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## Original Contribution

# Under the Weather: Legionellosis and Meteorological Factors

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**Abstract:** The incidence of legionellosis, caused by the bacteria *Legionella* which are commonly found in the environment, has been increasing in New Jersey (NJ) over the last decade. The majority of cases are sporadic with no known source of exposure. Meteorological factors may be associated with increases in legionellosis. Time series and case-crossover study designs were used to evaluate associations of legionellosis and meteorological factors (temperature (daily minimum, maximum, and mean), precipitation, dew point, relative humidity, sea level pressure, wind speed (daily maximum and mean), gust, and visibility). Time series analyses of multi-factor models indicated increases in monthly relative humidity and precipitation were positively associated with monthly legionellosis rate, while maximum temperature and visibility were inversely associated. Case-crossover analyses of multi-factor models indicated increases in relative humidity occurring likely before incubation period was positively associated, while sea level pressure and visibility, also likely preceding incubation period, were inversely associated. It is possible that meteorological factors, such as wet, humid weather with low barometric pressure, allow proliferation of *Legionella* in natural environments, increasing the rate of legionellosis.

**Keywords:** *Legionella*, weather, precipitation, humidity, sea level pressure, visibility

## INTRODUCTION

Legionellosis can take two forms: a self-limiting flu-like illness called Pontiac Fever or a more severe, potentially fatal pneumonia called Legionnaires' Disease. Legionellosis is caused by the naturally occurring bacteria *Legionella*, which are ubiquitous in the environment and reproduce in high numbers inside free-living amoeba in warm (25–45°C), stagnant water. *Legionella pneumophila* serogroup 1 is the most common etiologic agent or serogroup of

legionellosis (Yu et al. 2002). The primary human exposure route to *Legionella* is thought to be the inhalation of aerosolized water containing high concentrations of the microorganism, and aspiration may also be an important mode of transmission. Legionellosis cannot be transmitted between people or by swallowing contaminated water. Older adults, smokers, and individuals with immunocompromised conditions and comorbidities are at higher risk of legionellosis. Incidence of legionellosis may be greatest during the summer and fall months (Neil and Berkelman 2008).

*Legionella* have been identified in many different kinds of water and water systems, such as hot- and cold-water

taps and showers, creeks, ponds, whirlpool spas, cooling towers, and evaporative condensers of large air-conditioning systems (World Health Organization 2007). Outbreaks of legionellosis have been linked to spas, cooling towers, humidifiers, respiratory therapy devices, and misters. Investigations have not been able to identify a common exposure in the majority of cases. Up to 80% of cases are sporadic with no known source (Hicks et al. 2007).

The occurrence of legionellosis without a common exposure (such as a building or facility) indicates that a broader common exposure may exist. Researchers have hypothesized that the incidence of legionellosis may be associated with weather patterns, such as increased rainfall, humidity, temperature, water vapor pressure, and cloud cover (Fisman et al. 2005; Conza et al. 2013; Dunn et al. 2013). Warm, wet weather conditions may contribute to the proliferation of *Legionella* in the environment.

Studies of the presence of the bacterium following rainfall have had mixed results. In natural environments, *L. pneumophila* have been isolated in puddles (Sakamoto et al. 2009) and floodwaters (Schalk et al. 2012) following rainfall. In another study of potable water, increased rainfall was not associated with a change in *L. pneumophila* serogroup 1 isolation rates but was associated with a decrease in other serogroups (Rivera et al. 2009). Thus, it remains unclear whether rainfall impacts the proliferation of the bacterium. Additionally, soil is an important reservoir of *Legionella* and has been linked to disease (van Heijnsbergen et al. 2014; Wallis and Robinson 2005). *Legionella* proliferation in soil and increased risk of disease may be correlated with meteorological factors since *Legionella* growth is particularly associated with damp soil (Sakamoto 2015). Previous studies have found associations between legionellosis incidence and humidity, temperature, and rainfall (Fisman et al. 2005; Dufresne et al. 2012; Ricketts et al. 2012; Conza et al. 2013; Garcia-Vidal et al. 2013) though others found no association with humidity (Herrera-Lara et al. 2013). These mixed results indicate a need for greater understanding of the relationship between weather and legionellosis.

