Incidence of Norovirus-Associated Diarrhea, Shanghai, China, 2012–2013

Jianxing Yu,[1] Chuchu Ye,[1] Shengjie Lai,[1] Weiping Zhu, Zike Zhang, Qibin Geng, Caoyi Xue, Weizhong Yang, Shuyu Wu, Aron J. Hall, Qiao Sun, Zhongjie Li

We conducted sentinel-based surveillance for norovirus in the Pudong area of Shanghai, China, during 2012–2013, by analyzing 5,324 community surveys, 408,024 medical records, and 771 laboratory-confirmed norovirus infections among 3,877 diarrhea cases. Our analysis indicated an outpatient incidence of 1.5/100 person-years and a community incidence of 8.9/100 person-years for norovirus-associated diarrhea.

Norovirus is the most common cause of gastroenteritis (i.e., diarrhea or vomiting) (*1*). Diarrhea represents the second greatest burden of infectious disease in the world, and globally, ≈20% of diarrhea cases are associated with norovirus infection (*2*). China is one of the 15 highest-burden countries for diarrhea in the world (*3*). To guide the planning, implementation, and evaluation of disease control programs, nationwide sentinel-based surveillance for diarrhea across all age groups has been conducted in China since 2009, in which the prevalence of norovirus is monitored regularly (*4*). However, incidence rates of norovirus are not readily available from previous studies because of the lack of population denominators (*4*,*5*). To assess the population-based burden of norovirus disease based on this surveillance platform, we conducted community surveys and reviewed medical records for diarrhea in the Pudong New Area (a district of the city of Shanghai, China) during 2012–2013. We then estimated age-stratified rates for norovirus-associated diarrhea.

Author affiliations: Division of Infectious Disease, Key Laboratory of Surveillance and Early-Warning on Infectious Disease, Chinese Center for Disease Control and Prevention, Beijing, China (J. Yu, S. Lai, Z. Zhang, Q. Geng, W. Yang, Z. Li); Ministry of Health Key Laboratory of Systems Biology of Pathogens and Dr. Christophe Mérieux Laboratory, CAMS-Fondation Mérieux, Institute of Pathogen Biology, Academy of Medical Sciences of China and Peking Union Medical College, Beijing (J. Yu); Research Base of Key Laboratory of Surveillance and Early-Warning on Infectious Disease, Pudong New Area Center for Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Shanghai, China (C. Ye, W. Zhu, C. Xue, Q. Sun); State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China (Z. Zhang); State Key Laboratory of Virology, Wuhan University College of Life Sciences, Wuhan, China (Q. Geng); Centers for Disease Control and Prevention, Beijing, China (S. Wu); Centers for Disease Control and Prevention, Atlanta, Georgia, USA (A.J. Hall)

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The Study

We conducted surveillance for diarrhea (defined as ≥3 passages of watery, loose, bloody, or mucoid stools within a 24-hour period) at outpatient clinics (mainly enteric, pediatric, and internal medicine clinics) of 10 sentinel hospitals in Pudong during February 1, 2012–December 31, 2013. We determined the catchment population, market share of sentinel hospitals, and weighted proportion of persons with diarrhea in the community who sought medical care by conducting the age-stratified Hospital Utilization and Attitudes Survey among respondents residing in Pudong (online Technical Appendix, https://wwwnc.cdc.gov/EID/article/23/2/16-1153-Techapp1.pdf). In total, an estimated population of 1,722,580 was under surveillance during the study period.

We obtained the number of outpatient visits for diarrhea each year at 10 sentinel hospitals by reviewing and analyzing medical records. We extracted medical records of acute gastroenteritis (AGE), encoded as A00–A09 or K52.9 by the International Classification of Diseases, 10th Revision (ICD-10), from 10 sentinel hospitals' hospital information systems (HIS) in 2012 and 2013. In total, 408,024 episodes of AGE were identified (189,645 in 2012 and 218,379 in 2013). To validate these AGE records with diarrhea cases likely meeting the study case definition, we ascertained numbers of diarrhea cases at 7 sentinel hospitals' enteric clinics during February 2012–December 2013 (online Technical Appendix). We identified 39,365 AGE episodes at these clinics and identified 28,030 eligible diarrhea case-patients during the same period. We used the ratio of 0.712 (28,030/39,365) as a contractive factor to narrow down the ICD-10–coded AGE episodes to diarrhea cases likely meeting the study case definition (Figure 1). After validation, we estimated that 290,513 (408,024 × 0.712) diarrhea case-patients visited the 10 sentinel hospitals in 2012 and 2013.

