Characterizing Norovirus Transmission from Outbreak Data, United States

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Norovirus is the leading cause of acute gastroenteritis outbreaks in the United States. We estimated the basic (R_0) and effective (R_e) reproduction numbers for 7,094 norovirus outbreaks reported to the National Outbreak Reporting System (NORS) during 2009–2017 and used regression models to assess whether transmission varied by outbreak setting. The median R_0 was 2.75 (interquartile range [IQR] 2.38–3.65), and median R_e was 1.29 (IQR 1.12–1.74). Long-term care and assisted living facilities had an R_0 of 3.35 (95% CI 3.26–3.45), but R_0 did not differ substantially for outbreaks in other settings, except for outbreaks in schools, colleges, and universities, which had an R_0 of 2.92 (95% CI 2.82–3.03). Seasonally, R_0 was lowest (3.11 [95% CI 2.97–3.25]) in summer and peaked in fall and winter. Overall, we saw little variability in transmission across different outbreaks settings in the United States.

Norovirus is the most common cause of outbreaks of acute gastroenteritis (AGE) in the United States (*1*,*2*). The Centers for Disease Control and Prevention (CDC) collects data on AGE outbreaks through the National Outbreak Reporting System (NORS). During 2009–2017, norovirus was the suspected or confirmed etiology of 47% of AGE outbreaks reported to NORS (*3*). The size and severity of outbreaks varies across different settings, times of year, and genotypes, suggesting norovirus transmissibility is variable across different outbreak settings and contexts (*4*). Generally, the transmission potential of infectious diseases is influenced by the infectiousness of the pathogen, the duration of infectiousness, and the number of susceptible contacts exposed during the infectious period (*5*).

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The reproduction number is a metric for quantifying transmissibility of a pathogen. The basic reproduction number (R_0) is the average number of secondary cases that arise from a primary case in a completely susceptible population. The effective reproduction number (R_e) quantifies the average number of secondary cases that arise from a primary case in a population that is not completely susceptible. R_e varies over the course of an outbreak as the proportion of the susceptible population changes (*6*,*7*). R_0 and R_e are not just metrics of the biologic properties of pathogens but also measures of the transmissibility of a pathogen within a specific population or setting (*8*,*9*).

Several transmission modeling studies in different settings have estimated R_0 and R_e of norovirus, but a large variation in these estimates occurs and R_0 ranges from 1.1–7.2 (*10*). Much of the R_0 variation likely is due to differences in the structures, population mixing assumptions, and data between transmission models in different settings (*10*). Generally, model estimates from community surveillance data result in an R_0 of ≈2, but estimates from outbreak data tend to be higher and more variable. The variability of estimates from models that use outbreak data likely are driven by context; outbreaks might occur in populations that are not representative of the population as a whole and transmission likely is higher in these settings than in the community (*4*).

We estimated R_0 and R_e for thousands of norovirus outbreaks in the United States. We evaluated whether R_0 was associated with setting, season, year, or geographic region. In addition, we assessed whether norovirus was suspected or confirmed as the cause of the outbreak.

Methods

Data

We obtained data on all norovirus outbreaks during 2009–2017 from NORS and CaliciNet (*11*). We defined

an outbreak as ≥2 epidemiologically linked cases of suspected or laboratory-confirmed norovirus. NORS data consist of web-based reports of all foodborne, waterborne, and enteric disease outbreaks transmitted by contact with environmental sources, infected persons or animals, or unknown modes of transmission reported by state, local, and territorial public health agencies. This web-based reporting system collects epidemiologic information, including the dates; settings, such as long-term care facilities, child daycare facilities, hospitals, and schools; geographic location of the outbreak; the estimated total number of cases; and exposed population (*2*). For settings that report staff and guest case numbers, we included these data in the estimated total number of cases and exposed population. CaliciNet data consists of sequence-derived genotypes and epidemiologic data from norovirus outbreaks submitted from local, state, and federal public health laboratories. We obtained CaliciNet genotypes that were linked to outbreak data we acquired from NORS.

For all outbreaks reported to NORS, data are collected on the total estimated primary cases, including all laboratory-confirmed and suspected primary cases. These data exclude cases associated with secondary illnesses, such as person-to-person norovirus transmission in households after a restaurant-based outbreak. However, data for calculating attack rates, specifically the number of exposed persons and the subset of the exposed persons who became ill, are only collected for outbreaks with person-to-person, environmental, or unknown transmission modes. In addition, data collected from outbreaks might not be documented consistently across a report. For example, outbreaks for which setting-specific information on the total number of guests and staff that are reported to be ill, referred to as total ill, might not match the reported total estimated primary cases. During 2009–2017, a total of 17,822 suspected and confirmed norovirus outbreaks were reported to NORS. We excluded 10,728 outbreaks based on the following criteria, which we imposed hierarchically: transmission was not person-to-person (n = 3,866); the outbreak exposure occurred in multiple states (n = 8); the outbreak occurred in Puerto Rico (n = 3), which we excluded because of small sample size; the size of total exposed population or major setting were not reported (n = 5,573); the total estimated primary cases and the total ill among the exposed population were not equal (n = 1,231); or the total estimated primary cases or the total ill among the exposed population were reported to be greater than the total exposed population size (n = 47) (Appendix Figure 1, https://wwwnc.cdc.gov/EID/article/26/8/19-1537-App1.pdf). In all, 7,094 norovirus outbreaks met our inclusion criteria in subsequent analyses (Appendix Table 1). We did not use imputation techniques to infer values for missing data because no good proxy variables inferred missing data for major settings and exposed population size.

Estimating R_0 and R_e

We used the final size method to calculate R_0, R_e, and associated SEs (*12*; Appendix). The final size method calculates R_0 and R_e based on 3 variables: the total population size of the outbreak (*N*), the total number of cases in the outbreak (*C*), and the number of susceptible persons at the start of the outbreak (*S*). In our calculations, *C* was informed by NORS outbreak data for the estimated total number ill and *N* by the exposed population. NORS data does not include nor can it inform the number of susceptible persons at the start of an outbreak. Therefore, to estimate *S*, we used norovirus challenge study data on the percent of persons that become infected and develop AGE after challenge with virus. Across all published studies, the weighted average of participants in whom gastroenteritis developed after challenge is 47% (range 27%–80%; Appendix Table 1) (*13*–*19*). We assumed *S* is the number of persons susceptible to disease, as opposed to infection. To calculate *S*, we multiplied 47% by *N* and rounded to the nearest integer. For 890 outbreaks, the total number of cases, *C*, was greater than our estimated *S*; for these outbreaks we set *S* equal to *C*, corresponding to a 100% attack rate. We also calculated *S* assuming 27% and 80% of *N* were susceptible to assess the sensitivity of our model results to this parameter.

Regression Analysis

After estimating R_0, R_e, and associated SEs for each norovirus outbreak, we fit a linear regression model to the log-transformed estimated reproduction numbers to assess whether outbreak setting, census region, season, year, suspected or confirmed norovirus, or genotype were associated with transmissibility. All variables were categorical, where the reference was assigned as the group with the most outbreaks reported, except for the suspected or confirmed variable, for which we set the referent to outbreaks with confirmed norovirus etiology. We used weighted least squares combined with estimated standard errors to produce robust estimates accounting for heteroscedasticity and non–normally distributed model residuals by using the estimatr package in R version 3.4.2 (*20*,*21*). We included the following variables in our models: outbreak setting; census region;

meteorological season, defined as spring (March 1–May 31), summer (June 1–August 31), fall (September 1–November 30), or winter (December 1–February 28); year, defined as July–June; whether norovirus was suspected or confirmed; and norovirus genotype, categorized as GI, GII.4, or GII.non4.

For outbreaks for which we calculated R_0 and R_e, we had norovirus genotype data for only 22% (1,571). In a preliminary analysis, we fit a univariate linear regression model to estimate R_0 by norovirus genotype alone and by norovirus genotype and year and found no evidence for variation (Appendix). Given these results and the small sample size, we did not include norovirus genotype in our models and performed model selection on the remaining variables. To determine which variables to include, we used a forward selection process and selected the model with the lowest Akaike information criterion and Bayes information criterion values.

Sensitivity Analysis

We tested the sensitivity of our regression model results to different modeling approaches and different assumptions of the percent susceptible at the start of an outbreak. We also fit a logistic regression model of binary transmission and a negative binomial regression of the final outbreak size by using the log-transformed exposed population size as a measure of the attack rate of an outbreak. Thus, we could make comparisons between the models to see if the results from modeling continuous transmission were consistent with the results of modeling binary transmission and attack rates. In addition, we ran all the regression models again using the assumption that 27% and 80% susceptible at the start of an outbreak, which corresponds to the minimum and maximum percent susceptible to AGE from published challenge studies (Appendix Table 2).

