Atypical Manifestations of Cat-Scratch Disease, United States, 2005–2014

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Learning Objectives

Upon completion of this activity, participants will be able to:

- Assess the epidemiology of atypical CSD in the United States, based on an analysis of data from the 2005 to 2014 MarketScan national health insurance claims databases
- Describe the clinical features of atypical CSD in the United States, based on an analysis of data from the 2005 to 2014 MarketScan national health insurance claims databases
- Describe the clinical and public health implications of the epidemiology and clinical features of atypical CSD in the United States, based on an analysis of data from the 2005 to 2014 MarketScan national health insurance claims databases

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Atypical manifestations that can be severe and difficult to diagnosis develop in 5%–20% of patients with cat-scratch disease. To clarify the epidemiology of atypical cat-scratch disease in the United States, we analyzed data from the 2005–2014 MarketScan national health insurance claims databases by using the International Classification of Diseases, 9th Revision, Clinical Modification, codes for cat-scratch disease and selected atypical manifestations: retinitis/neuroretinitis, conjunctivitis, neuritis, encephalitis, hepatosplenic disease, osteomyelitis, erythema nodosum, and endocarditis. Atypical cat-scratch disease accounted for 1.5% of all cases, resulting in an average annual incidence of 0.7 cases/100,000 population. Atypical cat-scratch disease was associated with increased risk for hospitalization (risk ratios 8.77, 95% CI 6.56–11.72) and occurred most often in female patients 10–14 years of age. Ocular (48.7%), hepatosplenic (24.6%), and neurologic (13.8%) manifestations were most common among patients. A more comprehensive understanding of atypical cat-scratch disease can improve patient diagnosis and potentially elucidate pathophysiology of the disease.

Cat-scratch disease, a zoonotic bacterial infection, occurs worldwide and is caused by *Bartonella henselae*, a fastidious, intracellular gram-negative bacillus (*1*). Cats are the major reservoir of *B. henselae* and are infected by *Ctenocephalides felis* cat fleas. Although most cats infected with *B. henselae* are asymptomatic, signs such as fever and myocarditis might develop in some cats (*2*,*3*). Humans usually become infected through the scratches or bites of infected cats. *B. henselae* has also been shown to infect dogs (*4*), in some cases resulting in canine endocarditis (*5*–*7*). Although some human cases of cat-scratch disease have been linked to canine–human transmission (*8*–*12*), further research is needed to clarify the public health significance of *B. henselae* infection in dogs.

The true burden of cat-scratch disease in the United States is unknown because it is not a reportable condition; however, efforts have been made to estimate its incidence in the United States. In 1993, an analysis of hospital discharge data estimated a nationwide incidence of hospitalized cases of 0.77–0.86 cases/100,000 population annually (*13*). A subsequent study that examined a database of national health insurance claims during 2005–2013 found that incidence of cat-scratch disease in the United States was highest in southern states (6.4 cases/100,000 population) and in children 5–9 years of age (9.4 cases/100,000 population) (*14*).

Cat-scratch disease typically manifests as fever and an erythematous papule at the site of the cat scratch or bite, followed by lymphadenopathy in the regional lymph nodes that drain the area of inoculation (*15*). The papule usually appears 3–10 days after inoculation and can persist for several weeks, with regional lymphadenopathy developing 1–3 weeks postinoculation (*1*). From 80% to 95% of cases of cat-scratch disease are consistent with this typical presentation, and the remainder of cases manifest as atypical and more severe symptoms (*16*,*17*).

Atypical manifestations of cat-scratch disease can involve the eyes, nervous system, heart, liver, spleen, skin, or musculoskeletal system and might result in major illness (*1*,*15*). When cat-scratch disease involves the eye, the anterior compartment might be affected by Parinaud oculoglandular syndrome, and the posterior compartment might be affected by retinitis, retinochoroiditis, optic neuritis, uveitis, and vitritis (*18*–*20*). Nervous system involvement most commonly manifests as encephalopathy, but seizures, nerve palsies, neuritis, myelitis, and cerebellar ataxia have also been reported (*21*,*22*).

Endocarditis is more often seen in adults with cat-scratch disease than in children, although preexisting valvular disease puts children at increased risk for this complication (*1*). *Bartonella* infection can also cause abdominal pain and microabscesses in the liver and spleen (*23*), and in immunocompromised hosts can result in bacillary peliosis hepatis (*24*). In addition to the classic erythematous papule at the site of inoculation, erythema nodosum and bacillary angiomatosis are reported dermatologic manifestations of atypical infection (*25*,*26*). Osteolytic lesions, osteomyelitis, and arthritis have also been associated with cat-scratch disease (*16*,*24*,*26*). A study in 1998 found cat-scratch disease to be the third leading cause of prolonged fever of unknown origin in children, and a history of cat exposure was frequently absent (*27*).

Atypical manifestations of *B. henselae* infection can be severe, difficult to diagnose, and lead to lasting impairment. It is unclear why certain patients develop atypical cat-scratch disease, and little is known about its epidemiology. Improved understanding of atypical cat-scratch disease could lead to better recognition of cases by clinicians and inform efforts to understand the pathophysiology of this disease. The purpose of this study was to better characterize the rare and serious complications of this nonreportable zoonotic infection by using nationwide insurance claims data.

Methods

To identify potential cases of atypical cat-scratch disease, we conducted a retrospective analysis of

persons enrolled in the Truven Health MarketScan Commercial Claims and Encounters Database (Truven Health Analytics, https://www.ibm.com) during 2005–2014. The MarketScan Commercial Claims and Encounters Database includes persons <65 years of age covered by select employer-sponsored health insurance plans in all 50 states and contains administrative claims data on outpatient visits, inpatient admissions, and emergency department visits. Demographically, the MarketScan population generally mirrors the US population, with a slight overrepresentation of persons 50–59 years of age and a slight underrepresentation of persons 20–29 years of age (*28*).

