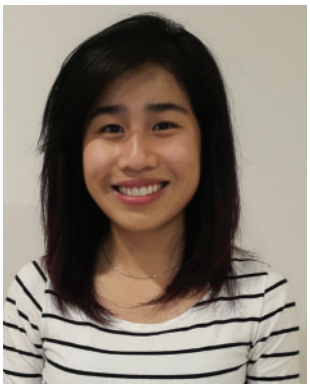
Norovirus and cruise ships




Jennifer H Lun[A,D], *Kelly-Anne Ressler*[B,E], *Mark J Ferson*[B,C,F] *and Peter A White*[A,G]

[A]School of Biotechnology and Biomolecular Sciences, Faculty of Science, University of New South Wales, Sydney, NSW, Australia

[B]Public Health Unit, South Eastern Sydney Local Health District, Randwick, NSW, Australia

[C]School of Public Health and Community Medicine, University of New South Wales, Kensington, NSW, Australia

[D]Email: j.lun@unsw.edu.au

[E]Email: KellyAnne.Ressler@health.nsw.gov.au

[F]Email: Mark.Ferson@health.nsw.gov.au

[G]Email: p.white@unsw.edu.au

Acute gastroenteritis (AGE) is one of the most common diseases of humans in both developed and developing countries. Despite the improved safety of food handling and prevention strategies, it remains one of the most significant health burdens on society[1]. An estimated 1.8 million AGE-associated deaths occur annually worldwide[2,3], making it the leading cause of mortality among children under the age of five years. In this article, we examine recent trends in emerging noroviruses, the ability of the virus to cause outbreaks on cruise ships and discuss the factors that influence its on-board spread.

The main agents responsible for acute gastroenteritis include viruses, bacteria, parasites and chemical agents. Across the globe, norovirus is estimated to cause 677 million gastroenteritis cases and 212 000 deaths per year[4]. In Australia, norovirus is now the leading cause of viral gastroenteritis following the introduction of rotavirus vaccine to the National Immunisation Program in 2006 and infects around 2.2 million people each year[5]. Illness is generally self-limiting, but can be severe in vulnerable populations; including children, elderly and immunocompromised individuals[6,7]. The main transmission routes are person to person, through the faecal-oral route, or consumption of contaminated food and water. Norovirus is highly infectious compared to other viruses, with 100–1000 virions sufficient to infect a healthy individual[8]. In addition, norovirus is resistant to freezing, heating and can tolerate commonly used disinfectants, including alcohol and quaternary ammonium compounds better than other viruses[9,10]. The combination of these properties allows norovirus to survive in external environments for long periods. The virus often attacks in closed or semi-closed environments such as cruise ships, nursing homes, childcare centres and hospitals[11,12].

Norovirus was first identified in an elementary school outbreak in Norwalk, Ohio in 1968[13], although it took four more years before Albert Kapikian finally discovered the virus in the faecal matter of infected individuals stored from the Norwalk outbreak[14]. Norovirus is a non-enveloped 27–35 nm icosahedral virion, encapsulating a single stranded RNA genome of 7.5 kilobase pairs. Its genome contains three open reading frames (ORF1-3), encoding seven non-structural proteins and two capsid proteins. Based on the full-length capsid amino acid sequences, norovirus can be categorised into seven genogroups (GI–GVI) and further divided into more than 40 genotypes[15]. Only GI, GII and GIV have been shown to cause disease in humans, with GII the most common (90% of cases), followed by GI (5–10%), whilst GIV is rare. Although many genotypes have now been identified, one important one known as GII, genotype 4 (GII.4), is the cause of ~70% of all norovirus infections and has been responsible for all six pandemics of norovirus–associated gastroenteritis[16].

Similar to influenza A, the evolution of norovirus is attributed to two main forces; antigenic drift and antigenic shift. Antigenic drift

results in amino acid divergence in the protruding (P) domain of the viral capsid, allowing escape from herd immunity acquired through previous norovirus infections. Antigenic shift or recombination, is also implicated in the emergence of new viruses and is achieved through the exchange of genetic material between strains when a co-infection occurs. The common location for norovirus recombination is at the ORF1/ORF2 overlapping region, spanning the structural and non-structural region[17]. Both of these mechanisms drive the evolution of GII.4 viruses and have been implicated in the emergence of the GII.4 pandemic variants over the past two decades[16]. The first pandemic spread of a GII.4 variant was recognised in mid-1990s[18], namely the GII.4 US 95/96 variant. This variant dominated for several years until a new GII.4 strain (Farmington Hills 2002) emerged and became predominant[19]. Since then, four new GII.4 pandemics variants have emerged around every 2–3 years and include; Hunter 2004[20], Den Haag 2006b[21], New Orleans 2009[22] and Sydney 2012[23,24]. Previous studies have shown GII.4 strain is the most commonly identified genotype on cruise ships[25].