To measure the proportion of diarrhea episodes associated with norovirus, physicians working at outpatient clinics of the 10 sentinel hospitals screened visiting patients for

[1]These authors contributed equally to this article.

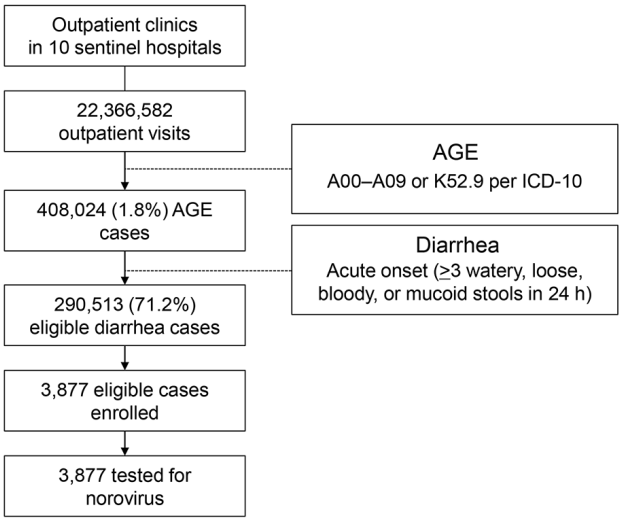

Figure 1. Registration, enrollment, and testing of diarrhea case patients in Pudong New Area, Shanghai, China, 2012–2013. (A pilot study was conducted during the first month of the year 2012. No case enrollment was conducted during that period.) AGE, acute gastroenteritis; ICD-10, International Classification of Diseases, 10th Revision.

eligibility of enrollment; the first 1–3 eligible diarrhea case-patients for each week in each sentinel hospitals were recruited by using a convenience sampling method. Fecal specimens were collected for enrolled case-patients and tested for norovirus genogroups GI and GII in the local public health laboratory by using reverse transcription PCR (RT-PCR) assays as described previously (*4*). In total, we enrolled 3,877 diarrhea case-patients (2,235 in 2012 and 1,642 in 2013). We detected norovirus in 771 cases (19.9%). We observed no significant difference in norovirus detection between surveillance years (19% in 2012 vs. 21% in 2013). However, detection of norovirus was significantly different between age groups (22% in persons ≥5 years of age vs. 12% in children <5 years of age; p<0.001) (Table 1). The highest norovirus detection rates were in October (35%–38%) and the lowest in June (5%–6%), but a secondary peak in detection occurred in March (19%–34%) (Figure 2).

We calculated outpatient incidence rates for norovirus-associated diarrhea in Pudong as the number of outpatient visits associated with norovirus divided by the total population at risk, which was based on total episodes of AGE in sentinel hospitals, the contractive factor used to narrow down the total episodes of ICD-10–coded AGE to diarrhea cases likely meeting the study case definition, the percentage of diarrhea case-patients with norovirus, and the total study catchment population. We estimated community incidence rates by dividing the number of outpatient visits associated with norovirus by the product of population at risk and the proportion of persons with diarrhea in the community who sought medical care, based on results of the Hospital Utilization and Attitudes Survey. We calculated 95% CIs by using bootstrap methods with 1,000 samples for each rate.

