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Cooling towers influence in an urban environment: A predictive model to control and prevent *Legionella* risk and Legionellosis events

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ABSTRACT

Cooling towers (CTs) are used to dissipate excess heat from water by evaporation, common in large facilities as hospital, companies, and hotels.

The main risk attributed to CTs is represented by *Legionella*, a Gram-negative bacterium associated with a severe form of pneumonia known as Legionnaires' disease (LD). The infection route is by inhalation of aerosols reaching the lower respiratory tract.

Despite several events associated with CTs, the knowledge in this field is still limited.

The aim of this study was to develop a predictive model of bioaerosol dispersion using PM_{10} particles as a proxy, to generate risk maps of *Legionella* spread in the surrounding area in several weather and microbiological conditions.

The *Legionella* contamination in the CT basin was 40938 ± 24523 cfu/L, with four peaks independent of the season, associated with an increase in air minimum temperature values (+1–2 °C) and a high relative humidity (66–100%) preceded by rainfall (0.2–30.6 mm/day).

The model revealed that the most extensive bioaerosol spread is predicted in winter and summer, with an increase in *Legionella* risk at a distance of up to 1.5 km from the CT.

This method represents a novel integrated approach for the prevention and management of LD risk in CTs.

1. Introduction

Cooling towers (CTs) are specialized heat exchangers used to remove excess heat by evaporation of water [1]. These devices are generally part of air conditioning, ventilation and/or heating systems of most commercial, industrial, residential and hospital buildings. Due to their characteristics, such as semi-open water basins and constant water temperatures (20–35 °C), CTs are recognized as ideal environments for microbial growth and sources for dissemination of human pathogens [2–4]. The main public health risk associated with CTs is Legionnaires' disease (LD), a severe and potentially fatal pneumonia caused by *Legionella* [5]. The *Legionellaceae* family consists of the single genus *Legionella*, which includes more than 64 species, divided into more than 70 different serogroups (SGs) [6]. *Legionella* is a ubiquitous Gram-negative bacterium, living both in natural and artificial aquatic ecosystems, the latter including hot water plumbing, showerheads, faucets, hot tubs, as well as CTs [7–10]. *Legionella* can survive in a range of temperatures between 5.7 and 63 °C with an optimal growth temperature between 25 and 40 °C [11,12]. More than 80% of LD cases are caused by *Legionella pneumophila* SG 1 (*Lp*1), while the remaining 20%

Abbreviations: BAC, Baltimore Aircoil Company; CTs, Cooling towers; Cys-, without L-cysteine; Cys+, with L-cysteine; DTM, digital terrain elevation; IEM, Iowa Environment Mesonet; *Lp*1, *Legionella pneumophila* SG 1; SE, standard error; SGs, serogroups.

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are caused by other serogroups and species, such as *L. anisa*, *L. bozemanii*, *L. dumoffii*, *L. jordanis*, *L. longbeachae*, *L. micdadei* [13]. LD is usually contracted through inhalation of aerosols containing *Legionella* bacteria, produced when water droplets with size lower than 0.5 μm generated by contaminated water systems are aerosolized [14,15]. However, the exclusive occurrence of *Legionella* in water distribution systems or in devices supplied by water is a condition necessary but not sufficient to cause LD [16]. There are several risk factors correlated to LD risk, such as male sex, advanced age (>65y), cigarette smoking, presence of chronic diseases and immunodeficiency [8].

In Italy, the incidence of LD in 2020 amounted to 34.3 cases per million inhabitants. According to data from the Italian Institute of Health, among the 2074 cases notified, 87.4% were classified as community-acquired, 6.4% were travel-associated, 6% were hospital and other health care facilities linked [17]. Although the criteria for case definition is well established [18], the LD diagnosis is commonly based on urinary antigen and other commercial tests, able to detect mainly infection by *Lp*1. Therefore, due to the difficulties linked to culture techniques necessary to isolate *Legionella* from respiratory samples, as well as to the low sensitivity and specificity of the diagnostic tests, the disease remains currently underestimated [7]. Other relevant issues are linked to the localization of the source of infection, especially when the disease is acquired in communities (homes, hotels, social activities) where the *Legionella* surveillance is poorly applied, and the preventive measures are missing. The problems with notification have increased also with the ongoing SARS-CoV-2 pandemic situation started in 2020 that has probably led to an underestimation of LD diagnosed cases especially due to the similarity of the COVID-19 symptoms with the pulmonary forms caused by *Legionella* [19–21].

Independently of the device, the production and mechanisms of aerosol dispersion are exactly the same. CTs are stated as the most common sources of worldwide *Legionella* outbreaks mainly for their capacity to disperse contaminated aerosols over long distances. Problems of particular interest are plume rise/deflection, condensation, and drift deposition, mainly in the case of inadequate maintenance and disinfection treatments, with consequent *Legionella* development. The CTs produce a plume containing bio-contaminated droplets capable to spread in the atmosphere in relation to CT design and meteorological conditions [22]. Several studies reported that the CT plumes can spread also over several kilometers of distance from the source [23–29]. Therefore, CTs represent a risk not only for people residing in proximity of the CT area, but also for other people downwind the CT plumes [30].

In addition, many studies reported that the dispersion of aerosol emitted from CTs can be promoted under specific meteorological conditions characterized by the presence of stagnant air masses and thermal inversions, high air temperature and relative humidity, the latter being associated with precipitation and/or damp weather conditions [31–36].

Looking at the CTs involvement in *Legionella* diseases, Murcia (Spain) experienced Europe's greatest community-borne outbreak in July 2001 with almost 800 cases, 449 of which were confirmed, and six fatalities. The infection outset was found to be a cooling tower [24].

In Italy, several LD outbreaks linked to CTs have been identified since 1995. The first major epidemic occurred in August 1995 in Sestri Levante (NW Italy) with 34 confirmed cases. On that occasion, cases of disease were detected within a radius of 3 km, and, for the first time, a cooling tower was identified as the source of the infection [37]. Between August and October 2003, another LD outbreak, caused by a CT, occurred in Rome (central Italy), with 15 confirmed cases [38]. Moreover, in Cesano Maderno (NW Italy), a small industrial area within Milan conurbation, an outbreak of LD occurred between December 2005 and August 2008, with 43 cases and 5 deaths distributed over a period of three years, with two peaks in June and October 2006. Only retrospective analyses of prevalent wind direction have been able to suggest that the likely source of this uncommon outbreak was a hidden CT [39]. Furthermore, from July to August 2006, an outbreak of 15 confirmed LD cases was detected in Venice (NE Italy). Even though the source of the epidemic was not identified, no more cases were observed after the disinfection of the cooling towers identified as positive for *Legionella* in the city center [40]. In addition, another very interesting LD outbreak was the one occurred in Parma (northern Italy) between August and October 2016. Forty out of the 41 cases were confirmed as related to the epidemic. Although it has not been possible to identify with certainty the environmental source responsible for the epidemic, it has not been excluded that some CTs located nearby the affected area may have played a key role in triggering the outbreak [41].

No further outbreak events related to CTs have been reported in last more recent years in Italy, though this does not mean that they did not occur. The cumulative data of LD cases in Italy indicate their systematic growth from 2017 on. Unfortunately, it is not possible to argue whether the growth depended on the prevalence of the microorganism or was rather attributable to an improved higher accuracy in the LD infection diagnosis and notification [17].

Several characteristics make CTs an important source of *Legionella*: elevated air temperature and humidity ranges are extremely advantageous to the development of biofilms, growth of heterotrophic bacteria and amoebae, while carbon and nutrients from atmospheric sources inside a large volume of stagnant water exposed to the atmosphere provide the suitable nutrient substrate for the ingrowth of any microbiological community, *Legionella* included, the latter taking advantage of its opportunistic behavior [3,42,43]. In addition, insufficient biocide treatment, poor maintenance programs, lack of control measures and failure of system equipment may further increase the risk for the colonization of CTs by *Legionella* [44]. National and International Guidelines regarding the prevention and control of Legionellosis [45] contain references for employers regarding CT construction and their management. Additional installation Guidelines are suggested by Spain directive [46,47].