Results

Of the 7,094 norovirus outbreaks included in our final dataset, 75% (5,335) occurred in long-term care and assisted living facilities and 57% (4,016) occurred in winter. The median outbreak size was 28 cases (interquartile range [IQR] 16–47) and the median attack rate was 22% (IQR 11%–36%) (Table 1). The median R_0 was 2.75 (IQR 2.38–3.65) and the median R_e was 1.29 (IQR 1.12–1.74).

Model Selection and Regression Analysis

The final selected model included the following variables: major setting, census region, season, year, and whether norovirus was suspected or confirmed (Akaike information criterion = 5,803; Bayes information criterion = 5,968) (Appendix Table 3). For long-term care and assisted living facilities, R_0 was 3.35 (95% CI 3.26–3.45). R_0 for outbreaks in all other settings did not differ substantially, except for outbreaks in schools, colleges, and universities, in which R_0 was slightly reduced, 2.92 (95% CI 2.82–3.03) (Table 2; Appendix Figure 2). We found that R_0 differed substantially by outbreak status; suspected norovirus outbreaks had a lower R_0, 3.02 (95% CI 2.94–3.10), than that for confirmed outbreaks (R_0 = 3.35 [95% CI 3.26–3.45]).

Estimated R_0 varied only slightly by census region and was lowest in the northeast (R_0 = 3.00 [95% CI 2.92–3.08]). Season and year also contributed to changes in the R_0. Estimated R_0 was highest in winter (3.35 [95% CI 3.26–3.45]) and fall (3.37 [95% CI 3.24–3.50]) and lowest during the summer months (3.11 [95% CI 2.97–3.25]). Outbreaks reported during January 2009–June 2012 all had higher estimated R_0 (range for individual seasonal years 3.77–3.93) than the reference period, July 2016–June 2017 (Table 2; Appendix Figure 2). Our findings were generally robust to assumptions about the proportion susceptible at the start of the outbreak and whether we modeled the outcome of R_0, R_e, or final outbreak size (Appendix Tables 4–6, Figure 3).

Discussion

By using a large national outbreak dataset, we investigated transmission patterns of norovirus outbreaks. Our analysis led to several key findings. First, reported norovirus outbreaks in the United States have modest R_0 (2.75 [IQR 2.38–3.65]) and R_e (1.29 [IQR 1.12–1.74]) values. Second, we found that R_0 and R_e did not vary across most settings, except for outbreaks in schools, colleges, and universities, which had lower estimated transmission values. Third, we found higher transmission in laboratory-confirmed outbreaks relative to suspected outbreaks and higher transmission for outbreaks occurring in the winter months relative to summer months.

Our finding that norovirus outbreaks in the United States have modest transmission values is somewhat surprising. In a recent review of norovirus modeling studies, Gaythorpe et al. (*10*) found R_0 estimates for norovirus were 1.1–7.2. Of note, R_0 and R_e estimates from transmission modeling studies that analyzed data from norovirus outbreaks were high, but variability between studies was high; R_e estimates were ≈1–14 (*22*–*24*). Our estimates are within the reproduction numbers estimated by using transmission models of norovirus based on outbreak data (*22*,*25*).

Table 1. Norovirus outbreaks with exposed population size reported to the National Outbreak Reporting System, United States, 2009–2017*

Characteristics	No. (%)	Median attack rate, % (IQR)	Median final size, % (IQR)	Median R_0 (IQR)
All outbreaks	7,094 (100)	22 (11–36)	28 (16–47)	2.75 (2.38–3.65)
Major setting				
Child day care	272 (4)	21 (13–36)	18 (11–29)	2.67 (2.39–3.60)
Hospital or healthcare facility	271 (4)	22 (11–38)	19 (11–34)	2.70 (2.33–3.59)
Long-term care or assisted living facility	5,335 (75)	23 (13–36)	30 (17–47)	2.81 (2.42–3.76)
Other	350 (5)	20 (10–36)	24 (15–40)	2.66 (2.35–3.60)
Private home or residence	42 (1)	66 (50–91)	9 (6–16)	3.80 (2.26–4.92)
Restaurant	77 (1)	50 (27–64)	10 (6–16)	3.12 (2.53–4.31)
School, college, or university	747 (11)	12 (6–24)	42 (19–80)	2.41 (2.24–2.92)
Season				
Winter	4,016 (57)	22 (12–36)	30 (17–51)	2.80 (2.40–3.77)
Fall	808 (11)	21 (11–37)	26 (15–47)	2.72 (2.36–3.63)
Spring	1,964 (28)	20 (11–35)	27 (15–44)	2.69 (2.37–3.57)
Summer	306 (4)	17 (9–33)	19 (11–32)	2.57 (2.29–3.33)
Outbreak status				
Confirmed	3,114 (44)	26 (15–40)	35 (20–55)	2.99 (2.51–4.22)
Suspected	3,980 (56)	18 (9–31)	24 (14–40)	2.59 (2.32–3.27)
Census region				
Northeast	1,898 (27)	17 (9–29)	31 (17–53)	2.58 (2.30–3.23)
Midwest	2,205 (31)	25 (13–39)	26 (15–44)	2.87 (2.44–3.98)
South	2,224 (31)	23 (12–38)	29 (17–47)	2.81 (2.39–3.93)
West	767 (11)	21 (13–34)	28 (16–44)	2.75 (2.42–3.57)
Year				
2009 Jan–Jun†	243 (3)	28 (15–42)	35 (20–55)	3.09 (2.50-4.56)
2009 Jul–2010 Jun	275 (4)	29 (15–45)	35 (19–57)	3.17 (2.51–4.77)
2010 Jul–2011 Jun	592 (8)	29 (16–44)	32 (19–54)	3.12 (2.54–4.58)
2011 Jul–2012 Jun	679 (10)	27 (15–40)	35 (19–59)	3.01 (2.52–4.29)
2012 Jul–2013 Jun	967 (14)	21 (12–36)	28 (16–46)	2.73 (2.38–3.61)
2013 Jul–2014 Jun	913 (13)	20 (11–33)	29 (18–51)	2.68 (2.38–3.45)
2014 Jul–2015 Jun	941 (13)	21 (11–35)	28 (16–46)	2.74 (2.3–3.61)
2015 Jul–2016 Jun	1,007 (14)	17 (9–32)	25 (14–42)	2.57 (2.31–3.29)
2016 Jul–2017 Jun	1,070 (15)	19 (10–31)	26 (14–42)	2.63 (2.33–3.24)
2017 Jul–Dec†	407 (6)	20 (10–34)	22 (14–38)	2.66 (2.33–3.55)

*IQR, interquartile range.
†Partial norovirus years included in this analysis. The National Outbreak Reporting System was established in January 2009, and the first year of this analysis is 2009 January–June. At the time of analysis, we received data through December 2017.

However, our estimates are higher than those from several studies that estimated reproduction numbers by using population-level transmission models (*26*–*29*), suggesting that transmission of norovirus in outbreak settings is higher than sporadic transmission in the community.

From our main analysis, we found that outbreaks in schools, colleges, and universities had lower estimated transmission, but transmission varied little across all other settings. Relative to outbreaks in long-term care and assisted living facilities, outbreaks that occurred in private homes or residences and restaurants had higher final sizes, and schools, colleges, and universities had lower estimated attack rates. Our finding that outbreaks in the winter had higher estimated transmissibility than outbreaks that occurred in summer is likely a factor of the strong wintertime seasonality of noroviruses in the United States (*30*,*31*). Consistent with this finding are the observations that norovirus case and outbreak reports are inversely correlated with temperature (*30*,*31*) and that survival of norovirus surrogate viruses, such as murine norovirus and feline calicivirus, declines with increasing temperatures (*32*,*33*).

