P0353

Incidence and severity of norovirus-associated acute gastroenteritis in adults with underlying conditions in the United States: initial results from the ORION study

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ORION
Observational Research on the Impact and Outcomes of Norovirus

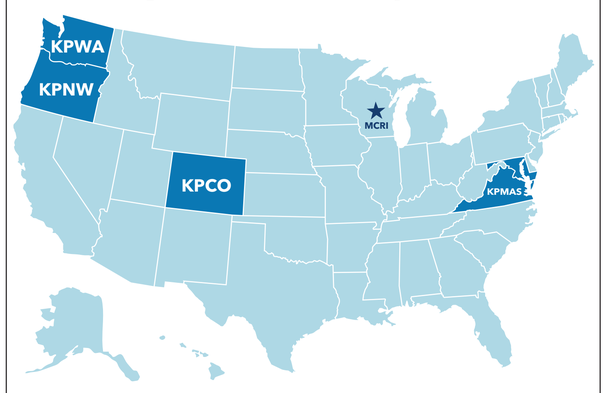
Background

- The 'Observational Research on the Impact and Outcomes of Norovirus' (ORION) Study aims to better understand the occurrence and severity of norovirus acute gastroenteritis (AGE) among a community cohort of adults, particularly those with underlying conditions.
- The goals of this interim analysis are to:
  - Estimate the incidence of AGE, including that due to norovirus, and assess the relationship between AGE and the presence of underlying conditions; and
  - Describe symptoms and severity of AGE illness episodes, overall and by type and number of underlying conditions.

Methods

- Study design: Prospective, community cohort of 3,555 adults ≥18 years recruited from four Kaiser Permanente (KP) health plan regions in the United States (**Figure 1**)
  - Exclusion: opting out of research, cognitive impairment, or non-English speaking
  - Over-recruitment of individuals with underlying conditions (shown in **Table 1**) recorded in the electronic health record during the year prior to enrollment
- Study observation period: 1 April 2025 – 30 April 2026
  - Interim analysis observation period: 1 April 2025 – 28 February 2026
- Weekly assessment of new AGE episodes, as defined by participant-reported onset of vomiting or diarrhea within previous 7 days
  - Home self-collection of stool specimens for RT-PCR multiplex testing and genotyping at Marshfield Clinic Research Institute
  - Exposures defined as number of additional household members, and contact with either a person with vomiting or diarrhea or a child <5 years of age in the week prior to AGE illness
  - Severe AGE defined as ≥6 episodes of vomiting or diarrhea within a 24-hour period or reported hospitalization due to AGE
- We calculated:
  - Cumulative incidence (episodes per 1,000 person years [PY]) and 95% confidence intervals (CI) through bootstrapping with 1,000 replicates; and
  - Age-, sex-, and exposure-adjusted incidence rate ratios (aIRR) using modified Poisson regression.

Figure 1: ORION Study Sites[1]



[1]Study participant recruitment and follow-up occurs at Kaiser Permanente Colorado (KPCO), Mid-Atlantic States (KPMAS), Northwest (KPNW), and Washington (KPWA); stool specimen testing occurs at Marshfield Clinic Research Institute (MCRI).

Results

Table 1: Distribution of all-cause and norovirus AGE episodes among ORION participants, 1 Apr 25-28 Feb 26

