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Q Fever in the United States: Summary of Case Reports from Two National Surveillance Systems, 2000–2012

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Abstract. Q fever is a worldwide zoonosis historically associated with exposure to infected livestock. This study summarizes cases of Q fever, a notifiable disease in the United States, reported to the Centers for Disease Control and Prevention through two national surveillance systems with onset during 2000–2012. The overall incidence rate during this time was 0.38 cases per million persons per year. The reported case fatality rate was 2.0%, and the reported hospitalization rate was 62%. Most cases (61%) did not report exposure to cattle, goats, or sheep, suggesting that clinicians should consider Q fever even in the absence of livestock exposure. The prevalence of drinking raw milk among reported cases of Q fever (8.4%) was more than twice the national prevalence for the practice. Passive surveillance systems for Q fever are likely impacted by underreporting and underdiagnosis because of the nonspecific presentation of Q fever.

INTRODUCTION

Coxiella burnetii is the etiologic agent of Q fever, a zoonotic illness historically associated with exposure to infected livestock, particularly sheep, cattle, and goats. The organism is highly infectious and shed in large numbers in milk and during parturition.[1] It is resistant to desiccation, heat, and disinfection; and, it is capable of being transferred long distances by wind, which complicates diagnosis and control, and that causes concern that *C. burnetii* could be used as a tool for bioterrorism.[2–9] Inhalation of infectious organisms is widely recognized as the most prevalent route of exposure; transmission by ingestion of unpasteurized milk, tick bite, sexual contact, and transfusion of infected blood products have rarely been implicated in rare human infections.[10–14] Large outbreaks associated with inhalational exposure have occurred in slaughterhouses, auction yards, dairies, military units, laboratories, and households.[15–21]

In humans in the United States, acute Q fever most commonly presents as a flu-like illness, more rarely as hepatitis or pneumonia; asymptomatic infections have also been documented.[22,23] In addition to the acute illness, Q fever can cause chronic infection. Chronic infection occurs rarely (< 5%) and may present months to years after an acute infection. Chronic Q fever typically manifests as blood-culture negative endocarditis or infection of a vascular aneurysm or vascular prosthesis.[22,24–26] Doxycycline is recommended for patients with acute Q fever to shorten the duration of symptoms, but the recommended treatment of chronic Q fever is a long-term (≥ 18 months) combination of doxycycline and hydroxychloroquine.[27,28]

Q fever was added to the list of nationally notifiable infectious diseases in 1999 for the United States.[29] The original case definition was updated in 2008, and the single reporting category of Q fever was divided into acute Q fever and chronic Q fever.[30] Here, we summarize all cases of Q fever reported with onset during 2000–2007 and all cases reported under the newer case definition with onset during 2008–2012 to two national surveillance systems. Previously, we summarized reports from a single national surveillance system from 1978 to 2004; and, this past report overlaps with our report for 2000–2004.[31]

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METHODS

Case definition 2000–2007.[29]

- "Acute Infection: A febrile illness usually accompanied by rigors, myalgia, malaise, and retrobulbar headache. Severe disease can include acute hepatitis, pneumonia, and meningoencephalitis. Clinical laboratory findings may include elevated liver enzyme levels and abnormal chest film findings. Asymptomatic infections may also occur.
- Chronic Infection: Potentially fatal endocarditis may evolve months to years after acute infection, particularly in persons with underlying valvular disease. A chronic fatigue-like syndrome has been reported in some Q fever patients."

Confirmed cases are clinically compatible or epidemiologically linked cases with a documented seroconversion, isolation of *C. burnetii* by culture, demonstration of *C. burnetii* by immunohistochemistry (IHC), or detection of nucleic acids by polymerase chain reaction (PCR). Probable cases are clinically compatible or epidemiologically linked cases with only a single, positive serological result (as defined by the testing laboratory).

Case definition 2008–2012.[30]

- "Acute Q fever: Acute fever and one or more of the following: rigors, severe retrobulbar headache, acute hepatitis, pneumonia, or elevated liver enzyme levels.
- Chronic Q fever: Newly recognized, culture-negative endocarditis, particularly in a patient with previous valvulopathy or compromised immune system, suspected infection of a vascular aneurysm or vascular prosthesis, or chronic hepatitis, osteomyelitis, osteoarthritis, or pneumonitis in the absence of other known etiology."

Confirmed laboratory evidence for acute Q fever was changed from the 2000 to 2007 case definition: documenting a seroconversion is limited to indirect immunofluorescent assay (IFA) phase II immunoglobin G (IgG) titers. Supportive laboratory evidence of acute Q fever requires an IFA phase II IgG titer of at least 1:128 or a positive enzyme-linked immunosorbent assay (ELISA), dot-ELISA, or latex agglutination.

Laboratory confirmation of a chronic Q fever case requires a single IFA phase I IgG titer of at least 1:800, a PCR positive result, isolation by culture, or demonstration by IHC. Supportive laboratory evidence of chronic Q fever requires a single IFA phase I IgG titer of at least 1:128 but < 1:800. To meet the case definition a case must fall into one of four categories:

- A confirmed acute Q fever case must have laboratory-confirmed evidence and either must be clinically compatible or epidemiologically linked to a laboratory-confirmed case.
- A probable acute Q fever case must have laboratory supportive evidence and must be clinically compatible.
- A confirmed chronic Q fever case must have laboratory-confirmed evidence and be clinically compatible.
- A probable chronic Q fever case must have laboratory supportive evidence and be clinically compatible.

