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

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Abbreviations

Acronym	Meaning
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
HBGA	Histo-blood group antigen
HICPAC	Healthcare Infection Control Practices Advisory Committee
HIV	Human immunodeficiency virus
Km	Kilometer
LUX	Light-upon-extension
Ml	Milliliter
MMWR	Morbidity and Mortality Weekly Report

Acronym	Meaning
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
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

Acronym	Meaning
TN	True negative
TP	True positive
UV	Ultraviolet
Vs	Versus

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 healthcare settings. 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. Guidance for norovirus outbreak management and disease prevention in non-healthcare settings can be found at Updated Norovirus Outbreak Management and Disease Prevention Guidelines (https://www.cdc.gov/mmwr/pdf/rr/rr6003.pdf).

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, published material addressing three key questions were examined:

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?

Key questions are described within the Evidence Review section (p.26).

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 under ***Summary of Recommendations*** and described further in the ***Methods*** section (p.22) and Umscheid et al. [This link is no longer active: "Updating the Guideline Methodology of the Healthcare Infection Control Practices Advisory Committee (HICPAC)". Similar information may be found at Umscheid CA, Agarwal RK, Brennan PJ, Healthcare Infection Control Practices Advisory Committee. Updating the guideline development methodology of the Healthcare Infection Control Practices Advisory Committee (HICPAC). American journal of infection control. 2010;38(4):264-273.] for the process used to grade quality of evidence and implications of category designation. 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 this systematic review of the evidence were included in the ***Summary of Recommendations*** if they were deemed critical to the target users of this guideline. Unlike recommendations informed by the 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.

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 prioritized for 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 defined search strategy that will be used for periodic reviews to ensure that the guideline is updated as new information becomes available.

II. Summary of Recommendations

Table 1. HICPAC Categorization Scheme for Recommendations

Rating	Description
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.

Patient Cohorting and Isolation Precautions

1. Avoid exposure to vomitus or diarrhea. Place patients on Contact Precautions in a single occupancy room if they have symptoms consistent with norovirus gastroenteritis. **(Category IB)** (Key Question 1.A.1)

    1a. When patients with norovirus gastroenteritis cannot be accommodated in single occupancy rooms, efforts should be made to separate them from asymptomatic patients. Dependent upon facility characteristics, approaches for cohorting patients during outbreaks may include placing patients in multi-occupancy rooms, or designating patient care areas or contiguous sections within a facility for patient cohorts. **(Category IB)** (Key Question 3C.4.b)

2. During outbreaks, place patients with norovirus gastroenteritis 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 3.C.4.a)

    2a. Consider longer periods of isolation or cohorting precautions for complex medical patients (e.g., those with cardiovascular, autoimmune, immunosuppressive, 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 1.A.2.a)

    2b. Consider extending the duration of isolation or cohorting precautions for outbreaks among infants and young children (e.g., under 2 years), even after resolution of symptoms, as there is a potential for prolonged viral shedding and environmental contamination. Among infants, there is evidence to consider extending contact precautions for up to 5 days after the resolution of symptoms. **(Category II)** (Key Question 3.A.1)

3. 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 3.A.2)

4. Consider minimizing patient movements within a ward or unit during norovirus gastroenteritis outbreaks. **(Category II)** (Key Question 3.C.4.c)

    4a. Consider restricting symptomatic and recovering patients from leaving 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 3.C.4.c.1)

5. Consider suspending group activities (e.g., dining events) for the duration of a norovirus outbreak. **(Category II)** (Key Question 3.C.4.d)

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

Hand Hygiene

7. Actively promote adherence to hand hygiene among healthcare personnel, patients, and visitors in patient care areas affected by outbreaks of norovirus gastroenteritis. **(Category IB)** (Key Question 3.C.1.a)

8. During outbreaks, use soap and water for hand hygiene after providing care or having contact with patients suspected or confirmed with norovirus gastroenteritis. **(Category IB)** (Key Question 3.C.1.b)

   8a. For all other hand hygiene indications (e.g., before having contact with norovirus patients) refer to the 2002 HICPAC Guideline for Hand Hygiene in Health-Care Settings (https://www.cdc.gov/mmwr/PDF/rr/rr5116.pdf), which includes the indications for use of FDA-compliant alcohol-based hand sanitizer. **(Category IB)** (Key Question 3.C.1.b.1)

      8a.1 Consider ethanol-based hand sanitizers (60-95%) as the preferred active agent compared to other alcohol or non-alcohol based hand sanitizer products during outbreaks of norovirus gastroenteritis. **(Category II)** (Key Question 3.C.1.b.2)

   8b. 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 3.C.1.b.3)

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

Patient Transfer and Ward Closure

10. Consider the closure of wards to new admissions or transfers 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 3.C.6)

