衞生防護中心
Centre for Health Protection

Scientific Committee on Enteric Infections and Foodborne Diseases

Update on Norovirus-associated Acute Gastroenteritis Outbreaks in Hong Kong

Purpose

This paper provides an update on the global and local epidemiology of acute gastroenteritis (AGE) outbreaks associated with norovirus (NoV) and reviews the public health measures for prevention and control of the disease in Hong Kong.

Background

The virus

2. NoV belongs to the family *Caliciviridae*. Caliciviruses are non-enveloped, positive-sense, single-stranded RNA viruses and consist of five genera, namely, *Norovirus*, *Sapovirus*, *Lagovirus*, *Nebovirus* and *Vesivirus*[1]. NoV is classified into at least seven genogroups (GI–GVII), among which, only GI, GII and GIV are known to infect humans[2,3]. Antigenic drift and shift of NoV result in replacement of the dominant circulating viruses with new variants approximately every three years, often leading to an increase in outbreaks worldwide[2,4].

The disease

3. NoV is highly contagious and can be transmitted by ingesting food or water contaminated with the virus; contact with contaminated objects, vomitus or faeces from infected persons; or aerosol spread with contaminated droplets of splashed vomitus[5].

4. A person usually develops symptoms 12 to 48 hours after exposure to NoV[5]. Common symptoms include nausea, vomiting, diarrhoea, abdominal pain, fever and malaise. The symptoms are usually self-limiting and most people will recover within one to three days[5]. However, severe NoV infections can lead to hospitalisation, increased morbidity and even death in infants, children, the elderly and immunocompromised hosts[3]. In immunocompromised hosts, NoV can lead to persistent infection, resulting in prolonged virus shedding and gastrointestinal disease that can be debilitating and life-threatening[6].

5. NoV is a common causative agent of foodborne infection as well as the most important pathogen of sporadic gastroenteritis, institutional AGE outbreaks and global epidemics of AGE[3]. NoV-associated institutional AGE outbreaks have been reported in child care centres (CCC), kindergartens (KG), schools, residential care homes for the elderly (RCHE), hospitals and cruise ships[5,7].

Laboratory diagnosis[3]

6. NoV can be identified using electron microscopy (EM) by visualising the shape and size of intact viral particles during examination of a very small amount of stool sample. However, EM has low sensitivity for small round-structured viruses and cannot differentiate NoV, sapovirus and astrovirus due to similar shapes and sizes.

7. Antigenic detection assays have been developed for direct detection of NoV antigen due to its rapid, relatively inexpensive and simple protocol, and the fact that it is highly adoptable for use. However, the number of antigen detection assays remains limited for NoV because of the absence of broadly recognising antibodies that can capture and detect conserved viral antigens in these highly diversified viruses.

8. Nucleic acid testing (NAT) methods based on reverse

transcription-polymerase chain reaction (RT-PCR) are currently considered the gold standard for laboratory detection of NoV. These NAT amplification methods are very sensitive and have become increasingly important for accurate detection of NoV in clinical samples.

Management and prevention

9. There is no specific treatment for NoV infection and the mainstay of management is supportive treatment and prevention of dehydration[5]. There is no vaccine against NoV. To prevent NoV-associated AGE, general measures to prevent AGE, including maintaining good personal, food and environmental hygiene, should be adopted[5].

Global situation

10. Worldwide, NoV is the leading cause of AGE outbreaks[4]. Though most deaths due to NoV infection occur in developing countries, NoV is a problem in both low- and high-income countries[4]. NoV infections and outbreaks are usually more common in the cooler winter months. About half of all cases occur from December to February in countries in the northern hemisphere and June to August in countries in the southern hemisphere[4].

11. The commonest NoV strain, genogroup II genotype 4 (GII.4), was a major cause of outbreaks worldwide. Analysis of 16,635 NoV sequences obtained from outbreak investigations and sporadic gastroenteritis cases from 2005 to November 2016 from 19 countries in Europe, Asia, Oceania and Africa showed that 8.2% and 91.7% belonged to genotype GI and GII, respectively[8]. GII.4 drift variants emerged with two- to three-year periodicity up to 2012. For example, in late 2009, the pandemic variant GII.4 New Orleans 2009 emerged in Italy, became predominant during 2010-2011 and continued to circulate in a sporadic fashion until April 2013[9]. In March 2012, a new GII.4 NoV strain, named GII.4 Sydney 2012, was identified in Australia[10]. In late 2012, surveillance systems showed an increase in NoV activity globally and molecular data suggested that this increase was related to the emergence of the GII.4 Sydney 2012 strain[11].