In New Jersey, the number of legionellosis cases began unexpectedly increasing in May 2013 (16 cases, compared to a ten-year average of 7.8 cases in May), with a peak in June 2013 (58 cases, compared to a ten-year average of 14.5 cases in June). This late spring peak differed from the most often observed seasonal incidence peak from June through October (CDC 2011) and appeared to correspond with

abnormally high levels of rainfall in May and June of that year. We explored associations of meteorological factors on increases in legionellosis events using two different research designs: case-crossover and time series.

## MATERIALS AND METHODS

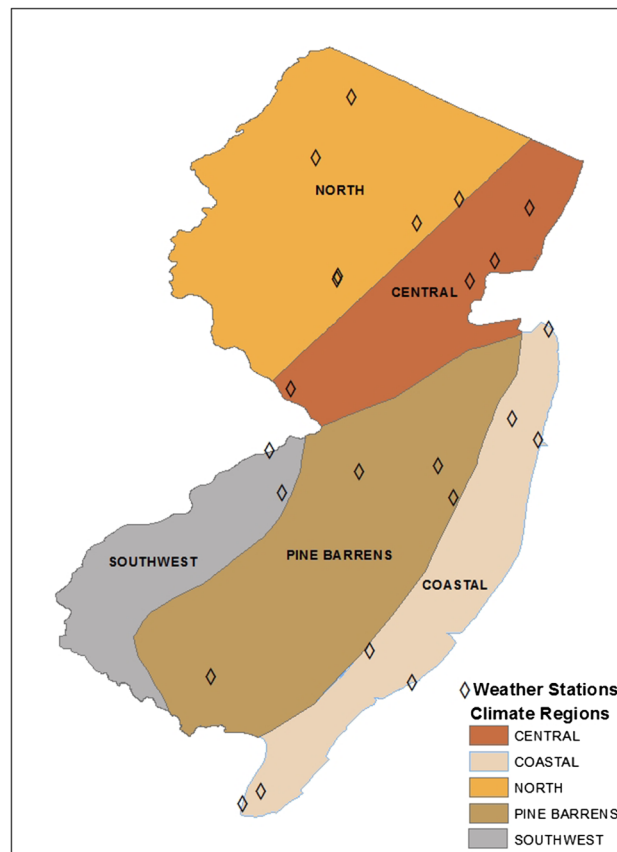
### Cases

Cases of legionellosis diagnosed in New Jersey are reportable to the New Jersey Department of Health (NJDOH). In New Jersey, laboratory confirmation of legionellosis is required by regulation to be sent to local health departments within 24 h of diagnosis and local health departments subsequently investigate cases and report them to the state health department. Legionellosis is confirmed when a case meets one of the following laboratory diagnosis criteria: culture isolation of any *Legionella* organism, detection of specific *L. pneumophila* serogroup 1 antigen in urine, or certain seroconversion criteria. NJDOH maintains the Communicable Disease Reporting and Surveillance System (CDRSS) of all reported cases of New Jersey residents with all reportable diseases, including legionellosis. Cases of legionellosis in CDRSS from 2003 to 2013 were included in this study. Those cases reported to be out of the state during the entire incubation period (2–10 days prior to illness onset) were excluded.

### Meteorology

Data on daily measures of the meteorological factors including mean, maximum and minimum temperature, mean dew point, mean sea level pressure, mean station pressure, mean visibility, mean wind speed, maximum sustained wind gust, and precipitation were obtained for 26 weather stations located in New Jersey available from the global summary of the day (GSOD) data from the National Climatic Data Center (2014). Mean relative humidity was calculated from temperature and dew point data.

New Jersey was divided into five climate regions described by the Office of the New Jersey State Climatologist (Fig. 1). Each station was geocoded to a climate region, and available daily values of meteorological factors from each station were averaged within each climate region. Each legionellosis case was assigned to one of the five identified climate regions based on address and, respectively, assigned the meteorological values in the given climate region.



**Figure 1.** Climate region map of New Jersey with weather stations with available global summary of the day data (GSOD).

