Risk Assessment Group

CONSULTATIVE SIGNAL ASSESSMENT
PRIMARY RISK ASSESSMENT
EVIDENCE BASED RISK ASSESSMENT
PUBLIC HEALTH EVENT ASSESSMENT

LEGIONELLA OUTBREAK, OOST VLAANDEREN

Date of the signal	Date of the PHEA	Signal provider	Experts consultation	Method
07/05/2019	17/05/2019	AZG	**Permanent experts:** Dr Valeska Laisnez (AZG), Dr Romain Mahieu (COCOM-GGC), Dr Paul Pardon (FOD), Dr Carole Schirvel (AViQ), Dr S. Lokietek (AViQ), Dr. C. Theugels (LNE), Ms M. Thomas (Ost Belgie), Dr Sophie Quoilin (Sciensano). **Specific experts :** Prof. Dr D. Piérard (VUB), Dr N. Hammami (AZG), Dr S. Jacquinet (Scidensano), Ms S. Klamer (Sciensano).	eMail
Date of update	Closing date			

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Signal	On 07th May 2019, an outbreak of legionellosis has been identified by the Agentschap Zorg en Gezondheid after the notification of 7 cases in two days in the same city, Evergem, in the North of Gent. **Situation on 22/05/2019:** 25 cases with 24 confirmed cases First case notification on 6th May. The date of onset of cases was between 29th April and 18th May. All are confirmed cases by urine antigen positive in all patients, some of them also PCR and/or culture positive on a respiratory sample. The patients are geographically clustered, especially with regard to their place of residence or, for some, their working area.

Hazard description	
Criteria	Description
Cause	Legionellosis is a respiratory disease caused by Legionella.
Reservoir	Legionella bacteria are common and found naturally in environmental water sources (living in t° 5-60° but multiplying between 20 and 50, ideally 35°) such as rivers, lakes and reservoirs, usually in low numbers. The bacteria can multiply in man-made aquatic systems like cooling towers, evaporative condensers, humidifiers, decorative fountains, hot water systems and similar systems.
Transmission	Legionella is transmitted via aerosolization and inhalation of small droplets (< 5µm). No human-to-human transmission but exposition can be large mainly if legionella is spread by a cooling tower.
Epidemiology	In Belgium, more than 200 cases are diagnosed each year with an estimated incidence of 2/100.000 inhabitants a year with a peak during summertime. Brussels Capital Region is slightly more affected than the other regions. Since 2009, an increasing trend is observed. Sex ratio M/F is 2.5/1, most affected age group is among the 40+. Incubation period: usually between 2 and 10 days, max. 20 days. Recent studies show an association between temperature and temperature precipitation and atmospheric pressure with the risk of occurrence of legionellosis, especially if the temperature increases simultaneously with rainfall (1, 2, 3). This association has been put in evidence in Belgium (see annex). Large explosive outbreaks in the community are mostly associated with cooling towers or wet air-conditioning system used in buildings or structures that have complex water systems, like hotels and resorts, long-term care facilities, hospitals, and cruise ships. Such large outbreaks are described (not exhaustive list): • France in 2004: 86 cases and 18 deaths (CFR: 21%), associated with cooling tower, • UK in 2012: 92 cases and 4 deaths (CFR: 4%), possibly associated with cooling tower, • UK in 2010: 22 cases and 2 deaths (CFR: 9%), unknown, • Spain in 2012: 18 cases and 3 deaths (CFR: 16%), plumbing system in a hotel, • Portugal in 2014: 375 cases and 12 deaths (CFR: 3.2%), associated with cooling tower, • Portugal in 2017: 56 cases and 6 deaths (CFR: 11%), associated with cooling tower, In Belgium, we faced two major events associated with Legionella both in 1999: • Houffalize: 7 cases and 1 death (CFR: 14%), warm water system in a hotel, • Kapellen: 93 cases and 5 deaths (CFR: 5%), bubble bath in trade fair.
Severity	Legionellosis can be severe in patients having underlying conditions, immunocompromised people; in elderly; smoking; alcoholism; … Case-fatality rate estimated on Belgian data is about 5 to 8% (up to 15% in Heymann). Antibiotic treatment is effective.
Exposure	The infective dose is unknown, but it can be assumed low in sensitive subjects, with cases of disease occurring after brief exposures or at a distance of up to 3 km or more

(12 Km described during the outbreak in France) from the place of origin of the outbreaks.