12. After 2012, the GII.4 Sydney 2012 capsid seemed to persist through recombination[8]. The novel recombinant of GII.P16–GII.4 Sydney 2012 variant was detected in 2014 in Germany and the Netherlands, and again in 2016

in Japan, China and the Netherlands. The novel GII.P17-GII.17 recombinant, first reported in Asia in 2014, circulated widely in Europe from 2015 to 2016[8].

United States

13. In the United States, the total number of NoV outbreaks recorded by the National Outbreak Reporting System (NORS) from 2009 to 2012 ranged from under 100 cases recorded in August (over the four years) to over 900 cases recorded in January (over the four years)[12]. From 2009 to 2012, healthcare facilities, including nursing homes and hospitals, were the most common settings among NoV outbreaks reported to NORS (62.7%). The other settings included restaurants or banquet facilities (22.1%), schools or day-care facilities (6.1%), private residences (1.9%) and other/multiple settings (7.2%)[13].

14. Most NoV outbreaks in the United States had been caused by the GII.4 strains with each of the other genotypes causing less than 7% of the outbreaks[14]. In 2012, the GII.4 Sydney 2012 strain spread rapidly nationwide, causing an increasing number of outbreaks[10]. From September to December 2012, a total of 141 (53%) of the 266 NoV outbreaks reported to the electronic laboratory surveillance network of the Centers for Disease Control and Prevention of the United States were caused by the GII.4 Sydney 2012 strain[10].

United Kingdom

15. In the United Kingdom, NoV infection is not a notifiable disease. Public Health England receives voluntary reports of outbreaks in hospitals, schools, care homes, hotels, etc.[15]. The number of NoV-associated AGE outbreaks typically peaks between December and March each year[16].

16. Analysis of faecal samples from 592 NoV outbreaks occurring in England between May 2012 and June 2013 showed that 485 (82%) belonged to the genetically diverse GII.4 genocluster. The emergence of NoV strains genetically related to the GII.4 Sydney 2012 strain in England during the 2012/13 season replaced the GII.4 New Orleans 2009 strain as the most commonly detected variant of GII.4 strains[16]. Whilst the emergence of the GII.4 Sydney 2012 strain coincided with an early peak in the number of NoV outbreaks, there was not an overall increase in NoV activity compared to the previous season[16].

Japan

17. In Japan, cases of infectious gastroenteritis (including those caused

by NoV) are reported from approximately 3,000 paediatric sentinel sites in the country[17]. For the 2015/16 season, there were 1,545 NoV detections from infectious gastroenteritis patients aged 15 years or below[17]. The GII.4, GII.3 and GII.17 strains constituted 31%, 15% and 5% of the NoV detections, respectively. An expansion of GII.17, a new genotype similar to GII.P17-GII.17 Kawasaki 308, was observed. For the 2016/17 season (as of 26 December 2016), a remarkable increase in detections of GII.2 strains was reported. Among the 157 outbreaks reported, 47% were associated with the GII.2 strains[17].

Mainland China

18. Analysis of 983 NoV sequences obtained in Mainland China from 1999 to 2011 showed that most of the NoV sequences from distinct geographical regions appeared to be closely related, and 90% of NoV sequences were obtained from the coastal regions[18]. GII.4 was shown to be the most prevalent genotype, accounting for 64.4% of all genotypes, followed by GII.12 (13.9%) and GII.3 (7.0%)[18]. In October 2012, the GII.4 Sydney 2012 strain caused an increase of sporadic cases in Shanghai[19].

19. In Guangdong, NoV-associated AGE outbreaks were highly seasonal, with more than 90% of the outbreaks being reported from November to March[20]. From January 2013 to October 2014, the commonest genotype of NoV detected from samples of AGE outbreaks was the GII.4 Sydney 2012 strain[19]. In November 2014, a new genotype GII.17 was first detected in Guangzhou and spread rapidly thereafter[19]. From November 2014 to January 2015, outbreaks related to the NoV GII.17 strain were reported in ten cities of Guangdong Province and represented 83% of all outbreaks[19]. In November 2016, another new recombinant GII.2 NoV (GII.P16-GII.2) strain emerged in Guangdong and was associated with an increase in the number of AGE outbreaks[20].

Taiwan

20. In Taiwan, the GII.4 Sydney 2012 strain caused 65% of reported NoV-associated AGE outbreaks from January 2012 to December 2013 and had almost completely replaced the previously dominant GII.4 New Orleans 2009 strain since April 2012[21]. From the 2014/15 season to September 2016, a previously uncommon genotype, GII.17, became the predominant genotype causing NoV-associated AGE outbreaks in Taiwan[22]. Since September 2016, a new GII.P16-GII.2 strain has replaced GII.17 as the predominant strain causing

NoV-associated AGE outbreaks[22].