Several differences we found might be driven by surveillance biases rather than differences in norovirus transmission. Suspected norovirus outbreaks without a laboratory-confirmed outbreak etiology had lower transmission than laboratory-confirmed norovirus outbreaks, perhaps because suspected outbreaks are not investigated as well as confirmed outbreaks and have lower rates of case ascertainment. Outbreaks reported in the south had higher estimated R_0 and R_e relative to outbreaks in the northeast, which might be related to differences in the quality of reporting between these regions. For example, if surveillance in certain regions only captured larger, more easily detectable outbreaks with higher attack rates, this could bias our estimates of transmissibility upwards. Tremendous variability exists in outbreak reporting between states, ≈100-fold difference between the highest and lowest reporting states, which

likely affects the observed outbreak characteristics we included (*34*). Similarly, NORS has been collecting outbreak reports since January 2009, but in August 2012 CDC began a concerted effort to improve norovirus outbreak reporting to NORS and CaliciNet with the introduction of NoroSTAT (*35*,*36*). Thus, our finding that norovirus outbreaks reported before August 2012 were larger and had higher estimated R_0 and R_e values might be related to CDC's efforts to capture outbreaks that previously would not have been reported, such as smaller outbreaks. Further, because the transmission mode can be difficult to identify for norovirus outbreaks, our analysis might have included outbreaks for which the mode of transmission was misclassified as person-to-person. Larger outbreaks with higher transmission are more likely to be reported, and our results might not reflect transmission in smaller outbreaks. In addition, the exposed population size is difficult to quantify and is not consistently reported to NORS. Thus, the differences we found in estimated attack rates across different settings could be due to true variability in the exposed population size across settings or variability in the reliable reporting of the exposed population size. However, our analysis restricted to outbreaks in long-term care and assisted living facilities found the same trends among the variables for outbreak status, census region, season, and year as our analysis of all outbreaks, which suggests the results are robust.

Table 2. Estimated log-linear change in R_0 from the intercept for linear regression of log transformed R_0 for norovirus outbreaks reported to the National Outbreak Reporting System, United States, 2009–2017

Category	Estimated log-linear change in R_0 (95% CI)
Intercept	3.35 (3.26–3.45)
Major setting	
Long-term care or assisted living facility	Referent
Child day care	0.99 (0.95–1.03)
Hospital or healthcare facility	0.93 (0.90–0.97)
Other	0.97 (0.93–1.01)
Private home or residence	0.99 (0.82–1.19)
Restaurant	1.01 (0.91–1.11)
School, college, or university	0.87 (0.85–0.89)
Season	
Winter	Referent
Fall	1.00 (0.98–1.03)
Spring	0.98 (0.96–1.00)
Summer	0.93 (0.89–0.96)
Outbreak status	
Confirmed	Referent
Suspected	0.90 (0.88–0.92)
Census region	
South	Referent
Northeast	0.89 (0.87–0.91)
Midwest	1.00 (0.97–1.02)
West	0.98 (0.95–1.01)
Year	
2009 Jan–Jun	1.16 (1.10–1.23)
2009 Jul–2010 Jun	1.17 (1.11–1.23)
2010 Jul–2011 Jun	1.16 (1.12–1.21)
2011 Jul–2012 Jun	1.12 (1.08–1.16)
2012 Jul–2013 Jun	1.04 (1.01–1.07)
2013 Jul–2014 Jun	1.02 (0.99–1.06)
2014 Jul–2015 Jun	1.05 (1.02–1.08)
2015 Jul–2016 Jun	1.02 (0.99–1.05)
2016 Jul–2017 Jun	Referent
2017 Jul–Dec	1.04 (1.00–1.09)

Our study has several additional limitations. First, our process of data selection might have introduced bias into our analyses. We excluded outbreaks that occurred in multiple states, which are likely to have higher transmissibility given the larger geographic range involved; however, only 8 multistate outbreaks occurred during the study period, thus the bias is likely negligible. A substantial proportion of the dataset, 5,573 (31%) outbreaks, had to be excluded because the exposed population size was not reported. Excluding these outbreaks could introduce bias if the exposed population size is more likely to be reported for outbreaks with smaller, or larger, exposed population sizes. We only included outbreaks with person-to-person transmission; thus, our estimates of transmissibility are not generalizable to norovirus outbreaks where transmission occurs via other modes, such as foodborne, waterborne, or environmental transmission.

A second set of limitations relates to the final size method. This method assumes a susceptible-infected-recovered type infection in a homogenously mixing population (*12*), but this simplification likely does not reflect true mixing patterns. In addition, we might observe different mixing patterns in each of the different outbreak settings, such as older persons in long-term care facilities versus young children in childcare. The final size method also underestimates reproduction numbers for outbreaks with high attack rates. For example, in private homes, attack rates are high, but exposed population sizes are small. If everyone in the household is infected, then no additional infections can occur in the home. Thus, the final size method cannot capture any additional transmission that could have happened if the exposed population size had been larger, such as a higher number of persons in the household. Becker termed this limitation the "wasted infection potential" (*37*). Further, the final size method does not account for the effect of control measures. For some of the outbreaks represented in our dataset, control measures were most likely implemented, such as isolating ill persons and cleaning contamination. Such interventions likely would reduce the number ill, and the estimated R_0 would be lower than the R_0 in the absence of control measures.

In addition, the final size method assumes that the proportion of susceptible persons is known at the start of an outbreak; however, the level of susceptibility to norovirus is not well known. Certain host genetic factors are associated with the ability of norovirus to establish an infection within a human host (*38*–*41*), leading to variable susceptibility to norovirus infection (*42*–*44*). Secretor-negative persons have nonfunctional fucosyltransferase-2 genes, causing infection failure for norovirus genogroups I and II type 4 (*38*,*40*,*41*,*45*,*46*). Our estimates of R_0 and R_e assume that 47% of the population in our dataset is susceptible at the start of all outbreaks. However, the proportion susceptible varies among outbreaks and potentially over time and age as the distribution of circulating norovirus genotypes change. Further, our regression model estimates were sensitive to our assumption of the percent susceptible at the start of an outbreak. When we assumed 47% and 80% of the population was susceptible, the estimated transmissibility of norovirus in private homes or residences and restaurants was higher than transmissibility in long-term care and assisted living facilities. However, when we assumed 27% of the population was susceptible at the start of an outbreak, the association between private homes or residences and restaurants reversed. These settings then had lower estimated transmission relative to outbreaks in long-term care and assisted living facilities because the population size that can be infected is much lower, thus reducing the estimates of R_0 and R_e. For example, if a household had 15 persons, the maximum possible R_0 assuming 27% susceptibility is 4, which is lower than the average predicted R_0 for outbreaks in the reference group. Therefore, the results for private homes or residences and restaurants, where exposed population sizes are lower, should be interpreted with caution because transmission values in these settings might be underestimated. We also assumed that only symptomatic persons contribute to transmission in our calculation; persons with asymptomatic norovirus infections can contribute to transmission, but they likely are not as infectious as persons with symptomatic infections (*22*,*47*).

Finally, our main analysis does not account for norovirus genotype. Because of the limited data available on outbreak genotype we were not able to fully assess whether certain genotypes were more transmissible. As more genotyping data become available, future studies should investigate transmissibility.

We estimated reproduction numbers by using the final size method for >7,000 outbreaks from a national outbreak reporting system, then used these estimates to examine factors associated with norovirus transmission. Our analyses suggest that norovirus transmission rates are modest. Such modest rates of R_e suggest there are opportunities for effective control measures to curtail transmission of norovirus. However, challenges remain. Transmission by asymptomatic persons, which we did not account for in this analysis and generally goes undetected in surveillance, can limit the effectiveness of traditional control methods focused on ill persons, even for pathogens with modest transmission (*48*).

Overall, we found limited variation in R_0 and R_e for reported norovirus outbreaks in the United States, particularly across different settings. Our findings highlight the need for better data on the total exposed population sizes in outbreaks, which heavily influence estimates of attack rates, R_0, and R_e, to further refine estimates of these outbreak factors.

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EID Podcast
Tickborne Ehrlichia in North Carolina

While caring for patients in North Carolina, Dr. Ross Boyce began to suspect that tickborne *Ehrlichia* was being underdiagnosed. His study showed that *Ehrlichia*, despite being relatively common, was only tested for in about a third of patients thought to have a tickborne illness.

In this EID podcast, Dr. Ross Boyce, an infectious disease physician at the University of North Carolina at Chapel Hill, examines the prevalence and diagnosis of *Ehrlichia* in North Carolina.

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EMERGING INFECTIOUS DISEASES

Article DOI: https://doi.org/10.3201/eid2608.191537

Characterizing Norovirus Transmission from Outbreak Data, United States

Appendix

Estimating Basic and Effective Reproduction Numbers

We calculated basic reproduction (R_0), effective reproduction (R_e), and the associated standard errors (SE) for each outbreak. We used equations proposed by Becker (*1*) that use the final epidemic size

$$R_0 = \frac{N-1}{C} \sum_{i=S-C+1}^{S} \frac{1}{i}$$

$$SE(R_0) = \frac{N-1}{C} \sqrt{\sum_{i=S-C+1}^{S} \frac{1}{i^2} + \frac{CR_0^2}{(N-1)^2}}$$

where *N* is the total population size, *C* is the total number of cases in the outbreak, and *S* is the number of susceptible persons at the start of the outbreak. R_e is calculated by replacing *N* with *S* in the first equation above. SE(R_e) is calculated by replacing *N* with *S* and R_0 with R_e in the second equation shown above. The final size method assumes a susceptible-infected-recovered type infection with a closed, homogenously mixing population (*1*).

