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Original article

Travel-associated cases of Legionnaires' disease in the United States, 2015–2016☆

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ABSTRACT

Background: Recent travel is associated with ~20% of reported Legionnaires' disease (LD) cases worldwide.
Methods: We analyzed LD cases reported to the Centers for Disease Control and Prevention (CDC) during 2015–2016. Travel-associated cases met case criteria for confirmed LD in someone who spent ≥1 night away from home during the 10 days before symptom onset. Most analyses were limited to travel-associated, public accommodation stay (TAPAS) cases. We used reported travel dates to estimate the number of TAPAS cases acquired during travel.
Results: Of 12,200 LD cases reported among U.S. residents, 12.3% were travel-associated; 8.7% were TAPAS. Median patient age for TAPAS cases was 61 years; 64.4% were male; 67.3% were white; 77.9% were non-Hispanic; 96.1% were hospitalized; 4.5% died. Among 887 TAPAS cases involving U.S. destinations, an estimated 29.8% were acquired during travel; 4.28 TAPAS cases were reported, and an estimated 1.10 TAPAS cases were acquired during travel, per 10,000,000 hotel room nights booked. Sixty-eight U.S. TAPAS clusters were detected.
Conclusions: While acquisition during travel accounted for a relatively small proportion of all LD cases, clusters of TAPAS cases were frequently detected. Prompt notification of these cases to CDC facilitates cluster detection and expedites intervention.

1. Introduction

Legionellosis comprises Legionnaires' disease (LD) (a severe pneumonia), Pontiac fever (a milder, self-limited illness), and extrapulmonary legionellosis (a *Legionella* infection outside the lungs). LD often requires hospitalization and has a case fatality rate of approximately 10%. Risk factors include older age (≥50 years), current or former smoking, a weakened immune system, and chronic lung conditions [1–3]. The incubation period of LD is approximately 5–6 days, but ranges from 2 to 10 or 2–14 days have been observed [4–6]. Reported LD has been on the rise in the United States since 2000 [7,8].

People can develop LD when they inhale aerosolized water containing *Legionella*. Although the bacteria are found naturally in freshwater environments at low levels, building water systems that are not adequately maintained provide an opportunity for *Legionella* to grow and spread [9]. Travel away from home, particularly lodging in accommodations with poorly maintained water systems, is a known risk factor for LD [9,10]. Public accommodations such as hotels, resorts, and

Abbreviations: CDC, Centers for Disease Control and Prevention; CSTE, Council of State and Territorial Epidemiologists; LD, Legionnaires' disease; NNDSS, National Notifiable Diseases Surveillance System; SLDSS, Supplemental Legionnaires' Disease Surveillance System; TAPAS, travel-associated, public accommodation stay [case of Legionnaires' disease].

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cruise ships often have cooling towers, hot tubs, decorative fountains, showers, and other devices that can aerosolize water and transmit *Legionella* to occupants if not properly maintained [11]. Implementing effective water management programs can reduce risk of *Legionella* growth and transmission to building occupants [12,13]. Among outbreaks associated with building water systems investigated by the Centers for Disease Control and Prevention (CDC) from 2000 to 2014, nearly 90% were caused by problems preventable with an effective water management program [9].

Multiple LD cases associated with the same accommodation can indicate an exposure source in the building or cruise ship; however, detecting travel-associated clusters can be challenging. Because the incubation period of LD is long, disease onset usually occurs after infected travelers disperse from the travel destination and return home, often to different public health jurisdictions, where they seek medical care and may be diagnosed with LD. To facilitate detection of travel-associated LD clusters, U.S. public health jurisdictions report travel-associated cases in their residents to CDC.

The last detailed analysis of travel-associated cases of LD in the United States incorporated data on cases occurring during 2005–2006 [14]. Here, we describe reported LD cases among U.S. residents associated with travel to a public accommodation during 2015–2016, the most recent period for which data were available.

2. Material and methods

2.1. Definitions

We defined and classified LD cases according to the Council of State and Territorial Epidemiologists (CSTE) criteria in effect during 2015–2016 (Fig. 1), which were approved in 2005 [15] and underwent administrative formatting changes in 2009 [16]. A travel-associated case was defined as one in which the patient spent ≥1 night away from home (excluding healthcare and congregate living settings) during the 10 days before symptom onset (i.e., the exposure period). An accommodation visit was defined as an overnight stay at a unique location. For example, if a patient stayed in two different hotels during travel in the same destination jurisdiction, this would constitute two public accommodation visits. A travel-associated cluster was defined as two or more cases associated with a stay at the same accommodation within 12 months. An accommodation was classified as private if any of the following words appeared in its name or description on the case report form: "Brother," "Cabin," "Camp," "Cottage," "Cousin," "Daughter," "Family," "Friend," "Grandson," "Mobile," "Mother," "Motor home," "Niece," "Parent," "Private," "Relative," "Sister," "Son," "Townhouse," "Trailer," "Truck"; otherwise, the accommodation was assumed to be public. Home-sharing services (e.g., Airbnb) were considered public accommodations. If the accommodation name and description were missing, the accommodation type was classified as unknown. Most of our analyses focused on travel-associated, public accommodation stay (TAPAS) cases. The travel destination is the jurisdiction in which the patient spent the night away from home. U.S. jurisdictions included the 50 states (excluding New York City), New York City, and the District of Columbia. U.S. territories included American Samoa, Guam, the Northern Mariana Islands, Puerto Rico, and the U.S. Virgin Islands. Non-U.S. jurisdictions included independent nations.

