GUIDELINE FOR THE PREVENTION AND CONTROL OF NOROVIRUS GASTROENTERITIS OUTBREAKS IN HEALTHCARE SETTINGS

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Acknowledgement

HICPAC thanks the following members who served on the HICPAC Norovirus Gastroenteritis Guideline subcommittee during the guideline development process: Alexis Elward and Keith M. Ramsey.

HICPAC thanks the following outside experts for reviewing a draft of this guideline: John Boyce, Hospital of St. Raphael, New Haven, CT; Aron Hall, NCIRD, CDC; L. Clifford McDonald, DHQP, CDC; and Umesh Parashar, NCIRD, CDC. The opinions of the reviewers might not be reflected in all of the recommendations contained in this document.

Disclosure of Financial Interests and Relationships

The authors T.M., C.A.U., R.K.A., I.L., G.K., and K.B.S. report no actual or potential conflicts of interest. C.A.U., R.K.A. and I.L. received funding from the CDC to support the guideline development process.

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Abbreviations

AIDS	Acquired immune deficiency syndrome
BAS	Basic science study
°C	Celsius
CaCV	Calicivirus
CCU	Cardiac/coronary care unit
CDC	Centers for Disease Control and Prevention
CI	Confidence interval
CICU	Cardiac/coronary intensive care unit
CSTE	Council of State and Territorial Epidemiologists
DES	Descriptive study
DHQP	Division of Healthcare Quality Promotion
DIAG	Diagnostic study
DNA	Deoxyribonucleic acid
ECL	Electrochemiluminescence
EFORS	Electronic Foodborne Outbreak Reporting System
EIA	Enzyme immunoassay
ELISA	Enzyme-linked immunoassay
EM	Electron microscopy
EPA	Environmental Protection Agency
FBDSS	Foodborne Disease Outbreak Surveillance System
FCV	Feline calicivirus
FDA	Food and Drug Administration
FN	False negative
FP	False positive
GRADE	Grading of Recommendations Assessment, Development, and Evaluation

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HBGA	Histo-blood group antigen
HICPAC	Healthcare Infection Control Practices Advisory Committee
HIV	Human immiunodeficiency virus
Km	Kilometer
LUX	Light-upon-extension
Ml	Milliliter
MMWR	Morbidity and Mortality Weekly Report
MNV	Murine norovirus
N/A	Not applicable
NASBA	Nucleic acid sequence-based amplification
NCIRD	National Center for Immunization and Respiratory Diseases
NIH	National Institutes of Health
NLV	Norwalk-like virus
No	Number
NORS	National Outbreak Reporting System
NPV	Negative predictive value
OBS	Observational study
OR	Odds ratio
ORF	Open reading frame
P	P value
PCR	Polymerase chain reaction
PPE	Personal protective equipment
PPM	Part per million
PPV	Positive predictive value
RCT	Randomized controlled trial
RHD	Rapid humidifying device

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RIA	Radioimmunoassay
RF	Reduction factor
RR	Relative risk
RT	Room temperature
RT-LAMP	Reverse transcription loop-mediated amplification assay
RT-PCR	Reverse transcriptase polymerase chain reaction
SD	Standard deviation
SPIEM	Solid-phase immune electron microscopy
SR	Systematic review
SRFV	Small round featureless virus
SRSV	Small round structured virus
TCID	Tissue culture infective dose
TE	Transcriptional enhancement
TEM	Transmission electron microscopy
TN	True negative
TP	True positive
UV	Ultraviolet
Vs	Versus

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I. Executive Summary

Norovirus gastroenteritis infections and outbreaks have been increasingly described and reported in both non-healthcare and healthcare settings during the past several years. In response, several states have developed guidelines to assist both healthcare institutions and communities on preventing the transmission of norovirus infections and helped develop the themes and key questions to answer through an evidence-based review. This guideline addresses prevention and control of norovirus gastroenteritis outbreaks in the healthcare setting. The guideline also includes specific recommendations for implementation, performance measurement, and surveillance. Recommendations for further research are provided to address knowledge gaps identified during the literature review in the prevention and control of norovirus gastroenteritis outbreaks.

This document is intended for use by infection prevention staff, physicians, healthcare epidemiologists, healthcare administrators, nurses, other healthcare providers, and persons responsible for developing, implementing, and evaluating infection prevention and control programs for healthcare settings across the continuum of care. The guideline can also be used as a resource for societies or organizations that wish to develop more detailed implementation guidance for prevention and control of norovirus gastroenteritis outbreaks for specialized settings or populations.

To evaluate the evidence on preventing and controlling norovirus gastroenteritis outbreaks in healthcare settings, we examined published material addressing three key questions:

1. What host, viral, or environmental characteristics increase or decrease the risk of norovirus infection in healthcare settings?
2. What are the best methods to identify an outbreak of norovirus gastroenteritis in a healthcare setting?
3. What interventions best prevent or contain outbreaks of norovirus gastroenteritis in the healthcare setting?

Explicit links between the evidence and recommendations are available in the Evidence Review in the body of the guideline and Evidence Tables and GRADE Tables in the Appendices. **It is important to note that the Category I recommendations are all considered strong and should be implemented;** it is only the *quality* of the evidence underlying the recommendation that distinguishes between levels A and B. Category IC recommendations are required by state or federal regulation and may have any level of supporting evidence. The categorization scheme used in this guideline is presented in Table 1: Summary of Recommendations and described further in the Methods section. The Implementation and Audit section includes a prioritization of recommendations (i.e., high-priority recommendations that are essential for every healthcare facility) in order to provide facilities more guidance on implementation of these guidelines. A list of recommended performance measures that can potentially be used for reporting purposes is also included.

Evidence-based recommendations were cross-checked with those from other guidelines identified in an initial systematic search. Recommendations from other guidelines on topics not directly addressed by our systematic review of the evidence were included in our Summary of Recommendations if they were deemed critical to the target users of this guideline. Unlike recommendations informed by our search of primary studies, these recommendations are stated independently of a key question.

The Summary of Recommendations includes recommendations organized into the following categories: 1) Patient Cohorting and Isolation Precautions, 2) Hand Hygiene, 3) Patient Transfer and Ward Closure, 4) Indirect Patient Care Staff - Food Handlers in Healthcare, 5) Diagnostics, 6) Personal Protective Equipment, 7) Environmental Cleaning, 8) Staff Leave and Policy, 9) Visitors, 10) Education, 11) Active Case-finding, and 12) Communication and Notification.

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Areas for further research identified during the evidence review are outlined in the Recommendations for Further Research. This section includes gaps that were identified during the literature review where specific recommendations could not be supported because of the absence of available information that matched the inclusion criteria for GRADE. These recommendations provide guidance for new research or methodological approaches that should be used in future studies

Readers who wish to examine the primary evidence underlying the recommendations are referred to the Evidence Review in the body of the guideline, and the Evidence and GRADE Tables in the Appendices. The Evidence Review includes narrative summaries of the data presented in the Evidence and GRADE Tables. The Evidence Tables include all study-level data used in the guideline, and the GRADE Tables assess the overall quality of evidence for each question. The Appendices also contain a clearly delineated search strategy that will facilitate more frequent, periodic updates to ensure that the guideline remains a timely resource as new information becomes available.

II. Summary of Recommendations

Table 1. HICPAC Categorization Scheme for Recommendations	
Category IA	A strong recommendation supported by high to moderate quality evidence suggesting net clinical benefits or harms.
Category IB	A strong recommendation supported by low-quality evidence suggesting net clinical benefits or harms, or an accepted practice (e.g., aseptic technique) supported by low to very low-quality evidence.
Category IC	A strong recommendation required by state or federal regulation.
Category II	A weak recommendation supported by any quality evidence suggesting a tradeoff between clinical benefits and harms.
Recommendation for further research	An unresolved issue for which there is low to very low-quality evidence with uncertain tradeoffs between benefits and harms.

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PATIENT COHORTING AND ISOLATION PRECAUTIONS

1.A.1 Avoid exposure to vomitus or diarrhea. For a recognized outbreak, use Contact Precautions for patients with symptoms consistent with norovirus gastroenteritis. Sporadic cases of norovirus can be managed under Standard Precautions with provisions to reduce staff, visitor, and patient exposures to vomitus or diarrhea. **(Category IB)** (Key Question 1A)

> 1.A.2.a Consider longer periods of isolation or cohorting precautions for complex medical patients, especially those with cardiovascular, autoimmune, or renal disorders, as they can experience protracted episodes of diarrhea and prolonged viral shedding. Patients with these or other comorbidities have the potential to relapse and facilities may choose longer periods of isolation based on clinical judgment. **(Category II)** (Key Question 1A)

3.A.1 Consider extending the duration of isolation or cohorting precautions for outbreaks among infants, even after resolution of symptoms, as there is potential for prolonged viral shedding and environmental contamination. Among infants, extending Contact Precautions for up to 5 days after the resolution of symptoms is suggested. **(Category II)** (Key Question 3A)

3.C.4.a During outbreaks, patients with norovirus gastroenteritis should be cohorted or placed on Contact Precautions for a minimum of 48 hours after the resolution of symptoms to prevent further exposure of susceptible patients **(Category IB)** (Key Question 3C)

3.C.4.b During suspected or confirmed outbreaks, preferentially place patients with norovirus gastroenteritis on Contact Precautions and into private rooms equipped with at least one dedicated handwashing sink and toilet or commode. If these provisions are not available, patients may be cohorted into groups of those who are symptomatic, exposed but asymptomatic, and unexposed with access to separate toilets or commodes for each group. Alternatively, all patients within a hospital unit or section may be placed under Contact Precautions. **(Category IB)** (Key Question 3C)

3.C.4.c Minimize patient movements within a ward or unit. Symptomatic and recovering patients should not leave the patient-care area unless it is for essential care or treatment, to reduce the likelihood of environmental contamination and transmission of norovirus in unaffected clinical areas. **(Category II)** (Key Question 3C)

3.C.4.d Suspend group activities (e.g., dining events) during an uncontrolled outbreak of norovirus gastroenteritis. **(Category II)** (Key Question 3C)

3.C.5.b Staff who have recovered from recent suspected norovirus infection associated with this outbreak may be best suited to care for exposed or symptomatic patients. **(Category II)** (Key Question 3C)

HAND HYGIENE

3.C.1.a Perform handwashing, using soap and water, according to Standard Precautions (i.e, prior to contact with patients, medication preparation, preparation or consumption of food, insertion of invasive devices, after touching contaminated equipment, removing personal protective equipment (PPE;e.g., gloves), or toileting activities with patients with symptoms of norovirus infection (cf: http://www.cdc.gov/mmwr/PDF/rr/rr5116.pdf). **(Category IB)** (Key Question 3C)

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3.C.1.b. Areas affected by outbreaks of norovirus gastroenteritis should actively promote adherence with hand hygiene among healthcare personnel, patients, and visitors. **(Category IB)** (Key Question 3C)

3.C.1.b.1 During outbreaks, use of soap and water is the preferred method of hand hygiene. Consider FDA-approved alcohol-based hand sanitizers as a supplemental method of hand hygiene during outbreaks of norovirus gastroenteritis when hands are not visibly soiled and have not been in contact with diarrheal patients, contaminated surfaces, or blood or other body fluids. **(Category II)** (Key Question 3C)

3.C.1.b.3 Ethanol-based hand sanitizers (60-95%) are preferred as a supplemental method of hand hygiene compared to other alcohol or non-alcohol based hand sanitizer products during outbreaks of norovirus gastroenteritis. **(Category II)** (Key Question 3C)

PATIENT TRANSFER AND WARD CLOSURE

3.C.6 Closure of wards to new admissions or transfers is suggested as a measure to attenuate the magnitude of an outbreak of norovirus gastroenteritis. The threshold for ward closure varies and depends on risk assessments by infection prevention personnel and facility leadership. **(Category II)** (Key Question 3C)

3.C.11 During outbreaks, patients on Contact Precautions for norovirus can be transferred or discharged to skilled nursing facilities as needed. If receiving facilities are unable to provide adequate cohorting or isolation provisions, it may be prudent to postpone transfers until arrangements are made for appropriate isolation or cohorting. Expedite the discharge of symptomatic or recovering patients who are medically suitable for discharge to their place of residence. **(Category II)** (Key Question 3C)

Implement systems to designate patients with symptomatic norovirus and to notify receiving healthcare facilities or personnel prior to transfer of such patients within or between facilities. (Category II)

INDIRECT PATIENT CARE STAFF – FOOD HANDLERS IN HEALTHCARE

1.C.3.a To prevent food-related outbreaks of norovirus gastroenteritis in healthcare settings, food handlers should perform hand hygiene prior to contact with or the preparation of food items and beverages. **(Category IB)** (Key Question 1C)

1.C.3.b Personnel who prepare or distribute food or work in the vicinity of food should be excused from work if they develop symptoms of acute gastroenteritis consistent with norovirus infection. Personnel should not return to these activities until a minimum of 48 hours after the resolution of symptoms or longer as required by local health regulations. **(Category IB)** (Key Question 1C)

3.B.2 All shared food items for patients or staff should be removed from clinical areas for the duration of the outbreak. **(Category IB)** (Key Question 3B)

DIAGNOSTICS

1.C.1 Develop and institute facility policies to enable rapid clinical and virological confirmation of suspected cases of symptomatic norovirus infection and promptly implement control measures to reduce the magnitude of outbreaks in a healthcare facility **(Category II)** (Key Question 1C)

2.A.1 In the absence of clinical laboratory diagnostics or in the case of delay in obtaining laboratory results, use Kaplan's clinical and epidemiologic criteria to identify a norovirus gastroenteritis outbreak (see Table 4 for Kaplan's criteria). **(Category IA**) (Key Question 2A)

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2.B Submit stool specimens as early as possible during a suspected norovirus gastroenteritis outbreak and ideally from individuals during the acute phase of illness (within 2-3 days of onset). It is suggested that healthcare facilities consult with state or local public health authorities regarding the types of and number of specimens to obtain for testing. **(Category II**) (Key Question 2B)

2.C Facilities should follow up-to-date and local laboratory protocols for testing clinical specimens for suspected cases of viral gastroenteritis. Refer to the Centers for Disease Control and Prevention (CDC) for the most current recommendations for norovirus diagnostic testing (http://www.cdc.gov/ncidod/dvrd/revb/gastro/norovirus-factsheet.htm). **(Category IB**) (Key Question 2C)

Routine collecting and processing of environmental swabs during a norovirus outbreak is not required. When supported by epidemiologic evidence, environmental sampling may be useful to highlight specific sources of contamination during investigations. **(Category II)**

Specimens obtained from vomitus may be submitted for laboratory identification of norovirus when fecal specimens are unavailable. Testing of vomitus as compared to fecal specimens may be less sensitive due to lower detectable viral concentrations. **(Category II)**

PERSONAL PROTECTIVE EQUIPMENT

1.C.4 If norovirus infection is suspected, healthcare personnel and visitors should wear PPE to reduce the likelihood of exposure to, or contamination by vomitus or fecal material when caring for patients with symptoms of norovirus infection. Gloves and gowns are recommended for the care of patients on Contact Precautions and according to Standard Precautions for any contact with body fluids, non-intact skin, or contaminated surfaces. **(Category IB)** (Key Question 1C)

3.C.2.a Use a surgical or procedure mask, and eye protection if there is a risk of splashes to the face during the care of patients, particularly among those who are vomiting. **(Category IB)** (Key Question 3C)

3.C.2.b Clinical and environmental services staff, as well as visitors, should wear gloves and gowns when entering areas under isolation or cohorting. **(Category IB)** (Key Question 3C)

ENVIRONMENTAL CLEANING

3.B.1 Perform routine cleaning and disinfection of frequently touched environmental surfaces and equipment in isolation and cohorted areas, as well as high traffic clinical areas. Cleaning should include, but is not limited to, commodes, toilets, hand/bedrailing, faucets, telephones, door handles, computer equipment, and kitchen preparation surfaces. Staff should adhere to established healthcare facility policies, which guide effective cleaning and disinfection of patient equipment using EPA-registered cleaning and disinfecting agents with activity against norovirus or norovirus surrogates (http://www.epa.gov/oppad001/list_g_norovirus.pdf). **(Category IB)** (Key Question 3B)

3.C.12.a Clean and disinfect shared equipment with an appropriate EPA-registered product between patient uses, and follow the manufacturer's recommendations for contact times and application. Consider using a chlorine-based agent like sodium hypochlorite, but other agents like hydrogen peroxide, citric acid, quaternary ammonium, and chlorine dioxide products have also been approved. The EPA lists registered products with activity against norovirus on their website (http://www.epa.gov/oppad001/list_g_norovirus.pdf). Ensure that EPA-labeled products are approved for use in healthcare settings. **(Category IB)** (Key Question 3C)

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3.C.12.b.1 Increase the frequency of cleaning and disinfection of patient care areas and frequently touched surfaces during outbreaks of norovirus gastroenteritis. Unit level cleaning may be increased up to twice daily, with frequently touched surfaces cleaned and disinfected up to three times daily using EPA-approved products for healthcare settings. **(Category IB)** (Key Question 3C)

3.C.12.b.2 Clean and disinfect surfaces starting from the areas with a lower likelihood of norovirus contamination (e.g., tray tables, counter tops) to areas with highly contaminated surfaces (e.g., toilets, bathroom fixtures). Change mop heads when new solutions are prepared, or after cleaning large spills of emesis or fecal material. **(Category IB)** (Key Question 3C)

3.C.12.c.1 Discard disposable patient-care items from patient rooms after patients on isolation for norovirus gastroenteritis are discharged or transferred to a healthcare facility. Unused linens remaining in a patient room should be laundered before use on another patient. **(Category II)** (Key Question 3C)

3.C.12.c.2 No additional provisions for the use of disposable patient service items such as utensils or dishware are required for patients with symptoms of norovirus infection. Silverware and dishware may undergo normal processing and cleaning using standard procedures. Staff handling soiled patient-service items should use Standard Precautions. **(Category II)** (Key Question 3C)

3.C.12.d.1 Avoid the use of upholstered furniture and rugs or carpets in patient care areas, as these objects are difficult to clean and disinfect completely. If this option is not possible, we suggest immediately cleaning soilage, such as emesis or fecal material, from upholstery, using a manufacturer-approved cleaning agent or detergent. Opt for seating in patient-care areas that can withstand routine cleaning and disinfection. **(Category II)** (Key Question 3C)

3.C.12.d.2 Steam cleaning of upholstered furniture present in patient rooms is suggested upon patient discharge. Consider discarding items that cannot be appropriately cleaned. Appropriate PPE should be used during these activities. **(Category II)** (Key Question 3C)

3.C.12.d.3 Change privacy curtains when they are visibly soiled and upon patient discharge or transfer. **(Category II)** (Key Question 3C)

3.C.12.d.4 Handle soiled linens carefully, without agitating them, to avoid dispersal of virus. Wear appropriate PPE, such as gloves, to minimize the likelihood of personal contamination. **(Category IB)** (Key Question 3C)

3.C.12.d.5 No additional provisions, such as the practice of double bagging, incineration, or modifications for laundering are recommended for linen. Staff handling soiled linens should adhere to Standard Precautions. **(Category II)** (Key Question 3C)

3.C.12.e.1 Clean surfaces and patient equipment prior to the application of a disinfectant. Presence of residual organic and protein loads on surfaces reduces the overall effectiveness of disinfectants. Follow manufacturer's recommendations for optimal disinfectant dilution, application, and surface contact time. **(Category IB)** (Key Question 3C)

STAFF LEAVE AND POLICY

3.C.3 Facilities should develop and adhere to sick leave policies for healthcare personnel symptomatic with norovirus infection. Ill staff members should be excluded from work for a minimum of 48 hours after the resolution of symptoms. Once staff return to work, adherence to hand hygiene must be maintained. **(Category IB)** (Key Question 3C)

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3.C.5.a Establish protocols for staff cohorting in the event of an outbreak of norovirus gastroenteritis, where staff care for one patient cohort on their ward (i.e., symptomatic, exposed but asymptomatic, or unexposed), and do not move between patient cohorts. **(Category IB)** (Key Question 3C)

3.C.5.c Exclude non-essential staff, students, and volunteers from working in areas experiencing outbreaks of norovirus gastroenteritis. **(Category IB)** (Key Question 3C)

VISITORS

3.C.7.a Visitor policies should be established for acute gastroenteritis (e.g., norovirus) outbreaks. **(Category IB)** (Key Question 3C)

3.C.7.b Restrict non-essential visitors from affected areas during outbreaks of norovirus gastroenteritis. For those facilities that proceed with continued visitor privileges, screening visitors for symptoms consistent with norovirus infection is encouraged. **(Category IB)** (Key Question 3C)

EDUCATION

3.C.8.a Healthcare facilities should provide education to staff, patients, and visitors about symptoms, preventing infection, and modes of transmission of norovirus at the start of and throughout the duration of an outbreak. **(Category IB)** (Key Question 3C)

3.C.8.b Consider providing educational sessions and making resources available on the prevention and management of norovirus before outbreaks occur, as part of annual trainings, and when sporadic cases are detected. **(Category II)** (Key Question 3C)

ACTIVE CASE-FINDING

3.C.9.a Begin active case-finding when a cluster of acute gastroenteritis cases is detected in the healthcare facility. Use a defined case definition to populate line lists to track both exposed and symptomatic patients and staff. Collect relevant epidemiological, clinical, and demographic data as well as information on patient location and outcomes. **(Category IB)** (Key Question 3C)

COMMUNICATION AND NOTIFICATION

3.C.10 Develop written policies that specify the chains of communication needed to manage and report outbreaks of norovirus gastroenteritis. Key stakeholders such as clinical staff, environmental services, laboratory administration, healthcare facility administration and public affairs, as well as state or local public health authorities, should be included in the framework. **(Category IB)** (Key Question 3C)

3.C.9.b Notify appropriate local and state health departments, as required by state and local public health regulations, if an outbreak of norovirus gastroenteritis is suspected. **(Category IC)** (Key Question 3C)

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III. Implementation and Audit

Prioritization of Recommendations

Although it is important to note that the Category I recommendations in this guideline are all considered strong recommendations and should be implemented, it may not be feasible to implement all 28 category I recommendations concurrently. This section provides healthcare facilities guidance by focusing on those recommendations chosen by a consensus of experts based on strength of recommendation as well as on the likely impact of the strategy in preventing norovirus gastroenteritis outbreaks. Note that a limited number of Category II recommendations are included as priority implementation strategies. While these recommendations currently are limited by the strength of the available evidence, they were identified as key activities in preventing transmission of norovirus in healthcare settings.

Priority Recommendations

2.A.1 In the absence of clinical laboratory diagnostics or in the case of delay in obtaining laboratory results, use Kaplan's clinical and epidemiologic criteria to identify a norovirus gastroenteritis outbreak. **(Category IA**) (Key Question 2A)

1.A.1 Avoid exposure to vomitus or diarrhea. For a recognized outbreak, use Contact Precautions for patients with symptoms consistent with norovirus gastroenteritis. Sporadic cases of norovirus can be managed under Standard Precautions with provisions to reduce staff, visitor, and patient exposures to vomitus or diarrhea. **(Category IB)** (Key Question 1A)

3.C.3 Facilities should develop and adhere to sick leave policies for healthcare personnel symptomatic with norovirus infection. Ill staff members should be excluded from work for a minimum of 48 hours after the resolution of symptoms. Once staff return to work, adherence to hand hygiene must be maintained. **(Category IB)** (Key Question 3C)

3.C.5.a Establish protocols for staff cohorting in the event of an outbreak of norovirus gastroenteritis, where staff care for one patient cohort on their ward (i.e., symptomatic, exposed but asymptomatic, or unexposed), and do not move between patient cohorts. **(Category IB)** (Key Question 3C)

3.C.9.b Notify appropriate local and state health departments, as required by state and local public health regulations, if an outbreak of norovirus gastroenteritis is suspected. **(Category IC)** (Key Question 3C)

3.C.12.b.1 Increase the frequency of cleaning and disinfection of patient care areas and frequently touched surfaces during outbreaks of norovirus gastroenteritis. Unit level cleaning may be increased up to twice daily, with frequently touched surfaces cleaned and disinfected up to three times daily using EPA-approved products for healthcare settings. **(Category IB)** (Key Question 3C)

3.C.1.b.1 During outbreaks, use of soap and water is the preferred method of hand hygiene. Consider FDA-approved alcohol-based hand sanitizers as a supplemental method of hand hygiene during outbreaks of norovirus gastroenteritis when hands are not visibly soiled and have not been in contact with diarrheal patients, contaminated surfaces, or blood or other body fluids. **(Category II)** (Key Question 3C)

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3.C.11 During outbreaks, patients on Contact Precautions for norovirus can be transferred or discharged to skilled nursing facilities as needed. If receiving facilities are unable to provide adequate cohorting or isolation provisions, it may be prudent to postpone transfers until arrangements are made for appropriate isolation or cohorting. Expedite the discharge of symptomatic or recovering patients who are medically suitable for discharge to their place of residence. **(Category II)** (Key Question 3C)

Performance Measures

Use of performance measures may assist individual healthcare facilities, as well as local and state health departments to recognize increasing and peak activities of norovirus infection, and may allow for prevention and awareness efforts to be implemented rapidly or as disease incidence escalates. Evaluate fluctuations in the incidence of norovirus in healthcare settings using the National Outbreak Reporting System (NORS) (http://www.cdc.gov/outbreaknet/nors/). This system monitors the reporting of waterborne, foodborne, enteric person-to-person, and animal contact-associated disease outbreaks to CDC by state and territorial public health agencies. This surveillance program was previously used only for reporting foodborne disease outbreaks, but it has now expanded to include all enteric outbreaks, regardless of mode of transmission. Additionally, CDC is currently implementing a national surveillance system (CaliciNet) for genetic sequences of noroviruses; this system may also be used to measure changes in the epidemiology of healthcare-associated norovirus infections.

IV. Recommendations for Further Research

Our literature review revealed that many of the studies addressing strategies to prevent norovirus gastroenteritis outbreaks in healthcare facilities were not of sufficient quality to allow firm conclusions regarding the benefit of certain interventions. Future studies of norovirus gastroenteritis prevention should:

1. Include primary analytic research (e.g. analysis which identifies the impact of specific or bundled infection control interventions),
2. Use of controls or comparison groups in both clinical and laboratory settings,
3. Compare surrogate and human norovirus strains, focusing on the differences in their survival and persistence after cleaning and disinfection, and compare the natural history of disease in animal models to that in human norovirus infections,
4. Consider healthcare-focused risk factors (e.g the impact of isolation vs. cohorting practices, duration of isolation, hand hygiene policies during outbreaks of norovirus, etc.)
5. Be statistically powered to detect clinically relevant differences that may exist,
6. Evaluate clinically relevant outcomes, and
7. Focus on infection control-interventions and associated outcomes.

The following are specific areas recommended for further research (see also recommendations under the category of No recommendation/unresolved issue in the Evidence Review):

1. Assess the benefit of using the Kaplan criteria as an early detection tool for outbreaks of norovirus gastroenteritis in healthcare settings and examine whether the Kaplan criteria are differentially predictive of select strains of norovirus.
2. Determine correlations between prolonged shedding of norovirus after symptoms have subsided and the likelihood of secondary transmission of norovirus infection.
3. Identify a satisfactory animal model for surrogate testing of norovirus properties and pathogenesis. Translate laboratory findings into practical infection prevention strategies.
4. Quantify the effectiveness of cleaning and disinfecting agents against norovirus or appropriate surrogates.
5. Evaluate effectiveness and reliability of novel environmental disinfection strategies such as fogging, UV irradiation, vapor-phase hydrogen peroxides, and ozone mists to reduce norovirus contamination.

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6. Assess the utility of medications that may attenuate the duration and severity of norovirus illness.
7. Evaluate the effectiveness of FDA-approved hand sanitizers against norovirus or appropriate surrogates, including viral persistence after treatment with non-alcohol based products.
8. Develop methods to evaluate norovirus persistence in the environment, with a focus on persistent infectivity.
9. Determine the role of asymptomatic shedding (among recovered persons and carriers) in secondary transmission.
10. Evaluate the duration of protective immunity and other protective host factors, including histo-blood group antigens (HBGA) and secretor status.
11. Assess the contribution of water or food sources to outbreaks of norovirus gastroenteritis in healthcare settings.

V. Background

Norovirus is the most common etiological agent of acute gastroenteritis and is often responsible for outbreaks in a wide spectrum of community and healthcare settings. These single-stranded RNA viruses belong to the family *Caliciviridae*, which also includes the genera Sapovirus, Lagovirus, and Vesivirus.[1] Illness is typically self-limiting, with acute symptoms of fever, nausea, vomiting, cramping, malaise, and diarrhea persisting for 2 to 5 days.[2,3] Noteworthy sequelae of norovirus infection include hypovolemia and electrolyte imbalance, as well as more severe medical presentations such as hypokalemia and renal insufficiency. As most healthy children and adults experience relatively mild symptoms, sporadic cases and outbreaks may be undetected or underreported. However, it is estimated that norovirus may be the causative agent in over 23 million gastroenteritis cases every year in the United States, representing approximately 60% of all acute gastroenteritis cases.[4] Based on pooled analysis, it is estimated that norovirus may lead to over 91,000 emergency room visits and 23,000 hospitalizations for severe diarrhea among children under the age of five each year in the United States.[5,6]

Noroviruses are classified into five genogroups, with most human infections resulting from genogroups GI and GII.[6] Over 80% of confirmed human norovirus infections are associated with genotype GII.4.[7,8] Since 2002, multiple new variants of the GII.4 genotype have emerged and quickly become the predominant cause of human norovirus disease.[9] As recently as late 2006, two new GII.4 variants were detected across the United States and resulted in a 254% increase in acute gastroenteritis outbreaks in 2006 compared to 2005.[10] The increase in incidence was likely associated with potential increases in pathogenicity and transmissibility of, and depressed population immunity to these new strains.[10] CDC conducts surveillance for foodborne outbreaks, including norovirus or norovirus-like outbreaks, through voluntary state and local health reports using the Foodborne Disease Outbreak Surveillance System (FBDSS). CDC summary data for 2001-2005 indicate that caliciviruses (CaCV), primarily norovirus, were responsible for 29% of all reported foodborne outbreaks, while in 2006, 40% of foodborne outbreaks were attributed to norovirus.[11] In 2009, the National Outbreak Reporting System (NORS) was launched by the CDC after the Council of State and Territorial Epidemiologists (CSTE) passed a resolution to commit states to reporting all acute gastroenteritis outbreaks, including those that involve person-to-person or waterborne transmission.

Norovirus infections are seen in all age groups, although severe outcomes and longer durations of illness are most likely to be reported among the elderly.[2] Among hospitalized persons who may be immunocompromised or have significant medical comorbidities, norovirus infection can directly result in a prolonged hospital stay, additional medical complications, and, rarely, death.[10] Immunity after infection is strain-specific and appears to be limited in duration to a period of several weeks, despite the fact that seroprevalence of antibody to this virus reaches 80-90% as populations transition from childhood to adulthood.[2] There is currently no vaccine available for norovirus and, generally, no medical treatment is offered for norovirus infection apart from oral or intravenous repletion of volume.[2]

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Food or water can be easily contaminated by norovirus, and numerous point-source outbreaks are attributed to improper handling of food by infected food-handlers, or through contaminated water sources where food is grown or cultivated (e.g., shellfish and produce). The ease of its transmission, with a very low infectious dose of <10 -100 virions, primarily by the fecal-oral route, along with a short incubation period (24-48 hours) [12,13], environmental persistence, and lack of durable immunity following infection, enables norovirus to spread rapidly through confined populations.[6]

Institutional settings such as hospitals and long-term care facilities commonly report outbreaks of norovirus gastroenteritis, which may make up over 50% of reported outbreaks.[11] However, cases and outbreaks are also reported in a wide breadth of community settings such as cruise ships, schools, day-care centers, and food services, such as hotels and restaurants. In healthcare settings, norovirus may be introduced into a facility through ill patients, visitors, or staff. Typically, transmission occurs through exposure to direct or indirect fecal contamination found on fomites, by eating foods prepared by ill food-handlers, by contact with body fluids or skin surfaces, or by exposure to aerosols of norovirus from vomiting persons.[2,6] Healthcare facilities managing outbreaks of norovirus gastroenteritis may experience significant costs relating to isolation precautions and PPE, ward closures, supplemental environmental cleaning, staff cohorting or replacement, and sick time.

The pathogenesis of human norovirus infection

The P2 subdomain of the viral capsid is the likely binding site of norovirus, and is the most variable region on the norovirus genome.[14] The P2 ligand is the natural binding site with human HBGA, which may be the point of initial viral attachment.[14] HBGA is found on the surfaces of red blood cells and is also expressed in saliva, in the gut, and in respiratory epithelia. The strength of the virus binding may be dependent on the human host HBGA receptor sites, as well as on the infecting strain of norovirus. Infection appears to involve the lamina propria of the proximal portion of the small intestine,[15] yet the cascade of changes to the local environment is unknown.

Clinical diagnosis of norovirus gastroenteritis is common, and, under outbreak conditions, the Kaplan Criteria are often used to determine whether gastroenteritis clusters or outbreaks of unknown etiology are likely to be attributable to norovirus.[16] These criteria are:

1. Submitted fecal specimens negative for bacterial and if tested, parasitic pathogens,
2. Greater than 50% of cases reporting vomiting as a symptom of illness,
3. Mean or median duration of illness ranging between 12 and 60 hours, and
4. Mean or median incubation period ranging between 24 and 48 hours.

The current standard for norovirus diagnostics is reverse transcriptase polymerase chain reaction (RT-PCR), but clinical laboratories may use commercial enzyme immunoassays (EIA), or electron microscopy (EM).[6] ELISA and transmission electron microscopy (TEM) demonstrate high sensitivity but lower specificities against the RT-PCR gold standard. The use of enzyme-linked immunosorbent assays (ELISA) and EM together can improve the overall test characteristics—particularly test specificity.[17] Improvements in PCR have included the development of multiple nucleotide probes to detect a spectrum of genotypes as well as methods to improve detection of norovirus from dilute samples or low viral loads and those containing PCR-inhibitors.[18] While the currently available diagnostic methods are capable, with differing degrees of sensitivity and specificity, of detecting the physical presence of human norovirus from a sample, its detection does not directly translate into information about residual infectivity.

A significant challenge to controlling the environmental spread of norovirus in healthcare and other settings is the paucity of data available on the ability of human strains of norovirus to persist and remain infective in environments after cleaning and disinfection.[19] Identifying the physical and chemical properties of norovirus is limited by the fact that human strains are presently uncultivable *in vitro*. The majority of research evaluating

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the efficacy of both environmental and hand disinfectants against human norovirus over the past two decades has primarily utilized feline calicivirus (FCV) as a surrogate. It is still unclear whether FCV is an appropriate surrogate for human norovirus, with some research suggesting that human norovirus may exhibit more resistance to disinfectants than does FCV.[20] Newer research has identified and utilized a murine norovirus (MNV) surrogate, which exhibits physical properties and pathophysiology more similar to those of human norovirus.[20] Currently, the Environmental Protection Agency (EPA) offers a list of approved disinfectants demonstrating efficacy against FCV, and the Federal Drug Administration (FDA) is responsible for evaluating hand disinfectants with label-claims against FCV as a surrogate for human norovirus (among other epidemiologically significant pathogens). It is unknown whether there are variations of physical and chemical tolerances to disinfectants and other virucidal agents among the various human norovirus genotypes. Other research pathways are evaluating the efficacy of fumigants, such as vapor phase hydrogen peroxides, as well as fogging methods as virucidal mechanisms to eliminate norovirus from environmental surfaces.

VI. Scope and Purpose

This guideline provides recommendations for the prevention and control of norovirus gastroenteritis outbreaks in healthcare settings. All patient populations and healthcare settings have been included in our review of the evidence. The guideline also includes specific recommendations for implementation, performance measurement, and surveillance strategies. Recommendations for further research are also included to address the knowledge gaps relating to norovirus gastroenteritis outbreak prevention and management that were identified during the literature review.

To evaluate the evidence on preventing and managing norovirus gastroenteritis outbreaks, we examined data addressing three key questions:

1. What host, viral, or environmental characteristics increase or decrease the risk of norovirus infection in healthcare settings?
2. What are the best methods to identify an outbreak of norovirus gastroenteritis in a healthcare setting?
3. What interventions best prevent or contain outbreaks of norovirus gastroenteritis in the healthcare setting?

This document is intended for use by infection prevention staff, healthcare epidemiologists, healthcare administrators, nurses, other healthcare providers, and persons responsible for developing, implementing, and evaluating infection prevention and control programs for healthcare settings across the continuum of care. The guideline can also be used as a resource for societies or organizations that wish to develop guidance on prevention or management of outbreaks of norovirus gastroenteritis for specialized settings or populations.

VII. Methods

This guideline was based on a targeted systematic review of the best available evidence on the prevention and control of norovirus gastroenteritis outbreaks in healthcare settings. We used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach[21-24] to provide explicit links between the available evidence and the resulting recommendations. Our guideline development process is outlined in *Figure 1.*

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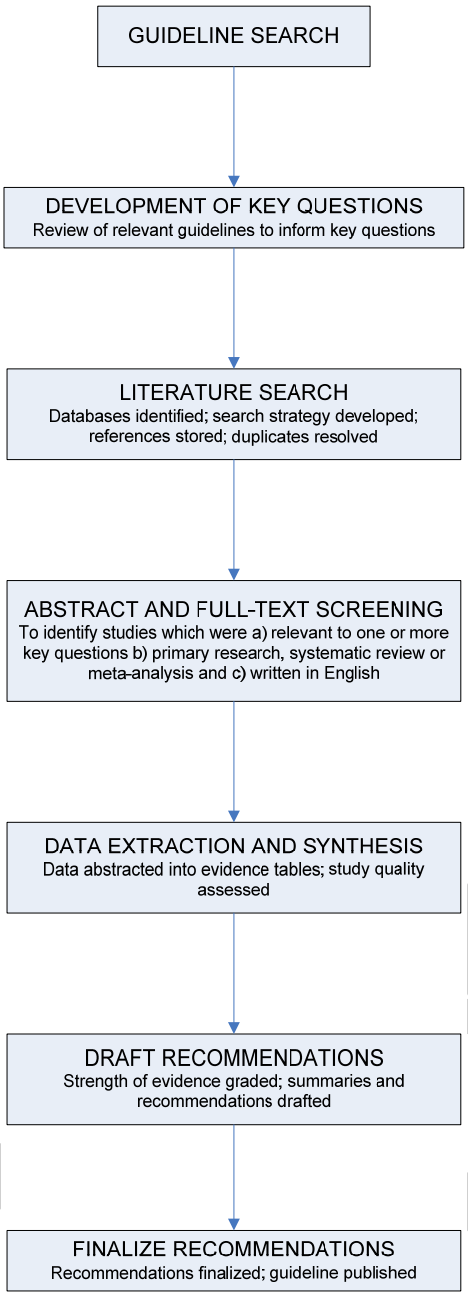
Figure 1. The Guideline Development Process



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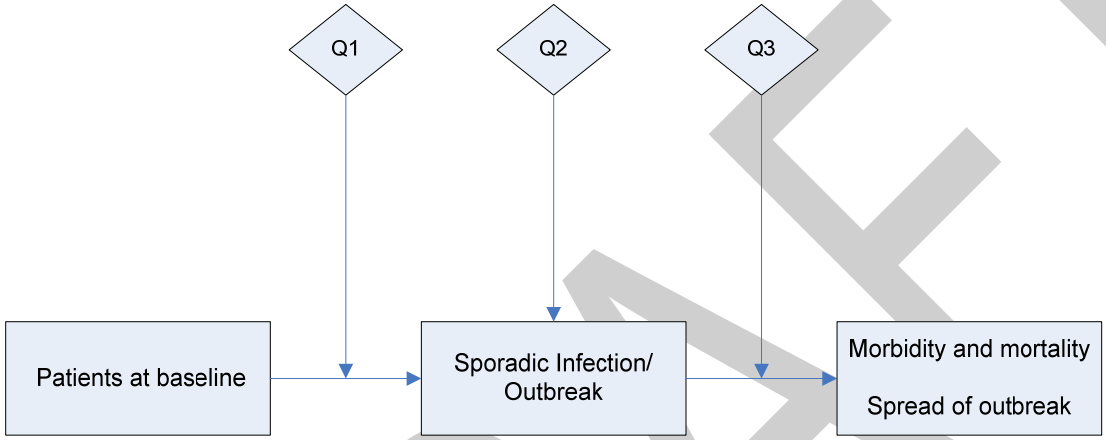
Development of Key Questions

We first conducted an electronic search of the National Guideline Clearinghouse, MEDLINE, EMBASE, the Cochrane Health Technology Assessment Database, the NIH Consensus Development Program, and the National Institute for Health and Clinical Excellence, the Scottish Intercollegiate Guidelines Network and the United States Preventive Services Task Force databases for existing national and international guidelines relevant to norovirus. The strategy used for the guideline search and the search results can be found in *Appendix 1A.* A preliminary list of key questions was developed from a review of the relevant guidelines identified in the search.[25-49] Key questions were put in final form after vetting them with a panel of content experts and HICPAC members. An analytic framework depicting the relationship among the key questions is included in *Figure 2*.

Figure 2. Norovirus Analytic Framework



Literature Search

Following the development of the key questions, search terms were developed for identifying literature most relevant to those questions. For the purposes of quality assurance, we compared these terms to those used in relevant seminal studies and guidelines. These search terms were then incorporated into search strategies for the relevant electronic databases. Searches were performed in MEDLINE, EMBASE, CINAHL, the Cochrane Library, Global Health and ISI Web of Science (all databases were searched to the end of February 2008), and the resulting references were imported into a reference manager, where duplicates were resolved. The detailed search strategy used for identifying primary literature and the results of the search can be found in *Appendix 1B*.

Study Selection

Titles and abstracts from references were screened by a single reviewer (T.M. or K.B.S.). Full text articles were retrieved if they were 1) relevant to one or more key questions, 2) primary research, systematic reviews or meta-analyses, and 3) written in English. To be included, studies had to measure ≥ 1 clinically relevant outcome. For Key Questions 1 and 3, this included symptoms of norovirus infection, or stool antigen, virus, or EM results. For Key Question 2, this included any study published after 1997 that reported test characteristics (e.g., sensitivity, specificity, predictive values, likelihood ratios). Outbreak descriptions were included if: 1) norovirus was confirmed as the cause by EM, PCR, or antigen tests AND 2) the outbreak occurred in a healthcare setting and included a list of interventions or practices used to prevent or contain the outbreak OR 3) the outbreak occurred in any setting, but the report included statistical analyses. Full-text articles were screened by two independent reviewers (T.M., and I.L., or K.B.S.) and disagreements were resolved by discussion. The results of this process are depicted in *Figure 3.*

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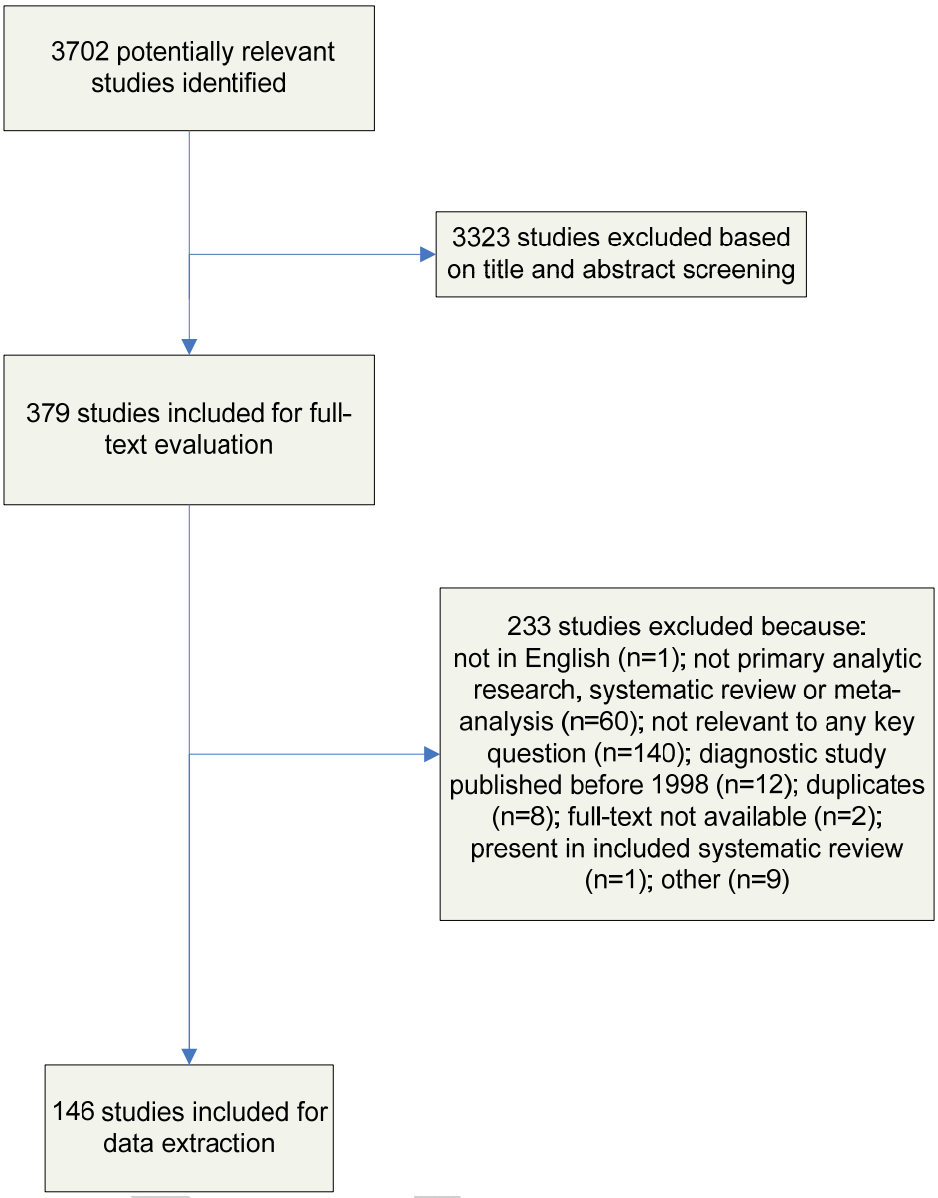
Figure 3. Results of the Study Selection Process



Data Extraction and Synthesis

For those studies meeting inclusion criteria, data on the study author, year, design, objective, population, setting, sample size, power, follow-up, and definitions and results of clinically relevant outcomes were extracted into standardized data extraction forms (*Appendix 3*). From these, three evidence tables were developed, each of which represented one of our key questions *(Appendix 2)*. Studies were extracted into the

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most relevant evidence table. Then, studies were organized by the common themes that emerged within each evidence table. Data were extracted by a single author (R.K.A or I.L.) and cross-checked by another author (R.K.A or I.L.). Disagreements were resolved by the remaining authors. Data and analyses were extracted as originally presented in the included studies. Meta-analyses were performed only where their use was deemed critical to a recommendation and only in circumstances in which multiple studies with sufficiently homogenous populations, interventions, and outcomes could be analyzed. Systematic reviews were included in our review. To avoid duplication of data, we excluded primary studies if they were also included in a systematic review captured by our search. The only exception to this was if the primary study also addressed a relevant question that was outside the scope of the included systematic review. Before exclusion, data from the primary studies that we originally captured were abstracted into the evidence tables and reviewed. We also excluded systematic reviews that analyzed primary studies that were fully captured in a more recent systematic review. The only exception to this was if the older systematic review also addressed a relevant question that was outside the scope of the newer systematic review. To ensure that all relevant studies were captured in the search, the bibliography was vetted by a panel of content experts. For the purposes of our review, statistical significance was defined as $p \leq 0.05$.

Grading of Evidence

First, the quality of each study was assessed using scales adapted from existing methodology checklists,[50-54] and scores were recorded in the evidence tables. *Appendix 4* includes the sets of questions we used to assess the quality of each of the major study designs. Descriptive studies were those without a control or comparator group, including case series and ecologic studies. Basic science studies comprised research conducted *in vitro*. Other study designs like prospective and retrospective controlled trials and RCTs were defined using standard definitions, and criteria used in their classification were outlined in *Appendix 4*. Next, the quality of the evidence base was assessed using methods adapted from the GRADE Working Group.[21-24] In summary, GRADE tables were developed for each of the interventions or questions addressed within the evidence tables. Included in the GRADE tables were the intervention of interest, any outcomes listed in the evidence tables that were judged to be clinically important, the quantity and type of evidence for each outcome, the relevant findings, and the GRADE of evidence for each outcome,as well as an overall GRADE of the evidence base for the given intervention or question. For therapy or harm questions, the initial GRADE of evidence for each outcome was deemed high if the evidence base included an RCT or a systematic review of RCTs, low if the evidence base included only observational studies, or very low if the evidence base consisted only of expert opinion or uncontrolled studies. The initial GRADE could then be modified by eight criteria. Criteria that can decrease the GRADE of an evidence base include shortcomings in quality, consistency, directness, or precision and publication bias. Criteria that can increase the GRADE include a large magnitude of effect, a dose-response gradient, or inclusion of unmeasured confounders that would increase the magnitude of effect (*Table 2)*. Studies equivalent to RCTs (e.g., a controlled study not requiring randomization, like a study in genetically identical mice) would also start out as high level evidence, but would often lose points for indirectness. For questions regarding diagnostic measures (e.g., sensitivity or predictive values) or descriptive measures (e.g., prevalence or incidence), the initial GRADE of evidence can be high even if the evidence base only includes descriptive study designs, like cross-sectional studies.[24] The initial GRADE can then be modified by criteria similar to those used for therapy or harm questions. GRADE definitions are as follows:[21,22]

1. High - further research is very unlikely to change confidence in the estimate of effect
2. Moderate - further research is likely to affect confidence in the estimate of effect and may change the estimate
3. Low - further research is very likely to affect confidence in the estimate of effect and is likely to change the estimate
4. Very low - any estimate of effect is very uncertain

After determining the GRADE of the evidence base for each outcome of a given intervention or question, we calculated the overall GRADE of the evidence base for that intervention or question. The overall GRADE was

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based on the lowest GRADE for the outcomes deemed critical to making a recommendation. For questions that had no outcomes that were deemed critical by the working group, no overall GRADE was assigned to the evidence.

Table 2: Rating the Quality of Evidence Using the GRADE Approach

Type of Evidence	Initial Grade	Criteria to Decrease Grade	Criteria to Increase Grade	Overall Quality Grade
RCT	High	Quality Serious (-1 grade) or very serious (-2 grades) limitation to study quality Consistency Important inconsistency (-1 grade) Directness Some (-1 grade) or major (-2 grades) uncertainty about directness Precision Imprecise or sparse data (-1 grade) Publication bias High risk of bias (-1 grade)	Strong association Strong (+1 grade) or very strong evidence of association (+2 grades) Dose-response Evidence of a dose-response gradient (+1 grade) Unmeasured Confounders Inclusion of unmeasured confounders increases the magnitude of effect (+1 grade)	High Moderate Low Very low
Observational study	Low			
Any other evidence (e.g., expert opinion)	Very low			

Formulating Recommendations

Narrative evidence summaries were then drafted by the working group using the evidence and GRADE tables. One summary was written for each theme that emerged under each key question. The working group used the narrative evidence summaries to develop guideline recommendations. Factors determining the strength of a recommendation included 1) the values and preferences we used to determine which outcomes were critical, 2) the harms and benefits that emerge by weighing the critical outcomes, and 3) the overall GRADE of the evidence base for the given intervention or question (Table 3).[23] If weighing the critical outcomes for a given intervention or question resulted in a net benefit or a net harm, then a Category I Recommendation was formulated to recommend strongly for or against the given intervention. If weighing the critical outcomes for a given intervention or question resulted in a tradeoff between benefits and harms, then a Category II Recommendation was formulated to recommend that providers or institutions consider the intervention when deemed appropriate. If weighing the critical outcomes for a given intervention or question resulted in an uncertain tradeoff between benefits and harms, then a No Recommendation was formulated to reflect this uncertainty.

Table 3. Formulating Recommendations

HICPAC Recommendation	Weighing Benefits and	Quality of Evidence

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	Harms for Critical Outcomes	
STRONG (I)	Interventions with net benefits or net harms	IA – High to Moderate IB – Low to Very Low (Established Practice) IC – High to Very Low (Regulatory)
WEAK (II)	Inteventions with tradeoffs between benefits and harms	High to Very Low
No recommendation/ unresolved issue	Uncertain tradeoffs between benefits and harms	Low to Very Low

For Category I recommendations, levels A and B represent the quality of the evidence underlying the recommendation, with A representing high to moderate quality evidence and B representing low to very low-quality evidence but established standards (e.g., aseptic technique, education and training). For IB recommendations, although there may be low to very low-quality evidence directly supporting the benefits of the intervention, the theoretical benefits are clear, and the theoretical risks are marginal. Level C represents practices required by state or federal regulation, regardless of the quality of evidence. It is important to note that the strength of a Category IA recommendation is equivalent to that of a Category IB or IC recommendation; it is only the quality of the evidence underlying the IA recommendation that makes it different from a IB.

In some instances, multiple recommendations emerged from a single narrative evidence summary. The new HICPAC categorization scheme for recommendations is provided in Table 1, which is reproduced below.

Table 1. HICPAC Categorization Scheme for Recommendations	
Category IA	A strong recommendation supported by high to moderate quality evidence suggesting net clinical benefits or harms.
Category IB	A strong recommendation supported by low-quality evidence suggesting net clinical benefits or harms, or an accepted practice (e.g., aseptic technique) supported by low to very low-quality evidence.
Category IC	A strong recommendation required by state or federal regulation.
Category II	A weak recommendation supported by any quality evidence suggesting a tradeoff between clinical benefits and harms.
Recommendation for further research	An unresolved issue for which there is low to very low-quality evidence with uncertain tradeoffs between benefits and harms.

Category I recommendations are defined as strong recommendations with the following implications:

1. For patients: Most people in the patient's situation would want the recommended course of action and only a small proportion would not; request discussion if the intervention is not offered.
2. For clinicians: Most patients should receive the recommended course of action.
3. For policymakers: The recommendation may be adopted as policy.

Category II recommendations are defined as weak recommendations with the following implications:

1. For patients: Most people in the patient's situation would want the recommended course of action, but many would not.
2. For clinicians: Different choices will be appropriate for different patients and clinicians must help each patient to arrive at a management decision consistent with her or his values and preferences
3. For policymakers: Policy making will require substantial debate and involvement of many stakeholders.

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Our evidence-based recommendations were cross-checked with those from guidelines identified in our original systematic search. Recommendations from previous guidelines for topics not directly addressed by our systematic review of the evidence were included in our "Summary of Recommendations" if they were deemed critical to the target users of this guideline. Unlike recommendations informed by our literature search, these recommendations are not linked to a key question. These recommendations were agreed upon by expert consensus and are designated either IB if they represent a strong recommendation based on accepted practices (e.g., aseptic technique) or II if they are a suggestion based on a probable net benefit despite limited evidence.

The wording of each recommendation was carefully selected to reflect the recommendation's strength.[55] We used the active voice when writing Category I recommendations - the strong recommendations. Phrases like "do" or "do not" and verbs without conditionals were used to convey certainty. We used a more passive voice when writing Category II recommendations - the weak recommendations. Words like "consider" and phrases like "is preferable," "is suggested," or "is not suggested" were chosen to reflect the lesser certainty of the Category II recommendations. Rather than a simple statement of fact, each recommendation is actionable, describing precisely a proposed action to take.

The category "No recommendation/unresolved issue" was most commonly applied to situations in which either 1) the overall quality of the evidence base for a given intervention was low to very low and there was no consensus on the benefit of the intervention or 2) there was no published evidence on outcomes deemed critical to weighing the risks and benefits of a given intervention. If the latter was the case, those critical outcomes were noted at the end of the relevant evidence summary.

Recommendations included in this guideline have been formulated to be consistent with policies from the U.S. FDA and EPA. All recommendations were approved by HICPAC, and are focused only on efficacy, effectiveness, and safety, yet, the optimal use of these guidelines should include a consideration of the costs relevant to the local setting of guideline users.

Reviewing and Finalizing the Guideline

After a draft of the tables, narrative summaries, and recommendations was completed, the working group shared the draft with the expert panel for review in depth. While the expert panel was reviewing this draft, the working group completed the remaining sections of the guideline, including the executive summary, background, scope and purpose, methods, summary of recommendations, and recommendations for guideline implementation, audit, and further research. The working group then made revisions to the draft based on feedback from members of the expert panel and presented the entire draft guideline to HICPAC for review. The CDC then submitted the guideline for clearance and posted it on the Federal Register for public comment. After a period of public comment, the guideline was revised accordingly, and the final guideline was published and posted on the HICPAC website.

Updating the Guideline

Future revisions to this guideline will be dictated by new research and technological advancements for preventing and managing norovirus gastroenteritis outbreaks, and will occur at the request of HICPAC.

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VIII. Evidence Review

Question 1: What host, viral or environmental characteristics increase or decrease the risk of norovirus infection in healthcare settings?

To answer this question, we reviewed the quality of evidence for risk factors examined in 57 studies. In areas in which the outcome of symptomatic norovirus infection was available, we considered it to be the critical outcome in decision-making. The evidence for this question consisted of one systematic review,[56] 51 observational,[57-62,62-64,64-77,77-107] and 4 descriptive studies,[108-111] as well as one basic science study.[112] The paucity of randomized controlled trials (RCT) and the large number of observational studies greatly influenced the quality of evidence supporting the conclusions in the evidence review. Based on the available evidence, the risk factors were categorized as host, viral or environmental characteristics. Host characteristics were further categorized into demographics, clinical characteristics, and laboratory characteristics. Environmental characteristics were further categorized into institution, pets, diet, and exposure. The findings of the evidence review and the grades for all clinically relevant outcomes are shown in Evidence and Grade Table 1.

Q1.A Person characteristics

Q1.A.1 Demographic characteristics

We found low-quality evidence to support age as a risk factor for norovirus infection,[57-60,62-64] and very low-quality evidence to support black race as a protective factor.[64] Three studies indicated that persons over the age of 65 may be at greater risk than younger patients for prolonged duration and recovery from diarrhea in healthcare settings.[57-59] Studies including children under the age of five showed an increased risk of household transmission as well as asymptomatic infection compared with older children and adults.[60,62]

A single but large-scale observational study among military personnel found blacks to be at lower risk of infection than whites.[64] Very low-quality evidence failed to demonstrate meaningful differences in the risk of infection corresponding to strata on the basis of educational background (in the community setting).[61] Based upon very low-quality evidence, outbreaks originating from patients were more likely to affect a large proportion of patients than were outbreaks originating from staff.[56] Exposure to vomitus and diarrheal patients increased the likelihood that long-term care facility staff would develop norovirus infection.[66]

Our search did not identify studies that established a clear association between sex and symptomatic norovirus infection or complications of norovirus infection.[57,59, 79, 98] Low-quality evidence from one prospective controlled trial did not identify sex as a significant predictor of symptomatic norovirus in univariate analyses.[57] There is low-quality evidence suggesting that sex is not a risk factor for protracted illness or complications of norovirus infection including acute renal failure and hypokalemia.[57]

Q1.A.2 Clinical characteristics

Review of the available studies revealed very low-quality evidence identifying clinical characteristics as risk factors for norovirus infection.[57,60,65,68] One small study found hospitalized children with human immunodeficiency virus (HIV) and chronic diarrhea were more likely to have symptomatic infection with small round structured virus (SRSV) than those without HIV and affected with chronic diarrhea.[68] Adult patients with symptomatic norovirus receiving immunosuppressive therapy or admitted with underlying trauma were at risk for a greater than 10% rise in their serum creatinine.[57] Norovirus-infected patients with cardiovascular disease or renal transplant patients were at greater risk for a decrease in their potassium levels by greater than 20%.[57] Observational, univariate study data also supported an increased duration of diarrhea (longer than two days) among hospitalized patients of advanced age and those with malignancies.[57] Our search did not reveal data

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on the risk of norovirus acquisition among those co-infected with other acute gastrointestinal infections, such as *C. difficile*.

