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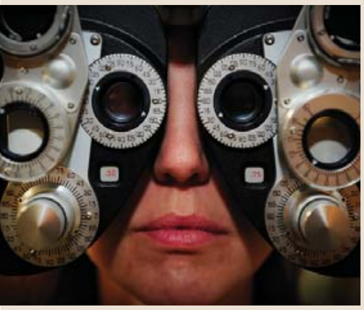

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Characterizing the Relationship Between Tick Bites and Lyme Disease in Active Component U.S. Armed Forces in the Eastern United States

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Lyme disease (LD) is the most commonly diagnosed vector-borne illness in the U.S. Analysis of ticks that are removed from patients (rather than collected from the environment) may inform LD surveillance. In this ecological study, LD rates among active component U.S. Armed Forces in the eastern U.S. were compared with tick data from the U.S. Army Public Health Command Human Tick Test Kit Program (HTTKP) covering the same geographic region. In the population of service members in the study sample, mean annual LD incidence was 52.2 per 100,000 person-years (95% CI ± 7.6 per 100,000) between 1 January 2006 and 31 December 2012. A 10% increase in the rate of ticks submitted to the HTTKP corresponded to an increase in LD incidence of 5.7% ($p<0.01$). Where *Borrelia burgdorferi* infection of *Ixodes scapularis* ticks was high (20% or greater tick infection prevalence), tick removal rates explained 53.7% of the annual variation in LD incidence ($p=0.01$). These data support using location-specific rates of ticks removed while feeding on active component service members to complement LD surveillance.

Lyme disease (LD) is the most commonly diagnosed vector-borne illness both in the U.S. military and in the general U.S. population.[1,2] For an infection to occur, the causative spirochete, *Borrelia burgdorferi,* must be transmitted in the saliva of a vector tick during feeding.[3] In the U.S., *Ixodes scapularis* (eastern U.S.) and *Ixodes pacificus* (Pacific Coast) are the vectors of LD. Although the mechanics of infection are straightforward, the surveillance of human disease remains challenging. In areas where LD is endemic, for example, high rates of infection are often accompanied by decreased case reporting (underreporting bias).[4] Syndromic surveillance efforts are, in turn, complicated by the wide range of clinical pathology that is attributable to *B. burgdorferi* infection **(Table 1)**. Finally, serologic surveillance is limited by the fact that tests are not universally ordered, are not required for diagnosis, exhibit a time lag to positivity following acute infection, require two-step testing (confirmatory Western blot), and may have difficulty distinguishing incident from resolved infection.[5]

In some cases, overreporting of LD may also occur. The Infectious Disease Society of America (IDSA) recommends that patients presenting with tick bites receive prophylactic treatment for LD when the local prevalence of *B. burgdorferi* infection in *I. scapularis* ticks is known to be high (greater than 20% of ticks infected).[5] In cases where providers elect to administer prophylaxis, either based on these IDSA recommendations or some other assessment of elevated risk, there is no designated ICD-9-CM code to reflect this situation. Such clinical encounters may be coded as LD cases, resulting in an overestimation of true disease burden (misclassification bias).

Because LD is a vector-borne illness, the use of entomological data to inform surveillance efforts may be beneficial. Multiple studies have demonstrated a strong positive correlation between *B. burgdorferi* infection in vector ticks (referred to as the entomological infection prevalence [EIP]) and LD.[6–8] In areas where LD is an emerging threat (e.g., along parts of the Canada–New York State border) a significant positive correlation has been demonstrated between counts of *I. scapularis* ticks and disease incidence.[9] A recent large-scale analysis of more than 300 locations confirmed a positive correlation between EIP and LD but demonstrated variability in the ability of tick data to predict LD in areas where LD is not known to be endemic.[10]