Norovirus is notorious for causing outbreaks on cruise ships all over the world, affecting hundreds of passengers and leads to considerable economic costs for the industry[26–30]. The cruise ship industry has an important economic benefit to Australia, bringing in thousands of passengers each year from their hinterlands to port cities, resulting in an estimated tourist income of $1.74 billion[31]. Since 2007, the number of cruise ship arrivals into Sydney has trebled and their destinations abroad have doubled, with an average of 200 cruise ships berthing in Sydney each year, peaking at 320 in 2016 (Table 1). Despite the strict sanitation measures on ships, around 5.3% (yearly range 3.1%–9.0%) of ship arriving in Sydney have reported outbreaks of gastroenteritis (unpublished data, Public Health Unit, SESLHD), with norovirus commonly identified as the main culprit (Table 1). A recent investigation in the United State, from 2008 to 2014, showed norovirus is responsible for 97% (92/95) of acute gastroenteritis on cruise ships[25]. In fact, cruise ships have been touted as sentinel surveillance settings for new norovirus strains, with pandemics ensuing soon after the number of cruise ship outbreaks increase.

In attempts to prevent norovirus outbreaks on cruise ships and help eliminate the risks person-to-person spread associated with buffet style meals, some cruise ship companies have rolled out dine-in restaurants with designated wait-staff. Hand washing and the use of hand sanitisers is another strategy for outbreak prevention on ships[32,33]. In Australia, on-board gastroenteritis outbreaks exceeding a threshold of 3% of the ship's passengers and crews affected are required under the Biosecurity Act 2015 (Commonwealth) to be reported to the Australian Department of Agriculture and Water Resources (DAWR). Following this notification, DAWR Biosecurity Officers inform the state or territory health authority, with subsequent implementation of prevention and control protocols. Among other things, these include: cleaning of infected cabins and more frequent laundering of linen; increased cleaning and disinfection in common areas, including the cruise terminal; deployment of external public health sanitation squads and delayed boarding of new passengers to allow additional sanitation activities. Two major classes of disinfectant are used on board cruise ships to ensure

Table 1. Cruise ship arrivals in Sydney and number/cause of reported acute gastroenteritis (AGE) outbreaks 2007–2016 (source: Cruise Ship Health Surveillance Program, Public Health Unit, SESLHD).

		Norovirus	AGE other cause	AGE unknown cause	Total AGE outbreaks	Total no. of arrivals
Arrival year	2007	3 (3.0%)	0	6 (6.0%)	9 (9.0%)	99
	2008	6 (5.9%)	0	0	6 (5.9%)	102
	2009	1 (0.9%)	0	4 (3.7%)	5 (4.6%)	109
	2010	3 (2.2%)	0	4 (2.9%)	7 (5.1%)	136
	2011	2 (1.0%)	0	5 (2.6%)	7 (3.7%)	191
	2012	6 (2.8%)	0	8 (3.7%)	14 (6.5%)	214
	2013	4 (1.6%)	1 (0.4%)	12 (4.8%)	17 (6.8%)	250
	2014	7 (2.6%)	1 (0.4%)	6 (2.2%)	14 (5.2%)	268
	2015	4 (1.4%)	0	5 (1.8%)	9 (3.2%)	278
	2016	4 (1.3%)	1 (0.3%)	5 (1.6%)	10 (3.1%)	320
Total		40	3	55	98	1967

inactivation of virions, hydrogen peroxide and chlorine based sanitisers, and they can be used for decontamination of both non-food contact surfaces and food-contact surfaces.