However, the outbreak cases described above highlight how generally it is difficult to unambiguously identify the source of infection promptly and with confidence. This occurs due to the poor availability of clinical isolates and of their comparison with the environmental ones, but also to the lack of a CTs register [48].

In community-acquired outbreaks, early identification and disinfection of the infections source are essential to prevent their spread and further cases. In fact, many of the outbreaks associated with CTs are preventable, therefore the introduction of suitable regulations at the national scale might significantly reduce morbidity and mortality caused by LD. In this respect, it is important to point out that only in Lombardy, the Italian Region including Milan, there is a regional Directive [49] establishing the mandatory notification of CTs in a register, whereas elsewhere in Italy the register is missing despite its institution is recommended by the *Legionella* National Guidelines [45].

A very useful approach recently emerged during worldwide LD outbreak investigations, is the set-up of an aerosol dispersion model capable of identifying potential sources of contamination. As shown for some epidemiological events in Italy [37–41], this approach allows, starting from the spatial distribution of LD cases and meteorological data of the days before the onset of disease symptoms, to spatially locate risk areas, in relation to the transport and dispersion of aerosol during the infection period [23,26,50–53].

Therefore, the application of a dispersion model to the range of potential local sources enables the identification of the source better matching the LD cases notified. Dispersion modeling simulations have been shown to be valuable tools to support classical epidemiological, environmental and microbiological investigation for the identification of LD sources [26,27,29,53]; unfortunately, so far this approach is used only as a post-event diagnostic tool and it has never been used in forecasting mode in order to assess whether a particular source might represent a risk of potentially upcoming outbreaks.

Therefore, in the light of the Italian epidemiological *Legionella* events linked to CTs, the aim of this study is to set up, for the first time as a preventive approach and in the absence of actual LD cases, a predictive model to study the spread of droplets containing *Legionella* from the stream plume of a hospital CT located near the city center of Bologna, Italy. The novelty of the present study, with respect to previous ones, lies in setting up a preventive approach and risk determination working in absence of cases rather than applied to diagnose the source of a LD outbreak. The chosen CT was involved in a *Legionella* environmental surveillance program in the period 2013–2020, and the influence of its activity linked to the dispersion of contaminated particles was studied to map several areas of risk for the population in relation to CT location (area around the CT) and under varying local meteorological conditions.

Despite the widely recognized hazard and diffusion of LD, some aspects of the *Legionella* phenomenology are still poorly investigated. In particular, very limited studies are available concerning the risk assessment from a *Legionella* spread at any spatial scale, therefore the relationships among *Legionella* and the other bacterial community within the CT environment remain still scarcely explored.

This work therefore reflects the need for integrating the missing information as outlined above. To better assess the *Legionella* risk across the study area, the microbiological dynamics inside the CT, linked to the interactions between *Legionella* and *Pseudomonas aeruginosa*, beyond their correlation with the water temperature measured, were also investigated. Moreover, in relation to the level of contamination found, a predictive *Legionella* spread dispersion model, able to predict the increase of *Legionella* risk in the area surrounding the CT, was elaborated.

In this framework the dispersion model has been applied in the reasonable hypothesis that *Legionella* is aero-transported in a PM_{10} matrix acting as the vector of the infection [54,55]. PM_{10} defined as an aerosol suspension composed of particles/droplets with an aerodynamical diameter equal to or less than 10 μm (down to the nm size) is one of the most popular aerosol metrics. The size range of particles in PM_{10} suitably fits and therefore includes both viruses and bacteria enabling transport and consequent transmission. Aerosol transmission of infectious diseases has recently drawn the attention of the both the public and the administrators worldwide, since the still on-going SARS-CoV-2 epidemics has been demonstrated to populate the submicron aerosol fraction highly represented in PM_{10}. In this framework it is to note that recently some authors remarkably detected the simultaneous occurrence of *Legionella* and SARS-CoV-2 on the same aerosol samples [56,57].

This approach might therefore represent a novel model design to apply in the framework of *Legionella* prevention and control protocols extendable also to other emerging infections, with the aim of reducing the risk of its spread while prompting the maintenance and disinfection procedures, at the basis of water safety planning and management.

2. Material and methods

2.1. Cooling tower structure and characteristics

The CT investigated in this study is located on the rooftop of a hospital building located in the center of Bologna, Italy (Fig. S1).

This CT is an open cooling tower, model VTL-E 245-P, produced by Baltimore Aircoil Company (BAC) (Jessup, MD, USA), installed in 2013 to serve the air conditioning circuit of the facility.

The main technical characteristics of the CT are reported in Table S1.

The CT operations consist in the forced recirculation of warm water (1) from the facility at the top of the tower, dropping it through a spray system (2) into the heat exchanger below for cooling (3) and collecting the cooled water (7) in the basin at the bottom (6). The heat exchange is achieved thanks to a centrifugal fan (4), allowing ambient air (5) to blow upwards through the tower. The contact in countercurrent between the warm processed water and cold air allows water cooling thanks to the evaporation process and the associated exchange of latent heat. Eventually the warm saturated air (8) leaves the tower after passing through the drift eliminators (9), which remove water droplets from the air (Fig. S2).

2.2. Study area and topography

Though no outbreaks have been associated with the CT herein investigated, we have chosen it as a case study for its particular position, placed within a densely populated conurbation. The CT, in fact, besides laying within the inhabited center, is located at the bottom of a hilly area. The hills, in this case, may represent a real obstacle to air masses circulation, leading to modification of the plume pattern emitted from the CT and potentially favoring even the stagnation of the bio-contaminated droplets emitted, right at the level of the urban area, thus potentially leading to an increased risk of exposure for inhabitants living downwind the facility.

Bologna (44°29′ N; 11°20′ E) (Fig. 1) is a mid-size town (391,412 inhabitants as of 2020, reaching 1.019.539 extending to the metropolitan area), capital city of the Emilia-Romagna region.

The city is situated in the core of the Po Valley, which is considered as one of the areas in Europe with the poorest air quality [58], owing to the high population density and intensive economic development leading to an overall huge emissive spectrum. Bologna is basically located in the plain though its southern side has been urbanistically expanded towards the Northern Apennines range, locally named as the Bologna Hills, contributing to significantly shape the local landscape. Its geographical position, the presence of the hills to the south and its complex topography, together with its morphology typical of a number of European cities characterized by a historical, densely-built center surrounded by residential and industrial areas [59,60] greatly affects the dispersion pattern of pollutants and of aerosolized particles emitted in the city. In particular, the study area of this work is in the Santo Stefano district, with 64.559 inhabitants/m^2, laying against the Bologna hills.

2.3. Physical and chemical analyses

The physical and chemical parameters of the CT water basin were measured during seven years of the study, and include temperature, pH, hardness, alkalinity, conductivity, and disinfectant residues.

Temperature, pH, hardness, alkalinity, and conductivity were measured monthly during the study.

Regarding the disinfection treatment, two types of disinfectants are applied: one adopted for the continuous disinfection processing called WTD823 (Water Team SRL, Cesena, Italy) and the other used only during chemical shock treatments of the CT, called WTD817 (Water Team SRL, Cesena, Italy). In detail, the WTD823 is a stabilized alkaline sodium hypochlorite aqueous solution. The WTD817 disinfectant is a solution of bronopol and methylchloroisothiazolinone and methylisothiazolinone (3:1).