Although these studies support a potential role of tick data to supplement LD surveillance, they are limited by tick-drag sampling methods to assess vector parameters. Tick-drag sampling (or environmental sampling) is a well-established convenience sampling method to estimate local-level vector population densities. Important limitations of this technique are as follows: 1) it can collect only ticks that are living freely in the environment (not feeding or interacting with a host); 2) because of logistical considerations, it tends to sample only small geographic areas; and 3) it tends to collect a biased sample of ticks.[11] In a military context, the movement of service members throughout large training areas and between installations makes it improbable that tick drags will be conducted in all the potential areas where exposure may occur. Furthermore, military-specific occupational tasks (which often involve increased time spent outdoors and in close proximity to wooded and grassy areas) may increase

TABLE 1. Stages and selected symptoms of Lyme disease

Stage	Selected symptoms
Acute, localized	Erythema migrans ("target lesion")
	Prodromal syndrome (fatigue, malaise, fever, chills, headache, muscle ache)
Early, disseminated	Musculoskeletal, non-specific (myalgia, arthralgia)
	Erythema migrans ("target lesion")—may be multiple
	Neurologic (facial nerve palsy, meningitis [lymphocytic], encephalitis)
	Cardiac (AV blockade)
Late, disseminated	Arthrtitis
	Neurologic (peripheral neuropathy, encephalomyelitis)

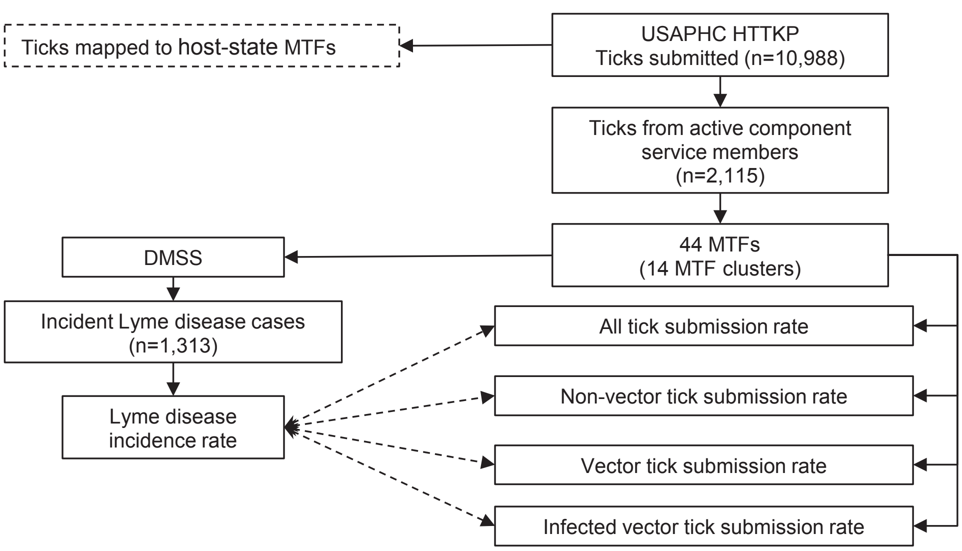
Adapted from:

1. Wright WF1, Riedel DJ, Talwani R, Gilliam BL. Diagnosis and management of Lyme disease. *Am Fam Physician*. 2012 Jun 1;85(11):1086–1093.
2. Lyme disease among U.S. military members, active and reserve component, 2001–2008. *MSMR*. 2009; 16(27):2–4.

the risk of tick exposure in ways not captured by conventional tick-drag models.[12]

Given the limitations of passive LD surveillance and the complexity involved in environmental tick sampling over large geographic areas, having installation-specific data on the ticks that are biting service members would be valuable. Moreover, understanding the relationship between these ticks and incident LD may help inform surveillance and prevention within the military. The Human Tick Test Kit Program (HTTKP) administered through the Tick-Borne Disease Laboratory of the U.S. Army Public Health Command (USAPHC) is a Department of Defense research program that identifies ticks removed from service members and their dependents and tests them for diseases transmissible to humans.[13,14] The objective of this study is to characterize the relationship between ticks removed during human feeding and voluntarily submitted to the HTTKP and the rate of incident LD among active component service members. The hypotheses are that tick removal rates are correlated with incident LD, and that the correlation is stronger for vector ticks versus any tick and is strongest for the subset of vector ticks that are proven to be infected with *B. burgdorferi*.

