P0354

Medically attended acute gastroenteritis among those with underlying conditions in the United States, 2023-2024

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Background

- Norovirus is the leading cause of acute gastroenteritis (AGE) in the United States[1,2]
- The impact of underlying medical conditions on the occurrence and severity of norovirus AGE has not been well studied.
- The goal of this analysis was to characterize the incidence and severity of medically attended AGE (MAAGE) among adults, including that due to norovirus, by type and number of underlying conditions.

Methods

Study Design and Observation Period:

- Prospective cohort, 15 November 2023 – 30 September 2024

Population:

- Kaiser Permanente Northwest (KPNW; Oregon / Washington, USA) health plan members, age ≥18 years
  - Inclusion criteria: incident MAAGE encounter, defined by ICD-10 code
  - Exclusion criteria: no registered health plan email address, unable to provide informed consent for participation, or previous opt-out of health plan research activities

Methods:

- Daily electronic health record (EHR) abstraction to identify eligible MAAGE encounters
- Electronic recruitment of participants via informed consent and completion of enrollment survey
  - Illness symptoms and exposure characteristics were assessed on survey.
- Self-collection of stool specimens by participants at home, with real-time RT-PCR testing for norovirus at the Oregon Health Authority's public health laboratory
- Severe NoV episodes defined as:
  - ≥6 episodes of vomiting within a 24-hour period; or
  - ≥6 episodes if diarrhea within a 24-hour period; or
  - Hospital admission or receipt of intravenous rehydration therapy.
- 9 underlying medical conditions (specified in Table 1) were defined by ICD-10 code and identified within 12 months prior to eligible MAAGE encounter through EHR abstraction
  - We considered individual underlying conditions (not mutually exclusive) as well as cumulative number of conditions (mutually exclusive)
  - We also identified the overall number of non-inpatient medical encounters during same time period
- Cumulative incidence rates (IR; episodes per 1,000 person-years) of all-cause and norovirus MAAGE disease estimated with 95% confidence intervals (CI) calculated using bootstrapping with 1,000 replicates.
- Adjusted incidence rate ratios (aIRR) for overall and severe disease estimated using modified Poisson regression models.
  - Adjusted by age, sex, presence of a medical encounter within 12 months prior to index MAAGE, and participant-reported exposure.

Results

Figure 1: Cumulative incidence of all-cause (a) and NoV+ (b) MAAGE among KPNW adults, 15/11/23-30/9/24, by type and number of underlying conditions

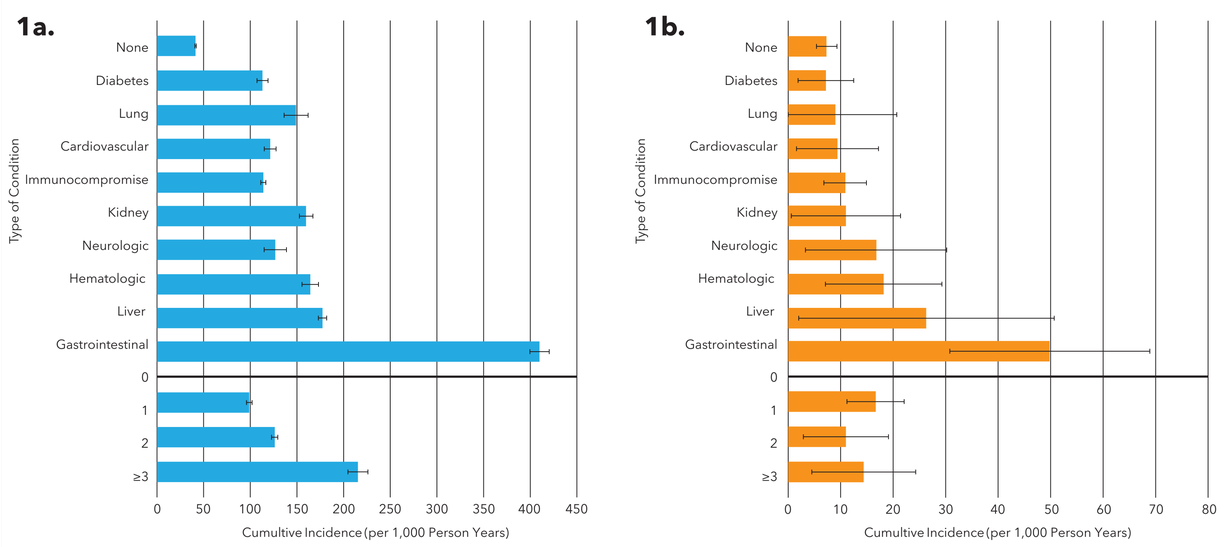


Table 2: Symptoms and severity of all-cause and NoV-MAAGE among SAGE participants, by number of underlying conditions[1]

