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
Norovirus and Healthcare Facilities: How to Keep the Virus Out, and What to do When it Gets in
Prof. Ben Lopman, Emory University, and Prof. Miren Iturriza-Gomara, University of Liverpool
A Webber Training Teleclass

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

Age Specific Clinical Outcomes of Norovirus in the United States

- ED Visits
- Hospitalizations
- Deaths

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Norovirus disease burden in the United States

<table>
<thead>
<tr>
<th>Event</th>
<th>Annual estimate</th>
<th>Lifetime risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deaths</td>
<td>800</td>
<td>1 in ~6,000</td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>71,000</td>
<td>1 in ~60</td>
</tr>
<tr>
<td>Emergency department visits</td>
<td>400,000</td>
<td>1 in ~9</td>
</tr>
<tr>
<td>Outpatient visits</td>
<td>1.8 million</td>
<td>1 in ~2</td>
</tr>
<tr>
<td>Cases</td>
<td>19 to 21 million</td>
<td>5 times</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Event</th>
<th>Event per 10,000 population &lt; 5yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalizations</td>
<td>Norovirus 8</td>
</tr>
<tr>
<td>ED Visits</td>
<td>Norovirus 141</td>
</tr>
<tr>
<td>Outpatient Visits</td>
<td>Norovirus 318</td>
</tr>
</tbody>
</table>

Payne et al, NEJM, 2013

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Global prevalence of norovirus among cases of AGE

- Under 5 (n=79): 0.18 (0.15 to 0.20)
- Over 5 (n=20): 0.18 (0.13 to 0.24)
- Mixed (n=94): 0.19 (0.17 to 0.21)
- Inpatient (n=113): 0.17 (0.15 to 0.19)
- Outpatient (n=35): 0.20 (0.16 to 0.24)
- Community (n=16): 0.24 (0.18 to 0.30)
- Other (n=23): 0.19 (0.14 to 0.28)
- HMD (n=26): 0.14 (0.11 to 0.16)
- LMD (n=79): 0.19 (0.16 to 0.22)
- Developed (n=70): 0.20 (0.17 to 0.22)
- Pandemic (n=61): 0.19 (0.16 to 0.22)
- Endemic (n=114): 0.18 (0.16 to 0.20)
- Overall (n=175): 0.18 (0.17 to 0.20)


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 losses

Outbreaks in health care facilities


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

Person-to-person 69%
Foodborne 23%
Environmental 0.3%
Waterborne 0.3%
Unknown 7%


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

Long-Term Care Facilities 59%
Restaurants 17%
Schools 5%
Caterer/Banquet Facility 5%
Hospitals 3%
Private Residence 2%
Daycares 2%
Other/Multiple 7%


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Setting of 1115 Norovirus Outbreaks in Six European Counties, 2002

Virology and Clinical Disease

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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

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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 polypeptide, 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**

<table>
<thead>
<tr>
<th>MNV</th>
<th>HuNV*</th>
<th>Function</th>
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</thead>
<tbody>
<tr>
<td>N51/2</td>
<td>p48 (N-term)</td>
<td>Replication complex formation, contributes to persistence in MNV infections</td>
</tr>
<tr>
<td>NS3</td>
<td>NTPase (2C-like)</td>
<td>RNA helicase/NTPase</td>
</tr>
<tr>
<td>NS4</td>
<td>p22 (3A-like)</td>
<td>Replication complex formation</td>
</tr>
<tr>
<td>NS5</td>
<td>VPg</td>
<td>Genome-linked protein involved in translation and replication</td>
</tr>
<tr>
<td>NS6</td>
<td>Pro (3C-like)</td>
<td>Protease</td>
</tr>
<tr>
<td>NS7</td>
<td>Pol/3Dpol</td>
<td>RdRp</td>
</tr>
<tr>
<td>VP1</td>
<td>VP1</td>
<td>Major capsid protein</td>
</tr>
<tr>
<td>VP2</td>
<td>VP2</td>
<td>Minor capsid protein</td>
</tr>
<tr>
<td>VF1</td>
<td>No equivalent</td>
<td>Virulence factor</td>
</tr>
</tbody>
</table>
Outline of the norovirus life cycle.

(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).
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.

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

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

There is transient malabsorption of d-xyllose, 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 cytolytic 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.


<table>
<thead>
<tr>
<th>Host</th>
<th>Virus Strain</th>
<th>Route</th>
<th>In Vivos Viral Antigen</th>
<th>Intestinal Disease</th>
<th>Fecal Shedding [dpi]</th>
<th>Vomiteria</th>
<th>Stomach Trophism</th>
<th>Small Intestinal Trophism</th>
<th>Large Intestinal Trophism</th>
<th>MLN Trophism</th>
<th>Peripheral Tissue Trophism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Humans</td>
<td>HuNoV</td>
<td>parent</td>
<td>intestinal monocytes, lamina propria cells</td>
<td>severe diarrhea and vomiting</td>
<td>yes (vomiting)</td>
<td>N/A</td>
<td>+</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Chimpanzees</td>
<td>HuNoV GL 1</td>
<td>parent</td>
<td>intestinal OC and D cells</td>
<td>asymptomatic</td>
<td>(2-42)</td>
<td>–</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>+</td>
</tr>
<tr>
<td>Gerbil</td>
<td>HuNoV GL 4</td>
<td>parent</td>
<td>IECs</td>
<td>mild diarrhea</td>
<td>+ [1-4]</td>
<td>+</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Gerbil</td>
<td>HuNoV GL 4</td>
<td>parent</td>
<td>IECs and intestinal Mφ</td>
<td>mild diarrhea</td>
<td>+ [1-6]</td>
<td>+</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Balb/c RAC/cyt/v? mice</td>
<td>HuNoV GL 4 pass</td>
<td>intestinal</td>
<td>Mφ in spleen and liver</td>
<td>asymptomatic</td>
<td>N/A</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>Wild-type mice</td>
<td>HuNoV</td>
<td>parent</td>
<td>intestinal Mφ and DDCs</td>
<td>asymptomatic</td>
<td>+ [1-750]</td>
<td>N/A</td>
<td>+/?</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Interferon-?? mice</td>
<td>HuNoV</td>
<td>parent</td>
<td>Mφ and DDCs; IECs</td>
<td>severe diarrhoea, weight loss</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Malnourished mice</td>
<td>HuNoV</td>
<td>parent</td>
<td>N/A</td>
<td>+ [1-750]</td>
<td>N/A</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Characteristics of NoV animal models

