A positive association between cryptosporidiosis notifications and ambient temperature, Victoria, Australia, 2001–2009

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ABSTRACT

Increased temperatures provide optimal conditions for pathogen survival, virulence and replication as well as increased opportunities for human–pathogen interaction. This paper examined the relationship between notifications of cryptosporidiosis and temperature in metropolitan and rural areas of Victoria, Australia between 2001 and 2009. A negative binomial regression model was used to analyse monthly average maximum and minimum temperatures, rainfall and the monthly count of cryptosporidiosis notifications. In the metropolitan area, a 1 °C increase in monthly average minimum temperature of the current month was associated with a 22% increase in cryptosporidiosis notifications (incident rate ratio (IRR) 1.22; 95% confidence interval (CI) 1.13–1.31). In the rural area, a 1 °C increase in monthly average minimum temperature, lagged by 3 months, was associated with a 9% decrease in cryptosporidiosis notifications (IRR 0.91; 95% CI 0.86–0.97). Rainfall was not associated with notifications in either area. These relationships should be considered when planning public health response to ecological risks as well as when developing policies involving climate change. Rising ambient temperature may be an early warning signal for intensifying prevention efforts, including appropriate education for pool users about cryptosporidiosis infection and management, which might become more important as temperatures are projected to increase as a result of climate change.

Key words | climate change, cryptosporidiosis, gastroenteritis, rainfall, temperature

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INTRODUCTION

Climate is one of many factors that can affect the transmission of micro-organisms, with outbreaks occurring both interannually and seasonally (or other calendar periods), for many infectious diseases (Fisman 2007; Koelle 2009). Rainfall or ambient temperature has been implicated in outbreaks of cholera, *Salmonella* spp., *Escherichia coli*, *Campylobacter* spp., *Giardia* spp., *Shigella* spp., typhoid, cryptosporidiosis, leptospirosis and a number of viruses (Curriero *et al.* 2001; Lipp *et al.* 2002; Zell 2004; Diaz 2006; Fisman 2007; Senior 2008; Semenza & Menne 2009). Possible explanations for this relationship between climate and infectious disease include increased reproduction and longer transmission periods of micro-organisms in warmer weather, changes in ecological balances, as well as climate-related migration and activity of humans, hosts and vectors (Fisman 2007; Semenza & Menne 2009).

There is now substantial evidence that the world is experiencing accelerated climate change, with evident increases in global average air and ocean temperatures, widespread melting of snow and ice and rising global average sea level (IPCC 2007). While Eastern Australia has become significantly drier and North-Western Australia has become significantly wetter since 1950, Australia has experienced an average warming trend of 0.9 °C over the last century (CSIRO 2007a). The Commonwealth Scientific and Industrial Research Organisation has predicted that the average surface temperature will increase by 1.0–5.0 °C by 2070 (CSIRO 2007a). The impact for Victoria is projected

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to be an increase in summer temperatures of 0.6–2 °C by 2030, up to 5 °C by 2070 (CSIRO 2007b). This has implications for future disease control, not only for Australia but globally, if warmer temperatures are associated with increases in infectious diseases such as cryptosporidiosis. Indeed, positive associations between food- and water-borne pathogens and temperature have been reported in the literature (D'Souza *et al.* 2004; Kovats *et al.* 2004; Naumova *et al.* 2007; Zhang *et al.* 2007; Lake *et al.* 2008; Britton *et al.* 2010a).

Cryptosporidium spp., a parasite that is an important cause of gastroenteritis worldwide, has previously been associated with rainfall (Curriero *et al.* 2001; Diaz 2006). A large cryptosporidiosis outbreak that occurred in Milwaukee, Wisconsin, USA, in 1993 was preceded by heavy rains which affected drinking water filtration (Ford *et al.* 2009). Heavy rains and flooding have also been implicated in cryptosporidiosis outbreaks through the excessive demand placed on sewage water treatment plants (Lipp *et al.* 2002) and through contamination of recreational water by the washing of pathogens or nutrients into source waters (Fisman 2007). While the associations between temperature of the current or previous month and routine notifications of 'food poisoning', including salmonellosis have been reported (Bentham & Langford 1995; D'Souza *et al.* 2004; Britton *et al.* 2010a), there are conflicting results on the association between cryptosporidiosis, ambient temperature and rainfall (Lake *et al.* 2008; Britton *et al.* 2010b).