	All-Cause MAAGE					NoV-MAAGE				
	Overall N (%)	Zero N (%)	One N (%)	Two N (%)	≥Three N (%)	Overall N (%)	Zero N (%)	One N (%)	Two N (%)	≥Three N (%)
TOTAL	834	388	230	120	96	121	68	37	10	6
Diarrhea[1]	760 (91)	343 (88)	210 (91)	115 (96)	92 (96)	112 (93)	62 (91)	34 (92)	10 (100)	6 (100)
≥6 episodes	359 (47)	165 (48)	102 (49)	54 (47)	38 (41)	56 (50)	28 (45)	21 (62)	4 (40)	3 (50)
>4 days duration	320 (42)	136 (40)	91 (43)	52 (45)	41 (45)	18 (16)	7 (11)	7 (21)	1 (10)	3 (50)
Vomiting[1]	419 (50)	202 (52)	123 (53)	52 (43)	42 (44)	94 (78)	56 (82)	27 (73)	9 (90)	2 (33)
≥4 episodes	220 (53)	106 (52)	64 (52)	29 (56)	21 (50)	68 (72)	38 (68)	21 (78)	7 (78)	2 (100)
≥4 days duration	47 (11)	16 (8)	21 (17)	4 (8)	6 (14)	4 (4)	3 (5)	1 (4)	0 (0)	0 (0)
Prescription antiemetics	237 (28)	132 (34)	53 (23)	29 (24)	23 (24)	56 (46)	36 (53)	17 (46)	2 (20)	1 (17)
Intravenous hydration	48 (6)	13 (3)	20 (9)	8 (7)	7 (7)	6 (5)	3 (4)	2 (5)	0	1 (17)
Severe Disease[2]	445 (53)	211 (54)	122 (53)	66 (55)	46 (48)	77 (64)	43 (63)	25 (68)	6 (60)	3 (50)

[1] % with diarrhea and vomiting are of overall episodes; number of episodes and duration % are out of those reporting diarrhea and vomiting, respectively.
[2] Excludes 4 individuals with all-cause MAAGE whose severity score could not be calculated due to missing responses.

Table 1: Characteristics of adult SAGE participants with all-cause and norovirus MAAGE, compared to the underlying KPNW study population

	KPNW Population N (%)	All-Cause MAAGE N (%)	Norovirus MAAGE N (%)
Overall	358,896	834	121
Sex			
Female	201,074 (56)	603 (72)	98 (64)
Male	157,822 (44)	231 (28)	54 (35)
Age			
18-59	248,271 (69)	559 (67)	84 (69)
60+	110,625 (31)	275 (33)	37 (31)
Underlying comorbidities			
Cardiovascular	19,824 (6)	67 (8)	5 (4)
Gastrointestinal	13,152 (4)	186 (22)	22 (18)
Kidney	16,355 (5)	58 (7)	4 (3)
Diabetes	29,333 (8)	103 (12)	6 (5)
Hematologic	22,785 (6)	90 (11)	10 (8)
Immunocompromise	51,058 (14)	201 (24)	18 (15)
Liver	5,981 (2)	36 (4)	5 (4)
Lung	10,066 (3)	34 (4)	2 (2)
Neurologic	8,749 (2)	43 (5)	5 (4)
None	249,801 (70)	388 (47)	68 (56)
Number of comorbidities			
0	249,801 (70)	388 (47)	68 (56)
1	67,185 (19)	230 (28)	37 (31)
2	25,273 (7)	120 (14)	10 (8)
≥3	16,637 (5)	96 (12)	6 (5)
Health care visit prior to illness[1]			
Yes		827 (99)	121 (100)
No		7 (1)	0 (0)
AGE contact prior to illness[2]			
Yes		109 (13)	43 (36)
No		388 (47)	36 (30)
Unknown		337 (40)	42 (35)
Household size[3]			
0		118 (14)	11 (9)
1		270 (32)	37 (31)
2		196 (24)	31 (26)
3+		250 (30)	42 (35)
Health status prior to illness[4]			
0-65		208 (25)	15 (12)
66-75		174 (21)	18 (15)
76-85		232 (28)	41 (34)
86-100		204 (25)	47 (39)

[1]Any health care encounter within 12 months prior to index MAAGE encounter
[2]Reported contact with someone with vomiting or diarrhea in the week prior to illness
[3]Number of individuals living in same household as, but excluding, SAGE participant
[4]Approximate quartiles of perceived health status among participants included with all-cause MAAGE, as assessed by the EQ-5D-5L Visual Acuity Scale. 0=worst imaginable health state and 100=best imaginable health state. Excludes 16 individuals who did not complete this question. All norovirus MAAGE participants completed this question.

Figure 2: Adjusted incidence rate ratios (aIRR) for all-cause and NoV+ MAAGE, by underlying type and number of underlying conditions[1]

