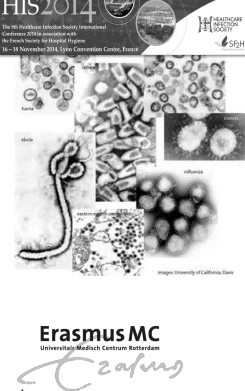


# Norovirus Understanding diversity in relation to detection, healthcare impact, control and prevention

Prof. Marion Koopmans, Erasmus University of Rotterdam, The Netherlands  
Broadcast live from the 2014 Healthcare Infection Society conference, Lyon, France



Rijksinstituut voor Volksgezondheid en Milieu  
Ministerie van Volksgezondheid, Welzijn en Sport

**Norovirus**  
Understanding diversity in relation to detection, healthcare impact, control and prevention

Marion Koopmans  
m.koopmans@erasmusmc.nl  
@MarionKoopmans

Lyon 2014

www.webbertraining.com November 17, 2014

### Norovirus background

- Most common etiology of acute gastro-enteritis
- Transmission person-to-person, environmental, foodborne, waterborne, zoonotic?
- Mostly mild illness, self limiting
- More severe disease in persons with co-morbidities
  - Cardiovascular patients (OR 17.1, 2.2-403)
  - Renal transplant recipients (OR 13.1, 7-281)
  - Age >65 (OR 11.6, 1.9-204)
  - Immunosuppression (OR 5.7, 1.8-20.1)
- Sporadic cases and outbreaks
- Short-lived immunity

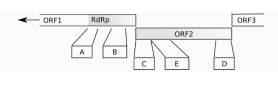
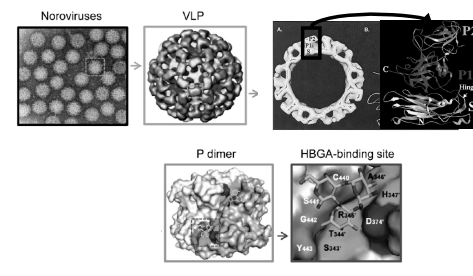
### Visualization by Immune Electron Microscopy of a 27-nm Particle Associated with Acute Infectious Nonbacterial Gastroenteritis

ALBERT Z. KAPLAN, RICHARD C. WYATT, RAFAEL DOLIN, THOMAS S. THORNHILL, ANTHONY B. KALICA, and ROBERT M. CHANOCK

Received for publication 1 August 1972

A 27-nm particle was observed by immune electron microscopy in an infectious stool filtrate derived from an outbreak in Newark, Ohio, of acute infectious nonbacterial gastroenteritis. Both experimentally and naturally infected individuals developed serological evidence of infection; this along with other evidence suggested that the particle was the etiologic agent of Newark gastroenteritis.

**1990: Jiang et al; sequence of the Norwalk virus genome**

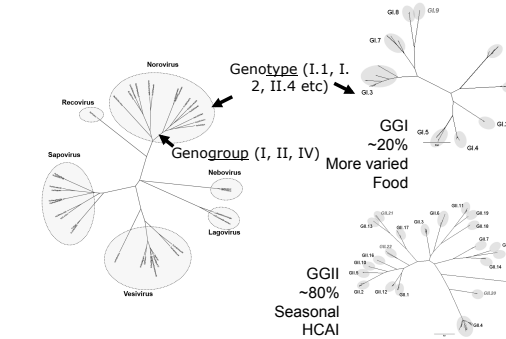



Jiang and Tan, 2010

### Norovirus diagnostics

- No cell culture model (?)
- RT-PCR based for individual patients
  - Conserved genome targets
  - Note genetic diversity > validation of PCR assays is difficult (GI14 and GI13 most commonly detected in patients)
  - QCMD quality control panels
- ELISA for outbreak diagnostics (insufficient sensitivity for case-based diagnostics)
- Genotyping
  - May be used in outbreak investigations
  - Capsid and polymerase gene based

### Family, genus, genogroups, genotypes, variants



Genotype (I.1, I.2, II.4 etc)

Genogroup (I, II, IV)

GGI ~20% More varied Food

GII ~80% Seasonal HCAI

Dominant Variant (GII.4)

