











Associations between extreme precipitation, drinking water, and protozoan acute gastrointestinal illnesses in four North American Great Lakes cities (2009–2014)

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ABSTRACT

Climate change is already impacting the North American Great Lakes ecosystem and understanding the relationship between climate events and public health, such as waterborne acute gastrointestinal illnesses (AGIs), can help inform needed adaptive capacity for drinking water systems (DWSs). In this study, we assessed a harmonized binational dataset for the effects of extreme precipitation events (≥ 90 th percentile) and preceding dry periods, source water turbidity, total coliforms, and protozoan AGIs – cryptosporidiosis and giardiasis – in the populations served by four DWSs that source surface water from Lake Ontario (Hamilton and Toronto, Ontario, Canada) and Lake Michigan (Green Bay and Milwaukee, Wisconsin, USA) from January 2009 through August 2014. We used distributed lag non-linear Poisson regression models adjusted for seasonality and found extreme precipitation weeks preceded by dry periods increased the relative risk of protozoan AGI after 1 and 3–5 weeks in three of the four cities, although only statistically significant in two. Our results suggest that the risk of protozoan AGI increases with extreme precipitation preceded by a dry period. As extreme precipitation patterns become more frequent with climate change, the ability to detect changes in water quality and effectively treat source water of varying quality is increasingly important for adaptive capacity and protection of public health.

Key words: climate change, cryptosporidiosis, giardiasis, Great Lakes, public health, water quality

HIGHLIGHTS

- We examined binational source water quality of the North American Great Lakes, as measured at the intakes of four drinking water systems (DWSs), along with the precipitation on the risk of cryptosporidiosis and giardiasis in the populations served by the DWSs.
- When preceded by a dry period, an extreme precipitation week increased the relative risk of acute gastrointestinal illness after 1 and 3–5 weeks for three of the four PWSs studied.

INTRODUCTION

Drinking water safety is a foundational pillar of our modern societies, however, drinking water-associated diseases continue to occur worldwide, including in high-income countries (Benedict *et al.* 2017; Moreira & Bondelind 2017). *Cryptosporidium* and *Giardia* are ubiquitous waterborne protozoan parasites that are responsible for endemic and epidemic acute gastrointestinal illnesses (AGIs) globally, producing symptoms of cramps, diarrhea, and vomiting, and can be fatal to children and people with weakened immune systems (Collinet-Adler & Ward 2010; Efstratiou *et al.* 2017).

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Around the North American Great Lakes, nearly 8.5 million Canadians across the Province of Ontario and 30 million Americans across eight states rely upon the surface waters of the Great Lakes for their drinking water supply (Environment and Climate Change Canada and U.S. Environmental Protection Agency 2021), which are protected by comparable laws in both countries. The presence of *Cryptosporidium* and *Giardia* in the surface waters of Lake Ontario (Edge *et al.* 2013), the St. Lawrence River (Payment *et al.* 2000), and other surface water bodies used for public water supplies across the United States (Ongerth 2013) has been documented. In response to major waterborne disease outbreaks in the United States and Canada traced to contaminated source water (MacKenzie *et al.* 1994; Hrudefy *et al.* 2003), the US Environmental Protection Agency (EPA) and the Ontario Ministry of the Environment strengthened drinking water rules applicable to surface water supplies, which require disinfection and 99.99% (4-log) removal/inactivation of viruses, 99.9% (3-log) removal/inactivation of *Giardia lamblia*, and 99% (2-log) removal of *Cryptosporidium* and additional treatment for water systems vulnerable to source water contamination, among other protective measures (EPA 2006; Ontario 2020). However, despite continual improvements in water quality monitoring and treatment technologies, waterborne protozoan AGIs remain major public health concerns. Across Ontario and the United States, thousands of cases of cryptosporidiosis and giardiasis are regularly reported through all months of the year and are primarily transmitted by waterborne sources (drinking water and recreational water) and occasionally other exposures (person-to-person contact, animal contact, and foodborne) (Gharpure *et al.* 2019; Conners *et al.* 2021; Public Health Ontario 2021). Furthermore, the burden of protozoan AGI is projected to grow with increasing climate change impacts (Lal *et al.* 2013; Chhetri *et al.* 2019).

Extreme rain events and their negative impacts on water resources and human health are expected to be more common across North America and globally given current long-term climate change projections (Caretta *et al.* 2022). Climate change is already impacting the Great Lakes ecosystem as demonstrated by warmer air and water temperatures, greater frequency and intensity of severe storms patterns (e.g., more frequent dry spells followed by extreme precipitation events), increased variability in lake level fluctuations (i.e., record highs and lows), decreased annual average ice cover, and growing migration of pests, diseases, and invasive species from warmer regions (Bartolai *et al.* 2015; Wuebbles *et al.* 2019). Consequently, cases of waterborne diseases increase after heavy precipitation events (Thomas *et al.* 2006; Patz *et al.* 2008; Chhetri *et al.* 2017). More frequent extreme storm events flush pathogens from the watershed, release pollutants from flood events, increase turbidity from large-scale runoff events, and cause more frequent combined sewer overflows (CSOs) (Kistemann *et al.* 2002; Krometis *et al.* 2007; Olds *et al.* 2018). The deluge of pathogens, sediments, and other contaminants from the watershed impairs the quality of the receiving water bodies, which may temporarily overwhelm drinking water treatment and contribute to increased AGI. The projected increase of heavy precipitation and CSO events is a considerable threat to source water quality. Most of the communities served by combined sewer systems in the United States are in the Northeast and Great Lakes regions (EPA 2016), and CSO events are reported across Canada annually (Statistics Canada 2019). CSOs dump a mixture of untreated wastewater and urban runoff into receiving water bodies used for recreation and sources of drinking water, which has been shown to be a significant source of microbial contaminants (Madoux-Humery *et al.* 2016), including large concentrations of *Cryptosporidium* and *Giardia* (Gibson *et al.* 1998), and contaminants of emerging concern (Baker *et al.* 2022). Following CSO events, there have been increased AGI cases reported (Jagai *et al.* 2015; Brokamp *et al.* 2017).