In 2016, three new recombinant viruses emerged in Australia: GII.P4 New Orleans 2009/GII.4 Sydney 2012, GII.P16/GII.4 Sydney 2012 and GII.P16/GII.2. Due to the lack of herd immunity against these novel hybrid viruses, an increase in gastroenteritis outbreaks was observed in the population in the winter period. Over the past six years, 12 cruise ship outbreaks were investigated further to identify the aetiological agent. The GII.4 Sydney pandemic norovirus was responsible for five (42%), and the newly identified recombinant GII.P16/GII4 Sydney 2012 caused two (17%) (Table 2). In recent times, the impact of pandemic Sydney 2012 variant has declined, likely due to increased herd immunity, but viruses with the capsid GII.4 Sydney have continued to thrive in the semi-closed cruise ship environment and remain a scourge to both passengers and the cruise ship industry alike.

Cruise ships are also commonly susceptible to subsequent outbreaks once an initial outbreak has struck. A study in Europe of 13 ships over a 28-week period showed each ship had between 1 and 12 outbreaks (mean = 3.46)[34]. In the case of cruise ship outbreaks, great debate surrounds whether the norovirus outbreak was sourced through embarking passengers, or if the virus was already on board from the previous outbreak. After the first infection is introduced on to a ship, an outbreak is likely to ensue through person-to-person transmission. With the regular changing of passengers, noroviruses on board that avoid disinfection could repeatedly infect a new susceptible population and even exhaustive control measures might not be enough to avoid this. A number of risk factors for repeated outbreaks have been identified: these include possible contact between boarding and disembarking passenger groups, inappropriate cleaning for norovirus elimination[35], and passengers refusing to be isolated to prevent further transmission of the virus[36].

Table 2. Cruise ship norovirus outbreaks and responsible genotypes.

Outbreak date	Norovirus genotype responsible	
	Polymerase genotype	Capsid genotype
10/2012	ND	GII.4 Sydney 2012
11/2012	ND	GII.4 2006b
12/2012	ND	GII.4 New Orleans 2009
3/2013	ND	GII.4 Sydney 2012
2/2014	GII.P16	GII.13
12/2014	GII.Pe	GII.4 Sydney 2012
11/2015	GII.Pe	GII.4 Sydney 2012
12/2015	GII.P16	GII.4 Sydney 2012
2/2016	GII.Pe	GII.4 Sydney 2012
7/2016	GII.P16	GII.4 Sydney 2012
8/2016	GII.P4 New Orleans 2009	GII.4 Sydney 2012
2/2017	GI.P3	GI.3

ND, not determined.

In conclusion, norovirus is a common cause of gastroenteritis on cruise ships due to the closed setting, its low infectious dose and its ability to survive in the environment. Norovirus evolves through antigenic drift and shift to create new strains capable of escaping herd immunity, resulting in increases in outbreaks of AGE around the globe. These emerging viruses often appear early on cruise ships[34,37], therefore active surveillance is vital to protect ship's passengers and prevent outbreaks.

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Biographies

Jennifer Lun is a PhD student in the School of Biotechnology and Biomolecular Sciences at UNSW. Her PhD research has focused on understanding circulating norovirus strains and the evolutionary mechanisms that have facilitated the emergence of pandemic viruses.

Kelly-Anne Ressler is an Epidemiologist with the South Eastern Sydney Public Health Unit, holding a Bachelor of Science Nutrition and a Masters of Public Health from the University of Wollongong. Kelly has been employed by the Public Health Unit since 1998 and provides epidemiological advice to members of the infectious diseases, immunisation and environmental health teams. Since 2004, Kelly has coordinated the Cruise Ship Health Surveillance Program, which collects health surveillance data and provides response to outbreaks of infectious disease on board international vessels entering Sydney Harbour. Kelly also has an interest in the epidemiology of sexually transmitted infections, particularly syphilis in men who have sex with men, but also in the investigation and control of foodborne disease outbreaks and emerging infections.

Professor Mark Ferson is a public health physician and paediatrician. He is the Director of the Public Health Unit, South Eastern Sydney Local Health District, and the Chair of the NSW Infectious Diseases Network, which is tasked with promoting high standards, open communication and consistency of practice across the state's Public Health Units. He is public health medicine subspecialty editor for the *Internal Medicine Journal* and the ASID representative on the editorial board for *Communicable Diseases Intelligence*. Mark's research interests are in the epidemiology and control of infectious diseases, with a particular focus on childcare settings, childhood vaccination, gastroenteritis viruses and the exanthemata, and on public health law and history.

Peter White is a Professor in the School of Biotechnology and Biomolecular Sciences at UNSW. His research interests include molecular epidemiology, antiviral development, viral discovery and the replication of positive-sense viruses.