Clarke et al. 2010; Verhoef et al., 2011; Kroneman et al., 2013

A Webber Training Teleclass  
www.webbertraining.com

# Norovirus Understanding diversity in relation to detection, healthcare impact, control and prevention

Prof. Marion Koopmans, Erasmus University of Rotterdam, The Netherlands  
 Broadcast live from the 2014 Healthcare Infection Society conference, Lyon, France

Typing tool and nomenclature; [www.noronet.nl](http://www.noronet.nl)

Report: Genotype and subtype assignment  
 Downloadable: Phylogenetic tree against reference strains, Alignment, PAUP log file

Downloadable results + reference sequences in multiple file formats

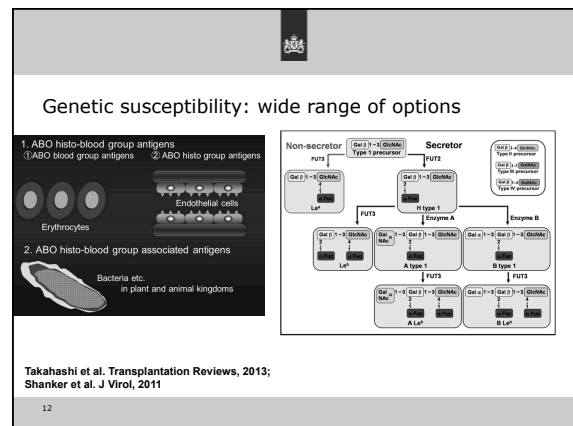
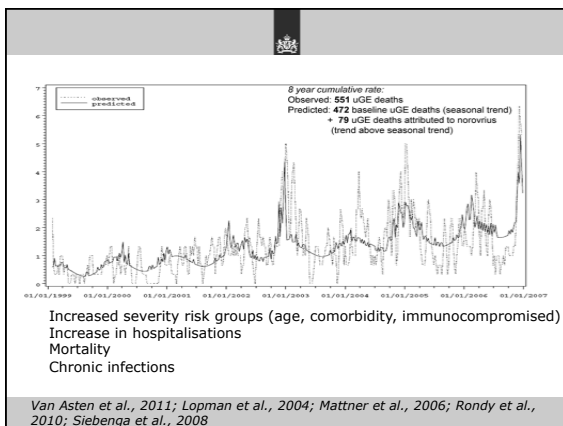
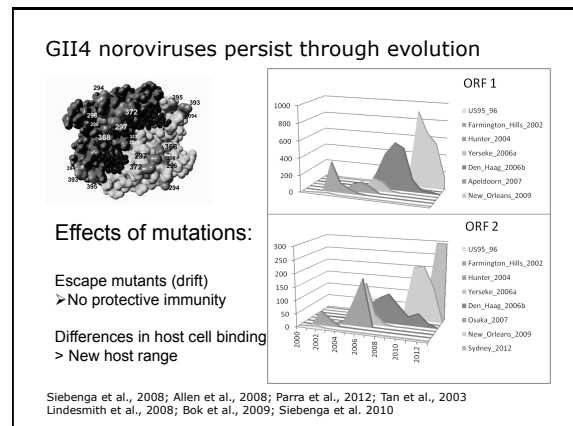
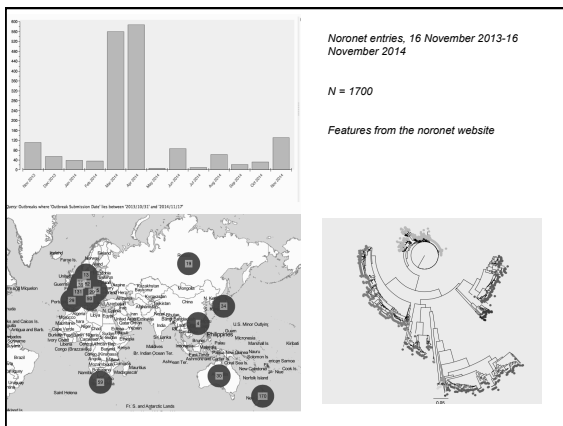
Tutorial

Details of method

Tables of the reference sequences for each taxonomic level

Batch job option (e.g. retyping of up to 10.000 sequences to adapt to standardized nomenclature)