Local situation

21. In Hong Kong, the Centre for Health Protection (CHP) of the Department of Health encourages institutions to report suspected institutional outbreaks of AGE including those associated with NoV to CHP for investigation and control. An outbreak is classified as AGE outbreak when the main presenting symptoms are acute onset of diarrhoea with or without vomiting in the absence of a common food source. Other common symptoms include abdominal pain and fever. Viruses such as NoV and rotavirus are common causes of seasonal increase in institutional AGE outbreaks.

Institutional AGE outbreaks

22. From 2008 to 2018 (as of 30 June 2018), CHP recorded a total of 1,625 institutional AGE outbreaks affecting a total of 16,619 persons. Among these 1,625 outbreaks, 830 (51.1%) were confirmed, with the majority caused by NoV (684 outbreaks, 82.4%), followed by rotavirus (94 outbreaks, 11.3%), *Clostridium difficile* (26 outbreaks, 3.1%) and other agents including *Salmonella* and sapovirus (26 outbreaks, 3.1%).

23. From 2008 to 2017, the annual number of NoV-associated AGE outbreaks ranged from 17 to 136. A total of 8,339 persons were affected with the annual number ranging from 216 to 1,675 (Figure 1). In the first six months of 2018, a total of 18 NoV-associated AGE outbreaks have been recorded, affecting 202 persons.

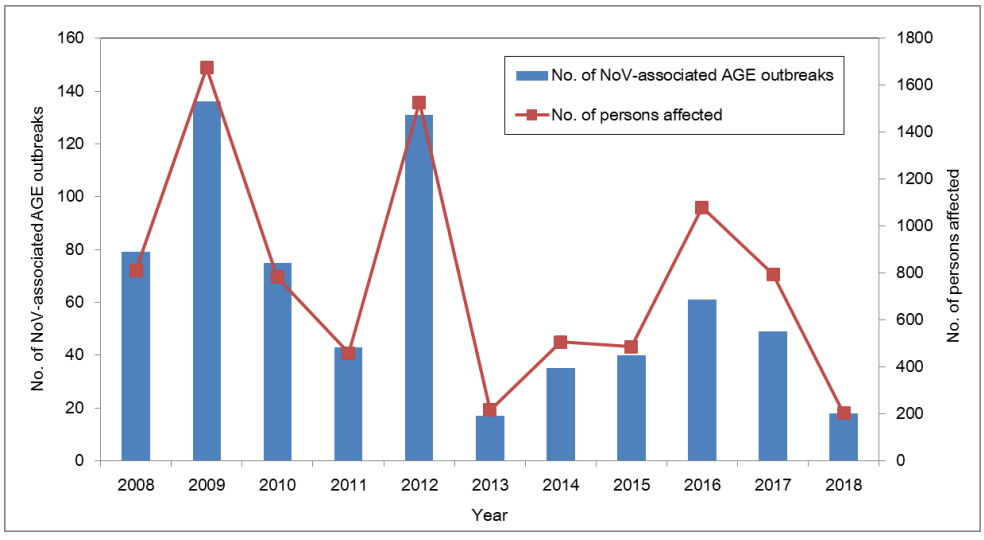

Figure 1. Annual number of NoV-associated AGE outbreaks and number of persons affected, 2008 to 2018 (as of 30 June 2018)

24. From 2008 to 2012, cyclical increase in the number of NoV-associated AGE outbreaks every two to three years was observed. The increases in the number of NoV-associated AGE outbreaks in 2009 and 2012 coincided with the emergence of new strains[23,24]. From 2013 to 2018, no significant increase in NoV-associated AGE outbreaks was observed in spite of the emergence of new strains of NoV in 2014 and 2016[25,26] (Figure 2).