Billing codes from outpatient, inpatient, and emergency department visits are assigned by either a clinician or billing specialist according to the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM), and procedures are captured as either ICD-9-CM codes, Current Procedure Terminology codes, or Healthcare Common Procedure Coding System codes. Because the International Classification of Diseases, 10th Revision, Clinical Modification, was not officially adopted in the United States until 2015, those codes were not included.

We identified cat-scratch disease cases by extracting all enrollee visit records during the study period with an ICD-9-CM code for cat-scratch disease (078.3). The first instance of a 078.3 diagnosis code in a patient record was considered the index event. Atypical manifestations of interest were selected for analysis if they had recorded precedent in the literature as a complication of cat-scratch disease and distinct, clearly discernable ICD-9-CM codes associated with the specific manifestation. Based on these criteria, the known complications of cat-scratch diseases included for analysis were endocarditis, osteomyelitis, erythema nodosum, conjunctivitis, retinitis/neuroretinitis, encephalitis, neuritis, and hepatosplenic disease.We included ICD-9-CM codes associated with optic neuritis in the retinitis/neuroretinitis category. Encounters with an ICD-9-CM code for cat-scratch disease and an accompanying diagnostic code to indicate the anatomic location of a wound or inoculation site for *B. henselae* were also flagged for analysis and were categorized as either head or neck region, arm or shoulder region, leg or hip region, or torso region. We compiled a detailed list of all ICD-9-CM codes used to identify atypical manifestations of cat-scratch disease (Appendix Table, https://wwwnc.cdc.gov/EID/article/26/7/20-0034-App1.pdf).

We extracted insurance billing records of enrollees with ICD-9-CM codes for cat-scratch disease and selected manifestations at either the same encounter or within a 30-day window of one another. These records were evaluated along with previous and subsequent records by 2 independent reviewers (R.J.M. and C.A.N.) to ensure that the clinical picture was consistent with the coded atypical manifestation based on diagnosis codes, procedure codes, and provider types. If plausible alternative causes of the selected manifestation or likely coding errors were identified, we did not include the enrollee record as an atypical case. In cases of discordance, a third reviewer (Paul Mead) determined final categorization based on record review.

We included persons with an ICD-9-CM code for cat-scratch disease but without accompanying atypical manifestation as typical cases for comparison. Residence in a rural area was assigned if an enrollee did not reside in a metropolitan statistical area, as designated by the US Office of Management and Budget. Because previous research has identified increases in cat-scratch disease in late summer, fall, and January (*13*,*14*,*29*), we categorized month of onset as either late summer and fall, January, or all other months for analysis.

We performed descriptive and comparative statistical analyses by using JMP version 13.2.1 (https://www.jmp.com) and SAS version 9.3 (https://www.sas.com). We used Pearson χ^2 tests or Fisher exact tests for comparisons of categorical variables. To compare the conditional probability of having atypical cat-scratch disease across strata of potential variables of interest (e.g., sex, age category), we calculated risk ratios (RRs) and associated 95% CIs. Human subjects review at the Centers for Disease Control and Prevention determined that institutional review board approval was not required for this study.

Results

Study Population and Incidence

During 2005–2014, the MarketScan database contained a median of 44,488,485 (range 16,159,068–53,131,420) enrollees each year. Of 14,824 cat-scratch disease cases identified from MarketScan during this period, 224 (1.5%) cases were classified as atypical (Table 1). The average annual incidence of atypical cat-scratch disease diagnoses during the study period was 0.7 cases/100,000 population.

Atypical cat-scratch disease was most common among adults 15–49 years of age (47.3%), and patients with atypical cat-scratch disease were more likely to be hospitalized than those with typical manifestations ($p<0.0001$).

Table 1. Characteristics of patients with cat-scratch disease and risk factors for development of atypical cat-scratch disease, United States, 2005–2014

Characteristic	Typical disease, no. (%), n = 14,600	Atypical disease, no. (%), n = 224	Risk ratio (95% CI)*
Sex			
M	5,583 (38.2)	94 (42.0)	1.17 (0.90–1.52)
F	9,017 (61.8)	130 (58.0)	Referent
Age, y			
Child ≤14	4,678 (32.0)	81 (36.2)	1.20 (0.91–1.57)
Adult, 15–49	6,421 (44.0)	106 (47.3)	Referent
Adult, 50–64	3,501 (24.0)	37 (16.5)	0.63 (0.44–0.90)
Month of onset			
Late summer and fall†	5,470 (37.5)	93 (41.5)	1.18 (0.90–1.56)
January	1,490 (10.2)	22 (9.8)	1.03 (0.65–1.64)
All other months‡	7,640 (52.3)	109 (48.7)	Referent
Hospitalized	487 (3.3)	56 (25)	8.77 (6.56–11.72)
Residence in southern state	7,732 (53.0)	129 (57.6)	1.20 (0.93–1.57)
Residence in rural area	3,235 (22.1)	51 (22.8)	1.06 (0.78–1.45)

*Outcome for risk ratio calculations was development of atypical cat-scratch disease.
†August, September, October, and November.
‡February, March, April, May, June, July, and December.

Distribution by Age and Sex

Children ≤14 years of age accounted for 36.2% of atypical cat-scratch disease diagnoses overall; 26 cases (11.4%) were in female patients 10–14 years of age (Figure 1). Among female patients 10–14 years of age, 16 patients (61.5%) had ocular manifestations (13 retinitis/neuroretinitis and 3 conjunctivitis), and 6 patients (23.1%) had hepatosplenic disease.