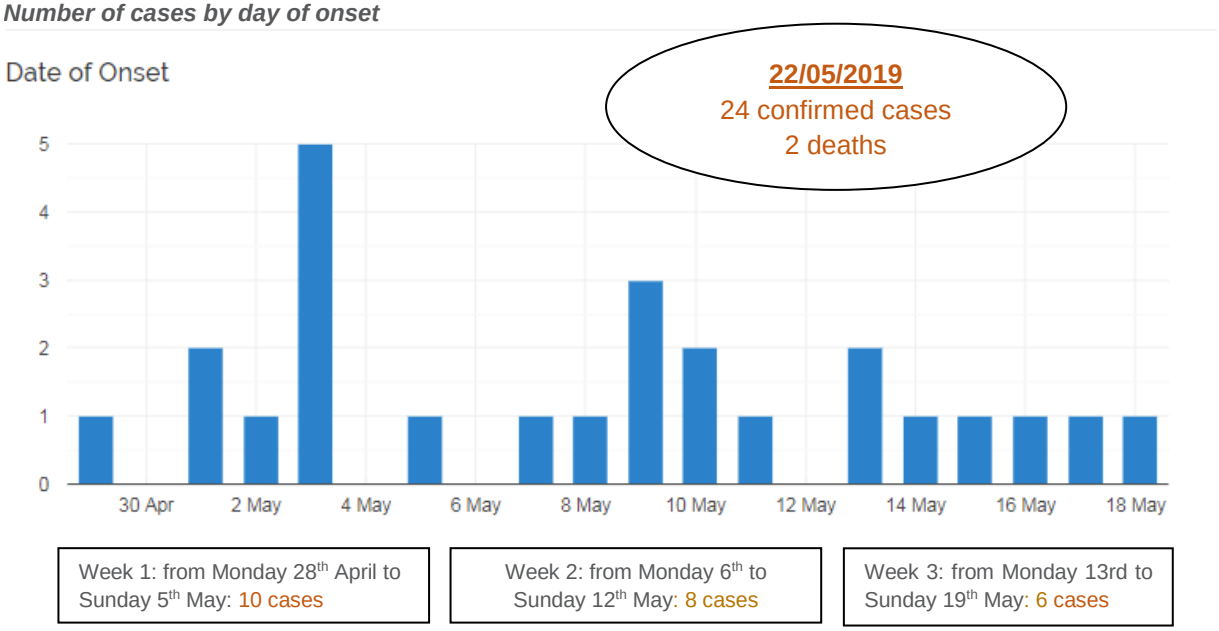
The probability of outbreak depends on :

- bacterial concentrations in the water source,
- production and spread of aerosols,
- host-related factors such as age, pre-existing conditions,
- virulence of the particular strain of Legionella,
- meteorological conditions.

Most infections do not cause illness.

Hazard characterisation

Criteria	Description
Time	**Case definition**: ***Confirmed case*** : a person living or working in a 12 Km radius around the Langerbrugge eiland, between 19th April and the 16th May, having a compatible clinical picture and laboratory confirmation (e.g.: urinary antigen test, culture). ***Probable case :*** a person having stayed less than 100 minutes or living/working outside the 12 Km radius around the Langerbrugge eiland, between 19th April and the 16th May, having a compatible clinical picture and laboratory confirmation (e.g.: urinary antigen test, culture). Based on this case definition: there 24 confirmed cases and 1 probable. **Epidemic curve**: https://www.wiv-isp.be/epidemio/epistat/legi.aspx 20/05/2019: First case date of onset 29th April and last case 18th May ***Number of cases by day of onset***



Week 1: from Monday 28th April to Sunday 5th May: 10 cases

Week 2: from Monday 6th to Sunday 12th May: 8 cases

Week 3: from Monday 13rd to Sunday 19th May: 6 cases

If we consider a mean incubation period of 2 to 10 days, and the onset for the index case on 19th April with a last case on 18th May, the incriminated period start on 19th April (29th April – 10 days) until 16th May (18th May -2 days). It is not possible to define the most likely period of exposure while this outbreak is probably not a point source outbreak meaning that persons are exposed to the same source over a brief time. Here the exposure is more spread over time what is coherent in case of an outbreak due to an environmental contamination by a cooling tower or air conditioning system.

