Added value of this study

Our study describes the epidemiological features and evolution of 45 infectious diseases (an increase from the previous report of 18 diseases) from 2004 to the end of 2008, when major special national science and technology projects on prevention and control in China were initiated, then from 2009 up to 2013. To our knowledge, our report covers the longest period studied in post-SARS China. The increasing trend in overall incidence of infectious diseases levelled off after 2009; the annual percentage change in 2009–13 (2·3%) was significantly lower than that in 2004–08 (6·2%).

Implications of all the available evidence

The incidence and mortality of infectious diseases has varied significantly in the post-SARS era. Effective prevention and control strategies are needed for diseases with the highest yearly incidence, including hand, foot, and mouth disease, tuberculosis, and hepatitis B, and those with the fastest rates of increase—ie, hydatid disease (echinococcosis), hepatitis C, and syphilis. The Chinese Government now has the authority to enforce joint multisectoral integrated prevention and control by collaboration between different departments and levels of administrations.

specific incidence and mortality trends of 45 notifiable infectious diseases from 2004 to 2013 in China and to investigate the overall effectiveness of current prevention and control strategies.

Methods

Data collection

The Chinese Government established a routine reporting system for selected infectious diseases in the 1950s,[3] with data available for 31 provinces in mainland China, covering a population of about 1·3 billion people. This system has been web-based since 2003 and operates through administrative grading responsibility and territorial management. The number of notifiable infectious diseases included in the reporting system increased from 18 before 1978 to 39 after 2013.[14,15] The 39 notifiable infectious diseases are divided into three classes (A, B, and C), and these are described in the appendix (p 1). Clinicians complete a standard case report card for infectious diseases. Epidemic reports are time-sensitive; all class A infectious diseases and pulmonary anthrax and SARS in class B should be reported through the network within 2 h of diagnosis, whereas the remaining class B and C infectious diseases should be reported within 24 h.[15,16]

Procedures

We extracted data from the notifiable infectious disease report database, which was open and available from the public health science data centre of the Chinese Center for Disease Control and Prevention and the official website of National Health and Family Planning Commission during the study period.[14,17] We obtained incidence and mortality data for the 39 notifiable infectious diseases, stratified by date (month and year), sex, age, and province. To further assess the epidemiological features of the 39 notifiable infectious diseases, we substratified viral hepatitis into hepatitis A, hepatitis B, hepatitis C, and hepatitis E; the combination of bacterial and amoebic dysentery into two separate categories of bacterial dysentery and amoebic dysentery; the combination of typhoid and paratyphoid into separate groups for typhoid and paratyphoid; and seasonal influenza into traditional seasonal influenza and influenza A H1N1 (2009 pandemic H1N1 influenza). Therefore, we assessed 45 infectious diseases, including their subtypes, in this study.

Statistical analysis

We defined incidence (per 100 000) as the number of annual incident cases divided by the population size; overall mortality (per 100 000) as the number of deaths per year divided by the total population size; and the case-fatality ratio (per 1000) as the number of annual deaths divided by the number of annual incident cases. We described seasonal distribution with a radar diagram based on monthly incidence. We standardised the incidence and case-fatality ratio for each infectious disease, from 0 to 1 according to percentile rank, and further represented data as thermodynamic diagrams.

See Online for appendix

We used joinpoint regression models (appendix p 2)[18] to examine incidence trends from 2004 to 2013 and to

	Cases (n)*	Yearly incidence (per 100 000)†	Deaths (n)*	Case-fatality ratios (per 1000)	Seasonal feature
Total	54 984 661	417·98	132 681	2·41	April to September
HFMD	9 035 966	114·48	2712	0·30	April to July (May to June)‡
Hepatitis B	10 730 323	81·57	7620	0·71	Not significant
Tuberculosis	10 567 049	80·33	29 508	2·79	January to May
Other§	7 305 601	55·54	500	0·07	June to December (July to August)‡
Mumps	3 212 659	24·42	23	0·007	April to July (May to June)‡
Bacterial dysentery	3 190 263	24·25	632	0·20	May to October
Syphilis	2 729 518	20·75	671	0·25	Not significant
Gonorrhoea	1 355 604	10·31	13	0·01	Not significant
Hepatitis C	1 227 325	9·33	1228	1·00	Not significant
Seasonal influenza	811 835	6·17	71	0·09	March to April, September to December
Measles	668 103	5·08	392	0·59	March to June
Acute haemorrhagic conjunctivitis	537 391	4·09	1	0·002	September
Hepatitis A	525 982	4·00	204	0·39	Not significant
Rubella	517 830	3·94	5	0·01	April to June
Influenza A H1N1	164 892	3·13	877	5·32	September to December (November)‡
HIV infection	408 955	3·11	48 199	117·86	Not significant
Scarlet fever	320 374	2·44	9	0·03	May to June, November to December
Brucellosis	287 120	2·18	10	0·04	March to July
Malaria	242 317	1·84	236	0·97	June to October (July to October)‡
Hepatitis E	218 418	1·66	358	1·64	January to May
Typhoid	145 875	1·11	66	0·45	May to October
Haemorrhagic fever	136 280	1·04	1500	11·01	October to December (November)‡
Paratyphoid	69 092	0·53	16	0·23	May to October
Encephalitis	37 485	0·28	1696	45·25	July to August
Schistosomiasis	36 047	0·27	15	0·42	July to August
Typhus	27 152	0·21	4	0·15	June to November
Pertussis	26 150	0·20	21	0·80	May to August
Amoebic dysentery	25 357	0·19	8	0·32	May to September
Hydatid disease	24 037	0·18	10	0·42	Not significant
Rabies	23 008	0·17	22 597	982·14	June to November
Neonatal tetanus	16 534	0·13	1638	99·07	Not significant
ECM	10 390	0·079	937	90·18	January to April
Dengue	7958	0·06	1	0·13	September to October
Leptospirosis	7587	0·058	204	26·89	August to September (September)‡
Anthrax	3730	0·028	47	12·60	July to August
Leprosy	3542	0·027	20	5·65	January to April (January)‡
Kala-azar	3247	0·025	11	3·39	Not significant
Cholera	2102	0·016	8	3·81	August to October
Poliomyelitis	20	0·0015	1	50·00	July to September
Avian influenza H7N9	19	0·0014	1	52·63	December
SARS¶	10	0·00076	1	100·00	April
Plague	58	0·00049	22	379·31	June to July, October
Avian influenza H5N1	39	0·00033	28	717·95	January to April, October to November (January)‡
Filariasis	19	0·00029	1	52·63	Not significant
Diphtheria	3	0·00011	0	0·00	May to July

*Total numbers for 10 years. †Average for 10 years. ‡Period in parentheses represents a more typical seasonal feature and the incidence of each disease is more concentrated during this period. §Infectious diarrhoeal diseases other than cholera, bacterial dysentery, amoebic dysentery, typhoid, and paratyphoid. ¶SARS data were not adequate for determining seasonal distribution. ECM=epidemic cerebrospinal meningitis. HFMD=hand, foot, and mouth disease. SARS=severe acute respiratory syndrome.

