

# Trend and disease burden of bacillary dysentery in China (1991–2000)

Xuan-yi Wang,<sup>a</sup> Fangbiao Tao,<sup>b</sup> Donglou Xiao,<sup>c</sup> Hyejon Lee,<sup>a</sup> Jacqueline Deen,<sup>a</sup> Jian Gong,<sup>d</sup> Yuliang Zhao,<sup>e</sup> Weizhong Zhou,<sup>f</sup> Weiming Li,<sup>g</sup> Bing Shen,<sup>h</sup> Yang Song,<sup>i</sup> Jianming Ma,<sup>j</sup> Zheng-mao Li,<sup>c</sup> Zijun Wang,<sup>c</sup> Pu-yu Su,<sup>b</sup> Nayoon Chang,<sup>a</sup> Jun-hong Xu,<sup>i</sup> Pei-ying Ouyang,<sup>k</sup> Lorenz von Seidlein,<sup>a</sup> Zhi-yi Xu,<sup>a</sup> & John D Clemens<sup>a</sup>

**Objective** We aimed to determine the burden of bacillary dysentery in China, its cross-regional variations, trends in morbidity and mortality, the causative bacterial species and antimicrobial resistance patterns.

**Methods** We extracted and integrated governmental statistics and relevant medical literature published from 1991 to 2000. Data were also collected from one general hospital each for the six provinces and Jin-an district, Shanghai, representative of six geographical regions and a modern city.

**Findings** In 2000, 0.8–1.7 million episodes of bacillary dysentery occurred of which 0.5 to 0.7 million were treated at health-care facilities and 0.15–0.20 million patients were hospitalized. The highest morbidity and mortality rates were among the youngest and oldest age groups. Bacillary dysentery peaked during the summer months. The major causative species was *Shigella flexneri* (86%) and the predominant *S. flexneri* serotype was 2a (80%). About 74–80% of *Shigella* isolates remained susceptible to fluorinated quinolones.

**Conclusion** We conclude that while morbidity and mortality due to bacillary dysentery has decreased considerably in China in the past decade due to increasing access to affordable health care and antibiotics, a considerable burden exists among the youngest and oldest age groups and in regions with low economic development. We suggest that while a vaccine would be effective for short- and medium-term control of bacillary dysentery, improved water supply, sanitation, and hygiene are likely to be required for long-term control.

Bulletin of the World Health Organization 2006;84:561–568.

Voir page 567 le résumé en français. En la página 567 figura un resumen en español.

يمكن الاطلاع على الملخص بالعربية في صفحة 568.

## Introduction

Globally, morbidity and mortality due to diarrhoea has decreased from 4.6 million deaths in 1982 to 3.3 million in 1992 to 2.5 million in 2003.<sup>1–3</sup> A review published in 1999 reported that bacillary dysentery caused by *Shigella* species (*S. flexneri*, *S. sonnei*, *S. boydii*, and *S. dysenteriae*) remains a major source of diarrhoea, especially in developing countries. It also reported that of the 164.7 million episodes of shigellosis (*Shigella*-related diarrhoea) occurring worldwide each year, 163.2 million were in developing countries; however, the review included sparse data from China.<sup>4</sup>

China, a developing country with the largest population in the world, has made significant socioeconomic progress over the past decade. Many indicators show that the health status of the average Chinese has improved considerably. For example, life expectancy in China increased from 57.0 years in 1957 to 71.4 years in 2000.<sup>5</sup> Even so diarrhoeal diseases remain an important public health problem. A cross-sectional survey conducted in 1988 estimated that of the 84 million diarrhoeal episodes that occurred in China annually, 25% affected children less than five years of age. The survey also found that *Shigella* is one

of the principle etiologic organisms for diarrhoea.<sup>6</sup> A live oral *Shigella* vaccine which was developed and produced in China in 1997 reportedly provides 60–70% protection against *S. flexneri* 2a and *S. sonnei* infections.<sup>7</sup>

A continuing analysis of the disease burden of bacillary dysentery would be required for effective treatment and prevention policies, health prioritization debates, and cost–benefit assessments to enable rational decisions on research, prevention and control activities. We reviewed the burden of bacillary dysentery in China with data from existing sources to determine the trends in morbidity

<sup>a</sup> International Vaccine Institute, San 4-8 Bongcheon-7 dong, Kwanak-gu, Seoul, Republic of Korea 151-818. Correspondence to this author (email: xywang@ivi.int).

<sup>b</sup> School of Public Health, Anhui Medical University, Hefei, Anhui Province, China.

<sup>c</sup> Department of Disease Control, Ministry of Health, China.

<sup>d</sup> Center for Disease Control and Prevention, Guangxi Province, China.

<sup>e</sup> Center for Disease Control and Prevention, Hebei Province, China.

<sup>f</sup> Center for Disease Control and Prevention, Jiangsu Province, China.

<sup>g</sup> Center for Disease Control and Prevention, Jilin Province, China.

<sup>h</sup> Center for Disease Control and Prevention, Jin-an District, Shanghai, China.

<sup>i</sup> Center for Disease Control and Prevention, Sichuan Province, China.

<sup>j</sup> Center for Disease Control and Prevention, Xinjiang Province, China.

<sup>k</sup> Department of Molecular Medical Virology, Shanghai Medical College, Fudan University, Shanghai, China.

Ref. No. 05-023853

(Submitted: 11 May 2005 – Final revised version received: 19 October 2005 – Accepted: 26 October 2005)

and mortality, the high-risk populations, bacterial species, serotypes and antimicrobial resistance patterns.