Surveillance systems. State and local public health departments report cases of Q fever to the Centers for Disease Control and Prevention (CDC) through the National Notifiable Disease Surveillance System (NNDSS). These data include reporting category, place of residence, date of onset, and demographics: sex, age, race, and ethnicity. Although California only reported confirmed and probable cases, whether a case was classified as confirmed or probable was not always transmitted to NNDSS by California. Therefore, some cases of Q fever reported through NNDSS have an unknown case classification and are not included in the number of probable or confirmed reports.

In addition to the data collected by NNDSS, state and local public health departments also report epidemiological data, clinical data, and laboratory data about cases by paper case report forms (CRFs). Additional data collected by CRFs include patient occupation, patient pregnancy status, history of animal contact, exposure to parturient animals and unpasteurized milk, clinical signs and syndromes, pre-existing medical conditions, whether hospitalized, whether the case survived or died, and results of serologic and other diagnostic testing.

Data analysis. Hypothesis testing was performed at a significance level of 0.05. The exact binomial test was used to test equality of binomial proportions. The exact χ^2 test was used to test equality of multinomial proportions. Fisher's exact test was used to assess independence of the row and column effects in contingency tables. The Cochran-Armitage test was used to assess trends in contingency tables. The Cochran-Armitage tests the null hypothesis of independence of row and column effects, similar to Fisher's exact test, in tables with two rows and multiple columns. However, the Cochran-Armitage test for trend uses a two-sided alternative hypothesis of increasing or decreasing column proportions with increasing column rank. To reduce computation time, estimated *P* values from Monte-Carlo simulations were used for Fisher's exact test with contingency tables larger than 2 × 2, for the exact χ^2 test, and the Cochran-Armitage test for trend. Calculation of reported incidence rates (IRs) used the United States Census Bureau population estimates from 2000 to 2012.[32,33] Because Q fever was not notifiable in some states during certain years, those populations were not considered at risk for calculating IR: Alaska (2000, 2005–2006), Arkansas (2000–2001), District of Columbia (2011–2012), Delaware (2000–2001), Illinois (2000), Indiana (2001), Iowa (2000–2002, 2005–2012), Louisiana (2005), Maryland (2000–2001), Massachusetts (2000–2001), Mississippi (2000–2001), New Hampshire (2007–2012), New York (2000), Oklahoma (2000, 2002–2003, 2007–2008), Ohio (2000–2001), Pennsylvania (2000–2001, 2003–2004), Rhode Island (2000–2001), Texas (2000–2001), Vermont (2000–2002, 2004–2012), Virginia (2000–2001), and West Virginia (2002–2005). Reported IRs were calculated as the number of Q fever cases per million persons per year (MPY). Because of the large proportion of missing data for race and ethnicity, IR were not calculated or compared for these demographics. All analyses were performed using SAS 9.3.[34] Reported occupations were classified as agricultural occupations according to the U.S. Bureau of Labor Statistics'(BLS) Standard Occupational Classification system.[35]

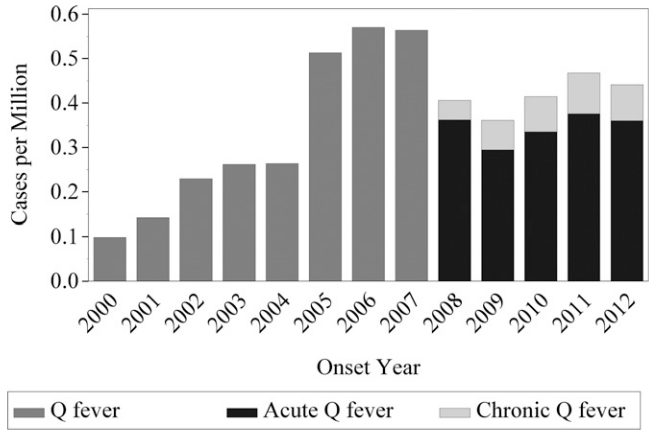

FIGURE 1. Reported incidence rate of Q fever cases per million persons per year. Cases were reported to the National Notifiable Disease Surveillance System, and the population at risk was calculated from the Census Bureau population estimates.[32,33] Cases were reported as Q fever from 2000 to 2007 and as acute or chronic Q fever for 2008–2012.