2.2. Case reporting

U.S. jurisdictions report all diagnosed cases of LD to CDC through the National Notifiable Diseases Surveillance System (NNDSS), which is considered the gold standard for case counts; data include patient demographic characteristics and limited epidemiologic information. For most cases, additional data, including patient exposure history (in particular, travel), hospitalization and outcome, and laboratory diagnostic information, are reported separately to the Supplemental Legionnaires' Disease Surveillance System (SLDSS) at CDC; however, not all NNDSS cases are reported in SLDSS [7]. Non-U.S. jurisdictions can also report cases to SLDSS if the patient is diagnosed there. To facilitate detection of travel-associated LD clusters, CSTE recommends that all travel-associated cases be reported to CDC through SLDSS within 7 days of notification [15]. While nearly all travel-associated cases involving a destination other than the jurisdiction of the patient's residence were reported to SLDSS, approximately half of U.S. jurisdictions did not report travel-associated cases that involved only within-jurisdiction-of-residence travel promptly to CDC. However, approximately half of these eventually reported all cases to SLDSS as time and resources allowed; therefore, approximately 25% of jurisdictions may not have reported all travel-associated cases that involved only within-jurisdiction-of-residence travel to SLDSS. For this analysis, we assumed that all travel-associated cases were reported to SLDSS.

Completeness of reporting non-travel-associated cases to SLDSS varies by year and jurisdiction. To reduce the potential for bias, analyses involving non-travel-associated cases in SLDSS were restricted to years and jurisdictions in which ≥90% of NNDSS cases were reported to SLDSS. These jurisdictions are referred to as complete reporters.[1]

2.3. Cluster detection

Jurisdictions report accommodation information for travel-associated cases to CDC through SLDSS. When notification of a travel-associated case is received at CDC, SLDSS is reviewed for other cases associated with a stay at the same accommodation within the previous 12 months. CDC notifies destination jurisdictions of all travel-associated cases, as well as any travel-associated clusters that are detected.

2.4. Inclusion criteria

We included cases meeting the CSTE criteria for a confirmed case of LD among U.S. residents that occurred during 2015 or 2016. We included clusters that were first detected during 2015 or 2016, regardless of when the first case occurred. Cases occurring in non-U.S. residents, but not cases occurring after 2016, were included for cluster detection and cluster size analysis.

2.5. Estimated number of TAPAS cases acquired in the destination

It is unlikely that, for every reported TAPAS case, particularly those associated with brief visits, infection was acquired in the destination. Therefore, we estimated the number of TAPAS cases for which infection was acquired in the destination, using a modeled incubation period probability distribution and the specific days of the exposure period each patient spent in the destination.

Estimating the number of people infected with *Legionella* while visiting a given jurisdiction depends on the incubation period of LD, which is variable, and not known for each individual patient. Previous work modeled the incubation period distribution by fitting a 2-parameter gamma probability density function to documented patient incubation periods in a large, well-characterized outbreak [4,17]. The

[1] 2015 complete reporters: Alabama, Colorado, Connecticut, Florida, Georgia, Hawaii, Iowa, Kansas, Kentucky, Maine, Michigan, Minnesota, Mississippi, Missouri, New Hampshire, New Mexico, New York City, New York State, North Dakota, Ohio, Pennsylvania, Rhode Island, South Carolina, Texas, Vermont, Virginia, Washington, West Virginia, Wisconsin, and Wyoming. 2016 complete reporters: Alabama, Alaska, Arizona, Arkansas, Colorado, Connecticut, Delaware, Florida, Georgia, Hawaii, Illinois, Iowa, Kansas, Kentucky, Maine, Michigan, Minnesota, Mississippi, Missouri, Montana, New Hampshire, New Jersey, New York City, New York State, Ohio, Pennsylvania, Rhode Island, South Carolina, Utah, Vermont, Virginia, Washington, West Virginia, Wisconsin, and Wyoming.

Council of State and Territorial Epidemiologists Case Definition and Classification of Legionnaires' Disease

- Clinical description
  - Illness characterized by fever, myalgia, cough, and clinical or radiographic pneumonia
- Laboratory criteria
  - Confirmed
    - By culture: isolation of any *Legionella* organism from respiratory secretions, lung tissue, pleural fluid, or other normally sterile fluid.
    - By detection of *Legionella pneumophila* serogroup 1 antigen in urine using validated reagents.
    - By seroconversion: fourfold or greater rise in specific serum antibody titer to *Legionella pneumophila* serogroup 1 using validated reagents.
  - Suspect
    - By seroconversion: fourfold or greater rise in antibody titer to specific species or serogroups of *Legionella* other than *L. pneumophila* serogroup 1 (e.g., *L. micdadei*, *L. pneumophila* serogroup 6)
    - By seroconversion: fourfold or greater rise in antibody titer to multiple species of *Legionella* using pooled antigen and validated reagents.
    - By the detection of specific *Legionella* antigen or staining of the organism in respiratory secretions, lung tissue, or pleural fluid by direct fluorescent antibody staining, immunohistochemistry, or other similar method, using validated reagents.
    - By detection of *Legionella* species by a validated nucleic acid assay.
- Case classification
  - Confirmed: a clinically compatible case that meets at least one of the confirmatory laboratory criteria
  - Suspect: a clinically compatible case that meets at least one of the presumptive laboratory criteria

Fig. 1. Council of State and Territorial Epidemiologists case definition and classification of Legionnaires' disease.
The criteria used to define and classify cases of Legionnaires' disease in place at the time the cases in this study occurred are shown [16].

authors reported that shape parameter $a = 4.96$ and scale parameter $b = 1.27$ gave the best fit to that outbreak's incubation period distribution, and we assumed that our patients' incubation periods followed the same form.

We used this model to calculate the probability that a patient would have an incubation period of each of 1 through 10 days (Fig. 2). For example, the modeled probability of a 1-day incubation period (i.e., infection occurring on the day before symptom onset) is 0.022, or 2.2%. Similarly, the probability that a patient was infected within the 5 days (i.e., on day 1, 2, 3, 4, or 5) prior to symptom onset is 0.516, or 51.6%. Because our travel-associated case definition required at least a 1-night stay away from home during the 10 days before symptom onset, the probability of an incubation period shorter than 1 day or longer than 10 days (0.067) was excluded (Fig. 2).