## Methods

### Government statistics: national level

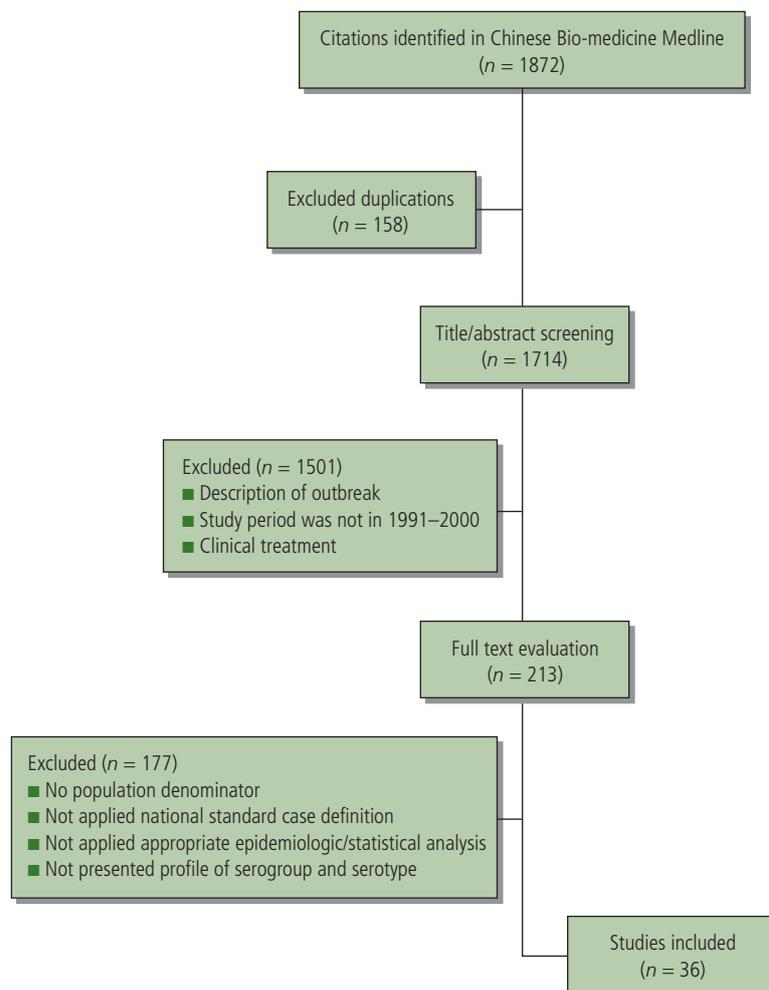
China has two national surveillance systems for infectious diseases — the National Noticeable Infectious Disease Reporting system (NIDR) and the National Sentinel Disease Surveillance Points system (DSP).<sup>8</sup>

The NIDR system involves all health-care facilities at the village, township, county, and city levels. The Law on the Prevention and Control of Infectious Diseases (SCSNPC, 1989)<sup>8</sup> requires health-care staff to report any of the 24 infectious diseases, including bacillary dysentery, to the Chinese Center for Disease Control and Prevention (CDC) where data are collected and analysed every month. The Department of Disease Control in the Ministry of Health then issues annual reports based on these data.

The DSP system was started in 1978 to complement and augment the NIDR. In 1990 a stratified three-stage cluster probability sampling was designed for re-selection of surveillance sites, to improve representativeness considering the variations in geographical features, inequality of economic development and the uneven health-care services in different regions of China. The system consists of 145 sites and covers around 1% of the total population of China (around 10 million people).<sup>8–11</sup> The representativeness of the sample was established through an index, including gross national product, literacy rate, birth rate, infant death rate, rough death rate, ratio of the age groups 0–14 years and over 65 years to the total population, ratio of labour in the industry to that in the total population, and ratio of labour in agriculture to that in the total population.<sup>10,11</sup> To ensure a consistent and high quality of surveillance, standard operating procedures were developed and implemented as well as training, monitoring and supervision of staff were included in this system.<sup>11</sup> DSP data are used to adjust national reports based on the NIDR system, which may be less complete. The World Bank has used DSP data due to its relatively high accuracy.<sup>8,9</sup>

Before 2001, the *International classification of diseases*, ninth revision (ICD-9)

Fig. 1. Eligibility of epidemiologic studies for inclusion in the systematic review



WHO 06.11

was used in China for the classification of disease and cause of death<sup>11</sup> in both the NIDR and DSP systems. Under the ICD-9 codes for dysentery, both bacillary dysentery and amoebic dysentery are included. We included only bacillary dysentery data collected between 1991 and 2000. Due to lack of age-specific morbidity and mortality data in the NIDR system annual report, we used data from the DSP system for the description of age-specific mortality and morbidity. We calculated the mean rates for the periods 1991–95 and 1996–2000 based on the numerators and denominators provided by the database.

### Government statistics: regional level

The mainland is customarily grouped into six geographical regions according to similarity of geographical parameters. There are considerable differences in

the socioeconomic status of these six regions with those in east China, where more than 70% of China's population resides, having higher economic status than those in north-west China where economic progress has not been as rapid. To explore the cross-regional variations in bacillary dysentery rates, we selected six provinces — one province from each of the six geographical regions, similar to the geographical sampling designed for the DSP system<sup>10–12</sup> and Jin-an district from Shanghai to represent the most modern Chinese urban area (Table 1).

### Hospitalization data

Hospital data on inpatient–outpatient ratios and duration of hospitalizations were collected from one general hospital for each of the six provinces and Jin-an district, Shanghai for the year 2000. We searched patient logbooks, medical records, discharge diagnosis forms and

laboratory registrations for the terms bacillary dysentery and shigellosis.