Table 1. Norovirus test results among diarrhea case-patients, by sex, surveillance year, and age group, Pudong New Area, Shanghai, China, 2012–2013

Variable	Positive, no. (%)	Negative, no. (%)	p value
Total	771 (100)	3,106 (100)	
Sex			0.278
M	426 (21)	1,646 (79)	
F	345 (19)	1,460 (81)	
Surveillance year			0.074
2012	422 (19)	1,813 (81)	
2013	349 (21)	1,293 (79)	
Age group			<0.001
0–11 mo	30 (10)	277 (90)	
12–23 mo	23 (16)	124 (84)	
24–59 mo	28 (13)	184 (87)	
5–24 y	69 (18)	306 (82)	
25–44 y	268 (21)	1,028 (79)	
45–64 y	263 (24)	828 (76)	
≥65 y	90 (20)	359 (80)	

We estimated the annual outpatient incidence rates of norovirus-associated diarrhea in Pudong to be 1.3/100 person-years (95% CI 1.2–1.4) in 2012 and 1.6/100 person-years (95% CI 1.4–1.8) in 2013, with an average rate of 1.5/100 person-years (95% CI 1.4–1.6) for the 2 years combined (Table 2). Children <2 years of age (7.4/100 person-years, 95% CI 5.4–9.3) and adults ≥65 years of age (2.6/100 person-years, 95% CI 2.0–3.2) exhibited increased rates of outpatient visits, compared with adults 25–44 years of age (1.0/100 person-years, 95% CI 0.9–1.1) (Table 2). The annual community incidence rates for norovirus-associated diarrhea were 8.1/100 person-years (95% CI 7.2–9.0) in 2012 and 9.8/100 person-years (95% CI 8.7–11.0) in 2013, with an average rate of 8.9/100 person-years (95% CI 8.2–9.7) for the 2 years combined.

Conclusions

This 2-year study provides age-stratified incidence rates for norovirus infections among medically attended diarrhea

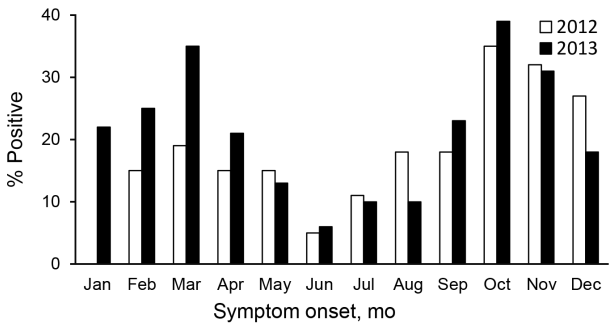

Figure 2. Proportion of norovirus detected among diarrhea case patients in outpatient settings, by month of symptom onset, Pudong New Area, Shanghai, China, 2012–2013.

Table 2. Estimated outpatient and community incidence of norovirus-associated diarrhea, by surveillance year, age group of patients, and season, Pudong New Area, Shanghai, China, 2012–2013

Variable	Outpatient incidence, no. cases/100 person-years (95% CI)	Community incidence, no. cases/100 person-years (95% CI)
Surveillance year		
2012	1.3 (1.2–1.4)	8.1 (7.2–9.0)
2013	1.6 (1.4–1.8)	9.8 (8.7–11.0)
2 y combined	1.5 (1.4–1.6)	8.9 (8.2–9.7)
Age group		
0–11 mo	8.4 (5.8–11.6)	20.3 (13.8–27.9)
12–23 mo	6.8 (4.2–9.6)	14.7 (9.2–20.8)
24–59 mo	1.4 (1.0–2.0)	2.5 (1.7–3.5)
5–24 y	1.1 (0.8–1.3)	8.8 (7.0–10.8)
25–44 y	1.0 (0.9–1.1)	13.0 (11.6–14.7)
45–64 y	1.7 (1.5–1.9)	3.2 (2.8–3.6)
≥65 y	2.6 (2.0–3.2)	7.8 (6.1–9.5)
Season		
Spring, Mar–May	1.2 (1.0–1.4)	7.9 (6.7–9.0)
Summer, Jun–Aug	0.8 (0.7–1.0)	4.9 (3.9–6.0)
Autumn, Sep–Nov	2.3 (2.1–2.5)	13.4 (11.7–15.1)
Winter, Dec–Feb	1.7 (1.4–1.9)	10.5 (8.8–12.3)

patients in Pudong, Shanghai. We used a sentinel-based surveillance approach and combined multiple data sources to generate incidence, including 5,324 community surveys, 408,024 retrospectively collected electronic medical records, and 771 laboratory-confirmed norovirus infections identified among 3,877 diarrhea cases. Each year in Pudong, ≈1 in 11 persons became ill with norovirus-associated diarrhea in the community (corresponding to 526,000 cases) and ≈1 in 67 persons visited a healthcare provider for norovirus-associated diarrheal illness (corresponding to 88,000 ambulatory visits). These findings suggest that norovirus was a substantial burden on the community and healthcare system of Pudong.