## Study Designs

Associations with legionellosis and monthly meteorological values were estimated using a time series study design, and associations with daily meteorological values were estimated using a case-crossover design. Both time series and case-crossover study designs have been popularly used for estimating effects with acute health effects and air pollution and have been shown to be comparable (Fung et al. 2003). Both study designs however have unique characteristics that may make them more advantageous than the other. Time series design controlled for long-term influences and trends in the data using month and year allowing for the examination of the monthly, short-term associations, while case-crossover study design allows examination of daily, short-term associations to be examined. Legionellosis cases were geocoded to census tract based on residential address. For time series study design, monthly case counts were summed across census tracts for each climate region. Census tract populations were provided from the 2010 U.S. Census Bureau and population was estimated for each climate region.

For case-crossover study design, bi-directional control sampling was used in which the day exactly a week before and a week after a case's day of symptom onset were assigned as control days. Selection before and after the case day avoids bias to temporal trends while selection by week avoids any effects of day of week (Navidi 1998; Navidi et al. 1999; Fung et al. 2003; PHASE 2007). Since each case served as their own control, individual-level confounding factors which remain constant over short period of time (e.g., age, race, gender) were controlled for, and time trends were controlled for by dividing the study period into fixed 21-day strata (the last stratum in the study period was only 18 days) (PHASE 2007). If a control-day fell outside of the case-day stratum, a new control was selected either 2 weeks before the case day or 2 weeks after the case day, whichever day was in the same stratum of the case day.

Due to the incubation period from exposure to symptom onset, lag windows were explored as suggested by Fisman et al. 2005: "likely during incubation" for the average of lag days 1 through 5; "likely preceding incubation" for the average of lag days 6 through 10; and

“preceding incubation” for the average of lag days 11 through 15.

## Data Analysis

Poisson generalized linear regression models were used to estimate rate ratios (RR) and 95% confidence intervals (CI) of monthly meteorological factors and monthly rate of legionellosis in the time series study analysis (SAS, 2002–2008). Census tract population data were offset in the regression. Month, year, and region were included in all models. Single-meteorological variable models for time series analyses explored associations between each meteorological variable, without control for other meteorological variables, and monthly rates of legionellosis.

Conditional logistic regression was used to estimate odds ratios (OR) and 95% CI for the associations between symptom onset and the lag periods for each meteorological variable in the case-crossover design (Navidi 1998; Tolbert et al. 2000; Boutin-Forzano et al. 2004; Villeneuve et al. 2007). The selection of lag period for each meteorological variable was based on the evaluation of effect magnitudes and Akaike Information Criteria (AIC) for model fit. Effect estimates are presented as different unit increases for each of the meteorological variables and are listed in Tables 2 and 3.

Multivariate models for both time series and case-crossover analyses explored associations of meteorological factors while controlling for other meteorological factors. Due to missing daily values (>19%), mean station pressure was dropped. Due to instances of high correlation and corresponding concerns of collinearity, only factors with a Pearson correlation  $r < 0.50$  were included in the full model. To limit the impact of collinearity for both study designs, only one of three temperature measures (i.e., minimum, maximum or mean) was included, and only mean wind speed was included, while both maximum sustained wind speed and maximum wind gust were excluded. In the case-crossover, mean wind speed was not included as the lag period occurred before the lag periods selected for the other meteorological factors. For time series, ‘Full Model A’ did not include dew point, while ‘Full Model B’ did not include maximum temperature or relative humidity. For case-crossover analysis, ‘Full Model A’ did not include relative humidity, while ‘Full Model B’ did not include dew point. Using backward elimination, removing any variable with a  $P$  value  $< 0.2$ , a final reduced model was selected from each ‘full model.’

To assess potential impact of season, a sensitivity analysis was restricted to warmer months, those with a monthly average of 50°F or higher (April through October). Month as a variable was not adjusted for in the time series analysis when season was restricted to avoid over-control for seasonality.

