

Association between Combined Sewer Overflow Events and Gastrointestinal Illness in Massachusetts Municipalities with and without River-Sourced Drinking Water, 2014–2019

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BACKGROUND: Combined sewer overflow (CSO) events release untreated wastewater into surface waterbodies during heavy precipitation and snowmelt. Combined sewer systems serve ~40 million people in the United States, primarily in urban and suburban municipalities in the Midwest and Northeast. Predicted increases in heavy precipitation events driven by climate change underscore the importance of quantifying potential health risks associated with CSO events.

OBJECTIVES: The aims of this study were to *a*) estimate the association between CSO events (2014–2019) and emergency department (ED) visits for acute gastrointestinal illness (AGI) among Massachusetts municipalities that border a CSO-impacted river, and *b*) determine whether associations differ by municipal drinking water source.

METHODS: A case time-series design was used to estimate the association between daily cumulative upstream CSO discharge and ED visits for AGI over lag periods of 4, 7, and 14 days, adjusting for temporal trends, temperature, and precipitation. Associations between CSO events and AGI were also compared by municipal drinking water source (CSO-impacted river vs. other sources).

RESULTS: Extreme upstream CSO discharge events (>95th percentile by cumulative volume) were associated with a cumulative risk ratio (CRR) of AGI of 1.22 [95% confidence interval (CI): 1.05, 1.42] over the next 4 days for all municipalities, and the association was robust after adjusting for precipitation [1.17 (95% CI: 0.98, 1.39)], although the CI includes the null. In municipalities with CSO-impacted drinking water sources, the adjusted association was somewhat less pronounced following 95th percentile CSO events [CRR = 1.05 (95% CI: 0.82, 1.33)]. The adjusted CRR of AGI was 1.62 in all municipalities following 99th percentile CSO events (95% CI: 1.04, 2.51) and not statistically different when stratified by drinking water source.

DISCUSSION: In municipalities bordering a CSO-impacted river in Massachusetts, extreme CSO events are associated with higher risk of AGI within 4 days. The largest CSO events are associated with increased risk of AGI regardless of drinking water source. <https://doi.org/10.1289/EHP14213>

Introduction

In >700 municipalities in the United States, combined sewer systems (CSS) collect residential and nonresidential sewage, industrial waste, and stormwater that flow together to a wastewater treatment facility. CSS discharge untreated combined wastewater into rivers and lakes when the volume of water in the common collection pipe exceeds treatment capacity, potentially posing risks to the health of communities and ecosystems downstream of discharge points. Discharge events—called combined sewer overflow (CSO) events—are driven by heavy precipitation and runoff from snowmelt.^{1,2} Observed and predicted increases in the intensity and frequency of precipitation events due to climate change in the Northeast and Midwest, where most CSS in the United States are located, underscore

the importance of understanding and addressing the health risks associated with CSO events.^{3–5}

CSO events introduce viral, bacterial, and protozoan pathogens, as well as chemical and physical contaminants, to surface waterbodies.^{1,2,6–14} Compared with dry weather conditions, CSO events can lead to one to two orders of magnitude increases in the concentration of waterborne pathogens and fecal indicator organisms in receiving waterbodies.^{2,6,15} Exposure to sewage-associated pathogens can lead to gastrointestinal, respiratory, and soft tissue infections among recreational and drinking water users.^{16–21} The association between fecal contamination of surface waters and gastrointestinal illness is well documented in settings with modern wastewater infrastructure,^{22–25} as is the relationship between precipitation, which is the primary driver of CSO events, and gastrointestinal illness.^{26–28} However, relatively little research has been conducted to determine the direct association between CSO events and health outcomes.

The few studies that have investigated the relationship between CSO events and health outcomes suggest a link between discharge events and acute gastrointestinal illness (AGI). Research has demonstrated elevated rates of AGI following large-volume CSO events among residents of Atlanta, Georgia,²⁹ and increased odds of AGI among children living near CSO outfalls in Cincinnati, Ohio, after any CSO event.³⁰ Studies of recreational use of CSO-impacted waterbodies suggest that the risk of AGI among swimmers can increase up to five times after a CSO event compared with when no CSO event occurred³¹ and that the likelihood that recreators will develop AGI can vary widely by activity and level of water contact.⁹ CSO events in drinking water sources may also pose a risk to community health. A study in the Milwaukee, Wisconsin, metropolitan area found a higher rate of pediatric cases of AGI following partially treated sewage discharge events in a drinking water source.³² In

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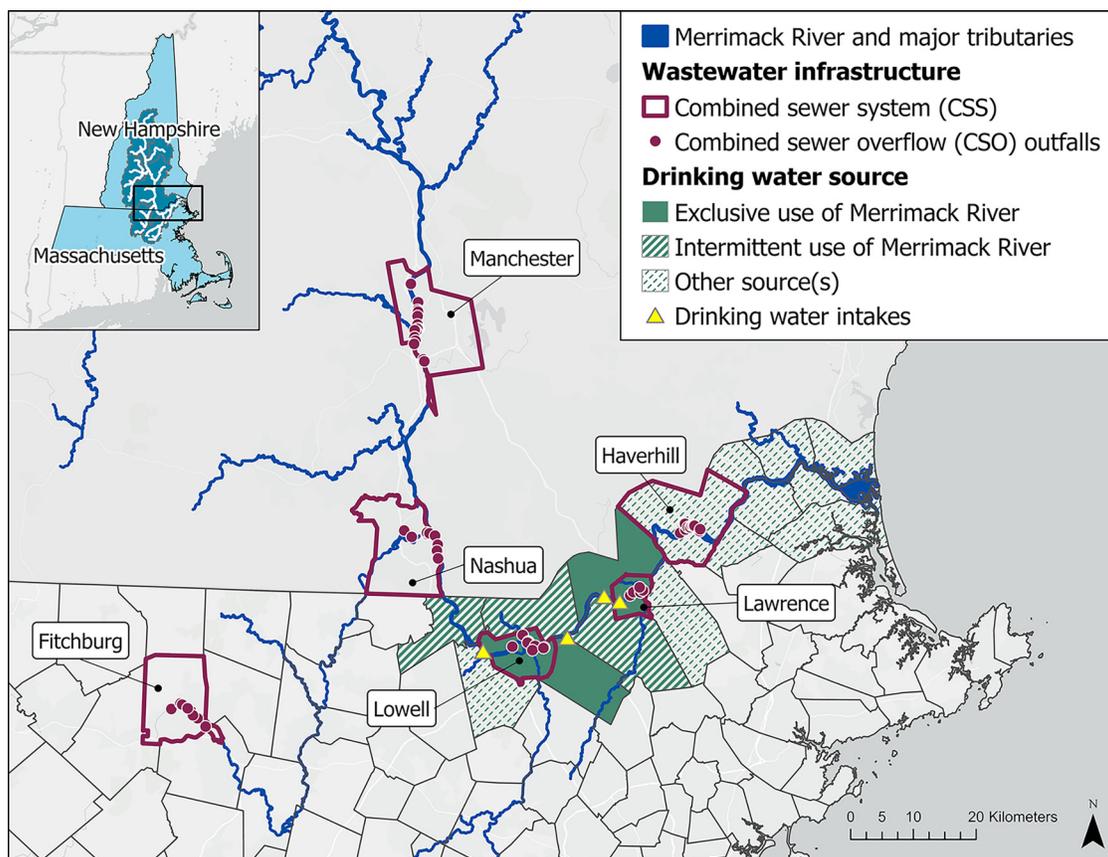


Figure 1. Map of the study area in the lower reaches of the Merrimack River. Map created in ArcGIS Pro (version 3.1.2; Esri) with publicly available data from the US Environmental Protection Agency, US Geological Survey, US Census Bureau, and Massachusetts Bureau of Geographic Information.

