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ORIGINAL ARTICLE

A prospective comparative study of children with gastroenteritis: emergency department compared with symptomatic care at home

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Abstract

Little is known about the epidemiology and severity of gastroenteritis among children treated at home. We sought to compare illness severity and etiology between children brought for emergency department (ED) care to those managed at home (i.e., community). Prospective cohort study of children enrolled between December 2014 and December 2016 in two pediatric EDs in Alberta, Canada along with children treated at home after telephone triage (i.e., community). Primary outcomes were maximal frequency of vomiting and diarrhea in the 24-h pre-enrollment period; secondary outcomes included etiologic pathogens, dehydration severity, future healthcare visits, and treatments provided. A total of 1613 patients (1317 ED, 296 community) were enrolled. Median maximal frequency of vomiting was higher in the ED cohort (5 (3, 10) vs. 5 (2, 8); $P < 0.001$). Proportion of children with diarrhea and its 24-h median frequency were lower in the ED cohort (61.3 vs. 82.8% and 2 (0, 6) vs. 4 (1, 7); $P < 0.001$, respectively). In regression analysis, the ED cohort had a higher maximum number of vomiting episodes pre-enrollment (incident rate ratio (IRR) 1.25; 95% CI 1.12, 1.40) while the community cohort had higher maximal 24-h period diarrheal episodes (IRR 1.20; 95% CI 1.01, 1.43). Norovirus was identified more frequently in the community cohort (36.8% vs. 23.6%; $P < 0.001$). Children treated in the ED have a greater number of vomiting episodes; those treated at home have more diarrheal episodes. Norovirus is more common among children treated symptomatically at home and thus may represent a greater burden of disease than previously thought.

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Introduction

Acute gastroenteritis (AGE) is a common childhood illness [1]. In high-income countries, morbidity and healthcare resource use are the greatest concern with nearly 179 million cases of AGE occurring each year in the USA [2, 3]. However, the vast majority (up to 90%) of affected individuals are cared for at home by their caregivers [4]. Although these children do not exert a direct burden on the healthcare system, affected children are important given their enormous burden of disease, role as primary reservoir of transmission, and economic implications [4].

While the severity of disease [5, 6] and etiologic pathogens [7, 8] among children who seek hospital care have been described, these children may not represent children who do not seek medical care. Although hospitalized children represent < 1% of children with AGE, they account for 60% of pediatric stool cultures performed [9, 10]. Moreover, traditional testing of children with AGE has amplified our knowledge gap with testing limited to children with diarrhea; those with isolated vomiting do not have specimens tested, and thus, the etiology of this common ED complaint is under-represented.

To address these gaps, we conducted a prospective comparative cohort study that included children brought for ED care (ED cohort) and those receiving only care at home (community cohort) and included children with isolated vomiting. We hypothesized that children with AGE treated symptomatically at home by their caregivers (i.e., community cohort) would differ in terms of illness severity and relative distribution of pathogens from those brought for ED care. Understanding these differences will assist in guiding public health policies (e.g., vaccine development) and clinical management.

Materials and methods

Population studied

This was a secondary analysis of a large prospective cohort study [11] that included two distinct cohorts of children with AGE who were consecutively recruited by the Alberta Provincial Pediatric EnTeric Infection TEam (APPETITE) [11]. Children in the ED cohort were recruited in person in the EDs of two pediatric tertiary care institutions—the Alberta Children's Hospital (Calgary, Alberta) and Stollery Children's Hospital (Edmonton, Alberta). Participants in the community cohort, i.e., managed at home, were recruited by nurses staffing a province-wide triage telephone advice resource available to provide information, guidance and care recommendations to residents of Alberta (Health Link provided by Alberta Health Services) [12, 13]. They employ a standardized protocol to determine the appropriate care pathway enabling them to triage over 750,000 calls annually; nearly 50% of callers are recommended to provide ongoing care at home. Those receiving the latter recommendation were recommended to provide oral rehydration therapy and to monitor for the development of dehydration; no antiemetic agents were administered. Caregivers were also asked if their contact information could be shared with the study team. Families who agreed were subsequently contacted and recruited by telephone. Caregivers of children deemed to require medical assessment were ineligible [14]. These children were recruited to enable an assessment of etiologic pathogens among the large pool of children with AGE who do not seek medical care. Approvals were obtained from the Health Research Ethics Boards of the University of Calgary and of the University of Alberta.