### Published literature

To explore the profile of the causative species and serotypes, locally and internationally published papers were identified through a literature search using the keywords *Shigella*, bacillary dysentery, dysentery and diarrhoea. We searched the Chinese Bio-medicine Medline (CBM) for nationally published articles and Medline for international medical literature. The results were checked and reviewed independently by two investigators according to the following inclusion criteria (Fig. 1):

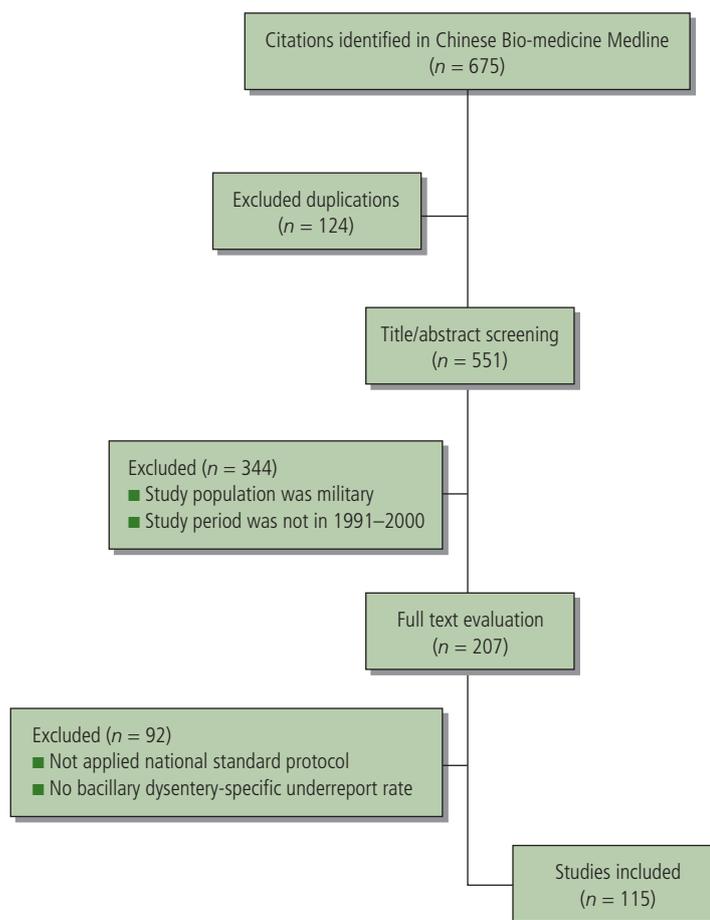
1. published between 1991 and 2000;
2. not an outbreak study;
3. not on clinical treatment;
4. use of a clear population denominator;
5. application of the national standard case definition (see below);
6. application of appropriate epidemiological and statistical analyses;
7. presented the profile of serogroup or serotype.

The inter-observer agreement between the two reviewers for title/abstract and full-text evaluation was very high (kappa 0.86 and 0.90,  $P < 0.05$ ). Eventually, 36 papers that fulfilled the inclusion criteria were included in this review.

### Underreporting

Although the DSP system was created to minimize underreporting, it is still thought to underestimate the morbidity from infectious diseases. The Ministry of Health thus developed a general protocol that uses standardized surveys to assess this underreporting. Results from these community- and hospital-based underreporting surveys, that more accurately estimate the amount of total

Fig. 2. Eligibility of underreporting studies for inclusion in the systematic review



WHO 06.12

versus treated infectious diseases,<sup>11</sup> are published in the national literature. We searched the CBM dataset using keywords, infectious disease/report, infectious disease/underreporting, epidemic information/report and epidemic information/underreporting. We also had the results screened independently by the same two investigators (who processed

the epidemiological literature) for the following standard inclusion criteria (Fig. 2):

1. published between 1991 and 2000;
2. not military data;
3. application of the national standard protocol for underreporting survey;
4. presented the specific underreporting rates of bacillary dysentery.

Table 1. The incidence and community-based underreporting of bacillary dysentery in China, by geographical regions, 1991–2000

Region of China	Province included in the region	Representative province/district	Median under-reporting rate <sup>a</sup>	Incidence/10 000 <sup>b</sup>
North	Beijing, Tianjin, Hebei, Shanxi, Inner Mongolia	Hebei	0.597	11.84
North-east	Liaoning, Jilin, Heilongjiang	Jilin	0.506	11.97
East	Jiangsu, Zhejiang, Anhui, Fujian, Jiangxi, Shandong	Jiangsu	0.445	11.90
Centre and south	Henan, Hubei, Hunan, Guangdong, Guangxi, Hainan	Guangxi	0.707	17.87
South-west	Sichuan, Guizhou, Yunnan, Chongqing, Xizang	Sichuan	0.628	17.28
North-west	Shan-xi, Gansu, Qinghai, Ningxia, Xinjiang	Xinjiang	0.447	18.37
Shanghai <sup>c</sup>		Jin-an District	0.000	9.23

<sup>a</sup> Underreporting rate = No. of unreported cases/(reported cases + unreported cases).

<sup>b</sup> Data are from seven Centres for Disease Control and Prevention and were corrected for regional underreporting.

<sup>c</sup> Shanghai was isolated from the east region as representative of the most modern Chinese urban area.

Table 2. Case–fatality rates, morbidity and mortality in China due to bacillary dysentery, 1991–2000

Year	NIDR Data <sup>a</sup>					DSP Data <sup>b</sup>	
	Cases	Deaths	Fatality rate (1/10 000)	Morbidity (1/10 000)	Mortality (1/10 000)	Morbidity (1/10 000)	Mortality (1/10 000)
1991	1 318 482	1155	8.8	11.6	0.010	23.1	0.031
1992	916 366	682	7.4	8.0	0.006	19.6	0.029
1993	628 833	426	6.8	5.5	0.004	13.3	0.012
1994	874 465	515	5.9	7.5	0.004	18.0	0.015
1995	864 346	440	5.1	7.3	0.004	18.1	0.010
1996	784 407	383	4.9	6.6	0.003	14.8	0.004
1997	715 191	354	4.9	6.0	0.003	12.3	0.008
1998	687 946	353	5.1	5.5	0.003	11.1	0.024
1999	595 877	221	3.7	4.8	0.002	10.4	0.000
2000	503 170	156	3.1	4.1	0.001	7.8	0.001

<sup>a</sup> From Noticeable Infectious Diseases Reporting (NIDR) system annual reports, Ministry of Health, China.