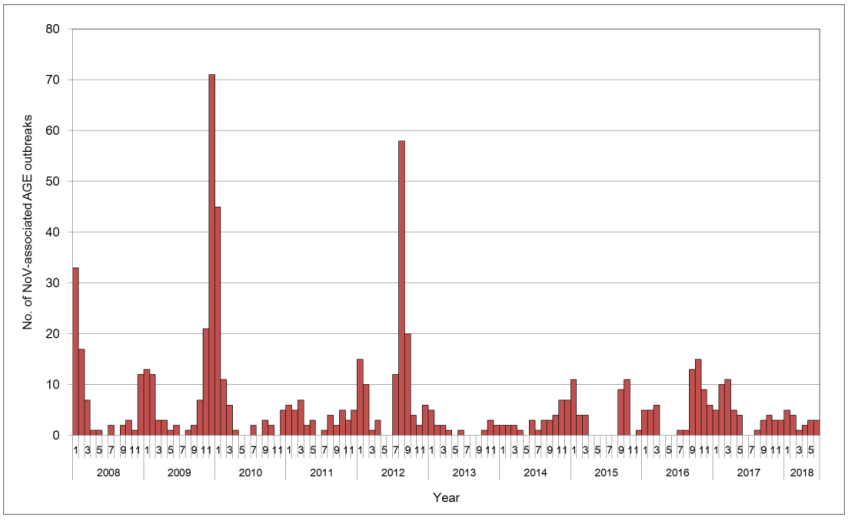

Figure 2. Monthly number of NoV-associated AGE outbreaks, 2008 to 2018 (as of 30 June 2018)

25. NoV-associated AGE outbreaks occurred throughout the year. Of the 666 outbreaks recorded from 2008 to 2017, over half (336, 50.5%) occurred in the winter months from December to February (Figure 3). The usual peak occurred in winter except for the year 2012, when the AGE and NoV activities reached a high level atypically during the summer months from July to September (Figure 2). In 2012, the number of NoV-associated AGE outbreaks peaked at 58 in August. The number decreased to 20 in September and returned to baseline in October[27]. A novel recombinant GII.4 strain, named "2012v", was associated with this early epidemic outside the usual winter season[28].

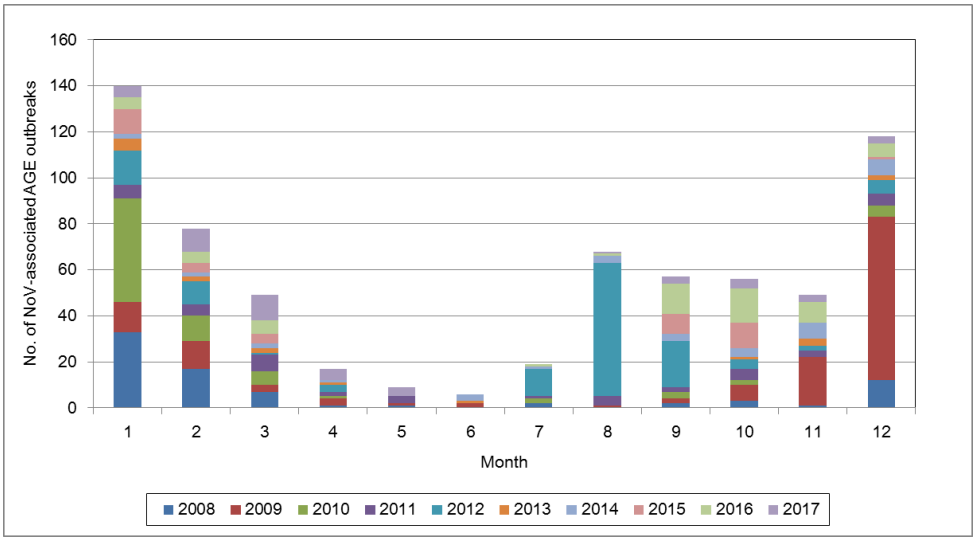

Figure 3. Cumulative number of NoV-associated AGE outbreaks by month, 2008 to 2017

26. Among the 684 NoV-associated AGE outbreaks recorded between 2008 and 2018 (as of 30 June 2018), the majority (354, 51.8%) occurred in RCHE, followed by CCC/KG (151, 22.1%), hospitals (51, 7.5%), residential care homes for persons with disabilities (RCHD) (38, 5.6%) and primary schools (35, 5.1%). The remaining 55 outbreaks occurred in other institutions (e.g. correctional institutions, secondary schools, special schools, eating premises, etc.) (Figure 4).