Genogroup and genotype analysis

Among the outbreaks for which we calculated R_0 and R_e only 1,571 outbreaks (22%) had data on norovirus genotype. We fit a linear regression model to the log transformed estimate of R_0 to assess whether the following genogroup and genotypes were associated transmissibility: genogroup I (GI), genogroup II genotype 4 (GII.4) and genogroup II non-genotype 4 (GII.non4). We found that R_0 varied little for outbreaks of GI (R_0 = 3.50 [95% CI 3.32, 3.68]), GII.4 (R_0 = 3.46 [95% CI 3.38, 3.55]) and GII.non4 (R_0 = 3.26 [95% CI 3.11, 3.41]).

In addition to the univariate regression analysis of genogroup and genotype, we also fit a linear regression model to the log transformed estimate of R_0 with predictor variables for

genotype and year to assess whether GII.4 noroviruses had different effects on transmissibility at the time when new strains emerged (i.e., GII.4 New Orleans in the 2009/2010 season and GII.4 Sydney in the 2012/2013 season). There was not sufficient evidence to suggest that R_0 differed for outbreaks of GII.4 during the norovirus seasons when GII.4 New Orleans (R_0 = 4.00 [95% CI 3.53, 4.54]) or GII.4 Sydney (R_0 = 3.38 [95% CI 3.24, 3.53]) relative to GII.4 outbreaks reported in seasons when no new strains emerged (R_0 = 3.38 [95% CI 3.19, 3.58]). (Appendix Table 4)

Alternative Models

We assessed two alternative approaches for modeling norovirus transmission: a logistic regression to model a binary transmission outcome (i.e., high versus low transmission) and a negative binomial regression to model the final size of outbreaks, adjusting for exposed population size (i.e., modeling attack rates). For our logistic regression, we used the first and third tertiles of estimated values of R_0 and R_e, assuming the percent susceptible was 47%, to determine the cutoffs for our outcome of interest: low versus high transmission. We excluded outbreaks with transmission values within the second tertile and focus our logistic regression comparison between the lowest and highest tertiles of transmission. The third tertile of R_0 and R_e values were 3.23 and 1.52, respectively.

The trends of transmissibility across our variables of interest (outbreak setting, census region, season, year, whether norovirus was suspected or confirmed and norovirus genotype) from our main regression analysis of a continuous transmission outcome were consistent across the logistic regressions of high R_0 (R_0>3.23) and R_e (R_e>1.52) and linear regression of R_e values. (Appendix Table 5) The trends of transmissibility were consistent for most of our variables of interest in the negative binomial model of final outbreak sizes; however, private homes or residences and restaurants had a much more pronounced effect on the attack rate of outbreaks, relative to long-term care and assisted living facilities (RR = 2.35 (95% CI 1.85, 3.01) and RR = 1.67 (95% CI 1.40, 2.01), respectively). As the exposed population size is difficult to quantify, and thus may not be reported reliably, we analyzed the subset of outbreaks that occurred within long-term care and assisted living facilities with our regression models. The patterns found among the variables for outbreak status, census region, season and year were consistent with what was found analyzing the full dataset. (Appendix Table 6)

Percent Susceptible

We tested the sensitivity of our results to the assumption of the percent susceptible start of an outbreak by running all the regression models assuming the percent susceptible at the start was 27% and 80%, which represent the minimum and maximum estimates of the percent susceptible to AGE from published challenge studies, respectively (Appendix Table 2). By adjusting our assumption of the percent susceptible at the start of the outbreak to 27% and 80%, the median R_0 was 6.04 (IQR 4.53, 9.38) and 1.43 (IQR 1.33, 1.61), respectively, while the median R_e was 1.82 (IQR 1.24, 3.83) and 1.14 (IQR 1.07, 1.29), respectively. Assuming the proportion susceptible was 27% we found that outbreaks in long-term care and assisted living facilities were more likely to have R_0 >8.05 and R_e>3.24 relative to all other settings. (Appendix Table 5, Appendix Table 6, Appendix Figure 2) When the percent susceptible was 80% we found that outbreaks in long-term care and assisted living facilities had increased odds of having R_0 >1.54 and R_e>1.23 compared to hospitals/other healthcare facilities, schools/colleges/universities, and other settings. Outbreaks in private homes or residences and restaurants had higher odds of having R_0 >1.54 and R_e>1.23 relative to long-term care and assisted living facilities, however the confidence intervals are wide due to small sample sizes. (Appendix Table7, Appendix Table 8, Appendix Figure 2) Trends in the variables for census region, season, year, and whether norovirus was suspected or confirmed for the models assuming 27% and 80% susceptibility were consistent with the models assuming 47% susceptibility. (Table 2, Appendix Table 7, Appendix Table 8)

Appendix Table 1. Descriptive characteristics of norovirus outbreaks that met our inclusion criteria and those outbreaks that were excluded from this analysis

Characteristics	No. (%)	Median attack rate (IQR)*	Median final size (IQR)
All Outbreaks	10,728 (60)	22 (10–44)	20 (10–39)
Major setting			
Child day care	168 (2)	21 (16–36)	16 (10–26)
Hospital/healthcare facility	316 (3)	24 (9–54)	16 (8–28)
Long-term care/assisted living facility	3,596 (34)	21 (10–42)	25 (14–43)
Other	493 (5)	24 (11–42)	19 (9–40)
Private home/residence	81 (1)	61 (40–95)	8 (5–13)
Restaurant	259 (2)	41 (17–68)	8 (4–13)
School/college/university	562 (5)	12 (6–26)	30 (13–69)
Missing	5,253 (49)	30 (14–43)	18 (8–36)
Season			
Winter	5,597 (49)	22 (10–4)	23 (11–44)
Fall	1,390 (13)	20 (10–40)	18 (8–35)
Spring	3,137 (30)	21 (10–43)	19 (9–36)
Summer	868 (8)	23 (10–41)	14 (7–26)
Outbreak Status			
Confirmed	4,875 (55)	22 (11–42)	23 (11–42)
Suspected	5,853 (45)	21 (9–44)	18 (9–36)
Census region			
Northeast	2,667 (25)	11 (6–24)	24 (12–47)

Characteristics	No. (%)	Median attack rate (IQR)*	Median final size (IQR)
Midwest	3,964 (37)	33 (17–62)	19 (9–36)
South	1,863 (17)	21 (10–40)	22 (10–45)
West	2,207 (21)	25 (13–41)	17 (8–32)
Multistate	16 (0.1)	30 (10–39)	14 (8–54)
Puerto Rico	11 (0.1)	12 (7–24)	18 (8–30)
Year			
2009 Jan–Jun†	630 (6)	32 (20–55)	25 (13–46)
2009 Jul–2010 Jun	914 (9)	22 (10–41)	22 (10–39)
2010 Jul–2011 Jun	1,079 (10)	29 (14–46)	25 (13–48)
2011 Jul–2012 Jun	1,107 (10)	15 (6–35)	22 (10–47)
2012 Jul–2013 Jun	1,405 (13)	23 (9–51)	22 (10–40)
2013 Jul–2014 Jun	1,240 (12)	21 (9–43)	20 (9–39)
2014 Jul–2015 Jun	1,224 (11)	25 (13–46)	20 (9–38)
2015 Jul–Jun 2016	1,279 (12)	17 (9–38)	17 (8–32)
2016 Jul–2017 Jun	1,397 (13)	21 (10–37)	18 (9–34)
2017 Jul–Dec†	456 (40)	21 (10–41)	16 (8–31)
Genogroup and genotype			
GII.4	1,550 (14)	27 (13–48)	23 (11–38)
GII.non4	774 (7)	23 (11–44)	19 (9–34)
GI	436 (4)	26 (15–53)	21 (10–40)
Missing	7,968 (74)	20 (9–41)	20 (10–10)

*****The medians and IQRs for attack rates were calculated for the subset of outbreaks where both the exposed population size and total estimated primary cases were reported. Among the 10,728 outbreaks excluded from our primary analysis, 8,903 outbreaks were missing data for the exposed population size.
†Two partial norovirus years included in this analysis. NORS was established in January 2009, thus the first year of this analysis is January–June 2009. At the time of analysis, we received data through December 2017, thus the final year of this analysis is July–Dec 2017.

