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Seasonal variation of acute gastro-intestinal illness by hydroclimatic regime and drinking water source: a retrospective population-based study

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ABSTRACT

Acute gastro-intestinal illness (AGI) is a major cause of mortality and morbidity worldwide and an important public health problem. Despite the fact that AGI is currently responsible for a huge burden of disease throughout the world, important knowledge gaps exist in terms of its epidemiology. Specifically, an understanding of seasonality and those factors driving seasonal variation remain elusive. This paper aims to assess variation in the incidence of AGI in British Columbia (BC), Canada over an 11-year study period. We assessed variation in AGI dynamics in general, and disaggregated by hydroclimatic regime and drinking water source. We used several different visual and statistical techniques to describe and characterize seasonal and annual patterns in AGI incidence over time. Our results consistently illustrate marked seasonal patterns; seasonality remains when the dataset is disaggregated by hydroclimatic regime and drinking water source; however, differences in the magnitude and timing of the peaks and troughs are noted. We conclude that systematic descriptions of infectious illness dynamics over time is a valuable tool for informing disease prevention strategies and generating hypotheses to guide future research in an era of global environmental change.

Key words | acute gastro-intestinal illness, climate change, ecological determinants, seasonality

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INTRODUCTION

> 'Whoever wishes to investigate medicine properly, should proceed thus: in the first place to consider the seasons of the year, and what effects each of them produces, for they are not all alike, but differ much from themselves in regard to their changes.'
>
> Hippocrates (Lloyd *et al.* 1978)

Acute gastro-intestinal illness (AGI) is a major cause of mortality and morbidity worldwide (Prüss *et al.* 2002). Estimates suggest that AGI infections cause four million cases of diarrhea worldwide each year (WHO 2000). In developing nations, diarrhea is the third leading cause of death (WHO 2008). Although mortality due to AGI in developed nations is relatively low, the morbidity, associated socio-economic costs, and burden to the health care system remain high (Payment & Riley-Buckley 2002; Majowicz *et al.* 2006; Fleury *et al.* 2009). Additionally, major waterborne outbreaks such as the Walkerton, Ontario example in 2001 are reminders of the potentially devastating population health impacts of waterborne AGI (Ali 2004; Eggertson 2008). Despite the fact that AGI is currently responsible for a huge burden of disease throughout the world and is a major public health problem, important knowledge gaps exist in terms of its epidemiology. Specifically, an understanding of seasonality, the systematic periodic occurrence of illness, and those factors driving seasonal variation remain poorly understood (Grassly & Fraser 2006; Naumova 2006; Fisman 2007; Lal *et al.* 2012).

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The causes and consequences of seasonal variation in infectious disease occurrence have intrigued medical professionals and epidemiologists for more than a century (i.e. Ransome (1880); Lloyd *et al.* (1978)). More recently, increasing concerns regarding global environmental change, globalization and 'an apparent surge in infectious disease emergence' and re-emergence have inspired a renewed interest in the seasonality of infectious illness (Fisman 2012; Lal *et al.* 2012). The dynamics of AGI are surely influenced by a complex interaction of ecological, social, and biological determinants; however, waterborne AGI in particular is mediated by ecological factors that influence drinking water quality and quantity (Eisenberg *et al.* 2007; Institute of Medicine (US) 2009; Lal *et al.* 2012). Ecological drivers have not been adequately explored due to the dominant public health paradigm that is largely focused on individual level risk factors (McMichael 1999; March & Susser 2006; Ruiz-Moreno *et al.* 2007; Eisenberg *et al.* 2012; Lal *et al.* 2012).

The role of hydroclimatology, a term commonly used to describe the dominant climatic drivers for watershed responses (Allen *et al.* 2010), is one such ecological factor that has not been adequately explored to date. Recent advances have been made with regards to our understanding of cholera epidemiology, in part due to increased interest and research pertaining to environmental drivers of seasonality, including hydroclimatology (Bertuzzo *et al.* 2012). The work of Akanda *et al.* (2011) and Bertuzzo *et al.* (2012) has highlighted ways in which distinct hydroclimatic regimes can influence pathogen transmission and disease occurrence in different ways, resulting in distinct seasonal patterns of illness at the population level. Hydroclimatology may play a role in driving the seasonality of AGI. Other potentially important ecological drivers of seasonality include drinking water source, agricultural and other land use activities, and variations in wild animal populations. Herein, we examine the dynamics of AGI over time and across different hydroclimatic regimes and drinking water sources to explore whether and how these factors may drive seasonality of AGI.

A better understanding of AGI seasonality, those factors driving disease dynamics, and differences in seasonality across settings is key to disease prevention at the population level. More specifically, this knowledge can facilitate the prediction and forecasting of longer-term changes in the risk of illness, inform effective disease prevention and control strategies, and improve the accuracy of early warning systems (Pascual & Dobson 2005; Altizer *et al.* 2006). Infectious diseases that vary seasonally demonstrate some form of climatic dependence and are most likely to be influenced by climate change and variability. Hence, a greater understanding of seasonal variation can play an important role in the climate change adaptation process (McMichael 2003; Fleury *et al.* 2006; WHO 2010). Furthermore, an in-depth understanding of past and current seasonal variation in infectious illness epidemiology can provide a baseline for monitoring the early impacts of climate change on health (Martens & McMichael 2002). Lastly, exploring disease dynamics, and specifically how these vary by relevant factors and across different settings, can generate hypotheses and highlight future research priorities.