11. Consider limiting transfers to those for which the receiving facility is able to maintain Contact Precautions; otherwise, it may be prudent to postpone transfers until patients no longer require Contact Precautions. During outbreaks, medically suitable individuals recovering from norovirus gastroenteritis can be discharged to their place of residence. **(Category II)** (Key Question 3.C.11)

12. 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 IC)**

Indirect Patient Care Staff – Food Handlers in Healthcare

13. To prevent food-related outbreaks of norovirus gastroenteritis in healthcare settings, food handlers must perform hand hygiene prior to contact with or the preparation of food items and beverages (This link no longer active: http://www.fda.gov/Food/GuidanceRegulation/RetailFoodProtection/FoodCode/). **(Category IC)** (Key Question 1.C.3.a)

14. Personnel who work with, prepare or distribute food must be excluded from duty if they develop symptoms of acute gastroenteritis. 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 (This link no longer active: http://www.fda.gov/Food/GuidanceRegulation/RetailFoodProtection/FoodCode/). **(Category IC)** (Key Question 1.C.3.b)

15. Remove all shared or communal food items for patients or staff from clinical areas for the duration of the outbreak. **(Category IB)** (Key Question 3.B.2)

Diagnostics

16. Consider the development and adoption of facility policies to enable rapid clinical and virological confirmation of suspected cases of symptomatic norovirus infection while implementing prompt control measures to reduce the magnitude of a potential norovirus outbreak. **(Category II)** (Key Question 1.C.1)

17. 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 3 for Kaplan's criteria). **(Category IA**) (Key Question 2.A.1)

18. Further research is needed to compare the Kaplan criteria with other early detection criteria for outbreaks 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 2.A.1)

19. Consider submitting 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 2.B)

20. Use effective laboratory diagnostic protocols for testing of suspected cases of viral gastroenteritis (e.g., refer to the Centers for Disease Control and Prevention (CDC)'s Updated Norovirus Outbreak Management and Disease Prevention Guidelines (https://www.cdc.gov/mmwr/pdf/rr/rr6003.pdf)). **(Category IB)** (Key Question 2.C)

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

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

Personal Protective Equipment

23. If norovirus infection is suspected, adherence to PPE use according to Contact and Standard Precautions is recommended for individuals entering the patient care area (i.e., gowns and gloves upon entry) to reduce the likelihood of exposure to infectious vomitus or fecal material. **(Category IB)** (Key Question 1.C.4)

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

25. More research is needed to evaluate the utility of implementing Universal Gloving (e.g., routine use of gloves for all patient care) during norovirus outbreaks. **(No recommendation/unresolved issue)**

Environmental Cleaning

26. Perform routine cleaning and disinfection of frequently touched environmental surfaces and equipment in isolation and cohorted areas, as well as high-traffic clinical areas. Frequently touched surfaces include, but are not limited to, commodes, toilets, faucets, hand/bedrailing, telephones, door handles, computer equipment, and kitchen preparation surfaces. **(Category IB)** (Key Question 3.B.1)

27. Clean and disinfect shared equipment between patients using EPA-registered products with label claims for use in healthcare. Follow the manufacturer's recommendations for application and contact times. The EPA lists products with activity against norovirus on their website (Selected EPA-registered Disinfectants (https://www.epa.gov/pesticide-registration/selected-epa-registered-disinfectants)). **(Category IC)** (Key Question 3.C.12.a)

28. Increase the frequency of cleaning and disinfection of patient care areas and frequently touched surfaces during outbreaks of norovirus gastroenteritis (e.g., increase ward/unit level cleaning to twice daily to maintain cleanliness, with frequently touched surfaces cleaned and disinfected three times daily using EPA-approved products for healthcare settings). **(Category IB)** (Key Question 3.C.12.b.1)

29. 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 a new bucket of cleaning solution is prepared, or after cleaning large spills of emesis or fecal material. **(Category IB)** (Key Question 3.C.12.b.2)

30. Consider discarding all disposable patient-care items and laundering unused linens from patient rooms after patients on isolation for norovirus gastroenteritis are discharged or transferred. Facilities can minimize waste by limiting the number of disposable items brought into rooms/areas on Contact Precautions. **(Category II)** (Key Question 3.C.12.c.1)

31. No additional provisions for using disposable patient service items such as utensils or dishware are suggested for patients with symptoms of norovirus infection. Silverware and dishware may undergo normal processing and cleaning using standard procedures. **(Category II)** (Key Question 3.C.12.c.2)

32. Use Standard Precautions for handling soiled patient-service items or linens, including the use of appropriate PPE. **(Category IB)** (Key Question 3.C.12.c.3)

33. Consider avoiding 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, immediately clean 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 3.C.12.d.1)

34. Consider steam cleaning of upholstered furniture in patient rooms upon discharge. Consult with manufacturer's recommendations for cleaning and disinfection of these items. Consider discarding items that cannot be appropriately cleaned/disinfected. **(Category II)**(Key Question 3.C.12.d.2)