RESULTS

NNDSS. A total of 1,366 confirmed and probable cases of Q fever were reported through NNDSS with year of onset from 2000 to 2012, and the overall reported IR was 0.38 cases per MPY. Broken down by reporting category, 732 cases of

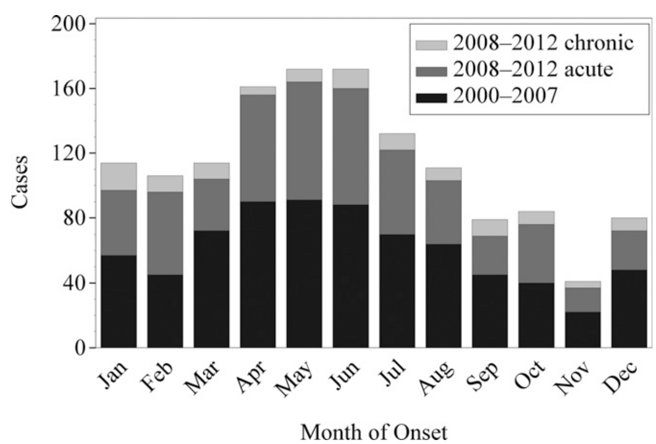

FIGURE 2. Frequency of reported cases of Q fever versus month of onset of symptoms. Cases were reported to the National Notifiable Disease Surveillance System. Cases were reported as Q fever from 2000 to 2007 and as acute or chronic Q fever for 2008–2012.

Q fever were reported from 2000 to 2007 (IR = 0.35). From 2008 to 2012, 635 cases of Q fever were reported (IR = 0.42), including 512 cases of acute Q fever (IR = 0.35) and 110 cases of chronic Q fever (IR = 0.07). The reported annual incidence rate of Q fever increased during 2000–2007 ($P < 0.0001$, Figure 1). However, the combined annual incidence rate of acute and chronic Q fever did not change during 2000–2008 ($P = 0.13$, Figure 1).

Across the 2000–2012 reporting period, the incidence of Q fever varied significantly by month ($P < 0.0001$) and peaked in May and June (Figure 2). When chronic Q fever cases were examined separately, however, the monthly incidence during

Table 1
Division and state incidence rates (IR) of Q fever in cases per million persons per year, as reported through the Nationally Notifiable Disease Surveillance System, 2000–2012*

Division state	Q fever, 2000–2007 IR (N)	Acute Q fever, 2008–2012 IR (N)	Chronic Q fever, 2008–2012 IR (N)	Q fever, 2000–2012 IR (N)
New England	0.34 (31)	0.05 (3)	0.02 (1)	0.23 (35)
Connecticut	0.04 (1)			0.02 (1)
Maine	1.53 (16)	0.15 (1)	0.15 (1)	1.05 (18)
Massachusetts	0.36 (14)	0.06 (2)		0.22 (16)
New Hampshire				
Rhode Island				
Vermont				
Mid Atlantic	0.11 (28)	0.27 (55)	0.09 (19)	0.22 (102)
New Jersey	0.09 (6)	0.41 (18)	0.07 (3)	0.24 (27)
New York	0.10 (13)	0.23 (22)	0.14 (14)	0.21 (49)
Pennsylvania	0.18 (9)	0.24 (15)	0.03 (2)	0.23 (26)
W.N. Central	0.67 (94)	0.60 (52)	0.19 (17)	0.72 (163)
Iowa				
Kansas	0.41 (9)	0.63 (9)	0.07 (1)	0.53 (19)
Minnesota	0.35 (14)	0.30 (8)		0.33 (22)
Missouri	0.96 (44)	0.40 (12)	0.10 (3)	0.78 (59)
Nebraska	1.36 (19)	0.88 (8)	1.09 (10)	1.60 (37)
North Dakota	0.39 (2)		0.30 (1)	0.35 (3)
South Dakota	0.97 (6)	3.68 (15)	0.49 (2)	2.25 (23)
E.N. Central	0.34 (109)	0.31 (73)	0.05 (12)	0.35 (194)
Illinois	0.57 (50)	0.19 (12)	0.03 (2)	0.42 (64)
Indiana	0.18 (8)	0.12 (4)	0.03 (1)	0.17 (13)
Michigan	0.15 (12)	0.34 (17)	0.08 (4)	0.25 (33)
Ohio	0.33 (23)	0.10 (6)	0.03 (2)	0.25 (31)
Wisconsin	0.36 (16)	1.20 (34)	0.11 (3)	0.73 (53)
S. Atlantic	0.21 (83)	0.17 (52)	0.02 (6)	0.20 (141)
Delaware		0.22 (1)		0.13 (1)
District of Columbia	0.66 (3)	1.69 (3)		0.95 (6)
Florida	0.16 (22)	0.10 (9)		0.13 (31)
Georgia	0.10 (7)	0.25 (12)		0.16 (19)
Maryland	0.39 (13)	0.14 (4)		0.27 (17)
North Carolina	0.32 (22)	0.38 (18)		0.34 (40)
South Carolina	0.12 (4)	0.04 (1)	0.04 (1)	0.11 (6)
Virginia	0.24 (11)	0.07 (3)	0.10 (4)	0.21 (18)
West Virginia	0.14 (1)	0.11 (1)	0.11 (1)	0.18 (3)
E.S. Central	0.52 (70)	0.10 (9)	0.07 (6)	0.38 (85)
Alabama		0.13 (3)	0.04 (1)	0.07 (4)
Kentucky	1.03 (34)	0.09 (2)	0.23 (5)	0.75 (41)
Mississippi	0.17 (3)			0.09 (3)
Tennessee	0.70 (33)	0.13 (4)		0.47 (37)
W.S. Central	0.29 (57)	0.45 (80)	0.12 (22)	0.42 (159)
Arkansas	0.18 (3)	0.96 (14)		0.54 (17)
Louisiana	0.16 (5)			0.09 (5)
Oklahoma	0.28 (4)	0.27 (4)	0.20 (3)	0.38 (11)
Texas				
Mountain	0.89 (140)	0.69 (76)	0.17 (19)	0.88 (235)
Arizona	0.29 (13)	0.37 (12)	0.12 (4)	0.38 (29)
Colorado	1.78 (65)	1.03 (26)	0.20 (5)	1.56 (96)
Idaho	0.54 (6)	0.13 (1)	0.13 (1)	0.42 (8)
Montana		3.43 (17)	0.61 (3)	1.62 (20)
Nevada	1.25 (23)	0.44 (6)		0.91 (29)
New Mexico	1.38 (21)	1.07 (11)	0.10 (1)	1.30 (33)
Utah	0.05 (1)	0.14 (2)	0.29 (4)	0.21 (7)
Wyoming	2.70 (11)	0.36 (1)	0.36 (1)	1.89 (13)
Pacific	0.32 (120)	0.50 (124)	0.03 (8)	0.40 (252)
Alaska		0.28 (1)		0.15 (1)
California	0.37 (105)	0.54 (100)	0.01 (2)	0.44 (207)
Hawaii		0.59 (4)		0.24 (4)
Oregon	0.42 (12)	0.47 (9)	0.05 (1)	0.46 (22)
Washington	0.06 (3)	0.30 (10)	0.15 (5)	0.22 (18)

