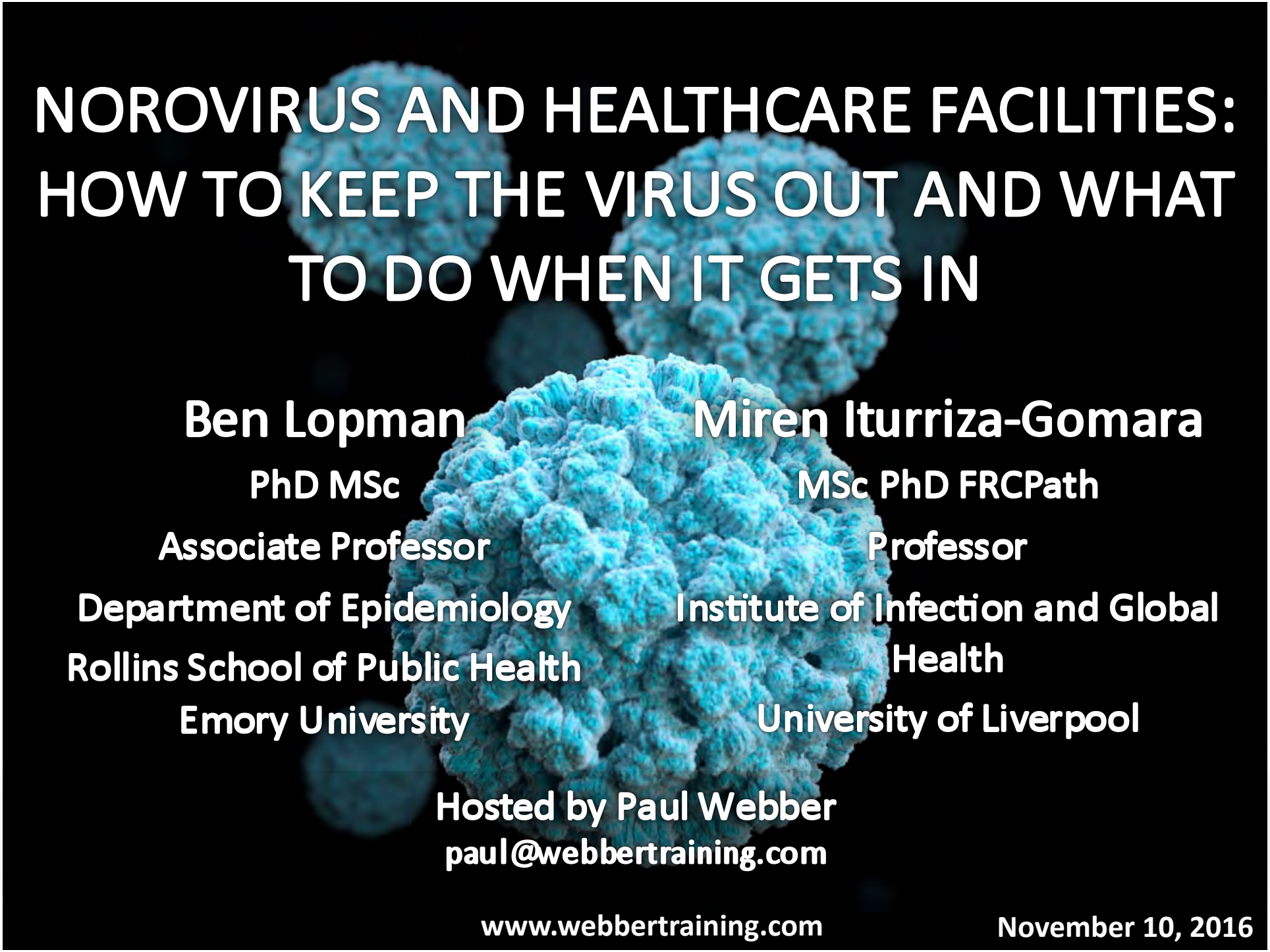
NOROVIRUS AND HEALTHCARE FACILITIES: HOW TO KEEP THE VIRUS OUT AND WHAT TO DO WHEN IT GETS IN



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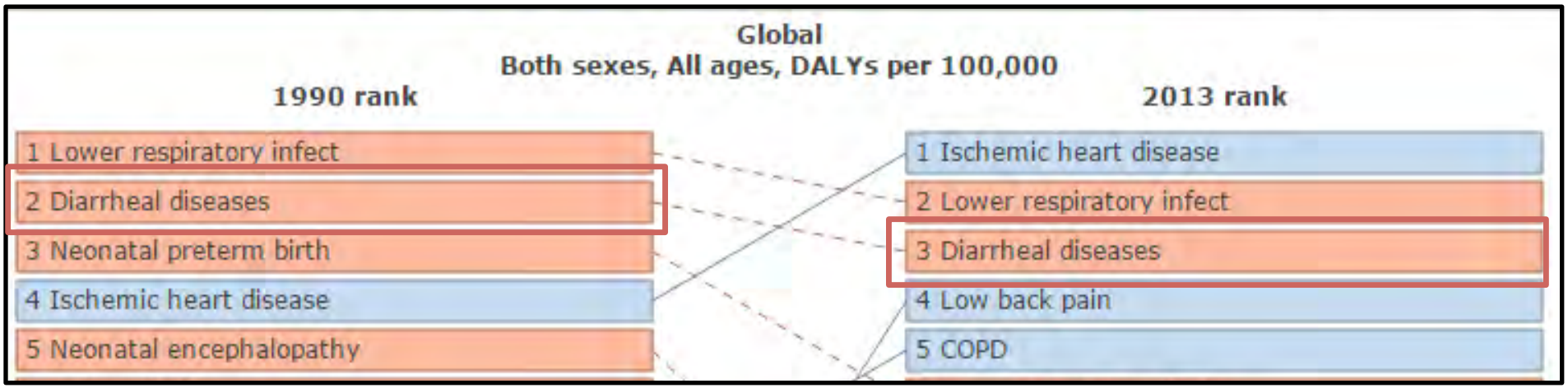
Outline

1. Global burden and epidemiology
2. Outbreaks in health care facilities
3. Control

1. Virology
2. Clinical Disease
3. Vaccines

Global burden and epidemiology

Progress against diarrheal diseases…



…much work to be done still

Nearly 1 million under 5 deaths/year

Rotavirus : 250,000 to 500,000

Norovirus: 70,000 to 200,000

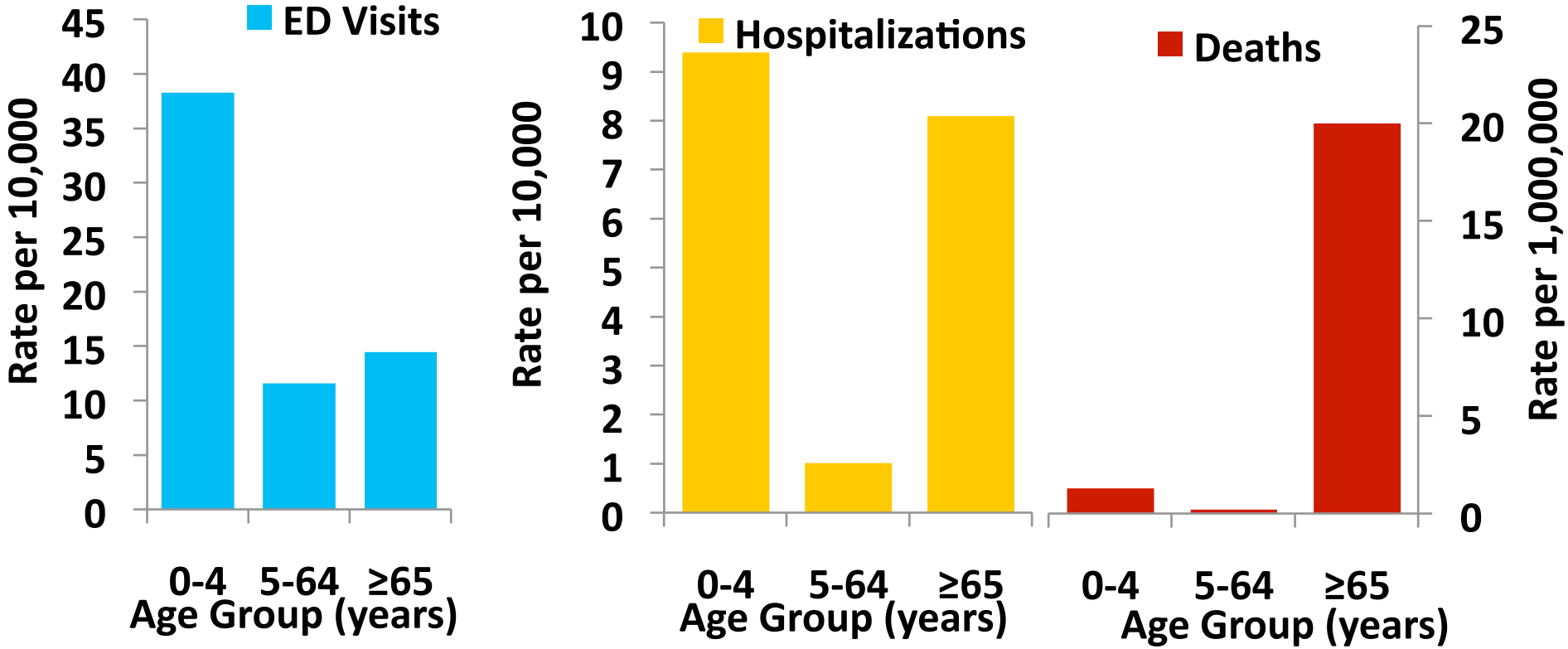
Challenges in estimating [global] burden of norovirus

Diagnostics: availability	Diagnostics: interpretation
Not coded for in ICD-data	Sub-clinical cases
Little surveillance	Few community studies

PLOS MEDICINE

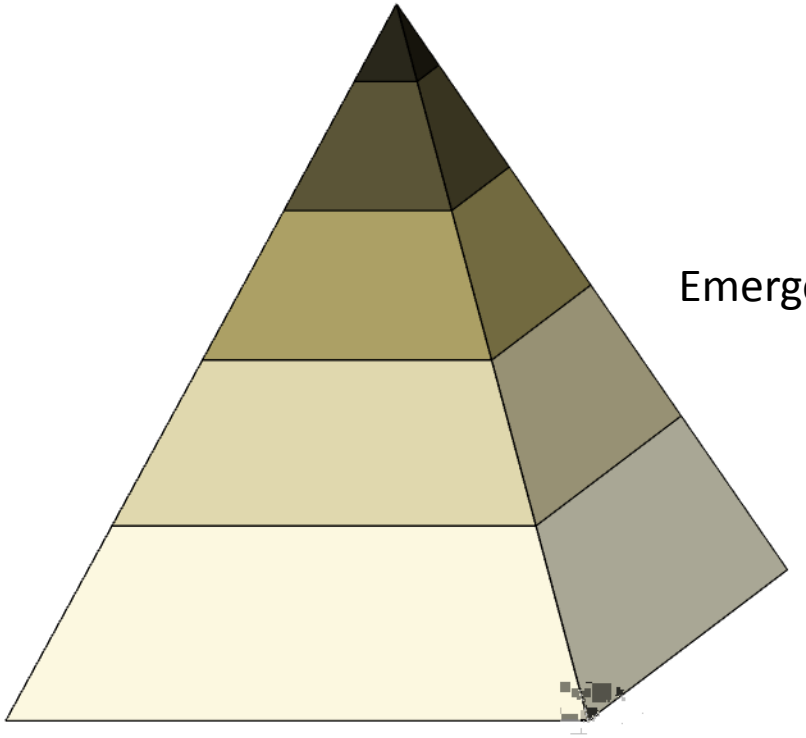
Lopman, Steele, Parashar, PLOS Medicine, 2016

Age Specific Clinical Outcomes of Norovirus in the United States



Hall, Curns, McDonald, Parashar, Lopman, 2012 CID
Lopman, Hall, Curns, Parashar, 2011 CID
Gastañaduy, Hall, Curns, Parashar, Lopman, 2013 JID