Nearly half of all patients with atypical cat-scratch disease were younger adults (15–49 years of age). When we compared older adults with younger adults, older adults (50–64 years of age) had a decreased risk for having atypical cat-scratch disease (RR 0.63, 95% CI 0.44–0.90) (Table 1).

Seasonality

Atypical cat-scratch disease diagnoses increased from August through March, and diagnoses were concentrated during August–October (33.5% of diagnoses) and January–March (29.5% of diagnoses) (Figure 2), although neither diagnosis in late summer and fall or diagnosis in January were found to be risk factors for development of atypical cat-scratch disease (Table 1). Trends in atypical cat-scratch disease diagnoses were similar to trends in typical cat-scratch disease diagnoses. However, typical cat-scratch disease had less defined peak periods, and diagnoses decreased sharply after January.

Geographic Distribution and Residence in Rural Area

Most (57.6%) cases of atypical cat-scratch disease occurred in the southern region of the United States (57.6%), followed by the midwest (16.5%) and northeast (12.5%) regions (Figure 3). The geographic distribution of atypical cases did not differ significantly from cases of typical cat-scratch disease.

Residence in a rural area was not a risk factor for development of atypical cat-scratch disease (RR 1.06, 95% CI 0.78–1.45). Also, the proportion of patients with atypical cat-scratch disease living in a rural area did not differ from the proportion of patients with typical cat-scratch disease living in a rural area (p = 0.70).

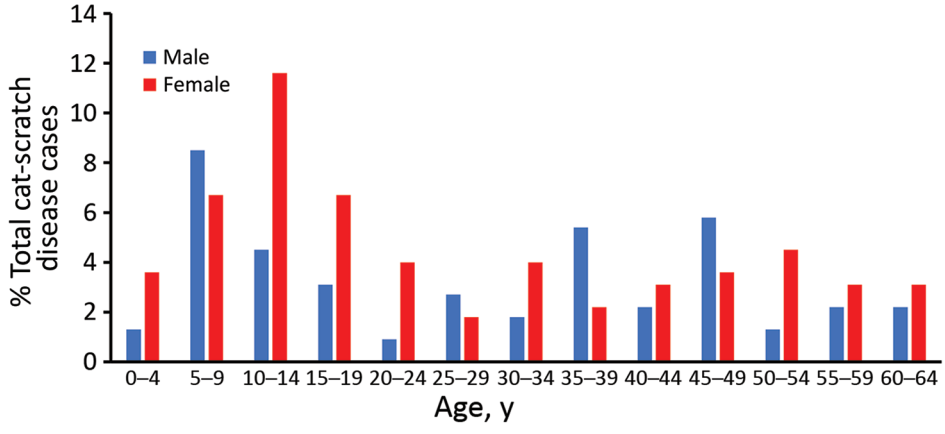

Figure 1. Age and sex distribution of patients with atypical cat-scratch disease, United States, 2005–2014.

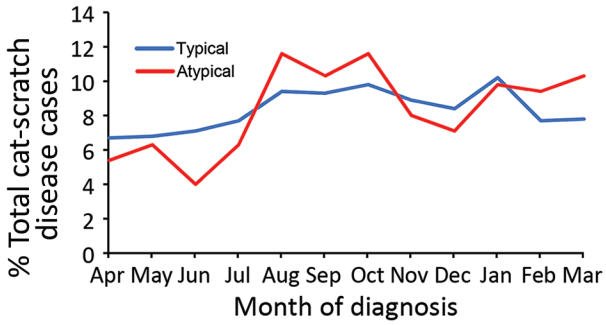

Figure 2. Seasonal variation of atypical and typical cat-scratch disease by month of diagnosis, United States, 2005–2014.

Atypical Manifestations by Type

Among 224 patients with atypical cat-scratch disease, 109 (48.7%) had ocular manifestations (retinitis/neuroretinitis or conjunctivitis), 55 (24.6%) had hepatosplenic disease, and 31 (13.8%) had neurologic manifestations (neuritis or encephalitis). The remaining 33 (14.7%) case-patients had osteomyelitis, erythema nodosum, or endocarditis (Table 2). Among patients with ocular manifestations, 82.6% had retinitis/neuroretinitis; most (64.5%) patients with neurologic manifestations had encephalitis. Three (1.3%) patients with atypical cat-scratch disease had >1 manifestation: 1 patient with osteomyelitis and hepatosplenic disease; 1 patient with endocarditis and hepatosplenic disease; and 1 patient with osteomyelitis, encephalitis, and hepatosplenic disease.

Children ≤14 years of age were at increased risk for hepatosplenic disease (RR 1.76, 95% CI 1.04–2.99) and osteomyelitis (RR 3.81, 95% CI 1.28–11.37) compared with persons ≥15 years of age. Older adults (50–64 years of age) were less likely to show development of ocular manifestations (retinitis/neuroretinitis and conjunctivitis) than younger adults (15–49 years of age) (RR 0.49, 95% CI 0.28–0.85).

Among persons with ocular (retinitis/neuroretinitis and conjunctivitis) manifestations, most diagnoses were made during August–October (31.2%) and January–March (35.8%). Among persons with neurologic (neuritis and encephalitis) manifestations, diagnoses were concentrated during October (22.6%). We observed no notable trends in seasonality of diagnoses for other manifestations of atypical cat-scratch disease (Figure 4). We also observed no differences in geographic distribution or rurality by manifestation of atypical cat-scratch disease.