Table 1: **Incidence and mortality data for 45 notifiable infectious diseases**

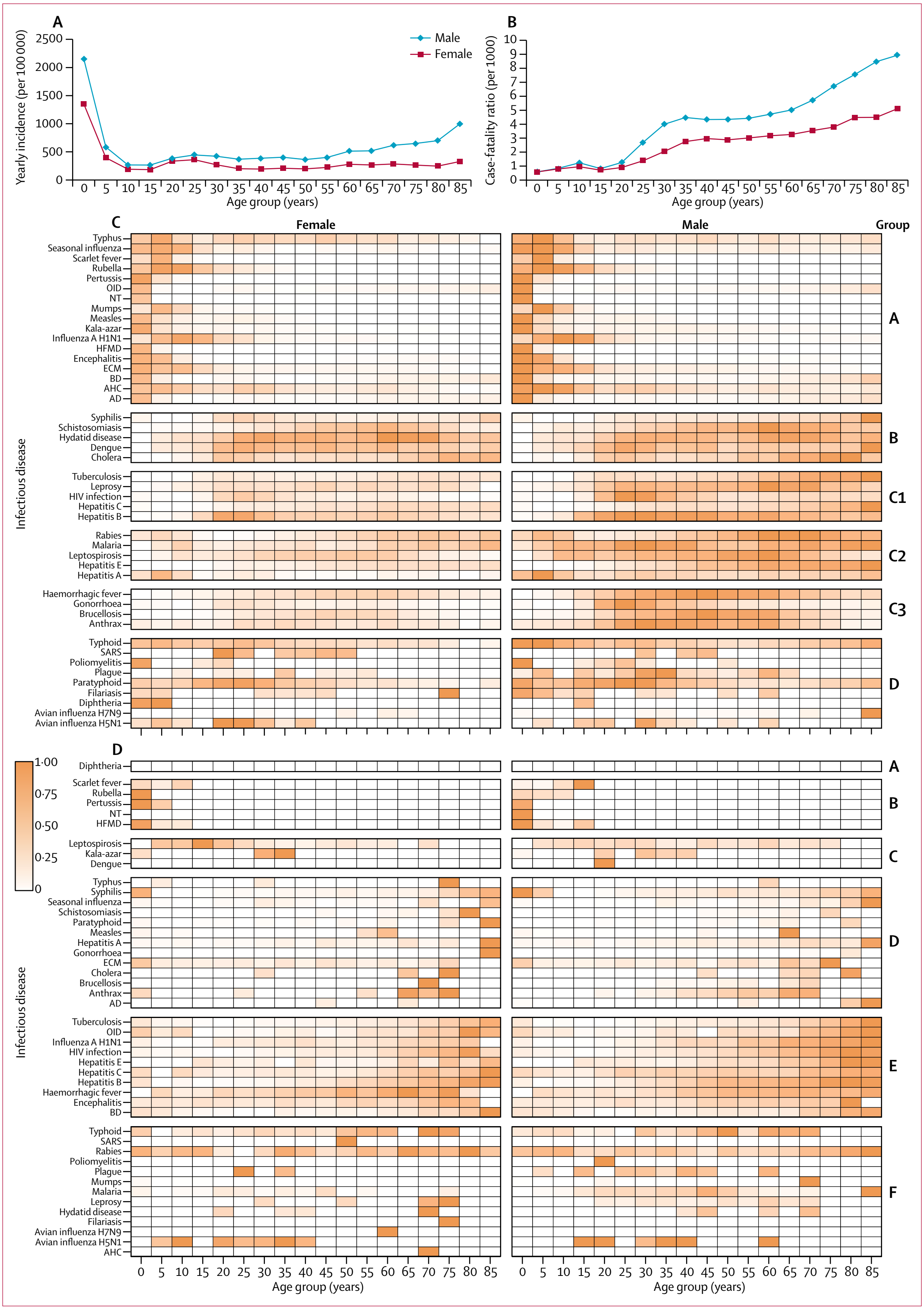

Figure 1: **Incidence and case-fatality ratios of 45 infectious diseases, by sex and age**

(A) Overall yearly incidence of 45 infectious diseases, by sex and age. (B) Overall yearly case-fatality ratios of 45 infectious diseases by sex and age. (C) Incidence of 45 infectious diseases by sex and age. Infectious diseases are grouped according to whether they had high incidence among children (group A), high incidence among adults (group B), increasing incidence trends by age and especially significant among men (group C1), high incidence among males in all age groups (group C2), high incidence among middle-aged men (group C3), and no significant features in terms of incidence by sex and age (group D). (D) Case-fatality ratios of 45 infectious diseases by sex and age. Infectious diseases are grouped according to whether they had no fatality in any age group (group A), high case-fatality ratios among children (group B), high case-fatality ratios among young people and middle-aged adults (group C), high case-fatality ratios among elderly people (group D), increasing trends in case-fatality ratios with age (group E), and no significant features in terms of case-fatality ratios by sex and age (group F). The incidence and case-fatality ratio for each infectious disease were standardised from 0 to 1 according to percentile rank, and represented by the colour scale (from 0 to 1; where 1 is the highest rate and 0 is the lowest rate). AD=amoebic dysentery. AHC=acute haemorrhagic conjunctivitis. BD=bacterial dysentery. ECM=epidemic cerebrospinal meningitis. HFMD=hand, foot, and mouth disease. NT=neonatal tetanus. OID=infectious diarrhoeal diseases other than cholera, bacterial dysentery, amoebic dysentery, typhoid, and paratyphoid. SARS=severe acute respiratory syndrome.