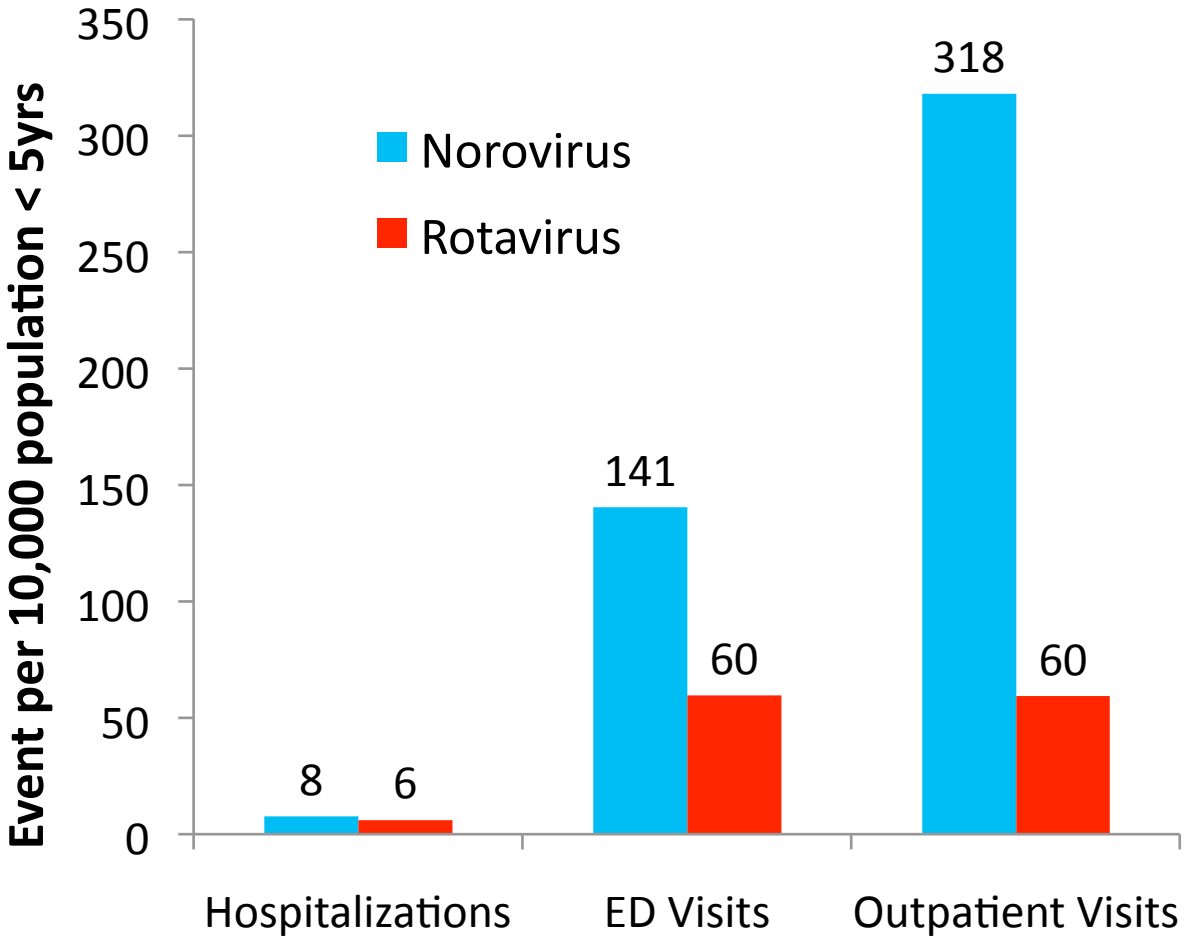
Norovirus disease burden in the United States



	Annual estimate	Lifetime risk
Deaths	800	1 in ~6,000
Hospitalizations	71,000	1 in ~60
Emergency department visits	400,000	1 in ~9
Outpatient visits	1.8 million	1 in ~2
Cases	19 to 21 million	5 times

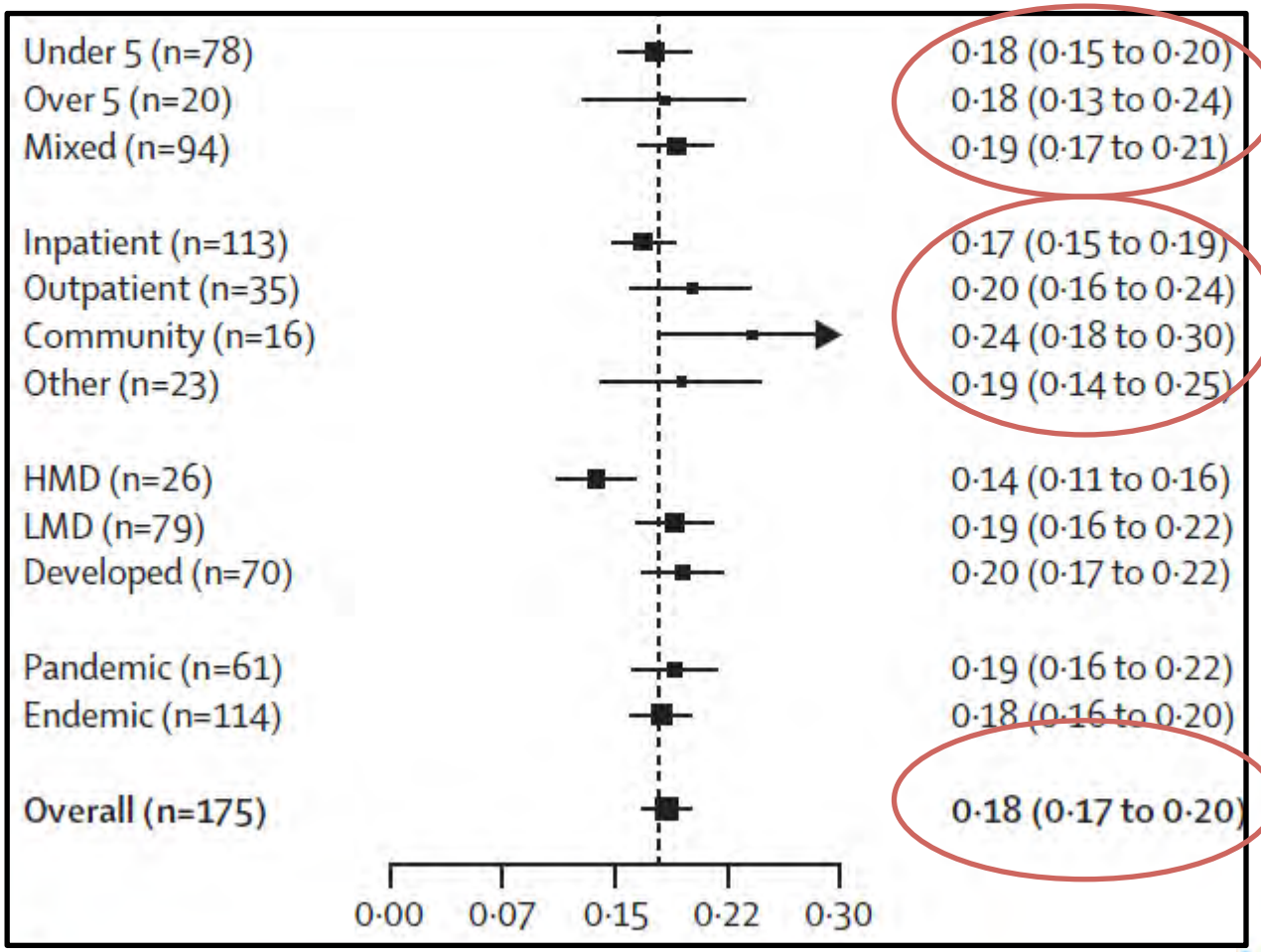
Hall, Lopman, Payne, Patel, Gastañaduy, Vinjé, Parashar,2013 EID
Hall, Curns, McDonald, Parashar, Lopman, 2012 CID
Lopman, Hall, Curns, Parashar, 2011 CID
Gastañaduy, Hall, Curns, Parashar, Lopman, 2013 JID
Scallan et al, 2010 EID

Norovirus and Rotavirus Hospitalization, ED and outpatient rates
0 – 4 year olds
2009 to 2010



Payne et al, NEJM, 2013

Global prevalence of norovirus among cases of AGE



World Health Organization

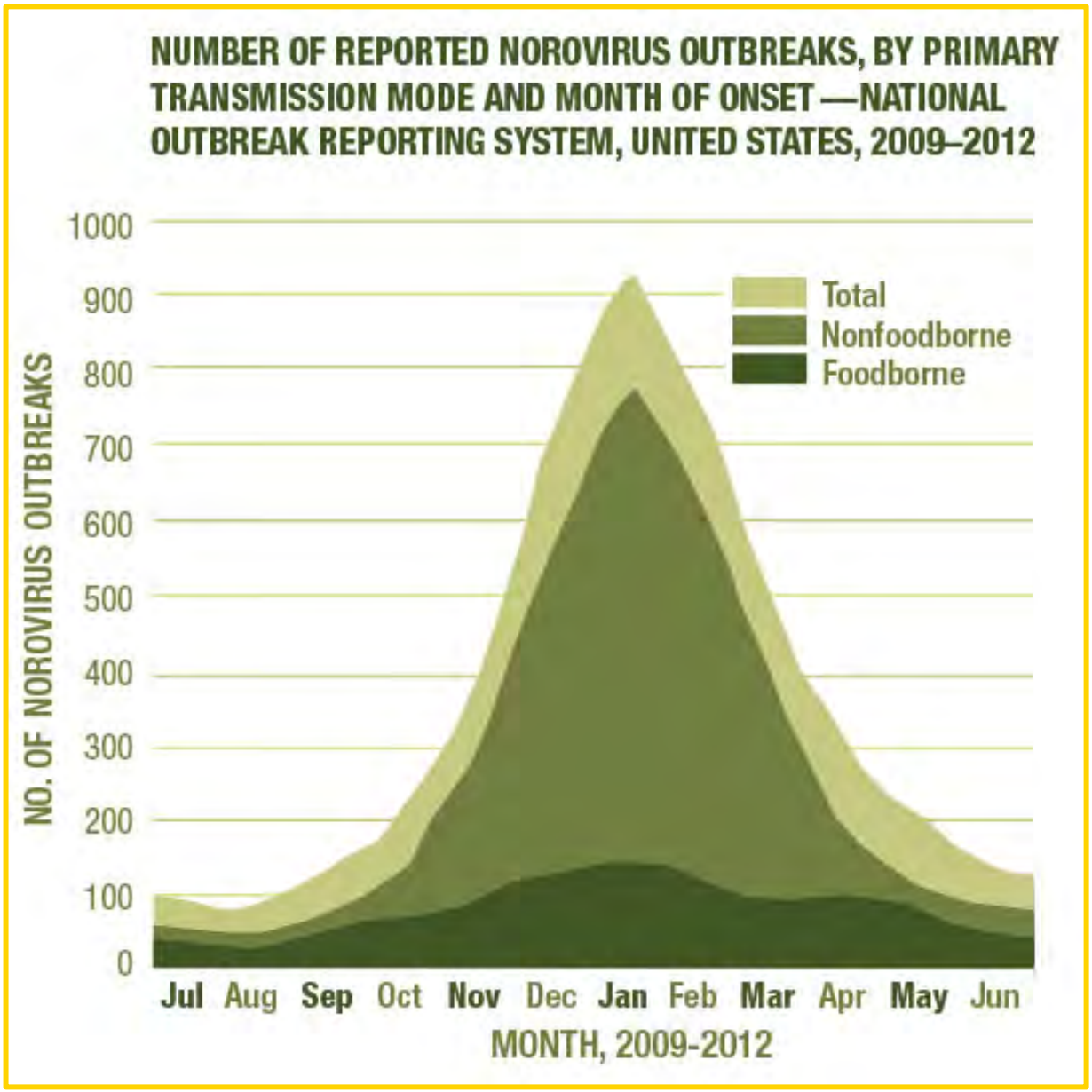
Ahmed, Hall, Robinson, Verhoef, Premkumar, Parashar, Koopmans, Lopman, *Lancet Infectious Diseases*, 2014

Global Burden of Norovirus

- WHO Foodborne Disease Burden Epidemiology Group (FERG)
- Global and regional age-stratified estimates of deaths, and DALYs
- Norovirus ranking as foodborne hazard:
  - #1 cause of foodborne illness
  - #4 cause of foodborne deaths
  - #5 cause of foodborne DALYs
- Total norovirus burden annually:
  - 685 million cases; 200 million in children <5
  - 212,489 deaths; 54,214 in children <5
  - 85% of illnesses and 99% of deaths occur in developing countries
  - $60 billion in direct health system costs and productivity loses