Massachusetts, increased risk of AGI was observed following extreme precipitation events in a region with a CSO-impaired drinking water source, whereas the risk of AGI did not change following similar precipitation events in other regions of the state.³³ Importantly, neither of the studies involving a CSO-impacted drinking water source used CSO event data in their analyses but, instead, respectively used partially treated sewage discharge events or precipitation data to characterize exposure.^{32,33} In all studies, the association between discharge events and reported AGI has a lag of 2 to 8 days (d), which could be due to pathogen travel time in the waterbody, timing of recreational activity, drinking water treatment and distribution, pathogen infection and incubation, or decision to seek care.^{29,30,32,33}

There remain key gaps in our understanding of the association between CSO events and health, including the robustness of the association, relevant exposure pathways, and the role of precipitation events. Accordingly, we sought to assess the association between CSO events and emergency department (ED) visits for AGI in the Massachusetts municipalities that border the Merrimack River, a drinking water and recreational resource for surrounding communities. We evaluate whether the association between CSO events and AGI differs by municipal drinking water source and after adjusting for precipitation events. We hypothesize that *a*) upstream CSO events increase risk of AGI in downstream municipalities after adjusting for precipitation, and *b*) the risk of AGI in municipalities that exclusively source their drinking water from the Merrimack River is more strongly associated with upstream CSO discharge than in municipalities with other drinking water sources. This study builds on the work by Jagai et al.—led by one of the coauthors of the present analysis—that was conducted in the same region of Massachusetts³³ by leveraging a self-matched study design, incorporating CSO discharge

volume data in the exposure classification, stratifying municipalities by drinking water source, and analyzing outcome data from more recent years. To our knowledge, this is the first study to directly investigate the role of drinking water source in the association between CSO event discharge volume and AGI.

Methods

Study Site

The Merrimack River flows 185 km through New Hampshire and northern Massachusetts before flowing into the Atlantic Ocean.³⁴ At 12,976 km², the Merrimack watershed is the fourth largest in New England and home to >2.6 million people.³⁴ More than 500,000 people rely on the Merrimack as a drinking water source, and it is a regional recreational resource for many more.³⁵

The main stem of the Merrimack River flows through five of the six CSS municipalities in the watershed (Figure 1). The sixth CSS community in the watershed is located 82 km upstream from the confluence with the main stem of the Merrimack River along a tributary and was not included in the present study because of its distance from the main stem of the river. Four municipalities in Massachusetts exclusively source their drinking water from the river, while three intermittently depend on the Merrimack River as a drinking water source (Table S1). All 17 Massachusetts municipalities that border the Merrimack River were included in this study.

Exposure Data and Classification

US Environmental Protection Agency (EPA) Region 1 and the City of Manchester, New Hampshire, provided daily CSO event data for the study period. Locations of CSO outfalls are documented and

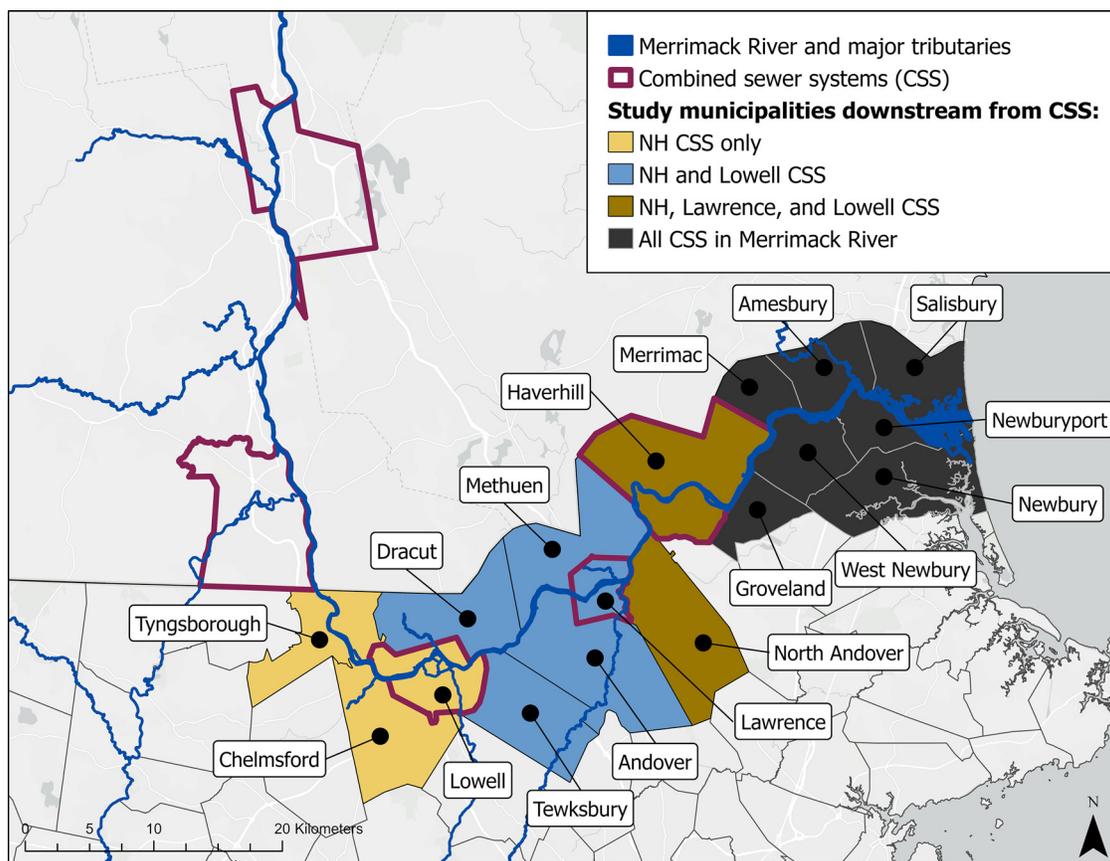


Figure 2. Study municipalities ($n = 17$) and their spatial relationships to combined sewer system (CSS) municipalities. Cumulative daily upstream combined sewer overflow (CSO) discharge volume was calculated for each study municipality as the sum of CSO discharge released from upstream CSS municipalities each day. Map created in ArcGIS Pro (version 3.1.2; Esri) with publicly available data from the US Environmental Protection Agency, US Geological Survey, US Census Bureau, and Massachusetts Bureau of Geographic Information. Note: NH, New Hampshire.

publicly available via an online dashboard accessible at www.epa.gov/merrimackriver/about-merrimack.³⁵ CSO event data were aggregated by municipality and date, yielding a time series of total daily CSO discharge volume per CSS municipality. Cumulative daily upstream CSO discharge volume was calculated for each study municipality as the sum of CSO discharge released from upstream CSS municipalities each day. Figure 2 shows the 17 study municipalities and their spatial relationships to CSS.

Total daily precipitation (in inches) and mean daily temperature (in degrees Fahrenheit) were estimated using PRISM (Parameter-elevation Relationships on Independent Slopes Model) Climate Data.³⁶ A recent study comparing PRISM data to US Climate Reference Network precipitation data found that the two datasets had good comparisons across different seasons and most regions in the United States, including the Northeast, with absolute daily differences of ~ 5 mm between most modeled and measured estimates.³⁷ The centroid for each municipality in the study was used to identify the corresponding 4-km² PRISM grid cell and generate a daily time series of total precipitation and average temperature for each municipality. Cross-correlations were performed to determine how closely and at what point in the time-series precipitation and CSO discharge were most correlated.

Study days were categorized in one of the following ways: a) extreme CSO/precipitation events (≥ 95 th percentile events on the basis of cumulative daily upstream CSO discharge or total daily precipitation, respectively), b) all other CSO/precipitation events (< 95 th percentile events), or c) no CSO/precipitation events. Days with no CSO/precipitation events were used as the referent category. By characterizing CSO discharge volume and

precipitation categorically, risk of AGI following the largest CSO/precipitation events were compared with risk of AGI following days without any events.

Outcome Data

Statewide ED visit data for Massachusetts were obtained from the Center for Health Information and Analysis (CHIA), a state-level agency that collects and normalizes patient-level and financial data from all hospitals across Massachusetts. The Massachusetts Acute Hospital Case Mix Database contains data on ED visits, as well as hospital inpatient discharges and outpatient observation stays for patients who originated in the ED.³⁸ Data available for each visit include the date, municipality of residence, patient age and sex (used for descriptive statistics only), and primary and secondary diagnoses as defined by the *International Classification of Diseases (ICD) 9th*³⁹ or 10th revision.⁴⁰ Claims were deidentified and visits were assumed for analysis to represent separate individuals. Claims data were available from 1 January 2014 through 30 September 2019.