## RESULTS

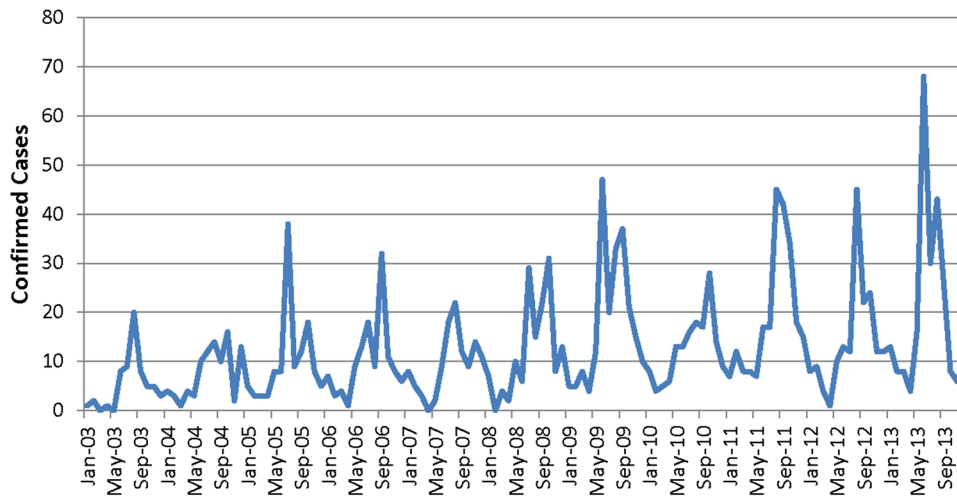
The study included 1665 cases of legionellosis. Among cases, 66.8% were males, and 78.5% were over the age of 50 years. Cases occurred most often from June through October, and over half resided in the Central region, which was expected due to the population distribution of New Jersey (Table 1; Fig. 2).

### Time Series Analysis

Models of single-meteorological variables, adjusted for month, year, and region, found mean monthly relative humidity, dew point, gust, and precipitation, were positively associated with monthly rate of legionellosis ( $P$  value  $< 0.05$ ), while visibility, mean temperature, and maximum temperature were inversely associated (Table 2). Two multivariate “full models” were created using non-correlated exposures (Table 2). When included in a multivariate model and following backward elimination, increases in relative humidity and precipitation were positively associated with legionellosis rate (RR = 1.28, 95% CI 1.14–1.43 for each 10% increase, and RR = 1.09 95% CI 1.03–1.17 for each 0.1 inch increase, respectively), while maximum

**Table 1.** Demographics of Legionellosis Cases.

Total	<i>n</i> = 1665	%
Male	1113	66.8
Age		
< 50	356	21.4
≥ 50	1307	78.5
Unknown	2	0.1
Region		
Central	886	53.2
Southwest	259	15.6
North	240	14.4
Coastal	147	8.8
Pine Barrens	133	8.0



**Figure 2.** Legionellosis cases by onset month and year in New Jersey, 2003–2013.

**Table 2.** Time Series Study Design Adjusted RR and 95% CI of Associations of Monthly Meteorological Factors and Monthly Rate of Legionellosis for Full Year and Restricted to April–October.