In Australia, increases in cryptosporidiosis tend to occur in the warmer months and over irregular cycles (DoHA 2011). In Victoria, large increases in cryptosporidiosis notifications were observed in 2006 and 2009; this interannual nature of cryptosporidiosis has been observed in other Australian jurisdictions (Kent *et al.* 2011). The aim of this study was to therefore determine whether there was an association between cryptosporidiosis notifications, temperature and rainfall in metropolitan and rural Victoria regions between 2001 and 2009.

MATERIALS AND METHODS

Cryptosporidiosis notifications for Victoria for the period 2001–2009 were obtained from the Victorian Department of Health Notifiable Infectious Diseases Surveillance System. Notification data tend to underestimate the incidence of disease due to under-reporting of cases (Britton *et al.* 2010a); however, the association between cryptosporidiosis and weather should be unaffected as it is unlikely that these variables are correlated.

For a case to be confirmed, laboratory definitive evidence is required, the criterion of which is the detection of *Cryptosporidium* spp. oocysts. To analyse the data by date of infection, the calculated onset date for each notification was adjusted by the average incubation period of cryptosporidiosis, which is 7 days.

Victoria is the most southern state in mainland Australia and the smallest, making up approximately 227,000 km^2 (GA 2010). Victoria's main city, Melbourne, is a large metropolitan area covering approximately 10,000 km^2 and surrounded by largely rural area (CM 2013). It is the second most populous city in Australia, with a population of 4.25 million people (ABS 2013a). Two areas within Victoria were analysed, Eastern Metropolitan Region (one of the five Melbourne metropolitan regions) and a rural region, Gippsland, herein referred to as 'Metro' and 'Rural'. The 'Metro' area is Melbourne's second largest metropolitan region in terms of population, extending from Melbourne's inner eastern suburbs to outer eastern semi-rural mountainous areas and covering an area of approximately 3,000 km^2 (DEECD 2012). The 'Rural' area is even larger, covering 43,000 km^2 (DEPI 2014), with considerable variation in rainfall: from an approximate annual mean average of 600 mm (24 in) in the central plains to 1,800 mm (71 in) in the mountains (BOM 2014). These were chosen as they had the highest notification rate of all metropolitan and rural regions (Kent *et al.* 2011).

Mean monthly maximum and minimum temperature and mean monthly rainfall data were obtained from the Bureau of Meteorology (BOM 2012) using weather station data for Dunns Hill (latitude 37.88 °S and longitude 145.34 °E) and East Sale airport (latitude 38.12 °S and longitude 147.13 °E), to represent the weather patterns of 'Metro' and 'Rural', respectively.

To allow for overdispersion in the data, negative binomial regression was used for model fitting, using incident rate ratio (IRR). The IRR was calculated using the number of notifications rather than incidence rates and is therefore an estimation based on the assumption that a comprehensible linear relation exists between number of cases and incidence rate. The mean monthly temperature and rainfall data were modelled as explanatory variables for cryptosporidiosis notifications with temperature lags of 0–2 months. To reduce the Type 1 error that can occur when simultaneous tests are performed on a single data set, a Bonferroni correction was applied to each climate variable for each area. As there were four comparisons for each analysis of climate by area, the correction applied was $p < 0.0125$.

An adjusted analysis was also conducted to reduce the influence of large numbers due to the occasional major outbreak of cryptosporidiosis. This included an indicator variable for 'outbreak month' defined as months with counts greater than two standard deviations from the 9-year mean monthly count. In addition, dummy variables to control for season (referent 'spring' (September–November)), long-term trends (referent year 2001) and count of cryptosporidiosis notifications in the month previous to exposure were added to the model.

Ethics approval was not required as the study used routinely collected data of a notifiable condition, which were de-identified when extracted from the surveillance system.

