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Supplemental Material

Multiple Sources of the Outbreak of Legionnaires' Disease in Genesee County, Michigan, in 2014 and 2015

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Figure S1. Crude incidence of Legionnaires' disease per 100.000 over the years 2009 – 2017 in the United State of America (USA, blue (National Notifiable Diseases Surveillance System)), in Michigan (without Genesee County MI-GC, green) and in Genesee County, MI (Genesee County, orange) based on recorded LD cases in the Michigan Disease Surveillance System and United States Census Bureau population data.

Figure S2. Results of free chlorine monitoring at eight fixed monitoring sites (1-8) in the distribution network throughout Flint. These sites were shops, businesses or community service centers where a City of Flint official went to take measurements and samples. X-axes show months in 2014 and 2015 (m-yy); y-axes show free chlorine concentration in mg per L. Red line is 0.2 mg/l, recommended best practice (American Water Works Association, 2007).

Figure S3. Results of the Gaussian plume model: spatial distribution of the highest impact aerosol sources (shown as squares), and the number of cases that are potentially impacted by each aerosol source (shown as color/shade) evaluated with intermediate aerosol concentration threshold $(>0.0001 \text{g/m}^2)$. Aerosol exposure during hospital stays and visits were excluded.

References

Independent review panel

A panel of independent experts was invited to provide critical and frank review of the design of the outbreak investigation, the strength of evidence and completeness of the investigation and the results, conclusions and recommendations, the transparency of the study, appropriate use of data and methods, scientific quality and integrity. Three meetings were organized, in the design phase, mid-term and at the end of the study, in which the design, methods, results and conclusions were presented and reviewed. The manuscript of the paper was also reviewed by the expert panel.

The panel consisted of:

- Dr Mark Dworkin (University of Illinois at Chicago)
- Dr Lisa Fitzpatrick (George Washington University)
- Dr Philippe Hartemann (University of Lorraine, France)
- Dr Paul Hunter (University of East Anglia, England)
- Dr Tim Wade (US Environmental Protection Agency)

Panel members (except TW) were compensated upfront for the time they dedicated to the review.

Pasquill Stability Category	X (km)	а	b
A* (Extremely unstable)	<0.10	122.80	0.9447
	0.10-0.15	158.08	1.0542
	0.16-0.20	170.22	1.0932
	0.21-0.25	179.52	1.1262
	0.26-0.30	217.41	1.2644
	0.31-0.40	258.89	1.4094
	0.41-0.50	346.75	1.7283
	0.51-3.11	453.85	2.1166
	>3.11	**	**
B* (Moderately unstable)	<0.20	90.673	0.93198
	0.21-0.40	98.483	0.98332
	>0.40	109.30	1.09710
C* (Slightly unstable)	All	61.141	0.91465
D (Neutral)	<0.30	34.459	0.86974
	0.31-1.0	32.093	0.81066
	1.01-3.0	32.093	0.64403
	3.01-10	33.504	0.60486
	10.01-30	36.650	0.56589
	>30	44.053	0.51179
E (Slightly stable)	<0.10	24.260	0.8366
	0.11-0.30	23.331	0.81956
	0.31-1.0	21.628	0.75660
	1.01-2.0	21.628	0.63077
	2.01-4.0	22.534	0.57154
	4.01-10	24.703	0.50527
	10.01-20	26.970	0.46713
	20.01-40	35.420	0.37615
	>40	47.618	0.29592
F (Very stable)	<0.20	15.209	0.81558
	0.21-0.7	14.457	0.78407
	0.71-1	13.953	0.68465
	1.01-2	13.953	0.63227
	2.01-3	14.823	0.54503
	3.01-7	16.187	0.46490
	7.01-15	17.836	0.41507
	15.01-30	22.651	0.32681
	30.01-60	27.074	0.27436
	>60	34.219	0.21716

Table S1 Parameter values for horizontal atmospheric stability

* If the calculated value of σ_z exceeds 5000 m, σ_z is set to 5000 m. ** σ_z is equal to 5000 m.

 Table S2 Parameter values for vertical atmospheric stability

Pasquill Stability Category	С	d
A (Extremely unstable)	24.167	2.5334
B (Moderately unstable)	18.333	1.8096
C (Slightly unstable)	12.5	1.0857
D (Neutral)	8.333	0.72382
E (Slightly stable)	6.25	0.54287
F (Very stable)	4.1667	0.36191

Table S3. Clinical Legionella pneumophila isolates ID, hospital A exposure status, Sequence type,NCBI SAMN number.