35. During outbreaks, change privacy curtains when they are visibly soiled and upon patient discharge or transfer. **(Category IB)** (Key Question 3.C.12.d.3)

36. Handle soiled linens carefully, without agitating them, to avoid dispersal of virus. Use Standard Precautions, including the use of appropriate PPE (e.g., gloves and gowns), to minimize the likelihood of cross-contamination. **(Category IB)** (Key Question 3.C.12.d.4)

37. Double bagging, incineration, or modifications for laundering are not indicated for handling or processing soiled linen. **(Category II)** (Key Question 3.C.12.d.5)

38. Clean surfaces and patient equipment prior to the application of a disinfectant. Follow the manufacturer's recommendations for optimal disinfectant dilution, application, and surface contact time with an EPA-approved product with claims against norovirus. **(Category IC)** (Key Question 3.C.12.e.1)

39. 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 3.C.12.e.2)

40. 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 3.C.12.e.3)

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

Staff Leave and Policy

42. Develop and adhere to sick leave policies for healthcare personnel who have symptoms consistent with norovirus infection. **(Category IB)** (Key Question 3.C.3)

    42a. Exclude ill personnel from work for a minimum of 48 hours after the resolution of symptoms. Once personnel return to work, the importance of performing frequent hand hygiene should be reinforced, especially before and after each patient contact. **(Category IB)** (Key Question 3.C.3.a)

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

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

Visitors

45. Establish visitor policies for acute gastroenteritis (e.g., norovirus) outbreaks. **(Category IB)** (Key Question 3.C.7.a)

46. Restrict non-essential visitors from affected areas of the facility during outbreaks of norovirus gastroenteritis. **(Category IB)** (Key Question 3.C.7.b)

    46a. For those affected areas where it is necessary to have continued visitor privileges during outbreaks, screen and exclude visitors with symptoms consistent with norovirus infection and ensure that they comply with hand hygiene and Contact Precautions. **(Category IB)** (Key Question 3.C.7.b.1)

Education

47. Provide education to staff, patients, and visitors, including recognition of norovirus symptoms, preventing infection, and modes of transmission upon the recognition and throughout the duration of a norovirus gastroenteritis outbreak. **(Category IB)** (Key Question 3.C.8.a)

48. 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 3.C.8.b)

Active Case-Finding

49. Begin active case-finding when a cluster of acute gastroenteritis cases is detected in the healthcare facility. Use a specified case definition, and implement 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 3.C.9.a)

Communication and Notification

50. 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 3.C.10)

    50a. Provide timely communication to personnel and visitors when an outbreak of norovirus gastroenteritis is suspected and outline what policies and provisions need to be followed to prevent further transmission **(Category IB)** (Key Question 3.C.10.a)

51. As with all outbreaks, 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 3.C.9.b)

III. Implementation and Audit

Prioritization of Recommendations

Category I recommendations in this guideline are all considered strong recommendations and should be implemented. If it is not feasible to implement all of these recommendations concurrently, e.g., due to differences in facility characteristics such as nursing homes and other non-hospital settings, priority should be given to the recommendations below. A limited number of Category II recommendations are included, and while these currently are limited by the strength of the available evidence, they are considered key activities in preventing further transmission of norovirus in healthcare settings.

Patient Cohorting and Isolation Precautions

1. Avoid exposure to vomitus or diarrhea. Place patients on Contact Precautions in a single occupancy room if they present with symptoms consistent with norovirus gastroenteritis. **(Category IB)** (Key Question 1.A.1)

Hand Hygiene

8. During outbreaks, use soap and water for hand hygiene after providing care or having contact with patients suspected or confirmed with norovirus gastroenteritis. **(Category IB)** (Key Question 3.C.1.b)

Patient Transfer and Ward Closure

11. Consider limiting transfers to those for which the receiving facility is able to maintain Contact Precautions; otherwise, it may be prudent to postpone transfers until patients no longer require Contact Precautions. During outbreaks, medically suitable individuals recovering from norovirus gastroenteritis can be discharged to their place of residence. **(Category II)** (Key Question 3.C.11)

Diagnostics

17. 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 2.A.1)

Environmental Cleaning

28. Increase the frequency of cleaning and disinfection of patient care areas and frequently touched surfaces during outbreaks of norovirus gastroenteritis (e.g., consider increasing ward/unit level cleaning to twice daily to maintain cleanliness, with frequently touched surfaces cleaned and disinfected three times daily using EPA-approved products for healthcare settings). **(Category IB)** (Key Question 3.C.12.b.1)

Staff Leave and Policy

42. Develop and adhere to sick leave policies for healthcare personnel who have symptoms consistent with norovirus infection. **(Category IB)** (Key Question 3.C.3)