The concentration of antiscalant/corrosion inhibitor and disinfectant supplied in the CT water return line, was empirically quantified by setting the disinfectant dosing pumps. Regarding the operational concentration, the WTD823 concentration was set up to 30 mg/L, instead the shock treatment was performed using WTD817 through a continuous dosage at a concentration of 500 mg/L, following the manufacturer's instructions.

The monthly maintenance visits were planned by hospital stakeholders to register physical and chemical parameters other than to control the CT operational functions.

Physical and chemical parameters, expressed as the mean value ± standard error (SE), were measured during samples collection for the entire period of the study, and were showed in Table 1.

2.4. Water sampling and microbiological analysis

Following the *Legionella* risk assessment plan in agreement with the national and regional (Emilia Romagna) Guidelines [45,61] to assess the *Legionella* contamination, the CT was monitored twice or three times per year in relation to the water quality results obtained. From 2013 to 2020 a total of 18 water samples (2 L each) was collected from CT water basin.

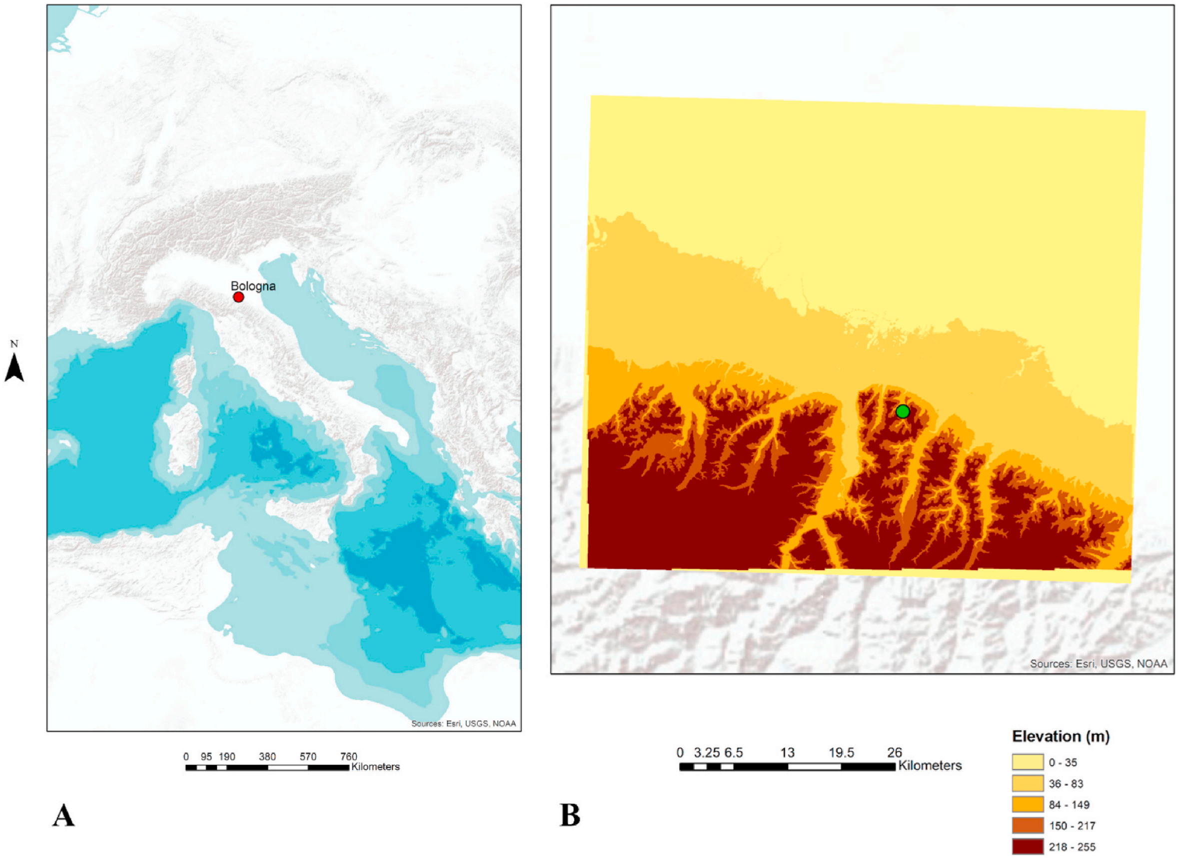

Fig. 1. Map representing a) location of the city of Bologna (red dot) within Italy; b) topography of the study area (green dot) and its surroundings (source: digital terrain model, cartographic archive, Geoportale Emilia-Romagna). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 1
Mean value of physical and chemical parameters of CT water basin.

Temperature (°C)	pH	Hardness (°f)	Alkalinity (ppm)	Conductivity (μS/cm)
24.0 ± 1.2	8.0 ± 0.0	140 ± 7	168 ± 5	513 ± 11

All samples were collected according to the standard method UNI EN ISO 19458:2016 as suggested by the Italian Guidelines [45,62]. During the sampling, water temperature was measured and recorded. All the samples were kept refrigerated at 4 °C until the analysis, which was carried out on the same day. All the water samples were analyzed for *Legionella* spp. and *P. aeruginosa.*

For the detection and enumeration of *Legionella*, culture was performed in accordance with ISO 11731:2017 [63]. An aliquot of 100 μl, of filtered, and treated by heat and acid samples were directly plated onto the *Legionella* GVPC selective medium (Thermo Fisher Scientific, Oxoid, Ltd., Basingstoke, U.K.). All plates were incubated aerobically at 35 ± 2 °C and 2.5% CO_2. The culture takes from 10 to 15 days, with visual observation every two days. The presumptive colonies were enumerated and sub-cultured on BCYE agar with (Cys+) and without (Cys-) L-cysteine (Thermo Fisher Scientific, Diagnostic, Ltd., Basingstoke, UK).

Legionella growth was observed only on BCYE Cys+. These colonies (at least five different colonies for each plate) were identified using the *Legionella* latex test kit (*Legionella* latex test kit; Thermo Fisher Scientific, Ltd. Basingstoke, UK), based on the manufacturer's instructions. Moreover, the identification was confirmed by MALDI-TOF MS (Bruker Daltonik GmbH, Bremen, Germany). The contamination found was expressed as colony-forming units/liter (cfu/L).

The same samples (100 mL) were simultaneously analyzed for the presence of *P. aeruginosa,* which is not only an efficient biofilm indicator, but has also the ability to inhibit *Legionella* growth during culture, preventing the risk of producing inaccurate results [64]. The analysis was carried out according to UNI EN ISO 16266:2008 [65], using the standard membrane filter technique and the membrane was cultured on *Pseudomonas* selective agar (PSA, Biolife, Milan, Italy), incubated at 36 ± 1 °C for 48 h. Suspect colonies with green-blue fluorescence under a Wood's lamp (ultraviolet light (UV) at 365 nm), were then sub-cultured on Nutrient agar (NA, Biolife, Milan, Italy) for 18–24 h and subjected to biochemical identification conducted by using the RapID™ NF Plus kit (Thermo Fisher Scientific) according to the manufacturer's instructions. For sake of completeness, oxidase reactions tests were also performed. The results were finally expressed in cfu/100 mL.

2.5. Setup of the dispersion model

The dispersion of infectious aerosols from the CT was simulated with a quasi-Gaussian dispersion model, the ADMS-Urban [66,67]. The topography of the area surrounding the CT was considered using digital terrain elevation (DTM) data provided by the Emilia-Romagna Region (https://geoportale.regione.emilia-romagna.it/catalogo/dati-cartografici/altimetria/layer-2) with a resolution of 5 × 5 m. Since inhalation of *Legionella*-contaminated droplets occurs in the presence of aerosols sizing 10 μm or smaller [14,15], in this work the dispersion of *Legionella* was simulated using PM_{10} aerosols as a proxy in analogy with Faccini et al. [53].