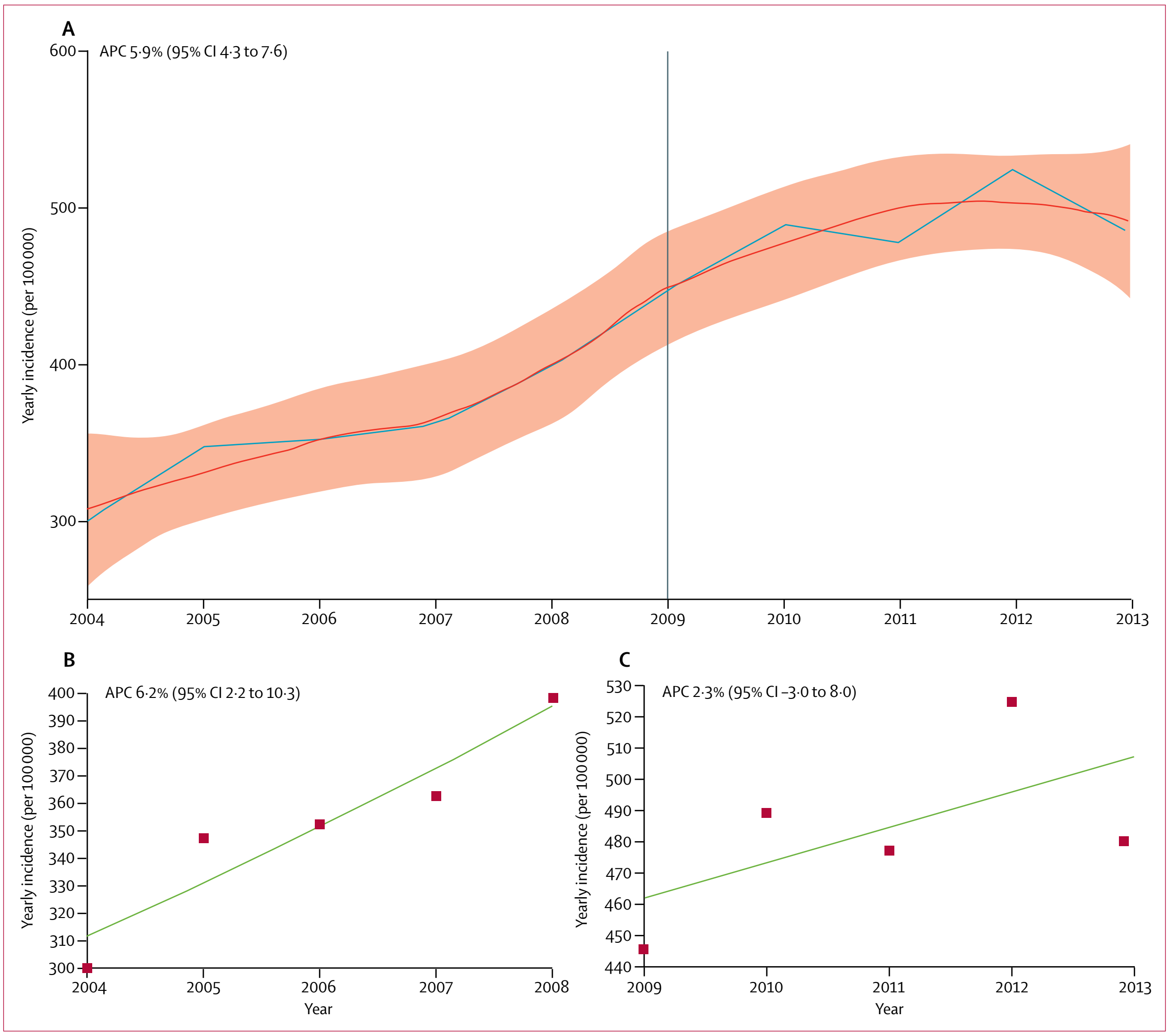

Figure 2: **Joinpoint regression showing trends in overall incidence of 45 infectious diseases**
(A) Trend in overall incidence from 2004 to 2013. Red line denotes the overall incidence and orange shading denotes the 95% CI. Blue line denotes observed incidence. Solid vertical line at 2009 denotes the end of the first 5 years of the study and the beginning of the second 5 years. (B) Yearly APC in incidence and overall trend, from 2004 to 2008. Red squares denote the observed values and green line the slope of the APC. (C) Yearly APC in incidence and overall trend, from 2009 to 2013. Red squares denote the observed values and green line the slope of the APC. APC=annual percentage change.

identify changes in trends between the first 5 years of the study period (2004–08) and the last 5 years (2009–13). We expressed trends as annual percentage changes (appendix p 2). We used the *Z* test to assess whether an annual percentage change was significantly different from zero. In describing trends, we used the terms increase and decrease when the slope (annual percentage change) was significant ($p<0·05$). We used the term stable to refer to a non-significant annual percentage change ($p\geq0·05$) and indicated that the incidence was maintained at a perennially stable level or that the incidence was perennially unreported or only reported sporadically.

We used IBM SPSS Modeler (version 14.1) for data extraction, sorting, and cleaning, and IBM SPSS Statistics (version 21), *R* project, and Joinpoint (version 4.3.1) for further data analysis.

Role of the funding source

The funder had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all data in the study and had final responsibility for the decision to submit for publication.