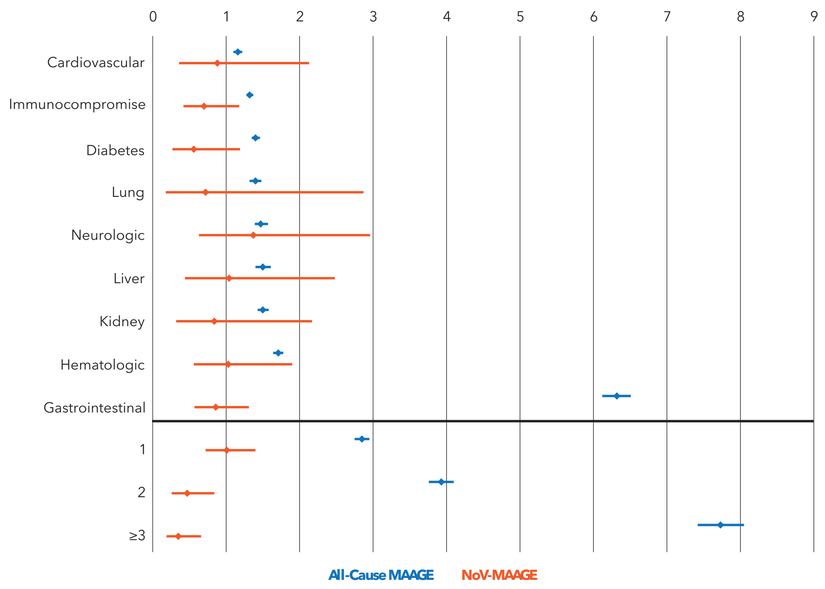
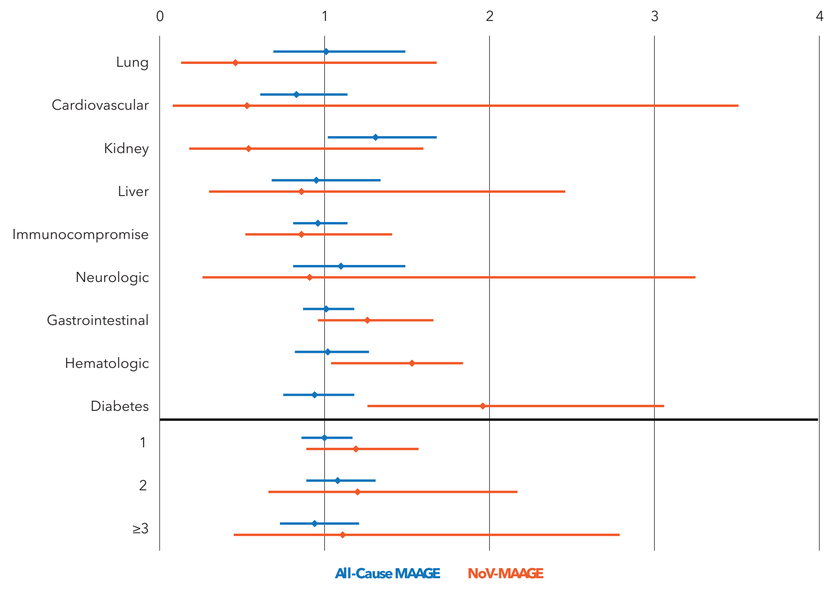


Figure 3: Adjusted incidence rate ratios (aIRR) for all-cause and NoV+ severe MAAGE, by underlying type and number of underlying conditions[1]



[1]aIRRs for individual comorbidities are compared to those who are otherwise healthy in individual models; aIRRs for number of comorbidities are compared to those reporting zero. All aIRR estimates have been adjusted by age, sex, health care utilization in year prior to illness (any vs. none), household size, contact with someone with vomiting or diarrhea in week prior to illness onset, and perceived overall health status.

Results

- Study population characteristics are shown in **Table 1**.
- **We observed an all-cause MAAGE IR of 66.8 (66.0, 67.6) and a norovirus AGE IR of 9.9 (8.1, 11.7) episodes per 1,000 PY.**
- The incidence of all-cause MAAGE was higher among those with any underlying condition and increased with the number of conditions identified. This was seen in unadjusted incidence rates (**Figure 1a**) and when adjusting for age, sex, health care use in prior year, exposures within a week of illness onset, and perceived health status (**Figure 2**).
  - Though the incidence rates of norovirus MAAGE were similar by number of underlying conditions (**Figure 1b**), this relationship was inversely related upon adjustment (**Figure 2**).
- Roughly half of all-cause MAAGE and two-thirds of norovirus MAAGE was characterized as severe (**Table 2**)
  - We observed no pattern in the proportion or markers of severe disease by type or number of conditions
- Chronic kidney disease was significantly associated with severe, all-cause MAAGE; diabetes and hematologic diseases were associated with severe norovirus MAAGE (**Figure 3**)

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Conclusions

- The presence of underlying conditions was associated with increased occurrence of all-cause MAAGE in our study.
- Findings on the association between severe disease and underlying conditions were mixed; However, severe norovirus MAAGE was significantly higher among those with diabetes and hematologic disease.
- Our work adds substantially to previous findings in this nascent area of study of the burden of norovirus among those with underlying conditions epidemiology.[3]
  - A strength of our study was our ability to adjust for underlying patterns of health care utilization and factors related to exposures and contact patterns that were not accounted for in previous research;
  - Our study is limited to medically attended episodes, so our findings may not be generalizable to the relationship between non-medically attended episodes and underlying conditions.
- Further work is needed to understand the role of underlying conditions in the occurrence and pathophysiology of norovirus AGE.

Funding

Funding for this study was provided through an institutional research collaborative agreement between Moderna, Inc. and the Kaiser Permanente Center for Health Research.

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