*Population at risk was calculated from the Census Bureau population estimates.[32,33]

2008–2012 was not significantly different ($P = 0.25$, Figure 2). The IR of Q fever from 2000 to 2012 varied by U.S. census division, which are nine groups of geographically related states ($P < 0.0001$). The highest reported IR was from the Mountain division (IR = 0.88, 235 cases) and the West North Central division (IR = 0.72, 163 cases) (Table 1). The IR increased with age group to a maximum of 0.63 cases per MPY among 60–64 year olds, and then decreased with age group ($P < 0.001$, Figure 3).

The male-to-female ratio was 3.0:1 for cases reported during 2000–2007 ($P < 0.0001$). During 2008–2012, the male-to-female ratio was 2.9:1 for acute Q fever ($P < 0.0001$), and 3.7:1 for chronic Q fever ($P < 0.0001$, Table 2). During 2000–2012, the majority of cases (63%) were reported as white race, and 32% of cases were reported with unknown race (Table 2). Most cases (56%) were reported as non-Hispanic ethnicity, and 32% of cases were reported with unknown ethnicity (Table 2). Three hundred and thirteen cases (23%) were reported with neither race nor ethnicity.

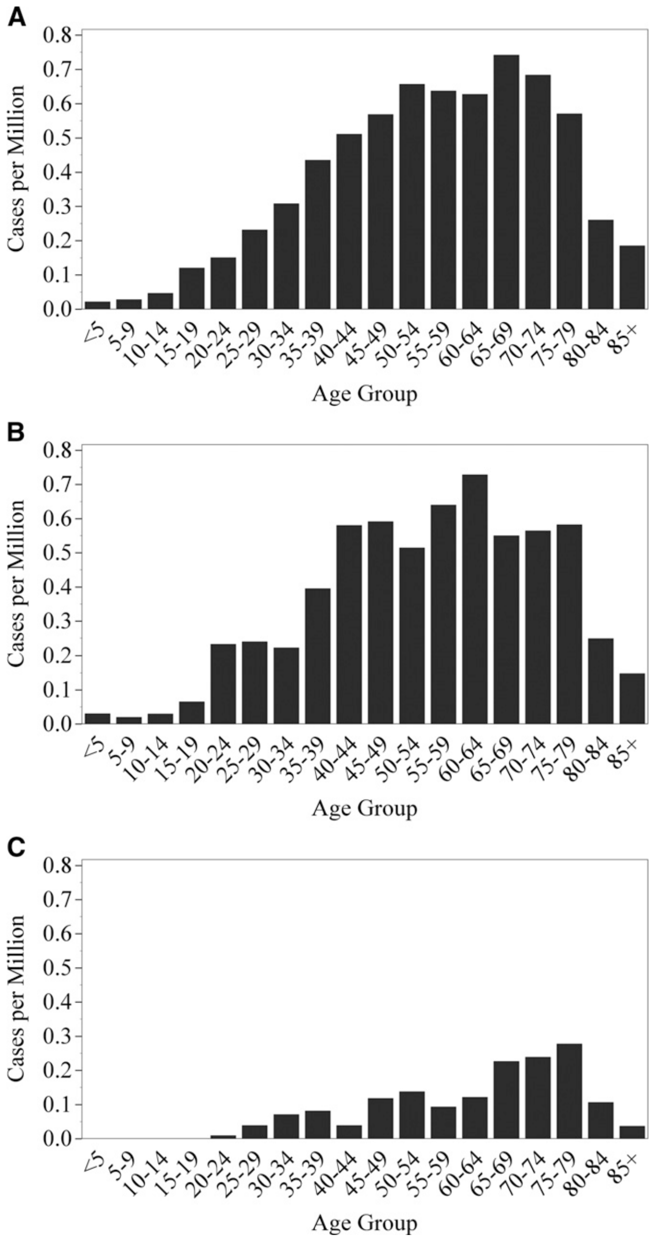

FIGURE 3. Reported incidence rate of Q fever per million persons per year by age group. (**A**) Q fever, 2000–2007. (**B**) Acute Q Fever, 2008–2012. (**C**) Chronic Q fever, 2008–2012. Cases were reported to the National Notifiable Disease Surveillance System and the population at risk was calculated from the Census Bureau population estimates.[32,33]