Results

Between January, 2004, and December, 2013, a total of 54 984 661 cases of 45 infectious diseases were reported, resulting in an average incidence of 417·98 cases per 100 000 per year. The infectious diseases with the highest yearly incidence were hand, foot, and mouth disease (114·48 cases per 100 000), hepatitis B (81·57 cases per 100 000), and tuberculosis (80·33 cases per 100 000; table 1; appendix pp 3, 4), which together accounted for

	Trend	Annual percentage change (95% CI)	p value*
Total	Increase	5·9% (4·3 to 7·6)	<0·05
Plague†	Decrease	–65·0% (–86·1 to –11·6)	<0·05
Cholera	Decrease	–27·8% (–42·6 to –9·3)	<0·05
Hepatitis A	Decrease	–14·8% (–17·6 to –11·9)	<0·05
Hepatitis B	Stable	0·8% (–1·1 to 2·9)	0·4
Hepatitis C	Increase	19·2% (15·9 to 22·6)	<0·05
Hepatitis E	Increase	7·0% (4·6 to 9·4)	<0·05
Bacterial dysentery	Decrease	–10·9% (–11·7 to –10·0)	<0·05
Amoebic dysentery	Decrease	–10·8% (–13·6 to –7·8)	<0·05
Typhoid	Decrease	–13·2% (–17·5 to –8·6)	<0·05
Paratyphoid	Decrease	–17·6% (–20·9 to –14·1)	<0·05
HIV infection	Increase	16·3% (11·5 to 21·2)	<0·05
Gonorrhoea	Decrease	–8·5% (–11·7 to –5·1)	<0·05
Syphilis	Increase	16·3% (13·8 to 18·8)	<0·05
Poliomyelitis†	Stable	7·0% (–27·6 to 58·3)	0·7
Measles	Stable	–14·8% (–27·8 to 0·5)	0·1
Pertussis	Decrease	–9·6% (–14·1 to –4·8)	<0·05
Diphtheria†	Stable	–2·0% (–14·8 to 12·8)	0·8
ECM	Decrease	–27·2% (–29·9 to –24·4)	<0·05
Scarlet fever	Stable	8·8% (–0·5 to 18·9)	0·1
Haemorrhagic fever	Decrease	–7·5% (–10·9 to –4·0)	<0·05
Rabies	Decrease	–8·2% (–12·3 to –3·8)	<0·05
Leptospirosis	Decrease	–14·3% (–18·9 to –9·4)	<0·05
Brucellosis	Increase	14·1% (9·0 to 19·4)	<0·05
Anthrax	Decrease	–11·0% (–12·7 to –9·4)	<0·05
Typhus	Decrease	–7·4% (–9·5 to –5·3)	<0·05
Encephalitis	Decrease	–13·9% (–20·3 to –6·9)	<0·05
Kala-azar	Stable	–5·6% (–13·2 to 2·8)	0·2
Malaria	Decrease	–26·1% (–33·7 to –17·6)	<0·05
(Continued from previous column)			
Dengue	Stable	18·4% (–21·2 to 77·8)	0·4
Neonatal tetanus	Decrease	–18·2% (–19·1 to –17·3)	<0·05
Tuberculosis	Decrease	–2·8% (–5·1 to –0·5)	<0·05
SARS†	Stable	–6·8% (–29·9 to 23·8)	0·6
Schistosomiasis	Increase	10·5% (5·9 to 15·4)	<0·05
Filariasis†	Decrease	–68·8% (–86·5 to –27·6)	<0·05
Hydatid disease	Increase	24·0% (12·0 to 37·2)	<0·05
Leprosy	Increase	4·7% (0·8 to 8·6)	<0·05
Seasonal influenza	Stable	11·4% (–3·6 to 28·8)	0·1
Mumps	Increase	6·3% (1·6 to 11·2)	<0·05
Rubella	Stable	3·7% (–12·2 to 22·5)	0·7
Acute haemorrhagic conjunctivitis	Stable	10·6% (–33·3 to 83·4)	0·7
Other‡	Increase	6·6% (3·3 to 10·0)	<0·05
Avian influenza H5N1†§	Stable	24·5% (–5·4 to 63·8)	0·1
HFMD†§	Stable	49·7% (–3·8 to 132·7)	0·1
Influenza A H1N1†§	Stable	671·4% (–36·3 to 9243·0)	0·1
Avian influenza H7N9†§	Stable	14·8% (–23·3 to 71·8)	0·5

(Table 2 continues in next column)

A normal (Z) distribution was used to assess significance of the annual percentage change, and the parametric method was used to calculate 95% CIs. ECM=epidemic cerebrospinal meningitis. HFMD=hand, foot, and mouth disease. SARS=severe acute respiratory syndrome. *Joinpoint program provides significant values as p<0·05. †When incidence data contained zero, we substitute the zero with 1% of the smallest incidence. ‡Infectious diarrhoeal diseases other than cholera, bacterial dysentery, amoebic dysentery, typhoid, and paratyphoid. §HFMD, influenza A H1N1, and avian influenza H7N9 were emerging during the period of study, and avian influenza H5N1 was emerging in 2003 according to a previous report.

***Table 2:* Annual percentage change in incidence of 45 infectious diseases, from 2004 to 2013**

66% (276·38 of 417·98 cases) of the overall incidence. 35 of 45 infectious diseases were characterised by seasonal distribution, particularly acute haemorrhagic conjunctivitis (September), rubella (April to June), influenza A H1N1 (September to December), and dengue (September to October; table 1; appendix pp 5, 6).

Among the 54 984 661 cases of infectious disease, 132 681 deaths were recorded, representing an average yearly mortality of 1·01 deaths per 100 000 and case-fatality ratio of 2·41 deaths per 1000 cases per year. The infectious diseases with the highest mortality in terms of yearly case-fatality ratio were rabies (982·14 deaths per 1000 cases), avian influenza A H5N1 (717·95 deaths per 1000 cases), and plague (379·31 deaths per 1000 cases; table 1; appendix pp 3, 4).

Overall yearly incidence of the 45 infectious diseases was highest among male individuals compared with females, across all age groups, and incidence was highest among children younger than 10 years and was lowest among those aged 10–20 years (figure 1A; appendix p 7). Overall yearly case-fatality ratios of the 45 infectious diseases were highest among men older than 20 years compared with their female counterparts, and they were lowest among children younger than 10 years and were highest among elderly patients older than 80 years, showing an increasing trend with rising age (figure 1B; appendix p 7).