FIGURE 1. Schematic representation of data elements used in this analysis



USAPHC HTTKP=United States Army Public Health Command Human Tick Test Kit Program; DMSS=Defense Medical Surveillance System; MTF=military treatment facility

METHODS

This was an ecological study exploring the relationships between two independent datasets (**Figure 1**). The Defense Medical Surveillance System (DMSS) was used to identify all active component service members in the U.S. with an incident diagnosis of LD between 1 January 2006 and 31 December 2012. The surveillance case definition was any medical encounter (inpatient or outpatient) with a diagnosis of LD (ICD-9: 088.81) in any diagnostic position, or any reportable medical event of LD. Incidence date was defined as the earliest event that satisfied these surveillance criteria. An individual could be counted only once as an incident case during the study period.

Geographic data were obtained for each case as defined by the member's unit ZIP code at the time of diagnosis. Unit ZIP codes were used as a proxy for the location of the Military Treatment Facility (MTF) closest to the patient. The sum of active component person-time (years) at each location was used to calculate MTF-specific LD incidence rates. MTFs with rates based on fewer than five cases were excluded (unstable rates), as were cases originating from MTFs outside the continental U.S.

LD incidence rates were compared annually by predetermined demographic categories. Incidence rate ratios and 95% confidence intervals were calculated.

Tick data submitted by the above identified MTFs were obtained from the USAPHC's HTTKP. *I. pacficus* ticks were not included in the analysis, which focused on *I. scapularis* in the LD endemic areas of the eastern U.S. (accounts for more than 95% of cases reported to the Centers for Disease Control and Prevention [CDC] annually).[2] MTFs that submitted fewer than five specimens during the surveillance period were excluded from further analysis. Information on species of tick and the results of polymerase chain reaction testing for *B. burgdorferi* were available within the HTTKP dataset.[15,16] Tick submissions were divided by the same denominator used to calculate LD rates to obtain MTF-specific tick submission rates.

LD rates, tick submission rates, and MTF locations (via ZIP codes) were loaded into a geographic information system, ArcGIS 10.2 (Esri, Redlands, CA), and joined to Esri-provided maps of the U.S. To ensure that de-identified data could not compromise individual patients' confidentiality, MTFs that diagnosed fewer than 10 LD cases in any surveillance year were aggregated into MTF clusters based on proximity. The geographic center of each cluster was calculated using the mean distance function in ArcGIS and mapped **(Figure 2)**. To further preserve confidentiality, Coast Guard data were aggregated with the Navy.

Tick submission and LD rates were log transformed and simple linear regressions were conducted for all relationships of interest by using two-tailed Pearson correlation coefficients. Kolmogorov-Smirnov testing was used to assess normality of the datasets after transformation. When correlations met the threshold for significance, adjustment for repeated measures sampling was performed. Both between- and within-cluster correlation coefficients were calculated to account for potential correlation among repeated measures for the same cluster.[17] An α level of 0.05 was used to determine significance for all tests performed. Analysis was conducted in SPSS 22.0 (IBM, Armonk, NY) with the assistance of the Uniformed Services University of the Health Sciences (USUHS) Biostatistics Consulting Center. The study was reviewed by the USUHS Office of Research and deemed to be exempt from the requirement for an institutional review board.

FIGURE 2. Geographic distribution of the 14 military treatment facility (MTF) clusters

MTF cluster	Individual component MTFs
A	Dover AFB/Aberdeen Proving Ground/Fort Detrick/Fort Meade/Carlisle Barracks
B	Fort Riley/Fort Sill/Fort Leavenworth/Fort Leonard Wood
C	Joint Base Langley-Eustis/Fort Monroe/Naval Station Norfolk/Fort Lee
D	Fort Monmouth/Naval Weapons Station Earle/Joint Base MDL/Picatinny Arsenal/West Point
E	Marine Corps Air Station Cherry Point/MCB Camp Lejeune/Fort Jackson
F	Fort Knox/Fort Campbell
G	Fort Bragg
H	Hanscom AFB/Fort Drum
I	Pentagon DTHC/DC Army Corps of Engineers/Joint Base Andrews
J	Naval Submarine Base New London/Naval Station Newport
K	Walter Reed NMMC
L	Fort Belvoir/Henderson Hall/Fort Myer
M	Fort Stewart/NAS Jacksonville/Eglin AFB/Redstone Arsenal
N	Fort McCoy/Camp Ripley/Wright-Patterson AFB