Place

The first cases appeared in the city of Evergem in the north of Gent, East Flanders. Among the cases who were not living in Evergem, 7 have a working activity in the industrial zone located along the canal.

Attack rate:

Evergem: 2.56/10.000 inhabitants (39.000 inhabitants, based on postcode 9940)

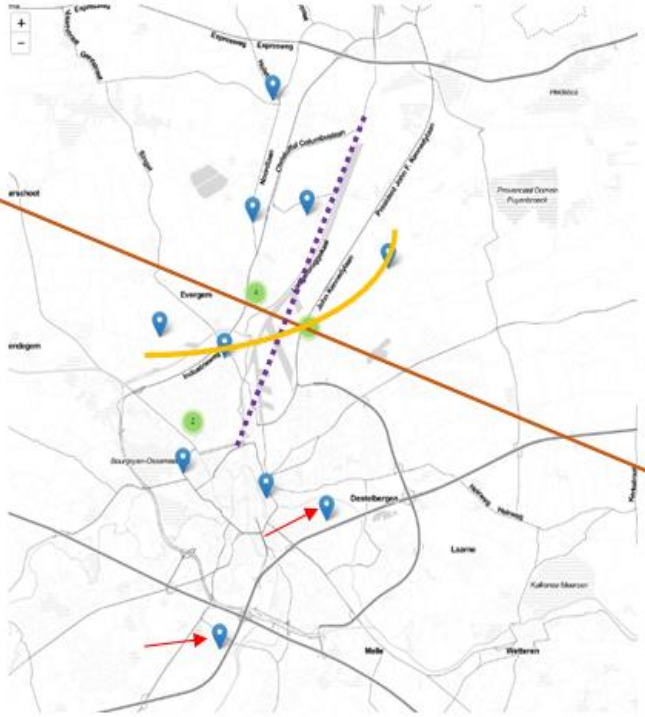
Ghent municipality: 0.24/10.000 inhabitants (250.000 inhabitants, based on postcode 9000).

Evolution in the outbreak:

If we take into account the situation after two weeks (until 16th of May), the radius of cases is about a 10 on 20 Km around this industrialised zone.

A difference in the characteristics of the patients based on their place of residence is also observed. Cases living in Evergem are more likely to be retired or disabled with a higher mean age compared to the cases living in Gent.

Two patients can be considered like outliers



Above the line :

9 patients are inactive (Pension/Disability) – Staying home and then more exposed or reliable to the demography of the neighbourhood?

6 patients have underlying conditions or are smoker and alcoholic (67%)

Mean age: 66 y

6 cases during the first week (67%)

Under the line:

11 patients and among them 9 are active + index case who is inactive with underlying conditions.

4 patients have underlying conditions (36%).

Mean age: 45 y

5 patients during the second week (56%)

→ Only two patients do not mentioned contact in axis ····· where other cases are living or working.

Persons

Clinical situation at 22/05/209: 25 cases all diagnosed by urinary antigen test and 9 patients had respiratory analysis. All respiratory samples that become positive for PCR (6) or culture (1) are sent to the NRC.

24 patients were hospitalised with a clinical picture compatible with Legionella infection.

Severity: 6 patients stayed in Intensive care unit (25%) and among them 5 cases occurred during the first week what is in line with pre-existing underlying conditions in these patients.

Case fatality rate: 8.3%, 2 patients died.