To estimate the expected number of TAPAS cases for which infection was acquired in a jurisdiction, we used arrival and departure information to determine which days prior to symptom onset a patient spent in the jurisdiction. We then calculated the probability that infection was acquired on those specific days, using the model-derived probabilities associated with each of those days. For example, if a patient spent the first 5 days prior to symptom onset in jurisdiction A, we allocated 0.516 expected patients to jurisdiction A. If that patient also spent days 6

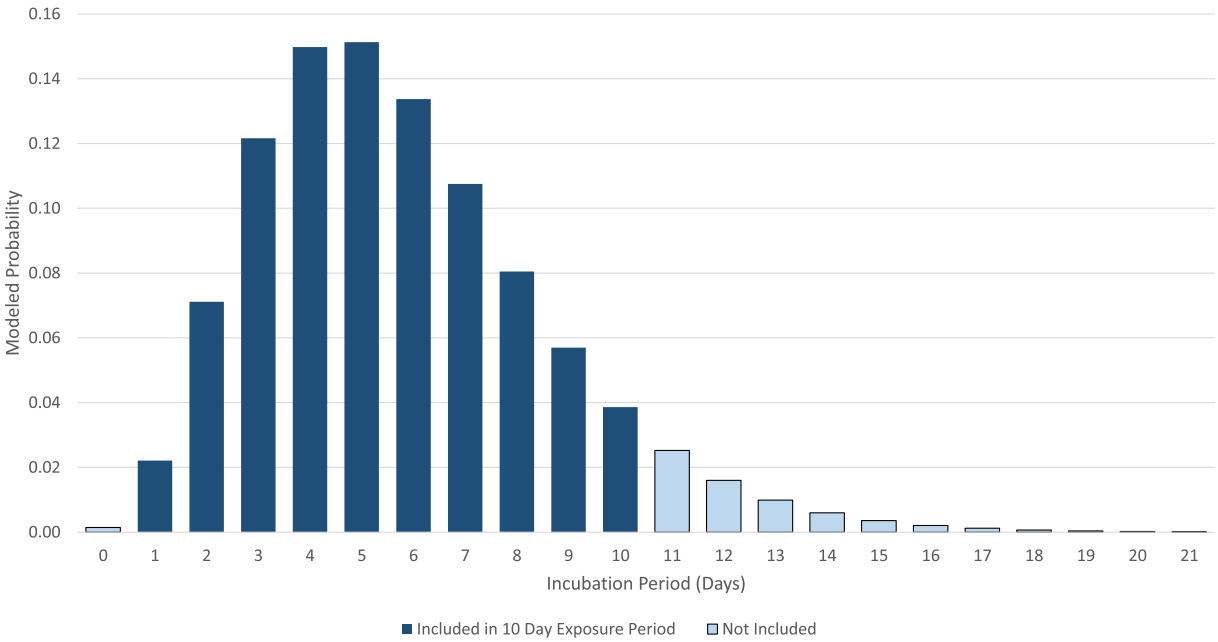


Fig. 2. Modeled incubation period probability distribution of Legionnaires' disease.
The modeled incubation period probability distribution of Legionnaires' disease is shown. Incubation period in days is plotted across the horizontal axis. For example, under the gamma model, the probability that a patient's incubation period is 1 day is 0.022, or 2.2%. Our travel-associated case definition included incubation periods of length 1 day through 10 days. The probability of a patient having an incubation period of those lengths (93.3%) is shown in dark shaded bars; the probability of a longer or shorter incubation period (6.7%) is shown in light shaded bars.

through 10 prior to symptom onset in jurisdiction B, we allocated 0.417 expected patients to jurisdiction B. After performing this allocation procedure for every patient, we estimated the total number of TAPAS cases for which infection was acquired in each jurisdiction as the sum of these values. Cases missing dates of stay did not contribute to our estimated number of cases.

2.6. Estimated number of hotel room nights booked

The total number of hotel rooms available and average occupancy by jurisdiction for 2015 and 2016 were provided by the American Hotel and Lodging Association. For each jurisdiction and year, we multiplied the number of rooms available by the average annual occupancy by the number of days in that year (365 for 2015 and 366 for 2016) to estimate the number of hotel room nights booked by jurisdiction. The number of hotel room nights booked served as a proxy measure of public accommodation travel volume, which we used as a denominator for standardizing the raw number of reported TAPAS cases across jurisdictions.

3. Results

3.1. Cases

During 2015–2016, 12,200 LD cases in U.S. residents were reported to NNDSS (Table 1). Of these, 1,499 (12.3%) occurred in patients who reported an overnight stay away from home, either inside or outside the United States, during the 10 days prior to symptom onset. Among these patients, 1,064 (71.0%) reported staying in at least one public accommodation (TAPAS); 401 stayed only in private accommodations; and 34 had unknown accommodation types. Of all LD cases reported among U.S residents during 2015–2016, 8.7% (1,064/12,200) occurred in patients who reported ≥1 overnight stay in a public accommodation during the 10 days prior to symptom onset. Among patients who reported staying in public accommodations, 1,029 stayed only in hotels/motels/resorts/home-shares, 16 only sailed on a cruise, and 19 reported both.

TAPAS cases in U.S. residents were associated with travel in 51 of 52 U.S. jurisdictions (887 patients), 2 U.S. territories (6 patients), 37 non-U.S. jurisdictions (131 patients), and international waters on a cruise voyage (35 patients); 128 patients visited more than one jurisdiction (Table S1). The median number of TAPAS cases by U.S. destination (including Delaware, which had 0 cases) was 12.5 (range: 0–117) (Fig. 3a). TAPAS cases were associated with 1,171 public accommodation visits in U.S. jurisdictions, 6 accommodation visits in U.S. territories, 181 accommodation visits in non-U.S. jurisdictions, and 35 cruise voyages; 121 patients visited more than one accommodation per jurisdiction. The median number of public accommodation visits by U.S. jurisdiction was 15 (range: 0–138).

