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Mass Shock-dosing of Cooling Towers in Response to A *Legionella pneumophila* Outbreak: Did it Work?

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Abstract

Between January and June 2012, a moderate-sized *Legionella pneumophila* serogroup 1 (Lp1) outbreak occurred in Auckland, New Zealand, which involved 19 cases, with two deaths. Initial investigation did not reveal a common source. Poorly maintained cooling towers were a likely cause, and mass shock dosing of all such towers with biocide was undertaken in April 2012 and repeated after an almost identical outbreak in the autumn of 2013. Our aim was to assess whether shock dosing of towers affected disease incidence. A time-series analysis, using regression discontinuity, of the notified Lp1 cases from 2007 to October 2014 was carried out.

A total of 84 out of 92 cases of Lp1 were available for analysis. Seasonal trend decomposition showed an excess of cases in the autumn of 2012 and 2013, with a decline in 2014. Poisson regression showed an average log-linear annual increase in monthly notifications by 40% (95% confidence interval (CI): 17% to 68%), with an average 46% decline (95% CI: 74% decrease to 13% increase) comparing cases before April 2012 to those that occurred afterward. In dispersed outbreaks in urban settings, we conclude that this study supports mass shock dosing of cooling towers to limit disease occurrence.

Keywords: Cooling towers; Regression; Mass shock-dosing; Disease

Introduction

Legionnaires' disease is an uncommon cause of bacterial pneumonia in New Zealand. The pathogen occurs naturally in soil and water, and over 50 different species and 70 different serogroups have been identified. Globally, *Legionella pneumophila* (predominantly serogroup 1) causes the majority of infections [1]. In New Zealand, *L. pneumophila* and *L. longbeachae* are the most common species, accounting for 37.8% (340/900) and 37.7% (339/900) of cases respectively for all laboratory-proven legionellosis identified over the period between 2006 and 2010 [2]. *L. longbeachae* cases rise each year in spring and summer in New Zealand, associated with gardening activity. *L. pneumophila* cases tend to rise in late summer to winter, probably related to higher rainfall, lower winds, and higher humidity, but possibly also due to cooling towers being switched off and cleaned, which typically happens at the end of summer, with the release of biofilm during cleaning. *L. pneumophila* grows in water, and has an affinity for man-made warm water systems.

Survival and growth of *Legionella* species is temperature-dependent, being dormant below 20°C, active between 20 and 46°C [3], and an increasing rate of decline and death at temperatures of 50°C and above [3-5]. The mode of transmission is inhalation of aerosolized organisms [4]. In New Zealand, cases of legionellosis are notified to public health authorities, either from clinicians, or via direct electronic notification of positive laboratory tests.

In New Zealand, five outbreaks have occurred since the early 1970s; four of which were traceable to a point source (a building cooling tower, a display spa pool, a marina waterblaster and a local rain water system) [6]. In early 2012, a disseminated outbreak occurred in the Auckland region, consisting of 19 cases of *L. pneumophila* serogroup 1 (Lp1) occurring between 1 January 2012 and 1 July 2012. Three cases had sputum tested by sequence-based typing of the genetic profiles of the organism. Two matched, and one was unique. Water samples from homes were obtained from twelve cases, with one residential spa pool positive for *L. pneumophila*, while the other 11 cases' homes were negative. Three cooling towers and one car wash were positive for *Legionella*, however the sequence based typing did not match those of the clinical samples. Geospatial analysis did not show indicate a likely point source.

The lack of any point source led the public health unit via a media release (3 April 2012) and letter from the Auckland Council (13 April 2012) to request all cooling tower owners in the Auckland region to shock dose their systems. An estimated 60 to 70% of commercial and industrial wet cooling systems were treated within three days. It was estimated that almost all were treated within four weeks [7]. A similar outbreak also occurred in 2013, with repeat mass shock-dosing undertaken in April 2013. Shock dosing is expected to render *Legionella* species undetectable for between one to thirty days with considerable variability, depending on the characteristics of the tower (one study reported a mean of 14 days, with standard deviation 13 days, based on a sample of experiments undertaken on 9 contaminated towers with chlorinated phenolic thioether [8]).