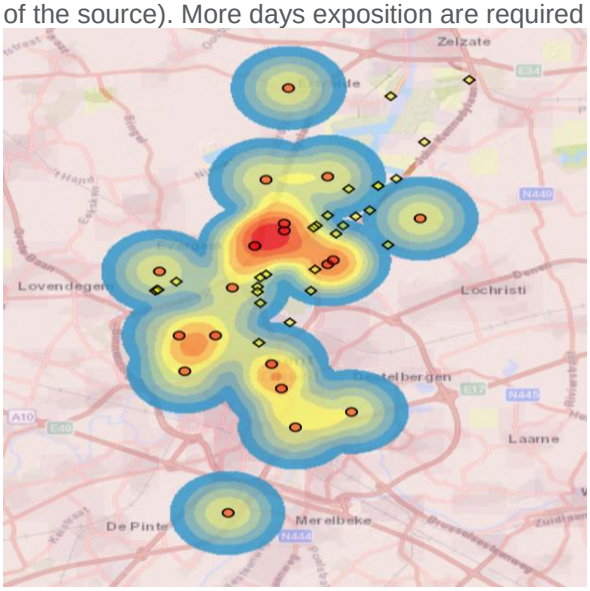
Mean age: 55 y with a median of 52 y (22-90).

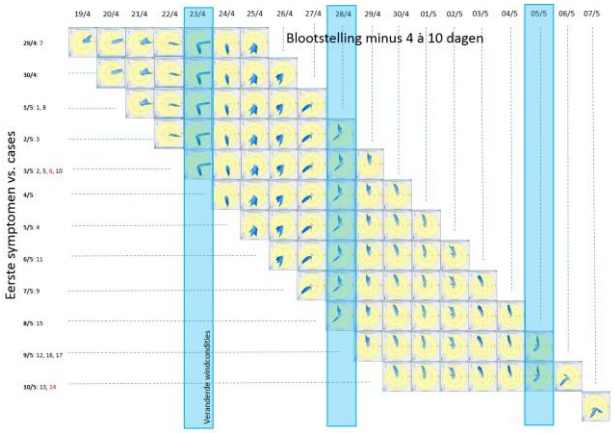
Sex ratio M/F: 5/1

Risk factors for the 24 confirmed cases

	< 65 Y	> 65 Y	% /risk factors
No risk factors	3	2	/
Smokers	3	0	18%
Smoking/alcoholism	2	0	12%
Underlying pathologies	2	6	44%
Unknown	4	2	/
Total at risk patients*	70% (n=10)	75% (n=8)	72%

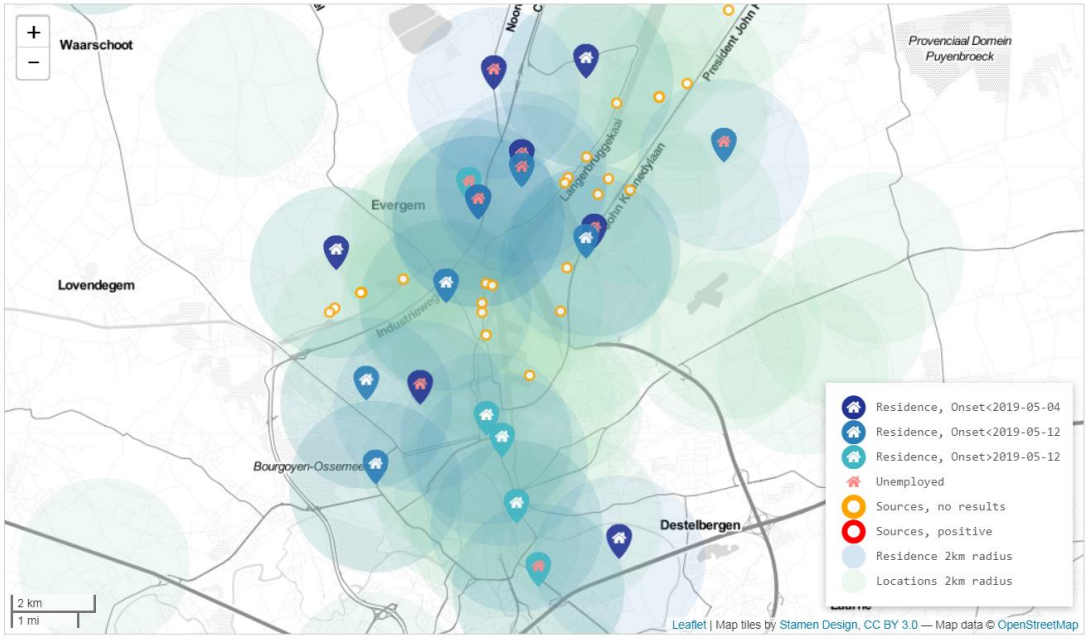
*Based on the number of available information

