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Impact of Norovirus in the cruise ship industry

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Griffith University is a top ranking University, based in South East Queensland, Australia. Griffith University hosts the Griffith Institute for Tourism, a world-leading institute for quality research into tourism. Through its activities and an external Advisory Board, the Institute links university-based researchers with the business sector and organisations, as well as local, state and federal government bodies. For more information, visit http://www.griffith.edu.au/griffith-institute-tourism.

1. Executive Summary

Norovirus can be a potentially and highly communicable disease which is usually manifested by an acute onset of diarrhoea, abdominal cramps, nausea and vomiting in both adults and children (Desselberger and Gray 2013). Norovirus transmission is spread primarily person-to-person by the faecal-oral route including contact with contaminated surfaces and transmission via aerosolised vomit. Most Norovirus-associated gastroenteritis outbreaks occur where individuals live, work or play in close proximity such as aged-care facilities, hospitals and childcare centres (Hall *et al.* 2013) and therefore can affect the most vulnerable in the community such as the elderly, immune-compromised patients and young children (Eden *et al.* 2014). Norovirus outbreaks also occur on cruise ships, as detailed in this report.

Noroviruses are the most common causes of both epidemic and endemic viral enteritis in the United States of America (US[1]) and worldwide, taking over from rotaviruses due to the marked reduction in the prevalence of rotavirus infection following successful vaccine development (Hall *et al.* 2011, Hall *et al.* 2013).

A survey conducted by OzFoodNet found that approximately 17.2 million Australians experience episodes of gastroenteritis every year (OzFoodNet 2012). Between 2000 and 2008 there were 2,923 Norovirus outbreaks (Australian Government Department of Health and Ageing 2010).

Foodborne gastroenteritis accounts for approximately $811 million annually in productivity, lifestyle and premature mortality costs (81% of estimated total cost of $1,003 million). Seven other foodborne illnesses account for the balance of 19% and, of these, listeriosis and reactive arthritis are the major contributors to costs (Australian Government Department of Health and Ageing 2008).

Noroviruses are the most common cause of viral gastrointestinal outbreaks on cruise ships with the most common mode of transmission being person to person. Nonetheless, spread via contaminated food or water or by contact with contaminated surfaces are known modes of transport (Ericsson *et al.* 2003).

Infections can reoccur on successive cruises, a phenomenon which might result from new, susceptible passengers boarding in different ports along the voyage and thus, rather than the infection running its course during one cruise (or sector), the outbreak can continue over a period of several cruises (or sectors) (Ericsson *et al.* 2003).

International health regulations require cruise operators to report the presence of any notifiable and quarantinable diseases on their ship before they enter port. In response to requests that not all ships doctors are regularly updated on Quarantine Laws, the International Health Regulations are being revised to make these regulations more responsive to current and emerging infectious diseases and to place more responsibility put on ship owners to report and keep their crews updated (Ferson and Ressler 2005).

Due to the perceived nature of Norovirus related gastroenteritis being that of a disease that is short lived and self-limiting, the development of specific antiviral measures has been slow.

[1] United States of America.

The increasing recognition of its life-threatening status in immunocompromised patients, who often require prolonged hospitalization, has stimulated new research to develop an effective antiviral therapy (Kaufman *et al.* 2014). Currently, most medical treatment involves lessening the impact of the Norovirus symptoms while waiting for the patient to stop shedding the virus (Norovirus Working Group 2007).

The duration of Norovirus immunity and the limited cross protection post infection are key challenges in developing vaccination and determining the health and economic values of a vaccines and, ultimately, for developing a vaccination strategy (in terms of target age groups and frequency of immunization) (Bartsch *et al.* 2012).

Although there are no commercially available prophylactics against Norovirus, one area that has been explored is the use of Nutraceuticals (nutritionally enhanced food) such as probiotics. However, more research needs to be done to determine their efficacy in lessening symptoms and reducing the number of days an individual is typically stricken with the infection."

Contents

2. Introduction

Noroviruses are a major cause of epidemic – acute gastroenteritis and diarrhoea – in children and adults which presents acute onset of diarrhoea, abdominal cramps, nausea and vomiting (Desselberger and Gray 2013). Norovirus transmission is spread primarily person-to-person by the faecal-oral route, contact with contaminated surfaces, and transmission via aerosolised vomit.

Noroviruses are in some ways the perfect human pathogens. These viruses possess essentially all of the attributes of an ideal infectious agent: highly contagious, rapidly and prolifically shed, constantly evolving, evoking limited immunity, and only moderately virulent, allowing most people with intact immune systems who are infected to recover fully, thereby maintaining a large susceptible pool of hosts (Hall 2012).

Most Norovirus-associated gastroenteritis outbreaks occur in aged-care facilities, hospitals and childcare centres (Hall *et al.* 2013) and therefore affect the most vulnerable in the community such as the elderly, immune-compromised patients and young children (Eden *et al.* 2014).

There is currently no specific treatment for Norovirus infection (Tan and Jiang 2008, Dai *et al.* 2012, Desselberger and Gray 2013).

Norovirus is one of the leading causes of diarrhoea outbreaks on cruise ships. Due to the close living quarters, and shared dining areas, as well as large passenger turnovers, controlling Norovirus outbreaks on cruise ships can be challenging. Norovirus can easily be brought on board when ships dock and due to its ability to persist on surfaces can infect consecutive cruises (Centers for Disease Control and Prevention 2014).

The following report is a review of the latest research into Norovirus and the effects on the cruise ship industry.

3. Norovirus

3.1 Norovirus Basics

3.1.1 What is it?

The Human Enteric Caliciviruses (HECVs) are recognized as the major causative agents of outbreaks of acute nonbacterial gastroenteritis in developed countries and is estimated to cause almost half of all cases of acute gastroenteritis, globally (Patel *et al.* 2009, Eden *et al.* 2014). HECVs are divided into two genera, the genus Norovirus (Norovirus, formerly known as 'Norwalk-like viruses') and the genus Sapovirus (SaV, formerly known as 'Sapporo-like viruses') (Duizer *et al.* 2004).

Norwalk-like (NLV) or small round structured virus (SRSV), the causative agent for Norovirus, was first defined in 1968 from samples taken from a primary school in Norwalk, Ohio (US). However, Norovirus was first recognised as early as 1929 and was called the "*Winter Vomiting Disease*" (Zahorsky 1929, Adler and Zickl 1969, Kapikian *et al.* 1972, Norovirus Working Group 2007).

Noroviruses belong to the family Caliciviridae (see Figure 1) and are divided into five genogroups (GG). The genogroups that cause disease in humans are: GGI, GGII and GGIV with the vast majority of human illness caused by strains of the GGI and GGII genotypes (Nordgren 2009, Siebenga *et al.* 2009) and in particular, the GII.4 strains are responsible for most human Norovirus outbreaks, including pandemics (Leon and Moe 2006).

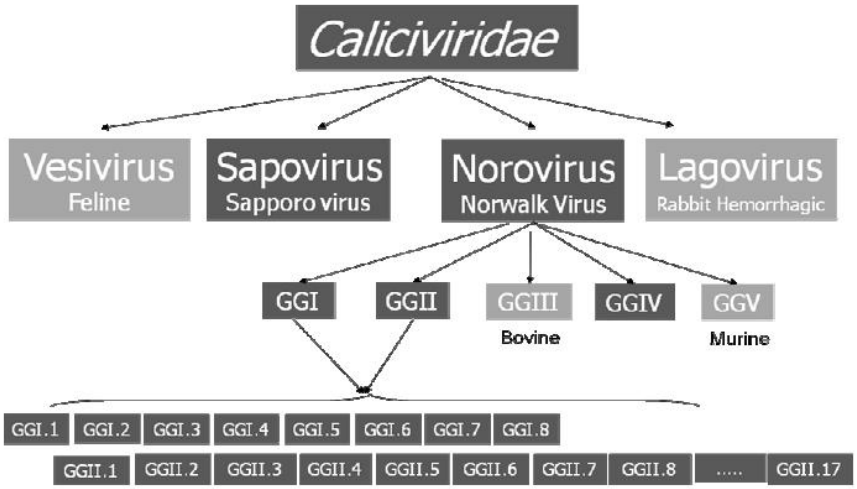

Figure 1 The Caliciviridae family, with human pathogenic groups marked in darker grey (Nordgren 2009)

During the 21st Century, new GII.4 strains have emerged every two to three years. New strains replace previously predominant strains, often leading to increased outbreak activity (Ong 2013). According to the Centers for Disease Control and Prevention (CDC) (2013) and the Health Protection Agency (2013) a new GII.4 Norovirus strain was identified in Australia in March 2012 and named GII.4 Sydney. This new strain has replaced the previously predominant strain, GII.4 New Orleans, in the USUS and UK (Ong 2013) and has caused major gastroenteritis outbreaks in multiple countries (van Beek *et al.* 2013).

3.1.2 What does it cause?

Norovirus presents as acute onset of diarrhoea, abdominal cramps, nausea and vomiting (Atmar and Estes 2006, Desselberger and Gray 2013). Other symptoms may include headache, chills, low grade fever, muscle aches and tiredness. The illness has an incubation period of 15-48 hours and symptoms last between 24-48 hours (Norovirus Working Group 2007). Gastroenteritis is responsible for increased strain on health-care services, increased loss of productivity and general social disruption (Hall *et al.* 2006). Norovirus is the only documented human enteric virus to cause epidemics of gastroenteritis (Siebenga *et al.* 2009).

According to Kaplan *et al.* (1982) the symptoms described for Norovirus-associated gastroenteritis include the following: nausea (79%), vomiting (69%), diarrhoea (66%), abdominal cramps (30%), headache (22%), low-grade fever (37%), chills (32%) and myalgias (26%).

3.1.3 How is it transmitted?

Norovirus is transmitted primarily person to person by the faecal oral route and contact with contaminated surfaces (see Figure 2). According to McIver McIver 2005), Norovirus transmission occurs via:

- contact with persons with gastroenteritis;
- being in semi-closed environments, such as buses or airplanes, with people who are ill with gastroenteritis;
- visiting or working in a health care facility during an outbreak;
- contact with areas that have been contaminated by vomiting and/or faeces; and,
- consumption of contaminated food, by poor food-handling hygiene or cultivation of filter-feeding shellfish in contaminated environments.

According to Figure 2 an infection results in intestinal pathology, with the virus then being shed via stool or vomit of individuals with symptoms, as well as the stool of individuals who do not show symptoms. Some individuals may have acquired immunity in previous infections.

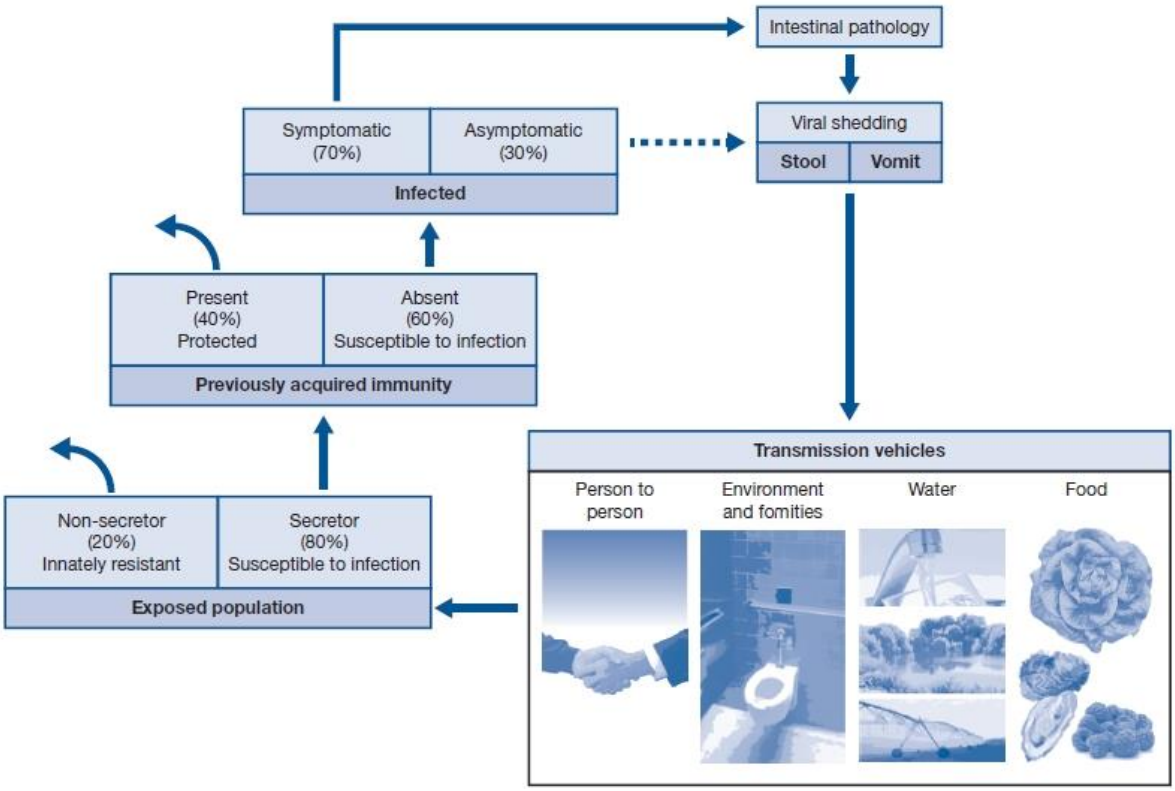

Figure 2 The cycle of Norovirus transmission begins with infected individuals, including both symptomatic and asymptomatic infections (taken from Hall *et al.* 2013)

Increased Norovirus transmission has been recorded from car dealerships, sports games, commercial ice, well water, cruise ships, military training camps, neonatal intensive care units, day care centres and nursing homes (Payne 2013). Even single vomiting incidents in crowded environments have been associated with outbreaks of Noroviruses (Evans *et al.* 2002, Thornley *et al.* 2011, Wikswo *et al.* 2011). With the ease and increase in international travel, international travellers have been identified as vectors due to the similarity of strains between outbreaks across the world (World Health Organization 2010).