Hospitalization of Atypical Case-Patients

Patients with atypical cat-scratch disease were more likely to be hospitalized than patients with typical cat-scratch disease (RR 8.77, 95% CI 6.56–11.72) (Table 1). Among patients with atypical cat-scratch disease, children ≤14 years of age accounted for 60.7% of hospitalizations and had an increased risk for hospitalization compared with adults 15–49 years of age (RR 2.34, 95% CI 1.44–3.79). A total of 57.1% of the hospitalizations occurred during August–November, and we found an overall increased risk for hospitalization during this period when compared with all other months, except for January (RR 1.88, 95% CI 1.15–3.05) (Table 3).

Increased risks of hospitalization were found for neurologic manifestations (neuritis and encephalitis) (RR 1.88, 95% CI 1.15–3.08), hepatosplenic disease (RR 2.30, 95% CI 1.49–3.55), and osteomyelitis (RR 2.13, 95% CI 1.20–3.82). Ocular manifestations (retinitis/neuroretinitis and conjunctivitis) were associated with decreased risk for hospitalization (RR 0.23, 95% CI 0.12–0.43).

Location of Wound

Information on wound location was available for only 10 (4.5%) patients with atypical cat-scratch disease. Among these persons, 2 with conjunctivitis, 1 with encephalitis, and 2 with hepatosplenic disease had a wound on the head or neck; 1 with osteomyelitis and 3 with hepatosplenic manifestations had a wound on the arm or shoulder; 1 with endocarditis had a wound on the leg or hip;

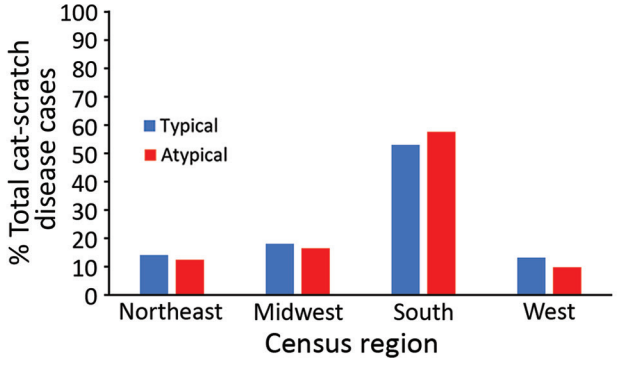

Figure 3. Proportions of typical and atypical cat-scratch disease by US Census region, United States, 2005–2014. Northeast: Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont, New Jersey, New York, Pennsylvania. Midwest: Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, South Dakota, Ohio, Wisconsin. South: Arkansas, Delaware, Florida, Georgia, Louisiana, Maryland, North Carolina, Oklahoma, South Carolina, Texas, Virginia, West Virginia, Alabama, Hawaii, Kentucky, Mississippi, Oregon, Tennessee. West: Alaska, Arizona, California, Colorado, Idaho, Montana, Nevada, New Mexico, Utah, Washington, Wyoming, Puerto Rico, Virgin Islands.

Table 2. Demographic characteristics for patients by manifestation of atypical cat-scratch disease, United States, 2005–2014

Characteristic	No. (%)	Sex, no. (%)		Age category, y, no. (%)			Hospitalized, no. (%)
		M	F	0–14	15–49	50–64	
Atypical disease	224*	94 (42.0)	130 (58.0)	81 (36.2)	106 (47.3)	37 (16.5)	56 (25.0)
Ocular disease	109 (48.7)	46 (48.9)	63 (48.5)	33 (40.7)	60 (56.6)	16 (43.2)	10 (17.9)
Retinitis/neuroretinitis	90 (40.2)	36 (38.3)	54 (41.5)	23 (28.4)	53 (50.0)	14 (37.8)	8 (14.3)
Conjunctivitis	19 (8.5)	10 (10.6)	9 (6.9)	10 (12.3)	7 (6.6)	2(5.4)	2 (3.6)
Hepatosplenic disease	55 (24.6)	24 (25.5)	31 (23.8)	25 (30.9)	21 (19.8)	9 (24.3)	24 (42.9)
Neurologic disease	31 (13.8)	13 (13.8)	18 (13.8)	12 (14.8)	13 (12.3)	6 (16.2)	13 (23.2)
Encephalitis	20 (8.9)	12 (12.8)	8 (6.2)	12 (14.8)	8 (7.5)	0 (0)	13 (23.2)
Neuritis	11 (4.9)	1 (1.1)	10 (7.7)	0 (0)	5 (4.7)	6 (16.2)	0 (0)
Osteomyelitis	14 (6.3)	6 (6.4)	8 (6.2)	9 (11.1)	4 (3.8)	1 (2.7)	7 (12.5)
Erythema nodosum	11 (4.9)	2 (2.1)	9 (6.9)	4 (4.9)	5 (4.7)	2 (5.4)	4 (7.1)
Endocarditis	8 (3.6)	4 (4.3)	4 (3.1)	1 (1.2)	4 (3.8)	3 (8.1)	2 (3.6)

*A total of 228 manifestations of atypical cat-scratch disease were seen among 224 patients. Three patients had >1 manifestation; 1 patient had osteomyelitis and hepatosplenic disease;1 patient had endocarditis and hepatosplenic disease; and 1 patient had osteomyelitis, encephalitis, and hepatosplenic disease.

and 1 with endocarditis had a wound on an unspecified limb.

Discussion

Using US nationwide insurance claims data, we identified and characterized 224 atypical cases of cat-scratch disease during 2005–2014 and estimated an average annual incidence of 0.7 cases/100,000 population. Nearly half of all atypical cat-scratch disease cases had ocular manifestations, most of which were retinitis/neuroretinitis. Atypical cat-scratch disease was most prevalent among female patients 10–14 years of age, who most commonly had ocular manifestations.