In our study, outpatient rates of norovirus-associated diarrhea were consistent between the 2 consecutive surveillance years of 2012 and 2013. The average annual incidence for norovirus-associated outpatient visits was estimated to be 1.5/100 person-years, which was broadly consistent although slightly higher than that reported in studies conducted in other countries, such as the United States (0.4–1.2/100 person-years) (*6*), the United Kingdom (0.48–0.6/100 person-years) (*7*), Germany (0.29–1.07/100 person-years) (*8*), and the Netherlands (0.5–1.5/100 person-years) (*9*). The average prevalence of norovirus across all age groups in our study was 19.9%, similar to the global estimate of 20% from outpatient studies by Ahmed et al. (*2*). This prevalence was higher when compared with some other studies that were conducted in other countries (4.4%–16%) (*6*–*8*). We believe that high exposure to norovirus in our study population might have been a source of the elevated rates. The new norovirus GII.4 variant Sydney_2012 emerged during our study period and has caused several outbreaks in eastern China since 2012 (*10*,*11*). Although sequencing information was lacking in our study and we have only 2 years of surveillance data, given the elevated rates and substantial burden of norovirus in our study population, we should remain vigilant and continue to monitor norovirus, ideally with genotype information, in future studies.

Acknowledgments

We wish to thank all the patients, nurses, clinicians, and laboratory, research, and administrative staff who took part in our active surveillance study at 10 sentinel hospitals.

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Dr. Yu is an epidemiologist at Institute of Pathogen Biology, Chinese Academy of Medical Sciences and Peking Union Medical College in China. Dr. Yu's work focuses on the epidemiology of enteric and respiratory viral infections, including norovirus and rotavirus.

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Addresses for correspondence: Zhongjie Li, Division of Infectious Disease, Key Laboratory of Surveillance and Early-Warning on Infectious Disease, Center for Disease Control and Prevention of China, 155 Changbai Rd, Changping District, Beijing, China, 102206; email: lizj@chinacdc.cn; Qiao Sun, Shanghai Pudong New Area Center for Disease Control and Prevention, 3039 Zhangyang Rd, Shanghai, China, 200136; email: qsun@pdcdc.sh.cn

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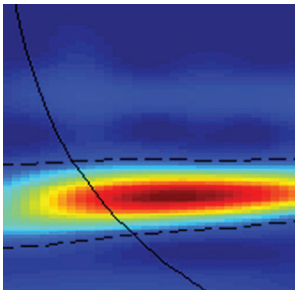

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- Real-time Microbiology Laboratory Surveillance System to Detect Abnormal Events and Emerging Infections, Marseille, France
- Underrecognition of Dengue during 2013 Epidemic in Luanda, Angola
- Health Care–Associated Infection Outbreak Investigations in Outpatient Settings, Los Angeles County, California, USA, 2000–2012
- Influenza A Viruses of Human Origin in Swine, Brazil
- Response Strategies against Meningitis Epidemics after Elimination of Serogroup A Meningococci, Niger
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- Development of Framework for Assessing Influenza Virus Pandemic Risk
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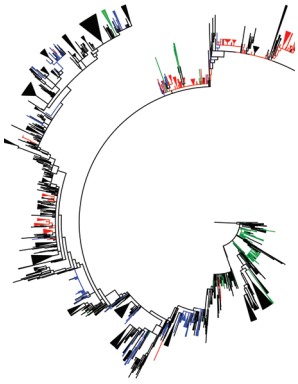

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Incidence of Norovirus-Associated Diarrhea, Shanghai, China, 2012–2013

Technical Appendix

Hospital Utilization and Attitudes Survey (HUAS)

To define the catchment population for 10 hospitals that conducted diarrhea surveillance from February 1, 2012 through December 31, 2013 at Pudong New Area of Shanghai City, a cross-sectional survey (hospital utilization and attitudes survey [HUAS]) was conducted among 5,324 community residents of Pudong. Face-to-face interviews were conducted separately among 2 age strata, children aged <5 years and people aged ≥5 years. Diarrhea episodes (defined as ≥3 passages of watery, loose, bloody, or mucoid stools within a 24-hour period) and health care utilization practices (whether they consulted a doctor and where they consulted) in the previous 4 weeks before interview were assessed.