Appendix Table 2. Data from published norovirus challenge studies on the number of participants challenged with norovirus and the number of challenged participants who subsequently developed acute gastroenteritis*

			Acute gastroenteritis	
Study (reference)	Secretor-negative screening	No. challenged	No.	Proportion
Dolin 1972 (*2*)	Secretors not screened	12	9	0.75
Wyatt 1974 (*3*)	Secretors not screened	23	16	0.70
Parrino 1977 (*4*)	Secretors not screened	12	6	0.50
Treanor 1988 (*5*)	Secretors not screened	10	8	0.80
Johnson 1990 (*6*)	Secretors not screened	42	25	0.60
Graham 1994 (*7*)	Secretors not screened	50	34	0.68
Lindesmith 2003 (*8*)	Secretor-negatives included	77	21	0.27
Lindesmith 2005 (*9*)	Secretor-negatives included	15	7	0.47
Atmar 2008 (*10*)	Secretor-negatives excluded	21	11	0.52
Leon 2011 (*11*)	Secretor-negatives excluded	15	5	0.33
Atmar 2011 (*12*)	Secretor-negatives excluded	41	29	0.71
Seitz 2011 (*13*)	Secretor-negatives excluded	13	10	0.77
Frenck 2012 (*14*)	Secretor-negatives included	40	12	0.30
Bernstein 2015 (*15*)	Secretor-negatives excluded	98	29	0.30
Overall		469	222	0.47†

*We assume that the average proportion that develop AGE across all studies, weighted by total number of participants in each study, is the proportion that are susceptible to norovirus in our calculations of R_0 and R_e.
†Average proportion susceptible weighted by number of participants.

Appendix Table 3. Estimated log linear change in R_0 (95% CI) from the estimated R_0 for the intercept for each model in a forward selection process for a linear regression model of log transformed R_0 values*

Model variable	Model 1	Model 2	Model 3	Model 4	Model 5
Intercept	3.22 (3.19–3.25)	3.44 (3.39-3.49)	3.57 (3.50–3.64)	3.61 (3.53–3.68)	3.35 (3.26–3.45)
Child day care	0.95 (0.91–0.99)	0.99 (0.95–1.03)	0.98 (0.94–1.02)	0.98 (0.94–1.02)	0.99 (0.95–1.03)
Hospital or healthcare facility	0.94 (0.90–0.98)	0.93 (0.89–0.97)	0.94 (0.90–0.98)	0.94 (0.90–0.98)	0.93 (0.90–0.97)
Other	0.96 (0.92–1.00)	0.96 (0.93–1.00)	0.95 (0.91–0.99)	0.97 (0.93–1.01)	0.97 (0.93–1.01)
Private home or residence	1.00 (0.84–1.19)	0.99 (0.83–1.18)	0.98 (0.81–1.17)	0.99 (0.82–1.19)	0.99 (0.82–1.19)
Restaurant	1.02 (0.93–1.12)	1.01 (0.92–1.11)	1.00 (0.91–1.09)	1.00 (0.91–1.10)	1.01 (0.91–1.11)
School, college, or university	0.84 (0.82–0.87)	0.88 (0.86–0.90)	0.86 (0.84–0.88)	0.86 (0.84–0.88)	0.87 (0.85–0.89)
Suspected outbreak	–	0.88 (0.87–0.90)	0.88 (0.87–0.90)	0.89 (0.87–0.90)	0.90 (0.88–0.92)
Region 1	–	–	0.89 (0.87–0.91)	0.89 (0.87–0.91)	0.89 (0.87–0.91)
Region 2	–	–	0.99 (0.97–1.02)	0.99 (0.97–1.02)	1.00 (0.97–1.02)
Region 4	–	–	0.96 (0.93–0.99)	0.96 (0.93–0.99)	0.98 (0.95–1.01)
Fall	–	–	–	1.00 (0.97–1.03)	1.00 (0.98–1.03)
Spring	–	–	–	0.97 (0.95–0.99)	0.98 (0.96–1.00)
Summer	–	–	–	0.92 (0.88–0.95)	0.93 (0.89–0.96)

Model variable	Model 1	Model 2	Model 3	Model 4	Model 5
Jan 2009–Jun 2009	–	–	–	–	1.16 (1.10–1.23)
Jul 2009–Jun 2010	–	–	–	–	1.17 (1.11–1.23)
Jul 2010–Jun 2011	–	–	–	–	1.16 (1.12–1.21)
Jul 2011–Jun 2012	–	–	–	–	1.12 (1.08–1.16)
Jul 2012–Jun 2013	–	–	–	–	1.04 (1.01–1.07)
Jul 2013–Jun 2014	–	–	–	–	1.02 (0.99–1.06)
Jul 2014–Jun 2015	–	–	–	–	1.05 (1.02–1.08)
Jul 2015–Jun 2016	–	–	–	–	1.02 (0.99–1.05)
Jul 2017–Dec 2017	–	–	–	–	1.04 (1.00–1.09)
Fitting Metrics					
Akaike information criterion	6,237	6,049	5,935	5,920	5,803
Bayes information criterion	6,291	6,111	6,017	6,023	5,968

*The Akaike information criterion, Bayes information criterion, and adjusted R^2 are presented for each model.

Appendix Table 4. Estimated log-linear change in R_0 from the intercept for linear regression of log transformed R_0 by genotype and year

Characteristics	Estimated log-linear change in R_0 (95% CI)
Intercept	3.38 (3.19–3.58)
Genogroup or genotype	
GII.4	Referent
GI	1.01 (0.95–1.07)
GII.non4	0.94 (0.89–0.99)
Year	
Jan 2009–Jun 2009	0.98 (0.76–1.25)
Jul 2009–Jun 2010	1.18 (1.03–1.35)
Jul 2010–Jun 2011	1.11 (1.01–1.21)
Jul 2011_Jun 2012	1.00 (0.93–1.08)
Jul 2012–Jun 2013	1.00 (0.93–1.07)
Jul 2013–Jun 2014	1.02 (0.95–1.10)
Jul 2014–Jun 2015	1.02 (0.95–1.10)
Jul 2015–Jun 2016	0.98 (0.91–1.06)
Jul 2016–Jun 2017	Referent
Jul 2017–Dec 2017	1.14 (1.01–1.28)

Appendix Table 5. Risk ratios of attack rates, estimated log-linear change in R_0 and R_e relative to the intercept from linear regression of the log transformed reproduction numbers and odds ratios of an outbreak with high transmission from logistic regression*

Characteristics	RR of attack rates (95% CI)	OR of R_0>3.23 (95% CI)	Estimated log-linear change in R_e (95% CI)	OR of R_e>1.52 (95% CI)†
Intercept	0.27 (0.26–0.29)	1.75 (1.41–2.18)	1.63 (1.58–1.68)	1.72 (1.39–2.13)
Major setting				
Long-term care, assisted living facility	Referent	Referent	Referent	Referent
Child day care	1.08 (0.98–1.19)	1.03 (0.74–1.42)	1.00 (0.95–1.05)	1.11 (0.80–1.53)
Hospital or healthcare facility	0.94 (0.86–1.03)	0.62 (0.45–0.85)	0.94 (0.89–0.98)	0.65 (0.48–0.89)
Other	0.98 (0.90–1.06)	0.73 (0.55–0.96)	0.98 (0.93–1.02)	0.74 (0.56–0.98)
Private home or residence	2.35 (1.85–3.01)	1.80 (0.88–3.87)	1.31 (1.14–1.51)	8.47 (3.22–29.27)
Restaurant	1.67 (1.40–2.01)	1.41 (0.78–2.62)	1.10 (0.99–1.22)	1.96 (1.09–3.67)
School, college, or university	0.67 (0.63–0.71)	0.29 (0.23–0.36)	0.86 (0.83–0.88)	0.30 (0.24–0.38)
Season				
Winter	Referent	Referent	Referent	Referent
Fall	0.99 (0.94–1.05)	1.00 (0.81–1.23)	1.01 (0.97–1.04)	0.97 (0.79–1.19)
Spring	0.97 (0.93–1.01)	0.90 (0.78–1.04)	0.98 (0.95–1.00)	0.89 (0.77–1.04)
Summer	0.86 (0.79–0.95)	0.65 (0.47–0.88)	0.92 (0.88–0.96)	0.62 (0.45–0.85)
Outbreak Status				
Confirmed outbreak	Referent	Referent	Referent	Referent
Suspected outbreak	0.82 (0.79–0.85)	0.43 (0.37–0.49)	0.89 (0.87–0.91)	0.42 (0.37–0.47)
Census region				
South	Referent	Referent	Referent	Referent
Northeast	0.77 (0.74–0.81)	0.44 (0.37–0.52)	0.88 (0.85–0.90)	0.45 (0.38–0.53)
Midwest	1.07 (1.02–1.11)	1.02 (0.87–1.20)	1.00 (0.98–1.03)	1.03 (0.88–1.20)
West	0.99 (0.93–1.05)	0.95 (0.76–1.19)	0.97 (0.93–1.00)	0.94 (0.75–1.17)
Year				
Jan 2009–Jun 2009	1.34 (1.21–1.48)	2.49 (1.73–3.62)	1.20 (1.12–1.28)	2.50 (1.73–3.63)
Jul 2009–Jun 2010	1.37 (1.25–1.52)	2.59 (1.82–3.73)	1.22 (1.15–1.30)	2.55 (1.79–3.65)
Jul 2010–Jun 2011	1.34 (1.25–1.45)	2.64 (2.01–3.49)	1.20 (1.14–1.25)	2.58 (1.97–3.39)
Jul 2011–Jun 2012	1.24 (1.15–1.33)	2.12 (1.63–2.77)	1.14 (1.09–1.19)	2.16 (1.66–2.81)