RESULTS

During the surveillance period, a total of 1,313 incident cases of LD were identified from 2,218,559 person-years of active component U.S. military follow-up at 14 MTF clusters. The corresponding incidence rate for the sample was 59.2 per 100,000 person-years (95% CI ± 8.3 per 100,000) during the entire surveillance period (annual mean 52.2 per 100,000; 95% CI ± 7.6). Rates were significantly higher in women and in white non-Hispanics, and there was a trend to increasing incidence with both increasing age and increasing rank **(Table 2)**. In terms of military-specific demographic variables, LD incidence was significantly higher in the Navy/Coast Guard than in the Army (rate ratio [RR]: 1.7; 95% CI 1.43–1.97), the Air Force (RR: 1.3; 95% CI 1.14–1.58), or in the Marine Corps (RR: 1.0; 95% CI 0.82–1.18).

During the same surveillance period, a total of 11,282 tick specimens were removed from patients at the 14 MTF clusters and submitted to the HTTKP; 2.7% of specimens were excluded (determined not to be ticks, consisted of tick fragments insufficient to allow for identification, or belonged to a group of infrequently encountered species). The remaining 10,988 specimens were not evenly distributed geographically **(Figure 3)**. A total of 2,115 (23.1%) of the submitted ticks were removed from active component service members. The breakdown of tick species appeared to vary by MTF cluster location, with the majority of *I. scapularis* ticks coming from more northerly latitudes **(Figure 4)**.

Including multiple measurements per MTF cluster, the overall correlation between tick submission and LD incidence was strong (0.796, $p<0.01$) **(Table 3)**. In fact, the log-transformed tick submission rate explained more than 63% of the variance in log-transformed LD incidence by MTF cluster **(Figure 5)**. After adjusting for repeated measures, the within-MTF-cluster correlation between annual LD incidence and both "all tick" and "non-vector

FIGURE 3. Geographic distribution of major tick species submitted to the Human Tick Test Kit Program, 2006–2012