Noroviruses are a major cause of foodborne diseases worldwide and will soon be the most common cause of severe paediatric gastroenteritis now that rotaviruses (the previous leading cause) is being treated with vaccines (Atmar and Estes 2006, Koo *et al.* 2010). Nearly a third of documented gastroenteritis cases were due to contaminated food. In Australia this equates to an estimated minimum 5 million cases of foodborne gastroenteritis annually (Hall *et al.* 2005, Australian Government Department of Health and Ageing 2008). Norovirus outbreaks are frequently associated with bivalve shellfish such as oysters (Huppatz *et al.* 2008, Wang and Deng 2012, Thebault *et al.* 2013). In addition outbreaks are linked to the contamination of water with infected faecal matter, or from an infected food handler working with freshly prepared produce such as salads or fruit (Kendall *et al.* 2013).

Although Noroviruses are not able to multiply outside of their host, they are able to survive in certain situations for long periods. Noroviruses have been shown to persist in the guts of oysters growing in contaminated waters. For example, the virus itself can attach to oyster

tissues such as gills and digestive glands making it difficult to eliminate from contaminated oysters (Wang and Deng 2012).

Factors that contribute to as well as promote widespread endemic Norovirus infection and epidemic disease, particularly in confined institutional settings, include:

- short incubation time (median 1.2 days) (Lee *et al.* 2013);
- high virulence and infectivity (Kroneman A *et al.* 2008, Teunis *et al.* 2008, Greig and Lee 2009, Seitz *et al.* 2009, Hall *et al.* 2011);
- strong resistance to common disinfectants (Park *et al.* 2010);
- persistence on surfaces and in water (Seitz *et al.* 2009); and
- faecal shedding of virus, which may last up to 1–2 months in infected persons who have resolved symptoms and are otherwise healthy (Glass *et al.* 2009, Hall *et al.* 2011, Morillo *et al.* 2012, Hall *et al.* 2013, Koo *et al.* 2013;).

Table 1 examines the factors that promote the environmental transmission of Norovirus.

Table 1 Factors that promote the environmental transmission of Norovirus (taken from Lopman *et al.* 2012, page 98)

Factor	Evidence	Key references/examples
Large human population pool	Incidence in developed countries is approximately 5% per year for all ages and 20% per year in children under the age of 5 years.	de Wit *et al.* 2001, Phillips *et al.* 2010, Hall *et al.* 2011, Scallan *et al.* 2011
Copious shedding in faeces disseminated by contact with infected surfaces (including humans, e.g. by handshaking)	Peak shedding is typically 105–109 particles/g of stool, but may be as high as 10(11).	Atmar *et al.* 2008, Gallimore *et al.* 2006
Widespread and rapid dissemination by vomit	Settings where outbreaks occur may have been and continue to be widely contaminated; the virus can be found on a range of surfaces. Outbreaks spread rapidly due to aerosolisation of virus via vomitus, which also serves to contaminate environments for future exposures.	Cheesbrough *et al.* 1997, Cheesbrough *et al.* 2000, Marks *et al.* 2000, Marks *et al.* 2003, O'Neill and Marks 2005, Gallimore *et al.* 2006, Gallimore *et al.* 2008, Atmar *et al.* 2011,
Prolonged shedding	In experimentally infected adults, virus can be detected for a median of 4 weeks and up to 8 weeks (by RT-PCR). Virus can be detected for up to 3 weeks after the onset of symptoms in approximately 25% of community-acquired infections.	Cheesbrough *et al.* 1997, Rockx *et al.* 2002, Gallimore *et al.* 2003,
Environmental stability	On the basis of observations made in outbreaks, Norovirus particles may remain infectious for 2 weeks on environmental surfaces and over 2 months in water. Cool, dry conditions appear to be most favourable for survival of infectious virus.	Cheesbrough *et al.* 1997, Lopman *et al.* 2009, Seitz *et al.* 2009
Resistance to chemical disinfection	Chemical disinfection of surfaces may be a key point of the transmission cycle for intervention, but due to the absence of an infectivity assay for human Norovirus, determining the	Park *et al.* 2010, Park and Sobsey 2011

	effectiveness of various chemicals has been based on cultivable surrogate viruses.	
Diverse range of fomites can become contaminated	Both high- and low-touch surfaces may become contaminated by both faecal matter or vomit. Food (though not strictly a fomite) may become contaminated in a similar way by infected food handlers.	Cheesbrough *et al.* 2000, Gallimore *et al.* 2006, de Wit *et al.* 2007, Gallimore *et al.* 2008, Barrabeig *et al.* 2010, Boxman *et al.* 2011

Environmental conditions also play an important role in transmission (Gallimore *et al.* 2003, Widdowson *et al.* 2004, Isakbaeva *et al.* 2005, Verhoef *et al.* 2008). Norovirus has been shown to survive ambient temperatures on stainless steel surfaces for several weeks (Liu *et al.* 2008), and was found to be transmitted to over seven other surfaces (Barker *et al.* 2004). As little as one gram of contaminated faeces may contain approximately 5 billion infectious doses, with as little as 18 viral particles needed to cause an infection in humans (Teunis *et al.* 2008).

On cruise ships, Norovirus has been detected on general environmental surfaces as well as on surfaces in restrooms during infection outbreaks (Verhoef *et al.* 2008). Multiple outbreaks on cruise ships from identical strains of Norovirus (Gallimore *et al.* 2003, Widdowson *et al.* 2004, Isakbaeva *et al.* 2005, Verhoef *et al.* 2008) and subsequent genetic sequencing, indicated that environmental contamination plays an important role in transmission (Carling *et al.* 2009).

Some of the leading causes of outbreaks on cruise ships have been attributed to inadequate temperature control, infected food handlers, contaminated raw ingredients, cross-contamination, and inadequate heat treatment (Lawrence 2004; Rooney *et al.* 2004). Waterborne outbreaks have been associated with specific deficiencies in water handling, uploading from unsafe sources, water tank contamination, defective backflow prevention, and cross-contamination between potable and non-potable water (Cramer *et al.* 2008).

3.1.4 How is Norovirus identified?

The identification of Norovirus is complicated by the fact that it cannot be cultured in the laboratory. As a result there is no one reliable standard testing procedure (Fisman *et al.* 2009). Traditional identification has relied on electron microscopy to show characteristic viral particles in clinical specimens, however this method is both expensive and time consuming (Richards *et al.* 2003, Castriciano *et al.* 2007). The diagnostic test of choice is Reverse-transcription polymerase chain reaction of suspected stools (Koopmans 2008), but unfortunately many laboratories are unable to conduct these tests (Koo *et al.* 2010). Therefore, where there is a cruise ship outbreak, swabs must be dispatched to the nearest land-side laboratory capable of analysing such swabs once the ship reaches port. Given that ships often call into remote ports and ports in developing nations, laboratories may be some distance away or even in a different country, thereby contributing to delays in analysis.

Without the single reliable use of a test, different definitions have been used in Norovirus outbreak diagnosis (Duizer *et al.* 2007):

- if 2 or more samples are found positive (Richards *et al.* 2003);
- 50% or more of samples test positive (Lopman *et al.* 2003); and

- clinical appearance of a nonbacterial gastroenteritis with at least 1 sample positive for Norovirus and other laboratory tests negative for bacterial and parasitic agents (Fankhauser *et al.* 1998).

3.1.5 Who is at risk?

Norovirus outbreaks are commonly identified in populations living, working or playing in spaces of containment including:

- restaurant patrons (Centers for Disease Control and Prevention 2007; Daniels *et al.* 2000),
- children (Patel *et al.* 2009);
- the elderly (Green *et al.* 2002);
- the immunocompromised (Roddie *et al.* 2009);
- military personnel (Hyams *et al.* 1993, Sharp *et al.* 1995);
- travellers to developing countries (Ajami *et al.* 2010, Koo *et al.* 2010);
- passengers of cruise ships (Widdowson *et al.* 2004);
- residents of healthcare facilities such as
    - nursing homes (Green *et al.* 2002, Calderon-Margalit *et al.* 2005) and
    - hospitals (Johnston *et al.* 2007), and
- other populations housed in close quarters (Yee *et al.* 2007).

The majority of Norovirus-associated gastroenteritis outbreaks occur within institutional settings, such as aged-care facilities, hospitals and childcare centres (Hall *et al.* 2013), probably because of their pattern of contagion[2]. As indicated above, the most vulnerable in the community include the elderly, immune-compromised and young children (Eden *et al.* 2014) (see

[2] It is important to note that individual cases often remain unrecorded, in contrast to 'outbreaks' that receive substantial attention.

Table 2). In outbreaks among haematology and oncology patients, virus shedding on average was up to 3 weeks longer than median symptom duration, with some patients shedding for months and even up to 1 year, (Simon *et al.* 2006, Ludwig *et al.* 2008, Capizzi *et al.* 2011). As such the emergence of the entity called ‘chronic Norovirus gastroenteritis’ (Bok and Green 2012) has been noted.

Table 2 Clinical differences in Norovirus infection in immunocompetent and immunocompromised populations (Kaufman *et al.* 2014)

	Immunocompetent	Immunocompromised
Acuity	• Usually sudden	• Usually sudden
Vomiting	• Usually present • Usually <1 day	• Variable • Often Absent
Diarrhoea	• Sometimes absent • Watery • Usually 1-4 days • Variably dehydrating	• Watery • Variable 1 week to >6 months • Almost always dehydrating
Faecal Shedding	• <1 week to 2 months	• 2 to >12 months
Mortality	• Rare	• Up to 25%

Those that are immunosuppressed are at a higher risk of infection and death than patients whose immune systems are intact (Mattner *et al.* 2006, Arias *et al.* 2013, Hall *et al.* 2013). This population can include, for example, patients that have undergone chemotherapy (Schwartz *et al.* 2011), recuperating from surgery (Greig and Lee 2012), newborns (Greig and Lee 2012), children (Patel *et al.* 2009) and the elderly (Fretz *et al.* 2009). Although difficult to pinpoint, Noroviruses cause up to 200,000 deaths annually in children under 5 years of age in developing countries (Patel *et al.* 2009).

Figure 3 shows the three geographical risk zones that have been identified as at-risk areas (DuPont 2008). Risk also appears to be linked to geography, location and movement. For example, on the whole, those travelling from resource-rich to resource-poor settings are at greatest risk of infection due to lower quality sanitation (Patel *et al.* 2009, Hearn and Doherty 2014). Compared with other genotypes, GII.4 outbreaks are associated with more hospitalisations and deaths (Desai *et al.* 2012).