    42a. Exclude ill personnel from work for a minimum of 48 hours after the resolution of symptoms. Once personnel return to work, the importance of performing frequent hand hygiene should be reinforced, especially before and after each patient contact. **(Category IB)** (Key Question 3.C.3.a)

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

Communication and Notification

51. As with all outbreaks, 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 3.C.9.b)

Performance Measures for Health Departments

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) (https://www.cdc.gov/nors/index.html) [Current version of this document may differ from original.]. 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

The literature review for this guideline 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 in healthcare settings should include:

1. Analyses of the impact of specific or bundled infection control interventions,
2. Use of controls or comparison groups in both clinical and laboratory trials,
3. Comparisons of 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. Assessment of 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. Statistically powerful studies able to detect small but significant effects of norovirus infection control strategies or interventions, and
6. Quantitative assessments of novel, and practical methods for effective cleaning and disinfection during norovirus outbreaks.

The following are specific areas in need of further research in order to make more precise prevention recommendations (see also recommendations under the category of No recommendation/unresolved issue in the Evidence Review):

Measurement and Case Detection

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.

Host Contagiousness and Transmission

1. Determine correlations between prolonged shedding of norovirus after symptoms have subsided and the likelihood of secondary transmission of norovirus infection.
2. Assess the utility of medications that may attenuate the duration and severity of norovirus illness.
3. Determine the role of asymptomatic shedding (among recovered persons and carriers) in secondary transmission.
4. Evaluate the duration of protective immunity and other protective host factors, including histo-blood group antigens (HBGA) and secretor status.
5. Assess the contribution of water or food sources to outbreaks of norovirus gastroenteritis in healthcare settings.

Environmental Issues

1. Quantify the effectiveness of cleaning and disinfecting agents against norovirus or appropriate surrogates.
2. 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.
3. Develop methods to evaluate norovirus persistence in the environment, with a focus on persistent infectivity.
4. Identify a satisfactory animal model for surrogate testing of norovirus properties and pathogenesis. Translate laboratory findings into practical infection prevention strategies.

Hygiene and Infection Control

1. Evaluate the effectiveness of FDA-approved hand sanitizers against norovirus or appropriate surrogates, including viral persistence after treatment with non-alcohol based products.
2. Assess the benefits and impact of implementing Universal Gloving practices during outbreaks of norovirus gastroenteritis

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]

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) (Updated Norovirus Outbreak Management and Disease Prevention Guidelines (https://www.cdc.gov/mmwr/pdf/rr/rr6003.pdf)) 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 ingestion of fecally-contaminated food or water, 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 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 the 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, three key questions were examined and addressed:

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 professional societies or organizations that wish to develop guidance on prevention or management of outbreaks of norovirus gastroenteritis for specialized settings or populations.

VII. Methods

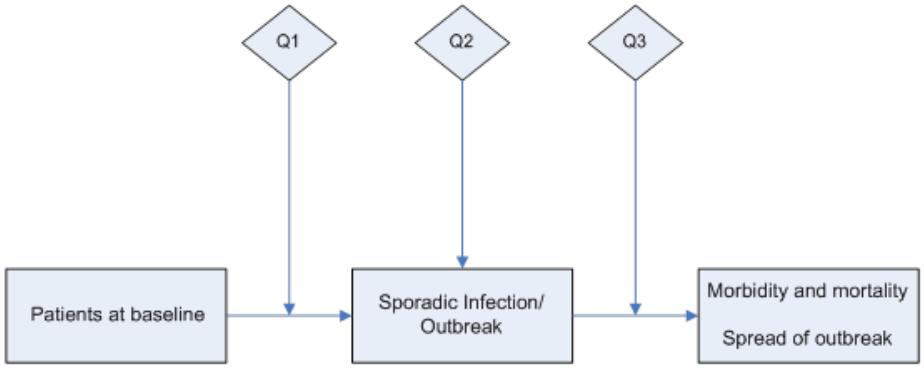
This guideline was based on a targeted systematic review of the best available evidence on the prevention and control of norovirus gastroenteritis outbreaks in healthcare settings. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used[21-24] to provide explicit links between

the available evidence and the resulting recommendations. Methods and/or details that were unique to this guideline are included below.

Development of Key Questions

First, 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 was conducted 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 1*.

Figure 1. 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, these terms were compared 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.