In order to estimate PM_{10} emissions from the CT, the construction and working parameters of the CT (see Section 2.1) were used with a refinement of the EPA method [68] calculating particulate matter emissions from wet CTs [69–71]. Briefly, with respect to the simpler EPA approach based on the calculated drift loss and the estimated total dissolved solids to calculate total PM emissions, this method considers explicitly the size of the emitted particles accounting also for the localized deposition. The CT was simulated as a point source. Table 2 presents the input variables used for the setup of the forecast dispersion model.

It can be observed that the input variables contain geometrical characteristics of the tower and other variables measured or estimated during the sampling, but no explicit data from the *Legionella* sampling contamination described above entered directly in the dispersion model, thus making the predictive model independent on the level of *Legionella* contamination value. For the purpose of assessing a variable risk of spreading a hypothetically bio-contaminated aerosol to the surrounding area under different meteorological conditions, we have considered hourly meteorological data (wind speed and direction, air temperature, cloud cover, air relative humidity, precipitation) measured at a nearby synoptic meteorological station, located at Bologna airport, during eight consecutive years (2013–2020). Meteorological data were obtained from the Iowa Environment Mesonet (IEM) (https://mesonet.agron.iastate.edu/request/download.phtml).

The seasonal risk of spreading the PM_{10} aerosols was estimated as weighted seasonal overlays using the "fuzzy or" overlay spatial technique, widely used in multicriteria spatial modeling for estimating the maximum value of the sets (in our case, the seasonal averages) the cell location belongs to Refs. [72,73]. In general, the "fuzzy" overlay method allows the analysis of the possibility of a phenomenon belonging to multiple sets in a multicriteria overlay analysis. The "or" specifies instead the type of method used to combine the data (options available are the "fuzzy and", "fuzzy or", "fuzzy product", "fuzzy sum", and "fuzzy gamma"). Specifically, the "fuzzy or" overlay type returns the maximum value of the sets the cell location belongs to. Accordingly, in our case the selection of this technique stands in the fact that it returns the maximum seasonal risk of adverse events [74], in this case represented by *Legionella* being aerotransported in the PM_{10} matrix emitted from the CT, an approach recognized as best suited for vulnerability assessment [75].

2.6. Statistical analysis

R Statistical Software (version 4.1.2, "Bird Hippie" R Foundation for Statistical Computing, Vienna, Austria) was used to carry out the statistical analyses. Frequency distribution of the variable was studied by means of the Shapiro–Wilk test. Spearman's rho rank correlations were calculated for each pairwise combination of variables in the samples analyzed (*Legionella* spp., *P. aeruginosa* and temperature).

Specifically, Spearman's rho coefficient was used to classify the correlation found according to Asuero et al. [76], as follows:

- 0.00 to ±0.29: Little if any correlation.
- ±0.30 to ±0.49: Low correlation;
- ±0.50 to ±0.69: Moderate correlation;
- ±0.70 to ±0.89: High correlation;
- ±0.90 to ±1.00: Very high correlation;

Table 2
Input variables for the setup of the dispersion model.

Input variable	Value
Tower height (m)	3.3
Tower lenght (m)	3.65
Volumetric flux of release (m^3/s)	27.8
Temperature of release (°C)	21–26
Drift loss (%)	0.044
Circulating water flow rate (gpm)	4.00E+05
Total dissolved solids (ppm)	18500
Density of TDS solids (g/cc)	2.5

The significance of all statistical tests was set at 95% ($p \leq 0.05$).

To optimize the fruition of the graphical model output, the level of contamination for *Legionella* and *P. aeruginosa* data were converted into log10 cfu/L (Log cfu/L) and Log cfu/100 mL.

3. Results

The data reported concerns physico-chemical and microbiological characterization of the CT water samples, collected in the period 2013–2020 in the framework of a systematic monitoring campaign aiming at optimizing the CT operation management within a hospital facility.

In detail, Table 1 reports the physico–chemical parameters measured expressed as mean values ± SE.

The data regarding the microbiological parameters (*Legionella* and *P. aeruginosa*) analyzed in the 18 water samples collected from the CT during the studied period are reported as the annual contamination level and expressed as cfu/L for *Legionella* and cfu/100 mL for *P. aeruginosa*.

With respect to the temperature measured, it is possible to observe that the mean temperature was 24 ± 4.9 °C, ranging between 7 and 31 °C (minimum and maximum, observed in the 2017).

The relation between microbiological contamination found with water temperature values measured is displayed in Fig. 2.

The *Legionella* CT mean contamination was 40938 ± 24523 cfu/L. The contamination was observed during the whole monitoring period except for the end of 2018 until 2020, when the level of contamination decreased below the detection limit (<50 cfu/L).

Fig. 2 shows how in 4/18 samples (22%) the *Legionella* contamination level was above the limit allowed by the Italian Guideline fixed to 1000 cfu/L (red dotted line) [45], showing a mean of 183250 ± 81582 cfu/L. Samples with contamination levels exceeding the threshold limit were detected in 2014, 2016 (twice) and 2017.

During the sampling period, the species identified was *Lp*1. Samples with contamination levels exceeding the threshold limit were detected in 2014, 2016 and 2017.

Regarding the 14 (out of 18, i.e., 78%) samples under the threshold limit, the mean contamination was 277.71 ± 91.72 cfu/L. The *Legionella* concentration discovered required no further action other than a review of risk management practices, according to Italian and Regional Guidelines [45].

Except for the period 2018–2020, when no contamination was reported, the value of contamination remained nearly constant throughout the study period.

Relevant data were observed also for *P. aeruginosa,* contributing significantly to the CT bio-contamination, as it was always detected throughout the whole monitoring, with a mean concentration of 599 ± 175 cfu/100 mL. Remarkably, the contamination of *P. aeruginosa* disappeared in the same period in line with the *Legionella* behavior observed.

Considering that the CT has an annual operational activity schedule, the contamination found for both microbiological parameters was evaluated based on the seasonal variations, considering the sampling performed in each season (Fig. 3).

The results showed *Legionella* contamination with wide oscillations (from 0 to 380000 ufc/L), that generally remain close to the Guidelines Limit (≤3 Log ufc/L) including some samples negative for *Legionella* (below the detection limit of technique (<50 ufc/L)), in detail: 2/5 in winter, 2/4 in spring and autumn and 2/3 in summer.

The four samples above the risk level, with a peak of 10^5 cfu/L, appear to be independent of the season/year (one in 2014 and 2017, and two in 2016) (Figs. 2–4). Conversely the presence of *P. aeruginosa* was always observed at high concentration with peaks over 1000 ufc/100 mL, showing oscillations independent of the season.

Aiming to assess the occurrence of potential correlation between *Legionella* and *P. aeruginosa* as well as with temperature, a correlation matrix was built (Fig. 5).