Dates of stay were available for at least one accommodation visit for 84.0% (745/887) of patients who stayed in a U.S. jurisdiction and for 86.5% (1,013/1,171) of U.S. accommodation visits. The median number of nights within the 10 days before disease onset that patients spent in a U.S. accommodation was 2 (range: 1–10). The total number of nights during both 2015 and 2016 that patients spent in a U.S. destination was 2,688, and the median number of nights patients spent by U.S. destination was 28 (range: 0–485) (Table S1). After assigning expected cases to destinations using the gamma model, the total estimated number of patients infected during travel in a U.S. destination was 264.7, and the median estimated number of patients infected during travel by jurisdiction was 2.9 (range: 0.0–48.0) (Fig. 3b). The same three jurisdictions had the most reported TAPAS cases and the highest estimated number of patients infected during travel in the jurisdiction. For U.S. jurisdictions, the estimated percentage of reported TAPAS cases acquired during travel in a U.S. destination was 29.8% (264.7/887) overall and 35.5% (264.7/745) for cases with dates of stay available; these respective percentages were 54.4% (3.3/6) and 65.3% (3.3/5) for U.S. territories; 47.2% (61.8/131) and 53.7% (61.8/115) for non-U.S. jurisdictions; and 40.9% (14.3/35) and 44.7% (14.3/32) for cruise voyages (Table S1).

Table 1
Confirmed Legionnaires' disease cases, United States residents, 2015–2016.

	N	%
All confirmed NNDSS[a] cases	12,200	100.0
Cases with a travel exposure, SLDSS[b]	1,499	12.3
Cases with at least one public accommodation stay (TAPAS)	1,064	71.0
Hotel/motel/resort	1,029	96.7
Cruise ship	16	1.5
Both	19	1.8
Cases with all private accommodations	401	26.8
Cases with unknown accommodation types	34	2.3

[a] National Notifiable Diseases Surveillance System.
[b] Supplemental Legionnaires' Disease Surveillance System.

The total number of reported TAPAS cases and estimated number of TAPAS cases for which infection was acquired in the destination per 10 million hotel room nights booked were 4.28 and 1.10, respectively, for U.S. jurisdictions; the median numbers by U.S. jurisdiction were 4.68 (range: 0.00–9.84) and 0.99 (range: 0.00–4.20) (Fig. 3c). The jurisdictions with the most reported TAPAS cases and highest estimated number of patients infected during travel in the jurisdiction changed after standardizing for travel volume.

Within complete reporting jurisdictions, there were 7,974 confirmed cases of LD, of which 761 (9.5%) were TAPAS cases.

Median patient age was 61 years (range: 9–98) for TAPAS cases, compared to 62 years (range: 0–103) for non-TAPAS cases (Table 2a). The percentage of cases in males was similar for TAPAS (64.4%) and non-TAPAS (60.7%) cases. Compared to non-TAPAS cases, a higher percentage of patients were white (67.3% vs. 58.5%), and a lower percentage were Black/African American (15.0% vs. 20.5%) for TAPAS cases. The percentage of TAPAS cases in Hispanics (2.4%) was less than half that of non-TAPAS cases (5.7%).

The proportion of patients hospitalized was similar for TAPAS cases (96.1%) and non-TAPAS cases (96.7%) (Table 2b). Among the 77.9% of patients for whom outcome data were available, the case fatality rate for TAPAS cases (4.5%) was lower than that for non-TAPAS cases (9.4%) (rate ratio: 0.48; 95% confidence interval: 0.33–0.70).

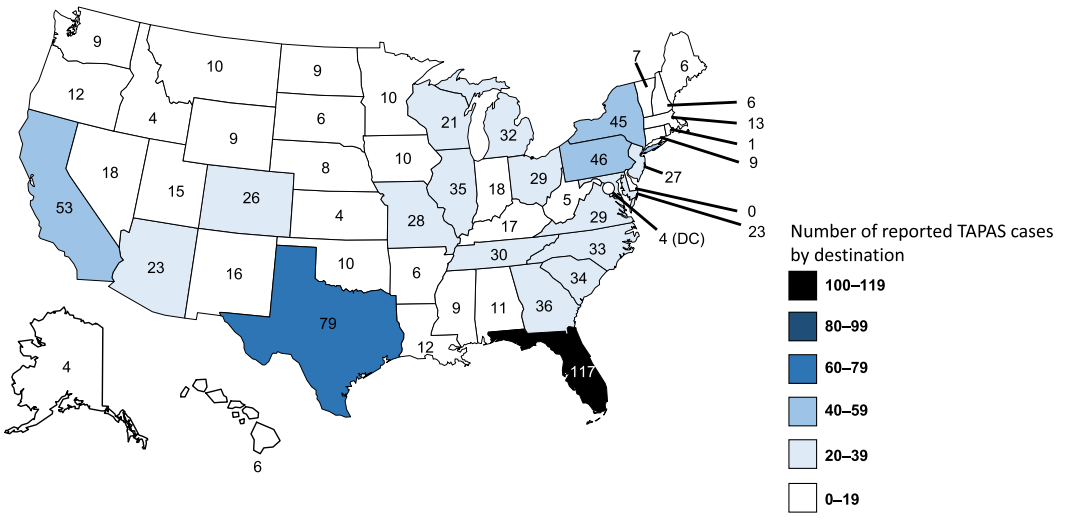
Within complete reporting jurisdictions, disease onset for most LD cases occurred during the summer through early fall months for both TAPAS and non-TAPAS cases (Fig. 4). However, for TAPAS cases, a higher proportion had onset during the spring months and a lower proportion had onset during the fall months compared to non-TAPAS cases.