Q1.A.3 Laboratory characteristics

Q1.A.3.a Antibody levels

There was very low-quality evidence to support the limited protective effects of serum antibody levels against subsequent norovirus infection.[74-76] In two challenge studies, adult and pediatric subjects with prior exposure to norovirus showed higher antibody titers than found in previously unexposed subjects after initial infection and after challenge.[74,76] The detection of preexisting serum antibody does not appear to correlate with protection against subsequent norovirus challenge, nor did increasing detectable pre-existing antibody titres correlate with attenuations in the clinical severity of disease.[7475] In one study, symptoms such as vomiting, nausea, headaches, and arthralgia were correlated with increasing antibody titres.[74] In a serial challenge study, 50% of participants (n=6) developed infection, and upon subsequent challenge 27-42 months later, only those same participants developed symptoms. A third challenge 4-8 weeks after the second series resulted in symptoms in just a single volunteer.[76] Pre-existing antibody may offer protection to susceptible persons only for a limited window of time, on the order of only a few weeks. Our search revealed neither data on the persistence of immunity to norovirus nor elevations in antibody titers that were consistently suggestive of immunity.

Q1.A.3.b Secretor genotype

Review of the outlined studies demonstrated high-quality evidence to support the protective effects of human host non-secretor genotypes against norovirus infection.[70-72,113] Two observational studies and one intervention study examined volunteers with and without the expression of the secretor (FUT2) genotype after norovirus challenge.[70-72] Statistically significant differences were reported with secretor-negative persons demonstrating a greater likelihood of protection against, or innate resistance to symptomatic and asymptomatic norovirus infection than seen in persons with secretor-positive genotypes. Our search did not reveal data on the dose-response effects of norovirus in persons with homozygous and heterozygous secretor genotypes. Because the FUT2-mediated secretor positive phenotype appears to confer susceptibility to subsequent norovirus infection following challenge, there is an association between this phenotype and measurable circulating antibody (suggesting prior infection) in the population. One study estimated that 80% of the population is secretor-positive (or susceptible to norovirus) and 20% is secretor-negative (resistant to norovirus challenge independent of inoculum dose). Among susceptible persons, approximately 35% are protected from infection. This protection is potentially linked to a memory-mediated rapid mucosal IgA response to norovirus exposure that is not seen in the other 45% of susceptibles, who demonstrate delayed mucosal IgA and serum IgG responses.[72] Although elevated antibody levels following infection appear to confer some protective immunity to subsequent challenge, paradoxically, measurable antibody titers in the population may be a marker of *increased* susceptibility to norovirus because of the association between such antibodies and FUT2-positive status.

Q1.A.3.c ABO phenotype

We found low-quality evidence suggesting any association of ABO blood type with the risk of norovirus infection.[69,72,73,77,78,114,115] An RCT suggested that persons with histo-blood group type O was associated with an increased risk of symptomatic or asymptomatic norovirus infection among secretor-positive patients.[72] Binding of norovirus to the mucosal epithelium may be facilitated by ligands associated with type-O blood. The other blood types—A, B, and AB—were not associated with norovirus infection after controlling for secretor status. Three studies showed no protective effect of any of the blood types against norovirus.[69,77,78] Our search did not reveal prospective cohort data to correlate the role of ABO blood types with risk of norovirus infection.

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Q1.B Viral characteristics

There was very low-quality evidence to suggest an association of virus characteristics with norovirus infection.[57,108-110] Very low-quality descriptive evidence suggested that increases in overall norovirus activity may result from the emergence of new variants among circulating norovirus strains, and strains may differ in pathogenicity, particularly among GII.3 and GII.4 variants.[108-110] In recent years, GII.4 strains are increasingly reported in the context of healthcare-associated outbreaks, but further epidemiologic and laboratory studies are required to expand on this body of information. Our search did not identify studies examining genotypic characteristics of viruses associated with healthcare-acquired norovirus infection.

Q1.C Environmental characteristics

Q1.C.1 Institutional characteristics

We found very low-quality evidence to support the association of institutional characteristics with symptomatic norovirus infection.[82,99] Among two observational studies, the number of beds within a ward, nurse understaffing, admission to an acute care hospital (compared to smaller community-based facilities), and having experienced a prior outbreak of norovirus gastroenteritis within the past 30 days were all possible risk factors for new infection.[82,99] These increased institutional risks were identified from univariate analyses in pediatric and adult hospital populations. There were statistically significant increased risks of infection among those admitted to geriatric, mental health, orthopedic, and general medicine wards. Our search did not reveal data on the comparative risks of infection among those admitted to private and shared patient rooms.

Q1.C.2 Pets

Review of the outlined studies demonstrated very low-quality evidence to support exposure to pets (e.g., cats and dogs) as a risk factor for norovirus infection.[61] One case-control study examined pet exposure among households in the community and concluded that the effect of cats was negligible.[61] The single study did not demonstrate any evidence of transmission between pets and humans of norovirus infection. Our search did not reveal studies that evaluated the impact of therapy pets in healthcare settings during outbreaks of norovirus gastroenteritis or data examining domestic animals as reservoirs for human infection.

Q1.C.3 Diet

There was low-quality evidence to suggest that extrinsically contaminated food items are commonly implicated as vehicles of norovirus exposure in healthcare settings.[61,77,80,84,86,87,89-97,100-102,104-107,111] Nineteen observational studies itemized statistically significant food sources implicated in community outbreaks.[80,81,84,86,87,89-97,100,101,104-106] Common to most of these food sources was a symptomatic or asymptomatic food-handler. Sauces, sandwiches, fruits and vegetables, salads, and other moisture-containing foods were most often cited as extrinsically contaminated sources of outbreaks of norovirus gastroenteritis. Importantly, these data reflected the breadth of foods that can become contaminated. Tap water and ice were also associated with norovirus contamination during an outbreak with an ill food-handler. This literature review did not identify studies that examined the introduction of intrinsically contaminated produce or meats as a nidus for norovirus infection and dissemination within healthcare facilities.

Q1.C.4 Proximity to infected persons

This review demonstrated high-quality evidence to suggest that proximity to infected persons with norovirus is associated with increased risk of symptomatic infection.[61,62,64,79,83,88,98,103,111] Eight observational studies found statistically significant factors that elevate the risk of infection such as proximate exposure to an infected source within households or in crowded quarters increased infection risk, as did exposures to any or frequent

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vomiting episodes [61,62,64,79,83,88,98,103]. These data suggest person-to-person transmission is dependent on close or direct contact as well as shorter-range aerosol exposures. One observational study established a linear relationship between a point source exposure and attack rate based on proximity to an infected and vomiting source.[88] Our search did not identify studies that quantified the spatial radius necessary for transmission to successfully occur.

Q1 Recommendations

1.A.1 Avoid exposure to vomitus or diarrhea. For a recognized outbreak, use Contact Precautions for patients with symptoms consistent with norovirus gastroenteritis. Sporadic cases of norovirus can be managed under Standard Precautions with provisions to reduce staff, visitor, and patient exposures to vomitus or diarrhea. **(Category IB)** (Key Question 1A)

1.A.2.a Consider longer periods of isolation or cohorting precautions for complex medical patients, especially those with cardiovascular, autoimmune, or renal disorders, as they can experience protracted episodes of diarrhea and prolonged viral shedding. Patients with these or other comorbidities have the potential to relapse and facilities may choose longer periods of isolation based on clinical judgment. **(Category II)** (Key Question 1A)

1.C.1 Develop and institute facility policies to enable rapid clinical and virological confirmation of suspected cases of symptomatic norovirus infection and promptly implement control measures to reduce the magnitude of outbreaks in a healthcare facility **(Category II)** (Key Question 1C)

1.C.3.a To prevent food-related outbreaks of norovirus gastroenteritis in healthcare settings, food handlers should perform hand hygiene prior to contact with or the preparation of food items and beverages. **(Category IB)** (Key Question 1C)

1.C.3.b Personnel who prepare or distribute food or work in the vicinity of food should be excused from work if they develop symptoms of acute gastroenteritis consistent with norovirus infection. Personnel should not return to these activities until a minimum of 48 hours after the resolution of symptoms or longer as required by local health regulations. **(Category IB)** (Key Question 1C)

1.C.4 If norovirus infection is suspected, healthcare personnel and visitors should wear personal protective equipment (PPE) to reduce the likelihood of exposure to, or contamination by vomitus or fecal material when caring for patients with symptoms of norovirus infection. Gloves and gowns are recommended for the care of patients on Contact Precautions and according to Standard Precautions for any contact with body fluids, non-intact skin, or contaminated surfaces. **(Category IB)** (Key Question 1C)

Question 2: What are the best methods to identify an outbreak of norovirus gastroenteritis in a healthcare setting?

To address this question, we critically reviewed studies that provided test characteristics for the diagnosis of norovirus or outbreaks of norovirus gastroenteritis. The available data examined the use of clinical criteria for the diagnosis of an outbreak of norovirus, methods of specimen collection for the diagnosis of a norovirus outbreak, and characteristics of tests used to diagnose norovirus. The evidence consisted of 33 diagnostic

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studies.[17,18,116-146] The findings from the evidence review and the grades of evidence for clinically relevant outcomes are shown in Evidence and Grade Table 2.

Q2.A Clinical Criteria

We found moderate quality evidence from a single diagnostic study supporting the use of the Kaplan criteria to detect outbreaks of norovirus gastroenteritis.[16,116] Of 362 confirmed gastroenteritis outbreaks with complete clinical or laboratory data, the sensitivity of the Kaplan Criteria to detect an outbreak of norovirus gastroenteritis without an identified bacterial pathogen was 68.2%, with a specificity of 98.6%. The positive predictive value (PPV) was 97.1% and the negative predictive value was 81.8%. Individual criteria, such as vomiting among >50% of a patient cohort, brief duration of illness (12-60 hours), or mean incubation time of 24-48 hours, demonstrated high sensitivities (85.8-89.2%), but specificities were low (60.7-69.6%). The use of additional criteria, such as the ratios of fever-to-vomiting and diarrhea-to-vomiting, provided sensitivities of 90.1% and 96.6%, and specificities of 46.6% and 44.5%, respectively. Applied to the 1141 outbreaks of unconfirmed etiology, suspected norovirus or bacterial sources with complete data, the Kaplan criteria estimated that 28% of all 1998-2000 CDC-reported *foodborne* outbreaks might be attributable to norovirus. Our search did not identify studies that have assessed the utility of the Kaplan criteria in healthcare-associated outbreaks of norovirus gastroenteritis.

Q2.B Specimen Collection

There was low-quality evidence from three diagnostic studies outlining the minimum number of stool samples from symptomatic patients required to confirm an outbreak of norovirus gastroenteritis.[117,119,120,122,123] Obtaining a positive EIA result from two or more submitted samples demonstrated a sensitivity of 52.2-57%, with a peak in sensitivity when at least one from a total of six submitted samples was positive for norovirus (71.4-92%). Specificity was 100% when at least one positive EIA was obtained from a minimum of two submitted stool samples.

Using a reverse transcriptase polymerase chain reaction (RT-PCR) method, if at least one positive test was identified among 2 to 4 submitted stool specimens from symptomatic persons, the test sensitivity was greater than 84%. When 5-11 stool samples were submitted and at least 2 were confirmed as positive, the sensitivity of PCR was greater than 92%. When at least one stool specimen was submitted for identification, PCR confirmed norovirus as the causative agent in a larger proportion of outbreaks than those using EM or ELISA methods, and is currently the Gold Standard. Our evaluation was unable to determine how diagnostic test characteristics are affected by the timing of specimen collection relative to the disease process.

Q2.C Diagnostic Methods

We summarized 28 diagnostic studies[17,18,118-120,122,124-139,141-145,147] and 1 descriptive study[121] that evaluated the test characteristics of EIA such as ELISA, EM, reverse transcriptase PCR, and nucleic acid sequence-based amplification (NASBA) in the detection of norovirus in human fecal specimens. Test characteristics for the most common or commercially-available norovirus diagnostics are summarized in the following Table.

Q2 Recommendations

2.A.1 In the absence of clinical laboratory diagnostics or in the case of delay in obtaining laboratory results, use Kaplan's clinical and epidemiologic criteria to identify a norovirus gastroenteritis outbreak. **(Category IA**) (Key Question 2A)

2.A.2 Further research is needed to compare the Kaplan criteria with other early detection criteria for outbreaks

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of norovirus gastroenteritis in healthcare settings, and to assess whether additional clinical or epidemiologic criteria can be applied to detect norovirus clusters or outbreaks in healthcare settings. **(No recommendation/unresolved issue)** (Key Question 2A)

2.B Submit stool specimens as early as possible during a suspected norovirus gastroenteritis outbreak and ideally from individuals during the acute phase of illness (within 2-3 days of onset). It is suggested that healthcare facilities consult with state or local public health regarding the types of and number of specimens to obtain for testing. **(Category II**) (Key Question 2B)

2.C Facilities should follow up-to-date and local laboratory protocols for testing clinical specimens for suspected cases of viral gastroenteritis. Refer to the Centers for Disease Control and Prevention (CDC) for the most current recommendations for norovirus diagnostic testing (http://www.cdc.gov/ncidod/dvrd/revb/gastro/norovirus-factsheet.htm). **(Category IB**) (Key Question 2C)

Table 3. Test Characteristics for Norovirus in Fecal Specimens

Diagnostic method	Reference standard	Quantity and type of evidence	Findings*			
			Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Kaplan criteria	PCR	1 DIAG [116]	68	99	97	82
EIA/ELISA	PCR	10 DIAG [17,118-120,123-128,139]	31 – 90	65 – 100	52 – 100	56-97
EM	PCR	2 DIAG [17,119]	24 – 58	98-99	88-94	71-91
NASBA	PCR	1 DIAG [144]	100	50	-	-

* Range from studies that reported test characteristics
Negative predictive Value, NPV; Positive predictive value, PPV

Table 4. Kaplan Criteria[16]

1) Vomiting in more than half of symptomatic cases

2) Mean (or median) incubation period of 24 to 48 hours

3) Mean (or median) duration of illness of 12 to 60 hours

4) No bacterial pathogen isolated in stool culture

Question 3: What interventions best prevent or contain outbreaks of norovirus gastroenteritis in the healthcare setting?

To address this question, we critically reviewed 69 studies[58,63,66,79,83-85,87,89,92,102,103,112,148-203] for evidence of interventions that might prevent or attenuate an outbreak of norovirus. The available data dealt with viral shedding, recovery of norovirus, and components of an outbreak prevention or containment program, including the use of medications. The evidence consisted of 1 randomized controlled trial,[202] 1 systematic review,[153] 20 basic science studies,[112,162,163,185-201] 43 descriptive studies,[58,63,79,83-85,87,89,92,102,103,149-152,154-161,165-184] and 4 observational studies.[66,148,164,203] The findings from the evidence review and the grades of evidence for clinically relevant outcomes are shown in Evidence and Grade Table 3.

Q3.A Viral Shedding

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Our search did not identify studies demonstrating direct associations between viral shedding and infectivity. However, there was low-quality evidence to support an association between age and duration of viral shedding.[149,150] One observational study suggested that children under the age of six months may be at an increased risk of prolonged viral shedding (greater than two weeks), even after the resolution of symptoms.[148] Other findings suggest that infants can shed higher titers of virus than levels reported in other age groups.[149] We also found high-quality evidence demonstrating viral shedding in asymptomatic subjects, and low-quality evidence demonstrating that shedding can persist for up to 22 days following infection and 5 days after the resolution of symptoms.[150-152] Our search did not identify studies that correlated other factors to duration of viral shedding.

Q3.B Recovery of Norovirus

Q3.B.1 Fomites

We found low-quality evidence positively associating fomite contamination with norovirus infection.[153-159,161,163,194] Similarly, there was low-quality evidence demonstrating transfer of norovirus from fomites to hands.[194] One basic science study demonstrated that norovirus on surfaces can be readily transferred to other fomites (telephones, taps, door handles) via fingertips even when virus has been left to dry for 15 minutes in 30-50% of opportunities.[194] There was moderate quality evidence examining the norovirus contamination of the environment.[153-159,161,163] A single systematic review evaluated 5 outbreaks with environmental sampling data.[153] Three of those outbreaks confirmed environmental contamination with norovirus. Of the over 200 swabs examined from the 5 outbreaks in this review, 36% identified norovirus contamination on various fomites such as curtains, carpets, cushions, commodes and toilets, furnishings and equipment within 3-4 feet of the patient, handrails, faucets, telephones, and door handles. Between two outbreaks that collected 47 environmental samples, norovirus was not detected. Additional studies detected norovirus on kitchen surfaces, elevator buttons, and other patient equipment. [154-157, 194]

There was low-quality evidence regarding the duration of norovirus persistence.[154,155,157-159,161] Norovirus can persist in a dried state at room temperature for up to 21-28 days and, in a single observational study, was undetectable in areas of previously known contamination after 5 months had elapsed.[159] Laboratory studies comparing FCV and MNV-1 also demonstrated persistence of virus in both dried and in fecal suspensions for a minimum of seven days on stainless steel preparations at 4ºC and at room temperature.[20] Within a systematic review, it was observed that norovirus may remain viable in carpets up to 12 days, despite regular vacuuming.[153] Similarly, a cultivable surrogate for human strains of norovirus (FCV) was detected on computer keyboards and mice, as well as telephone components up to 72 hrs from its initial inoculation.[156] Our search did not find studies in which the recovery of norovirus from fomites, food, and water sources was directly associated with transmission of infection in healthcare settings; however transmission from these sources has been well documented in other settings.

Q3.B.2 Foods and Food Preparation Surfaces

We found low-quality evidence suggesting that foods and food-preparation surfaces is a significant source of norovirus transmission in healthcare settings.[112,162,163] There was moderate quality evidence among three basic science studies to suggest that norovirus can be recovered from foods such as meats and produce as well as from utensils and non-porous surfaces (e.g., stainless steel, Formica, ceramics) upon which foods are prepared.[112,162,163] Two of these studies, comprised of low-quality evidence, suggested that the transfer of diluted aliquots of norovirus from stainless steel surfaces to wet and dry food, and through contaminated gloves was detectable using PCR methods. Norovirus transfer was statistically more efficient when it was inoculated onto moist surfaces compared to dry ones.[162,163]

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There was low-quality evidence to suggest that norovirus persists for longer periods in meats compared to other foods and non-porous surfaces, both at 4ºC and at room temperature.[112] There was moderate quality evidence demonstrating that over a period of 7 days after application, both human norovirus genogroup I and a surrogate (FCV) could be detected among all surfaces tested.[112,162] Within the first hour, the log10 of FCV titers declined by 2-3, with an additional drop of 2-4 after 48 hours elapsed.[162] Food and food-preparation areas can serve as a common source of contamination with norovirus in the absence of cleaning and disinfection.

Q3.B.3 Water

Our search did not identify studies that measured the contribution of norovirus-contaminated water to outbreaks in the healthcare setting. However, there was moderate quality evidence to suggest that norovirus could be recovered from water.[155,158,160] Among three outbreaks that examined water as a source, one identified norovirus in 3 of 7 water samples.[160] In outbreaks in the community, which were outside the scope of this review, contaminated surface water sources, well water, and recreational water venues have been associated with outbreaks of norovirus gastroenteritis.[204]

Q3.C Components of an Outbreak Prevention/Containment Program

As with most infection-prevention and control activities during outbreaks in healthcare settings, multiple strategies are instituted simultaneously. Thus, it is difficult to single out particular interventions that may be more influential than others, as it is normally a combination of prudent interventions that reduce disease transmission. Numerous studies cite the early recognition of cases and the rapid implementation of infection control measures as key to controlling disease transmission. The following interventions represent a summary of key components in light of published primary literature and addressed in seminal guidelines on outbreaks of norovirus gastroenteritis.

Q3.C.1 Hand Hygiene

Q3.C.1.a Handwashing with soap and water

We found very low-quality evidence to confirm that handwashing with soap and water prevents symptomatic norovirus infections.[63,66,79,85,89,102,103,165,166,168-171,173-177,183] Several descriptive studies emphasized hand hygiene as a primary prevention behavior and promoted it simultaneously with other practical interventions. Several outbreaks centered in healthcare augmented or reinforced hand hygiene behavior as an early intervention and considered it an effective measure aimed at outbreak control.[103,165,168,170,174,176,177,183] The protocols for hand hygiene we reviewed included switching to the exclusive use of handwashing with soap and water, and a blend of handwashing with the adjunct use of alcohol-based hand sanitizers. Additional guidance is available in the 2003 HICPAC Guidelines for Hand Hygiene (http://www.cdc.gov/mmwr/PDF/rr/rr5116.pdf).

Q3.C.1.b Alcohol-based hand sanitizers

We found very low-quality evidence to suggest that hand hygiene using alcohol-based hand sanitizers may reduce the likelihood of symptomatic norovirus infection.[66,87,169,171,205] Several studies used FDA-approved alcohol-based hand antiseptics during periods of norovirus activity as an adjunct measure of hand hygiene.[66,87,168,169,171,205,206] Two studies used a commercially available 95% ethanol-based hand sanitizer along with handwashing with soap and water; but without a control group and with hand hygiene comprising one of several interventions, the relative contribution of hand hygiene to attenuating transmission was difficult to evaluate.[169,171] In the laboratory, even with 95% ethanol products, the maximum mean reduction in log10 titer reduction was 2.17.[189] Evidence to evaluate the efficacy of alcohol-based hand disinfectants consisted of basic science studies using FCV as a surrogate for norovirus. Moderate quality evidence supported ethanol as a superior active ingredient in alcohol-based hand disinfectants compared to 1-propanol.[189,191,193,196] The use

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of hand sanitizers with mixtures of ethanol and propanol have shown effectiveness against FCV compared to products with single active ingredients (70% ethanol or propanol) under controlled conditions.[189] There were no studies available to evaluate the effect of non-alcohol based hand sanitizers on norovirus persistence on skin surfaces.

Q3.C.1.c Role of artificial nails

Very low-quality evidence suggested that the magnitude in reduction of a norovirus surrogate (FCV) using a spectrum of soaps and hand disinfectants was significantly greater among volunteers with natural nails compared to those with artificial nails.[197] A subanalysis showed that longer fingernails were associated with consistently greater hand contamination. Further evidence summarizing the impact of artificial and long fingernails in healthcare settings can be found in the HICPAC Guidelines for Hand Hygiene in Healthcare Settings (http://www.cdc.gov/Handhygiene/).

Q3.C.2 Personal Protective Equipment

Very low-quality evidence among 1 observational[66] and 13 descriptive studies[167-173,176-179,181,183] support the use of personal protective equipment (PPE) as a prevention measure against symptomatic norovirus infection. A single retrospective study failed to support the use of gowns as a significantly protective measure against norovirus infection during the outbreak among staff but did not consider the role of wearing gowns in avoiding patient-to-patient transmission.[66] Mask or glove use was not evaluated in the self-administered questionnaire used in the study. Several observational and descriptive studies emphasized the use of gloves and isolation gowns for routine care of symptomatic patients, with the use of masks recommended when staff anticipated exposure to emesis or circumstances where virus may be aerosolized.[167-173,176-179,181,183] The use of PPE was advocated for both staff and visitors in two outbreak studies.[169,179]

Q3.C.3 Leave Policies for Staff

We found very low-quality evidence among several studies to support the implementation of staff exclusion policies to prevent symptomatic norovirus infections in healthcare settings.[84,85,92,165,167-169,172,174,176,177,179-181,183,184] Fifteen descriptive studies emphasized granting staff sick time from the time of symptom onset to a minimum of 24 hours after symptom resolution.[84,85,92,167-169,172,176,177,179,180,183,184] The majority of studies opted for 48 hours after symptom resolution before staff could return to the workplace.[84,92,167,169,172,176,177,179,180,183,184] One study instituted a policy to exclude symptomatic staff from work until they had remained symptom-free for 72 hours.[168] While selected studies have identified the ability of persons to shed virus for protracted periods post-infection, it is not well understood whether virus detection translates to norovirus infectivity. Our search was unable to determine whether return to work policies were effective in reducing secondary transmission of norovirus in healthcare facilities.

Q3.C.4 Isolation/Cohorting of Symptomatic Patients

We found very low-quality evidence among several descriptive studies to support patient cohorting or placing patients on Contact Precautions as an intervention to prevent symptomatic norovirus infections in healthcare settings.[87,166-171,173,176,177,179-182,184] No evidence was available to encourage the use of Contact Precautions for sporadic cases, and the standard of care in these circumstances is to manage such cases with Standard Precautions (http://www.cdc.gov/ncidod/dhqp/pdf/guidelines/Isolation2007.pdf). Fifteen descriptive studies used isolation precautions or cohorting practices as a primary means of outbreak management.[87,166-171,173,176,177,179-182,184] Patients were cared for in private rooms, physically grouped into cohorts of symptomatic, exposed but asymptomatic, or unexposed within a ward, or alternatively, with entire wards placed under Contact Precautions. Exposure status typically was based on a person's symptoms and/or physical and temporal proximity to norovirus activity. A few studies cited restricting patient movements within the ward,

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suspending group activities, and special considerations for therapy or other medical appointments during outbreak periods as adjunct measures to control the spread of norovirus.[63,169,182,183]

Q3.C.5 Staff Cohorting

Very low-quality evidence supported the implementation of staff cohorting and the exclusion of non-essential staff and volunteers to prevent symptomatic norovirus infections.[87,103,165,168-170,172,173,177,179,180,182,183] All studies addressing this topic were descriptive. Staff were designated to care for one cohort of patients (symptomatic, exposed but asymptomatic, or unexposed). Exposed staff were discouraged from working in unaffected clinical areas and from returning to care for unexposed patients before, at a minimum, allowing 48 hours from their last putative exposure to elapse.[177] Our search did not identify healthcare personnel other than nursing, medical, environmental services, and paramedical staff who were assigned to staff cohorting. There were no identified studies that evaluated the infectious risk of assigning recovered staff as caregivers for asymptomatic patients.

Q3.C.6 Ward Closure

We found low-quality evidence supporting ward closure as an intervention to prevent symptomatic norovirus infections.[85,164-166,168,173,176-179,183,184] Ward closure focused on temporarily suspending transfers in or out of the ward, and discouraged or disallowed staff from working in clinical areas outside of the closed ward. One prospective controlled study evaluating 227 ward-level outbreaks between 2002 and 2003 demonstrated that outbreaks were significantly shorter (7.9 vs. 15.4 days, $p<0.01$) when wards were closed to new admissions.[164] The mean duration of ward closure was 9.65 days, with a loss of 3.57 bed-days for each day the ward was closed. The duration of ward closure in the descriptive studies examined was dependent on facility resources and magnitude of the outbreaks. Allowing at least 48 hours from the resolution of the last case, followed by thorough environmental cleaning and disinfection was common before re-opening a ward. Other community-based studies have used closures as an opportunity to perform thorough environmental cleaning and disinfection before re-opening. Two studies moved all patients with symptoms of norovirus infection to a closed infectious disease ward and then performed thorough terminal cleaning of the vacated area.[170,172] In most instances, it was preferable to minimize patient movements and transfers in an effort to contain environmental contamination.

Q3.C.7 Visitor Policies

We found very low-quality evidence demonstrating the impact of restriction and/or screening of visitors for symptoms consistent with norovirus infection.[168,170,173,182,183] In two studies, visitors were screened for symptoms of gastroenteritis using a standard questionnaire or evaluated by nursing staff prior to ward entry as part of multi-faceted outbreak control measures.[168,170] Other studies restricted visitors to immediate family, suspended all visitor privileges, or curtailed visitors from accessing multiple clinical areas.[182,183] We failed to identify research that considered the impact of different levels of visitor restrictions on outbreak containment.

Q3.C.8 Education

We found very low-quality evidence on the impact of staff and/or patient education on symptomatic norovirus infections.[166,168,169,172,173,182] Six studies simply described education promoted during outbreaks.[166,168,169,172,173,182] Content for education included recognizing symptoms of norovirus, understanding basic principles of disease transmission, understanding the components of transmission-based precautions, patient discharges and transfer policies, as well as cleaning and disinfection procedures. While many options are available, the studies we considered used posters to emphasize hand hygiene and conducted one-on-one teaching with patients and visitors, as well as holding departmental seminars for staff. We failed to identify research that examined the impact of educational measures on the magnitude and duration of outbreaks of

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norovirus gastroenteritis, or what modes of education were most effective in promoting adherence to outbreak measures.

Q3.C.9 Surveillance

We found very low-quality evidence to suggest that surveillance for norovirus activity was an important measure in preventing symptomatic infection.[58,84,166,170] Four descriptive studies identified surveillance as a component of outbreak measurement and containment. Establishing a working case definition and performing active surveillance through contact tracing, admission screening, and patient chart review were suggested as actionable items during outbreaks. Our search was unable to determine whether active case-finding and tracking of new norovirus cases were directly associated with shorter outbreaks or more efficient outbreak containment.

Q3.C.10 Policy Development and Communication

We found very low-quality evidence of the benefit of established written policies and a pre-arranged communication framework in facilitating the prevention and management of symptomatic norovirus infections.[63,84,172,182-184] Six descriptive studies outlined the need for mechanisms to disseminate outbreak information and updates to staff, laboratory liaisons, healthcare facility administration, and public health departments. [63,84,172,182-184] Our search did not find studies demonstrating that facilities with written norovirus policies already in place had fewer or shorter outbreaks of norovirus gastroenteritis.

Q3.C.11 Patient Transfers and Discharges

We found very low-quality evidence examining the benefit of delayed discharge or transfer for patients with symptomatic norovirus infection.[172,179,183,184] Transfer of patients after symptom resolution was supported in one study but discouraged unless medically necessary in three others. Discharge home was supported once a minimum of 48 hours had elapsed since the patient's symptoms had resolved. For transfers to long-term care or assisted living, patients were held for five days after symptom resolution before transfer occurred. Our search was unable to identify studies that compared the impact of conservative patient discharge policies for recovered, asymptomatic patients.

Q3.C.12 Environmental Disinfection

Q3.C.12.a Targeted surface disinfection

We found very low-quality evidence to support cleaning and disinfection of frequently touched surfaces to prevent symptomatic norovirus infection.[79,153,168,183] One systematic review[153] and three descriptive studies[79,168,183] highlighted the need to routinely clean and disinfect frequently touched surfaces (e.g., patient and staff bathrooms and clean and dirty utility rooms, tables, chairs, commodes, computer keyboards and mice, and items in close proximity to symptomatic patients). One systematic review[153] and two descriptive studies[102,177,183,184] supported-steam cleaning carpets once an outbreak was declared over. Within the review, a single case report suggested that contaminated carpets may contain viable virus for a minimum of twelve days even after routine dry vacuuming.[153] Routine cleaning and disinfection of non-porous flooring were supported by several studies, with particular attention to prompt cleaning of visible soiling from emesis or fecal material.[153,168] There were no studies directly addressing the impact of surface disinfection of frequently touched areas on outbreak prevention or containment.

Q3.C.12.b Process of environmental disinfection

We found very low-quality evidence supportive of enhanced cleaning during an outbreak of norovirus gastroenteritis.[168,170,177,179] Several studies cited increasing the frequency of cleaning and disinfection during

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outbreaks of norovirus gastroenteritis.[168,170,177,179] Ward-level cleaning was performed once to twice per day, with frequently touched surfaces and bathrooms cleaned and disinfected more frequently (e.g., hourly, once per shift, or three times daily). Studies also described enhancements to the process of environmental cleaning. Environmental services staff wore PPE while cleaning patient-care areas during outbreaks of norovirus gastroenteritis.[176,177,179,205] Personnel first cleaned the rooms of unaffected patients and then moved to the symptomatic patient areas [159]. Adjunct measures to minimize environmental contamination from two descriptive studies included labeling patient commodes and expanding the cleaning radius for enhanced cleaning within the immediate patient area to include other proximal fixtures and equipment.[170,177] In another study, mop heads were changed at an interval of once every three rooms.[168] Our search did not identify whether there was an association with enhanced cleaning regimens during outbreaks of norovirus gastroenteritis and the attenuation in outbreak magnitude or duration.

Q3.C.12.c Patient-service items

We found very low-quality evidence to support the cleaning of patient equipment or service items to reduce symptomatic norovirus infections.[168,172,177] Three descriptive studies suggested that patient equipment/service items be cleaned and disinfected after use, with disposable patient care items discarded from patient rooms upon discharge.[168,172,177] A single descriptive study used disposable dishware and cutlery for symptomatic patients.[172] Our search did not identify studies that directly examined the impact of disinfection of patient equipment of outbreaks of norovirus gastroenteritis.

Q3.C.12.d Fabrics

We found very low-quality evidence examining the impact of fabric disinfection on norovirus infections.[153,168,177,183] One systematic review[153] and three descriptive studies[168,177,183] suggested changing patient privacy curtains if they are visibly soiled or upon patient discharge. One descriptive study suggested that soiled, upholstered patient equipment should be steam cleaned[135, 159]. If this was not possible, those items were discarded. Two descriptive studies emphasized careful handling of soiled linens to minimize re-aerosolization of virus.[177,183] Wheeling hampers to the bedside or using hot soluble hamper bags (e.g., disposable) were suggested mechanisms to reduce self-contamination. Our search did not identify studies that examined the direct impact of disinfection of fabrics on outbreaks of norovirus gastroenteritis or whether self-contamination with norovirus was associated with new infection.

Q.3.C.12.e Cleaning and disinfection agents

The overall quality of evidence on cleaning and disinfection agents was very low.[63,83,87,89,153,167,168,170,174,176-179,182,184] The outcomes examined were symptomatic norovirus infection, inactivation of human norovirus, and inactivation of FCV. Evidence for efficacy against norovirus was usually based on studies using FCV as a surrogate. However, FCV and norovirus exhibit different physiochemical properties and it is unclear whether inactivation of FCV reflects efficacy against human strains of norovirus. One systematic review[153] and 14 descriptive studies[63,83,87,89,167,168,170,174,176-179,182,184] outlined strategies for containing environmental bioburden. The majority of outbreaks were managed with sodium hypochlorite in various concentrations as the primary disinfectant. The concentrations for environmental cleaning among these studies ranged from 0.1% to 6.15% sodium hypochlorite.

We found moderate quality evidence examining the impact of disinfection agents on human norovirus inactivation.[187,194,201] Three basic science studies evaluated the virucidal effects of select disinfectants against norovirus.[187,194,201] A decline of 3 in the log10 of human norovirus exposed to disinfectants in the presence of fecal material, a fetal bovine serum protein load, or both was achieved with 5% organic acid after 60 minutes of contact time, 6000 ppm free chlorine with 15 minutes of contact time, or a 1 or 2% peroxide solution for 60 minutes.[187] This study also demonstrated that the range of disinfectants more readily inactivated FCV than human norovirus samples, suggesting that FCV may not have equivalent physical properties to those of human

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norovirus. One basic science study demonstrated a procedure to eliminate norovirus (genogroup II) from a melamine substrate using a two step process - a cleaning step to remove gross fecal material, followed by a 5000-ppm hypochlorite product with a one minute contact time.[194] Cleaning with a detergent, or using a disinfectant alone failed to eliminate the virus.

We also found moderate quality evidence examining the impact of disinfection agents on the human norovirus surrogate, FCV.[185,187,188,190-192,198-200] Nine basic science studies evaluated the activity of several disinfectants agents against FCV.[185,187,188,190-192,198-200] Only a single study showed equivalent efficacy between a quaternary ammonium compound and 1000 ppm hypochlorite on non-porous surfaces.[188] In contrast, selected quaternary ammonium based-products, ethanol, and a 1% anionic detergent were all unable to inactivate FCV beyond a reduction of 1.25 in the log10 of virus, compared to 1000 ppm and 5000 ppm hypochlorite, 0.8% iodine, and 0.5% glutaraldehyde products.[200] 4% organic acid, 1% peroxide, and >2% aldehyde products showed inactivation of FCV but only with impractical contact times exceeding 1 hour.[187]

Studies of disinfecting non-porous surfaces and hands evaluated the efficacy of varying dilutions of ethanol and isopropanol and determined that 70-90% ethanol was more efficacious at inactivating FCV compared to isopropanol, but unable to achieve a reduction of 3 in the log10 of the viral titer (99.9%), even after 10 minutes of contact.[191] Other studies have shown that combinations of phenolic and quaternary ammonium compounds and peroxyacetic acid were only effective against FCV if they exceeded the manufacturers' recommended concentrations by a factor of 2 to 4.[199] The included basic science studies agents demonstrating complete inactivation of FCV were those containing hypochlorite, glutaraldehyde, hydrogen peroxide, iodine, or >5% sodium bicarbonate active ingredients. Not all of these products may be feasible for use in healthcare settings.

In applications to various fabrics (100% cotton, 100% polyester, and cotton blends), FCV was inactivated completely by 2.6% glutaraldehyde, and showed >90% reductions of FCV titers when phenolics, 2.5% or 10% sodium bicarbonate, or 70% isopropanol were evaluated.[190] In carpets consisting of olefin, polyester, nylon, or blends, 2.6% glutaraldehyde demonstrated >99.7% inactivation of FCV, with other disinfectants showing moderate to modest reductions in FCV titers.[190] The experimental use of monochloramine as an alternative disinfectant to free chlorine in water treatment systems only demonstrated modest reductions in viral titer after 3 hours of contact time. Our search did not evaluate publications using newer methods for environmental disinfection, such as ozone mist from a humidifying device, fumigation, UV irradiation, and fogging.

Our search was not able to evaluate well-designed studies that compared virucidal efficacy of products on human norovirus, FCV, or other surrogate models among commonly used hospital disinfectants agents to establish practical standards, conditions, concentrations, and contact times. Ongoing laboratory studies are now exploring murine models as a surrogate that may exhibit greater similarity to human norovirus than FCV. Forthcoming research using this animal model may provide clearer direction regarding which disinfectants reduce norovirus environmental contamination from healthcare environments, while balancing occupational safety issues with the practicality of efficient and ready-to-use products.

Q3.D Medications

We identified very low-quality evidence suggesting that select medications may reduce the risk of illness or attenuate symptoms of norovirus.[202,203] Among elderly psychiatric patients, those on antipsychotic drugs plus trihexyphenidyl or benztropine were less likely to become symptomatic, as were those taking psyllium hydrophilic mucilloid.[203] The pharmacodynamics to explain this outcome is unknown, and it is likely that these medications may either be a surrogate marker for another biologically plausible protective factor, or may impact norovirus through central or local effects on gastrointestinal motility. Those who received nitazoxanide, an anti-protozoal drug, were more likely to exhibit longer periods of norovirus illness than those patients who received placebo.[202] Our search did not identify research that considered the effect of anti-peristaltics on the duration or outcomes of norovirus infection.

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Q3 Recommendations

3.A.1 Consider extending the duration of isolation or cohorting precautions for outbreaks among infants, even after resolution of symptoms, as there is potential for prolonged viral shedding and environmental contamination. Among infants, extending Contact Precautions for up to 5 days after the resolution of symptoms is suggested. **(Category II)** (Key Question 3A)

3.A.2 Further research is needed to understand the correlation between prolonged shedding of norovirus and the risk of infection to susceptible patients **(No recommendation/unresolved issue)** (Key Question 3A)

3.B.1 Perform routine cleaning and disinfection of frequently touched environmental surfaces and equipment in isolation and cohorted areas, as well as high traffic clinical areas. Cleaning should include, but is not limited to, commodes, toilets, hand/bedrailing, faucets, telephones, door handles, computer equipment, and kitchen preparation surfaces. Staff should adhere to established healthcare facility policies which guide effective cleaning and disinfection of patient equipment, using EPA-registered cleaning and disinfecting agents with activity against norovirus or norovirus surrogates (http://www.epa.gov/oppad001/list_g_norovirus.pdf). **(Category IB)** (Key Question 3B)

3.B.2 All shared food items for patients or staff should be removed from clinical areas for the duration of the outbreak. **(Category IB)** (Key Question 3B)

3.C.1.a Perform handwashing, using soap and water, according to Standard Precautions (i.e, prior to contact with patients, medication preparation, preparation or consumption of food, insertion of invasive devices, after touching contaminated equipment, removing personal protective equipment (PPE; e.g., gloves), or toileting activities with patients with symptoms of norovirus infection (cf: http://www.cdc.gov/mmwr/PDF/rr/rr5116.pdf). **(Category IB)** (Key Question 3C)3.C.1.b. Areas affected by outbreaks of norovirus gastroenteritis should actively promote adherence with hand hygiene among healthcare personnel, patients, and visitors. **(Category IB)** (Key Question 3C)

3.C.1.b.1 During outbreaks, use of soap and water is the preferred method of hand hygiene. Consider FDA-approved alcohol-based hand sanitizers as a supplemental method of hand hygiene during outbreaks of norovirus gastroenteritis when hands are not visibly soiled and have not been in contact with diarrheal patients, contaminated surfaces, or blood or other body fluids. **(Category II)** (Key Question 3C)3.C.1.b.2 Further research is required to directly evaluate the efficacy of alcohol-based hand sanitizers against human strains of norovirus, or against a surrogate virus with properties convergent with human strains of norovirus. **(No recommendation/unresolved issue)** (Key Question 3C)

3.C.1.b.3 Ethanol-based hand sanitizers (60-95%) are preferred as a supplemental method of hand hygiene compared to other alcohol or non-alcohol based hand sanitizer products during outbreaks of norovirus gastroenteritis. **(Category II)** (Key Question 3C)

3.C.2.a Use a surgical or procedure mask, and eye protection if there is a risk of splashes to the face during the care of patients, particularly among those who are vomiting. **(Category IB)** (Key Question 3C)

3.C.2.b Clinical and environmental services staff, as well as visitors, should wear gloves and gowns when entering areas under isolation or cohorting. **(Category IB)** (Key Question 3C)

3.C.3 Facilities should develop and adhere to sick leave policies for healthcare personnel symptomatic with norovirus infection. Ill staff members should be excluded from work for a minimum of 48 hours after the resolution of symptoms. Once staff return to work, adherence to hand hygiene must be maintained.

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(Category IB) (Key Question 3C)

3.C.4.a During outbreaks, patients with norovirus gastroenteritis should be cohorted or placed on Contact Precautions for a minimum of 48 hours after the resolution of symptoms to prevent further exposure of susceptible patients **(Category IB)** (Key Question 3C)

3.C.4.b During suspected or confirmed outbreaks, preferentially place patients with norovirus gastroenteritis on Contact Precautions and into private rooms equipped with at least one dedicated handwashing sink and toilet or commode. If these provisions are not available, patients may be cohorted into groups of those who are symptomatic, exposed but asymptomatic, and unexposed with access to separate toilets or commodes for each group. Alternatively, all patients within a hospital unit or section may be placed under Contact Precautions. **(Category IB)** (Key Question 3C)

3.C.4.c Minimize patient movements within a ward or unit. Symptomatic and recovering patients should not leave the patient-care area unless it is foressential care or treatment, to reduce the likelihood of environmental contamination and transmission of norovirus in unaffected clinical areas. **(Category II)** (Key Question 3C)

3.C.4.d Suspend group activities (e.g., dining events) during an uncontrolled outbreak of norovirus gastroenteritis. **(Category II)** (Key Question 3C)

3.C.5.a Establish protocols for staff cohorting in the event of an outbreak of norovirus gastroenteritis, where staff care for one patient cohort on their ward (i.e., symptomatic, exposed but asymptomatic, or unexposed), and do not move between patient cohorts. **(Category IB)** (Key Question 3C)

3.C.5.b Staff who have recovered from recent suspected norovirus infection associated with this outbreak may be best suited to care for exposed or symptomatic patients. **(Category II)** (Key Question 3C)

3.C.5.c Exclude non-essential staff, students, and volunteers from working in areas experiencing outbreaks of norovirus gastroenteritis. **(Category IB)** (Key Question 3C)

3.C.6 Closure of wards to new admissions or transfers is suggested as a measure to attenuate the magnitude of an outbreak of norovirus gastroenteritis. The threshold for ward closure varies and depends on risk assessments by infection prevention personnel and facility leadership. **(Category II)** (Key Question 3C)

3.C.7.a Visitor policies should be established for acute gastroenteritis (e.g., norovirus) outbreaks. **(Category IB)** (Key Question 3C)

3.C.7.b Restrict non-essential visitors from affected areas during outbreaks of norovirus gastroenteritis. For those facilities that proceed with continued visitor privileges, screening visitors for symptoms consistent with norovirus infection is encouraged. **(Category IB)** (Key Question 3C)

3.C.8.a Healthcare facilities should provide education to staff, patients, and visitors about symptoms, preventing infection, and modes of transmission of norovirus at the start of, and throughout the duration of an outbreak. **(Category IB)** (Key Question 3C)

3.C.8.b Consider providing educational sessions and making resources available on the prevention and management of norovirus before outbreaks occur, as part of annual trainings, and when sporadic cases are detected. **(Category II)** (Key Question 3C)

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3.C.9.a Begin active case-finding when a cluster of acute gastroenteritis cases is detected in the healthcare facility. Use a defined case definition to populate line lists to track both exposed and symptomatic patients and staff. Collect relevant epidemiological, clinical, and demographic data as well as information on patient location and outcomes. **(Category IB)** (Key Question 3C)

3.C.9.b Notify appropriate local and state health departments, as required by state and local public health regulations, if an outbreak of norovirus gastroenteritis is suspected. **(Category IC)** (Key Question 3C)

3.C.10 Develop written policies that specify the chains of communication needed to manage and report outbreaks of norovirus gastroenteritis. Key stakeholders such as clinical staff, environmental services, laboratory administration, healthcare facility administration and public affairs, as well as state or local public health authorities, should be included in the framework. **(Category IB)** (Key Question 3C)

3.C.11 During outbreaks, patients on Contact Precautions for norovirus can be transferred or discharged to skilled nursing facilities as required. If receiving facilities are unable to provide adequate cohorting or isolation provisions, it may be prudent to postpone transfers until arrangements are made for appropriate isolation or cohorting. Prioritize the discharge of symptomatic or recovering patients awaiting discharge to their place of residence. **(Category II)** (Key Question 3C)

3.C.12.a Clean and disinfect shared equipment with an appropriate EPA-registered product between patient uses and follow the manufacturer's recommendations for contact times and application. Consider using a chlorine-based agent like sodium hypochlorite, but other agents like hydrogen peroxide, citric acid, quaternary ammonium, and chlorine dioxide products have also been approved. The EPA lists registered products with activity against norovirus on their website (http://www.epa.gov/oppad001/list_g_norovirus.pdf). Ensure that EPA-labeled products are approved for use in healthcare settings. **(Category IB)** (Key Question 3C)

3.C.12.b.1 Increase the frequency of cleaning and disinfection of patient care areas and frequently touched surfaces during outbreaks of norovirus gastroenteritis. Unit level cleaning may be increased up to twice daily, with frequently touched surfaces cleaned and disinfected up to three times daily using EPA-approved products for healthcare settings. **(Category IB)** (Key Question 3C)

3.C.12.b.2 Clean and disinfect surfaces starting from the areas with a lower likelihood of norovirus contamination (e.g., tray tables, counter tops) to areas with highly contaminated surfaces (e.g., toilets, bathroom fixtures). Change mop heads when new solutions are prepared, or after cleaning large spills of emesis or fecal material. **(Category IB)** (Key Question 3C)

3.C.12.c.1 Discard disposable patient-care items from patient rooms after patients on isolation for norovirus gastroenteritis are discharged or transferred to a healthcare facility. Unused linens remaining in a patient room should be laundered before use on another patient. **(Category II)** (Key Question 3C)3.C.12.c.2 No additional provisions for the use of disposable patient service items such as utensils or dishware are required for patients with symptoms of norovirus infection. Silverware and dishware may undergo normal processing and cleaning using standard procedures. Staff handling soiled patient-service items should use Standard Precautions. **(Category II)** (Key Question 3C)

3.C.12.d.1 Avoid the use of upholstered furniture and rugs or carpets in patient care areas, as these objects are difficult to clean and disinfect completely. If this option is not possible, we suggest immediately cleaning soilage, such as emesis or fecal material, from upholstery, using a manufacturer-approved cleaning agent or detergent. Opt for seating in patient-care areas that can withstand routine cleaning and disinfection. **(Category II)** (Key Question 3C)

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3.C.12.d.2 Steam cleaning of upholstered furniture present in rooms upon patient discharge is suggested. If items cannot be appropriately cleaned, consider discarding these items. Appropriate personal protective equipment should be used during these activities. **(Category II)** (Key Question 3C)

3.C.12.d.3 Change privacy curtains when they are visibly soiled and upon patient discharge or transfer. **(Category II)** (Key Question 3C)

3.C.12.d.4 Handle soiled linens carefully, without agitating them, to avoid dispersal of virus. Wear appropriate PPE, such as gloves, to minimize the likelihood of personal contamination. **(Category IB)** (Key Question 3C)

3.C.12.d.5 No additional provisions, such as the practice of double bagging, incineration, or modifications for laundering are recommended for linen. Staff handling soiled linens should adhere to Standard Precautions. **(Category II)** (Key Question 3C)

3.C.12.e.1 Clean surfaces and patient equipment prior to the application of a disinfectant. Presence of residual organic and protein loads on surfaces reduces the overall effectiveness of disinfectants. Follow manufacturer's recommendations for optimal disinfectant dilution, application, and surface contact time. **(Category IB)** (Key Question 3C)

3.C.12.e.2 More research is required to clarify the effectiveness of cleaning and disinfecting agents against norovirus, either through the use of surrogate viruses or the development of human norovirus culture system. **(No recommendation/unresolved issue)** (Key Question 3C)

3.C.12.e.3 More research is required to clarify the effectiveness and reliability of fogging, UV irradiation, and ozone mists to reduce norovirus environmental contamination. **(No recommendation/unresolved issue)** (Key Question 3C)

3.C.12.e.4 More research is required to evaluate the virucidal capabilities alcohol-based as well as non-alcohol based hand sanitizers against norovirus. **(No recommendation/unresolved issue)** (Key Question 3C)

3.D Further research is required to evaluate the utility of medications that may attenuate the duration and severity of norovirus illness. **(No recommendation/unresolved issue)**(Key Question 3D)

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IX. Appendices

Guideline for Prevention and Management of Norovirus Outbreaks in Healthcare Settings

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APPENDIX 1A: SEARCH STRATEGY FOR GUIDELINES

Database	
National Guideline Clearinghouse	http://www.guideline.gov/
MEDLINE	OVID
EMBASE	OVID
Cochrane Library	Wiley Interscience
NIH Consensus Development Program	http://consensus.nih.gov/
National Institute for Health and Clinical Excellence	http://www.nice.org.uk/
Scottish Intercollegiate Guidelines Network	http://www.sign.ac.uk/
USPSTF	http://www.ahrq.gov/clinic/uspstfix.htm

NATIONAL GUIDELINE CLEARINGHOUSE

Keyword	Search Results
norovirus	2
Norwalk	6
"viral gastroenteritis"	6

MEDLINE

#	Search History	Results
1	exp norovirus/	1196
2	(norwalk or norovirus).mp.	1680
3	small round structured virus$.mp.	192
4	exp Virus Diseases/ and exp Gastroenteritis/	6314
5	((virus$ or viral) adj10 gastroenteritis).mp.	2121
6	or/1-5	8414
7	limit 6 to (guideline or practice guideline)	13

Platform

EMBASE

#	Search History	Results
1	exp norovirus/	516
2	(norwalk or norovirus).mp.	1494
3	exp Small Round Structured Virus/	33
4	((virus$ or viral) adj10 gastroenteritis).mp.	2884

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5	exp Viral Gastroenteritis/	142
6	or/1-5	3383
7	exp Practice Guideline/	127276
8	6 and 7	42

COCHRANE LIBRARY

#	Search History	Results
#1	MeSH descriptor norovirus, this term only	3
#2	norovirus OR Norwalk	54
#3	(#1 OR #2) *Restricted to Technology Assessments*	0

NIH Consensus Development Program

No relevant guidelines were found

National Institute for Health and Clinical Excellence

Keyword	Search Results
norovirus	0
Norwalk	0
gastroenteritis	0

Scottish Intercollegiate Guidelines Network

No relevant guidelines were found

USPSTF

No relevant guidelines were found

25 relevant guidelines identified[25-48,49]

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APPENDIX 1B: SEARCH STRATEGY FOR SYSTEMATIC REVIEWS/PRIMARY LITERATURE

Database	Number of Hits*
MEDLINE (1950 to 2008 Week 5)	2324
EMBASE (1980 to 2008 Week 5)	1533
CINAHL (1987 to 2007 Dec Week 1)	160
Global Health (1910 to Dec 2007)	1064
Cochrane Library	33
ISI Web of Science	1463
Total (after removing duplicates)	**3702**

* On 02/07/2008

MEDLINE

#	Searches	Results
PHASE 1: SEARCH TERMS FOR NOROVIRUS		
1	exp norovirus/	1257
2	(norovirus$ or norwalk).mp. [mp=title, original title, abstract, name of substance word, subject heading word]	1773
3	(small round structured virus$ or SRSV).mp. [mp=title, original title, abstract, name of substance word, subject heading word]	205
4	norwalk-like virus$.mp.	353
5	winter vomiting disease.mp.	20
PHASE 2: SEARCH TERMS FOR CALICIVIRUS AND RESTRICTED VIRAL GASTROENTERITIS TERMS		
6	exp Caliciviridae/ or exp Calicivirus, Feline/ or calicivirus.mp. or exp Caliciviridae Infections/	2421
7	exp virus diseases/ and exp gastroenteritis/ and (exp disease outbreaks/ or outbreak$.mp. or exp horizontal disease transmission/ or exp health facilities/)	1112
8	(virus or viral).mp. and exp gastroenteritis/ and (exp disease outbreaks/ or outbreak$.mp. or exp horizontal disease transmission/ or exp health facilities/)	900

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9	((virus or viral) adj5 gastroenterit$).mp. and (exp disease outbreaks/ or outbreak$.mp. or exp horizontal disease transmission/ or exp health facilities/)	297
10	(nosocomial adj5 gastroenteritis).mp.	53
11	(epidemic adj5 gastroenteritis).mp.	200
12	(non?bacterial adj5 gastroenteritis).mp.	145
13	exp virus diseases/ and exp diarrhea/ and (exp disease outbreaks/ or outbreak$.mp. or exp horizontal disease transmission/ or exp health facilities/)	491
14	(virus or viral).mp. and exp diarrhea/ and (exp disease outbreaks/ or outbreak$.mp. or exp horizontal disease transmission/ or exp health facilities/)	351
15	((virus or viral) adj5 diarrhea).mp. and (exp disease outbreaks/ or outbreak$.mp. or exp horizontal disease transmission/ or exp health facilities/)	217
PHASE 3: COMBINING PHASES AND APPLYING LIMITS		
16	or/1-15	4160
17	(addresses or bibliography or biography or clinical conference or comment or congresses or consensus development conference or consensus development conference nih or dictionary or directory or duplicate publication or editorial or festschrift or historial article or interview or lectures or legal cases or news or newspaper article or patient education handout).pt.	853201
18	16 not 17	4067
19	limit 18 to (humans and english language)	2324

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EMBASE

#	Searches	Results
1	exp NOROVIRUS/	588
2	exp Norwalk Gastroenteritis Virus/	745
3	(norovirus$ or norwalk).mp.	1588
4	exp Small Round Structured Virus/	33
5	(small round structured virus$ or SRSV).mp.	161

6	norwalk-like virus$.mp.	309
7	winter vomiting disease.mp.	8
8	exp CALICIVIRUS/	2578
9	exp Viral Gastroenteritis/	188
10	or/1-9	3002
11	(book or conference paper or editorial or note or proceeding).pt.	1019316
12	10 not 11	2735
13	limit 12 to (human and english language)	1533

CINAHL

#	Searches	Results
1	(norovirus$ or norwalk).mp.	152
2	(small round structured virus$ or SRSV).mp.	14
3	norwalk-like virus$.mp.	42
4	winter vomiting disease.mp.	1
5	calicivirus.mp.	21
6	or/1-5	162
7	limit 6 to english	160

GLOBAL HEALTH

#	Searches	Results
1	exp norovirus/	929
2	(norovirus$ or norwalk).mp.	1112
3	(small round structured virus$ or SRSV).mp.	299

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4	norwalk-like virus$.mp.	303
5	winter vomiting disease.mp.	547
6	or/1-5	1360
7	limit 6 to english language	1064

COCHRANE LIBRARY

#	Searches	Results
#1	MeSH descriptor norovirus explode all trees	10
#2	MeSH descriptor Norwalk virus explode all trees	5
#3	(norovirus*): ti,ab,kw OR (norwalk): ti,ab,kw	33
#4	(small round structured virus*): ti,ab,kw OR (SRSV): ti,ab,kw	0
#5	(norwalk-like virus*): ti,ab,kw	6
#6	(winter vomiting disease): ti,ab,kw	1
#7	#1 OR #2 OR #3 OR #4 OR #5 OR #6	33

ISI WEB OF SCIENCE

Searches	Results
Topic=(norovirus) OR Topic=(norwalk) OR Topic=(small round structured virus) OR Topic=(norwalk-like virus) OR Topic=(winter vomiting disease) Timespan=All Years. Databases=SCI-EXPANDED, SSCI, A&HCI. Refined by: Document Type=(ARTICLE OR REVIEW) & Languages=(ENGLISH)	1463

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APPENDIX 2: EVIDENCE, GRADE AND STUDY QUALITY ASSESSMENT TABLES

Q1: What person, virus or environmental characteristics increase or decrease the risk of norovirus infection in healthcare settings?