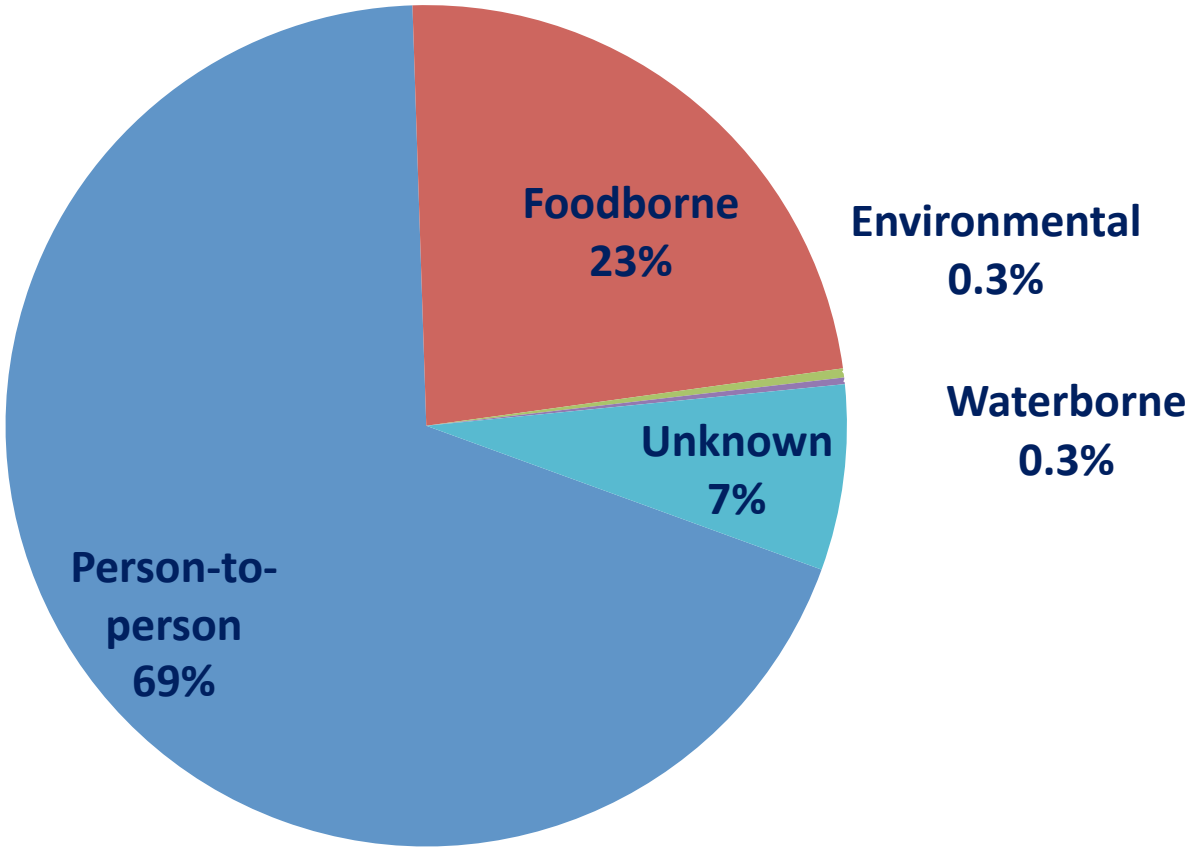
Pires 2015 PLoS One; Kirk 2015 PLoS Med; Bartsch 2016 PLoS One; Hall 2016 Exp Rev Vac

Outbreaks in health care facilities



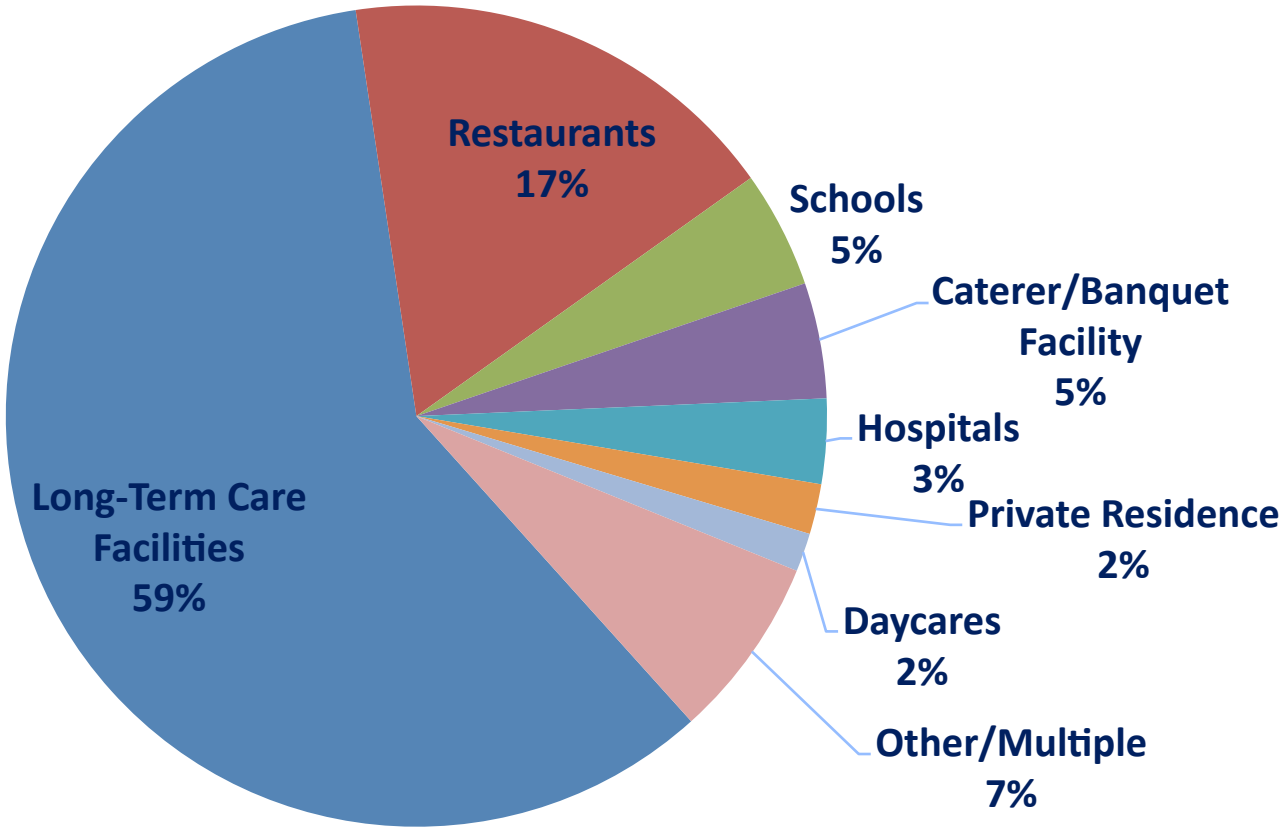
http://www.cdc.gov/norovirus/trends-outbreaks.html

Transmission Mode of Norovirus Outbreaks, NORS, 2009-2012 (N=4,318)



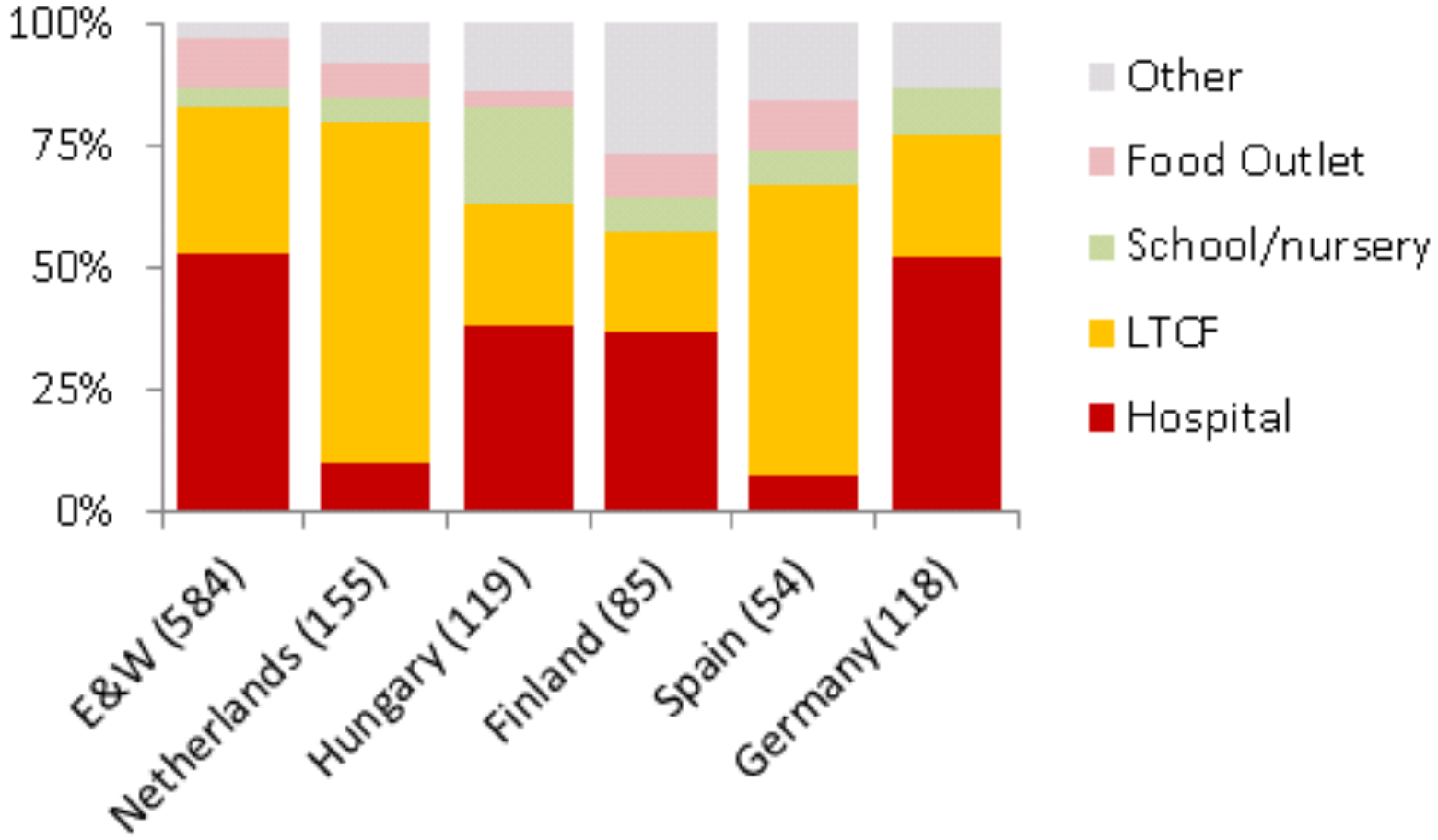
Hall et al, MMWR Morb Mortal Wkly Rep. 2014

Setting of Norovirus Outbreaks, NORS, 2009-2012 (N=3,243)



Hall et al, MMWR Morb Mortal Wkly Rep. 2014

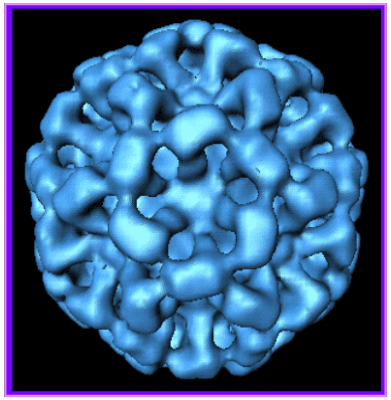
Setting of 1115 Norovirus Outbreaks in Six European Counties, 2002



Lopman 2004 Lancet

Virology and Clinical Disease

Noroviruses



- *Caliciviridae*
- Non-enveloped small round structured viruses (28-35 nm diameter)
- Genome: + sense ssRNA ~ 7.5k
- Endemic in children

- The most common cause of outbreaks of gastroenteritis in the UK
- Burden to health service
  - seasonal appearance
  - cost: £115m/year in nosocomial outbreaks

  (Lopman et al 2005)

Norovirus
Clinical manifestations

Nausea - 79%
Vomiting - 69%
Diarrhoea - 66%
Fever - 37%
Chills - 32%
Abdominal cramps - 30%
Myalgias -26%
Headache - 22%
Sore throat - 18%