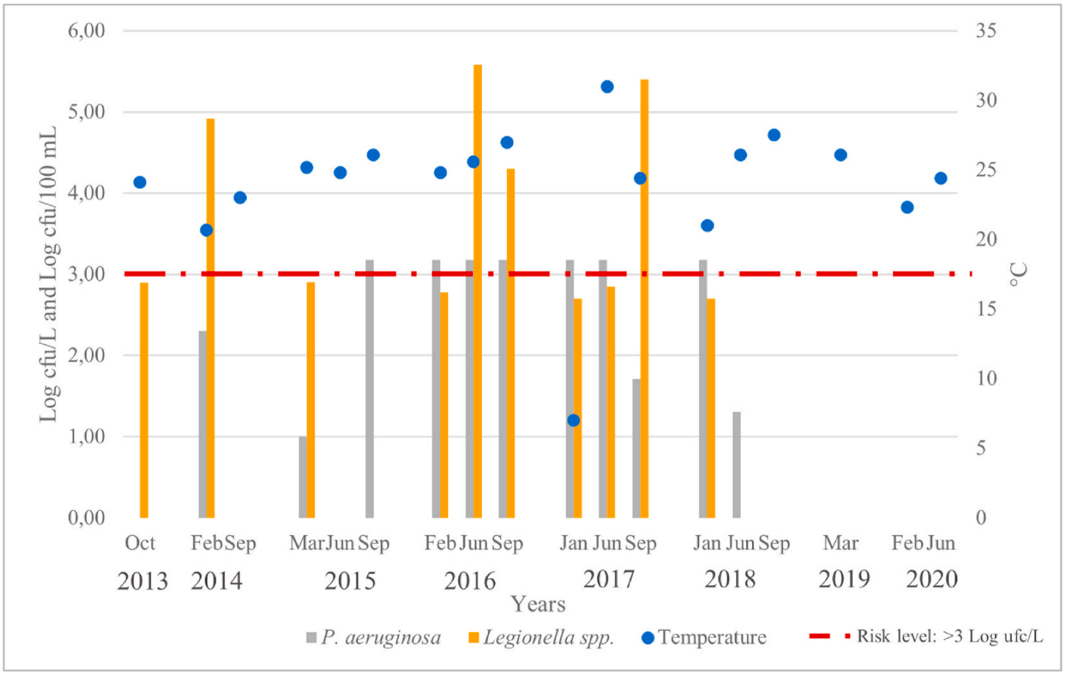

Fig. 2. Microbiological contamination (orange/grey bars on the left y-axis) and temperature of CT water basin samples (blue dots on the right y-axis) during the study period. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

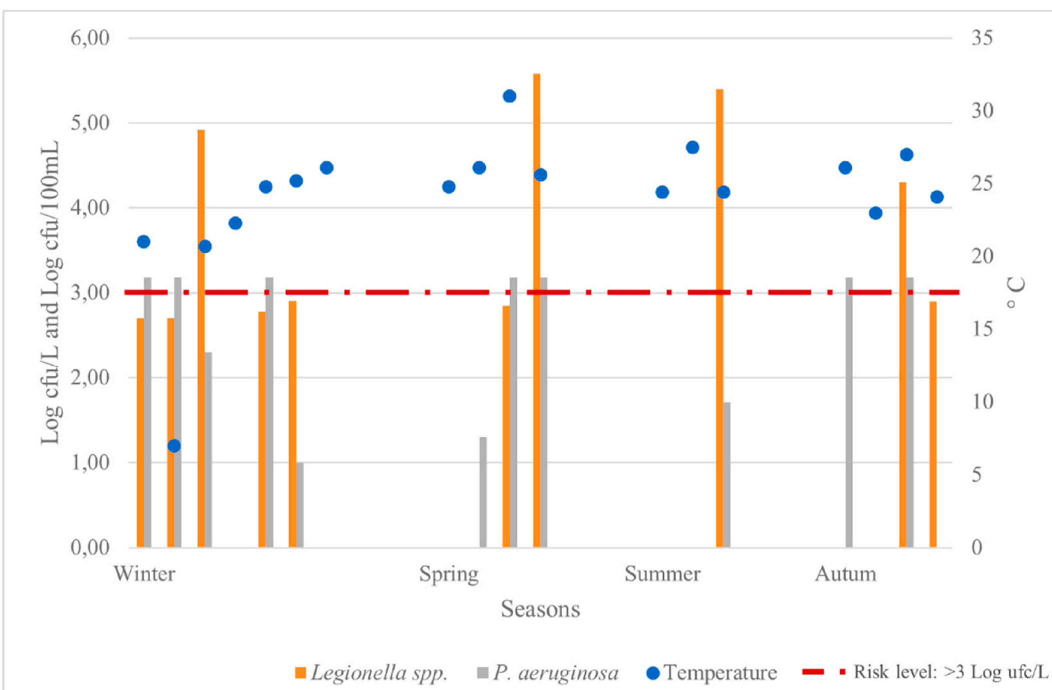

Fig. 3. Microbiological contamination distribution on the basis of season. Relation with temperature values measured in the CT water basin.

The data showed little or no correlation between both microbiological parameters and temperature without statistical significance. On the other hand, the correlation between *Legionella* and *P. aeruginosa* was positive with a statistically significant level ($p = 2.7 \times 10^{-2}$), which suggests how both bacteria concentrations simultaneously increased in the CT environment.

Regarding the data of the four peaks, displayed in Fig. 6, the relationship between *Legionella* and *P. aeruginosa* showed only little or no correlation, while a high positive correlation was observed between *P. aeruginosa* and temperature (0.74), suggesting how the increase in temperature promotes the *P. aeruginosa* growth.

A more in-depth analysis of these four samples was performed in relation to the meteorological conditions recorded. The meteorological data recorded at nearby meteorological stations provided by the Regional Environmental Protection Agency during the days of simultaneously high concentration of *Legionella* and *P. aeruginosa* (3/02/2014, 6/6/2016, 29/09/2016, 11/09/2017) revealed the occurrence of relatively higher values of both air temperature (especially the minima) and

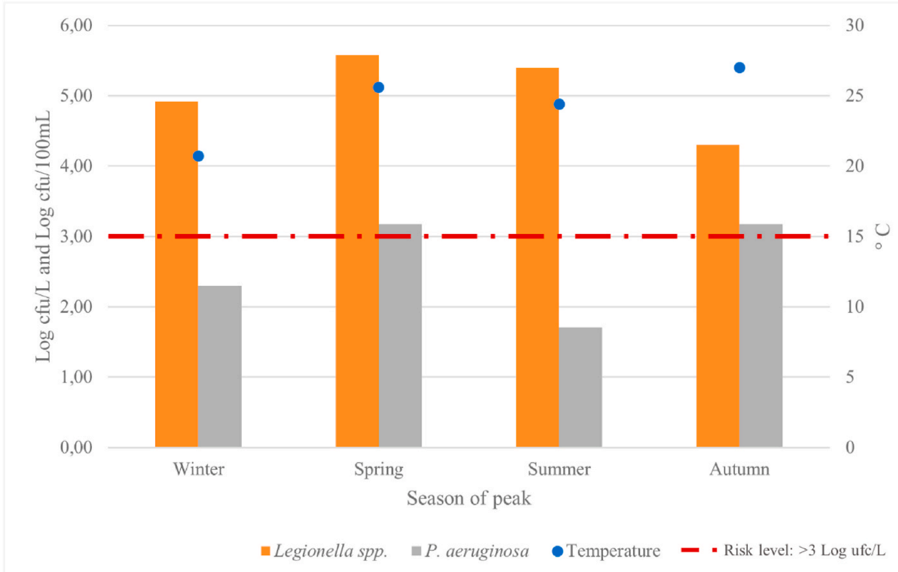

Fig. 4. The four seasonal peaks above the risk level of *Legionella* contamination distribution in relation with *P. aeruginosa* contamination distribution and temperature values measured in the CT water basin.