EVIDENCE TABLE Q1

Person characteristics

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Demographic characteristics						
MMWR; 2008 [79]	Prospective controlled study. 1,3,4	To investigate an outbreak at an elementary school.	Students and staff at an elementary school in Washington DC in February 2007. Students – median age 8 years (range 3-12 years); 55% female. Staff – median age 41 years (range 13-66 years); 92% female. 266 – 207 students and 59 staff.	**Symptomatic norovirus infection** *Bivariate analysis: All results RR (95% CI); p value* Being a student – 0.94 (0.66-1.34); 0.76 Being female – 1.13 (0.82-1.56); 0.52 Having an ill contact – 1.76 (1.16-2.67); 0.01 Classroom J (first) – 1.94 (1.34-2.80); 0.02 Library use: 0.94 (0.58-1.52); 0.87 Library computer use: 1.08 (0.41-2.84); 1.00 **Interventions implemented** District of Columbia Department of Health recommended -more thorough handwashing - cleaning all shared environmental surfaces with a diluted (1:50 concentration) household bleach -cleaning computer equipment (i.e., mice and keyboards) -excluding ill persons from school for at least 72 hours after resolution of illness	A case of gastrointestinal illness was defined as illness in a student or staff member with nausea, vomiting, or diarrhea, who was at the school February 2-18, 2007. Power and sample size not reported.	017_IL
Mattner, F; 2006 [57]	Prospective controlled study 1,3,4,6,7	To characterize risk factors for the clinical complications of norovirus infections (e.g. vomiting, diarrhea, potassium decrease, creatinine increase, C-	All individuals working in or admitted to five wards (psychiatry, nephrology, gastroenterology, cardiology and trauma) at a university hospital in Germany in the period	**Clinical features in patients** (study duration 3 months) Diarrhea – 79/84; 95% Vomiting – 57/84; 68% Somnolence – 2/84; 2% Serum creatinine increase > 10% – 22/84; 26% Serum potassium decrease > 20% – 7/84; 8%	Diarrhea was defined as three or more episodes of loose stools in a 24 hr period. Cases were considered to be norovirus-positive if	358_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		reactive protein increase)	from the onset of clinical symptoms of the first patient until 2 days after the last patient became symptom free. All patients and staff members who were affected with a sudden onset of diarrhea and/or vomiting were included as cases. Patients admitted with clinical signs were regarded as index cases, and patients admitted ≥48 hrs before developing clinical signs were regarded as nosocomial cases. 84 patients (72 acquired infection nosocomially) and 79 staff members (60 nurses). 3 norovirus positive patients were excluded from risk factor analysis. N for risk factor analyses was 53 for all outcomes except C reactive protein increase (N=52)	**Comparisons of attack rates in patients and nurses** (study duration 3 months) *All results are attack rate (%) in patients vs. nurses; P value* Psychaitry ward – 78 vs. 88; <0.01 Nephrology ward – 32% in the first period and 33% in the second period in patients. Data for nurses not given Gastroenterology – 27 vs. 90; <0.01 Cardiology – 42 vs. 44; 0.87 Trauma – 35 vs. 83; <0.01 Total – 38 vs. 76; <0.01 **Risk factors for complications of norovirus** (study duration 3 months) *VOMITING>1 DAY:* *Univariate analysis: All results OR; P value* Age > 65 years – 1.84; 0.30 Male gender – 0.91; 1.00 Underlying cardiovascular disorders – 2.7; 0.13 Underlying gastrointestinal disorders – 0.34; 0.31 Underlying autoimmune disease – 0.81; 1.00 Underlying renal disorders – 0.95; 1.00 Renal transplant – 1.31; 0.75 Underlying malignancy – P value 0.18; OR not reported Underlying trauma – 1.14; 1.00 Immunosuppressive therapy – 0.92; 1.00 Community acquired norovirus – 2.36; 0.19 *Multivariate analysis: All results OR (95% CI)* Underlying cardiovascular disorders – 7.17(1.59-51.2) Community acquired norovirus – 5.54(1.04-42.8) *DIARRHEA>2 DAYS:* *Univariate analysis: All results OR; P value* Age > 65 years – 3.58; 0.01 Male gender – 2.15; 0.12 Underlying cardiovascular disorders – 2.80; 0.15 Underlying gastrointestinal disorders – 0.22; 0.03 Underlying autoimmune disease – 4.67; 0.24 Underlying renal disorders – 1.77; 0.39 Renal transplant – 1.71; 0.54	samples from at least two patients from the same ward were positive by norovirus-specific RT-PCR. Power and sample size not reported	

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Underlying malignancy – 0.07; 0.01 Underlying trauma – 0.27; 0.053 Immunosuppressive therapy – 1.29; 0.79 Community acquired norovirus – 3.09; 0.06 *Multivariate analysis: All results OR (95% CI)* Age > 65 years – 11.56(1.89-224.00) Underlying malignancy – 0.02(0.00-0.19) Underlying trauma – 0.05(0.00-0.55) *POTASSIUM DECREASE >20%:* *Univariate analysis: All results OR; P value* Age > 65 years – 0.94; 1.00 Male gender – 0.90; 1.00 Underlying cardiovascular disorders – 5.17; 0.06 Underlying gastrointestinal disorders – 0.46; 0.67 Underlying autoimmune disease – 0.98; 1.00 Underlying renal disorders – 1.74; 0.71 Renal transplant – 3.91; 0.09 Underlying malignancy – P value 0.58; OR not reported Underlying trauma – P value 0.19; OR not reported Immunosuppressive therapy – 2.83; 0.25 Community acquired norovirus – 0.48; 0.68 *Multivariate analysis: All results OR (95% CI)* Underlying cardiovascular disorders – 17.10(2.17-403.00) Renal transplant – 13.02(1.63-281.00) *CREATININE INCREASE >10%:* *Univariate analysis: All results OR; P value* Age > 65 years – 1.04; 1.00 Male gender – 1.79; 0.24 Underlying cardiovascular disorders – 0.60; 0.42 Underlying gastrointestinal disorders – 1.93; 0.36 Underlying autoimmune disease – 4.50; 0.12 Underlying renal disorders – 1.44; 0.59 Renal transplant – 3.53; 0.07 Underlying malignancy – 0.93; 1.00 Underlying trauma – 0.07; <0.01 Immunosuppressive therapy – 5.74; <0.01		

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Community acquired norovirus – 5.07; 0.01 *Multivariate analysis: All results OR (95% CI)* Immunosuppressive therapy – 5.67(1.78-20.1) *C REACTIVE PROTEIN >58 MG:* *Univariate analysis: All results OR; P value* Age > 65 years – 0.81; 0.79 Male gender – 2.63; 0.11 Underlying cardiovascular disorders – 0.32; 0.06 Underlying gastrointestinal disorders – 1.54; 0.55 Underlying autoimmune disease – 3.71; 0.14 Underlying renal disorders – 2.13; 0.19 Renal transplant – 1.33; 0.76 Underlying malignancy – 2.96; 0.25 Underlying trauma – 0.23; 0.35 Immunosuppressive therapy – 3.38; 0.06 Community acquired norovirus – 2.30; 0.23 *Multivariate analysis: All results OR (95% CI)* Underlying malignancy – 9.07(1.17-193.00) Immunosuppressive therapy – 5.37(1.62-19.9)		
Lopman, BA; 2004 [58]	Prospective controlled study 1,2,3,4	To describe norovirus outbreaks in residential homes or hospitals of principally older individuals.	Patients in hospitals and nursing homes in England. Cases were hospital patients, nursing home residents, and health care staff with ≥2 episodes of vomiting, ≥3 episodes of diarrhea, or both during a 24-hour period. Those with symptoms due to incontinence or ingestion of laxative drugs were excluded. 271 outbreaks – 33 in nursing homes and 238 in hospital units. 4378 cases – 2154	**Duration of symptomatic illness** Hospital patients vs. hospital staff, nursing home staff, and nursing home residents (75th percentile); p value – 3 days (5 days) vs. 2 days (3 days); p<0.001 Recovery was slowest in the oldest age group (≥85 years) of hospitalized patients - 40% symptomatic after 4 days	Outbreak is defined as ≥ 2 cases in a hospital functional care unit with dates of onset within 7 days of each other. Power and sample size not reported. Promotion of active surveillance (2-tiers of clinical symptoms) to detect cases as a means of prevention of outbreaks	642_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			hospitalized patients, 1360 hospital care staff, 505 nursing home residents, and 358 nursing home staff.			
Rodriguez-Guillen, L; 2005 [60]	Prospective controlled study 2,4	To investigate the frequency of human CaCV (norovirus and sapovirus) in stool samples from adults and children with HIV.	Adults and children with and without HIV from Venezuela. Stool samples – 240 from adults and 81 from children. Subjects – 209 adults and 65 children.	**Detection in children vs adults; p value** CaCV – 62/159 vs 10/81; <0.0001 Novorivus GI – 4% detected exclusively from adults norovirus GII – 20% vs 4%; <0.01 **Detection in HIV positive vs negative subjects; p value** Adults – 22/108 vs 6/51; NS Children – 22/43 vs 9/38; 0.0111 **Detection in subjects with vs without diarrhea** HIV positive adults – 3/32 vs 10/76; 0.4234 HIV negative adults – 3/26 vs 3/25; 0.6468 HIV positive children – 11/18 vs 11/25; 0.2681 HIV negative children – 5/17 vs 4/21; 0.3565	Diarrhea defined as the occurrence of three or more bowel movements within a 24 hour period with decrease in stool consistency. Outcomes determined using RT-PCR. Power and sample size not reported.	502_IL
Lee, N; 2007 [59]	Retrospective controlled study 1,2,3,4,6,7	To study the association between fecal viral concentration and clinical manifestations of GII.4 norovirus infection. Risk factors for prolonged diarrhea were also studied.	Patients ≥16 yrs of age at 2 regional hospitals in Hong Kong. Mean age 60 years; 37.5% male. 44 enrolled; 40 analyzed	**Factors associated with higher median fecal viral concentration (during a 2 year study period)** *Univariate analysis (All results P value)* Age ≥ 65 yrs – 0.06 Female gender – 0.71 Pre-existing medical conditions – 0.52 Prolonged duration of diarrhea – <0.01 Frequency of vomiting – 0.22 Frequency of fever – 0.38 *Correlation analysis (All results Spearman correlation coefficient, P value)* Total duration of diarrhea – 0.47; <0.01 Total frequency of vomiting – 0.34; 0.04 **Risk factors for prolonged duration of diarrhea (during a 2 year study period)** *Univariate analysis (All results P value)* Age ≥ 65 yrs – <0.05 Pre-existing medical conditions – <0.05 Frequency of fever – 0.01	Cases were included for analysis if stool samples were collected ≤ 96 hours from symptom onset. Diarrhea was defined as having ≥ 3 loose stools per day. Diagnosis of norovirus infection and its quantitation were based on RT-PCR assay of stool samples. Prolonged diarrhea was defined as ≥ 4 days of diarrhea Power and sample size not reported Correlation between	2416_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Multivariate analysis (All results OR; 95% CI) Fecal viral concentration (per log_{10} copies) – 9.56(1.18-77.57) Age (per year) – 1.15(1.03-1.28)	norovirus concentration and duration of illness (not severity)	
de Wit, M; 2003 [61]	Retrospective controlled study (nested case-control study) 1,3,4,6,7	To identify risk factors for norovirus infection	Patients registered at a general practice network in Netherlands. Cases were those persons identified in the community cohort with gastroenteritis and a matched control was selected from the cohort members without gastroenteritis at that time. Median age of case patients was 2 years. Other demographic characteristics were not reported. 152 case-control pairs	**Symptomatic norovirus infection** *All results OR(95% CI) unless otherwise noted* *All case-control pairs* *Univariate analysis* Poor food-handling hygiene (as a score) – 1.3(1.0-1.5); P<0.05 Low education level vs. intermediate education level – 1.9(0.9-4.0) High education level vs. intermediate education level – 2.2(1.2-3.9) Participant to day care center – 1.7(0.9-3.3) Household member to daycare center – 2.0(1.0-3.9) Household member to primary school – 1.6(1.0-2.7) Pets in household – 0.6(0.4-1.0) Cat as pet – 0.6(0.4-1.0) 1 household member with gastroenteritis vs. none – 3.7(1.7-8.0) >1 household member with gastroenteritis vs. none – 13.1(3.9-34.7) Child household contact – 5.2(1.8-15.3) Adult household contact – 4.4(2.0-9.6) Contact with person outside household with gastroenteritis – 11.4(4.7-27.3) Consumption of fish in the week before onset of symptoms – 1.8(1.0-3.2) Consumption of barbecued food in the week before onset of symptoms – 0.2(0.05-1.0) *Multivariate analysis* Poor food-handling hygiene (as a score) – 1.3(1.0-1.7); P<0.05 1 household member with gastroenteritis vs. none – 1.2(0.3-4.2) >1 household member with gastroenteritis vs. none – 10.9(2.0-60.5) Contact with person outside household with gastroenteritis – 12.7(3.1-51.8) *Population attributable risk (%) (based on multivariate odds ratios)* Poor food handling hygiene – 47 Number of household members with gastroenteritis – 17 Contact with person outside household with gastroenteritis – 56 *<1 year to 4 years (105 case-control pairs)* *Univariate analysis* Poor food-handling hygiene (as a score) – 1.2(0.9-1.5) ≥ 1 household members with gastroenteritis – 4.4(2.2-9.2)	Samples were tested for norovirus by RT-PCR Cases and controls were matched by age, degree of urbanization, region and date of inclusion Selection of variables into the multivariable model was backwards manually, based on the log likelihood ratio; a significance level of 0.05 was used. Food handling hygiene was determined using a questionnaire that included items on acquisition and preparation of food. Power and sample size not reported	763_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Contact with person outside household with gastroenteritis – 17.7(5.1-61.1) *Multivariate analysis* Poor food-handling hygiene (as a score) – 1.2(0.9-1.7) ≥ 1 household members with gastroenteritis – 2.7(0.8-8.9) Contact with person outside household with gastroenteritis – 10.9(2.2-54.6) *Population attributable risk (%) (based on multivariate odds ratios)* Poor food-handling hygiene (as a score) – 46 ≥ 1 household members with gastroenteritis – 27 Contact with person outside household with gastroenteritis – 51 *≥ 5 years (46 case-control pairs)* *Univariate analysis* Poor food-handling hygiene (as a score) – 1.3(0.9-1.9) ≥ 1 household members with gastroenteritis – 15.0(2.0-113.6) Contact with person outside household with gastroenteritis – 5.9(1.7-20.1) *Multivariate analysis* Poor food-handling hygiene (as a score) – 1.3(0.8-2.2) ≥ 1 household members with gastroenteritis – 1.1(0.1-15.9) Contact with person outside household with gastroenteritis – 12.1(1.0-147.3) *Population attributable risk (%) (based on multivariate odds ratios)* Poor food-handling hygiene (as a score) – 63 ≥ 1 household members with gastroenteritis – 4 Contact with person outside household with gastroenteritis – 60		
Gotz, H; 2001 [62]	Retrospective controlled study 1,3,4	To describe an outbreak in which secondary transmission into households by individuals occurred	Children and staff at 30 child centers (either a day care facility for preschool children or an after-school center for young children) in Sweden and their household contacts. Child center cases – 79 adults (mean age 41 yrs) and 114 children (mean age 5 yrs) Household cases – 58 adults (mean age 36 yrs)	**Symptoms** *All results adults vs. children - % reporting symptoms; P value* Diarrhea – 71.5 vs. 52.0; <0.01 Vomiting – 64.1 vs. 80.6; <0.01 Nausea – 96.8 vs. 93.1; 0.22 Stomach pain – 87.7 vs. 88.7; 0.82 Headache – 63.6 vs. 43.5; 0.01 Chills – 44.3 vs. 20.8; <0.01 Fever – 44.7 vs. 35.2; 0.20 Myalgia – 48.2 vs. 17.5; <0.01 **Symptomatic norovirus infection - Primary attack rate** Adults vs. children – 68/127 vs. 74/386; P<0.01	Primary case: a person in the child center who became ill and who had diarrhea, vomiting or nausea during the first 3 days of the outbreak Secondary case: a person who became ill from day 4 through day 12 of the outbreak Secondary household case: a person who became ill at >6 h but <10 days after the	1024_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			and 21 children (mean age 7 yrs) 775	Children 0-5 yrs old vs. 6-10 yrs old – 44/204 vs. 30/179; P=0.23 **Symptomatic norovirus infection - Secondary attack rate** Adults vs. children – 11/59 vs. 40/312; P=0.23 Children 0-5 yrs old vs. 6-10 yrs old – 27/160 vs. 12/149; P=0.02 **Risk factors for household transmission of symptomatic norovirus infection** *All results RR(95% CI) unless otherwise noted* Children (vs. adults) – 3.8(1.9-7.6) Exposure to vomiting – 2.4(1.0-5.5) Exposure to diarrhea – 0.8(0.5-1.3) Increased frequency of vomiting – P<0.01 Size of household – P=0.14 Onset of illness at child center (vs. onset of illness at home) – 0.9(0.6-1.6) **Median incubation period for primary cases** 34 hours (range 2-61 hours) **Median serial interval** (between a case in the chid center and the linked household cases) Overall – 73 hours (range 4-198 hours) Counting only the first case in each household – 59 hours (range 4-198 hours) Truncating at 96 hours – 52 hours (4-96 hours)	onset of disease in the corresponding patient who acquired the infection in the child center. Norwalk like virus (NLV) was confirmed using EM, used PCR for genotyping Power and sample size not reported 524/775 subjects (68%) returned the questionnaire	
Oppermann, H; 2001 [63]	Retrospective controlled study 1,2,3,4	To identify risk factors for a gastroenteritis outbreak.	Guests and staff at a mother and child health clinic in Germany. 166 guests and 49 staff met case definition. Data available for 164 guests and 47 staff.	**Symptomatic norovirus infection - Attack Rates** Guests 44% - adults 27% and children 54% Staff 23.4% **Symptomatic norovirus infection** *All results affected vs. not affected; p value* Children – 3.5 years vs. 6.3 years; <0.001 Adults – 32 years vs. 33 years; NS **Interventions** -At the start of each cure period guests should be instructed to wash hands after using the bathroom and prior to meals. Patients should immediately tell doctors about any gastrointestinal symptoms. -Persons with GI symptoms should have as little contact as possible with other guests of the health clinic and not use common facilities such as indoor	Case definition was someone who stayed at the health clinic from October 27 to November 17, 1999 and had vomiting and/or diarrhea one day after his/her arrival at the earliest. NLV and astroviruses detected using PCR.	1041_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				swimming pools including cleaning personnel should be told immediately when GI disease is suspected and be given instructions about appropriate protective measures. -The rooms of the diseased persons, especially lavatories, should be cleaned daily using a virucidal disinfectant. Vomitus should be disinfected immediately. -If an outbreak is suspected, the public health department should be notified.		
Sharp, TW; 1995 [64]	Retrospective controlled study 1,3,4,6,7	To identify risk factors for an outbreak onboard an aircraft carrier.	Crew members aboard an aircraft carrier. 4500 male crew members. Questionnaire results available for 2,618 shipboard personnel. Mean age 27 years (range, 17-59)	**Symptomatic norovirus infection - Attack rates (n=4500)** 13% with symptomatic infection 8% sought medical attention; almost all missed at ≥1 day work **Symptomatic norovirus infection** **Univariate analysis (n=2618)** *All results variable – attack rate; unadjusted OR (95% CI)* Age range (years) 17-19 – 17.6%; Reference 20-39 – 14.3%; 0.93 (0.6-1.5) 40-59 – 11.5%; 0.73 (0.4-1.2) 40-59 – 9.3%; 0.57 (0.3-1.2) Race White – 14.3%; Reference Black – 8.8%; 0.58 (0.4-0.85) Other – 17.2%; 1.24 (0.9-1.74) Rank Junior enlisted – 13.8%; Reference Senior enlisted – 10.7%; 0.74 (0.4-1.3) Officers – 9.4%; 0.65 (0.4-1.09) Number of persons in sleeping compartment 1-10 – 7.1%; Reference 11-50 – 8.6%; 1.23 (0.7-2.3) 51-100 – 15.5%; 2.39 (1.4-4.3) >100 – 18.6%; 2.98 (1.7-5.3) **Multivariate analysis (n=2618)** *All results variable – adjusted OR (95% CI)* Age (by year) – 0.98 (0.97-0.99) Race White – Reference Black – 0.6 (0.3-0.9) Other – 1.0 (0.7-1.3)	Power and sample size not reported. Gastroenteritis was defined as anyone reporting either vomiting or water stools with at least one of the following: nausea, fever, headaches, chills, or myalgias. Gastroenteritis was associated with at least a fourfold increase in Norwalk virus antibody levels measured by ELISA. Norwalk virus like particles were also seen using immune EM in 2/6 stools.	1513_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Number of persons in sleeping compartment 1-10 – Reference 11-50 – 1.1 (0.5-1.7) 51-100 – 2.8 (1.2-3.4) >100 – 2.8 (1.2-3.4) **Pre-outbreak antibody levels and subsequent acute gastroenteritis** *All results pre-outbreak antibody titer – No. developing illness/total No. (%)* <50 – 2/14 (14%) 50-200 – 9/28 (32%) 400-800 – 8/20 (40%) 1600-3200 – 11/35 (31%) ≥6400 – 2/12 (17%) All – 32/109 (29%) **Pre-outbreak antibody levels and subsequent fourfold or more titer rise** *All results pre-outbreak antibody titer – No. with fourfold or more titer rise/total No. (%)* <50 – 6/14 (43%) 50-200 – 12/28 (43%) 400-800 – 5/20 (25%) 1600-3200 – 9/35 (26%) ≥6400 – 2/12 (17%) All – 23/109 (31%) **Pre-outbreak antibody levels and subsequent fourfold or more titer rise with acute gastroenteritis** *All results pre-outbreak antibody titer – No. with fourfold or more titer rise and developing illness/total No. (%)* <50 – 2/14 (14%) 50-200 – 5/28 (18%) 400-800 – 4/20 (20%) 1600-3200 – 4/35 (11%) ≥6400 – 1/12 (8%) All – 16/109 (15%)		
Clinical characteristics						
Mattner, F; 2005 [56]	Systematic review	To investigate the effect of the index case (i.e.,	All published nosocomial norovirus outbreaks with	**Index case in outbreaks** Patient vs. staff – 20/30 (67%) vs. 10/30 (33%)	Sources include Medline search from 1962-2004	520_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
	1,2,3	patient vs. staff) on infection risk and outbreak size.	proven or suspected person-to-person transmission. Inclusion for statistical analyses limited to outbreaks with epidemic curves for each ward and outbreaks where the index case could be identified. 1033 individuals among 30 outbreaks included in the study.	**Symptomatic norovirus infection** *All results index case: patient vs.staff (95% CI for difference in mean); p value (30 wards included)* Mean number of affected patients – 27.75 vs 11.5 (5.1-27.0); 0.006 Mean number of affected staff – 11.75 vs 12.8 (-9.0 -6.9); 0.78 Mean number of overall affected individuals – 39.5 vs 24.3 (1.1-29.0); 0.36 *All results index case: patient vs. staff; OR (95% CI); p value (7 wards included)* Number of affected patients - 154/356 vs. 21/153; 4.79 (1.82-8.28); <0.0005 Number of affected staff – 79/224 vs. 36/136; 1.51 (0.92-2.49); 0.08	using search terms: "norovirus", "Norwalk virus", "small round structured virus", and "outbreak"; Outbreak Worldwide Database; German data in Epidemiologisches Bulletin; data from personal communication with a German teaching hospital; and author's own data. Power and sample size not reported.	
Mattner, F; 2006 [57]	Prospective controlled study 1,3,4,6,7	To characterize risk factors for the clinical complications of norovirus infections (e.g. vomiting, diarrhea, potassium decrease, creatinine increase, C-reactive protein increase)	All individuals working in or admitted to five wards (psychiatry, nephrology, gastroenterology, cardiology and trauma) at a university hospital in Germany in the period from the onset of clinical symptoms of the first patient until 2 days after the last patient became symptom free. All patients and staff members who were affected with a sudden onset of diarrhea and/or vomiting were included as cases. Patients admitted with clinical signs were regarded as index cases, and patients admitted ≥48 hrs before developing clinical signs were regarded as nosocomial cases	**Clinical features in patients** (study duration 3 months) Diarrhea – 79/84; 95% Vomiting – 57/84; 68% Somnolence – 2/84; 2% Serum creatinine increase > 10% – 22/84; 26% Serum potassium decrease > 20% – 7/84; 8% **Comparisons of attack rates in patients and nurses** (study duration 3 months) *All results are attack rate (%) in patients vs. nurses; P value* Psychaitry ward – 78 vs. 88; <0.01 Nephrology ward – 32% in the first period and 33% in the second period in patients. Data for nurses not given Gastroenterology – 27 vs. 90; <0.01 Cardiology – 42 vs. 44; 0.87 Trauma – 35 vs. 83; <0.01 Total – 38 vs. 76; <0.01 **Risk factors for complications of norovirus** (study duration 3 months) *VOMITING>1 DAY:* *Univariate analysis: All results OR; P value* Age > 65 years – 1.84; 0.30 Male gender – 0.91; 1.00 Underlying cardiovascular disorders – 2.7; 0.13 Underlying gastrointestinal disorders – 0.34; 0.31	Diarrhea was defined as three or more episodes of loose stools in a 24 hr period. Cases were considered to be norovirus-positive if samples from at least two patients from the same ward were positive by norovirus-specific RT-PCR. Power and sample size not reported	358_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			84 patients (72 acquired infection nosocomially) and 79 staff members (60 nurses). 3 norovirus positive patients were excluded from risk factor analysis. N for risk factor analyses was 53 for all outcomes except C reactive protein increase (N=52)	Underlying autoimmune disease – 0.81; 1.00 Underlying renal disorders – 0.95; 1.00 Renal transplant – 1.31; 0.75 Underlying malignancy – P value 0.18; OR not reported Underlying trauma – 1.14; 1.00 Immunosuppressive therapy – 0.92; 1.00 Community acquired norovirus – 2.36; 0.19 *Multivariate analysis: All results OR (95% CI)* Underlying cardiovascular disorders – 7.17(1.59-51.2) Community acquired norovirus – 5.54(1.04-42.8) *DIARRHEA>2 DAYS:* *Univariate analysis: All results OR; P value* Age > 65 years – 3.58; 0.01 Male gender – 2.15; 0.12 Underlying cardiovascular disorders – 2.80; 0.15 Underlying gastrointestinal disorders – 0.22; 0.03 Underlying autoimmune disease – 4.67; 0.24 Underlying renal disorders – 1.77; 0.39 Renal transplant – 1.71; 0.54 Underlying malignancy – 0.07; 0.01 Underlying trauma – 0.27; 0.053 Immunosuppressive therapy – 1.29; 0.79 Community acquired norovirus – 3.09; 0.06 *Multivariate analysis: All results OR (95% CI)* Age > 65 years – 11.56(1.89-224.00) Underlying malignancy – 0.02(0.00-0.19) Underlying trauma – 0.05(0.00-0.55) *POTASSIUM DECREASE >20%:* *Univariate analysis: All results OR; P value* Age > 65 years – 0.94; 1.00 Male gender – 0.90; 1.00 Underlying cardiovascular disorders – 5.17; 0.06 Underlying gastrointestinal disorders – 0.46; 0.67 Underlying autoimmune disease – 0.98; 1.00 Underlying renal disorders – 1.74; 0.71 Renal transplant – 3.91; 0.09		

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Underlying malignancy – P value 0.58; OR not reported Underlying trauma – P value 0.19; OR not reported Immunosuppressive therapy – 2.83; 0.25 Community acquired norovirus – 0.48; 0.68 *Multivariate analysis: All results OR (95% CI)* Underlying cardiovascular disorders – 17.10(2.17-403.00) Renal transplant – 13.02(1.63-281.00) *CREATININE INCREASE >10%:* *Univariate analysis: All results OR; P value* Age > 65 years – 1.04; 1.00 Male gender – 1.79; 0.24 Underlying cardiovascular disorders – 0.60; 0.42 Underlying gastrointestinal disorders – 1.93; 0.36 Underlying autoimmune disease – 4.50; 0.12 Underlying renal disorders – 1.44; 0.59 Renal transplant – 3.53; 0.07 Underlying malignancy – 0.93; 1.00 Underlying trauma – 0.07; <0.01 Immunosuppressive therapy – 5.74; <0.01 Community acquired norovirus – 5.07; 0.01 *Multivariate analysis: All results OR (95% CI)* Immunosuppressive therapy – 5.67(1.78-20.1) *C REACTIVE PROTEIN >58 MG:* *Univariate analysis: All results OR; P value* Age > 65 years – 0.81; 0.79 Male gender – 2.63; 0.11 Underlying cardiovascular disorders – 0.32; 0.06 Underlying gastrointestinal disorders – 1.54; 0.55 Underlying autoimmune disease – 3.71; 0.14 Underlying renal disorders – 2.13; 0.19 Renal transplant – 1.33; 0.76 Underlying malignancy – 2.96; 0.25 Underlying trauma – 0.23; 0.35 Immunosuppressive therapy – 3.38; 0.06 Community acquired norovirus – 2.30; 0.23		

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Multivariate analysis: All results OR (95% CI) Underlying malignancy – 9.07(1.17-193.00) Immunosuppressive therapy – 5.37(1.62-19.9)		
Lopman, BA; 2004 [58]	Prospective controlled study 1,2,3,4	To describe norovirus outbreaks in residential homes or hospitals of principally older individuals.	Patients in hospitals and nursing homes in England. Cases were hospital patients, nursing home residents, and health care staff with ≥2 episodes of vomiting, ≥3 episodes of diarrhea, or both during a 24-hour period. Those with symptoms due to incontinence or ingestion of laxative drugs were excluded. 271 outbreaks – 33 in nursing homes and 238 in hospital units. 4378 cases – 2154 hospitalized patients, 1360 hospital care staff, 505 nursing home residents, and 358 nursing home staff.	**Duration of illness** Hospital patients vs. hospital staff, nursing home staff, and nursing home residents (75th percentile); p value – 3 days (5 days) vs. 2 days (3 days); p<0.001 Recovery was slowest in the oldest age group (≥85 years) of hospitalized patients - 40% symptomatic after 4 days	Outbreak is defined as ≥ 2 cases in a hospital functional care unit with dates of onset within 7 days of each other. Power and sample size not reported. Promotion of active surveillance (2-tiers of clinical symptoms) to detect cases as a means of prevention of outbreaks	642_IL
Rodriguez-Guillen, L; 2004 [60]	Prospective controlled study 2,4	To investigate the frequency of human CaCV (norovirus and sapovirus) in stool samples from adults and children with HIV.	Adults and children with and without HIV from Venezuela. Stool samples – 240 from adults and 81 from children. Subjects – 209 adults and 65 children.	**Detection in children vs adults; p value** CaCV – 62/159 vs 10/81; <0.0001 Novorivus GI – 4% detected exclusively from adults norovirus GII – 20% vs 4%; <0.01 **Detection in HIV positive vs negative subjects; p value** Adults – 22/108 vs 6/51; NS Children – 22/43 vs 9/38; 0.0111 **Detection in subjects with vs without diarrhea** HIV positive adults – 3/32 vs 10/76; 0.4234 HIV negative adults – 3/26 vs 3/25; 0.6468 HIV positive children – 11/18 vs 11/25; 0.2681	Diarrhea defined as the occurrence of three or more bowel movements within a 24 hour period with decrease in stool consistency. Outcomes determined using RT-PCR. Power and sample size not reported.	502_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				HIV negative children – 5/17 vs 4/21; 0.3565		
Thea, D; 1993 [65]	Prospective controlled study 1,3,4	To determine the prevalence of enteric viruses and their relation to diarrhea, wasting and immunosuppression among HIV infected and uninfected persons.	Adult general medical patients admitted to a hospital in Zaire. 57% were HIV positive. 10/198 patients had SRSV infection. 234 enrolled, 198 analyzed	**Presence of diarrhea in patients shedding norovirus** Of 10 patients shedding norovirus, 2 had acute diarrhea, 2 had chronic diarrhea and 6 had no diarrhea **Presence of HIV infection in patients shedding norovirus** Of 10 patients shedding norovirus, 5 had HIV infection (1 Stage III and 4 Stage IV) and 5 did not. **Asymptomatic norovirus infection - Viral shedding** *Association with HIV infection* HIV positive vs. HIV negative – 17% vs. 18%; P=0.82 Viral shedding vs. no viral shedding (Stage III HIV positive) – P=0.80 Viral shedding vs. no viral shedding (Stage IV HIV positive/AIDS) – P=0.79 *Association with degree of immunocompromise (defined by CD4/CD8 ratio)* *All results P values for test of trend towards greater frequency of shedding among lower CD4/CD8 quintiles* Overall – P=0.14 Among HIV positive – 0.07 Among HIV negative – 0.45	norovirus was detected by EM. HIV Stages: I: Asymptomatic II: Mild disease III: Moderate disease IV: Acquired immune deficiency syndrome (AIDS) Power and sample size not reported	1606_RA
Lee, N; 2007 [59]	Retrospective controlled study 1,2,3,4,6,7	To study the association between fecal viral concentration and clinical manifestations of GII.4 norovirus infection. Risk factors for prolonged diarrhea were also studied.	Patients ≥16 yrs of age at 2 regional hospitals in Hong Kong. Mean age 60 years; 37.5% male. 44 enrolled; 40 analyzed	**Factors associated with higher median fecal viral concentration (during a 2 year study period)** *Univariate analysis (All results P value)* Age ≥ 65 yrs – 0.06 Female gender – 0.71 Pre-existing medical conditions – 0.52 Prolonged duration of diarrhea – <0.01 Frequency of vomiting – 0.22 Frequency of fever – 0.38 *Correlation analysis (All results Spearman correlation coefficient, P value)* Total duration of diarrhea – 0.47; <0.01 Total frequency of vomiting – 0.34; 0.04 **Risk factors for prolonged duration of diarrhea (during a 2 year study period)** *Univariate analysis (All results P value)*	Cases were included for analysis if stool samples were collected ≤ 96 hours from symptom onset. Diarrhea was defined as having ≥ 3 loose stools per day. Diagnosis of norovirus infection and its quantitation were based on RT-PCR assay of stool samples. Prolonged diarrhea was defined as ≥ 4 days of diarrhea	2416_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Age ≥ 65 yrs – <0.05 Pre-existing medical conditions – <0.05 Frequency of fever – 0.01 *Multivariate analysis (All results OR; 95% CI)* Fecal viral concentration (per log_{10} copies) – 9.56(1.18-77.57) Age (per year) – 1.15(1.03-1.28)	Power and sample size not reported Correlation between norovirus concentration and duration of illness (not severity)	
Marx, A; 1999 [66]	Retrospective controlled study 1,3,4	To assess risk factors for gastroenteritis associated with Norwalk-like viruses (NLVs)	Residents and employees at a geriatric long term care facility. 68% residents were female, median age was 83 yrs (range 65-106). 78% of employees were female, median age was 36 yrs. Study was conducted in Washington State. 91 residents and 97 employees	*All results RR(95% CI); P value for the presence of risk factor* **Risk factors for symptomatic norovirus infection among residents** Physical dependence – 3.5(1.0-12.9);0.02 Respiratory therapy – 2.3(0.8-6.4); 0.20 Antibiotics – 1.6(1.0-2.8); 0.20 Chronic infections – 1.6(0.9-3.0); 0.40 Tube feeding – 1.3(0.7-2.6); 0.70 Disoriented – 1.2(0.8-1.8); 0.60 Diuretics – 0.4(0.2-0.9); 0.02 **Risk factors for symptomatic norovirus infection among employees** Exposure to vomitus – 2.6(1.1-6.5); 0.03 Gastroenteritis in household – 2.3(1.4-3.6); 0.01 Exposure to residents with gastroenteritis – 2.2(1.0-4.9); 0.05 Resident care – 1.4(0.8-2.5); 0.30 Tap water – 0.9(0.5-1.5); 0.60 Ice – 0.7(0.4-1.2); 0.20 **Symptomatic norovirus infection (Effect of protective measures among nursing staff)** Gowning – 0.4(0.1-1.4) Strict hand washing – 0.7(0.2-1.3) Use of hand-disinfection gel – 0.8(0.4-1.4) Laundering work clothes daily – 1.2(0.7-1.3)	A case of acute gastroenteritis was defined as an individual with onset of vomiting or diarrhea during the study period (Feb 12 – Mar 20 1996); diarrhea was defined as ≥2 loose or watery stools in a 24 hr period. A single NLV strain of genogroup II genetically related to Toronto virus was the only pathogen identified. NLVs were identified by EM in stool and vomitus specimens and further characterized by RT-PCR and nucleotide sequencing. Data on residents was collected through medical records. 90 of 97 employees completed a self-administered questionnaire Power and sample size not reported	1237_RA
Caceres, V; 1998 [67]	Retrospective controlled study 1,3,4	To identify the etiologic agent and risk factors associated with a hospital ward outbreak of gastroenteritis.	Patients and staff on a medical-surgical ward in South Carolina where the index case (a nursing staff member) worked. Overall demographics not reported.	**Symptomatic norovirus infection - Attack rate** (during the study period) Staff vs. patients – 28/89 vs. 10/91; RR(95% CI) = 2.9(1.5-5.5) **Symptomatic norovirus infection among staff** *All results RR(95% CI) (comparisons not clear, assume the opposite of the risk factor given)* Stayed in hospital overnight – 2.0(1.0-3.9)	A case was defined as a staff member or patient who had acute onset of vomiting and diarrhea from January 5-13, 1996 as recorded in patient charts.	1324_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			89 staff and 91 patients	Assisted ill patients – 1.1(0.6-2.2) Worked longer hours – 1.8(1.0-3.5) Used staff bathroom on ward – 22/61 vs. 0/1; RR undefined Ate in cafetaria – 1.5(0.7-3.1) Brought own food – 1.1(0.6-2.1) Consumed water from ward – 1.4(0.7-2.8) Consumed ice from ward – 1.1(0.2-5.5) Changing bed sheets without golves – 1.7(0.7-4.0) Changing urine catheters without gloves – 0/0 vs. 17/54; RR undefined Turning patients without gloves – 0.8(0.4-1.9) **Symptomatic norovirus infection among household members** Case staff vs. non-case staff – 5/27 vs. 7/69; 1.8(0.6-5.3) **Symptomatic norovirus infection among patients** *All results RR(95% CI) (comparisons not clear, assume the opposite of the risk factor given)* ED vs. admitted directly from home – 1.3(0.4-4.5) Regular diet - 1.4(0.4-4.4) Full ambulation – 2.6(0.7-9.5) Physical therapy – 0.8(0.2-2.9) Urinary catheter care – 1.2(0.4-4.0) Nasogastric tube care – 0/5 vs. 10/86; RR undefined Wound care – 0/24 vs. 10/67; RR undefined Respiratory care – 5.7(1.8-18.1) **Risk of symptomatic norovirus infection associated with patient nurse exposures** *All results RR(95% CI)* Patients – on a shift with an assigned primary nurse who had onset of illness in the preceding 48h vs. not – 14% vs. 0%; RR undefined Nurses – on a shift with an assigned primary patient who had onset of illness in the preceding 48h vs. not – 0.3(0.1-1.1) **Discharge diagnoses of vomiting, diarrhea or viral gastroenteritis** Month of outbreak vs. same month previous year – 79/3567 vs. 63/3982; P<0.05 **Etiologic agent** EM identified SRSV in 9 of 9 stool samples	A patient was considered to be exposed if he or she had been taken care of by a case-nurse (an assigned nurse who was a primary caretaker) who had developed the illness in the preceding 48 hours. Staff exposure was ascertained if care of a symptomatic patient occurred within 48 hours All stool and vomit specimens were obtained within 48 hours after the onset of gastroenteritis. Specimens were examined by EM for viral particles and by RT-PCR for SRSV RNA Power and sample size not reported	

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Cegielski, J; 1994 [68]	Controlled study based on a cross-sectional survey None	To determine whether specific viruses were associated with HIV infection	HIV infected and HIV uninfected Tanzanian children admitted with chronic diarrhea, and controls without diarrhea aged 15 months to 5 years. Consecutive sample (n=59) Not reported	**Asymptomatic norovirus infection** HIV infected children with chronic diarrhea vs. HIV uninfected children with chronic diarrhea – 4/21 vs. 1/32; Prevalence Ratio (90% CI) – 6.09(1.03-36.14) Rotavirus and coronavirus particles were not associated with HIV infection.	Enteric viruses were identified by EM of fecal specimens. Asymptomatic infection defined as presence of SRSV Power and sample size not reported	1525_RA
Laboratory Characteristics						
Halperin, T; 2008[69]	Prospective controlled study 1,3,4	To determine if norovirus genogroup II susceptibility is related to ABO phenotype.	Sick soldiers and healthy contacts in military units in Israel during outbreaks during February 2003 and January 2005. All soldiers were male and 18-22 years old. 138 cases and 166 healthy subjects.	**Symptoms** Attack rate – 20%. Nausea and/or emesis – 75% Diarrhea – 69% Stomachache – 65% Fever – 17% **ABO distribution** A – 36.5% AB – 11.8% B – 20% O – 31.6% **Risk Factor compared to blood type O** *All results – Symptomatic infection OR (95% CI); Fever OR (95% CI)* A – 0.58 (0.33-1.01); 2.14 (0.68-6.74) AB – 0.48 (0.20-1.14); OR N/A B – 0.72 (0.37-1.38); 3.08 (0.89-10.67)	Cases had emesis, nausea, or stomachache. Healthy contacts served in the same company as the case patients, had no GI symptoms, and were in the compound for at least the 3 days prior to the outbreak. Power and sample size not reported.	5114_IL
Hutson, A; 2005 [70]	Prospective controlled study 1,2,3,4	To evaluate whether secretor status was associated with resistance to norovirus infection.	Volunteers experimentally challenged with norovirus. Demographic characteristics not reported. Study was conducted in Texas. 51	**Asymptomatic norovirus infection (following challenge)** Secretor positive vs. secretor negative – 42/43 vs. 0/8; statistical differences were not reported **Symptomatic norovirus infection (following challenge)** Secretor positive vs. secretor negative – 29/43 vs. 0/8; statistical differences were not reported	norovirus infection was defined as four-fold or greater increase in norovirus specific serum antibody titer (ELISA) or norovirus antigen shedding [ELISA, radioimmunoasay (RIA) or RT-PCR] Secretor genotype was	468_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
					assessed by testing PCR products obtained from deoxyribonucleic acid (DNA) extracted from archived sera. FUT2 gene typically associated with non-secretor status (norovirus resistant) and in 20% of Caucasians. Study did not characterize participants by ethnicity, only FUT2 genotyping. Power and sample size not reported	
Thorven, M; 2005 [71]	Prospective Controlled Study 1,3,4	To investigate if the FUT2 secretor gene was associated with resistance to nosocomial and sporadic outbreaks caused by genogroup II noroviruses	Symptomatic and asymptomatic individuals from nosocomial and sporadic outbreaks of genogroup II norovirus. Blood donors in Sweden were used as a second control group. Patient demographics not described. Study was conducted in Sweden. 115	**Secretor Status** Outbreak 1 (Internal Medicine Ward; N=50) *Symptomatic patients:* Homozygous secretors – 47% Heterozygous secretors – 53% Secretor negative – 0% *Asymptomatic patients:* Secretor negative – 19% (Number of patients for each category was not reported) Outbreak 2 (Pediatrics Ward; N=28) *Symptomatic patients:* Secretor negative – 0/7 *Asymptomatic patients:* Secretor negative – 9/21 Outbreak 3 (Orthopedic Ward; N=18) *Symptomatic patients:* Secretor negative – 0/12 *Asymptomatic patients:* Secretor negative – 3/6 Community Outbreaks (N=19) *Symptomatic patients:*	A patient with gastroenteritis was defined as a patient with vomiting (≥ once/24 h) and/or diarrhea (≥ 2 watery stools/24 h) norovirus was detected in stool using RT-PCR. The DNA from saliva was sequenced for secretor genotype using sequence-specific primers and PCR. Power and sample size not reported	400_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Homozygous secretors – 7/15 Heterozygous secretors – 8/15 Secretor negative – 0/15 *Asymptomatic patients:* Homozygous secretors – 2/4 Heterozygous secretors – 2/4 Secretor negative – 0/4 <u>Cumulative data</u> Homozygous non secretor status Symptomatic patients vs. non-symptomatic patients – 0/53 vs. 18/62; P<0.01 Symptomatic patients vs. blood donors – 0/53 vs. 21/104; P<0.01		
Lindesmith, L; 2003 [72]	Prospective controlled study 1,2,3,4	To investigate the role of secretor status and acquired immunity in Norwalk virus infection. Volunteers received doses of Norwalk virus inoculum ranging from 10 to 3 × 10^8 PCR detectable units.	Volunteers dosed with Norwalk virus. 49% male; 71% white, 23% black and 6% other races; average age 30 yrs (range 20-49). Study was conducted in North Carolina. 77	**Asymptomatic norovirus infection (following challenge)** Secretor positive vs. secretor negative – 34/55 vs. 0/22; P<0.01 Blood types <u>Among O blood type</u> Secretor positive – RR 1.56; P<0.05 Secretor negative – No events; P>0.05 Overall – RR 1.89; P<0.05 <u>Among A blood type</u> Secretor positive – RR 0.79; P>0.05 Secretor negative – No events; P>0.05 Overall – RR 0.54; P<0.05 <u>Among B blood type</u> Secretor positive – RR 0.66; P>0.05 Secretor negative – No events; P>0.05 Overall – RR 0.82; P>0.05 <u>Among AB blood type</u> Secretor positive – No events; P>0.05 Secretor negative – No events; P>0.05 Overall – P>0.05 **Symptomatic norovirus infection** O blood type– P>0.05	Norovirus infection was defined as viral RNA detected in stool or a ≥4-fold increase in Norwalk-virus specific serum IgG. Symptomatic infection was defined as an infected subject with vomiting or diarrhea (>2 unformed stools in 24 hours). Secretor genotype was determined through PCR amplification of DNA extracted from saliva. Data on immunity was not not extracted as it was not clinically relevant (antibody titers) Comparison group for RR unclear. Power and sample size not reported	830_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Hutson, A; 2002 [73]	Prospective controlled study 1,2,3,4	To investigate the role of ABO phenotype in norovirus susceptibility	Volunteers experimentally challenged with norovirus. Demographic characteristics not reported. Study was conducted in Texas. 51	*All results OR (95% CI); P value by Fisher's exact for the presence of blood type and the risk of infection* **Asymptomatic norovirus infection (following challenge)** O – 11.80(1.3-103.00); 0.01 A – 0.63(0.14-2.70); 0.70 B – 0.27(0.04-1.90); 0.21 AB – 0(0-1.10); 0.03 A/AB combined – 0.25(0.05-1.20); 0.13 B/AB combined – 0.10(0.02-0.56); 0.01 **Symptomatic norovirus infection (following challenge)** O – 0.89(0.23-3.40); 1.0 A – 3.90(0.72-21.00); 0.16 B – 0(0-0.99); 0.03	norovirus infection was defined as four-fold or greater increase in norovirus specific serum antibody titer (ELISA) or norovirus antigen shedding (ELISA, RIA or RT-PCR) Asymptomatic infection was defined as the absence of vomiting and/or diarrhea and a low overall symptom score (abdominal cramps, chills, body ache, headache, nausea and fever) Comparison group for OR unclear. Power and sample size not reported	954_RA
Graham DY, 1994[74]	Prospective controlled study 1,3,4	To evaluate the clinical features and virologic and immunologic responses following oral administration of Norwalk virus.	8 volunteer studies between July 1985 and January 1990 where medical students and staff of the Texas Medical Center were administered norovirus. 21 women, 30 men 19-39 years old 43 white, 6 black, 1 Hispanic, and 1 East Indian. N=50 subjects	**Infection status measured by serum antibody response** After norovirus challenge, 9 (18%) uninfected vs. 41 (82%) infected. Of those infected, 82% with vs. 60% without preexisting antibody; p>0.2. Of those infected, Group 4 subjects had higher preexisting antibody titers than uninfected subjects; p=0.004 Uninfected subjects had lower preexisting antibody titers than infected subjects; p<0.001 Of those infected, there were increases in geometric mean titers after infection (p<0.01) and the increase in convalescent titers were higher in subjects with vomiting (Groups 3 and 5 vs. 2 and 4; p=0.016) or with vomiting and diarrhea (Group 5 vs. 2-4, p=0.02) *All results: No (%) subjects with pre-existing Norwalk virus antibody titers of levels <10 vs. 10 vs. 40 vs. 160 vs. 640 vs 2560 who have the characteristic of interest* Seroconversion: 3/5 (60) vs. 4/7 (57) vs. 13/17 (76) vs. 16/16 (100) vs. 4 /4(100) vs. 0/1; p value=0.065 Viral shedding: 2 (40) vs. 2 (29) vs. 12 (70) vs. 16 (100) vs. 3 (75) vs 1 (100); p value=0.0012	ELISA to detect norovirus specific antibodies and antigen in stool. Biotin-avidin ELISA, RIA, RT-PCR, and dot blot hybridization to detect antigen in stool. Norovirus infection defined as ≥ 4 fold increase in serum antibody titer or excretion of virus. Diarrhea defined as watery stools (unformed stools not considered diarrhea). Asymptomatic infection defined as no vomiting or diarrhea and a symptom	1563_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Diarrhea: 2 (40) vs. 1 (14) vs. 10 (59) vs. 7 (44) vs. 3 (75) vs. 1 (100); p value=NS Vomiting: 2 (40) vs. 1 (14) vs. 7 (41) vs. 5 (31) vs. 1 (25) vs 0; p value=NS Nausea: 2 (40) vs. 1 (14) vs. 11 (65) vs. 10 (62) vs. 4 (100) vs. 0; p=0.065 Cramps: 2 (40) vs. 1 (14) vs. 12 (70) vs. 10 (62) vs. 2 (50) vs. 0; p value=NS Headache: 4 (80) vs. 3 (42) vs. 12 (70) vs. 9 (56) vs. 3 (75) vs. 0; p value=NS Chills: 1 (20) vs. 0 vs. 5 (29) vs. 3 (19) vs. 1 (25) vs. 0; p value=NS Fever: 1 (20) vs. 0 vs. 4 (23) vs. 3 (19) vs. 1 (25) vs. 0; p value=NS *Virologic parameters of infection* 64% patients with symptomatic infection vs. 32% with asymptomatic infection had stools with positive antigen Earliest positive sample occurred at 15 hours Peak of stool viral shedding 25-72 hours after inoculation Most infected volunteers shed viral antigen continuously from their first positive sample until the last sample obtained Longest antigen shedding was 7 days after inoculation and 1 asymptomatic subject shed antigen 6 days after inoculation *All results No. positive/no. tested stool samples (%); Mean no. stools/person/day in Uninfected vs. Infected (asymptomatic) vs. Infected (symptomatic) patients at different time points* Day 0: 0/5; 0.6 vs. 0/7; 0.5 vs. 0/10; 0.4 Day 1: 0/6; 0.7 vs. 0/16; 1.2 vs. 12/51 (24); 1.8 Day 2: 0/7; 0.8 vs. 9/17 (53); 1.3 vs. 81/109 (74); 3.9 Day 3: 0/13; 1.4 vs. 5/9 (56); 0.7 vs. 40/44 (91); 1.6 Day 4: 0/1; NC vs. 2/3 (67); NC vs. 16/22 (73); NC Day 5: 0/4; NC vs. 1/3 (33); NC vs. ½ (50); NC Day 6: 0/2; NC vs. 1/1 (100); NC vs. 5/5 (100); NC Day 7: 0/1; NC vs. NS; NC vs. 2/2 (100); NC Total: 0/39; NC vs. 18/56 (32); NC vs. 157/245 (64); NC NC - not calculated because not all stools collected after subjects discharged NS – no samples received. *Clinical features of subjects relative to infection status* Incubation time to onset of symptoms: 24-38 hours Duration of illness: 2-3 days Diarrhea: occurred earliest at 15 hours and latest at 55 hours after inoculation.	score of ≤4 in an infected subject. Symptomatic infection defined as a composite symptom score of ≥ 5 in an infected subject. Patients who vomited or had diarrhea had symptomatic infection. Subjects divided into 5 groups: Group 1 - uninfected Group 2 - asymptomatic or mildly symptomatic (no vomiting or diarrhea) Group 3 - symptomatic (vomiting but no diarrhea) Group 4 - symptomatic (no vomiting but watery diarrhea) Group 5 - symptomatic (vomiting and watery diarrhea) Clinical scores: symptoms were graded using a 5 point score with 0 (absence of symptom) and 5 (most severe iscomfort with symptom). Compositescores tabulated for 72 hour period after inoculation (maximum score 35). Power and sample size not reported.	