Children had a high incidence of 17 infectious diseases (categorised as group A in figure 1C): typhus, seasonal influenza, scarlet fever, rubella, pertussis, other infectious diarrhoeal diseases (ie, other than cholera, bacterial dysentery, amoebic dysentery, typhoid, and paratyphoid), neonatal tetanus, mumps, measles, kala-azar (visceral leishmaniasis), influenza A H1N1, hand, foot, and mouth disease, encephalitis, epidemic cerebrospinal meningitis, bacterial dysentery, acute haemorrhagic conjunctivitis, and amoebic dysentery. Adults had a high incidence of syphilis, schistosomiasis, hydatid disease (echinococcosis), dengue, and cholera (denoted group B in figure 1C). Furthermore, tuberculosis, leprosy, HIV infection, hepatitis C, and hepatitis B (group C1) showed an increasing trend of incidence by age, which was especially noticeable among men; rabies, malaria, leptospirosis, hepatitis E, and hepatitis A (group C2) showed high yearly incidence among males in all age groups; and

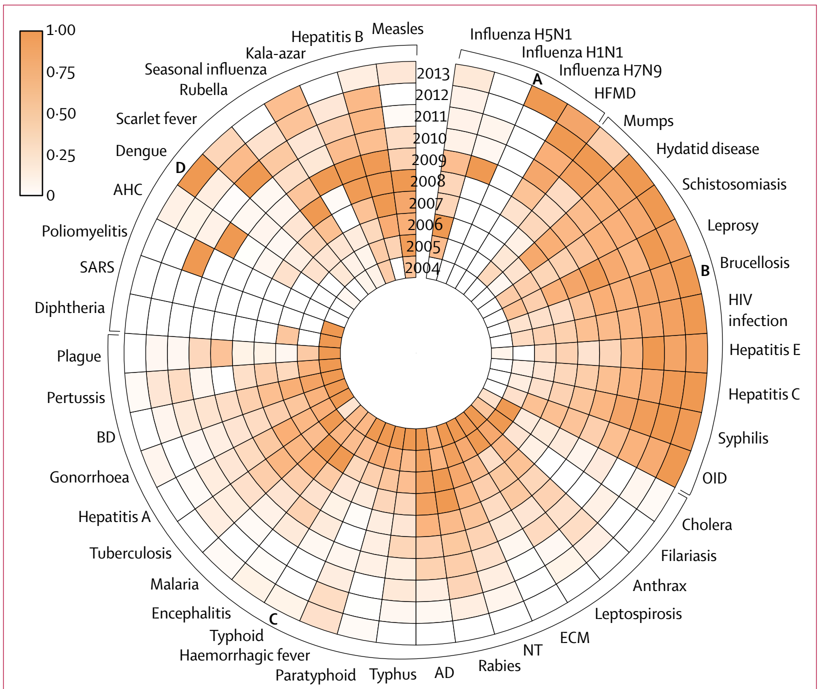

***Figure 3:* Trends in incidence for 45 infectious diseases, from 2004 to 2013**

Every concentric circle represents 1 year, starting with 2004 in the centre. Infectious diseases are grouped according to emerging status (group A), increasing (group B) or decreasing (group C) trends, or stable status (group D). The incidence and case-fatality ratio for each infectious disease were standardised from 0 to 1 according to percentile rank, and represented by the colour scale (from 0 to 1; where 1 is the highest rate and 0 is the lowest rate). HFMD=hand, foot, and mouth disease. AD=amoebic dysentery. AHC=acute haemorrhagic conjunctivitis. BD=bacterial dysentery. ECM=epidemic cerebrospinal meningitis. NT=neonatal tetanus. OID=infectious diarrhoeal diseases other than cholera, bacterial dysentery, amoebic dysentery, typhoid, and paratyphoid. SARS=severe acute respiratory syndrome.

haemorrhagic fever, gonorrhoea, brucellosis, and anthrax showed the highest incidence among middle-aged men (group C3).

Case-fatality ratios were high among children for five infectious diseases (denoted group B in figure 1D): scarlet fever, rubella, pertussis, neonatal tetanus, and hand, foot, and mouth disease. Young adults had high case-fatality ratios for leptospirosis, kala-azar, and dengue (denoted group C in figure 1D), and the case-fatality ratios for typhus, syphilis, seasonal influenza, schistosomiasis, paratyphoid, measles, hepatitis A, gonorrhoea, epidemic cerebrospinal meningitis, cholera, brucellosis, anthrax, and amoebic dysentery (group D) were high for middle-aged individuals. Ten infectious diseases showed an increasing trend of case-fatality ratios with age (group E): tuberculosis, other infectious diarrhoeal diseases, influenza A H1N1, HIV infection, hepatitis E, hepatitis C, hepatitis B, haemorrhagic fever, encephalitis, and bacterial dysentery. Data for incidence and case-fatality were further analysed by stratification of sex, age group, the diseases themselves, and transmission routes (appendix pp 8–15).

During the study period, the average overall incidence of the 45 infectious diseases increased from 300·54 cases per 100 000 in 2004 to 483·63 cases per 100 000 in 2013 (figure 2A). The joinpoint regression indicated an annual percentage change of 5·9% (95% CI 4·3 to 7·6; $p<0·05$; table 2). However, the increasing trend varied across different periods, and the trend changed after 2009. The annual percentage change was 6·2% (95% CI 2·2 to 10·3; $p<0·05$) from 2004 to 2008 and 2·3% (–3·0 to 8·0; $p>0·05$) from 2009 to 2013, indicating a significant decrease in the second 5-year period (figure 2B, 2C). During the study period, the average case-fatality ratio increased from 1·86 deaths per 1000 cases in 2004 to 2·58 deaths per 1000 cases in 2013 (appendix p 16). However, the trend was not significant after 2005; specifically, no increasing trend was noted after 2009.

Ten of the 45 infectious diseases showed significantly increasing trends in incidence from 2004 to 2013: hydatid disease, hepatitis C, HIV infection, syphilis, brucellosis, schistosomiasis, hepatitis E, other infectious diarrhoeal diseases, mumps, and leprosy (denoted as group B in figure 3). In particular, hydatid disease, hepatitis C, syphilis, and HIV infection showed the fastest rates of growth, with annual percentage changes of 24·0% (95% CI 12·0 to 37·2), 19·2% (15·9 to 22·6), 16·3% (13·8 to 18·8), and 16·3% (11·5 to 21·2), respectively (table 2). Moreover, 20 infectious diseases showed significantly decreasing trends in incidence from 2004 to 2013 (denoted as group C in figure 3). In particular, filariasis, plague, and cholera showed the fastest reductions, with annual percentage changes of –68·8% (95% CI –86·5 to –27·6), –65·0% (–86·1 to –11·6), and –27·8% (–42·6% to –9·3), respectively (table 2). Although hand, foot, and mouth disease, influenza A H1N1, and avian influenza H7N9 were emerging during the study period, and avian influenza H5N1 was first noted in 2003,[7] these diseases showed stable trends after emerging (table 2).