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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 (e.g. 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 vitro there 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.
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>
<thead>
<tr>
<th>Characteristic</th>
<th>Immunocompetent Hosts</th>
<th>Immunocompromised Hosts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence</td>
<td>Leading cause of gastroenteritis worldwide</td>
<td>Not established; estimated at about 1/10 to 1/100</td>
</tr>
<tr>
<td>Seasonality</td>
<td>Peak in winter months</td>
<td>Year-round</td>
</tr>
<tr>
<td>Clinical features</td>
<td>Acute onset, duration of 24 to 48 hr</td>
<td>Acute onset, indefinite duration</td>
</tr>
<tr>
<td>Viral shedding</td>
<td>20 to 40 days</td>
<td>Weeks to years</td>
</tr>
<tr>
<td>Level of virus</td>
<td>$10^6$ to $10^9$ genome copies per gram of stool</td>
<td>$10^6$ to $10^9$ genome copies per gram of stool, depending on level of immunosuppressive therapy</td>
</tr>
<tr>
<td>Evolution of virus in host</td>
<td>Small number of stable variants</td>
<td>Markedly diverse variants</td>
</tr>
<tr>
<td>Tissue tropism</td>
<td>Small intestine</td>
<td>Small intestine</td>
</tr>
<tr>
<td>Complications</td>
<td>Dehydration</td>
<td>Dehydration, malnutrition, dysfunction of intestinal barrier</td>
</tr>
<tr>
<td>Treatment</td>
<td>Infection is usually self-limiting; rehydration, if needed</td>
<td>No virus-specific treatment is available; supportive care, adjustment of immunosuppressive therapy</td>
</tr>
<tr>
<td>Prognosis</td>
<td>Usually excellent, but the infection can be life-threatening</td>
<td>Poor to excellent; chronic infection is common</td>
</tr>
</tbody>
</table>

Epidemiology

Norovirus Diversity and Classification

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HuNoV Genotype distribution

(A) All ages: n = 55 studies;
Ahmed et al[7]

- GII.4 62% (57-68%)
- GII.noni4 33% (28-38%)
- GII 2% (1-3%)

(B) <5 yrs of age: n = 37 studies;
Hoa Tran et al[85]

- GII.4 67%
- GII.noni4 29%

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
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Norovirus recombination:
Mixing of genomes of two viruses

Hawaii virus

Mexico virus

Hawaii / Mexico recombinant virus

Hawaii/Mexico
Recombinant norovirus

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Possible recombinant strains have been detected throughout Europe

<table>
<thead>
<tr>
<th>Polymerase</th>
<th>Derivation</th>
<th>Pol Lineage</th>
<th>Capid</th>
<th>Country</th>
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<tr>
<td>Hawaii</td>
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<td>Seacroft</td>
<td>FR</td>
<td>1999</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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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Mechanisms generating diversity among noroviruses

Genetic drift

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

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### Pandemic

GI14 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.

Normal winter season
- GI14 predominates
- GI14 variants emerge
- GI14 variant is selected, out of season outbreaks occur, becomes epidemic
- Return to normal season, wide diversity at the beginning, narrowing as season progresses.

Unusual summer activity
- Lack of herd immunity to a new variant
- Population protected in the short term against variant GI14
- Population susceptible to other genotypes due to short-term immune protection.

Epidemic winter season
- GI14 variant is selected, out of season outbreaks occur, becomes epidemic
- Return to normal season, wide diversity at the beginning, narrowing as season progresses.

Normal winter season
- Narrowing diversity
- GI14 predominates
- GI14 variants emerge
- GI14 variant is selected, out of season outbreaks occur, becomes epidemic
- Return to normal season, wide diversity at the beginning, narrowing as season progresses.

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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 \(\text{Al(OH)}_3\)
  - 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

<table>
<thead>
<tr>
<th>Illness Severity Infected</th>
<th>Vaccine (N=50)</th>
<th>Placebo (N=48)</th>
<th>% Reduction (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any</td>
<td>20.0%</td>
<td>37.5%</td>
<td>47% (-4%, 73%)</td>
</tr>
<tr>
<td>Mod-severe</td>
<td>6.0%</td>
<td>18.8%</td>
<td>68% (-11%, 91%)</td>
</tr>
<tr>
<td>Severe</td>
<td>0%</td>
<td>8.3%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Bernstein 2015 JID

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Norovirus and Healthcare Facilities: How to Keep the Virus Out, and What to do When it Gets in
Prof. Ben Lopman, Emory University, and Prof. Miren Iturriza-Gomara, University of Liverpool
A Webber Training Teleclass

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?


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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
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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](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)
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