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				All results: No. (%) subjects with antibody responses 0 vs. 4 vs. 16 vs. 64 vs. 256 fold with the characteristic of interest; total No. subjects with antibody response Diarrhea: 1/10 (10) vs. 0/3 vs. 9/15 (60) vs. 11/17 (65) vs. 3/5 (60); 24/50 (59); p value=NS Vomiting: 0 vs. 0 vs. 4 (27) vs. 9 (53) vs. 3 (60); 16 (39); p value=0.02 Nausea: 1 (10) vs. 0 vs. 10 (67) vs. 13 (76) vs. 4 (80); 27 (66); p value≤0.02 Cramps: 0 vs. 1 (33) vs. 10 (67) vs. 12 (71) vs. 4 (80); 27 (66) ; p value=NS Headaches/body aches: 4 (40) vs. 0 vs. 11 (73) vs. 12 (71) vs. 4 (80); 27 (66); p value=0.04 Chills: 0 vs. 0 vs. 4 (27) vs. 5 (29) vs. 1 (20); 10 (24); p value=0.08 Fever: 0 vs. 0 vs. 3 (20) vs. 3 (18) vs. 3 (60); 9 (22) ; p value=NS **Antigen vs. antibody detection** *All results: Patients with given clinical scores who had the following antigen response/antibody response (+/+ vs -/+ vs +/- vs. -/-)* Clinical score 0-2 (uninfected): 0 vs 0 vs 0 vs 9 Clinical score 0 (asymptomatic infection): 4 vs 4 vs 0 vs 0 Clinical score 1-4 (mild symptomatic infection): 4 vs 1 vs 0 vs 0 Clinical score 5-24: 26 vs 1 vs 1 vs 0 Total: 34 vs 6 vs 1 vs 9 Antibody detection may be more sensitive than antigen detection		
Nakata, S; 1985 [75]	Prospective controlled study 1,2,3	To determine if clinical illness correlates with pre-existing CaCV serum antibody.	Human CaCV outbreak in a Japanese orphanage during October 1982. 41	**Symptomatic infection** Preexisting serum CaCV antibody – present 3/18 vs. absent 18/23; p<0.01	All patients except one, who only had vomiting, had diarrhea. Power and sample size not reported.	1960_IL
Parrino, TA; 1977 [76]	Prospective controlled study 1,2,3,4,5	To examine immunity in viral gastroenteritis.	Male volunteers, 30-47 years of age, were challenged with Norwalk virus and had symptoms, jejunal biopsies, and serum antibodies evaluated. 12	**Baseline** All subjects had normal baseline biopsy samples. **First challenge** 6/12 developed gastroenteritis. 4/5 symptomatic volunteers who had antibody levels checked had increase in serum Norwalk antibodies that waned over time. 3/3 asymptomatic patients who had antibodies checked did not have increase in serum antibody. 3/5 symptomatic volunteers had abnormal biopsies. 2/5 asymptomatic volunteers had normal biopsies.	Patients were considered clinically ill if they had vomiting and/or diarrhea with one or more associated signs and symptoms. Two investigators characterized subjects as clinically ill without knowledge of serologies or small bowel biopsy results.	2228_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Second challenge (27-42 months later) 6/12 who were symptomatic after the first challenge were symptomatic again with jejunal lesions after the second challenge. 6/12 who were previously asymptomatic were asymptomatic without jejunal lesions. 3/3 asymptomatic patients who had antibody levels checked did not have increase in serum antibody. **Third challenge** *Only performed in 4/6 volunteers who twice became symptomatic; 4-8 weeks after second challenge* 1 was symptomatic. 3 were asymptomatic.	Two investigators characterized subjects without knowledge of serologic findings and prior to biopsy results. Immune-electron-microscopy technique was performed for measurement of Norwalk serum antibody using the 8FIIa Norwalk filtrate as antigen. Power and sample size not reported.	
Fretz, R; 2005 [77]	Retrospective controlled study 1,2,3,6,7	To identify risk factors for sporadic norovirus infections.	All patients of general practitioners in German-speaking parts of Switzerland. Cases (mean age 32.7 years; median age 34 years; range 1.1-69.3 years) were subjects who resided in the study area who had an episode of diarrhea and/or vomiting, consulted a practitioner in the study area, had stool samples negative for *Campylobacter, Shigella, Salmonella*, and other gastroenteric pathogens, had stool samples positive for norovirus genogroup I or II. Cases excluded subjects <6 months or >75 years, patients with possible nosocomial disease, and patients who were part of a norovirus	**Symptoms** (study duration 2 years) Diarrhea – 124/126 (98.4%). Vomiting – 84/126 (66.7%). Nausea – 85/126 (67.5%) Fever – 57/126 (45.2%) Headache – 45/126 (35.7%) Abdominal cramps – 87 (69%) Other – 46 (36.5%) **Mean duration of symptomatic illness** 7.3 days (SD, 6.2 days; range 0.25-28 days) **Symptomatic norovirus infection** *Multivariable analysis* *Consumption of food and beverages OR (95% CI); p value* Mineral water – 1.00 (0.46-2.16); 1.00 Salad – 1.25 (0.34-2.65); 0.74 Raw berries – 0.75 (0.17-3.35); 0.71 Tap water – 1.33 (0.56-3.16); 0.51 Sweet beverages – 1.06 (0.55-2.05); 0.87 *Personal contacts OR (95% CI); p value* Household with children ≤2 years) – 1.00 (0.29-3.45); 1.00 Household with children ≤ 5 years – 0.75 (0.26-2.16); 0.59 Household with children ≤ 10 years – 0.75 (0.26-2.16): 0.59	Power and sample size reported as 70 matched case-control pairs to detect an OR of 2.9 (alpha 0.05; power 0.80; 0.5 probability of an event in the exposed group). Period between the start of symptoms and completion of the patient questionnaire averaged 29 days (median 24 days).	506_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			outbreak. Controls (mean age 33.2 years; median age 37.1 years; range 1.3-70.1 years) were identified through each patient, were the same sex and age group (defined as 5 year intervals over 5-20 years and 10 year intervals over 20-60 years), lived within 10 kilometer (km) of the case, and had not consulted a general practitioner for gastrointestinal illness or symptoms in the month prior to the questionnaire. 126 cases met study inclusion criteria. 73 matched case-control pairs.	Household with children ≤ 65 years – 0.75 (0.17-3.35); 0.71 Household with children > 1 person – 1.50 (0.53-4.21); 0.44 Household with children > 2 person – 0.77 (0.34-1.75); 0.53 Household with children > 3 person – 0.71 (0.32-1.61); 0.53 Household with children > 4 person – 1.14 (0.41-3.15); 0.53 **Symptomatic norovirus infection** *ABO histo-blood group OR (95% CI); p value - conditional logistic regression* Type A: 1.34 (0.55-3.42); 0.49 Type B: 0.33 (0.07-1.65); 0.15 Type O: 1.00 (0.40-2.52); 0.49 Type AB: 1.50 (0.25-8.98); 0.65 Type A/AB: 1.44 (0.62-3.38); 0.39 Type B/AB: 0.63 (0.20-1.91); 0.40 **Symptomatic norovirus infection** *ABO histo-blood group OR (95% CI)*; p value – *random effects logistic regression* Type A: 1.20 (0.55-2.61); 0.64 Type B: 0.28 (0.07-1.13); 0.07 Type O: 1.11 (0.51-2.45); 0.79 Type AB: 1.89 (0.35-10.2); 0.46 Type A/AB: 1.39 (0.64-3.00); 0.40 Type B/AB: 0.59 (0.21-1.70); 0.32		
Meyer, E; 2004 [78]	Retrospective controlled study 1,2,3,4	To determine if O phenotype is more commonly found in patients from norovirus outbreaks compared to blood donors.	Cases were subjects with vomiting, nausea, and/or diarrhea from two nosocomial norovirus outbreaks at a German university hospital. Controls were blood donors in Southwest Germany. 95 cases and 45 controls.	**Symptomatic norovirus infection** *% blood donors vs. % outbreaks with particular ABO phenotype; p value* Type O – 41.2 vs. 22; 0.01 Type A – 43.3 vs 58; 0.52 Type B – 10.7 vs 11; 1.00 Type AB – 4.8 vs 9; 0.34	Power and sample size not reported.	729_IL

Virus characteristics

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Tu ET, 2008 [108]	Descriptive study 3,4	To describe the emergence of new GII.4 variants during the early 2006 epidemic period in Australia and New Zealand.	Fecal samples from gastroenteritis outbreaks in Australia and New Zealand in early 2006. 231 fecal samples were obtained from patients with acute gastroenteritis from Australia and New Zealand through the surveillance network between December 2005 through August 2006. 87 outbreaks. N=186 sequenced samples.	*<u>norovirus genotype (%) in outbreaks</u>* GII.2 (0.5%) GII.3 (9%) GII.4 (86%) GII.5 (0.5%) GII.12 (2%) GII.16 (2%) *<u>Genotype (%) by Location</u>* *New South Wales, Australia (n=119 sequenced strains)* GII.4 2006a (57.1%) GII.4 2006b (17.6%) GII.4 US95/96 (13.4%) GII.4 Hunter (2.5%) GII.b/GII.3 (4.2%) GII.3 (1.7%) GII.4/GII.12 (2.5%) GII.2 (08%) *Queensland, Australia (n=11)* GII.b/GII.3 (45.5%) GII.3 (36.3%) GII.4 2006a (18.2%) *Victoria, Australia (n=14)* GII.4 2006a (100%) *New Zealand (n=42)* GII.4 2006a (73.8%) GII.4 Hunter (11.9%) GII.16 (7.1%) GII.b/GII.3 (2.4%) GII.5 (2.4%) GII.4/GII.12 (2.4%) Two GII.4 variants identified: 2006a (61.8%) and 2006b (11.3%).	Fecal samples tested using RT-PCR. Power and sample size not reported.	5120_IL
Mattner, F; 2006 [57]	Prospective controlled study 1,3,4,6,7	To characterize risk factors for the clinical complications of norovirus infections (e.g. vomiting, diarrhea, potassium decrease,	All individuals working in or admitted to five wards (psychiatry, nephrology, gastroenterology, cardiology and trauma) at a university hospital in Germany in the period from the onset of clinical	**Clinical features in patients** (study duration 3 months) Diarrhea – 79/84; 95% Vomiting – 57/84; 68% Somnolence – 2/84; 2% Serum creatinine increase > 10% – 22/84; 26% Serum potassium decrease > 20% – 7/84; 8%	Diarrhea was defined as three or more episodes of loose stools in a 24 hr period. Cases were considered	358_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		creatinine increase, C-reactive protein increase)	symptoms of the first patient until 2 days after the last patient became symptom free. All patients and staff members who were affected with a sudden onset of diarrhea and/or vomiting were included as cases. Patients admitted with clinical signs were regarded as index cases, and patients admitted ≥48 hrs before developing clinical signs were regarded as nosocomial cases 84 patients (72 acquired infection nosocomially) and 79 staff members (60 nurses). 3 norovirus positive patients were excluded from risk factor analysis. N for risk factor analyses was 53 for all outcomes except C reactive protein increase (N=52)	**Comparisons of attack rates in patients and nurses** (study duration 3 months) *All results are attack rate (%) in patients vs. nurses; P value* Psychaitry ward – 78 vs. 88; <0.01 Nephrology ward – 32% in the first period and 33% in the second period in patients. Data for nurses not given Gastroenterology – 27 vs. 90; <0.01 Cardiology – 42 vs. 44; 0.87 Trauma – 35 vs. 83; <0.01 Total – 38 vs. 76; <0.01 **Risk factors for complications of norovirus** (study duration 3 months) *VOMITING>1 DAY:* *Univariate analysis: All results OR; P value* Age > 65 years – 1.84; 0.30 Male gender – 0.91; 1.00 Underlying cardiovascular disorders – 2.7; 0.13 Underlying gastrointestinal disorders – 0.34; 0.31 Underlying autoimmune disease – 0.81; 1.00 Underlying renal disorders – 0.95; 1.00 Renal transplant – 1.31; 0.75 Underlying malignancy – P value 0.18; OR not reported Underlying trauma – 1.14; 1.00 Immunosuppressive therapy – 0.92; 1.00 Community acquired norovirus – 2.36; 0.19 *Multivariate analysis: All results OR (95% CI)* Underlying cardiovascular disorders – 7.17(1.59-51.2) Community acquired norovirus – 5.54(1.04-42.8) *DIARRHEA>2 DAYS:* *Univariate analysis: All results OR; P value* Age > 65 years – 3.58; 0.01 Male gender – 2.15; 0.12 Underlying cardiovascular disorders – 2.80; 0.15 Underlying gastrointestinal disorders – 0.22; 0.03 Underlying autoimmune disease – 4.67; 0.24 Underlying renal disorders – 1.77; 0.39	to be norovirus-positive if samples from at least two patients from the same ward were positive by norovirus-specific RT-PCR. Power and sample size not reported	

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Renal transplant – 1.71; 0.54 Underlying malignancy – 0.07; 0.01 Underlying trauma – 0.27; 0.053 Immunosuppressive therapy – 1.29; 0.79 Community acquired norovirus – 3.09; 0.06 *Multivariate analysis: All results OR (95% CI)* Age > 65 years – 11.56(1.89-224.00) Underlying malignancy – 0.02(0.00-0.19) Underlying trauma – 0.05(0.00-0.55) *POTASSIUM DECREASE >20%:* *Univariate analysis: All results OR; P value* Age > 65 years – 0.94; 1.00 Male gender – 0.90; 1.00 Underlying cardiovascular disorders – 5.17; 0.06 Underlying gastrointestinal disorders – 0.46; 0.67 Underlying autoimmune disease – 0.98; 1.00 Underlying renal disorders – 1.74; 0.71 Renal transplant – 3.91; 0.09 Underlying malignancy – P value 0.58; OR not reported Underlying trauma – P value 0.19; OR not reported Immunosuppressive therapy – 2.83; 0.25 Community acquired norovirus – 0.48; 0.68 *Multivariate analysis: All results OR (95% CI)* Underlying cardiovascular disorders – 17.10(2.17-403.00) Renal transplant – 13.02(1.63-281.00) *CREATININE INCREASE >10%:* *Univariate analysis: All results OR; P value* Age > 65 years – 1.04; 1.00 Male gender – 1.79; 0.24 Underlying cardiovascular disorders – 0.60; 0.42 Underlying gastrointestinal disorders – 1.93; 0.36 Underlying autoimmune disease – 4.50; 0.12 Underlying renal disorders – 1.44; 0.59 Renal transplant – 3.53; 0.07 Underlying malignancy – 0.93; 1.00 Underlying trauma – 0.07; <0.01		

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Immunosuppressive therapy – 5.74; <0.01 Community acquired norovirus – 5.07; 0.01 *Multivariate analysis: All results OR (95% CI)* Immunosuppressive therapy – 5.67(1.78-20.1) *C REACTIVE PROTEIN >58 MG:* *Univariate analysis: All results OR; P value* Age > 65 years – 0.81; 0.79 Male gender – 2.63; 0.11 Underlying cardiovascular disorders – 0.32; 0.06 Underlying gastrointestinal disorders – 1.54; 0.55 Underlying autoimmune disease – 3.71; 0.14 Underlying renal disorders – 2.13; 0.19 Renal transplant – 1.33; 0.76 Underlying malignancy – 2.96; 0.25 Underlying trauma – 0.23; 0.35 Immunosuppressive therapy – 3.38; 0.06 Community acquired norovirus – 2.30; 0.23 *Multivariate analysis: All results OR (95% CI)* Underlying malignancy – 9.07(1.17-193.00) Immunosuppressive therapy – 5.37(1.62-19.9)		
Adamson, WE; 2007 [109] 3,4	Descriptive study	To determine if the increased number of norovirus cases in Scotland during early 2006 was due to the emergence of a new norovirus variant	A representative number of norovirus cases from outbreaks in Scotland were analyzed at the West of Scotland Specialist Virology Centre laboratory 149 samples were GII genotype 4	**norovirus GII genotype 4 variants** (study duration 19 months) 1/2005-2/2006 vs 3/2006-8/2006: 69/84 (82%) GII-4 v3 vs 61/77 (79%) GII-4 v4		
Gallimore, CI; 2004 [110] 3,4	Descriptive study	To determine if norovirus was present during a 2002 outbreak in a pediatric tertiary hospital and determine the strains in symptomatic vs. asymptomatic patients.	Staff and patients in a pediatric tertiary hospital during a norovirus outbreak in June-July 2002. 9 symptomatic (6 patients and 3 staff members). 99 asymptomatic (12 patients and 87 staff members). Point prevalence survey.	**norovirus strains** Symptomatic vs. asymptomatic patients and staff– 9/9 (100%) GII-3a vs 27/99 (27%) GII-4.	Asymptomatic excretion of norovirus can occur. However, in this case, the strain did not cause nosocomial infection and may suggest either low level excretion or commensal carriage	673_IL

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Environmental characteristics

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
MMWR; 2008 [79]	Prospective controlled study. 1,3,4	To investigate an outbreak at an elementary school.	Students and staff at an elementary school in Washington DC in February 2007. Students – median age 8 years (range 3-12 years); 55% female. Staff – median age 41 years (range 13-66 years); 92% female. 266 – 207 students and 59 staff.	**Symptomatic norovirus infection** *Bivariate analysis: All results RR (95% CI); p value* Being a student – 0.94 (0.66-1.34); 0.76 Being female – 1.13 (0.82-1.56); 0.52 Having an ill contact – 1.76 (1.16-2.67); 0.01 Classroom J (first) – 1.94 (1.34-2.80); 0.02 Library use: 0.94 (0.58-1.52); 0.87 Library computer use: 1.08 (0.41-2.84); 1.00 **Interventions implemented** District of Columbia Department of Health recommended -more thorough handwashing - cleaning all shared environmental surfaces with a diluted (1:50 concentration) household bleach -cleaning computer equipment (i.e., mice and keyboards) -excluding ill persons from school for at least 72 hours after resolution of illness	A case of gastrointestinal illness was defined as illness in a student or staff member with nausea, vomiting, or diarrhea, who was at the school February 2-18, 2007. Power and sample size not reported.	017_IL
MMWR, 2007 [80]	Prospective controlled study 1,2,3,4	To investigate source of norovirus gastroenteritis outbreak at a family reunion.	Family reunion in Grant county, West Virginia, October 2006. 39 included in cohort study: 19 are cases and 20 are controls.	*Risk factor – unadjusted RR (95% CI); p value* Food consumed Scalloped potatoes – RR 2.80 (1.14-6.86); 0.01 Ham – RR 2.19 (0.63-7.60); 0.24 Chicken – RR 2.16 (0.97-4.81); 0.04 Chocolate cheese ball – RR 2.14 (1.26-3.65); 0.04 – only eaten by 7 individuals Onion dip – RR 1.65 (0.88-3.07): 0.23 Meatballs – RR 1.54 (0.79-3.03); 0.21 Green beans – RR 1.44 (0.76-2.73); 0.27 Cream cheese roll-ups – RR 1.43 (0.77-2.65); 0.29 Cheese ball – RR 1.43 (0.72-2.83); 0.66 Chip dip – RR 1.33 (0.69-2.54); 0.42 Buterscotch cake – RR 1.24 (0.61-2.52); 0.71 Cole slaw – RR 1.17 (0.60-2.30); 0.65 Deviled eggs – RR 1.11 (0.59-2.10); 0.75 Pasta salad – RR 1.04 (0.57-1.89); 0.90 Broccoli salad – RR 1.04 (0.52-2.07); 0.92 Chocolate cake – RR 1.03 (0.36-2.94); 1.00 Pinch-me cake – RR 1.03 (0.36-2.92); 1.00	12/13 stool specimens tested positive for norovirus genogroup II by RT-PCR. Power and sample size not reported.	3864_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Sugar cookies – RR 1.00 (0.42-2.39); 1.00 Coffee – RR 1.00 (0.46-2.19); 1.00 Soda – RR 0.90 (0.47-1.70); 0.74 Spicy rice casserole – RR 0.89 (0.39-1.77); 1.00 Parsley potatoes – RR 0.83 (0.39-1.77); 0.63 Potato casserole – RR 0.74 (0.37-1.50); 0.40 Raw vegetables – RR 0.74 (0.34-1.62); 0.43 Pecan cake – RR 0.70 (0.27-1.83); 0.69 Coffee creamer – RR 0.69 (0.13-3.54); 1.00 Mandarin orange cake – RR 0.63 (0.19-2.04); 0.66 Macaroni salad – RR 0.53 (0.22-1.28); 0.11 Turkey – RR 0.40 (0.0-2.39); 0.35 Baked beans – RR 0.38 (0.11-1.34); 0.12 Fruit cocktail – N/A Other risk factors Contact with ill person – RR 2.27 (1.01-5.07); 0.03 At home A prereunion gathering – RR 1.57 (0.87-2.81); 0.24 At home B prereunion gathering – RR 0.92 (0.46-1.81); 0.80		
Costas L, 2007 [81] 1,2,3,4,6,7	Prospective controlled study	To investigate a norovirus outbreak among hospital staff.	Healthcare workers at a hospital in Barcelona, Spain. 31/38 cases available for interview. 31 unmatched healthcare workers selected as controls	*Risk factor – OR (95% CI); p value* Rice salad with cocktail sauce – OR 4.11 (1.14-14.72); 0.03 Waterborne source – OR 0.675 (0.237-1.924) September 12th (when rice salad with cocktail sauce served) – OR 3.37; p=0.07	norovirus identified from stool samples – testing used not defined. Power and sample size not reported.	IL_6577
Lopman, BA; 2005 [82] 1,2,3,4,6,7	Prospective controlled study	To evaluate institutional factors related to gastroenteritis outbreaks in hospitals.	Outbreaks occurring in 3 hospital administrations (NHS trusts) in England. These trusts include 4 major acute hospitals and 11 community hospitals, which comprise 171 inpatient functional care units.	**Outbreak rates** (study duration 52 weeks) *Overall* 227 outbreaks in 113 units – 1.33 outbreaks/unit-year *Hospital Type* Acute center vs. community – 1.5 (1.3-1.8) vs. 0.9 (0.7-1.2); 0.0002 *All results are rate (95% CI)* Unit specialty; p<0.0001 Other types – 1.0 (0.8-1.3) General medical – 2.5 (1.9-3.2) Geriatric – 1.9 (1.4-2.6) Surgical – 1.2 (0.8-1.8) Orthopaedics – 1.9 (1.2-2.9)	Power and sample size not done. noroviruses were detected in 65% of all outbreaks where specimens were available.	511_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Mental health – 0.7 (0.3-1.5) No previous outbreak vs. previous outbreak – 0.9 (0.8-1.1) vs. 2.4 (2.0-2.9); p<0.0001 Month following outbreak vs. rest of follow-up period – 3.3 (2.4-4.6) vs. 1.3 (1.1-1.5); p<0.0001 **Outbreak risk factors** (study duration 52 weeks) *All results are HR (95% CI); p value* *Univariate analysis* Number of beds in unit (per additional 10 beds) – 1.50 (1.25-1.81); <0.0001 Average length of stay (per additional week) – 0.96 (0.92-1.00); 0.04 Unit in acute centre vs. community hospital – 1.80 (1.31-2.49); 0.0002 Previous outbreak – 2.00 (1.50-2.67); 0.0001 Month following outbreak vs. other time – 2.05 (1.41-2.98); <0.0001 General medicine vs. geriatric vs. orthopaedics – 2.48 (1.76-3.49) vs. 1.94 (1.32-2.85) vs.1.90 (95% CI 1.17-3.08); <0.0001 *Multivariable analysis* Number of beds in unit (per additional 10 beds) – 1.22 (0.96-1.55); 0.10 Average length of stay (per additional week) – 0.89 (0.80-0.99); 0.041 Previous outbreak – 0.88 (0.62-1.25); 0.47 Hospital ward type – p=0.006 General medicine – 1.71 (1.11-2.63) Geriatric – 2.55 (1.52-4.25) Surgical – 0.79 (0.48-1.29) Orthopaedics – 1.43 (0.82-2.49) Mental Health – 2.30 (0.36-14.9)		
Evans, M; 2002 [83]	Prospective controlled study 1,3,4	To describe an outbreak of norovirus gastroenteritis following vomiting by an attendee at a concert	Primary school children attending a concert at a metropolitan concert hall. Demographic characteristics not provided. 1229 children from 15 primary schools	**Description of outbreak** Following the vomiting, cleaning was done with an ordinary vacuum cleaner the following day. No hypochlorite based product was used. The index case was seated in tier 13. **Auditorium seating as a risk factor for symptomatic norovirus infection** (follow-up not clearly reported) Children seated in tiers 9-13 vs. children seated elsewhere – 199/387 vs. 58/797; RR(95% CI) = 7.1(5.4-9.2)	A case was defined as a person who had attended the concert hall and had developed vomiting and/or diarrhea within 24-72 hrs of the visit. NLV was confirmed in fecal samples using RT-PCR	897_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
					Power and sample size not reported	
Lachlan, M; 2002 [84]	Prospective controlled study 1,3,4	To describe an outbreak of norovirus gastroenteritis and lessons learned.	Persons with a connection to a hotel linked to the outbreak or ill contacts of people who were unwell and had a connection with the hotel. 112 potentially exposed, 79 cases	**Symptomatic norovirus infection - Food specific attack rates** Beef sandwich – 1.35(1.08-1.67) Cheese sandwich – 1.33(1.06-1.67) Egg sandwich – 1.49(1.18-1.88) Ham sandwich – 1.39(1.14-1.69) Lamb sandwich – 1.46(1.28-1.66) Tuna sandwich – 1.27(1.02-1.60) Sausage sandwich – 1.01(0.77-1.32) Soup – 1.28(1.00-1.64), P<0.05 Parsley garnish – 0.71(0.18-2.83) Tomato garnish – 1.15(0.82-1.61) Hot chocolate – 1.45(1.28-1.65) Tea – 1.04(0.81-1.33) Coffee – 1.36(1.10-1.67) Ice – 1.25(1.00-1.57) Other drinks – 1.52(1.12-2.05) After applying a critical P value (<0.003) with Bonferroni correction, only egg sandwich and drinks from the bar (other drinks) were found to be statistically significant. **Lessons from the outbreak** 1. Outbreak control team meetings that are formally minuted with action points being highlighted on a flipchart 2. Good liaison with laboratory services to agree on clear pathways for the delivery and analysis of samples that became available during normal working hours or were processed over the weekend. 3. Rapid virological confirmation to reassure the public that appropriate control measures were in place and handle the media interest. 4. Joint visit to the outbreak premises by protective services and public health representatives to facilitate clear and open communication between all parties and secure a voluntary agreement from the hotel owner to cease all food preparation. 5. Food handlers should remain off work from onset of illness	A case was defined as someone with symptoms of diarrhea, vomiting or abdominal pain or any combination of these more than once in 24 hours and a connection with the hotel where the outbreak started. norovirus was confirmed by EM	942_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				until 48 hours after diarrhea and vomiting have ceased 6. All those involved in carrying out interviews and analyzing data working from one site and through one computer network to improve the efficiency of working through contact lists, allowing rapid assessment of the epidemic curve and symptom pattern and the results of RR calculations of the foodstuffs.		
Love, S; 2002 [85]	Prospective controlled study 1,3,4	To describe an outbreak of gastroenteritis and procedures implemented to control it.	Guests and employees of a Virginia hotel. There were 3 groups: Group A: Attendees of a business conference (n=110); median age of cases (n=34) 52 years; 59% cases female Group B: Physicians and their families (n=95); median age of cases (n=11) 31 years; 73% cases female Group C: Retired persons (n=310); median age of cases (n=15) 71 years; 60% cases female 60 cases	**Risk factors for symptomatic norovirus infection** (follow-up unclear) Attending reception: RR(95% CI) – 2.1(1.1-4.0) Eating coleslaw at picnic: RR(95% CI) – 3.6(1.0-13.6) **Interventions** Infection control measures instituted: 1. Employees who were ill in the past two weeks or had an ill child in diapers were excluded from work for 1 day. Employees who were currently ill with vomiting or diarrhea were told not to work for 1 day after resolution of symptoms 2. All employees were instructed about hygiene and hand washing 5 days after initial cases 3. The facility was closed for 8 h to permit thorough cleaning of all food service areas and guest rooms. New guests were not accepted until all guestrooms, bathrooms, and common rooms were thoroughly cleaned 7 days after initial cases 4. All cold food requiring hand-preparation was excluded from the menu. No open bowls of food such as chips or popcorn were served 7 days after initial cases **Response to intervention** (at two week follow-up) The hotel reported no further ill guests or employees	A case was defined as vomiting or diarrhea in a hotel attendee or staff. norovirus confirmed by RT-PCR Power and sample size not reported.	915_IL
Anderson, AD; 2001 [86]	Prospective controlled study 1,3,4	To identify the source of a gastroenteritis outbreak at a car dealership.	Multistate investigation involving catered meals given to car dealerships spanning 13 states. Median age 37 years (range 3-89 years). 753 banquet attendees. 333 met case definition.	**Symptomatic norovirus infection** *Univariate analysis* *All results are RR (95% CI)* Any salad – 3.8 (2.5-5.6) Rotini pasta salad – 3.0 (2.4-3.7) Potato salad –1.6 (1.3-1.9) Bow-tie pasta salad –1.5 (1.3-1.8) Vegetable salad – 1.7 (1.4-1.9) Condiments – 1.4 (1.2-1.7) Dips – 1.3 (1.1-1.5) Cheeses – 1.3 (1.1-1.5)	Case was a person who attended a "banquet dinner" at one of the dealerships and developed vomiting or diarrhea (≥3 loose stools within 24 hours). 2/15 caterers had elevated norovirus immunoglobulins. 16 specimens that were	1003_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Snacks –1.0 (0.8-1.1) Meats – 1.1 (0.7-2.0) Desserts – 1.2 (1.0-1.4) Breads – 1.4 (1.1-1.9)	sequenced showed a common outbreak strain. Power and sample size not reported.	
Cunney RJ, 2000 [87]	Prospective controlled study 1,2,3,4	To investigate a hospital NLV outbreak.	Hospital outbreak N= 95 persons: 47 patients and 48 staff.	**Infection control practices** -Affected patients were cohorted -Admissions to and transfers from the geriatric ward were stopped -70% alcohol hand rub supplemented routine hand washing -Affected staff sent home until 48 hours after symptoms subsided -Decontamination procedures changed from standard phenolic solution to 2% hypochlorite solution **Food source** Drinking water from the hospital water supply: 16 symptomatic and 6 nonsymptomatic (p=0.1)	12 (13%) containing SRSV were solid phase immune electron microscopy (SPIEM) positive for NLV 25 (27%) sampes contained small round featureless virus (SRFV) identified by direct EM and were negative on SPIEM Power and sample size not reported.	1197_IL
Marks, P; 2000 [88]	Prospective controlled study 1,3,4	To describe an outbreak of gastroenteritis following a meal in a hotel during which one of the diners vomited	Diners attending an evening dinner at a large hotel in the UK. Demographic characteristics not reported 126; 52 cases	**Symptoms** (% of ill subjects reporting symptoms) Nausea – 58 Diarrhea and vomiting – 42 Vomiting without diarrhea – 21 Diarrhea without vomiting – 21 Abdominal pain – 40 Fever – 38 **Time of onset of symptoms** 83% of those who became ill did so between 13 and 48 hours after the meal and 59% between 25 and 48 hours. Of the 14 people who reported precise times for the onset of their illness, the mean time from exposure to onset of symptoms was 33 hours and the median 35 hours. **Symptomatic norovirus infection - Attack rate in %** (at each of the tables) The lady who vomited was seated at table 2	NLV was confirmed using EM and RT-PCR 83 of 126 guests (66%) returned completed questionnaires Power and sample size not reported	1122_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Table 1 – 71 Table 2 – 91 Table 3 – 56 Table 4 – 50 Table 5 – 40 Table 6 – 25 There was a signifiant relationship between distance from the vomiter and the risk of becoming ill (P<0.01) with no significant deviation from that trend (P=0.68)		
Lo SV, 1994 [89]	Prospective controlled study 1,2,3,4	To investigate a SRSV gastroenteritis outbeak in 4 hospitals served by one central kitchen.	4 hospitals - 1 acute district general hospital and 3 smaller peripheral hospitals with long-stay and rehabilitation patients 81 patients and 114 staff in 4 hospitals Buffet lunch cohort study: N=41 completed quesionnaire Patient case-control study: N= 23/24 cases and 35/36 controls completed questionnaires. Staff case-control study: N= 22/27 cases and 49/54 controls completed questionnaire.	***Buffet lunch study*** *Food - RR (95% CI)* Ham and tomato – RR 1.0 (0.6-1.7) Cheese and pickle – RR 0.8 (0.4-1.9) Turkey salad – RR 2.4 (1.4-4.1) Tuna – RR 1.2 (0.7-2.0) Sausage roll – RR 1.1 (0.6-1.8) Cheese and pineapple – RR 1.0 (0.6-1.8) Sausage mushroom – RR 1.6 (0.-2.9) Fresh fruit – RR 0.8 (0.3-2.3) Meringue – RR 0.9 (0.5-1.4) Orange juice – 1.0 (0.48-2.0) Wine – 1.0 (0.51-2.1) ***Patient case-control study*** ***Risk factor*** *Food - OR (95% CI)* March 7th Beel cobble – OR 0 (0-1.7) Beef crumble – OR 1.6 (0-11.5) Mince – OR 0.7 (0.1-3.9) Sausage and onion – OR 0.3 (0.1-1.3) Cheese pie – OR 0.2 (0-1.6) Lamb salad – OR 0.4 (0.05-2.4) Tuna salad – OR 6.6 (1.0-71.6); p<0.05 Any salad – OR 1.8 (0.5-6.8) Corn beef sandwich – OR 1.6 (0.1-23) Any sandwich OR 4.6 (0.6-39) March 8th Cod – OR 1 (0.3-3.5)	A cohort study of staff who attended a retirement buffet lunch, a patient case-control study based at the district general hospital, and a nursing staff case-control study at the district general hospital were performed. Fecal samples underwent bacteriological examination, routine EM, and immuno-EM. Power and sample size not reported.	1540_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Chicken curry – OR 0.8 (0.2-2.8) Flaked fish – OR 0.7 (0.01-15) Lamb casserole – OR 0.9 (0.2-3.9) Mushroom pizza – OR 0.3 (0.01-3.9) Savoury lamb – OR 1 (0.1-9.7) Beef salad – OR 3.2 (0.2-97) Chicken salad – OR 2.5 (0.3-31) Any salad – OR 4.7 (0.9-30); p <0.05 Salmon sandwich – OR 0.2 (0-2.2) Any sandwich – OR 0.4 (0.04-2.3) March 9th Pork casserole - OR 1.5 (0.4-5.7) Chicken pie – OR 0.3 (0.1-1.5) Minced chicken – OR 0.2 (0-1.6) Cawl – OR 1.6 (0.2-13) Fishcake – OR 0.5 (0.1-2.5) Egg salad – OR 0.3 (0-3.9) Cheese salad – OR 2.2 (0.2-4.8) Any salad – OR 1.1 (0.2-4.8) Ham sandwich – OR 0.5 (0.01-6.7) Any sandwich – OR 1 (0.1-9.7) *Staff case-control study* No statistically significant associations found. 1 food handler who prepared the salad had a child who was ill 2 days prior and the food handler became ill the day following food preparation. *Infection control practices* Closure of the central kitchen Disposal of all remaining food Discontinuing all hospital admissions and ward transfers Daily ward cleaning with 2% hypochlorite Emphasis on hand washing		
Patterson T, 1993 [90]	Prospective controlled study 1,2,3,4,67	To investigate an SRSV gastroenteritis outbreak at a conference.	Outbreak at an international AIDS conference. April 23, 1990. N=226/283 (80%) delegates replied to the questionnaire.	*Risk factor – Unadjusted RR (95% CI); p value – the foods prepared by potential source (foodhandler) italicized* Wednesday, April 18, 1990 Canapes – RR 1.21 (0.80-1.84); 0.44 *Celery – RR 1.16 (0.76-1.79); 0.59* Sausage – RR 1.2 (1.01-2.30); 0.07	SRSV visualized on EM in 2/5 samples. A member of the catering staff attended a children's party April 15th where there	1625_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Thursday, April 19, 1990 buffet Chicken drumsticks – RR 1.66 (1.08-2.55); 0.03 Green salad – RR 1.42 (0.87-2.31); 0.20 Tomato and chive salad – RR 0.79 (0.51-1.23); 0.36 *Ham – RR 2.18 (1.38-3.44); <0.001* Vegetable pie – RR 0.76 (0.46-1.25); 0.34 Coleslaw – RR 0.84 (0.52-1.37); 0.59 *Coleslaw and rice – RR 1.27 (0.80-2.02); 0.38* Thursday, April 19, 1990 civic reception *Melon – RR 1.19 (0.78-1.82); 0.51* *Sole – RR 1.12 (0.73-1.70); 0.70* *Lamb – RR 1.23 (0.80-1.89); 0.42* Vegetables – RR 1.31 (0.85-2.01); 0.28 *Chocolate roulade – RR 0.97 (0.64-1.48) 0.98* Cheese – RR 1.04 (0.67-1.63) Friday, April 20, 1990 buffet *Coronation chicken – RR 3.51 (2.23-5.52); <0.0001* Green salad – RR 1.78 (1.12-2.84); 0.018 Vegetable quiche – RR 1.07 (0.70-1.63); 0.88 *Potato salad – RR 1.45 (0.95-2.21); 0.11* Curried rice – RR 1.43 (0.93-2.19); 0.13 Tomato and chive salad – RR 1.02 (0.73-1.43); 0.99 Chicken and ham pie – RR 1.25 (0.80-1.96); 0.43 Coleslaw – RR 1.13 (0.48-2.66); 0.76 Highest attack rates for coronation chicken and ham prepared by suspected source (foodhandler). Adjusted analyses found only cornocation chicken was associated with illness: *Coronation chicken – RR 3 (1.9-4.8); <0.0001*	was a child with gastrointestinal illness.April 17th the staff member had vomiting and diarrhea, came to work, and was sent home. She returned on April 19th asymptomatic and helped prepare meals for the conference. Power and sample size not reported.	
Alexander WJ, 1986 [91]	Prospective controlled study 1,2,3,4	To investigate a norovirus outbreak at a college campus.	College campus in Jefferson County, Alabama in November 1981 N=92	**Patient-control analysis of foods eaten and development of illness (Meal: Item – No. of discardant pairs (patients vs. controls); p value** Noon, Nov 15th: fried chicken – 2 vs. 4; NS Noon, Nov 16th: chicken/dumplings – 2 vs. 8; NS Noon, Nov 16th: corn – 6 vs. 3; NS Noon, Nov 16th: BBQ beef – 3 vs. 0; NS Noon, Nov 16th: lettuce – 11 vs. 2; 0.02<p<0.05 Evening, Nov 16th: lettuce - 7 vs. 1; NS Noon, Nov 17th: mashed potatoes - 4 vs. 1; NS	Serologic evidence of Norwalk virus infection. Power and sample size not reported.	1935_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Noon, Nov 17th: lettuce – 8 vs. 4; NS Evening, Nov 17th: lettuce – 9 vs. 2; NS		
de Wit, M; 2007 [92]	Retrospective controlled study 1,3,4,6,7	To describe an outbreak of gastroenteritis caused by a baker infected with norovirus who continued to work in his bakery having washed his hands and disinfected countertops.	Staff of a department in the Netherlands who attended a reception where the outbreak was reported. Median age 39 years; 45% female. 800-900 employees; 231 reported diarrhea or vomiting	**Symptoms** Diarrhea and vomiting – 76% Diarrhea only – 12% Vomiting only – 12% Median time to onset of symptoms – 31 hours **Symptomatic norovirus infection** *All results OR(95% CI)* *Univariate analysis* Coffee – 0.3(0.1-0.9) Tea – 0.7(0.2-2.0) Milk – 1.3(0.9-1.9) Butter milk – 1.1(0.7-1.8) Orange juice – 1.2(0.8-1.6) Champagne – 1.6(1.1-2.3) Cheese – 1.5(1.1-2.2) Brie – 1.1(0.7-1.8) Ham – 1.5(1.0-2.2) Beef – 1.2(0.8-1.9) Tuna salad – 1.6(1.1-2.4) Salmon salad – 2.2(1.0-4.5) Egg salad – 1.4(0.9-2.1) Raisin roll – 0.9(0.6-1.3) Increasing number of rolls – 2.0(1.6-2.4) *Multivariate analysis* Coffee – 0.4(0.1-0.8) Raisin roll – 0.5(0.3-0.8) Number of rolls – 2.0(1.5-2.5) **Intervention implemented** Sick food handlers excluded from work for 48hrs and reinforcement of hygiene measures	A case was defined as a member of the departmental staff who attended the reception and reported diarrhea (3 or more loose stools a day) or vomiting in the 72 hours following the reception. A control was defined as a member of the department staff attending the reception without diarrhea or vomiting in the 72 hours following the reception. norovirus infection was confirmed using RT-PCR The estimated response rate for questionnaires among cases was nearly 100%. The estimated response rate among controls was 40-50% Power and sample size not reported	4084_RA
MMWR; 2007 [93]	Retrospective controlled study	To identify the source of a restaurant outbreak.	Subjects who ate at a Michigan restaurant in January/February 2006 during a norovirus outbreak. Cases – median age	**Symptomatic norovirus infection** *All results in OR (95% CI)* Antipasti platter – 2.96 (1.08-8.14) Garlic mashed potatoes – 4.05 (1.37-11.99)	Case for the descriptive study was a patron who had eaten food at the restaurant between January 19-	046_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
	1,2,3,4		40 years (range 1-92 years); 58.5% female. 364 patrons met case definition for the descriptive study. The case control study included 45 cases and 91 controls.	Several food service workers reported to work ill including one line cook who vomited at the work station. **Interventions:** -Food prepared during January 27-30th was discarded -Ill employees were excluded from work for at least 72 hours after symptoms had subsided. -Facility was cleaned extensively.	February 3, 2006 and developed vomiting or diarrhea within 10-50 hours. A case for the employee was an employee with vomiting or diarrhea during that time period. For the analytic study, case patron was someone who had eaten at the restaurant from January 28-29 and developed vomiting or diarrhea 10-50 hours after eating. A control was a patron with the same exposure but no gastrointestinal illness. Power and sample size not reported.	
Rizzo C, 2007 [94] 1,2,3,4,6,7	Retrospective controlled study	To investigate risk factors for a norovirus outbreak in a resort.	Resort in Puglia region of Italy during a three week period in July 2005. 400 guests during outbreak 150 guests available at the start of investigation and 41 (27.3%) cases identified. N= 41 cases and 41 matched controls.	*Risk factor – cases # (%) vs. controls # (%): OR (95% CI); p value* *Only variables included in conditional logistic model have multivariate OR listed* Ice – 21 (51%) vs. 12 (29%): univariate OR 4.1 (0.9-7.1); 0.04 multivariate OR 16.4 (1.8-250.9); 0.04 Eggs – 2 (5%) vs. 8 (19%): univariate OR 2.3 (0.1-1.7); 0.12 Grilled sausage – 21 (51%) vs. 25 (61%): univariate OR 0.7 (0.2-1.7); 0.17 Ham – 1 (2%) vs. 5 (12%): univariate OR 2.8 (0.1-1.7); 0.09 Grilled meat – 11 (27%) vs. 15 (37%): univariate OR 3.5 (0.1-1.1); 0.06 Snacks – 20 (49%) vs. 19 (46%): univariate OR 0.1 (0.4-2.8); 0.15 Raw mussels – 22 (54%) vs. 13 (31%): univariate OR 3.9 (0.9-6.8); 0.04 multivariate OR 25.5 (1.5-442.9); =0.03	18/20 (90%) fecal samples were positive for norovirus by RT-PCR 3 samples confirmed GGII norovirus. One matched control was selected for each case assuming 25% exposed controls, 80% power to detect OR 4.1, alpha error of 5%.	3_IL
Schmid, D; 2007 [95]	Retrospective controlled study	To identify the source of a norovirus outbreak at a telephone	Cases were employees or external persons who ate lunch at the canteen of the telephone	**Symptomatic norovirus infection - Attack rate** 182/325 (56%)	Gastroenteritis was defined as someone with symptoms of diarrhea (≥3 stools in 24	031_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
	1,3,4,6,7	company.	company in Austria and developed gastroenteritis. 325	**Symptomatic norovirus infection** *Demographic characteristics* Age – cases 38.4 years (SD 11.33) vs controls 34.5 years (SD 12.7); p=0.004 Female – RR 1.23 (95% CI 1.02-1.5); p=0.054 *Working days* *Univariate analysis: All results RR (95% CI); p value* Monday – 0.06 (0.02-0.2) Tuesday – N/A Wednesday – 18.82 (11.82-29.96); <0.001 Thursday – 2.14 (1.65-2.79); <0.001 *Multivariate analysis: All results RR (95% CI)* Monday – 0.08 (0.02-0.25) Tuesday – N/A Wednesday – 3.05 (2.18-4.28) Thursday – 1.89 (1.27-2.81) *Day-by-day food specific analysis* *Univariate analysis: All results RR (95% CI)* Monday salad – N/A Monday potatoes – 0.94 (0.09-10.17) Tuesday potatoes – 0.66 (0.39-1.14) Tuesday compote – 1.40 (0.77-2.54) Tuesday salad – 2.51 (0.61-10.31) Wednesday rice with beans –1.39 (1.04-1.85) Wednesday salad – 3.44 (1.24-9.59) Thursday semolina dumpling soup – 2.94 (1.57-5.52) Thursday roast pork –1.72 (0.96-3.07) Thur sday potatoes –1.37 (0.81-2.32) Thursday sauerkraut –1.86 (1.06-3.26) Thursday salad – 1.04 (0.64-1.7) *Multivariate analysis: All results RR (95% CI); p value* Monday salad – N/A Monday potatoes – 0.78 (0.05-13.67); 0.87 Tuesday potatoes – 0.80 (0.37-1.71); 0.57 Tuesday compote – 1.11 (0.50-2.43); 0.80 Tuesday salad – 2.19 (0.73-6.52); 0.16	hours) and/or projectile vomiting after January 15, 2006. Power and sample size not reported. Most likely source of outbreak was a kitchen assistant who prepared the salad.	

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Wednesday rice with beans –1.24 (0.96-1.61); 0.1 Wednesday salad – 2.82 (1.00-7.94); 0.05 Thursday semolina dumpling soup – 2.53 (1.32-4.83); 0.01 Thursday roast pork – 1.46 (0.55-3.88); 0.45 Thursday potatoes – 0.51 (0.29-0.92); 0.02 Thursday: sauerkraut – 1.91 (0.78-4.68); 0.16 Thursday salad – 1.77 (1.17-2.69); 0.01 **Interventions implemented** Closure of kitchen		
Payne, J; 2006 [207]	Retrospective controlled study 1,3,4	To summarize an outbreak investigation into three norovirus outbreaks and a cluster of community cases. The primary outcome was identifying the source of norovirus illness.	Cases of norovirus outbreak associated with a national submarine sandwich franchise restaurant in Michigan. The 3 outbreaks were at a school staff luncheon, publishing company staff luncheon and a social service organization luncheon. Community cases were also reported. 170 cases	**Symptomatic norovirus infection** School staff luncheon – 23/29; 80% Publishing company staff luncheon – 55/95; 58% Social service organization luncheon – 9/18; 50% Community cases – 25/28; 90% **Predominant symptoms** School staff luncheon – diarrhea (87%) and vomiting (74%) Publishing company staff luncheon – diarrhea (94%) and vomiting (83%) Social service organization luncheon – diarrhea (78%) and vomiting (78%) Community cases – diarrhea (92%) and vomiting (80%) **Source of symptomatic norovirus infection** School staff luncheon – 22/23 cases reported eating lettuce; no specific food item was significantly associated with the illness Publishing company staff luncheon – lettuce – 11.24(1.30-95.2); jalapeno peppers – 3.45(1.04-11.40); onions – 3.09(1.27-7.80) Social service organization luncheon – no specific food item was significantly associated with the illness Community cases – no specific food item was significantly associated with the illness A food handler employed by the restaurant was identified as the source of illness. He had returned to work within a few hours of having symptoms of gastrointestinal illness while he was still excreting norovirus in the stools and lettuce was sliced each morning by him.	A case was defined as illness in a person who ate the suspect meal during the outbreak and became ill 8-56 hrs later with vomiting or diarrhea and two of the following: documented fever, abdominal cramps or nausea Cases were identified when the county health department was notified of the outbreak. Power and sample size not reported	326_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Fretz, R; 2005 [77]	Retrospective controlled study 1,2,3,6,7	To identify risk factors for sporadic norovirus infections.	All patients of general practitioners in German-speaking parts of Switzerland. Cases (mean age 32.7 years; median age 34 years; range 1.1-69.3 years) were subjects who resided in the study area who had an episode of diarrhea and/or vomiting, consulted a practitioner in the study area, had stool samples negative for *Campylobacter, Shigella, Salmonella*, and other gastroenteric pathogens, had stool samples positive for norovirus genogroup I or II. Cases excluded subjects <6 months or >75 years, patients with possible nosocomial disease, and patients who were part of a norovirus outbreak. Controls (mean age 33.2 years; median age 37.1 years; range 1.3-70.1 years) were identified through each patient, were the same sex and age group (defined as 5 year intervals over 5-20 years and 10 year intervals over 20-60 years), lived within 10 km of the case, and had not consulted a general practitioner for gastrointestinal illness or symptoms in the month prior to the questionnaire. 126 cases met study inclusion criteria. 73 matched case-control pairs.	**Symptoms** (study duration 2 years) Diarrhea – 124/126 (98.4%). Vomiting – 84/126 (66.7%). Nausea – 85/126 (67.5%) Fever – 57/126 (45.2%) Headache – 45/126 (35.7%) Abdominal cramps – 87 (69%) Other – 46 (36.5%) **Mean duration of symptomatic illness** 7.3 days (SD, 6.2 days; range 0.25-28 days) **Symptomatic norovirus infection** *Multivariable analysis* *Consumption of food and beverages OR (95% CI); p value* Mineral water – 1.00 (0.46-2.16); 1.00 Salad – 1.25 (0.34-2.65); 0.74 Raw berries – 0.75 (0.17-3.35); 0.71 Tap water – 1.33 (0.56-3.16); 0.51 Sweet beverages – 1.06 (0.55-2.05); 0.87 *Personal contacts OR (95% CI); p value* Household with children ≤2 years) – 1.00 (0.29-3.45); 1.00 Household with children ≤ 5 years – 0.75 (0.26-2.16); 0.59 Household with children ≤ 10 years – 0.75 (0.26-2.16): 0.59 Household with children ≤ 65 years – 0.75 (0.17-3.35); 0.71 Household with children > 1 person – 1.50 (0.53-4.21); 0.44 Household with children > 2 person – 0.77 (0.34-1.75); 0.53 Household with children > 3 person – 0.71 (0.32-1.61); 0.53 Household with children > 4 person – 1.14 (0.41-3.15); 0.53 **Symptomatic norovirus infection** *ABO histo-blood group OR (95% CI); p value - conditional logistic regression* Type A: 1.34 (0.55-3.42); 0.49 Type B: 0.33 (0.07-1.65); 0.15 Type O: 1.00 (0.40-2.52); 0.49 Type AB: 1.50 (0.25-8.98); 0.65 Type A/AB: 1.44 (0.62-3.38); 0.39 Type B/AB: 0.63 (0.20-1.91); 0.40	Power and sample size reported as 70 matched case-control pairs to detect an OR of 2.9 (alpha 0.05; power 0.80; 0.5 probability of an event in the exposed group). Period between the start of symptoms and completion of the patient questionnaire averaged 29 days (median 24 days).	506_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Symptomatic norovirus infection *ABO histo-blood group OR (95% CI)*; p value – *random effects logistic regression* Type A: 1.20 (0.55-2.61); 0.64 Type B: 0.28 (0.07-1.13); 0.07 Type O: 1.11 (0.51-2.45); 0.79 Type AB: 1.89 (0.35-10.2); 0.46 Type A/AB: 1.39 (0.64-3.00); 0.40 Type B/AB: 0.59 (0.21-1.70); 0.32		
Grotto, I; 2004 [97]	Retrospective controlled study	To investigate an outbreak on an Israeli military base. 1,3,4	Soldiers at Israel Defense Force training center. 159: 84 males and 75 females. 40 cases and 44 controls for the case control study.	**Risk factor of meals, selected food items, and dining facilities:** *All results – OR (95% CI)* Breakfast Dec 20, 1999 – 1.68 (0.55-5.20) Fresh vegetable salad that meal – 2.62 (0.99-6.96) Lunch Dec 20, 1999 – 4.11 (0.96-24.52) Fresh vegetable salad that meal – 4.38 (1.51-13.35) Dinner Dec 20, 1999 – 0.59 (0.05-5.45) Breakfast Dec 21, 1999 – 1.29 (0.49-3.43) Vegetable salad at that meal – 2.86 (1.05-7.88) Lunch Dec 21, 1999 – 0.70 (0.25-1.91) Dinner Dec 21, 1999 – 0.15 (0.05-0.44) Restaurant – 0.34 (0.13-0.92) Eating at least one meal at a restaurant located off base on Dec 20-21 – 0.34 (0.13-0.92) One food handler was reported being ill and vomiting 2 days before the outbreak. This food handler was not excluded from work and was not present during the iinvestigation.	Cases were defined as any base personnel who during the week of December 19-26, 1999 suffered diarrhea (3 or more loose stools in 24 hours), vomiting or abdominal pain, with or without fever (>37.5 degrees Celsius).	576_IL
de Wit, M; 2003 [61]	Retrospective controlled study (nested case-control study) 1,3,4,6,7	To identify risk factors for norovirus infection	Patients registered at a general practice network in Netherlands. Cases were those persons identified in the community cohort with gastroenteritis and a matched control was selected from the cohort members without gastroenteritis at that time. Median age of case patients was 2 years. Other demographic characteristics were not reported.	**Symptomatic norovirus infection** *All results OR(95% CI) unless otherwise noted* *All case-control pairs* *Univariate analysis* Poor food-handling hygiene (as a score) – 1.3(1.0-1.5); P<0.05 Low education level vs. intermediate education level – 1.9(0.9-4.0) High education level vs. intermediate education level – 2.2(1.2-3.9) Participant to day care center – 1.7(0.9-3.3) Household member to daycare center – 2.0(1.0-3.9) Household member to primary school – 1.6(1.0-2.7) Pets in household – 0.6(0.4-1.0)	Samples were tested for norovirus by RT-PCR Cases and controls were matched by age, degree of urbanization, region and date of inclusion Selection of variables into the multivariable model was backwards manually, based on the log likelihood ratio; a	763_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			152 case-control pairs	Cat as pet – 0.6(0.4-1.0) 1 household member with gastroenteritis vs. none – 3.7(1.7-8.0) >1 household member with gastroenteritis vs. none – 13.1(3.9-34.7) Child household contact – 5.2(1.8-15.3) Adult household contact – 4.4(2.0-9.6) Contact with person outside household with gastroenteritis – 11.4(4.7-27.3) Consumption of fish in the week before onset of symptoms – 1.8(1.0-3.2) Consumption of barbecued food in the week before onset of symptoms – 0.2(0.05-1.0) *Multivariate analysis* Poor food-handling hygiene (as a score) – 1.3(1.0-1.7); P<0.05 1 household member with gastroenteritis vs. none – 1.2(0.3-4.2) >1 household member with gastroenteritis vs. none – 10.9(2.0-60.5) Contact with person outside household with gastroenteritis – 12.7(3.1-51.8) *Population attributable risk (%) (based on multivariate odds ratios)* Poor food handling hygiene – 47 Number of household members with gastroenteritis – 17 Contact with person outside household with gastroenteritis – 56 *<1 year to 4 years (105 case-control pairs)* *Univariate analysis* Poor food-handling hygiene (as a score) – 1.2(0.9-1.5) ≥ 1 household members with gastroenteritis – 4.4(2.2-9.2) Contact with person outside household with gastroenteritis – 17.7(5.1-61.1) *Multivariate analysis* Poor food-handling hygiene (as a score) – 1.2(0.9-1.7) ≥ 1 household members with gastroenteritis – 2.7(0.8-8.9) Contact with person outside household with gastroenteritis – 10.9(2.2-54.6) *Population attributable risk (%) (based on multivariate odds ratios)* Poor food-handling hygiene (as a score) – 46 ≥ 1 household members with gastroenteritis – 27 Contact with person outside household with gastroenteritis – 51	significance level of 0.05 was used. Food handling hygiene was determined using a questionnaire that included items on acquisition and preparation of food. Power and sample size not reported	

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				<u>≥ 5 years (46 case-control pairs)</u> *Univariate analysis* Poor food-handling hygiene (as a score) – 1.3(0.9-1.9) ≥ 1 household members with gastroenteritis – 15.0(2.0-113.6) Contact with person outside household with gastroenteritis – 5.9(1.7-20.1) *Multivariate analysis* Poor food-handling hygiene (as a score) – 1.3(0.8-2.2) ≥ 1 household members with gastroenteritis – 1.1(0.1-15.9) Contact with person outside household with gastroenteritis – 12.1(1.0-147.3) *Population attributable risk (%) (based on multivariate odds ratios)* Poor food-handling hygiene (as a score) – 63 ≥ 1 household members with gastroenteritis – 4 Contact with person outside household with gastroenteritis – 60		
Marks, P; 2003 [98]	Retrospective controlled study 1,3,4,6,7	To describe an outbreak of NLV gastroenteritis during which vomiting occurred in some, but not all, classrooms and thus investigate the importance of vomiting as a mode of transmission of NLV, and the likelihood that environmental contamination played a role in the spread of the outbreak.	Children in a primary school and nursery in the UK. Age range 4-11 yrs. 492	**Symptomatic norovirus infection – Attack rates** (during the study period) *Based on sex [All results % (95% CI)]* Male – 30.4(25.1-36.2) Female – 31.3(25.7-37.6) *Based on age group [All results % (95% CI)]* 3-<4 yr – 20.0(9.5-37.3) 4-<5 yr – 25.9(16.3-38.4) 5-<6 yr – 44.8(32.7-57.5) 6-<7 yr – 52.3(37.9-66.2) 7-<8 yr – 39.0(27.6-51.7) 8-<9 yr – 28.3(18.5-40.8) 9-<10 yr – 27.0(18.2-38.1) 10-<11 yr – 22.2(13.7-33.9) 11-<12 yr – 16.7(8.3-30.6) *Vomiting episodes within classrooms as a risk factor [All results OR(95% CI) unless otherwise noted]* Attack rates increased with the number of vomiting episodes to which pupils were exposed (Chi-squared for linear trend – 37.8; P<0.01)	Cases were defined as follows: • for those pupils who returned a questionnaire: those who reported either diarrhea or vomiting or both • for those pupils who did not return a questionnaire: those who were absent from school with symptoms compatible with NLV infection Secondary cases were defined as other household members reporting by questionanaire diarrhea or vomiting after a pupil had been ill.	798_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				1 episode vs. none – Unadjusted: 2.7(1.6-4.5); Adjusted*: 5.1(2.2-11.6) 2 episodes vs. none – Unadjusted: 3.0(1.5-5.8); Adjusted*: 3.9(1.8-8.6) 3 episodes vs. none – Unadjusted: 10.4(4.8-22.4); Adjusted*: 14.6(5.9-36.5) *Exposure to another child vomiting as a risk factor [All results OR(95% CI)]* Unadjusted: 3.9(2.2-7.0); Adjusted*: 4.1(1.8-9.3) **Median time from exposure to onset of illness in days**(during the study period) 3 pupils vomiting on the same day vs. vomiting occurring only once – 1 vs. 14; P<0.01 **Symptomatic norovirus infection - Secondary attack rates** (during the study period) Adults – 17% Children – 46% Overall – 30% (*Adjusted for sex, age and building in which the classroom was situated)	Airborne transmission is implicated but in the discussion the authors state that aerosolization (eg droplets) from vomiting children may be the method of transmission. Outbreak was confirmed using EIA or PCR for selected specimens Completed questionnaires were returned for 289 pupils (response rate 59%) Study period was 25 June to 16 July 2001 Power and sample size not reported	
Stegenga, J.; 2002 [99] 1,3,4	Retrospective controlled study	To examine the relationship between nurse staffing levels and the rate of nosocomial viral gastrointestinal infections in a general pediatrics population	Patients on a general pediatrics ward in Toronto, Canada. Demographic characteristics not provided. 37	**Symptomatic norovirus infection** *All results Pearson correlation coefficient with norovirus gastroenteritis, P value* Monthly night patient-to-nurse ratio – 0.56; <0.05 Monthly day patient-to-nurse ratio – 0.50; <0.05 Monthly patient census – 0.51; <0.05 Monthly nursing hours per patient day: – 0.38; 0.14 **Symptomatic norovirus infection at 72 hours** *(infections per 1000 patient days)* Nursing hours/patient-day<10.5 vs. >10.5 – 6.39 vs. 2.17; RR(95% CI) = 2.94(2.16-4.01) *All results preinfection period vs. non-preinfection period; P value* **Mean nursing hours per patient day** 12.5 vs. 13.0; <0.05 **Mean nursing hours worked per patient day**	norovirus gastroenteritis was defined according to CDC definition Analysis was done under the assumption of a 72 hr incubation period for norovirus gastroenteritis. The cut-off point for 10.5 nursing hrs per patient day was chosen because the authors deemed this to represent a level of staffing that was inappropriately low, but occurred frequently enough to provide a comparison with more appropriate staffing levels.	963_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				390 vs. 376; <0.01 **Mean patient census** 31.7 vs. 29.5; <0.01 **Day patient-to-nurse ratio** 3.31 vs. 3.32; P>0.05 **Night patient-to-nurse ratio** 3.26 vs. 3.16; P<0.05	The 72 hour period prior to each infection was considered as pre-infection period and all other periods were considered post-infection. Overall, 92 days were defined as pre-infection period and 363 days were defined as non pre-infection period. Power and sample size not reported	
Gotz, H; 2001 [62]	Retrospective controlled study 1,3,4	To describe an outbreak in which secondary transmission into households by individuals occurred	Children and staff at 30 child centers (either a day care facility for preschool children or an after-school center for young children) in Sweden and their household contacts. Child center cases – 79 adults (mean age 41 yrs) and 114 children (mean age 5 yrs) Household cases – 58 adults (mean age 36 yrs) and 21 children (mean age 7 yrs) 775	**Symptoms** *All results adults vs. children - % reporting symptoms; P value* Diarrhea – 71.5 vs. 52.0; <0.01 Vomiting – 64.1 vs. 80.6; <0.01 Nausea – 96.8 vs. 93.1; 0.22 Stomach pain – 87.7 vs. 88.7; 0.82 Headache – 63.6 vs. 43.5; 0.01 Chills – 44.3 vs. 20.8; <0.01 Fever – 44.7 vs. 35.2; 0.20 Myalgia – 48.2 vs. 17.5; <0.01 **Symptomatic norovirus infection - Primary attack rate** Adults vs. children – 68/127 vs. 74/386; P<0.01 Children 0-5 yrs old vs. 6-10 yrs old – 44/204 vs. 30/179; P=0.23 **Symptomatic norovirus infection - Secondary attack rate** Adults vs. children – 11/59 vs. 40/312; P=0.23 Children 0-5 yrs old vs. 6-10 yrs old – 27/160 vs. 12/149; P=0.02 **Risk factors for household transmission of symptomatic norovirus infection** *All results RR(95% CI) unless otherwise noted* Children (vs. adults) – 3.8(1.9-7.6) Exposure to vomiting – 2.4(1.0-5.5) Exposure to diarrhea – 0.8(0.5-1.3) Increased frequency of vomiting – P<0.01	Primary case: a person in the child center who became ill and who had diarrhea, vomiting or nausea during the first 3 days of the outbreak Secondary case: a person who became ill from day 4 through day 12 of the outbreak Secondary household case: a person who became ill at >6 h but <10 days after the onset of disease in the corresponding patient who acquired the infection in the child center. NLV was confirmed using EM, used PCR for genotyping Power and sample size not reported 524/775 subjects (68%)	1024_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Size of household – P=0.14 Onset of illness at child center (vs. onset of illness at home) – 0.9(0.6-1.6) **Median incubation period for primary cases** 34 hours (range 2-61 hours) **Median serial interval** (between a case in the chid center and the linked household cases) Overall – 73 hours (range 4-198 hours) Counting only the first case in each household – 59 hours (range 4-198 hours) Truncating at 96 hours – 52 hours (4-96 hours)	returned the questionnaire	
Becker KM, 2000 [100]	Retrospective controlled study 1,2,3,4,6,7	To investigate norovirus outbreak at a football game.	Football game in Florida. norovirus outbreak primarily involved members of the North Carolina football team during a game in Florida. N=108 members of the North Carolina team and support staff interviewed. 54 with illness: 43 primary cases and 11 secondary cases.	*Meal risk factor – Unadjusted RR (95% CI)* Lunch 9/18 – RR 4.1 (1.6-10.0) Dinner 9/18 – RR 1.2 (0.7-2.2) Late dinner 9/18 – RR 1.2 (0.8-1.8) Breakfast 9/19 – RR 0.9 (0.6-1.5) Lunch 9/19 – RR 1.1 (0.7-1.7) Rate of attack among those who ate box lunch 9/18 – 62% *Lunch 9/18 food specific risk factor – OR (95% CI)* Sandwich – unadjusted OR 2.6 (1.2-5.5); adjusted OR 4.9 (1.3-18.9) Apple – unadjusted OR 1.6 (1.1-2.3); adjusted OR 2.4 (0.6-9.3) Candy bar – unadjusted OR 1.8 (1.0-3.2); adjusted OR 1.6 (0.5-5.0) Rate of attack among those with ate sandwich – 71%	All 4 stool samples obtained from North Carolina patients were positive for norovirus like virus on EM. All 4 samples and ½ stool samples from players on Florida team were positive for norovirus-like virus of genogroup I on RT-PCR. RT-PCR products had identical sequences. Power and sample size not reported	1101_IL
Parashar, U; 1998 [101]	Retrospective controlled study 1,3,4	To determine the etiologic agent, source of infection and mode of spread of a gastroenteritis outbreak.	Employees of a manufacturing company in Ohio. Demographic characteristics not reported. 325	**Symptomatic norovirus infection - Food specific attack rates** (at < 1 week after outbreak) *All results RR(95% CI)* Sandwiches – 14.1(2.0-97.3) Ice – 1.5(1.0-2.3) Tap water – 1.5(1.1-2.2) Chips – 1.4(0.9-2.1) Cookies – 1.4(0.9-2.1) Bottled soda – 1.3(0.9-1.9) Canned soda – 1.3(0.8-2.0) One of the food handlers who prepared the sandwiches reported	A case was defined by the presence of vomiting or diarrhea (≥ 3 loose stools in 24 hrs). NLV was confirmed by EM and RT-PCR Power and sample size not reported	1288_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				gastroenteritis that had subsided 4 days earlier		
McEvoy, M; 1996 [102]	Retrospective controlled study 1,3,4	To describe an outbreak of norovirus gastroenteritis.	Passengers and crew of 4 cruises in the western Mediterranean. Median age of cases 55 years; 13/23 males 46 (23 cases and 23 controls)	**Risk factors for symptomatic norovirus infection** (matched pairs analysis) *All results OR; P value* Gala dinner – 0.20; 0.22 Salad – 1.00; 0.77 Fruit – 0.56; 0.42 Eggs – 0.50; 0.38 Table – 1.33; 1.00 Taps – OR not calculable; 0.24 Ice (tap water) – 0.56; 0.42 Teeth (tap water) – 1.00; 0.77 Pool – 0.71; 0.77 Chicken – 0.50; 0.39 Prawns – 0.29; 0.18 Meat – 1.14; 1.00 Cream – 0.67; 0.75 **Interventions** 1. Hygiene measures were introduced in the galley 2. When the passengers disembarked for a short period, the cabins were cleaned with a chlorine based disinfectant 3. Soft furnishings were removed for steam cleaning from all cabins whose occupants had reported illness. At the same time, the crew and staff quarters, including communal bathrooms and lavatories, were cleaned in the same way. **Response to outbreak** After control measures were implemented, fewer than 10 cases of diarrhea and/or vomiting were detected on each of the fifth and sixth cruises	A primary cabin case (the first case to have occurred in a cabin) was defined as a passenger on the ship from 27 May to 2 June with diarrhea (≥3 loose stools in a 24 hour period) and/or vomiting. Controls were matched to cases by sex and age (within 10 years) norovirus was identified by EM and RT-PCR in fecal specimens 277/1100 questionnaires were completed and returned. Power and sample size not reported.	1410_RA
Sharp, TW; 1995 [64]	Retrospective controlled study 1,3,4,6,7	To identify risk factors for an outbreak onboard an aircraft carrier.	Crew members aboard an aircraft carrier. 4500 male crew members. Questionnaire results available for 2,618 shipboard personnel. Mean age 27 years (range, 17-	**Symptomatic norovirus infection - Attack rates (n=4500)** 13% with symptomatic infection 8% sought medical attention; almost all missed at ≥1 day work **Univariate analysis (n=2618)** *All results variable – attack rate; unadjusted OR (95% CI)* Age range (years)	Power and sample size not reported. Gastroenteritis was defined as anyone reporting either vomiting or water stools with at least one of the following:	1513_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			59)	17-19 – 17.6%; Reference 14.3%; 0.93 (0.6-1.5) 20-39 – 11.5%; 0.73 (0.4-1.2) 40-59 – 9.3%; 0.57 (0.3-1.2) Race White – 14.3%; Reference Black – 8.8%; 0.58 (0.4-0.85) Other – 17.2%; 1.24 (0.9-1.74) Rank Junior enlisted – 13.8%; Reference Senior enlisted – 10.7%; 0.74 (0.4-1.3) Officers – 9.4%; 0.65 (0.4-1.09) Number of persons in sleeping compartment 1-10 – 7.1%; Reference 11-50 – 8.6%; 1.23 (0.7-2.3) 51-100 – 15.5%; 2.39 (1.4-4.3) >100 – 18.6%; 2.98 (1.7-5.3) **Multivariate analysis (n=2618)** *All results variable – adjusted OR (95% CI)* Age (by year) – 0.98 (0.97-0.99) Race White – Reference Black – 0.6 (0.3-0.9) Other – 1.0 (0.7-1.3) Number of persons in sleeping compartment 1-10 – Reference 11-50 – 1.1 (0.5-1.7) 51-100 – 2.8 (1.6-3.4) >100 – 2.8 (1.6-3.4) **Pre-outbreak antibody levels and subsequent acute gastroenteritis** *All results pre-outbreak antibody titer – No. developing illness/total No. (%)* <50 – 2/14 (14%) 50-200 – 9/28 (32%) 400-800 – 8/20 (40%) 1600-3200 – 11/35 (31%) ≥6400 – 2/12 (17%) All – 32/109 (29%)	nausea, fever, headaches, chills, or myalgias. Gastroenteritis was associated with at least a fourfold increase in Norwalk virus antibody levels measured by ELISA. Norwalk virus like particles were also seen using immune EM in 2/6 stools.	