Meteorological factors*	Unit	Single-meteorological variable		Full Model A		Final Model A		Full Model B		Final Model B	
		RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
<i>Full year</i>											
Mean temperature	10°F	0.81	0.66–1.00	–	–	–	–	–	–	–	–
Min temperature	10°F	1.16	0.96–1.41	–	–	–	–	–	–	–	–
Max temperature	10°F	1.02	0.95–1.10	<b>0.76</b>	<b>0.62–0.92</b>	<b>0.77</b>	<b>0.64–0.93</b>	–	–	–	–
Dew point	10°F	1.19	1.00–1.42	–	–	–	–	1.02	0.83–1.25	–	–
Relative humidity	10%	<b>1.37</b>	<b>1.23–1.52</b>	<b>1.22</b>	<b>1.07–1.40</b>	<b>1.28</b>	<b>1.14–1.43</b>	–	–	–	–
Precipitation	0.1 in	<b>1.16</b>	<b>1.10–1.23</b>	<b>1.10</b>	<b>1.02–1.18</b>	<b>1.09</b>	<b>1.03–1.17</b>	<b>1.14</b>	<b>1.07–1.22</b>	<b>1.14</b>	<b>1.07–1.21</b>
Sea level pressure	5 mb	0.88	0.76–1.02	1.05	0.89–1.23	–	–	0.97	0.82–1.14	–	–
Visibility	5 mi	<b>0.80</b>	<b>0.72–0.88</b>	0.66	0.35–1.23	–	–	<b>0.43</b>	<b>0.24–0.77</b>	<b>0.40</b>	<b>0.24–0.69</b>
Wind speed	1 knot	0.99	0.90–1.09	1.00	0.90–1.12	–	–	0.97	0.88–1.08	–	–
Gust	1 knot	<b>1.05</b>	<b>1.01–1.10</b>	–	–	–	–	–	–	–	–
<i>April–October</i>											
Mean temperature	10°F	<b>1.43</b>	<b>1.33–1.53</b>	–	–	–	–	–	–	–	–
Min temperature	10°F	<b>1.47</b>	<b>1.38–1.58</b>	1.09	0.99–1.21	1.09	0.99–1.21	–	–	–	–
Max temperature	10°F	<b>1.37</b>	<b>1.28–1.47</b>	–	–	–	–	–	–	–	–
Dew point	10°F	<b>1.54</b>	<b>1.44–1.64</b>	–	–	–	–	<b>1.20</b>	<b>1.08–1.33</b>	<b>1.19</b>	<b>1.07–1.31</b>
Relative humidity	10%	<b>2.12</b>	<b>1.92–2.35</b>	<b>1.73</b>	<b>1.51–1.99</b>	<b>1.69</b>	<b>1.48–1.93</b>	–	–	–	–
Precipitation	0.1 in	<b>1.29</b>	<b>1.22–1.37</b>	<b>1.14</b>	<b>1.06–1.23</b>	<b>1.14</b>	<b>1.05–1.23</b>	<b>1.26</b>	<b>1.18–1.35</b>	<b>1.26</b>	<b>1.18–1.34</b>
Sea level pressure	5 mb	0.93	0.81–1.06	0.88	0.75–1.04	0.90	0.77–1.05	1.10	0.95–1.29	–	–
Visibility	5 mi	<b>0.13</b>	<b>0.07–0.24</b>	1.44	0.72–2.88	–	–	0.64	0.34–1.22	–	–
Wind speed	1 knot	<b>0.63</b>	<b>0.59–0.68</b>	<b>0.81</b>	<b>0.73–0.91</b>	<b>0.82</b>	<b>0.73–0.91</b>	<b>0.74</b>	<b>0.66–0.83</b>	<b>0.72</b>	<b>0.65–0.80</b>
Gust	1 knot	<b>0.90</b>	<b>0.87–0.94</b>	–	–	–	–	–	–	–	–

Values in bold are statistically significant at a significance level of 5%.

temperature was inversely associated (RR = 0.77, 95% CI 0.64–0.93 for each 10°F increase). In a separate final model, precipitation was again positively associated with

legionellosis rate (RR = 1.14, 95% CI 1.07–1.21 for each 0.1 inch increase), and visibility was inversely associated (RR = 0.40, 95% CI 0.24–0.69 for each 5 mile increase).

When the seasonal period for analysis was restricted to April through October, single-weather variable analyses (adjusted for year and region) revealed that mean relative humidity, dew point, precipitation, and all temperature variables were positively associated with legionellosis rate and visibility, and all wind factors were inversely associated (Table 2). Following backward elimination of 'Full Model A' including minimum temperature and sea level pressure, relative humidity and precipitation remained positively associated with monthly legionellosis incidence rate (RR = 1.69, 95% CI 1.48–1.93 for each 10% increase, RR = 1.14, 95% CI 1.05–1.23 for each 0.1 inch increase, respectively), while wind speed was inversely associated (RR = 0.82, 95% CI 0.73–0.91 for each 1 knot increase) (Table 2). Following backward elimination of 'Full Model B' which included sea level pressure and visibility, the factors dew point and precipitation were positively associated (RR = 1.19, 95% CI 1.07–1.31 for each 10°F increase; RR = 1.26, 95% CI 1.18–1.34, 0.1 inch increase, respectively), while wind speed was inversely associated (RR = 0.72, 95% CI 0.65–0.80 for each 1 knot increase).