This paper analyses variations in the incidence of AGI in British Columbia (BC), Canada over the period of 1999–2010 in order to answer the following questions: (1) Does the incidence of AGI in BC, Canada illustrate a seasonal pattern? (2) Does the seasonal pattern of AGI in BC differ according to hydroclimatic regime and drinking water source? and (3) Has the incidence of AGI in BC changed over time? Several different methods are applied in order to provide a complete picture and robust understanding of seasonality in AGI incidence. To the best of our knowledge, this is the first study to describe and compare seasonal patterns of AGI by hydroclimatic regime and drinking water source.

METHODS

Design

We conducted a retrospective, population-based study to assess the seasonality of reported and laboratory confirmed AGI cases from January 1, 1999 to January 1, 2010 in targeted communities in the province of BC. This study was approved by the Simon Fraser University (SFU) Research Ethics Board for the use of secondary data.

Setting

BC, Canada was selected as the setting for this work for several reasons. First, the province offers a rich diversity of hydroclimatology and drinking water sources, thus acting as a unique case study to examine the seasonal patterns of gastrointestinal illness across these factors (Allen *et al.* 2010). Second, a province-wide surveillance system, the Integrated Public Health Information System (iPHIS), operational since the late 1990s, offered access to laboratory-confirmed illness data of high quality and adequate time span for the analysis for seasonal disease dynamics. Third, despite the fact that AGI rates are higher in this province than the rest of the country, a knowledge gap exists with regards to seasonality of infectious AGI in this setting (Davies & Mazumder 2003).

The hydroclimatology of BC can be broadly classified as rainfall-dominated (pluvial) and snowmelt-dominated (nival) (Allen *et al.* 2010). Rainfall-dominated regimes are found primarily in coastal lowland areas and snowmelt-dominated regimes occur in the interior plateau and mountain regions (Eaton & Moore 2010). The hydrology of rainfall-dominated regimes is characterized by seasonal changes in rainfall, with peak streamflow and groundwater recharge occurring during the rainy winter months (November–February) and the lowest monthly streamflows and groundwater levels occurring in the late summer and early fall (July–September) (Eaton & Moore 2010). On the other hand, hydrological processes in snowmelt-dominated regimes are controlled primarily by melting snowpack and glaciers. Thus, the hydrology of snowmelt-dominated regimes is characterized by the highest flows occurring in the spring and early summer, and the lowest flows in the late summer and throughout the winter (Eaton & Moore 2010).

Drinking water sources in BC include groundwater, surface water, or a mixture of groundwater and surface water (hereafter referred to as mixed water). Approximately 30% of BC residents rely on groundwater for drinking water (Government of Canada 2007).

Eight study communities were selected from across the province of BC for this analysis. These eight communities were selected to represent different combinations of hydroclimatic regimes and drinking water sources relevant across the province, as illustrated in Figure 1.

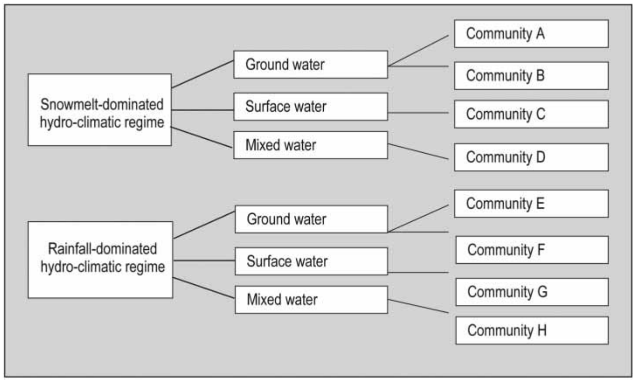

Figure 1 | Hydroclimatic regimes and drinking water sources across the study communities.

Case data

Physicians in BC are mandated to report cases of notifiable waterborne illness to regional public health authorities, who in turn report cases to the BC Centre for Disease Control through iPHIS. Five potentially waterborne AGI pathogens are included in this study: *Campylobacter, Salmonella, verotoxigenic Escherichia coli, Giardia, and Cryptosporidium*. The first three are bacterial pathogens while the latter two are protozoan. Reported cases along with information on age at onset of illness, sex, disease type, serotype, episode date, report date, address, and a unique identifier were extracted from the iPHIS system for the selected study communities.

A total of 89 cases (3.9% of all reported cases) were excluded. Cases were excluded if they were identified as travel cases (identified by disease subtypes known to be only travel related), or were identified as clearly outside of the study community after geocoding the cases (for example, on a nearby island or more than 75 km from the center of the study community). We expect that travel cases remain in our dataset as the travel variable was poorly populated.

Linking cases to a drinking water source

Cases were geocoded by street address and postal code of residence using a geographic information system (GIS) in ArcMap10.0 (ESRI, Redlands, CA, USA). A spatial join function was then performed to assign each case to a specific drinking water system based on land parcel information, ultimately linking each case to a drinking water source. More specifically, we gathered spatial data indicating water service areas for the various drinking water systems within each study community, and province-wide layers indicating the location of groundwater wells and surface water extraction points. Information about small community systems was gathered from community water managers and manually added to the GIS. Using these spatial datasets, we assumed that all cases linked to a residential land parcel located within a drinking water system service area were serviced by that system, and thus we assigned the case the associated water source *unless* there was an active surface water extraction license, groundwater well, or small community system linked to the land parcel. This method of linking case data to a drinking water system and source is adapted from the work of Jones *et al.* (2006).

Generating time-series

We generated monthly times-series with rates expressed as the number of cases per month per 100,000 population for the entire dataset and for cases disaggregated by hydroclimatic regime and drinking water source.