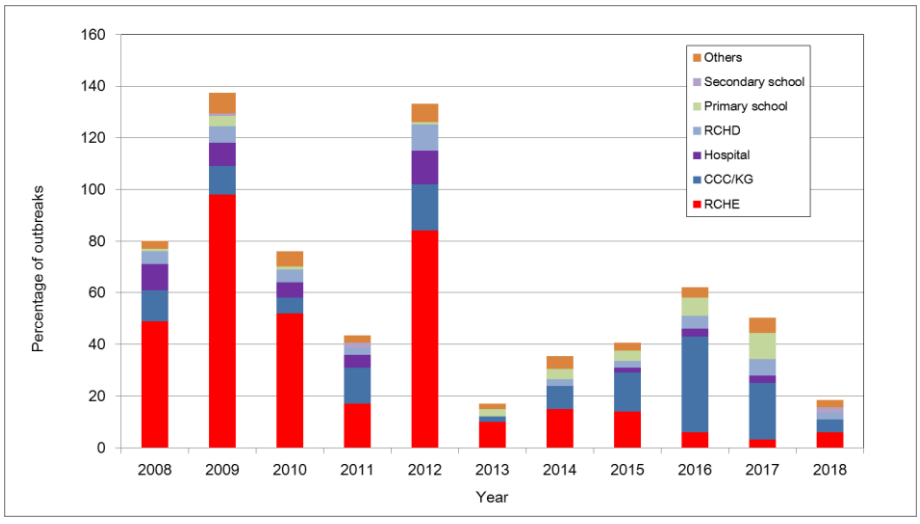

Figure 4. Annual number of NoV-associated AGE outbreaks by place of occurrence, 2008 to 2018 (as of 30 June 2018)

27. The number of persons affected in the NoV-associated AGE

outbreaks ranged from two to 181 with a median of ten persons per outbreak. Three hundred and twenty-eight (48.0%) outbreaks affected two to nine persons, while 268 (39.2%) outbreaks affected ten to 19 persons. Only 88 (12.9%) outbreaks affected 20 or more persons (Table 1).

Year	No. of persons affected			
	2 to 9	10 to 19	20 or above	Median (Range)
2008	46	26	7	9 (2 to 33)
2009	68	50	18	9.5 (2 to 105)
2010	39	30	6	9 (3 to 43)
2011	21	18	4	10 (2 to 30)
2012	67	49	15	9 (2 to 69)
2013	6	9	2	11.5 (4 to 27)
2014	12	17	6	12 (3 to 39)
2015	16	18	6	11 (3 to 39)
2016	23	23	15	11 (3 to 150)
2017	21	20	8	11 (4 to 181)
2018 (as of 30 June)	9	8	1	9.5 (2 to 53)
Total	328	268	88	10 (2 to 181)

Table 1. Number of persons affected in NoV-associated AGE outbreaks, 2008 to 2018 (as of 30 June 2018)

28. Of the 8,541 persons affected in NoV-associated AGE outbreaks, 1,734 (20.3%) required hospitalisation. The majority (1,112, 64.1%) of the hospitalised patients were from AGE outbreaks that occurred in RCHE. The percentage of affected persons requiring hospitalisation decreased from 19.2%-29.6% during the period between 2008 and 2012 to 9.2%-15.8% in recent years (2014-2017) (Figure 5), which was likely due to the decrease in proportion of outbreaks involving RCHE (Figure 4). Two fatal cases were recorded in 2008, involving a 97-year-old woman and a 95-year-old woman from two different NoV-associated AGE outbreaks occurring in two different RCHE. Both patients had underlying medical illnesses.

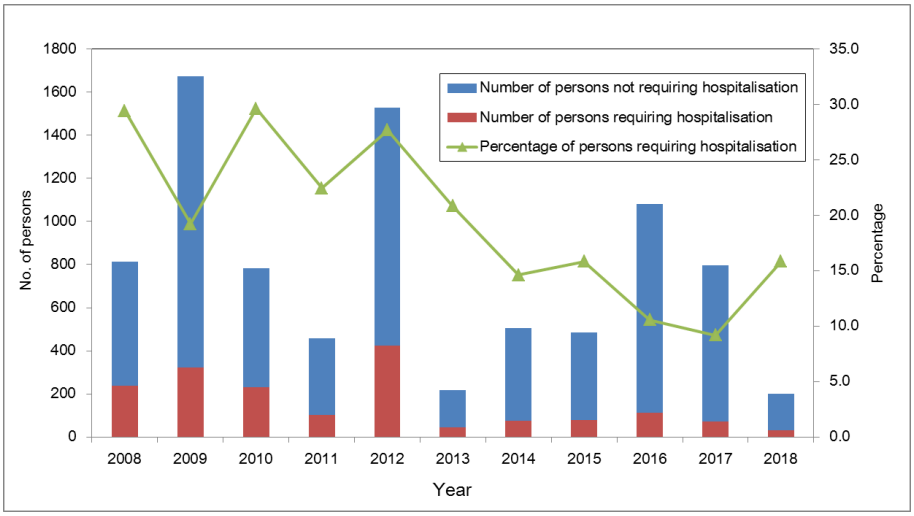

Figure 5. Number and percentage of affected persons requiring hospitalisation, 2008 to 2018 (as of 30 June 2018)

AGE activity detected in syndromic and sentinel surveillance

29. Seasonal pattern of AGE activity was also detected in the Accident and Emergency Departments (AED) communicable diseases syndromic surveillance system and sentinel surveillance system based at RCHE (Figures 6 to 7). From 2008 to 2018 (as of 30 June 2018), the weekly average consultation rate (per 1,000 coded cases) of AGE syndrome group based at AED was 105.8 (range: 76.4 to 194.8). From 2008 to 2018 (as of 30 June 2018), the weekly average number of residents (per 1,000 residents) with acute diarrhoea and vomiting detected in sentinel RCHE were 0.16 (range: 0.00 to 1.02) and 0.45 (range: 0.14 to 1.42) respectively.