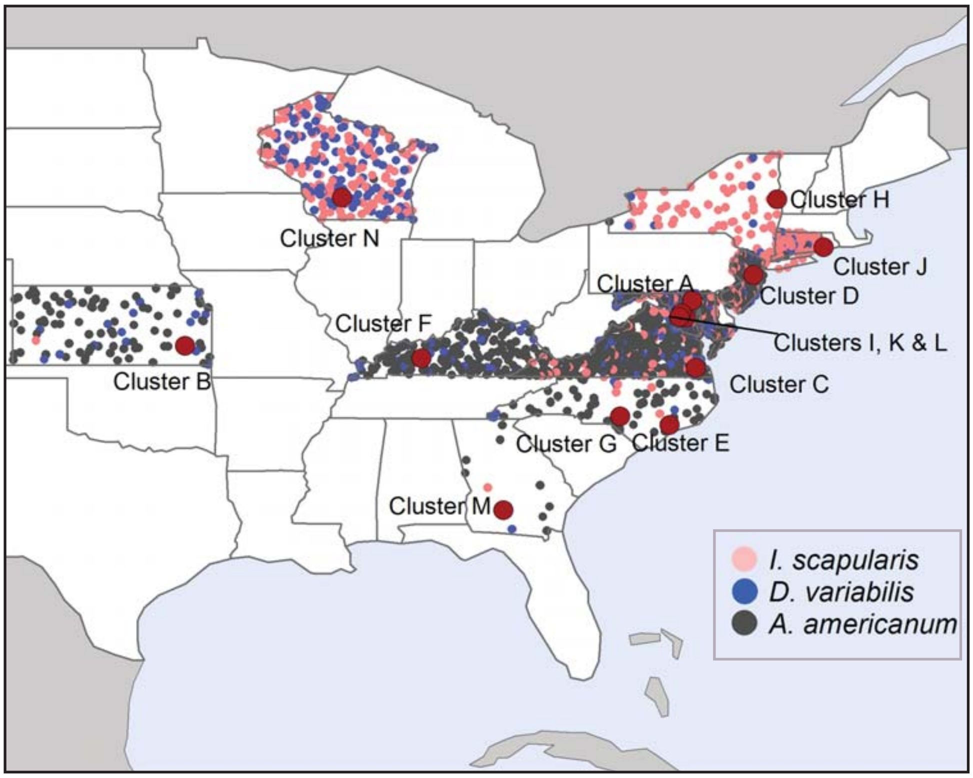


FIGURE 4. Proportional species composition of ticks found biting active component service members and submitted to the Human Tick Test Kit Program from select military treatment facility (MTF) clusters, 2006–2012