These increasing climate change impacts require greater adaptive capacity and coordinated actions across governments to mitigate their expected worsening effects and to best protect public health. In the Great Lakes region, Bassil & colleagues (2015) identified eight key factors impacting binational environmental and health databases as barriers to conduct objective assessments of environmental health threats, particularly climate change, on public health. These factors included limited availability, accessibility, and gaps in data harmonization, stakeholder collaboration, policy and strategic alignment, resource adequacy, environmental-human health indicators, and binational data exchange networks. This study examined challenges related to limited availability, accessibility, and gaps in data harmonization, and binational data exchange networks.

Based on binational data assembled by the International Joint Commission (Health Professionals Advisory Board 2021), the purpose of this study was to evaluate the utility of routine monitoring of environmental and health data from multiple jurisdictions to inform climate change-relevant health indicators. We did this by assessing the associations of precipitation and water quality indicators with reported cases of protozoan AGI (cryptosporidiosis and giardiasis) in residents of four cities (two in Canada and two in the United States) that rely on the surface waters of the North American Great Lakes for their drinking water supply. Our study is unique in that we successfully obtained, harmonized, and assessed data from multiple jurisdictions across a transboundary watershed over the same time period of January 1, 2009 through August 31, 2014 (5 years and 8 months).

METHODS

Study areas and drinking water treatment processes

We examined precipitation data, surface water quality indicators, and cases of cryptosporidiosis and giardiasis from four cities along the shores of the North American Great Lakes: Hamilton and Toronto, Ontario along the north shore of Lake Ontario and Milwaukee and Green Bay, Wisconsin along the west shore of Lake Michigan. These four cities were chosen because they each have drinking water systems (DWSs) that rely on the surface waters of the Great Lakes and provided data from the DWSs and well-established public health surveillance programs.

Using those data, we assessed the effect of extreme precipitation events and surface water quality indicators on protozoan AGI incidence in these four cities on both sides of the Great Lakes Basin. Cases of cryptosporidiosis and giardiasis were chosen for human health outcomes given prior evidence that extreme precipitation events (≥ 90 th percentile) increase the risk of these diseases and they are largely waterborne (Curriero *et al.* 2001). Sporadic cases of protozoan AGI were studied instead of outbreaks because these cases are more frequent than outbreaks (Bylund *et al.* 2017; Nic Lochlainn *et al.* 2019) and more likely to be related to weather or climate factors than outbreaks, which are generally linked to short-term point-source events (Gharpure *et al.* 2019; Conners *et al.* 2021). All four cities' DWSs consistently monitor for two source water quality indicators (total coliforms and turbidity) allowing for analysis of trends with the protozoan AGI case data.

The geographic areas included in this study were defined by the postal codes roughly corresponding to the DWS service areas of the Green Bay Water Utility, Hamilton Water, Milwaukee Water Works, and Toronto Water. Service area maps were requested from the four DWSs, and protozoan AGI cases from postal codes that overlapped the service areas were included.

All four DWSs obtain their source water from the offshore surface waters of the adjacent Great Lake. Toronto Water has four drinking water treatment plants (DWTPs) with seven active source water intakes withdrawing water from Lake Ontario offshore of the Greater Toronto Area from Etobicoke to Scarborough. Hamilton Water has one DWTP with two active source water intakes in Lake Ontario. Milwaukee Water Works has two DWTPs with two active source water intakes withdrawing water from Lake Michigan. Green Bay Water Utility has one DWTP with one active source water intake located offshore of Kewaunee, Wisconsin, withdrawing water from Lake Michigan. Six of these eight DWTPs use the conventional treatment process of coagulation and flocculation, sedimentation, filtration, disinfection, and fluoridation, with some variation in the chemical inputs. The other two DWTPs, Toronto Water's Horgan DWTP and Island DWTP, use direct filtration (i.e., omit sedimentation prior to filtration). During the study period, half of these DWTPs used ozone disinfection (Green Bay Water Utility, both of Milwaukee Water Works' DWTPs, and Toronto Water's Horgan DWTP, beginning in 2013) while Hamilton Water and Toronto Water's other three DWTPs (Clark, Harris, and Island) did not use ozone disinfection (HPAB 2021).

Datasets

For health data, a request for the reported (laboratory-confirmed) cases of cryptosporidiosis and giardiasis as well as health risk factors (travel history, use of bottled water, recreational water exposure, and daycare center use) for the postal codes served by the DWSs from 2003 through 2016 was sent to the public health agencies – Public Health Ontario (PHO) and the Wisconsin Department of Health Services (WDHS). Cases were extracted from their respective databases based on the episode date. From PHO, protozoan AGI cases and health risk factors from September 2003 through August 2014 were provided. From WDHS, reported cases of protozoan AGI and health risk factors were provided from digitized records from January 2009 through March 2017. The overlapping protozoan AGI cases data that were provided, from January 1, 2009 through August 31, 2014, defined our study period. To calculate incidence, population data were obtained from the 2011 Canadian census and the 2010 US census for the postal codes corresponding with the DWS service areas, which defined our study areas. Details of the study areas are shown in Table 1.