RESULTS

Cryptosporidiosis notifications increased over the study period by 15% for 'Metro' (IRR 1.15; 95% confidence interval (CI) 1.07–1.23; $p = 0.001$); there was no increase observed for the 'Rural' area ($p = 0.559$) (Figure 1). When outbreak months were removed from the analysis, the increase in notifications was reduced to 6% for 'Metro' (IRR = 1.06; 95% CI 1.00–1.12).

There was seasonal variation for cryptosporidiosis counts and both temperature variables, for both areas, but trends were not as clear for rainfall (Figure 1). Figure 2 shows the monthly patterns averaged across all 9 years for each area. The peak mean maximum and minimum temperature for each area occur in January. The peak of cryptosporidiosis notifications occurs 2 months after both temperature peaks in 'Metro' and 3 months after the lowest mean maximum and minimum temperatures in 'Rural'. For both areas, no clear trend for rainfall was found as a number of peaks were detected (Figure 2). These observations would suggest that mean temperatures of the current and previous month were not as good a predictor of notifications as the mean temperatures lagged by 2–3 months. This was confirmed for both areas by comparing the fit of the regression model with the various lagged periods.

For the 'Metro' area, unadjusted univariate analysis showed that a 1 °C increase in mean maximum monthly temperature lagged 2 months was associated with a 16% increase in cryptosporidiosis notifications; for mean minimum monthly temperature there was a 30% increase in notifications (Table 1). These associations were stronger than for the current or previous months. When each temperature model was adjusted for the indicator variables – outbreak month, season, long-term trends and count of notifications in the previous month – the association between increases in mean maximum and minimum temperature lagged 2 months and increase in notification weakened (11% and 19%, respectively) (Table 1). For mean maximum temperature, the effect of lagging by 2 months did not substantially change the relationship found for the current or previous months. However, the relationship with mean monthly minimum temperatures lagged by 2 months was marginally weaker than for the current month (22% increase in notifications). Lagging maximum temperatures by 3 months did not improve the fit of the regression model and weakened it for minimum temperatures (data not shown).

The relationship between temperature and cryptosporidiosis notifications differed in the 'Rural' area. Unadjusted, univariate analysis showed that a 1 °C increase in mean maximum monthly temperature lagged by 3 months was associated with a 4% decrease in cryptosporidiosis notifications, which increased to a 8% decrease in notifications after adjusting for the indicator variables (Table 1). For mean minimum monthly temperature lagged by 3 months a 1 °C increase was associated with a 5% decrease in cryptosporidiosis notifications in the unadjusted model and a 9% decrease in notifications in the adjusted model (Table 1). There was no significant association with either temperature variable for the current, previous or 2 months prior with cryptosporidiosis notifications (data not shown).

No association was found with rainfall for any area examined (data not shown).