Individuals were included in the analysis if they had AGI, entered a Massachusetts hospital through the ED during the study period, and their permanent or temporary municipality of residence was in the study area. Cases of AGI were defined as any visit that included one or more of the following as a primary or secondary diagnosis: specified and unspecified infectious intestinal diseases (ICD-9 codes: 001–009 or ICD-10 codes: A00–A09), other and unspecified noninfectious gastroenteritis (ICD-9 code: 558.9 or ICD-10 code: K52.9), vomiting (ICD-9 codes: 787.0, 787.01, 787.03 or ICD-10 codes: R11.1, R11.10–R11.12, R11.2), and diarrhea (ICD-9 code: 787.91 or ICD-10 code:

R19.7). Daily AGI cases were aggregated to the municipal level based on residence for each study municipality over the study period. This study was designated as exempt from review by the Boston University Medical Campus Institutional Review Board (IRB) because the outcome dataset comprised deidentified data (IRB no. H-42193).

Statistical Analysis

A case time-series design was used to assess associations between CSO/precipitation events and daily municipality-level cases of AGI. The case time-series design is a self-matched method that allows for assessment of short-term risks of intermittent exposure events by comparing outcomes that occur at different times within individuals or small areas, such as municipalities.^{41,42} This approach allows for investigation of potentially lagged relationships and provides control for time-invariant characteristics by design, similar to other self-matched designs.^{41,42}

The case time-series model (model 1) is specified as follows:

$$g[E(y_{it})] = \xi_{i(k)} + f(x_{it}, l) + ns(temp, f) + I(federal\ holiday), \quad (1)$$

where y_{it} is the number of AGI cases in municipality i at time t . The baseline risks for different risk sets (e.g., temporal strata; $k = 1, 2, \dots, k_i$) are represented by $\xi_{i(k)}$. The temporal strata used to define within-municipality comparison included year, month, and day of week. The function $f(x_{it}, l)$ specifies the association with the exposure in municipality i at time t along the lag dimension l . A uniform weighted lag structure was used that assumes that the probability of illness is constant across the lag period. The term $ns(temp, f)$ describes a natural spline of average daily temperature with f degrees of freedom (3 degrees of freedom was assumed). The temporal strata in the case time-series model control for temporal trends across years, months, and days of the week, but $I(federal\ holiday)$ was included as an indicator for public federal holidays because patterns of ED use may differ on holidays.^{43,44} Results generated by the case time-series model include cumulative exposure–response relationships reported as cumulative risk ratio (CRR) as well as exposure–lag–response associations reported as daily risk ratio (DRR) over the lag period. CRR represents an adjusted estimate comparing the number of cases over the lag period after an extreme event occurs to the number of cases over the same lag period after days when no event occurs (reference days). Days of extreme events are temporally matched to reference days by day of the week, month, and year.

Model 1 was used to estimate the association between extreme CSO events and AGI and, separately, to estimate the association between extreme precipitation events and AGI (2 distinct models). Model 1 was also applied to the same two exposure metrics (CSO and precipitation events) stratified by municipal drinking water source: *a*) exclusive use of the Merrimack River as a drinking water source, or *b*) exclusive use of other drinking water sources (4 additional model iterations).

Precipitation is a driver of CSO events, and studies suggest that both precipitation and CSO events are independently associated with AGI.^{29,45} Model 2 included extreme precipitation as a potential confounder in the association between CSO events and AGI:

$$g[E(y_{it})] = \xi_{i(k)} + f_C(x_{it}, l) + f_P(x_{it}, l) + ns(temp, f) + I(federal\ holiday). \quad (2)$$

Model 2 components are the same as in model 1 except there are two functions— $f_C(x_{it}, l)$ and $f_P(x_{it}, l)$ —that specify associations with extreme CSO discharge and precipitation events, respectively, in municipality i at time t along the lag dimension l . Model 2 was

applied to a model for all municipalities in the study, as well as groups stratified by municipal drinking water source (3 models total). A 7-d lag period was chosen *a priori* for models 1 and 2 based on previous studies.^{29,33} Analyses were conducted in R (version 4.2.1; R Development Core Team) with version 2.4.7 of the *dlnm* package.⁴⁶

Sensitivity Analysis

Models for all municipalities were tested with 4- and 14-d lag periods to consider different lagged relationships between exposure metrics and AGI. Four- and 14-d lag periods were selected post hoc based on exploratory analyses. The definition of extreme CSO and precipitation events used in our categorical exposure variables was assessed by testing 90th, 95th, and 99th percentile cutoffs. Three municipalities in the study area rely on the Merrimack River as a drinking water source intermittently, but data on how frequently or what proportion of drinking water needs are met by use of the Merrimack in these municipalities were not available, and the number of AGI cases from these municipalities was not sufficiently large for an independent analysis. The relationship between exposure events and AGI in municipalities that used any water from the Merrimack (exclusively and intermittently) was assessed as a sensitivity analysis. Finally, the association between individual municipality CSO discharge volumes and AGI in downstream municipalities was evaluated to account for bias that may be introduced by using a cumulative measure of upstream discharge.

Results

Descriptive Statistics

Over the course of the study period, CSS municipalities released a total of 3,012.6 million gallons (Mgal) of CSO discharge into the Merrimack River (Table S2). CSO events occurred in at least one CSS in the watershed on 447 d (21%) of the study period (1 January 2014–31 September 2019). Both the frequency and size of CSO events varied among municipalities, with Manchester and Lowell contributing ~83% of total CSO discharge volume to the system. Cumulative daily upstream CSO discharge volume was highly variable during the study period, ranging from <0.1 Mgal to 189.0 Mgal with the 95th percentile value at 27.3 Mgal and the 99th percentile at 78.7 Mgal (Figure S1).

Precipitation events occurred in at least one of the municipalities in the study area on 972 d (46%) of the study period (Table S2). Precipitation events ranged from <2.54 mm of daily accumulation to 118.6 mm daily, with a 95th percentile value of 31.5 mm and a 99th percentile value of 50.0 mm. A positive correlation was observed between daily municipality-level precipitation and upstream cumulative CSO discharge on the day of the events ($r = 0.53$) (Figure S2).

Massachusetts EDs documented 100,206 cases of AGI among residents of the study municipalities over the study period (Table 1). AGI patients were majority female (59.9%), and ~30% of patients were in age groups most susceptible to AGI (adults >65 and children <5 years of age).²⁰ Figure 3 shows the per capita rate of AGI among all study municipalities over the study period compared with the overall rate of AGI in the state of Massachusetts per the CHIA dataset.³⁸

Model Results

All municipalities. In models adjusted for temporal trends and temperature but not adjusted for precipitation, the CRR of AGI was 22% higher [1.22; 95% confidence interval (CI): 1.05, 1.42] in the 4 d following 95th and 63% higher [1.63 (95% CI: 1.07, 2.47)] in the 4 d following 99th percentile CSO events compared with days with no CSO events when considering all municipalities (Figure 4A). A marginal association that was not statistically

Table 1. Descriptive statistics for cases of acute gastrointestinal illness (AGI) in 17 Massachusetts municipalities bordering the Merrimack River, 1 January 2014–30 September 2019. *N* = 100,206 total AGI cases.

Characteristic ^a	<i>n</i> (%)
Cases of AGI by year	
2014	16,079 (16.0)
2015	16,881 (16.8)
2016	16,903 (16.9)
2017	17,727 (17.7)
2018	18,141 (18.1)
2019 (through 30 September)	14,475 (14.4)
Average number of cases of AGI per year	17,427
Cases of AGI by sex	
Female	59,989 (59.9)
Male	40,216 (40.1)
Unknown	1 (0.0)
Cases of AGI by age group (y)	
<5	14,845 (14.8)
5–19	15,094 (15.1)
20–64	53,999 (53.9)
≥65	16,268 (16.2)
Cases of AGI by municipal drinking water source	
Merrimack River exclusively (4 municipalities)	64,278 (64.2)
Merrimack River intermittently (3 municipalities)	7,649 (7.6)
Other sources (10 municipalities)	28,279 (28.2)

Note: AGI, acute gastrointestinal illness; ED, emergency department; ICD, International Classification of Diseases.