Risk characterisation	
Criteria	Description
Production and spread of aerosols	Presence of Legionella in cooling towers and air-conditioning systems is known and infrastructure must - have containment plan with regular sampling and cleaning procedure, - notify their infrastructure to a central register. A list of these infrastructures is available in Flanders and they have been mapped. A first set of 17 cooling towers were sampled, started on 9-10th May. Double check with companies if disinfection was implemented on 16th of May. Currently all companies (first set of 17 and second set of 9) are requested to perform weekly disinfection until the end of the outbreak. The risk area has been delineated on the basis of geographical proximity to the cases considering that the concentration is probably higher around the source (first cases closer of the source). More days exposition are required if living farest of the source (5).  ***Map ECDC***
Bacterial concentrations in the water source	96 samples have been taken between 9th May and 17th May in 17 industrial sites. Results of the culture are pending.
Host-related factors such as age, pre-existing conditions	Most of the patients have underlying conditions.
Strain: virulence and characterisation	National reference centre will - characterise the strain in human samples - compare human and environmental sources if strains are identified.
Meteorological conditions	In April following the KMI (https://www.meteo.be/nl/klimaat/klimatologisch-overzicht/2019/april) Relative humidity : 66% (nl= 72): dry conditions, droplets do not spread far. Fee precipitation: 36 mm (nl: 51.3): few precipitation Temperature: 11°C (nl: 9.8°C) Mean speed wind in April: 3.3 m/sec while the normal is 3.7 m/sec: limited speed of wind. Main direction of the wind in April was East. AZG did a mapping of the wind direction in the zone from the first possible day of exposition. This chart highlights two changes in the direction of the wind between the 19th April and the 7th May.



Contribution of climatic conditions to the outbreak is probably limited.

Conclusion	The source is probably related to a cooling tower or wet air-conditioning system. To find Legionella in cooling tower or wet air-conditioning system is expected even after disinfection. Exposed population: population living or working in about a 12 Km radius around the source. More cases are expected. No risk of international spread but foreigners staying in the zone could be infected. Confirmation of the source after: - microbiological match between human and environmental strains and/or - very high level of contamination in an infrastructure or major variations in Legionella contamination in an infrastructure

Public health impact	
Criteria	Description
Risk	Large outbreak of Legionella is unusual but expected as Legionella is present in water and because there are a lot of cooling towers or wet air-conditioning systems. The zone around the canal is at risk due to the presence of a high density of industries. The risk can be characterised as medium because - no person-to-person transmission but case fatality rate in patients with risk factors can be as high as 20%, - decreasing trend between first to third week (even if a second wave cannot be excluded), - main control measures already taken but the possibility remains that the source is still active. Considering the clustering effect and the industrialised place, the source of infection is probably located in the southern zone of the canal Gent and cooling towers remain the main suspect. It is possible that - the source will be never clearly identified, - several waves of cases will be observed possible.
Measures	Control measures already taken: • Date 13/05: Information to the population of region Gent and Evergem to seek medical care if suggestive symptoms. • Date 7/05 : Circular letter sent to GP/hospital of region Gent, Evergem, Lochristi and Zelzate (with regular updates, at least once a week) • Epidemic inquiry in two rounds (generic and detailed daily trips) among the cases • Between 7th and 15th May: 17 + 9 companies have been identified as potentially at risk to be the source of the outbreak and samples have been taken before they disinfected their installations. The results are still pending. • Companies have been asked to notify possible sources and to disinfect them. Zone at risk delimited based on the proximity with the living place/working place of the cases. • AZG send data on human cases to Sciensano for mapping (by localisation of cases, status, chronology, …) and epidemiological analysis: maps are available on a specific interactive page in Epistat: https://www.wiv-isp.be/epidemio/epistat/legi.aspx by using usual login and pw. ***Map Sciensano***  • AZG and VITO will analyse (waiting for approval of attorney) the localisation data of the mobile of patients who are not living or working in the incriminated zone.