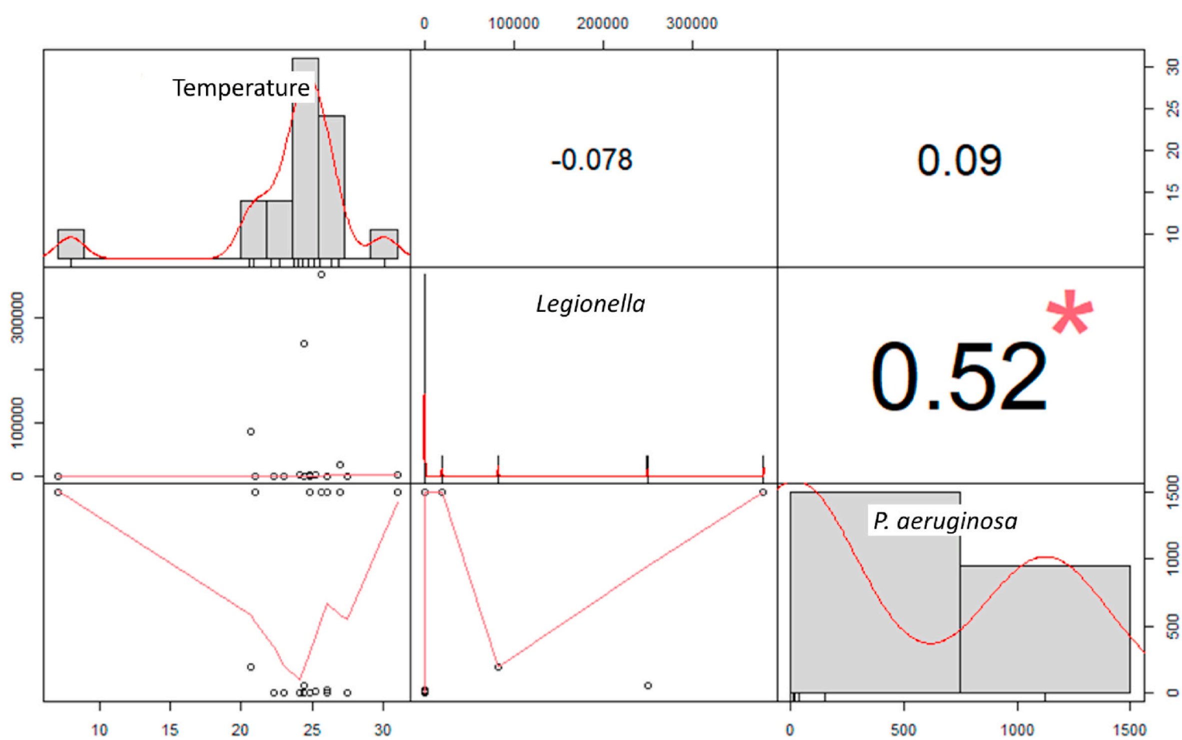

Fig. 5. Correlation matrix of *Legionella* vs *P. aeruginosa* concentration (mean contamination), and water temperature values. In the upper right corner (above the diagonal) the Spearman correlation coefficients are presented together with the *p* significance value (the * indicates *p* significance value < 0.05); in the lower left corner (below the diagonal) the scatterplots of the couples of variables are presented together with a fitted line (in red); along the diagonal the histogram (grey bars) and the fitted population distribution (in red) of each of the three variables are presented. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

relative humidity on the sampling day and on the preceding days. The air minimum temperature values generally increase of about 1–2 °C with respect to the previous days (6.2 °C and 6.6 °C on 3/2/2014 and 2/2/2014 respectively *vs* 5 °C and 4.7 °C recorded on 1/2/2014 and 4/2/2014; 14 °C and 17.6 °C on 29/09/2016 and 30/9/2016 *vs* 12.9 °C and 13.6 °C recorded on 26 and 27/09/2016), relative humidity values were in the range of 66–100% compared to the relatively drier range of 40–70% measured on the previous days. In addition, these samples were always associated with rainfall events on the previous 1–4 days (in the range of 0.2–31 mm/day). The details and plots of data recorded are provided in the supplementary material section (Figs. S3–S5). Fig. 7 shows the results of the dispersion modeling of the PM_{10} plume emitted from the CT during the 2013–2020 period, according to the different seasons.

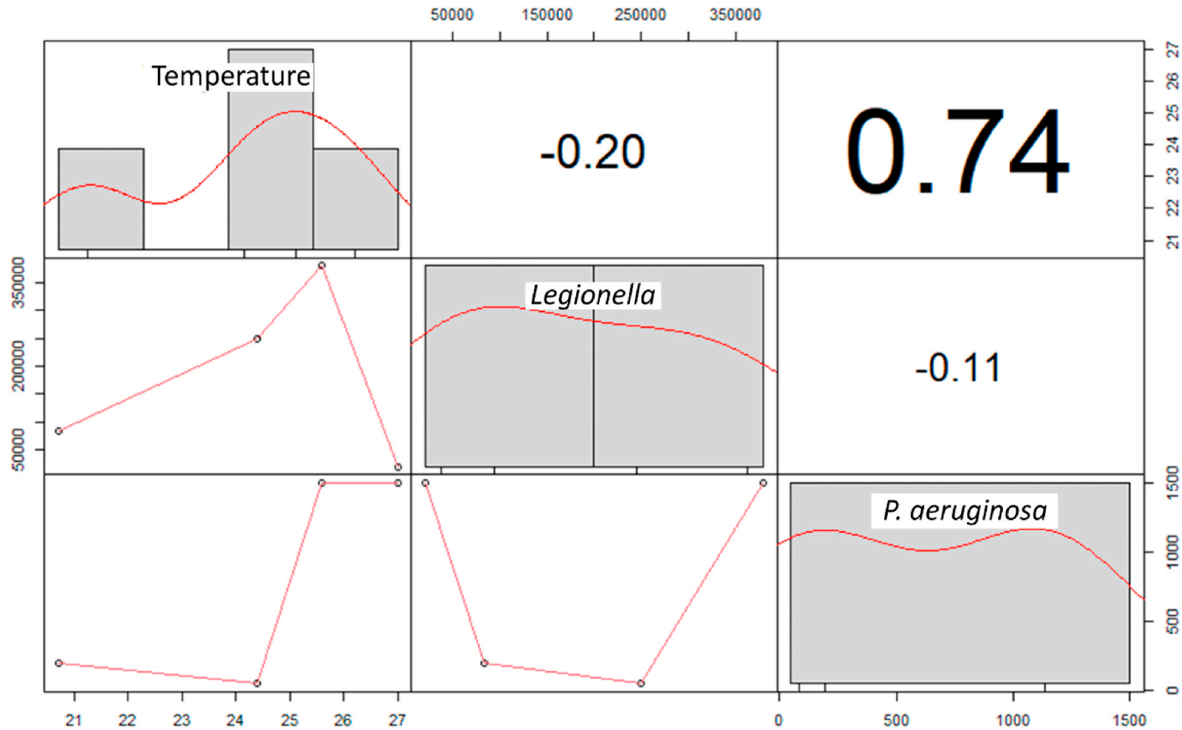

Fig. 6. Correlation matrix of the four peaks value. *Legionella vs P. aeruginosa* concentration (mean contamination), and water temperature values. In the upper right corner (above the diagonal) were showed the Spearman correlation coefficients are presented together with the *p* significance value (the * indicates *p* significance value < 0.05); in the lower left corner (below the diagonal) were showed the scatterplots of the couples of variables are presented together with a fitted line (in red); along the diagonal represented the histogram (grey bars) and the fitted population distribution (in red) of each of the three variables are presented. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