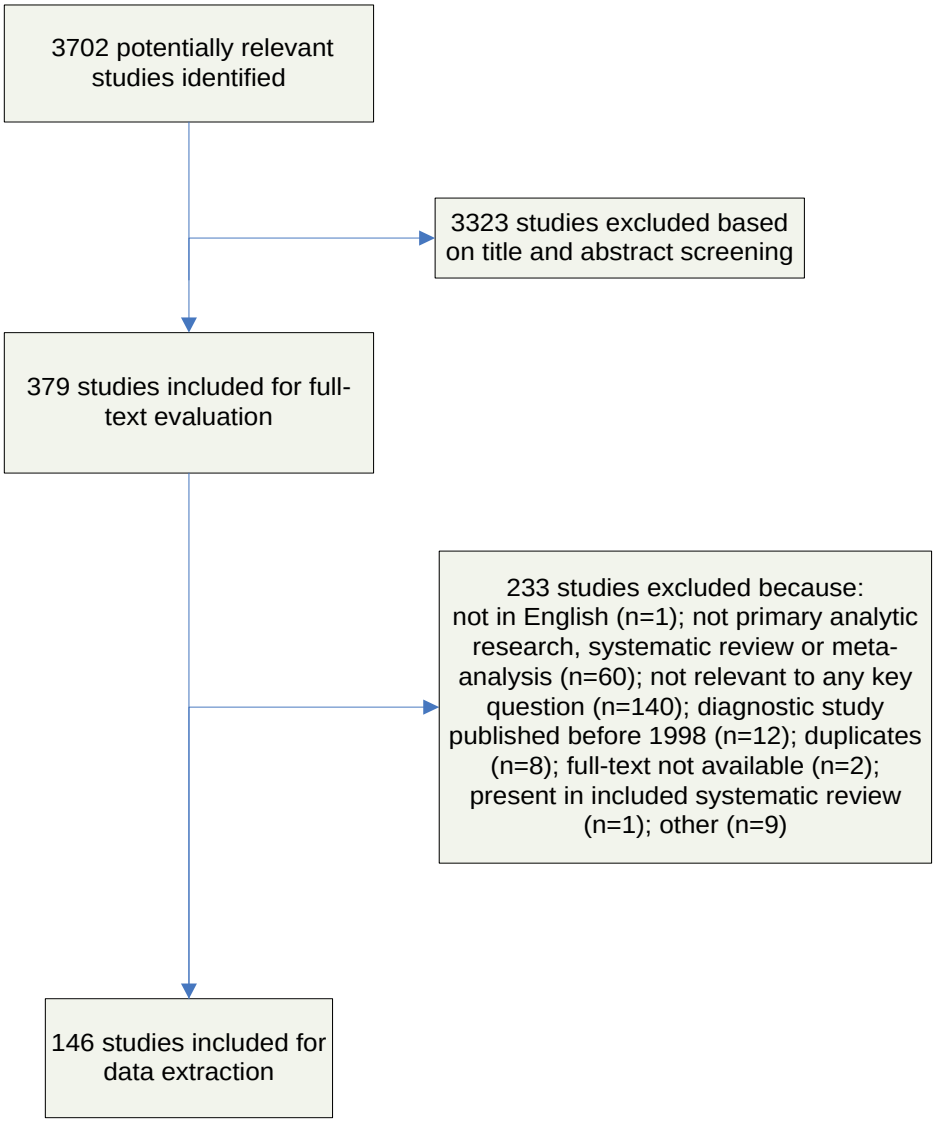
To be included, studies had to measure ≥ 1 clinically relevant outcome. For Key Questions 1 and 3, this included symptoms of norovirus infection, or stool antigen, virus, or EM results. For Key Question 2, this included any study published after 1997 that reported test characteristics (e.g., sensitivity, 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 2.*

Figure 2. 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 the key questions *(Appendix 2)*. Studies were extracted into the 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 this review. To avoid duplication of data, primary studies were excluded if they were also included in a systematic review captured through the broader search strategy. 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 primary studies that were originally captured were abstracted into the evidence tables and reviewed. Systematic reviews that analyzed primary studies that were fully captured in a more recent systematic review were excluded. 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 the review, statistical significance was defined as $p \leq 0.05$.

For all other methods (i.e., Grading of Evidence, Formulation of Recommendations, and Finalizing of the Guideline) please refer to the [This link is no longer active: “Guideline Methods supplement” Similar information may be found at Umscheid CA, Agarwal RK, Brennan PJ, Healthcare Infection Control Practices Advisory Committee. Updating the guideline development methodology of the Healthcare Infection Control Practices Advisory Committee (HICPAC). American journal of infection control. 2010;38(4):264-273.]

Updating the Guideline

Future revisions to this guideline will be dictated by new research and technological advancements for preventing and managing norovirus gastroenteritis outbreaks.

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, the quality of evidence was evaluated among risk factors identified in 57 studies. In areas for which the outcome of symptomatic norovirus infection was available, this was considered 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

Low-quality evidence was available 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 patients with diarrhea increased the likelihood that long-term care facility staff would develop norovirus infection.[66]

The 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.[65,68] 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 having had a renal transplant 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] This

search did not reveal data 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 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 a few weeks. The search strategy did not reveal 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. This 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

There was 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] The search strategy did not reveal prospective cohort data to correlate the role of ABO blood types with risk of norovirus infection.