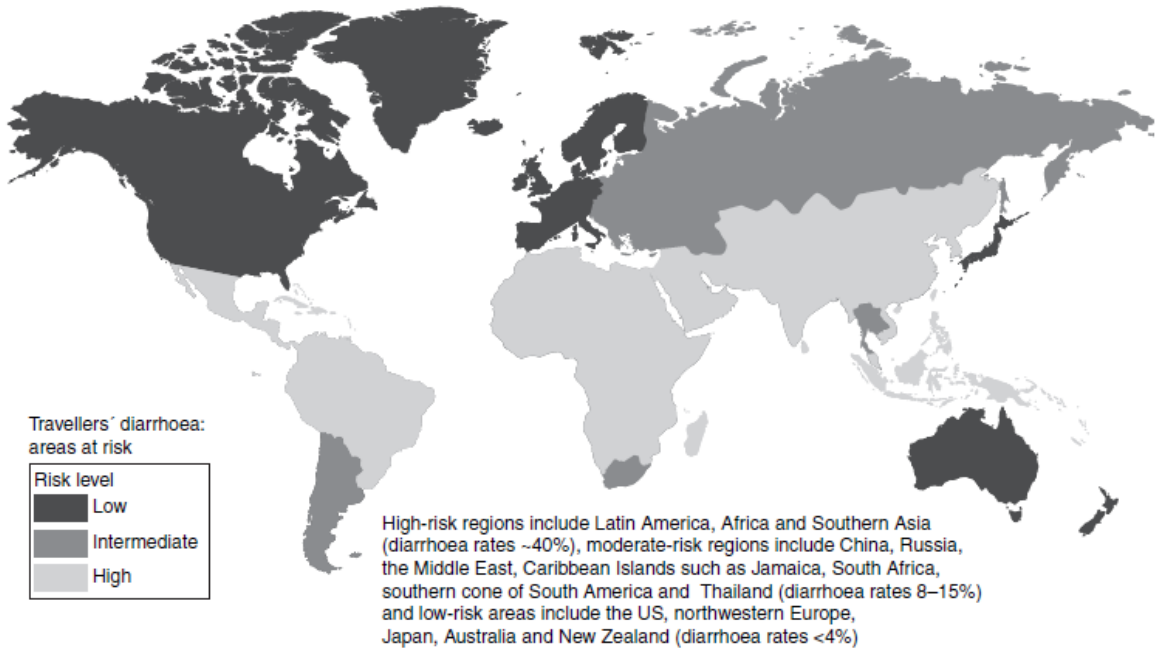

Figure 3 Variation in risk of acquiring traveller's diarrhoea among international visitors from low-risk regions (DuPont 2008, page 743).

3.2 Norovirus Treatment and Prevention

Currently, there is no specific treatment for Norovirus infection (Tan and Jiang 2008, Dai *et al.* 2012, Desselberger and Gray 2013). Norovirus infection cannot be treated with antibiotics because it is a viral (not a bacterial) infection (Centers for Disease Control and Prevention 2011) and there are currently no vaccines or antivirals available (Tan and Jiang 2010). Because Norovirus may be difficult to diagnose (e.g., to differentiate from food poisoning), patients admitted to hospital who actually have Norovirus may unwittingly trigger outbreaks with increases in infectious patients into hospital wards without being correctly diagnosed (Beersma *et al.* 2012).

The safeguarding of food and water supplies and the rigorous and timely application of outbreak management and infection control measures are the main keys to preventing the spread of Norovirus, especially until large-scale effective vaccination and specific treatments become available (Ong 2013).

Due to the perceived nature of Norovirus-related gastroenteritis as being a disease that is short lived and self-limiting, the development of specific antiviral measures has been slow. The increasing recognition of its life-threatening status in immunocompromised patients who often require prolonged hospitalization has stimulated new research to develop an effective antiviral therapy (Kaufman *et al.* 2014). Currently, most medical intervention is limited to supporting the patient while waiting for the patient to stop shedding the virus (Norovirus Working Group 2007).

3.2.1 Vaccine Research

Vaccine research in the last decade has proven promising, with increased studies looking at developing a licensed vaccine or antivirals (Arias *et al.* 2013).

Currently, animal-based models are being used to increase our understanding of Norovirus infections (Wang *et al.* 2005, Wobus *et al.* 2006, Souza *et al.* 2008, Bok *et al.* 2011); however, no small animal-based model for Norovirus mimics the disease manifestations observed in humans (Wobus *et al.* 2006, Tan and Jiang 2010, Bok *et al.* 2011). As a result, human outbreaks and volunteer studies have been the primary source for existing knowledge of NV epidemiology and pathogenesis, respectively (Glass *et al.* 2009, Fankhauser *et al.* 2002, Atmar *et al.* 2008).

A targeted healthcare setting vaccine candidate is under development and could reduce hospital-acquired infection (Desselberger and Gray 2013) along with several others (Atmar *et al.* 2011, Blazevic *et al.* 2011, Velasquez *et al.* 2011).

Norovirus Virus Like Particles (VLP) have been suggested as a vaccine candidate (Atmar and Estes 2012). Vaccination with Norovirus VLP vaccines have been shown to induce antibodies that block virus-derived VLP carbohydrate binding in a human clinical study (Richardson *et al.* 2013). In particular, an experimental oral challenge study showed an intramuscular (IM) bivalent Norovirus GI.1/GII.4 Virus Like Particle (VLP) vaccine protected against vomiting and diarrhoea (Bernstein *et al.* 2013).

Norovirus-specific IgY (Immunoglobulin Y) was identified as a potentially useful option for large-scale production of Norovirus-specific antibodies for therapeutic use against Noroviruses (Dai *et al.* 2012). The route of inoculation is one of the main factors influencing the efficacy of a vaccine. Intranasally inoculated VLPs induced a protective immune response in volunteers subsequently challenged with Norovirus, leading to a 47% reduction in the occurrence of gastro enteritis in vaccinated volunteers (Atmar *et al.* 2011). High levels of specific IgA antibodies against Human-Norovirus were detected, further supporting this route of inoculation to induce a robust mucosal protection. The advantages of an approach based on intranasal delivery are its ease of administration and the stimulation of mucosal dendritic cells facilitating a local immune response (Guerrero *et al.* 2001).

The duration of Norovirus immunity and the limited cross-protection post-infection are key challenges in developing vaccinations and determining the health and economic values of a vaccines and, ultimately, for developing a vaccination strategy (in terms of target age groups and frequency of immunization) (Bartsch *et al.* 2012). However Atmar *et al.* 2011) have shown that a two-dose, intranasally administered, VLP vaccine provided homologous protection against gastroenteritis and infection, thus showing it may be possible to use a vaccination strategy to prevent Norovirus infection.

3.2.1.1 Passive Immunisation

Passive immunization[3] remains an effective strategy to prevent and treat infectious diseases. Oral administration of antibodies has been described previously (Cooper and Paterson 2001). Passive immunization may prove a useful option for high-risk populations, whose immunity may be immature or weakened such as young children, the elderly, and immunocompromised patients (Dai *et al.* 2012).

3.2.1.2 Immunity

There is currently a lack of prolonged cross-protective immunity following infection due to the diverse nature and rapid evolution of the Norovirus group (Hall 2012). Volunteer studies indicate that immunity to Noroviruses seems to be short lived and that immunity to one strain does not provide good protection from infection with others (Wyatt *et al.* 1974, Parrino *et al.* 1977, Johnson *et al.* 1990, Matsui and Greenberg 2000). In general immunity is short-lived (<2 years), and the duration of protection after vaccination remains to be determined (Glass *et al.* 2009). The existence of long-term immunity is more controversial but multiple studies found protective responses against GI.1 were present six months after challenge in some but not all individuals (Debbink *et al.* 2012).

3.2.2 Anti-virals Research

The lack of knowledge of the measurable correlate of immunity that corresponds with human protection against Norovirus infections currently hinders progress for an effective antiviral solution to Noroviruses (Koo *et al.* 2010). With previous studies showing antibody-mediated immunity to be short-lived and the antigenic drift of Noroviruses, there has been limited widespread protection with Norovirus vaccines. The success of such vaccines will be dependent upon vigilant surveillance for the predominant circulating Norovirus genotypes for

[3] *Passive immunization* employs preformed antibodies provided to an individual that can prevent or treat infectious diseases and is used when there is a high risk of infection and insufficient time for the body to develop its own immune response.

which vaccinations should be prepared, similar to current influenza vaccinations (Koo *et al.* 2010). Human volunteer studies have been performed to assess inactivation techniques for Human-Norovirus, but these studies are expensive to perform and logistically-complicated, limiting their use and the amount of data that can be obtained (Leon *et al.* 2011). As a result, assessment of Norovirus inactivation is typically evaluated using research surrogates, such as murine Norovirus (Kingsley *et al.* 2007), feline calicivirus (Duizer *et al.* 2004, Tree *et al.* 2005) and Tulane virus (Li *et al.* 2013).

3.2.2.1 Current Clinical Trials

Table 3 is a current list (as at 28th March, 2014) of the clinical trials for Norovirus vaccines.

Table 3 Clinical trials for Norovirus[4] (US National Institutes of Health 2014)

Clinical trials for Norovirus	
Dose Range Evaluation of Norovirus Challenge Pool (GII.4, CIN-1)	
Condition:	Norovirus Infections
Intervention:	Biological: Norovirus challenge pool (GII.4, CIN-1)
Safety and Immunogenicity of Norovirus GI.1/GII.4 Bivalent VLP Vaccine	
Condition:	Norovirus
Interventions:	Biological: Hepatitis A Vaccine; Biological: Norovirus Bivalent VLP Vaccine
Viral Infections in Healthy and Immunocompromised Hosts	
Conditions:	Virus Infections; Respiratory Viruses; Norovirus; Suspected Viral Infections
Intervention:	
Secondary Lactose Intolerance Due to Chronic Norovirus Infection	
Condition:	Chronic Diarrhoea
Intervention:	Behavioural: Lactose H2 breath test (LH2BT)

3.2.3 Nutraceutical Research/ Prophylactic

A Nutraceutical is a nutritionally enhanced food. The term was coined by Stephen DeFelice in 1979 as a food, or parts of food, that provide medical or health benefits, including the prevention and treatment of disease (Gad 2001). Although there is no commercially available prophylactics against Norovirus, one area that has been explored is the use of glycosylated hydrogels (Zhang *et al.* 2006). The incorporation of human blood group antigens (HBGAs), which are the receptor molecules for Human-Norovirus, enables the trapping of viral particles in the hydrogel (Tan and Jiang 2011, Atmar and Estes 2012).

3.2.3.1 Probiotics

Probiotics are cell preparations or microbial cells that have a beneficial effect on the health and wellbeing of the host. Probiotics have the potential to reduce the duration and severity of diarrhoea and thus may be a safe intervention (Allen *et al.* 2004). Probiotics are commonly used as medication, even though they may have been originally developed as a food option (Kolader *et al.* 2013). Many different probiotic organisms, doses, treatment durations, study

[4] See http://clinicaltrials.gov/search/open/condition=%22Norovirus%22

populations, designs, settings, and aetiologies have been described favouring their potential use (Kolader *et al.* 2013) including Noroviruses (Rubio-del-Campo *et al.* 2014).

3.2.4 Current Control Options

Even though the literature does not confirm it, infection control procedure are a key element in controlling Norovirus outbreaks (Harris *et al.* 2010). Outbreak control measures focus on interruption of person-to-person transmission and removal of sources of infection (food, water, food-handlers), along with measures to improve environmental hygiene (Desselberger and Gray 2013).

For example, in relation to food management, neutralising infected oysters with high-pressure inactivation (600 MPa) has shown to be effective in oysters seeded with Human-Norovirus in volunteer studies (Richards 2012). The advantage of this method is that it is a non-chemical option.

In terms of transmission management, and controversially, it has been suggested the use of alcohol-based sanitizers could be a risk factor for Norovirus outbreaks in hospitals rather than a treatment as they have low-effectivity against Norovirus (Said *et al.* 2008 Lopman *et al.* 2012), suggesting this approach has limitations (Carling *et al.* 2009). Washing hands with soap and water reduces transmission, however, hand sanitizers are less effective than washing with ordinary soap and water (Edmonds *et al.* 2012). Furthermore, enhanced collaboration between cruise passenger ships and sanitary organisations will help prevent the occurrence of communicable diseases aboard passenger ships through integrated hygiene programmes (Mouchtouri *et al.* 2010).