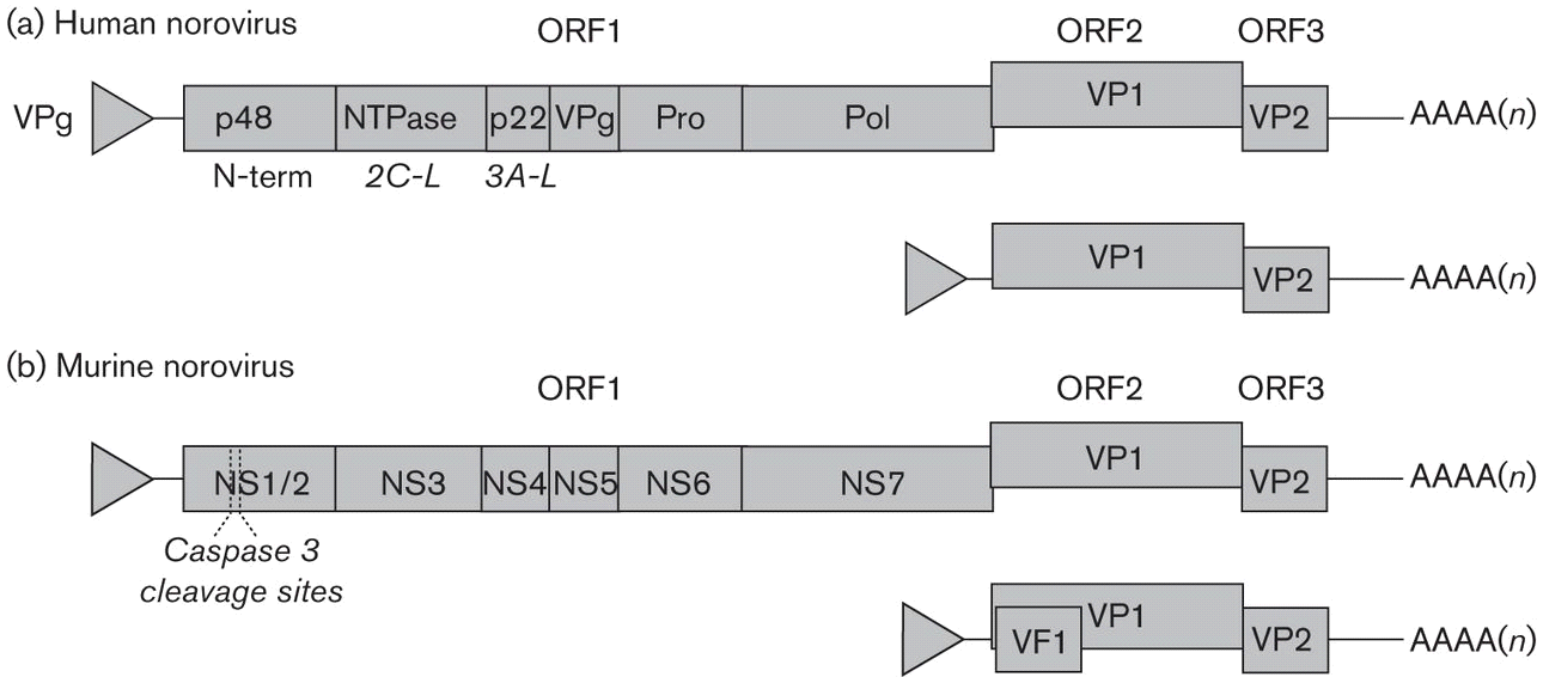
Incubation period: 10-50h
Duration of symptoms: 24-48h

High attack rate

Low infectious dose
(10 virus particles)

Asymptomatic infections
are common

NoV Genome Organisation

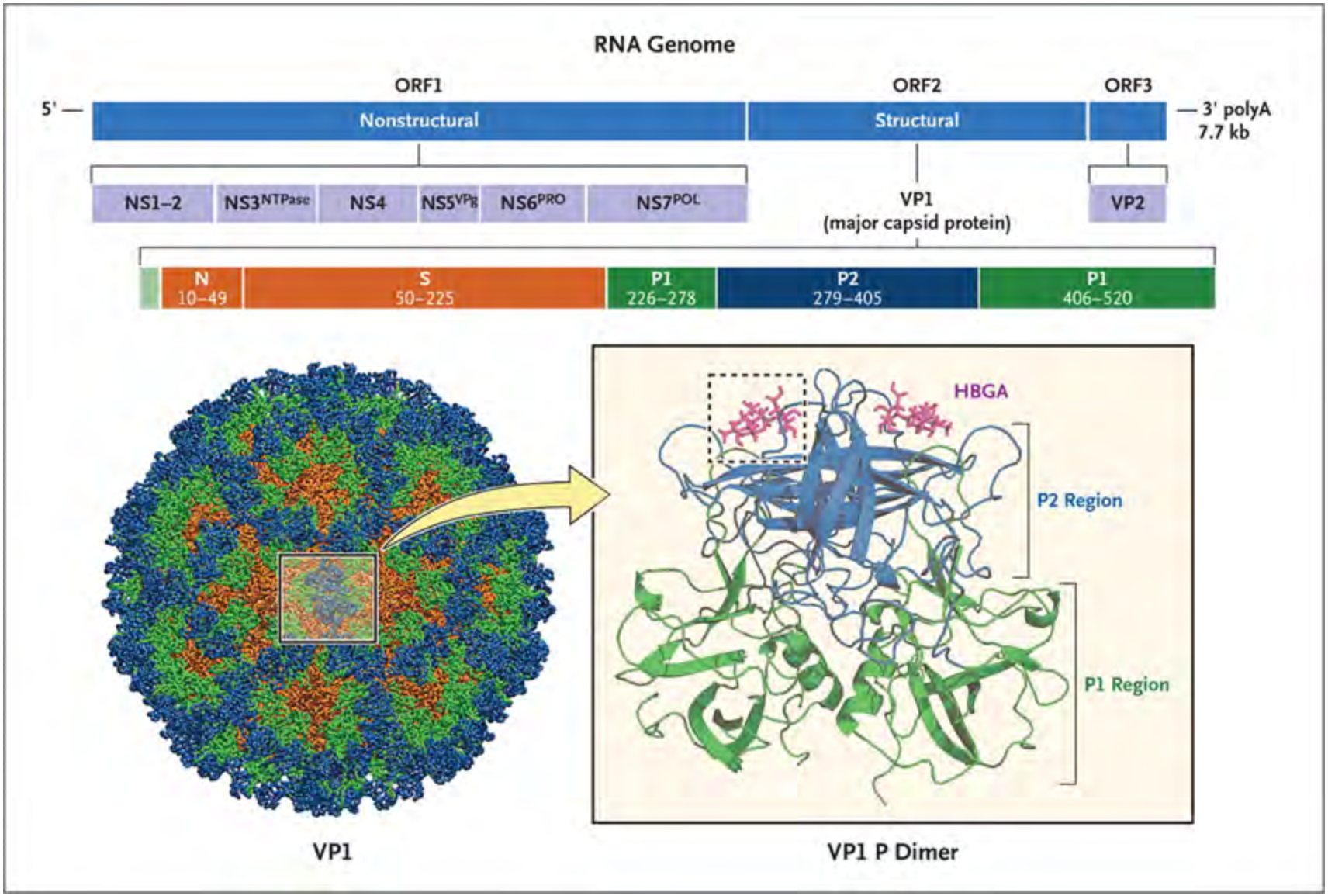


The HuNV genome is covalently attached to VPg (NS5) with a poly(A) tail and is divided into three ORFs, common to all noroviruses. ORF1 is translated as a polyprotein, which is cleaved by the viral protease NS6 to produce the NS proteins. ORF2 and ORF3 are translated from a subgenomic RNA.

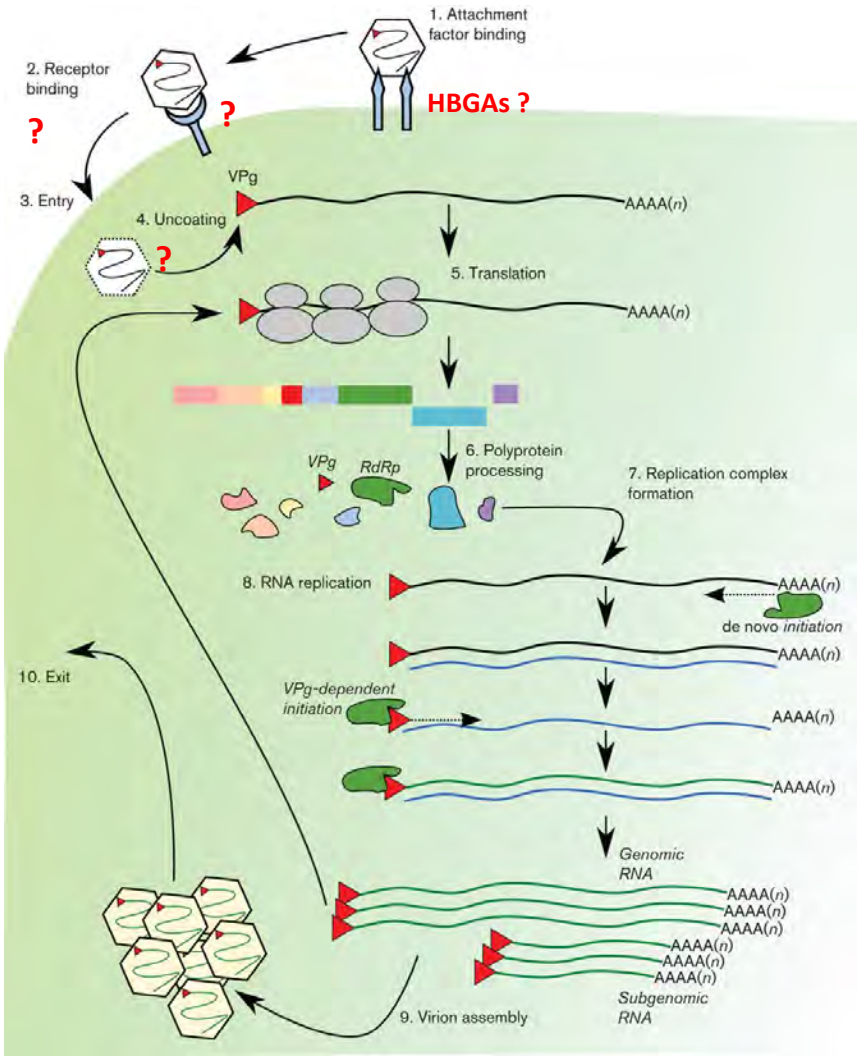
MNV has an additional alternative fourth ORF. ORF4 overlaps with ORF2 and is also translated primarily from the subgenomic RNA into the virulence factor 1 (VF1) protein.

Nomenclature for HuNV and MNV proteins and their functions

MNV	HuNV*	Function
NS1/2	p48 (N-term)	Replication complex formation, contributes to persistence in MNV infections
NS3	NTPase (2C-like)	RNA helicase/NTPase
NS4	p22 (3A-like)	Replication complex formation
NS5	VPg	Genome-linked protein involved in translation and replication
NS6	Pro (3C-like)	Protease
NS7	Pol/3Dpol	RdRp
VP1	VP1	Major capsid protein
VP2	VP2	Minor capsid protein
VF1	No equivalent	Virulence factor


RNA Genome
ORF1
ORF2
ORF3
5' —
Nonstructural
Structural
— 3' polyA
7.7 kb
NS1–2
NS3NTPase
NS4
NS5VPg
NS6PRO
NS7POL
VP1
(major capsid protein)
VP2
N
10–49
S
50–225
P1
226–278
P2
279–405
P1
406–520
HBGA
P2 Region
P1 Region
VP1
VP1 P Dimer

Outline of the norovirus life cycle.



Thorne L G , and Goodfellow I G J Gen Virol 2014;95:278-291

(1) HuNV and MNV are thought to attach to the cell surface using various carbohydrate attachment factors. **This is not sufficient to mediate entry and binding to an unidentified protein receptor is thought to be required**.

(2). Entry (3) and uncoating (4) proceed through as-yet-undefined pathways.

(5) The viral genome is translated, through interactions with VPg at the 5′ end of the genome (red triangle) and the cellular translation machinery.

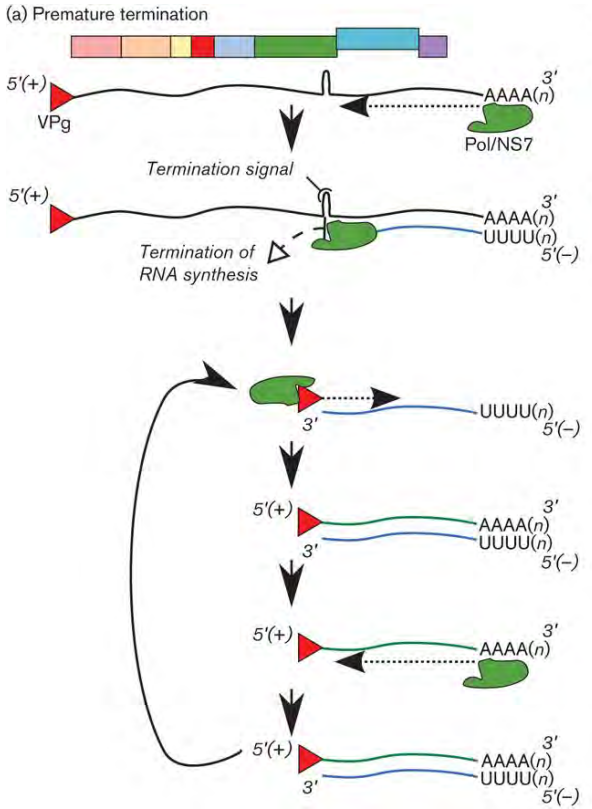
(6) The ORF1 polyprotein is co- and post-translationally cleaved by the viral protease NS6.

(7) The replication complex is formed by recruitment of cellular membranes to the perinuclear region of the cell (not shown), through interactions in part with NS1/2 and NS4.

(8) Genome replication occurs via a negative-strand intermediate, and genomic and subgenomic RNA are generated by the viral RdRp (NS7), using both *de novo* and VPg-dependent mechanisms of RNA synthesis.