The aim of this study was to retrospectively consider, using statistical analysis of reported cases, whether shock dosing had limited the extent of the epidemic.

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Methods

Data

Notified, confirmed cases of Lp1 resident in the greater Auckland region were extracted from a nationally administered database (Episurv) between the dates of 1 January 2007 to 31 August 2014. Descriptive analysis characterized the demographic features and geographic location of the cases. The criteria for notification consisted of a clinically compatible illness, along with laboratory evidence of Lp1 infection. Laboratory evidence of Lp1 infection comprised: a positive *Legionella* urinary antigen test (UAT); isolation or demonstration of Lp1 bacteria or antigen in sputum, tissue or other body fluid; a four-fold or greater rise on paired immunofluorescence in serum to a detectable titre of 1:256 or greater; or a stable high detectable titre of 1:1024 or greater in convalescent serum.

Analysis

Data were aggregated into the number of cases reported by month. To standardise the length of each month, cases reported on the 29th to 31st of each month were discarded.

Time-trend analysis consisted of seasonal-trend decomposition, a loess technique, which results in a time series being split into three components: seasonal variation, trend and remainder. The trend component was of greatest interest.

A Poisson model

was also implemented, which had three components: a seasonal component (with time scaled to a unit, and multiplied by $2^*\pi$ so that a complete cycle completes in one calendar year), calendar time and a term for a binary variable which was assigned a value of 1 for data collected after a time point and 0 for values collected before, which represents the effect of the combined 2012 and 2013 shock dosing.

The structure of the model was therefore:

$$\ln(\text{Lp1}_t) = \beta_0 + \beta_1 t + \beta_2 \sin(2\pi\, t) + \beta_3 \cos(2\pi\, t) + \beta_4 t + \beta_5 intervention + \varepsilon_t$$

Where:

t is the calendar time expressed in years and months (e.g. February 2012 = 2012+2/12)

Lp1_t is the monthly count of Lp1 notified cases at a calendar time.

"*intervention*" is a binary variable which is assigned one for a value recorded later than an intervention date and 0 for a value recorded earlier. The intervention period was considered around the time of the first mass-shock dose, so that data collected after the time of the first shock dose, including the second shock dose, was considered part of the post-intervention period.

ε_t is the residual at time *t*.

Beta coefficients were exponentiated to yield incidence rate ratios.

From this calculation, the amplitude α of the seasonality component may be calculated by

$$\alpha = \sqrt{\beta_2^{\,2} + \beta_3^{\,2}}$$

The peak maxima or minima is found by solving for *t*

$$t = \arctan\left(\frac{\beta_2}{\beta_3}\right)\frac{T}{2\pi}$$

Where *T* is the time interval described by one cosine function (here, one year) [9]. The other peak or trough will then be half a cycle (6 months) after the first.

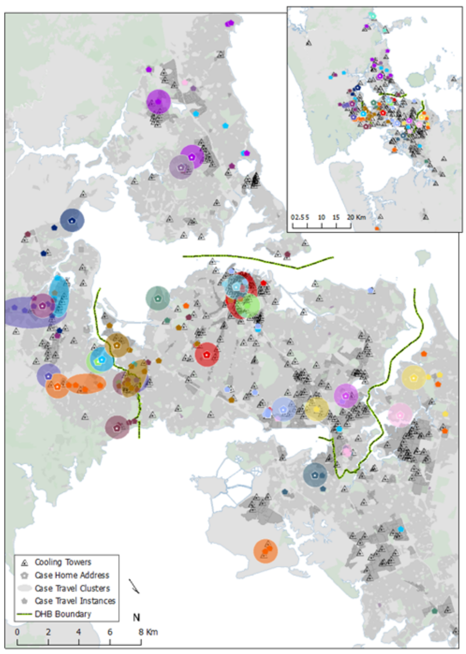
A likelihood ratio test was carried out to assess whether over-dispersion was present, comparing a Poisson to a negative binomial regression model. A two-sided *p*-value of < 0.05 was considered statistically significant. An autocorrelation and partial autocorrelation analysis of the residuals was conducted to consider evidence of pseudo replication.

