

# Norovirus Illnesses in Children and Adolescents



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## KEYWORDS

• Norovirus • Gastroenteritis • Diarrhea • Vomiting • Outbreaks

## KEY POINTS

- Norovirus is a leading cause of both endemic and epidemic gastroenteritis in the United States and globally.
- Norovirus causes approximately 4.2 million illnesses; 815,000 outpatient visits; 130,000 emergency department visits; 24,600 hospitalizations; and 38 deaths annually in children in the United States.
- Most of the global childhood mortality from norovirus illness occurs in developing countries.
- Early assessment of dehydration status and treatment aimed at correcting fluid status are key to preventing severe outcomes from norovirus illness.
- Vaccines against norovirus illness and strategies for defining the target population, vaccination schedule, and delivery mechanism for vaccination are under development.

## BACKGROUND

Norovirus is a leading cause of acute gastroenteritis in the United States<sup>1</sup> and globally<sup>2</sup>. Although norovirus infection causes illness in all age groups, incidence rates are highest among young children.<sup>1,3</sup> In several countries that have introduced national rotavirus vaccination programs, norovirus has replaced rotavirus as the leading cause of medically attended<sup>4-8</sup> and community<sup>8,9</sup> pediatric gastroenteritis. Approximately 99% of the 212,000 annual deaths caused by norovirus occur in developing countries.<sup>10</sup> Although deaths are rare in the United States, norovirus is responsible for approximately 24,000 hospitalizations; 132,000 emergency room visits; and 925,000 outpatient visits in children less than 18 years, at an estimated cost of more than \$200 million.<sup>11,12</sup> With norovirus vaccines under development,<sup>13</sup> a review of the virology, epidemiology, clinical presentation, diagnosis, treatment, and prevention of pediatric norovirus is described herein.

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Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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## NOROVIRUS VIROLOGY

Noroviruses are a genetically diverse group of viruses in the *Caliciviridae* family that cause acute gastroenteritis.<sup>14</sup> The first norovirus was described when a viral particle was observed by electron microscopy in a stool sample derived from a 1968 outbreak in Norwalk, Ohio, leading to the initial name of Norwalk virus.<sup>15</sup> Norwalk virus was the first virus shown to cause gastroenteritis. Since then, other Norwalk-like viruses have been discovered; currently, noroviruses are classified into genogroups GI to GVII.<sup>16</sup> Genogroups GI, GII, and, to a lesser extent, GIV, are known to cause human disease. Globally, viruses of the GII.4 genotype are the leading cause of norovirus disease,<sup>17</sup> include new variants that emerge every 2 years to 4 years,<sup>18,19</sup> and are associated with greater symptom severity and health care burden.<sup>20</sup>

## CLINICAL PRESENTATION AND DISEASE COURSE

Norovirus infections cause acute gastroenteritis, presenting as acute-onset vomiting and/or diarrhea. When present, diarrhea is typically watery and nonbloody and may be accompanied by abdominal cramps, nausea, and fever.<sup>21</sup> Constitutional symptoms, including low-grade fever, generalized myalgias, malaise, headache, and chills, frequently occur. The incubation period lasts 12 hours to 48 hours, and the duration of clinical symptoms is typically 12 hours to 72 hours. Asymptomatic norovirus infection, identified through stool shedding of norovirus in patients without gastroenteritis, has been found in 3% to 10% of children and adults.<sup>22</sup> Although most infections result in full recovery,<sup>23</sup> severe outcomes, such as hospitalization and death, occur, particularly among children ages less than 5 years, adults ages greater than 65 years, and immunocompromised hosts.<sup>1,24–26</sup>

### ***Severity of Norovirus Illness in Children***

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A meta-analysis of norovirus-associated gastroenteritis in children aged less than 5 years worldwide found that approximately 70% of cases occur within the 6-month to 23-month age range, and fewer than 15% occur before 6 months.<sup>27</sup> In this analysis, the proportion of cases among children less than 12 months increased from community to outpatient to inpatient settings, suggesting that infants more often have severe disease or are more likely to seek medical care and be hospitalized. Gastroenteritis caused by norovirus is generally milder than illness caused by rotavirus.<sup>28</sup> Children less than 5 years diagnosed with norovirus gastroenteritis after presenting to 3 US children's hospitals participating in active surveillance had fewer days of diarrhea, fewer diarrhea episodes, less fever, fewer abnormal behavioral signs, and less hospitalization than those diagnosed with rotavirus.<sup>29</sup> In contrast, children with norovirus gastroenteritis had more days of vomiting and more vomiting episodes than those with an unknown etiology.

### ***Norovirus in Immunocompromised Children***

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Typically, norovirus outbreaks in hospitalized children with immunocompromising conditions occur by community-acquired infection in an index patient followed by nosocomial transmission to other patients and hospital staff.<sup>30–32</sup> In both retrospective and prospective studies, children with norovirus infection after solid organ or stem cell transplantation are at risk for prolonged viral shedding,<sup>33–37</sup> diarrhea greater than 14 days,<sup>33,34,36–40</sup> and severe outcomes.<sup>33,34,36,37,39,40</sup> Hospitalizations from norovirus gastroenteritis in these studies did not follow the typical seasonal pattern of norovirus.

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