3.2.4.1 Preventative approaches

Some preventative approaches include: γ-irradiation, thermal inactivation, steam-ultrasound, UV radiation, chloride or ozone disinfection, and electron beam irradiation (Richards 2012). However, due to the lack of an available cell culture system to detect any remaining infectivity, the vast majority of such studies are conducted with Norovirus surrogates (Arias *et al.* 2013). Some research has suggested the use of antimicrobial copper surfaces in high risk areas such as closed environments including health care facilities and cruise ships as a mechanism to reduce the spread of Norovirus (Kevil and Warnes 2013).

3.2.4.2 Control and Effectiveness

Control measures currently implemented are targeted at slowing down and containing outbreaks in closed or semi-closed environments such as hospitals, care homes or cruise ships. Quarantine of infected individuals, enhanced environmental decontamination and enhanced hand hygiene are the most common measures currently in place (Lopman *et al.* 2012).

In hospital-acquired (nosocomial) infections, the most frequent recommendations include isolation/cohorting of infected individuals, enhanced hand washing, and implementation of infection control measures (Greig and Lee 2012). On cruise ships, the best control measures

are extensive disinfection, good food and water handling practices, isolating ill persons, providing paid sick leave for ill crew, and promoting hand washing with soap and water among passengers (Isakbaeva *et al.* 2005) and the supplemental use of hand santisers, required as passengers enter food service areas and board or re-board their ships at each port.

According to Carling *et al.* 2009, an objective evaluation of public restroom environmental hygiene on 56 cruise ships found that around a third of selected bathroom area objects were cleaned on a daily basis. Therefore, better cleaning may prevent or moderate Norovirus outbreaks on cruise ships. More recent years have seen improvements in practices.

Further research suggests detergent based cleaning without adequate disinfection may increase rather than reduce transmission. Effective control of Norovirus outbreaks requires a combination of decontamination of the environment (particularly contact surfaces) and implementation of a thorough hand washing technique. Hand washing alone is not effective if recontamination occurs (Barker *et al.* 2004).

Norovirus is remarkably resistant to several commonly used disinfectants and some advocate for the use of chlorine (sodium hypochlorite) as a disinfectant wherever possible (Kingsley *et al.* 2014).

3.3 Norovirus worldwide

Noroviruses are the most common causes of both epidemic and endemic viral enteritis in the US and worldwide, taking over from rotaviruses due to the marked reduction in the prevalence of rotavirus infection following successful vaccine development (Hall *et al.* 2011, Hall *et al.* 2013).

GII.4 variants have also caused the six pandemics of Norovirus-associated acute gastroenteritis since 1995, all of which were initiated by the emergence of Norovirus GII.4 variants including (Eden *et al.* 2014):

- *US 1995/96* in 1996 (Noel *et al.* 1999, White *et al.* 2002);
- *Farmington Hills 2002* in 2002 (Widdowson *et al.* 2004);
- *Hunter 2004* in 2004 (Bull *et al.* 2006);
- *Den Haag 2006b* in 2007–2009 (Tu *et al.* 2008, Eden *et al.* 2010);
- *New Orleans 2009* in 2009–2012 (Vega *et al.* 2011, Tra *et al.* 2013); and, most recently
- the *Sydney 2012* variant (Eden *et al.* 2013, van Beek *et al.* 2013).

The emergence of these GII.4 variants often coincides with dramatic increases in the occurrence of both community-acquired and institutional outbreaks of acute gastroenteritis, as exemplified in late 2012 with the emergence of *Sydney 2012* (Bennett *et al.* 2013, Fonager *et al.* 2013, van Beek *et al.* 2013).

New emerging strains have been shown to be able to be rapidly detected thanks to Norovirus surveillance systems established in Europe, Japan and the United States (Lindesmith *et al.* 2012). For example, *NoroNet*, is an informal network of scientists working in public health institutes or universities sharing virological, epidemiological and molecular data on Norovirus (http://www.rivm.nl/en/Topics/N/NoroNet). The major aim of this network

to detect trends and identify possible (foodborne) outbreaks by sharing epidemiological and molecular data of Norovirus outbreaks (van Beek *et al.* 2013).

3.3.1 Globally

It is estimated that over 1.8 million deaths of children under the age of 5 have been caused by gastroenteritis in general (Hall *et al.* 2013). Specifically, and as mentioned further above, a recent review of Noroviruses (Patel *et al.* 2009) has shown that there has been over a million hospital admissions worldwide; with approximately 900,000 clinic visits and over 200,000 deaths of children under 5 years of age in developing countries (Ong 2013). Globally, it appears there is an increase in Norovirus activity in late 2012 (Eden *et al.* 2014) (see Figure 4). This increase is related to the emergence of Norovirus genotype II.4, termed *Sydney 2012* (Health Protection Agency 2013) (see Figure 5). Similarly, two articles published recently in *Eurosurveillance* and *CDC MMWR* reported that the latest surveillance data in Europe and the US demonstrate an increased activity of Norovirus in late 2012 that relates to the new Norovirus genotype II.4 variant, Sydney 2012 (CDC 2013, van Beek *et al.* 2013), described in section 3.3.

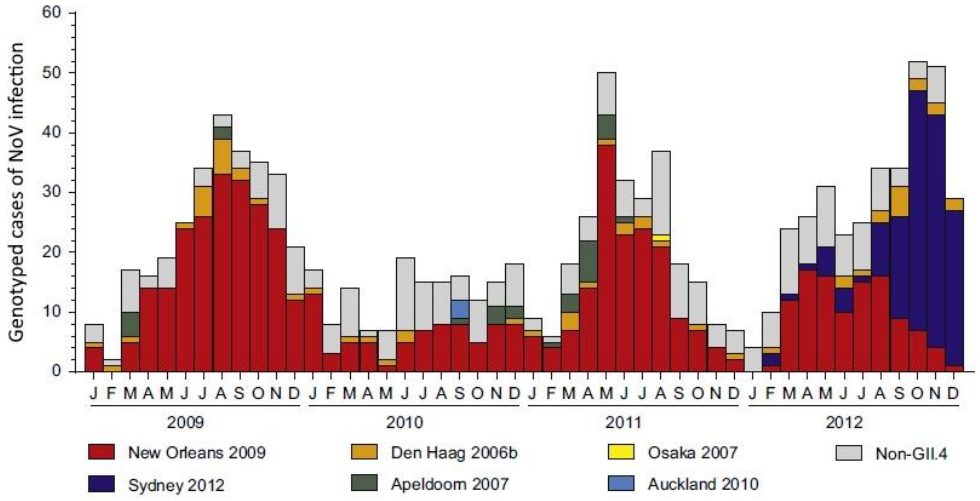

Figure 4 Prevalence of circulating Norovirus genotypes in the Oceania region (Eden *et al.* 2014).

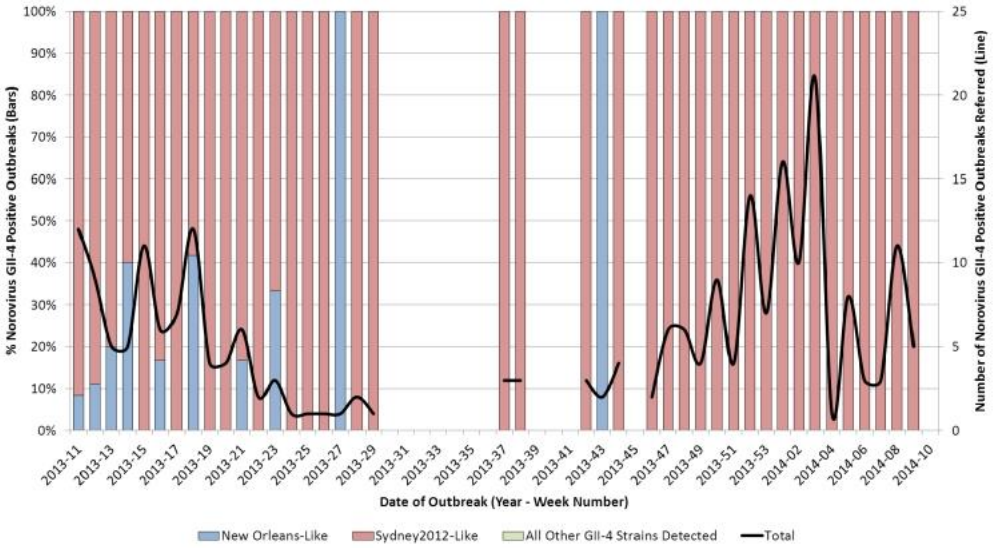

Figure 5 **GII-4 Norovirus strains detected (by week) among Norovirus confirmed outbreaks (all settings) (Week 11, 2013 to Week 11, 2014) (Health Protection Agency 2013).**

The genotyping results for Australia and New Zealand were combined and then plotted by month between 2009 and 2012 to highlight the cause of each Norovirus epidemic as well as the shift in prevalence between New Orleans 2009 and Sydney 2012 that occurred during late 2012. The prevalence of each GII.4 variants is shown with non-GII.4s grouped separately and coloured according to the key provided (Eden *et al.* 2014). Table 4 shows the reported Norovirus outbreaks / sporadic cases by sample year from 2010 to 2013.

Table 4 **Number of reported Norovirus outbreaks / sporadic cases by sample year (van Beek *et al.* 2013)**

	2010	2011	2012	2013	TOTAL
AUSTRALIA			2		2
AUSTRIA	54	32	16		102
BELGIUM	14	6	28		48
CHILE			4		4
CHINA		77			77
DENMARK	11	23	28		62
FINLAND	283	94	61	6	444
FRANCE	215	204	146		565
GERMANY	50	62	74	8	194
HONG KONG			3	1	4
HUNGARY	91	83	48	5	227
IRELAND	7		4		11
ITALY	1				1
JAPAN	41	24	84	11	160
NETHERLANDS	662	491	460	72	1685
NEW ZEALAND			216	34	250
RUSSIAN FEDERATION		6	20	5	31
SLOVENIA			1		1
SOUTH AFRICA	34	53	14	4	105
SPAIN	61	36	23		120
SWEDEN	24	64	32		120
UNITED KINGDOM	9	6			15
Total	1557	1261	1264	146	4228

3.3.2 United States of America (US)

Norovirus is responsible for up to 50% of all foodborne gastroenteritis outbreaks in the US (Widdowson *et al.* 2004) and over 90% of all gastroenteritis cases (Glass *et al.* 2009).

Hall *et al.* 2013 report that each year on average in the US, Norovirus:

- causes 19–21 million cases of acute gastroenteritis (inflammation of the stomach or intestines or both);
- leads to 1.7–1.9 million outpatient visits and 400,000 emergency department visits, primarily in young children; and,
- contributes to about 56,000–71,000 hospitalizations and 570-800 deaths (lifetime risk equal to 1 in 146 5000–7000), mostly among young children and the elderly.

3.3.3 United Kingdom (UK)

In England and Wales, the Health Protection Agency Communicable Disease Surveillance Centre operates a surveillance system for gastroenteritis outbreaks, in conjunction with a standardized testing approach (Danial *et al.* 2011).

3.3.4 Australia and the South Pacific

In Australia it is estimated that over 17 million episodes occur annually (Hall *et al.* 2006, Kirk *et al.* 2010). In 2000, by adapting the Centers for Disease Control and Prevention's (CDC) FoodNet model of active surveillance, Australia improved its national surveillance of gastrointestinal and foodborne illness. The OzFoodNet surveillance network applies concentrated efforts at the national and local levels to investigate and understand foodborne disease and to provide better evidence for minimizing the number of cases of foodborne illness in Australia (Kirk *et al.* 2008).

In 2009, OzFoodNet sites reported an 18% increase in outbreaks of gastrointestinal disease from the year before (1820 compared with 1545). The majority of outbreaks in 2009 were transmitted from person-to-person (82%) and were most frequently caused by Norovirus (52%) (OzFoodNet 2009).

Each year in Australia, there is an estimated 1.8 million cases of Norovirus infection. A Melbourne study has found that prevalence is highest during spring and summer. If the source is contaminated food this may be reportable in some states (Australian Government Department of Health and Ageing 2010). A survey conducted by OzFoodNet found approximately 17.2 million Australians experienced episodes of gastroenteritis every year (OzFoodNet 2012). Between 2000 and 2008, there were 2923 Norovirus outbreaks affecting 86,570 people (Australian Government Department of Health and Ageing 2010) (Figure 6).