<sup>b</sup> From Disease Surveillance Points (DSP) system annual reports, Ministry of Health, China.

The inter-observer agreement between the two reviewers for the title/abstract and full-text screening was very high (kappa 0.93 and 0.95,  $P < 0.05$ ).

A total of 115 articles presented specific underreporting rates of bacillary dysentery from the six geographical regions. Of these, 43 papers described community-based underreporting rates, 87 reported hospital-based underreporting rates and some reported both. Published articles that fulfilled the inclusion criteria in our analysis were from 23 provinces or municipalities.

Since the NIDR and DSP data are based on reports from all health-care facilities, all reported cases would be “treated cases”. The median community-based underreporting rate was used to estimate the total incidence rate (corrected rate = original rate/(1 – underreporting rate)),<sup>11</sup> and the median hospital-based underreporting rate was applied to correct the treated incidence rate.

### Sensitivity analysis

We conducted a sensitivity analysis, using data from 2000 as an example, to estimate the possible variation in bacillary dysentery morbidity. The 25% and 75% percentiles of community- and hospital-based underreporting rates were used to calculate the range of total and treated bacillary dysentery cases. The proportion of inpatients and outpatients, derived from the seven selected hospitals, was used to estimate the total inpatients and outpatients.

### Loss of work-days

We calculated the number of days lost due to bacillary dysentery as the product of episodes and mean number of work-days lost per episode. The same calculation was applied to disease episodes for adults and children because it is still customary in China for parents to accompany their children during hospitalization. Therefore, hospitalization of

children would mean loss of work-days for the adults who accompany them.

### Case definition of bacillary dysentery

A suspected case of bacillary dysentery was defined as an acute diarrhoeal episode with at least one of following symptoms: fever, abdominal pain, tenesmus, tenderness in the left lower quadrant and bloody or mucus stool. The clinical diagnosis of bacillary dysentery was confirmed when in addition to the symptoms mentioned above, the microscopic examination of the stool showed more than 15 white blood cells and some red blood cells per high-power field (x 400). The laboratory diagnosis was confirmed if a *Shigella* species was isolated from a stool culture.<sup>13</sup>

## Results

### Morbidity and mortality rates

Data from both the NIDR and DSP systems showed that morbidity of treated episodes and mortality due to bacillary dysentery decreased from 1991 to 2000. Morbidity decreased by about 3-fold while mortality decreased approximately 10- and 31-fold, respectively (Table 2). In 2000, morbidity due to treated bacillary dysentery was 0.001 per 10 000 and the case–fatality rate was 0.03% (NIDR data, Table 2).

### Age-specific mortality and morbidity

The incidence of treated bacillary dysentery was highest among children under 10 years of age (DSP data, Table 3). The

Table 3. Morbidity and mortality of bacillary dysentery in China, by age, 1991–2000

Age group (years)	Morbidity (1/10 000)		Mortality (1/10 000)	
	1991–1995	1996–2000	1991–1995	1996–2000
≤ 1	38.55	38.59	0.19	0.07
1–4	58.58	39.55	0.07	0.05
5–9	24.48	13.88	0.02	0.01
10–19	9.75	6.85	0.01	0.00
20–29	14.08	7.87	0.00	0.00
30–39	15.34	9.70	0.00	0.01
40–49	15.02	9.39	0.01	0.00
50–59	15.31	9.28	0.02	0.00
≥ 60	15.43	10.38	0.06	0.01

Source: Annual reports of the Diseases Surveillance Points (DSP) system, Ministry of Health, China.

decrease in the incidence of treated bacillary dysentery over the past 10 years was most rapid among children less than 10 years old with the exception of children under one year of age for whom incidence has remained stable.

### Underreporting

A median of 54% of total bacillary dysentery cases (interquartile ratios (IQR), 37–70%) was missed by the NIDR system as found from the review of 43 published community-based surveys. The median underreporting rate of hospital-based surveillance was 15% (IQR, 5–28%). Table 1 shows the regional variance in community-based underreporting rates by geographical regions.

### Hospitalizations

Hospital data from the seven study areas showed that 72% of bacillary dysentery patients who presented to hospitals were treated as outpatients and 28% were hospitalized (Table 4 (web version only, available at: <http://www.who.int/bulletin>)). The median duration of hospitalization for bacillary dysentery was 5 days (25% and 75% percentiles: 4 and 5 days) (Table 4).

### Sensitivity analysis of proportion of treated/total incidence and disease burden

After applying community- and hospital-based underreporting rates, the incidence of total and treated bacillary dysentery increased by 117% and 17%, respectively in the year 2000 (Table 5 (web

Table 6. Sensitivity analysis of bacillary dysentery disease burden in China, 2000

	Low	High
Total morbidity (1/10 000) <sup>a</sup>	6.5	13.8
Treated morbidity (1/10 000) <sup>a</sup>	4.3	5.7
Total bacillary dysentery episodes <sup>b</sup>	807 697.9	1 714 804.9
Treated bacillary dysentery episodes <sup>c</sup>	534 323.3	708 289.0
Episodes treated as outpatients <sup>d</sup>	384 712.7	509 968.1
Episodes treated as inpatients <sup>e</sup>	149 610.5	198 320.9
Episodes treated at home <sup>f</sup>	273 374.7	1 006 515.9
Lost work-days due to hospitalization <sup>g</sup>	748 052.6	991 604.6

Note. The 25% and 75% percentiles of community- and hospital-based underreporting rates were used to calculate the range of total and treated bacillary dysentery cases.

<sup>a</sup> Data are from Table 5.

<sup>b</sup> Calculated by multiplying total morbidity by total population (1 242 612 226) in 2000.<sup>14</sup>

<sup>c</sup> Calculated by multiplying treated morbidity by total population in 2000.