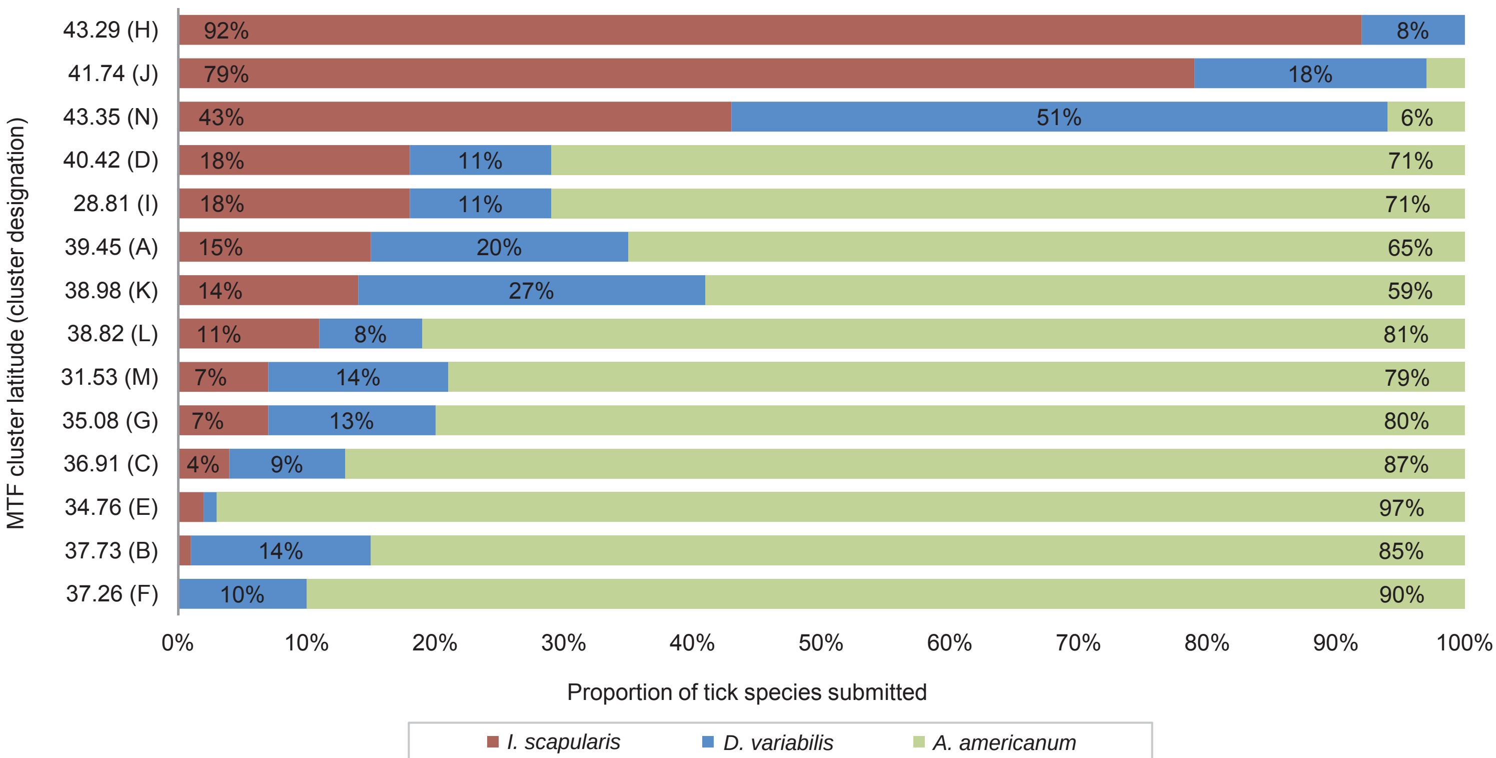


TABLE 2. Incidence rates[a] of Lyme disease (LD), active component, U.S. Armed Forces, 2006–2012

	2006		2007		2008		2009	
	LD rate (95% CI)	IRR (95% CI)	LD rate (95% CI)	IRR (95% CI)	LD rate (95% CI)	IRR (95% CI)	LD rate (95% CI)	IRR (95% CI)
Annual incidence	52.3 (44.1–60.5)	-	44.3 (36.8–51.8)	-	52.9 (44.9–60.9)	-	56.1 (47.9–64.3)	-
Age group								
<20	35.6 (13.5–57.7)	Ref	38.4 (15.7–61.1)	Ref	33.9 (12.9–54.9)	Ref	53.0 (25.2–80.7)	Ref
20–29	25.8 (18.0–33.6)	0.7 (0.4–1.4)	36.5 (27.3–45.8)	1.0 (0.5–1.8)	43.4 (33.6–53.2)	1.3 (0.7–2.5)	40.4 (31.1–49.7)	0.8 (0.4–1.4)
30–39	69.9 (51.4–88.4)	2.0 (1.0–3.9)	35.5 (22.4–48.7)	0.9 (0.5–1.9)	52.6 (36.9–68.3)	1.6 (0.8–3.1)	70.9 (52.8–89.0)	1.3 (0.8–2.4)
40+	171.2 (123.3–219.1)	4.8 (2.4–9.5)	119.6 (79.4–159.8)	3.1 (1.6-6.2)	127.8 (87.2–168.5)	3.8 (1.9–7.6)	108.7 (72.2–145.3)	2.1 (1.1–3.8)
Sex								
Female	61.2 (38.1–84.3)	1.2 (0.8–1.8)	61.3 (38.2–84.5)	1.5 (1.0–2.3)	97.4 (69.0–125.9)	2.2 (1.5–3.0)	75.3 (50.4–100.3)	1.4 (1.0–2.1)
Male	50.7 (42.0–59.5)	Ref	41.4 (33.5–49.3)	Ref	45.2 (37.1–53.3)	Ref	52.8 (44.2–61.4)	Ref
Race/ethnicity								
Black, non-Hispanic	22.9 (10.5–35.4)	0.4 (0.2–0.6)	14.5 (4.5–24.6)	0.3 (0.1–0.5)	21.1 (9.1–33.0)	0.3 (0.2–0.6)	36.8 (21.1–52.6)	0.5 (0.3–0.8)
Other	36.1 (19.4–52.8)	0.6 (0.3–0.9)	33.7 (17.7–49.7)	0.6 (0.4–1.0)	32.0 (16.8–47.2)	0.5 (0.3-0.8)	22.3 (9.7–35.0)	0.3 (0.2–0.6)
White, non-Hispanic	65.2 (53.8–76.6)	Ref	55.5 (45.1–66.0)	Ref	67.3 (56.0–78.5)	Ref	70.0 (58.7–81.4)	Ref
Service								
Army	40.8 (31.4–50.2)	Ref	33.9 (25.6–42.3)	Ref	56.3 (45.7–66.8)	Ref	57.7 (47.08–68.25)	Ref
Navy/ Coast Guard	83.2 (53.4–113.0)	2.0 (1.3–3.1)	56.6 (31.8–81.5)	1.7 (1.0–2.8)	61.7 (35.9–87.5)	1.1 (0.7–1.7)	59.7 (33.5–85.8)	1.0 (0.6–1.7)
Air Force	81.6 (55.3–107.9)	2.0 (1.4–3.0)	43.1 (23.7–62.4)	1.3 (0.8–2.2)	55.8 (33.5–78.1)	1.0 (0.6–1.5)	63.4 (39.5–87.3)	1.1 (0.7–1.7)
Marine Corps	42.0 (21.4–62.6)	1.0 (0.6–1.8)	88.3 (57.2–119.4)	2.6 (1.7–4.0)	26.6 (10.9–42.2)	0.5 (0.3–0.9)	39.7 (21.3–58.0)	0.7 (0.4–1.1)
Military occupation								
Combat-specific	36.7 (22.3–51.1)	Ref	52.7 (35.5–70.0)	Ref	50.7 (33.9–67.5)	Ref	58.5 (40.8–76.2)	Ref
Health care	63.7 (34.3–93.2)	1.7 (1.0–3.1)	59.6 (31.3–87.9)	1.1 (0.6–2.0)	74.8 (43.5–106.1)	1.5 (0.9–2.5)	56.8 (29.8–83.7)	1.0 (0.6–1.7)
Other	55.9 (45.6–66.3)	1.5 (1.0–2.4)	39.3 (30.7–48.0)	0.7 (0.5–1.1)	50.6 (41.1–60.1)	1.0 (0.7–1.5)	55.2 (45.3–65.1)	0.9 (0.7–1.3)
Rank								
Enlisted	40.6 (32.7–48.5)	Ref	33.4 (26.3–40.6)	Ref	41.6 (33.8–49.4)	Ref	44.8 (36.8–52.8)	Ref
Officer	111.0 (81.6–140.3)	2.7 (2.0–3.8)	100.1 (72.1–128.1)	3.0 (2.1–4.3)	110.6 (81.9–139.3)	2.7 (1.9–3.7)	115.4 (85.9–144.8)	2.6 (1.9–3.5)