For source water quality data, sampling results for turbidity, total coliforms, *Escherichia coli*, *Cryptosporidium parvum*, *G. lamblia*, nitrates, water temperature, and pH were requested from 2003 through 2016. The DWSs provided sampling results for most of these parameters over this period, but only turbidity and total coliforms were consistently monitored with comparable (i.e., harmonized) sampling frequencies by all four DWSs.

Weather data were obtained from the National Oceanic and Atmospheric Administration (NOAA) and Environment and Climate Change Canada (ECCC) web data portals for the nearest weather station to each city (Table 1). The climate for all

Table 1 | Summary characteristics of study cities

Case city	Green Bay, WI	Hamilton, ON	Milwaukee, WI	Toronto, ON
Drinking water source	Lake Michigan	Lake Ontario	Lake Michigan	Lake Ontario
DWS service area population	231,820	551,778	864,060	2,615,047
Köppen–Geiger climate classification	Dfb – humid continental climate	Dfb – humid continental climate	Dfb – humid continental climate	Dfb – humid continental climate
Weather station name	Kewaunee, WI	Hamilton A	Milwaukee Mitchell International Airport	Toronto East York Dustan
Weather station location (decimal degrees)	44.462, –87.504	43.167, –79.933	42.955, –87.904	43.7, –79.34
Weather station elevation	180.7 m (592.8 ft)	238 m (780.8 ft)	204.2 m (669.9 ft)	125 m (410.1 ft)
Mean annual temperature	12.0 °C (53.5 °F)	8.4 °C (47.0 °F)	13.0 °C (55.5 °F)	9.0 °C (48.0 °F)
Mean annual precipitation	750 mm (29.53 in)	835 mm (32.87 in)	884 mm (34.81 in)	831 mm (32.72 in)

four cities is classified as humid continental climate (Dfb) by the Köppen–Geiger system (Kottek *et al.* 2006) and have similar mean annual air temperatures and precipitation amounts, which suggests direct comparison is feasible. Lake current data were obtained through the NOAA Great Lakes Coastal Forecasting System (GLCFS) for coordinates near the intakes.

Model components

We applied distributed lag non-linear regression models (DLNMs) to examine how precipitation and water indicators were associated with protozoan AGI case counts in each of the four cities. Models were developed individually for each DWS's DWTP (eight total) to incorporate the water quality indicators measured at the DWS's source water intakes and examine the relationship between weather (extreme precipitation and precipitation pattern), source water quality indicators (total coliforms and turbidity), and the city-wide weekly cumulative cases for cryptosporidiosis and giardiasis combined.

An ecological time-series study design was used to assess the relationship between reported cases of cryptosporidiosis and giardiasis (dependent variables) in the population served by their respective DWS and the following environmental independent variables:

- Extreme precipitation week (weekly cumulative precipitation ≥ 90 th percentile);
- Precipitation patterns (dry periods or wet periods) and abrupt precipitation week – i.e., extreme precipitation week (≥ 90 th percentile) following a dry period (defined below);
- Air and water temperature;
- Source water quality indicators of turbidity and total coliforms;
- Lake current direction (onshore or offshore) near the location of the source water intakes.

Due to variations in the frequency of data reporting, all variables were aggregated to weekly frequency to enable harmonized comparisons compatible with the time-series study design and statistical analysis. Cases of protozoan AGI (cryptosporidiosis and giardiasis) were aggregated to 7-day (i.e., weekly) cumulative values. Precipitation was aggregated to 7-day cumulative values. Snowfall was converted to its liquid water equivalent according to the formula: snowfall (mm)/10 = liquid water equivalent (mm). Cumulative precipitation was the sum of rainfall (mm) and snowfall's liquid water equivalent (mm). Air temperature was aggregated to a three-week trailing mean. Source water temperature, turbidity, and total coliforms were aggregated to 7-day mean values.

Extreme precipitation weeks were defined as those meeting or exceeding the 90th percentile of the weekly precipitation distribution across the study period. Use of the 90th percentile cutoff was based on expected increases in source water microbial and turbidity loads following extreme events (Curriero *et al.* 2001; Kistemann *et al.* 2002; Edge *et al.* 2013; Bush *et al.* 2014). Precipitation pattern (dry vs. wet periods) was examined to identify abrupt precipitation weeks (i.e., extreme precipitation week following a dry period). Precipitation pattern was normalized to location using the method of Chhetri & colleagues (2017) – an even distribution of weeks falling in 'dry' and 'wet' periods. Based on the weather data, the best fit for

defining dry periods for Green Bay and Milwaukee was at least 40 days of no precipitation in the previous 60 days. The best fit for defining dry periods for Hamilton and Toronto was at least 35 days without precipitation in the previous 60 days.

Modeled weekly lake current velocity data (speed and direction) at the surface and a depth of 10 m for locations near each DWTP's intake were obtained from NOAA GLCFS. The lake current velocity's directional component was calculated to a weekly average and used to determine a lake current onshore/offshore factor, which was included in the model parameterization exercises.

Statistical analysis

The association between the dependent variable (cryptosporidiosis and giardiasis cases) and independent variables (cumulative precipitation, precipitation pattern, source water turbidity, source water total coliforms, and lake current velocity, direction, and onshore or offshore factor) were tested using a DLNM with a Poisson outcome. Numerous models were fitted using quasi-maximum likelihood to select covariates (e.g., air and water temperature, turbidity, total coliforms, and lake currents) and modeling parameters (e.g., degrees of freedom for spline functions). The best fitting model was determined using the quasi-Akaike's information criterion (qAIC) goodness-of-fit statistic.

The population attributable risk (PAR) is reported as an estimate of the proportion of combined cryptosporidiosis and giardiasis cases in the population that is attributable to extreme precipitation. Relative risk (RR) is approximated from PAR using the relationship $PAR = RR - 1/RR \times 100\%$ (Gasparrini & Leone 2014). Statistical significance was accepted at an α level of 0.05.