Trends in hospitalizations of patients with cat-scratch disease highlight the severity of atypical cat-scratch disease compared with typical cat-scratch disease. Atypical cat-scratch disease appears to be particularly severe among children ≤14 years of age, who had an increased risk for hospitalization. Adults 50–64 years of age had the lowest risk for development of atypical cat-scratch disease and specifically ocular manifestations. Reasons that older adults might have complications associated with cat-scratch disease less often than other age groups are unclear and require further study.

Severity of cat-scratch disease in children has been previously documented. In a study conducted by Reynolds et al., ≈25% of hospitalizations of children for cat-scratch disease were caused by complications associated with atypical cat-scratch disease; neurologic and hepatosplenic complications were most common (*30*). Although children in our study were also particularly at risk for hepatosplenic disease, neurologic and hepatosplenic complications were associated with increased risk for hospitalization in our overall study population, indicating that these manifestations are particularly severe for all age groups. Encephalitis was the most common neurologic manifestation in our population, which was also consistent with findings of Reynolds et al., in which most hospitalizations of children for neurologic complications of cat-scratch disease were caused by encephalitis or encephalopathy (*30*). Thus, physicians should consider cat-scratch disease in patients who have encephalitis or new onset hepatosplenic abnormalities, especially children.

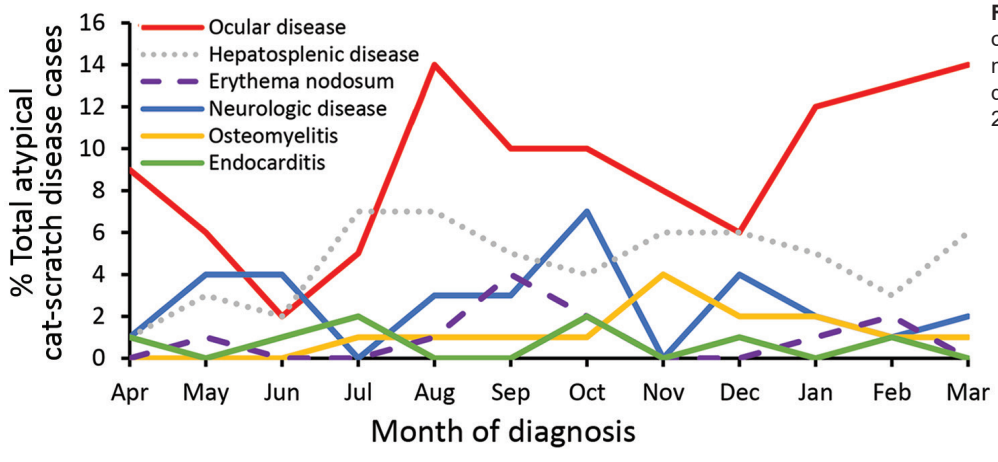

Figure 4. Seasonal variation of atypical cat-scratch disease manifestations by month of diagnosis, United States, 2005–2014.

Table 3. Demographic characteristics for patients hospitalized with atypical cat-scratch disease and associated risk factors for hospitalization, United States, 2005–2014

Characteristic	Hospitalized, no. (%), n = 56	Not hospitalized, no. (%), n = 168	Risk ratio (95% CI)
Sex			
M	26 (46.4)	68 (40.5)	1.19 (0.76–1.89)
F	30 (53.6)	100 (59.5)	Referent
Age, y			
Child ≤14	34 (60.7)	47 (28.0)	2.34 (1.44–3.79)
Younger adult, 15–49	19 (33.9)	87 (51.8)	Referent
Older adult, 50–64	3 (5.4)	34 (20.2)	0.45 (0.14–1.44)
Month of onset			
Late summer and fall*	32 (57.1)	61 (36.3)	1.88 (1.15–3.05)
January	4 (7.1)	18 (10.7)	0.99 (0.38–2.62)
All other months†	20 (35.7)	89 (53.0)	Referent
Residence in southern state	36 (64.3)	93 (55.4)	1.33 (0.82–2.14)
Residence in rural area	11 (19.6)	40 (23.8)	1.26 (0.71–2.26)

*August, September, October, and November.
†February, March, April, May, June, July, and December.

Previous studies have documented the highest rates of cat-scratch disease in late summer and fall and a separate peak often seen in January (*13*,*14*,*29*). One such study found that rates of *B. henselae* seropositivity among samples submitted to Mayo Clinic Laboratories over a 10-year period were highest during September–January, with the highest annual rates in January (*29*). Typical cat-scratch disease diagnoses in our study followed similar seasonal patterns to those previously reported. However, atypical cat-scratch disease appeared more concentrated during August–October and January–March. The reasons for this finding are unclear but might include delays in diagnosis of atypical cat-scratch disease. For example, patients who contract cat-scratch disease and had complications during January might not be given a diagnosis of atypical cat-scratch disease at that time because they do not show classic symptoms or their symptoms take time to develop and care-seeking is delayed.

Furthermore, a recent case series of ocular manifestations of cat-scratch disease reported that 9 of 10 patients had symptoms ≤3 months before showing development of ocular complications and that 3 patients had been originally given misdiagnoses of etiologies other than cat-scratch disease (*31*). Given that ocular manifestations of cat-scratch disease were most common in our study, increased diagnoses of atypical cat-scratch disease through March could be a sign of delayed diagnoses, particularly for manifestations that are less severe, such as those involving the eye.

Trends related to geographic distribution of cases did not differ between atypical and typical cat-scratch disease. Similar to findings from 3 previous studies that reported the highest incidences of cat-scratch disease in the southern United States (*13*,*14*,*30*), in our study, most typical (53.0%) and atypical (57.6%) cat-scratch disease cases occurred in patients residing in this region. In addition, a national survey of US healthcare providers found that those in the Pacific and southern regions of the United States were more likely to have been given a diagnosis of cat-scratch disease than in other regions (*32*). These findings are further supported by studies that have found higher average *B. henselae* seroprevalences and active bacteremia in pet cats from warmer, more humid climates, including the southern United States (*33*,*34*). Thus, healthcare providers in regions with climates that support flea abundance should be aware of the risk for cat-scratch disease and be able to recognize its atypical manifestations.