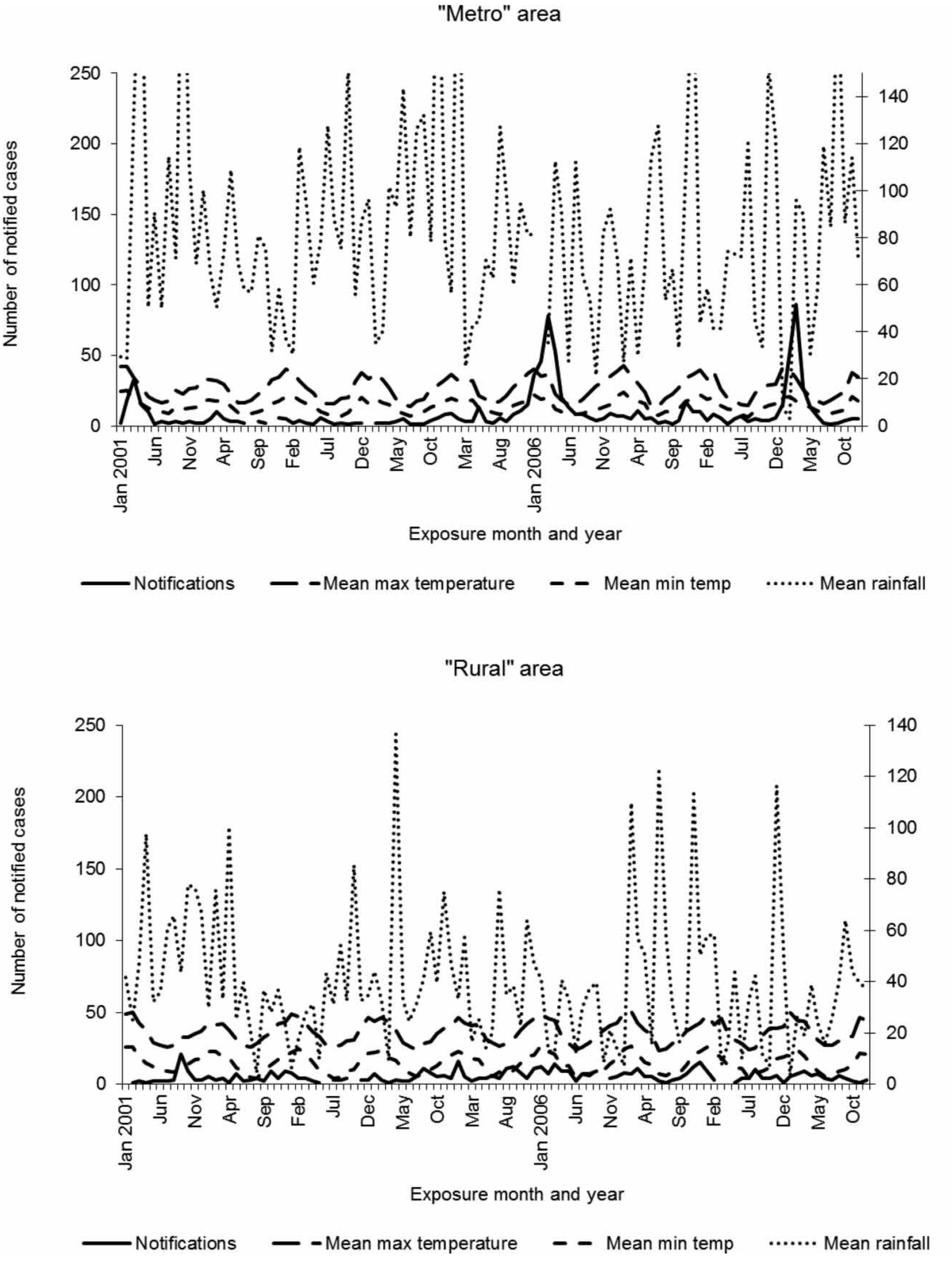

Figure 1 | Monthly cryptosporidiosis notifications and mean monthly climate variables for metropolitan and rural regions, Victoria, Australia, 2001–2009.