All statistical analyses were performed using Microsoft[®] Excel[®] for Office 365, R (R Core Team, v.3.5.3, 2018) and RStudio (RStudio, Inc., v.1.2.5033[©] 2009–2019) software using package *dlm* (Gasparrini 2011).

RESULTS

A total of 3,791 cases of cryptosporidiosis ($n = 545$) and giardiasis ($n = 3,246$) were reported across the four study areas from January 1, 2009 through August 31, 2014 (Table 2). Residents within the Green Bay Water Utility service area had the highest incidence rate of cryptosporidiosis over the 68-month study period (4.27 cases per 10,000 residents). Residents within the Toronto Water service area had the highest incidence of giardiasis (8.84 cases per 10,000 residents) and highest incidence of combined AGI (9.94 cases per 10,000 residents). Residents within the Hamilton Water service area had the lowest incidence of combined AGI (5.46 per 10,000 residents).

The number of combined protozoan AGI cases reported per week ranged from 0 to 6 for Green Bay (Figure 1(a)) and Hamilton (Figure 1(b)), 0 to 10 for Milwaukee (Figure 1(c)), and 1 to 20 for Toronto (Figure 1(d)). The highest number of weekly combined protozoan AGI cases were from July to September, which aligns with the wettest months of the year (Figure 2). However, AGI cases were routinely recorded in every month of the year across all study sites reflecting the sporadic nature of the cases. Total weekly precipitation ranged from 0 to 177 mm for Green Bay (Figure 2(a)), 0 to 100 mm for Hamilton (Figure 2(b)), 0 to 168 mm for Milwaukee (Figure 2(c)), and 0 to 99 mm for Toronto (Figure 2(d)).

Model analysis

Regression analyses among the source water quality indicators and weather indicators showed no correlation; neither between within-group or between-groups (source water quality indicators and weather indicators). Results of the regression analyses are shown in the Supplementary Material (Supplement – available online). To facilitate direct comparison of model

Table 2 | Cases and incidence of cryptosporidiosis and giardiasis for each drinking water system service area from January 1, 2009 through August 31, 2014

DWS service area	Laboratory-confirmed cases			Incidence per 10,000 residents		
	Cryptosporidiosis	Giardiasis	Combined	Cryptosporidiosis	Giardiasis	Combined
Green Bay Water Utility	99	93	192	4.27	4.01	8.28
Hamilton Water	36	265	301	0.65	4.80	5.46
Milwaukee Water Works	122	577	699	1.41	6.68	8.09
Toronto Water	288	2,311	2,599	1.10	8.84	9.94
Overall	545	3,246	3,791	1.28	7.61	8.89