### Case-Crossover Analysis

For each single-meteorological variable model, a lag window was selected. For each meteorological factor, the lag window of days 6–10 ("likely preceding incubation period") had the lowest AIC and the highest effect estimate, with the exception of average and maximum temperature and wind speed which had the lowest AIC occurring for the lag window of days 11–15 ("preceding incubation"). For average temperature, since the magnitude of the effect estimate was strongest for lag days 6–10 and the AIC values were similar, the lag period days 6–10 was selected for addition into multivariate analysis.

Single-meteorological variable models found each meteorological factor was statistically significantly associated with increased odds of legionellosis (Table 3). Mean, minimum and maximum temperature, dew point, precipitation, and relative humidity were positively associated, while sea level pressure, visibility, and wind speed were inversely associated (Table 3).

Following backward elimination of 'Full Model A,' which included minimum temperature, dew point, and precipitation, 'Final Model A' found sea level pressure and visibility were statistically significantly inversely associated (OR = 0.91, 95% CI 0.88–0.94 for each 5 millibar increase and OR = 0.69, 95% CI 0.59–0.80 for each 5 mile increase,

respectively). Reduction of 'Full Model B,' which included minimum temperature, relative humidity, precipitation, and visibility, resulted in sea level pressure (OR = 0.91, 95% CI 0.88–0.94, for each 5 millibar increase) and relative humidity (OR = 1.08, 95% CI 1.04–1.11, for each 10% increase) remaining in the reduced model. Restriction of the seasonal period for analysis to warm weather months did not result in any meaningful differences compared to the full-year models, with the possible exception of visibility (Table 3).

## DISCUSSION

This state-wide investigation utilizing two study designs to examine a wide variety of meteorological factors found positive associations of legionellosis and monthly precipitation and humidity and inversely associated monthly visibility. Daily humidity and dew point were positively associated with legionellosis, and daily visibility and sea level pressure were inversely associated. Both study designs found associations with measures of temperature to be inconsistent. To our knowledge, this is the largest study of legionellosis and meteorological factors.

Risk of contracting legionellosis depends on three factors: pathogen proliferation, aerosol exposure, and susceptible population. Since *Legionella* is ubiquitous in the environment, given the right meteorological conditions it can be hypothesized that *Legionella* could amplify in the environment and result in more human exposure. Particular weather conditions may allow for *Legionella* bacteria to aerosolize, and to remain in the air for a sustained period of time, potentially increasing both the duration and intensity of exposure.

Monthly precipitation was strongly associated with increased monthly rates of legionellosis; however, this association was not found for daily precipitation measures. The association between precipitation and legionellosis may require an extended latency period, such that a rainy month is more indicative of an environment that would result in increased *Legionella* growth as compared to measures of daily precipitation. Increased precipitation in the environment may allow amplification of *Legionella* in soil, puddles, and surface water such as lakes, streams, and rivers, and surface water which serves as a drinking water source may increase water distribution system occurrence, and precipitation could possibly result in increased growth in outdoor structures such as cooling towers. Associations

**Table 3.** Case-Crossover Study Design Adjusted OR and 95% CI of Associations of Meteorological Factors and Risk of Legionellosis for Full Year and Restricted to April–October.