Eligibility criteria included the following: < 18 years of age, AGE defined by ≥ 3 episodes of vomiting and/or diarrhea in the preceding 24 h, and < 7 days of symptoms [15]. Children were excluded if they had been previously enrolled during the prior 14 days, presented due to an acute psychiatric issue, had a neutrophil count < 1.0×10^9/L, or needed emergent ED medical interventions (i.e., resuscitation room or Canadian Emergency Department Triage and Acuity Scale 1). Consenting caregivers also had to agree to complete a follow-up survey 14 days later. Eligible children in both study groups submitted a stool specimen and two rectal swab specimens.

Outcomes and outcome measures

The primary outcome, disease severity, was defined as the maximal frequencies each of (1) vomiting and (2) diarrhea in any 24-h period prior to enrollment. Secondary outcomes included (1) etiologic enteropathogens and (2) other markers of disease severity including dehydration severity as assessed by caregivers employing the Clinical Dehydration Scale score [16–18] (Online Table 1), frequency and duration of vomiting and diarrhea both pre- and post-enrollment, future healthcare visits, and treatments provided. Symptoms included in this analysis were those reported at the time of the ED visit (ED Cohort) and telephone recruitment (community cohort), respectively.

Clinical data collection

Trained research assistants administered a structured survey to eligible consented families/caregivers. Fourteen days following enrollment, participants completed a follow-up survey. Surveys were administered either by telephone or

electronically. Those opting for electronic follow-up received daily e-mail reminders for up to 3 days. If the electronic survey was not completed after these reminders, participants were contacted by telephone. Clinical Dehydration Scale score assignment was based on caregiver report for all participants.

Specimen collection and laboratory methodology

ED cohort Two Flocked swabs (FLOQSwab, Copan Italia, Italy) were inserted sequentially into the rectum of each participant and rotated 360° once. One swab was placed into a dry, sterile tube, and the other was inserted into 2-mL modified Cary-Blair transport media, FecalSwab (Copan Italia, Italy). Bulk stool specimens were collected in sterile containers (V302-F, Starplex Scientific Inc., Ontario). If a bulk stool specimen was not provided before ED discharge, caregivers were instructed to collect a specimen at home. Specimens collected at home were stored at room temperature for up to 12 h and then retrieved by a study-funded courier and transported to the local laboratory in cooler boxes containing ice packs.

Community cohort Stool collection kits containing two rectal swabs, a stool container, and instructions were couriered to the home. Caregivers were asked to collect the first stool sample produced and perform the rectal swabs at the same time following enrollment.

Diagnostic testing

Specimens collected from both cohorts underwent identical testing. Enteric bacterial culture was performed on stool specimens and the rectal swabs collected in modified Cary-Blair transport media upon receipt at the laboratory. Residual stool specimens and dry rectal swabs from all patients were stored at − 80 °C until tested using nucleic acid amplification assays. All testing performed was blinded to clinical data. Detailed molecular and routine culture methods employed are described in Appendix A.

Both specimens (i.e., swab and stool) were tested if provided for all patients. A patient was classified as positive for a given pathogen if either the swab or stool tested positive using any assay. All positive results were assumed to be true positives, i.e., negative results obtained for the same pathogen in a different specimen type or testing method for the same patient were classified as false negatives. Swabs, tested in the absence of stool, have demonstrated comparable diagnostic accuracy [19, 20].

Statistical analysis

Data were summarized with frequencies and percentages for categorical variables and medians and interquartile ranges (IQR) for continuous variables. For the primary outcomes, we performed negative binomial regression models using the maximal number of vomiting and diarrheal episodes per a 24-h period before enrollment as dependent variables, respectively, adjusting for age, presence of chronic disease, antibiotic use in the preceding 60 days, symptom duration at enrollment, season at enrollment, and the individual enteropathogen targets. In the regression models, we tested interaction effects for co-detected enteropathogen combinations that were identified in a minimum of 10 participants, and interaction effect between participant age and the detection of *Clostridioides difficile*. All independent variables and interaction terms were entered into the model simultaneously; we only retained interaction terms with significant effect ($P < 0.05$) in the final model. Goodness-of-fit was assessed using Akaike information criterion.