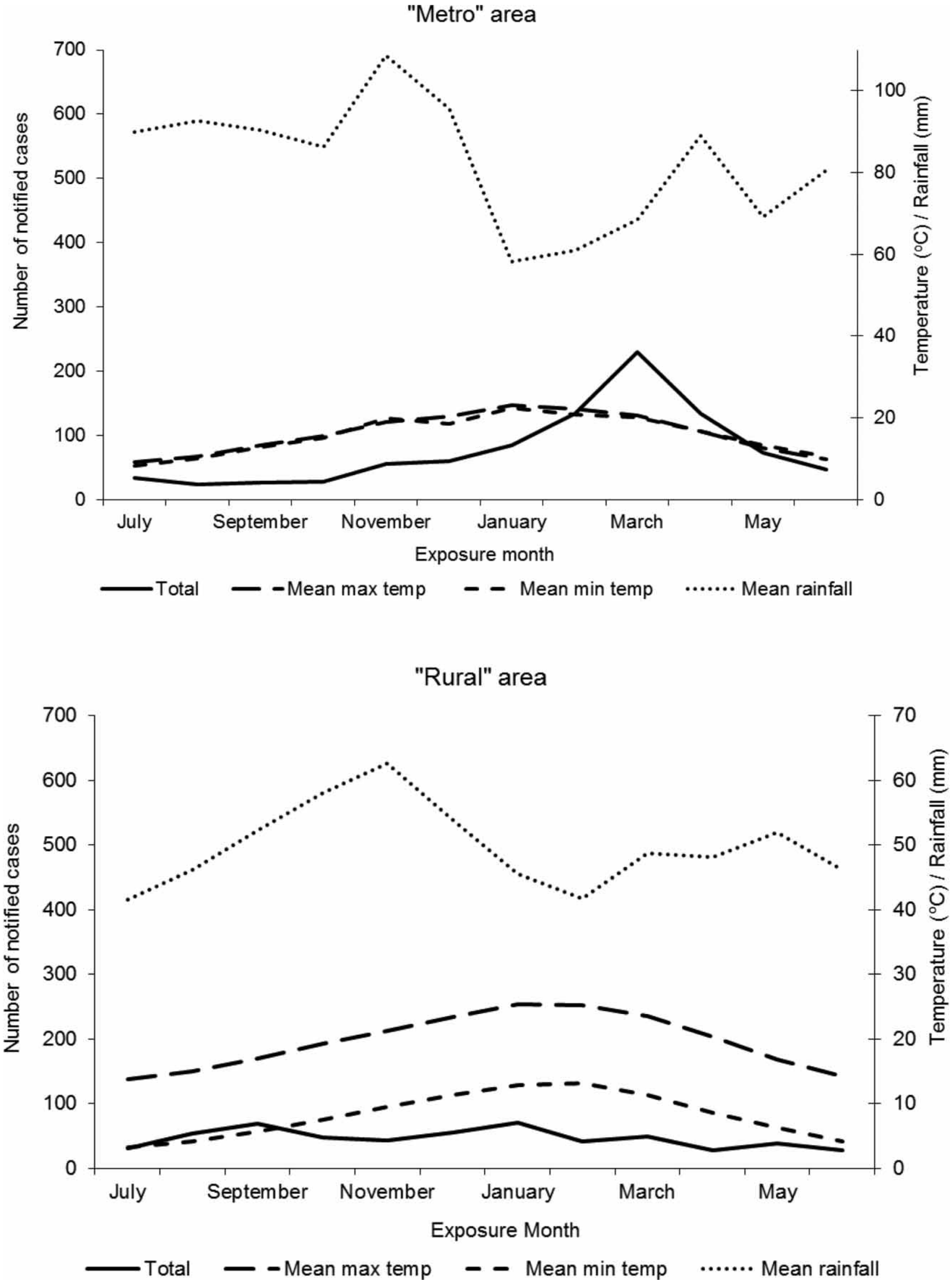

Figure 2 | Monthly cryptosporidiosis notifications and mean monthly climate variables for metropolitan and rural regions, Victoria, Australia, averaged for each month, 2001–2009.

Table 1 | IRR with 95% CI for the relationship between each climate variable and cryptosporidiosis notifications for a 'Metro' and 'Rural' area in Victoria, 2001–2009

		Risk with 1 °C rise in mean monthly temperature			
		Unadjusted model		Adjusted model[a]	
Area	Temperature variable	IRR	95% CI	IRR	95% CI
'Metro'	Mean max current month	1.10**	1.05–1.14	1.10**	1.06–1.15
	Mean max previous month	1.14**	1.10–1.18	1.10**	1.04–1.15
	Mean max lagged 2 months	1.16**	1.12–1.20	1.11**	1.05–1.18
	Mean min current month	1.21**	1.13–1.30	1.22**	1.13–1.31
	Mean min previous month	1.28**	1.20–1.36	1.15 *	1.06–1.26
	Mean min lagged 2 months	1.30**	1.21–1.38	1.19**	1.08–1.31
'Rural'	Mean max lagged 3 months	0.96*	0.93–0.99	0.92*	0.88–0.97
	Mean min lagged 3 months	0.95*	0.92–0.98	0.91*	0.86–0.97

[a] Adjusted by 'outbreak month', season, year and cryptosporidiosis count in the previous month.

$*p \leq 0.0125$.

$**p < 0.001$.

DISCUSSION

This study found that both mean maximum and minimum temperatures were positively associated with cryptosporidiosis notifications in the metropolitan area, with the strongest relationship with mean minimum temperature. These findings are supported by research from New Zealand, Australia and the USA, which found temporal associations between increases in temperature and cryptosporidiosis notifications (Hu *et al.* 2007; Naumova *et al.* 2007; Lake *et al.* 2008).