CRFs. A total of 709 reports of Q fever were submitted to the CDC by CRF with onset during 2000–2012, and 474 of these reports (67%) were unique cases—not duplicates of another report—that met the Council of State and Territorial Epidemiologists (CSTE) case definition. The most frequently reported symptoms among the 474 cases included fever (95%), malaise (70%), headache (60%), myalgia (50%), and cough (37%), although symptoms varied by acute versus chronic case status (Table 3). Of the 440 cases reported during 2000–2012 with information on hospitalization, 271 cases reported being hospitalized, yielding a reported hospitalization rate (HR) of 62%. The HR was not the same for Q fever during 2000–2007, acute Q fever from 2008 to 2012, and chronic Q fever during 2008–2012 ($P = 0.0001$); the HR for chronic Q fever cases during 2008–2012 was 80%. During 2000–2012, the HR increased with age ($P = 0.0003$). There was no association with HR and reported race category ($P = 0.18$). However, the HR of blacks, Asians, and American Indians grouped together (78%) was higher than the HR of whites alone (59%, $P = 0.04$). The HR among Hispanics (76%) was greater than the HR among non-Hispanics (57%, $P = 0.01$). The HR was not significantly different by gender ($P = 0.16$).

A total of nine fatal Q fever cases were reported among 428 cases with known outcome, yielding a case fatality rate (CFR) of 2.10%. An additional five fatal reports did not meet the CSTE case definition: four reports were not clinically compatible and a fifth report was submitted without sufficient laboratory evidence. Fatal cases were reported with endocarditis, pneumonia, or encephalitis (Table 4). During 2008–2012, the CFR for acute Q fever (0.5%) was different than the CFR of chronic Q fever (4.5%, $P = 0.03$). The reported CFR was similar among males and females ($P = 0.24$). The CFR increased with age group ($P = 0.047$), and fatal cases were not reported among those younger than 40. The CFR was not different among race groups ($P = 0.23$). There were no fatal cases reported among Asians or American Indians. The difference in the CFR among blacks (8.0%) compared with the CFR among whites was not statistically significant (1.8%, $P = 0.10$). The CFR among Hispanics (1.8%) was not significantly different than among non-Hispanics (2.4%, $P = 1$).

No cases of Q fever were reported among pregnant woman during 2000–2012. Pre-existing medical conditions were reported for 167 cases (35%) during the overall study period. During 2000–2007, 24 cases (14%) reported valvular heart disease or vascular graft. During 2008–2012, 4 acute cases (2.0%) reported valvular heart disease or vascular graft, and 30 chronic cases (30%) reported valvular heart disease or vascular graft.

Among all reports, the most common occupation reported for 2000–2012 was rancher (17%), followed by working in the military (8%) (Table 5). Of the 292 reports listing an occupation, 106 reports (36%) were categorized as agricultural workers as defined by the BLS. Of the 38 reported cases in the military, 36 cases (95%) reported travel to a foreign country: 32 to Iraq (84%), 2 to Afghanistan (5%), 1 to Israel (3%), 1 to Kuwait (3%), and 1 to Germany (3%). In contrast, only 9.2% of cases not in the military reported travel to a foreign country

Table 2

Age, ethnicity, race, sex, and case definition of cases of Q fever as reported through case report forms (CRFs) and through the Nationally Notifiable Disease Surveillance System (NNDSS), by reporting category, 2000–2012