3.2. Clusters

During 2015–2016, 78 TAPAS clusters involving U.S. residents were identified (Table S1). Sixty-eight clusters were detected in 34 U.S. destination jurisdictions; 4 clusters were detected in 3 non-U.S. jurisdictions; and 6 clusters were detected on cruise voyages. The median number of clusters identified per U.S. jurisdiction was one (range 0–10). A total of 202 cases were associated with the 78 clusters. The median cluster size was two cases (range: 2–10) (Fig. 5). Of the 68 clusters occurring within U.S. destination jurisdictions, 45 (66.2%) involved no patients with a common jurisdiction of residence.

4. Discussion

Among all reported LD cases in U.S. residents during 2015–2016, less than 10% of patients reported travel with a public accommodation stay within the 10 days prior to disease onset. During 1980–1998 and 2005–2009, 21% and 24%, respectively, of reported LD cases in the United States were classified as travel-associated [18,19]. An analysis of



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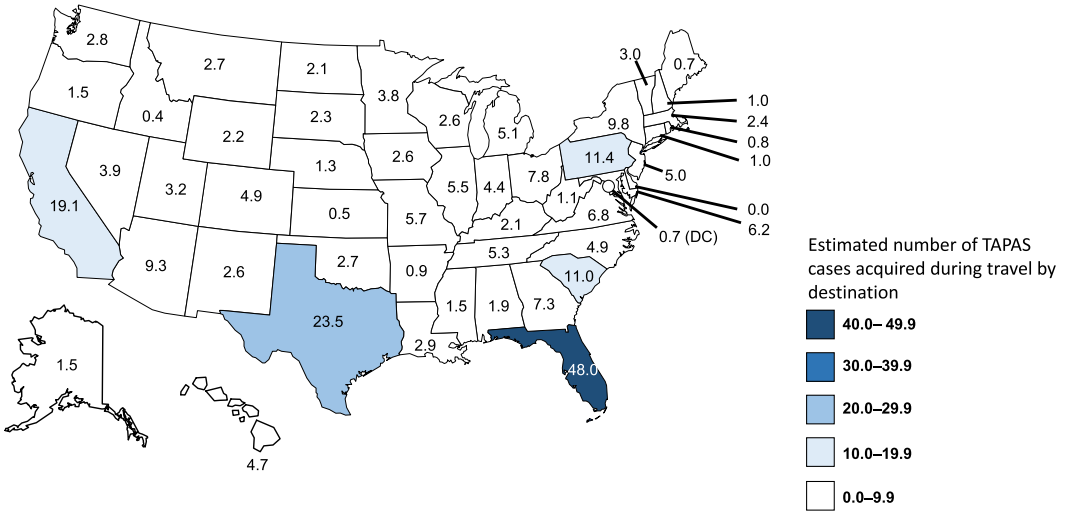

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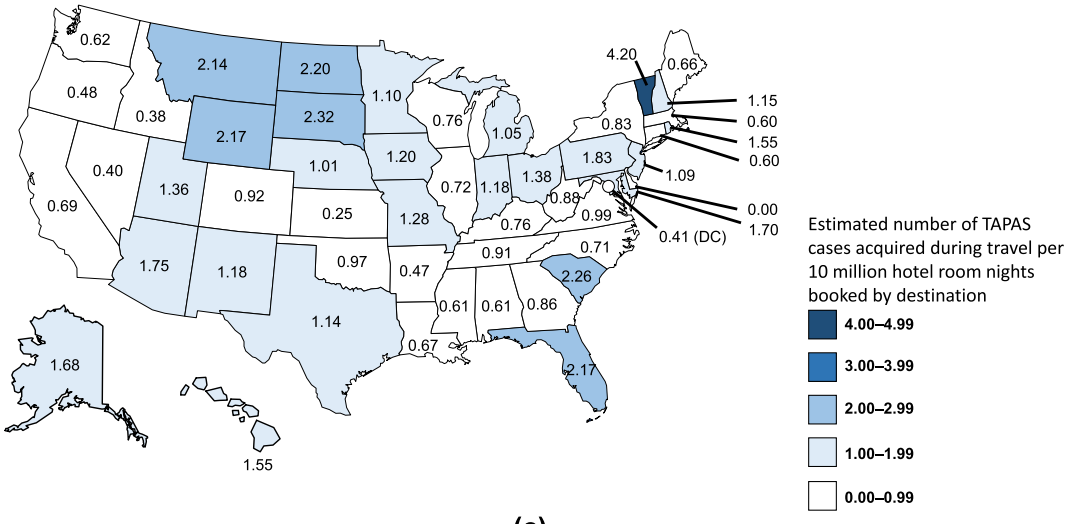

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Fig. 3. United States travel destinations reported by travel-associated public accommodation stay Legionnaires' disease cases, United States residents, 2015–2016.

A. Number of reported travel-associated public accommodation stay (TAPAS) cases, by destination, 2015–2016. While 887 patients reported a U.S. destination, 112 were counted as a case in more than 1 jurisdiction because they visited more than 1 jurisdiction.

B. Estimated number of travel-associated public accommodation stay (TAPAS) cases acquired during travel, by destination, 2015–2016. Patients who visited more than one destination contributed to the estimate of each jurisdiction visited.

C. Estimated number of travel-associated public accommodation stay (TAPAS) cases acquired during travel per 10 million hotel room nights booked, by destination, 2015–2016. Patients who visited more than one destination contributed to the estimate of each jurisdiction visited.

Table 2a
Demographics by travel status, United States jurisdictions reporting ≥90% of cases[a], 2015–2016.