Meteorological factors*	Unit	Univariate		Full Model A		Final Model A		Full Model B		Final Model B	
		RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
<i>Full year</i>											
Mean temperature	10°F	<b>1.15</b>	<b>1.08–1.22</b>	—	—	—	—	—	—	—	—
Min temperature	10°F	<b>1.17</b>	<b>1.11–1.23</b>	0.96	0.84–1.09	—	—	1.04	0.98–1.11	—	—
Max temperature	10°F	<b>1.10</b>	<b>1.05–1.16</b>	—	—	—	—	—	—	—	—
Dew point	10°F	<b>1.16</b>	<b>1.11–1.21</b>	1.11	0.98–1.25	—	—	—	—	—	—
Relative humidity	10%	<b>1.26</b>	<b>1.18–1.35</b>	—	—	—	—	1.03	0.99–1.08	<b>1.08</b>	<b>1.04–1.11</b>
Precipitation	0.1 in	<b>1.03</b>	<b>1.02–1.04</b>	1.01	1.00–1.03	—	—	1.01	1.00–1.02	—	—
Sea level pressure	5 mb	<b>0.90</b>	<b>0.87–0.93</b>	<b>0.92</b>	<b>0.89–0.95</b>	<b>0.91</b>	<b>0.88–0.94</b>	<b>0.85</b>	<b>0.80–0.91</b>	<b>0.91</b>	<b>0.88–0.94</b>
Visibility	5 mi	<b>0.61</b>	<b>0.52–0.71</b>	0.83	0.68–1.01	<b>0.69</b>	<b>0.59–0.80</b>	0.85	0.68–1.06	—	—
<i>April–October</i>											
Mean temperature	10°F	1.06	0.99–1.13	—	—	—	—	—	—	—	—
Min temperature	10°F	<b>1.09</b>	<b>1.02–1.16</b>	0.87	0.74–1.01	—	—	<b>0.92</b>	<b>0.85–0.99</b>	—	—
Max temperature	10°F	1.05	0.99–1.11	—	—	—	—	—	—	—	—
Dew point	10°F	<b>1.10</b>	<b>1.04–1.16</b>	1.09	0.94–1.03	—	—	—	—	—	—
Relative humidity	10%	<b>1.10</b>	<b>1.06–1.13</b>	—	—	—	—	<b>1.06</b>	<b>1.01–1.11</b>	<b>1.07</b>	<b>1.04–1.11</b>
Precipitation	0.1 in	<b>1.03</b>	<b>1.02–1.04</b>	1.01	0.99–1.02	—	—	1.00	0.99–1.02	—	—
Sea Level pressure	5 mb	<b>0.88</b>	<b>0.85–0.92</b>	<b>0.89</b>	<b>0.85–0.93</b>	<b>0.90</b>	<b>0.86–0.93</b>	<b>0.79</b>	<b>0.73–0.86</b>	<b>0.90</b>	<b>0.86–0.93</b>
Visibility	5 mi	<b>0.60</b>	<b>0.51–0.72</b>	0.94	0.89–0.98	<b>0.93</b>	<b>0.90–0.96</b>	0.80	0.62–1.03	—	—

Values in bold are statistically significant at a significance level of 5%.

\*Lag window of days 6–10 (“likely preceding incubation period”).

with precipitation have been found previously in the Mid-Atlantic Region (Hicks et al. 2007), and in a case–control study in Barcelona, Spain (Garcia-Vidal et al. 2013). In a study of precipitation and Legionnaires’ disease in Taiwan, precipitation was associated with increased risk of disease, but no significant associations were found with relative humidity (Chen et al. 2014). Detections of *Legionella* and rainwater puddles on roads and floods after rainfall (Sakamoto et al. 2009; Schalk et al. 2012; Kanatani et al. 2013) may also be a suggestive of amplification of *Legionella* in the environment with increased rainfall. Also *Legionella* growth in soils may be correlated with increased moisture in the environment (Sakamoto 2015).

Monthly and daily humidity and dew point were also found to be associated with increased risk of legionellosis. Moisture in the air may allow *Legionella* to remain suspended in aerosolized droplets for longer time periods, possibly increasing exposure to bacteria via inhalation. Multivariate time series analyses highlight that when monthly measures of meteorological factors are included in a single model, wet, humid environments, and/or wet, low

visibility environments remain statistically significantly associated with increased rates of legionellosis. The relationship with relative humidity and increased incidence of Legionnaire’s Disease has previously been shown (Fisman et al. 2005; Karagiannis et al. 2009). Vapor pressure, a meteorological factor analogous to relative humidity, was associated with increased risk of Legionnaires’ disease in two regions in Switzerland, but not precipitation, wind, relative humidity, or radiation (Conza et al. 2013).