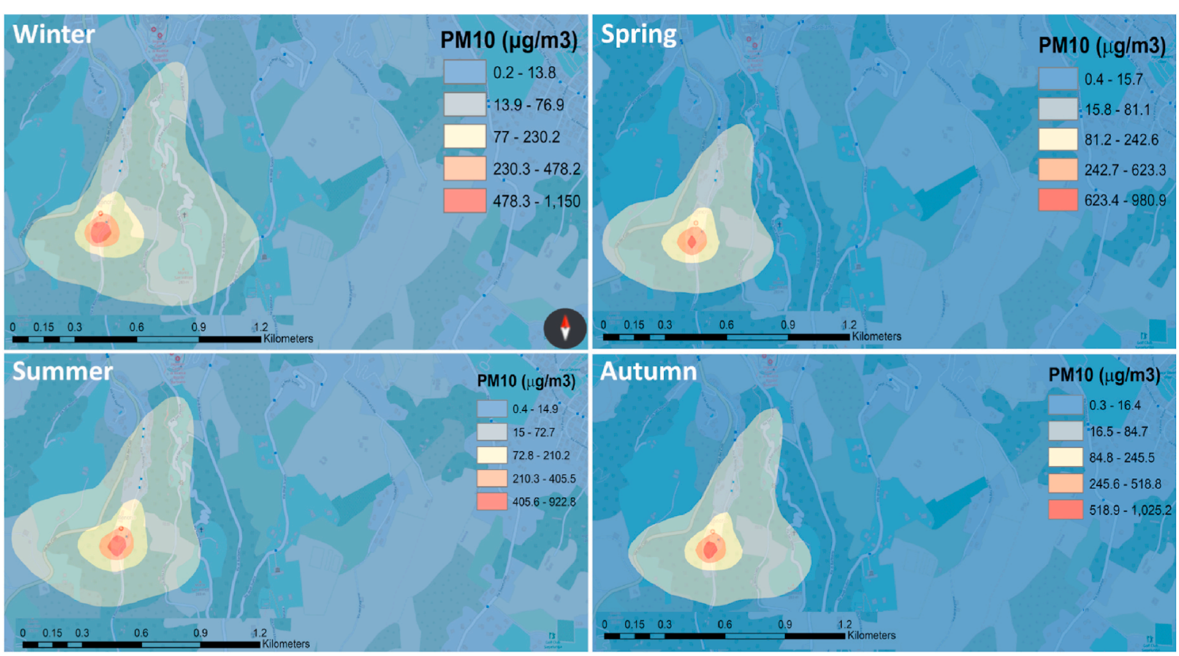

Fig. 7. Maximum risk of *Legionella* spread aerotransported in the PM_{10} matrix as estimated by the dispersion model and with the "Fuzzy Or" Overlay spatial technique for the period between 2013 and 2020 in the four seasons. The red dot indicates the position of the CT; the color scale indicates the PM_{10} concentration range indicated in the legend on the top right of each map. The map in the background is from OpenStreetMap contributors. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

The results highlight that, though the largest part of the PM_{10} matrix used as a proxy for *Legionella* concentrates in the close surroundings of the CT (150–300 m distance), a non-negligible portion of it disperses over the inhabited areas in all seasons. In particular, a remarkable spread of very high PM_{10} concentration values is observed during the winter and autumn seasons. The high concentrations observed in winter and autumn are most likely connected to the different prevailing meteorological conditions impacting on the study site. Indeed, the air pollutant concentrations observed downwind emission sources are a function of atmospheric stability, air temperature lapse rate, atmospheric inversions, atmospheric mixing heigh, dispersion from emission sources. Specifically, the winter and autumn seasons are often associated with the prevalence of stagnant weather conditions, characterized by low mixing height, marked stability and atmospheric inversions inhibiting the vertical dispersion of pollutants (thus, also PM_{10}) emitted and formed at ground level by the different pollutant sources.

The larger extension of the red, yellow, and green areas generated from the modelled plumes during the winter and summer (Fig. 7) suggests that during these seasons, PM_{10} may reach inhabited areas at longer distances from the CT, thus increasing the risk of infections from LD (total average extension of the PM_{10} plume transport about 1.5 km (area of 2.25 km^2) in winter as compared to the average of 850 m (area of 0.7 km^2) of the other seasons.

The change in the annual expansion of the plume emitted by the tower is connected to the different prevailing weather conditions impacting on the study site during the analyzed period (see the results of the dispersion model for each year and season in Figs. S6–S13).Indeed, the larger expansion range observed in winter and summer seasons can be associated with the different thermal plume rise and higher dispersion recorded during these seasons in the study period, and precisely in years from 2017 until 2020 (Supplementary Figs. S10–S13). Specifically, the increase in the expansion range observed from 2017 to 2020 can be attributed to the generally higher atmospheric stability and dispersion observed during these years with respect to the previous ones.

For sake of clarity, it is to note that no actual case of legionellosis was reported during the study period in the hospital where the CT is located and around the area of study.

4. Discussion

From an engineering point of view, CTs are among the most widely and consistently used systems for the removal of excess heat by evaporation of water. However, from a microbiological perspective, CTs contribute to bacterial spread through the plume dispersal. The bacterial spread may likely affect human health as demonstrated by worldwide reported outbreaks [31,77,78]. As concerns some of described outbreaks, the limits found during the reported epidemiological investigations, aiming to discover the source of infection and matching the environmental strain with the human one, are linked to two main issues: i) the lack of a CT register, despite it is recommended by both the International and Italian Guidelines since 2015 [45–47] and ii) the CTs disinfection shock treatment often carried out during outbreaks, may alter the analytical results hampering the *Legionella* isolation.

Commonly, the various national policies have introduced specific directives enforcing the CT notification, supplemented by CT planimetry together with its technical characteristics, only following the identification of an outbreak. This is the case of the recent Italian outbreak occurred in Parma [41] and Bresso in 2019 [53].

Currently in Italy, the only available data reporting a mandatory census of domestic and industrial pressure equipment (e.g., water, gas, water vapor, etc.) are supplied by the National Institute for Insurance Against Industrial Injuries portal (INAIL website), thought the notification in Certification and Verification of Plants and Equipment application (CIVA) [79], by contrast the hospital CT are not included.

The data reported by literature focuses on CT maintenance and monitoring as the main strategy to prevent the risk of LD. Briefly, the spread of *Legionella* can be minimized by a systematic water quality testing, limitation of water stagnation, detection and correction of process leaks into the cooling system providing nutrients to the bacterial microbiome, maintaining overall system cleanliness, applying scale and corrosion inhibitors and controlling the overall microbial population. Moreover, the diffusion of bacteria from a CT should be contained by means of high-efficiency drift eliminators at the air outlet to prevent blow-off and dispersal of contaminated droplets to the surrounding environment [80].

Currently, no specific guidance on the frequency of sampling of the CT is reported. Therefore, the *Legionella* control in this environment, when required by the risk assessment plan, is at the facility manager's discretion. The evaluation of *Legionella* as a new parameter to estimate water quality for human consumption, according to the approach of water safety plan as prescribed by the new European Union (EU) Directive 2020/2184, would contribute to improve the CT water supply management and limit the bacteria water input flow [81].

In this study, despite the CT was subjected to periodic maintenance measures, visits and a routine sampling program, the evidence of contamination of *Legionella* and *P. aeruginosa* in the samples clearly demonstrated how it may represent a significant biological hazard for downwind urban areas. Despite no clusters or outbreaks have been so far reported for this CT, the elaboration of the dispersion forecasting risk model together with the identification of actual environmental risk factors support the need for enforcing improved protocols in the management of the CT in order to prevent potential future outbreaks.

The study of CT risk considers simultaneously the CT characteristics including its location and operational activity, the physical and chemical parameters beside the microbiological ones as well as the climatological conditions of the affected district. This study, to our knowledge, represents the first attempt to develop a risk map around the CT area and the derivation of guidelines for the development of a solid preventive approach considering all risk factors, with respect to application of dispersion model study that generally were applied during the outbreaks to trace and diagnose the source of infection [29,82].

Starting from the examination on water temperature, the CT temperature measured during the 7 years study (24.0 ± 4.9 °C) was in line with the temperature of semi-open water basins (20–35 °C) reported in literature [2–4]. The CT water temperature generally is higher than that of the cold-water distribution system (<20 °C). The range found is high enough to promote the *Legionella* survival and proliferation [12] and explains the level of contamination found. Moreover, the constant values registered support the absence of correlation found between *Legionella*, *P. aeruginosa* and temperature. The significant correlation found between *Legionella* and *P. aeruginosa* ($p = 2.7 \times 10^{-2}$) demonstrates how the CT is able to promote the generation of an ecological niche where *Legionella* finds protection from local physical, chemical and mechanical stress [83].