^aCases: ED visits in Massachusetts hospitals for AGI defined as any visit with one or more of the following as a primary or secondary diagnosis: specified and unspecified infectious intestinal diseases (ICD-9 codes: 001–009 or ICD-10 codes: A00–A09), other and unspecified noninfectious gastroenteritis (ICD-9 code: 558.9 or ICD-10 code: K52.9), vomiting (ICD-9 codes: 787.0, 787.01, 787.03 or ICD-10 codes: R11.1, R11.10–R11.12, R11.2), and diarrhea (ICD-9 code: 787.91 or ICD-10 code: R19.7). All cases had a permanent or temporary municipality of residence in the study area.

significant was observed between 90th percentile CSO events and AGI [CRR = 1.07 (95% CI: 0.96, 1.19)]. No increase in risk was observed following CSO events below the 90th percentile. These associations remained largely unchanged among all municipalities after adjusting for precipitation, with a 17% increase in CRR of AGI in the 4 d after 95th percentile CSO events [1.17 (95% CI: 0.98, 1.39)] and a 62% increase after 99th percentile CSO events [1.62 (95% CI: 1.04, 2.51)] (Figure 4B). Extreme precipitation was also associated with a 13% increase in CRR of AGI in the 4 d following 95th percentile precipitation events [1.13 (95% CI: 1.00, 1.27)], and a marginal increase following 99th percentile precipitation events [1.07 (95% CI: 0.82, 1.41)] (Figure 4C). Results of all models, including those that assessed the association between extreme events and AGI among municipalities that use any water from the Merrimack and those that used a 7- or 14-d lag period, are included in Tables S3, S4, and S5, respectively. Results from the 7- and 14-d lag period models followed a pattern similar to the results of the 4-d lag period models, with an increase in CRR of AGI observed after extreme CSO events when adjusting for precipitation, although none of the associations between extreme CSO events and AGI were statistically significant [e.g., 7-d lag: CRR = 1.12 (95% CI: 0.89, 1.41)] after 95th percentile CSO events and 1.70 (95% CI: 0.95, 3.06) after 99th percentile CSO events among all municipalities; 14-d lag: 1.20 (95% CI: 0.84, 1.70) after 95th percentile CSO events and 1.49 (95% CI: 0.61, 3.64) after 99th percentile CSO events among all municipalities) (Tables S4 and S5).

Stratification by drinking water source. We did not observe a difference in the unadjusted CRR of AGI in municipalities with different drinking water sources following 95th percentile CSO events after stratification by drinking water source [Merrimack River: CRR = 1.19 (95% CI: 0.97, 1.46); Other sources: 1.19 (95% CI: 0.93, 1.54)] (Figure 4A). After adjusting for precipitation, CRR of AGI was only marginally elevated following 95th percentile

CSO events among municipalities that exclusively get their drinking water from the river [CRR = 1.05 (95% CI: 0.82, 1.33)], whereas the CRR of AGI among municipalities that do not use the Merrimack River as a drinking water source was slightly higher [1.27 (95% CI: 0.94, 1.70)] (Figure 4B). The CRR of AGI was elevated regardless of drinking water source after 99th percentile CSO events compared with days with no CSO events [Merrimack River: CRR = 1.57 (95% CI: 0.86, 2.88); Other sources: 1.84 (95% CI: 0.88, 3.85)] (Figure 4B).

Daily relative risk. Comparison of DRRs of AGI in municipalities with different drinking water sources over the 4-d lag period showed that the magnitude of the strongest observed increase in DRR was approximately the same between drinking water groups [Merrimack River: DRR = 1.36 (95% CI: 1.05, 1.76); Other sources: 1.45 (95% CI: 1.07, 1.96)], but occurred on different days within that period (Figure 5; Table S6). The strongest association between extreme CSO events and AGI was observed 2 d after an event among municipalities that use the Merrimack as their exclusive drinking water source, and 1 d after an event among municipalities with other drinking water sources. A similar temporal pattern was observed in the 4 d following 95th percentile CSO events, although the magnitudes of the associations were attenuated (Figure S3, Table S6).

Sensitivity analyses. Results from the sensitivity analysis assessing the relationship between CSO events from individual CSS municipalities and cases of AGI in downstream municipalities are shown in Table S7. Elevated CRR of AGI was observed among downstream municipalities 4 d after CSO events in Manchester [1.09 (95% CI: 0.93, 1.29)] and Lowell [1.16 (95% CI: 0.95, 1.42)], although neither of these associations were statistically significant.

Discussion

In this analysis of the association between CSO events and ED visits for AGI, we observed higher risk of AGI in the 4 d following extreme CSO events compared with days with no CSO events. Results were robust to adjustment for potential confounding by precipitation. The magnitude of the associations observed in the present analysis were similar to or larger than those found in previous studies, although methodological differences and study populations make direct comparisons difficult. Using a similar self-matched study design, Brokamp et al. found a 16% higher odds of AGI after any CSO event among children living within 500 m of a CSO outfall [odds ratio = 1.16 (95% CI: 1.04, 1.30)].³⁰ This study differed in notable ways from our study, including the spatial approach to exposure classification, pediatric study population, and the binary classification of CSO events, but the magnitude of the association was similar to the CRR we observed following 95th percentile CSO events. On the other hand, Miller et al. did not use a self-matched study design and found a smaller but more precise association between large CSO events and AGI after adjusting for precipitation among Atlanta residents of all ages [rate ratio = 1.09 (95% CI: 1.03, 1.14)].²⁹ The definition of a large CSO event used by Miller et al. was ≥56.6 Mgal of discharge, which falls in the range between 95th (27.3 Mgal) and 99th percentile (78.7 Mgal) CSO discharge events in our study. In an earlier analysis in the Merrimack Valley region of Massachusetts that used extreme precipitation as a proxy for CSO events, Jagai et al. found a 13% increase in cumulative risk of AGI following extreme precipitation events [equivalent to 50.0 mm, CRR = 1.13 (95% CI: 1.00, 1.28)].³³ This result is remarkably similar to the association observed in this analysis between 95th percentile precipitation events (equivalent to 31.5 mm) and the cumulative risk of AGI over 4 d observed in our study. Overall, we found that the strength of the associations observed in this study between 95th percentile CSO or precipitation events and AGI were fairly consistent with