<sup>d</sup> Treated episodes times 72% (from Table 4).

<sup>e</sup> Treated episodes times 28% (from Table 4).

<sup>f</sup> Total episodes minus treated episodes.

<sup>g</sup> Inpatients treated for bacillary dysentery times 5 days (from Table 4).

version only, available at: <http://www.who.int/bulletin>). After extracting the NIDR data in 2000 for sensitivity analysis of disease burden and applying the proportion of inpatients found in the seven hospitals, we estimated that 0.8 to 1.7 million episodes of bacillary dysentery occurred in China in 2000. Of these, 0.5 to 0.7 million episodes were treated at health-care facilities and 149 611 to 198 321 were hospitalized for treatment (Table 6).

### Seasonality

In China, the majority of bacillary dysentery cases occurred during the summer months in 1991–2000 (Fig. 3). In

Guangxi Province the illness peaked in June, in Xinjiang, Hebei, and Jilin Provinces it peaked between July and August, and in Sichuan and Jiangsu Provinces and in the city of Shanghai it peaked in September (NIDR data from provincial CDCs).

### Regional variance

Comparison of bacillary dysentery rates from the seven areas, after correction for community-based underreporting rates in each province (as shown in Table 1), showed that the highest morbidity due to bacillary dysentery was in Xinjiang Province (18.4 per 10 000), followed by Guangxi (17.9 per 10 000) and Sichuan (17.3 per 10 000) Provinces. The incidence in Jilin, Jiangsu and Hebei were quite similar. The lowest morbidity due to bacillary dysentery occurred in Jin-an District, Shanghai (9.2 per 10 000; NIDR data from provincial CDCs).

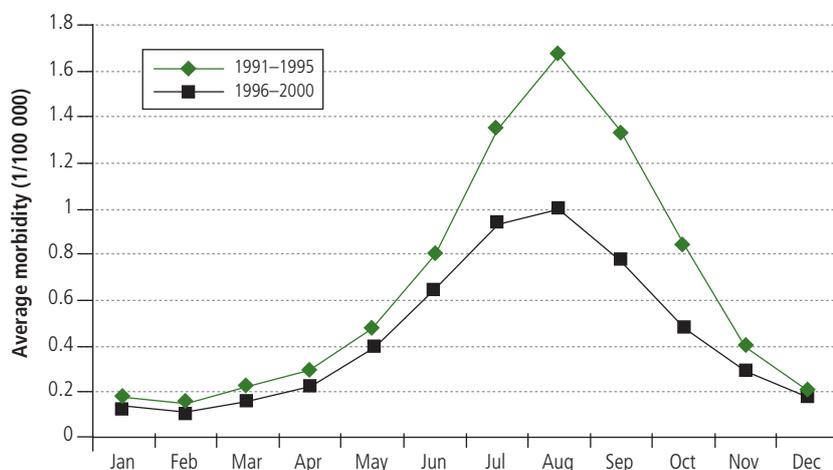
### Causative species and serotypes

Over the past 10 years, *S. flexneri* (median 86%; IQR 75–94%) was the predominant serogroup followed by *S. sonnei* (median 12%; IQR 5–22%), *S. dysenteriae* (median 0%; IQR 0% and 1.1%), and *S. boydii* (median 0%; IQR 0–1%). The predominant serotype among *S. flexneri* was *S. flexneri* 2a (80%; Table 7).

### Antimicrobial resistance

Hospital data from the seven areas showed that a high proportion of *Shigella* isolates are no longer susceptible to

Fig. 3. The seasonality of *Shigella* infections throughout China, 1991–2000



Source: Noticeable Infectious Diseases Reporting (NIDR) system annual reports, Ministry of Health, China.

WHO 06.13

ampicillin and trimethoprim/sulfamethoxazole, former first-line drugs for the treatment of shigellosis, and that the percentage of isolates susceptible to fluorinated quinolones had decreased to 74–80%. *Shigella* isolates, however, continued to be susceptible to gentamicin, the most widely used antibiotic for treatment of bacillary dysentery in China (Table 8).

## Discussion

Rapid economic development and the subsequent improvement of water supply and sanitation in the past decade resulted in decreased morbidity (three-fold) and mortality (10- and 31-fold) from treated bacillary dysentery in China during 1991–2000. Despite this decrease the number of bacillary dysentery cases occurring each year in China remains unacceptably high. Our findings showed that 0.8 to 1.7 million episodes of bacillary dysentery occurred in 2000, of which 0.5 to 0.7 million episodes were treated at health-care facilities, and 0.15 to 0.20 million patients were hospitalized. Bacillary dysentery caused the loss of 0.75 to 0.99 million work-days in China, which translates into considerable economic damage.

Bacillary dysentery continues to cause the greatest morbidity and mortality among children. Its incidence did not change much in infants (age less than one year) between 1991 and 2000. Our results showed a u-shaped pattern of age-specific morbidity with children and older people having the highest bacillary dysentery incidence rates. This age-related pattern of incidence conforms to those reported by two prospective surveillance studies.<sup>15,16</sup> Thus, we believe that future preventive interventions to control bacillary dysentery, such as vaccinations, should target children and older people.

To explore the regional variations, we compared the incidence of total bacillary dysentery in the seven selected areas. The disease burden due to bacillary dysentery was greater in north-west, north, and south-west China than in east China. This finding suggests an inverse correlation of dysentery burden and economic indicators. Approximately, 70% of the Chinese population lives in east China, which has the highest economic indicators (e.g. gross domestic product and per capita income). In contrast, north-west China remains less developed

Table 7. Distribution of *Shigella flexneri* serotypes in China, 1991–2000

Serotype	No. of isolates	Median % (interquartile ratio)
1a	272	1.7 (0.4–7.8)
1b	325	0.6 (0.2–6.2)
1c	15	0.0 (0.0–0.1)
2a	6468	80.0 (69.1–90.4)
2b	152	3.4 (0.1–6.1)
3a	255	0.6 (0.0–4.5)
3b	57	0.0 (0.0–0.2)
3c	9	0.0 (0.0–0.2)
4	230	2.5 (1.7–4.1)
5	30	0.4 (0.0–0.6)
6	73	0.5 (0.0–1.6)
x	70	0.7 (0.2–1.4)
y	126	1.7 (1.0–2.4)

and economic progress is much slower compared to east China.