This study had several limitations. First, although MarketScan is a large database of insurance claims data from persons covered by employer-sponsored insurance, it is a convenience sample and may not accurately represent the characteristics of all persons in the United States. For example, trends we see in atypical cat-scratch disease by geographic region and rural residence might be biased by differences in coverage and access to care that are not accounted for here. Furthermore, MarketScan does not include data for adults ≥65 years of age, military personnel, uninsured persons, or Medicaid/Medicare enrollees. These specific populations might show varying degrees of cat-scratch disease severity or risk that are not captured in our results. In addition, because only persons <65 years of age are included in the database, the proportion of children who have cat-scratch disease might be artificially inflated. The number of patients who had atypical cat-scratch disease was small, especially when broken down by manifestation. Thus, it is difficult to draw conclusions regarding risk factors for specific manifestations of atypical cat-scratch disease and hospitalization within these groups.

Furthermore, misclassification could have occurred when ICD-9-CM codes were used to classify atypical cat-scratch disease for several reasons. ICD-9-CM codes are subject to error from the clinicians and billing specialists who enter them. In addition, we excluded records that fit our criteria for manifestations of atypical cat-scratch disease but lacked additional supporting information, which could have caused us to underestimate the true burden of atypical cat-scratch disease. Last, codes for some known atypical cat-scratch disease manifestations, such as pulmonary complications and thrombocytopenia, were excluded because of etiologic ambiguity in enrollee records.

In conclusion, our findings indicate that atypical cat-scratch disease in the United States follows trends similar to those for typical cat-scratch disease but is more prevalent and severe among children ≤14 years of age and is least likely to occur in older adults (50–64 years of age). In addition, differences in seasonality of diagnoses were seen, which might be an indication that diagnosis of atypical cat-scratch disease is often delayed. Ocular (retinitis/neuroretinitis and conjunctivitis) and hepatosplenic complications were the most common manifestations of atypical cat-scratch disease. Improved understanding of atypical cat-scratch disease might lead to better recognition of cases by clinicians, as well as inform efforts to clarify the pathophysiology of this disease.

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Atypical Manifestations of Cat-Scratch Disease, United States, 2005–2014

Appendix

Appendix Table. ICD-9-CM codes and descriptions used to identify atypical manifestations of cat-scratch disease*

ICD-9-CM code	Description
3689	Unspecified visual disturbance
22803	Hemangioma of retina
36011	Sympathetic uveitis
36100	Retinal detachment with retinal defect, unspecified
36101	Recent retinal detachment, partial, with single defect
36102	Recent retinal detachment, partial, with multiple defects
36103	Recent retinal detachment, partial, with giant tear
36104	Recent retinal detachment, partial, with retinal dialysis
36105	Recent retinal detachment, total or subtotal
3612	Serous retinal detachment
36189	Other forms of retinal detachment
3619	Unspecified retinal detachment
36213	Changes in vascular appearance of retina
36229	Other nondiabetic proliferative retinopathy
36230	Retinal vascular occlusion, unspecified
36254	Macular cyst, hole, or pseudohole
36281	Retinal hemorrhage
36282	Retinal exudates and deposits
36283	Retinal edema
36289	Other retinal disorders
3629	Unspecified retinal disorder
36321	Pars planitis
36370	Choroidal detachment, unspecified
36371	Serous choroidal detachment
36372	Hemorrhagic choroidal detachment
3638	Other disorders of choroid
3639	Unspecified disorder of choroid
36405	Hypopyon
36901	Better eye: total vision impairment; lesser eye: total vision impairment
36902	Better eye: near-total vision impairment; lesser eye: not further specified
36903	Better eye: near-total vision impairment; lesser eye: total vision impairment
36904	Better eye: near-total vision impairment; lesser eye: near-total vision impairment
36905	Better eye: profound vision impairment; lesser eye: not further specified
36906	Better eye: profound vision impairment; lesser eye: total vision impairment
36907	Better eye: profound vision impairment; lesser eye: near-total vision impairment
36908	Better eye: profound vision impairment; lesser eye: profound vision impairment
36910	Moderate or severe impairment, better eye, impairment level not further specified
36911	Better eye: severe vision impairment; lesser eye: blind, not further specified
36912	Better eye: severe vision impairment; lesser eye: total vision impairment
36913	Better eye: severe vision impairment; lesser eye: near-total vision impairment
36914	Better eye: severe vision impairment; lesser eye: profound vision impairment
36915	Better eye: moderate vision impairment; lesser eye: blind, not further specified
36916	Better eye: moderate vision impairment; lesser eye: total vision impairment
36917	Better eye: moderate vision impairment; lesser eye: near-total vision impairment
36918	Better eye: moderate vision impairment; lesser eye: profound vision impairment
36920	Moderate or severe impairment, both eyes, impairment level not further specified
36921	Better eye: severe vision impairment; lesser eye; impairment not further specified
36922	Better eye: severe vision impairment; lesser eye: severe vision impairment
36923	Better eye: moderate vision impairment; lesser eye: impairment not further specified
36924	Better eye: moderate vision impairment; lesser eye: severe vision impairment