The variable 'episode date' (defined as the date of symptom onset) was used to derive the day, month, and year of illness occurrence, and then to generate monthly time-series representing the number of cases per month over the 132-month study period. Monthly rates were then generated using total population at risk derived from census data as the denominator. Population at risk within each community was estimated spatially using aggregates of dissemination area population totals – the smallest administrative unit with census derived data. Population at risk was calculated at two points during the 11-year study period, 2001 and 2006, and an average population at risk over the study period was generated.

We also estimated population at risk totals for the different hydroclimatic regimes and water sources of interest. To generate population totals for each hydroclimatic regime, we pooled the population counts for those communities located in snowmelt-dominated regimes and for those communities located in rainfall-dominated regimes. This pooling approach could not be used to generate population at risk estimates for each drinking water source, because communities D and H (Figure 1) are characterized by some entirely groundwater systems, some entirely surface water systems, and others that are a mix of both groundwater and surface water. In these cases, information from local community officials and water managers regarding service populations for all community water systems was used to estimate the proportion of the total population serviced with each type of water source. This proportion was then applied to the total population of communities D and H to estimate the population in these two communities supplied with groundwater, surface water, and mixed water. The calculations were then used to generate total estimated population at risk for each drinking water source.

Analysis

We used time-series plots, monthly plots, negative binomial models, and spectral analysis as visual and statistical tools to characterize the seasonal and secular trends in the AGI time-series. Analysis involved the use of several graphical and statistical techniques to triangulate findings and provide a more robust understanding of disease dynamics. We applied each of these methods to the full dataset and to the dataset disaggregated by cases occurring in each hydroclimatic regime and linked to each drinking water source. By examining seasonal variation in the times-series disaggregated by these selected factors, seasonal patterns under different conditions were evaluated.

(1) *Time-series plots:* To reflect trends in AGI data, we plotted the 11-year time-series of monthly AGI incidence. The time-series was smoothed using the three-month moving average, a basic smoothing technique, to enhance interpretation of trends (Zeger *et al.* 2004). By superimposing the time-series disaggregated by hydroclimatic regime and drinking water source, similarities and differences across these factors could be explored.
(2) *Monthly plots*: Total monthly incidence over the 11-year study period was calculated and plotted. Again, we superimposed the total monthly incidence over the 11-year study period disaggregated by hydroclimatic regime and drinking water source. Also, negative binomial regression models using PROC GLM were used to test statistical significance of monthly variation. A negative binomial was used rather than a Poisson model due to over-dispersion in the data as indicated by deviance factors greater than 1 (Osgood 2000). The month with the lowest number of

cases was used as the reference month as per convention (Naumova et al. 2000).

(3) *Spectral analysis:* Spectral analysis is useful for detecting periodicities (dominant cyclical patterns) in time-series and to test data for seasonality (Cryer & Chan 2008). We constructed a periodogram to identify influential periodicities present in the AGI data. We also tested the statistical significance of seasonal patterns using two formal tests: the Fisher–Kappa (FK) test and the Bartlett Kolmogorov–Smirnov (BKS) test. The FK tests the hypothesis that the series is white noise against the alternative hypothesis that the series contains a periodic component of unspecified frequency. The BKS tests the null hypothesis that the series is white noise, or that there is no periodicity.

(4) *Annual plots:* Finally, we examined secular trends in the data using simple plots of illness rates across the 11-years in the study period. Additionally, a negative binomial regression model was used to test the statistical significance of variation across years relative to 1999.

Table 1 | Characteristics of all AGI cases, 1999–2010

Characteristic	No. of Cases ($n = 2308$)	% of Total
Pathogen type		
Bacterial	1,805	78.2
Protozoan	458	21.8
Hydroclimatic regime		
Snowmelt-dominated	1,081	47.0
Rainfall-dominated	1,227	53.1
Water source		
Groundwater	700	30.3
Surface water	1,011	43.8
Mixed water	597	25.9

Statistical analyses were carried out using SAS software, version 9 (SAS Institute, Inc., Cary, North Carolina) and graphs were created using Microsoft Excel.

RESULTS

During the study period from January 1, 1999 to January 1, 2010 2,308 cases of AGI were reported to iPHIS after excluding known travel cases and cases outside the study communities. Of the total 2,308 cases, 1,805 cases (78%) were caused by bacterial pathogens and 458 cases (22%) were caused by protozoan pathogens (Table 1). The incidence of AGI across age categories is bimodal with one peak among children less than 5 and another between the ages of 20–30. A similar pattern is seen for males and females (Figure 2).

Time-series plots

Visual examination of the time-series plots for all cases illustrates a clear pattern in the data characterized by annual cyclical peaks and troughs (Figure 3(a)). The timing and amplitude of the peak rates clearly vary from year to year. In some years, the time-series illustrates a bimodal peak, a large peak in the summer followed by a second smaller

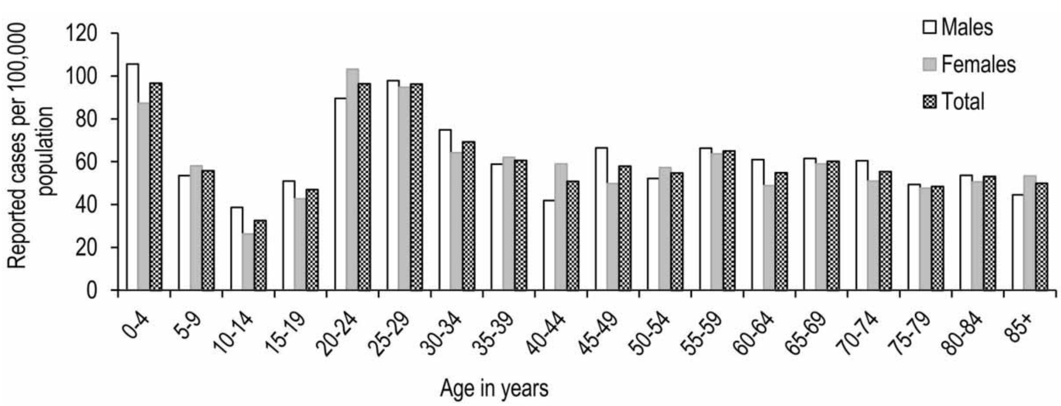

Figure 2 | AGI rates per 100,000 by sex and age, 1999–2010.