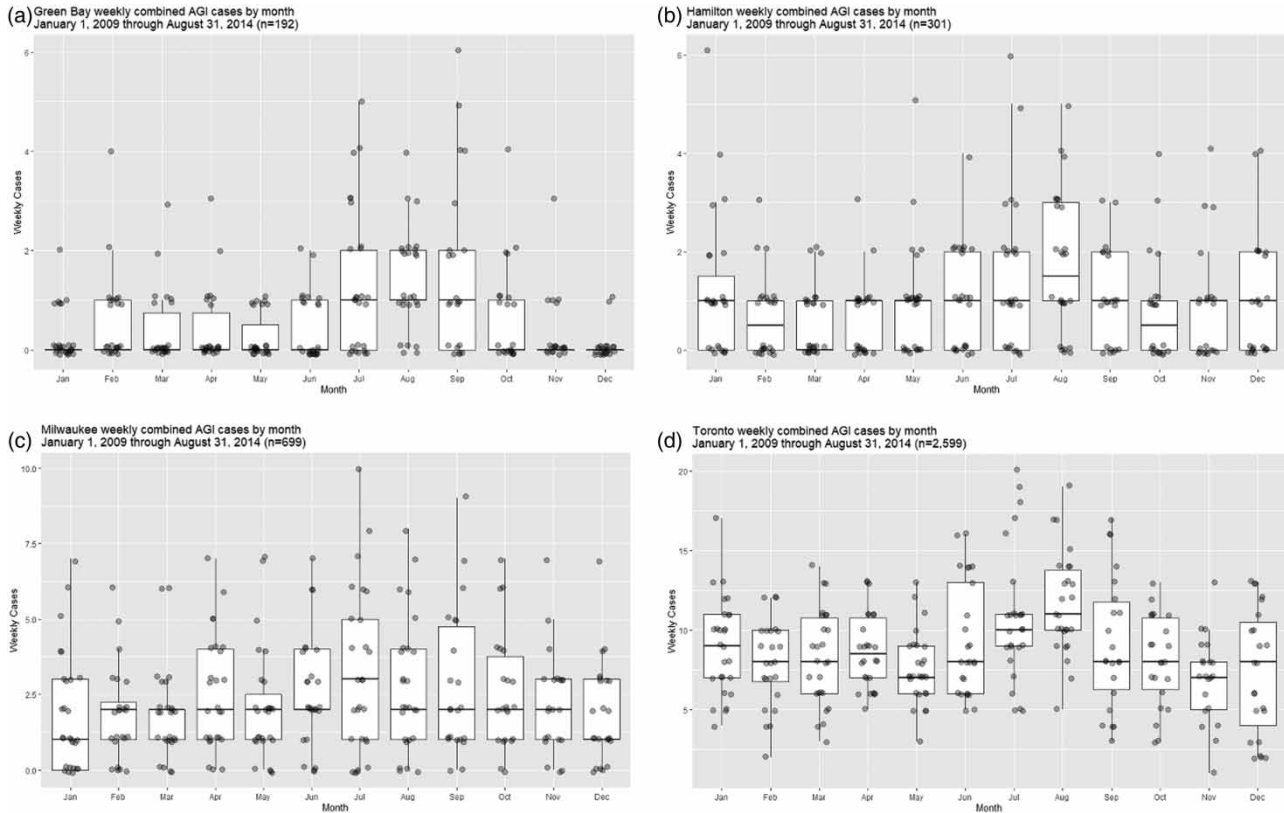


Figure 1 | Boxplots of weekly combined AGI (cryptosporidiosis and giardiasis) cases, grouped by month, for the four case cities. *Note:* the upper whisker extends from the hinge to the highest value that is within $1.5 \times$ IQR of the hinge, where IQR is the interquartile range. Dots represent weekly data points of combined protozoan AGI cases.

results, the final model for all eight DWTPs used these same parameters. From the model parameterization exercises, air temperature (3-week trailing average), surface water temperature (weekly average), and lake current velocity (speed, direction, and onshore/offshore factor) did not improve model fit and were dropped from the final model. The model parameters that produced the best fit for most of the eight DWTPs' datasets and thus comprised the final model's parameters were variables for combined protozoan AGI cases, precipitation, precipitation pattern (wet or dry), source water turbidity and total coliforms, seasonality in cryptosporidiosis and giardiasis (Fourier term), and a factor for public holidays to adjust for their potential impacts on healthcare access. Detailed parameterization of the DLNMs is presented in the Supplementary Material (Supplement – available online).

The population attributable risk of protozoan AGI following an abrupt precipitation week (i.e., extreme precipitation week following a dry period) was modeled from each DWTP's dataset (eight total) and are displayed in Figure 3. For Green Bay, there was no visible trend or statistically significant change to population attributable risk following abrupt precipitation weeks (Figure 3(a)). Hamilton presented the greatest increase in relative risk for AGI. The relative risk was significantly increased 3–5 weeks after abrupt precipitation weeks (Figure 3(b)). There was some variation in the model results for Milwaukee and Toronto, which have multiple DWTPs (two and four, respectively) resulting in multiple streams of data being tested. The two models for Milwaukee's DWTPs showed an increased trend in relative risk that peaked 3–6 weeks after abrupt precipitation weeks, although were not statistically significant (Figure 3(c) and (d)). A peak relative risk 1 week after abrupt precipitation weeks was seen in Toronto's four models (Figure 3(e)–(h)), but only the model for Toronto Island was statistically significant (Figure 3(h)). This was followed by shorter peaks in relative risk around 6 weeks but were not statistically significant.

DISCUSSION

This analysis describes a connection between abrupt precipitation weeks (i.e., extreme precipitation week following a dry period) and protozoan AGI in the populations served by two of the four DWSs with the primary source of surface water