Mortality from bacillary dysentery was lower in China compared with that reported from other countries. The morbidity of treated bacillary dysentery episodes in the past decade in industrialized countries was estimated to be 1.8 to 6.5 per 100 000 population with an average case–fatality rate of 0.2%.<sup>4</sup> NIDR data from the Department of Disease Control, Ministry of Health, China showed that while the morbidity of treated bacillary dysentery was higher than in industrialized countries (41 to 116 per 100 000 population), the mean case–fatality rate was much lower (0.06%). A prospective *Shigella* disease burden study conducted in a rural setting showed an incidence rate of 4.4/1000/year, but with no related deaths or sequelae.<sup>15</sup> A likely explanation for this low mortality is the cheap and convenient health-care system in China with common diseases like bacillary dysentery being treated promptly even in rural areas.<sup>17–19</sup> In 1998, there were at least seven doctors per 1000 population in urban and at least one doctor per 1000 population in rural areas of China.<sup>20</sup>

In China, the use of antimicrobial drugs was poorly regulated up to 2004 and overuse of antibiotics remains a big problem. In rural areas, consultations are usually free and health-care providers derive income from the sale of medicine. These factors resulted in antibiotics being prescribed with little restraint and perhaps caused the emergence of strains resistant to multiple antimicrobials. By analysing hospital data, we found that in 2000 more than half the *Shigella* isolates from the seven hospitals were resistant

to ampicillin and trimethoprim/sulfamethoxazole, and 20% and 5% were resistant to ciprofloxacin and norfloxacin, respectively. The emergence of resistance to fluoroquinolones raises serious questions regarding adequate treatment of shigellosis in the future. A surprising finding was that most *Shigella* isolates were susceptible to gentamicin even though oral gentamicin is widely used to treat bacillary dysentery in China.<sup>15</sup> Even while the therapeutic benefit of gentamicin for bacillary dysentery, especially if administered orally, is controversial,<sup>21</sup> intravenous administration of gentamicin is reserved for patients who are unable to take the medication orally, such as infants.

Our study had a few limitations, such as the selected areas and hospitals not being representative of the region and the varied socioeconomic status even within regions. Nonetheless, we believe that precise numbers may not be as important as the patterns and trends emerging from our analysis, which we consider are accurate and representative. Our study probably underestimated the true burden of bacillary dysentery because the existing surveillance systems capture only dysentery, resulting in watery diarrhoeal episodes caused by *Shigella* infections to be missed. In a recent prospective surveillance study only 44% of shigellosis cases presented with dysentery.<sup>15</sup>

## Conclusion

Our study found that there is a considerable burden of bacillary dysentery in China, especially among the youngest and the oldest population groups and

those in the low economic regions. While critical and continuing analysis of illness and disease burden is essential for the development of national treatment and prevention policies, we suggest that a vaccine, which can protect against shigellosis, could help control the disease burden in the short- and medium-term. For long-term control, improved water supply, sanitation, and hygiene are likely to be required. ■

### Acknowledgements

We thank the following organizations and individuals for their help and assistance: the Department of Disease Control, Ministry of Health, China for allowing us to use national statistics on bacillary dysentery; and Dr Yu-hua Ruan, Dr Yi-xin He and Dr Zhen-jing

Table 8. Antimicrobial resistance of *Shigella* strains isolated in seven hospitals in China, in 2000: median percentage of resistant and sensitive strains

Antibiotic	No. tested	% resistant (range)
Ampicillin	409	53 (36.8–57.3)
Gentamicin	232	13 (0–25.0)
Trimethoprim/sulfamethoxazole	407	62.0 (56.7–77.3)
Ciprofloxacin	209	20.0 (5.5–27.3)
Norfloxacin	234	4.9 (0–16.5)
Chloramphenicol	405	18.0 (15.1–36.9)

Note. Data are from the clinical laboratories in seven hospitals.

Huang (Chinese Center for Disease Control and Prevention) for help in data collection.

**Funding:** This study was supported by the Diseases of the Most Impoverished

Program, funded by the Bill and Melinda Gates Foundation and coordinated by the International Vaccine Institute, Seoul, Republic of South Korea.

**Competing interests:** none declared.

### Résumé

#### Evolution de la dysenterie bacillaire et charge de morbidité due à cette maladie en Chine (1991-2000)

**Objectif** L'étude visait à déterminer la charge de dysenterie bacillaire en Chine, les variations interrégionales, les tendances de la morbidité et de la mortalité, les agents étiologiques bactériens et les schémas de résistance aux antimicrobiens.

**Méthodes** Les statistiques publiques et les documents médicaux pertinents publiés de 1991 à 2000 ont été extraits et pris en compte dans l'étude. On a également recueilli des données auprès d'un hôpital général de chacune des six provinces considérées et du district de Jin an à Shanghai, ces hôpitaux étant représentatifs de six régions géographiques et d'une ville moderne.

**Résultats** En 2000, 0,8 à 1,7 million d'épisodes de dysenterie bacillaire ont été enregistrés, dont 0,5 à 0,7 million ont été traités dans des établissements de soins et 150 000 à 200 000 ont donné lieu à des hospitalisations. Les taux de morbidité et de mortalité les plus élevés ont été relevés parmi les classes d'âge correspondant aux plus jeunes et aux plus âgés. La dysenterie bacillaire a atteint

un pic au cours des mois d'été. Le principal agent étiologique était *Shigella flexneri* (86 %) et le sérotype prédominant de *S. flexneri* était le sérotype 2a (80 %). De 74 % à 80 % des isoléments de *Shigella* étaient sensibles aux quinolones fluorés.