In general, increased temperatures may provide the optimal conditions for pathogen survival, virulence and replication, particularly when ambient overnight temperatures are warmer (Fisman 2007). In particular, *Cryptosporidium* spp. oocysts can persist in the environment and can be readily dispersed throughout the environment through increased rainfall events (King & Monis 2007). However, the oocysts are highly susceptible to inactivation with higher (>15 °C) environmental temperatures. Therefore, the observed relation between mean maximum and minimum temperatures and cryptosporidiosis in the metropolitan area may not be due to pathogen survival, virulence and replication, as overnight temperatures may exceed this level and day temperatures certainly would. The relationship is more likely to be explained by human behaviour as recreational water activity, camping and hiking are more common in the warmer months (Britton *et al.* 2010a). Certainly, cryptosporidiosis infection has been implicated in the use of swimming pools which may be more accessible in urban areas (Peuch *et al.* 2001; CDC 2007, 2009; Shields *et al.* 2008). However, this study also highlights the differential effect of temperature on notifications in metropolitan versus rural areas and would suggest that differing transmission modes may be at play.

The relationship between cryptosporidiosis and temperature was reversed for the rural area. The negative association between cryptosporidiosis notifications and temperature increased as the period of warmer temperatures was prolonged, with negligible difference in risk between mean maximum and minimum temperature. This finding is supported by a New Zealand study, which found that a 1 °C increase in current average temperature was associated with a 2% decrease in notifications (Britton *et al.* 2010b). This effect is comparable to the non-significant effect of unlagged temperatures on notifications in the present study. In the Victorian rural area, an increase in cryptosporidiosis notifications is seen in spring, which is a time of increased agriculture and livestock husbandry (Kent *et al.* 2011). In New Zealand, peak notifications also occur in the spring, and are associated with increased exposure to livestock (Lake *et al.* 2008). It would appear that cryptosporidiosis notifications are environmental exposures rather than behavioural activities as in urban areas.

The present study also found the associations were stronger for temperature in the current and 2 months prior to infection compared with the previous month or 3 months prior. Lake *et al.* (2008) found that the cryptosporidiosis rate in New Zealand was positively associated with temperatures in the current or previous month, rather than lags of 2 or 3 months. In another study from Massachusetts, USA, cryptosporidiosis notifications peaked about 40 days after peaks in temperature (Naumova *et al.* 2007). Reasons for the temporal delay in these studies have been attributed to differences in transmission routes, amplification of infection from person-to-person spread, survival of pathogens in the environment at different times of the year, differences in incubation periods, disease manifestation and/or testing practices (Naumova *et al.* 2007). In the present study, the lag period is not likely to be the result of delays in reporting as illness onset time was recorded in the surveillance system.

Rainfall has been strongly associated with cryptosporidiosis in a number of studies (Curriero *et al.* 2001; Patz 2001; Rose *et al.* 2001; Britton *et al.* 2010b) where it has been suggested that a number of events have to occur simultaneously to result in an outbreak. These include contamination of source water, transport of contaminant to water intake, insufficient treatment and exposure to contaminant (Fisman 2007). For example, the 1993 Milwaukee outbreak of cryptosporidiosis occurred as a result of simultaneous adverse events: heavy rainfall and subsequent runoff, with an inadequate coagulation-filtration process (Rose *et al.* 2001). The present study did not find an association between cryptosporidiosis and rainfall in any area examined. A New Zealand study using national level data also did not find an association between rainfall and cryptosporidiosis (Lake *et al.* 2008), while another New Zealand study, which used smaller census area units (Britton *et al.* 2010b), found a positive association. Analysis of larger areas does not take into account geographic variations in climate. The 'Metro' area examined in this study is a large area of approximately 3,000 km^2. Rainfall associations may be found in Victorian studies if smaller areas were examined or if the adverse events described above were to occur simultaneously.