(9) The replicated genomes are translated (within the replication complex) or packaged into the capsid, VP1, for virion assembly and exit (10).

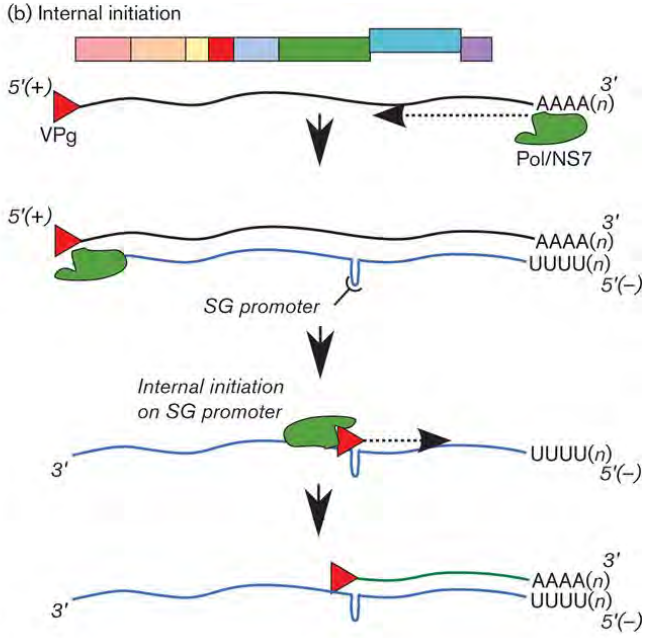
Mechanisms of norovirus subgenomic RNA synthesis



I. The presence of a termination signal upstream of the VP1-coding region results in premature termination during negative-sense RNA synthesis by the viral RNA polymerase (NS7/Pol).

II. The resulting negative-sense subgenomic RNA (blue) is then used for VPg-dependent RNA synthesis to produce a subgenomic dsRNA.

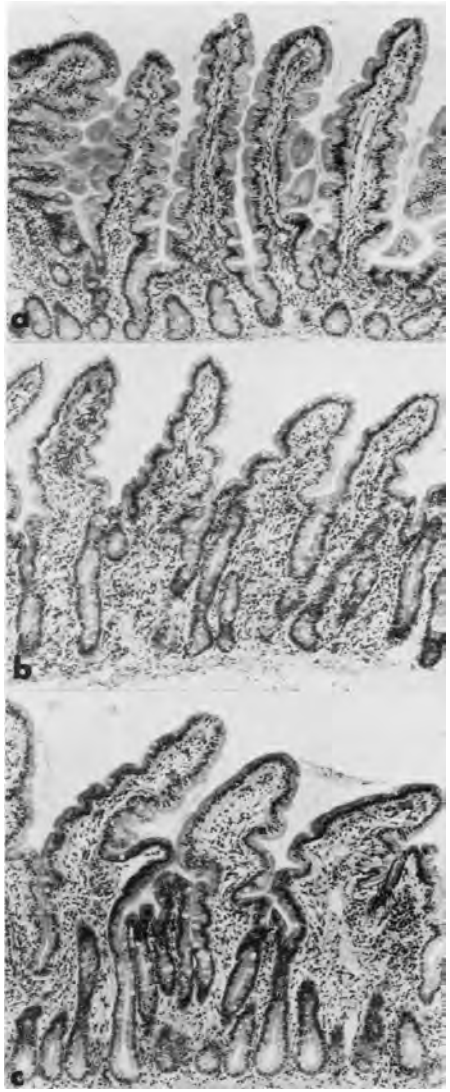
III. The newly synthesized positive-sense 'daughter' subgenomic RNA (green) can then be used as a template for the synthesis of negative-sense subgenomic RNA. These in turn function as templates for additional rounds of 'daughter' subgenomic RNA synthesis.



I. (b) The internal initiation model relies on the VPg-dependent subgenomic RNA synthesis occurring on a promoter sequence present downstream of the VP1-coding region on the negative-sense RNA

II. The viral RNA polymerase initiates RNA synthesis, presumably in a VPg-dependent manner, to produce new 'daughter' VPg-linked subgenomic RNA (green), which may in turn function as a template for additional rounds of subgenomic RNA synthesis as in the premature termination model.

Pathogenesis



The pathological basis of human norovirus-induced diarrhoea is not well understood.

Norovirus infection leads histopathological changes in the small intestine including broadening and blunting of the villi.

There is transient malabsorption of d-xylose, fat, and lactose, which could be related to shortened microvilli and decreased brush border enzyme activity

Intestinal inflammation is modest, with the exception of a significant increase in intraepithelial cytotoxic T cells reported in one small cohort of naturally infected subjects

The available data suggest that human norovirus-induced diarrhoea is not caused by structural damage of the intestinal wall but instead by alterations of secretory and/or absorptive processes.

Human norovirus infections are typified by a high incidence of vomiting episodes but the underlying pathophysiology of this manifestation is also undefined. One study of infected volunteers noted a marked delay in gastric emptying, possibly due to abnormal gastric motor function.

Biopsies of the Small Intestine before and after Oral Ingestion of Norwalk Agent (Hematoxylin and Eosin Stain X100).
(a) Before ingestion villi are tall, and the cellularity of the lamina propria is normal.
(b) Two days after ingestion the villi are shortened, the crypts are hypertrophied and contain increased numbers of mitoses, and the cellularity of the lamina propria is increased.
(c) Six days after ingestion shortened villi, hypertrophied crypts and increased mitoses persist.

David S. Schreiber, M.D., Neil R. Blacklow, M.D., and Jerry S. Trier, M.D. N Engl J Med 1973; 288:1318-1323June 21, 1973DOI: 10.1056

Characteristics of NoV animal models

Host	Virus Strain	Route	In Vivo Viral Antigen	Intestinal Disease	Fecal Shedding (dpi)	Viremia	Stomach Tropism	Small Intestinal Tropism	Large Intestinal Tropism	MLN Tropism	Peripheral Tissue Tropism
Humans	HuNoVs	peroral	intestinal monocytes, lamina propria cells	severe diarrhea and vomiting	yes (widely variable)	+/?	N/A	+	N/A	N/A	N/A
Chimpanzees	HuNoV GI.1	peroral; intravenous	intestinal DC and B cells	asymptomatic	+ (2–42)	–	N/A	+	N/A	N/A	+
Gnotobiotic pigs	HuNoV GII.4	peroral	IECs	mild diarrhea	+ (1–4)	+	N/A	+	N/A	N/A	N/A
Gnotobiotic calves	HuNoV GII.4	peroral	IECs and intestinal M?b	mild diarrhea	+ (1–6)	+	N/A	+	N/A	N/A	N/A
Balb/c RAG/γc?/? mice	HuNoV GII.4 pool	intraperitoneal	M?b in spleen and liver	asymptomatic	–	N/A	+	+	+	+	+
Wild-type mice	MuNoVs	peroral	intestinal M? and DCb	asymptomatic	+ (1–?56)	N/A	+/?	+	+	+	+/?
Interferon?/? mice	MuNoVs	peroral	M? and DCb; IECs	severe diarrhea	+	+	+	+	+	+	+
Malnourished mice	MuNoVs	peroral	N/A	modest weight loss	+ (1–?50)	N/A	+	+	+	+	+

NoVs Infect Innate Immune Cells

- Upon crossing the epithelial barrier, viral particles next encounter immune cells in the lamina propria and lymphoid follicles, including Peyer's patches, although intestinal epithelial cells are also infected in case of bovine NoV .

- MuNoV replicates in antigen-presenting dendritic cells and macrophages *in vitro* in a lytic cycle. *In vivo*, MuNoV antigen is detectable in cells morphologically resembling dendritic cells and macrophages and in cells positive for the macrophage marker F4/80.

- HuNoV appears to target intestinal immune cells *in vivo* consistent with the tropism of MuNoV: Viral antigen was detected in intestinal lamina propria cells from a biopsy sample of a HuNoV-infected person and inactivated HuNoV particles bind to lamina propria cells in human intestinal tissue sections.

NoVs Infect Adaptive Immune Cells *In Vitro*.

- In addition to macrophages and dendritic cells, B cells were recently identified as targets of NoV infection

Enteric Bacteria Serve as a Co-Factor for NoV Infection:

- Both HuNoV and MuNoV productively infect B cell lines *in vitro*, establishing the first cell culture system for HuNoV.
- B cell infection appears to be distinct from macrophage or dendritic cell infection in that no cytopathic effect is observed in infected cultures.
- Enteric bacteria can enhance viral infections (eg poliovirus, reovirus, and mouse mammary tumor virus infections are reduced in antibiotic-treated or germ-free mice).
- Antibiotic treatment of mice results in a significant reduction in MuNoV yield in the intestine when compared to untreated mice.
- Thus, commensal bacteria can stimulate MuNoV infections *in vivo* and may influence the immune response to viral infection. Although enteric bacteria are not required for MuNoV infection *in vitro* , they significantly enhance HuNoV infection of B cells *in vitro*.

Potential mechanism(s) of bacterial enhancement of enteric virus infection

- Binding to bacterial lipopolysaccharide (LPS) is one mechanism (eg Polio) but LPS does not enhance HuNoV infection of B cells in vitro.

- Instead, HBGA-expressing bacteria and free HBGA stimulate HuNoV infection of B cells, while non-HBGA-expressing bacteria do not:

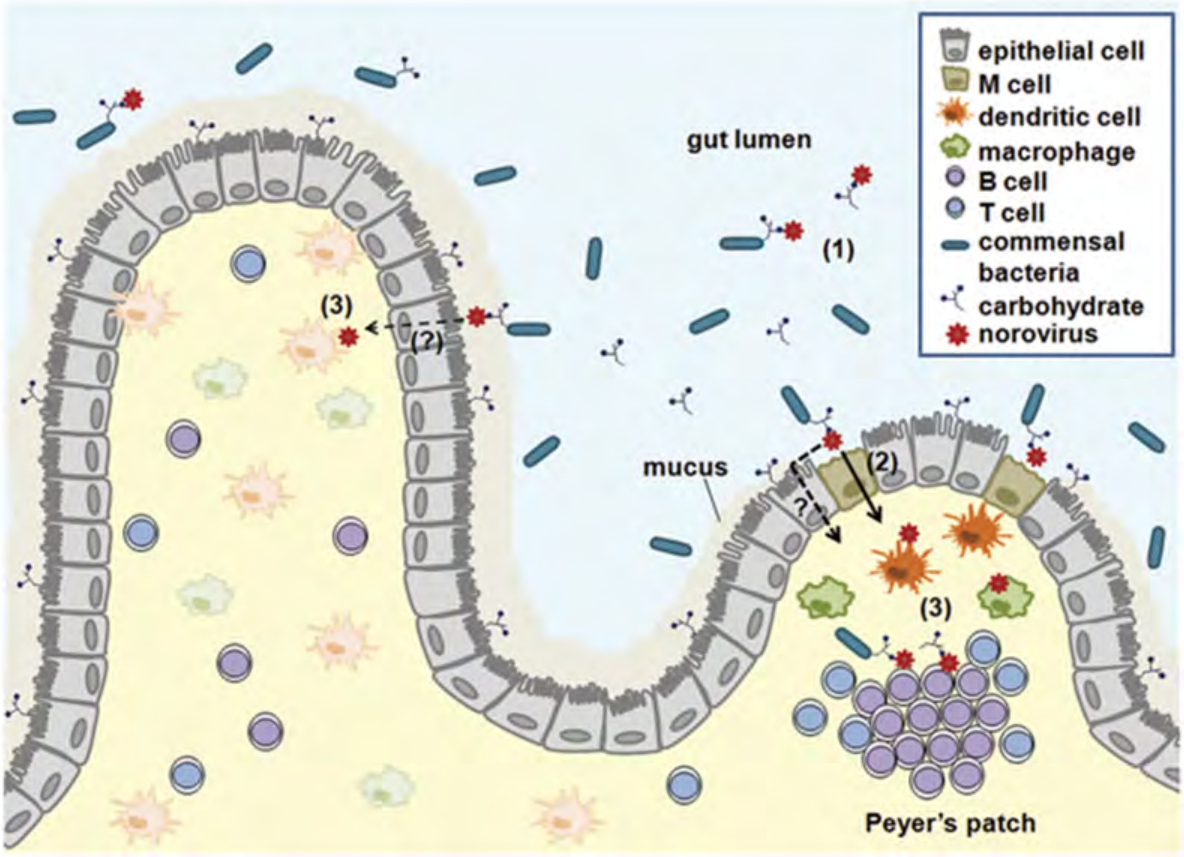
- HBGAs are neutral carbohydrates found on proteins or lipids that are bound by individual HuNoV strains and their expression correlates with a person's susceptibility to infection. However, expression of appropriate HBGAs on enterocytes in culture does not mediate infection.