Characteristics	RR of attack rates (95% CI)	OR of R_0>3.23 (95% CI)	Estimated log-linear change in R_e (95% CI)	OR of R_e>1.52 (95% CI)†
Jul 2012–Jun 2013	1.08 (1.01–1.15)	1.26 (0.99–1.59)	1.05 (1.01–1.09)	1.29 (1.02–1.63)
Jul 2013–Jun 2014	1.04 (0.97–1.11)	1.19 (0.93–1.52)	1.04 (1.00–1.07)	1.18 (0.93–1.51)
Jul 2014–Jun 2015	1.08 (1.01–1.15)	1.33 (1.05–1.68)	1.06 (1.02–1.10)	1.32 (1.04–1.66)
Jul 2015–Jun 2016	1.05 (0.98–1.12)	1.14 (0.91–1.44)	1.03 (1.00–1.07)	1.15 (0.91–1.44)
Jul 2016–Jun 2017	Referent	Referent	Referent	Referent
Jul 2017–Dec 2017	1.05 (0.96–1.14)	1.40 (1.03–1.90)	1.04 (0.99–1.09)	1.33 (0.98–1.80)

*Assuming the percent susceptible at the start of an outbreak is 47%.
†Logistic regression compares outbreaks with transmission in the third tertile (Re>1.52) to outbreaks in the first tertile (Re<1.17) and does not include Re values in second tertile. Linear and negative binomial regressions use full dataset.

Appendix Table 6. Estimated log-linear change in basic and effective reproduction numbers relative to the intercept from linear regression*

		Basic reproduction number		Effective reproduction number	
Characteristics	RR of attack rates (95% CI)	Estimated log-linear change (95% CI)	OR of R_0>3.23 (95% CI)†	Estimated log-linear change (95% CI)	OR of R_e>1.52 (95% CI)†
Intercept	0.28 (0.26–0.30)	3.39 (3.28–3.51)	2.01 (1.56–2.60)	1.63 (1.57–1.7)	2.00 (1.55–2.57)
Season					
Winter	Referent	Referent	Referent	Referent	Referent
Fall	0.99 (0.92–1.06)	1.00 (0.96–1.03)	0.92 (0.71–1.20)	1.00 (0.95–1.04)	0.90 (0.69–1.16)
Spring	0.96 (0.92–1.00)	0.97 (0.95–1.00)	0.87 (0.73–1.03)	0.97 (0.94–1.00)	0.87 (0.73–1.03)
Summer	0.83 (0.73–0.93)	0.90 (0.86–0.95)	0.55 (0.36-0.85)	0.90 (0.85–0.95)	0.54 (0.35–0.84)
Outbreak Status					
Confirmed outbreak	Referent	Referent	Referent	Referent	Referent
Suspected outbreak	0.81 (0.78–0.84)	0.89 (0.87–0.91)	0.39 (0.34-0.45)	0.89 (0.86–0.91)	0.39 (0.34–0.45)
Census Region					
South	Referent	Referent	Referent	Referent	Referent
Northeast	0.69 (0.66–0.73)	0.86 (0.84–0.88)	0.31 (0.25–0.37)	0.84 (0.82–0.86)	0.31 (0.26–0.38)
Midwest	1.00 (0.95–1.05)	0.98 (0.95–1.00)	0.83 (0.69–0.99)	0.99 (0.96–1.02)	0.81 (0.67–0.97)
West	0.96 (0.90–1.03)	0.96 (0.93–1.00)	0.89 (0.67–1.18)	0.96 (0.92–1.00)	0.89 (0.67–1.17)
Year					
Jan 2009–Jun 2009	1.47 (1.32–1.63)	1.20 (1.13–1.28)	3.39 (2.22–5.23)	1.26 (1.17–1.35)	3.41 (2.24–5.25)
Jul 2009–Jun 2010	1.46 (1.31–1.63)	1.21 (1.14–1.29)	3.04 (1.98–4.74)	1.28 (1.19–1.38)	2.92 (1.91–4.51)
Jul 2010–Jun 2011	1.43 (1.32–1.55)	1.20 (1.15–1.25)	3.27 (2.39–4.50)	1.25 (1.19–1.32)	3.13 (2.30–4.29)
Jul 2011–Jun 2012	1.28 (1.19–1.38)	1.14 (1.10–1.19)	2.39 (1.76–3.25)	1.17 (1.12–1.23)	2.35 (1.74–3.19)
Jul 2012–Jun 2013	1.10 (1.03–1.18)	1.05 (1.02–1.09)	1.35 (1.03–1.78)	1.07 (1.03–1.11)	1.35 (1.03–1.78)
Jul 2013–Jun 2014	1.08 (1.01–1.17)	1.04 (1.00–1.08)	1.29 (0.97–1.74)	1.05 (1.01–1.10)	1.28 (0.95–1.71)
Jul 2014–Jun 2015	1.16 (1.08–1.24)	1.07 (1.04–1.11)	1.59 (1.21–2.08)	1.09 (1.05–1.14)	1.56 (1.19–2.04)
Jul 2015–Jun 2016	1.08 (1.01–1.16)	1.02 (0.99, 1.06)	1.19 (0.9–1.58)	1.05 (1.00–1.09)	1.19 (0.90–1.57)
Jul 2016–Jun 2017	Referent	Referent	Referent	Referent	Referent
Jul 2017–Dec 2017	1.09 (0.99–1.20)	1.06 (1.01–1.12)	1.56 (1.08–2.27)	1.06 (1.00–1.13)	1.50 (1.04–2.16)

*Odds ratios of outbreaks with R_0>3.23 and R_e>1.52, final size adjusting for exposed population size among long-term care or assisted care facilities, assuming 47% susceptible at the start of the outbreak. R_0, basic reproduction number; R_e, estimated reproduction number.
†Logistic regression compares outbreaks with transmission in the third tertile (R_0>3.23, R_e>1.52) to outbreaks in the first tertile (R_0<2.48, R_e<1.17), and does not include R_e values in second tertile. Linear and negative binomial regressions use full dataset.

Appendix Table 7. Estimated log-linear change in basic reproductive number (R_0) from linear regression and odds ratios of outbreaks with high R_0 assuming 27% and 80% susceptible at the start of the outbreak*

	27% Susceptible		80% Susceptible	
Characteristics	Estimated log-linear change in R_0 (95% CI)	OR of R_0>8.05 (95% CI)†	Estimated log-linear change in R_0 (95% CI)	OR of R_0>1.54 (95% CI)†
Intercept	7.42 (7.18–7.68)	2.05 (1.66–2.54)	1.57 (1.54–1.60)	1.78 (1.43–2.22)
Major Setting				
Long-term care or assisted living facility	Referent	Referent	Referent	Referent
Child day care	0.92 (0.88–0.97)	0.64 (0.45–0.89)	1.02 (0.99–1.05)	1.11 (0.80–1.55)
Hospital or healthcare facility	0.85 (0.81–0.89)	0.46 (0.33–0.64)	0.99 (0.96–1.02)	0.66 (0.48–0.91)
Other	0.91 (0.87–0.95)	0.54 (0.40–0.72)	0.99 (0.96–1.02)	0.77 (0.58–1.01)
Private home or residence	0.53 (0.43–0.65)	0.02 (0.00–0.12)	1.17 (1.05–1.31)	5.17 (2.22–14.21)
Restaurant	0.69 (0.61–0.77)	0.17 (0.09–0.33)	1.08 (1.01–1.16)	1.78 (0.99–3.31)
School, college, or university	0.85 (0.82–0.88)	0.32 (0.25–0.39)	0.93 (0.91–0.94)	0.30 (0.24–0.38)
Season				
Winter	Referent	Referent	Referent	Referent
Fall	0.97 (0.94–1.01)	0.91 (0.74–1.12)	1.00 (0.98–1.01)	0.94 (0.77–1.16)
Spring	0.97 (0.94–0.99)	0.80 (0.69–0.93)	0.99 (0.98–1.00)	0.88 (0.76–1.02)
Summer	0.90 (0.86–0.95)	0.54 (0.39–0.75)	0.97 (0.94–1.00)	0.62 (0.45–0.85)
Outbreak Status				
Confirmed outbreak	Referent	Referent	Referent	Referent