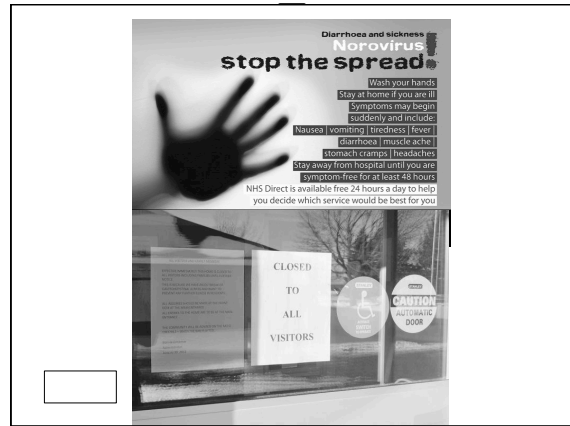
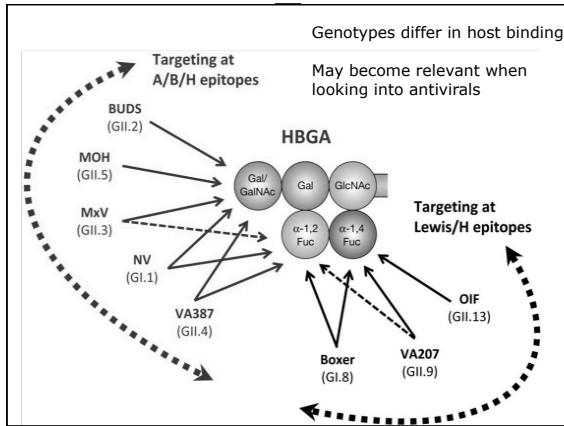
<http://www.rivm.nl/en/Topics/N/NoroNet>



A Webber Training Teleclass  
[www.webbertraining.com](http://www.webbertraining.com)

# Norovirus Understanding diversity in relation to detection, healthcare impact, control and prevention

Prof. Marion Koopmans, Erasmus University of Rotterdam, The Netherlands  
Broadcast live from the 2014 Healthcare Infection Society conference, Lyon, France



*Epidemiol. Infect.* (2012), **140**, 1151–1160. © Her Majesty the Queen in right of Canada 2012  
doi:10.1017/S0950268811000271

## REVIEW ARTICLE

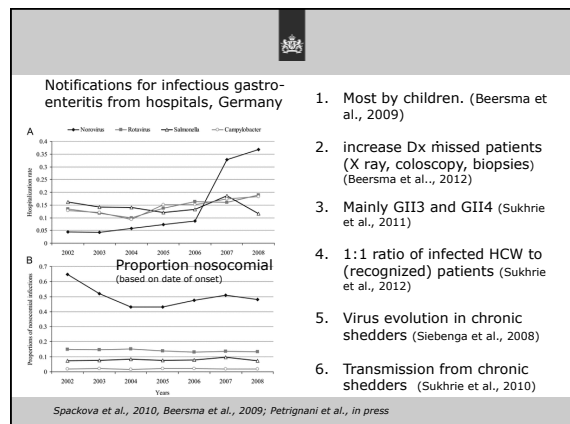
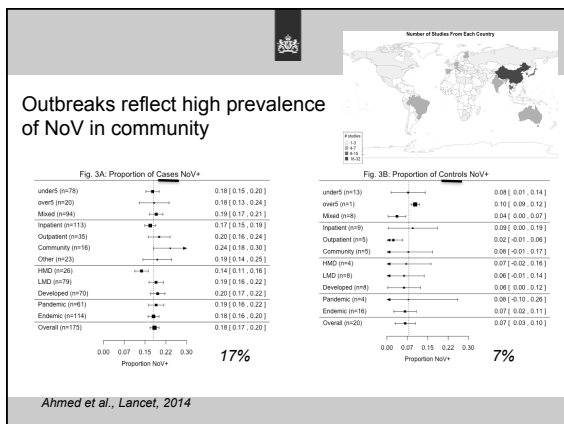
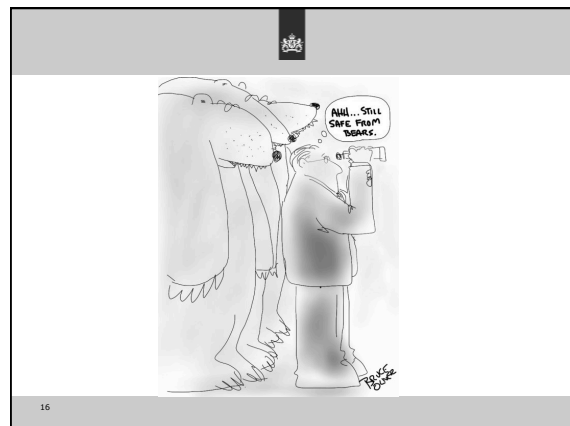
### A review of nosocomial norovirus outbreaks: infection control interventions found effective