HUAS results are shown in Technical Appendix Table. The weighted monthly prevalence of diarrhea in the community of Pudong was 4.1% (95% CI 3.6–4.7), corresponding to an incidence rate of 0.54 episodes/person-year. Among respondents reporting one or more newly occurred episode of diarrhea in the previous month, 21.2% reported that they had consulted a doctor or sought medical care as a result of the diarrhea. In total, 1,722,580 persons were estimated to comprise the catchment of these 10 hospitals that conducted surveillance for diarrhea during 2012–2013 (Technical Appendix Table). The catchment population consisted of 29% of the registered population in Pudong, and was very close to the market share of these 10 hospitals (27% of total population in Pudong) (*1*), calculated as the outpatient/emergency department visits of 10 hospitals (10.1 million) divided by the total outpatient/emergency department visits of Pudong (37.5 million) in year 2012.

Retrieving and Validation of Acute Gastroenteritis (AGE) Records from the Hospital Information System (HIS) of 10 Sentinel Hospitals (SHs) in Pudong

Retrieving of AGE records

To help measure occurrence and characterize distribution of diarrhea cases by time, place, and population, data on outpatient visits were obtained from the Hospital Information System (HIS) of 10 sentinel hospitals (SHs) that conducted surveillance for diarrhea in Pudong during February 1, 2012 to December 31, 2013. Data were anonymized by dropping the name of patients before use so that the identity of any individual could not be uncovered. Acute gastroenteritis (AGE) records (encoded as A00–A09 or K52.9 by the *International Classification of Diseases, 10th Revision*, or had any of the terms "diarrhea, enteritis, gastroenteritis, ileitis, jejunitis or sigmoiditis" in diagnoses) were extracted and analyzed for study purposes.

During our study period of 2012–2013, 408,024 (2%) records of AGE were retrieved from 22,366,582 records of outpatient visits in HIS of 10 SHs in Pudong (Technical Appendix Table 2). 189,645 (46%) AGE visits were obtained in 2012, and 218,379 (54%) in 2013. Most (32%) of the AGE visits were among children aged <5 years (Technical Appendix Figure 1). The seasonal pattern for occurrence of AGE visits was different by age group, with peaks in winter months for children aged <5 years and peaks in summer for other age groups (Technical Appendix Figure 2).

Validation of AGE Records

To help validate retrospectively collected AGE records, eligible diarrhea case patients (defined as ≥3 passages of watery, loose, mucoid, or bloody stools within a 24 hour period) were also reported in selected outpatient clinics (enteric clinics) at 7 SHs during the study period, which were selected based on the willingness of the hospitals to participate. The ratio of reported diarrhea cases to ICD-coded AGE records from HIS in the same enteric clinics during 2012–2013 were used to scale down the total episodes of AGE from any cause to newly occurred diarrhea cases likely meeting our study case definition.

During our study period of 2012–2013, 28,030 cases of eligible diarrhea were reported at enteric clinics of the 7 SHs. In the same period, 39,365 ICD-coded records of AGE were retrieved from the HIS of the same enteric clinics. Thus, 71.2% (28030/39365) of ICD-coded AGE episodes were likely eligible diarrhea cases for inclusion in our surveillance study. This

ratio (0.712) was used as a contractive factor to scale down the total episodes of ICD-coded AGE among all 10 SHs included in the full surveillance study to the estimated number of newly occurred diarrhea cases likely meeting our case definition.