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Pre-outbreak antibody levels and subsequent fourfold or more titer rise *All results pre-outbreak antibody titer – No. with fourfold or more titer rise/total No. (%)* <50 – 6/14 (43%) 50-200 – 12/28 (43%) 400-800 – 5/20 (25%) 1600-3200 – 9/35 (26%) ≥6400 – 2/12 (17%) All – 23/109 (31%) **Pre-outbreak antibody levels and subsequent fourfold or more titer rise with acute gastroenteritis** *All results pre-outbreak antibody titer – No. with fourfold or more titer rise and developing illness/total No. (%)* <50 – 2/14 (14%) 50-200 – 5/28 (18%) 400-800 – 4/20 (20%) 1600-3200 – 4/35 (11%) ≥6400 – 1/12 (8%) All – 16/109 (15%)		
Chadwick, PR; 1994 [103]	Retrospective controlled study 1,3,4,6,7	To determine risk factors for small round structured virus infection during an outbreak at an elderly care unit.	Healthcare workers at an elderly care unit. Cases – mean age 36 years (range 21-58 years). Controls – mean age 39 years (range 18-59 years). 90% questionnaire responders were female. 103 questionnaires returned.	**Clinical features** Overall attack rate – 34% *Attack rates among healthcare subspecialties* Nursing – 40% Pharmacists – 34% Doctors – 0% Staff absent from work due to illness – 75% Duration of absence – median 2 days (range 1-9 days) **Risk factors for symptomatic infection** *Univariate analysis* Nearby vomiting – 50% exposed staff vs. 20% unexposed staff; OR 3.89 (95% CI 1.4-11); p=0.007 Number of exposures to nearby vomiting – p=0.032 Contact with ill patients – 42% exposed staff vs. 13% unexposed staff; OR 4.71 (95% CI 0.94-46); p=0.07 Number of close contacts with ill patients – p=0.023	Case was a patient or staff at the hospital with vomiting or ≥2 loose stools in a 24 hour period. Power and sample size not reported. Aerosolization of vomit may have been important in infection transmission during the outbreak.	1555_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Cleaning vomit – OR 1.96 (95% CI 0.46-9.8); p=0.49 Cleaning diarrhea – OR 4.67 (96% CI 0.49-225); p=0.22 *Multivariate analysis* Nearby vomiting was the only significant risk factor **Interventions Implemented** Handwashing emphasized Restricted transfers from affected wards Ward closures Staff cohorting Disinfection with chlorine-based products Attribute declining attack rates among subsequent wards to infection control measures		
Reid, JA; 1988 [104]	Retrospective controlled study 1,3,4	To investigate an outbreak of NLV.	Subjects affected by outbreak in a United Kingdom hotel in October of 1987. Over 164 people affected – 40 staff, over 70 resident guests, and 54 people attending functions. 32 cases and 100 controls completed questionnaire for case-control study.	**Symptomatic norovirus infection - Food specific attack rates** *All results: Consumption vs. no consumption; p value* *Function 2* *Smoked trout – 5/7 (71%) vs. 0/9 (0%); <0.005 Soup – 0/9 (0%) vs. 5/7 (63%); <0.005 *Cold meats* *Ham – 1/7 (14%) vs. 4/7 (57%); NS *Beef – 2/5 (40%) vs. 3/10 (30%); NS *Chicken – 2/4 (50%) vs. 3/12 (25%); NS *Tongue – ½ (50%) vs. 3/12 (25%); NS *Turkey – 2/4 (50%) vs. 2/9 (22%); NS *Pork – 1/1 (100%) vs. 4/14 (29%); NS Turkey and rice – 5/11 (45%) vs. 0/5 (0%); 0.11 *Salads* Coleslaw – 1/4 (25%) vs. 4/12 (33%); NS *Waldorf – 5/10 (50%) vs 0/6 (0%); 0.09 *Tomato and cucumber – 3/10 (30%) vs 1/5 (20%); NS *Mixed - 2/8 (25%) vs 2/7 (29%); NS *Rice - 4/6 (67%) vs 1/10 (10%); 0.04 *Function 3*	*Foods prepared by chef who was still excreting virus 48 hours after his symptoms. Cases were guest at the hotel from October 17-24 who had gastrointestinal disease defined by the presence of vomiting, or diarrhea (3 or more loose stools in 24 hours) or abdominal pain and nausea, or fever and either abdominal pain or nausea. reported to managementbut who had not been interviewed. Norwalk-like virus identified by EM. Power and sample size not reported.	1847_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				*Mixed seafood – 22/28 (79%) vs 0 (0%) Baked poussin – 21/27 (78%) vs 1/1 (100%); NS Courgettes – 18/22 (82%) vs 4/6 (67%); NS Cauliflower – 19/25 (76%) vs 3/3; NS Black Forest gateaux – 19/25 (76%) vs. 3/3 (100%); NS Cream topping – 16/20 (80%) vs. 6/8 (75%); NS Cream (with coffee) – 9/12 (75%) vs. 13/16 (81%); NS Cocoa almonds: 13/15 (87%) vs 9/13 (69%); NS Table water: 6/8 (75%) vs 16/20 (80%); NS		
Iversen, AM; 1987 [105]	Retrospective controlled study 1,3,4	To identify the source of two outbreaks caused by a small round structured virus.	Two outbreaks occurred in the banqueting suite of a London hotel. First dinner -280 guests. Second dinner – 114 guests.	**Symptomatic norovirus infection - Food specific attack rates:** *All results –consumption vs. no consumption; p value* *First outbreak* Melon – 197/220 vs. 0/5; 0.000006 Beef – 196/223 vs. 4/5; NS Potatoes – 196/218 vs. 3/9; NS Horseradish sauce – 142/161 vs. 58/67; NS Blackforest gateau –184/207 vs. 16/21; NS Cream – 180/202 vs. 19/26; NS *Second outbreak* Trout – 51/92 vs. 5/9; NS Horseradish sauce – 31/35 vs. 25/39; 0.026 Vermicelli consommé – 54/66 vs. 2/8; 0.004 Duck – 55/70 vs. 2/5; NS Potatoes – 52/68 vs. 4/6; NS Ice cream soufflé – 53/67 vs. 3/7; NS	Case was someone with abdominal pain, nausea, vomiting, or diarrhea in a week after dinner. Chef was likely source of outbreaks. Power and sample size not reported.	1881_IL
White, KE; 1986 [106]	Retrospective controlled study 1,3,4,6,7	To conduct a foodborne outbreak investigation.	Attendees at 8 banquets at a single Minnesota hotel. 383 attendees.	**Symptomatic norovirus infection - Attack rate** 220/383 (57%) developed gastroenteritis. **Food-specific attack rate** *Univariate analysis – All results % ill among exposed vs % ill among unexposed; OR; p value* *Banquet A* Potato salad – 57% vs. 30%; 3.2; 0.05 Fried chicken – 54% vs. 27%; 3.1; 0.06 Cranberry sauce – 86% vs. 34%; 11.6; 0.01 Fruit salad – 59% vs. 32%; 3; 0.07	Case was defined as individual who developed diarrhea (≥ 3 loose stools within 24 hours) or vomiting within 3 days of consuming a meal prepared by food service of the hotel or after contact with primary case. Power and sample size not reported.	1921_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Banquet B Potato salad – 82% vs. 65%; 2.5; 0.04 Coleslaw – 84% vs. 57%; 4.0; 0.0007 *Banquet C* Tossed salad – 56% vs. 13%; 9.0; 0.007 *Multivariate analysis – All results RR; p value* *Banquet A* Potato salad – 10.6; 0.010 Fried chicken – 4.1; 0.086 Cranberry sauce – 7.5; 0.062 Fruit salad – 7.7; 0.026 *Banquet B* Potato salad – 2; 0.177 Coleslaw – 3.8; 0.004 *Banquet C* Tossed salad – N/A		
Kaplan JE, 1982 [107]	Retrospective controlled study 2,4	To describe Norwalk oubreaks and assess how often Norwalk virus was implicated in outbreaks of acute nonbacterial gastroenteritis.	Records of gastroenteritis outbreaks investigated for a viral cause by the CDC from 1976-1980 and where serologic tests available. 7 additional norovirus outbreaks confirmed through 1980 at the NIH but not investigated by CDC.	**Overall** 31/74 outbreaks (42%) investigated by the CDC were norovirus related 17/74 outbreaks (23%) with possible involvement of the norovirus 26/74 (35%) not due to norovirus virus **Analysis of confirmed norovirus outbreaks** *norovirus outbreak characteristics* norovirus outbreaks: 38 confirmed including 7 not investigated by CDC 10 in camps and recreational areas, 7 in elementary schools 4 on cruise ships, 4 in nursing homes, 4 in colleges/universities, 4 in restaurants, 3 in small families, and 2 in larger communities. 3 in countries other than US, 4 on cruise ships at sea. Outbreaks occurred all months of the year. *Source of norovirus outbreak* Common source of infection: 31 outbreaks. 17 possible vehicle of transmission: water in 13 outbreaks (municipal water systems in 2 outbreaks, semipublic water supplies in 7, stored water on cruise ships in 2, and recreational swimming in 2 outbreaks) and food in 4 (2 with oysters and 2 with salad).	Common source of infection if a vehicle of transmission was incriminated by epidemiologic analysis or if the peak onset of illness occurred during the first 2 days of the outbreak. Primary person to person transmission presumed when no vehicle of transmission identified and when the peak onset of illness occurred after the second day of the outbreak; this was shown in some outbreaks by geographic clustering of cases. Secondary person to person	2077_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Primary person to person transmission: 7 outbreaks Secondary person to person transmission (attack rates 4% to 32%): 20/ 23 common source and 3/3 person to person outbreaks for which evidence available. Secondary attack rate highest among children<10 years of age in a single outbreak where information available. *Duration of norovirus outbreak* Outbreak duration: median 7 days (range, 1 day to 3 months) Of 24 common source outbreaks for which information available, 12 lasted 5-9 days. Outbreaks of longer duration included 7 in which successive weekly outbreaks occurred among newly introduced populations and 1 nationwide epidemic associated with eating raw oysters Of the 5 perton to person transmitted outbreaks where information available, 4 lasted 5-9 days. *Number of infected persons and attack rates* Infected persons ranged from 2 to 2000. Largest outbreaks in communities, schools, recreational areas, and on cruise ships (median, 348; range, 19-2000) Smallest outbreaks in families and nursing homes (median, 19 cases; range 2-43) *All results: Common source outbreak vs. Person to person transimssion* No. affected persons – median, 236 (range, 6-2000) vs. median 38 (range 2-559). Attack rates – median, 60% (range 23%-93%) vs. median 39% (range 31% to 42%). Attack rates did not differ significantly with age or sex in the 6 outbreaks in which information was available. *Prevalence and duration of symptoms* *All results (#outbreaks which noted symptom): median % patients with symptom (range)* Nausea (30): 79 (51-100) Vomiting (34): 69 (25-100) Diarrhea (34): 66 (21-100) Abdominal cramps (30): 71 (17-90) Headache (22): 50 (17-80)	transmission was evidenced in both types of outbreaks by the finding of illness in family members or roommates not exposed to the primary location of the outbreak. Incubation period determined by measuring either the interval between exposure to a common source and onset of illness or the intervals between onset of illness in primary and secondary cases. Serologic testing by RIA and results of stool testing by immune EM or RIA/ An outbreak of gastroenteritis was considered to be caused by norovirus if at least 50% of the serum pairs from cases had a fourfold or greater rise in Norwalk antibody titer between acute and convalescent phases. Power and sample size not reported.	

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Fever (29): 37 (13-71) Chills (14): 32 (5-74) Myalgias (14): 26 (11-73) Sore throat (7): 18 (7-32) From 5 outbreaks, vomiting more frequent than diarrhea among children; and diarrhea more frequent than vomiting among adults. In 6 elementary school outbreaks, vomiting occurred in median 75% and diarrhea in median 46% of all children In 4 ourbreaks on cruise ships (affecting mostly adults), vomiting and diarrhea occurred in 51% and 85% cases respectively Duration of illness from 29 outbreaks ranged from 2 hours to several days. The mean (or median) time was 24- 48 hours in 19 outbreaks and 12- 60 hours in 26/28 outbreaks In 6 outbreaks, a small percent of persons (15% or less) were ill longer than 3 days Off 22 outbreaks that recorded incubation period of illness, range was 4-77 hours Mean (or median) incubation period was 24- 48 hours in 20/ 22 outbreaks. **Analysis of outbreaks possibly caused by norovirus virus** 17 outbreaks occurred in all seasons of the year 11 in nursing homes, 3 in camps or recreational areas, 2 in elementary schools, and 1 in college. Of 15 outbreaks in which information is available, 6 were common source infection (including 1 waterborne) and 9 primary person to person transmission (geographic clustering of cases in 2 outbreaks) Secondary transmission (attack rates, 33% to 40%) in 2/3 common source outbreaks and 6/6 person to person outbreaks where information available Outbreaks in the possibly norovirus virus category similar to in the confirmed norovirus category in duration of illness, prevalence of symptoms, and incubation period *All results: % (No. with characteristic/total number of outbreaks) among*		

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				those with Norwalk infection vs. possibly Norwalk infection vs. not Norwalk infection Duration of illness from 12 to 60 hours: 93 (28) vs. 92 (12) vs 84 (19) Vomiting ≥ 50% cases: 89 (27/30) vs. 90 (10/17) vs. 50 (18/26) Diarrhea ≥ 50% cases: 74 (27) vs. 70 (10) vs. 94 (18) Headache ≥ 50% cases: 50 (18) vs. 25 (4) vs. 38 (13) Incubation period from 24 to 48 hours: 91 (22) vs. 80 (5) vs. 78 (9) **Analysis of norovirus negative outbreaks** 26 outbreaks occurred all months of the year 5 in nursing homes, 5 in restaurants, 4 in residential communities, 4 on cruise ships, 3 in hospitals, 2 in camps or recreational areas, and 2 in colleges. 14/21 outbreaks in which information was available were relate to a common source; 7 were waterborne an 3 were foodborne (salads) 7 outbreaks were primary to primary person to person transmission; geographic clustering was found in 2 of these. Secondary transmission (attack rates 11% to 48%) in 7/7 common source outbreaks and in 2/2 person to person outbreaks for which information was available Outbreaks not due to norovirus virus similar to those due to norovirus in duration of illness, prevalence of symptoms, and incubation period		
Blanton LH, 2006 [111]	Descriptive Study 1,2,3,4	To describe epidemiologic data from outbreaks of acute gastroenteritis occurring between July 2000 and June 2004 where samples were sent to the CDC.	226 confirmed outbreaks. 184 (81%) had CaCV detected. Genogroup II norovirus strains were the most abundant (79%), followed by genogroup I norovirus strains (19%)	**CaCV** *Settings* 65% of CaCV outbreaks in nursing homes, retirement centers, and hospitals 38% outbreaks in schools and day-care centers 58% outbreaks in vacation settings including cruise ships *Transmission* Person to person transmission (55%) vs. foodborne transmission (18%); p<0.001 **norovirus** During 2002-2003 CaCV season, Farmington Hills sequivar was responsible for 36% all confirmed norovirus outbreaks and 44% of all GII outbreaks	RT-PCR used. Power and sample size not reported.	371_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Mattison, K; 2007 [112]	Basic Science Study Not applicable (N/A)	To assess virus survival in foods and on sufaces. FCV was used as a surrogate for norovirus to investigate its survival.	Food (lettuce, strawberry, ham) and metal surfaces. Study was conducted in Canada. N/A	**Survival of virus** *At 30 min* Lettuce – 20% Strawberry – 1% Ham – 43% Metal disk – 11% *At 7 days* There was a signifiant reduction in viral titer after 7 days for all samples at both room temperature (RT) and 4°C (P<0.05). **Comparison of virus survival at RT and 4°C (on day 7)** Lettuce – undetectable at RT; 1% survival at 4°C; statistical differences were not reported Strawberry – undetectable at both RT and 4°C; survived for 5 days at 4°C, compared with survival of 1 day at RT; statistical differences were not reported Ham – P>0.05 Metal disk – P>0.05 **Comparison of virus survival among the different samples** The survival on ham was significantly greater when compared to all other surfaces at both temperatures (P<0.05)	Power and sample size not reported	154_RA

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GRADE TABLE Q1 WHAT PERSON, VIRUS OR ENVIRONMENTAL CHARACTERISTICS INCREASE OR DECREASE THE RISK OF NOROVIRUS INFECTION IN HEALTHCARE SETTINGS?

Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
Person characteristics														
Demographic characteristics														
Age	Symptomatic norovirus infection*	3 OBS [62-64]	Primary attack rate was significantly increased in adults when compared with children in 1 OBS in the community setting. Secondary attack rate was significantly increased in children aged 0-5 years compared with those aged 6-10 years. Children were a possible risk factor for household transmission when compared with adults[62] Increase in age was an independent protective factor in 1 OBS among aircraft crew members [64]Children who were affected were significantly younger in 1 OBS at a mother and child health clinic [63]	Low	0	0	0	0	0	0	0	0	Low	Low
	Asymptomatic norovirus infection	1 OBS [60]	Children were a possible risk factor for detection of CaCV and norovirus GII strain when compared with adults in 1 OBS in the community setting [60]	Low	0	0	0	-1	0	0	0	0	Very Low	
	Duration of illness*	2 OBS [57,59] 1 DES [58]	Age ≥ 65 years was an independent risk factor for increased duration of diarrhea in 2 OBS in the healthcare setting [57,59] Recovery was slowest in the oldest age group ≥ 65 years in 1 DES in the nursing home setting [58]	Low	0	0	0	0	0	0	0	0	Low	
Gender	Symptomatic norovirus infection*	1 OBS[79]	Gender was not a risk factor for symptomatic norovirus infection[79]	Low	0	0	0	0	0	0	0	0	Low	Low
	Acute kidney	1 OBS[57]	Gender was not a risk factor for acute kidney disease[57]	Low	0	0	0	0	0	0	0	0	Low	

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Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
	disease													
	Duration of illness	1 OBS[57]	Gender was not associated with increased duration of illness[57]	Low	0	0	0	0	0	0	0	0	Low	
	Hypokalemia	1 OBS[57]	Gender was not a risk factor for hypokalemia[57]	Low	0	0	0	0	0	0	0	0	Low	
Race	Symptomatic norovirus infection*	1 OBS [64]	Black race (compared with white) was an independent protective factor in 1 OBS among aircraft crew members [64]	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
Education	Symptomatic norovirus infection*	1 OBS [61]	Education level was not a risk factor in 1 OBS in the community setting [61]	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
Patient characteristics	Symptomatic norovirus infection*	2 OBS [66,67]	Patients who were exposed to case nurses had a greater risk than those who were not in 1 OBS in the healthcare setting. Respiratory care lack of nasogastric tube care and lack of wound care were possible risk factors [67] OBS in a long term care facility, physical dependence was a possible risk factor and use of diuretics was a possible protective factor [66]	Low	0	-1	0	0	0	0	0	0	Very Low	Very low
Staff characteristics	Symptomatic norovirus infection*	1 SR [56] 2 OBS [66,67]	Patient-indexed outbreaks affected significantly more patients than staff-indexed outbreaks in 1 SR. Staff were similarly affected by both outbreak index category groups [56] Nurses who were exposed to case patients did not have a significantly different risk of infection from those who were not in 1 OBS in the healthcare setting. Being a staff member was a possible risk factor [67]. Exposure to vomitus, gastroenteritis in household and exposure to residents with gastroenteritis were possible risk factors among employees in 1 OBS in a long term care facility [66]	Low	0	0	0	0	0	0	0	0	Low	Low
	Duration of illness	1 OBS [58]	Hospital patients had a significantly increased duration of illness compared to a combined group consisting of hospital staff, nursing home staff and nursing home residents in 1 OBS [58]	Low	0	0	0	-1	0	0	0	0	Very Low	

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Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
Clinical characteristics														
HIV	Symptomatic norovirus infection*	1 OBS [68]	HIV infected children with chronic diarrhea were a possible risk factor compared with HIV uninfected children with chronic diarrhea in 1 OBS in the healthcare setting [68]	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
	Asymptomatic norovirus infection	2 OBS [60,65]	HIV positive children were a possible risk factor compared with HIV negative children in 1 OBS in the community setting. HIV positive adults were not a risk factor [60] Presence of HIV infection or the degree of immunocompromise was not a risk factor in 1 OBS in the healthcare setting [65]	Low	0	0	0	0	0	0	0	0	Low	
Immune co-morbidities	Acute kidney disease*	1 OBS [57]	Immunosuppresive therapy was an independent risk factor for an increase in serum creatinine in 1 OBS in the healthcare setting [57]	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
Other co-morbidities	Duration of illness*	1 OBS [57]	Presence of underlying cardiovascular disorders was an independent risk factor for increased duration of vomiting in 1 OBS in the healthcare setting. Underlying malignancy and underlying trauma were independent risk factors for an increased duration of diarrhea. Presence of underlying gastrointestinal disorders was a possible risk factor for increased duration of diarrhea [57]	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
	Acute kidney disease	1 OBS [57]	Presence of underlying cardiovascular disorders and renal transplant were independent risk factors for potassium decrease in 1 OBS in the healthcare setting. Underlying trauma was a possible risk factor for an increase in serum creatinine [57]	Low	0	0	0	-1	0	0	0	0	Very Low	
Laboratory characteristics														
Antibody levels	Symptomatic norovirus/ CaCV infection*	3 OBS [74-76]	4/5 volunteers ill with norovirus showed a serum antibody rise in 1 OBS. After a second challenge, a pronounced antibody rise was again detected in these 4 subjects. The fifth ill subject maintained persistently elevated antibody levels at all times [76] Pre-existing serum CaCV antibody were a possible protective factor in 1	Low	0	-1	0	0	0	0	0	0	Very Low	Very Low

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Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
			OBS in a Japanese orphanage [75] Uninfected subjects had a lower preexisting antibody titer than infected subjects in 1 OBS. As the antibody titer increased, the incidence of vomiting, nausea, headache/body aches increased [74]											
Secretor genotype	Symptomatic norovirus infection*	2 OBS [70,71]	FUT2 non-secretor genotype was significantly associated with resistance to nosocomial and sporadic outbreaks of norovirus in 1 OBS [71] Presence of secretor positive genotype was associated with an increased risk in 1 OBS among volunteers challenged with norovirus [70]	Low	0	0	0	0	0	+2	0	0	High	High
	Asymptomatic norovirus infection	2 OBS [70,72]	Presence of secretor positive genotype was associated with an increased risk in 1 OBS among volunteers challenged with norovirus [70] Presence of secretor positive genotype was a possible risk factor in 1 OBS among volunteers challenged with norovirus [72]	Low	0	0	0	0	0	+2	0	0	High	
ABO phenotype	Symptomatic norovirus infection*	5 OBS [69,72,73,77,78]	Blood group O was not a risk factor in 1 OBS among volunteers challenged with norovirus [72] None of the blood types were risk factors in 2 OBS [69,77], one of which involved nosocomial and sporadic outbreaks [77] and the other involved military units [69] Blood group O was a possible protective factor in 1 OBS in the healthcare setting, although selection bias may be present [78] Blood group B was a possible protective factor in 1 OBS among volunteers challenged with norovirus [73]	Low	0	-1	0	0	0	0	0	0	Very Low	Very Low

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Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
	Asymptomatic norovirus infection	2 OBS [72,73]	In 1 OBS among volunteers challenged with norovirus, blood group O was a possible risk factor both overall and among secretor positive patients. Blood group A was a possible protective factor overall, but not after controlling for secretor status [72] Presence of a B HBGA (B and AB blood groups combined) was a possible protective factor, as was blood group AB in 1 OBS among volunteers challenged with norovirus. Blood group O was a possible risk factor [73]	Low	0	-1	0	0	0	0	0	0	Very Low	
Virus characteristics														
Virus characteristics	Duration of illness*	1 OBS [57]	Community acquired norovirus was an independent risk factor for increased duration of vomiting in 1 OBS in the healthcare setting [57]	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
	Acute kidney disease	1 OBS [57]	Community acquired norovirus was a possible risk factor for an increase in creatinine [57]	Low	0	0	0	-1	0	0	0	0	Very Low	
	Undefined norovirus infections*	3 DES [108-110]	An increase in norovirus activity coincided with the emergence of a new GII-4 variantin 1 DES [109] GII-3a strain was identified in 100% symptomatic patients while GII-4 was identified in 27% asymptomatic patients and staff in 1 DES [110] G-II.4 strain was the predominant strain associated with outbreaks of norovirus in Australia in 1 DES [108]	Very Low	0	0	0	0	0	0	0	0	Very Low	
Environmental characteristics														
Institution characteristics	Symptomatic norovirus infection*	2 OBS [82,99]	An increase in average length of stay was an independent protective factor, general medicine ward and geriatric ward were independent risk factors in 1 OBS in the healthcare setting. Number of beds in a unit, having a previous outbreak, month following outbreak and acute care unit were possible risk factors. Surgical and mental health wards were not risk factors [82]	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low

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Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
			Nurse understaffing was a possible risk factor in 1 OBS in a pediatrics ward [99]											
Pets	Symptomatic norovirus infection*	1 OBS [61]	Pets in household and cats as pets were not risk factors in 1 OBS in the community setting [61]	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low

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Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
Diet †	Symptomatic norovirus infection*	23 OBS[61,77,80,81,84,86,89-95,97,100-102,104-107,207] and 1 DES[111]	Of 17 norovirus outbreaks in 1 OBS where a possible vehicle of transmission was identified, water was implicated in 13 (municipal water systems in 2, semipublic water supplies in 7, stored water on cruise ships in 2, and recreational swimming in 2); and food in 4 (2 with oysters and 2 with salad) [107] Person to person transmission (55%) occurred more often than food transmission (18%) in 1 DES[111] Coffee and raisin roll were independent protective factors and the number of rolls eaten was an independent risk factor in 1 OBS in the community setting where a baker continued to work despite being infected [92] Poor food-handling hygiene was independent risk factor in 1 OBS in the community setting [61] Lettuce, jalapeno peppers and onions were possible risk factors in 1 OBS in the community setting. A food handler who returned to work within a few hours of illness was identified as the source [207] Sandwiches, ice and tap water were possible risk factors in 1 OBS in the community setting. A food handler was implicated [101] Salad on Wednesday and Thursday, semolina dumpling soup on Thursday were independent risk factors and potatoes on Thursday were independent protective factors in 1 OBS in the community setting [95] Antipasti platter and garlic mashed potatoes were possible risk factors in 1 OBS in the community setting [93] Any salad, pasta salad, potato salad, vegetable salad, condiments, dips, cheese and bread were possible risk factors in 1 OBS in the community setting [86]	Low	0	0	0	0	0	0	0	0	Low	Low

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Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
	Symptomatic norovirus infection*	23 OBS[61,77,80,81,84,86,89-95,97,100-102,104-107,207] and 1 DES[111]	Vegetable salad was a possible risk factor in 1 OBS in the community setting. A food handler was the source of the outbreak [97] Eating smoked trout and rice salad and not eating soup were possible risk factors in 1 OBS in the community setting [104] Melon and vermicelli consommé were possible risk factors in 1 OBS in the community setting. Horseradish sauce was a possible risk factor in one outbreak reported in the study [105] In 1 OBS that reported outbreaks at banquets, potato salad, coleslaw and fruit salad were independent risk factors, cranberry sauce and tossed salad were possible risk factors [106] Lettuce was a possible risk factor in 1 OBS in the community setting [91] Ice and raw mussels were independent risk factors in 1 OBS in the community setting [94] Turkey salad, tuna salad and any salad were possible risk factors in 1 OBS. A possibly infected food handler was implicated [89] Coronation chicken was an independent risk factor in 1 OBS [90] Sandwich was an independent risk factor in 1 OBS [100] Scalloped potatoes, chicken and chocolate cheese roll were possible risk factors in 1 OBS [80] Rice salad with cocktail sauce was a possible risk factor in 1 OBS [81] Drinking water from the hospital water supply was not associated in 1 OBS [87] Beef, cheese, egg, ham, lamb, tuna sandwiches, soup, hot chocolate and coffee were found to be possible risk factors in 1 OBS [84] None of the foods were found to be risk factors in 2 OBS [77,102]										

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Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
	Survival of CaCV	1 BAS [112]	Ham was a possible risk factor in 1 BAS [112]	Very Low	0	0	0	0	0	0	0	0	Very Low	
Proximity to infected persons	Symptomatic norovirus infection*	8 OBS [61,62,64,79,83,88,98,103] and 1 DES[111]	Exposure to more than one household member with gastroenteritis was an independent risk factor overall, but not when divided into two groups of age < or ≥5 years in 1 OBS in the community setting. Contact with person outside household with gastroenteritis was an independent risk factor overall and in the two age-groups [61] > 50 persons in a sleeping compartment was an independent risk factor in 1 OBS among aircraft crew members. ≤ 50 persons was not a risk factor [64] Exposure to vomiting and increased frequency of vomiting were possible risk factors in 1 OBS in the community setting. Exposure to diarrhea and the size of the household were not risk factors [62] Exposure to vomiting and increased frequency of vomiting were independent risk factors in 1 OBS in the community setting [98] Distance from the vomiter was a possible risk factor in 2 OBS in the community setting [83,88] Nearby vomiting was an independent risk factor in 1 OBS among healthcare workers. Number of exposures to nearby vomiting and number of close contacts with ill patients were possible risk factors [103] Having an ill contact was a possible risk factor in 1 OBS [79] Person to person transmission (55%) occurred more often than food transmission (18%) in 1 DES [111]	Low	0	0	0	0	0	+1	+1	0	High	High

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Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
	Time to illness	1 OBS [98]	Significantly decreased with exposure to increased frequency of vomiting in 1 OBS in the community setting [98]	Low	0	0	0	-1	0	0	0	0	Very Low	

RCT – randomized controlled trial; OBS – observational study (prospective or retrospective controlled); DES – descriptive study (case series, case report, uncontrolled data in an observational study); BAS – basic science study
* These outcomes are considered the most critical by the guideline developers.
** These modifiers can impact the GRADE by 1 or 2 points
† Rules for "not a risk factor" were not applied

Note: Definitions: "Independent risk factor" implies a variable was significant in a multivariate analysis; "possible risk factor" implies (1) it was significant in a univariate analysis and a multivariate analysis was not performed, or (2) it was significant in a univariate analysis but not in the multivariate analysis, but there were <10 events per variable examined in the multivariate analysis; "not a risk factor" implies that (1) it was not significant in a univariate/multivariate analysis when only one analysis was reported, and (2) there were > 10 events per variable examined in the univariate or multivariate analysis.

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Q2: What are the best methods to identify a norovirus outbreak in a healthcare setting?

EVIDENCE TABLE Q2

Clinical criteria

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Turcios, R; 2006 [116]	Diagnostic study 1,2	To examine how well the Kaplan's criteria, fever-to-vomiting ratio, diarrhea-to-vomiting ratio, and each component of the Kaplan criteria discriminated between outbreaks due to norovirus and due to bacterial agents. Kaplan's criteria are: 1. Vomiting in more than half of affected persons 2. Mean (or median) incubation period of 24-48 hrs 3. Mean (or median) duration of illness of 12-60 hrs 4. No bacterial pathogen in stool culture Another objective was to estimate the proportion of all outbreaks reported to the CDC between 1998 and 2000 that could be attributed to norovirus by using the Kaplan criteria alone. The gold standard for comparison was a confirmed norovirus or bacterial etiology by clinical microbiological testing and molecular biological testing.	Outbreaks reported to the CDC between 1998 and 2000. For testing the criteria, only outbreaks of confirmed etiology for which complete data were available were used. Out of a total of 4050 outbreaks, confirmed etiology with complete data were available for 362.	*All results % (95% CI) for each criterion* **Sensitivity** Kaplan criteria – 68.2(60.0-75.5) % of patients with vomiting – 88.5(82.0-93.0) Duration of illness – 85.8(78.9-90.8) Incubation period – 89.2(82.8-93.5) Fever-to-vomiting ratio – 90.1(83.6-94.3) Diarrhea-to-vomiting ratio – 96.6(91.9-98.7) **Specificity** Kaplan criteria – 98.6(95.6-99.6) % of patients with vomiting – 60.7(53.8-67.3) Duration of illness – 65.0(58.1-71.3) Incubation period – 69.6(62.9-75.6) Fever-to-vomiting ratio – 46.6(39.3-53.9) Diarrhea-to-vomiting ratio – 44.5(37.7-51.5) **Likelihood ratio** Kaplan criteria – 48.7 % of patients with vomiting – 2.2 Duration of illness – 2.4 Incubation period – 2.9 Fever-to-vomiting ratio – 1.7 Diarrhea-to-vomiting ratio – 1.7 **PPV** Kaplan criteria – 97.1(91.2-99.3) % of patients with vomiting – 60.9(54.0-67.4) Duration of illness – 62.9(55.8-69.5) Incubation period – 67.0(59.9-73.4) Fever-to-vomiting ratio – 55.7(49.0-62.2) Diarrhea-to-vomiting ratio – 55.3(48.9-61.3)	Power and sample size not reported.	348_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				NPV Kaplan criteria – 81.8(76.4-86.2) % of patients with vomiting – 88.4(81.9-92.9) Duration of illness – 86.9(80.4-91.5) Incubation period – 90.3(84.5-94.2) Fever-to-vomiting ratio – 86.3(77.7-92.0) Diarrhea-to-vomiting ratio – 94.9(87.9-98.1) **Outbreaks attributable to norovirus using Kaplan criteria** 28%		

Specimen collection

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Duizer, E; 2007 [117]	Diagnostic study 2,3	To use statistical analysis in determining 1) the minimum number of positive stool samples using RT-PCR or ELISA (IDEIA) compared to a hypothetical gold standard needed to declare norovirus as the causative agent of a gastroenteritis outbreak and 2) the probability of finding this minimum number of positive samples for varying numbers of tested samples.	N/A	**# Positive samples needed to assign norovirus as the causative agent** ELISA: 1 positive for 2-6 samples tested RT-PCR: 1 positive for 2-4 samples tested 2 positive for 5-11 samples tested **Sensitivity (%) for detecting a norovirus outbreak for various numbers of tested samples** ELISA: 57% for 2 tested samples 72% for 3 tested samples 88% for 5 tested samples 92% for 6 tested samples RT-PCR: 84% for 2 tested samples >90% for 3 tested samples	*Parameters* Defined outbreak as caused by norovirus if the prevalence is >8% Hypothetical gold standard: sensitivity 100%; specificity 100%. RT-PCR: sensitivity 72%; specificity 99%. IDEIA: sensitivity 41%; specificity 98%. Minimum # positive samples needed is the number of positive samples where there is >95% probability of	044_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				92% for 5 tested samples 96% sensitivity for 6 tested samples	attaining a prevalence ≥8%. IDEIA NLV (Dakocytomation Ltd., Ely, UK).	
Gray, JJ; 2007 [118]	Diagnostic study 2,3	To determine test characteristics for IDEIA and RIDA-SCREEN.	Stool samples from patients with symptoms of gastroenteritis collected during the 2004-2005 and 2005-2006 norovirus seasons and evaluated in this European multicenter study. 2,254 samples from 273 outbreaks. 274 samples collected in sporadic cases. 144 samples had other enteric pathogens identified.	**Test characteristics** IDEIA: Sensitivity 58.93% (95% CI 56.12-61.68%) Specificity 93.91% (95% CI 92.23-95.25%) PPV 92.30% NPV 64.90% RIDA-SCREEN: Sensitivity 43.81% (95% CI 41.01-46.65%) Specificity 96.27% (95% CI 95.00-97.38%) PPV 93.70% NPV 58.20% **Sensitivity for differing number of samples tested** The sensitivity for outbreak diagnosis improved when ≥6 samples tested. IDEIA: 3 vs. 6 samples tested (z=±3.191; p=0.0014) RIDA-SCREEN: 3 vs. 6 samples tested (z=±3.828; p=0.0001) **Range of norovirus genotypes detected** *All samples: Genotype - IDEIA vs. RIDASCREEN No [(%) samples genotype detected (95% CI)]; p value* GI-1 – 4 [80.00% (37.55-96.36%)] vs. 3 [60.00% (23.07-88.24%)]; 0.49 GI-2 – 11 [84.62% (57.77-95.67%)] vs. 2 [15.38% (4.33-42.23%)]; 0.0002 GI-3 – 12 [42.86% (26.51-60.93%)] vs. 9 [32.14% (17.93-50.66%)]; 0.4 GI-4 – 2 [100.00% (34.24-100.00%)] vs. 0 [0.00% (0.00-65.76%)]; 0.3 GI-5 – 3 [37.50% (13.68-69.43%)] vs. 0 [0.00% (0.00-32.44%)]; 0.2 GI-6 – 5 [71.43% (35.89-91.78%)] vs. 0 [0.00% (0.00-35.43%)]; 0.02 GI-7 – 0 [0.00% (0.00-79.35%)] vs. 0 [0.00% (0.00-79.35%)]; >0.5 GII-1 – 7 [87.50% (52.91-97.76%)] vs. 0 [0.00% (0.00-32.44%)]; 0.0024 GII-2 – 8 [50.00% (28.00-72.00%)] vs. 4 [25.00% (10.18-49.50%)]; 0.2 GII-3 – 30 [57.69% (44.19-70.13%)] vs. 11 [21.15% (12.24-34.03%)]; 0.0003 GII-4 – 203 [67.44% (61.96-72.49%)] vs. 186 [61.79% (56.19-67.10%)];	IDEIA norovirus (Oxoid; Thermo Fisher Scientific, Ely, UK). RIDASCREEN norovirus (R-Biopharm, Darmstadt, Germany) RT-PCR was the reference standard.	053_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				0.17 GII-5 – 2 [33.33% (9.68-70.00%)] vs. 3 [16.67% (3.01-56.35%)]; >0.5 GII-6 – 2 [22.22% (6.32-54.74%)] vs. 0 [0.00% (0.00-29.91%)]; 0.4 GII-7 – 20 [68.97% (50.77-82.72%)] vs. 5 [17.24% (7.6-34.55%)]; 0.002 GII-8 – 0 [0.00% (0.00-79.35%)] vs. 0 [0.00% (0.00-79.35%)]; >0.5 GIV-1 – 0 [0.00% (0.00-48.99%)] vs. 0 [0.00% (0.00-48.99%)]; >0.5 rGII – 10 [52.63% (31.71-72.67%)] vs. 2 [10.53% (2.94-31.39%)]; 0.01 IDEIA showed reactivity to a broader range of genotypes than the RIDASCREEN norovirus assay, which showed genotype-dependent sensitivities.		
Richards, A; 2003 [119]	Diagnostic Study 1,2	To determine the test characteristics of ELISA and EM in detecting norwalk-like virus (NLV) infection when compared with PCR	Fecal samples collected from patients involved in outbreaks of gastroenteritis in the UK 531 fecal samples	**Test characteristics (%) of ELISA vs. PCR** Sensitivity – 55.5(51.1-60.0) Specificity – 98.3(97.1-99.9) PPV – 95.0(CI not reported) NPV – 76.9 (CI not reported) **Test characteristics (%) of EM vs. PCR** Sensitivity – 23.9(19.5-28.1) Specificity – 99.2(98.3-100) PPV – 93.9(CI not reported) NPV – 70.7(CI not reported) **Identification of NLV as the cause of an outbreak** (% of outbreaks) *When the causative agent was defined by ≥ 2 positive samples* EM – 7.2 ELISA – 18.6 PCR – 41.5 *When the causative agent was defined by ≥ 1 positive samples* EM – 19.6 ELISA – 47.8 PCR – 62.8 **Sensitivity; Specificity of ELISA based on number of samples collected** 2 samples – 52.9; 100 ≥4 – 69.2; 100 ≥6 – 71.4; 100 **Other results**	Power and sample size not reported.	848_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Agreement between ELISA and PCR – 81.8% (Kappa = 0.57) Sensitivity of ELISA was significantly increased when compared with EM (P<0.01)		

Diagnostic methods – Fecal specimens

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
EIA/ELISA						
Khamrin, P; 2008 [120]	Diagnostic Study 1,2	To evaluate the test characteristics of immunochromatography and ELISA (Denka) when compared with monoplex RT-PCR for detection of norovirus from stool specimens.	Infants and children with acute gastroenteritis in Japan 503 fecal specimens	**Test characteristics of immunochromatography and ELISA** *Immunochromatography vs. RT-PCR* TP – 90 TN – 375 False positive (FP) – 14 False negative (FN) – 24 Sensitivity – 78.9% Specificity – 96.4% PPV – 86.5% NPV – 94.0% Accuracy – 92.4% *ELISA vs. RT-PCR* TP – 103 TN – 375 FP – 14 FN – 11 Sensitivity – 90.4% Specificity – 96.4% PPV – 88.0% NPV – 97.2% Accuracy – 95.0% **Accuracy of norovirus genotype detection**	Immunochromatography takes 20 min. ELISA takes 4 hrs. Power and sample size not reported Prevalence not reported	2351_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				All results listed as positives detected/true positives *Immunochromatography vs. RT-PCR* GI/1 – 1/2 GII/3 – 13/14 GII/4 – 75/95 GII/6 – 1/3 *ELISA vs. RT-PCR* GI/1 – 2/2 GII/3 – 12/14 GII/4 – 86/95 GII/6 – 3/3		
Wiechers, C; 2008 [121]	Descriptive study 1,2,3	To describe a cluster of positive IDEIA cases which were unable to be confirmed using RT-PCR or EM.	Infants in a level III neonatal intensive care unit in Germany during November 2003. 43 infants screened. 163 stool samples obtained.	**# positive/# tested samples** IDEIA: 46/163 samples from 22/43 infants were positive. RT-PCR: 0/11 samples with enough volume were positive. EM: 0/11 samples were positive. **Variables associated with IDEIA positive samples** Stools with and without blood: 11/46 vs. 1/117; p<0.001 Age of patients with IDEIA positive vs. negative samples: median 34.9 weeks (range 28.6-40.9) vs. 36.6 weeks (range 29.4-66.9); p<0.001.	RT-PCR (QIAGEN, Hilden, Germany). IDEIA NLV kit (DakoCytomation Ltd., Ely, UK).	5118_IL
Castriciano S, 2007 [122]	Diagnostic Study 1,2,3	To compare RIDASCREEN norovirus EIA to IDEIA NLV GI/GII	66 positive and 162 negative stool samples 228 total samples	**Test characteristics: Test – Positive (% sensitivity; CI) vs. Negative (% specificity; CI)** RT-PCR: 65 (98.5; 91.9-99.7) vs. 162 (100; 97.7-100) RIDASCREEN: 53 (80.3; 69.2-88.1) vs. 162 (100; 97.7-100) IDEIA-NLV: 40 (60.6; 48.5-71.5) vs. 162 (100; 97.7-100) EM: 24 (36.4; 25.8-48.4) vs. 157 (96.9; 93.0-98.7)	Used stools that had previously been screened by EM and stored at -70 C. Re-tested using RT-PCR.	143_IL
Gray, JJ; 2007 [118]	Diagnostic study 2,3	To determine test characteristics for IDEIA and RIDA-SCREEN.	Stool samples from patients with symptoms of gastroenteritis collected during the 2004-2005 and 2005-2006 norovirus seasons and evaluated in this European	**Test characteristics** IDEIA: Sensitivity 58.93% (95% CI 56.12-61.68%) Specificity 93.91% (95% CI 92.23-95.25%) PPV 92.30% NPV 64.90% RIDA-SCREEN: Sensitivity 43.81% (95% CI 41.01-46.65%) Specificity 96.27% (95% CI 95.00-97.38%)	IDEIA norovirus (Oxoid; Thermo Fisher Scientific, Ely, UK). RIDASCREEN norovirus (R-Biopharm, Darmstadt, Germany) RT-PCR was the reference standard.	053_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			multicenter study. 2,254 samples from 273 outbreaks. 274 samples collected in sporadic cases. 144 samples had other enteric pathogens identified.	PPV 93.70% NPV 58.20% **Sensitivity for differing number of samples tested** The sensitivity for outbreak diagnosis improved when ≥6 samples tested. IDEIA: 3 vs. 6 samples tested (z=±3.191; p=0.0014) RIDA-SCREEN: 3 vs. 6 samples tested (z=±3.828; p=0.0001) **Range of norovirus genotypes detected** *All samples: Genotype - IDEIA vs. RIDASCREEN No [(%) samples genotype detected (95% CI)]; p value* GI-1 – 4 [80.00% (37.55-96.36%)] vs. 3 [60.00% (23.07-88.24%)]; 0.49 GI-2 – 11 [84.62% (57.77-95.67%)] vs. 2 [15.38% (4.33-42.23%)]; 0.0002 GI-3 – 12 [42.86% (26.51-60.93%)] vs. 9 [32.14% (17.93-50.66%)]; 0.4 GI-4 – 2 [100.00% (34.24-100.00%)] vs. 0 [0.00% (0.00-65.76%)]; 0.3 GI-5 – 3 [37.50% (13.68-69.43%)] vs. 0 [0.00% (0.00-32.44%)]; 0.2 GI-6 – 5 [71.43% (35.89-91.78%)] vs. 0 [0.00% (0.00-35.43%)]; 0.02 GI-7 – 0 [0.00% (0.00-79.35%)] vs. 0 [0.00% (0.00-79.35%)]; >0.5 GII-1 – 7 [87.50% (52.91-97.76%)] vs. 0 [0.00% (0.00-32.44%)]; 0.0024 GII-2 – 8 [50.00% (28.00-72.00%)] vs. 4 [25.00% (10.18-49.50%)]; 0.2 GII-3 – 30 [57.69% (44.19-70.13%)] vs. 11 [21.15% (12.24-34.03%)]; 0.0003 GII-4 – 203 [67.44% (61.96-72.49%)] vs. 186 [61.79% (56.19-67.10%)]; 0.17 GII-5 – 2 [33.33% (9.68-70.00%)] vs. 3 [16.67% (3.01-56.35%)]; >0.5 GII-6 – 2 [22.22% (6.32-54.74%)] vs. 0 [0.00% (0.00-29.91%)]; 0.4 GII-7 – 20 [68.97% (50.77-82.72%)] vs. 5 [17.24% (7.6-34.55%)]; 0.002 GII-8 – 0 [0.00% (0.00-79.35%)] vs. 0 [0.00% (0.00-79.35%)]; >0.5 GIV-1 – 0 [0.00% (0.00-48.99%)] vs. 0 [0.00% (0.00-48.99%)]; >0.5 rGII – 10 [52.63% (31.71-72.67%)] vs. 2 [10.53% (2.94-31.39%)]; 0.01 IDEIA showed reactivity to a broader range of genotypes than the RIDASCREEN norovirus assay, which showed genotype-dependent sensitivities.		
Wilhelmi de Cal, I; 2007 [123]	Diagnostic study 2,3	To evaluate IDEIA and Ridascreen compared to RT-PCR for norovirus antigen detection.	The study included stool samples from children <5 years of age with acute gastroenteritis who were admitted to a hospital in Spain between October 1, 2002 and April 1,	**Samples positive for norovirus** 39 samples positive by RT-PCR. Concordant results with 3 methods in 77 (65.8%) samples. Discordant results with 3 methods in 40 (34.2%) samples. 18/39 samples underwent genotyping and sequence analysis: 1 had Sapovirus and 17 were norovirus genogroup II. **Test characteristics** IDEIA:	IDEIA NVL assay (DakoCytomation, Ely, UK). Ridascreen NLV (R-BioPharm, Darmstadt, Germany). RT-PCR assay (One-Step RT-PCR Kit, QIAGEN, Valencia, CA, USA).	144_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			2004. Stools collected 24-48 hrs after admission with a diagnosis of acute gastroenteritis 117 samples that were negative for bacterial pathogens, rotaviruses, adenoviruses, and astroviruses were tested for Caliciviridae by RT-PCR, IDEIA, and Ridascreen.	Sensitivity 76.9% Specificity 85.9% PPV 73.2% NPV 88.2% Agreement 82.9% Kappa index 0.6203 Ridascreen: Sensitivity 59% Specificity 73.1% PPV 52.3% NPV 78.1% Agreement 68.4% Kappa index 0.3103		
De Bruin, E; 2006 [124]	Diagnostic study 2,3	To evaluate IDEIA and Ridascreen EIAs compared to RT-PCR for the diagnosis of acute gastroenteritis outbreaks.	Two panels of stool samples collected from Dutch gastroenteritis surveillance (1999 - 2003). Panel 1: 158 fecal samples from 23 outbreaks, including confirmed Rotavirus and Astrovirus outbreaks that had been tested for norovirus by RT-PCR in 2002 and 2003. Panel 2: 19 samples positive	**Agreement between ELISAs and RT-PCR** Positive in all tests – 10/158 (6%) Negative in all tests – 71/158 (45%) Discrepant results – 77/158 (49%) **Detection of norovirus Samples with ELISA kits** *1. ELISA (Dako kit) vs. RT-PCR (All samples)* TP – 28 TN - 81 FN – 46 FP – 3 Sensitivity – 37.8% Specificity – 96.4% PPV – 90.3% NPV – 63.8% *2. ELISA (Dako kit) vs. RT-PCR (norovirus positive outbreaks)* <u>Criterion A – Two or more norovirus positive samples per outbreak to identify the causative agent</u> TP – 30 TN – 40	RT-PCR protocol followed by Southern blot hybridization was the reference standard. IDEIA (DakoCytomation Ltd., Ely, UK). Ridascreen (R-biopharm AG, Darmstadt, Germany). Prevalence not reported	238_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			for norovirus by RT-PCR: 6 samples of 5 different genogroup I strains, 12 samples of 6 genogroup II strains, and 1 genogroup IV strain. These stool samples were collected from Dutch gastroenteritis surveillance from 1999 to 2002.	FP – 1 FN – 43 <u>Criterion B – 50% or more norovirus positive samples per outbreak to identify the causative agent</u> TP – 24 TN – 63 FP – 7 FN – 38 *3. ELISA (Ridascreen kit) vs. RT-PCR* TP – 27 TN - 74 FN – 47 FP – 10 Sensitivity – 36.5% Specificity – 88.1% PPV – 73.0% NPV – 61.2% *4. ELISA (Ridascreen kit) vs. RT-PCR (norovirus positive outbreaks)* <u>Criterion A – Two or more norovirus positive samples per outbreak to identify the causative agent</u> TP – 35 TN – 39 FP – 2 FN – 38 <u>Criterion B – 50% or more norovirus positive samples per outbreak to identify the causative agent</u> TP – 29 TN – 62 FP – 8 FN – 33 **Detection of norovirus outbreaks with ELISA kits** *1. ELISA (Dako kit) vs. RT-PCR* <u>Criterion A – Two or more norovirus positive samples per outbreak to identify the causative agent</u> TP – 8		

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				TN – 8 FP – 0 FN – 7 <u>Criterion B – 50% or more norovirus positive samples per outbreak to identify the causative agent</u> TP – 5 TN – 11 FP – 0 FN – 7 *2. ELISA (Ridascreen kit) vs. RT-PCR* <u>Criterion A – Two or more norovirus positive samples per outbreak to identify the causative agent</u> TP – 9 TN – 8 FP – 0 FN – 6 <u>Criterion B – 50% or more norovirus positive samples per outbreak to identify the causative agent</u> TP – 4 TN – 11 FP – 0 FN – 8 RIDASCREEN not able to discriminate between groups 17% of PCR-identified Genogroup I 58% of PCR-identified Genogroup II 0% of PCR-identified by Genogroup IV 74/158 samples confirmed NLV via PCR and Southern Blot Of these, 28/74 confirmed with Dako and 27/74 with RIDAscreen 84/158 samples were negative by PCR 3/84 negative by PCR were positive using Dako 10/84 negative by PCR were positive using RIDAscreen Dako: 96% specificity Ridascreen: 88% specificity		