J. D. GREIG\* AND M. B. LEE†

\* *Science to Policy Unit, The Laboratory for Foodborne Zoonoses, Public Health Agency of Canada, Guelph, Ontario, Canada*  
† *School of Occupational and Public Health, Ryerson University, Toronto, Ontario, Canada*

(Accepted 23 November 2011; first published online 4 January 2012)

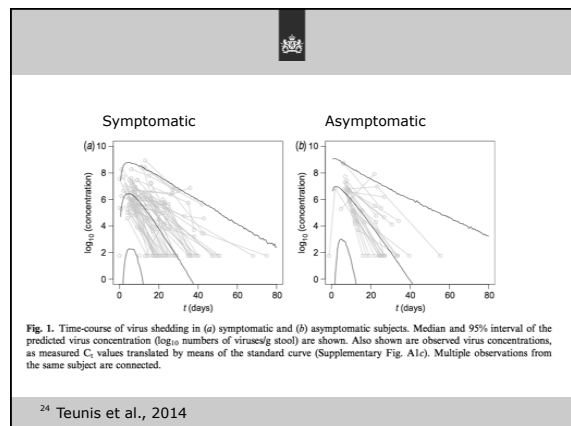
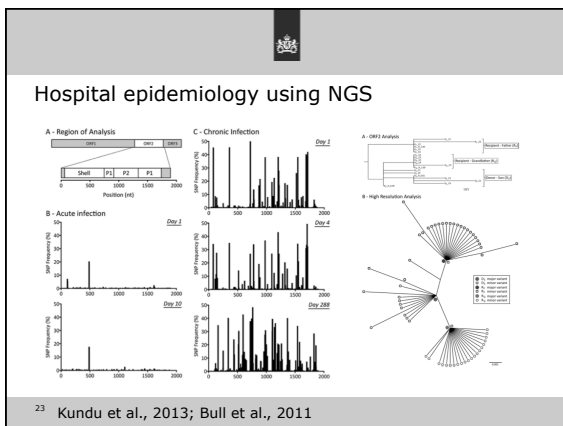
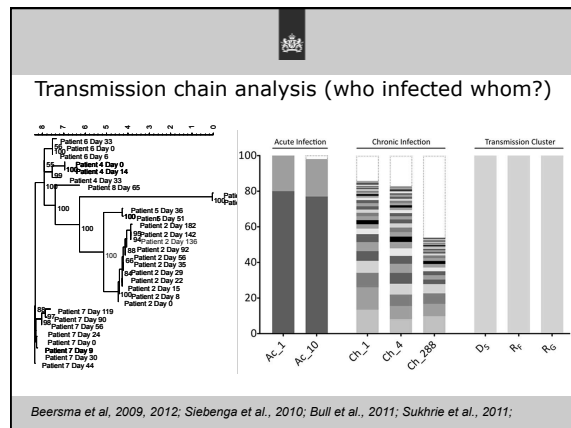
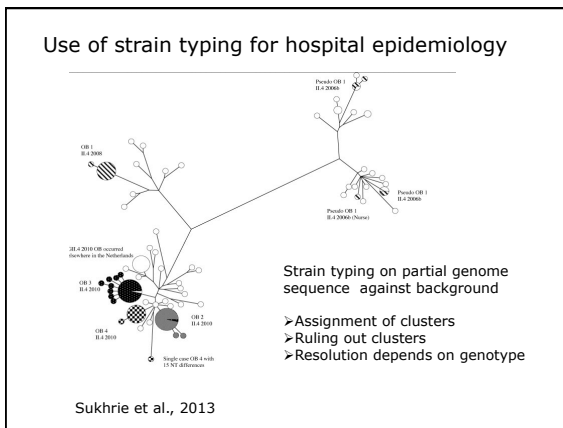
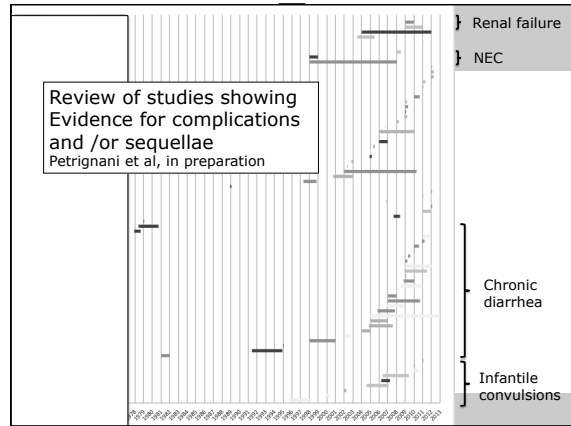
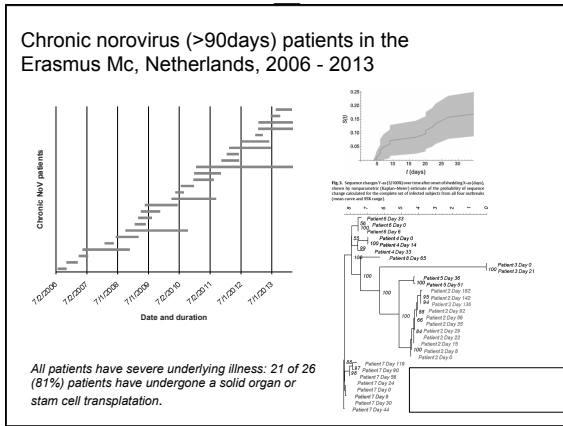
1. Rapid identification
2. Immediate implementation of infection control measures
3. Debate on alcohol based disinfectants (no model)
4. Experimental evidence for decontamination with H<sub>2</sub>O<sub>2</sub>
5. Preclinical evidence for post exposure prophylaxis