- Some pathogenic and commensal enteric bacteria also express carbohydrates indistinguishable from human HBGAs, and HuNoV particles bind to HBGA-expressing bacteria. Interaction of HuNoV with free or bacteria-bound HBGAs enhances attachment to, and infection of, B cells (MuNoV binds carbohydrates such as sialic acids which are abundant on the surface of enteric bacteria)

- Bacteria may also play additional roles in vivo by enhancing the transcytosis of NoVs across the intestinal epithelium. While HuNoV and MuNoV can be transcytosed across polarized cells in the absence of bacteria in vitrothere are additional physical barriers (e.g., a thick mucus lining) impeding their access to the epithelium in the complex environment of the intestinal lumen.

- To overcome such physical barriers, NoVs may bind to motile bacteria that can traverse the mucus layer. Conversely, it is possible that NoVs actively drive transcytosis of commensal bacteria.

Model for Infection

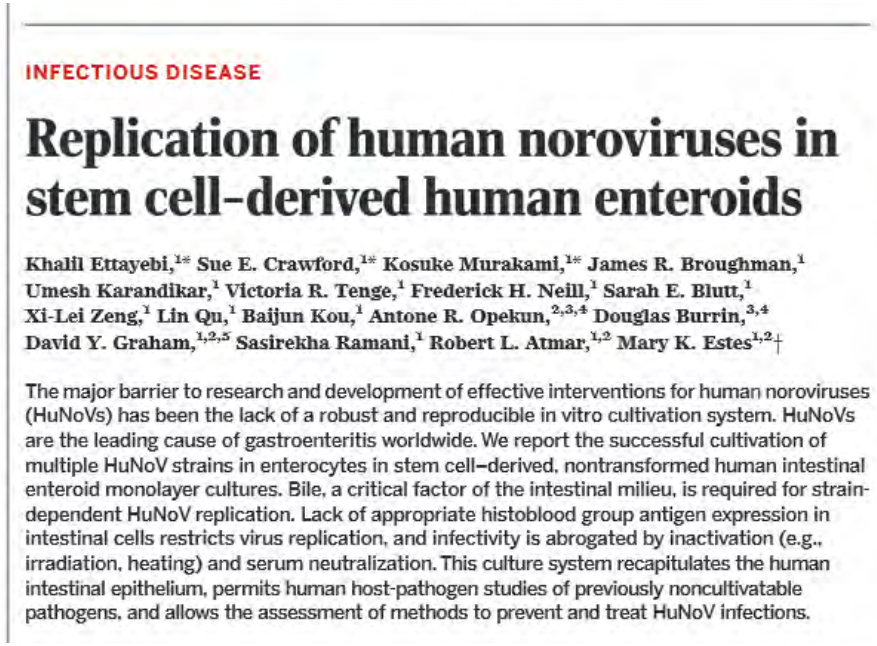


(1) NoVs bind carbohydrates expressed on enterocytes and secreted into the gut lumen. Enteric bacteria can express similar carbohydrates. NoVs may bind to such carbohydrates in any of these contexts.

(2) NoVs are transcytosed across the intestinal epithelium via M cells and additional as-yet-to-be-identified pathways.

(3) Following transcytosis, NoVs infect dendritic cells, macrophages, and B cells. Depending on the species, infection can occur in the presence or absence of carbohydrates. Free carbohydrates or bacterially expressed carbohydrates may be cotranscytosed with the virus. Immune cell infection and putative concomitant viral-bacterial antigen presentation during NoV infections could have significant consequences on the nature and magnitude of antiviral immune responses.

Plos Pathogens Volume: 11 Issue: 2 (2015-02-01) ISSN: 1553-7366



INFECTIOUS DISEASE

Replication of human noroviruses in stem cell–derived human enteroids

Khalil Ettayebi,[1*] Sue E. Crawford,[1*] Kosuke Murakami,[1*] James R. Broughman,[1] Umesh Karandikar,[1] Victoria R. Tenge,[1] Frederick H. Neill,[1] Sarah E. Blutt,[1] Xi-Lei Zeng,[1] Lin Qu,[1] Baijun Kou,[1] Antone R. Opekun,[2,3,4] Douglas Burrin,[3,4] David Y. Graham,[1,2,5] Sasirekha Ramani,[1] Robert L. Atmar,[1,2] Mary K. Estes[1,2†]

The major barrier to research and development of effective interventions for human noroviruses (HuNoVs) has been the lack of a robust and reproducible in vitro cultivation system. HuNoVs are the leading cause of gastroenteritis worldwide. We report the successful cultivation of multiple HuNoV strains in enterocytes in stem cell–derived, nontransformed human intestinal enteroid monolayer cultures. Bile, a critical factor of the intestinal milieu, is required for strain-dependent HuNoV replication. Lack of appropriate histoblood group antigen expression in intestinal cells restricts virus replication, and infectivity is abrogated by inactivation (e.g., irradiation, heating) and serum neutralization. This culture system recapitulates the human intestinal epithelium, permits human host-pathogen studies of previously noncultivatable pathogens, and allows the assessment of methods to prevent and treat HuNoV infections.

A new in vitro tool for NoV replications and immune/vaccine studies

- This is a biologically relevant model
- The model can be targeted to represent specific populations and genetic backgrounds
- Secretor/non-secretor status driven susceptibility recapitulates epidemiological data
- Provides a tool to study neutralising antibody responses as a correlate for protection

Characteristics of Norovirus Gastroenteritis in Immunocompetent versus Immunocompromised Hosts.

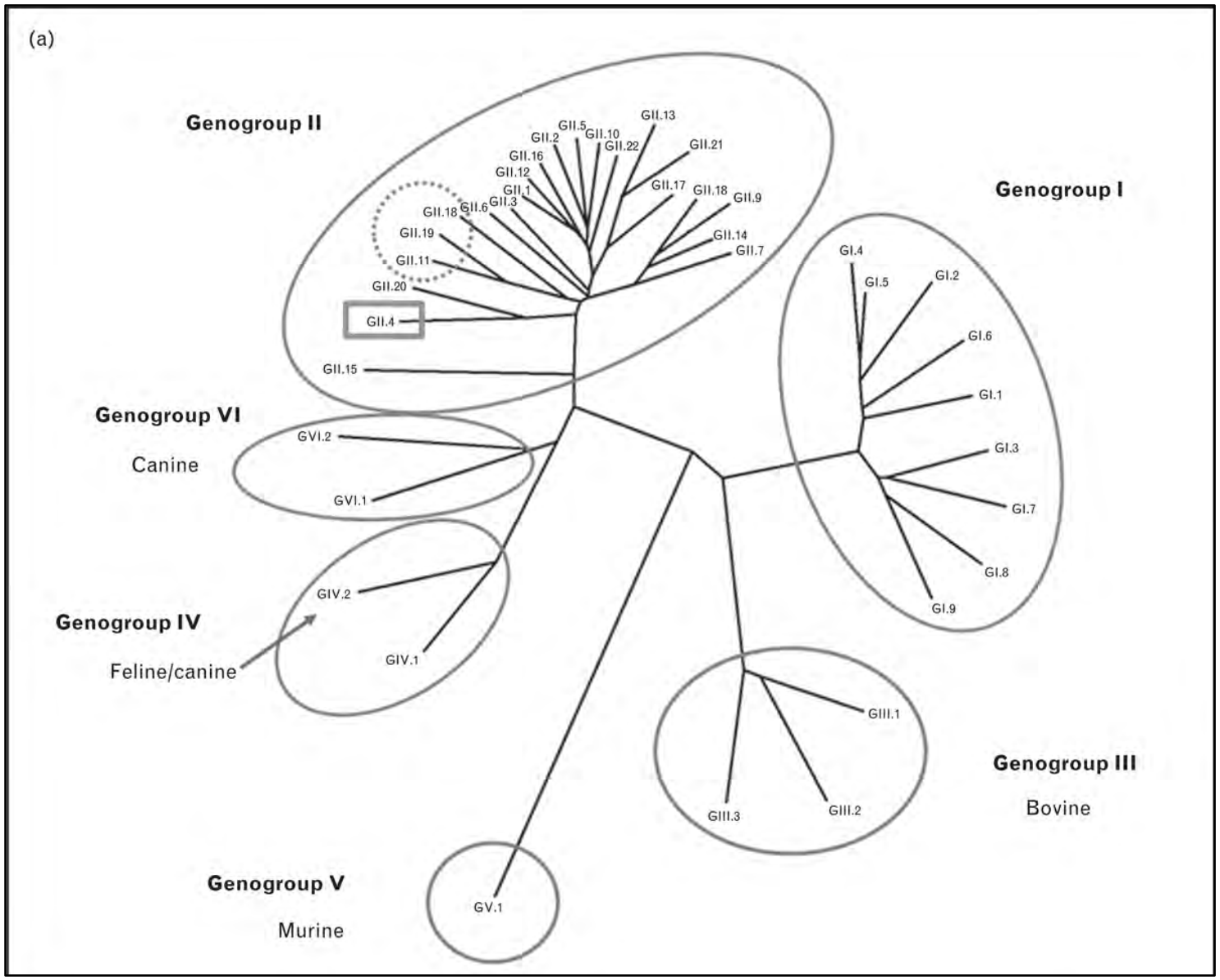
Table 2. Characteristics of Norovirus Gastroenteritis in Immunocompetent versus Immunocompromised Hosts.

Characteristic	Immunocompetent Hosts	Immunocompromised Hosts
Prevalence	Leading cause of gastroenteritis worldwide	Not established; estimated at about 17 to 18%
Seasonality	Peak in winter months	Year-round
Clinical features	Acute onset, duration of 24 to 48 hr	Acute onset, indefinite duration
Viral shedding	20 to 40 days	Weeks to years
Level of virus	10^8 to 10^9 genome copies per gram of stool	10^5 to 10^8 genome copies per gram of stool, depending on level of immunosuppressive therapy
Evolution of virus in host	Small number of stable variants	Markedly diverse variants
Tissue tropism	Small intestine	Small intestine
Complications	Dehydration	Dehydration, malnutrition, dysfunction of intestinal barrier
Treatment	Infection is usually self-limiting; rehydration, if needed	No virus-specific treatment is available; supportive care, adjustment of immunosuppressive therapy
Prognosis	Usually excellent, but the infection can be life-threatening	Poor to excellent; chronic infection is common

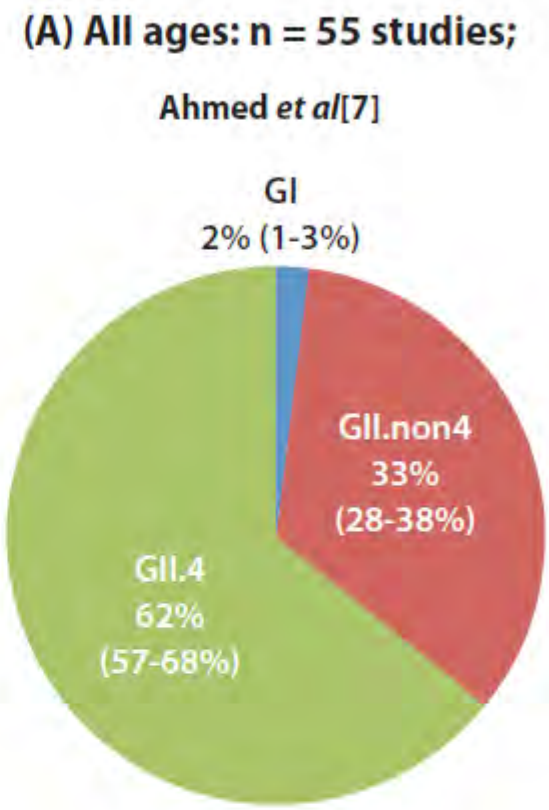
Bok K, Green KY. N Engl J Med 2012;367:2126-2132