	ORION Participants N (%)	AGE Episodes N (%)	Norovirus Episodes N (%)
TOTAL	**3,555**	**1,173**	**68**
Sex			
Female	2,078 (58)	769 (66)	41 (60)
Male	1,477 (42)	404 (34)	27 (40)
Age			
18-34 yrs	529 (15)	191 (16)	13 (19)
35-49 yrs	908 (26)	376 (32)	20 (29)
50-64 yrs	870 (24)	257 (22)	12 (18)
65-74 yrs	727 (20)	219 (19)	12 (18)
75+ yrs	521 (15)	130 (11)	11 (16)
Underlying comorbidity[1]			
Obesity	837 (24)	340 (29)	11 (16)
Cardiovascular disease	654 (18)	225 (19)	12 (18)
Liver disease	437 (12)	132 (11)	5 (7)
Kidney disease	585 (16)	173 (15)	6 (9)
Diabetes	664 (19)	246 (21)	7 (10)
Neurologic disorders	394 (11)	129 (11)	4 (6)
Immunocompromise	1,427 (40)	473 (40)	25 (37)
Hematologic disease	721 (20)	262 (22)	12 (18)
Chronic GI disease	854 (24)	338 (29)	21 (31)
Pulmonary disease	412 (12)	143 (13)	9 (13)
None	383 (11)	81 (7)	12 (18)
Comorbidity Summary			
0	383 (11)	81 (7)	12 (18)
1	1,231 (35)	404 (34)	29 (43)
2	917 (26)	300 (26)	13 (19)
3+	1,024 (29)	388 (33)	14 (21)
Number of People in Household			
Missing	11 (0)	2 (0)	1 (1)
0	570 (16)	174 (15)	7 (10)
1	1,323 (37)	406 (35)	21 (31)
2	759 (21)	255 (22)	14 (21)
3+	892 (25)	336 (29)	25 (37)
Contact with Someone with V/D			
Yes		151 (13)	38 (56)
No		1,022 (87)	30 (44)
Contact with child <5 yrs.			
Yes		74 (6)	26 (38)
No		1,099 (94)	42 (62)

[1]Underlying conditions are not mutually exclusive. GI=gastrointestinal

Figure 2: Incidence of all-cause AGE among ORION participants, overall and by sex, age, and number of underlying conditions

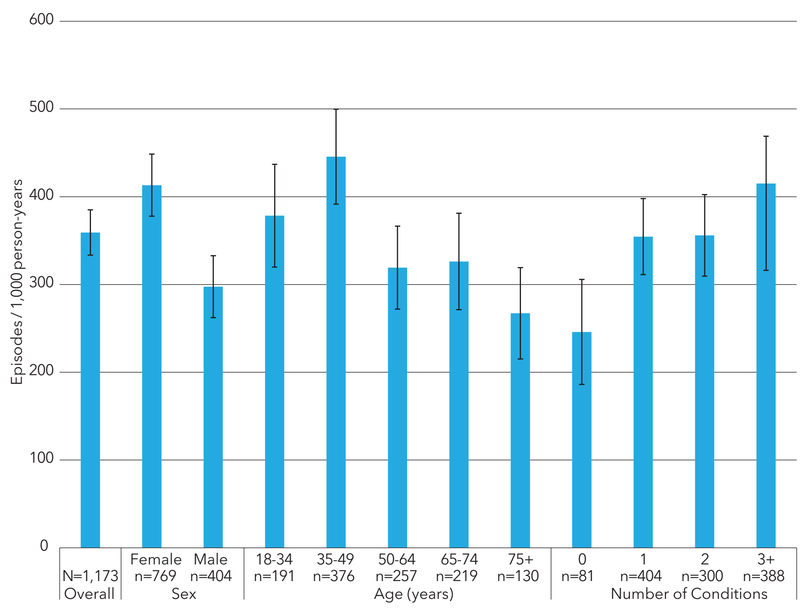


Figure 3: Incidence of norovirus AGE among ORION participants, overall and by sex, age, and number of underlying conditions