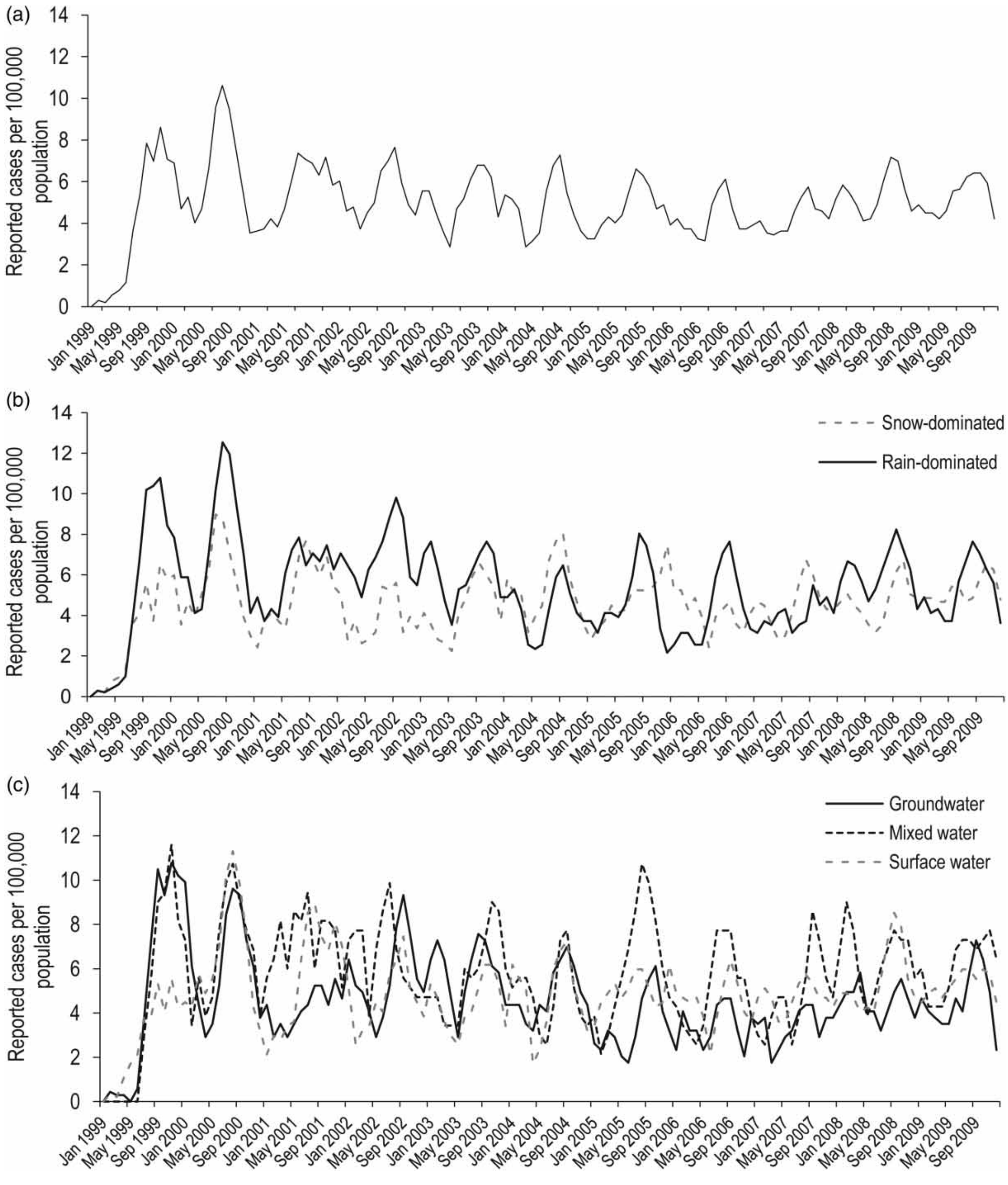

Figure 3 | Time-series of monthly AGI rates (1999–2010); (a) for all cases, (b) by hydroclimatic regime, and (c) by water source.

peak in the fall, while in other years there is a single summertime peak. There is a range of peaks across the years; however, more than half of the years in the study period illustrate a peak incidence in July and all years show peak incidence in the summer or fall months.

Cyclical patterns remain, although the amplitude and timing of peaks and troughs differ when the cases are disaggregated by a hydroclimatic regime (Figure 3(b)) and drinking water source (Figure 3(c)). However, it is difficult to identify any consistent patterns in the time-series plots across these factors. For example, in some years the seasonal cycles in Figure 3(b) show an earlier peak among those cases occurring in snow-dominated regimes compared to those cases occurring in the rainfall-dominated regimes, while in other years the opposite is the case. Aside from the consistently higher peaks among those cases linked to a mixed water source, there are no clear or consistent trends looking at the time-series disaggregated by drinking water source.