ICD-9-CM code	Description
36925	Better eye: moderate vision impairment; lesser eye: moderate vision impairment
3693	Unqualified visual loss, both eyes
36960	Profound impairment, one eye, impairment level not further specified
36961	One eye: total vision impairment; other eye: not specified
36962	One eye: total vision impairment; other eye: near-normal vision
36963	One eye: total vision impairment; other eye: normal vision
36964	One eye: near-total vision impairment; other eye: vision not specified
36965	One eye: near-total vision impairment; other eye: near-normal vision
36966	One eye: near-total vision impairment; other eye: normal vision
36967	One eye: profound vision impairment; other eye: vision not specified
36968	One eye: profound vision impairment; other eye: near-normal vision
36969	One eye: profound vision impairment; other eye: normal vision
36970	Moderate or severe impairment, one eye, impairment level not further specified
36971	One eye: severe vision impairment; other eye: vision not specified
36972	One eye: severe vision impairment; other eye: near-normal vision
36973	One eye: severe vision impairment; other eye: normal vision
36974	One eye: moderate vision impairment; other eye: vision not specified
36975	One eye: moderate vision impairment; other eye: near-normal vision
36976	One eye: moderate vision impairment; other eye: normal vision
3698	Unqualified visual loss, one eye
3699	Unspecified visual loss
37221	Angular blepharoconjunctivitis
37222	Contact blepharoconjunctivitis
37289	Other disorders of conjunctiva
3729	Unspecified disorder of conjunctiva
37700	Papilledema, unspecified
37702	Papilledema associated with decreased ocular pressure
37703	Papilledema associated with retinal disorder
37732	Retrobulbar neuritis (acute)
37742	Hemorrhage in optic nerve sheaths
37749	Other disorders of optic nerve
3688	Other specified visual disturbances
4387	Late effects of cerebrovascular disease, disturbances of vision
37239	Other conjunctivitis
3410	Neuromyelitis optica
3630	Focal chorioretinitis and focal retinochoroiditis (fill)
3631	Disseminated chorioretinitis and disseminated retinochoroiditis (fill)
3632	Other and unspecified forms of chorioretinitis and retinochoroiditis (fill)
3684	Visual field defects (fill)
3725	Conjunctival degenerations and deposits (fill)
3770	Papilledema (fill)
3771	Optic atrophy (fill)
3772	Other disorders of optic disc (fill)
3773	Optic neuritis (fill)
3790	Scleritis and episcleritis (fill)
3792	Disorder of vitreous body (fill)
3799	Unspecified disorder of eye and adnexa (fill)
36900	Profound impairment, both eyes, impairment level not further specified
36012	Panuveitis
36212	Exudative retinopathy
36231	Central retinal artery occlusion
36232	Retinal arterial branch occlusion
36233	Partial retinal arterial occlusion
36234	Transient retinal arterial occlusion
36235	Central retinal vein occlusion
36236	Venous tributary (branch) occlusion
36241	Central serous retinopathy
36300	Focal chorioretinitis, unspecified
36301	Focal choroiditis and chorioretinitis, juxtapapillary
36303	Focal choroiditis and chorioretinitis of other posterior pole
36304	Focal choroiditis and chorioretinitis, peripheral
36305	Focal retinitis and retinochoroiditis, juxtapapillary
36306	Focal retinitis and retinochoroiditis, macular or paramacular
36307	Focal retinitis and retinochoroiditis of other posterior pole
36308	Focal retinitis and retinochoroiditis, peripheral
36310	Disseminated chorioretinitis, unspecified
36311	Disseminated choroiditis and chorioretinitis, posterior pole
36312	Disseminated choroiditis and chorioretinitis, peripheral
36313	Disseminated choroiditis and chorioretinitis, generalized

ICD-9-CM code	Description
36314	Disseminated retinitis and retinochoroiditis, metastatic
36315	Disseminated retinitis and retinochoroiditis, pigment epitheliopathy
36403	Secondary iridocyclitis, infectious
37600	Acute inflammation of orbit, unspecified
37701	Papilledema associated with increased intracranial pressure
372	Disorders of conjunctiva
3720	Acute conjunctivitis (fill)
37201	Serous conjunctivitis, except viral
37202	Acute follicular conjunctivitis
37203	Other mucopurulent conjunctivitis
37204	Pseudomembranous conjunctivitis
3722	Blepharoconjunctivitis, unspecified
37220	Blepharoconjunctivitis, unspecified
3723	Other and unspecified conjunctivitis (fill)
37230	Conjunctivitis, unspecified
37261	Granuloma of conjunctiva
3773	Optic neuritis (fill)
37730	Optic neuritis, unspecified
37739	Other optic neuritis
36320	Chorioretinitis, unspecified
7301	Chronic osteomyelitis (fill)
73010	Chronic osteomyelitis, site unspecified
73011	Chronic osteomyelitis, shoulder region
73012	Chronic osteomyelitis, upper arm
73013	Chronic osteomyelitis, forearm
73014	Chronic osteomyelitis, hand
73015	Chronic osteomyelitis, pelvic region and thigh
73016	Chronic osteomyelitis, lower leg
73017	Chronic osteomyelitis, ankle and foot
73018	Chronic osteomyelitis, other specified sites
73019	Chronic osteomyelitis, multiple sites
73030	Periostitis, without mention of osteomyelitis, site unspecified
73031	Periostitis, without mention of osteomyelitis, shoulder region
73032	Periostitis, without mention of osteomyelitis, upper arm
73033	Periostitis, without mention of osteomyelitis, forearm
73034	Periostitis, without mention of osteomyelitis, hand
73035	Periostitis, without mention of osteomyelitis, pelvic region and thigh
73036	Periostitis, without mention of osteomyelitis, lower leg
73037	Periostitis, without mention of osteomyelitis, ankle and foot
73038	Periostitis, without mention of osteomyelitis, other specified sites
73039	Periostitis, without mention of osteomyelitis, multiple sites
73000	Acute osteomyelitis, site unspecified
73001	Acute osteomyelitis, shoulder region
73002	Acute osteomyelitis, upper arm
73003	Acute osteomyelitis, forearm
73004	Acute osteomyelitis, hand
73007	Acute osteomyelitis, ankle and foot
73009	Acute osteomyelitis, multiple sites
73022	Unspecified osteomyelitis, upper arm
73023	Unspecified osteomyelitis, forearm
73024	Unspecified osteomyelitis, hand
73027	Unspecified osteomyelitis, ankle and foot
73029	Unspecified osteomyelitis, multiple sites
37603	Orbital osteomyelitis
73005	Acute osteomyelitis, pelvic region and thigh
73028	Unspecified osteomyelitis, other specified sites
73025	Unspecified osteomyelitis, pelvic region and thigh
73008	Acute osteomyelitis, other specified sites
73021	Unspecified osteomyelitis, shoulder region
73026	Unspecified osteomyelitis, lower leg
7302	Unspecified osteomyelitis
73020	Unspecified osteomyelitis, site unspecified
73005	Acute osteomyelitis, pelvic region and thigh
73028	Unspecified osteomyelitis, other specified sites
73025	Unspecified osteomyelitis, pelvic region and thigh
73006	Acute osteomyelitis, lower leg
73008	Acute osteomyelitis, other specified sites
73021	Unspecified osteomyelitis, shoulder region
73026	Unspecified osteomyelitis, lower leg