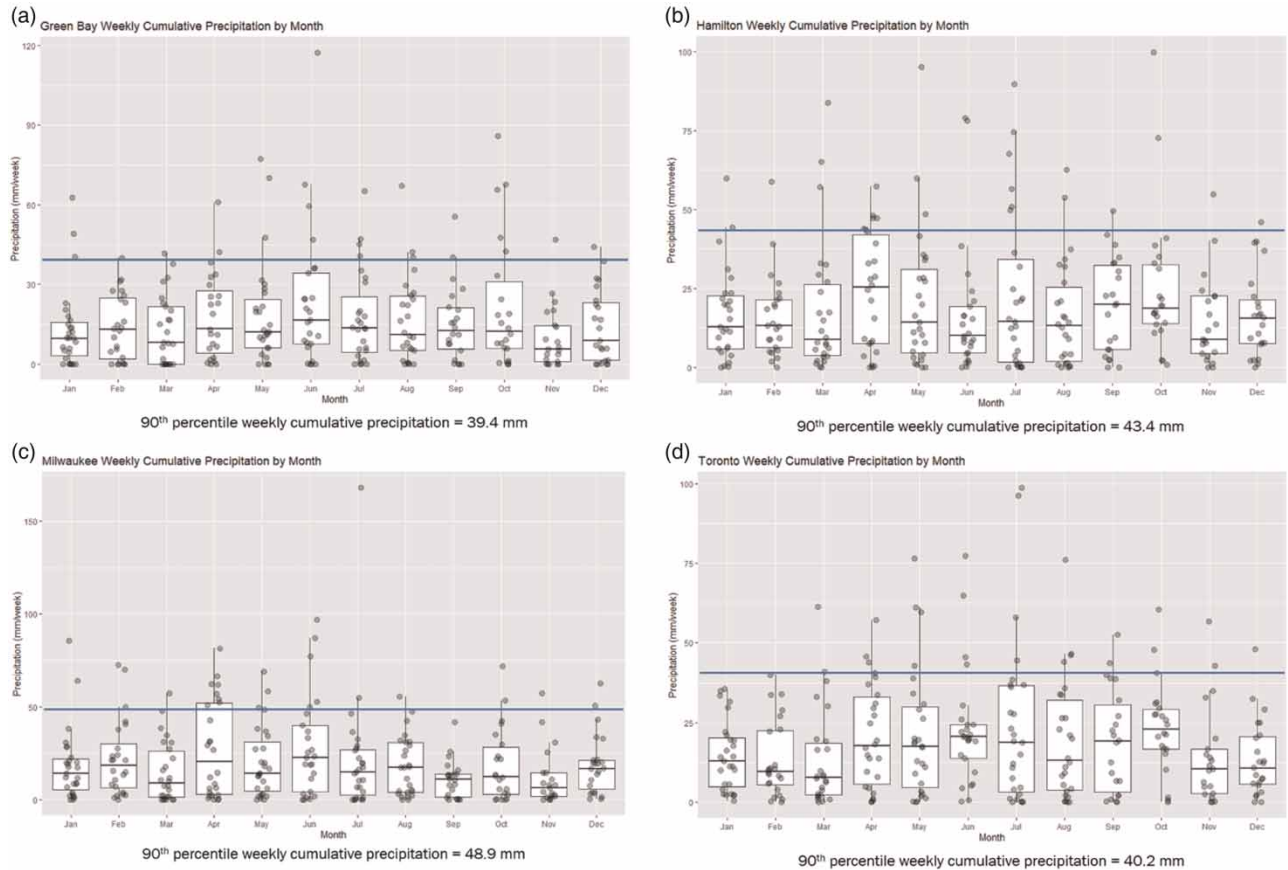


Figure 2 | Boxplots of weekly cumulative precipitation, grouped by month, for the four case cities. *Note:* the upper whisker extends from the hinge to the highest value that is within $1.5 \times$ IQR of the hinge, where IQR is the interquartile range. Dots represent weekly data points. The blue line indicates the 90th percentile of precipitation across the 68-month study period. Please refer to the online version of this paper to see this figure in colour: <http://dx.doi.org/10.2166/wh.2022.018>.

from the North American Great Lakes described here. Furthermore, this work demonstrated that integrated, comparable binational environmental and human health data can be obtained and used for research and modeling to inform the protection of overall human health in the Great Lakes region, which was previously identified as a substantial impediment (Bassil *et al.* 2015).

While other studies have noted that incidence of cryptosporidiosis and giardiasis are sensitive to rain events (Lake *et al.* 2005; Britton *et al.* 2010; Lal *et al.* 2013), this is the first study to our knowledge in the Great Lakes region that has examined source water quality indicators, as measured at DWS source water intakes, along with precipitation, on the risk of protozoan AGI (cryptosporidiosis and giardiasis) in the populations served by those DWSs. Our results add to previous studies that demonstrated an association between heavy precipitation following dry periods and increases in diarrheal diseases (Levy *et al.* 2016; Chhetri *et al.* 2017). This phenomenon may be due to extended dry periods that contribute to soil compaction and a retention of contaminants in the watershed, which when followed by a heavy precipitation event, enables overland runoff into sources of drinking water, leading to increased turbidity and pathogen loads (Lake *et al.* 2005; Krometis *et al.* 2007) and consequently can temporarily overload drinking water treatment processes allowing pathogens to pass through to the distribution system and ultimately to residents' taps where they are consumed resulting in AGI (Fox & Lytle 1996; Moreira & Bondelind 2017). Chlorine-based disinfectants that are used to comply with disinfection treatment requirements and to achieve the required minimum disinfectant residual in the distribution system are not effective at inactivation of *Cryptosporidium* and *Giardia* (Betancourt & Rose 2004), which emphasizes the importance of source water protection and removing these protozoa in the treatment process preceding chlorination.

The variation in the effect sizes, statistical significance, and lag time for peak risk for each city may be due to differences in the drinking water treatment processes, distribution system factors, and variation in AGI reporting. The DWSs that use ozone