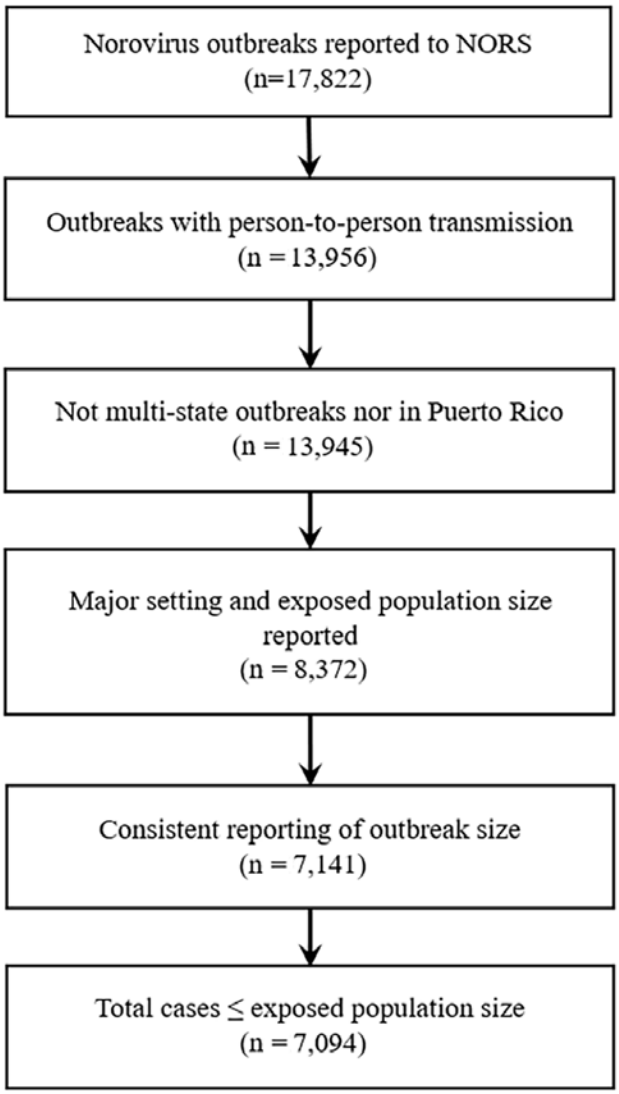
Characteristics	27% Susceptible		80% Susceptible	
	Estimated log-linear change in R_0 (95% CI)	OR of R_0>8.05 (95% CI)†	Estimated log-linear change in R_0 (95% CI)	OR of R_0>1.54 (95% CI)†
Probable outbreak	0.87 (0.85–0.89)	0.45 (0.40–0.51)	0.95 (0.94–0.96)	0.42 (0.37–0.48)
Census Region				
South	Referent	Referent	Referent	Referent
Northeast	0.93 (0.91–0.96)	0.55 (0.47–0.65)	0.93 (0.92–0.95)	0.44 (0.37–0.52)
Midwest	0.99 (0.97–1.02)	0.93 (0.80–1.09)	1.01 (1.00–1.03)	1.03 (0.88–1.21)
West	1.03 (0.99–1.06)	1.10 (0.88–1.37)	0.98 (0.96–1.00)	0.95 (0.76–1.19)
Year				
Jan 2009–Jun 2009	1.12 (1.06–1.20)	2.05 (1.42–3.00)	1.10 (1.06–1.14)	2.62 (1.80–3.83)
Jul 2009–Jun 2010	1.11 (1.05–1.18)	1.86 (1.30–2.67)	1.12 (1.08–1.16)	2.64 (1.85–3.82)
Jul 2010–Jun 2011	1.11 (1.07–1.16)	1.95 (1.49–2.57)	1.09 (1.06–1.12)	2.59 (1.97–3.43)
Jul 2011–Jun 2012	1.13 (1.08–1.18)	2.09 (1.62–2.72)	1.06 (1.04–1.08)	2.15 (1.65–2.81)
Jul 2012–Jun 2013	1.02 (0.99–1.06)	1.13 (0.90–1.41)	1.02 (1.00–1.04)	1.33 (1.05–1.69)
Jul 2013–Jun 2014	1.01 (0.98–1.05)	1.12 (0.88–1.42)	1.02 (1.00–1.04)	1.20 (0.94–1.54)
Jul 2014–Jun 2015	1.03 (0.99–1.07)	1.26 (1.00–1.59)	1.03 (1.01–1.05)	1.37 (1.08–1.73)
Jul 2015–Jun 2016	1.00 (0.96–1.03)	1.01 (0.80–1.26)	1.03 (1.01–1.05)	1.12 (0.88–1.41)
Jul 2016–Jun 2017	Referent	Referent	Referent	Referent
Jul 2017–Dec 2017	1.04 (0.99–1.09)	1.22 (0.91–1.65)	1.01 (0.99–1.03)	1.31 (0.97–1.78)

*OR, odds ratio; R_0, basic reproduction number; R_e, estimated reproduction number.
†Logistic regression compares outbreaks with transmission in the third tertile (S = 27%(N): R_0>8.05; S = 80%(N): R_0>1.54) to outbreaks in the first tertile (S = 27%(N): R_0<4.96; S = 80%(N): R_0<1.36) and does not include R_0/R_e values in second tertile. Linear and negative binomial regressions use full dataset.

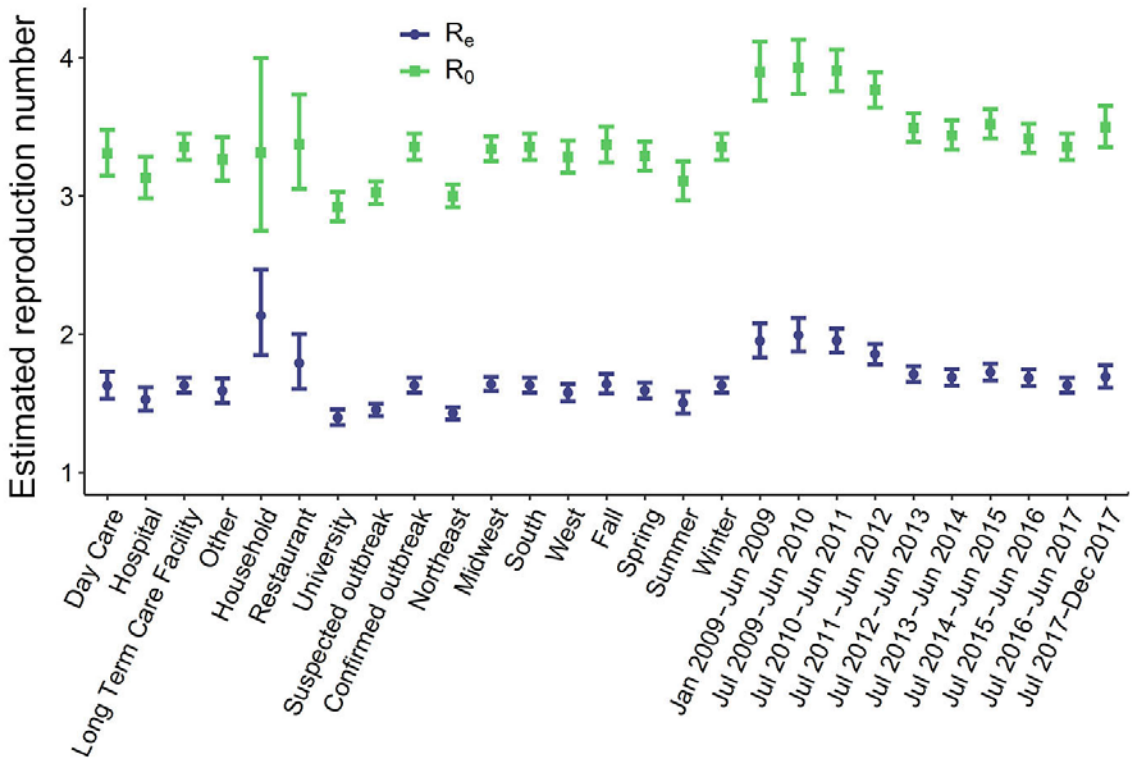
Appendix Table 8. Estimated log-linear change in R_e (95% CI) from linear regression and odds ratios of outbreaks with high R_e assuming 27% and 80% susceptible at the start of the outbreak