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. This 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

Very low-quality evidence was available 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 infections.[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. The review process 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. This search strategy 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 such as proximate exposure to an infected source within households or in crowded quarters increased infection risk, as did exposures to any or frequent 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 short-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] This search process 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. Place patients on Contact Precautions in a single occupancy room if they have symptoms consistent with norovirus gastroenteritis. (Category IB) (Key Question 1A)

1.A.2.a Consider longer periods of isolation or cohorting precautions for complex medical patients (e.g., those with cardiovascular, autoimmune, immunosuppressive, 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 Consider the development and adoption of facility policies to enable rapid clinical and virological confirmation of suspected cases of symptomatic norovirus infection while implementing prompt control measures to reduce the magnitude of a potential norovirus outbreak. (Category II) (Key Question 1C)

1.C.3.a To prevent food-related outbreaks of norovirus gastroenteritis in healthcare settings, food handlers must perform hand hygiene prior to contact with or the preparation of food items and beverages (FDA Food Code (http://www.fda.gov/Food/GuidanceRegulation/RetailFoodProtection/FoodCode/) Current version of this document may differ from original.). (Category IC) (Key Question 1C)

1.C.3.b Personnel who work with, prepare or distribute food must be excluded from duty if they develop symptoms of acute gastroenteritis. 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 (FDA Food Code (http://www.fda.gov/Food/GuidanceRegulation/RetailFoodProtection/FoodCode/) Current version of this document may differ from original.). (Category IC) (Key Question 1C)

1.C.4 If norovirus infection is suspected, adherence to PPE use according to Contact and Standard Precautions is recommended for individuals entering the patient care area (i.e., gowns and gloves upon entry) to reduce the likelihood of exposure to infectious vomitus or fecal material. (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, studies that provided test characteristics for the diagnosis of norovirus or outbreaks of norovirus gastroenteritis were critically reviewed. 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 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

There was 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. The search strategy 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] In modeling analyses using a hypothetical test demonstrating 100% sensitivity and 100% specificity, 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. This 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

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 were summarized. Test characteristics for the most common or commercially-available norovirus diagnostics are summarized in the following Box.

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 (see Table 3 for Kaplan's criteria). **(Category IA**) (Key Question 2A)

2.A.2 Further research is needed to compare the Kaplan criteria with other early detection criteria for outbreaks 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 Consider submitting 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 Use effective laboratory diagnostic protocols for testing of suspected cases of viral gastroenteritis (e.g., refer to the Centers for Disease Control and Prevention (CDC)'s Updated Norovirus Outbreak Management and Disease Prevention Guidelines [https://www.cdc.gov/mmwr/pdf/rr/rr6003.pdf]). **(Category IB)** (Key Question 2C)

Table 2. Test Characteristics for Norovirus in Fecal Specimens

Diagnostic method	Reference standard	Quantity and type of evidence	Findings * (%) Sensitivity	Findings * (%) Specificity	Findings * (%) Positive Predictive Value	Findings * (%) Negative Predictive Value
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	n/a	n/a

* Range from studies that reported test characteristics

Table 3. 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, 69 studies[58,63,66,79,83-85,87,89,92,102,103,112,148-203] were critically reviewed 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 Tables for Question 3 in the Appendix.

Q3.A Viral Shedding

This review 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]

High-quality evidence was available to demonstrate the presence of 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] The search strategy employed did not identify studies that correlated other clinical factors to duration of viral shedding.

Q3.B Recovery of Norovirus

Q3.B.1 Fomites

There was 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 in 30-50% of opportunities even when virus has been left to dry for 15 minutes.[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. However, in two outbreaks from which 47 environmental samples were collected, 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] This search strategy 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

There was low-quality evidence suggesting that foods and food-preparation surfaces are significant sources 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, laminate, 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]

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

This search strategy 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, multiple strategies are instituted simultaneously during outbreaks in healthcare settings. 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

Very low-quality evidence was available 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 that were 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 2002 HICPAC Guideline for Hand Hygiene in Health-Care Settings (https://www.cdc.gov/mmwr/PDF/rr/rr5116.pdf).

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

Very low-quality evidence was available 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-compliant 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.[193] 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, particularly when simulated organic loads (e.g. fecal material) were used in conjunction with exposure to norovirus.[189,191,193,196] The use 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 Guideline for Hand Hygiene in Health-Care Settings (https://www.cdc.gov/mmwr/PDF/rr/rr5116.pdf).

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

There was 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. The literature 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

There was 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 (See 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings (https://www.cdc.gov/infectioncontrol/guidelines/isolation/)). 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 single occupancy (e.g., 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, 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 was designated to care for one cohort of patients (symptomatic,

exposed but asymptomatic, or unexposed). Exposed staff was 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] The search strategy 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

Low-quality evidence was available to support 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, studies defended that it was preferable to minimize patient movements and transfers in an effort to contain environmental contamination.