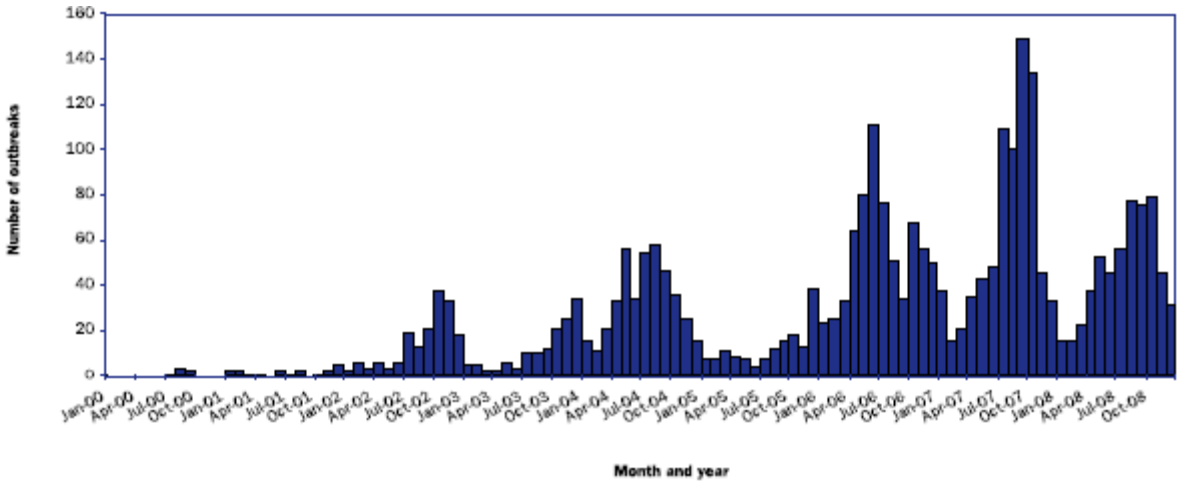

Figure 6 Number of outbreaks due to Norovirus spread by different modes of transmission in Australia, by month of onset of first case, 2000–08.

In the Australian state of New South Wales, a distinct peak in Norovirus activity was observed each year around August during the late-winter period during the period 2009 and 2012; however, the magnitude of the peaks varied. Specifically, a sharp increase in the number of Norovirus outbreaks was observed between August and October 2009, with 84 outbreaks recorded in September, representing a more than twofold increase compared to the average number of outbreaks (n=41) in the peak winter months for 2010, 2011 and 2012 (Eden *et al.* 2014) (see Figure 7).

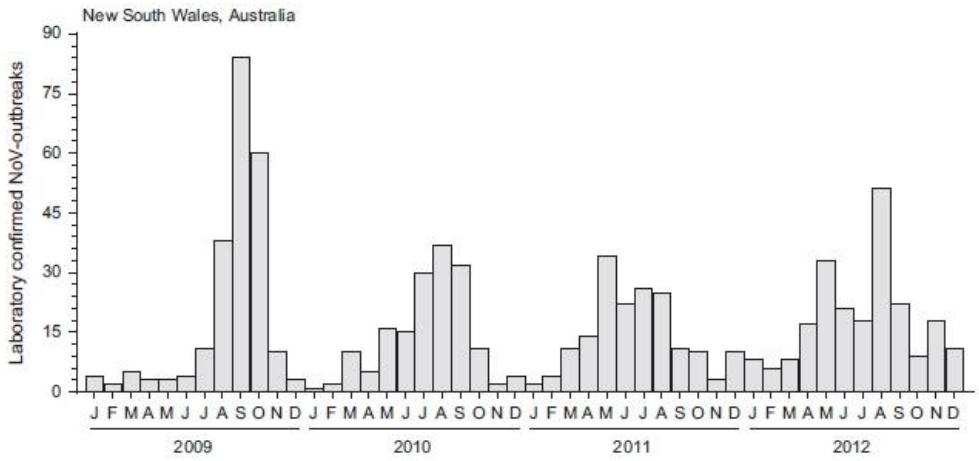

Figure 7 Laboratory confirmed number of monthly Norovirus outbreaks in Australia between 2009 and 2012 (adapted from (Eden *et al.* 2014).

According to Figure 7 annual peaks in activity were observed during the late winter period in Australia except in 2011 where the peak in activity occurred during autumn (adapted from Eden *et al.* 2014). Between 1st Jan – 31st Mar 2012, OzFoodNet sites reported 441 outbreaks of enteric illness, including those transmitted by contaminated foods. In total, these outbreaks affected 7,027 people of whom 242 were hospitalised and 18 died. Forty-

eight percent of these outbreaks occurred in residential aged care facilities (OzFoodNet 2014).

3.4 Costs

According to (Bartsch *et al.* 2012, page 5):

- There was an estimated 16.7 million Norovirus gastroenteritis cases in the USUS, costing over $5 billion annually.
- A vaccine protecting 50% of the population would result in between 1 to 2 million cases averted, but would result in additional cost to develop the vaccine
- cost-savings could occur if the vaccine offered protection for 48 months and cost $25 with an efficacy ≥50% or cost ≤$50 with an efficacy ≥75%.
- Vaccines with these characteristics could reduce the total US costs of Norovirus between hundreds of millions or several billions of dollars a year.

In the US, the cost of Norovirus-associated hospitalizations has been estimated at approximately $500 million, while foodborne Norovirus cost due to healthcare and lost productivity has been estimated at $2 billion (Batz *et al.* 2011).

A case study by Ong (2013) showed that a Norovirus outbreak in early 2004 at Johns Hopkins Hospital (USUS) involved 365 patients and health workers. It resulted in closure to an intensive care unit (ICU), coronary care unit (CCU) and psychiatry ward. Visitors were not allowed into the infected areas and nursing staff were not permitted to attend shared eating facilities. The cost of the outbreak was estimated at over $600,000 for lost revenue due to closures, cleaning, equipment replacement and payment of sick leave and overtime.

Outbreaks in the United Kingdom have been estimated to cost the National Health Service (NHS) an estimated £1 billion annually (Lopman *et al.* 2004).

In Australia, according to Australian Government Department of Health and Ageing (2008):

- Foodborne gastroenteritis accounts for approximately $811 million annually (81% of all productivity, lifestyle and premature mortality costs, estimated total cost of $1,003 million). Seven other foodborne illnesses account for the balance of 19% and, of these, listeriosis and reactive arthritis are the major contributors to costs
- The estimated total cost of health care services is $221.9 million. Of this total, gastroenteritis accounts for an estimated $199.8 million (90.0%). The other seven diseases account for the remaining $22.1 million (10.0%), with irritable bowel syndrome contributing most to the costs. Visits to emergency departments, GPs and specialists account for two-thirds of all costs.

4. Noroviruses and Cruise Ships

For centuries, ships have transmitted infections or vectors that affect the quality of food products carried (Rowbotham 1998, Cayla *et al.* 2001, Babic-Erceg *et al.* 2003, Rooney *et al.* 2004, Mouchtouri *et al.* 2010, Schlaich *et al.* 2010). As spaces of containment, ships provide the setting for person-to-person or animal-to-human disease transmission of water and foodborne diseases and thus impact on human population health (Hadjichristodoulou *et al.* 2013). The transmission of these infections or vector is exacerbated when ships move from country to country where different standards of hygiene are practised and diseases surveillance practices vary (Hadjichristodoulou *et al.* 2013). Outbreaks occur on cruise ships and in terminals (Koo *et al.* 1996, Centers for Disease Control and Prevention 2012).

Norovirus is one of the leading causes of diarrhoea outbreaks on cruise ships, accounting for over 90% of such cases. Due to the close living quarters, and shared dining areas, as well as large passenger turnovers, controlling Norovirus outbreaks on cruise ships is challenging. Norovirus can be brought on board when ships dock, and due to its ability to persist on surfaces, can infect passengers on consecutive cruises (Centers for Disease Control and Prevention 2014).

Outbreaks have been recognised on cruise ships for over 20 years, however management and reporting of and between countries is not consistent. Notwithstanding this, dramatic improvements in sanitation and operational procedures aboard cruise ships have been seen this millennium compared with the state of sanitation and procedures in the mid-1970s. The US Centers for Disease Control and Prevention's Vessel Sanitation Program, which conducts regular cruise ship inspections, has shown a significant increase in median ship sanitation scores in the 2000s (Lawrence 2004).

Passengers and crew aboard cruise ships are frequently affected by Norovirus outbreaks (Cramer *et al.* 2006). The virus is generally introduced on board by passengers or crew infected before embarkation but might also result from food items contaminated before loading or persistently contaminated environmental surfaces from previous cruises. The virus might also be acquired when ships dock in countries where sanitation might be inadequate, either through contaminated food or water or passengers becoming infected while docked (Centers for Disease Control and Prevention 2011).

An expert panel report of the European Center for Disease Prevention and Control (Stockholm, Sweden, September 2006) was issued in response to increasing numbers of Norovirus on European cruise ships. It concluded that in order to control Norovirus outbreaks on cruise ships a set of guidelines on basic hygiene is needed (European Centre for Disease Prevention and Control 2006).

4.1 Prevalence of Norovirus on cruise ships

4.1.1 World Wide

The following case study documents a perfect example of cruise ship outbreak, according to Isakbaeva *et al.* 2005, page 154):

> "*An outbreak of Norovirus gastroenteritis affected passengers on two consecutive cruises of ship X and continued on 4 subsequent cruises despite a 1-week*

sanitization. We documented virus transmission by food and person-to-person contact, persistence of virus despite sanitization on-board, introduction of new strains, and seeding of an outbreak on land. Like other outbreaks of viral gastroenteritis on cruise ships (Gunn et al. 1980, Ho et al. 1989, Herwaldt et al. 1994, Khan et al. 1994, McEvoy et al. 1996, Widdowson et al. 2004), this outbreak affected several hundred people, was transmitted by multiple modes, and recurred on subsequent cruises."

Like other gastroenteritis outbreaks in closed and crowded settings, outbreaks on cruise ships usually have multiple routes of transmission and thus prove particularly challenging to identify and control (Sharp *et al.* 1995, Kuusi *et al.* 2002).

Table 5 shows Norovirus and/or unknown outbreaks reported on a sample of international cruise ship voyages from January 2011 to July 2015.