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Okitsu-Negishi, S; 2006 [125]	Diagnostic study 2,3	To evaluate the RIDASCREEN norovirus ELISA kit compared to RT-PCR.	503 stool samples collected from infants and children with acute sporadic gastroenteritis who visited 6 pediatric clinics in Japan from July 2004 to March 2005.	**Test characteristics for RIDASCREEN** Sensitivity - 76.3% Specificity - 94.9%. PPV - 81.3% NPV – 93.2% 90.7% agreement FP - 20 TP -87 FN - 27 TN - 369 Sensitivity by norovirus genotype *All results – # positive/# tested (%)* GI/1 – 1/2 (50%) GII/3 – 3/13 (23.1%) GII/4 – 82/96 (85.4%) GII/6 – 1/3 (33.3%)	RT-PCR was the reference standard. RIDASCREEN (R-Biopharm AG, Darmstadt, Germany). Power and sample size not reported. Prevalence not reported	228_IL
Burton-MacLeod, JA: 2004 [126]	Diagnostic study 2,3	To assess two enzyme-linked immunosorbent assay kits, SRSV (II)-AD and IDEIA, compared to RT-PCR.	104 stool samples with norovirus: 4 genogroup I subgroups and 10 genogroups II subgroups from 35 outbreaks that occurred in the US June 1999-2002. 33 samples with other enteric viruses from children <5 years of age with diarrhea. SRSV (II)-AD also tested with 6 Sapovirus positive samples from	**Test characteristics** SRSV (II)-AD: Sensitivity 80% Specificity 69% 77% agreement Sensitivities > 70% for 10/14 subgroups Cross-reacted with samples containing norovirus GI and GII subgroups; as well as samples with human Sapovirus. Detected 59% of the GII antigens in the GI wells and 63% of the GI antigens in the GII wells. IDEIA: Sensitivity 39% Specificity 100% 54% agreement Sensitivities >70% for 3/14 subgroups. GII/2, GII/5, GII/6, and GII/n may not be detected by IDEIA. Discriminated between norovirus GI and GII antigens. Detected no GII antigens in the GI wells and only 7% of GI antigens in the GII wells.	SRSV (II)-AD (Denka Seiken Co. Ltd., Tokyo, Japan). IDEIA NLV (DakoCytomation Ltd., Ely, UK). RT-PCR was the reference standard. Power and sample size not reported.	660_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			patients in an outbreak.			
Christen, A; 2003 [127]	Diagnostic study 2,3,4	To evaluate IDEIA compared to RT-PCR in detecting norovirus.	39 stool samples from a prior case-control study conducted in Switzerland. 24 additional samples previously PCR tested by a German Laboratory.	**Swiss samples** TP – 9 TN – 15 FN - 12 FP - 3 *IDEIA Test characteristics* Sensitivity 0.43 Specificity 0.83 PPV 0.75 NPV 0.56 Relative trueness 0.62 False positive 0.17 False negative 0.57 Concordance index Kappa 0.25 **German samples** TP – 6 TN – 11 FN - 7 FP – 0 *IDEIA Test characteristics* Sensitivity 0.46 Specificity 1.00 PPV 1.00 NPV 0.61 Relative trueness 0.71 False positive 0.00 False negative 0.54 Concordance index Kappa 0.44	IDEIA NLV ELISA (Dako-Cytomation, Ely, UK). RT-PCR was the reference standard. Power and sample size not reported. Prevalence not reported Differences in sensitivities may have resulted from differences in storage of samples (4ºC for <3 days versus -20ºC for long term storage as recommended by the manufacturer). Some samples had been stored for many weeks at 4ºC.	4519_IL
Gunson, R; 2003; [128]	Diagnostic study 1	To compare a real-time polymerase chain reaction (PCR) and a newly developed EIA for the	Stool samples were collected from outbreaks and sporadic	**Positive samples detected** *1. PCR* Overall – 26 Among sporadic cases – 5	Power and sample size not reported. Prevalence not reported	757_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		detection of norovirus. Negative or discrepant PCR results were investigated using EM and a different, not real time PCR.	cases/unidentified outbreaks, no timeframe specified 70 stool samples	*2. EIA* Overall – 10 Among sporadic cases – 3 All PCR samples could be confirmed using the second PCR. The EIA detected two positive samples that were negative by the PCR. Neither of these samples could be confirmed using the second PCR or EM. EIA Positive Negative Real-time PCR Positive 8 18 Negative 2 42 **Test characteristics (%)** Sensitivity – 30.8 Specificity – 95.5 PPV – 80.0 NPV – 70.0		
Rabenau, H; 2003 [17]	Diagnostic Study 1,2	To compare the sensitivity and specificity of: 1. ELISA when compared with a) TEM and PCR or b) PCR only 2. TEM when compared with a) ELISA and PCR or b) PCR only	Inhabitants and employees of homes for the elderly (in Frankfurt, Germany) aged 20 to >60 years; 73% females, 42% > 60 yrs. 244 stool samples from 227 patients	**Test characteristics (%) for ELISA** *When compared with TEM and PCR* Sensitivity – 50.0 Specificity – 96.2 PPV – 68.0 NPV – 92.2 (True Positive[TP] – 17; True Negative[TN] – 202; FP – 8; FN – 17) *When compared with PCR only* Sensitivity – 31.3 Specificity – 94.9 PPV – 60.0 NPV – 84.9 (TP – 15; TN – 186; FP – 10; FN – 33) **Test characteristics (%) for TEM** *When compared with ELISA and PCR* Sensitivity – 88.2 Specificity – 99.0 PPV – 93.8 NPV – 98.1 (TP – 30; TN – 208; FP – 2; FN – 4) *When compared with PCR only*	Power and sample size not reported. Prevalence not reported	801_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Sensitivity – 58.3 Specificity – 98.0 PPV – 87.5 NPV – 90.6 (TP – 28; TN – 192; FP – 4; FN – 20) **Test characteristics (%) for PCR** *When compared with ELISA and TEM* Sensitivity – 94.1 Specificity – 92.4 PPV – 66.7 NPV – 99.0 (TP – 32; TN – 194; FP – 16; FN – 2)		
Richards, A; 2003 [119]	Diagnostic Study 1,2	To determine the test characteristics of ELISA and EM in detecting norwalk-like virus (NLV) infection when compared with PCR	Fecal samples collected from patients involved in outbreaks of gastroenteritis in the UK 531 fecal samples	**Test characteristics (%) of ELISA vs. PCR** Sensitivity – 55.5(51.1-60.0) Specificity – 98.3(97.1-99.9) PPV – 95.0(CI not reported) NPV – 76.9 (CI not reported) **Test characteristics (%) of EM vs. PCR** Sensitivity – 23.9(19.5-28.1) Specificity – 99.2(98.3-100) PPV – 93.9(CI not reported) NPV – 70.7(CI not reported) **Identification of NLV as the cause of an outbreak** (% of outbreaks) *When the causative agent was defined by ≥ 2 positive samples* EM – 7.2 ELISA – 18.6 PCR – 41.5 *When the causative agent was defined by ≥ 1 positive samples* EM – 19.6 ELISA – 47.8 PCR – 62.8 **Sensitivity; Specificity of ELISA based on number of samples collected** 2 samples – 52.9; 100 ≥4 – 69.2; 100 ≥6 – 71.4; 100	Power and sample size not reported. Prevalence not reported	848_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Other results Agreement between ELISA and PCR – 81.8% (Kappa = 0.57) Sensitivity of ELISA was significantly increased when compared with EM (P<0.01)		
EM						
Rabenau, H; 2003 [17]	Diagnostic Study 1,2	To compare the sensitivity and specificity of: 1. ELISA when compared with a) TEM and PCR or b) PCR only 2. TEM when compared with a) ELISA and PCR or b) PCR only	Inhabitants and employees of homes for the elderly (in Frankfurt, Germany) aged 20 to >60 years; 73% females, 42% > 60 yrs. 244 stool samples from 227 patients	**Test characteristics (%) for ELISA** *When compared with TEM and PCR* Sensitivity – 50.0 Specificity – 96.2 PPV – 68.0 NPV – 92.2 (True Positive[TP] – 17; True Negative[TN] – 202; FP – 8; FN – 17) *When compared with PCR only* Sensitivity – 31.3 Specificity – 94.9 PPV – 60.0 NPV – 84.9 (TP – 15; TN – 186; FP – 10; FN – 33) **Test characteristics (%) for TEM** *When compared with ELISA and PCR* Sensitivity – 88.2 Specificity – 99.0 PPV – 93.8 NPV – 98.1 (TP – 30; TN – 208; FP – 2; FN – 4) *When compared with PCR only* Sensitivity – 58.3 Specificity – 98.0 PPV – 87.5 NPV – 90.6 (TP – 28; TN – 192; FP – 4; FN – 20) **Test characteristics (%) for PCR** *When compared with ELISA and TEM* Sensitivity – 94.1 Specificity – 92.4 PPV – 66.7	Power and sample size not reported. Prevalence not reported	801_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				NPV – 99.0 (TP – 32; TN – 194; FP – 16; FN – 2)		
Richards, A; 2003 [119]	Diagnostic Study 1,2	To determine the test characteristics of ELISA and EM in detecting norwalk-like virus (NLV) infection when compared with PCR	Fecal samples collected from patients involved in outbreaks of gastroenteritis in the UK 531 fecal samples	**Test characteristics (%) of ELISA vs. PCR** Sensitivity – 55.5(51.1-60.0) Specificity – 98.3(97.1-99.9) PPV – 95.0(CI not reported) NPV – 76.9 (CI not reported) **Test characteristics (%) of EM vs. PCR** Sensitivity – 23.9(19.5-28.1) Specificity – 99.2(98.3-100) PPV – 93.9(CI not reported) NPV – 70.7(CI not reported) **Identification of NLV as the cause of an outbreak** (% of outbreaks) *When the causative agent was defined by ≥ 2 positive samples* EM – 7.2 ELISA – 18.6 PCR – 41.5 *When the causative agent was defined by ≥ 1 positive samples* EM – 19.6 ELISA – 47.8 PCR – 62.8 **Sensitivity; Specificity of ELISA based on number of samples collected** 2 samples – 52.9; 100 ≥4 – 69.2; 100 ≥6 – 71.4; 100 **Other results** Agreement between ELISA and PCR – 81.8% (Kappa = 0.57) Sensitivity of ELISA was significantly increased when compared with EM (P<0.01)	Power and sample size not reported Prevalence not reported	848_RA
PCR						
Nordgren, J; 2008 [129]	Diagnostic study 2,3	To evaluate 2 novel light-upon-extension (LUX) RT-PCR assays for norovirus genogroup I and II detection	61 stool samples from Sweden. 42 samples from	**Positive samples** *Overall* - 99% correlation between LUX RT- PCR and TaqMan RT-PCR. LUX RT-PCR – 47/103 Conventional PCR – 39/103	TaqMan based RT-PCR described by Kageyama, conventional PCR described by Zintz were used as the	5115_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		and quantification.	Nicaragua. A reference panel of 15 stool samples from Sweden used for external validation of norovirus.	TaqMan RT-PCR – 48/103 *Swedish samples* LUX RT-PCR and TaqMan RT-PCR – 18/61 (100% correlation). *Nicaraguan samples* LUX RT-PCR – 29/42 TaqMan RT-PCR – 30/42 Conventional PCR – 25/42 IDEIA – 24/42 *Reference panel* LUX RT-PCR correctly identified all (n=11) coded controlled specimens. **Detection level** LUX RT- PCR detected ≤ 10^1 to 10^7 genes/reaction, with a theoretical lower limit of ≤ 20,000 viruses/gm of stool.	reference standards for both the Swedish and Nicaraguan samples. IDEIA (DakoCytomation, Copenhagen, Denmark) was used as a reference for the Nicaraguan specimens. Power and sample size not reported.	
DeMedici, D; 2007 [130]	Diagnostic study 1,2,3	To compare IDEIA, a published RT-PCR, and an RT-boosted-PCR in detecting norovirus in stools collected after the end of a gastroenteritis outbreak.	Samples obtained from an outbreak in Italy in December 2002 where 202 patients developed vomiting and/or diarrhea after eating oysters. 41 stool samples.	**Positive samples** ELISA – 6/41 RT-PCR – 6/41 RT-boosted-PCR – 23/41 Results of RT-PCR vs. ELISA (χ^2=0.17; p>0.05). RT-boosted-PCR vs. RT-PCR and ELISA (χ^2=15.06 and 13.47; p<0.05 for both).	IDEIA NLV kit (Dako, Ely, UK) Power and sample size not reported.	049_IL
Hymas, W; 2007 [131]	Diagnostic study 2,3	To evaluate a novel one step real-time eclipse RT-PCR designed to detect norovirus genogroups I and II compared to conventional CDC TaqMan assay.	29 stool samples and 9 RNA samples provided from Utah and North Carolina.	**Correlation between eclipse RT-PCR and TaqMan PCR** 97% overall agreement *By genotype:* Genotype I: 100% correlation Positive by both tests – 4 Negative by both tests – 32 Genotype II: 91% correlation Positive by both tests – 25 Negative by both tests – 10 Discordant results - 3 1 stool sample was positive by eclipse RT-PCR but negative by TaqMan PCR.	CDC Taqman assay was the reference standard. Power and sample size not reported.	130_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				2 samples were positive by eclipse RT-PCR but indeterminate by TaqMan PCR. **Limit of detection and cross reactivity** Sensitivity for GI and GII was approximately 50 copies/reaction.		
Logan, C; 2007 [132]	Diagnostic study 2,3	To test real-time RT-PCR compared to EM in detecting viral gastroenteritis, including norovirus, Sapovirus, and human Astrovirus.	Stool samples from pediatric patients with diarrhea and/or vomiting received at a microbiology laboratory in Ireland, from February 2004-April 2005. 140 stool samples from symptomatic patients. 25 stool samples from asymptomatic patients.	**Positive results** Enteric viruses were detected in 53/140 (38%) samples by RT-PCR vs. 10/140 (8%) by EM. Detection of norovirus increased 200% using RT-PCR over EM. All norovirus samples were genogroup II/4. **Agreement between EM and RT-PCR** *norovirus* Positive by both tests – 5 Negative by both tests – 109 Discordant results – 26 4 were positive by EM but negative by RT-PCR. 22 were negative by EM but positive by RT-PCR. **Test characteristics (%) of RT-PCR vs EM** Sensitivity – 55.6 Specificity – 83.2 PPV – 18.5 NPV – 96.5	EM was the reference standard. Power and sample size not reported.	008_IL
Menton, JF; 2007 [133]	Diagnostic study 1,3	To evaluate a real-time RT PCR and a Reverse Line Blot Hybridization assay developed based on the open reading frame (ORF)1-ORF2 region. The assays were validated using a reference stool panel and then used to investigate two outbreaks of gastroenteritis.	Reference stool panel contained 5 genotypes of GI norovirus and 9 genotypes of GII norovirus. 56 samples from two norovirus outbreaks in Irish hospitals in 2005 and 2006.	**Level of detection** GI – 10^7 to 10^1 molecules of plasmid DNA GII – 5 x 10^7 to 5 x 10^1 molecules of plasmid DNA **Positive results** 26/56 samples positive. All belonged to the GII/4 variant.	Power and sample size not reported.	052_IL
Wolf, S; 2007 [134]	Diagnostic study 2,3	To evaluate a multiplex real-time RT-PCR that distinguishes between norovirus genogroups I, II, and III and targets the	Real time RT-PCR assays evaluated against 45 RNA stool samples collected from	**Positive results** Multiplex real time RT-PCR positive for norovirus GI/1, GI/2, GI/3, GI/4, GI/5, GI/6, G1/7, GII/8, GII/10, GII/12, and GII/17 in different matrices (stool samples, treated and raw sewage, source water, and treated drinking water).	Kageyama real time RT-PCR compared to the multiplex real time RT-PCR. A new bovine NLV,	068_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		junction between open reading frames 1 and 2 compared to Kageyama real time RT-PCR.	2001-2006 known to be positive for norovirus including: 34 human stool samples from New Zealand, 6 raw and 3 treated sewage samples, and single samples of contaminated drinking water and source water. 28 stool samples collected from asymptomatic cattle in May 2006 from farms in New Zealand.	**Agreement between the multiplex real time RT-PCR vs. Kageyama real time RT-PCR** All samples positive by Kageyama RT-PCR also positive by multiplex RT-PCR. Norovirus GI – 2/25 (8%) negative by Kageyama RT-PCR but positive by multiplex RT-PCR. Norovirus GII – 3/17 (18%) negative by Kageyama RT-PCR but positive by multiplex RT-PCR. **Cycle threshold (C_T) values** In 16/20 norovirus GI samples and 26/28 norovirus GII samples positive by both assays, C_T values for the multiplex assay were on average -2.4 C_T U lower than for the Kageyama assay. Remaining 6 samples had higher C_T values using the multiplex assay: 3/3 GI/3 specimens, on average +3.9 C_T U 1/1 GI/7 specimen, +3.5 C_T U 1/1 GII/1 specimen, +3.3 C_T U 1/1 GII/12, +1.4 C_T U **Level of detection** Multiplex real-time RT-PCR detects <10 copies/reaction of norovirus GI/1, GII/3, and GIII/1. Calculated efficiency values of the assay were 0.93, 0.90, and 1.04 based on the slopes of the standard curves of 3.59, 3.60, and 3.23.	Bo/NLV/Norsewood/2006/NZL was identified using multiple real-time RT-PCR. Power and sample size not reported.	
Yoda, T; 2007 [135]	Diagnostic study 2,3	To evaluate a one-step reverse transcription loop-mediated isothermal amplification (RT-LAMP) assay in comparison to routine RT-PCR.	94 samples from Japan obtained during 2004-2006 which had previously been analyzed for bacterial and enteric viruses .	**Agreement between RT-LAMP (OPH) vs. RT-PCR (Eiken)** *All results – RT-LAMP (OPH) vs. RT-PCR (Eiken) # positive/# samples* GI/1 – 1/1 vs. 1/1 GI/3 – 7/7 vs. 3/7 GI/4 – 3/3 vs. 3/3 GI/8 – 4/4 vs. 4/4 GI/11 – 2/2 vs. 0/2 GI/12 – 8/8 vs. 2/8 GII/2 – 10/10 vs. 10/10 GII/3 – 10/10 vs. 10/10 GII/4 – 10/10 vs. 10/10 GII/6 – 10/10 vs. 10/10 GII/12 – 2/2 vs. 2/2 GII/1 – 3/5 vs. 4/5 GII/5 – 4/4 vs. 4/4 GII/7 – 3/3 vs. 3/3	EC NLV GI and GII detection kits (Eiken Chemical Co., Ltd.) Power and sample size not reported.	167_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Sensitivity tests *All results –No. of copies in clinical sample – sensitivity RT-LAMP (OPH) vs. sensitivity RT-PCR (Eiken)* GI/3 – 8 x 10^5 – 8 x 10^1 vs. 8 x 10^4 GI/8 – 8 x 10^4 – 8 x 10^{-1} vs. 8 x 10^{-1} GII/2 – 7 x 10^4 – 7 x 10^0 vs. 7 x 10^1 GII/3 – 8 x 10^3 – 8 x 10^1 vs. 8 x 10^3 GII/4 – 5 x 10^6 – 5 x 10^1 vs. 5 x 10^1 GII/6 – 2 x 10^5 – 2 x 10^2 vs. 2 x 10^2 The results of RT-LAMP correlated well to RT-PCR.		
Antonishyn, NA; 2006 [136]	Diagnostic study 2,3	To evaluate a one-step real-time multiplex RT-PCR compared to conventional PCR.	150 stool samples from cases of acute nonbacterial gastroenteritis between November 2004-March 2005. 50 archived samples used to compare TaqMan PCR with a separate RT using random primers or a single-step RT-PCR. 100 samples used to compare sensitivity of multiplex PCR with conventional RT-PCR.	**Agreement between one-step multiplex RT-PCR vs. conventional PCR** Both tests positive - 59 Both tests negative - 27 Discordant results – 14 14 were negative by conventional RT-PCR but positive using one-step real-time RT-PCR. Sensitivity of multiplex RT-PCR 19% higher than manual extraction with conventional RT-PCR.	Power and sample size not reported.	223_IL
Trujillo, A; 2006 [18]	Diagnostic study 2	To compare the test characteristics of Taqman RT-PCR with conventional RT-PCR for the detection of GI, GII and GIV strains	Stool specimens from sporadic cases and outbreaks of gastroenteritis. Water samples from outbreaks of	**Test characteristics of Taqman RT-PCR vs. conventional RT-PCR** *Stool specimens* TP – 65 TN – 27 FP – 0 FN – 0	Power and sample size not reported	4225_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			gastroenteritis in the US. 92 stool samples and 33 water samples	By means of serially diluted norovirus RNA transcripts, a potential detection limit of < 10 transcript copies per reaction mixture was observed with the GII assay and a potential detection limit of < 10 transcript copies per reaction mixture was observed with the GI assay. *Water specimens* 8/33 specimens were found to be positive. No test characteristics were reported		
Hohne, M; 2004 [137]	Diagnostic study 2,3	To evaluate a one-tube RT-PCR method, which would prevent the product carryover, in comparison to an in-house RT-PCR.	70 positive stool samples from outbreaks in Germany and 34 European samples collected over a 4 year period (1997-2000).	**Positive detection by one-tube RT-PCR of previously identified positive stool samples** Overall 93% detection including isolates of 4 different GGI and 7 different GGII genotypes. German outbreaks – 66/70 (94.3%) samples were positive including those of 6 different GGII genotypes and 2 different GGI genotypes. European samples –31/34 (91%) samples were positive including those of 4 different GGI genotypes and 7 different GGII genotypes.	Samples had previously been diagnosed positive via PCR or EM.	3090_IL
Rohayem, J; 2004 [138]	Diagnostic study 2,3	To evaluate a single-step multiplex RT-PCR compared to simplex RT-PCR for norovirus, Astrovirus, and Adenovirus.	460 stool samples from infants or children in Germany with non-Rotavirus acute gastroenteritis during 14 months (March 1997 to May 1998): 257 archived samples 203 rotavirus-negative samples collected prospectively	**Detection limit of the multiplex RT-PCR** Detection limit of 10^2 copies for norovirus and Astrovirus RNA transcript, and adenovirus plasmid DNA. **Positive tests** *Retrospective collection (n=257)* norovirus: Simplex RT-PCR – 17 (6.6%) Multiplex RT-PCR – 17 (6.6%)	IDEIA Astrovirus and norovirus genogroup I and II, Dako, Germany. Acute gastroenteritis defined as ≥ 1 episode of diarrhea (watery or loose stools in a 24 hour period), with vomiting and/or other symptoms (fever, nausea, abdominal pain, and/or cramps).	668_IL
Schmid, M; 2004 [139]	Diagnostic study 2,3	To evaluate a real-time RT-PCR assay on the LightCycler (LC) with SYBR Green detection and melting curve analysis (T_m)	52 stool samples from Germany between January-April 2003:	**Positive cases** Antigen ELISA – 18/52 (34.6%) samples positive Real-time PCR and nPCR – 26/52 (50%) samples positive **Agreement between real-time PCR, antigen ELISA, and nPCR**	RIDASCREEN Norwalk-like virus kit (R-Biopharm, Darmstadt, Germany) and well-established nested PCR used as reference standards.	655_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		compared to RIDASCREEN.	38 from patients in gastroenteritis outbreaks 14 single sporadic cases in children <5 years of age 13.1% were < 10 years of age, 39.5% between 10-60 years, and 47.4% were > 60 years old	Positive by all three tests – 9 Negative by all three tests – 17 Positive by real-time PCR and nPCR but negative by ELISA – 17 Positive by ELISA but negative by real-time PCR and nPCR – 9 100% correlation between real-time PCR and nPCR. **Test characteristics compared to nested PCR** ELISA – sensitivity 9/26 (34.6%) and specificity 17/26 (65.3%) Real-time PCR – sensitivity 26/26 (100%) and specificity 26/26 (100%) Difference in sensitivity between ELISA and real-time PCR (34.6% vs. 100%; p<0.001) PCR-based procedures are more sensitive and specific than antigen ELISA.		
Vinje J, 2003 [140]	Diagnostic study 2,3	To evaluate the performance of 5 different RT-PCR assays for the detection of norovirus in an international collaborative study.	5 laboratories in 5 countries in the European consortium tested stool specimens collected over a 4 year period (1997 to 2000) from both outbreaks and sporadic cases of gastroenteritis and had previously been tested by RT-PCR and EM. 91 stool samples – 82 norovirus positive and 9 controls	**Overall characteristics** Norovirus detected by at least 1 RT-PCR assay in 69 (84%) of the samples that originally tested positive. Overall sensitivity: 52-73% overall Overall sensitivity by genotype: 54-100% for genogroup I vs. 58-85% for genogroup II Overall sensitivity by test: p1 67% vs. p2 59% vs. p5 52% vs. p6 73% vs. p13 60% 64% of false-negative results in a set of diluted stools (n=20) that may have lost quality upon storage. Sensitivity improved when these samples were excluded. No single assay was best although the p1 assay demonstrated the most satisfactory overall performance. **Sensitivity by genotype** GI genotype: p1 100%, p2 54%, p5 85%, p6 92%, p13 85% GII genotype: p1 75%, p2 75%, p5 58%, p6 85%, p13 69%	PCR assays: Laboratory p1 use primer pair JV12-JV13 Laboratory p2 use NVp110 followe by PCR with the primers NVp110, Ni, an NVp69 Laboratory p5 used two RT-PCR assays with E3-Ni an E3-Ando primer pairs respectively Laboratory p6 use nested RT-PCR assay format Laboratory p13 use single tube RT-PCR targeting the 3' en of ORF1 (region B)	IL_836
Tatsumi, M; 2002 [141]	Diagnostic study 1,2	To determine the sensitivity and specificity of RT-PCR-ELISA for detecting Norwalk virus when compared with conventional PCR	Children aged 2 months to 14 years (mean age 28.7 months) admitted with acute gastroenteritis. Study was	**Test characteristics** All 46 stool specimens that were positive for viruses other than Norwalk by RT-PCR-Southern hybridization were identified as such by RT-PCR-ELISA All 30 stool specimens that were positive for Norwalk virus by RT-PCR-Southern hybridization were identified as such by RT-PCR-ELISA	Power and sample size not reported	911_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			conducted in Japan. 93 children; 154 stool samples	In terms of detection limits, the sensitivity of RT-PCR-ELISA was the same as that of conventional PCR with Southern hybridization and was 10-100 times more sensitive than the conventional PCR. In 93 other stool specimens from hospitalized patients, 20% samples were found to be positive with RT-PCR-ELISA and 13% were found to be positive with conventional PCR.		
O'Neill, H; 2001 [142]	Diagnostic study 1	To assess the use of nRT-PCR in detecting norovirus	31 outbreaks in various settings including nursing homes, small district hospitals, large general hospitals, a ferry ship, hotels, restaurants and staff canteens. Study was conducted in the UK. Total N not reported	**Number of samples positive for norovirus** (follow-up not reported) *All results number positive/number tested; percentage positive* Ferry ship – 8/10; 80 (All 10 specimens negative for virus by EM) Country hotel – 14/17; 82 (2 positive by EM) Nursery school – 7/12; 50 City hotel – 3/3; 100 Restaurant – 8/32; 25 Restaurant – 7/7; 100 Large hospital – 14/116; 12 Psychiatric hospital – 27/35; 77 Restaurant – 5/5; 100 Large hospital – 16/58; 27 Medical ward – 9/17; 53 District hospital – 8/32; 25 Medical ward – 3/5; 60 Nursing home – 2/2; 100 Nursing home – 2/2; 100 Large Hospital – 7/37; 19 District hospital – 2/2; 100 Care of elderly ward – 9/12; 75 Nursing home – 2/5; 40 Hotel – 8/10; 80 Hotel – 6/12; 50 Large area hospital – 12/67; 18 Hotal – 3/3; 100 Regimental reunion – 9/11; 82 Leisure center – 4/6 - 66	Power and sample size not reported Simultaneous testing with EM was done only for the first two outbreaks	983_RA
NASBA						
Jean, J; 2003 [143]	Diagnostic study	To evaluate the sensitivity of NASBA primers specific	Stool specimens from regional	**Sensitivity of NASBA derived RT-PCR** Comparable to other RT-PCR protocols. Consistent detection of viral RNA by RT-	Power and sample size not reported	5780_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
	2	for the GII norovirus adapted for RT-PCR and the effect of transcriptional enhancement (TE) both followed by electrochemiluminescence (ECL).	gastroenteritis outbreaks. Study conducted in North Carolina Not reported	PCR was obtained up to approximately -7 log_{10} dilution with ECL readings ranging from 3.2 to 3.6 log_{10} **Sensitivity of NASBA derived RT-PCR/TE** A detection limit of ≥1 log_{10} was observed with ECL readings ranging from 4.3 to >7.0 log_{10}		
Greene, S; 2003 [144]	Diagnostic study 1,2	To determine the test characteristics of a rapid NASBA when compared with RT-PCR for the detection of Norwalk-like viruses (NLV)	Volunteers challenged with norovirus. Demographics not reported. Study setting unclear. 15 stool specimens	**Detection limits** The NASBA assay could consistently detect 10^5-10^2 detectable units of NLV RNA in a stool filtrate. **Cross-reactivity** Cross-reactivity studies with a representative panel of other enteric pathogens were negative **Sensitivity** 100% **Specificity** 50% **Accuracy** 67%	Power and sample size not reported	856_RA

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Diagnostic methods – Food specimens

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
PCR						
Tian, P; 2006 [145]	Diagnostic Study 2	To develop a sensitive RT – Immuno PCR method for detecting norovirus capsid protein in food samples	Food samples contaminated with norovirus. Study was conducted in the US. N/A	**Detection limit of RT-Immuno PCR compared with ELISA and conventional RT-PCR** Viral RNA could be detected in samples diluted 1000 fold when compared with ELISA and 10-100 fold when compared with RT-PCR using fecal and food samples	Power and sample size not reported	4285_RA

Diagnostic methods – Water specimens

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
PCR						
Wolf, S; 2007 [134]	Diagnostic study 2,3	To evaluate a multiplex real-time RT-PCR that distinguishes between norovirus genogroups I, II, and III and targets the junction between open reading frames 1 and 2 compared to Kageyama real time RT-PCR.	Real time RT-PCR assays evaluated against 45 RNA samples collected from 2001-2006 known to be positive for norovirus including: 34 human stool samples from New Zealand 6 raw and 3 treated sewage samples Single samples of contaminated drinking water and source water. 28 stool samples collected from asymptomatic cattle in May 2006 from farms in New Zealand.	**Positive results** Multiplex real time RT-PCR positive for norovirus GI/1, GI/2, GI/3, GI/4, GI/5, GI/6, G1/7, GII/8, GII/10, GII/12, and GII/17 in different matrices (stool samples, treated and raw sewage, source water, and treated drinking water). **Agreement between the multiplex real time RT-PCR vs. Kageyama real time RT-PCR** All samples positive by Kageyama RT-PCR also positive by multiplex RT-PCR. norovirus GI – 2/25 (8%) negative by Kageyama RT-PCR positive by multiplex RT-PCR. norovirus GII – 3/17 (18%) negative by Kageyama RT-PCR positive by multiplex RT-PCR. **Cycle threshold (C_T) values** In 16/20 norovirus GI samples and 26/28 norovirus GII samples positive by both assays, C_T values for the multiplex assay were on average -2.4 C_T U lower than for the Kageyama assay. Remaining 6 samples had higher C_T values using the multiplex assay: 3/3 GI/3 specimens, on average +3.9 C_T U 1/1 GI/7 specimen, +3.5 C_T U 1/1 GII/1 specimen, +3.3 C_T U 1/1 GII/12, +1.4 C_T U **Level of detection** Multiplex real-time RT-PCR detects <10 copies/reaction of norovirus	Kageyama real time RT-PCR compared to the multiplex real time RT-PCR. A new bovine NLV, Bo/NLV/Norsewood/2006/NZL was identified using multiple real-time RT-PCR.	068_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				GI/1, GII/3, and GIII/1 N/A. Calculated efficiency values of the assay were 0.93, 0.90, and 1.04 based on the slopes of the standard curves of 3.59, 3.60, and 3.23.		
Trujillo, A; 2006 [18]	Diagnostic study 2	To compare the test characteristics of Taqman RT-PCR with conventional RT-PCR for th edetection of GI, GII and GIV strains	Stool specimens from sporadic cases and outbreaks of gastroenteritis. Water samples from outbreaks of gastroenteritis in the US. 92 stool samples and 33 water samples	**Test characteristics of Taqman RT-PCR vs. conventional RT-PCR** *Stool specimens* TP – 65 TN – 27 FP – 0 FN – 0 By means of serially diluted norovirus RNA transcripts, a potential detection limit of < 10 transcript copies per reaction mixture was observed with the GII assay and a potential detection limit of < 10 transcript copies per reaction mixture was observed with the GI assay. *Water specimens* 8/33 specimens were found to be positive. No test characteristics were reported	Power and sample size not reported	4225_RA
Concentration method						
Beuret, C; 2003[146]	Diagnostic study None	To test a method for concentration of enteric viruses from water, whereby viruses are directly lysed after filtration on a negatively charged membrane. This method does not have the rinsing, elution, centrifugation and flocculation steps used in older protocols.	Water samples. Study was conducted in Switzerland. Not reported	**Detection limit** A sensitivity of a 10^6 fold dilution could be detected for norovirus which compared favorably to the older protocol	Power and sample size not reported	5853_RA

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GRADE TABLE Q2 WHAT ARE THE BEST METHODS TO IDENTIFY A NOROVIRUS OUTBREAK IN A HEALTHCARE SETTING?

Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**		
Kaplan criteria	Sensitivity*	1 DIAG [116]	68%	High	0	0	0	-1	0	Moderate	Moderate
	Specificity*	1 DIAG [116]	99%	High	0	0	0	-1	0	Moderate	
	PPV*	1 DIAG [116]	97%	High	0	0	0	-1	0	Moderate	
	NPV*	1 DIAG [116]	82%	High	0	0	0	-1	0	Moderate	
Specimen collection	Number of positive samples needed*	1 DIAG [117]	Using ELISA, 1 positive sample for 2-6 samples tested was needed to assign norovirus as the causative agent Using RT-PCR, 1 positive sample for 2-4 samples tested or 2 positive samples for 5-11 samples tested were needed to assign norovirus as the causative agent	High	-1	0	0	-1	0	Low	Low
	Sensitivity*	2 DIAG [117,119]	ELISA: 2 tested samples – 53-57%; 3 tested samples – 72%; ≥4 tested samples – 69%; 5 tested samples – 88%; 6 tested samples – 92%; ≥6 tested samples – 71% RT-PCR: 2 tested samples – 84%; 3 tested samples – >90%; 5 tested samples – 92%; 6 tested samples – 96%	High	-1	0	0	0	0	Moderate	
	Specificity*	1 DIAG [119]	ELISA: 2 to ≥6 samples – 100%	High	-1	0	0	-1	0	Low	

* These outcomes are considered the most critical by the guideline developers.
** These modifiers can impact the GRADE by 1 or 2 points

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Q3: What patient interventions best prevent or contain norovirus outbreaks in the healthcare setting?

EVIDENCE TABLE Q3

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Virus shedding						
Murata, T; 2007 [148]	Prospective controlled study 2,3,4	To describe children infected with norovirus and duration of viral shedding.	Children with acute gastroenteritis who presented to a pediatric clinic in Japan. Median age 18 months (range 3 months to 7 years). 71 (59 included for analysis)	**Symptoms** Vomiting 94.9% Diarrhea 94.9% Fever 20.3% **Severity of illness** Overall duration of illness – median 5 days *All results children <2 years old vs 2-5 years old; p value* Duration of illness in days – 7 vs. 3.5; 0.0069 Maximum number of stools – 7 vs. 3; 0.0078 20 point severity score developed for rotavirus – 11 vs. 8; 0.0031 **Period of viral shedding (n=26)** Overall in days – median, 16 (range, 5-47) Patients ≤6 months of age vs >1 year old in days – 42 vs. 10; p=0.0475 Shedding > 2 weeks in children <1 year vs. 1 year vs. 2-3 years of age – 6/8 (75%) vs. 5/7 (71.4%) vs. 2/8 (25%) Patients ≤6 months – 3/5 shed for long periods (42, 44, and >47 days)	Acute gastroenteritis was defined as the presence of either diarrhea or vomiting at presentation between November 1, 2002 to December 31, 2002. norovirus was diagnosed using RT-PCR. Power and sample size not reported.	176_IL
Rockx, B; 2002 [149]	Prospective controlled study (with a nested case control design) 1,3,4	To describe the natural history of CaCV infections in humans.	The case definition of gastroenteritis was ≥ 3 loose stools in 24 h, vomiting ≥ 3 times in 24 h, loose stools with two additional symptoms or vomiting with two additional symptoms. Additional symptoms included diarrhea, vomiting,	**Ages affected (until day 22 after the onset of symptoms)** Proportion of norovirus gastroenteritis cases was highest in children (age 0.5-17 yrs; proportion 14-19%) and elderly (age ≥ 65 yrs; proportion 13%) **Clinical symptoms** Clinical manifestations reported by 99 cases with norovirus infection were: Diarrhea – 87% Vomiting – 74% Abdominal pain – 51% Abdominal cramps – 44% Nausea – 49%	Clinical information was obtained from medical diaries kept by patients during the 4 weeks after the onset of symptoms. norovirus was detected by RT-PCR. Power and sample size	934_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			nausea, fever, abdominal pain, abdominal cramps, and blood or mucus in stool. Healthy control subjects were selected for the same period and matched with cases by age and geographical location. Demographics not reported – community based population registered through the Netherlands Institute of Primary Health Care. Study conducted in Netherlands. 4860	Fever – 32% Mucus in stool – 19% Bloody stool – 0% **Median duration of symptoms (days)** Overall – 5 Age < 1 yr – 6 Age 1-4 yrs – 4 Age 5-11 yrs – 5 Age ≥ 12 yrs – 3 **Percentage of infected cases shedding virus** On day 1 – 78% On day 22 – 26% (Highest in newborns aged < 1 yr)	not reported	
Marshall, J; 2001 [150]	Descriptive study (Case report) N/A	To report a case excreting high levels of NLV in the absence of any clinical symptoms of gastroenteritis.	An elderly woman (71 yrs) who contracted norovirus infection during an outbreak in Australia 1	**Asymptomatic shedding** (day 2 and day 5 after resolution of symptoms) About 5 x 10^5 NLV virions per gram of feces were detected. These were closely related to Camberwell virus, a GII NLV	Stool specimens were analyzed using EM and RT-PCR	1056_RA
Hedlund, 1998; [151]	Descriptive study 1,2,3,4	To describe the role of NLV in pediatric diarrhea and describe asymptomatic shedding	All cases with stool samples positive for NLV 77 cases – 33 community acquired, 47 nosocomial	**Asymptomatic shedding** 5 of 17 children examined repeatedly excreted virus after the symptoms had subsided.	NLV identified by EM	3554_RA
Chiba, S; 1980 [152]	Descriptive study	To evaluate viral shedding and duration	Stool specimens were obtained from CaCV outbreaks in an	**Stool specimens positive for CaCV** Overall – 29/61 (48%)	Illness not defined	2140_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
	1,3,4	of illness.	orphanage in Sapporo, Japan. 61 stool samples.	*Symptomatic patients* *All results – positive/tested (%)* Obtained before onset of illness – 0/7 (0%) Obtained within 4 days after onset of illness – 18/19 (95%) Obtained days 5-10 – 7/14 (50%) *Asymptomatic patients* *All results – positive/tested (%)* 3/10 (30%)		
Recovery of norovirus						
Dalling, J; 2004 [153]	Systematic review 1,2,3,7	To identify if environmental contamination contributes to prolonged or recurring outbreaks and to clarify appropriate terminal cleaning measures.	Search of Health Electronic Resources Online in Northern England (HEROINE). Databases included Books@Ovid, MyOvid@Hand, journals@OvidFullText, Cochrane Database of Systematic Reviews, American College of Physicians Journal Club, DARE and CCTR, Allied and Complementary Medicine (AMED), Cumulative Index Nursing and Allied Health, EMBASE, PREMEDLINE and MEDLINE (1996 to present), British Nursing Index, and the National Research Register. Websites included the Department of Health, Public Health	**Transmission due to environmental contamination** Identified that environmental contamination occurred during outbreaks – 5/11 (55%) Environmental contamination considered cause of transmission – 9/11 (82%) Identified environmental contamination as cause of prolonged or recurring outbreaks – 0/11 (0%) **Environmental sampling** Identified environmental contamination – 3/5 studies 76/210 (36%) swabs positive from curtains, cushions, carpets, lockers, commodes, toilet rims, seats and handles, taps, basins, telephones, door handles, physiotherapy instrument handle, and horizontal surfaces above and below 1.5 meters including light fittings and mantelpieces. **Laboratory testing methods** Studies using RT-PCR – 100% Two studies recognized that RT-PCR positive for norovirus does not necessarily represent viable virus. **Sampling methods** *Methods of specimen collection* 3/5 studies used saline or transport medium moistened swabs for sampling; 0%, 31%, and 42% samples were positive. 1/5 studies used dry swabs; 0% samples were positive. 1/5 studies used wet and dry swabs; 13% samples were positive. There appeared to be more positive swabs in studies that used moistened swabs. *Timing of collection* Unclear in 3/5 studies whether swabs samples were collected before or after environmental cleaning.	Sample size and power not reported.	3958_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			Laboratory Service, CDC, Infection Control Nurses Association, and the World Health Organization. Search terms included ("Norwalk" OR "norovirus" OR "Winter Vomiting" OR "Viral gastroenteritis" OR "SRSV" OR "Calicivirus") AND ("Outbreak" OR "Management" OR "Environment" OR "Disinfect" OR "Decontaminate" OR "Decontamination" OR "Clean" OR "Contaminate" OR "Contamination" OR "Precautions" OR "Control"). Limited to English language. Articles excluded if unrelated to viral gastroenteritis or environmental contamination; or focused on the source of infection (i.e., food borne gastroenteritis) or laboratory diagnosis techniques. References of articles reviewed to identify additional relevant articles. Articles critiqued using	*Selection of sampling sites* 4/5 studies did not explain why certain sites were swabbed and did not identify total swabs taken from each site. **Virus survival** 1 study reported 21-28 day survival in a dried state at room temperature. 2 studies reported virus survival for at least 12 days; 1 paper repeated sampling and did not find virus in a previously contaminated environment after 5 months. 1 study suggested that carpets may have viable virus for at least 12 days that is not removed by routine vacuum cleaning. **Changing curtains** 2 studies recommend changing curtains, but there is no evidence examining impact of curtain changes on duration or recurrence of outbreaks. **Carpet decontamination** 3 studies advised steam cleaning of carpets but there is no evidence examining impact of steam cleaning on norovirus survival. 1 study recommended steam cleaning carpets and changing curtains as Category II "strongly recommended and viewed as effective by experts in the field and by the working group, based on strong rationale and suggestive evidence, even though definitive studies may not have been done." 1 study identified carpets as a cleaning priority due to high levels of norovirus by RT-PCR. **Cleaning and disinfection** 4 studies recommended and/or performed terminal cleaning. 3 papers recommended a cleaning or disinfectant agent; all recommended hypochlorite 1000 ppm. Chadwick et al. recommendations based on Doultree et al. which recommended glutaraldehyde 0.5% and iodine 0.8%, but not 75% ethanol, quarternary ammonia 1:10 and anionic detergent 1%. Doultree et al. gives no reference for the recommendation. 2/5 studies that studied environmental sampling reported decontamination methods; both used 500 ppm hypochlorite, which is no longer advised in current guidelines. 0/5 studies evaluated the effectiveness of currently used disinfectants. **Specific areas for decontamination** 4 studies listed recommendations including decontamination of frequently handled objects, taps, door handles, toilets and bathrooms, bath rails, toys, carpets, and surfaces		

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			a tool adapted from Cormack. 11 articles. 5 articles included data from environmental sampling.	contaminated by stools or vomit. The only area recommended by > 1 study was bathrooms, despite 2 papers identifying by swabs contamination of both toilets and door handles.		
Wu, H; 2005 [154]	Prospective controlled study 1,3,4	To identify the likely mode of transmission, characterize risk factors for illness, and evaluate for environmental contamination in a norovirus outbreak.	Residents and employees of a long term care facility in Philadelphia. 97% residents were male, median age 77 yrs (range 40-103), 87% had a cardiovascular or chronic pulmonary condition, 28% had a gastrointestinal disorder, 24% had diabetes and 70% had organic brain disease, dementia or a psychiatric disorder. 246 residents and 246 employees	**Cases (follow up 41 days)** 127 residents and 84 employees met the case definition. **Transfer to acute care hospital (follow up 41 days)** *All results RR(95% CI) with non-case residents used as control* All case residents – 2.2(1.1-4.3) Case-residents during the early period – 1.7(0.8-3.5) Case-residents during the late period – 3.8(1.8-8.0) **Mortality (follow up 41 days)** *All results RR(95% CI) with non-case residents used as control* All case residents – 1.2(0.5-2.9) Case-residents during the early period – 1.0(0.4-2.5) Case-residents during the late period – 2.1(0.8-5.9) **Positive stool or vomitus samples (follow up 41 days)** All 8 stool samples and 1 of 3 vomitus samples from cases tested positive for norovirus **Environmental contamination (follow up 41 days)** **10 samples tested, 5 positive and match clinical sample genotype** Positive swabs – toilet seat, dining room table, elevator button, bed rail, toilet seat and hand rails Negative swabs – table, elevator button, handrail, wheelchair, bedrail, bedside table	Cases were defined as: three or more occurrences of loose stools in a 24 hr period OR one or more episodes of unexplained vomiting OR a physician diagnosis of acute gastroenteritis Stool/virus samples and environmental swabs were tested with RT-PCR 181 employees (74%) returned the surveys. "Early period" was defined as symptom onset before or during the peak of the outbreak, while "late period" was defined as after the early period Power and sample size not reported	406_RA
Jones, E; 2007 [155]	Descriptive study 1,2,3,4	To describe the role of fomite contamination during a	Participants in three consecutive 5-night educational boating trips. 36/54 were females. Study was	**Positive fomites** Bathroom surfaces – 5/6 (83%) Kitchen surface samples – 2/5 (40%) Doorknob samples – 3/3 (100%)	Random samples from interior boat surfaces and toilet reservoirs were collected by swabbing surfaces.	95_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		norovirus outbreak	conducted in Arizona, USA 54	Samples of onboard potable water supplies were all negative	norovirus was confirmed using RT-PCR. Stool samples were not available.	
Clay, S; 2006 [156]	Descriptive Study 3	To assess the survival of FCV on fomites. FCV was used as a surrogate.	Fomites – keyboard keys, computer mouse, brass disks (as a representative for water faucets or door knobs), telephone buttons, telephone receiver and telephone wire. N/A	**Time to 90% reduction in viral titer (hrs) (follow up 144 hr)** Keyboard keys – 0 to 4 Computer mouse – 0 to 4 Brass – 0 to 4 Telephone buttons – 12 to 24 Telephone receiver – 4 to 8 Telephone wire – 0 to 4 **Time to undetectable virus (hrs) (follow up 144 hr)** Keyboard keys – 8 to12 Computer mouse – 24 to 48 Brass – 8 to 12 Telephone buttons – 48 to 72 Telephone receiver – 48 to 72 Telephone wire – 24 to 48	361_RA	
Gallimore, C; 2006 [157]	Descriptive Study 1,3	To determine if gastroenteric viruses were present on surfaces and equipment. Environmental sampling was done using swabs and subsequent nucleic acid extraction and RT-PCR assays.	Swab sites in a pediatric primary immunodeficiency unit that were chosen to represent areas commonly in contact with hands. Three patients were also studied (two were patients with immunodeficiency < 1 month of age; one was a 4 yr old patient with lactose intolerance) 11 swab sites and 3 patients	**Environmental swabs positive for norovirus (every 2 weeks during a 6 month period)** *All results number of positive swabs/number of swabs taken for each swab site* Staff toilet door handle – 1/14 Staff toilet taps – 4/14 Telephone outside rooms 3 and 4 which contained the patients– 1/14 Microwave oven – 3/14 Room 4 outside flow syringe pump – 3/14 Room 3 outside flow syringe pump – 3/14 Parents' phone – 5/14 Parents' room door handle – 2/14 Game console – 1/14 Parents' toilet door handle – 1/14 Parents' toilet taps – 4/14 Recommendation: consider chlorine-based disinfectant for hard surfaces **norovirus detected in stool of patients with PCR (during a 6 month period)** norovirus was detected in the stool of 1 of the 3 patients	360_RA	

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Kuusi, M; 2002 [158]	Descriptive study 1	To conduct an epidemiological, environmental and virological investigation of an outbreak.	Guests and staff at a rehabilitation center. Environmental samples were collected from water supply system, swimming pools, surfaces of 2 accommodation rooms with symptomatic guests, 2 sauna rooms, 2 bathrooms, 2 gym rooms, ultrasound treatment room, main entrance and restaurant. 280	**Positive environmental samples (during ~1 month)** Ultrasound physiotherapy instrument's handle A bathroom door handle in a room of a symptomatic guest A toilet seat in a room of a symptomatic guest A toilet seat in a public toilet for women The environmental strain was identical to the strain detected from patient samples. Water samples and swimming pools were negative.	Detected using RT-PCR	914_RA
Cheesbrough, J; 2000 [159]	Descriptive study 1,2,3,4	To investigate the pattern of norovirus contamination during and after an outbreak	Guests at a hotel in England. Demographic characteristics not reported. 144 environmental swabs	**Positive fomites during outbreak (61/144)** *All results positive fomites/total fomites; %* Carpet (known recent vomit) – 5/8; 62 *Carpet had been cleaned with detergent, water and then vacuumed prior to testing Carpet (no known recent vomit) – 9/12; 75 Toilet rims or seats – 8/11; 73 Toilet handles, taps, basins and surfaces – 13/33; 39 Horizontal surfaces (outside toilet) below 1.5 m, e.g. tables, ledges – 11/29; 37 Horizontal surfaces (outside toilet) above 1.5 m, e.g. mantle piece, light fittings – 6/12; 50 Frequently handled objects, phones, door handles – 7/29; 24 Soft furnishings, cushions, curtains, etc – 2/10; 20 **Post-outbreak follow-up** (5 months after outbreak) 0/144 positive samples	norovirus was confirmed by RT-PCR	1098_RA
Schvoerer, E; 1999 [160]	Descriptive study 3	To describe an outbreak of norovirus gastroenteritis	Patients at a re-education ward of a hospital in France. 6	**Symptoms** Nausea – 6/6 Vomiting – 2/6 Abdominal pain – 6/6 Fever – 2/6 **Positive water samples** 3/7 samples tested were positive for norovirus	norovirus was confirmed using RT-PCR on stool samples Outbreak was associated with contaminated drinking water	1280_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Positive stool samples 3/6 samples tested were positive for norovirus		
Green, J; 1998 [161]	Descriptive study 1,3	To describe a norovirus outbreak occurring in a hospital for the mentally ill	Patients and staff at a hospital for the mentally ill in the UK. The environmental sampling sites were all within dormitory 4, a bay in which symptomatic patients were cohort nursed. 28 patients and staff; 36 environmental swabs	**Positive environmental samples** 11/36(27%) environmental swabs collected on the affected ward were positive for SRSV on day 3 of outbreak. The sites shown to be contaminated included lockers, curtains and commodes, all in proximity to symptomatic patients	norovirus in environmental samples was characterized using RT-PCR	1317_RA
Mattison, K; 2007 [112]	Basic Science Study N/A	To assess virus survival in foods and on sufaces. FCV was used as a surrogate for norovirus to investigate its survival.	Food (lettuce, strawberry, ham) and metal surfaces. Study was conducted in Canada. N/A	**Survival of virus** *At 30 min* Lettuce – 20% Strawberry – 1% Ham – 43% Metal disk – 11% *At 7 days* There was a signifiant reduction in viral titer after 7 days for all samples at both room temperature (RT) and 4°C (P<0.05). **Comparison of virus survival at RT and 4°C (on day 7)** Lettuce – undetectable at RT; 1% survival at 4°C; statistical differences were not reported Strawberry – undetectable at both RT and 4°C; survived for 5 days at 4°C, compared with 1 day at RT; statistical differences were not reported Ham – P>0.05 Metal disk – P>0.05 **Comparison of virus survival among the different samples** The survival on ham was significantly greater when compared to all other surfaces at both temperatures (P<0.05)	154_RA	
D'Souza, D; 2006 [162]	Basic science study N/A	To investigate the stability of norovirus on various food	Stainless steel, formica and ceramic coupons sterilized by autoclaving were used	**Detection of virus** *1. norovirus* Could be detected on all 3 surfaces for up to 7 days post inoculation	Virus recovery was evaluated by RT-PCR (for norovirus and norovirus RNA) or by	337_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		preparation surfaces and to evaluate the degree of virus transfer from these surfaces to a model ready-to-eat food (lettuce). Artificial contamination was done with: 1) norovirus, 2) norovirus RNA, or 3) FCV.	as the environmental surfaces N/A	<u>*2. norovirus RNA*</u> Not detected on stainless steel beyond 24 hrs. Data for the other surfaces not reported <u>*3. FCV*</u> Could be detected on all 3 surfaces for up to 7 days post inoculation, with 6-7 log_{10} drop in virus titer over the 7 day period. There were no significant differences in recovery between the three surfaces tested (P>0.05). Statistically significantly higher recovery at time point 0 (P<0.05), but virus recovery at 1, 2, 4, 8 and 24 hours not significantly different from each other (P>0.05). Virus recovery at 24 and 48 hrs not significantly different from each other (P>0.05). Virus recovery at 7 days significantly lower from prior time points (P<0.05). **Virus transfer between stainless steel surfaces** *All results are number of lettuce samples testing positive for norovirus at 10, 30 and 60 min virus drying time* Dry lettuce – 9/9; 0/9; 0/9 Wet lettuce – 8/9; 6/9; 7/9 Pressure applied to the samples did not have a statistically significant effect on transfer. Significantly higher transfer to wet lettuce (P<0.01). For dry lettuce, the transfer at time 0 was statistically significantly higher than at times 30 and 60 min (P<0.05). For wet lettuce, the transfer at time 0 was statistically significantly higher than at times 10, 30 and 60 min (P<0.05).	plaque assay (for FCV) using feline kidney cells	
Paulson, DS; 2005 [163]	Basic science	Current food code requires food handlers to wear gloves when handling ready-to-eat food. The study objective was to evaluate the amount of virus transferred from contaminated surfaces to	A simulation study was performed to determine the amount of virus transferred from contaminated stainless steel surfaces, spatulas, forks, cutting boards, door knobs, and lettuce to vinyl food handler gloves. Objects were inoculated with CaCV strain F9 viral suspension, and air dried for 5 or 15	**Virus transferred** <u>*All results – Baseline; post-transfer recovery in virus log_{10} values*</u> *5 minute dry time* Average baseline – 5.9; post-transfer recovery – 4.7-5.4 Spatula – 5.9 ± 0.23; 5.4 ± 0.03 Lettuce – 5.9 ± 0.23; 5.1 ± 0.20 Fork – 5.9 ± 0.23; 5.3 ± 0.15 Cutting board – 5.9 ± 0.23; 5.3 ± 0.13 Door knob – 5.9 ± 0.23; 4.7 ± 0.07 Stainless steel coupon – 5.9 ± 0.23; 5.2 ± 0.11 *15 minute dry time – All results virus log_{10} values* Average baseline – 5.8; post-transfer recovery – 4.9-5.3 Spatula – 5.8 ± 0.31; 5.3 ± 0.15 Lettuce – 5.8 ± 0.31; 5.3 ± 0.04 Fork – 5.8 ± 0.31; 5.2 ± 0.23	As few as 10-100 viral particles may be sufficient to cause infection so there is definite risk for transmission by food handlers wearing gloves. Remaining questions: 1) How long can norovirus remain on inanimate surfaces and still be infectious and 2) how much virus is transferred from gloved	4356_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		gloved hands.	minutes. A gloved fingertip was pressed lightly into the contaminated area for 5-10 seconds. The baseline viral load on the test items and the viral load recovered from gloved hands post-transfer were assessed.	Cutting board – 5.8 ± 0.31; 5.2 ± 0.09 Door knob – 5.8 ± 0.31; 4.9 ± 0.18 Stainless steel coupon – 5.8 ± 0.31; 4.9 ± 0.13	hands to food?	
Components of an outbreak prevention/containment program						
Dalling, J; 2004 [153]	Systematic review 1,2,3,7	To identify if environmental contamination contributes to prolonged or recurring outbreaks and to clarify appropriate terminal cleaning measures.	Search of Health Electronic Resources Online in Northern England (HEROINE). Databases included Books@Ovid, MyOvid@Hand, journals@OvidFullText, , Cochrane Database of Systematic Reviews, American College of Physicians Journal Club, DARE and CCTR, Allied and Complementary Medicine, Cumulative Indsex Nursing and Allied Health, EMBASE, PREMEDLINE and MEDLINE (1996 to present), British Nursing Index, and the National Research Register. Websites included the	**Transmission due to environmental contamination** Identified that environmental contamination occurred during outbreaks – 5/11 (55%) Environmental contamination considered cause of transmission – 9/11 (82%) Identified environmental contamination as cause of prolonged or recurring outbreaks – 0% **Environmental sampling** Identified environmental contamination – 3/5 studies 76/210 (36%) swabs positive from curtains, cushions, carpets, lockers, commodes, toilet rims, seats and handles, taps, basins, telephones, door handles, physiotherapy instrument handle, and horizontal surfaces above and below 1.5 meters including light fittings and mantelpieces. **Laboratory testing methods** Studies using RT-PCR – 100% Two studies recognized that RT-PCR positive for norovirus does not necessarily represent viable virus. **Sampling methods** *Methods of specimen collection* 3 used saline or transport medium moistened swabs for sampling. 1 used dry swabs. 1 used wet and dry swabs. There were more positive swabs in studies that used moistened swabs. *Timing of collection* Unclear in 3 studies whether swabs were taken before or after environmental cleaning. *Selection of sampling sites*	Sample size and power not reported.	3958_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			Department of Health, Public Health Laboratory Service, CDC, Infection Control Nurses Association, and the World Health Organization. Search terms included (“Norwalk” OR “norovirus” OR “Winter Vomiting” OR “Viral gastroenteritis” OR “SRSV” OR “Calicivirus”) AND (“Outbreak” OR “Management” OR “Environment” OR “Disinfect” OR “Decontaminate” OR “Decontamination” OR “Clean” OR “Contaminate” OR “Contamination” OR “Precautions” OR “Control”). Limited to English language. Articles excluded if unrelated to viral gastroenteritis, environmental contamination, concentrated on the source of infection (i.e., food borne gastroenteritis), or laboratory diagnosis techniques. References of articles reviewed to	4 studies did not explain why certain sites were swabbed and did not identify total swabs taken from each site. **Virus survival** 1 study reported 21-28 day survival in a dried state at room temperature. 2 studies reported virus survival for at least 12 days; 1 paper repeated sampling and did not find virus in a previously contaminated environment after 5 months. 1 paper suggested that carpets may have viable virus for at least 12 days that is not removed by routine vacuum cleaning. **Changing curtains** 2 studies recommend changing curtains, but there is no evidence addressing whether changing curtains would prolong an outbreak. **Carpet decontamination** 3 studies advised steam cleaning of carpets but there is no evidence that it is effective for norovirus. 1 study identified carpets as a cleaning priority due to high levels of RT-PCR. 1 study recommended steam cleaning carpets and changing curtains as Category II “strongly recommended and viewed as effective by experts in the field and by the working group, based on strong rationale and suggestive evidence, even though definitive studies may not have been done.” **Cleaning and disinfection** 4 studies recommended and/or performed terminal cleaning. 3 papers recommended a cleaning or disinfectant agent; all recommended hypochlorite 1000 ppm. Chadwick recommendations based on Doultree article which recommended glutaraldehyde 0.5% and iodine 0.8%, but not 75% ethanol, quarternary ammonia 1:10 and anionic detergent 1%. The last study gives no reference for the recommendation. 2/5 studies that studied environmental sampling reported decontamination methods; both used 500 ppm hypochlorite, which is no longer advised in current guidelines. 0/5 studies evaluated the effectiveness of currently used disinfectants. **Specific areas for decontamination** 4 studies listed recommendations including decontamination of frequently handled objects, taps, door handles, toilets and bathrooms, bath rails, toys, carpets, and surfaces contaminated by stools or vomit. The only area recommended by > 1 study was bathrooms, despite 2 papers identifying contamination of both toilets and door handles by environmental swabs.		