Assessment	If we refer to the density of the cases during first two weeks, the zone of the harbour is plausible. If we refer to the outbreak occurred in the Nord Pas de Calais in 2004 during which they found associated cases up to 12 km around the source, a radius of patients distributed on a maximum distance of about 11 on 21 Km is plausible. The first measures taken are proportionated to the current situation. The first results from environmental samples will orientate the next steps: If positive results in environmental sampling: - incriminated societies will provided their logbooks in order to evaluate how their managed the risk of Legionella; - strains will be send to the NRC for comparison with human strains; - iterative samples from all these installations until the outbreak is eradicated; If microbiological concordance between human and environmental strains: the source is identified. - iterative samples from all the incriminated installations until the outbreak is eradicated. If new increase in the number of cases or if no microbiological concordance between the strains, depending of the epidemiological situation, additional measures will be discussed.
Additional measures	To evaluate if the radius has to be extended, based on localisation of the new cases; To list on a larger radius all other structures able to induce aerosolisation of contaminated droplets; To sample these infrastructures on a circle strategy; To broaden the type of societies to be investigated (e.g.: car washes, public drinking water network, private wells for drinking water, industrial drilling, water treatment plants, water jets and decorative fountains, cleaning equipment for sewerage networks and roads, canals, …); To maintain iterative samples from all these installations until the outbreak is eradicated; To sample domestic hot water circuits in the homes of all cases; To sample air; To contact ECDC with official request for support.

Update on 21st May: results from environmental sampling

For 5/17 companies : L. pneumophila is present and in 2 in very high concentration.
Inspection rounds started on 20th May in the 2 companies, on 21st May in two other companies.
The results of the other companies sampled on a later date are pending.

REFERENCES

1. Brandsema PS, Euser SM, Karagiannis I, Den Boer JW, Van Der Hoek W. Summer increase of Legionnaires' disease 2010 in The Netherlands associated with weather conditions and implications for source finding. Epidemiol Infect. 2014. Nov;142(11):2360-71. 5.
2. Hicks L. A., Rose JR., C. E., Fields B. S., Drees M. L., Engel J. P., Jenkins P. R., Rouse B. S., Blythe D., Khalifah A. P., Feikin D. R. & Whitney C. G. Increased rainfall is associated with increased risk for legionellosis. (2007). Epidemiology and Infection 135, pp.811 – 817. 6.
3. Beauté J, Sandin S, Uldum SA, Rota MC, Brandsema P, Giesecke J, Sparén P2. Short-term effects of atmospheric pressure, temperature, and rainfall on notification rate of communityacquired Legionnaires' disease in four European countries. Epidemiol Infect. 2016 Aug 30:1- 11.
4. "Surto de legionella com origem pelo menos numa das torres de arrefecimento do São Francisco Xavier" [Legionella outbreak with origin in at least one of the cooling towers of São Francisco Xavier]. Jornal de Negócios (in Portuguese). November 16, 2017. Retrieved November 24, 2017.
5. Epidémie de légionellose dans le Pas-de-Calais. Novembre 2003 à janvier 2004. Rapport de la mission d'appui. INVS. http://invs.santepubliquefrance.fr/publications/2004/legio_pas_de_calais/rapport_mission_pdc.pdf

ANNEXES

Weather dynamics explain part of the increase in reported domestic Legionellosis cases, Belgium 2010-2017

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Background: In many European countries, the number of reported domestic legionellosis cases is increasing. This might be linked to easier access to diagnostic methods and an increased awareness among physicians. There is increasing evidence that the number of legionellosis cases is associated with meteorological factors. In Belgium, the number of reported domestic legionellosis cases increased from 131 in 2010 towards 200 in 2017, with a peak of 217 cases in 2016. Over these 8 years, both the daily maximal temperature and the relative humidity showed an increasing trend. We aim to identify an association between the number of reported domestic legionellosis cases in Belgium and the selected meteorological variables.