Monthly plots

Figure 4 shows the monthly plots of AGI incidence. The monthly incidence for all cases (Figure 4(a)) illustrates a seasonal pattern with the trough occurring in April and a peak occurring from July to September (summertime). Statistically significant peak incidences were found in July (incidence risk ratio (IRR) = 2.21, 95% confidence interval (CI): 1.79–2.73), August (IRR = 2.00, 95% CI: 1.62–2.48) and September (IRR = 2.13, 95% CI: 1.72–2.64) (Table 2).

Among those cases occurring in rainfall-dominated regimes, the trough incidence occurs in April and the peak incidence occurs in September (IRR = 2.37, 95% CI: 1.78–3.17) (Table 2). In contrast, the trough among those cases in the snowmelt-dominated regime occurs in March and the peak incidence occurs in July (IRR = 2.36, 95% CI: 1.75–3.20) (Table 2) with a steady decline through the fall and winter (Figure 4(b)).

Monthly plots by drinking water source show that the timing of the peak occurs during different months of the summer and early fall across different drinking water sources (Figure 4(c)). Among those cases linked to a surface water source, the seasonal peak occurs in July–September (IRR-July = 2.44, 95% CI: 1.77–3.38; IRR-Aug = 2.16 95% CI: 1.55–3.01; IRR-Sept = 2.07 95% CI: 1.49–2.90) (Table 2). Similar patterns are seen in those cases linked to a groundwater source where the peak incidence also occurs from July through to September (IRR-July = 2.03, 95% CI: 1.40–2.93; IRR-Aug = 2.01, 95% CI: 1.39–2.90; IRR-Sept = 2.00, 95% CI: 1.38–2.9) (Table 2). For those cases linked to a mixed water source the peak incidence occurs in September (IRR = 2.41, 95% CI: 1.59–3.63), with another smaller peak in July (IRR = 2.09 95% CI: 1.37–3.17) (Table 2).

The magnitude of the peak of incidence is greatest among cases occurring in a rainfall-dominated hydroclimatic regime and linked to mixed water sources.

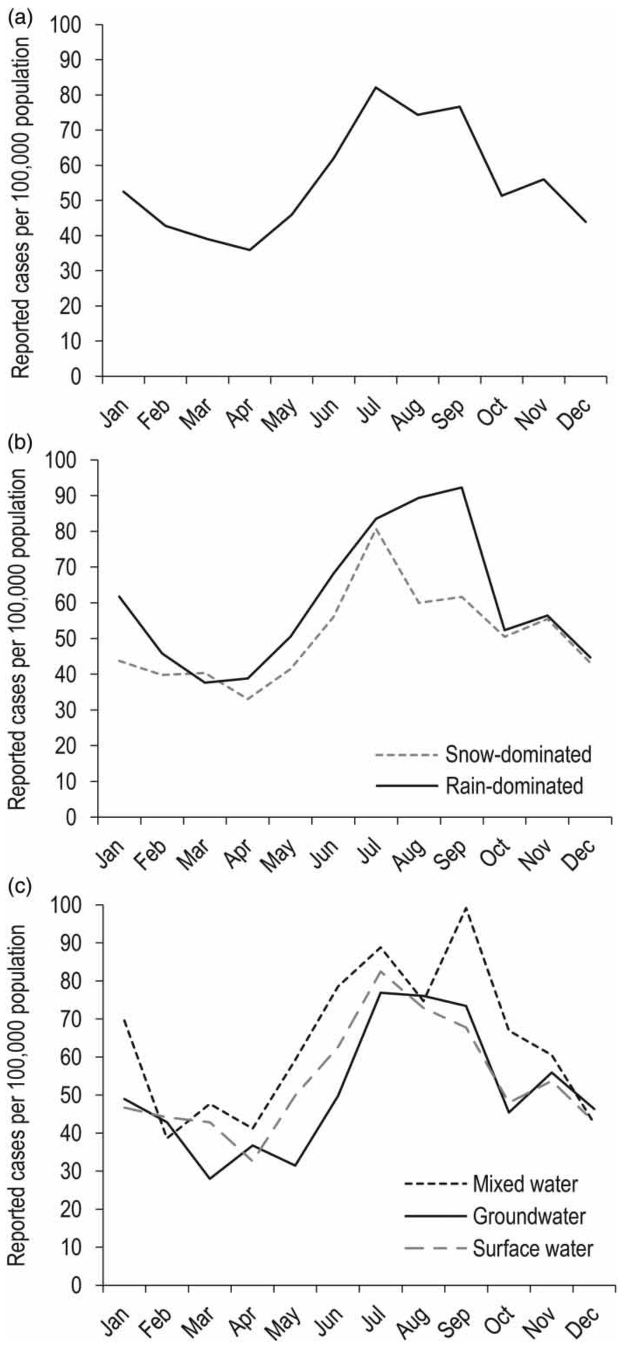

Figure 4 | Total monthly AGI rates (1999–2010); (a) for all cases, (b) by hydroclimatic regime, and (c) by water source.

Spectral analysis

The periodogram for all cases shows an annual (12-month) periodicity in the time-series as indicated by the large spectral density at 12 months in the periodogram (Figure 5). The same annual periodicity is seen in the time-series data when disaggregated by hydroclimatic regime and drinking water source (results not shown). The Fisher's κ and Bartlett–Kolmogorov–Smirnov tests confirm a statistical

Table 2 | Results of negative binomial for years, all cases, 1999–2010

		95% CI	
Year	IRR	Upper	Lower
2000	1.53[a]	1.26	1.85
2001	1.41[a]	1.16	1.72
2002	1.34[a]	1.10	1.64
2003	1.25[a]	1.02	1.53
2004	1.17	0.96	1.44
2005	1.20	0.98	1.47
2006	1.03	0.83	1.27
2007	1.05	0.85	1.30
2008	1.31[a]	1.08	1.60
2009	1.27[a]	1.04	1.55

[a]Indicates statistical significance, $p < 0.05$.
IRR is incidence risk ratio, CI is confidence interval.
1999 is the reference year.