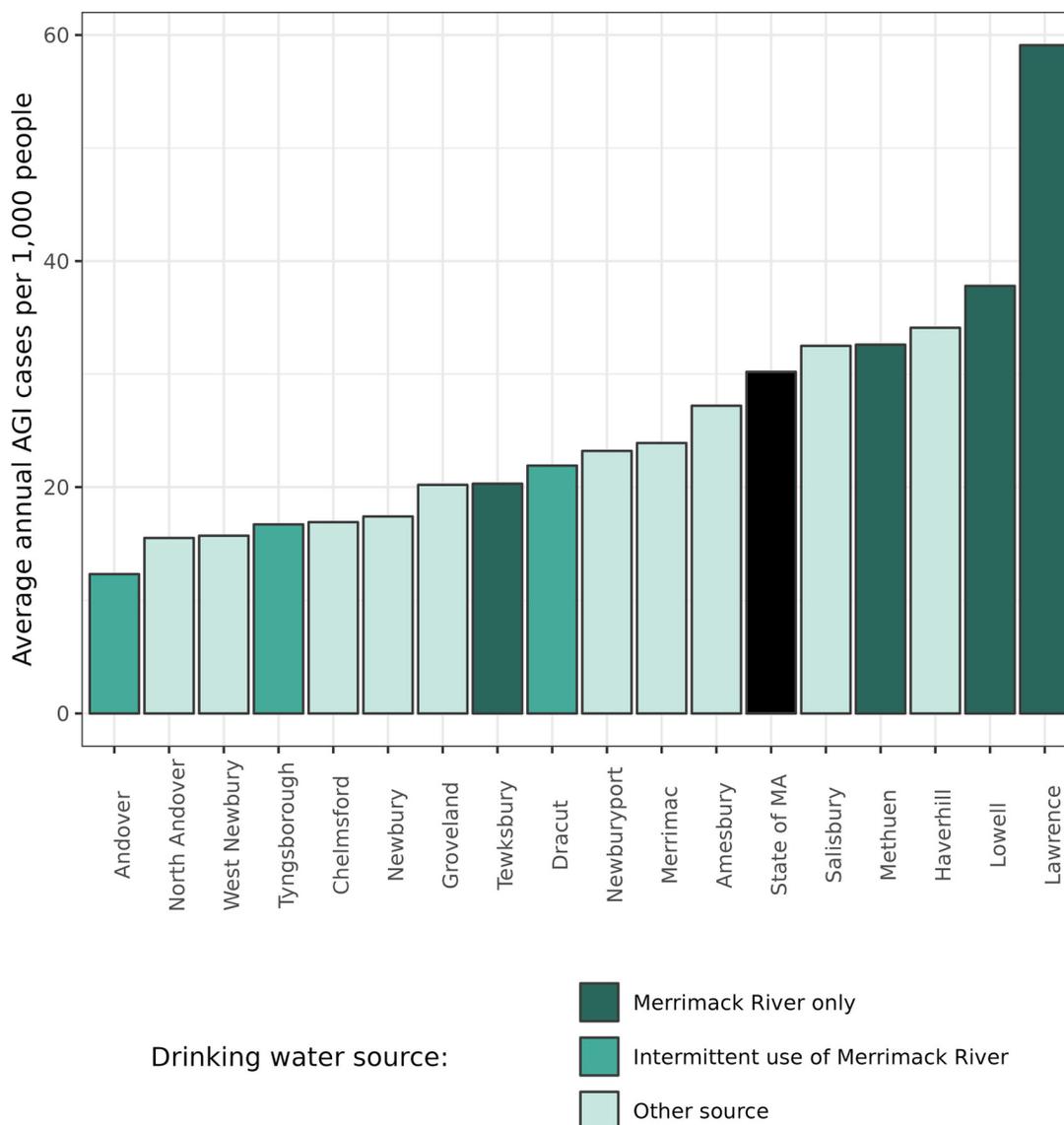


Figure 3. Average annual cases of acute gastrointestinal illness (AGI) per 1,000 people among study municipalities by drinking water source compared with background levels of AGI in the state of Massachusetts (MA). Annual population estimates for the state of MA and study municipalities were accessed through the American Community Survey 5-y estimates⁴⁷ and City and Town Population Totals⁴⁸ from the US Census Bureau. The data used to create this figure are included in Table S1. $N = 100,206$ total AGI cases between 1 January 2014 through 30 September 2019.

previous findings but that the CRR of AGI following 99th percentile CSO events was notably higher than what has been reported in similar studies.

The magnitude of cumulative CSO discharge volume was an important factor in the association between CSO events and AGI, with the largest associations observed following ≥ 95 th and ≥ 99 th percentile CSO events. Our findings suggest that a nonlinear dose-response relationship exists between upstream CSO discharge volume and AGI, a finding consistent with previous studies.^{29,33} Miller et al. similarly found that only large CSO events (≥ 75 th percentile CSO events by volume, equivalent to ≥ 56.5 Mgal) were significantly associated with AGI in the week following an event, but models estimating the association between any CSO event and AGI resulted in no association.²⁹ Jagai et al. found that only the most extreme precipitation events (99th percentile, equivalent to 50.0 mm) were significantly associated with increased cumulative risk of AGI; lower magnitude, nonstatistically significant associations were found for lower percentile precipitation events.³³ These results are particularly relevant given that the frequency and

intensity of extreme precipitation events (and extreme CSO events as a result) are expected to increase due to climate change in the Northeast and Midwest, where most CSS in the United States are located.³

We hypothesized that CSO events would be more strongly associated with risk of AGI among municipalities whose drinking water is sourced from the Merrimack River vs. municipalities that use other sources of water. However, in stratified analyses we found that the risk of AGI associated with CSO events was similar regardless of drinking water source. Although the adjusted estimates following extreme CSO events (95th and 99th percentile by volume) were less pronounced among municipalities using the Merrimack as their drinking water source compared with those with other sources, the overlap in the CIs between the associations for the two groups suggests that these estimates are not statistically significantly different. These results suggest that contaminated municipal drinking water may not be the only exposure pathway linking CSO events with AGI risk. The association between extreme precipitation and AGI risk was

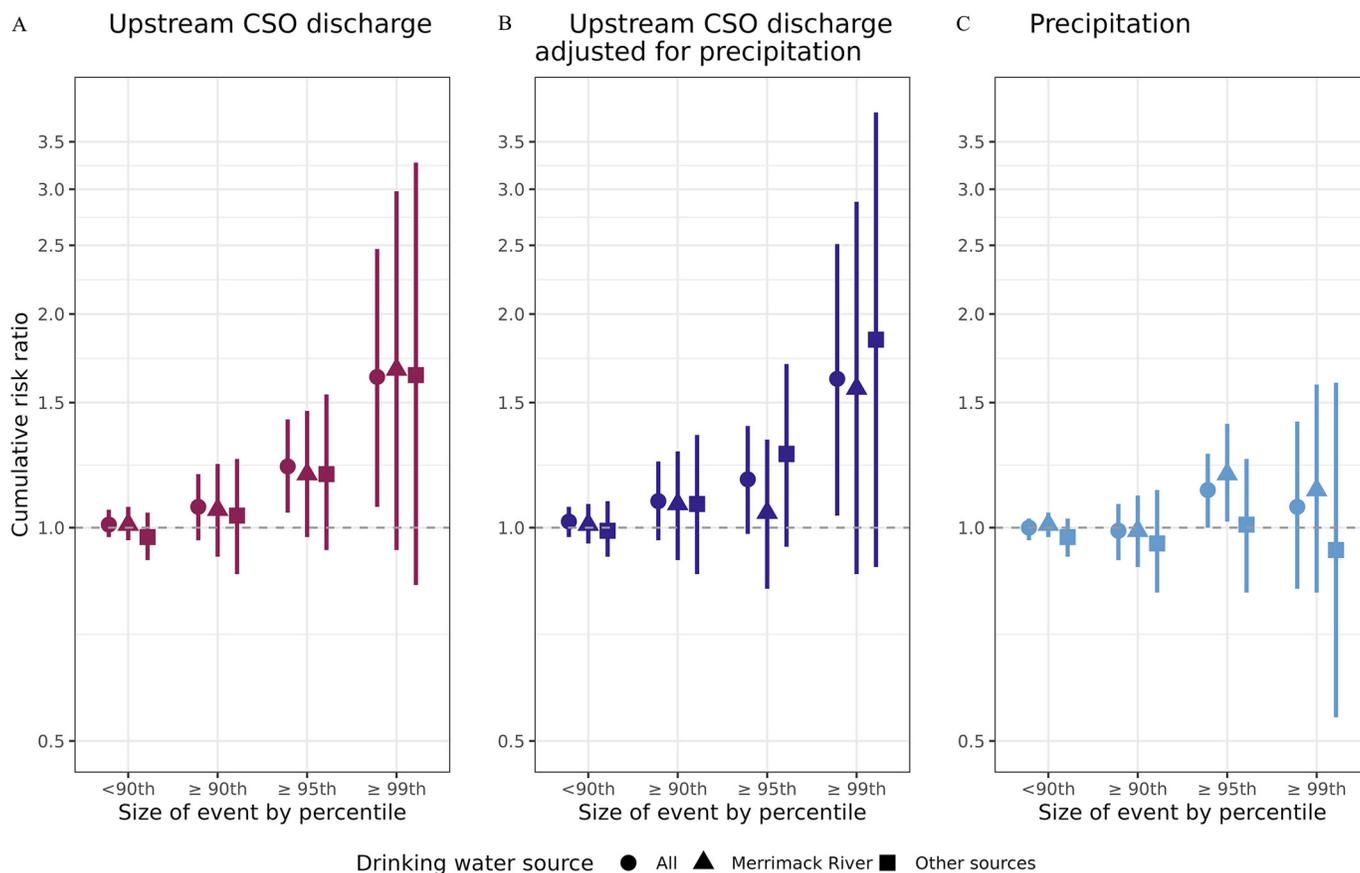


Figure 4. Cumulative risk ratio (CRR) of acute gastrointestinal illness (AGI) over the 4 d following (A) combined sewer overflow (CSO) events, (B) CSO events adjusting for precipitation, and (C) precipitation events. Model results are shown for all municipalities and by drinking water source (Merrimack River or other sources), as well as events of different sizes: <90th percentile, ≥90th percentile, ≥95th percentile, and ≥99th percentile events. Municipalities that intermittently use the Merrimack River as a drinking water source were included in the analysis for all municipalities but not in the drinking water stratification analysis. All analyses were conducted using case time-series models with covariates to adjust for average daily temperature and federal holidays. This figure corresponds to data in Table S3. $N = 100,206$ total AGI cases between 1 January 2014 through 30 September 2019.

slightly higher among municipalities sourcing drinking water from the Merrimack River, but the estimates remain statistically indistinguishable owing to their overlapping CIs. Although the differences between associations by strata are modest at best, it is possible that heavy precipitation could directly influence the risk of AGI among municipalities with surface water sources independent of CSO events. A number of studies have found an association between extreme precipitation and gastrointestinal illness in areas served by surface water sources without CSS,^{26,27} and a study in New Jersey found positive associations between rainfall and AGI among areas served by surface water but not groundwater sources.⁴⁹ Heavy precipitation can impact surface water sources by increasing turbidity and reducing water treatment efficacy, transporting pathogens from environmental reservoirs to surface water via runoff, and resuspending pathogens from riverine sediments.⁵⁰

The evidence in the literature is inconclusive on the potential for drinking water contamination after CSO events. Although it is conceptually possible for treated drinking water to be contaminated by CSO discharge,^{51,52} studies of health risks that incorporated drinking water source contamination following discharge events either did not include CSO event data in the exposure^{32,33} or found that controlling for CSO events as a binary covariate did not alter the association between precipitation and AGI.⁴⁵ Interviews of workers at drinking water treatment utilities located within 1.6 km downstream of CSO outfalls suggest that many drinking water utilities adjust treatment based on wet weather,

adding further complexity to any assessments of the association between CSO events and health outcomes in municipalities with CSO-impacted drinking water sources.¹ We are unaware of an accounting of how many municipalities have a drinking water source that is impacted by CSO discharge, so it is unclear how widespread this issue might be, although the results of this analysis suggest that drinking water contamination may not be the only important exposure pathway in a CSO-impacted river system. Understanding the critical exposure pathway(s) following CSO discharge events is an important direction for future work that has direct implications for infrastructure investment decisions and policies designed to protect public health under future climate scenarios.