The Mann-Whitney *U* test was used to compare the secondary outcomes of the Clinical Dehydration Scale scores at enrollment with the frequency and duration of diarrhea and vomiting. Non-normally distributed data for continuous variables were assessed by the Wilcoxon Rank Sum test. Analysis for future healthcare visits and treatments provided was summarized by count and percentage, with the Chi-square test or the Fisher's exact test as appropriate used for comparisons between groups.

We calculated two-tailed *P* values and set the significance level α at 0.05. To control for false discovery, we corrected *P* values using the Bonferroni correction within sets of tests. Statistical analyses were performed with IBM SPSS Statistics for Windows, version 24.0 (IBM Corp., Armonk, NY) and SAS 9.4 (SAS Institute Inc., Cary, NC).

Results

Subjects

Between December 9, 2014 and December 31, 2016, 1613 participants were enrolled: 81.6% (1317/1613) were recruited in EDs and 18.4% (296/1613) via Health Link (i.e., community cohort) (Fig. 1). Children enrolled in the EDs were older (20.8 months (IQR 11.2, 46.9) vs. 17.4 months (IQR 11.6, 30.0)), less likely to have submitted a bulk stool specimen (75.0% (988/1317) vs. 97.3% (288/296)), and less likely to have a primary care physician (91.4% (1203/1316) vs. 97.3% (288/296)) (Table 1). There was no significant seasonal variation in recruitment (Table 1).

Primary outcome

The proportion of children with isolated vomiting was higher in the ED cohort compared to the community cohort (38.7% vs. 17.2%), while the proportion of children with diarrhea was higher in the community cohort (82.8% vs. 61.3%). The

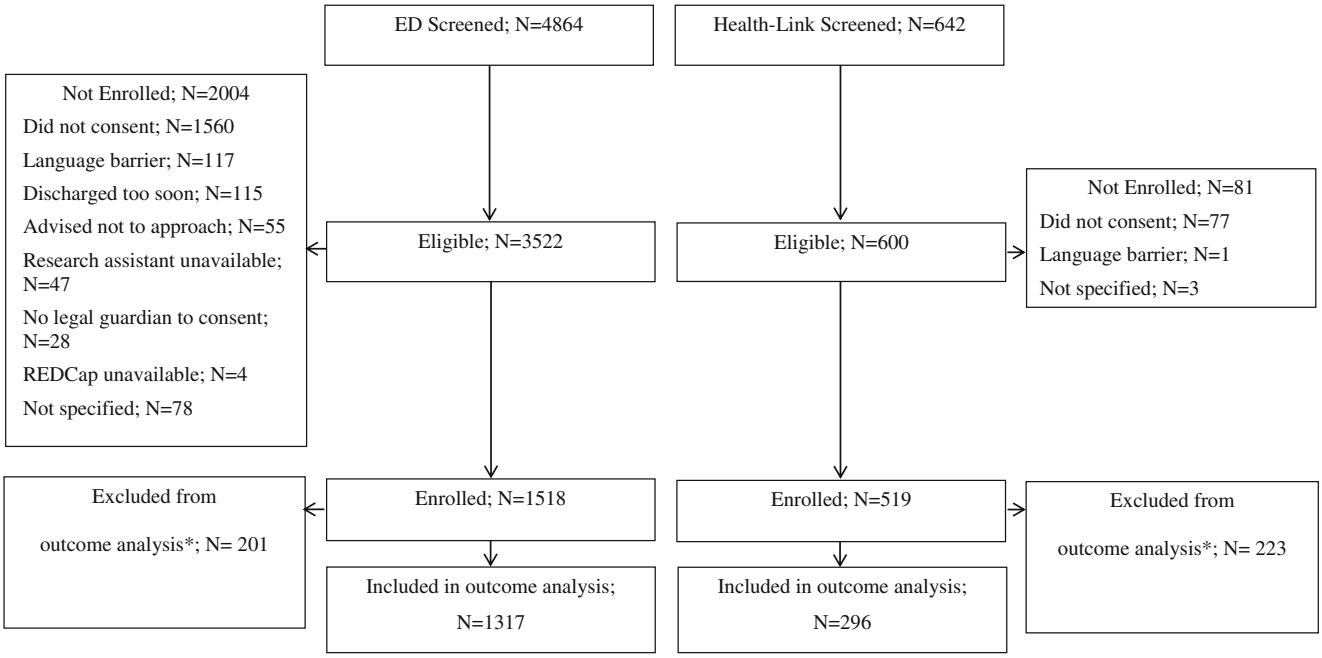

Fig. 1 Study subject participation. Asterisk, each subject may be excluded for one or more reasons