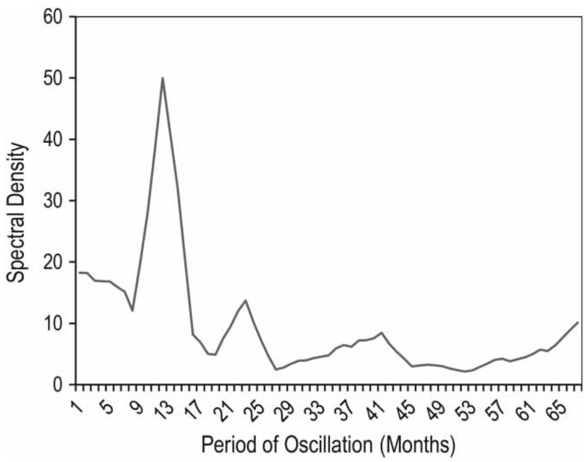

Figure 5 | Periodogram of monthly AGI. The peak in the periodogram indicates the dominant periodicity in the data (Fisman 2007).

significant seasonal pattern ($p < 0.01$) for all AGI overall (Table 3). This statistical significance remains when the cases are disaggregated by hydroclimatic regime and drinking water source (Table 3).

Annual plots

A non-linear trend is evident over the 11-year study period. Looking at the full dataset, there is a slight increase in risk relative to the reference year between 2001 and 2003, followed by a decrease between 2004 and 2007, and then another increase in risk during 2008 and 2009 (Figure 6(a)). The years 2004 to 2007 are not statistically significantly different from the 1999 reference period. Annual trends differ somewhat across the hydrological regimes and drinking water sources (see Figure 6(b) and (c); Table 2).

Table 3 | FK test and BKS test results

Time-series	FK	BKS
All GI Illness cases	18.02[b]	0.370[b]
Snowmelt-dominated cases	1.041[b]	0.193[a]
Rainfall-dominated cases	15.35[b]	0.403[b]
Groundwater cases	10.72[b]	0.284[b]
Surface water cases	10.73[b]	0.245[b]
Mixed water cases	10.78[b]	0.239[b]

[a]$p < 0.05$.
[b]$p < 0.01$.
FK test: the 5 and 1% critical values for the test are 5.93 and 6.56, respectively.

DISCUSSION

This study examined the seasonality of AGI in BC over an 11-year period using laboratory-confirmed case data from eight communities across the province. To our knowledge, this is the most comprehensive examination of AGI seasonality in BC and the first study anywhere to describe trends in AGI by hydroclimatic regime and drinking water source. Additionally, the majority of research examining the seasonality of AGI, and also research examining those factors that may drive these trends, originates from the USA, England, and Australia. There has been little research on the subject in BC. Targeted ecological studies at the regional level are needed to inform local decision-making, policy and action (Lal *et al.* 2012).

We used several different visual and statistical techniques to characterize seasonal patterns and our results consistently illustrate seasonality. These results are perhaps not surprising given that seasonal variation of AGI has been documented in numerous other settings (Naumova *et al.* 2000, 2007; Hall *et al.* 2006; Thomas *et al.* 2008; Zhang *et al.* 2008; White *et al.* 2009; Febriani *et al.* 2010; Harper *et al.* 2011; Lal *et al.* 2012). What is novel is consideration