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			identify additional relevant articles. Articles critiqued using a tool adapted from Cormack. 11 articles. 5 articles underwent environmental sampling.			
MMWR; 2008 [79]	Prospective controlled study. 1,3,4	To investigate an outbreak at an elementary school.	Students and staff at an elementary school in Washington DC in February 2007. Students – median age 8 years (range 3-12 years); 55% female. Staff – median age 41 years (range 13-66 years); 92% female. 266 – 207 students and 59 staff.	**Risk factors for symptomatic illness** *Bivariate analysis: All results RR (95% CI); p value* Being a student – 0.94 (0.66-1.34); 0.76 Being female – 1.13 (0.82-1.56); 0.52 Having an ill contact – 1.76 (1.16-2.67); 0.01 Classroom J (first) – 1.94 (1.34-2.80); 0.02 Library use: 0.94 (0.58-1.52); 0.87 Library computer use: 1.08 (0.41-2.84); 1.00 **Interventionsrecommended** District of Columbia Department of Health recommended -more thorough handwashing with soap and water or alcohol-based hand sanitisers - cleaning all shared environmental surfaces with a diluted (1:50 concentration) household bleach -cleaning computer equipment (i.e., mice and keyboards) -excluding ill persons from school for at least 72 hours after resolution of illness	A case of gastrointestinal illness was defined as illness in a student or staff member with nausea, vomiting, or diarrhea, who was at the school February 2-18, 2007. Power and sample size not reported.	017_IL
Lopman, BA; 2004 [58]	Prospective controlled study 1,2,3,4	To describe norovirus outbreaks in residential homes or hospitals of principally older individuals.	Patients in hospitals and nursing homes in England. Cases were hospital patients, nursing home residents, and health care staff with ≥2 episodes of vomiting, ≥3 episodes of diarrhea, or both during a 24-hour period. Those with symptoms due to incontinence or ingestion of laxative	**Duration of illness** Hospital patients vs. hospital staff, nursing home staff, and nursing home residents (75th percentile); p value – 3 days (5 days) vs. 2 days (3 days); p<0.001 Recovery was slowest in the oldest age group (≥85 years) of hospitalized patients - 40% symptomatic after 4 days	Outbreak is defined as ≥ 2 cases in a hospital functional care unit with dates of onset within 7 days of each other. Power and sample size not reported. Promotion of active surveillance (2-tiers of clinical symptoms) to detect cases as a	642_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			drugs were excluded. 271 outbreaks – 33 in nursing homes and 238 in hospital units. 4378 cases – 2154 hospitalized patients, 1360 hospital care staff, 505 nursing home residents, and 358 nursing home staff.		means of prevention of outbreaks	
Lopman, B; 2004 [164]	Prospective controlled study 1,2,3,4	To identify and report costs of gastroenteritis outbreaks in the UK from 2002 to 2003.	3 hospital systems in Avon, England. 2,154 patients and 1,360 healthcare staff from 227 unit outbreaks.	**Attack rates** 2,154 patients – 2.21 cases/1,000 hospital-days (95% CI 2.16-2.25). 1,360 healthcare staff – 0.47 cases/1,000 hospital-days (95% CI 0.45-0.50). Attack rates for staff members lower than for patients: 19.6% (95% CI 16.6%-22.7%) vs 46.8% (95% CI 40.9%-52.8%); p < 0.001. 227 unit outbreaks – 1.33 outbreaks/unit-year (95% CI 1.16-1.51). Units with outbreaks larger than those without outbreaks – 21.4 vs 12.6, p value < 0.0001. **Unit closure** Duration – mean 9.65 (95% CI 8.5-10.8) days; most extreme was a unit closed for 48 days. 3.57 (95% CI 1.86-5.2) bed-days lost for every day of unit closure. Estimated 5,443 bed-days lost from gastroenteritis outbreaks. **Costs** Empty beds – US $2.24 million or approximately $768,000/1,000 beds. Staff absence – $771,000 or $249,000/1,000 beds. Days of illness in working age men, women, and children – $106,000 or $36,000/1,000 beds. Bed-days lost plus staff absence – $3.15 million or $1.01 million/1,000 beds. By extrapolation, gastroenteritis outbreaks cost the English National Health Service US $184 million in one year (2002-2003). **Controlling outbreaks** Outbreaks contained faster when units rapidly closed to new admissions (within 4 days of the primary care): 7.9 vs 15.4 days; p=0.0023)	Outbreak defined as ≥ 2 cases in a functional care unit with dates of onset within 7 days of each other. Case was a patient or medical/nursing staff with vomiting (≥ 2 episodes of vomiting in a 24 hour period) OR diarrhea (≥ 3 loose stools in a 24 hour period) OR vomiting AND diarrhea (≥ 1 episodes of BOTH symptoms in a 24hour period) but excluding long standing diarrhea associated with disability or incontinence and diarrhea associated with laxative drugs. Costs derived from 1) bed-day loss from new admission restriction for affected units and	592_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
					2) staff absence from illness. Unit Costs of Health and Social Care 2002 report used to estimate the economic loss from empty beds and staff absence. British pounds (2002) converted to US dollars at the rate of 1 pound: $1.6 based on the 5 year average 1999-2003. norovirus detected in 63% outbreaks: confirmed etiologic agent in 61 outbreaks (50%) and detected in a single specimen in 16 outbreaks (13%).	
Billgren, M; 2002 [165]	Prospective controlled study 1,3,4	To describe outbreaks of norovirus gastroenteritis.	Ten hospitals representing 66% of the hospitals in Stockholm County., Sweden. These included medical and geriatric wards among others. Some medical and geriatric wards were randomly selected as controls. 211 wards	**Risk of an outbreak of norovirus gastroenteritis on a ward** Outbreak during the previous year (P<0.01) **Lessons learned** • Hospitals that applied stringent measures to viral spread such as avoiding transfer of patients and staff and emphasizing hygiene routines during the first week of a suspected outbreak could shorten and restrict the outbreak. In hospitals where these measures were introduced late, the outbreak spread to other wards. • It was not evident if other measures to any appreciable extent contributed to the shortening of the outbreaks. It was not obvious if measures such as keeping staff off duty until they had been asymptomatic for 48 h or closure to admission of new patients influenced the outcome of an outbreak.	The inclusion criteria for an outbreak were those of Kaplan in at least 3 persons during one week. Stool samples were analyzed using EM and RT-PCR Power and sample size not reported.	958_RA
Evans, M; 2002 [83]	Prospective controlled study 1,3,4	To describe an outbreak of norovirus gastroenteritis following vomiting by an	Primary school children attending a concert at a metropolitan concert hall. Demographic characteristics not provided.	**Description of outbreak** Following the vomiting, cleaning was done with an ordinary vacuum cleaner the following day. No hypochlorite based product was used. The index case was seated in tier 13. Several cases documented from exposure after initial concert, ie. index case not present but exposure continued	A case was defined as a person who had attended the concert hall and had developed vomiting and/or diarrhea within 24-72	897_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		attendee at a concert	1229 children from 15 primary schools	**Auditorium seating as a risk factor for norovirus infection** (follow-up not clearly reported) Children seated in tiers 9-13 vs. children seated elsewhere – 199/387 vs. 58/797; RR(95% CI) = 7.1(5.4-9.2)	hrs of the visit. NLV was confirmed in fecal samples using RT-PCR	
Lachlan, M; 2002 [84]	Prospective controlled study 1,3,4	To describe an outbreak of norovirus gastroenteritis and lessons learned.	Persons with a connection to a hotel linked to the outbreak or ill contacts of people who were unwell and had a connection with the hotel. 112 potentially exposed, 79 cases	**Symptomatic norovirus infection - Food specific attack rates** Beef sandwich – 1.35(1.08-1.67) Cheese sandwich – 1.33(1.06-1.67) Egg sandwich – 1.49(1.18-1.88) Ham sandwich – 1.39(1.14-1.69) Lamb sandwich – 1.46(1.28-1.66) Tuna sandwich – 1.27(1.02-1.60) Sausage sandwich – 1.01(0.77-1.32) Soup – 1.28(1.00-1.64), P<0.05 Parsley garnish – 0.71(0.18-2.83) Tomato garnish – 1.15(0.82-1.61) Hot chocolate – 1.45(1.28-1.65) Tea – 1.04(0.81-1.33) Coffee – 1.36(1.10-1.67) Ice – 1.25(1.00-1.57) Other drinks – 1.52(1.12-2.05) After applying a critical P value (<0.003) with Bonferroni correction, only egg sandwich and drinks from the bar (other drinks) were found to be statistically significant. **Lessons from the outbreak** 7. Outbreak control team meetings that are formally minuted with action points being highlighted on a flipchart 8. Good liaison with laboratory services to agree on clear pathways for the delivery and analysis of samples that became available during normal working hours or were processed over the weekend. 9. Rapid virological confirmation to reassure the public that appropriate control measures were in place and handle the media interest. 10. Joint visit to the outbreak premises by protective services and public health representatives to facilitate clear and open communication between all parties and secure a voluntary agreement from the hotel owner to cease all food preparation. 11. Food handlers should remain off work from onset of illness until 48 hours after diarrhea and vomiting have ceased	A case was defined as someone with symptoms of diarrhea, vomiting or abdominal pain or any combination of these more than once in 24 hours and a connection with the hotel where the outbreak started. norovirus was confirmed by EM	942_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				12. All those involved in carrying out interviews and analyzing data working from one site and through one computer network to improve the efficiency of working through contact lists, allowing rapid assessment of the epidemic curve and symptom pattern and the results of RR calculations of the foodstuffs.		
Love, S; 2002 [85]	Prospective controlled study 1,3,4	To describe an outbreak of gastroenteritis and procedures implemented to control it.	Guests and employees of a Virginia hotel. There were 3 groups: Group A: Attendees of a business conference (n=110); median age of cases (n=34) 52 years; 59% cases female Group B: Physicians and their families (n=95); median age of cases (n=11) 31 years; 73% cases female Group C: Retired persons (n=310); median age of cases (n=15) 71 years; 60% cases female 60 cases	**Risk factors for symptomatic norovirus infection** (follow-up unclear) Attending reception: RR(95% CI) – 2.1(1.1-4.0) Eating coleslaw at picnic: RR(95% CI) – 3.6(1.0-13.6) **Interventions** Infection control measures instituted: 5. Employees who were ill in the past two weeks or had an ill child in diapers were excluded from work for 1 day. Employees who were currently ill with vomiting or diarrhea were told not to work for 1 day after resolution of symptoms 6. All employees were instructed about hygiene and hand washing 5 days after initial cases 7. The facility was closed for 8 h to permit thorough cleaning of all food service areas and guest rooms. New guests were not accepted until all guestrooms, bathrooms, and common rooms were thoroughly cleaned 7 days after initial cases 8. All cold food requiring hand-preparation was excluded from the menu. No open bowls of food such as chips or popcorn were served 7 days after initial cases **Response to intervention** (at two week follow-up) The hotel reported no further ill guests or employees	A case was defined as vomiting or diarrhea in a hotel attendee or staff. norovirus confirmed by RT-PCR Power and sample size not reported.	915_RA
Lo SV, 1994 [89]	Prospective controlled study 1,2,3,4	To investigate a SRSV gastroenteritis outbeak in 4 hospitals served by one central kitchen.	4 hospitals - 1 acute district general hospital and 3 smaller peripheral hospitals with long-stay and rehabilitation patients 81 patients and 114 staff in 4 hospitals Buffet lunch cohort study: n=41 completed quesionnaire Patient case-control	*Buffet lunch study n=41* *Food - RR (95% CI)* Ham and tomato – RR 1.0 (0.6-1.7) Cheese and pickle – RR 0.8 (0.4-1.9) Turkey salad – RR 2.4 (1.4-4.1) Tuna – RR 1.2 (0.7-2.0) Sausage roll – RR 1.1 (0.6-1.8) Cheese and pineapple – RR 1.0 (0.6-1.8) Sausage mushroom – RR 1.6 (0.-2.9) Fresh fruit – RR 0.8 (0.3-2.3) Meringue – RR 0.9 (0.5-1.4) Orange juice – 1.0 (0.48-2.0) Wine – 1.0 (0.51-2.1) *Patient case-control study n=23 cases and 35 controls*	A cohort study of staff who attended a retirement buffet lunch, a patient case-control study based at the district general hospital, and a nursing staff case-control study at the district general hospital were performed. Fecal samples underwent bacteriological	1540_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			study: 23/24 cases and 35/36 controls completed questionnaires. Staff case-control study: 22/27 cases and 49/54 controls completed questionnaire.	*Risk factor* *Food - OR (95% CI)* March 7th Beel cobble – OR 0 (0-1.7) Beef crumble – OR 1.6 (0-11.5) Mince – OR 0.7 (0.1-3.9) Sausage and onion – OR 0.3 (0.1-1.3) Cheese pie – OR 0.2 (0-1.6) Lamb salad – OR 0.4 (0.05-2.4) Tuna salad – OR 6.6 (1.0-71.6); p<0.05 Any salad – OR 1.8 (0.5-6.8) Corn beef sandwich – OR 1.6 (0.1-23) Any sandwich OR 4.6 (0.6-39) March 8th Cod – OR 1 (0.3-3.5) Chicken curry – OR 0.8 (0.2-2.8) Flaked fish – OR 0.7 (0.01-15) Lamb casserole – OR 0.9 (0.2-3.9) Mushroom pizza – OR 0.3 (0.01-3.9) Savoury lamb – OR 1 (0.1-9.7) Beef salad – OR 3.2 (0.2-97) Chicken salad – OR 2.5 (0.3-31) Any salad – OR 4.7 (0.9-30); p <0.05 Salmon sandwich – OR 0.2 (0-2.2) Any sandwich – OR 0.4 (0.04-2.3) March 9th Pork casserole - OR 1.5 (0.4-5.7) Chicken pie – OR 0.3 (0.1-1.5) Minced chicken – OR 0.2 (0-1.6) Cawl – OR 1.6 (0.2-13) Fishcake – OR 0.5 (0.1-2.5) Egg salad – OR 0.3 (0-3.9) Cheese salad – OR 2.2 (0.2-4.8) Any salad – OR 1.1 (0.2-4.8) Ham sandwich – OR 0.5 (0.01-6.7) Any sandwich – OR 1 (0.1-9.7) *Staff case-control study* No statistically significant associations found.	examination, routine EM, and immuno-EM. Power and sample size not reported.	

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				1 food handler who prepared the salad had a child who was ill 2 days prior and the food handler became ill the day following food preparation. *Infection control practices* Closure of the central kitchen Disposal of all remaining food Discontinuing all hospital admissions and ward transfers Daily ward cleaning with 2% hypochlorite Emphasis on hand washing		
de Wit, M; 2007 [92]	Retrospective controlled study 1,3,4,6,7	To describe an outbreak of gastroenteritis caused by a baker infected with norovirus who continued to work in his bakery having washed his hands and disinfected countertops.	Staff of a department in the Netherlands who attended a reception where the outbreak was reported. Median age 39 years; 45% female. 800-900 employees; 231 reported diarrhea or vomiting	**Symptoms** Diarrhea and vomiting – 76% Diarrhea only – 12% Vomiting only – 12% Median time to onset of symptoms – 31 hours **Risk factors for symptomatic infection** *All results OR(95% CI)* *Univariate analysis* Coffee – 0.3(0.1-0.9) Tea – 0.7(0.2-2.0) Milk – 1.3(0.9-1.9) Butter milk – 1.1(0.7-1.8) Orange juice – 1.2(0.8-1.6) Champagne – 1.6(1.1-2.3) Cheese – 1.5(1.1-2.2) Brie – 1.1(0.7-1.8) Ham – 1.5(1.0-2.2) Beef – 1.2(0.8-1.9) Tuna salad – 1.6(1.1-2.4) Salmon salad – 2.2(1.0-4.5) Egg salad – 1.4(0.9-2.1) Raisin roll – 0.9(0.6-1.3) Increasing number of rolls – 2.0(1.6-2.4) *Multivariate analysis* Coffee – 0.4(0.1-0.8) Raisin roll – 0.5(0.3-0.8) Number of rolls – 2.0(1.5-2.5) **Intervention implemented**	A case was defined as a member of the departmental staff who attended the reception and reported diarrhea (3 or more loose stools a day) or vomiting in the 72 hours following the reception. A control was defined as a member of the department staff attending the reception without diarrhea or vomiting in the 72 hours following the reception. norovirus infection was confirmed using RT-PCR The estimated response rate for questionnaires among cases was nearly 100%. The estimated response rate among controls was 40-50% Power and sample size	4084_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Sick food handlers excluded from work for 48hrs and reinforcement of hygiene measures	not reported	
Hansen, S; 2007 [166]	Retrospective controlled study 1,3,4	To perform a systematic analysis of when ward closure was needed.	The Outbreak Database, which includes approximately 75% of all nosocomial outbreaks published in PubMed, was searched to identify how many outbreaks required closure. 1561 outbreaks	**Closure rates by ward** Overall – 194/1561 (12.4%) *All results – No. outbreaks with closure/No. outbreaks (rates); p value* General surgery – 44/346 (12.7%); NS Neonatology – 53/332 (16.0%); NS Internal medicine – 44/307 (14.3%); NS Pediatric ward – 8/132 (6.1%); 0.03 Hematology/oncology – 12/125 (9.6%); NS Geriatrics – 24/79 (30.3%); <0.001 General medicine – 3/76 (3.9%); 0.03 Hemodialysis – 5/76 (6.6%); NS Neurology/psychiatry – 7/66 (10.6%); NS Gynecology/obstetrics – 10/58 (17.2%); NS Transplantation units – 5/56 (8.9%); NS Orthopedics – 9/40 (22.5%); NS Neurosurgery – 9/39 (17.9%); 0.05 Urology – 5/38 (13.2%); NS **Closure rates by pathogen** *All results – No. outbreaks with closure/No. outbreaks (rates); p value* S. aureus – 23/223 (10.3%); NS Hepatitis virus – 6/150 (4.0%); 0.002 Pseudomonas spp – 10/130 (7.7%); NS Klebsiella spp – 10/115 (8.7%); NS Acinetobacter spp – 24/105 (22.9%); 0.02 Serratia spp – 14/94 (14.9%); NS Enterococci – 8/67 (11.9%); NS Enterobacter spp – 10/66 (15.2%); NS Streptococci – 19/63 (28.6%); 0.001 Salmonella spp – 4/56 (7.1%); NS Legionella spp – 2/48 (4.2%); NS norovirus – 15/34 (44.1%); <0.001 Clostridium spp – 4/34 (11.8%); NS Aspergillus spp – 5/25 (20.05%); NS Influenza/parainfluenza virus – 10/26 (38.5%); <0.001 Citrobacter spp – 3/12 (25.0%); NS Adenovirus – 3/11 (27.3%); NS	Any partial or total closure of an affected location for any duration included. Each closure rate compared to the overall closure rate. Power and sample size not reported.	141_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Shigella spp – 4/11 (36.4%); 0.04 Rotavirus – 7/27 (25.9%); 0.05 SARS – 4/12 (33.3%); NS **Closure rates by source of outbreak** *All results – No. outbreaks with closure/No. outbreaks (rates); p value* Patient – 66/395 (16.7%); 0.03 Environment – 24/194 (12.4%); NS Medical devices – 12/172 (7.0%); 0.04 Personnel – 17/154 (11.0%); NS Drugs – 3/73 (4.1%); 0.03 Food – 1/50 (2.0%); 0.03 Equipment for patient care – 5/35 (14.3%); NS Source not known – 80/518 (13.8%); NS **Closure rates by route of transmission** *All results – No. outbreaks with closure/No. outbreaks (rates); p value* Contact – 124/752 (16.5%); 0.01 Invasive techniques – 13/273 (4.8%); 0.01 Inhalation – 31/166 (18.7%); 0.02 Ingestions – 4/63 (6.3%); NS Mode not known – 41/404 (10.1%); NS **Closure rates by type of infection** *All results – No. outbreaks with closure/No. outbreaks (rates); p value* Bloodstream infections – 76/589 (12.9%); NS Gastrointestinal tract – 49/402 (12.2%); NS Pneumonia – 44/331 (13.3%); NS Surgical site infection – 21/195 (10.7%); NS Urinary tract – 23/190 (12.1%); NS Skin and soft tissue – 21/171 (12.3%); NS Other lower respiratory tract – 21/134 (15.7%); NS ENT – 24/109 (22.0%); 0.004 CNS – 23/95 (24.2%); 0.001 Other systemic infections – 7/49 (14.3%); NS Bones and joints – 5/44 (11.4%); NS Cardiovascular system – 4/34 (11.8%); NS **Duration** Duration of closure described in 32 outbreaks – median, 14 days (range, 3-56).		

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Interventions for all outbreaks, not limited to norovirus -Closure of entire unit (69.6%) -Infected or colonized patients isolated (66%) -Patient screening cultures and surveillance (58%) -Staff screening cultures and surveillance (49.5%) -Enforced hand hygiene (43.3%) -Reprocessing of devices (43.3%) -Healthcare worker education (24.2%) -Work load restriction (16.5%) -Vaccination (4.7%)		
Zingg, W; 2005 [167]	Retrospective controlled study 1,2,3,4,6,7	To describe a nosocomial norovirus outbreak, its management, and financial impact.	Patients at a Swiss university hospital. Age – mean 57.8 years. Sex – 56% male 16 case patients and 32 control patients.	**Symptomatic infection - Attack rate** 29.5%. **Costs** Overall – $40,675 *Laboratory testing* $2707 for laboratory tests (13 tested, 3 based on clinical symptoms) *Loss of revenue due to bed closures* $37,968 *Median numbers of occupied beds: Outbreak vs other non-outbreak periods* 29 beds/day in 2003 vs 42 beds/day in 2001, 43 beds/day in 2002, 42.5 beds/day (p=0.002, Mann-Whitney U test). Differences in median bed occupancy between peak incidence of illness and periods preceding and following (p<0.01). **Costs not included** *Nursing care* $10,300 (based on additional nursing care, in minutes) *Nursing care for case vs control patients – All results in median minutes/day; p value* Total – 74.3 vs 41.9; <0.05 Mobilization care – 105 vs 30; 0.05 Control of excretions – 202 vs 127.5; .54 Instructions – 30 vs 30; .42 Isolation measures – 180 vs 0;<0.0001 Difference due to need for isolation of infected cases (median, 180 minutes/day). *Lost productivity costs due to healthcare worker on sick leave*	Case was a patient or healthcare worker who developed acute diarrhea, nausea, and vomiting during the outbreak period; and had norovirus detected by RT-PCR in stool specimens. (12 definite cases; 3 probable cases with typical symptoms but not tested; and 1 with typical symptoms but norovirus RT-PCR negative.) Control was a patient hospitalized during the outbreak on the same medicine ward without symptoms of gastroenteritis, matched by age, sex, underlying disease category, and length of stay. Power and sample size	521_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				$12,807. *Infection control* $1408 **Interventions** -Infected patients isolated until 2 days after diarrhea resolved. -Gloves and gowns during direct patient contact until 2 days after the diarrhea resolved. -No new patient admissions or transfers. -Hand antisepsis and hand washing. -Rooms decontaminated with 0.5% hypochlorite after patient discharge. -Infected healthcare workers stayed home and were allowed to return to work 2 days after symptoms resolved. These measures did not completely prevent new cases, but there was a decrease in the incidence of new cases after these measures were implemented.	not reported.	
Oppermann, H; 2001 [63]	Retrospective controlled study 1,2,3,4	To identify risk factors for a gastroenteritis outbreak.	Guests and staff at a mother and child health clinic in Germany. Cases –166 guests and 49 staff. Data available – 164 guests and 47 staff.	**Symptomatic infection - Attack Rates** Guests 44% - adults 27% and children 54% Staff 23.4% **Age** *All results affected vs. not affected in years; p value* Children – 3.5 vs 6.3; <0.001 Adults – 32 vs 33; NS **Lessions Learned** **-Importance of early recognition of norovirus infection** Guests encouraged to wash hands after using the bathroom and prior to each meal. -Patients informed doctors immediately of any gastrointestinal symptoms. -Infected persons had limited contact with other guests and limited use of common facilities. -The staff was told immediately when gastroenteritis reported and instructed about appropriate protective measures. -The rooms of the infected persons, especially lavatories, were cleaned daily using a virucidal disinfectant. -Height of tables raised to prevent children from touching food -Newly arrived guests received meals in separate area from exposed guests -Vomitus disinfected immediately. -If an outbreak suspected, the public health department was to be notified.	Case was a person who stayed at the health clinic from October 27 to November 17, 1999 and had vomiting and/or diarrhea at earliest, one day after his/her arrival. NLV and Astroviruses detected using PCR. Power and sample size not reported.	1041_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Marx, A; 1999 [66]	Retrospective controlled study 1,3,4	To assess risk factors for gastroenteritis associated with Norwalk-like viruses (NLVs)	Residents and employees at a geriatric long term care facility. 68% residents were female, median age was 83 yrs (range 65-106). 78% of employees were female, median age was 36 yrs. Study was conducted in Washington State. 91 residents and 97 employees	**Attack rate** Residents – 52/91 (57%) Employees – 34/90 (35%) *All results RR(95% CI); P value for the presence of risk factor* **Risk factors for gastroenteritis among residents** Physical dependence – 3.5(1.0-12.9);0.02 Respiratory therapy – 2.3(0.8-6.4); 0.20 Antibiotics – 1.6(1.0-2.8); 0.20 Chronic infections – 1.6(0.9-3.0); 0.40 Tube feeding – 1.3(0.7-2.6); 0.70 Disoriented – 1.2(0.8-1.8); 0.60 Diuretics – 0.4(0.2-0.9); 0.02 **Risk factors for gastroenteritis among employees** Exposure to vomitus – 2.6(1.1-6.5); 0.03 Gastroenteritis in household – 2.3(1.4-3.6); 0.01 Exposure to residents with gastroenteritis – 2.2(1.0-4.9); 0.05 Resident care – 1.4(0.8-2.5); 0.30 Tap water – 0.9(0.5-1.5); 0.60 Ice – 0.7(0.4-1.2); 0.20 **Effect of protective measures among nursing staff** Gowning – 0.4(0.1-1.4) Strict hand washing – 0.7(0.2-1.3) Use of hand-disinfection gel – 0.8(0.4-1.4) Laundering work clothes daily – 1.2(0.7-1.3)	A case of acute gastroenteritis was defined as an individual with onset of vomiting or diarrhea during the study period (Feb 12 – Mar 20 1996); diarrhea was defined as ≥2 loose or watery stools in a 24 hr period. A single NLV strain of genogroup II genetically related to Toronto virus was the only pathogen identified. NLVs were identified by EM in stool and vomitus specimens and further characterized by RT-PCR and nucleotide sequencing. Data on residents was collected through medical records. 90 of 97 employees completed a self-administered questionnaire Power and sample size not reported	1237_RA
McEvoy, M; 1996 [102]	Retrospective controlled study 1,3,4	To describe an outbreak of norovirus gastroenteritis.	Passengers and crew of 4 cruises in the western Mediterranean. Median age of cases 55 years; 13/23 males 46 (23 cases and 23	**Risk factors for symptomatic norovirus infection** (matched pairs analysis) *All results OR; P value* Gala dinner – 0.20; 0.22 Salad – 1.00; 0.77 Fruit – 0.56; 0.42 Eggs – 0.50; 0.38 Table – 1.33; 1.00	A primary cabin case (the first case to have occurred in a cabin) was defined as a passenger on the ship from 27 May to 2 June with diarrhea (≥3 loose	1410_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			controls)	Taps – OR not calculable; 0.24 Ice (tap water) – 0.56; 0.42 Teeth (tap water) – 1.00; 0.77 Pool – 0.71; 0.77 Chicken – 0.50; 0.39 Prawns – 0.29; 0.18 Meat – 1.14; 1.00 Cream – 0.67; 0.75 **Interventions** 4. Hygiene measures were introduced in the galley 5. When the passengers disembarked for a short period, the cabins were cleaned with a chlorine based disinfectant 6. Soft furnishings were removed for steam cleaning from all cabins whose occupants had reported illness. At the same time, the crew and staff quarters, including communal bathrooms and lavatories, were cleaned in the same way. **Response to outbreak** After control measures were implemented, fewer than 10 cases of diarrhea and/or vomiting were detected on each of the fifth and sixth cruises	stools in a 24 hour period) and/or vomiting. Controls were matched to cases by sex and age (within 10 years) norovirus was identified by EM and RT-PCR in fecal specimens 277/1100 questionnaires were completed and returned. Power and sample size not reported.	
Chadwick, PR; 1994 [103]	Retrospective controlled study 1,3,4,6,7	To determine risk factors for small round structured virus infection during an outbreak at an elderly care unit.	Healthcare workers at an elderly care unit. Cases – mean age 36 years (range 21-58 years). Controls – mean age 39 years (range 18-59 years). 90% questionnaire responders were female. 103 questionnaires returned.	**Clinical features** Overall attack rate – 34% *Attack rates among healthcare subspecialties* Nursing – 40% Pharmacists – 34% Doctors – 0% Staff absent from work due to illness – 75% Duration of absence – median 2 days (range 1-9 days) **Risk factors for symptomatic infection** *Univariate analysis* Nearby vomiting – 50% exposed staff were infected vs. 20% unexposed staff; OR 3.89 (95% CI 1.4-11); p=0.007 Number of exposures to nearby vomiting – p=0.032 Contact with ill patients – 42% exposed staff were infected vs. 13% unexposed staff; OR 4.71 (95% CI 0.94-46); p=0.07 Number of close contacts with ill patients – p=0.023 Cleaning vomit – OR 1.96 (95% CI 0.46-9.8); p=0.49 Cleaning diarrhea – OR 4.67 (96% CI 0.49-225); p=0.22	Case was a patient or staff at the hospital with vomiting or ≥2 loose stools in a 24 hour period. Power and sample size not reported. Aerosolization of vomit may have been important in infection transmission during the outbreak. Exposure to nearby vomiting defined as vomiting occurring within 6 feet of the health care worker.	1555_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Multivariate analysis Nearby vomiting was the only significant risk factor **Interventions Implemented** Handwashing emphasized Restricted transfers from affected wards Ward closures Staff cohorting Disinfection with chlorine-based products Attribute declining attack rates among subsequent wards to infection control measures		
Johnston, CP; 2007 [168]	Descriptive study 1,2,3,4	To describe a norovirus outbreak	Patients and staff in coronary care and psychiatric units in a tertiary care hospital.. 355 cases – 90 patients and 265 health care workers Mean ages ± SD years – healthcare workers 36.2 ± 10.4 and patients 45.5 ± 23.4. Female – 83.8% healthcare workers and 47.8% patients.	**Descriptive** *Attack rates* Cardiac/coronary care unit (CCU) – 7/133 (5.3%) for patients and 29/97 (29.9%) for health care workers. Psychiatry unit – 39/233 (16.7%) for patients and 76/200 (38.0%) for health care workers. CCU - Employees used a total of 138 hours of sick leave and 18.5 hours of overtime. Psychiatry units – Despite routine infection control measures, additional cases occurred. **Costs** (US$) *Lost revenue* CCU – $147,507 Cardiac/coronary intensitve care unit (CICU) – $158,620 Psychiatry – $112, 242 *Additional costs* Cleaning – $96,961 Replacement of supplies – $53,075 Sick leave and overtime – $89,239 *Total* – $657,644 **Interventions** *At initial outbreak* -Healthcare workers educated on how to identify norovirus gastroenteritis, appropriate cleaning measures, and isolation protocols. -Infected healthcare workers returned to work 72 hours after symptom resolution. -Standard precautions and Contact Precautions of symptomatic patients. -Symptomatic patients in private rooms or cohorted together.	Cases were those with new onset vomiting and/or diarrhea during the outbreak period. Diarrhea was defined as ≥ 2 loose stools/24 hour period or unexplained increase in bowel movements. Norovirus genogroup II-4 variant detected. Economic analysis focused on the institutional costs of the outbreak from the Johns Hopkins Hospital Casemix administrative database. Costs included total lost revenue with closure of units to new admissions, attributable sick leave and overtime salary, cost of replacing	079_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				-In the emergency room, symptomatic patients cohorted together. -Frequent hand hygiene with either soap and water or alcohol based hand gel encouraged. -Healthcare workers at other institutions not allowed to care for patients at this institution (outbreak was citywide). -Closure of emergency department at a nearby hospital that had a gastroenteritis outbreak – the outbreak affected the entire city. -Nurse managers and infection control professionals screened patients and healthcare workers daily, reinforcing infection control practices. -Nurse managers screened all visitors for gastroenteritis, and if symptomatic, prohibited them from visiting patients in the units for 72 hours. -Sharing of food among healthcare workers was prohibited. -Aggressive cleaning measures implemented using 1:50 dilution of sodium hypochlorite (i.e., bleach). -Every shift, high touch surfaces (i.e., doorknobs, light switches, tables, counter tops, computer keyboards), and bathrooms (particularly toilets and fixtures) cleaned. -Daily, patient rooms (including walls, windows, beds, chairs, and ledges) cleaned; rooms of patients who vomited or had diarrhea were cleaned last. Floors were cleaned, replacing cleaning solutions and mop heads every 3 rooms. -At discharge, patient rooms, floors, patient dressers and overbed tables cleaned. Room contents were discarded, the room cleaned, and then restocked. -Surfaces soiled or grossly contaminated were cleaned, and curtains changed. *Additional interventions when additional cases identified (implemented 3 days after initial interventions)* -Visitors prohibited, unless extenuating circumstances. -Nurses on affected floors cohorted – one group cared for symptomatic patients and a second group for asymptomatic patients. -Gowns and gloves used until outbreak resolved. -No new admissions in several units because of staffing shortages. -CCU closed for 24 hours while extensive cleaning occurred. -All disposable supplies, including medical supplies, discarded. -Items with fabric surfaces, including furniture, that could not be disinfected were discarded. -All surfaces cleaned with sodium hypochlorite by two consecutive cleaning crews. -In the psychiatric unit, group sessions suspended and patients with gastroenteritis confined to their rooms and limited transport of patients to other hospital areas (implemented >1 month after initial interventions on psychiatric ward)	supplies, and cleaning expenses. Analysis limited to CICU, psychiatry units, and echocardiogram laboratory. Power and sample size not reported.	

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Leuenberger S; 2007 [169]	Descriptive study 1,2	To describe a norovirus outbreak in a Swiss hospital.	Patients in the geriatric and internal medicine wards where two outbreaks occurred. 77 persons in 2 buildings – 28 patients and 49 healthcare workers – 39 in building 1 including the geriatric ward and 38 in building 2, including the internal medicine, intensive care, surgery, orthopedic, and obstetrics and gynecology wards	**Interventions** -Public restaurant in building 1 closed due to an infected staff member. -Infected healthcare workers sent home for at least 48 hours. -Infected patients isolated and cohorted. -Movement of infected patients minimized. -Healthcare workers and visitors wore masks, gloves, and gowns. -Mandatory hand disinfection with a product that has 95% ethanol. -Daily surface disinfection.	Case was someone with sudden vomiting and diarrhea, abdominal cramps, fever below 38.5°C, and recovery within 48 hours. 4/18 samples tested positive for norovirus genogroup II cluster 4. Diagostic testing could not link the two outbreaks. The authors speculated that the large outbreak resulted from a more virulent and environmentally stable norovirus strain.	163_IL
Cheng, F; 2006 [170]	Descriptive study 1,2,3	To provide a practical action plan for effective infection control of a norovirus outbreak in acute pediatric wards	Patients, parents, visitors, health care workers or medical students who developed vomiting or diarrhea and were exposed to inpatients of a pediatric ward within four days of an outbreak. The setting was a university hospital in Hong Kong. There were 11 subjects, including 9 patients, 1 visitor and 1 medical student. Of	**Interventions** *1. Isolation of infected patients.* • Alert the hospital infection control team if ≥3 inpatients developed gastroenteritis after admission. • Cohort and isolate all symptomatic cases. • Patients exposed but remaining asymptomatic should stay in the original ward and should only be isolated if they develop clinical symptoms. • Stop admitting new patients to the ward in a suspected outbreak. *2. Disease surveillance and contact tracing.* • Define the surveillance period (e.g. four days before the onset of presentation of the index case for a suspected norovirus outbreak). • Establish a case definition for the outbreak. • Active surveillance and case finding for symptomatic inpatients. • Contact tracing of symptomatic cases among medical, nursing and allied health workers, and reviewing sick leave record of hospital staff. • Review admission records for phone contacts to trace symptomatic patients	Diarrhea was defined as changing from well-formed stool to ≥3 episodes of loose stools per day. Stool and rectal swab samples were evaluated using RT-PCR	282_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			these 6 were females and 5 were males. Age 4 mos. to 22 yrs	already discharged from the ward, and their parents and visitors. • Inform the University Health Service to trace medical students participating in the pediatric clerkship. *3. Infection control measures.* • Stringent contact precautions. • Enforce stringent hand hygiene policy in all pediatric wards. • Wear gloves, surgical masks and disposable plastic gowns when in contact with symptomatic patients or contaminated environment. • Remove toys and magazines displayed in the ward. *4. Environmental cleansing.* • Use concentrated disinfectant (hypochlorite solution 1000 ppm) for environmental cleansing. • Increase the frequency of routine cleansing in the ward (e.g. twice daily). • Widen the cleansing area to one square meter surrounding the contaminated area *5. Visiting policy* • Register all visitors and keep records for 14 days. • Restrict the number of visitors to two (i.e. parents only) for each inpatient. • All visitors should be screened by a standard questionnaire for symptoms and signs of gastroenteritis. *6. Staff management.* • Essential medical and paramedical staff who worked in affected ward were not allowed to work in unaffected clinical areas. • Non-essential personnel should not be allowed to enter the affected ward. • Symptomatic staff should discontinue clinical duties and seek medical advice immediately. *7. Others* • Posters about hand hygiene should be shown at the entrance of the ward. • Departmental seminars to educate staff on proper infection control measures and the clinical features of norovirus gastroenteritis. **Impact of Interventions** The outbreak was terminated within 3 days after the implementation of the infection control measures		
Simon, A; 2006 [171]	Descriptive study 1,2,3	To describe a norovirus outbreak.	Patients of a pediatric oncology unit in Germany. 14 males, 6 females. Median age 43 months (range 4-	**Outbreak description** 28.9% stool specimens tested positive for norovirus. Outbreak stopped with the start of the interventions **Viral shedding**	All tool samples tested with RT-PCR Viral shedding was defined as positive RT-	306_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			288 mos) 20 patients (11 outbreak, 9 sporadic) and 2 relatives	Median (Range) in days – 23(3-140) among 12 patients with >2 positive results who underwent weekly testing **Interventions** 1. Hand hygiene with 95% ethanol 2. Use of masks when in close contact with symptomatic patients 3. All patients were tested for norovirus and were isolated in cohorts if positive	PCR Nosocomial cases were identified as those with start of symptoms at least 24 hours after hospitalization	
Conway, R; 2005 [172]	Descriptive study None	To describe the management of an outbreak of norovirus.	Patients and staff at a tertiary care hospital. Demographic characteristics were not reported Sample size not reported	**Interventions** 1. Patients with loose or watery stools were reported to the Nursing Unit Manager or clinical coordinator for investigation. 2. Stool specimens or rectal swabs were collected on all patients. 3. Three wards managed the at-risk patients and patients who tested positive for norovirus during the outbreak. Patients were relocated and isolated from other patients, visitors and staff. 4. Barriers and signs were used to indicate entry and exit points for the isolated areas. 5. Dedicated nursing staff were allocated to care for these patients and skill mix and number of staff was assessed and allocated on a daily basis. 6. Nursing staff allocated to the care of these cohorts of patients were required to wear surgical scrubs, which were changed when leaving the ward. Any staff member entering the isolated area wore a disposable gown and gloves. 7. When dealing with explosive feces or projectile vomiting, a P2/N95 mask was worn to prevent staff from being affected by the aerosolization. 8. Upon leaving the isolated area all gowns, gloves and masks were disposed of and strict hand washing was enforced. 9. The Nursing Unit Manager assessed the cohorts of patients on a daily basis and provided an updated list. 10. Any patients who were symptom free for 48 hours were removed from the cohort and transferred to another area of the hospital. If cohort patients were being transferred to another facility, their discharges were delayed until the patients were symptom free for 48 hours. 11. Each ward involved in outbreak management was closed to any new admissions or transfers during the peak of the outbreak. To limit exposure to the outbreak, visitors were limited to only the immediate family. Children and elderly visitors were discouraged from visiting. 12. Education was provided to family members. 13. Disposable crockery and cutlery were arranged for the cohorts and kitchen staff were not permitted to enter the areas. The cleaning process in the kitchen was assessed and met the standard for cleaning the meal trays.	Cases were patients with loose or watery stools. norovirus confirmed using RT-PCR	3894_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				14. Affected staff members were advised to exclude themselves from work until symptom-free for 48 hours		
Cooper, E; 2005 [205]	Descriptive study 1,2,3	To describe a norovirus outbreak at a long term care facility.	Patients and staff on 3 wards in a 500 bed long term care facility in Australia. 52 patients and 11 staff.	**Interventions** The infection control team implemented the following measures consistent with the Victoria Department of Human Services guideline "Controlling an Outbreak of Gastroenteritis: Guidance for Institutions": -No patient transfers between wards or to other institutions. -Infected patients cohorted. -Hand hygiene encouraged and alcohol-based handrubs available by every bedside. -Gowns and gloves worn. -Detergent and water, followed by a 1,000-ppm solution of sodium hypochlorite used for cleaning. -Wards closed to new admissions. -Staff only scheduled to the same ward. -Visiting restricted. -Exposed food discarded. -Staff educated about how gastroenteritis spread, cleaning and disinfection procedures, isolation, transfers, and discharge. -Infected staff could not return to work until 48 hours after symptom resolution. -Contact information for the infection control team made available. The outbreak ended 32 days after the first symptoms of acute gastroenteritis identified.	norovirus genotype 2 detected on 2 of 3 wards. Power and sample size not reported.	5586_IL
Navarro, G; 2005 [174]	Descriptive study 1,2,3,4	To describe an outbreak in a long-term care unit in Spain.	Patients, residents, and staff in a long term care hospital in Spain. 82% female. Staff - 20-39 years old. Patients - 70-89 years old. 60 subjects – 32 patients, 19 staff members, 8 patients' relatives, and 1 relative of a staff member.	**Outbreak description** Incubation period of secondary cases – median 48 hours (range 1-7 days). Attack rate – 25.4% for patients and 41.3% for staff. Infected healthcare staff who cared for patients at symptom initiation - 84%; 78% of them were in charge of changing bed linens and moving patients. The outbreak was controlled in 21 days. **Interventions** -Hand hygiene and unit cleaning/disinfection re-emphasized. -Staff excluded from work while ill. -Hand washing with antiseptic soap (chlorhexidine or povidone-iodine). Handwashing involved wetting hands, using liquid soap, scrubbing 15 seconds, rinsing with water, and drying hands with a disposable paper towel. -Rooms cleaned with 1% aldehyde or 0.1% chlorine-free bleach.	Cases were those who developed diarrhea (≥2 episodes/24 hours) and/or vomiting after detection of the first case. Secondary cases were relatives of cases who developed symptoms within 24 hours of visiting an ill family member on the ward. This outbreak met Kaplan criteria.	522_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
					16/32 stool samples were positive for norovirus genotype 2. Power and sample size not reported.	
Schmid, D; 2005 [175]	Descriptive study 1,2,3,4	To describe an outbreak of norovirus affecting an Austrian nursing home and a hospital	Patients and staff of a nursing home and a nearby hospital in Austria. 88% female among nursing home cases and 68% female among hospital cases. In the nursing home, median age of staff cases was 41 years and that of resident cases was 82 years. In the hospital, median age of staff cases was 37 years and that of patients was 81 years. 25 cases in the nursing home and 28 cases in the hospital	**Attack rates** *Nursing home* Residents – 18/23(73.9%) Staff – 7/18(38.9%) *Hospital* Patients – 10/46(21.7%) Staff – 18/60(30.0%) **Response to outbreak** *Nursing home* Hygiene measures were implemented without waiting for virological confirmation. Two more cases among the residents occurred during the first two days after the measures were implemented. *Hospital* After a total of 16 cases had occurred in 7 days, the hospital authorities instituted control measures after virological confirmation. After these were implemented two staff and two patients fell ill.	The two institutional clusters met the Kaplan criteria for a norovirus outbreak	388_RA
Weber, D; 2005 [176]	Descriptive study 1,3,4	To describe an outbreak of norovirus.	A locked pediatric psychiatric unit in North Carolina. Age of patients 6-12 years. Sample size not reported	**Outbreak description** The index patient was a non-compliant 9 year boy with autism and mood disorders who frequently soiled the environment with fecal material. 3 of 4 patients, 10 of 38 permanently assigned staff, 3 staff temporarily floating from other psychiatric units, and five family members developed gastroenteritis. Symptoms reported by 13 staff members included loose or watery stools in 92%, nausea in 85%, abdominal pain in 77%, vomiting in 69% and fever in 31% **Interventions** 1. The unit was closed to all admissions 2. All staff with symptoms of gastroenteritis were given sick leave 3. Ill staff were not allowed to work until asymptomatic for at least 2 days 4. Staff were precluded from eating and drinking in the unit	Patients reported symptoms of gastroenteritis. norovirus was confirmed using RT-PCR in the index patient and 2 staff members.	405_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				5. The entire unit was treated as an isolation room with all staff performing hand hygiene and then donning gloves and a disposable gown 6. The unit was extensively cleaned and disinfected several times with 1:10 diluted hypochlorite (household bleach) 7. Hand hygiene with soap and water **Impact of interventions** (at 30 days after implementation) No subsequent cases of gastroenteritis were reported		
Lynn, S; 2004 [177]	Descriptive study 1,2,3,4	To describe outbreaks in two separate wards in a geriatric rehabilitation hospital and the role of infection control in limiting the spread.	Patients and staff in two wards in a geriatric rehabilitation hospital. 41 cases from the first outbreak. 24 cases from the second outbreak.	**First outbreak:** Attack rate – 57.1% for patients and 41% for staff. Outbreak duration – 14 days. Duration of ward closure – 11 days. Duration of staff sickness – mean, 1.2 days. Outcome – 1 patient died. **Second outbreak:** Attack rate – 56.5% for patients and 18% for staff. Outbreak duration – 16 days. Duration of ward closure – 6 days. Duration of staff sickness – mean, 3.5 days. **Interventions:** *Staffing guidelines* -Permanent staff worked in affected ward (wherever possible). -Staff needed to be symptom free for 48 hours before returning to work. -Staff without symptoms working in affected ward did not work anywhere else until 48 hours after completion of work in affected ward. -Casual staff who filled vacancies in affected ward remained there instead of also working on other wards. -Casual/bureau staff who had not worked in affected ward during the outbreak allocated to asymptomatic patients in non-infectious rooms. -All non-essential staff excluded when possible. *Precautions for any outbreak of vomiting and diarrhea* -Standard precautions at all times. -Hand hygiene stressed including when exiting ward. *Contact precautions* -Gloves and gown used when working in rooms with symptomatic patients. -Staff carried masks during acute outbreaks and used it if a patient had vomiting or	Cases were those with sudden onset of vomiting, with or without diarrhea. Other symptoms could include nausea, abdominal cramps, myalgia, headache, chills, and fever. The person had to have had contact with cases or in the environment/geographic area in which the outbreak was occurring. norovirus identified from stool sample using RT-PCR. Power and sample size not reported.	708_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				diarrhea or to clean up vomit. *Room placement* -Contact precautions per room. -No patients transfers to other rooms. -If a patient was moved, another patient was not moved into the original bed space until the remainder of the room was symptom free for 48 to 72 hours. *Linen* -Linen carrier taken to bedside -Hot water soluble bags and infectious labels used for soiled linen bags. *Cleaning guidelines* -Contaminated surfaces, carpet, flooring, and equipment promptly cleaned and disinfected. -Shared patient equipment cleaned with diluted Chlorwhite between usage. -Labeled individual commodes. -Toilets cleaned after use (wherever possible) with dilute Chlorwhite. *Empty rooms* -Terminally cleaned using Chlorwhite. -Steam clean carpets at >150 pounds per square inch (psi). -Bedside curtain changed when patient vomited or had diarrhea. *Cleaning staff for general cleaning* -Protective clothing while working. -Diluted sodium hypochlorite used for all horizontal surfaces including bedrails, handrails, door handles. -Toilets cleaned three times a day. *Sodium hypochlorite (Chlorwhite)* -1000 ppm = 10 mls per 500 ml water in spray bottle. -Solution made daily. -Bottle and pump cleaned with detergent and water before refilling.		
Khanna, N; 2003 [178]	Descriptive study None	To describe an outbreak of norovirus gastroenteritis.	Patients and healthcare workers at a university hospital in Switzerland. Demographic details not provided.	**Description of outbreak** There was no evidence for a water-borne, food-borne or environmental source. The source of the outbreak was most likely a patient admitted to the hospital. Once the outbreak was suspected, measures were instituted according to published guidelines, but the application of the guidelines proved difficult.	Patients suffered from clinical symptoms of acute gastroenteritis. norovirus was identified from fecal specimens by RT-PCR	787_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			63 cases	**Interventions** Interventions from published guidelines (Chadwick, JHI 2000) that were found to be feasible were: 1. Cohorting nurses 2. Wearing gloves and gown 3. Cautioning visitors 4. Increasing the frequency of routine ward, bathroom and toilet cleaning Interventions from guidelines that were found to be difficult or not feasible were: 1. Isolating symptomatic patients 2. Washing hands with soap after patient contact 3. Excluding affected staff from the ward immediately and until 48 hrs symptom free (this resulted in severe staff shortage) 4. Closing ward and avoiding transfer (exceeded hospital resources and frequently multiple wards were affected at the same time) 5. Using hypochlorite to disinfect hard surfaces (it was thought that hypochlorite may result in incompatibilities with surface composition not resistant with bleach)	Study period from 28 February to 20 March 2001	
McCall, J; 2002 [179]	Descriptive study 1,2,3,4	To describe an outbreak of norovirus.	Staff and patients of an acute elderly ward in Ireland. Demographic characteristics not reported. 58 cases	**Interventions** 1. Where possible symptomatic individuals were nursed in isolation and when no single rooms were available, cohort-nursed 2. Disposable plastic gown and gloves for staff and visitors; careful hand hygiene 3. Ward closed to admissions 4. Non-essential personnel excluded from ward 5. Transfers of patients to other wards and areas of the hospital were avoided unless medically essential 6. Not discharged to nursing or residential accommodations; discharge to patient's own home permitted 7. Frequency of routine ward, bathroom and toilet cleaning increased to hourly 8. Staff instructed that vomit and feces spillages be cleaned and disinfected promptly 9. Hypochlorite used to disinfect hard surfaces after cleaning 10. Staff who covered wide areas of the hospital advised to visit unaffected wards before affected wards 11. Medical rotations were altered to avoid cross cover between affected and unaffected wards 12. Staff advised that if they became unwell they should go off duty immediately and should be free of vomiting and diarrhea for 48 hrs before returning to work 13. Affected wards were not re-opened until 72 hours after the last new case and 72 hours after uncontained vomiting and diarrhea 14. Affected wards were terminally cleaned at the end of the outbreak	Case definition: A patient or staff member of the hospital who had acute onset of vomiting and/or diarrhea and who had a direct association with the elderly care ward without a negative sample. norovirus was confirmed using RT-PCR	890_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Response to intervention The control measures contained the spread of norovirus infection to one ward and stopped it in a few days		
Milazzo, A; 2002 [180]	Descriptive study 1,2,3,4	To describe an outbreak of norovirus gastroenteritis .	Residents and staff at an aged-care facility, 90/107 were females; 60% resided in the hostel, rest in the nursing home section. 107 residents, 75 staff	**Interventions** The interventions were based on published guidelines (Chadwick et al, JHI, 2000), specifically – staff were advised not to return to work for 48 hours after symptoms resolved.	A case was defined as a person living, working, visiting or epidemiologically linked to the aged-care facility with acute onset of diarrhea or vomiting between 14 August and 3 September 2000. Norovirus was confirmed with RT-PCR.	916_RA
Miller, M; 2002 [181]	Descriptive study 1,2,3,4	To describe an outbreak of norovirus gastroenteritis	Two aged care facilities and one hospital in Canberra., Australia Demographic characteristics not provided. 281 cases	**Description of outbreak** The outbreak lasted 32 days. Attack rates in the aged care facilities were 46.3%, 52.7% and that in the hospital was 55.2%. **Infection control challenges in the aged care facilities** 1. High pressure hoses in pan room 2. Lack of protective apparel in hose room 3. Lack of knowledge on body fluid spills 4. Limited access to spill kits 5. Lack of procedure for cleaning shower chairs 6. Inappropriate use of protective apparel when working with sick residents 7. Lack of adherence to staff sickness procedures 8. Transfers between institutions during outbreaks	Case definition: • at aged care facilities: a person who lived or worked at either institution and developed vomiting or diarrhea • at hospital: vomiting or diarrhea norovirus was detected using RT-PCR	879_RA
Hoyle, J; 2001 [182]	Descriptive study 1	To describe the challenges faced during an outbreak	Residents, staff and volunteers at a long term care facility in Australia. Demographic	**Interventions** 1. Education (especially about hand washing) 2. Collaborative development of an outbreak management guideline 3. Affected units were effectively quarantined until 14 days after the final case	A case was defined as any patient with diarrhea and/or vomiting within a 24	3979_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		and its management.	characteristics not reported. 76 residents; 25 staff and volunteers	report in each unit. Quarantine strategies included: • Restricting symptomatic residents to the affected unit • Restricting staff and volunteer movements from affected to unaffected units • Restricting visitors to one unit per visit • Affected staff, visitors and volunteers were deemed to be infectious for 48 hours after cessation of symptoms and were excluded from the facility • Physiotherapy and occupational and divisional therapy activities were limited to essential services only. Staff in affected units had to remain there • Instigating cleaning regimens for all allied health equipment • Gaining the cooperation of nursing staff in actively encouraging volunteers and visitors to utilize the clinical hand washing facilities 4. Allocating one nurse to care for the affected residents after providing care to his/her unaffected residents 5. Environmental cleaning – 1% sodium hypochlorite to wipe down surfaces for spills of vomitus and feces, thorough facility wide clean, all continence pads treated as infectious waste, additional mop heads allocated to all the units **Management issues identified** 1. Lack of isolation/cohorting facilities 2. Movements of nursing staff, allied health staff and large numbers of volunteers 3. Staff shortages 4. Lack of clear outbreak management policies and procedures 5. Perception of the signs of an outbreak (e.g. vomiting and diarrhea) as a normal situation 6. Issues with cleaning protocols and practices **Positive outcomes** 1. Development of realistic gastroenteritis management guidelines 2. Development of an effective infection control relationship with staff 3. Development of a positive relationship with the public health unit 4. Development of a holistic approach to infection control surveillance, infection management and prevention Anecdotally, the key interventions were sick leave for staff, limiting the movements of both staff and patients, and early ward closure	hour period. norovirus was confirmed to be the cause of the outbreak	