A Webber Training Teleclass  
www.webbertraining.com

# Norovirus Understanding diversity in relation to detection, healthcare impact, control and prevention

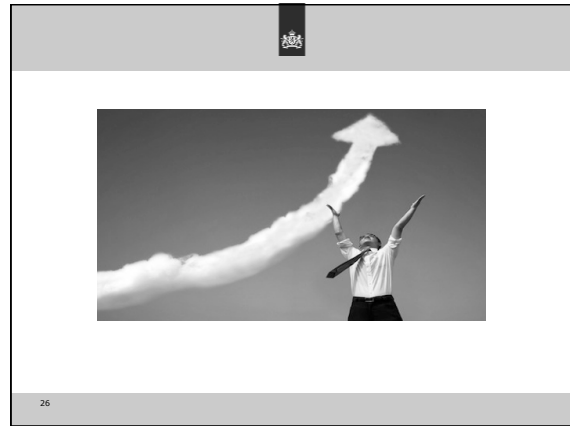
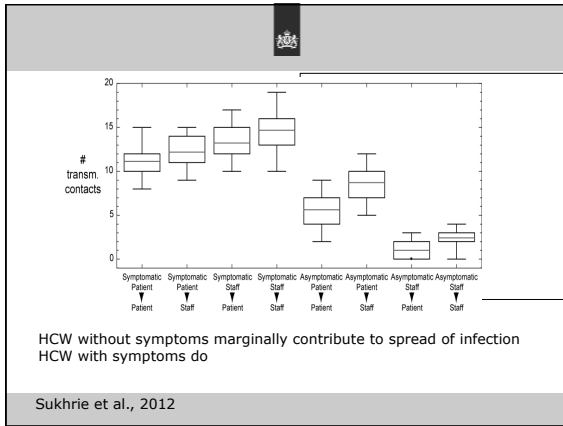
Prof. Marion Koopmans, Erasmus University of Rotterdam, The Netherlands  
Broadcast live from the 2014 Healthcare Infection Society conference, Lyon, France