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Technical Appendix Table 1. Healthcare utilization practices of diarrhea cases in the community of Pudong New Area, Shanghai, China, by age group*

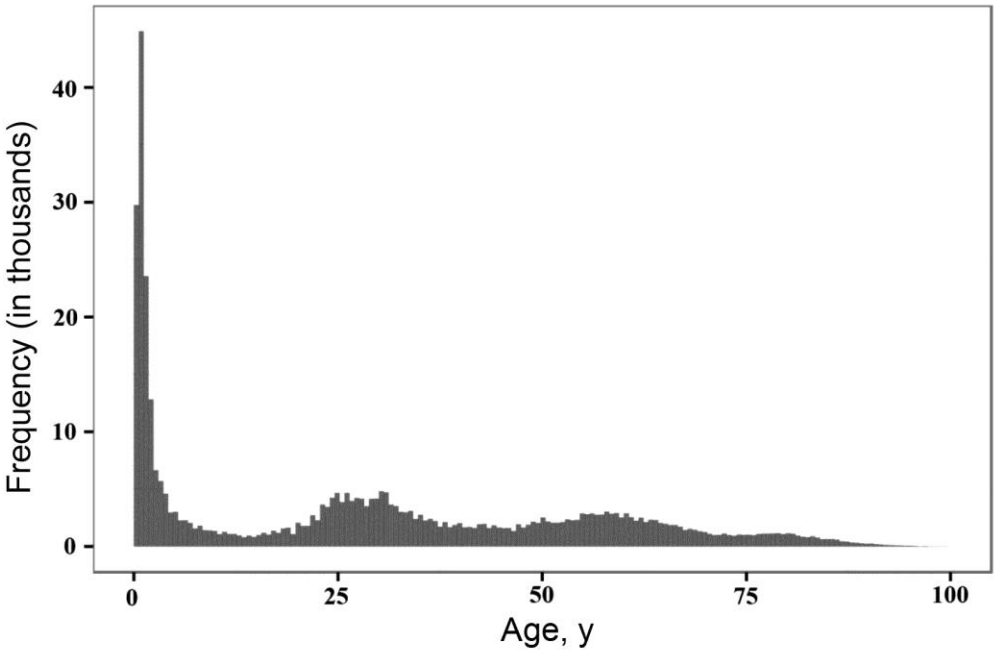
Age group	% Persons reported one or more newly occurred episodes of diarrhea in previous 4 weeks	% Persons with diarrhea who sought medical care	Estimated no. of persons who sought medical care for diarrhea at the 10 hospitals (% of total within the age group)†
0–11 mo, n = 397	11	42	25,594 (65)
12–23 mo, n = 458	6	46	31,934 (62)
24–59 mo, n = 1,348	3	58	96,040 (63)
5–24 year, n = 671	4	12	362,969 (30)
25–44 year, n = 1,372	5	8	701,827 (29)
45–64 year, n = 818	3	45	385,733 (25)
≥65 year, n = 274	5	45	118,483 (23)
Total, N = 5,338	4‡	21	1,722,580 (29)

*Unpublished data.
†The proportions in the brackets were calculated as the number of respondents who answered that they would like to seek medical care for diarrhea at the 10 hospitals divided by the total number of respondents interviewed within that age group. When multiplied by the registered population number at the middle term of year 2012 in Pudong, it produces the estimated number of catchment population in the column.
‡Weighted monthly prevalence.