	CRFs			NNDSS		
Characteristic	Q fever, 2000–2007	Acute Q fever, 2008–2012	Chronic Q fever, 2008–2012	Q fever, 2000–2007	Acute Q fever, 2008–2012	Chronic Q fever, 2008–2012
Age						
< 4	1 (0.6%)	1 (0.5%)		3 (0.4%)	3 (0.6%)	
5–9	1 (0.6%)			4 (0.5%)	2 (0.4%)	
10–19	4 (2.4%)	7 (3.4%)	1 (1%)	25 (3.4%)	10 (1.9%)	
20–29	20 (11.8%)	11 (5.4%)	8 (8%)	54 (7.4%)	50 (9.5%)	5 (4.5%)
30–39	17 (10.1%)	30 (14.6%)	12 (12%)	110 (15%)	61 (11.6%)	15 (13.6%)
40–49	41 (24.3%)	46 (22.4%)	16 (16%)	170 (23.2%)	125 (23.9%)	17 (15.5%)
50–59	32 (18.9%)	45 (22%)	19 (19%)	165 (22.5%)	118 (22.5%)	24 (21.8%)
60–69	21 (12.4%)	29 (14.1%)	22 (22%)	109 (14.9%)	94 (17.9%)	24 (21.8%)
70+	27 (16%)	16 (7.8%)	15 (15%)	88 (12%)	58 (11.1%)	25 (22.7%)
Unknown	5 (3%)	20 (9.8%)	7 (7%)	4 (0.5%)	3 (0.6%)	
Ethnicity						
Hispanic	8 (4.7%)	36 (17.6%)	16 (16%)	69 (9.4%)	78 (14.9%)	5 (4.5%)
Not Hispanic	118 (69.8%)	122 (59.5%)	63 (63%)	412 (56.3%)	294 (56.1%)	65 (59.1%)
Unknown	43 (25.4%)	47 (22.9%)	21 (21%)	251 (34.3%)	152 (29%)	40 (36.4%)
Race						
American Indian	1 (0.6%)	4 (2%)	2 (2%)	6 (0.8%)	6 (1.1%)	2 (1.8%)
Asian	2 (1.2%)	3 (1.5%)	1 (1%)			
Black	13 (7.7%)	7 (3.4%)	6 (6%)	35 (4.8%)	16 (3.1%)	1 (0.9%)
White	128 (75.7%)	158 (77.1%)	71 (71%)	459 (62.7%)	336 (64.1%)	70 (63.6%)
Unknown	25 (14.8%)	33 (16.1%)	20 (20%)	232 (31.7%)	166 (31.7%)	37 (33.6%)
Sex						
Female	45 (26.6%)	49 (23.9%)	19 (19%)	184 (25.1%)	132 (25.2%)	23 (20.9%)
Male	121 (71.6%)	154 (75.1%)	81 (81%)	545 (74.5%)	384 (73.3%)	86 (78.2%)
Unknown	3 (1.8%)	2 (1%)		3 (0.4%)	8 (1.5%)	1 (0.9%)
Classification						
Confirmed	41 (24.3%)	52 (25.4%)	48 (48%)	290 (39.6%)	153 (29.2%)	64 (58.2%)
Probable	128 (75.7%)	153 (74.6%)	52 (52%)	337 (46%)	305 (58.2%)	44 (40%)
Unknown				105 (14.3%)	66 (12.6%)	2 (1.8%)

($P < 0.0001$). The proportion of cases reporting hepatitis as a clinical syndrome was higher for those in the military (29%) than among those not in the military (11%, P = 0.003); whereas, the proportion of cases reporting pneumonia was not significantly different between those in the military (21%) and those not in the military (18%, P = 0.67).

A total of 314 reported cases (66%) noted exposure to any animal, and 185 reported cases (39%) had exposure to cattle,

Table 3

Frequency of symptoms among cases of Q fever as reported through case report forms, by reporting category, 2000–2012*

Symptom	Q fever, 2000–2007	Acute Q fever, 2008–2012	Chronic Q fever, 2008–2012	Q fever, 2000–2012
Fever	154 (91.1%)	205 (100%)	70 (70%)	429 (94.9%)
Malaise	120 (71%)	142 (69.3%)	55 (55%)	317 (70.1%)
Headache	90 (53.3%)	147 (71.7%)	36 (36%)	273 (60.4%)
Myalgia	83 (49.1%)	105 (51.2%)	39 (39%)	227 (50.2%)
Cough	52 (30.8%)	75 (36.6%)	38 (38%)	165 (36.5%)
Chills	26 (15.4%)	72 (35.1%)	14 (14%)	112 (24.8%)
Pneumonia	25 (14.8%)	25 (12.2%)	38 (38%)	88 (19.5%)
Endocarditis	34 (20.1%)	5 (2.4%)	35 (35%)	74 (16.4%)
Sweats	18 (10.7%)	46 (22.4%)	10 (10%)	74 (16.4%)
Retro orbital pain	11 (6.5%)	41 (20%)	14 (14%)	66 (14.6%)
Rash	26 (15.4%)	22 (10.7%)	11 (11%)	59 (13.1%)
Hepatitis	15 (8.9%)	18 (8.8%)	24 (24%)	57 (12.6%)
Anorexia	18 (10.7%)	25 (12.2%)	11 (11%)	54 (11.9%)
Fatigue	3 (1.8%)	23 (11.2%)	10 (10%)	36 (8%)
Nausea	5 (3%)	18 (8.8%)	7 (7%)	30 (6.6%)
Hepatomegaly	8 (4.7%)	15 (7.3%)	4 (4%)	27 (6%)
Weakness	10 (5.9%)	14 (6.8%)	2 (2%)	26 (5.8%)
Vomiting	3 (1.8%)	13 (6.3%)	6 (6%)	22 (4.9%)
Splenomegaly	9 (5.3%)	8 (3.9%)	4 (4%)	21 (4.6%)
Arthralgia	8 (4.7%)	9 (4.4%)	3 (3%)	20 (4.4%)
Diarrhea	1 (0.6%)	12 (5.9%)	6 (6%)	19 (4.2%)
Elevated liver enzymes	4 (2.4%)	14 (6.8%)		18 (4%)
Shortness of breath	1 (0.6%)	9 (4.4%)	5 (5%)	15 (3.3%)
Abdominal pain	4 (2.4%)	4 (2%)	5 (5%)	13 (2.9%)
Altered mental status		7 (3.4%)	4 (4%)	11 (2.4%)

*Only categories with at least 11 reports are presented here.