Table 5 Outbreak Updates for International Cruise Ships from 1st January, 2012 up till 1st July, 2015 (data does go back to 1994) (http://www.cdc.gov/nceh/vsp/surv/gilist.htm) (Centers for Disease Control and Prevention 2015)

2015					
Cruise Line	**Cruise Ship**	**Sailing Date**	**% sick passengers**	**% sick crew**	**Causative agent**
Princess Cruises	*Star Princess*	4/29 - 5/14	135 of 2588 (5.2%)	16 of 1093 (1.5%)	Norovirus
Oceania Cruises	*Oceania Marina*	4/21 - 5/7	69 of 1185 (5.8%)	11 of 769 (1.4%)	Norovirus
Holland America Line	*ms Maasdam*	4/17 - 5/1	67 of 1138 (5.9%)	12 of 578 (2.1%)	Norovirus
Princess Cruises	*Coral Princess*	4/12 - 4/27	99 of 1958 (5.1%)	12 of 881 (1.4%)	Norovirus
Royal Caribbean Cruise Line	*Legend of the Seas*	3/30 - 4/14	135 of 1746 (7.7%)	7 of 748 (0.9%)	Norovirus
Celebrity Cruises	*Celebrity Infinity*	3/29 - 4/13	106 of 2117 (5.0%)	6 of 964 (0.6%)	Norovirus
Norwegian Cruise Line	*Norwegian Pearl*	3/26 - 4/6	145 of 2472 (5.9%)	13 of 1062 (1.2%)	Norovirus
Celebrity Cruises	*Celebrity Equinox*	2/13 - 2/23	142 of 2896 (4.9%)	8 of 1209 (0.7%)	Norovirus
Royal Caribbean Cruise Line	*Grandeur of the Seas*	1/24 - 2/3	198 of 1948 (10.26%)	9 of 786 (1.2%)	Norovirus
2014					
Cruise Line	**Cruise Ship**	**Sailing Date**	**% sick passengers**	**% sick crew**	**Causative agent**
Princess Cruises	*Crown Princess*	10/18 - 11/16	158 of 3009 (5.3%)	14 of 1160 (1.2%)	Norovirus
Princess Cruises	*Crown Princess*	4/5 - 4/12	122 of 3161 (3.9%)	30 of 1176 (2.6%)	Norovirus and Enterotoxigenic *E. coli* (ETEC)
Royal Caribbean Cruise Line	*Grandeur of the Seas*	4/5 - 4/12	97 of 2120 (4.6%)	8 of 808 (1.0%)	Norovirus
Royal Caribbean Cruise Line	*Grandeur of the Seas*	3/28 - 4/5	111 of 2122 (5.2%)	6 of 790 (0.8%)	Norovirus
Holland America Line	*ms Veendam*	2/8 - 2/22	114 of 1273 (9.0%)	10 of 575 (1.7%)	Norovirus
Princess Cruise Lines	*Caribbean Princess*	1/25 - 2/1	181 of 3102 (5.8%)	11 of 1148 (1.0%)	Norovirus

Royal Caribbean Cruise Line	*Explorer of the Seas*	1/21 - 1/31	634 of 3071 (20.6%)	55 of 1166 (4.7%)	Norovirus
Norwegian Cruise Line	*Norwegian Star*	1/5 - 1/19	130 of 2318 (5.6%)	12 of 1039 (1.2%)	Norovirus
2013					
Cruise Line	**Cruise Ship**	**Sailing Date**	**% sick passengers**	**% sick crew**	**Causative agent**
Norwegian Cruise Line	*Norwegian Gem*	11/16 - 11/25	111 of 2600 (4.3%)	3 of 1064 (0.3%)	Norovirus
Celebrity Cruise Lines	*Celebrity Summit*	9/21 - 10/5	322 of 2112 (15.3%)	13 of 952 (1.4%)	Norovirus
Celebrity Cruise Lines	*Celebrity Millennium*	04/25 - 05/10	123 of 1963 (6.3%)	16 of 935 (1.7%)	Norovirus
Crystal Cruises	*Crystal Symphony*	04/29 - 05/06	125 of 816 (15.3%)	22 of 571 (3.9%)	Norovirus
Celebrity Cruises	*Celebrity Solstice*	04/08 - 04/25	183 of 2849 (6.4%)	2 of 1188 (0.2%)	Norovirus
Celebrity Cruises	*Celebrity Infinity*	03/17 - 04/01	101 of 2086 (4.8%)	17 of 927 (2.1%)	Norovirus
Princess Cruises	*Ruby Princess*	03/03 - 03/10	266 of 3129 (8.5%)	10 of 1189 (0.8%)	Norovirus
Royal Caribbean Cruise Line	*Vision of the Seas*	02/25 - 03/08	118 of 1991 (5.9%)	3 of 765 (0.4%)	Norovirus
2012					
Cruise Line	**Cruise Ship**	**Sailing Date**	**% sick passengers**	**% sick crew**	**Causative agent**
Cunard Line	*Queen Mary 2*	12/22-01/03	204 of 2613 (7.8%)	16 of 1255 (1.3%)	Norovirus
Princess Cruises	*Emerald Princess*	12/17-12/27	189 of 3235 (5.8%)	31 of 1189 (2.6%)	Norovirus
Prestige Cruise Holdings	*Oceania Riviera*	11/15-11/29	37 of 1019 (3.6%)	13 of 767 (1.7%)	Norovirus
Holland America Line	*Amsterdam*	11/11-12/5	85 of 791 (10.8%)	6 of 610 (1.0%)	Norovirus
Princess Cruises	*Ruby Princess*	10/09-10/28	149 of 2971 (5.0%)	14 of 1177 (1.2%)	Norovirus and Enterotoxigenic *E. coli* (ETEC)
Princess Cruises	*Dawn Princess*	08/21-09/13	114 of 1778 (6.4%)	11 of 851 (1.3%)	Norovirus
Royal Caribbean Cruise Line	*Rhapsody of the Seas*	08/24-08/31	153 of 2129 (7.2%)	6 of 812 (0.7%)	Norovirus
Carnival Cruise Line	*Carnival Glory*	08/06-08/11	205 of 3652 (5.6%)	3 of 1144 (0.3%)	Norovirus
Princess Cruises	*Sun Princess*	07/08-07/21	201 of 1918 (10.5%)	15 of 836 (1.8%)	Norovirus
Princess Cruises	*Ruby Princess*	02/26-03/04	129 of 3147 (4.1%)	9 of 1179 (0.8%)	Norovirus
Princess Cruises	*Crown Princess*	02/04-02/09	288 of 3078 (9.4%)	75 of 1178 (6.4%)	Norovirus
Celebrity Cruises	*Celebrity Silhouette*	01/29-02/10	178 of 2809 (6.3%)	11 of 1236 (0.9%)	Norovirus
Celebrity Cruises	*Celebrity Constellation*	01/28-02/11	102 of 1992 (5.1%)	12 of 946 (1.3%)	Norovirus
Princess Cruises	*Crown Princess*	01/28-02/04	364 of 3103 (11.7%)	32 of 1168 (2.7%)	Norovirus
P & O Cruises	*Aurora*	01/04-01/26	145 of 1727 (8.40%)	8 of 850 (0.9%)	Norovirus
Royal Caribbean Cruise Line	*Voyager of the Seas*	01/28-02/04	248 of 3139 (7.90%)	11 of 1192 (0.9%)	Norovirus

Note: Sailing dates are hyperlinked and clicking these will take you details about this outbreak report

4.1.2 Australia

In 2002, an increase in gastroenteritis outbreaks was found on cruise ships in the US and Australia (Australian Government Department of Health and Ageing 2010). From 1999-2003, three confirmed Norovirus outbreaks were reported on cruise ships visiting Sydney, caused by food poisoning acquired ashore or be shipboard person-to-person spread of Norovirus (Ferson and Ressler 2005, Australian Government Department of Health and Ageing 2010).

In December 2003, 200 passengers and crew had presented with gastroenteritis on a 10-day South Pacific cruise. Several specimens tested positive for Norovirus genogroup 1 (Ferson and Ressler 2005). In June 2006, outbreaks of Norovirus on cruise ships increased suddenly. Detection point source was not found due to the limited investigation of initial outbreaks and data sharing. The most probable explanation for the outbreaks is increased Norovirus activity in the community, which coincided with the emergence of two new FFII.4 variant strains in Europe and the Pacific (Verhoef *et al.* 2008).

From 2006-2011, the NSW cruise ship health surveillance program was notified of 45 outbreaks on board voyages arriving in Sydney. Sydney was the first Australian port of call for 33 of the trips. Twenty-nine of these were due to acute gastroenteritis, 15 were respiratory disease, and one was both gastro and respiratory disease (Ressler and Ferson 2011). Between 2006 and 2011 the NSW cruise ship health surveillance program report the total number of cases was 4,505 or an average of 14.5 cases per voyage of acute gastroenteritis, or 3.3 per 1,000 passengers/crew. These cases are reported on the pre-arrival report and are passengers and crew who have sought medical assistance. Therefore this figure is inconclusive as many people do need seek medical attention (Ressler and Ferson 2011). During November and December 2012, of 62 cruise ship voyages arriving in Sydney, Norovirus outbreaks were reported in 6 (NSW Department of Health 2013).

In Australia (as elsewhere), there are impediments to Australian regulation of this industry. The cruise companies that carry most Australian passengers are based in other countries, and none of the vessels are registered in Australia. There are currently no ‘large passenger vessels’ registered (or ‘flagged’) in Australia” (House of Representatives (Commonwealth of Australia) 2013). Despite Carnival and Royal Caribbean being American and British companies, their vessels are often registered outside those countries.

4.2 Outbreaks

4.2.1 What constitutes an outbreak?

While definitions differ, an outbreak is declared when >3.0% of the ship’s passengers or crew members report acute gatroenteritis to the ship’s infirmary (Centers for Disease Control and Prevention 2013) (see Table 6). Most outbreaks can be traced back to a single individual (Arias *et al.* 2013).

Table 6 Acute gastroenteritis threshold levels for outbreak response by industry and regulatory bodies (Ressler and Ferson 2011)

Organisation	Plan	Outbreak definition	Action
SESLHD Public Health Unit SES Cruise Ship Program	Level 1	Outbreak of <1% or case of other disease of quarantine concern on-board a ship that has passed environmental inspection within 12 months.	Verify heightened level of sanitation. Offer public health assistance as needed.
	Level 2	Outbreak of >1% or case of other disease of quarantine concern on-board a ship that has passed environmental inspection within 12 months	Epidemiological Investigation. Laboratory assessment. Verify heightened level of sanitation. Offer public health assistance as needed.
	Level 3	Outbreak of <1% or case of other disease of quarantine concern on-board a ship that has not passed environmental inspection within 12 months.	Epidemiological Investigation. Verify heightened level of sanitation. Consider environmental inspection.
	Level 4	Outbreak of >1% or case of other disease of quarantine concern on-board a ship that has not passed environmental inspection within 12 months.	Epidemiological Investigation. Laboratory assessment. Verify heightened level of sanitation. Environmental inspection.
AQIS	-	Greater than 3% of passengers and crew in the previous 21 days	Report to the Chief Quarantine Officer who requests further details or reports to the local Public Health Unit.
US Centres for Disease Control and Prevention	-	Greater than 3% of passengers and crew in the previous 21 days	Vessels must provide a separate notification to the Vessel Sanitation Program.
	-	Greater than 3% of passengers and crew	Outbreak updates are posted on the Vessel Sanitation Program website.

In general, two or more associated cases of diarrhoea and/or vomiting in a 24 hour period is considered to be an outbreak. Foodborne or waterborne outbreaks are the same except are considered caused by the consumption of common source of food or water within a specified time frame. Until epidemiological or microbiological investigations have been conducted it is often difficult to determine the source of an outbreak (Australian Government Department of Health and Ageing 2010).

Suspected case of Norovirus

A person presenting with three or more loose stools or bowel movements in a 24 hour period that are different from normal and/or two or more episodes of vomiting in a 24 hour period, is considered as a suspected case of Norovirus (Australian Government Department of Health and Ageing 2010).

Confirmed case of Norovirus

Confirmed cases of Norovirus infection must meet the suspected case definition above along with a positive laboratory test from one of the following definitive diagnostic tests:

1. detection of human Norovirus by antigen detection
2. detection of human Norovirus by Nucleic Acid Assays (NAAs)

3. visualisation of Norovirus by EM (Australian Government Department of Health and Ageing 2010) (see Figure 8)