R software (version 3.1.1), using the **glm** and **stl** functions were used for all analyses.

Results

A total of 92 cases of Lp1 were extracted over the study period from the surveillance database. The distribution of age of cases showed a right skew toward older age groups, with a mean age of 59 years, standard deviation of 17, and range between 2 and 90 years. Cases were 63% (28/92) male. Of the 92, only two were not treated in hospital, 87 required hospital treatment, and three had unknown treatment status. Seven deaths occurred as a result of infection, with two occurring during the first half of 2012. The deaths occurred in people aged between 45 and 89 years.

An informal analysis of the spatial distribution of the residential address of cases which occurred between 1 February 2012 to 30 June 2012, in relation to that of the location of cooling towers, did not show any obvious clustering around one likely source (Figure 1). The figure depicts a map of the Auckland region with the small pentagonal symbols with a white centre representing the location of the case's residence, and triangles denoting the location of known cooling towers. Shaded coloured ellipses and circles highlight areas of travel during the incubation period (two weeks before onset of symptoms). Solid coloured pentagons denote addresses visited during the case's incubation period, including work addresses. From this figure, it shows



DHB: District Health Board

Figure 1: Geographic distribution of cases, including home address, work address, other areas visited, and sites of cooling towers (see text for details).

that, during the high incidence period in 2012, cases resided in close proximity to cooling towers; however, no single cooling tower could be attributed to a majority of cases.

Once the length of months were standardised to 28 days, 84 cases were available for analysis. The number of cases observed per month ranged between zero and seven, with a median of 1, mean of 0.91 and standard deviation of 1.26 (Figure 2; upper plot [data]) (Figure 1).

Seasonal trend decomposition (Figure 2; lower three plots) showed an average annual excess of one monthly case occurring during the autumn months of April and May, with about half a case per month fewer reported in the winter months of July and August ('seasonal' series). The 'trend' component showed a gradual rise in case notifications of one extra case/month between 2007 to 2011. A clear excess of cases occurred in the autumn of 2012 and 2013, with a decline in incidence noted in 2014 (Figure 2).

Poisson regression of the monthly notifications (Figure 3 and Table 1) showed an average log-linear annual increase in monthly notifications of 40% (95% confidence interval (CI): 17% to 68%) over the study period, with an average 46% decline (95% CI: 74% decrease to 13% increase) comparing cases before the May 2012 mass shock dose to those occurring afterward, (assuming the log-linear annual increase continued). Varying this term to other time periods showed that the greatest evidence of a step change in notifications occurred in April 2012, which coincided with the timing of the shock dosing treatments of the cooling towers (Table 2).

The exponentiated amplitude α of the seasonal variation in the mean, attributable to the sine and cosine terms in the model, is 2.16, indicating a 236% (since sine and cosine vary between -1 and 1, then fluctuation is: 2*116%) seasonal fluctuation above and below the mean. The peak of the function is early March, with the low season early August (Tables 1 and 2).

A likelihood ratio test, comparing a Poisson distributed model with a negative binomial model, was not significant at the 5% level, indicating little evidence of overdispersion. Similarly, there was little evidence of pseudoreplication (autocorrelation) in the model residuals (Figure 3).

Discussion and Conclusion

The incidence of Lp1 has slowly increased in the Auckland region in the last seven years, with two recent moderate-sized outbreaks. After accounting for seasonality and overall trends, a statistical model supports an almost 46% decline in the number of cases after shock dosing in 2012, with a repeat dosing given in 2013 in response to an almost identical outbreak in that year. The decline is not statistically significant; however the modelling suggests an almost halving of incidence, given the background and seasonal trends. The time of the first shock dosing has the strongest support for a stepped decline in incidence, from the statistical model, comparing this time period to surrounding months.