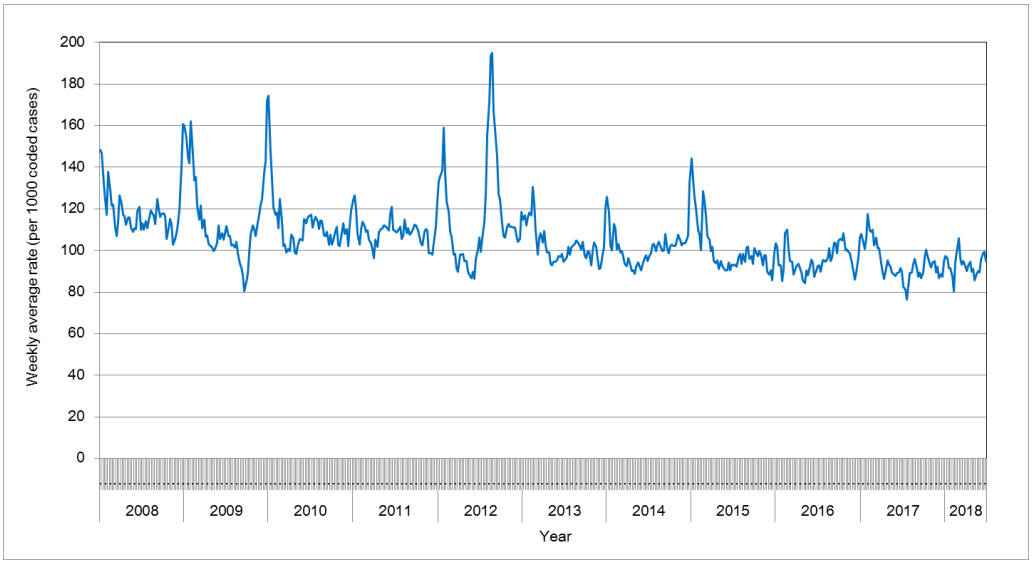

Figure 6. Weekly consultation rate of AGE syndrome group based at AED, 2008 to 2018 (as of 30 June 2018)

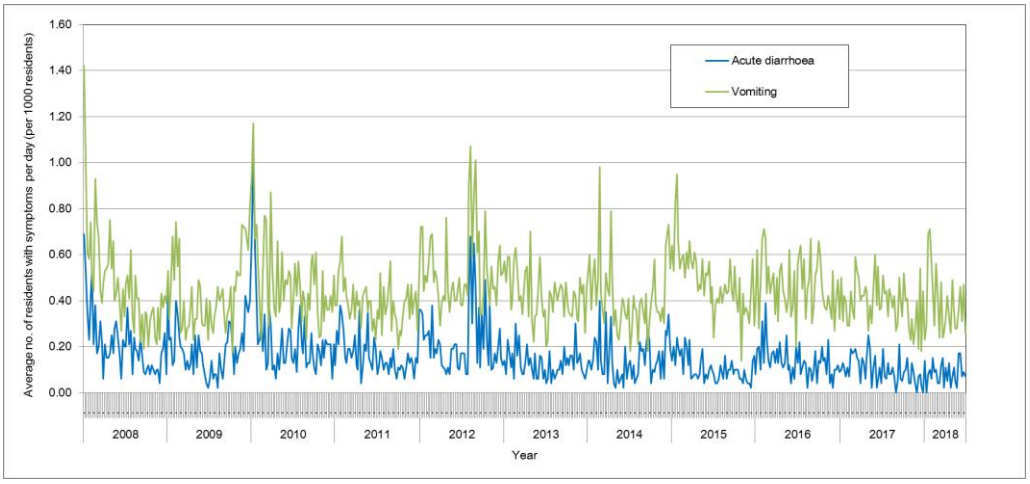

Figure 7. Weekly average number of residents with AGE symptoms (i.e. acute diarrhea and vomiting) at sentinel RCHE, 2008 to 2018 (as of 30 June 2018)

Hospital admission episodes in hospitals under Hospital Authority

30. Hospital admission episodes with principal diagnosis coded as "acute gastroenteropathy due to NoV" (ICD-CM 008.63) in hospitals under the Hospital Authority in the past decade showed peaks in 2009, 2012 and 2016, which coincided with the emergence of new strains (Figure 8).