Characteristics	27% Susceptible		80% Susceptible	
	Estimated log linear change in R_e (95% CI)	OR of R_e>3.24 (95% CI)†	Estimated log-linear change in R_e (95% CI)	OR of R_e>1.23 (95% CI)†
Intercept	2.41 (2.31–2.52)	1.88 (1.51–2.33)	1.25 (1.23–1.28)	1.67 (1.34–2.07)
Major Setting				
Long-term care or assisted living facility	Referent	Referent	Referent	Referent
Child day care	0.95 (0.89–1.01)	0.79 (0.56–1.11)	1.01 (0.98–1.05)	1.05 (0.75–1.45)
Hospital or healthcare facility	0.85 (0.80–0.90)	0.41 (0.29–0.58)	0.99 (0.96–1.02)	0.63 (0.46–0.86)
Other	0.91 (0.86–0.97)	0.65 (0.48–0.86)	0.99 (0.96–1.02)	0.76 (0.58–1.00)
Private home or residence	0.98 (0.85–1.14)	0.86 (0.24–3.04)	1.24 (1.12–1.37)	8.47 (3.22–29.28)
Restaurant	0.90 (0.80–1.01)	0.35 (0.16–0.74)	1.08 (1.01–1.16)	1.53 (0.86–2.78)
School, college, or university	0.79 (0.75–0.82)	0.27 (0.21–0.34)	0.93 (0.91–0.94)	0.31 (0.25–0.39)
Season				
Winter	Referent	Referent	Referent	Referent
Fall	0.98 (0.94–1.02)	0.89 (0.72–1.10)	1.00 (0.98–1.01)	0.97 (0.79–1.19)
Spring	0.96 (0.93–0.99)	0.82 (0.71–0.95)	0.99 (0.97–1.00)	0.90 (0.77–1.04)
Summer	0.87 (0.82–0.93)	0.53 (0.37–0.73)	0.97 (0.94–1.00)	0.63 (0.46–0.86)
Outbreak Status				
Confirmed outbreak	Referent	Referent	Referent	Referent
Suspected outbreak	0.82 (0.80–0.84)	0.41 (0.36–0.47)	0.95 (0.94–0.96)	0.42 (0.37–0.48)
Census Region				
South	Referent	Referent	Referent	Referent
Northeast	0.86 (0.83–0.89)	0.47 (0.40–0.56)	0.93 (0.92–0.95)	0.45 (0.38–0.53)
Midwest	1.01 (0.98–1.04)	0.95 (0.81–1.12)	1.02 (1.00–1.03)	1.01 (0.86–1.18)
West	0.99 (0.95–1.04)	0.98 (0.78–1.23)	0.98 (0.96–1.00)	0.92 (0.74–1.15)
Year				
Jan 2009–Jun 2009	1.25 (1.16–1.35)	2.64 (1.83–3.85)	1.10 (1.06–1.15)	2.66 (1.84–3.88)
Jul 2009–Jun 2010	1.27 (1.18–1.36)	2.57 (1.80–3.69)	1.12 (1.08–1.16)	2.64 (1.86–3.78)
Jul 2010–Jun 2011	1.24 (1.17–1.31)	2.61 (1.99–3.43)	1.09 (1.07–1.12)	2.56 (1.95–3.36)
Jul 2011–Jun 2012	1.20 (1.14–1.27)	2.21 (1.70–2.87)	1.06 (1.04–1.09)	2.22 (1.71–2.89)
Jul 2012–Jun 2013	1.05 (1.01–1.10)	1.31 (1.03–1.65)	1.02 (1.01–1.04)	1.30 (1.03–1.65)
Jul 2013–Jun 2014	1.03 (0.99–1.08)	1.29 (1.01–1.65)	1.02 (1.00–1.04)	1.25 (0.98–1.59)
Jul 2014–Jun 2015	1.07 (1.02–1.12)	1.33 (1.06–1.69)	1.03 (1.01–1.05)	1.34 (1.06–1.69)
Jul 2015–Jun 2016	1.02 (0.98–1.07)	1.12 (0.88–1.41)	1.03 (1.01–1.05)	1.15 (0.91–1.45)
Jul 2016–Jun 2017	Referent	Referent	Referent	Referent
Jul 2017–Dec 2017	1.05 (0.99–1.12)	1.41 (1.04–1.91)	1.01 (0.99–1.03)	1.37 (1.01–1.86)

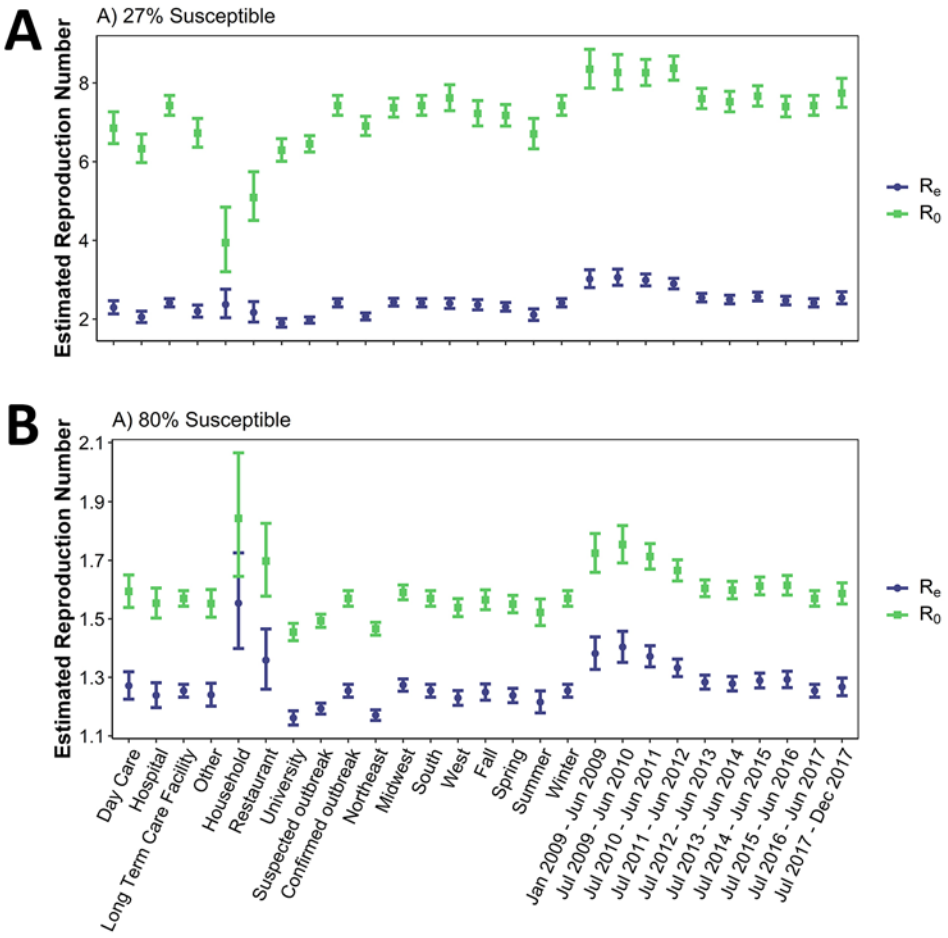
*OR, odds ratio; R_0, basic reproduction number; R_e, estimated reproduction number.
†Logistic regression compares outbreaks with transmission in the third tertile (S = 27%(N): R_e>3.24, S = 80%(N): R_e>1.23) to outbreaks in the first tertile (S = 27%(N): R_0<1.37, S = 80%(N): R_e<1.09), and does not include R_0/R_e values in second tertile. Linear and negative binomial regressions use full dataset.



Appendix Figure 1. Flowchart of outbreaks included in analysis.



Appendix Figure 2. Reproduction rate, and estimated reproduction rate for norovirus in the United States assuming the initial proportion susceptible is 47%. Blue circles indicate estimated reproductive rate. Green circles indicate basic reproduction rate. R_0, basic reproduction rate; R_e, estimated reproduction rate.



Appendix Figure 3. Estimated R_0 (green squares) and R_e (blue circles) assuming A) 27% susceptible and B) 80% susceptible at the start of the outbreak.

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