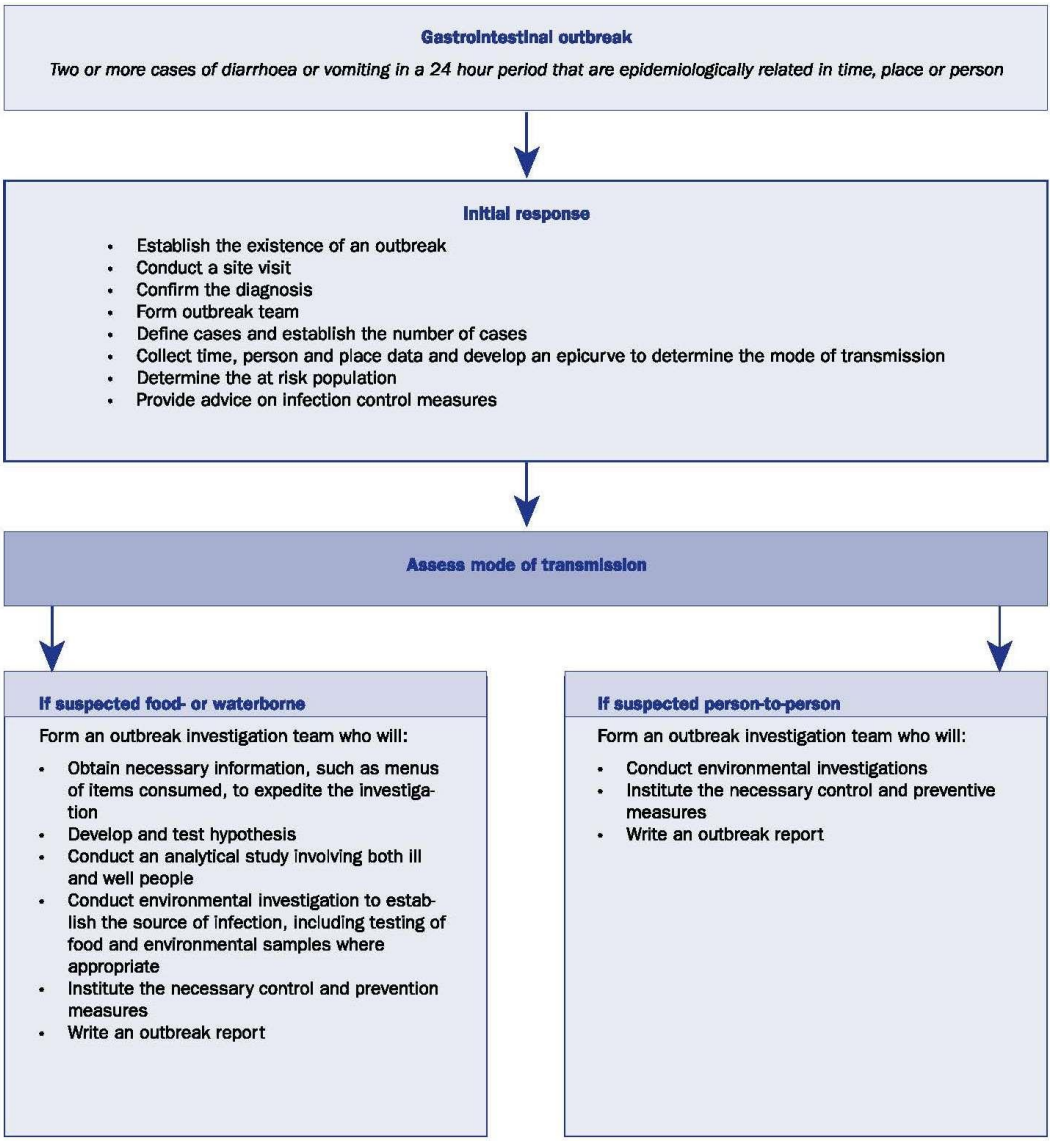

Figure 8 Flow chart – Investigation and management of gastroenteritis outbreaks (Australian Government Department of Health and Ageing 2010).

4.2.2 Who controls an outbreak?

Since cruise ships move from one country to another, leadership of infection investigations is usually difficult, thereby reducing effective outbreak control. To increase effective outbreak management, international agreement between public health authorities in different countries is needed to be able to assign one organisation to lead the control measures (Vivancos *et al.* 2010)

Responding to Outbreaks

The following Table 7 outlines the key points for investigation and response to Norovirus outbreaks.

Table 7 Key points for investigation and response to Norovirus outbreaks (taken directly from Centers for Disease Control and Prevention, 2011)

Key points
• Initiate investigations promptly, including collection of clinical and epidemiologic information, to help identify predominant mode of transmission and possible source. • Promote good hand hygiene, including frequent washing with soap and running water for a minimum of 20 seconds. If available, alcohol-based hand sanitizers (≥70% ethanol) can be used as an adjunct in between proper hand washings but should not be considered a substitute for soap and water hand washing. • Exclude ill staff in certain positions (e.g., food, childcare, and patient-care workers) until 48–72 hours after symptom resolution. In closed or institutional settings (e.g., long-term–care facilities, hospitals, and cruise ships), isolate ill residents, patients, and passengers until 24–48 hours after symptom resolution. In licensed food establishments, approval from the local regulatory authority might be necessary before reinstating a food employee following a required exclusion. • Reinforce effective preventive controls and employee practices (e.g., elimination of bare-hand contact with ready-to-eat foods and proper cleaning and sanitizing of equipment and surfaces). • After initial cleaning to remove soiling, disinfect potentially contaminated environmental surfaces using chlorine bleach solution with a concentration of 1,000– 5,000 ppm (1:50–1:10 dilution of household bleach (5.25%)) or other Environmental Protection Agency (EPA)–approved disinfectant.[5] In health-care settings, cleaning products and disinfectants used should be EPA-registered and have label claims for use in health care; personnel performing environmental services should adhere to the manufacturer's instructions for dilution, application, and contact time. • Collect whole stool specimens from at least five persons during the acute phase of illness (≤72 hours from onset) for diagnosis by TaqMan-based real-time reverse transcription-PCR (RT-qPCR), perform genotyping on Norovirus-positive stool specimens, and report results to CDC via CaliciNet (CDC's electronic Norovirus outbreak surveillance network). • Report all outbreaks of acute gastroenteritis to state and local health departments, in accordance with local regulations, and to CDC via the National Outbreak Reporting System (NORS).

Due to the variability in capacities, experience and resources available in Member State port health authorities (PHAs), education and training are critical to the coordination of cruise ship outbreak detection, reporting and response in Europe. SHIPSAN TRAINET (Ship sanitation training network) reported to plan producing training materials and training modules to be used by the Member States, and can be supported by ECDC, the European Program on Intervention Epidemiology Training (EPIET), and national field epidemiology training programs (European Centre for Disease Prevention and Control 2010).

[5] Agents registered as effective against Norovirus by EPA are available at www.epa.gov/oppad001/list_g_Norovirus.pdf. Evidence for efficacy against Norovirus usually is based on studies using feline calicivirus (FCV) as a surrogate. However, FCV and Norovirus exhibit different physiochemical properties, and whether inactivation of FCV reflects efficacy against Norovirus is unclear.

4.2.3 When is an outbreak defined as over?

According to the Norovirus Working Group (2012) the end of an outbreak for Infection Prevention and Control (IPC) is defined, on the basis of experience, as 48 hours after the resolution of vomiting and/or diarrhoea in the last known case and at least 72 hours after the initial onset of the last new case.

In Australia, there is no consistent guideline to when an outbreak is considered to be over. In general, Norovirus outbreaks can be declared over if no new cases have occurred in 72 hours from the onset of symptoms of the last case. However, this is a difficult generalisation as Norovirus has been detected in faeces many weeks after recovery (Australian Government Department of Health and Ageing 2010).

4.2.4 Examples of Outbreaks detected on cruise ships in Australia and the South Pacific

- *November 2012* - An unofficial Royal Caribbean blog website reported that crew members on board Royal Caribbean's mega-liner Voyager of the Seas (approximately 3,100 passengers) were facing a suspected Norovirus outbreak. It is reported that 135 passengers became sick during an 18-day cruise of Australia and New Zealand. The skipper appeared guarded when asked for comment. Passengers were alerted to the Norovirus problem by a notice posted in the ship's in-house daily programme, distributed to each cabin. Passengers also received a letter as they disembarked that informed that a number of passengers had experienced gastrointestinal illness during the cruise. Guests could not serve themselves from the buffet, and were handed knives and forks. Hand sanitisers were visible all over the ship. The whole ship was to be sanitised before the ship left Sydney for Auckland (Donoghue 2012; Royal Caribbean blog 2012). The Voyager of the Seas returned to Australia with what appears to be hundreds of cruise passengers infected with the Norovirus. The boarding of new passengers was thrown into chaos. A cruise line spokeswoman denied any connection between the long lines and the Norovirus, however a new passenger received a statement which gave the Norovirus outbreak as the reason for the delay in boarding (Homes and Schneider 2012).
- *October 2012* - The Fiji Health Ministry is reported that the Royal Caribbean's Rhapsody of the Seas has been the site of 51 cases of Norovirus, which prompted health officials to quarantine the cruise ship as it was docked at Suva Wharf (Fiji News 2012).
- *March 2010* - Sydney Morning Herald reports more than 240 Australian passengers on a cruise with the Dawn Princess to New Zealand were struck down with a gastro virus. The outbreak happened three days after it left Melbourne on December 29 with about 2000 passengers. Self-service buffet services were closed down with wait-staff assisting passengers at the buffet and infected passengers were quarantined after the outbreak. All passengers were allowed to leave the ship which ended its 13-night cruise in Melbourne (Edwards 2010).

Figure 9 shows the proportion (%) of ship's passengers and crew reported on pre-arrival reports with acute gastroenteritis for cruise ships entering Sydney Harbour, July 2006 to January 2014.

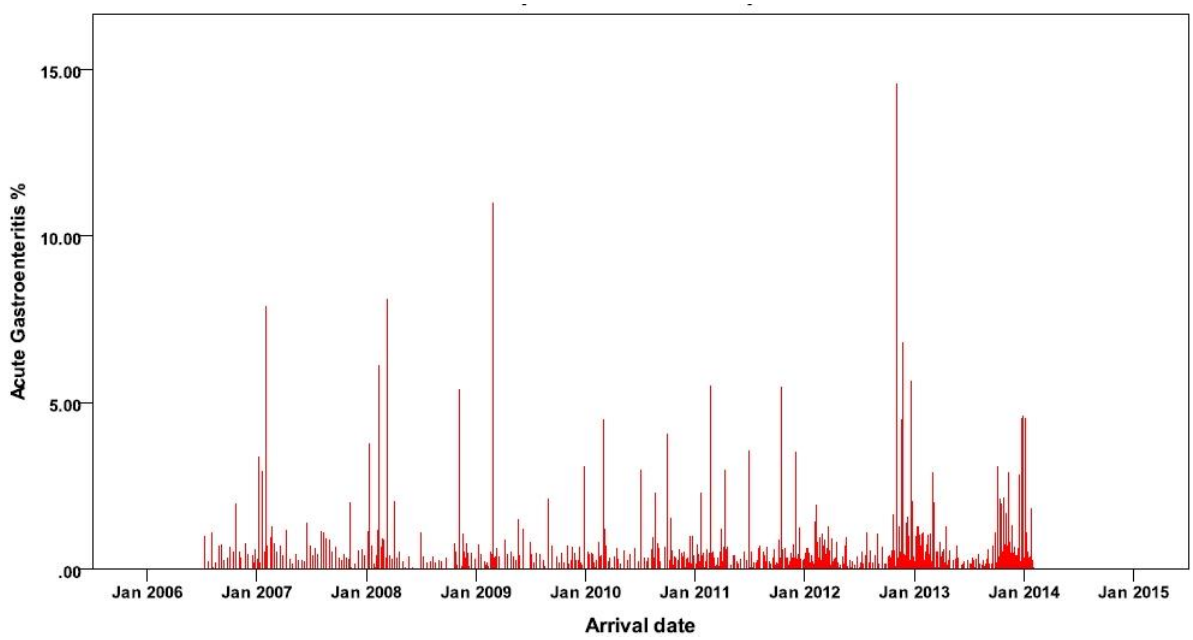

Figure 9 Proportion (%) of ship's passengers and crew reported on pre-arrival reports with acute gastroenteritis for cruise ships entering Sydney Harbour, July 2006 to January 2014 (South Eastern Sydney Local Health District Public Health Unit 2014).

4.3 Reporting

4.3.1 Reporting – Global

International health regulations require ships to report the presence of any notifiable and quarantinable diseases on their ship before they enter port. In response to requests that not all ships doctors are regularly updated on Quarantine Laws, international health regulations are being revised to make them more responsive to current and emerging infectious diseases and more responsibility put on ship owners to report and keep their crews updated (Ferson and Ressler 2005).

The US Vessel Sanitation Program (Centers for Disease Control and Prevention 2012), and the Southampton City Council Port Health Services (Southampton City Council Port Health Services 2012) provide reports on environmental health inspections and are available on their websites.

United States of America: Vessel Sanitation Program (VSP)

The Vessel Sanitation Program (VSP) was established in the 1970s by the Centers for Disease Control (CDC) as way to assist the cruise ship industry prevent and control the introduction, transmission, and spread of gastrointestinal illnesses (Centers for Disease Control and Prevention 2013). The VSP states that carriers arriving at US ports from foreign areas are subject to sanitary inspections to determine whether rodent, insect, or other vermin infestations exist, contaminated food or water, or other sanitary conditions requiring measures for the prevention of the introduction, transmission, or spread of communicable

diseases are present (Centers for Disease Control and Prevention 2013). Cruise ships participating in the program are required to report the total number of gastrointestinal illness cases (including zero cases) before the ship arrives at a US port. A separate notification is required when the illness count exceeds 3% of the total number of passengers or crew on-board. This reporting program and associated measures had led to a decrease in diarrhoea disease rates and outbreaks among cruise ship passengers (Centers for Disease Control and Prevention 2013; Cramer *et al.* 2003).