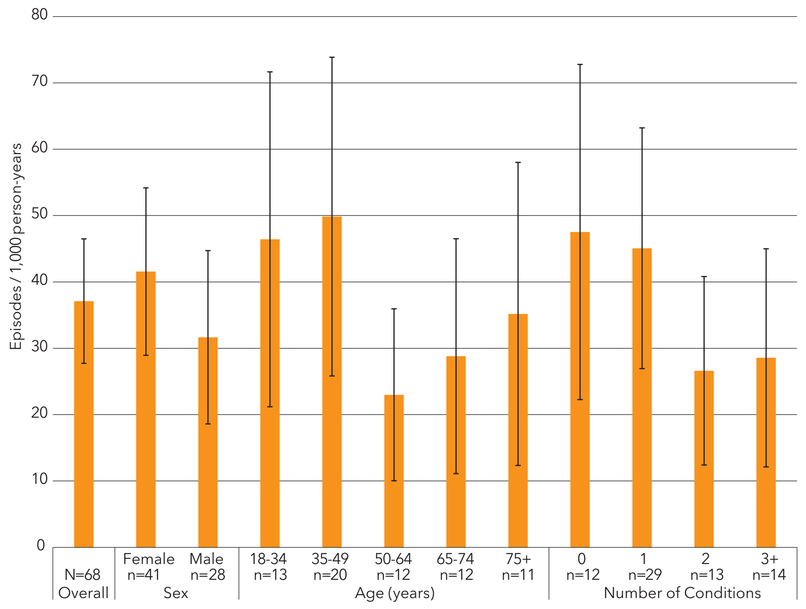
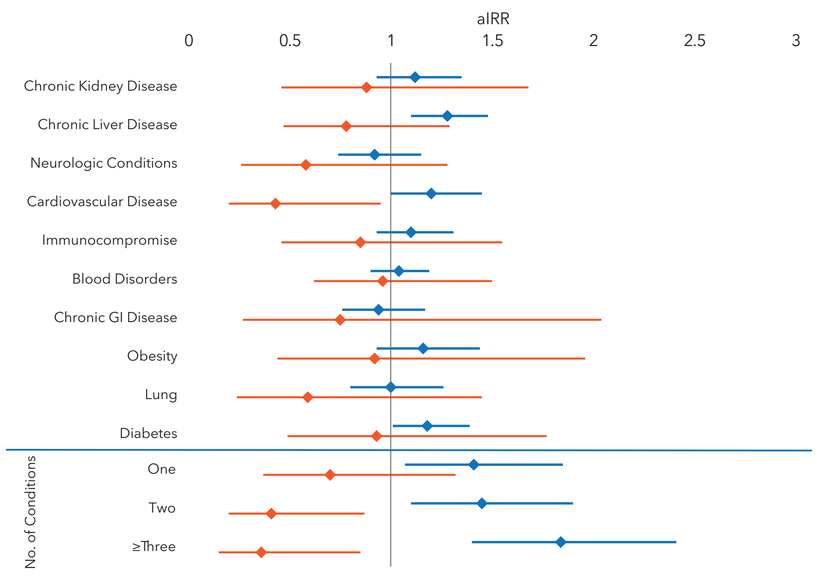
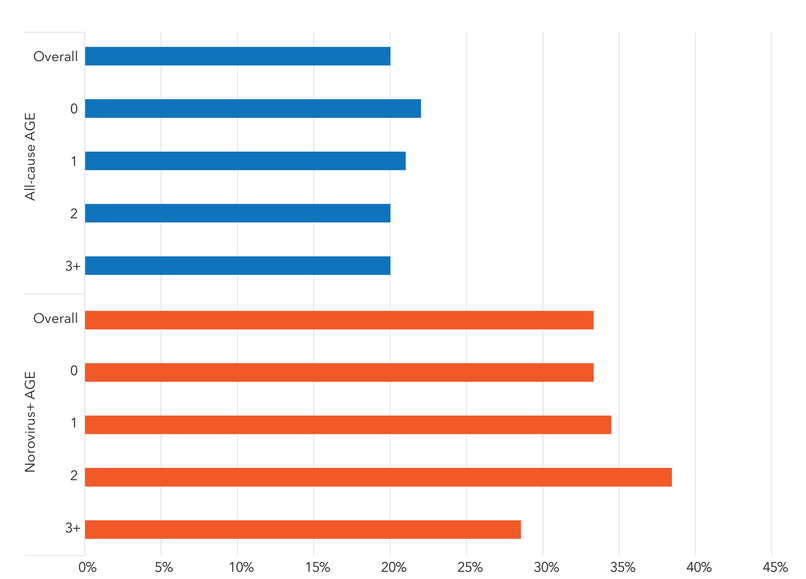


Figure 4: Age-, sex-, and exposure-adjusted incidence rate ratios (aIRR) for all-cause and norovirus AGE, by type and number of underlying conditions, compared to those with none[1]



[1]Exposures adjusted for number of household members, contact with someone with vomiting or diarrhea or contact with a child <5 years in the week prior to illness onset

Figure 5: Proportion of illnesses considered severe, by number of underlying conditions, among all-cause and norovirus AGE episodes.