Considering the *Legionella* surveillance, the CT was contaminated by *Lp* 1 (40938 ± 24523 ufc/L). The level of contamination varied during the years and seasons. Peaks exceeding the reference limit (1000 ufc/L or Log 3 ufc/L) [45] were observed during all seasons, suggesting the need of applying extraordinary maintenance protocols based on intervention such as: anti-scale and mechanical cleaning procedures on CT basin to remove the biofilm and support the disinfection [45]. Regarding *P. aeruginosa*, the trend of contamination level is in line with the *Legionella*'s one (599 ± 175 ufc/100 mL), but in this case no guidelines or directives treat the *P. aeruginosa* level in CT, considering that the CT water is not assimilated to drinking water for human consumptions.

In 2018 an extraordinary maintenance activity was implemented to control the remarkable microbial contamination detected as well as to solve some functional problems on CT. The activities consisted in a thorough clean-up of nozzles, filters, evaporative packs, internal components, and a complete renovation of CT water basin. These activities led to the breakdown of microbial contaminations under the technique detection limit (<50 ufc/L) (percentage of reduction of 100%) [45]. These findings are in line with the requirement of continuous maintenance program to avoid the arising of alert situation that can influence the CT functionality and increase the risk for personals and the urban area close the CT.

The monitoring performed during the period of study has permitted to study the trend of CT microbial contamination in relation to seasonal variation. No significant differences were found during the seasons, despite the four peaks of *Legionella* contamination, over the level of risk prescribed by National Guidelines [45]. These peaks were identified in different years: once in 2014 (winter) and 2017 (summer) and twice in 2016 (autumn and springer). The analysis of meteorological data registered in correspondence of the sampling data (recorded during the sampling day and the days preceding it), has allowed the identification of the coincidence of the four events of peak *Legionella* and *P. aeruginosa* above the risk level, with precipitation events characterized by an increase of relative humidity and air temperatures, especially in the minimum values. These observations agree with the literature, reporting the connection of *Legionella* outbreaks with elevated temperatures, relative humidity and rainfall [28,32,84].

A detailed analysis of the synoptic conditions and of air masses characteristics impacting the study area using both back-trajectories and the results of dust transport models showed that the peak events occurred also in combination with transport of desert dust to the study area (Figs. S14–S16). In particular, Figs. S14 and S15 present the dust optical depth simulated by two different transport models (BSC-DREAM 8b operated by the Barcelona Supercomputing Center and NAAPS from NOAA, respectively) during the days preceding four of the *Legionella* peaks presented in previous Fig. 4. Fig. S16 presents instead the dust surface concentration simulated by WMO SDS ensemble dust transport models and the back-trajectories calculated for another *Legionella* peak. All the Figures suggest very clearly that the study site was impacted by transport of desert dust from the North-African region in connection to the *Legionella* peaks were detected in the CT water. Though additional analyses and longer time series are needed to better document and investigate the role of desert dust transports in triggering bacteria outbreaks, this observation already suggests that the growth of bacteria inside the CT might be further promoted not only by particular local meteorological conditions, but also by contamination from exogeneous species transported together with the dust plume to the study area, in agreement with previous findings [85,86].

The elaboration and the introduction of a predictive dispersion model to study the spread of bacteria in relation to the variable meteorological conditions, such as air temperature, and wind flow, might help to contain the risk of infection across a community especially when the CTs are close to an urban area. The risk model implemented suggests indeed how the PM_{10} aerosols emitted by the CT disperse over the inhabited area in the surroundings of the CT, notably during the winter season. Indeed, during this season risks of contaminations appear higher, as suggested by the elevated concentrations of PM_{10} aerosols observed over an extended area relatively distant from the CT. As far as the current SARS-CoV-2 epidemic is concerned, extensive discussions have emerged about its transmission process, enlightening the role of ambient particles and droplets as a function of their wide range of size and of their fate in terms of micro and ambient meteorological implications [87,88]. Interestingly the complexity of aero-transported microorganisms and of coexisting infections, has brought to light some cases of human cross-infection between SARS-CoV-2 and *Legionella* [89]. Therefore, the extension of the modelling tools usually applied exclusively to physical and chemical parameters to the microbial field might become the basis for an efficient and up-to date-strategy to apply in the field of prevention of water and airborne related diseases [90]. As previously explained in the Introduction, the predictive dispersion model was applied in the reasonable hypothesis that *Legionella* is aero-transported in a PM_{10} matrix acting as the vector of the infection, as well documented in previous studies. While PM_{10} has been found to include a significant bacterial microbiome component [54] the present case suggests the need for some precautions. In fact, CTs in principle emit droplets. However, two conditions need to be evaluated. Firstly, CT droplets are actually both solutions and suspensions of a range of components resulting from the CT operations and management, as well as by mixing with ambient air always containing PM_{10}. Secondly, while the initial droplet dynamics out of the CT is controlled by inertial properties, specifically initial velocity, size, density and air viscosity, once released, evaporation of the aqueous phase is expected to vary as a function of temperature and to a lesser extent, of droplet expansion, leading to solid/moist residues, a behavior typical of ambient aerosol particles and of cloud processing. Finally, it is known that ambient aerosol is also remarkably hygroscopic as a function of its physico-chemical properties, which means that it always retains variable amounts of atmospheric moisture as a function of atmospheric conditions. Overall, therefore the choice of PM_{10} as a proxy of bacterial transport is more than justified. In addition, a previous study [77] has already compared the spatial distribution of LD with the exposure to PM_{10} emitted from the corresponding emitting sources, and showed that LD cases were in general connected to higher exposures to aerosols than controls. In parallel, therefore, the results of the dispersion model setup in this study suggest that the risk of LD in the residential area surrounding the CT may greatly increase and become significant under specific weather conditions impacting on the study site (e.g., with contamination promoted by high air temperature and relative humidity, transport of exogenous species with desert dust, and higher horizontal dispersion of the plume promoted by stagnant weather conditions and low mixing heights). In order to improve our results and considering the uncertainties presented previously, in the future we could evaluate to use the results of our simulations in the field, i.e., by directly analyzing *Legionella* contamination, but also in environmental samples collected downwind of it and as predicted by the dispersion model.

5. Conclusions

The recent international and national events linked to *Legionella* infection have highlighted how CTs represent a risk to public health. In the CT environment, the risk of *Legionella* colonization and proliferation is supported by the presence of large quantities of water, warm temperature and content of dissolved salts and the inefficient or poor maintenance and/or disinfection, favoring the survival of microorganisms and the presence of bacterial biofilm (e.g., *P. aeruginosa*).

To date, no study has attempted to develop predictive models for infectious risk mapping as a prevention tool, let alone there are predictive models of aerosol dispersion associated with CT functionality, maintenance activities or *Legionella* surveillance.

Therefore, the predictive model proposed in this study aims to define an approach, especially preventive, to be used not only by public health professionals involved in epidemiological investigations, but especially by stakeholders involved in design, installation, management, and environmental impact study of the CTs.

The elaboration and the introduction of a predictive risk model and the identification of the risk factors which promote the spread of bacteria over inhabited areas in terms of impacting meteorological conditions, including air temperature, wind flow, and occurrence of desert dust outbreaks might help to contain the risk of infection across a community especially when the CTs are close to an urban area and to draw consistent and updated guidelines for preventing the risks of contamination of *Legionella*.

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CRediT authorship contribution statement

Luna Girolamini: Writing – review & editing, Writing – original draft, Software, Methodology, Formal analysis, Data curation, Conceptualization. **Erika Brattich:** Writing – review & editing, Writing – original draft, Software, Methodology, Investigation, Data curation. **Federica Marino:** Writing – original draft, Formal analysis. **Maria Rosaria Pascale:** Formal analysis. **Marta Mazzotta:** Formal analysis. **Simona Spiteri:** Formal analysis. **Carlo Derelitto:** Formal analysis. **Laura Tositti:** Writing – review & editing, Methodology, Investigation.

Sandra Cristino: Writing – review & editing, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.buildenv.2022.109891.

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