The findings of this study suggest that CSO events and AGI were more strongly associated across the 4 d following an event compared with a longer lag period of 7 or 14 d. These findings are consistent with previous studies that found significant associations between sewage discharge events and AGI over lag periods from 2 to 8 d.^{29,30,32,33} A 4-d lag period is also consistent with the incubation times of some of the pathogens found in waterways contaminated with sewage,^{1,9,53} including noroviruses (12–48 h), rotavirus (1–3 d), *Shigella* (12 h–7 d), enterotoxigenic *Escherichia coli* (12–72 h), and *Cryptosporidium* (2–10 d).⁵³ Viral and protozoan waterborne pathogens can be infectious at low doses, persistent in environmental media, and less effectively removed by conventional drinking water treatment compared with bacteria.^{54,55} Another consideration with a short lag time is the time between CSO event

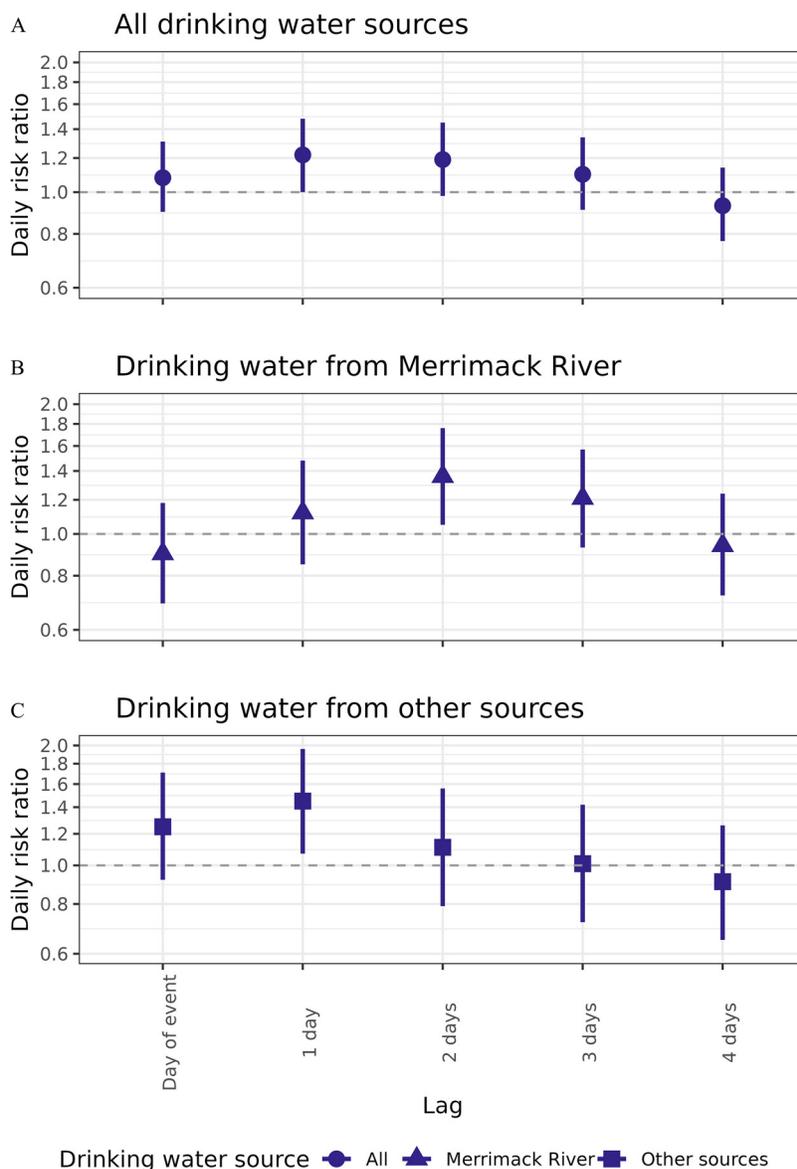


Figure 5. Daily risk ratio (DRR) of acute gastrointestinal illness (AGI) over a 4-d lag period following of 99th percentile combined sewer overflow (CSO) events and adjusted for precipitation in (A) municipalities with all drinking water sources, (B) municipalities that exclusively get their drinking water from the Merrimack River, and (C) municipalities that exclusively get their drinking water from sources other than the Merrimack. Municipalities that intermittently use the Merrimack River as a drinking water source were included in the analysis for all municipalities but not in the drinking water stratification analysis. All analyses conducted using case time-series models with covariates to adjust for average daily temperature and federal holidays. This figure corresponds to data in Table S6. $N = 100,206$ total AGI cases between 1 January 2014 through 30 September 2019.

and exposure, which could differ based on exposure pathway. It is possible that people exposed primarily through recreational activity or aerosolized pathogens could ingest contaminated water within hours after a CSO event, although our analysis was not spatially refined enough to assess the possibility of exposure through the latter pathway.

This study has a number of potential limitations. First, the analysis is limited by a lack of individual-level information on exposure, including rates of consumption or quality of drinking water, amount or timing of contact with recreational waters, and recreational surface water quality experienced by individuals within the study population. The lack of individual exposure data limits our ability to gain insights about specific exposure pathways. Moreover, the lack of information about local water contamination and potential local responses to CSO events (e.g., adjustments to drinking water treatment processes) may have led to substantial exposure misclassification and likely biased results toward the null hypothesis of no

association. Second, the AGI case data were deidentified, precluding identification of patients that may have been treated for AGI more than once. Our inability to account for the correlation among repeated episodes within an individual may have resulted in CIs that are perhaps too narrow. Third, people seeking care for AGI in the ED likely represent the most severe cases of gastrointestinal illness, given that $\leq 10\%$ of all cases of AGI come to medical attention in acute care settings.⁵⁶ Thus, it is unclear whether these results are generalizable to milder episodes of AGI or to other communities across the country.

This study also has some notable strengths. First, the case time-series design minimizes potential confounding by differences between municipalities and effectively controls for temporal trends. Second, by using daily measures of CSO discharge volume instead of approaches taken in other studies to measure CSO exposure, such as precipitation as a proxy for CSO events,³³ modeling CSO events as binary exposures,³⁰ or aggregating to a weekly time step,²⁹ this study

more directly evaluates the relationship between CSO discharge and health. Our use of daily CSO and precipitation data allowed for a refined temporal analysis in the days following an exposure event, and CSO volume data provided the opportunity to assess potential dose–response relationships between CSO discharge and AGI. We also considered the spatial relationship between CSS municipalities and downstream municipalities in our approach to assigning exposure. Although there are limitations to the characterization of exposure in this study introduced by considering upstream discharge, this approach is representative of how CSO discharge moves through the area and accumulates in downstream stretches of the river. The PRISM dataset provided spatial resolution of precipitation estimates that may account for heterogeneity in rainfall that is not captured by a regional weather station, the latter of which has been the source for precipitation data in other studies.^{29,33} Finally, reliance on the Merrimack River as a drinking water source downstream of CSO outfalls provided an opportunity to compare associations between municipalities that do and do not get their drinking water from this CSO-impacted source. To our knowledge, only three studies report the association between sewage-related discharge events and health outcomes in regions with modern wastewater infrastructure where drinking water intakes exist downstream of outfalls.^{32,33,45} In those studies, the exposure was either extreme rainfall as a proxy for CSO events,³³ undertreated sewage discharge events,³² or precipitation with CSO discharge included as a covariate.⁴⁵

Our findings suggest that extreme CSO events increase the risk of ED visits for AGI in downstream municipalities in the 4 d following an event and that a nonlinear dose–response relationship exists between CSO discharge and ED visits for AGI. The largest CSO events are associated with AGI across drinking water sources and concurrent precipitation levels, although we observed differences in the timing and magnitude of associations based on drinking water source. Although our study is ecological in design, our findings indicate that CSS may negatively impact public health. As precipitation events intensify as a result of climate change, large-volume CSO events may become more common and the risk of AGI in downstream municipalities may increase. Future work needed to inform CSO mitigation and improve climate change resiliency includes research clarifying the importance of different exposure pathways in the association between CSO events and AGI, expansion of this type of analysis to a regional or national scale to evaluate the robustness of the results across systems, and estimation of attributable cases of AGI following expected CSO events under future climate scenarios.