median maximal frequencies of vomiting (ED 5 (IQR 3, 10) vs. community cohort 5 (IQR 2, 8); $P = 0.001$) and diarrheal (ED 2 (IQR 0, 6) vs. community cohort 4 (IQR 1, 7); $P < 0.001$) episodes in any given 24-h period preceding enrollment differed between groups (Table 2; Online Fig. 1).

Factors independently associated with a higher maximum number of vomiting episodes prior to enrollment included ED cohort, age ≥ 24 months, the detection of rotavirus, norovirus, and sapovirus and non-summertime illness (Table 3). In the model for diarrheal episodes, factors independently associated with higher maximal number of diarrheal episodes prior to enrollment included community cohort, greater symptom duration, and detection of rotavirus, astrovirus, *Campylobacter*, *Salmonella*, and *Shigella* (Table 4).

Secondary outcomes

Norovirus was detected more commonly in the community cohort (36.8% (109/296) vs. 23.6% (311/1317); difference 13.2% 95% CI of the difference 7.3%, 19.4%; $P < 0.001$). No differences were identified in individual enteropathogens (Table 5). Viral pathogens (81.1% (240/296) vs. 64.0% (843/1317); difference 17.1%; 95% CI of the difference 21.9%, 11.6%; $P < 0.001$) and the overall enteropathogen detection rate were also higher in the community cohort (84.8% (251/296) vs. 71.1% (937/1317); difference 13.7%; 95% CI of the difference 8.5%, 18.1% $P < 0.001$).

The median Clinical Dehydration Scale score was higher among the ED cohort compared to the community cohort (3 (2, 4) vs. 1 (0, 2); $P < 0.001$) (Table 2). The proportion of children with vomiting during the follow-up period (59.0% (777/1317) vs. 56.1% (166/296); $P = 0.36$) and the duration of vomiting (ED 24.0 (0, 72.0) vs. community 24.0 (0, 66.0) h; $P = 0.36$) did not differ significantly between groups (Table 2; Online Table 2). During the follow-up period, the proportion of children with diarrhea was greater in the community cohort (ED 72.0% (948/1317) vs. community 82.4% (244/296); $P < 0.001$), as was its median duration (ED 48.0 (0, 120.0) vs. community 72.0 (24.0, 120.0) h; $P = 0.02$)).

During the follow-up period, the proportion of children brought for ED care (ED 7.9% (104/1317) vs. community 11.1% (33/296); $P = 0.08$) or to any healthcare provider (ED 34.5% (457/1317) vs. 34.5% (102/296); $P = 0.95$) did not differ between groups (Table 2). Intravenous fluid administration (ED 4.5% (59/1317) vs. community 0.7% (2/296); $P = 0.001$) and hospitalizations (ED 3.3% (43/1317) vs. community 0.7% (2/296); $P = 0.01$) were more frequent in the ED cohort.

Discussion

Our large, prospective pediatric sample from Alberta Province, Canada revealed phenotypic differences in the clinical features of children who are brought for ED care relative to those cared for at home by their caregivers in the community. In addition, although reported frequencies and durations of vomiting and diarrhea did not differ in a clinically meaningful way following recruitment (i.e., ED visit or phone contact), those brought for ED care were also more likely to receive intravenous rehydration and be hospitalized at a