Visibility, sea level pressure, and wind speed were all found to be inversely associated with legionellosis. Higher visibility indicates the absence of precipitation or fog, both of which may allow for *Legionella* to remain in the air and potentially increase exposure to the bacteria and disease onset. Also, it is possible that high visibility indicates less cloud coverage and more UV sunlight, restricting *Legionella* growth. Lower sea level pressure is associated with precipitation, and thus, an increase in pressure would indicate more precipitation and low humidity, explaining the inverse association. The effect of monthly wind speed is difficult to interpret. On one hand, increased wind would

allow for the spread of any aerosolized *Legionella*; however, the inverse association indicates that wind may disperse the bacteria resulting in a dose which may be too low to result in disease.

Minimum, average, and maximum temperature were assessed independently to estimate associations with legionellosis. Modeling of these daily temperature measures indicated minimum daily temperature to be the most predictive; however when additional meteorological variables were controlled for, minimum temperature was no longer associated. Modeling of monthly temperature measures had varying results. Because legionellosis is seasonal, the initial models were adjusted for month, which likely over adjusted the effect of temperature on disease. Results from single-meteorological variable models of month-adjusted full-year time series analyses appear very comparable to findings to case-crossover analyses with the exception of mean and maximum temperature—which were likely over-controlled for in the time series models. Overall, our findings are supported by research performed in a similar geographic region which found temperature appears to be less predictive of increased risk of legionellosis compared to wet, humid weather (Fisman et al. 2005; Brandsema et al. 2014). Other studies have found temperature to be associated with higher risk of community-acquired Legionnaires' disease (Conza et al. 2013), and associations with temperature were found in a small study ( $n = 78$ ) in Glasgow, Scotland (Dunn et al. 2013).

A time series and a case-crossover study design were used in this study to assess different possible relationships of legionellosis and meteorological factors across the state. The findings from the two different study designs appear to be generally comparable; however, there are some important differences between these designs. Primarily these designs evaluate different exposures—monthly versus daily measures of meteorological factors. Meteorological data were averaged from various stations over a month long period and exposure data was assigned based on month of onset and not necessarily month of exposure. Therefore, exposure variables may not accurately reflect the actual conditions that cases experienced during their exposure periods. Monthly measures were assigned to each case with symptom onset within the given month, regardless of whether onset was earlier or later in the month; therefore, monthly measures may not be reflective of each case's actual exposures preceding disease.

Weather conditions may have to occur before (i.e., be lagged) an individual's exposure to allow for bacterial amplification in the environment. Additionally, this lag would need to account for the latency from exposure to date of symptom onset of legionellosis. The case-crossover design used the following lag periods proposed by Fisman et al. 2005: "likely during incubation" for the average of lag days 1 through 5; "likely preceding incubation" for the average of lag days 6 through 10; and "preceding incubation" for the average of lag days 11 through 15, to investigate the exposure window of importance in increased risk of legionellosis. These lag period windows may not be the most indicative of risk period.

Much of the weather data were highly correlated preventing the addition of all potentially explanatory meteorological variables into a single model. These correlations differed for monthly versus daily exposure measures and this in turn affected the selection of variables for multivariate data analysis between the two study designs. Our study employed the use of 26 weather stations across the state broken into five climatic regions, creating a robust exposure classification. However, there was variability in station distribution and count within each of the regions, and some regions may have had better exposure classification.

## CONCLUSION

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In a large, geographically broad study, we found consistent positive associations of legionellosis with indicators of wet, humid weather, and inverse associations with high sea level pressure and high visibility—indicative of fair weather (Brandsema et al. 2014). There remains uncertainty as to the actual exposure mechanisms which result in these findings. Further research is needed to better understand how meteorological variables interact with each other and to elaborate on the exposure mechanism for which these factors relate to risk of legionellosis.

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## COMPLIANCE WITH ETHICAL STANDARDS

**CONFLICT OF INTEREST** The authors declare they have no conflict of interest.

**ETHICAL APPROVAL** “All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.”

**INFORMED CONSENT** For this study formal consent is not required.

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