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References

1. US EPA (US Environmental Protection Agency). 2004. Report to Congress on Impacts and Control of Combined Sewer Overflows and Sanitary Sewer Overflows [Fact sheet]. https://www.epa.gov/sites/default/files/2015-10/documents/csosortc2004_full.pdf [accessed 10 May 2023].

2. Madoux-Humery AS, Dorner S, Sauvé S, Aboufadi K, Galarneau M, Servais P, et al. 2016. The effects of combined sewer overflow events on riverine sources of drinking water. *Water Res* 92:218–227, PMID: 26866859, <https://doi.org/10.1016/j.watres.2015.12.033>.
3. US Global Change Research Program. 2018. Water. In: *Fourth National Climate Assessment*. <https://nca2018.globalchange.gov/chapter/3> [accessed 12 May 2023].
4. US EPA. 2020. Combined sewer overflow frequent questions. Published 14 October 2015. <https://www.epa.gov/npdes/combined-sewer-overflow-frequent-questions> [accessed 1 December 2020].
5. Harp RD, Horton DE. 2022. Observed changes in daily precipitation intensity in the United States. *Geophys Res Lett* 49(19):e2022GL099955, <https://doi.org/10.1029/2022GL099955>.
6. Rechenburg A, Koch C, Classen T, Kistemann T. 2006. Impact of sewage treatment plants and combined sewer overflow basins on the microbiological quality of surface water. *Water Sci Technol* 54(3):95–99, PMID: 17037139, <https://doi.org/10.2166/wst.2006.454>.
7. Passerat J, Ouattara NK, Mouchel JM, Rocher V, Servais P. 2011. Impact of an intense combined sewer overflow event on the microbiological water quality of the Seine River. *Water Res* 45(2):893–903, PMID: 20934197, <https://doi.org/10.1016/j.watres.2010.09.024>.
8. Madoux-Humery AS, Dorner S, Sauvé S, Aboufadi K, Galarneau M, Servais P, et al. 2013. Temporal variability of combined sewer overflow contaminants: evaluation of wastewater micropollutants as tracers of fecal contamination. *Water Res* 47(13):4370–4382, PMID: 23764588, <https://doi.org/10.1016/j.watres.2013.04.030>.
9. Donovan E, Unice K, Roberts JD, Harris M, Finley B. 2008. Risk of gastrointestinal disease associated with exposure to pathogens in the water of the Lower Passaic River. *Appl Environ Microbiol* 74(4):994–1003, PMID: 18156342, <https://doi.org/10.1128/AEM.00601-07>.
10. Hata A, Katayama H, Kojima K, Sano S, Kasuga I, Kitajima M, et al. 2014. Effects of rainfall events on the occurrence and detection efficiency of viruses in river water impacted by combined sewer overflows. *Sci Total Environ* 468–469:757–763, PMID: 24064345, <https://doi.org/10.1016/j.scitotenv.2013.08.093>.
11. Arnone RD, Walling JP. 2006. Evaluating *Cryptosporidium* and Giardia concentrations in combined sewer overflow. *J Water Health* 4(2):157–165, PMID: 16813009, <https://doi.org/10.2166/wh.2006.0013>.
12. Nickel JP, Fuchs S. 2019. Micropollutant emissions from combined sewer overflows. *Water Sci Technol* 80(11):2179–2190, PMID: 32198335, <https://doi.org/10.2166/wst.2020.035>.
13. Di Nunno F, Granata F, Parrino F, Gargano R, de Marinis G. 2021. Microplastics in combined sewer overflows: an experimental study. *J Mar Sci Eng* 9(12):1415, <https://doi.org/10.3390/jmse9121415>.
14. Treilles R, Gasperi J, Saad M, Rabier A, Breton J, Rocher V, et al. 2020. Macro and microplastics in stormwater and combined sewer overflows in Paris megacity. In: *Proceedings of the 2nd International Conference on Microplastic Pollution in the Mediterranean Sea. ICMPPMS 2019*. Cocco M, Di Pace E, Errico ME, Gentile G, Montarsolo A, Mossotti R, et al., eds. New York, NY: Springer International Publishing, 145–151.
15. Olds HT, Corsi SR, Dila DK, Halmo KM, Bootsma MJ, McLellan SL. 2018. High levels of sewage contamination released from urban areas after storm events: a quantitative survey with sewage specific bacterial indicators. *PLoS Med* 15(7):e1002614, PMID: 30040843, <https://doi.org/10.1371/journal.pmed.1002614>.
16. Fewtrell L, Kay D. 2015. Recreational water and infection: a review of recent findings. *Curr Environ Health Rep* 2(1):85–94, PMID: 25821715, <https://doi.org/10.1007/s40572-014-0036-6>.
17. Arnold BF, Wade TJ, Benjamin-Chung J, Schiff KC, Griffith JF, Dufour AP, et al. 2016. Acute gastroenteritis and recreational water: highest burden among young US children. *Am J Public Health* 106(9):1690–1697, PMID: 27459461, <https://doi.org/10.2105/AJPH.2016.303279>.
18. DeFlorio-Barker S, Wing C, Jones RM, Dorevitch S. 2018. Estimate of incidence and cost of recreational waterborne illness on United States surface waters. *Environ Health* 17(1):3, PMID: 29316937, <https://doi.org/10.1186/s12940-017-0347-9>.
19. Russo GS, Eftim SE, Goldstone AE, Dufour AP, Nappier SP, Wade TJ. 2020. Evaluating health risks associated with exposure to ambient surface waters during recreational activities: a systematic review and meta-analysis. *Water Res* 176:115729, PMID: 32240845, <https://doi.org/10.1016/j.watres.2020.115729>.
20. Reynolds KA, Mena KD, Gerba CP. 2008. Risk of waterborne illness via drinking water in the United States. *Rev Environ Contam Toxicol* 192:117–158, PMID: 18020305, https://doi.org/10.1007/978-0-387-71724-1_4.
21. Messner M, Shaw S, Regli S, Rotert K, Blank V, Soller J. 2006. An approach for developing a national estimate of waterborne disease due to drinking water and a national estimate model application. *J Water Health* 4(suppl 2):201–240, PMID: 16895092, <https://doi.org/10.2166/wh.2006.024>.
22. Collier SA, Deng L, Adam EA, Benedict KM, Beshearse EM, Blackstock AJ, et al. 2021. Estimate of burden and direct healthcare cost of infectious waterborne disease in the United States. *Emerg Infect Dis* 27(1):140–149, PMID: 33350905, <https://doi.org/10.3201/eid2701.190676>.