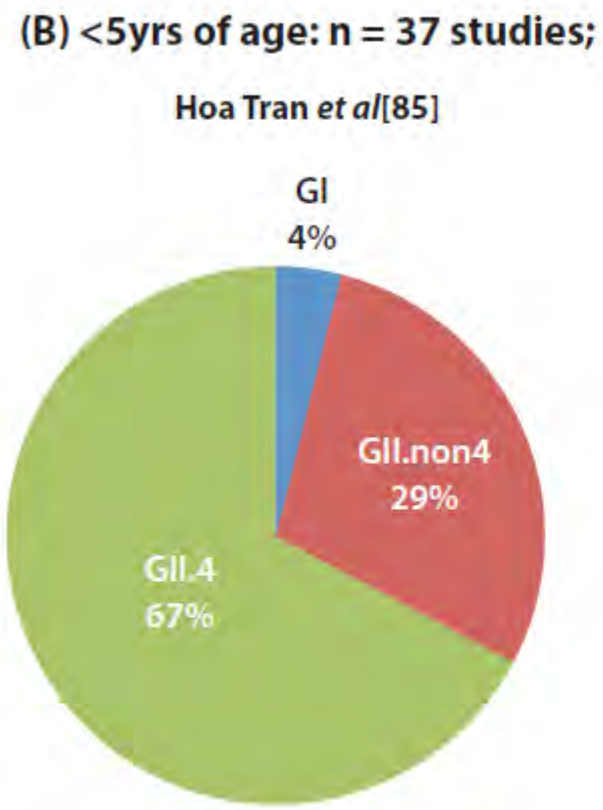
Epidemiology

Norovirus Diversity and Classification



HuNoV Genotype distribution





Mechanisms generating diversity among noroviruses

Genetic Recombination

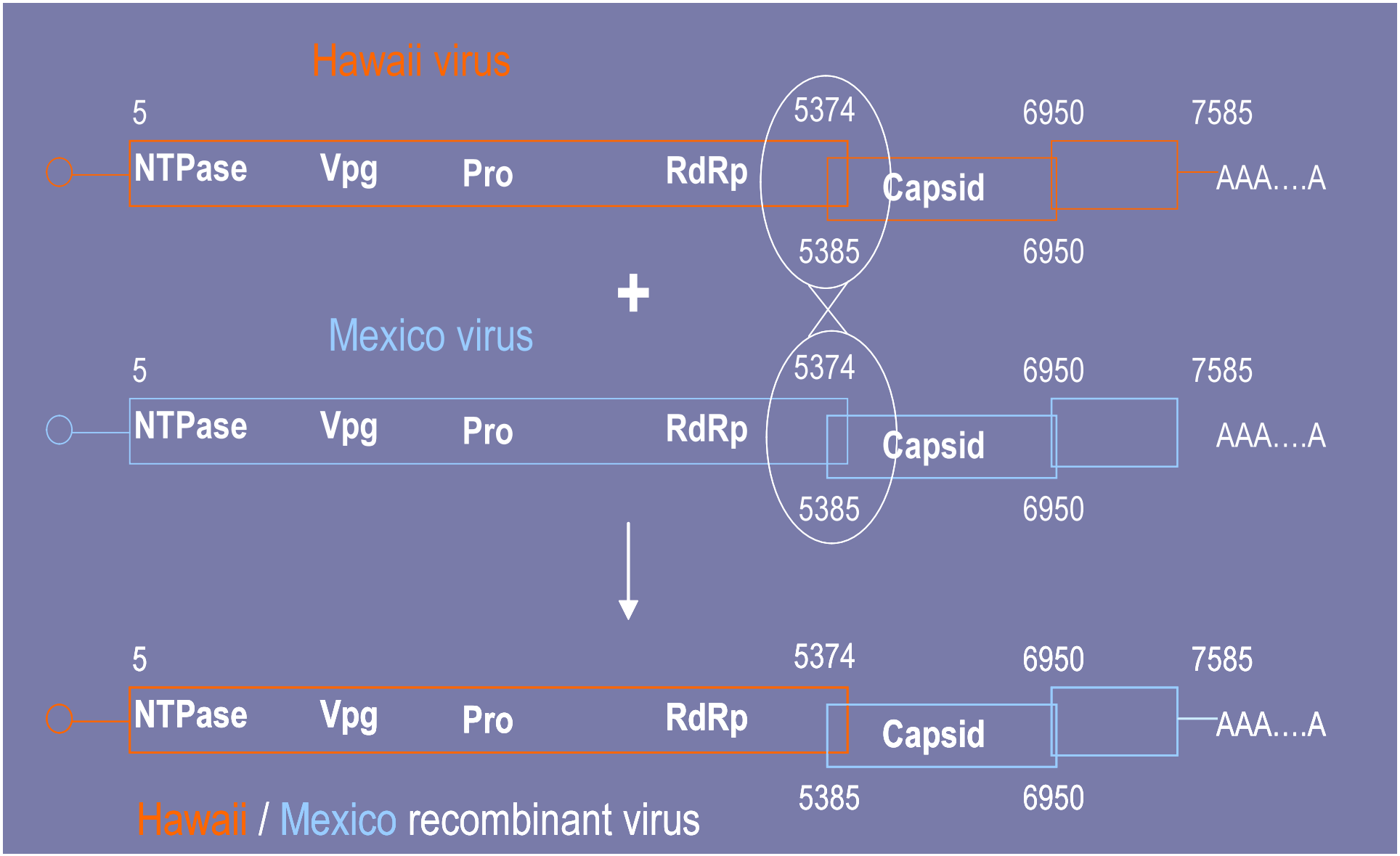
Requirements

- co-infection of a single cell
- relatedness of parental strains

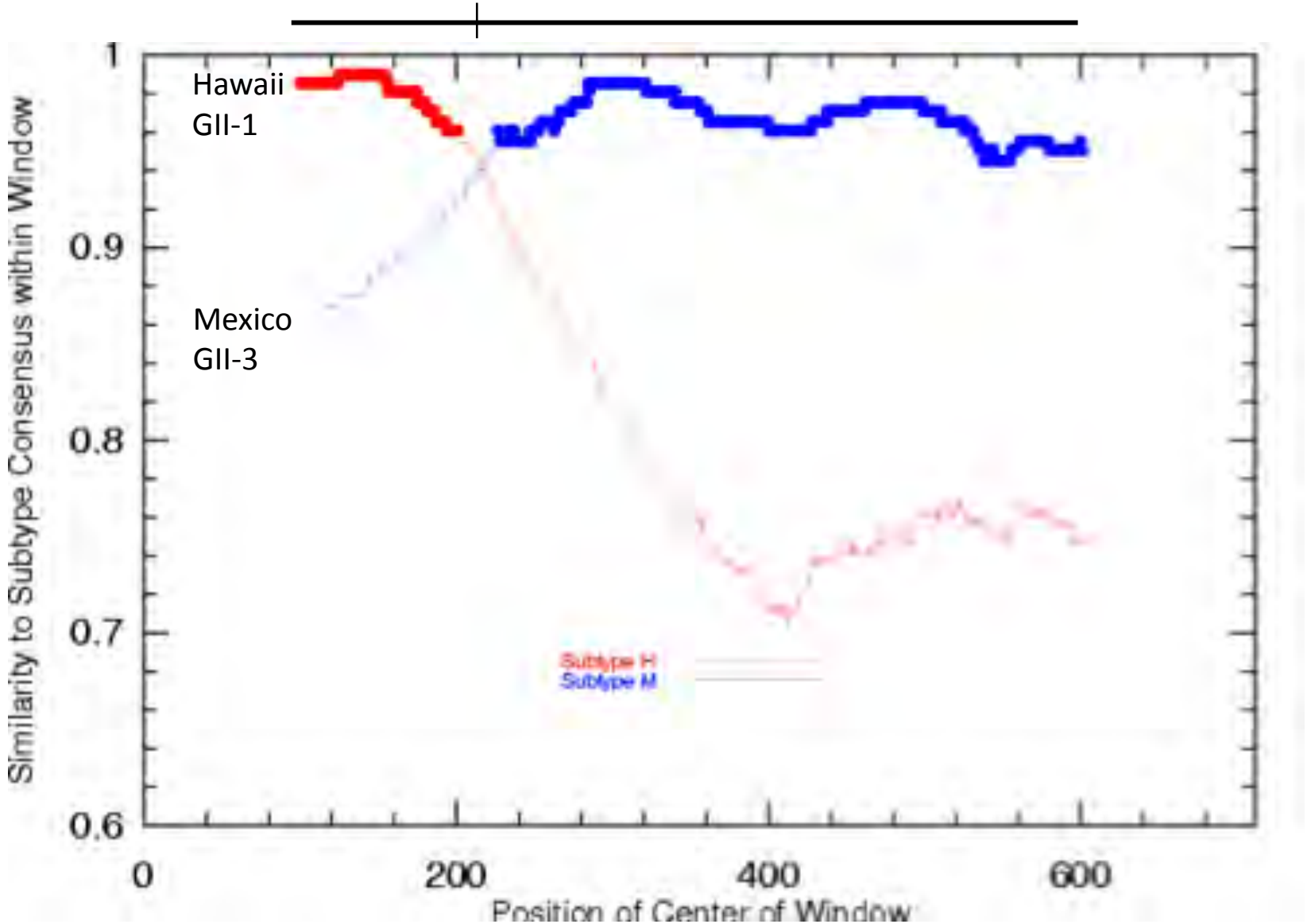
Noroviruses

- endemic co-circulation of genotypes
- faecal-oral route of transmission
- low infectious dose
    - waterborne and foodborne outbreaks
    - environmental survival
- limited heterotypic protection
- absence of long term immunity

Norovirus recombination: Mixing of genomes of two viruses



Hawaii/Mexico
Recombinant norovirus



Possible recombinant strains have been detected throughout Europe

Polymerase	Derivation POL Lineage	Capsid	Country	Year
Southampton		Hesse 3	GB	1995
Hawaii	I	Bristol	DE	1999
Hawaii	III	Toronto 24	FR	1998
Hawaii	III	Toronto 24	GB	2001
Hawaii	I	Hillingdon	GB	2002
Hawaii	II	Hillingdon	NL	2000
Harrow	II	Bristol	FR	2001
Harrow	I	Hawaii	DE	2001
Harrow	I	Hawaii	FR	2001
Harrow	I	Hawaii	GB	2001
Harrow	I	Hawaii	NL	2001
Harrow	I	Toronto 24	FR	2001
Harrow	I	Toronto 24	GB	2001
Harrow	I	Toronto 24	NL	2000
Harrow	II	Toronto 24	DE	2001
Harrow	II	Toronto 24	FR	2000
Harrow	II	Toronto 24	GB	2001
Bristol	II	Desert Shield	FR	2002
Leeds		Seacroft	GB	1999
Leeds		Amsterdam	NL	1999
Leeds		Seacroft	SE	1999
Leeds		Seacroft	FR	1999
Amsterdam	I	Seacroft	FI	1999

Recombination unlikely to have a major impact:

It occurs among co-circulating human viruses.

No evidence of transmission between species

No “new” antigens presented to the population

Mechanisms generating diversity among noroviruses

Genetic drift

The error prone nature of RNA replication leads to the accumulation of point mutations:

- Emergence of variant strains
- Emergence of antibody escape mutant strains

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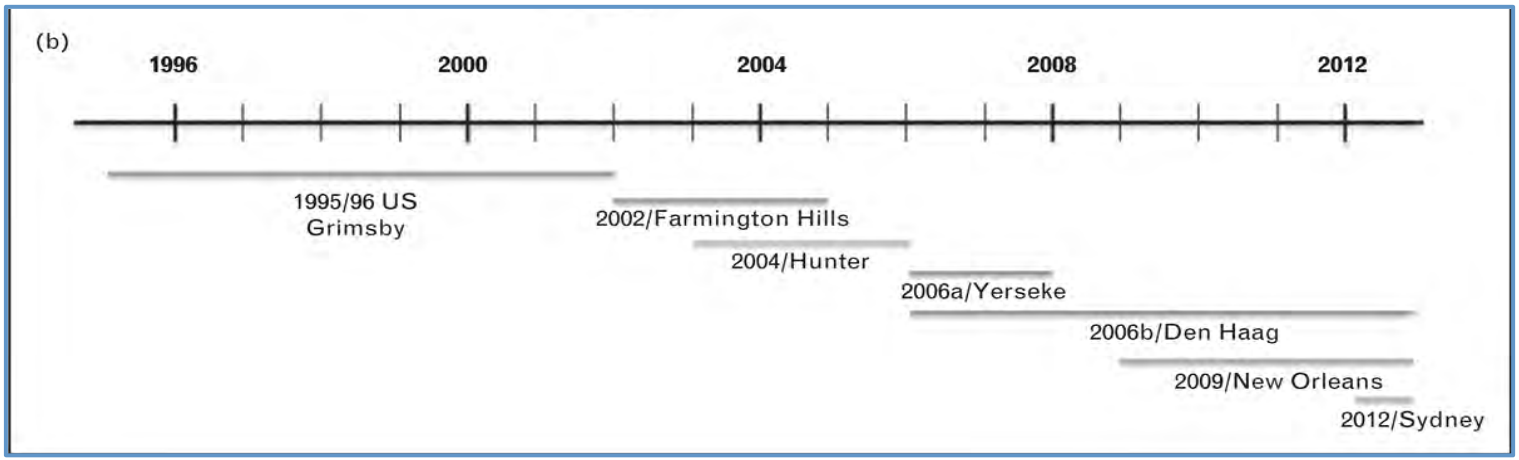
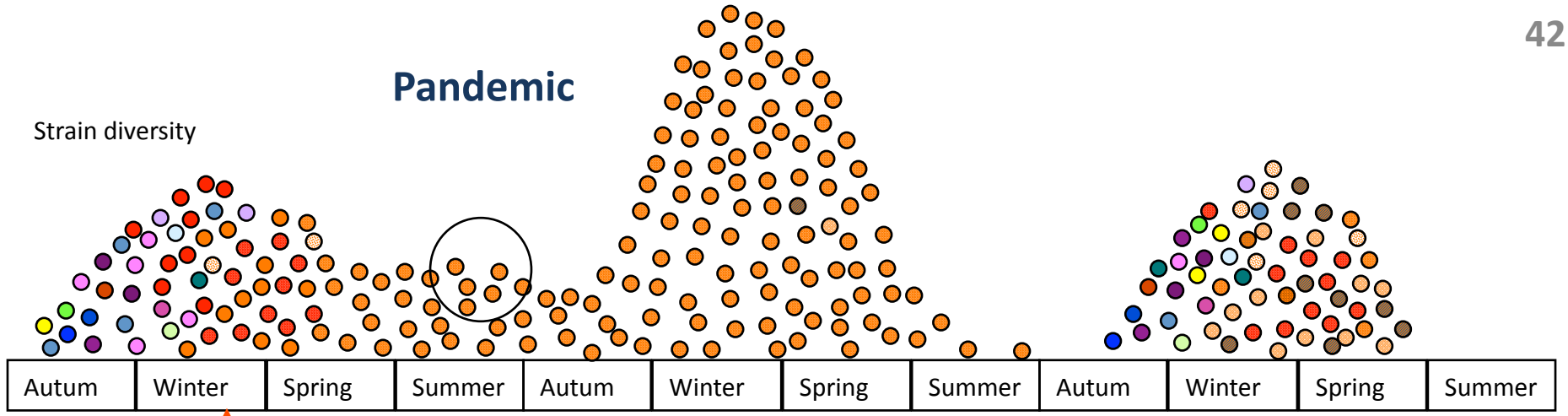


Pandemic



Narrowing diversity: GII4 predominates

GII4 variants emerge

GII4 variant is selected, out of season outbreaks occur, becomes epidemic

Lack of herd immunity to a new variant

Return to normal season, wide diversity at the beginning, narrowing as season progresses.