A limitation of time-series studies, using data from healthcare settings, is that diagnostic methods and clinical practice may change, leading to an apparent increase in notifications due to improved detection rather than increased burden of disease. The use of rapid mass treatment of cooling towers obviated more detailed sampling and matching of bacteria to the clinical specimens. This evidence would have further supported the use of shock dosing to reduce the burden of disease. Similarly, ecological analyses do not involve a control group, so the evidence for reduction is based on extrapolation of the underlying trend from previous years.

An overview of published dispersed outbreaks of Lp1 is presented in Table 3. Other dispersed outbreaks of Lp1 have resolved spontaneously. In Bloomington, U.S.A, for example [10], a dispersed outbreak was contained by shock dosing only one tower. Two outbreaks stopped although no control measures were performed [11,12], and one outbreak stopped before completion of the decontamination of towers [13].

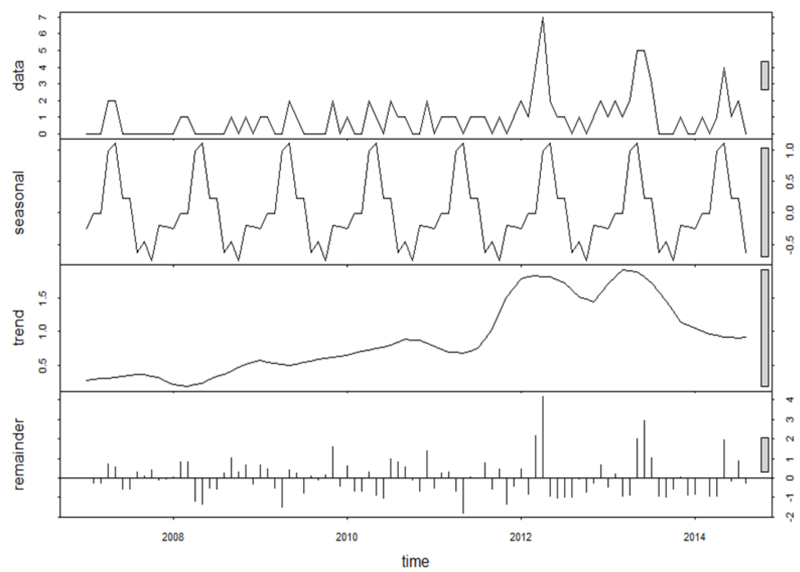


Figure 2: Seasonal trend decomposition of notified cases of *Legionella pneumophila* sero group 1 between January 2007 and August 2014.

Model term	Beta coefficient (95% CI)	Incidence rate ratio (95% CI)
sin(time * 2 * π)	0.74 (0.41 to 1.10)	-
cos(time * 2 * π)	-0.22 (-0.48 to 0.17)	-
Time (years)	0.34 (0.16 to 0.52)	1.40 (1.17 to 1.68)
Intervention†	-0.69 (-1.35 to 0.12)	0.54 (0.26 to 1.13)

†From May 2012 exposed, otherwise unexposed.

CI: confidence interval

Table 1: Incidence rate ratios derived from a Poisson regression model of monthly counts of *L. pneumophila* cases reported from the Auckland Region.

Month of discontinuity (2012; during or after month exposed, otherwise unexposed)	Incidence rate ratio (95% CI)
March	1.71 (0.75 to 4.03)
April	1.13 (0.52 to 2.53)
May	0.54 (0.26 to 1.13)
June	0.55 (0.27 to 1.14)
July	0.61 (0.30 to 1.25)
August	0.62 (0.31 to 1.27)

Table 2: Incidence rate ratios associated with a step change (regression discontinuity) in the number of monthly counts of *L. pneumophila* serogroup 1.