Q3.C.7 Visitor Policies

There was 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] The reviewed literature failed to identify research that considered the impact of different levels of visitor restrictions on outbreak containment.

Q3.C.8 Education

There was 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 that were reviewed used posters to emphasize hand hygiene and conducted one-on-one teaching with patients and visitors, as well as holding departmental seminars for staff. The literature reviewed failed to identify research that examined the impact of educational measures on the magnitude and duration of outbreaks of norovirus gastroenteritis, or what modes of education were most effective in promoting adherence to outbreak measures.

Q3.C.9 Surveillance

There was 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. There was no available literature 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

Very low-quality evidence was available to support the benefits of having 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] The search of the literature did not yield any studies to demonstrate that facilities with written norovirus policies already in place had fewer or shorter outbreaks of norovirus gastroenteritis.

Q3.C.11 Patient Transfers and Discharges

There was 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. The literature 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

Very low-quality evidence was available 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

There was 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 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] This literature search was not able to 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

There was 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] There were no identified studies that directly examined the impact of disinfection of patient equipment on outbreaks of norovirus gastroenteritis.

Q3.C.12.d Fabrics

Very low-quality evidence was available to examine 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. This literature 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.

There was found moderate quality evidence to examine 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 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.

Moderate quality evidence was available on 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 are 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. The literature search did not evaluate publications using newer methods for environmental disinfection, such as ozone mist from a humidifying device, fumigation, UV irradiation, and fogging.

This search strategy was unable to find 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

There was 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 are 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] The search strategy used in this review did not identify research that considered the effect of anti-peristaltics on the duration or outcomes of norovirus infection.

Q3 Recommendations

3.A.1 Consider extending the duration of isolation or cohorting precautions for outbreaks among infants and young children (e.g., under 2 years), even after resolution of symptoms, as there is a potential for prolonged viral shedding and environmental contamination. Among infants, there is evidence to consider extending contact precautions for up to 5 days after the resolution of symptoms. **(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. Frequently touched surfaces include, but are not limited to, commodes, toilets, faucets, hand/bedrailing, telephones, door handles, computer equipment, and kitchen preparation surfaces. **(Category IB)** (Key Question 3B)
3.B.2	Remove all shared or communal food items for patients or staff from clinical areas for the duration of the outbreak. **(Category IB)** (Key Question 3B)
3.C.1.a.	Actively promote adherence to hand hygiene among healthcare personnel, patients, and visitors in patient care areas affected by outbreaks of norovirus gastroenteritis. **(Category IB)** (Key Question 3C)
3.C.1.b.	During outbreaks, use soap and water for hand hygiene after providing care or having contact with patients suspected or confirmed with norovirus gastroenteritis. **(Category IB)** (Key Question 3C)
3.C.1.b.1.	For all other hand hygiene indications (e.g., when hands are not visibly soiled and have not been in contact with diarrheal patients, contaminated surfaces, or other body fluids) refer to the 2002 HICPAC Guideline for Hand Hygiene in Health-Care Settings (https://www.cdc.gov/mmwr/PDF/rr/rr5116.pdf), which includes the indications for use of FDA-compliant alcohol based hand sanitizer. **(Category IB)** (Key Question 3C)
3.C.1.b.2.	Consider ethanol-based hand sanitizers (60-95%) as the preferred active agent compared to other alcohol or non-alcohol based hand sanitizer products during outbreaks of norovirus gastroenteritis. **(Category II)** (Key Question 3C)
3.C.1.b.3.	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.2.a	Use a surgical or procedure mask and eye protection or a full face shield if there is an anticipated risk of splashes to the face during the care of patients, particularly among those who are vomiting. **(Category IB)** (Key Question 3C)
3.C.3	Develop and adhere to sick leave policies for healthcare personnel who have symptoms consistent with norovirus infection. **(Category IB)** (Key Question 3C)
3.C.3.a	Exclude ill personnel from work for a minimum of 48 hours after the resolution of symptoms. Once personnel return to work, the importance of performing frequent hand hygiene should be reinforced, especially before and after each patient contact. **(Category IB)** (Key Question 3C)
3.C.4.a	During outbreaks, place patients with norovirus gastroenteritis on Contact Precautions for a minimum of 48 hours after the resolution of symptoms to prevent further transmission. **(Category IB)** (Key Question 3C)
3.C.4.b	When patients with norovirus gastroenteritis cannot be accommodated in single occupancy rooms, efforts should be made to separate them from asymptomatic patients. Dependent upon facility characteristics, approaches for cohorting patients during outbreaks may include placing patients in multi-occupancy rooms, or designating patient care areas or contiguous sections within a facility for patient cohorts. **(Category IB)** (Key Question 3C)
3.C.4.c	Consider minimizing patient movements within a ward or unit during norovirus gastroenteritis outbreaks. **(Category II)** (Key Question 3C)