Materials/methods: The case-based information concerning the reported legionellosis cases was obtained from a combination of three surveillance systems: the laboratory sentinel surveillance network, the national reference center and the mandatory notifications. As a date variable, date of onset was used. Meteorological data was obtained from the weather institute (KMI) in Uccle, Brussels. Daily data was available for the daily average relative humidity (RH) and for the daily maximum temperature (Tmax). The meteorological variables were averaged per week. Time series analyses were performed using Poisson regression, adjusted for annual seasonality. RH and Tmax were included in the model with multiple time lags and interaction terms were included.

Results: There was an increasing trend over time, with 0.0013 legionellosis cases per week during 2010-2017, representing an increase of 14 cases per year. When adjusting for the meteorological components RH and Tmax, we still identify a significant increase over time, with 0.0011 cases per week during 2010-2017, representing an increase of 12 cases per year. We can thus conclude that the overall observed increase over time in the number of reported legionellosis cases is partly explained by the dynamics of these two meteorological variables over time.

Conclusions: We show an association between selected meteorological conditions (RH and Tmax) and the occurrence of domestic cases of legionellosis. The overall increase of reported legionellosis cases is partly explained by an increase in RH and Tmax. Overall, these associations may be useful in predicting periods of high risk and targeting public health interventions.

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Weather dynamics explain part of the increase in reported domestic legionellosis cases, Belgium 2010-2017

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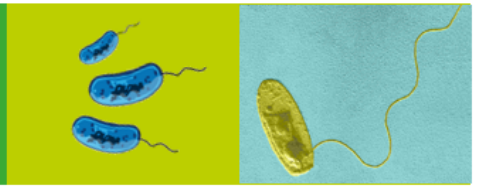


CONTEXT: In many European countries, the numbers of reported cases of domestic legionellosis are increasing. This might be linked to improved access to diagnostic methods and an increased awareness among physicians. Besides, there is increasing evidence that the number of legionellosis cases is associated with meteorological factors.

AIM: We aim to assess the association between the number of reported domestic legionellosis cases and selected meteorological variables in Belgium, during 2010-2017.

Methods

Data sources

- Case-based information concerning reported legionellosis cases was obtained from a combination of three surveillance networks:
  - the laboratory sentinel surveillance network,
  - the national reference center
  - the mandatory notifications.
- Meteorological data was obtained from the weather institute (KMI) Uccle, Brussels. Data was available for:
  - daily average relative humidity (RH) and
  - daily maximum temperature (Tmax).

Case definition

- Case definitions of the three surveillance networks were followed.
- Cases with known travel history during the incubation period were excluded from the analysis.

Data analysis

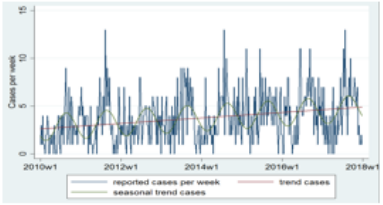
- Date of onset was used as date variable for cases.
- Meteorological variables were averaged per week.
- Values for Tmax and RH were categorized in quantiles or analysed as a continuous variable.
- Time series analyses were performed using Poisson regression, adjusted for annual seasonality.
- RH and Tmax were included in the model with multiple time lags and interaction terms were included.
- Data analysis was performed in STATA 14.1.

Results

In Belgium, the number of reported domestic legionellosis cases increased from 131 in 2010 towards 200 in 2017, with a peak of 217 cases in 2016.

Year	Imported	Domestic	Total
2010	0	131	131
2011	5	176	181
2012	15	150	165
2013	12	179	191
2014	21	176	197
2015	22	211	233
2016	26	217	243
2017	22	200	222
Total	123	1440	1563

Domestic and imported cases of legionellosis, Belgium 2010-2017.