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Cunney RJ, 2000 [87]	Prospective controlled study 1,2,3,4	To investigate a hospital NLV outbreak.	Hospital outbreak N= 95 persons: 47 patients and 48 staff.	**Infection control practices** -Affected patients were cohorted -Admissions to and transfers from the geriatric ward were stopped -70% alcohol hand rub supplemented routine hand washing -Affected staff sent home until 48 hours after symptoms subsided -Decontamination procedures changed from standard phenolic solution to 2% hypochlorite solution **Food source** Drinking water from the hospital water supply: 16 symptomatic and 6 nonsymptomatic (p=0.1)	12 (13%) containing SRSV were solid phase immune electron microscopy (SPIEM) positive for NLV 25 (27%) sampes contained small round featureless virus (SRFV) identified by direct EM and were negative on SPIEM Power and sample size not reported.	1197_IL
Russo, PL; 1997 [183]	Descriptive study 1,2,3,4	To evaluate two outbreaks.	Patients and staff at an extended-care facility for the elderly and an acute care ward with an elderly population. Area 1 – 40 patients and 20 staff. Area 2 – 18 patients and 14 staff. Mean age – 79.1 years (range, 19-99).	**Attack rates** *First outbreak* Wards B and C – 50% Ward A – 33% *Second outbreak* Ward X – 49% **Interventions** *Admissions and discharges* -No patients admitted to or discharged from wards until outbreak ceased. -Patients discharged home if symptom free for 48 hours, with information and education, provided by the infection control department, given to patients' caregivers. *Visitors* -Visitors restricted to immediate family. Children discouraged from visiting until outbreak ceased. *New cases or patients requiring transfer* -Information sent to infection control on new cases or patients requiring transfer because of clinical deterioration. *Staff illness* -Affected staff remained off work until symptom free for 48 hours.	Case was patient or staff with vomiting or ≥ 2 episodes of loose stools within a 24 hour period. Power and sample size not reported.	4006_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Nursing care -Single use gowns and gloves worn when attending to patients with diarrhea and/or vomiting. Gowns were removed and disposed in a linen skip. Gloves thrown away and hands washed. *Handwashing* -Wash or disinfect hands after each patient contact. -Catering and cleaning staff instructed in hygiene and handwashing procedures by ward nursing staff. *Restricting patient movements* -Patients should not attend other departments such as physiotherapy until the outbreak ceased. -Physiotherapy and occupational therapy limited to individual wards. *Staffing* -Staffing for each ward individualized. Staff should not be shared between wards. -Non-essential staff excluded until the outbreak ceased. *Environmental services staff* -Dedicated catering and cleaning staff required for the period of the outbreak. -Floors, locker, overbed tables, toilets, handwashing basins and taps, showers, surface areas in clean and dirty utility rooms cleaned with 100-200 ppm disinfectant containing sodium hypochlorite solution. -The infection control department determined when frequency of cleaning reduced. *Soiled linen* -Soiled linen placed in linen skip. Soiled linen should not be handled once in linen skip. Linen skips require frequent changing to prevent overfilling. Outcome: 2-3 weeks for the outbreaks declared over despite <24 hours for control measures to be implemented. Emphasized early notification and prompt staff furloughing **Costs (In outbreak 2 alone)** -Nursing staff sick leave - $7,600 -Bed closures - $10,600		
Stevenson, P; 1994 [184]	Descriptive study	To describe an outbreak in a hospital for	Patients and staff at a UK hospital for the elderly.	**Interventions** -Infected patients cohorted. -Special cleaning of toilet areas in affected wards.	Norwalk virus confirmed by EM.	1554_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
	1,2,3	the elderly.	95 patients and 69 staff (including 6 visitors) affected.	-Symptomatic staff excluded from work for 48 hours after symptom resolution. -Affected wards closed until 48 hour period with no new symptomatic patients or staff. -Patients needed 5 days of symptom resolution if being discharged to nursing home or elderly persons' home and 48 hours if returning to their own homes. **Enhanced Interventions** -Hospital closed 6 days after outbreak initiation until 4 days after the last case symptom free. -Cleaning regimen using hypochlorite solution (HAZ TABS) and alco-wipes. -Restricted staff cross-movement and patient communal gatherings. -Visiting restricted. -Discharges to nursing and residential homes stopped. -Guidelines and situation summary given to staff with daily updated press statements. -Wards symptom free for 4 days given a final deep clean with 2% hypochlorite solution (including carpets, curtains, walls, and other equipment) prior to reopening. -Reopening prohibited if any staff or patient had diarrhea or vomiting. If only diarrhea, assessment by duty medical officer done to establish if the patient was suffering from viral gastroenteritis.	A case was a patient or staff with vomiting or diarrhea, with or without other symptoms, at the hospital on or after October 25, 1991. Six visitors were included as staff members. Power and sample size not reported.	
Hudson, JB; 2007 [185]	Basic science	To evaluate the efficacy of ozone gas from a generator (Viroforce) in inactivating norovirus and its surrogate FCV in dried samples in an office, hotel room, and cruise liner cabin.	Virus samples (50-100uL) were dried in duplicate on surfaces including sterile plastic. Ozone level was maintained at 20-25 ppm for 20 minutes, the rapid humidifying device (RHD) was activated for a 5 minute burst of water vapor, both the generator and RHD were switched off for 10 minutes to allow for incubation in the humid atmosphere, and the scrubber was then turned on to remove all ozone gas. When ozone levels decreased to less than 1 ppm, the door was opened and	**Results from field test in office following standard ozone protocol** *All results: Fraction of control in Pfu (Log_{10}); Fraction of control in RT-PCR (Log_{10})* FCV :0.012 (-1.92); 0.029 (-1.54) FCV + FBS: 0.017 (-1.77); 0.021 (-1.68) FCV + stool: 0.015 (-1.82); 0.020 (-1.70) *All results: Fraction of control in RT-PCR (Log_{10})* norovirus sample 1: 0.070 (-1.15) norovirus sample 2: 0.055 (-1.26) norovirus sample 3: 0.046 (-1.34) **Results from field test in hotel room following standard ozone protocol** *All results: Fraction of control in Pfu (Log_{10}) ; Fraction of control in RT-PCR (Log_{10})* FCV, bathroom: 0 (<-4.0); 0.077 (-1.11) FCV, bed: <0.0002 (<-3.7); 0.077 (-1.11) FCV, table: 0 (<-4.0); 0.075 (-1.12) **Results from cruise liner cabin following standard ozone protocol** Treated (bathroom, bed, and table): <10^1 Pfu/mL; Surviving fraction <0.0002; RT-PCR surviving fraction 0.003-0.03 **Results on different surfaces following standard ozone protocol**	Norovirus measured by RT-PCR and FCV by QRT-PCR and virus infectivity assays. Feline bovine serum (FBS) Pfu = plaque forming units/mL **Control values** *Field test in office* *FCV infectivity* 5.1 x 10^4 Pfu/mL 116-218 ng RNA by PCR *norovirus infectivity* norovirus sample 1 = 58.15 ng RNA norovirus sample 2 = 129.5 ng RNA	122_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			test samples retrieved for testing.	*All results – fraction of control* Plastic – FCV infectivity ≤6 x 10^{-5}; FCV QRT-PCR 0.0013-0.0016; norovirus QRT-PCR 0.05-0.069 Fabric – FCV infectivity ≤3 x 10^{-4}; FCV QRT-PCR 0.0036-0.0048; norovirus QRT-PCR 0.056-0.065 Cotton – FCV infectivity ≤3 x 10^{-5}; FCV QRT-PCR 0.076-0.079; norovirus QRT-PCR 0.030-0.031 Carpet – FCV infectivity ≤4 x 10^{-5}; FCV QRT-PCR 0.0028-0.0032; norovirus QRT-PCR 0.042-0.059 Virus-containing samples dried onto hard and soft surfaces were equally vulnerable to ozone. Some potential toxicity issues, especially in areas with high traffic	norovirus sample 3 = 114.1 ng RNA *Field test in hotel room* *FCV infectivity* 8.0 x 10^4 Pfu/mL 415.5 ng RNA by PCR *Field test in cruise liner cabin* *FCV infectivity* 5.37 x 10^4 Pfu/mL *Field test for different surfaces* *FCV infectivity* 2.7-3.6 x 105 Pfu *FCV QRT-PCR* 18.7-57.3 ng RNA *norovirus QRT-PCR* 98.6-132.7 ng RNA	
Park GW, 2007 [186]	Basic Science	To evaluate the efficacy of sterilox hypochlorous acid (HOCl) solution (HAS) to reduce norovirus both in aqueous suspensions and on inanimate carriers. HOCl was further tested as a fog to decontaminate large spaces	No. 4 finish-polished stainless steel and ceramic tiles were used as representative nonporous andporous surfaces.	Exposing virus-contaminated carriers of ceramic tile (porous) and stainless steel (nonporous) to 20 to 200 ppm of HOCl solution resulted in ≥ 99.9% (≥ 3 $\log_{10}$) reductions of both infectivity and RNA titers of tested viruses within 10 min of exposure time. HOCl fogged in a confined space reduced the infectivity and RNA titers of norovirus, MNV, and MS2 on these carriers by at least 99.9% (3 $\log_{10}$) regardless of carrier location and orientation.	HOCl effectiveness was evaluated using nonculturable human norovirus measured by RT-PCR and two surrogate viruses, coliphage MS2 and MNV.	89_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Poschetto, LF; 2007 [187]	Basic science	To evaluate the efficacy of an organic acid (Venno Vet 1 Super), an aldehyde (Venno FF Super), a halogen compound (sodium hypochlorite solution), and peroxide (Oxystrong FG) in inactivating norovirus and FCV.	Known amounts of virus suspensions were incubated with disinfectants. Viral RNA levels were checked pre- and post-disinfection.	**Virucidal efficacies of disinfectants** *All results – minutes (titer in log_{10} RTPCRU/ml)* Organic acid (3%) FCV – 15 (5); 30 (5); 60 (5); 120 (5) norovirus – 15 (5); 30 (5); 60 (5); 120 (5) Organic acid (4%) FCV – 15 (3); 30 (2); 60 (2); 120 (2) norovirus – 15 (4); 30 (4); 60 (4); 120 (4) Organic acid (5%) norovirus – 15 (4); 30 (3); 60 (2); 120 (2) Aldehyde (0.1%) FCV – 15 (5); 30 (4); 60 (5); 120 (5) norovirus – 15 (5); 30 (5); 60 (5); 120 (5) Aldehyde (0.5%) FCV – 15 (4); 30 (4); 60 (3); 120 (3) norovirus – 15 (5); 30 (5); 60 (5); 120 (5) Aldehyde (1%) norovirus – 15 (4); 30 (4); 60 (4); 120 (4) Aldehyde (2%) norovirus – 15 (4); 30 (4); 60 (3); 120 (3) Halogen compound (1%) FCV – 15 (5); 30 (5); 60 (5); 120 (5) norovirus – 15 (4); 30 (3); 60 (3); 120 (4) Halogen compound (6,000 ppm free chlorine) FCV – 15 (2); 30 (2); 60 (2); 120 (2) norovirus – 15 (≤1); 30 (2); 60 (≤1); 120 (2) Halogen compound (1.2%) FCV – 15 (5); 30 (4); 60 (5); 120 (5) norovirus – 15 (4); 30 (4); 60 (4); 120 (4) Halogen compound (7,000 ppm free chlorine) FCV – 15 (2); 30 (2); 60 (≤1); 120 (2) norovirus – 15 (≤1); 30 (≤1); 60 (≤1); 120 (≤1) Peroxide (1%) FCV – 15 (2); 30 (3); 60 (2); 120 (2) norovirus – 15 (3); 30 (3); 60 (2); 120 (2) Peroxide (2%) FCV – 15 (2); 30 (2); 60 (2); 120 (2) norovirus – 15 (3); 30 (3); 60 (2); 120 (2) **Disinfectant concentrations and contact times associated with the greatest FCV**	The criterion normally set for virucidal efficacy is 99.9% (3 log_{10}) – these results are highlighted.	067_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				and norovirus titer reduction *All results Disinfectant [reduction factor (RF) in log10] – Conditions for FCV and norovirus* Organic acid (3) – FCV 4%, 30 minutes; norovirus 5%, 60 minutes Aldehyde (2) – FCV 0.5%, 60 minutes; norovirus 2%, 60-120 minutes Halogen compound (≥3) – FCV 1% (6,000 ppm free chlorine), 15 minutes; norovirus 1% (6,000 ppm free chlorine), 15 minutes Peroxide (3) – FCV 1%, 60 minutes or 2%, 15 minutes; norovirus 1%, 60 minutes or 2%, 60 minutes **Conclusions** All disinfectants, except the aldehyde, were effective on FCV. According to RT-PCR results, 5% organic acid, 1% peroxide, not less than 2% aldehyde with a contact time of 1 h, and a 1% halogen compound with 6,000 ppm of free chlorine and a contact time of 15 minutes, are required for safe disinfection.		
Jimenez, L; 2006 [188]	Basic science study N/A	To determine the virucidal effectiveness of R-82, a quarternary ammonium compound disinfectant. This was prepared as 1:256 dilutions in water with a hardness of 400 ppm calcium carbonate for 10 minutes. Hypochlorite concentrations of 100 ± 10 and 1000 ± 10 ppm were also analyzed as controls.	Feline calcivirus (FCV) suspensions. Study was conducted in New Jersey, US. N/A	**Reductions in FCV in log_{10} MPN/mL at 10 min contact time** *Initial testing* R-82 – 6.6 (complete inactivation) Hypochlorite 100 ± 10 ppm – 3.2 Hypochlorite 1000 ± 10 ppm – 6.6 (complete inactivation) *Confirmatory testing* R-82 – 6.4 (complete inactivation) Hypochlorite 100 ± 10 ppm – 2.8 Hypochlorite 1000 ± 10 ppm – 6.4 (complete inactivation)	The reduction of infectious virus (defined as FCV with cytopathic effects) were expressed as log_{10} most probable number (MPN)/mL. The log_{10} reduction for FCV was calculated as the difference between the disinfectant and plate recovery control.	3879_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Kramer, A; 2006 [189]	Basic science	To test the virucidal activity (reduction in viral titer) of a new hand disinfectant with reduced ethanol content (55%) in combination with 10% propan-1-ol, 5.9% propan-1.2-diol, 5.7% butan-1.3-diol and 0.7% phosphoric acid. For in vivo tests, the test product was compared with 70% ethanol, 70% propan-1-ol and standard hard water.	FCV strain F9 both in vitro and in vivo (fingerpad tests using human volunteers – 3 male, 4 female). 7	**Dilution of test product demonstrating virucidal efficacy (RF≥4) against FCV** 80% dilution for a contact time of 0.5 min **Reduction of FCV titers** *All results mean log10 RF; P value for comparison with test product* Test product vs. 70% ethanol – 2.38 vs. 0.68; P<0.01 Test product vs. 70% propan-1-ol – 2.38 vs. 0.74; P<0.01 Test product vs. standard hard water – 2.38 vs. 1.39; P<0.01	Virucidal efficacy was measured as log_{10} reduction in viral titers – called reduction factor (RF). A disinfectant solution was considered to have virucidal efficacy if, within the tested exposure period, the titre was reduced at least 10^4 fold (RF≥4)	374_RA
Malik, Y; 2006 [190]	Basic science study N/A	To evaluate five disinfectants against FCV on various carpets and fabrics to detect percentage inactivation of virus. The five disinfectants tested were:	*Fabrics* 1. 100% cotton 2. 100% polyester 3. Cotton blend (35:65 blend of cotton and polyester) *Carpets* 1. Olefin 2. Polyester 3. Nylon	All results are percentage inactivation of FCV at 1, 5 and 10 min **Fabrics** *1. 100% cotton* Metricide – 99.99; 99.99; 100.00 Microbac-II – 85.63; 73.40; 98.72 Sodium bicarbonate and quarternary ammonium compound – 86.20; 90.00; 97.34 GermEX – 98.26; 99.55; 99.86 Sodium bicarbonate and glutaraldehyde – 95.63; 99.12; 99.55 *2. 100% polyester* Metricide – 99.99; 99.99; 100.00 Microbac-II – 71.73; 98.32; 99.00	% virus inactivation = 100 – (amount of virus from disinfectant-treated pieces/amount of virus from negative-control pieces) × 100. Average of 3 experiments was used. Virus was grown in feline kidney cells.	313_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		1. Metricide – activated 2.6% glutaraldehyde (undiluted) 2. Microbac-II – 4.75% o-benzyl p-chlorophenol and 4.75% o-phenylphenol (1:128 dilution) 3. 10% sodium bicarbonate and 10% quarternary ammonium compound (1:32 dilution) 4. GermEX – 70% isopropanol (undiluted) 5. 2.5% sodium bicarbonate and 1.3% glutaraldehyde (1:32 dilution)	4. Blended carpet (85:15 blend of nylon and olefin) N/A	Sodium bicarbonate and quarternary ammonium compound – 94.56; 90.00; 92.40 GermEX – 82.17; 69.60; 91.60 Sodium bicarbonate and glutaraldehyde – 73.91; 83.52; 96.96 *3. Cotton blend* Metricide – 99.99; 99.99; 100.00 Microbac-II – 77.61; 86.20; 95.21 Sodium bicarbonate and quarternary ammonium compound – 99.00; 98.04; 95.43 GermEX – 99.00; 98.04; 96.30 Sodium bicarbonate and glutaraldehyde – 99.38; 99.25; 97.39 **Carpets** *1. Olefin* Metricide – 99.91; 99.97; 99.95 Microbac-II – 77.61; 84.25; 73.84 Sodium bicarbonate and quarternary ammonium compound – 0; 62.0; 83.83 GermEX – 60.95; 92.10; 97.00 Sodium bicarbonate and glutaraldehyde – 78.09; 88.00; 96.76 *2. Polyester* Metricide – 94.54; 100.00; 100.00 Microbac-II – 88.63; 88.29; 96.91 Sodium bicarbonate and quarternary ammonium compound – 82.72; 77.65; 95.53 GermEX – 88.63; 91.70; 78.72 Sodium bicarbonate and glutaraldehyde – 97.90; 95.10; 98.14 *3. Nylon* Metricide – 99.93; 99.95; 100.00 Microbac-II – 38.18; 36.95; 60.26 Sodium bicarbonate and quarternary ammonium compound – 0; 17.31; 17.21 GermEX – 52.72; 93.69; 91.72 Sodium bicarbonate and glutaraldehyde –67.27; 71.73; 90.00 *4. Blended carpet* Metricide – 80.00; 97.80; 99.68 Microbac-II – 55.17; 38.00; 68.39 Sodium bicarbonate and quarternary ammonium compound – 80.00; 38.00; 45.90 GermEX – 80.00; 73.80; 68.39 Sodium bicarbonate and glutaraldehyde – 97.58; 91.90; 90.00		

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Malik, Y; 2006 [191]	Basic science study N/A	To compare the virucidal activity of ethanol and isopropyl alcohol against dried feline calcivirus (FCV). Control was exposure to phosphate buffered saline (PBS).	F-9 strain of FCV. Study was conducted in US. N/A	**Percent virus reduction** *All results are reductions at a contact time of 1,3 and 10 minutes respectively at each concentration of the disinfectant in %* *Ethyl alcohol* 10 – 86.49; 91.16; 95.00 20 – 88.37; 88.37; 86.49 30 – 88.37; 81.65; 88.37 40 – 93.70; 99.19; 84.10 50 – 98.28; 97.55; 90.20 60 – 98.11; 98.65; 90.20 70 – 99.19; 98.41; 94.50 80 – 98.43; 98.50; 94.50 90 – 99.35; 97.49; 99.49 100 – 98.46; 97.65; 98.06 **Isopropyl alcohol** 10 – 95.07; 87.81; 87.81 20 – 80.29; 91.64; 80.83 30 – 90.46; 90.00; 83.13 40 – 99.30; 94.44; 94.75 50 – 99.59; 99.52; 99.12 60 – 99.84; 99.76; 99.79 70 – 97.57; 98.94; 99.47 80 – 97.37; 99.12; 99.46 90 – 97.37; 98.14; 99.57 100 – 97.36; 96.59; 96.65 Summary: Ethanol at 70% and 90% concentrations was most effective at killing FCV within 1 minute; isopropanol effective at 50% and 70% but none of the alcohols able to achieve 3 log reduction in FCV (>99.9% kill).	% virus reduction was calculated as [($V_{control}$ – $V_{treated}$)/ $V_{control}$] X 100	3891_RA
Malik, Y; 2006 [192]	Basic science study N/A	To evaluate the efficacy of the following compounds against FCV dried on a stainless steel surface: 1. Sodium Bicarbonate	F-9 strain of FCV. Study was conducted in US. N/A	**Percent virus reduction** *All results are reductions at a contact time of 1,3 and 10 minutes respectively at each concentration of sodium bicarbonate in %* 1 – 97.22; 97.22; 98.60 2 – 97.22; 98.14; 99.60 5 – 99.22; 99.40; 99.81 10 – 99.99; 99.99; ≥99.99 20 - 99.99; ≥99.99; ≥99.99 *All results are reductions at a contact time of 1,3 and 10 minutes respectively for each disinfectant*	% reduction = 100 – (virus counts eluted after test product treatment/virus counts eluted from control well disks) x 100	4234_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		1% + 1.3% glutaraldehyde 2. Sodium Bicarbonate 2.5% + 1.3% glutaraldehyde 3. Sodium Bicarbonate 1.0% + activated dialdehyde 4. Sodium Bicarbonate 2.5% + activated dialdehyde 5. Sodium Bicarbonate 2.0% + 2.0% hydrogen peroxide		Sodium Bicarbonate 1% + 1.3% glutaraldehyde – 99.99; 99.99; 99.99 Sodium Bicarbonate 2.5% + 1.3% glutaraldehyde – 99.99; 99.99; 99.99 Sodium Bicarbonate 1.0% + activated dialdehyde – 99.00; 99.00; 99.99 Sodium Bicarbonate 2.5% + activated dialdehyde – 99.99; 99.99; 99.99 Sodium Bicarbonate 2.0% + 2.0% hydrogen peroxide – 99.00; 99.00; 99.68		
Kampf, G; 2005 [193]	Basic science	To investigate the efficacy of 3 ethanol-based hand rubs against FCV on artificially contaminated hands.	German volunteers had their fingers contaminated with virus suspension with or without organic load and decontaminated with one of the 3 ethanol-based handrubs compared to 70% N-propanol or 70% ethanol to determine their efficacy against FCV. 4 volunteers.	**Reduction in FCV infectivity** *Mean log_{10} reduction factor hand rub (n=16), 70% ethanol (n=8): p value* Reference alcohols – N/A, 1.45; N/A Sterillium Virugaard – 2.17, 1.56; 0.17 Sterillium Rub – 1.25, 1.03; 0.20 Desderman N – 1.07, 1.27; 0.47 *Mean log_{10} reduction factor of hand rub (n=16), 70% propan-1-oll (n=8); p value* Reference alcohols – N/A, 0.95; N/A Sterillium Virugaard – 1.63, 0.95; 0.0003 Sterillium Rub – 1.43, 1.09; 0.03 Desderman N – 0.78, 0.97; 0.35 Summary: Ethanol superior to isopropan-1-ol	Cases received Sterillium Virugard, 95% ethanol, Sterillium Rub, 80% ethanol, or Deserman N, 75.1% ethanol. Controls received N-propanol (70%, w/w) and ethanol (70%, w/w), which have previously been described to be virucidal against FCV.	510_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Barker, J; 2004 [194]	Basic science	To study the transfer of norovirus from contaminated fecal material via fingers and cloths to other surfaces using RT-PCR and to assess the effectiveness of detergent and disinfectant based cleaning regimens.	A homogenized clinical fecal sample positive for norovirus genogroup II was used. A fecal sample negative for norovirus was used as a negative control. **Transfer of norovirus by fingers to surfaces** *Primary transfer* Fecal sample diluted in phosphate buffered saline was absorbed on toilet paper in a Petri dish. The experimenter's fingertips were pressed on to the contaminated tissue for 10 seconds, and dried for 15 seconds at room temperature. Contaminated fingers were then pressed on clean melamine surfaces for 10 seconds and left at room temperature for 15 minutes before testing for norovirus. *Secondary transfer* After allowing contaminated melamine surface to dry at room temperature for 15 minutes, clean dry	**Transfer of norovirus by fingers to surfaces** *Primary Transfer* 4 experiments using 8 clean melamine surfaces: 4 surfaces – all 4 experiments norovirus positive 2 surfaces – 3/4 experiments positive 1 surface – 1/4 experiments positive 1 surface – 0/4 experiments positive *Secondary Transfer* norovirus transferred from primary surface to 4/10 door handles, 5/10 telephone receivers, and 3/10 taps. **Cleaning and disinfection studies** Methods 1, 2 and 3 failed to eliminate norovirus in 14 experiments even when the cloth was re-soaked and the melamine surface rewiped. If the cloth was used to wipe a second clean surface, norovirus was recovered from that surface and from the fingers of study participants. Methods 4 and 5 eliminated norovirus from the surface in a portion of cases. When the surface tested negative, second surfaces and fingers also tested negative. norovirus could still be detected in 28% of surfaces at 5 minute and 21% after 1 minute. In cases where norovirus remained, there was 100% transfer to a second clean surface and 75% transfer to fingers. Method 6 completely eliminated norovirus.	Hypochlorite disinfectant/cleaner (HDC) containing 5000 ppm of available chlorine and 4% (w/v) of an anionic surfactant (supplied by Lever Brothers, Port Sunlight, UK).	628_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			fingers touched the surfaces and then touched a telephone receiver, a tap handle, and a door handle. Secondary surfaces were left at room temperature for 15 minutes before testing for norovirus. **Cleaning and disinfection studies** 6 melamine surfaces were contaminated with 10µL fecal sample and dried at room temperature for 15 minutes. They underwent the following protocols and were sampled for norovirus after cleaning: 1) Untreated control 2) Cleaning with cloth soaked in detergent solution for 10 seconds 3) Cleaning with used cloth initially soaked in detergent solution for 10 seconds, then later rinsed in detergent solution after use, and then used to rewipe the surface for 10 seconds. 4) Hypochlorite disinfectant/cleaner (HDC) applied to surface for 1 minute followed by wiping of			

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			surface with cloth soaked in detergent solution for 10 seconds. 5) Similar to 4, except HDC applied for 5 minutes. 6) Gross fecal matter removed from the surface by wiping with a cloth soaked in detergent solution for 10 seconds, followed by surface disinfection with HDC for 1 minute, followed by wiping of surface with cloth soaked in detergent solution for 10 seconds.			
Duizer E, 2004 [195]	Basic Science	To investigate the inactivation of the enteric canine CaCV no. 48 and the respiratory FCV F9.	N/A	**Thermal inactivation** Inactivation of CaCV and FCV: 4C: <1D inactivation in 2 weeks 20C: 3D inactivation 1 week Between 37 - 56C: 3D inactivation decreased from 24 hours to 8 minutes Heating to 71.3C: 3D inactivation in 1 minute Reduction of infectivity by five cycles of freezing and thawing was 0.44 ± 012 D for CaCV and 0.34 ± 0.18D for FCV **UV inactivation** 21 mJ/cm^2 for CaCV and 22mJ/cm^2 for FeCV: 2D inactivation 34 mJ/cm^2 for CaCV and FeCV: 3D inactivation **pH stability** pH<= 5 and pH>=10: >5D inactivation for CaCV pH 9: 4D reduction for FeCV and 3D reduction for CaCV pH 6: 2D reduction for FeCV and 4D reduction for CaCV pH<=2 and pH>=10: >5D inactivation for FCV	D = 1 $\log_{10}$, calculated by dividing the $TCID_{50}$ of the treated sample by the $TCID_{50}$ of the untreated sample	643_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Inactivation by 70% ethanol Inactivation of CaCV and FCV: <2D reduction in $TCID_{50}$ after 8 minutes 3D reduction after 30 minutes **Inactivation by sodium hypochlorite** Up to 30 ppm free chlorine: <1D inactivation 300 ppm: >3D inactivation for CaCV and <2D inactivation for FCV 3,000 ppm: complete inactivation (>5D) of FeCV and CaCV in 10 and 30 minutes at room temperature		
Gehrke, C; 2003 [196]	Basic science	To evaluate the efficacy of 3 types of alcohol against FCV as a surrogate for norovirus on fingertips.	**In vitro inactivation experiments** One part virus suspension mixed with one part double distilled water and eight parts alcohol in different concentrations to determine efficacy of alcohol products. **In vivo inactivation experiments** Fingertips of volunteers from Germany were artificially contaminated with FCV to determine the efficacy of virus elimination using different alcohol products. The tested alcohol products included ethanol, and 1- and 2-propanol.	**In vitro inactivation experiments** *All results Alcohol with concentration – Reduction in titer in log_{10} ID_{50} after different time periods; Time to ≥ 4 log_{10} reduction in titer* Ethanol 50% - 2.19 at 0.5 min, 3.65 at 1.0 min, ≥4.44 at 3.0 min, ≥4.50 at 5.0 min; 3.0 min Ethanol 70% - 3.55, ≥3.83, ≥5.00, ≥5.19; 3.0 min Ethanol 80% - 2.19, 2.97, 3.88, ≥4.25; 5.0 min 1-Propanol 50% - ≥4.13, ≥4.31, ≥5.13, ≥4.73; 0.5 min 1-Propanol 70% - ≥4.06, ≥4.06, ≥4.13, ≥4.13; 0.5 min 1-Propanol 80% - 1.90, ≥3.58, ≥4.13, ≥3.98; 3.0 min 2-Propanol 50% - 2.31, 3.22, ≥4.90, ≥5.47; 3.0 min 2-Propanol 70% - 2.35, 2.90, ≥3.92, ≥4.22; 5.0 min 2-Propanol 80% - 1.35, 1.27, 1.88, 2.38; >5.0 min *Extrapolated data* The following concentrations had the greatest virus-inactivating properties: Ethanol 67% after 1 min with a log_{10} reduction factor of 3.8. 2-Propanol 58% after 1 min with a log_{10} reduction factor of 4.9. 1-Propanol 60% after 30 sec with a log_{10} reduction factor of 4.3. **In vivo inactivation experiments** *All results Alcohol (concentration; exposure time; No. fingertips) – Reduction of FCV titer in log_{10} ID_{50} ± SD* Ethanol (70%; 30 sec; 16) – 3.78 ± 0.83 Ethanol (90%; 30 sec; 8) – 2.84 ± 0.64 1-Propanol (70%; 30 sec; 16) – 3.58 ± 0.92 1-Propanol (90%; 30 sec; 8) – 1.38 ± 0.33 2-Propanol (70%; 30 sec; 16) – 2.15 ± 0.50	730_IL	

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				2-Propanol (90%; 30 sec; 8) – 0.76 ± 0.19 Hard water (N/A; 30 sec; 36) – 1.23 ± 0.44 **Conclusions** In vitro experiments showed that 1-propanol was most effective The greatest efficacy did not occur at the highest concentrations (80%). In contrast to the in vitro studies, in vivo 70% ethanol showed the greatest efficacy.		
Lin, C; 2003 [197]	Basic science	To evaluate different hand washing agents against natural and artificial fingernails contaminated with Ecoli and CaCV.	Volunteers from Georgia with artificial and natural nails were artificially contaminated with ground beef containing E coli JM109 or artificial feces containing FCV to evaluate the efficacy of the following agents: handwashing with tap water, regular liquid soap (Ivory, Proctor and Gamble), antibacterial liquid soap, (Dial Gol, active ingredient triclosan) alcohol-based hand sanitizer gel (Purell, 62% ethanol), regular liquid soap followed by alcohol gel, and regular liquid soap plus a nailbrush. Average age – 45 5 with artificial nails – all female 5 with natural nails – 3 female and 2 male	**FCV** *All six handwashing procedures combined - Before vs after handwashing FCV in -log $TCID_{50}$ ± SD* Natural nail – 3.06 ± 0.47 vs 1.15 ± 0.75 Artificial nail – 3.69 ± 0.52 vs 2.18 ± 0.98 *All results for Handwashing agents – reductions in counts in - log $TCID_{50}$ ± SD* *Tap water* Natural nail – 1.97 ± 0.68 Artificial nail – 1.22 ± 0.86 *Soap* Natural nail – 1.82 ± 0.46 Artificial nail – 1.89 ± 0.31 *Antibacterial soap* Natural nail – 2.26 ± 0.42 Artificial nail – 1.65 ± 0.19 *Hand sanitizer* Natural nail – 0.86 ± 0.55 Artificial nail – 0.43 ± 0.47 *Soap plus sanitizer* Natural nail – 2.13 ± 0.93 Artificial nail – 1.85 ± 0.69 *Soap plus nailbrush* Natural nail – 2.54 ± 0.57 Artificial nail – 0.41 ± 0.79 **Combined data** Lower non-statistical reductions of Ecoli and FCV counts obtained for artificial vs natural	Highlighted p≤0.05	769_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				fingernails (p>0.05). Significantly higher Ecoli and FCV counts were recovered from hands with artificial vs natural nails before and after hand washing (p<=0.05). Microbial cell numbers were correlated with fingernail length, with greater numbers for those with longer nails (p>0.05). **Conclusions** Best practices for fingernail sanitation of food handlers may be to keep fingernails short , natural, and scrub with soap and nailbrush when washing hands.		
Nuanualsuwan,S ; 2002 [198]	Basic science study N/A	To evaluate ultraviolet (UV) inactivation of feline calcivirus (FCV) and to compare it to hepatitis A virus, poliovirus type 1 and two small, round coliphages (MS2 and φX174).	FCV and other viruses (hepatitis A virus, poliovirus type 1 and two small, round coliphages - MS2 and φX174). N	**Dose in mW s/cm^2 required to reduce viral titer by 1 log$_{10}$** FCV – 47.85 Hepatitis A Virus – 36.50 Poliovirus type 1 – 24.10 MS2 – 23.04 φX174 – 15.48 The UV inactivation curve of FCV was not statistically different from Hepatitis A virus (P>0.05), but was significantly different from Poliovirus type 1, MS2 and φX174 (P<0.05)	4603_RA	
Gulati, BR; 2001 [199]	Basic science	To use FCV as a surrogate to determine the potential efficacy of disinfectants against norovirus on fresh fruit and produce, and food-contact surfaces.	The following products were tested for their efficacy against FCV on artificially contaminated: *Stainless steel food contact surfaces* – 5.25% sodium hypochlorite (Fox-chlor, Jane Fox, Minn); 1.75% iodine and 6.5% phosphoric acid (Mikroklene, Ecolab, St. Paul, Minn); three quarternary ammonium	**1 minute contact time** **-Not effective in any of the tests and no further details given** **10 minute contact time** *Food contact surfaces* *All results – Log$_{10}$ FCV reduction ± SD* 9% QAC 1:200 (450 ppm) – 0.3 ± 0.05 9% QAC 1:100 (900 ppm) – 0.0 ± 0.0 9% QAC 1:50 (1800 ppm) – 2.3 ± 0.05 10% QAC 1:256 (400 ppm) – 0.7 ± 0.1 10% QAC 1:128 (800 ppm) – 1.0 ± 0.1 10% QAC 1:64 (1600 ppm) – 2.0 ± 0.05 5% QAC and 2% sodium bicarbonate 1:64 (780 ppm of QAC) – 0.4 ± 0.05 5% QAC and 2% sodium bicarbonate 1:32 (1560 ppm of QAC) – 3.3 ± 0.1	An agent was considered effective if the virus titer decreased at least 3 log$_{10}$ (99.9%) compared to untreated controls – significant results highlighted. Disinfectants and sanitizers diluted in sterile tap water immediately before use.	5985_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			compouns (QACs) (Microquat and Oasis 144, Ecolab and UMQ, Chemical Specialties Lab, Fairmont, Minn); 15% peroxyacetic acid and 11% hydrogen peroxide (Victory, Ecolab); and two phenolic products (Lysol IC, Reckitt an Colman, Montvale, NJ, and Microbac II, Ecolab) *Strawberry and lettuce* - 5.25% sodium hypochlorite (Fox-chlor), QAC (Oasis 144), and 15% peroxyacetic acid and 11% hydrogen peroxide (Victory). Products tested at one, two, or four times manufacturers' recommended concentrations for contact times of 1 and 10 minutes.	5% QAC and 2% sodium bicarbonate 1:16 (3120 ppm of QAC) – 3.4 ± 0.05 5.25% sodium hypochlorite (200 ppm of free chlorine) – 0.3 ± 0.05 5.25% sodium hypochlorite (400 ppm of free chlorine) – 0.3 ± 0.0 5.25% sodium hypochlorite (800 ppm of free chlorine) – 1.1 ± 0.05 15% peroxyacetic acid and 11% hydrogen peroxide 1:2000 – 0.4 ± 0.1 15% peroxyacetic acid and 11% hydrogen peroxide 1:1000 – 0.6 ± 0.05 15% peroxyacetic acid and 11% hydrogen peroxide 1:500 – 3.0 ± 0.0 1.75% iodine and 6.5% phosphoric acid (75 ppm of titratable iodine) – 0.0 ± 0.0 1.75% iodine and 6.5% phosphoric acid (150 ppm of titratable iodine) – 0.0 ± 0.0 1.75% iodine and 6.5% phosphoric acid (300 ppm of titratable iodine) – 2.0 ± 0.1 4.75% o-benzyl p-chlorophenol and 4.75% o-phenylphenol 1:256 – 1.5 ± 0.05 4.75% o-benzyl p-chlorophenol and 4.75% o-phenylphenol 1:128 – 6.2 ± 0.2 4.75% o-benzyl p-chlorophenol and 4.75% o-phenylphenol 1:64 – 7.0 ± 0.2 5% o-benzyl p-chlorophenol and 10.5% o-phenylphenol 1:200 – 0.4 ± 0.1 5% o-benzyl p-chlorophenol and 10.5% o-phenylphenol 1:100 – 0.4 ± 0.1 5% o-benzyl p-chlorophenol and 10.5% o-phenylphenol 1:50 – 5.6 ± 0.2 *Fresh produce* *All results – Log_{10} FCV reduction ± SD* 15% peroxyacetic acid and 11% hydrogen peroxide 1:2000 – Strawberry 0 ± 0.00; Lettuce 0 ± 0.00 15% peroxyacetic acid and 11% hydrogen peroxide 1:1000 – Strawberry 1.0 ± 0.1; Lettuce 2.0 ± 0.1 15% peroxyacetic acid and 11% hydrogen peroxide 1:500 – Strawberry 3.0 ± 0.06; Lettuce 3.0 ± 0.06 5.25% sodium hypochlorite (200 ppm of free chlorine) – Strawberry 0 ± 0.0; Lettuce 0 ± 0.0 5.25% sodium hypochlorite (400 ppm of free chlorine) – Strawberry 0 ± 0.0; Lettuce 0 ± 0.0 5.25% sodium hypochlorite (800 ppm of free chlorine) – Strawberry 1.0 ± 0.06; Lettuce 1.5 ± 0.05 10% n-alkyl (50% C14, 40% C12, 10% C16) imethyl benzyl ammonium chloride 1:512 (200 ppm) – Strawberry 0 ± 0.0; Lettuce 0 ± 0.0		

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				10% n-alkyl (50% C14, 40% C12, 10% C16) imethyl benzyl ammonium chloride 1:256 (400 ppm) – Strawberry 0 ± 0.0; Lettuce 0 ± 0.0 10% n-alkyl (50% C14, 40% C12, 10% C16) imethyl benzyl ammonium chloride 1:128 (800 ppm) – Strawberry 1.5 ± 0.1; Lettuce 2.0 ± 0.1 **Conclusions** None of the disinfectants were effective when used at manufacturer's recommended concentration for 10 minutes. Phenolic compounds used at 2-4 x the recommended concentration inactivated FCV on contact surfaces. Quarternary ammonium compound and sodium carbonate was effective on contact surfaces at twice the recommended concentration. Rinsing of produce with water reduced virus titer by 2 $\log_{10}$. On artificially contaminated produce, only peroxyacetic acid and hydrogen peroxide were effective when used at 4x manufacturer's recommended concentration for 10 minutes.		
Doultree, J; 1999 [200]	Basic science study N/A	To test glutaraldehyde, iodine, hypochlorite, a quarternary ammonium-based product, an anionic detergent and ethanol for disinfecting activity against FCV. The stability of FCV to increasing temperature in suspension and in dried state was also tested.	F9 strain of FCV. Study was conducted in Australia.	**Efficacy of disinfectants against FCV** 0.5% glutaraldehyde (Aidal) – complete inactivation Hypochlorite (Det-Sol 5000) – complete inactivation at 1000 and 5000 ppm Hypochlorite (White King) – complete inactivation at 5000 but not at 1000 ppm Quarternary ammonia (Pinocleen) – no reduction 75% ethanol – 1.25 $\log_{10}$ reduction 0.8% Iodine (Sanichick) – complete inactivation 1% anionic detergent – 0.5 $\log_{10}$ reduction **Heat inactivation of FCV** 56°C – Inactivated at 60 min, no reduction at 1 and 3 min 70°C – Inactivated at 5 min, detected at 1 and 3 min Boiling – Inactivated at 1 min **Survival based on state and temperature** *Suspension* 4°C – stable Room temperature – survived for ~20 days 37°C – survived for ~10 days *Dried state* 4°C – stable Room temperature – survived for ~28 days 37°C – survived for ~1-2 days	Complete inactivation represents no detection of FCV	6202_RA

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Shin, G; 1998 [201]	Basic science study N/A	To test the inactivation of norovirus using monochloramine (2 mg/L in 0.01M phosphate buffer solution at pH 8.0) and compare it to the inactivation of Poliovirus 1 and MS2.	Norovirus from the feces of infected human volunteers. Poliovirus 1 and MS2 viruses as controls. Study was conducted in the US. Not reported	**Reduction in viral titer at 3hr (measured by RT-PCR)** norovirus – 1 log_{10} Poliovirus 1 – 0 MS2 – 0 However, infectivity assays showed 1 log_{10} reductions in Poliovirus 1 and MS2 at 3h	6200_RA	
Medications						
Rossignol, JF; 2006 [202]	Randomized Controlled Trial 1,3,5,7,9	To evaluate nitazoxanide 500mg vs placebo given to adults or adolescents twice daily for 3 days for the resolution of symptoms due to viral gastroenteritis.	Patients at least 12 years of age with gastroenteritis presenting to outpatient clinics at a university hospital in Egypt. 50 outpatients.	**Symptoms** Nausea in patients with norovirus vs other viral infections – 6/13 (46%) vs 1/32 (3%); p=0.0013 **Time from first dose to symptom resolution** *All results nitazoxanide vs placebo in days (IQR); p value* Overall – 1.5 (0.5-2.5) vs 2.5 (1.5-4.5); <0.0001 For Rotavirus infection – 1.5 (0.5-1.5) vs 2.5 (1.5->6.5);0.0052 For norovirus infection – 1.5 (1.5-1.5) vs 2.5 (1.5-6.5); 0.0295	Patients with diarrhea (≥3 diarrheal stools per day) and stool-positive for rotavirus, norovirus, or adenovirus were eligible for enrollment. Outcome was resolution for at least 72 hours of all symptoms of viral gastroenteritis that were present at enrollment. A sample size of 19 patients per group, with a 0.05 level two-sided log-rank test for	212_IL

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Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
					equality of survival curves, had 80% power to detect a difference between an 85% response rate for 1 group and a 40% response rate for a second group at a given time. A sample size of 25 patients per group allowed for exclusion of up to 20% due to other identified causes of diarrhea.	
Gustafson, TL; 1983 [203]	Retrospective controlled study 1,2,3,4	To determine whether certain medications protected patients from symptomatic disease during a norovirus outbreak.	Patients and staff in a chronic-care hospital in Tennessee. Cases – 22 employees and 31 patients. Controls – 14 employees and 25 patients.	**Cases** 55% of elderly psychiatric patients and 61% of nursing employees. **Protective medications** *Attack rates; p values* Patients only on antipsychotic drugs vs on antipsychotic drugs plus trihexyphenidyl or benztropine – 71% vs 14%; 0.013 Patients on psyllium hydrophilic mucilloid vs not receiving psyllium: 27% vs 71%; 0.012	Two case definitions used: For hospital personnel – any person with vomiting or diarrhea (≥1 liquid stools/ day), or two of the following symptoms (abdominal pain, abdominal cramps, or nausea). For patients – any patient with vomiting or diarrhea. Power and sample size not reported.	2014_IL

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GRADE TABLE Q3 WHAT PATIENT INTERVENTIONS BEST PREVENT OR CONTAIN NOROVIRUS OUTBREAKS IN THE HEALTHCARE SETTING?

Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
Virus Shedding														
Virus shedding	Duration of shedding	2 DES [149,150]	78% of infected cases were shedding virus on day 1 compared to 26% on day 22 in 1 DES [149]. The rate was highest in newborns An elderly woman shed norovirus on day 2 and day 5 after resolution of symptoms [150]	High	0	0	0	-1	0	0	0	0	Moderate	-
	Factors associated with shedding	1 OBS [148] 1 DES [149]	Age ≤ 6 months was a possible risk factor when compared with age > 1 year for increased viral shedding in 1 OBS [148] The rate was highest in newborns 1 DES [149]	Low	0	0	0	0	0	0	0	0	Low	
	Asymptomatic shedding	3 DES [150-152]	Asymptomatic shedding was reported in 3 DES [150-152]	High	0	0	0	0	0	0	0	0	High	
Recovery of norovirus														
Fomites	Transfer of norovirus*	1 BAS [194]	One BAS demonstrated that norovirus-contaminated surfaces can be readily transferred to other fomites (telephones, taps, door handles) via fingertips even when virus has been left to dry for 15 minutes in 30-50% of opportunities [194]	High	0	0	-1	-1	0	0	0	0	Low	Low
	Duration of Recovery	1 SR [153] of DES 1 OBS[141]	norovirus remained viable in carpets up to 12 days despite regular vacuuming in 1 SR [153] norovirus was undetectable in areas of previously known contamination after 5 months had elapsed [141]	Low	0	0	0	0	0	0	0	0	Low	

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Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
	Location of norovirus/ FCV Recovery	1 SR [153] of DES 7 DES [154-159,161] 1 BAS [163]	36% of swabs were positive from curtains, cushions, carpets, lockers, commodes, toilet rims, seats and handles, taps, basins, telephones, door handles, physiotherapy instrument handles, and horizontal surfaces above 1.5 meters (i.e., mantle piece and light fittings where direct handling is unlikely) and below 1.5 meters (i.e., tables and ledges where direct handling may occur) in 1 SR [153] Other environmental surfaces identified were bathroom surfaces like toilet seats, handrails and taps; horizontal surfaces near toilets like tables, mantel pieces, light fittings; kitchen surfaces like dining room tables; elevator buttons; bed rails; doorknobs; game consoles; instrument handles (e.g., ultrasound); soft furnishings like cushions and curtains; lockers [154,155,157-159,161] FCV was recovered from computer keyboard and mouse; telephone buttons, receiver and wire in 1 DES [156]	High	0	-1	0	0	0	0	0	0	Moderate	
Foods and food preparation surfaces	Location of norovirus Recovery	3 BAS [112,162,163]	Norovirus was transferred via gloved hands and detected on foods like lettuce, strawberry and ham. norovirus was also detected on food preparation surfaces like stainless steel, ceramic and formica surfaces; spatula; fork; cutting board [112,162,163]	High	0	0	-1	0	0	0	0	0	Moderate	Low
	Transfer of norovirus*	2 BAS [162,163]	Significantly higher transfer to wet lettuce (P<0.01). For dry lettuce, the transfer at time 0 was statistically significantly higher than at times 30 and 60 min (P<0.05). For wet lettuce, the transfer at time 0 was statistically significantly higher than at times 10, 30 and 60 min (P<0.05) [162] Transferred via gloved hands in 1 BAS [163]	High	-0	0	-1	-1	0	0	0	0	Low	
	Factors associated with recovery	1 BAS [112]	In 1 BAS [112], its recovery on ham was significantly greater when compared to other food and surface items.	High	-0	0	-1	-1	0	0	0	0	Low	

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Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
	Duration of Recovery	2 BAS [112,162]	At room temperature and 4ºC, FCV titers were significantly reduced by Day 7 in 1 BAS [112] norovirus was detected on all plated sterile surfaces, with the most significant reduction in titer occurring after 24hrs without cleaning or disinfection. Over 7 days, observed 6-7 log10 reduction in recovery in 1 BAS [162]	High	0	0	-1	0	0	0	0	0	Moderate	
Water	Recovery of norovirus	3 DES [155,158,160]	norovirus was detected in water samples in 1 DES [160] and not detected in 2 DES [155,158]	High	0	0	0	-1	0	0	0	0	Moderate	-
Components of an Outbreak Prevention/Containment Program														
Hand hygiene														
Soap and water	Symptomatic norovirus infection*	1 OBS [66] 18 DES [63,79,85,89,102,103,165,166,168-171,174-177,183,205]	Handwashing was not associated with a significantly decreased risk in 1 OBS [66] Emphazised as an intervention in 17 DES [63,79,85,89,102,103,165,166,168-171,174-177,183,205]. Involved wetting hands, using liquid soap, scrubbing 15 seconds, rinsing with water, and drying hands with a disposable paper towel in 1 DES in the healthcare setting [174]. Guests were encouraged to wash hands after using the bathroom and prior to each meal in 1 DES at a mother and child health clinic [63]. Hygiene measures were implemented without waiting for virological confirmation in 1 DES in the healthcare setting [175]	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low

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Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
Alcohol-based hand sanitizers	Symptomatic norovirus infection*	4 DES [87,169,171,205]	Mandatory hand disinfection with a product that has 95% ethanol in 2 DES in the healthcare setting [169,171] 70% alcohol handrub supplemented by routine handwashing in 1 DES [87] Alcohol based handrubs were available by every bedside in 1 DES in the healthcare setting [205]	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low
	Inactivation of FCV	4 BAS [189,191,193,196]	Ethanol was found to be superior to propanol as a handwashing agent in 2 BAS [193,196] A new disinfectant with reduced ethanol content was more efficacious that ethanol and propranolol in 1 BAS [189]	High	0	0	-1	0	0	0	0	0	Moderate	
Artificial nails	Inactivation of FCV	1 BAS [197]	1 BAS concluded that food handlers should refrain from using artificial fingernails, keep fingernails short, and scrub with soap and nailbrush when washing hands [197]	Low	0	0	-1	0	0	0	0	0	Very Low	-
PPE														
PPE	Symptomatic norovirus infection*	1 OBS [66] 13 DES [167-172,176-179,181,183,205]	Wearing gowns was not associated with a significantly decreased risk among nursing staff in 1 OBS [66] Protective apparel like masks, gloves, gowns for staff especially when in contact with symptomatic patients were emphazised as an intervention in 13 DES [167-172,176-179,181,183,205] Protective apparel were recommended for both staff and visitors in 2 DES [169,179]	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
Leave policies for staff														
Leave policies for	Symptomatic norovirus	17 DES [84,85,92,165,167-169,172,174,176,177,179-	Emphazised as an intervention in 17 DES [84,85,92,165,167-	Very	0	0	0	0	0	0	0	0	Very Low	Very Low

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Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
staff	infection*	181,183,184,205	169,172,174,176,177,179-181,183,184,205 Staff were excluded from work until symptom free for 24 hours in 1 DES [85] Staff were excluded from work until symptom free for 48 hours in 11 DES [84,92,167,169,172,176,177,179,180,183,184] Staff were excluded from work until symptom free for 72 hours in 1 DES [168]	Low										
Isolation/cohorting of symptomatic patients														
Isolation of affected patients	Symptomatic norovirus infection*	15 DES [87,166-171,176,177,179-182,184,205]	Emphasized as an intervention in 15 DES [87,166-171,176,177,179-182,184,205] In 1 DES that provided detailed description of the intervention, all symptomatic patients were isolated, while those who remained asymptomatic were kept in the original ward and isolated only when they subsequently developed clinical symptoms [170]	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low
Staff cohorting														
Staff cohorting	Symptomatic norovirus infection*	13 DES [87,103,165,168-170,172,177,179,180,182,183,205]	Emphasized as an intervention in 13 DES [87,103,165,168-170,172,177,179,180,182,183,205] Nurses on affected floors cohorted in 1 DES - one group cared for symptomatic patients and a second group for asymptomatic patients [168] Essential medical and paramedical staff who worked in affected ward were not allowed to work in unaffected clinical areas and non-essential personnel were not allowed to enter the affected ward in 1 DES [170]	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low

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Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
			Staff without symptoms working in affected ward did not work anywhere else until 48 hours after completion of work in affected ward in 1 DES [177]											
Ward closure														
Ward closure	Symptomatic norovirus infection*	1 OBS [164] 11 DES [85,165,166,168,176-179,183,184,205]	Emphasized as an intervention in 1 OBS [164] and 11 DES [85,165,166,168,176-179,183,184,205] Outbreaks were contained significantly sooner when units were closed to new admissions within 4 days in 1 OBS [164] Hospital was closed 6 days after outbreak initiation until 4 days after the last case was symptom free in 1 DES [184] A hotel was closed for 8 h to permit thorough cleaning of all food service areas and guest rooms in 1 DES. New guests were not accepted until all guestrooms, bathrooms, and common rooms were thoroughly cleaned 7 days after initial cases [85]	Low	0	0	0	-1	0	1	0	0	Low	Low
Visitor policies														
Visitor policies	Symptomatic norovirus infection*	5 DES [168,170,182,183,205]	Restriction of visitors was emphasized as an intervention in 5 DES [168,170,182,183,205] Nurse managers screened all visitors for gastroenteritis, and if symptomatic, prohibited them from visiting patients in the units for 72 hours in 1 DES [168] Visitors were restricted to the immediate family and children were restricted from visiting in 1 DES [183] Visitors were restricted to two for each patient in 1 DES. All visitors were registered and records were kept for 14 days. All visitors were screened by a standard questionnaire for symptoms and signs of	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low

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Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
			gastroenteritis [170] Visitors were restricted to one unit per visit in 1 DES [182]											
Education														
Education	Symptomatic norovirus infection*	6 DES [166,168,169,172,182,205]	Education of healthcare workers was emphasized as an intervention in 5 DES [166,168,169,182,205] Possible topics included identification of norovirus, spread of gastroenteritis, cleaning and disinfection procedures, isolation, transfers, discharge. Education was provided to family members in 1 DES [172]	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low
Surveillance														
Surveillance	Symptomatic norovirus infection*	4 DES [58,84,166,170]	Emphasized as an intervention in 4 DES [58,84,166,170] Active surveillance and case finding after defining the surveillance period and establishing a case definition was recommended in 1 DES. Contact tracing among staff was done and admission records of patients were reviewed[170] Active surveillance was promoted using a two-tiered definition of cases and outbreaks in 1 DES [58]	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low
Policy Development and Communication														
Policy development and communication	Symptomatic norovirus infection*	6 DES [63,84,172,182-184]	Emphasized as an intervention in 6 DES [63,84,172,182-184]	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low
Patient Transfers and Discharges														
Patient discharges	Symptomatic norovirus	4 DES [172,179,183,184]	Transfer of patients after symptom resolution was supported in 1 DES [172], but discouraged in 3 DES [179,183,184] unless medically necessary.	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low

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Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
	infection*													
Environmental Disinfection														
Targeted surface disinfection	Symptomatic norovirus infection*	1 SR [153] of DES 3 DES [79,168,183]	Emphasized as an intervention in 1 SR [153] and 3 DES [79,168,183] for high touch surfaces (eg. patient and staff bathrooms and clean/dirty utility rooms, tables, chairs, commodes, computer keyboards/mice, and items in close proximity to symptomatic patients) and carpets	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low
Process of environmental disinfection	Symptomatic norovirus infection*	4 DES [168,170,177,179]	The frequency of routine ward, bathroom and toilet cleaning was increased to hourly and hypochlorite was used to disinfect hard surfaces after cleaning in 1 DES [179] Diluted sodium hypochlorite was used for all horizontal surfaces and toilets were cleaned three times daily in 1 DES [177] The routine cleansing of ward was increased to twice daily in 1 DES [170] Mop heads were changed every 3 rooms in 1 study [168]	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low
Cleaning/ disinfection of patient service items	Symptomatic norovirus infection*	3 DES [168,172,177]	Emphasized as an intervention in 3 DES [168,172,177]	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low
Cleaning/ disinfection of fabrics	Symptomatic norovirus infection*	1 SR [153] of DES 3 DES [168,177,183]	Changing patient curtains if visibly soiled in 1 SR [153] and 2 DES [168,177] One DES suggested that soiled, upholstered patient equipment should be steam cleaned. If this was not possible, these items were discarded [168] Careful handling of soiled linen to minimize re-aerosolization of virus in 2 DES [177,183]	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low

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Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
Cleaning and disinfection agents	Symptomatic norovirus infection*	1 SR [153] of 14 DES [63,83,87,89,167,168,170,174,176-179,182,184]	Emphasized as an intervention in 1 SR [153] and 12 DES [63,83,167,168,170,174,176-179,182,184] In one DES, concentrated hypochlorite (1000 ppm) was used for disinfection. The frequency of routine cleaning of the ward was increased and the cleansing area was widened to one square meter surrounding the infected area [170] Hypochlorite was used to disinfect hard surfaces after cleaning in 1 DES [179] 1% sodium hypochlorite was used to wipe down surfaces for spills of vomitus and feces, thorough facility wide cleaning was performed, all continence pads treated as infectious waste and additional mop heads allocated to all the units in 1 DES [182] Diluted sodium hypochlorite was used for all horizontal surfaces in 1 DES [177] Rooms were disinfected with 0.5% hypochlorite after patient discharge in 1 DES [167] Rooms were cleaned with 1% aldehyde or 0.1% chlorine-free bleach in 1 DES [174] Unit was disinfected several times with 1:10 diluted hypochlorite (household bleach) in 1 DES [176] Hypochlorite was used to disinfect hard surfaces in 1 DES [178] 2% hypochlorite solution used in 2 DES [87,89] Cleaning regimen used hypochlorite solution and alcohol wipes in 1 DES [184] An outbreak resulted when vomiting was cleaned with an ordinary vacuum cleaner without hypochlorite [83]	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low

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Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
	Inactivation of norovirus*	3 BAS [187,194,201]	5% organic acid, 1% peroxide, not less than 2% aldehyde with a contact time of 1 h or a 1% halogen compound with 6,000 ppm of free chlorine and a contact time of 15 minutes were required for safe disinfection in 1 BAS [187] Cleaning a contaminated surface with a cloth soaked in anionic detergent followed by cleaning with a combination of hypochlorite/detergent was found to the best cleaning regimen in 1 BAS. Cleaning with the detergent alone or the hypochlorite/detergent combination without prior cleaning failed to eliminate norovirus contamination [194] Treatment of water with monochloramine produced negligible reduction in norovirus titer in 1 BAS [201]	High	0	0	-1	0	0	0	0	0	Moderate	

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Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
	Inactivation of FCV	9 BAS [185,187,188,190-192,198-200]	An activated aldehyde based product was found to be the most effective disinfectant on all types of fabric and carpet in 1 BAS [190], although statistical differences were not reported A quarternary ammonium compound exhibited similar efficacy to hypochlorite 1000 ppm in 1 DES [188] Ethanol at 70% and 90% and isopropranol at 40-60% were effective at killing 99% of FCV within 1 min in 1 BAS [191] Sodium bicarbonate at concentrations of 5% and above was found to achieve 99% reduction in FCV titers, both alone and in combination with aldehyde or hydrogen peroxide in 1 BAS [192] FCV was more resistant to UV light when compared with hepatitis A virus, polio virus and round coliphages although statistical differences were not reported in 1 BAS [198] 0.5% glutaraldehyde, hypochlorite and 0.8% iodine completely inactivated FCV, but a quarternary ammonium compound, ethanol and a 1% anionic detergent did not in 1 BAS [200] 4% organic acid, 1% peroxide, not less than 2% aldehyde with a contact time of 1 h or a 1% halogen compound with 6,000 ppm of free chlorine and a contact time of 15 minutes were required for safe disinfection in 1 BAS [187] 1 BAS demonstrated that ozone from a portable commercial generator could inactivate norovirus and FCV [185] Phenolic compounds, peroxyacetic acid + hydrogen peroxide, and quarternary ammonium compound + sodium bicarbonate were effective at concentrations 2-4 times that recommended by the manufacturers in 1 BAS [199]	High	0	0	-1	0	0	0	0	0	Moderate	

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Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
Medications														
Medications	Symptomatic norovirus infection*	1 OBS [203]	Psychiatric patients who received trihexyphenidyl or benztropine in addition to antipsychotic drugs had a significantly decreased risk compared to those who received antipsychotic drugs alone Patients who received psyllium had a significantly decreased risk compared with those who did not.	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
	Time to symptom resolution*	1 RCT [202]	Significantly decreased in patients who received nitazoxanide when compared to those who did not.	High	0	0	-1	-1	0	0	0	0	Low	

RCT – randomized controlled trial; OBS – observational study (prospective or retrospective controlled); DES – descriptive study (case series, case report, uncontrolled data in an observational study); BAS – basic science study
* These outcomes are considered the most critical by the guideline developers.
** These modifiers can impact the GRADE by 1 or 2 points

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APPENDIX 3: DATA EXTRACTION TOOL

Author, Yr (Reference)

Study Design

Study Objective

Population and Setting

Power and Sample Size

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Results

Outcome definitions

Other comments

Relevant Questions: (√ all that apply)

Question 1: Question 2: Question 3: Question 4: Question 5:

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QUALITY ASSESSMENT

1. Systematic review

Search terms described
Databases searched described and two or more databases searched
Inclusion/exclusion criteria described
Number of included/excluded studies along with reasons of exclusion described
Studies screened by two independent reviewers for inclusion
Data extracted by two independent reviewers
Individual study quality assessed
Heterogeneity between study results assessed qualitatively and/or quantitatively
Publication bias assessed

2. Randomized controlled trial

Described as randomized
Randomization appropriately performed (e.g. random number table, computerized scheme)
Described as double-blind
Outcome assessor blinded
Study participant blinded (e.g. interventions identical in appearance)
Investigator blinded (e.g. opaque sealed envelopes)
Attrition described
Attrition smaller than 10-15% of assigned patients
Attrition appropriately analyzed (e.g. intention to treat analysis)

3. Prospective/retrospective controlled or pre-post studies

All study groups derived from similar source/reference populations
Attrition not significantly different across study groups
The measure of exposure is valid
The measure of outcome is valid
Investigators blinded to endpoint assessment
Potential confounders identified
Statistical adjustment for potential confounders done

4. Descriptive Study

Valid selection of study sample (consecutive or randomly selected subjects)
Criteria for inclusion/exclusion clearly stated
Outcomes measured in a valid manner
Effect estimates presented (e.g. proportions)

5. Diagnostic study

Valid selection of study sample (consecutive or randomly selected subjects)
Valid reference standard
Diagnostic test and reference standard performed independently in each subject
Diagnostic test and reference standard evaluated independently on each subject (blinding)

6. Economic evaluation

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Perspective defined (e.g. societal, payer, provider)
Time horizon defined
Decision tree(s) or rule(s) explicit
Sources of cost estimates presented
Sources of event rate estimates presented
Sensitivity analyses performed

7. Basic science study

N/A

8. Please mention any other relevant quality considerations:

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APPENDIX 4: QUALITY CHECKLISTS

I. SYSTEMATIC REVIEW

1. Search terms described
2. Databases searched described and two or more databases searched
3. Inclusion/exclusion criteria described
4. Number of included/excluded studies along with reasons of exclusion described
5. Studies screened by two independent reviewers for inclusion
6. Data extracted by two independent reviewers
7. Individual study quality assessed
8. Heterogeneity between study results assessed qualitatively and/or quantitatively
9. Publication bias assessed

II. RANDOMIZED CONTROLLED TRIAL

1. Described as randomized
2. Randomization appropriately performed (e.g. random number table, computerized scheme)
3. Described as double-blind
4. Outcome assessor blinded
5. Study participant blinded (e.g. interventions identical in appearance)
6. Investigator blinded (e.g. opaque sealed envelopes)
7. Attrition described
8. Attrition smaller than 10-15% of assigned patients
9. Attrition appropriately analyzed (e.g. intention to treat analysis)

III. PROSPECTIVE/RETROSPECTIVE CONTROLLED OR PRE-POST STUDIES

1. All study groups derived from similar source/reference populations
2. Attrition not significantly different across study groups
3. The measure of exposure is valid
4. The measure of outcome is valid
5. Investigators blinded to endpoint assessment
6. Potential confounders identified
7. Statistical adjustment for potential confounders done

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IV. Case Series

1. Valid selection of study sample (consecutive or randomly selected subjects)
2. Criteria for inclusion/exclusion clearly stated
3. Outcomes measured in a valid manner
4. Effect estimates presented (e.g. proportions)

V. Case Reports

N/A

VI. Diagnostic study

1. Valid selection of study sample (consecutive or randomly selected subjects)
2. Valid reference standard
3. Diagnostic test and reference standard performed independently in each subject
4. Diagnostic test and reference standard evaluated independently on each subject (blinding)

VII. Economic evaluation

1. Perspective defined (e.g. societal, payer, provider)
2. Time horizon defined
3. Decision tree(s) or rule(s) explicit
4. Sources of cost estimates presented
5. Sources of event rate estimates presented
6. Sensitivity analyses performed

VIII. Basic science study

N/A

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