	TAPAS[b] (Total = 761)		Non-TAPAS[c] (Total = 7,213)		
Demographic	N	%	N	%	p value
Median Age	61		62		0.0007
Age					
0–9	1	0.1	8	0.1	<0.0001
10–19	2	0.3	18	0.3	
20–29	16	2.1	147	2.0	
30–39	48	6.3	398	5.5	
40–49	101	13.3	791	11.0	
50–59	166	21.8	1,784	24.7	
60–69	249	32.7	1,810	25.1	
70–79	126	16.6	1,187	16.5	
80–89	46	6.0	821	11.4	
90+	4	0.5	240	3.3	
Not stated	2	0.3	9	0.1	
Sex					
Female	268	35.2	2790	38.7	0.1044
Male	490	64.4	4375	60.7	
Not stated	3	0.4	48	0.7	
Race					
American Indian/Alaska Native	5	0.7	25	0.4	<0.0001
Asian	10	1.3	67	0.9	
Black or African American	114	15.0	1,478	20.5	
Native Hawaiian/Other Pacific Islander	0	0.0	10	0.1	
White	512	67.3	4,222	58.5	
Multiple	0	0.0	10	0.1	
Not stated	120	15.8	1,401	19.4	
Ethnicity					
Hispanic	18	2.4	412	5.7	0.0004
Non-Hispanic	593	77.9	5,346	74.1	
Not stated	150	19.7	1,455	20.2	

[a] 2015 complete reporting states: Alabama, Colorado, Connecticut, Florida, Georgia, Hawaii, Iowa, Kansas, Kentucky, Maine, Michigan, Minnesota, Mississippi, Missouri, New Hampshire, New Mexico, New York City, New York State, North Dakota, Ohio, Pennsylvania, Rhode Island, South Carolina, Texas, Vermont, Virginia, Washington, West Virginia, Wisconsin, and Wyoming. 2016 complete reporting states: Alabama, Alaska, Arizona, Arkansas, Colorado, Connecticut, Delaware, Florida, Georgia, Hawaii, Illinois, Iowa, Kansas, Kentucky, Maine, Michigan, Minnesota, Mississippi, Missouri, Montana, New Hampshire, New Jersey, New York City, New York State, Ohio, Pennsylvania, Rhode Island, South Carolina, Utah, Vermont, Virginia, Washington, West Virginia, Wisconsin, Wyoming.

[b] Travel-associated, public accommodation stay cases.

[c] Cases with all private or unknown accommodations; or no, unknown, or missing travel status.

Table2b
Disease severity measures by travel status, United States jurisdictions reporting ≥90% of cases[a], 2015–2016.

	TAPAS[b]			Non-TAPAS[c]					
	Events	Cases	Rate (%)	Events	Cases	Rate (%)	Rate ratio	95% CI Lower Limit	95% CI Upper Limit
Hospitalization[d]	720	749	96.1	6,899	7,134	96.7	0.99	0.98	1.01
Death[e]	28	618	4.5	527	5,597	9.4	0.48	0.33	0.70

[a] 2015 complete reporting states: Alabama, Colorado, Connecticut, Florida, Georgia, Hawaii, Iowa, Kansas, Kentucky, Maine, Michigan, Minnesota, Mississippi, Missouri, New Hampshire, New Mexico, New York City, New York State, North Dakota, Ohio, Pennsylvania, Rhode Island, South Carolina, Texas, Vermont, Virginia, Washington, West Virginia, Wisconsin, and Wyoming. 2016 complete reporting states: Alabama, Alaska, Arizona, Arkansas, Colorado, Connecticut, Delaware, Florida, Georgia, Hawaii, Illinois, Iowa, Kansas, Kentucky, Maine, Michigan, Minnesota, Mississippi, Missouri, Montana, New Hampshire, New Jersey, New York City, New York State, Ohio, Pennsylvania, Rhode Island, South Carolina, Utah, Vermont, Virginia, Washington, West Virginia, Wisconsin, Wyoming.
[b] Travel-associated, public accommodation stay cases.
[c] Cases with all private or unknown accommodations; or no, unknown, or missing travel status.
[d] For 7,883/7,974 (98.9%) cases with hospitalization data.
[e] For 6,215/7,974 (77.9%) cases with outcome data.