3.C.4.c.1	Consider restricting symptomatic and recovering patients from leaving 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	Consider suspending group activities (e.g., dining events) for the duration of a norovirus outbreak. **(Category II)** (Key Question 3C)
3.C.5.a	Establish protocols for staff cohorting in the event of an outbreak of norovirus gastroenteritis. Ensure staff care for one patient cohort on their ward and do not move between patient cohorts (e.g., patient cohorts may include symptomatic, asymptomatic exposed, or asymptomatic unexposed patient groups). **(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 symptomatic patients until the outbreak resolves. **(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	Consider the closure of wards to new admissions or transfers 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	Establish visitor policies for acute gastroenteritis (e.g., norovirus) outbreaks. **(Category IB)** (Key Question 3C)
3.C.7.b	Restrict non-essential visitors from affected areas of the facility during outbreaks of norovirus gastroenteritis. **(Category IB)** (Key Question 3C)
3.C.7.b.1	For those affected areas where it is necessary to have continued visitor privileges during outbreaks, screen and exclude visitors with symptoms consistent with norovirus infection and ensure that they comply with hand hygiene and Contact Precautions. **(Category IB)** (Key Question 3C)
3.C.8.a	Provide education to staff, patients, and visitors, including recognition of norovirus symptoms, preventing infection, and modes of transmission upon the recognition and throughout the duration of a norovirus gastroenteritis 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)
3.C.9.a	Begin active case-finding when a cluster of acute gastroenteritis cases is detected in the healthcare facility. Use a specified case definition, and implement 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	As with all outbreaks, 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.10.a	Provide timely communication to personnel and visitors when an outbreak of norovirus gastroenteritis is identified and outline what policies and provisions need to be followed to prevent further transmission **(Category IB)** (Key Question 3C)
3.C.11	Consider limiting transfers to those for which the receiving facility is able to maintain Contact Precautions; otherwise, it may be prudent to postpone transfers until patients no longer require Contact Precautions. During outbreaks, medically suitable individuals recovering from norovirus gastroenteritis can be discharged to their place of residence. **(Category II)** (Key Question 3C)
3.C.12.a	Clean and disinfect shared equipment between patients using EPA-registered products with label claims for use in healthcare. Follow the manufacturer's recommendations for application and contact times. The EPA lists products with activity against norovirus on their website (Selected EPA-registered Disinfectants (https://www.epa.gov/pesticide-registration/selected-epa-registered-disinfectants) [Current version of this document may differ from original.]). **(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 (e.g., consider increasing ward/unit level cleaning to twice daily to maintain cleanliness, with frequently touched surfaces cleaned and disinfected 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 a new bucket of cleaning solution is prepared, or after cleaning large spills of emesis or fecal material. **(Category IB)** (Key Question 3C)
3.C.12.c.1	Consider discarding all disposable patient-care items and laundering unused linens from patient rooms after patients on isolation for norovirus gastroenteritis are discharged or transferred. Facilities can minimize waste by limiting the number of disposable items brought into rooms/areas on Contact Precautions. **(Category II)** (Key Question 3C)
3.C.12.c.2	No additional provisions for using disposable patient service items such as utensils or dishware are suggested for patients with symptoms of norovirus infection. Silverware and dishware may undergo normal processing and cleaning using standard procedures. **(Category II)** (Key Question 3C)
3.C.12.c.3	Use Standard Precautions for handling soiled patient-service items or linens, including the use of appropriate PPE. **(Category IB)** (Key Question 3C)
3.C.12.d.1	Consider avoiding 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, immediately clean 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	Consider steam cleaning of upholstered furniture in patient rooms upon discharge. Consult with manufacturer's recommendations for cleaning and disinfection of these items. Consider discarding items that cannot be appropriately cleaned/disinfected. **(Category II)**(Key Question 3C)
3.C.12.d.3	During outbreaks, change privacy curtains when they are visibly soiled and upon patient discharge or transfer. **(Category IB)** (Key Question 3C)

3.C.12.d.4	Handle soiled linens carefully, without agitating them, to avoid dispersal of virus. Use Standard Precautions, including the use of appropriate PPE (e.g., gloves and gowns), to minimize the likelihood of cross-contamination. **(Category IB)** (Key Question 3C)
3.C.12.d.5	Double bagging, incineration, or modifications for laundering are not indicated for handling or processing soiled linen. **(Category II)** (Key Question 3C)
3.C.12.e.1	Clean surfaces and patient equipment prior to the application of a disinfectant. Follow the manufacturer's recommendations for optimal disinfectant dilution, application, and surface contact time with an EPA-approved product with claims against norovirus. **(Category IC)** (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 of 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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