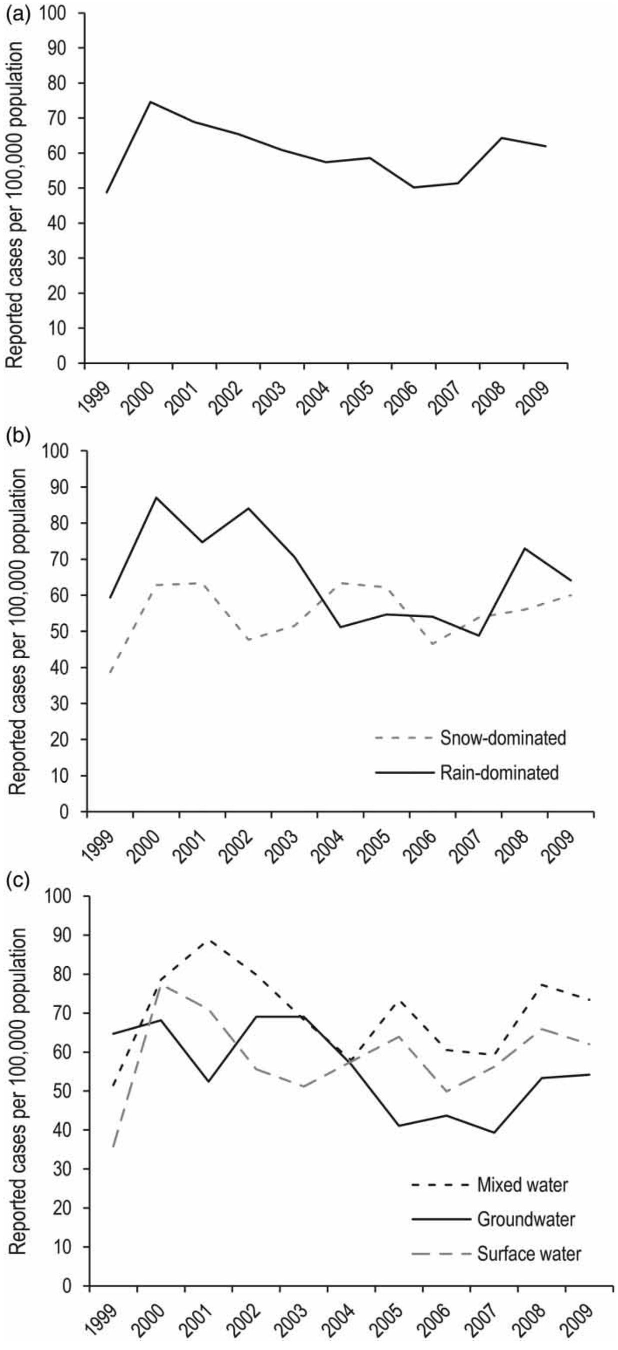

Figure 6 | Total annual AGI rates (1999–2010); (a) for all cases, (b) by hydroclimatic regime, and (c) by water source.

of the seasonal patterns by different hydroclimatic regimes and water source relevant in the context of BC. The seasonality of these diseases suggests that hydroclimatic factors such as temperature, precipitation, and runoff may influence disease occurrence.

Examining the time-series data disaggregated by the hydroclimatic regime and drinking water source enables a better understanding of the seasonal dynamics of AGI and can help generate hypotheses about possible mechanisms driving seasonal variation. Differences across the hydroclimatic regime and drinking water source are most easily identified in the monthly plots. Examining monthly plots disaggregated by the hydroclimatic regime demonstrates that the illness peak for those cases occurring in a rainfall-dominated regime occurs in September, compared to July for those cases occurring in a snowmelt-dominated regime. This may reflect differences in temperatures and hydrological patterns contributing to source water contamination at different times of the year in the two distinct regimes. Research indicates that source water microbial loads (both surface water and groundwater sources) are positively correlated with rainfall and may be influenced by the timing of precipitation and runoff events as well as temperature patterns (Atherholt *et al.* 1998; Kistemann *et al.* 2002).

The snowmelt-dominated hydroclimatic regime in BC is characterized by major runoff and groundwater recharge in the spring and early summer caused by warming temperatures that lead to rapid snowmelt; this is known as the spring freshet. At this time, the rivers run high and groundwater levels reach their maximum. Flooding is also a common occurrence. Runoff and groundwater recharge in the rainfall-dominated regimes is driven by precipitation, with streamflow and groundwater levels peaking through the late fall and early winter (Allen *et al.* 2010). Although the summertime peak in incidence is likely in part explained by higher temperatures which influence both human behavior and pathogen survival and replication, it is also plausible that the spring freshet in the snow-dominated watersheds causes runoff events and significant source water contamination contributing to the early summertime peak among those cases occurring in snowmelt-dominated watersheds. Rapid snowmelt may also overwhelm drinking water treatment systems (Naumova 2006). 'A rapid snowmelt, resultant runoff, and filtration system failure at the overloaded drinking water treatment plant were implicated with the largest known waterborne outbreak of cryptosporidiosis, which occurred in Milwaukee, Wisconsin in 1993' (Naumova 2006). Thomas *et al.* (2006) examined the association between spring freshet events and AGI outbreaks across Canada, but found no statistical significance (Thomas *et al.* 2006). Our results suggest that any association may have been masked by the inclusion of cases in both snowmelt-dominated and rainfall-dominated watersheds.

Fall precipitation may play a role in source water contamination and the fall incidence peak among those cases occurring in rainfall-dominated watersheds (Patz *et al.* 2008). Fall rains following the summertime drought are characteristic of rainfall-dominated watersheds and can lead to more severe runoff that is highly contaminated, thus posing a greater risk of contamination and illness (Charron *et al.* 2004). Additionally, high levels of rainfall onto saturated soil may facilitate the movement of pathogens over land and into drinking water sources (Lake *et al.* 2005; Britton *et al.* 2010). More research is needed to test and better understand the possible role of the spring freshet in snowmelt-dominated regimes, and precipitation in rainfall-dominated regimes in driving AGI transmission and seasonality.

Our results indicate that seasonal patterns vary across years. Inter-annual variability in seasonal patterns may suggest that ecological factors, such as weather and the hydrologic response of the watershed, which are known to vary across years, play a role in driving seasonal patterns. Interestingly, some evidence in settings where weather variability is limited both within years and across years points to limited variation in AGI rates (Araj *et al.* 1996). It is also possible that longer scale climatic processes such as the El Nino-Southern Oscillation (ENSO), a periodic fluctuation of atmospheric pressure and sea surface temperature in the equatorial Pacific Ocean, could influence inter-annual variation. Past research has found evidence for a relationship between ENSO and multiannual cycles of cholera (Pascual *et al.* 2000; Koelle *et al.* 2005; Hashizume *et al.* 2008). Time-series data longer than 11 years are needed to adequately explore the possible role of longer scale Earth system processes.

Other explanations are also possible, such as changes in reporting behavior from year to year (Zeger *et al.* 2004). Several studies have shown that reporting of infectious illness can be affected by factors such as publicized outbreaks in other settings or policy changes (Naumova *et al.* 2000). We expect environmental factors that vary across years are more relevant in this case as the reporting of notifiable diseases is required by law in BC (Hill 2012).

When interpreting these results, one must note that any effects of weather or hydrological variables on AGI occurrence would be lagged in time, likely on the scale of several weeks to months. Furthermore, it is a challenge to separate the effects of various factors driving seasonal illness patterns. More advanced statistical analysis is needed to tease out the effects of different potential environmental drivers of seasonality. Poisson time-series analyses using the generalized linear model (GLM) and the generalized additive model (GAM), which have been used extensively in air pollution research, are good candidates for further research. Case-crossover analysis may prove useful in examining the influence of more extreme events such as rapid snowmelt, extreme rainfall events, and flooding.