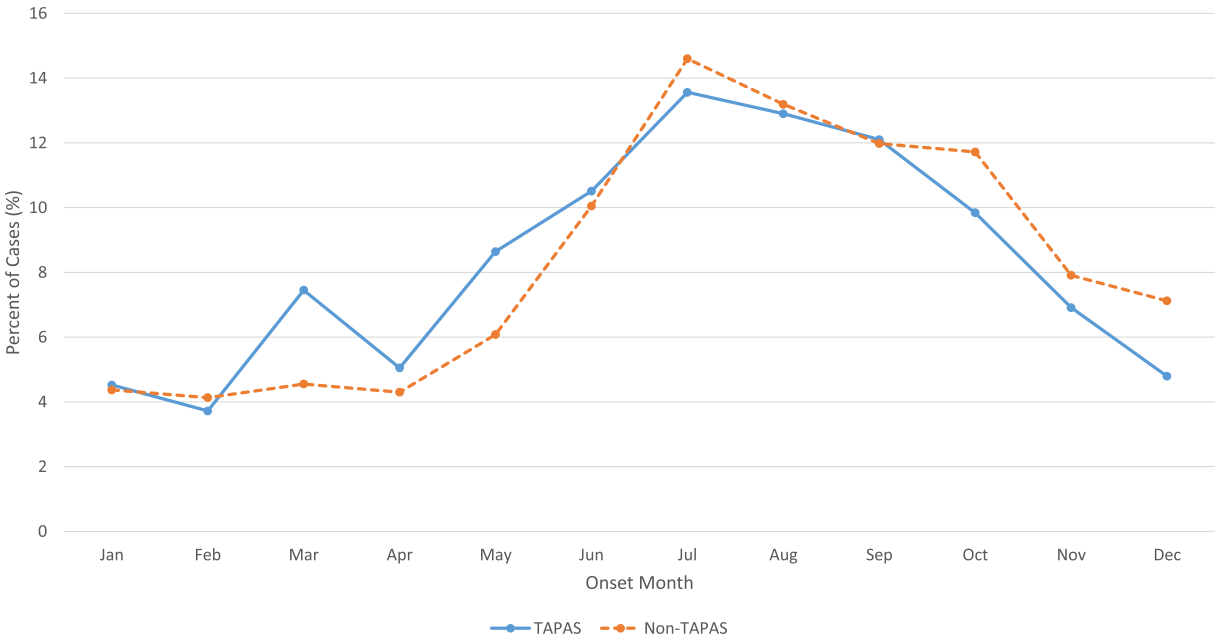

Fig. 4. Seasonality of reported Legionnaires' disease cases, among jurisdictions reporting ≥90% of Cases, 2015–2016.
The percentages of reported travel-associated public accommodation stay (TAPAS) and non-TAPAS cases of Legionnaires' disease occurring during 2015 and 2016 are plotted by month of symptom onset. TAPAS cases are represented by a solid line; non-TAPAS cases are represented by a dashed line.

LD cases in Europe during 2011–2015 determined that 20% were travel-associated [20]. However, because these studies employed definitions different from ours, results may not be directly comparable. Both U.S. studies considered cases to be travel-associated if travel occurred within 2 weeks (rather than 10 days) prior to disease onset, and used cases reported to SLDSS (rather than NNDSS) as a denominator; neither analyzed cases involving public accommodation visits as a specific subset. Travel history beyond 10 days was not collected for our cases; however, if we do not limit our travel-associated cases to those with a public accommodation stay and use all cases reported to SLDSS as a denominator in an attempt to replicate the same definition, 16.6% (1,499/9,053) of our cases would be travel-associated. The European study considered cases to be travel-associated if travel occurred 2–10 days before disease onset, and limited the denominator to cases with a known probable setting of infection, such as travel, healthcare, or community settings (rather than including cases missing this information). If the European study had included cases missing the probable setting of infection in the denominator, 17.5% of their cases would have been classified as travel-associated.

The number of reported TAPAS cases likely exceeds the number of cases for which infection was acquired during travel. While lodging in accommodations with inadequately maintained water systems is a risk factor for acquiring LD [9], it is not likely that the accommodation was the infection source for every reported TAPAS case. Potential infection sources exist outside the accommodation (e.g., a fountain at a restaurant), and the risk posed by the accommodation cannot be evaluated because most case reports for TAPAS cases contain few details about the potential exposure setting, other than the name and address of the accommodation and dates of travel. Furthermore, it is challenging to ascertain the jurisdiction of exposure based solely on surveillance data, particularly when patients spend only a few days at their destinations. However, absent a detailed exposure history, the likelihood that a jurisdiction was the source of a patient's infection increases with length of stay. The estimated number of TAPAS cases acquired in a U.S. jurisdiction was approximately 30%–35% of the total number of reported U.S. TAPAS cases; this percentage was higher for other areas of the world, likely because travel to these destinations tended to last longer.

This method of estimating the likelihood that a given location was the source of a patient's infection can be applied in other settings as well, particularly when clinical and environmental isolates are not available for comparison to assess source attribution. For example, if the only available information about a case is that the patient spent days 1

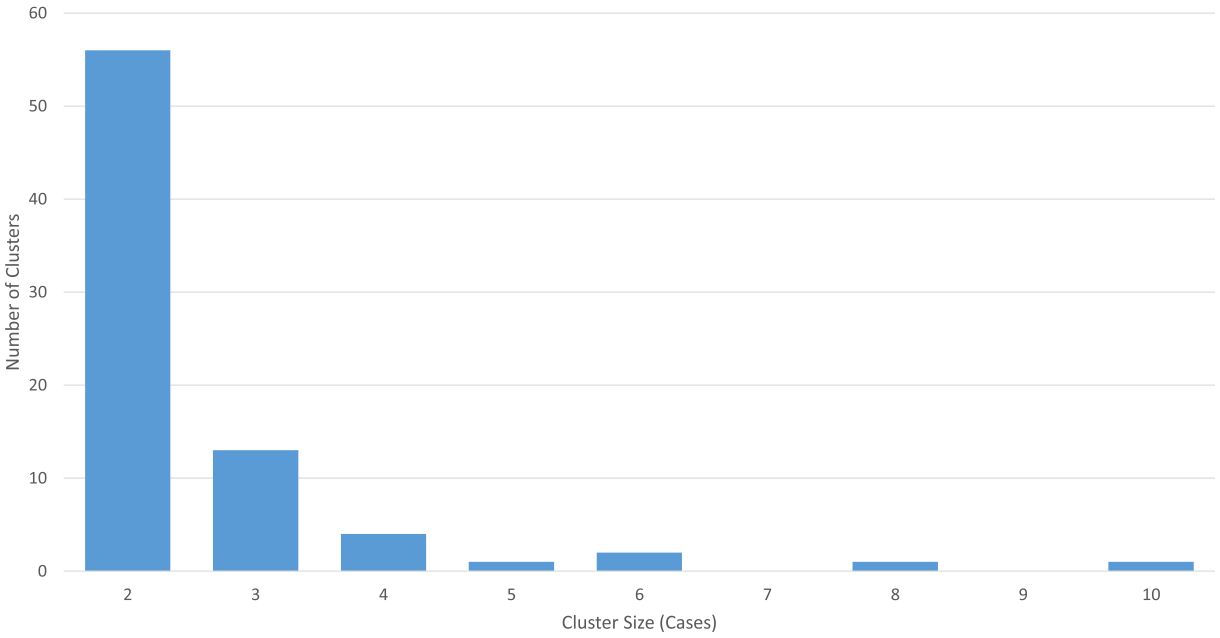

Fig. 5. Size of new travel-associated public accommodation stay clusters identified, 2015–2016.
The size of the 78 travel-associated public accommodation stay clusters newly identified during 2015 and 2016 are shown. Cluster size in number of cases is plotted across the horizontal axis.

through 5 prior to symptom onset in a hospital as an inpatient, the probability that the hospital was the infection source is 0.516 or 51.6%. Because inpatients do not leave the hospital, the LD case is linked to the facility as the only possible source, whereas a TAPAS case is linked to a destination jurisdiction and not necessarily the accommodation. However, when a cluster of more than one TAPAS case associated with an accommodation is identified, the likelihood that the accommodation is the source increases.