Table 1 Demographics at the time of enrollment

	All patients ($N = 1613$)		Emergency department cohort ($N = 1317$)		Community cohort ($N = 296$)		P value[a]
	Number	Value	Number	Value	Number	Value	
Age, median (IQR), months	1613	20.0 (11.3, 43.1)	1317	20.8 (11.2, 46.9)	296	17.4 (11.6, 30.0)	0.03
Sex-male, *N* (%)	1613	877 (54.4)	1317	709 (53.8)	296	168 (56.8)	0.37
Weight, median (IQR), kg	1607	11.3 (9.0, 15.5)	1314	11.4 (9.0, 16.2)	293	10.9 (9.1, 13.8)	0.06
Aboriginal, *N* (%)	1613	78 (4.8)	1317	67 (5.1)	296	11 (3.7)	0.37
Live on a reserve, *N* (%)	1613	9 (0.6)	1317	8 (0.6)	296	1 (0.3)	> 0.99
Travel outside Canada and the USA past 12 months, *N* (%)	1613	283 (17.5)	1317	244 (18.5)	296	39 (13.2)	0.08
Provincial zone of residence	1613		1317		296		< 0.001
North, *N* (%)		27 (1.7)		18 (1.4)		9 (3.0)	
South, *N* (%)		21 (1.3)		7 (0.5)		14 (4.7)	
Central, *N* (%)		25 (1.5)		10 (0.8)		15 (5.1)	
Calgary, *N* (%)		1104 (68.4)		891 (67.7)		213 (72.0)	
Edmonton, *N* (%)		434 (26.9)		389 (29.5)		45 (15.2)	
Other, *N* (%)		2 (0.1)		2 (0.2)		0	
Season of recruitment	1613		1317		296		0.80
Winter (Jan, Feb, Mar), *N* (%)		281 (17.4)		226 (17.2)		55 (18.6)	
Spring (Apr, May, June), *N* (%)		587 (37.0)		487 (37.0)		110 (37.2)	
Summer (July, Aug, Sept), *N* (%)		325 (20.1)		280 (21.3)		45 (15.2)	
Fall (Oct, Nov, Dec), *N* (%)		410 (25.4)		324 (24.6)		86 (29.1)	
Chronic medical illness, *N* (%)	1613	173 (10.7)	1317	149 (11.3)	296	24 (8.1)	0.12
Rectal swab sample received, *N* (%)	1613	1607 (99.6)	1317	1313 (99.7)	296	294 (99.3)	0.30
Stool sample received, *N* (%)	1613	1276 (79.1)	1317	988 (75.0)	296	288 (97.3)	< 0.001
Antibiotics past 60 days, *N* (%)	1613	245 (15.2)	1317	212 (16.1)	296	33 (11.1)	0.02
Primary care physician	1612		1316		296		< 0.001
None, *N* (%)		121 (7.5)		113 (8.6)		8 (2.7)	
Pediatrician, *N* (%)		430 (26.7)		387 (29.4)		43 (14.5)	
Family physician, *N* (%)		1054 (65.4)		810 (61.6)		244 (82.4)	
Do not know, *N* (%)		7 (0.4)		6 (0.5)		1 (0.3)	
Received rotavirus vaccine, *N* (%)	1613	503 (31.2)	1317	427 (32.4)	296	76 (25.7)	0.02

[a] Mann-Whitney *U* test was employed to compare age and weight. Chi-Square test was employed for comparison of other variables in the table; exact test was employed when cells had expected counts less than 5. P value < 0.004 was considered significant after correction via Bonferroni procedure for multiple comparisons ($n = 12$)

[b] Comparing emergency department and community care cohorts

subsequent visit. Lastly, norovirus was more frequently identified in children enrolled in the community cohort.

Most notably, children brought for ED care were more likely to have vomiting in the absence of diarrhea, to have experienced more vomiting episodes, and to have been assigned greater Clinical Dehydration Severity scores by their caregivers. On the other hand, children cared for at home had greater duration of diarrhea than those treated in the ED. Dehydration and/or the perception of dehydration is a significant factor in telephone nurse triage assessment and seeking care in an ED. Although the maximal frequency of vomiting did not differ significantly, children seeking ED care were more likely to have vomiting (Table 2), suggesting that the management of hydration status in the context of vomiting is more distressing to caregivers at home, while the converse was seen with respect to diarrhea.

The ED may serve as the choice location of care for some parents for a variety of reasons including perceived disease severity, lack of primary care access, anxiety, knowledge, and coping strategies. However, in general, EDs provide suboptimal education to caregivers of children with AGE as evidenced by an inverse correlation between the number of prior ED visits and caregiver knowledge when assessed using a gastroenteritis caregiver knowledge questionnaire [21]. Moreover, caregiver knowledge appears to be unrelated to formal education [21]. While more interventions were provided at subsequent ED visits to those in the ED cohort, we cannot decipher from our data if this reflects disease severity or natural tendency of ED physicians to “do more” in children with repeat ED visits. We hypothesize the latter is most likely given the overall very low rate of intravenous rehydration at the subsequent visit.