CI: confidence interval

Author	Place	Year	Cases	Management	Result
Broome [11]	Burlington, Vermont, USA	1977	69	Nil	Outbreak stopped
Helms [12]	Johnson County, Iowa, USA	1981	29	Nil	Outbreak stopped
Kool [13]	Los Angeles, California, USA	1997		Some CTs cleaned	Outbreak stopped
Mitchell [14]	Bolton, England	1988	60	Cleaning of a CT at a work site	No more cases
Heath [16]	Sydney, Australia	1995	11	51 towers cleaned	Uncertain
White [17]	Christchurch, NZ	2005	19	Mass shock dosing	Outbreak stopped
Carr [18]	Shropshire, England	2006	6	CT cleaned	Outbreak stopped
Pereira [19]	Norwich, England	2006	8	Super chlorination of 28 sites (including water fountains and car wash facilities)	Outbreak stopped
Keramarou [20]	The Valleys, South Wales	2010	22	Several CTs cleaned	Outbreak stopped

CT: cooling tower; NZ: New Zealand; USA: United States of America.

Table 3: Summary of dispersed *L. pneumophila* outbreaks.

An outbreak of Legionnaires' disease occurred in 1988 in Bolton, England, with 37 cases of pneumonic disease and 23 which were classified as non-pneumonic. Cases were strongly linked to employment at an engineering plant [14] with an odds ratio of 2.98 (95% CI: 1.20 to 7.58), comparing those who worked near or visited the north part of the factory, compared with locals and workers who did not, in a case-control study design. Factory and city cooling towers were cleaned and disinfected. Up to a year afterward, at the time the manuscript was written, no further cases were reported.

In Christchurch, New Zealand (population ~356,000), an outbreak of 19 cases of Lp1 occurred between April and August 2005, and resolved 12 days after a request for mass city-wide shock dosing of

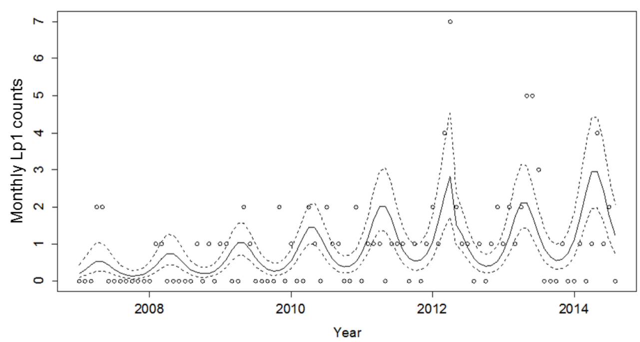


Figure 3: Poisson regression of predicted monthly Lp1 count (solid line), with 95% confidence interval (dashed line) and observed (standardised) monthly counts (open circles).

cooling towers by the local Public Health Unit [7,15]. No evidence of *Legionella* contamination was found in any of the 19 case's homes, urban drinking water wells, ornamental water features, or ponds. Four of the five cooling towers tested were positive for *Legionella,* including two samples of Lp1 from the same tower. However, the Public Health Unit requested shock-dose treatment before some of the sampling was performed. The sequence based typing from one cooling tower matched those of four of the case samples, which indicates that the cooling tower was a very likely source of these four cases. A case-control study was unable to identify risk factors for disease based on home addresses, or where people had visited in the 10 days before symptom onset.

To our knowledge, our study is the only one which undertakes a statistical analysis of time-trend data of the number of notifications (Table 3).

A systematic review of outbreaks of *L. pneumophila* traced to cooling towers reported that 10 of 19 outbreaks had a temporal association with inadequate cooling tower maintenance [21]. The author concluded that contaminated cooling towers were the likely sources of these outbreaks, and that mandatory registration and maintenance of these towers would help limit the severity and duration of outbreaks. To date, only cooling towers that are an integral part of buildings (such as air-conditioned office buildings) in New Zealand have a legal requirement for regular monitoring for *Legionella*; cooling towers used in industrial processes are not covered.

The study points to a number of barriers to *Legionella* control. When mass shock dosing was first implemented, no register of cooling towers was available. A list now exists in Auckland.

This study, along with other historic descriptions, suggests that in dispersed outbreaks, rapid shock dosing of cooling towers in an urban setting is likely to help limit disease occurrence. It corroborates the findings of a number of other studies that report resolution of Lp1 outbreaks after carrying out mass shock dosing of cooling towers. Further, the gradual rise in the incidence of Lp1 means that a case could be made for improved enumeration, monitoring and maintenance of cooling towers in Auckland to limit disease incidence.

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