While every U.S. jurisdiction (except Delaware) was associated with at least one TAPAS case, TAPAS cases were not uniformly distributed among jurisdictions. Destination jurisdictions with high numbers of reported TAPAS cases among travelers in the jurisdiction also had the highest estimated numbers of TAPAS cases acquired during travel in the jurisdiction. However, many of these jurisdictions also receive a high volume of visitors in general. Therefore, it was appropriate to standardize raw counts with a measure of travel volume. After standardizing for travel volume, TAPAS estimates by destination jurisdiction changed dramatically. While Florida, Texas, and California had the highest raw estimated number of TAPAS cases acquired, standardized estimates per 10 million hotel room nights booked were highest for Vermont, South Dakota, and South Carolina. Destination jurisdictions with the highest raw and standardized numbers of TAPAS cases were not, in general, located in the Middle Atlantic and East North Central divisions, which have the highest LD incidence by residence [7].

Our results show that for every 10 million hotel room nights booked, 4.28 TAPAS cases were reported, and an estimated 1.10 TAPAS cases were acquired in the destination jurisdiction. A similar rate of overall reported cases (3.0 reported cases/10 million nights spent) was found among European residents traveling in Europe [21].

We limited analyses involving non-TAPAS cases to data from complete reporting jurisdictions so that population estimates would not be biased. TAPAS cases and non-TAPAS cases were similar regarding patient age, sex, race, and ethnicity; some statistical differences that were observed may have resulted from large numbers, or may reflect population segments more likely to travel. While hospitalization rates were the same for TAPAS and non-TAPAS cases, the case fatality rate for TAPAS cases was half that of non-TAPAS cases. This might suggest that, while LD is a severe pneumonia that requires hospitalization for nearly all patients regardless of underlying health, patients who are more likely to travel may also tend to be healthier. Consistent with our findings, most European TAPAS cases during 2010 occurred in people in the 60–69 years of age group, and the case fatality rate was 4.7%; however, a higher percentage of European TAPAS cases (72.2%) occurred in men [22].

LD shows a summer through early fall seasonal pattern [7]. Our data show that this pattern holds true for both TAPAS and non-TAPAS cases, and the distribution of cases during these peak months was nearly identical. This implies that the increase in cases during the summer and early fall is not caused by the higher volume of travel during summer months. However, the percentage of cases occurring during the spring appears to be higher for TAPAS compared to non-TAPAS cases, possibly reflecting travel patterns of people at risk for LD.

In general, clusters of cases occurring in people who visited the same accommodation suggest the presence of a common exposure source. While most identified clusters were composed of only two cases, these clusters are important to identify, as they can serve as early warning signs that additional cases may occur if appropriate action is not taken. Without jurisdictions reporting all TAPAS cases to a central location at CDC through SLDSS, 66% of clusters in the United States might not have been detected because none of the patients shared a common jurisdiction of residence; each jurisdiction of residence would identify only a single case associated with the accommodation. This finding highlights the importance of CSTE's recommendation to state health departments to report all travel-associated LD cases to CDC within 7 days of the initial notification [15].

The available data and findings have several limitations. First, it is generally unknown whether the source of the patients' infections was the accommodation, and more broadly, the travel destination, which leaves the data subject to a misclassification bias. However, we attempted to minimize this limitation by estimating the expected number of TAPAS cases acquired during travel in the destination. Accommodation data were also subject to misclassification because accommodations were assumed to be public if a word from a list associated with private accommodations did not appear in the case report form. Accommodation visits missing dates of stay could not be used to estimate number of TAPAS cases acquired during travel in a destination,

thus reducing the estimated number of TAPAS cases acquired during travel. Also, the incubation period model predicts that 6.7% of patients would have been infected outside the window for which we collected travel history, resulting in further underestimation of TAPAS cases. We used an estimate of the number of hotel room nights booked as a proxy measure for total volume of travelers to a jurisdiction; however, the most appropriate measure of total travelers exposed in a destination would have included the average number of room occupants per night booked. Overall, insights into the epidemiology of LD would be enhanced if reporting of non-TAPAS cases to SLDSS were more complete.

Despite the limitations, these findings suggest that TAPAS cases represent a smaller fraction of all LD cases than previously reported; the number of TAPAS cases is low relative to the number of nights spent in public accommodations; and survival is higher for TAPAS compared to non-TAPAS cases [7,19]. If the percentage of patients infected during travel is lower than previously reported, and the majority of all cases lack a suspected exposure source (travel, healthcare setting, or senior/assisted living facility), this implies more patients were infected elsewhere, such as at their work or home [7]. While these data are encouraging, use of effective water management programs are still needed to minimize the risk for TAPAS cases by preventing *Legionella* growth and transmission associated with an accommodation [12,13]. Even if the burden of TAPAS cases is somewhat lower than previously reported, the human and financial costs associated with these cases and clusters can be substantial [23–25].

Clusters can indicate an exposure source within an accommodation where public health action can be taken to prevent additional cases. Even in instances where the accommodation may not have been the source of the cluster, the interaction between public health and the building manager is an opportunity to stress the importance of implementing a water management program. Prompt notification of travel-associated LD cases to CDC can maximize the number of clusters that are identified and thus, opportunities for public health intervention [15].

Declaration of competing interest

The authors do not report any commercial or other associations that might pose a conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tmaid.2020.101943.

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