**Conclusion** Malgré une baisse considérable de la morbidité et de la mortalité dues à la dysenterie bacillaire en Chine au cours de la dernière décennie, imputable à l'amélioration de l'accès à des soins de santé et à des antibiotiques à des prix abordables, une importante charge de morbidité subsiste chez les classes d'âge extrêmes et dans les régions faiblement développées sur le plan économique. Si un vaccin constituerait un moyen efficace à court et à moyen terme pour lutter contre la dysenterie bacillaire, il est probable que la lutte à long terme contre cette maladie exige une amélioration de l'approvisionnement en eau, des installations d'assainissement et de l'hygiène.

### Resumen

#### Disentería bacilar: tendencias y carga de morbilidad en China (1991–2000)

**Objetivo** Decidimos determinar la carga de disentería bacilar en China, las diferencias interregionales en ese sentido, las tendencias de la morbilidad y la mortalidad, las especies bacterianas causantes, y la distribución de la resistencia a los antimicrobianos.

**Métodos** Procedimos a extraer e integrar estadísticas gubernamentales y publicaciones médicas relacionadas aparecidas entre 1991 y 2000. También obtuvimos datos de un hospital general de cada una de las seis provincias consideradas y del distrito de Jin-an, Shanghai, como información representativa de seis regiones geográficas y una ciudad moderna.

**Resultados** En 2000 se produjeron entre 0,8 y 1,7 millones de episodios de disentería bacilar, de los cuales 0,5 - 0,7 millones fueron tratados en establecimientos de salud, y 0,15 - 0,20 millones fueron hospitalizados. Las mayores tasas de morbilidad y mortalidad fueron las registradas entre los grupos más jóvenes y en

las personas mayores. La disentería bacilar alcanzó la máxima cota en los meses de verano. La principal especie causante fue *Shigella flexneri* (86%), con la variante 2a como serotipo predominante (80%). Aproximadamente un 74% - 80% de las colonias de *Shigella* seguían siendo vulnerables a las quinolonas fluoradas.

**Conclusión** Aunque la morbimortalidad por disentería bacilar ha disminuido considerablemente en China durante el último decenio, gracias al mayor acceso a la atención sanitaria y los antibióticos, sigue habiendo una carga considerable de la enfermedad entre los grupos más jóvenes y de mayor edad, así como en las regiones con bajo desarrollo económico. En nuestra opinión, aunque una vacuna sería una opción eficaz para controlar la disentería bacilar a corto y medio plazo, todo control a largo plazo exigirá probablemente mejoras del abastecimiento de agua, el saneamiento y la higiene.

## ملخص

### اتجاهات وعبء الزحار العصوي في الصين (1991-2000)

الهدف: هدفنا هو التعرف على عبء الزحار العصوي في الصين، والاختلافات بين المناطق، واتجاهات الوفيات والمرضاة، وأنواع الجراثيم المسببة له وأمط المقاومة لمضادات المكروبات.

الطريقة: استخلصنا وأدرجنا الإحصائيات الحكومية والأدبيات الطبية الملائمة المنشورة في الفترة بين 1991 و2000. كما جمعنا معطيات من إحدى المستشفيات العامة في كلٍّ من الإمارات الستة ومقاطعة جين آن وشنغهاي لتمثل المناطق الجغرافية الستة والمدن العصرية.

الموجودات: لقد حدثت 0.8 – 1.7 مليون نوبة من الزحار العصوي في عام 2000، وولج 0.5 – 0.7 مليون نوبة منها في مرافق الرعاية الصحية فيما أدخل 0.15 – 0.25 مليون مريض إلى المستشفيات. وقد بلغت معدلات الوفيات والمرضى أعلى مستوياتها لدى المجموعات ذات الأعمار الصغيرة و الأعمار المتقدمة، وقد بلغت تلك المعدلات قيمتها في أشهر الصيف، وأكثر