Table 2 Comparison of clinical features—emergency departments versus community cohort at the time of enrollment and during 14-day follow-up

Symptom	All participants $n = 1613$	Emergency department cohort $n = 1317$	Community cohort $n = 296$	P value*
At enrollment				
Isolated vomiting (i.e., no diarrhea), *N* (%)	561 (34.8)	510 (38.7)	51 (17.2)	<0.001
Isolated diarrhea (i.e., no vomiting), *N* (%)	181 (11.2)	133 (10.1)	48 (16.2)	0.004
Both vomiting and diarrhea, *N* (%)	871 (54.0)	674 (51.2)	197 (66.6)	<0.001
Vomiting, *N* (%)	1432 (88.8)	1184 (89.9)	248 (83.8)	0.004
Vomiting duration, hours, median (IQR)	26.6 (8.6, 66.8)	24.7 (8.3, 65.2)	35.8 (14.2, 69.1)	0.012
Maximal no. of vomiting episodes per 24-h period**, median (IQR)	5 (3, 10)	5 (3, 10)	5 (2, 8)	0.001
Diarrhea, *N* (%)	1052 (79.9)	807 (61.3)	245 (82.8)	<0.001
Diarrhea duration, hours, median (IQR)	20.1 (0, 70.4)	11.4 (0, 70.0)	31.3 (10.7, 72.2)	<0.001
Maximal no. of diarrheal stools per 24-h period**, median (IQR)	3 (0, 7)	2 (0, 6)	4 (1, 7)	<0.001
Dehydration score, median (IQR)	3 (1, 4)	3 (2, 4)	1 (0, 2)	<0.001
14-Day follow-up period				
Healthcare visit, *n* (%)	559 (34.7)	457 (34.7)	102 (34.5)	0.95
ED visit, *n* (%)	137 (8.5)	104 (7.9)	33 (11.1)	0.08
Treatments received				
Intravenous fluids, *N* (%)	61 (3.7)	59 (4.5)	2 (0.7)	0.001
Hospitalization, *N* (%)	45 (2.8)	43 (3.3)	2 (0.7)	0.01

*P value < 0.007 was considered significant after correction via Bonferroni procedure for multiple comparisons ($n = 7$)

**Includes those subjects with no diarrhea or vomiting

Table 3 Negative binomial multivariable regression model identifying predictors of greater number vomiting episodes in any 24-h period prior to enrollment ($N = 1613$)

Parameter*	Incident rate ratio (95% CI)	P value
ED cohort	1.25 (1.12, 1.40)	< 0.001
Community care cohort	Ref	
Age ≥ 24 months	1.19 (1.09, 1.30)	< 0.001
Age < 24 months	Ref	
Baseline symptom duration, days	0.93 (0.91, 0.96)	< 0.001
Season		
Winter	Ref	
Spring	0.87 (0.77, 0.98)	0.02
Summer	0.70 (0.61, 0.81)	< 0.001
Fall	0.78 (0.68, 0.88)	< 0.001
Rotavirus positive	1.55 (1.39, 1.74)	< 0.001
Norovirus positive	1.43 (1.29, 1.58)	< 0.001
Astrovirus positive	0.66 (0.50, 0.87)	0.004
Sapovirus positive	1.20 (1.04, 1.38)	0.02
Campylobacter positive	0.50 (0.28, 0.88)	0.02
Salmonella positive	0.51 (0.37, 0.71)	< 0.001

Other variables in the model included: antimicrobial use in past 60 days, presence of chronic disease and presence of adenovirus, *C. difficile*, *Aeromonas* species, *E. coli* 0157, *E. coli* labile toxin, *E. coli* Shiga toxin, *Shigella* species, *Yersinia* species, *Cryptosporidium* species, *Entamoeba* species, and *Giardia* species

*Referent group for all pathogens was pathogen test negative. Full model shown in Online Table 3

We cannot be certain that there was no difference in dehydration between children who were brought for ED care than those cared for at home, as the score employed is not validated for use in the hands of caregivers, and even when used by trained healthcare providers, its measurement characteristics are suboptimal [18]. However, it is the best available tool to assess dehydration among children cared for at home. Other reasons for seeking care in ED may be the absence of a primary care physician, "convenience" of hours of ED operation, parental anxiety, and perceptions of "better" care. There may be small differences introduced into the study as recruitment from the community was higher in Calgary than Edmonton, the two major recruitment centers in the study.