Table 4
Demographics, whether hospitalized, and clinical syndrome for the nine fatal cases of Q fever reported through case report forms during 2000–2012

Age	Sex	Hospitalized	Endocarditis	Pneumonia	Hepatitis	Encephalitis
40–49	Male	+	+			
60–69	Female	+		+		
70+	Female	+	+			
70+	Female		+			
49–49	Male	+			+	
50–59	Male	+	+			
70+	Male	+		+		
50–59	Female	+		+		+
50–59	Male	+	+			

goats, or sheep. The most commonly reported animal contacts were cattle (25%), cats (22%), dogs (21%), goats (20%), and sheep (17%) during 2000–2012 (Table 6); 101 cases (22%) reported exposure to birthing animals. Thirty-eight cases (8.4%) reported exposure to unpasteurized milk, with 26 cases reporting the source: 16 reported exposure to cow's milk, 6 to goat's milk, and 4 were exposed to both cow and goat's milk. The reported prevalence of drinking raw milk among those reporting work in a dairy (53%) was significantly greater than the prevalence among those not reporting work in a dairy (6.5%, $P < 0.0001$). The prevalence of drinking raw milk was significantly greater among those reporting exposure to cattle (15%) than those not (5.8%, $P = 0.002$). Similarly, the reported prevalence of drinking raw milk among those working in agriculture (15%) was greater than those not (6%, $P = 0.003$). Among reported cases with exposure to unpasteurized milk, 4 cases (11%) reported no other risk factors for Q fever.

Because the clinical, epidemiological, and laboratory data required to apply the case definition are reported through the CRFs, whether a report met the case definition as confirmed or probable was known for all reports. During 2000–2007, 128 cases (76%) reported through CRF met the probable case definition, and 41 cases (24%) met the confirmed case definition. Among confirmed cases reported during this time period, a seroconversion was documented in 39 cases (95%); 3 cases (7.3%) were PCR positive, 2 cases (4.9%) were positive by IHC, and *C. burnetii* was isolated by culture in 1 case (2.4%). During 2008–2012, 153 acute cases (75%) met the probable case definition. Fifty-two acute cases (25%) met the confirmed case definition: a seroconversion was documented in 51 acute cases (98%), and 1 acute case (2%) was PCR positive. Fifty-two chronic cases (52%) met the probable case definition, and 48 chronic cases (48%) were laboratory confirmed. Of the cases reported during 2000–2007, 3 cases (1.8%) did not meet the new case definition for either chronic or acute Q fever.

DISCUSSION

The reported incidence of Q fever remains low in the United States compared with most nationally notifiable diseases, at 0.38 cases per MPY for 2000–2012. Historically, Q fever has been associated with occupational exposure to livestock, especially exposure to parturient animals.[23] In this study, 36% of employed cases reported an occupation related to agriculture, and 22% of cases reported exposure to birthing animals. However, < 0.5% of employed people in the United States work in agriculture.[36] The higher reported incidence rates in states from the Mountain division and the West North Central division may reflect increased exposure risk in these regions where livestock are more prevalent.[37,38] The observed seasonality of reported Q fever cases (especially acute Q fever), which peaks during May and June (Figure 2), corresponds with expected calving, lambing, and kidding seasons in the United States.[39–42] Although many cases of acute Q fever in the United States are likely attributed to direct animal exposure, windborne transmission of *C. burnetii* is also a likely mode of exposure, as one-third of cases reported no exposure to any animal. *Coxiella burnetii* is easily spread long distances by wind, and a 1–2 mile proximity to a livestock reservoir may be sufficient exposure for infection.[3,4,8] The largest documented epidemic of Q fever was primarily caused by airborne transmission of *C. burnetii* from infected goat farms to more highly populated areas in the Netherlands from 2007 through 2010.[43] A similar increase in incidence of Q fever during spring, attributed to windborne transmission following lambing season,

Table 5
Occupation and occupational setting of cases of Q fever as reported through case report forms, by reporting category, 2000–2012*

Occupation or occupational setting	Q fever, 2000–2007	Acute Q fever, 2008–2012	Chronic Q fever, 2008–2012	Q fever, 2000–2012
Unknown	39 (23.1%)	74 (36.1%)	40 (40%)	153 (33.8%)
Rancher	32 (18.9%)	39 (19%)	9 (9%)	80 (17.7%)
Military	15 (8.9%)	17 (8.3%)	6 (6%)	38 (8.4%)
Retired	10 (5.9%)	15 (7.3%)	13 (13%)	38 (8.4%)
Farm	7 (4.1%)	11 (5.4%)	3 (3%)	21 (4.6%)
Construction	5 (3%)	7 (3.4%)	5 (5%)	17 (3.8%)
Dairy	2 (1.2%)	10 (4.9%)	3 (3%)	15 (3.3%)
Office	8 (4.7%)	3 (1.5%)	2 (2%)	13 (2.9%)
Unemployed	6 (3.6%)	3 (1.5%)	3 (3%)	12 (2.7%)
Disabled	1 (0.6%)	5 (2.4%)	4 (4%)	10 (2.2%)
Driver	1 (0.6%)	4 (2%)	3 (3%)	8 (1.8%)
Student	4 (2.4%)	2 (1%)	1 (1%)	7 (1.5%)
Education	4 (2.4%)	1 (0.5%)		5 (1.1%)
Retail	3 (1.8%)	2 (1%)		5 (1.1%)
Veterinarian	2 (1.2%)	3 (1.5%)		5 (1.1%)
Custodian	3 (1.8%)		1 (1%)	4 (0.9%)
Laboratorian	2 (1.2%)		2 (2%)	4 (0.9%)
Nurse	2 (1.2%)	1 (0.5%)	1 (1%)	4 (0.9%)
Slaughterhouse		3 (1.5%)	1 (1%)	4 (0.9%)

*Only categories with at least four reports are presented here.