Overall yearly incidence and case-fatality ratios of the 45 infectious diseases varied greatly between geographic areas. The three provinces with the highest overall yearly incidence of the 45 infectious diseases were Beijing (753·45 cases per 100 000), Xinjiang (748·37 cases per 100 000), and Zhejiang (689·88 cases per 100 000). The three provinces with the highest overall yearly case-fatality ratios were Yunnan (7·65 deaths per 1000 cases), Guangxi (6·29 deaths per 1000 cases), and Guizhou (4·82 deaths per 1000 cases). Among the 45 infectious diseases, those with the highest incidence were mainly distributed across 19 provinces (figure 4A), and those with the highest case-fatality ratios were mainly distributed across 23 provinces (figure 4B).

Discussion

We report here the average overall yearly incidence, mortality, and case-fatality ratios of 45 infectious diseases in China from 2004 to 2013. The three infectious diseases with the highest incidence during this period were hand, foot, and mouth disease, hepatitis B, and tuberculosis. Trends in the incidence of major infectious diseases have varied in the past few years. Indeed, the incidence of dysentery, which was one of the three most common infectious diseases before 2006,[3,14] decreased substantially between 2004 and 2013 and was replaced by hand, foot, and mouth disease.

Globally, the incidence of the three main infectious diseases—hand, foot, and mouth disease, hepatitis B, and tuberculosis—varies greatly between countries. Large outbreaks of hand, foot, and mouth disease are not common in the USA, but in some countries in Asia, outbreaks are large and frequent.[19] In eastern Europe, Africa, and the Middle East, people with tuberculosis are mainly refugees, with a latent prevalence of 55%.[20] Geographically, the prevalence of hepatitis B differs greatly. In China, the proportion of HBsAg carriers was 7·18% in 2006, which is significantly higher than the proportion of carriers in countries in Europe and North America.[21]

In China, the high overall yearly incidence and mortality of the 45 infectious diseases could be related to high incidence and mortality in provinces near the remote Chinese border, such as Yunnan and Xinjiang. In these regions, a combination of factors can favour development and spread of infectious diseases—eg, different customs within the multiethnic population, limited access to health care, less efficient public health programmes and infrastructure, environmental degradation, and poverty. Furthermore, the reported yearly incidence, which is affected by detection levels and screening intensity, could vary between diseases and geographical areas.

In this study, significant seasonal features were noted for several infectious diseases, including acute haemorrhagic conjunctivitis, rubella, influenza A H1N1, and dengue. Seasonal features of infectious diseases are useful resources for inferring temporal and spatiotemporal transmission parameters, to better understand and predict the spread of disease.[22] However, the seasonality of infectious diseases could be affected by geographical differences; our results indicated that there were two epidemic peaks of seasonal influenza, whereas this infectious disease was reported to have a dual seasonal pattern between southern and northern China.[23]

Our findings indicated that overall yearly incidence of the 45 infectious diseases was high among male individuals and children, and overall yearly mortality was high for male individuals, children, and elderly people. Thus, specific strategies and measures should target these three populations. More than 95% of cases of childhood infectious disease are prevented by vaccines.[24] However, low perceptivity of disease risk by individuals can lead to reduced participation in vaccination programmes.[24] Vaccination programmes should strengthen society's understanding of infection and improve compliance with vaccination. A high incidence of infectious diseases in elderly people would be a great threat to public health and society in China, where 178 million people are older than 60 years, and this number is estimated to increase to approximately 423 million by 2050.[25] The incidence and case-fatality ratios of infectious diseases among people older than 60 years are roughly three times the current average.