The identification of norovirus in 36.8% of children treated at home was unanticipated, even compared to a recent meta-analysis suggesting community AGE having a prevalence of norovirus of 24% [22]. Similarly, a US cohort demonstrated that norovirus was the most common pathogen among children < 5 years old, incidence in outpatients of 152.2/1000 person years [23] while a similar cohort in England demonstrated similar incidence of 21.4/100 person years [24]. Since norovirus infection is typically associated with vomiting in younger children, and vomiting is associated with ED care seeking behavior, we anticipated that it would be more frequently seen in the ED cohort. However, the proportion of AGE associated with norovirus was significantly higher in the community. The norovirus detection rate is consistent with that reported in a smaller cohort that identified norovirus in 36% of children

Table 4 Negative binomial multivariable regression model with the maximal number of diarrheal episodes in any 24-h period prior to enrollment as the dependent variable ($N = 1612$)

Parameter*	IRR (95% CI)	*P* value
Community cohort	1.20 (1.01, 1.43)	0.04
ED cohort	Ref	
Baseline symptom duration, days	1.30 (1.25, 1.36)	< 0.001
Season		
Winter	Ref	
Spring	0.97 (0.80, 1.17)	0.73
Summer	1.31 (1.04, 1.64)	0.02
Fall	0.87 (0.70, 1.07)	0.19
Rotavirus positive	1.96 (1.62, 2.37)	< 0.001
Adenovirus positive	1.27 (1.04, 1.55)	0.02
Astrovirus positive	1.81 (1.19, 2.75)	0.005
Campylobacter positive	2.62 (1.22, 5.66)	0.01
Salmonella positive	2.80 (1.80, 4.37)	< 0.001
Shigella positive	8.21 (2.96, 22.79)	< 0.001
Interaction between (rotavirus positive)* (adenovirus positive)	0.57 (0.34, 0.96)	0.03

Other variables in the model included: age, antimicrobial use in past 60 days, the presence of chronic disease and presence of norovirus, sapovirus, *C. difficile*, *Aeromonas* species, *E. coli* 0157, *E. coli* labile toxin, *E. coli* Shiga toxin, *Shigella* species, *Yersinia* species, *Cryptosporidium* species, *Entamoeba* species, and *Giardia* species

*Referent group for all pathogens was pathogen test negative. Full model shown in Online Table 4

Table 5 Stool pathogen detection in emergency department and community cohorts

Pathogen	All participants $n = 1613$	Emergency department cohort $n = 1317$	Community cohort $n = 296$	*P* value[a]
Any enteropathogen, *N* (%)	1188 (73.7)	937 (71.1)	251 (84.8)	< 0.001
Any virus, *N* (%)	1083 (67.1)	843 (64.0)	240 (81.1)	< 0.001
Adenovirus, *N* (%)	268 (16.6)	217 (16.5)	51 (17.2)	0.73
Astrovirus, *N* (%)	40 (2.5)	29 (2.2)	11 (3.7)	0.15
Norovirus (I/II), *N* (%)	420 (26.0)	311 (23.6)	109 (36.8)	< 0.001
Rotavirus, *N* (%)	372 (23.1)	303 (23.0)	69 (23.3)	0.94
Sapovirus, *N* (%)	147 (9.1)	115 (8.7)	32 (10.8)	0.26
Any bacteria	281 (17.4)	234 (17.8)	47 (15.9)	0.50
Aeromonas, *N* (%)	15 (0.9)	15 (1.1)	0	0.09
Campylobacter, *N* (%)	11 (0.7)	7 (0.5)	4 (1.4)	0.13
C. difficile, *N* (%)	196 (12.2)	159 (12.1)	37 (12.5)	0.84
C. difficile in children ≥ 2 years of age, *N* (%)	24 (1.5)	23 (1.7)	1 (0.3)	0.11
E. coli O157, *N* (%)	7 (0.4)	7 (0.5)	0	0.36
Enterotoxigenic *E. coli* labile toxin, *N* (%)	4 (0.2)	3 (0.2)	1 (0.3)	0.56
Shiga toxin-producing *E. coli* (non-O157), *N* (%)	18 (1.1)	17 (1.3)	1 (0.3)	0.23
Salmonella, *N* (%)	34 (2.1)	29 (2.2)	5 (1.7)	0.82
Shigella, *N* (%)	6 (0.4)	6 (0.5)	0	0.60
Yersinia, *N* (%)	4 (0.2)	4 (0.2)	0	> 0.99
Any parasite	10 (0.6)	7 (0.5)	3 (1.0)	0.40
Cryptosporidium, *N* (%)	1 (0.1)	1 (0.1)	0	> 0.99
Entamoeba, *N* (%)	3 (0.2)	0	3 (1.0)	0.006
Giardia, *N* (%)	6 (0.4)	6 (0.5)	0	0.60