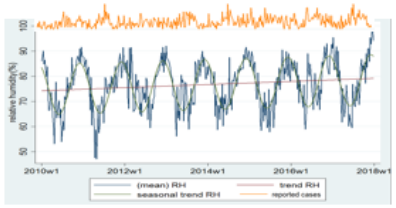
Adjusted for annual seasonality (26 and 52 weeks), there was an increasing trend over time during 2010-2017 for the number of domestic legionelloses, with a slope of 0.0013 cases per week, representing an increase of the annual number of cases with around 14 cases (Poisson regression).

	Adjusted IRR	95%CI	P-value
Trend	1.0011	1.0007-1.0016	0.000
RH, 2 week delay	1.037	1.018-1.055	0.000
Tmax, 2 week delay	1.089	1.018-1.165	0.000
Interaction Tmax*RH	0.999	0.998-1.000	0.01

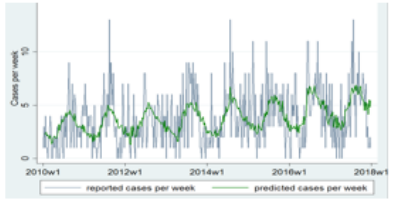
Multivariate model, adjusted for seasonality (26 and 52 weeks), providing incidence rate ratio (IRR), confidence interval (CI) for trend over time (per week), maximum temperature (Tmax, with two weeks delay) and relative humidity (RH, with two weeks delay).

Over these 8 years, both daily maximal temperature (Tmax) and relative humidity (RH) showed an increasing trend.

Adjusted for annual seasonality (26 and 52 weeks), there was an increasing trend over time during 2010-2017 for the Tmax, with a slope of 0.002 °C per week (linear regression).



Adjusted for annual seasonality (26 and 52 weeks), there was an increasing trend over time during 2010-2017 for the RH, with a slope of 0.009 percent per week (linear regression).



When adjusting for the meteorological components RH and Tmax in addition to annual seasonality (26 and 52 weeks), we still identify a significant increase over time during 2010-2017, with a slope of 0.0011 cases per week (Poisson regression), representing an increase of the annual number of cases with around 12 cases .

Discussion and limitations

- Meteorological conditions can be very local, and we included values from only one weather station, which was located centrally within the country but might not represent the conditions for the whole country.
- It would be interesting to include additional meteorological variables like atmospheric pressure, precipitation and wind speed.
- Time periods were fixed to weeks in our analysis: moving periods with flexible length of days might capture the associations better.
- The meteorological components are by definition modelling 'out-of-season' values, because the model was adjusted for annual seasonality.

Conclusions

- We show an association between selected meteorological conditions (RH and Tmax) and the occurrence of domestic cases of legionellosis in Belgium during 2010-2017.
- The observed overall increase in reported legionellosis is partly explained by the dynamics of RH and Tmax over time.
- The increase in legionellosis cases can not be explained completely by meteorological variables, and an increase in awareness and testing practices may contribute to the increase.

Recommendations

- We recommend further studies to model the spatial-temporal relationship between meteorological variables and legionellosis cases in Belgium.
- Regional infectious disease management teams and physicians might be more alert for cases of legionellosis around 14 days after out-of-season humidity and warm weather conditions.
- Real-time predictive models may be developed that may warn public health workers and physicians when weather conditions occur that imply increased risk of legionelloses.

EPIET

ACKNOWLEDGEMENTS

We acknowledge the KMI (royal meteorological institute) Belgium and Natalia Bustos Sierra for the meteorological data.

This work has been performed in the course of the EPIET program. We thank Ioannis Karagiannis and the facilitators for organising the time series training module and Els Duysburgh, Daniel Thomas, Amber Litzroth and Javiera Rebolledo for (co-) supervision of the EPIET program.

We acknowledge laboratories and physicians who participated to the surveillance network and Y. Dupont and G. Muyldermans for management of the laboratory surveillance network and data.

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