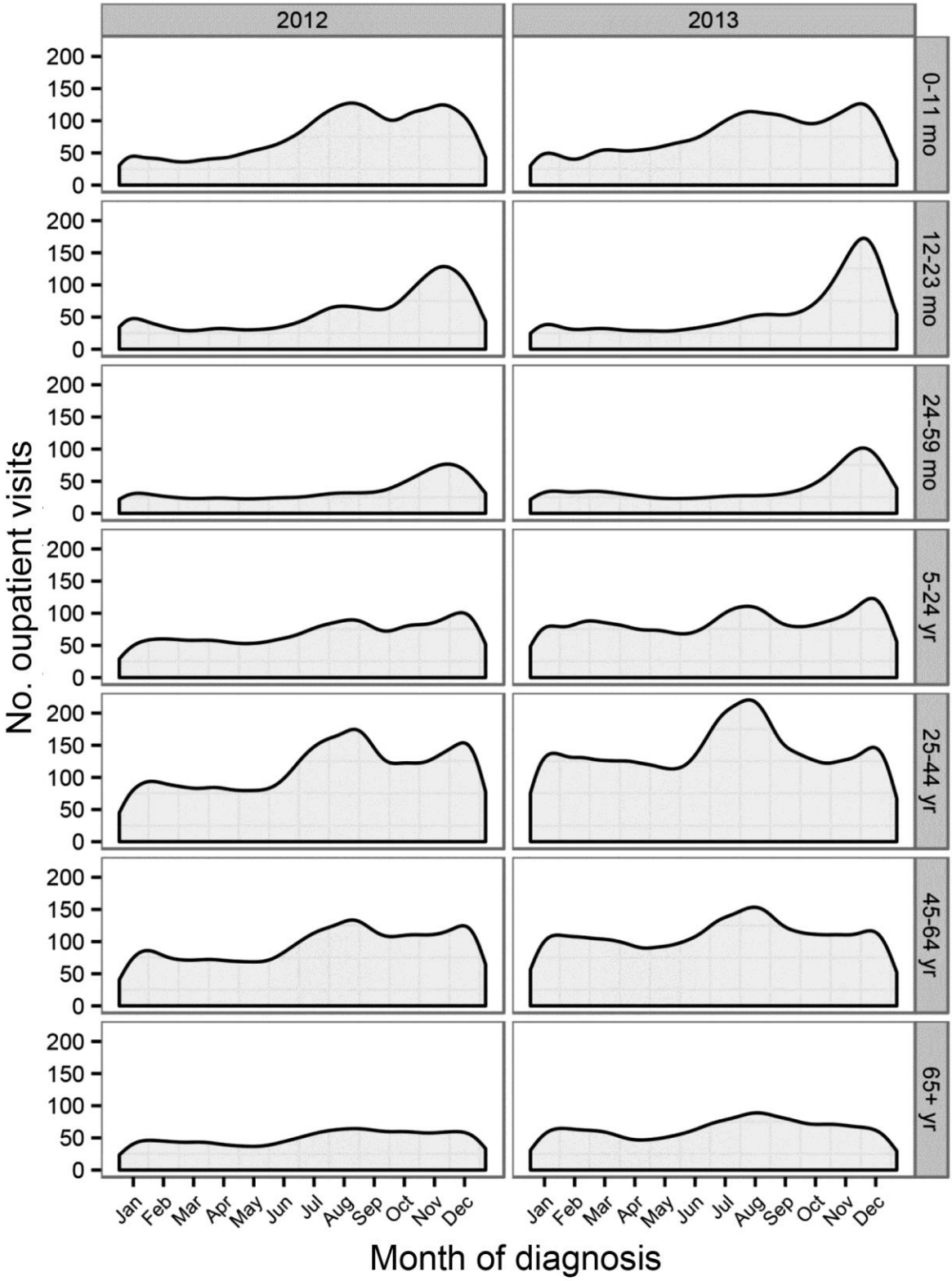
Technical Appendix Table 2. Outpatient visits with acute gastroenteritis (AGE)* diagnosed in 10 sentinel hospitals, Pudong New Area, Shanghai, China, 2012–2013

Age group	No. outpatient visits with AGE diagnoses	Total no. visits	AGE proportion of total, %
0–11 mo	59,182	802,997	7.4
12–23 mo	43,881	619,728	7.1
24–59 mo	28,980	1,482,024	2.0
5–24 y	58,999	3,007,685	2.0
25–44 y	95,614	5,083,752	1.9
45–64 y	77,137	6,249,896	1.2
≥65 y	43,078	4,973,896	0.9
Age unspecified	1,153	146,604	0.8
Total	408,024	22,366,582	1.8

*Acute gastroenteritis (AGE) = hospital outpatient medical records encoded as A00–A09 or K52.9 by the *International Classification of Diseases, 10th Revision*, or had characters “diarrhea, enteritis, gastroenteritis, ileitis, jejunitis or sigmoiditis” in diagnoses.



Technical Appendix Figure 1. Age distribution of outpatient visits with acute gastroenteritis, Pudong New Area, Shanghai, China, 2012–2013



Technical Appendix Figure 2. Number of outpatient visits with acute gastroenteritis, by date of diagnosis and age group, Pudong New Area, Shanghai, China, 2012–2013