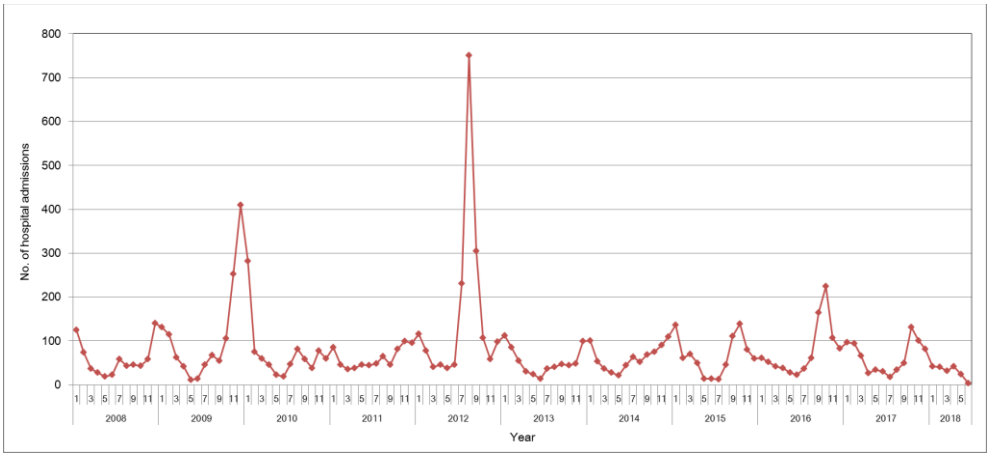

Figure 8. Monthly number of hospital admission episodes with principle diagnosis as acute gastroenteropathy due to NoV, 2008 to 2018 (as of 30 June 2018)

Laboratory surveillance

31. The Public Health Laboratory Services Branch (PHLSB) of CHP undertakes laboratory testing for gastroenteritis viruses. Laboratory data showed that from 2013 to June 2018, the monthly percentage of faecal specimens tested positive for NoV ranged from 1.76% to 25.80%. There was a consistent seasonal pattern with a higher percentage of faecal specimens tested positive for NoV in the cooler months (Figure 9).

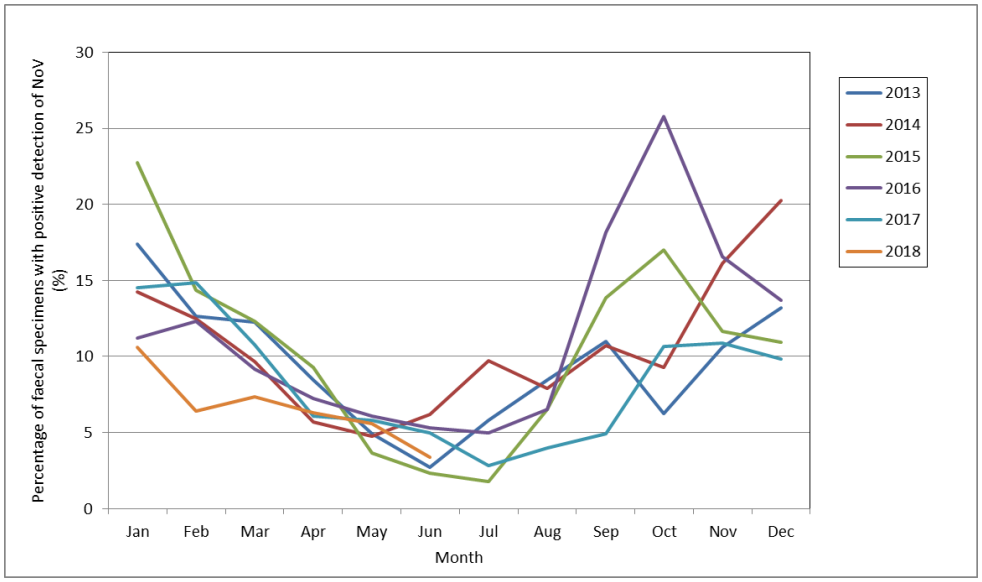

Figure 9. Percentage of faecal specimens with positive detection of NoV by PHLSB by year and month, 2013 to June 2018

32. Novel NoV strains had been reported in Hong Kong. In 2012, the novel recombinant GII.4 strain "2012v" emerged in Hong Kong[28], which was associated with the increase in number of NoV-associated AGE outbreaks and early epidemic outside the usual winter season. During the 2014/15 season, an emergent variant of a previously rare NoV GII.17 genotype, Kawasaki 2014, predominated in Hong Kong and outcompeted the GII.4 Sydney 2012 strain in hospitalised cases[29]. In 2016, a rapid increase in the number of GII.2 detections in hospitalised patients was observed since August, which coincided with the increased circulation of an uncommon recombinant norovirus genotype GII.P16-GII.2 reported in parts of Asia, including Mainland China and Japan, in the 2016/17 season[25].