New Zealand

While in New Zealand waters, the Master of a ship must inform the local Medical Officer of Health or a health protection officer when any person on board in any harbour at any time has symptoms which may be suspected to be caused by a notifiable infectious disease.

First arrival survey programme

- During the annual cruise season public health officials may visit passenger cruise vessels making more than one round-trip visit to New Zealand. This is to ensure that the appropriate processes are in place to protect the health of passengers and crew on entering New Zealand.

Shipping agents

- Health officers will notify shipping agents in advance of visiting a vessel. This enables shipping agents to advise vessels that the visit will take place, and ensures that public health officials receive the relevant security clearance.

Public health visits

- The health officer will board the cruise vessel approximately two hours after arrival. A copy of the New Zealand Maritime Declaration of Health will be required.
- The health officer will visit the vessel's medical facilities. The vessel's gastrointestinal surveillance log will be reviewed and the illness rates checked against those reported in the Advance Notice of Arrival and the 'no change in status' message. Where there are any discrepancies an explanation will be sought and the ship's officers will be reminded of their responsibility to notify cases of illness both on arrival and while in New Zealand waters (New Zealand Government Minister of Health 2011).

4.3.2 Australia

In states and territories Norovirus outbreaks will not necessarily be reported unless the medical practitioner suspects the source to be contaminated food. Managers of institutions may report outbreaks to health departments, while seeking advice on infection control issues. Other states and territories receive notifications of Norovirus outbreaks if the outbreak is in an institution or there is a cluster of gastrointestinal illness (Australian Government Department of Health and Ageing 2010).

4.3.2.1 Commonwealth

The *Australian Quarantine Act 1908* (Cwlth) requires mandatory reporting of specified quarantinable and infectious diseases using the "Quarantine Pre-arrival Report for Vessels." This Act is administered by the Australian Quarantine and Inspection Service (AQIS). Senior

disease control staff in each state health department are authorised human quarantine officers, linking the quarantine service and state-based disease control personnel (Gostin 2004) (Ferson and Ressler 2005)

OzFoodNet—an initiative of the Australian Government—was established in 2000 to determine the burden and causes of foodborne disease in Australia. It collects and summarises national data on the causes of outbreaks of foodborne illness and gastroenteritis. Quarterly and annual reports are published in the national journal, Communicable *Diseases Intelligence*. It is important to interpret outbreak data with caution, as Norovirus is not notifiable and changes in reporting may bias results over time (Australian Government Department of Health and Ageing 2010).

A CDNA working group developed the Guidelines for the public health management of gastroenteritis outbreaks due to Norovirus or suspected viral agents in Australia. The guidelines are designed to assist state and territory health departments and public health units manage outbreaks of gastroenteritis due to Norovirus or suspected viral agents and provide advice to aged care homes regarding management of suspected viral outbreaks. The guidelines complement existing state and territory protocols. The guidelines and were endorsed by CDNA and the Australian Health Protection Committee (AHPC) in early 2010 (OzFoodNet 2009, Australian Government Department of Health and Ageing 2010).

There are several websites which provide information and guidelines about infectious diseases, including Norovirus:

- *Staying healthy in child care: preventing infectious diseases in child care, 4th edition* National Health and Medical Research Council, Australian Government, December 2005 (*http://www.nhmrc.gov.au/publications/synopses/ch43syn.htm*)
- *Infection control guidelines for the prevention of transmission of infectious diseases in the health care setting,* Australian Government Department of Health and Ageing, January 2004 (*http://www.health.gov.au/internet/main/publishing.nsf/Content/icg-guidelines-index.htm*)
- *Australian guidelines for the prevention and control of infection in healthcare* – NHMRC 2010 (*http://www.nhmrc.gov.au/guidelines/publications/cd33*)

State/Territory Legislation

Statutory reporting of disease on international vessels is governed by state/territory public health legislation, Australian quarantine legislation and the International Health Regulations..

The *Australian Quarantine Act* 1908 requires mandatory reporting of specified quarantinable and infectious diseases using the “Quarantine Pre-arrival Report for Vessels (Pratique)”. This Act is administered by the Australian Quarantine and Inspection Service (AQIS). The International Health Regulations require all ships’ masters to report the presence of quarantinable diseases on the vessel before they enter port. However, ships’ doctors, who report on behalf of ships’ masters, have often not been aware of the *Quarantine Act* requirements to report other infectious diseases.

In Australia, generally, Norovirus infection in individual patients is not notifiable in any state or territory, therefore statistics are not available for the number of patients infected each year (Australian Government Department of Health and Ageing 2010).

In states and territories where only foodborne or waterborne illness is notifiable, Norovirus outbreaks will not necessarily be reported unless the medical practitioner suspects the source to be contaminated food (Australian Government Department of Health and Ageing 2010). State and territory health departments vary in their requirements and mechanisms for reporting Norovirus outbreaks or outbreaks of gastroenteritis and when outbreaks should be investigated (Australian Government Department of Health and Ageing 2010).

Table 8 State and Territory Legislation (statutory notification of infectious diseases acts)

State or Territory	Required?	Legislation
Nationally	No, nor is Gastro	***National Health Security Agreement 2008*** http://www.health.gov.au/casedefinitions
ACT	No, but Gastro illness cluster is	***Public Health Act 1997*** https://www.google.com.au/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&cad=rja&uact=8&ved=0CCkQFjAA&url=http%3A%2F%2Fwww.health.act.gov.au%2Fc%2Fhealth%3Fa%3Dsendfile%26ft%3Dp%26fid%3D1152510217&ei=arwvU4DLHYbxlAXpjYC4Cg&usg=AFQjCNEXjgMnNydBoh10FrDvfPiI4GO4hg
NSW	No, nor is Gastro	***Public Health Act 2010*** http://www.health.nsw.gov.au/Infectious/Pages/data.aspx
NT	No, but Gastro is	***Notifiable Diseases Amendment Act 1985*** http://www.health.nt.gov.au/library/scripts/objectifyMedia.aspx?file=pdf/20/49.pdf&siteID=1&str_title=Notifiable%20conditions%20to%20be%20reported%20in%20the%20NT.pdf
Qld	No, nor is Gastro	***Public Health Act 2005*** http://www.health.qld.gov.au/ph/documents/cdb/notif_conditions_rpt.pdf
SA	Unclear	***Public Health Act 2011*** http://www.sahealth.sa.gov.au/wps/wcm/connect/public+content/sa+health+internet/resources/notifiable+conditions+south+australian+public+health+act+2011?contentIDR=d73346804cacb033add9bda496684d9f&useDefaultText=1&useDefaultDesc=1
Tas	No, but Gastro in an institution is	***Public Health Act 1997*** http://www.dhhs.tas.gov.au/__data/assets/pdf_file/0003/53319/Notifiable_Diseases_Guideline_FINAL_Feb_2010.pdf
Vic	No, nor is Gastro	***Public Health and Wellbeing Act 2008*** http://ideas.health.vic.gov.au/notifying.asp
WA	No, nor is Gastro	***Health Act 1911*** http://www.public.health.wa.gov.au/3/284/2/notifiable_communicable_diseases.pm

Managers of institutions may also report outbreaks to health departments, while seeking advice on infection control issues. It will be at the discretion of the PHU how they wish to proceed with the report or investigation (Australian Government Department of Health and Ageing 2010).

Under Australian quarantine laws, ships are required to report gastroenteritis outbreaks to AQIS/DAFF Biosecurity before entering each port. For ships entering the Port of Sydney, this information is also provided to the Public Health Unit for South Eastern Sydney Local Health District. During November and December 2012, of 62 cruise ship voyages arriving in Sydney, Norovirus outbreaks were reported in 6 cases (NSW Department of Health 2013).

New South Wales (NSW)

The individual state of NSW is included here because it is Australia's principal turnaround port (along with Brisbane and Melbourne). In NSW, over the past decade, but particularly since 1998, staff of the South Eastern Sydney Public Health Unit (PHU) has worked with Sydney-based shipping lines operating international cruises to improve health surveillance on cruise ships. The major change has been from reporting of quarantinable diseases only when a case occurs to the routine reporting of all infectious diseases of public health interest for every cruise. A report must be filed even when there are no cases to report. Although this reporting is voluntary, it is consistent with the requirements of the *Public Health Act 1991* (NSW), the *Quarantine Act 1908* (Cwlth) and the International Health Regulations (Ferson and Ressler 2005).

The Cruise Ship Health Surveillance Program complies with the Australian Quarantine Act 1908 which requires that all vessels arriving in Australia from international waters submit quarantine pre-arrival reports to Australian Quarantine and Inspection Services (AQIS), through the ship's Australian agent, 12 to 96 hours prior to arrival in their first Australian Port. At the same time as sending pre-arrival reports to AQIS, the vessel masters, senior doctors or shipping agents also email these reports directly to the Public Health Unit when Sydney is the first Australian port (Ressler and Ferson 2011). Involvement in this program is by voluntary agreement.

Cruise ships visiting Australia are categorised as:

- Level 1 (report directly to the public health unit),
- Level 2 (will contact public health if the need arises), and
- Level 3 (do not know about the program run by AQIS, information can be forwarded to the Public Health Unit from AQIS) (Ressler and Ferson 2011).

Between July 2006 and June 2011, 566 voyages of 65 different ships carrying over 1.3 million passengers and crew were recorded in the program's databases as having docked in the ports of Sydney, i.e. Sydney itself, and Botany Bay. The program received pre-arrival reports from 258 (76%) of the 338 voyages made by ships whose operators agreed to participate. Of the 65 ships visiting Sydney over the five-year period, eight participated in the Level 1 program. An additional 10 ships were categorised in level 2, and the remaining 47 ships had not been approached to participate and were categorised as level 3. Pre-arrival reports for 21 ships that were not participating in the program were received either from AQIS when a ship was inspected by the Public Health Unit's Environmental Officers (Ressler and Ferson 2011).

4.3.2.2 States and Territories

The following table (

Table 9) details the state and territory information documents currently available dealing with Norovirus outbreaks.

Table 9 State and Territory Norovirus Information links

State or Territory	Title	Link
Australia	Guidelines for the public health management of gastroenteritis outbreaks due to norovirus or suspected viral agents in Australia, Appendix 1: further sources of information on norovirus	*http://www.health.gov.au/internet/publications/publishing.nsf/Content/cda-cdna-norovirus.htm-l~cda-cdna-norovirus.htm-l-app1*
ACT	Norovirus: Gastroenteritis	*http://www.health.act.gov.au/c/health?a=sendfile&ft=p&fid=276255991&sid=*
NT	Reporting of notifiable diseases by doctors.	*http://health.nt.gov.au/library/scripts/objectifyMedia.aspx?file=pdf/11/02.pdf&siteID=1&str_title=Notification%20form.pdf*
WA	Norovirus information for health professionals.	*http://www.public.health.wa.gov.au/3/609/3/Norovirus.pm*

4.4 Current control measure and treatment options

There are a number of aspects with public health significance that can influence the health of cruise ship passengers and crew members including food, water and air quality; the presence of vectors (such as mosquitos and ticks that can carry and transmit disease) and waste produced and carried on board; and even travellers' behaviour. Hazards that arise from these factors should be effectively managed in order to prevent disease occurrence. Scientific published papers that describe outbreaks and diseases related to ships contain useful information which can be used in planning preventive measures. Useful international guidance has been published by international and national organisations and authorities relevant to public health on ships (Mouchtouri *et al.* 2010). The WHO Guide to Ship Sanitation covers preventive environmental health management, disease surveillance, outbreak investigation, and routine inspection and audit. It provides a framework for policy making and local decision making (Mouchtouri *et al.* 2010).

5. Conclusion

Noroviruses are perhaps the perfect human pathogens. These viruses possess essentially all of the attributes of an ideal infectious agent: they are highly contagious, rapidly and prolifically shed, constantly evolving, evoking limited immunity, and only moderately virulent, allowing most of those infected to fully recover, thereby maintaining a large susceptible pool of hosts. With limited current vaccines or other treatments available, nutraceuticals and probiotics are an area warranting further investigation. They have the potential to reduce the duration and severity of diarrhoea and thus may be a safe intervention.

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