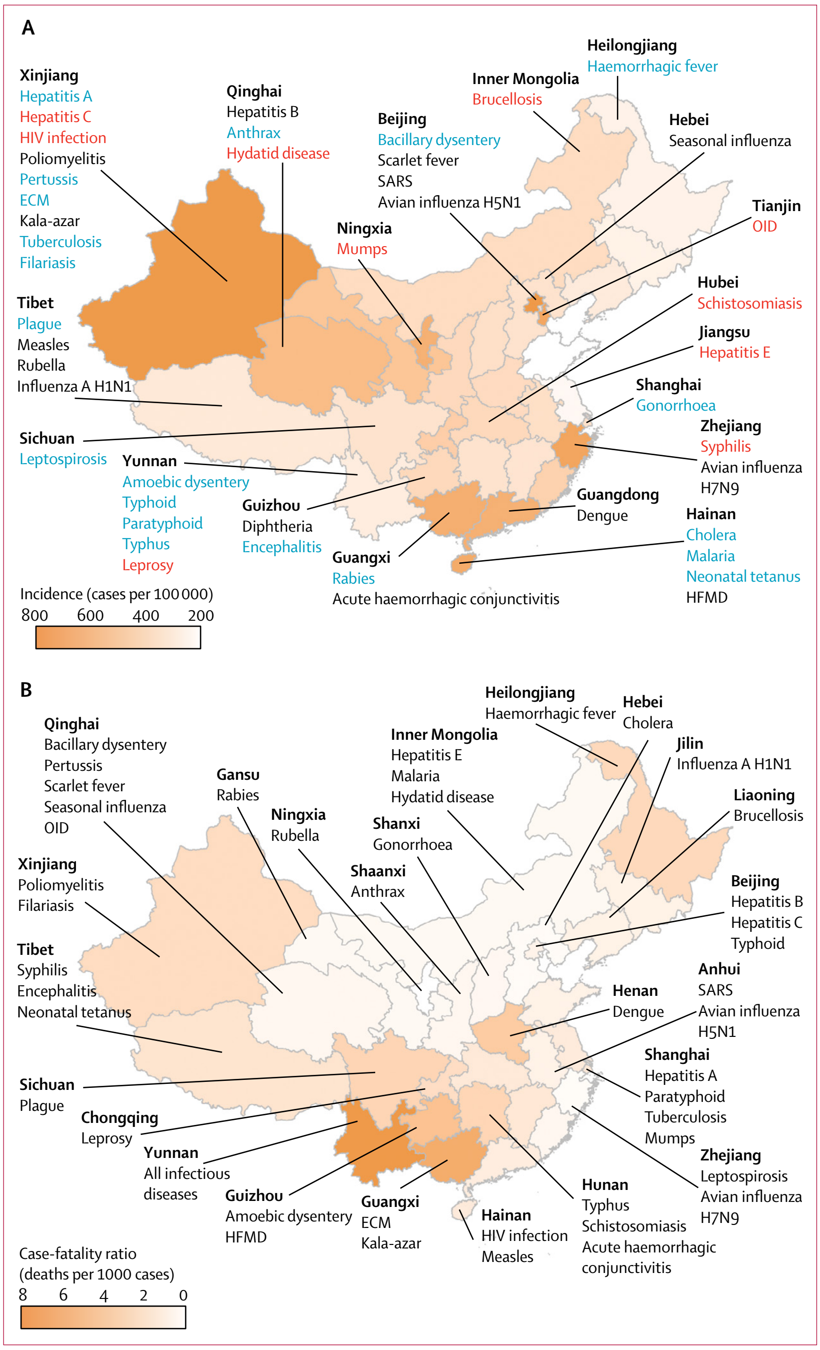

Figure 4: **Trends in incidence and case-fatality ratios of infectious diseases in different geographic areas of China**
(A) Incidence trends of the 45 infectious diseases in different Chinese provinces. The infectious diseases with the highest average incidence were distributed across the indicated provinces. Infectious diseases with increasing trends from 2004 to 2013 are presented in red; those with decreasing trends are in blue; and stable diseases are shown in black. (B) Case-fatality ratios of infectious diseases in different Chinese provinces. ECM=epidemic cerebrospinal meningitis. HFMD=hand, foot, and mouth disease. OID=infectious diarrhoeal diseases other than cholera, bacterial dysentery, amoebic dysentery, typhoid, and paratyphoid. SARS=severe acute respiratory syndrome.

In recent decades, the overall incidence and mortality of infectious diseases have shown a striking decline in China.[3] This sharp fall can be attributed to effective and large-scale public health interventions and large population-based vaccination programmes. However, the notable decreasing tendency of overall incidence was reversed in the past few years, with a gradual upward trend reported,[3] which we have confirmed in our study of 45 infectious diseases. Several factors could account for this increasing trend. First, the timeliness of reporting has improved, with fewer missing reports, which is attributable to great technological progress in laboratory detection and case identification. Moreover, diagnosis of infectious diseases has improved gradually in recent decades. In particular, use of PCR rapid diagnosis technologies has become widespread in hospitals at all levels. An improvement in diagnostic levels for infections would affect incidence.[26] Second, because of increasing antimicrobial resistance, augmented human connectivity, and changeable human behaviour, the threat of infection continues to rise.[2] In China, more than 10% of the population has moved from poor rural areas to urban centres in search of better economic opportunities, which promotes transmission of infectious diseases.[3] Furthermore, imported and emerging infectious diseases are correlated with socioeconomic, environmental, and ecological factors.[5] Specific strategies and measures should be designed to counteract increasing trends in hydatid disease, hepatitis C, HIV infection, syphilis, brucellosis, schistosomiasis, hepatitis E, other infectious diarrhoeal diseases, mumps, and leprosy—eg, early surveillance and warning with enhanced screening, massive vector control, expansion of vaccine immunisation programmes, and reduction or exemption of treatment costs for infectious diseases. However, some discrepancies with previous reports in trends of infectious diseases (eg, schistosomiasis) need to be studied specifically in the future.[27]

Although the overall yearly incidence of infectious diseases showed an increasing trend in China from 2004, fortunately, this trend changed after 2009. Furthermore, trends in incidence for 20 of 45 infectious diseases have decreased since 2004. After the 2003 SARS epidemic, the Chinese Government strengthened joint multisectoral cooperation and increased investments in infectious disease prevention and control. In particular, the major special national science and technology project on preventing and controlling infectious diseases began in China at the end of 2008,[13] with a total investment of about US$2·25 billion. The primary infectious diseases—including hepatitis B, tuberculosis, and HIV infection—have been contained effectively in a large-scale demonstration area (located in Zhejiang, Jiangsu, Shanghai, Shandong, Beijing, Gansu, Sichuan, Henan, Xinjiang, Guangdong, Yunnan, and Guangxi provinces), where the project has made improvements in perfecting, enhancing, and expanding screening, augmenting the vaccine immunisation programme, and reducing or exempting treatment costs for infectious diseases.[21,28,29] In the past several decades, China has implemented various strategies to prevent the spread of infectious diseases. Some strategies have been proven effective, which could also serve as a model for other developing countries. These strategies include improvements in the water supply and sanitation, improvements in the safety of blood collection, massive vector control, expanding the vaccine immunisation programme, and early surveillance and warning with enhanced screening.

Some limitations of our study should be mentioned. Based on data from the reporting system, reported yearly incidence affected by screening intensity could be underestimated. Second, incidence could also be underestimated because of ascertainment bias by self-selection, in which individuals with a specific infectious disease are more likely to avoid screening than are people without that infection. Third, overall yearly incidence of the 45 infectious diseases was affected by the constituent incidence of each infectious disease in each province; thus, overall incidence should be considered with reference to each infectious disease and province. Moreover, potential bias could affect incidence and mortality reporting because of variations in diagnostic standards, technical levels, and experimental conditions in different departments or institutions.

In conclusion, since the 2003 SARS outbreak, no complete, systematic, long-term, and comprehensive description of infectious disease characteristics and trends has been available in China. We have described the epidemiological features of and changes in 45 infectious diseases (expanded from a previous report of 18 infectious diseases) during the longest period studied in post-SARS China. Moreover, although the overall incidence of infectious diseases was increasing, this trend was inflected after 2009, and 20 of 45 infectious diseases showed decreasing trends since 2004. Furthermore, incidence and mortality have varied substantially in the post-SARS era. Hand, foot, and mouth disease, hepatitis B, and tuberculosis have the highest yearly incidence, and hydatid disease, hepatitis C, and syphilis show the fastest increases. Thus, personalised and precise strategies for prevention and control of these diseases should be applied for specific populations, with an emphasis on children, elderly people, male individuals, and people living in specific regions.

Contributors

LL and SY designed the study. SY, YL, JW, CD, YC, and YZ collected data. SY, JW, and YL analysed data. SY interpreted data and wrote the report. SY, JW, CD, YC, YZ, MD, CW, KX, JR, and BR revised the report from preliminary draft to submission. LL supervised the study.

Declaration of interests

We declare no competing interests.