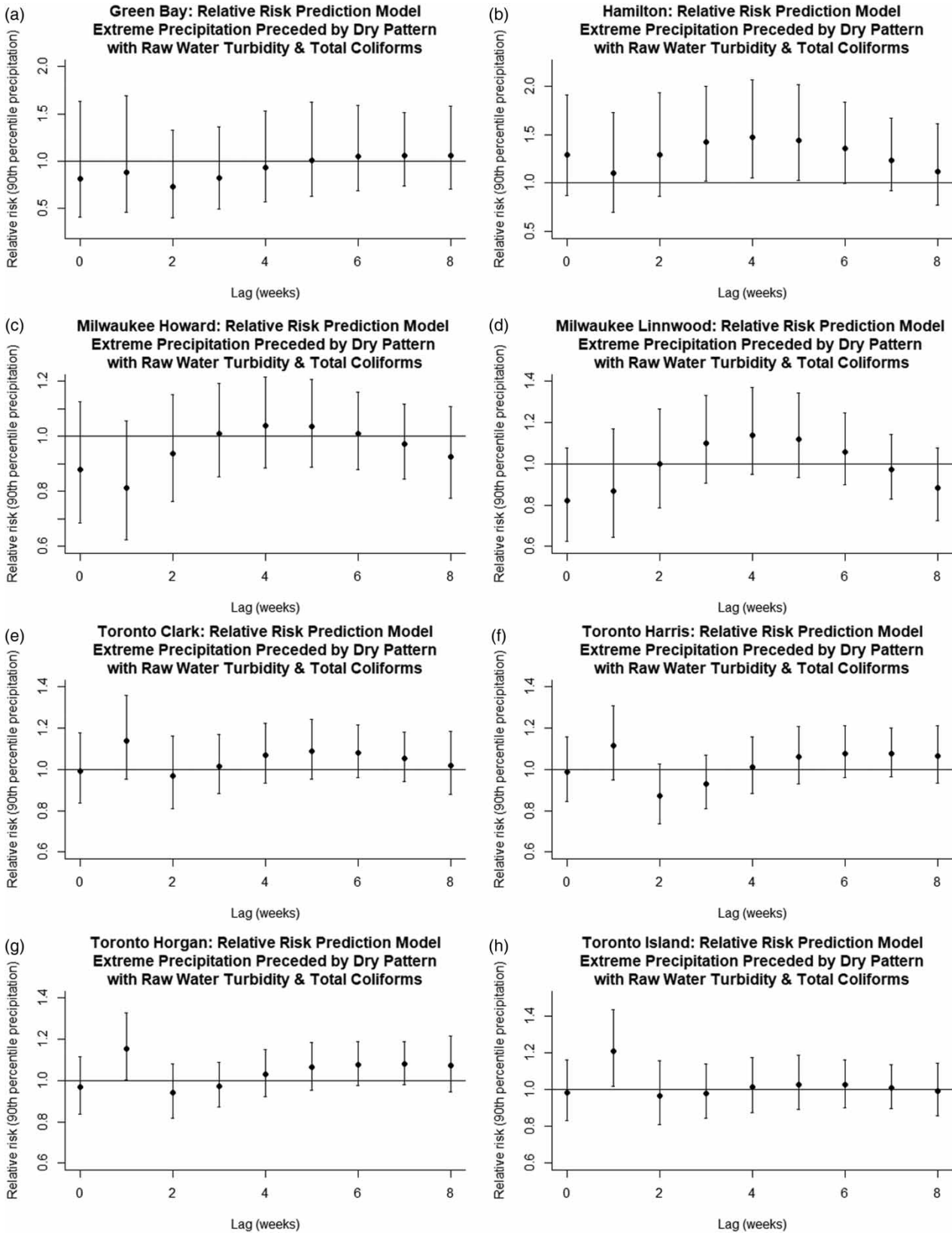


Figure 3 | Relative risk of AGI (cryptosporidiosis and giardiasis) following extreme precipitation (≥ 90 th percentile precipitation week) preceded by a dry period by DWTP.

disinfection (Green Bay Water Utility, both of Milwaukee Water Works' DWTPs, and the Toronto Water's Horgan DWTP) did not have a significant increase in relative risk, but the model for Hamilton Water which omits ozone disinfection did have a significant increase in relative risk 3–5 weeks after an abrupt precipitation spike. Previous studies have demonstrated that ozonation is effective at inactivating *Cryptosporidium* and *Giardia* (Morrison *et al.* 2022). Another difference among the water treatment processes is the use of direct filtration (i.e., no sedimentation prior to filtration) at Toronto Water's Horgan DWTP and Island DWTP, whereas the other six DWTPs we studied all use sedimentation prior to filtration (i.e., conventional treatment). The model for Toronto Island had a significant increase in relative risk one week after abrupt precipitation spikes. This may be due to direct filtration achieves less filtration and removal of pathogens than conventional treatment (Tfaily *et al.* 2015). Conversely, the model for Toronto Horgan did not have a significant increase in relative risk, which notably began using ozonation in 2013 covering the final third of our study period. Other potential explanatory factors are variation in water residence time in the distribution system (i.e., water age) (Tinker *et al.* 2009), distribution system deficiencies (Craun & Calderon 2001; Murphy *et al.* 2016), and differences in healthcare access, culturally-based responses to illnesses, and other diagnostic delays that contribute to delayed and underreporting of AGI (Sargeant Majowicz & Snelgrove 2008).

The power to achieve significant results in every model may have been limited given the modest number of reported protozoan AGI cases. This may be due in part to our choice to only use cases of cryptosporidiosis and giardiasis that were laboratory-confirmed, which are the most highly validated type of data but also most likely to underestimate the true disease incidence (Sargeant Majowicz & Snelgrove 2008). Other types of health outcomes data could be used in future studies but would sacrifice specificity. Likely, the most practical would be health data from syndromic surveillance of symptoms, such as emergency department chief complaints or other data associated with symptoms like sales of anti-diarrheal medications. Such systems are underway or under consideration across the United States and in Ontario (Public Health Ontario, Provincial Infectious Diseases Advisory Committee 2012; Papadomanolakis-Pakis *et al.* 2021; Centers for Disease Control and Prevention 2022). Alternately, future AGI incidence estimates may be available from systems that enable geographic queries of aggregated electronic health record data (Bacon *et al.* 2019). Although, a regional health data system is unlikely to be available around the entire perimeter of Great Lakes due to numerous jurisdictional barriers.

Notably, Green Bay had the fewest protozoan AGI cases across the study period ($n = 192$) relative to the other more populous cities and thus there was low statistical power to detect an effect. Green Bay is the only one of these four case cities that has a separate sanitary sewer system instead of a combined sewer system, alleviating the risk for CSO events that occur following heavy rainfall events, which are sources of pollution, including *Cryptosporidium* oocysts and *Giardia* cysts (Gibson *et al.* 1998), to receiving water bodies that are used for recreation and sources of drinking water. Unfortunately, measurements from sewer overflow events, whether from sanitary sewer overflows in Green Bay or CSO events in the other three case cities, were not available for this study because most sewer overflow outfalls in these cities are not metered but instead are modeled based on precipitation data.

It was not possible to compare the relative exposure contribution from multi-DWTP systems like Toronto (four DWTPs) and Milwaukee (two DWTPs) due to poor alignment of AGI cases geographic data at the postal code level with the DWTPs' service areas and the mixing of finished water from each DWTP in the distribution system. This limited the attribution between each DWTP's model results and protozoan AGI cases. To determine which AGI cases were of residents from within the DWTPs' service areas, more granular geographic information with the health data is needed (e.g., first three digits of the patient's street address to identify city block) as well as digital maps of the DWTPs' service areas and information about mixing in the distribution system (e.g., proportion of finished water from each DWTP in each pressure zone over time). With the postal code-level health data we received, we could not exclude AGI cases of individuals who reside in a postal code serviced by the DWS but outside of the DWS's service area, and thus likely included some AGI cases beyond the DWS service areas.