ICD-9-CM code	Description
73020	Unspecified osteomyelitis, site unspecified
4378	Other ill-defined cerebrovascular disease
4379	Unspecified cerebrovascular disease
2930	Delirium due to conditions classified elsewhere
2931	Subacute delirium
29389	Other specified transient mental disorders due to conditions classified elsewhere, other
2939	Unspecified transient mental disorder in conditions classified elsewhere
2948	Other persistent mental disorders due to conditions classified elsewhere
2949	Unspecified persistent mental disorders due to conditions classified elsewhere
3129	Unspecified disturbance of conduct
3207	Meningitis in other bacterial diseases classified elsewhere
32082	Meningitis due to gram-negative bacteria, not elsewhere classified
32089	Meningitis due to other specified bacteria
3209	Meningitis due to unspecified bacterium
3220	Nonpyogenic meningitis
32342	Other myelitis due to other infections classified elsewhere
32361	Infectious acute disseminated encephalomyelitis
32362	Other postinfectious encephalitis and encephalomyelitis
32363	Postinfectious myelitis
32382	Other causes of myelitis
3239	Unspecified causes of encephalitis, myelitis, and encephalomyelitis
32710	Organic hypersomnia, unspecified
32711	Idiopathic hypersomnia with long sleep time
32712	Idiopathic hypersomnia without long sleep time
32713	Recurrent hypersomnia
32714	Hypersomnia due to medical condition classified elsewhere
32719	Other organic hypersomnia
3332	Myoclonus
3449	Paralysis, unspecified
3568	Other specified idiopathic peripheral neuropathy
3570	Acute infective polyneuritis
78093	Memory loss
7811	Disturbances of sensation of smell and taste
7812	Abnormality of gait
7813	Lack of coordination
7814	Transient paralysis of limb
7961	Abnormal reflex
78039	Other convulsions
342	Flaccid hemiplegia
4374	Cerebral arteritis
345	Infantile spasms
436	Acute, but ill-defined, cerebrovascular disease
32341	Other encephalitis and encephalomyelitis due to other infections classified elsewhere
32381	Other causes of encephalitis and encephalomyelitis
37701	Papilledema associated with increased intracranial pressure
3483	Encephalopathy, not elsewhere classified (fill)
34830	Encephalopathy, unspecified
34839	Other encephalopathy
78097	Altered mental status
78002	Transient alteration of awareness
78009	Other alteration of consciousness
7800	Alteration of consciousness (fill)
780	General symptoms
7244	Thoracic or lumbosacral neuritis or radiculitis, unspecified
7292	Neuralgia, neuritis, and radiculitis, unspecified
7234	Brachial neuritis or radiculitis NOS
3343	Other cerebellar ataxia
3344	Cerebellar ataxia in diseases classified elsewhere
3412	Acute (transverse) myelitis
78931	Abdominal or pelvic swelling, mass, or lump, right upper quadrant
78941	Abdominal rigidity, right upper quadrant
78961	Abdominal tenderness, right upper quadrant
2895	Other diseases of spleen (fill)
28950	Disease of spleen, unspecified
28951	Chronic congestive splenomegaly
28953	Neutropenic splenomegaly
28959	Other diseases of spleen
570	Acute and subacute necrosis of liver
5719	Unspecified chronic liver disease without mention of alcohol

ICD-9-CM code	Description
5732	Hepatitis in other infectious diseases classified elsewhere
5733	Hepatitis, unspecified
5734	Hepatic infarction
5735	Hepatopulmonary syndrome
5738	Other specified disorders of liver
5739	Unspecified disorder of liver
7590	Anomalies of spleen
7904	Nonspecific elevation of levels of transaminase or lactic acid dehydrogenase
7905	Other nonspecific abnormal serum enzyme levels
7948	Nonspecific abnormal results of function study of liver
78901	Abdominal pain, right upper quadrant
28952	Splenic sequestration
7891	Hepatomegaly
7892	Splenomegaly
2894	Hypersplenism
572	Liver abscess and sequelae of chronic liver disease
5720	Abscess of liver
421	Acute and subacute endocarditis
4249	Acute and subacute endocarditis
6951	Erythema multiforme (fill)
6952	Erythema nodosum
2870	Allergic purpura

*ICD-9-CM, International Classification of Diseases, 9th revision, clinical modification; NOS, not otherwise specified.