Prevention and control of NoV-associated AGE outbreaks in Hong Kong

33. Prevention and control of NoV-associated AGE outbreaks comprise disease surveillance, outbreak control, laboratory surveillance, public education and risk communication.

Disease surveillance and outbreak control

34. CHP assesses the local situation of AGE in a comprehensive manner with information from different sources. CHP receives voluntary reporting of AGE outbreaks from various institutions, such as RCHE, other

residential homes, schools and hospitals. Apart from voluntary reporting by institutions, CHP also monitors the local AGE activity through the AED communicable diseases syndromic surveillance and sentinel surveillance systems based at General Out-patient Clinics, private doctors, Chinese Medicine Practitioners, CCC/KG and RCHE.

35. Upon receiving report of an AGE outbreak, CHP will conduct epidemiological investigation and implement control measures as appropriate. Health advice on outbreak prevention and control will be given to the institution. Symptomatic residents, students or staff will be encouraged to provide stool specimens for laboratory confirmation if tests have not been done yet. The institution will be put under medical surveillance. CHP will also inform and liaise with relevant government departments for outbreak control when necessary.

Laboratory surveillance

36. PHLSB will continue to publish the results of positive detection of gastroenteritis virus, including NoV, rotavirus, astrovirus, saprovirus and enteric adenovirus from faecal specimens on the CHP website regularly.

Public education and community engagement

37. The Central Health Education Unit of CHP has prepared a series of health education materials (e.g. pamphlets, posters and television announcements) to remind members of the public to maintain vigilance against NoV-associated AGE outbreaks. Feature articles on AGE are published in the on-line bi-weekly Communicable Diseases Watch from time to time to update healthcare professionals and members of the public on the latest situation of AGE.

38. The Infection Control Branch of CHP has published the "Guidelines on Prevention of Communicable Diseases in Schools/ Kindergartens/ Kindergartens-cum-Child Care Centres/ Child Care Centres" and "Guidelines on Prevention of Communicable Diseases in Residential Care Home for the Elderly" to provide practical guidelines to institutions for prevention of communicable diseases including NoV-associated AGE outbreaks.

Risk communication

39. Prior to the usual peak season of viral AGE, CHP will issue a press release to remind the general public to remain vigilant against the disease. CHP

will also issue letters to doctors, private hospitals, institutions, CCC/KG and schools to solicit their support in prevention and control of AGE. When an abnormal pattern is detected, CHP will also alert the public through different channels. For example, when the early peak of AGE and NoV activities in 2012 was observed, CHP issued a press release and letters to doctors, private hospitals, institutions, CCC/KG and schools to provide updates on the latest situation and remind management of institutions to step up personal and environmental hygiene. An article summarising the situation of the early peak was also published in the Communicable Diseases Watch. When large-scale AGE outbreaks, including those caused by NoV, are reported, CHP will issue press releases to appeal to the public and management of institutions to maintain strict personal and environmental hygiene.

Conclusion and recommendations

40. NoV is the leading cause of AGE outbreaks worldwide. Antigenic drift and shift of NoV result in replacement of the dominant circulating viruses with new variants approximately every few years, often causing global epidemics of AGE outbreaks.

41. In Hong Kong, the usual peak season of NoV-associated AGE outbreaks is in winter, with about half of the outbreaks occurring from December to February. Emergence of new NoV strains in 2009 and 2012 were associated with significant increases in the number of NoV-associated AGE outbreaks in Hong Kong in both years and an early epidemic outside the usual winter season in 2012.

42. CHP has implemented a series of public health measures for monitoring the local activity of NoV as well as prevention and control of NoV-associated AGE outbreaks, such as outbreak investigation and control, disease surveillance, laboratory surveillance, public education and timely risk communication.

43. As NoV keeps evolving with time and new strains may have the potential to cause an increase in the number of institutional outbreaks, it is important to maintain the current prevention and control measures and keep abreast of the latest global situation including circulating and emerging NoV strains.

Advice sought

44. Members are invited to note the information in this paper and advise on the enhancement of surveillance, prevention and control of NoV-associated AGE outbreaks in Hong Kong.

August 2018

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