ID	Hospital A exposure	Sequence type	NCBI SAMN No.
C01	Y	1	12730799
C02	Y	1	12706499
C03	Y (same patient as CO4)	1	11249681
C04	Y (same patient as CO3)	1	11249682
C05	Ν	44	12730802
C06	Ν	213	12730803
C07	Ν	213	12706498
C08	Ν	213	11249677
C09	Ν	222	12730806
C10	Ν	222	11249614
C11	Ν	222	11249679
C12	Ν	1941	11249678
C13	Ν	1941	11249680

ID	Site at Hospital A	Sequence type	NCBI SAMN No.
E01	Cooling tower	Novel	12684123
E02	Cooling tower	1	12684124
E03	Cooling tower	Novel	12684125
E04	Cooling tower	1	12684126
E05	Observation room 1	1	11100908
E06	Observation room 1	1	11101077
E07	Ice machine 1	1	12684127
E08	Patient room 1	1	12684128
E09	Patient room 2	1	12684129
E10	Patient room 2	1	12684130
E11	Ice machine 1	1	12684131
E12	Patient room 2	1	12684132
E13	Patient room 2	1	12684133
E14	Patient room 3	1	12684134
E15	Patient room 2	1	12684136
E16	Patient room 2	1	12684137
E17	Ice machine 1	1	12746497
E18	Patient room 1	1	12746498
E19	Patient room 2	1	12746499
E20	Patient room 2	1	12746500
E21	Drinking fountain 1	1	12684138
E22	Ice machine 1	1	12684139

 Table S4. Environmental Legionella pneumophila isolates from hospital A: ID, site, NCBI number

Table S5. Incidence rate ratio (IRR) of LD in Census block groups with a centroid >2 miles, 1-2 miles and <1 mile from aerosol sources (AS) in 2014 and 2015 using Genesee County population data (Census.gov 2015). Cases with onset between Dec 1, 2014 and Mar 1, 2015 were excluded as, generally, cooling towers are not operational in winter. A multilevel Poisson model was nested in Census block groups and adjusted for age group, sex, interaction factor for proximity and year. An interaction factor for City of Flint water at the residence and year was included to test for the sensitivity of the model to this exposure variable.

2014					
Cooling tower ID	Distance category (miles)	IRR	9!	5% CI	
AS01	> 2	1			
	1 - 2	4.28	1.64	11.19	
	0 - 1	3.73	1.07	13.06	
AS02	> 2	1			
	1 - 2	3.86	1.47	10.13	
	0 - 1	3.87	1.11	13.56	
AS05	> 2	1			
	1 - 2	3.79	1.43	10.01	
	0 - 1	6.57	2.04	21.21	
AS100	> 2	1			
	1 - 2	2.63	0.92	7.51	
	0 - 1	4.42	1.38	14.13	
AS102	> 2	1			
	1 - 2	1.72	0.53	5.59	
	0 - 1	4.68	1.57	13.95	

A. Adjusted for City of Flint water at the residence (See Figure 5)

2015					
Cooling tower ID	Distance category (miles)	IRR	9	5% CI	
AS01	> 2	1			
	1 - 2	0.94	0.21	4.25	
	0 - 1	1.89	0.39	9.25	
AS02	> 2	1			
	1 - 2	0.85	0.19	3.89	
	0 - 1	1.94	0.4	9.52	
AS05	> 2	1			
	1 - 2	1.34	0.38	4.72	
	0 - 1	1.27	0.15	10.34	
AS100	> 2	1			
	1 - 2	2.11	0.64	6.91	

	0 - 1	2.37	0.48	11.78
AS102	> 2	1		
	1 - 2	2.21	0.68	7.2
	0 - 1	2.29	0.46	11.33

B. Unadjusted for City of Flint water at the residence

L

Cooling tower ID	Distance category (miles)	IRR	9!	5% CI
AS01	> 2	1		
	1 - 2	6.75	2.82	16.16
	0 - 1	6.59	2.08	20.83
AS02	> 2	1		
	1 - 2	6.17	2.58	14.73
	0 - 1	6.83	2.16	21.59
AS05	> 2	1		
	1 - 2	5.68	2.30	14.02
	0 - 1	11.20	3.81	32.96
AS100	> 2	1		
	1 - 2	4.48	1.74	11.54
	0 - 1	8.09	2.83	23.13
AS102	> 2	1		
	1 - 2	3.02	1.01	9.05
	0 - 1	8.98	3.35	24.07

2015					
Cooling tower ID	Distance category (miles)	IRR	95	% CI	
AS01	> 2	1			
	1 - 2	0.91	0.21	3.89	
	0 - 1	1.77	0.40	7.82	
AS02	> 2	1			
	1 - 2	0.83	0.19	3.55	
	0 - 1	1.84	0.42	8.11	
AS05	> 2	1			
	1 - 2	1.31	0.39	4.40	
	0 - 1	1.21	0.16	9.26	
AS100	> 2	1			
	1 - 2	1.78	0.61	5.18	
	0 - 1	1.93	0.44	8.44	
AS102	> 2	1			
	1 - 2	1.88	0.65	5.47	
	0 - 1	1.86	0.42	8.17	



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Figure S3. Results of the Gaussian plume model: spatial distribution of the highest impact aerosol sources (shown as squares), and the number of cases that are potentially impacted by each aerosol source (shown as color/shade) evaluated with intermediate aerosol concentration threshold (>0.0001g/m²). Aerosol exposure during hospital stays and visits were excluded.

References

American Water Works Association, 2007. Partnership for safe water. Distribution. <u>https://www.awwa.org/AWWA-Articles/tech-tip-chlorine-residual-measurement</u>