There are no consistent discernible patterns in seasonality across those cases linked to different drinking water sources. Although we might expect to see some differences in patterns given that research has shown that water source mediates risk of illness in BC (Uhlmann *et al.* 2009; Teschke *et al.* 2010), our results may be limited by misclassification of drinking water source exposure. We are confident with the accuracy of our approach linking cases to their residential drinking water source because of high predictive values documented in a sensitivity analysis, but it may be that using residential drinking water source as a surrogate for all source water exposure is problematic. Individuals are likely to drink water from a different source at work or when they are away from their homes in the evening or weekends, such that the residential drinking water source may not be a good surrogate measure for exposure. This issue has been highlighted in the literature, but no solutions have been identified (Jones *et al.* 2006). This issue may be particularly relevant in our dataset as 64% of our cases originate from communities where there are drinking water systems supplied by groundwater, surface water, and a mix of the two within the community itself. For these communities, it is likely that individuals are exposed to different drinking water sources when drinking water in their residences and when drinking water in other settings in the community. Furthermore, trends in the data across different water sources may be influenced by foodborne cases which we would not expect to vary by water source. Although we had originally hoped to focus on the protozoan cases, which are very commonly waterborne pathogens, low case counts did not allow this approach. Future research should consider an analysis focused on specific pathogen groups (bacterial and protozoan) or pathogens whenever possible. Explicit attention to cryptosporidiosis and giardiasis, recognized by the World Health Organization (WHO) as 'neglected diseases', is called for (Savioli *et al.* 2006). Another limitation of this study, and which may warrant attention in future studies, is the need for attention to recreational exposures.

In addition to the knowledge generation and methodological contributions of this study, our efforts to compare seasonal patterns of AGI by hydroclimatic regime and drinking water source also contribute to an enhanced conceptual understanding of AGI as well as informing of practical recommendations. Although the combination of hydroclimatology and drinking water source is unlikely to represent the full complexity of factors driving AGI in BC, our explicit attention to interrelated ecological determinants indicates an approach grounded in systems thinking and complexity. The ecological factors that we have examined in this work may explain some seasonal variation, but clearly other factors also contribute to the seasonal dynamics of AGI in BC. Future research in BC and beyond may consider eco-bio-social approaches that have been applied to other re-emerging infectious diseases (see for example Arunachalam *et al.* (2010) and Kittayapong *et al.* (2012)) and should examine the important linkages between ecological and social factors when data permit.

With regards to the practical implications arising from these results, we suggest two specific practice and policy oriented recommendations. First, water managers, environmental health officers, and researchers should work together to identify locally-relevant conditions and times of the year when the risk of AGI illness may be heightened. In communities located in snow-dominated watersheds, early summer and the spring freshet are likely to be high-risk times. For those communities located in rain-dominated watersheds, late summer and early fall precipitation events are likely candidates. Second, microbiological and/or turbidity monitoring programs could be adapted to account for high-risk conditions and times, taking into account local conditions and water system characteristics. Increasing water supply and source testing during the spring freshet is an example. This testing could be used to inform early warning systems for the community and could also serve as data for future research.

There are both strengths and weaknesses in this study. The main strength is the use of different methods for characterizing seasonality. Often, temporal trends are examined using visual analysis of plotted time-series only; we have taken this approach but have used additional methods to generate richer and more robust findings. This study is unique because we have characterized seasonality by selected hydroclimatic regime and drinking water source. We have used a GIS to link cases to the hydroclimatic regime and drinking water source, allowing for analysis of seasonality across these factors. Finally, this study answers the increasingly common call for an interdisciplinary approach to infectious disease research. The study team is an interdisciplinary group bringing together knowledge from medicine, human ecology, public health, and earth sciences.

There are also important limitations to consider when interpreting these results. Although a diverse group of communities with different drinking water sources and geographic locations across the province was selected, it is possible that there are important differences between our study communities and other settings limiting the generalizability of this work. Another limitation is that the AGI case data used in these analyses likely under-represent the true number of illness cases. Under-reporting could introduce bias into the study if those cases captured in the data are systematically different than those cases not captured in the data. Additionally, our case data do not include information about foodborne versus waterborne transmission; such datasets do not exist in BC and are generally uncommon. Unfortunately, AGI data from surveillance systems rarely, if ever, include information about foodborne versus waterborne transmission pathways. Additionally, we have used the variable 'episode date' from the iPHIS reporting system to represent the date of onset of the gastrointestinal illness case. It is possible, however, that the 'episode date' in the reporting system is not reflective of the true date of onset which may introduce lag-time between case reporting and case occurrence. Finally, although we have excluded those cases known to be travel related, we suspect that travel-related cases remain in the dataset.

CONCLUSIONS

Seasonality represents a rich area for future research, particularly given widespread environmental degradation and our changing climate (Fisman 2007). These findings provide strong evidence for seasonality in general and differences in seasonality across selected ecological factors. This knowledge can provide insight into disease etiology and can contribute to public health policy-making and water resource management. Knowledge of the timing of disease peaks, for example, could allow public health programs to focus resources and preventative actions at certain times of the year. Furthermore, 'disease forecasting and warning systems could allow public health officials to alert the populace when specific meteorological conditions pose considerable risk to health' (Naumova 2006). We conclude that systematic descriptions of infectious disease dynamics over time is a valuable tool for generating hypotheses for future research, establishing climate change sensitivity and potentially informing of disease prevention strategies.

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