Acknowledgments

We thank the Chinese Center for Disease Control and Prevention for opening and sharing the Public Health Science Data Center. This study was supported by grants from the Key Joint Project for Data Center of the National Natural Science Foundation of China and Guangdong Provincial

Government (U1611264), the Mega-Project of National Science and Technology for the 12th Five-Year Plan of China (2011ZX10004-901, 2013ZX10004901, 2013ZX10004904, and 2014ZX10004008), the National Natural Science Foundation of China (81001271, 81672005), and the Fundamental Research Funds for the Central Universities.

References

1 World Health Organization. Global strategy for health for all by the year 2000. 1981. http://apps.who.int/iris/bitstream/10665/38893/1/9241800038.pdf (accessed March 15, 2017).

2 Heesterbeek H, Anderson RM, Andreasen V, et al. Modeling infectious disease dynamics in the complex landscape of global health. *Science* 2015; **347:** aaa4339.

3 Wang L, Wang Y, Jin S, et al. Emergence and control of infectious diseases in China. *Lancet* 2008; **372:** 1598–605.

4 World Health Organization. The world health report 2002: reducing risks, promoting healthy life. 2002. http://www.who.int/whr/2002/en/whr02_en.pdf?ua=1 (accessed March 15, 2017).

5 Jones KE, Patel NG, Levy MA, et al. Global trends in emerging infectious diseases. *Nature* 2008; **451:** 990–93.

6 Shaw K. The 2003 SARS outbreak and its impact on infection control practices. *Public Health* 2006; **120:** 8–14.

7 World Health Organization. Cumulative number of confirmed human cases of avian influenza A (H5N1) reported to WHO. Feb 14, 2017. http://www.who.int/influenza/human_animal_interface/HAI_Risk_Assessment/en/ (accessed Feb 16, 2017).

8 Yang SG, Cao B, Liang LR, et al. Antiviral therapy and outcomes of patients with pneumonia caused by influenza A pandemic (H1N1) virus. *PLoS One* 2012; **7:** e29652.

9 Wang HB, Yu WZ, Wang XQ, et al. An outbreak following importation of wild poliovirus in Xinjiang Uyghur Autonomous Region, China, 2011. *BMC Infect Dis* 2015; **15:** 34.

10 Chen Y, Liang W, Yang S, et al. Human infections with the emerging avian influenza A H7N9 virus from wet market poultry: clinical analysis and characterisation of viral genome. *Lancet* 2013; **381:** 1916–25.

11 Wei P, Cai Z, Hua J, et al. Pains and gains from China's experiences with emerging epidemics: from SARS to H7N9. *BioMed Res Int* 2016; **2016:** 5717108.

12 Cheng A, Wei H, Zuo G, Shen Y. Areas joint control of major disease. *J Prev Med Info* 2007; **23:** 2 (in Chinese). DOI:10.3969/j.issn.1006-4028.2007.01.030.

13 Ministry of Science and Technology (MOST) of the People's Republic of China. National medium and long-term science and technology development plan. http://www.most.gov.cn/mostinfo/xinxifenlei/gjkjgh/200811/t20081129_65774.htm (in Chinese; accessed Feb 9, 2006).

14 National Health and Family Planning Commission of the People's Republic of China. General situation of statutory infectious diseases in China in 2013. http://www.nhfpc.gov.cn/jkj/s3578/201402/26700e8a83c04205913a106545069a11.shtml (in Chinese; accessed Feb 13, 2014).

15 The Central People's Government of the People's Republic of China. Law of the People's Republic of China on prevention and treatment of infectious diseases (2004 revision). http://www.gov.cn/banshi/2005-05/25/content_971.htm (in Chinese; accessed May 25, 2005).

16 Wang L, Wang L, Yang G, Ma J, Wang L, QI X. China Information System for Disease Control and Prevention (CISDCP). 2016. http://www.pacifichealthsummit.org/downloads/HITCaseStudies/Functional/CISDCP.pdf (accessed March 16, 2017).

17 China Center for Disease Control and Prevention. The Public Health Science Data Center. http://www.phsciencedata.cn/Share/index.jsp (accessed June 15, 2016).

18 Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. *Stat Med* 2000; **19:** 335–51.

19 US Centers for Disease Control and Prevention. Hand, foot, and mouth disease (HFMD). https://www.cdc.gov/hand-foot-mouth/index.html (accessed Jan 6, 2017).

20 Ritz N, Brinkmann F, Santiago Garcia B, Tebruegge M, Kampmann B, on behalf of the Paediatric Tuberculosis Network European Trials group (ptbnet). Tuberculosis in young refugees. *Lancet* 2015; **386:** 2475–76.

21 Yang S, Yu C, Chen P, et al. Protective immune barrier against hepatitis B is needed in individuals born before infant HBV vaccination program in China. *Sci Rep* 2015; **5:** 18334.

22 Held L, Paul M. Modeling seasonality in space-time infectious disease surveillance data. *Biom J* 2012; **54:** 824–43.

23 Shu YL, Fang LQ, de Vlas SJ, Gao Y, Richardus JH, Cao WC. Dual seasonal patterns for influenza, China. *Emerg Infect Dis* 2010; **16:** 725–26.

24 van Panhuis WG, Grefenstette J, et al. Contagious diseases in the United States from 1888 to the present. *N Engl J Med* 2013; **369:** 2152–58.

25 Zhai C, Xie H, Jin L, Wang Q, Wang J. Research status of family caregivers of elderly chronic diseases. *Chin J Prev Control Chronic Dis* 2014; **22:** 3.

26 Li LM, Wang JH. Epidemiology, 3rd edn. Beijing: People's Medical Publishing House, 2014.

27 Wang X, Wang W, Wang P. Long-term effectiveness of the integrated schistosomiasis control strategy with emphasis on infectious source control in China: a 10-year evaluation from 2005 to 2014. *Parasitol Res* 2017; **116:** 521–28.

28 Li L. Standard operation procedure for major projects of national science and technology of infectious disease: the community comprehensive prevention and control of major infectious diseases. Beijing: Science Press, 2012: 3–13 (in Chinese).

29 Wang W, Zhao Q, Yuan Z, et al. Tuberculosis-associated mortality in Shanghai, China: a longitudinal study. *Bull World Health Organ* 2015; **93:** 826–33.v