Results

- We identified 1,173 all-cause AGE (359 [CI: 333, 385] per 1,000 PY), of which 686 had laboratory testing results and 68 were positive for norovirus (37 [28, 46] per 1,000 PY) episodes. Demographics, clinical conditions, and exposure characteristics are shown in **Table 1**.
- The incidence of all-cause AGE varied by age and increased with number of underlying conditions (**Figure 2**), while that of norovirus AGE was similar across all strata, although small samples limit our ability to detect differences (**Figure 3**).
- All-cause AGE was significantly higher – and norovirus AGE significantly lower – with an increasing number of underlying conditions, after adjusting for age, sex, and exposures (**Figure 4**).
- Norovirus AGE resulted in a higher proportion of severe illness than seen more generally among all-cause AGE, regardless of number of underlying conditions (**Figure 5**).
  - Symptom presence varied by number of underlying conditions in the norovirus population, although small numbers may have limited our ability to detect any such patterns (**Table 2**).
- Care-seeking increased among those with ≥1 comorbidities, compared to those with none, among all-cause and norovirus AGE populations (**Table 2**)

Conclusions

- Knowledge of norovirus epidemiology, including among those in high-risk groups, is vital for development of vaccines and related health policies.
- Norovirus AGE is reported as more severe than all-cause AGE, regardless of number of underlying conditions.
- Increased health care seeking for norovirus AGE episodes by number of underlying conditions suggests a higher burden of disease on this vulnerable population.
- We postulate that increasing age and comorbidity status impacts contact patterns, leading to lower exposure to norovirus and incidence of norovirus AGE.
  - The complex interaction of these factors is beyond the scope of this study.
- ORION will continue to gather data until the end of the 2025–2026 winter GI season and will conduct more robust analyses to build on these interim findings.
  - We will incorporate frailty and perceived health status into future analyses.

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Table 2: Severity and impact of all-cause and norovirus AGE episodes, by number of underlying conditions

	All-Cause AGE					Norovirus AGE				
	Overall N (%)	Zero N (%)	One N (%)	Two N (%)	≥Three N (%)	Overall N (%)	Zero N (%)	One N (%)	Two N (%)	≥Three N (%)
TOTAL	1173	81	404	300	388	68	12	29	13	14
Diarrhea	1003 (86)	68 (84)	336 (83)	253 (84)	346 (89)	57 (84)	11 (92)	25 (86)	10 (77)	11 (79)
≥6 episodes[1]	203 (20)	16 (24)	67 (20)	52 (17)	68 (18)	19 (33)	3 (27)	8 (32)	5 (39)	3 (27)
>4 days duration[1]	250 (25)	16 (24)	89 (27)	59 (45)	41 (45)	9 (16)	0 (0)	6 (24)	2 (20)	1 (9)
Vomiting	431 (37)	31 (38)	160 (40)	119 (40)	121 (31)	59 (87)	8 (67)	26 (90)	13 (100)	12 (86)
≥6 episodes[1]	47 (11)	2 (7)	19 (12)	12 (10)	14 (12)	8 (14)	1 (13)	3 (12)	1 (8)	3 (25)
≥4 days duration[1]	33 (8)	1 (3)	5 (3)	12 (10)	15 (12)	4 (7)	0 (0)	0 (0)	3 (23)	1 (8)
Nausea	649 (55)	42 (52)	241 (60)	164 (55)	202 (52)	61 (90)	10 (83)	26 (90)	12 (92)	13 (93)
Fatigue	691 (59)	46 (57)	245 (61)	169 (56)	231 (60)	66 (97)	12 (100)	28 (97)	13 (100)	13 (93)
Involuntary stool leakage	320 (27)	17 (21)	79 (20)	72 (24)	152 (39)	20 (29)	2 (17)	5 (17)	4 (31)	9 (64)
Fever	115 (10)	7 (9)	46 (11)	29 (10)	33 (9)	19 (28)	2 (17)	10 (34)	4 (31)	3 (21)
Sought care for AGE[2]	78 (9)	2 (3)	28 (10)	18 (9)	30 (11)	6 (12)	0 (0)	2 (12)	1 (11)	3 (27)

[1]% with diarrhea and vomiting are out of those completing the illness episode survey; number of episode and duration % are out of those reporting diarrhea and vomiting, respectively
[2]% who sought care are out of those who completed the Post-illness survey

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