[a] *P* value—comparison of emergency department vs community care cohort. *P* value < 0.0025 was considered significant after correction via Bonferroni procedure for multiple comparison ($n = 20$)

who were brought for medical evaluation [25]. A unique feature of our eligibility criteria was the inclusion of patients with isolated vomiting. This difference may have contributed to the large proportion of subjects presenting with norovirus disease, whose detection was an independent risk factor for increased vomiting frequency in our study [25]. This finding is important because pathogen burden of disease estimates often fail to address the implications of infection in non-healthcare settings, and our findings showing differing distribution of pathogens highlight the importance of collecting such data and its incorporation into burden of disease models.

Our study has potential limitations. The Health Link telephone triage service provides our research team with a potentially biased cohort. The caregivers are pre-consented with the most severely ill patients referred for medical care, which potentially precludes them from being involved in the study or led to their being enrolled in the ED cohort (i.e., confounding by indication). Moreover, the caregiver of children without a primary care physician could also be more likely to call the phone line which similarly might be more likely to refer them to the ED if no primary care physician was available to provide follow-up. Although the two comparison groups had significantly different sample sizes, given the large study sample, we had sufficient power to conduct the planned analyses. Although enrollment in the ED occurs in real time, the community cohort was contacted up to 24-h following the initial phone call, and while symptom data was collected at that time, specimen collection was routinely delayed by an additional 24-h.

Conclusions

Children brought for ED care differed from those cared for at home—they were more likely to experience intense vomiting while those cared for at home experienced a greater amount of diarrhea. Increased dehydration or the perception of dehydration was also seen among children treated in the ED. Perhaps most importantly with respect to public health is that a greater proportion of children cared for at home were infected with norovirus, highlighting the importance of better understanding community-based, pathogen-specific burden of disease.

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Contributor's statement Dr. Vanderkooi conceptualized and designed the study, acquired and interpreted the data, conducted the analyses, drafted the initial manuscript, provided administrative, technical or material support, and reviewed and revised the manuscript.

Dr. Freedman had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. He additionally obtained funding, conceptualized and designed the study, acquired and interpreted the data, conducted the analyses, drafted the initial manuscript, provided administrative, technical or material support, and reviewed and revised the manuscript.

Dr. Xie conducted the analyses, acquired and interpreted the data, provided administrative, technical or material support, and critically reviewed the manuscript for important intellectual content.

Drs Judy MacDonald, Shannon MacDonald and Payne conceptualized and designed the study, and critically reviewed the manuscript for important intellectual content.

Ms. Osterreicher conceptualized and designed the study, provided administrative, technical or material support, and critically reviewed the manuscript for important intellectual content.

Drs. Lee, Chui and Pang acquired and interpreted the data, obtained funding provided administrative, technical or material support, and critically reviewed the manuscript for important intellectual content.

Dr. Ali acquired and interpreted the data and critically reviewed the manuscript for important intellectual content.

Dr. Nettel-Aguirre provided statistical analysis and critically reviewed the manuscript for important intellectual content.

Dr. Drews acquired and interpreted the data and critically reviewed the manuscript for important intellectual content.

Dr. Louie conceptualized and designed the study, obtained funding and critically reviewed the manuscript for important intellectual content.

Ms. Kim and Lowerison provided administrative, technical or material support and acquired and interpreted the data.

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Compliance with ethical standards

Approvals were obtained from the Universities of Calgary and Alberta Health Research Ethics Boards. Informed consent was provided by caregivers or legal guardians; child assent was obtained as required

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Abbreviations AGE, acute gastroenteritis; ED, emergency department; IQR, inter-quartile range; IRR, incidence rate ratio

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