TABLE 6
Animal contact among cases of Q fever reported through case report forms by reporting category, 2000–2012*

Animal	Q fever, 2000–2007	Acute Q fever, 2008–2012	Chronic Q fever, 2008–2012	Q fever, 2000–2012
Cattle	33 (19.5%)	61 (29.8%)	19 (19%)	113 (25.0%)
Cats	39 (23.1%)	45 (22%)	17 (17%)	101 (22.3%)
Dogs	30 (17.8%)	45 (22%)	20 (20%)	95 (21.0%)
Goats	28 (16.6%)	50 (24.4%)	14 (14%)	92 (20.4%)
Sheep	18 (10.7%)	42 (20.5%)	17 (17%)	77 (17.0%)
Equine	14 (8.3%)	24 (11.7%)	4 (4%)	42 (9.3%)
Birds	12 (7.1%)	14 (6.8%)	3 (3%)	29 (6.4%)
Rabbits	10 (5.9%)	10 (4.9%)	4 (4%)	24 (5.3%)
Rodents	5 (3%)	7 (3.4%)	2 (2%)	14 (3.1%)
Pigs	3 (1.8%)	7 (3.4%)	1 (1%)	11 (2.4%)
Ticks	4 (2.4%)	5 (2.4%)	1 (1%)	10 (2.2%)
Deer	4 (2.4%)	2 (1%)	3 (3%)	9 (2.0%)

*Only categories with at least four reports are presented here.

has also been documented in France.[4] Clinicians should consider Q fever when appropriate despite an absence of direct exposure to livestock, including cases of community acquired pneumonia and other flu-like illnesses, especially when a potential risk factor for chronic Q fever is present.

In our data, 8% of cases reported a military occupation, yet military personnel account for only about 1% of the total United States population.[44] Eighty-four percent of the cases of Q fever among military personnel had traveled to Iraq; whereas, foreign travel was only 9% in other reported cases. In our data, military personnel were three times as likely as civilians to have reported hepatitis; yet, pneumonia was noted at similar proportions among military and civilian occupations. Differences in mode of transmission or variations in geographic strain virulence may be responsible for the higher rate of hepatitis observed among military service members.[22,45,46]

A higher proportion of reported cases were hospitalized among Hispanics than non-Hispanics. Furthermore, cases among blacks, Asians, and American Indians together were more likely to be hospitalized versus whites alone. This finding may represent an artifact of surveillance where cases of less serious disease among whites and non-Hispanics are more likely to receive laboratory diagnostics.

The prevalence of consuming raw milk among reported cases of Q fever from 2000 to 2012 was 8.4%, well above the national estimate of 3.0% for the prevalence of consuming raw milk.[47] This suggests that consuming raw milk may be an important risk for Q fever in the United States, and four of the cases reported through CRFs had no other known risk factor for Q fever. *Coxiella burnetii* is frequently detected in dairy products by PCR testing, and consuming unpasteurized dairy products may increase the risk of Q fever.[13,48–52] However, the strong association between drinking raw milk with working on a dairy, with working in agriculture, and with exposure to cattle indicates exposure to livestock and employment in an agricultural setting potentially confounds the association between raw milk consumption and Q fever in the general population.

These results are based upon passive surveillance at the national level, and the individual practices of state and local public health departments, laboratories, and clinics are diverse. Because infection with *C. burnetii* can be asymptomatic, mild, or easily mistaken for more common etiologies, reported cases of Q fever likely represent only a fraction of actual infections, and less severe cases and cases among people with inadequate access to healthcare are unlikely to be captured by passive reporting systems. Therefore, Q fever cases reported through passive surveillance often reflect a more severe clinical presentation, which is indicated by the high overall hospitalization rate of 62% and the 2.0% case fatality rate reported here. Seroprevalence of Q fever in the United States is estimated to be 3.1%.[53] Not all seropositive people have a history of Q fever, some may simply have exposure not leading to infection or have asymptomatic infections. The seroprevalence dwarves the reported incidence rate in the United States, suggesting the possibility of underreporting through national surveillance. In our concurrent report, we estimate that for every case of Q fever reported through CRFs there are at least 13 cases that go unreported.[54] The large proportion of missing data for race and ethnicity among reports from both surveillance systems precludes more meaningful comparison of race and ethnic groups. Similarly, the number of reported fatal cases is small, and the actual association between severe and fatal disease with sex, race, and ethnicity may be different than what has been reported. Despite these limitations, the data presented herein represent the most comprehensive summary for the trends in Q fever in the United States during 2000–2012.

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