- Population protected in the short term against variant GII4
- Population susceptible to other genotypes due to short-term immune protection.

GII4 dominate and have an advantage over other co-circulating genotypes.

- replicative advantage
- greater transmissibility associated with a lower infectious dose
- larger proportion of the population susceptible through inherited genetic factors,
- better survival of the virus in the environment,
- a mechanism that allows the virus to evade immune surveillance to some degree.

Vaccines

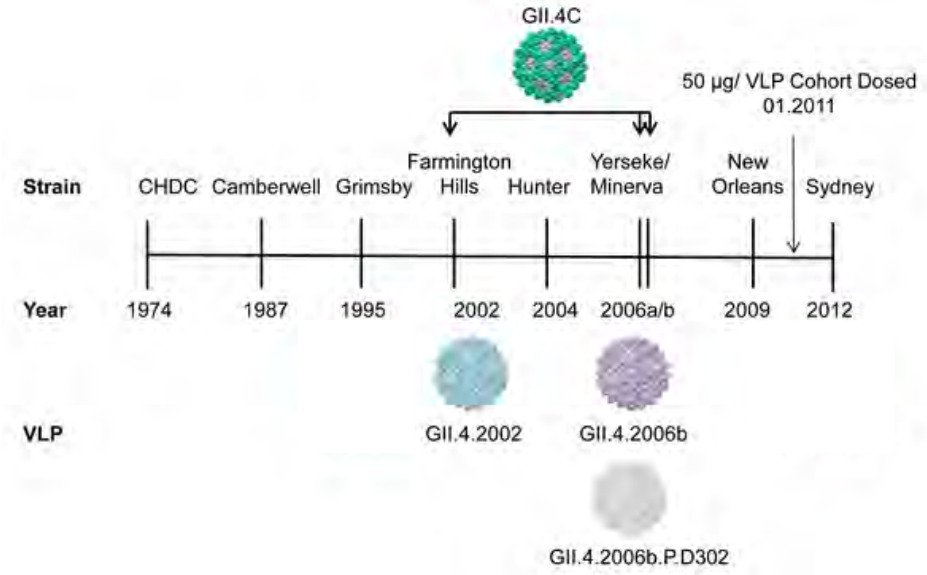
Norovirus vaccines showing promise

- A number of products being developed
  - virus-like particles (VLPs)
- The products with human efficacy data are being developed by Takeda Pharmaceuticals.
- Intranasal and intramuscular formulations tested in challenge studies
  - 47% (95% CI, 15%–67%) VE against norovirus gastroenteritis

Atmar et al. *NEJM*. 2011
Bernstein et al. *JID* 2014

Takeda Bivalent Norovirus VLP Vaccine

- GI.1
- GII.4 consensus
- Adjuvants
  - Alum
    - Aluminum hydroxide $Al(OH)_3$
  - MPL
    - 3-O-desacyl-4' monophosphoryl lipid A



Lindesmith et al, PLOS Med 2015

Takeda

IM bivalent (GI.1, GII.4) vaccine followed by challenge Per Protocol Efficacy Analysis

Illness Severity Infected	Vaccine (N=50)	Placebo (N=48)	% Reduction (95% CI)
Any	20.0%	37.5%	47% (-4%, 73%)
Mod-severe	6.0%	18.8%	68% (-11%, 91%)
Severe	0%	8.3%	100%

Bernstein 2015 JID

June 20, 2016

Takeda Pharmaceutical Company Limited

Takeda Initiates World's First Norovirus Vaccine Field Trial

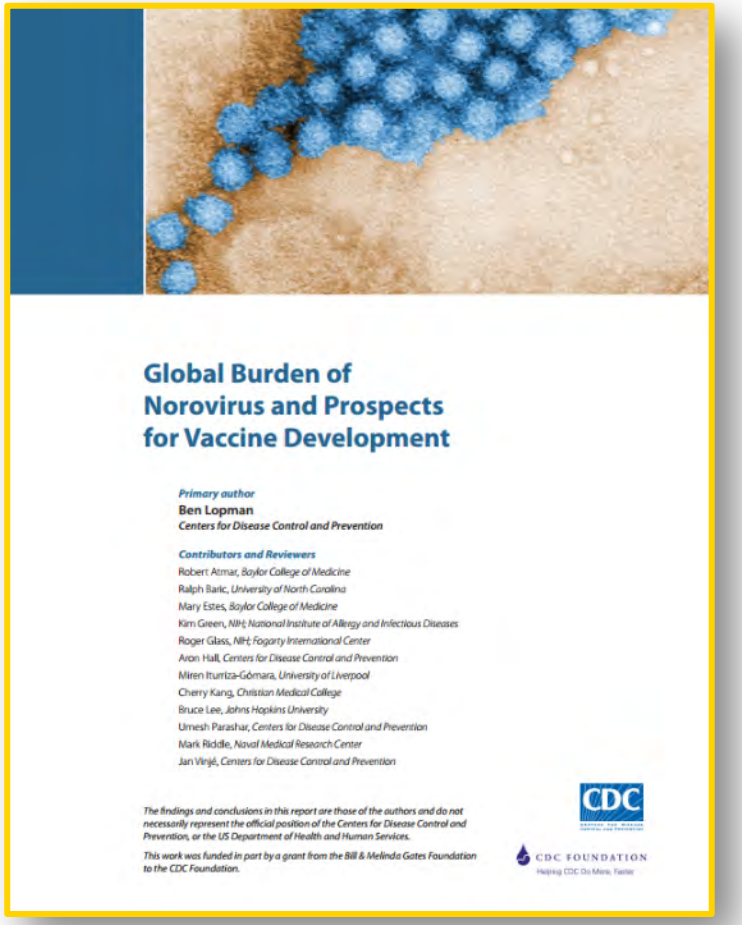
Vaccine candidate will target the leading cause of acute gastroenteritis around the globe

Osaka, Japan, June 20, 2016 – Takeda Pharmaceutical Company Limited [TSE: 4502], ("Takeda") today announced that it has dosed the first subject in a Phase 2b field efficacy trial of Takeda's norovirus vaccine candidate (TAK-214), the only norovirus vaccine candidate in human clinical trials.

The Phase 2b, double-blind, randomized, placebo-controlled trial involves healthy male or female adults aged 18 - 49 years. It will evaluate the efficacy of intramuscular administration of Takeda's norovirus vaccine candidate against moderate or severe acute gastroenteritis (AGE) due to norovirus, a common intestinal infection marked by watery diarrhea, vomiting, abdominal cramps, nausea and sometimes fever that may lead to clinically significant dehydration.[1,2]

Challenges for a norovirus vaccine

1. Role of prior infection history?
2. Duration of protection?
3. Protection against multiple genotypes?
4. Need to be updated to keep up with viral evolution?
5. Need for different vaccine formulation for certain groups?
6. Variation in human genetic susceptibility?



http://www.cdc.gov/norovirus/downloads/global-burden-report.pdf

Prevention and Control General

- Rapid reporting, response, and investigation
  - Identify mode of transmission and source of contamination
  - Collect appropriate specimens
- Promote appropriate hand hygiene
  - Wash with soap and water ≥ 20 seconds
  - Alcohol-based hand sanitizers?
- Prompt and thorough disinfection
  - Bleach solution for contaminated surfaces
  - Other EPA-approved disinfectants?
- Manage and exclude ill persons
  - ≥ 24-72 hrs after symptom resolution
  - Accommodating sick pay/leave policies for staff

Prevention and Control In healthcare settings

- Patient cohorting
  - Place patients with norovirus gastroenteritis on Contact Precautions for a minimum of 48 hours after the resolution of symptoms
- Personal Protective Equipment (PPE)
  - Gowns and gloves upon entry
- Patient Transfer and Ward Closure
  - Consider the closure of wards to new admissions or transfers
- Environmental Cleaning
  - Consider changing privacy curtains routinely and upon patient discharge or transfer.
- Rehydration therapy
  - Particular attention to children, elderly or otherwise vulnerable

CDC Home

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives. Protecting People.™

SEARCH

A-Z Index A B C D E F G H I J K L M N O P Q R S T U V W X Y Z #

Norovirus

Norovirus is a very contagious virus that can infect anyone. You can get it from an infected person, contaminated food or water, or by touching contaminated surfaces. The virus causes your stomach or intestines or both to get inflamed. This leads you to have stomach pain, nausea, and diarrhea and to throw up. These symptoms can be serious for some people, especially young children and older adults... **more**

Email page link
Print page

Contact Us:

Centers for Disease Control and Prevention
1600 Clifton Rd
Atlanta, GA 30333

800-CDC-INFO
(800-232-4636)
TTY: (888) 232-6348
Contact CDC-INFO

Norovirus Topics

About Norovirus
Overview about the virus, how it spreads, symptoms, treatment...

Preventing Norovirus Infection
You can help protect yourself and others from norovirus infection by following some simple tips...

For Food Handlers
Information about how norovirus spreads through contaminated food and water...

Trends and Outbreaks
Information about how common norovirus illness is, who gets infected, and when...

For Health Care Providers
Clinical features, transmission, diagnosis, disease burden, treatment...

Laboratory Testing
Types of laboratory testing done to diagnose norovirus infection, guidelines, reporting systems...

For Public Health Professionals
Information about burden of norovirus illness and outbreaks, surveillance & reporting, investigations...

Resources & References
Scientific articles and educational materials related to norovirus...

Protect Yourself from Norovirus!


Wash your hands often


Rinse fruits & vegetables


Cook shellfish thoroughly


Clean surfaces & wash laundry


When you're sick, don't prepare food or care for others

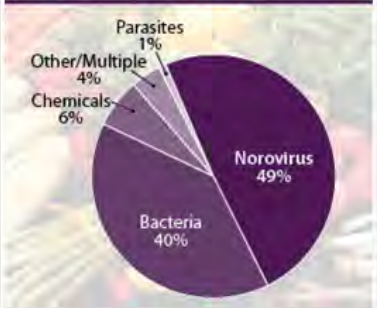
Share this widget | More info
www.cdc.gov/Norovirus

Many Names, Same Symptoms

You may hear norovirus illness called "food poisoning" or "stomach flu." It is true that food poisoning can be caused by noroviruses. But, other germs and chemicals can also cause food poisoning.

Norovirus illness is not related to the flu, which is a respiratory illness caused by influenza virus.

Known Causes of Foodborne Illness Outbreaks, U.S., 2006–2010



Symptoms

The most common symptoms are:

- diarrhea
- throwing up
- nausea
- stomach pain

Other symptoms include:

- fever
- headache

Norovirus prevention toolkit

http://www.cdc.gov/HAI/organisms/norovirus.html#a4

Guidelines

- Updated Norovirus Outbreak Management and Disease Prevention Guidelines
  - MMWR Recommendations and Reports
  - http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6003a1.htm
- Guideline for the Prevention and Control of Norovirus Gastroenteritis Outbreaks in Healthcare Settings
  - Healthcare Infection Control Practices Advisory Committee (HICPAC)
  - http://www.cdc.gov/hicpac/norovirus/002_norovirus-toc.html

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