A Webber Training Teleclass  
www.webbertraining.com

# Norovirus Understanding diversity in relation to detection, healthcare impact, control and prevention

Prof. Marion Koopmans, Erasmus University of Rotterdam, The Netherlands  
Broadcast live from the 2014 Healthcare Infection Society conference, Lyon, France



ANNOUËT | PERSPECTIVES

NOROVIRUS

## Enteric bacteria promote human and mouse norovirus infection of B cells

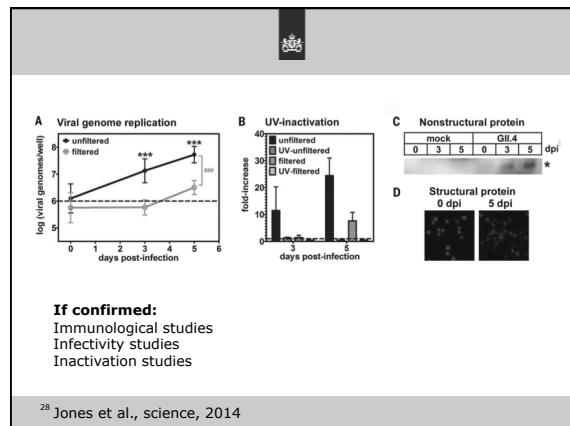
Melissa K. Jones,<sup>1,2</sup> Makiko Watanabe,<sup>1,2</sup> Shu Zhu,<sup>1</sup> Christina L. Greves,<sup>1,2</sup> Lisa R. Keres,<sup>1</sup> Katrina R. Grau,<sup>1</sup> Marian B. Gonzalez-Hernandez,<sup>2</sup> Nicole M. Irvine,<sup>2</sup> Christian R. Wilson,<sup>1</sup> Jan Vliet,<sup>1</sup> Scott A. Tiberius,<sup>1</sup> Shouwei M. Wang,<sup>1,2</sup> Stephanie M. Kasari<sup>1</sup>

The cell tropism of human noroviruses and the development of an in vitro infection model remain elusive. Although susceptibility to individual human norovirus strains correlates with an individual's histo-blood group antigen (HBGA) profile, the biological basis of this restriction is unknown. We demonstrate that human and mouse noroviruses infect B cells in vitro and likely in vivo. Human norovirus infection of B cells required the presence of HBGA-expressing enteric bacteria. Furthermore, mouse norovirus replication was reduced in vivo when the intestinal microbiota was depleted by means of oral antibiotic administration. Thus, we have identified B cells as a cellular target of noroviruses and enteric bacteria as a stimulatory factor for norovirus infection, leading to the development of an in vitro infection model for human noroviruses.

**Leaping the norovirus hurdle**  
Bacteria and B cells solve the problem of culturing human norovirus in the laboratory

Human norovirus culture in B cells, with bacterial extract containing HBGA

27



### Take home messages

- NoV infection is widely underdiagnosed
- NoV diagnostics should be routine, as part of hospital infection prevention policy
- Check product information for validation against uncommon genotypes
- Be aware of chronic norovirus in immunocompromised patients
- Strain typing / sequencing may inform hospital epidemiology or source tracking

29

### Acknowledgements

**RIVM**  
Dr Harry Vennema  
Annelies Kroneman  
Bas van der Veer  
Prof Peter Teunis  
Dr Erwin Duizer

**Erasmus University**  
Dr Thijs Beersma  
Jolanda Bogerman  
Dr Pieter Fraaij  
Susan Pas  
Dr Martin Schutten  
Prof Jan Henrik Richardus

**FSA**  
Dr Ingeborg Boxman

**PhD students**  
Dr Joukje Siebenga  
Dr Faizel Sukhrie  
Mariska Petrigiani  
Janko van Beek

**Global noronet and FBVE network**

www.noronet.nl  
Noronet partners  
Calicinet – Jan Vinje CDC US  
EpiSurv – Joanna Hewitt, NZ

30 November 18, 2014

A Webber Training Teleclass  
www.webbertraining.com

# Norovirus Understanding diversity in relation to detection, healthcare impact, control and prevention

Prof. Marion Koopmans, Erasmus University of Rotterdam, The Netherlands  
Broadcast live from the 2014 Healthcare Infection Society conference, Lyon, France