The increasing long-term trend for cryptosporidiosis notifications could also be explained by the fact that the Victorian population increased by an estimated 582,430 people between 2001 and 2009 (ABS 2013b). This equates to a 12.3% increase in population, the majority of which occurred in Victoria's capital, Melbourne. However, this study found a 15% increase in cryptosporidiosis notifications in the 'Metro' area over this time. Changes in notification practices over time could also have influenced this trend. The large number of notifications found in 2001 may be because cryptosporidiosis became notifiable in that year. Furthermore, the authors are not aware of changes in notification practices and testing procedures since cryptosporidiosis became notifiable. Changes in swimming pool use, namely, changes in installations of private swimming pools and in the use of public pools over the period of this study may also have contributed to the trend of increasing notifications over the period of the study. However, the authors were not able to find any statistics on this for Victoria. Future studies which explore the temperature-notification trend of notifiable diseases need to gather information on behaviour that may be associated with temperature and risk of infection. Nevertheless, the minimum temperatures for Victoria between 2000 and 2010 were, on average, 0.2 °C warmer than for any other decade since 1910 (DSE 2012).

The use of notifications data, which tend to underestimate the incidence of disease due to under-reporting of cases, is another limitation of this study. It has been estimated that about 10% of people with gastroenteritis visit a doctor and then only 10% will have a stool specimen taken (Padiglione & Fairley 1998). Therefore, the sample used may not represent all cases of cryptosporidiosis in Victoria, but rather the more severe cases. This also suggests that notifications may be misrepresented geographically, but by focussing on a smaller geographic area this may be reduced.

Using one weather station as the proxy for the weather in each area is a limitation of the study. Both the 'Metro' and 'Rural' areas are large and cover a wide range of topographies and so the weather data from one site provide only crude patterns. Although care was taken in selecting the weather station, this may not have been representative of weather patterns for all climate variables for that area. Selecting a weather station in a different site may have provided different findings. Future studies should focus on examining associations in smaller, more uniform topographical areas.

Even though these data may not represent all cases, surveillance data are the only ongoing routinely collected data and are therefore useful for monitoring disease over time. Despite these limitations, the strengths of association in this analysis, the consistency of findings in this study and that of other studies, and plausible biological pathways suggest that ambient temperature is causally related to cryptosporidiosis notifications. This study also highlights the differential association between temperature and cryptosporidiosis notifications in metropolitan and rural areas, which may be explained by differences in transmission pathways. In metropolitan areas, individuals are more likely to become infected in warm weather through person-to-person contact such as in water recreational activities; in rural areas, infections in cooler weather are more likely to occur through contact with livestock.

The positive relationship between temperature and cryptosporidiosis notifications found in the metropolitan area has implications for the present and future. Although a review of climate and disease outbreaks conducted by the World Health Organization in 2004 did not identify cryptosporidiosis as a candidate for an early warning system (WHO 2004), this study has shown that higher average monthly minimum temperatures may be a warning to health authorities of a risk of cryptosporidiosis. Strategies to minimise cryptosporidiosis outbreaks in the event of prolonged increased temperatures could include monitoring of ambient temperatures in metropolitan areas in early summer as part of cryptosporidiosis surveillance and educating the public on the added risks of hot weather on recreational activities. In addition, as cryptosporidiosis has often been associated with the use of public swimming pools in the USA, Australia and elsewhere, additional strategies include: educating users of the importance of hygiene; educating pool operators to adequately sanitise water/filters; clean up and water treatment after faecal accidents; restricting access of users/staff with diarrhoea; and educating users of their risks and responsibilities (Peuch *et al.* 2001; CDC 2007, 2009; Wheeler *et al.* 2007; Shields *et al.* 2008). As *Cryptosporidium* spp. is resistant to chlorine and can survive in swimming pools for a number of days, pool operators should be educated to install UV disinfection units following the filtration process to control the risk.

CONCLUSION

The future implications for the temperature–cryptosporidiosis relationship stem from the projections concerning global climate change. Given that climate models predict that the average temperature at the Earth's surface could increase from 1.1 to 6.4 °C by the end of this century; the ongoing effects of climate change suggest increases in cryptosporidiosis notifications (IPCC 2007). Consequently, focussing specific strategies on warm weather-related activities during times of increasing temperatures could aid adaptation to the risk of cryptosporidiosis due to climate change.

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