The number of reported cases of protozoan AGI in our study and their seasonality with a spike in cases during the summer months of July, August, and September were consistent with AGI incidence reports in Ontario and Wisconsin (Greig *et al.* 2001; Vrbova *et al.* 2012; WDHS 2018). Not all sporadic protozoan AGI cases are attributable to DWS water consumption (Bylund *et al.* 2017; Nic Lochlainn *et al.* 2019). However, numbers of cases reported here for colder months (i.e., October through April) imply that other common sources of exposure (e.g., recreational water, person-to-person, animal contact, and foodborne) are unlikely to explain many cases. Furthermore, a Fourier term was also included in the model to adjust for seasonality in AGI cases. Infections from non-DWS exposures would bias towards null results, increasing confidence that our results reflect interactions between weather and water quality as a major contributor. Further examination of the

observed spatial variation in disease incidence beyond DWS boundaries and other potential exposures (recreational water, person-to-person, and animal contact) could help address confounders. Using data from public health outbreak investigations may allow adjustment for confounding risk factors in future analyses. Additionally, in order to overcome the limits of low case numbers, greater monitoring of source water directly for protozoan oocysts could be used to examine the treatment log removals and risks as estimated with quantitative microbial risk assessment (Smeets *et al.* 2007).

This study was designed to assess the feasibility of using binational databases for the assessment of protozoan AGI risk from drinking water sourced from surface waters of the Great Lakes in relation to extreme precipitation events. It revealed that such an analysis is possible, despite the limitations of data access, availability, and harmonization as barriers (Bassil *et al.* 2015). In fact, a strength of our study was the ability to harmonize health, weather, and water quality data for 68 months across four cities in two nations. Notably, while more protozoan AGI data were provided (Ontario provided protozoan AGI data from October 2003 through August 2014 and Wisconsin provided protozoan AGI data from January 2009 through March 2017), for our ecological time-series study design, only the protozoan AGI data that overlapped (January 2009 through August 2014) could be used.

Most of the requested source water quality indicators (turbidity, total coliforms, *E. coli*, *C. parvum*, *G. lamblia*, nitrates, water temperature, and pH) were provided, but the sampling frequencies for the same indicator across the four DWSs varied widely – daily, weekly, monthly, and annually – and were not monitored over the same time periods. Thus, only the harmonized water quality data (turbidity and total coliforms) could be used in our ecological time-series study. Additionally, these variations in data granularity between study areas required aggregating all data (health, water, and weather) into weekly blocks, which may have impacted our models' results (Alarcon Falconi *et al.* 2020). Future studies should use finer resolution temporal (e.g., daily) and spatial (e.g., city block to match DWS service area) data to gain greater specificity.

To specifically identify vulnerabilities in the drinking water treatment and delivery process that may result in AGI, future investigations should analyze sample results for a uniform suite of indicators taken from source water intakes and treated water at both the point-of-entry to the distribution system and throughout the distribution system. Compared to source water quality, the treated water quality at the point-of-entry to the distribution system reflects treatment plant effectiveness, whereas treated water quality throughout the distribution system could reveal issues with the distribution system, such as back-siphonage of shallow groundwater or cross-contamination from nearby damaged sewerage pipes that can cause AGI (Craun & Calderon 2001; Murphy *et al.* 2016). Under current drinking water rules in both the United States and Ontario, there is not a consistent suite of indicators required to be monitored and reported across these three sampling locations to enable this analysis. We suggest a consistent suite of indicators include the pathogens in this study – *Cryptosporidium* and *Giardia* – and the other biological and chemical indicators of water quality (e.g., *E. coli*, turbidity, nitrates, atrazine, and cyanotoxins) that were previously recommended to the governments (HPAB 2014). Notably, the source water quality data we received demonstrate that these four DWSs sample for indicators beyond the regulatory monitoring and reporting requirements, which are used for DWSs' operational and research purposes. Thus, DWSs have more sampling data than the regulators and are important partners in understanding water quality from source to tap and protecting public health.

The challenges accessing health and water quality data underscore the importance of developing ongoing, longitudinal, granular, and consistently measured indicators across locations, regardless of nation, state, or province. Despite long-standing disease and environmental monitoring programs in both countries, much of the data for this study had to be assembled from a combination of federal (weather data), state/provincial (health data) and municipal (source water data) entities, which required a high level of effort. In each country and binationally, to our knowledge, no clearinghouse exists for drinking water quality from source to tap, which would reduce many of the barriers to conduct similar research.

CONCLUSIONS

Our results revealed a trend toward increased risk of protozoan AGI (cryptosporidiosis and giardiasis) following abrupt precipitation weeks (i.e., extreme precipitation week preceded by a dry period) for three of four large cities included in our study, though only statistically significant in two. As extreme weather events become more frequent with climate change, the ability to detect changes in water quality and effectively treat source water of varying quality is increasingly important for adaptive capacity and protection of public health. In evaluating future risk scenarios and infrastructure investments, governments and water treatment system managers should consider the potential implications of climate change on precipitation patterns and source water quality. This should be translated into improvements in monitoring and treatment needs for the full design life of

proposed water infrastructure (60–100 years) to become more resilient to climate-driven stressors and to mitigate these increasing risks to public health.

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ETHICS STATEMENT

The study protocol was approved by the appropriate Committee for the Protection of Human Participants by Simon Fraser University, British Columbia, Canada; study number: 2016s0607; approval date: November 4, 2020. The Denver Health and Hospital Authority Quality Improvement & Research Committee determined on June 25, 2018 that this work is not human subject research as defined in US 45 CFR 46 and thus exempt from further review.

DATA AVAILABILITY STATEMENT

Data cannot be made publicly available; readers should contact the corresponding author for details.

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