## References

1. Snyder JD, Merson MH. The magnitude of the global problem of acute diarrhoeal disease: a review of the active surveillance data. *Bull World Health Organ* 1982;60:605-13.
2. Bern C, Martinez J, de Zoysa I, Glass RI. The magnitude of the global problem of diarrhoeal disease: a ten-year update. *Bull World Health Organ* 1992;70:705-14.
3. Kosek M, Bern C, Guerrant RL. The global burden of diarrhoeal disease, as estimated from studies published between 1992 and 2000. *Bull World Health Organ* 2003;81:197-204.
4. Kotloff KL, Winickoff JP, Ivanoff B, Clemens JD, Swerdlow DL, Sansonetti PJ, et al. Global burden of Shigella infections: implications for vaccine development and implementation of control strategies. *Bull World Health Organ* 1999;77:651-66.
5. Ministry of Health, China. [Abstract of health statistics in China]. In Chinese. 2003.
6. Yu WL. [Survey on the prevention and treatment of diarrhea in parts of China]. In Chinese. *Zhong Hua Liu Xing Bing Xue Za Zhi* 1989;10:257-60.
7. Tu GL, Chui CF, Wang JY, Fu BN, Zhang WP, Zhang HJ, et al. [Double-blind field trial of oral live F 2a-Sonnie (FS) dysentery vaccine]. In Chinese. *Zhong Guo Sheng Wu Zhi Pin Xue Za Zhi* 1999;12:178-80.
8. Yang GH, Stroup DF, Thacker SB. National public health surveillance in China: implications for public health in China and the United States. *Biomed Environ Sci* 1997;10:1-13.
9. Yang GH, Zeng YM, Tang J, Huang ZJ, Chen AP. [Chinese disease surveillance points system]. In Chinese. *Ji Bing Jian Ce* 1995;10:327-9.
10. Yang GH, Zheng XW, Zeng G, Wang LS, Chen YL, Chen AP, et al. [Selection of DSP points in second stage and their presentation]. In Chinese. *Zhong Hua Liu Xing Bing Xue Za Zhi* 1992;13:197-201.
11. Dai ZC, Zheng XW, Qi XQ, Yang GH, Liu PL. [Disease Surveillance: methods and application]. In Chinese. Beijing: Huaxia Press; 1993.
12. Yang GH, Hu JP, Rao KQ, Ma JM, Rao C, Lopez AD. Mortality registration and surveillance in China: history, current situation and challenges. *Popul Health Metr* 2005;3:3-11.
13. Ministry of Health, China. [Collection of diagnostic criteria of infectious diseases and relevant regulations]. In Chinese. Beijing: Chinese Standard Press; 2003.
14. Department of Population, Social, Science and Technology Statistics, National Bureau of Statistics of China. [China Population Statistics Yearbook 2002]. In Chinese. Beijing: China Statistics Press; 2002.
15. Wang XY, Du L, von Seidlein L, Xu ZY, Zhang YL, Hao ZY, et al. Occurrence of shigellosis in the young and elderly in rural China: results of a 12-month population-based surveillance study. *Am J Trop Med Hyg* 2005;73:416-22.
16. Zhang WP, Liu MX, Zhang GJ, Han GE. [A population-based prospective surveillance on bacillary dysentery in Changge county, Henan province]. In Chinese. *Zhong Hua Liu Xing Bing Xue Za Zhi* 1997;18 Suppl 6B:92-4.
17. Gong XG, Hu SL, Chen XM, Wang WZ, Li JQ. [On prescription for outpatients made by the three-leveled health organization in impoverished areas]. In Chinese. *Zhong Guo Nong Cun Wei Sheng Shi Ye Guan Li* 1997;17:33-5.
18. Ou AH, Su YS, Liu TX, Long SL, Guo LJ, Yang SJ, et al. [Analysis of the expenditure on medical services in rural area]. In Chinese. *Zhong Guo Chu Ji Wei Sheng Bao Jian* 2000;14:9-11.
19. Zheng JZ, Han Y, Qin K, Hou TH. [Research about the relation of countryman's income and demands for health service]. In Chinese. *Zhong Guo Nong Cun Wei Sheng Shi Ye Guan Li* 2002;22:15-7.
20. Ministry of Health, China. [Research on national health services: an analysis report of the second national health services survey in 1998]. In Chinese. 2002.
21. Islam MR, Alam AN, Hossain MS, Mahalanabis D, Hye HK. Double-blind comparison of oral gentamicin and nalidixic acid in the treatment of acute shigellosis in children. *J Trop Pediatr* 1994;40:320-5.

Table 4. Ratios of inpatient–outpatient and hospitalization days due to bacillary dysentery in six provinces and Jin-an district in China, in 2000<sup>a</sup>

Region of China	Representative province/district	City or district from which hospital data were collected	Bacillary dysentery cases in the selected hospital in 2000 <sup>b</sup>			
			Total	Outpatients	Inpatients	Median number of days (IQR) <sup>c</sup>
				No. (%)	No. (%)	
North-west	Xinjiang	Urumchi	164	114 (70)	50 (30)	4.0 (3–7)
Shanghai	Jin-an	Jin-an	288	284 (99)	4 (1)	8.5 (6–11)
East	Jiangsu	Nantong	202	176 (87)	26 (13)	4.0 (3–5)
South-west	Sichuan	Chengdu	213	167 (78)	46 (22)	5.0 (3–6)
North-east	Jilin	Changchun	163	104 (64)	59 (36)	3.0 (2–4)
South	Guangxi	Nanning	122	88 (72)	34 (28)	5.0 (3–7)
North	Hebei	Baoding	322	195 (61)	127 (39)	5.0 (3–8)
Total			1474	1128 (77)	346 (23)	5.0 (4–5)

<sup>a</sup> Data of hospitalized bacillary dysentery cases were from medical records of the seven hospitals.

<sup>b</sup> Median proportions of bacillary dysentery episodes in outpatients and inpatients were 72% and 28%, respectively. Data are based on hospital registration book entries at the seven hospitals.

<sup>c</sup> IQR = interquartile ratios.

Table 5. Total and treated bacillary dysentery cases (1/10 000) in China, 1991–2000

Year	Crude incidence of bacillary dysentery <sup>a</sup>	Corrected for underreporting					
		Total incidence of bacillary dysentery <sup>b</sup>			Incidence of treated bacillary dysentery <sup>c</sup>		
		Baseline	Upper	Lower	Baseline	Upper	Lower
1991	11.6	25.1	39.0	18.4	13.6	16.1	12.2
1992	8.0	17.3	26.9	12.7	9.4	11.1	8.4
1993	5.5	11.9	18.5	8.7	6.4	7.6	5.8
1994	7.5	16.3	25.2	11.9	8.8	10.4	7.9
1995	7.3	15.8	24.5	11.6	8.6	10.1	7.7
1996	6.6	14.3	22.2	10.5	7.7	9.2	6.9
1997	6.0	13.0	20.1	9.5	7.0	8.3	6.3
1998	5.5	11.9	18.5	8.7	6.4	7.6	5.8
1999	4.8	10.4	16.1	7.6	5.6	6.7	5.0
2000	4.1	8.9	13.8	6.5	4.8	5.7	4.3

<sup>a</sup> Data are from Noticeable Infectious Diseases Reporting (NIDR) system annual reports, Ministry of Health, China.

<sup>b</sup> Calculated as follows: original rate/(1 – underreporting rate). The median (25%, 75% percentiles) of community-based underreporting rate was 54% (37%, 70%).

<sup>c</sup> Calculated as follows: original rate/(1 – underreporting rate). The median (25%, 75% percentiles) of hospital-based underreporting was 15% (5%, 28%).