23. Craun GF, Brunkard JM, Yoder JS, Roberts VA, Carpenter J, Wade T, et al. 2010. Causes of outbreaks associated with drinking water in the United States from 1971 to 2006. *Clin Microbiol Rev* 23(3):507–528, PMID: 20610821, <https://doi.org/10.1128/CMR.00077-09>.
24. Moreira NA, Bondelind M. 2017. Safe drinking water and waterborne outbreaks. *J Water Health* 15(1):83–96, PMID: 28151442, <https://doi.org/10.2166/wh.2016.103>.
25. Schuster CJ, Ellis AG, Robertson WJ, Charron DF, Aramini JJ, Marshall BJ, et al. 2005. Infectious disease outbreaks related to drinking water in Canada, 1974–2001. *Can J Public Health* 96(4):254–258, PMID: 16625790, <https://doi.org/10.1007/BF03405157>.
26. Curriero FC, Patz JA, Rose JB, Lele S. 2001. The association between extreme precipitation and waterborne disease outbreaks in the United States, 1948–1994. *Am J Public Health* 91(8):1194–1199, PMID: 11499103, <https://doi.org/10.2105/ajph.91.8.1194>.
27. Guzman Herrador BR, de Blasio BF, MacDonald E, Nichols G, Sudre B, Vold L, et al. 2015. Analytical studies assessing the association between extreme precipitation or temperature and drinking water-related waterborne infections: a review. *Environ Health* 14:29, PMID: 25885050, <https://doi.org/10.1186/s12940-015-0014-y>.
28. Exum NG, Betanzo E, Schwab KJ, Chen TYJ, Guikema S, Harvey DE. 2018. Extreme precipitation, public health emergencies, and safe drinking water in the USA. *Curr Environ Health Rep* 5(2):305–315, PMID: 29687348, <https://doi.org/10.1007/s40572-018-0200-5>.
29. Miller AG, Ebel S, Levy K. 2022. Combined sewer overflows and gastrointestinal illness in Atlanta, 2002–2013: evaluating the impact of infrastructure improvements. *Environ Health Perspect* 130(5):057009, PMID: 35580035, <https://doi.org/10.1289/EHP10399>.
30. Brokamp C, Beck AF, Muglia L, Ryan P. 2017. Combined sewer overflow events and childhood emergency department visits: a case-crossover study. *Sci Total Environ* 607–608:1180–1187, PMID: 28732397, <https://doi.org/10.1016/j.scitotenv.2017.07.104>.
31. Harder-Lauridsen NM, Kuhn KG, Erichsen AC, Mølbak K, Ethelberg S. 2013. Gastrointestinal illness among triathletes swimming in non-polluted versus polluted seawater affected by heavy rainfall, Denmark, 2010–2011. *PLoS One* 8(11):e78371, PMID: 24244306, <https://doi.org/10.1371/journal.pone.0078371>.
32. Redman RL, Nenn CA, Eastwood D, Gorelick MH. 2007. Pediatric emergency department visits for diarrheal illness increased after release of undertreated sewage. *Pediatrics* 120(6):e1472–e1475, PMID: 18055664, <https://doi.org/10.1542/peds.2007-0283>.
33. Jagai JS, Li Q, Wang S, Messier KP, Wade TJ, Hilborn ED. 2015. Extreme precipitation and emergency room visits for gastrointestinal illness in areas with and without combined sewer systems: an analysis of Massachusetts data, 2003–2007. *Environ Health Perspect* 123(9):873–879, PMID: 25855939, <https://doi.org/10.1289/ehp.1408971>.
34. US EPA. 2016. About the Merrimack. Published 15 August 2016. <https://www.epa.gov/merrimackriver/about-merrimack> [accessed 17 May 2023].
35. US EPA. 2019. Merrimack River Watershed. <https://epa.maps.arcgis.com/apps/MapSeries/index.html?appid=922e1c016c6e42b199f902d1c6b84bbd> [accessed 1 December 2020].
36. PRISM Climate Group. 2021. PRISM Climate Data. <https://prism.oregonstate.edu/> [accessed 18 March 2021].
37. Buban MS, Lee TR, Baker CB. 2020. A comparison of the U.S. Climate Reference Network precipitation data to the Parameter-Elevation Regressions on Independent Slopes Model (PRISM). *J Hydrometeorol* 21(10):2391–2400, <https://doi.org/10.1175/JHM-D-19-0232.1>.
38. CHIA (Center for Health Information and Analysis). 2021. Case Mix Data. <https://www.chiamass.gov/case-mix-data/> [accessed 20 March 2021].
39. WHO (World Health Organization). 1978. *International Statistical Classification of Diseases, Ninth Revision, Basic Tabulation List with Alphabetic Index*. <https://www.cdc.gov/nchs/icd/icd9cm.htm> [accessed 23 September 2022].
40. World Health Organization. 2019. ICD-10 Version:2019. <https://www.cdc.gov/nchs/icd/icd-10-cm.htm> [accessed 23 September 2022].
41. Gasparrini A. 2021. The case time series design. *Epidemiology* 32(6):829–837, PMID: 34432723, <https://doi.org/10.1097/EDE.0000000000001410>.
42. Gasparrini A. 2022. A tutorial on the case time series design for small-area analysis. *BMC Med Res Methodol* 22(1):129, PMID: 35501713, <https://doi.org/10.1186/s12874-022-01612-x>.
43. Zheng W, Muscatello DJ, Chan AC. 2007. Deck the halls with rows of trolleys . . . emergency departments are busiest over the Christmas holiday period. *Med J Aust* 187(11–12):630–633, PMID: 18072896, <https://doi.org/10.5694/j.1326-5377.2007.tb01451.x>.
44. Salazar A, Corbella X, Sánchez JL, Argimón JM, Escarrabill J. 2002. How to manage the ED crisis when hospital and/or ED capacity is reaching its limits. Report about the implementation of particular interventions during the Christmas crisis. *Eur J Emerg Med* 9(1):79–80, PMID: 11989505, <https://doi.org/10.1097/00063110-200203000-00019>.
45. Drayna P, McLellan SL, Simpson P, Li SH, Gorelick MH. 2010. Association between rainfall and pediatric emergency department visits for acute gastrointestinal illness. *Environ Health Perspect* 118(10):1439–1443, PMID: 20515725, <https://doi.org/10.1289/ehp.0901671>.
46. Gasparrini A. 2011. Distributed lag linear and non-linear models in R: the package dlnm. *J Stat Softw* 43(8):1–20, PMID: 22003319, <https://doi.org/10.18637/jss.v043.i08>.
47. US Census Bureau. 2021. American Community Survey 5-Year Data (2009–2019). <https://www.census.gov/data/developers/data-sets/acs-5year.html> [accessed 7 April 2021].
48. US Census Bureau. 2023. City and Town Population Totals: 2010–2019. <https://www.census.gov/data/tables/time-series/demo/popest/2010s-total-cities-and-towns.html> [accessed 11 May 2023].
49. Gleason JA, Fagliano JA. 2017. Effect of drinking water source on associations between gastrointestinal illness and heavy rainfall in New Jersey. *PLoS One* 12(3):e0173794, PMID: 28282467, <https://doi.org/10.1371/journal.pone.0173794>.
50. Chhetri BK, Takaro TK, Balshaw R, Otterstatter M, Mak S, Lem M, et al. 2017. Associations between extreme precipitation and acute gastro-intestinal illness due to cryptosporidiosis and giardiasis in an urban Canadian drinking water system (1997–2009). *J Water Health* 15(6):898–907, PMID: 29215354, <https://doi.org/10.2166/wh.2017.100>.
51. Sokolova E, Petterson SR, Dienus O, Nyström F, Lindgren PE, Pettersson TJR. 2015. Microbial risk assessment of drinking water based on hydrodynamic modelling of pathogen concentrations in source water. *Sci Total Environ* 526:177–186, PMID: 25931024, <https://doi.org/10.1016/j.scitotenv.2015.04.040>.
52. Taghipour M, Shakibaenia A, Sylvestre É, Tolouei S, Dorner S. 2019. Microbial risk associated with CSOs upstream of drinking water sources in a transboundary river using hydrodynamic and water quality modeling. *Sci Total Environ* 683:547–558, PMID: 31146060, <https://doi.org/10.1016/j.scitotenv.2019.05.130>.
53. CDC (Centers for Disease Control and Prevention). 2023. *Waterborne Disease Outbreak Investigation Toolkit*. <https://www.cdc.gov/healthywater/emergency/pdf/waterborne-disease-outbreak-toolkit-h.pdf> [accessed 19 May 2023].
54. Gibson KE. 2014. Viral pathogens in water: occurrence, public health impact, and available control strategies. *Curr Opin Virol* 4:50–57, PMID: 24440908, <https://doi.org/10.1016/j.coviro.2013.12.005>.
55. Betancourt WQ, Rose JB. 2004. Drinking water treatment processes for removal of *Cryptosporidium* and *Giardia*. *Vet Parasitol* 126(1–2):219–234, PMID: 15567586, <https://doi.org/10.1016/j.vetpar.2004.09.002>.
56. Schmidt MA, Groom HC, Rawlings AM, Mattison CP, Salas SB, Burke RM, et al. 2022. Incidence, etiology, and healthcare utilization for acute gastroenteritis in the community, United States. *Emerg Infect Dis* 28(11):2234–2242, PMID: 36285882, <https://doi.org/10.3201/eid2811.220247>.