[a]Incidence rate per 100,000 person-years
IRR=incidence rate ratio; CI=confidence interval

tick" submissions remained significant **(Table 4, Figures 6, 7)**. In this model, a 10% increase in the submission rate of ticks correlated with a 5.7% increase in LD and explained one-third of the total variation in rates (p<0.01).

The expected associations between the submission rates of *I. scapularis* ticks and LD and the submission rates of *B. burgdorferi*–infected *I. scapularis* ticks (infected vector ticks) and LD were not found to be significant.

Three independent subgroup analyses were conducted **(Table 5)**. The first subgroup analyzed were MTF clusters reporting annual EIPs 20% or greater (n=39). As previously noted, an EIP of 20% or greater is recognized by the IDSA as the threshold to initiate prophylactic treatment of patients with *I. scapularis* bites. In this subgroup, a strong correlation was noted between total tick submission rates and LD incidence explaining 53.7% of the variance in LD incidence rates. Thus, in endemic transmission zones, a 10% increase in the annual rate of tick submissions corresponded to a 7.3% increase in LD incidence **(Figure 8)**.

A second subgroup analysis (n=26) conducted for MTF clusters at risk for emerging LD infection as defined by an EIP=0% (*I. scapularis* ticks are biting active component service members but none of the ticks tested positive for *B. burgdorferi)* revealed no significant associations. The final subgroup analyzed MTF clusters that reported incident LD

TABLE 2 (cont.) Incidence rates[a] of Lyme disease (LD), active component, U.S. Armed Forces, 2006–2012

	2010		2011		2012		Total	
	LD rate (95% CI)	IRR (95% CI)	LD rate (95% CI)	IRR (95% CI)	LD rate (95% CI)	IRR (95% CI)	LD rate (95% CI)	IRR (95% CI)
Annual incidence	37.4 (30.9–44.0)	-	59.2 (50.9–67.5)	-	64.1 (55.4–72.8)	-	52.4 (49.4–55.4)	-
Age group								
<20	23.6 (4.7–42.5)	Ref	32.8 (10.1–55.5)	Ref	29.4 (7.6–51.2)	Ref	35.4 (26.9–44.0)	Ref
20–29	25.7 (18.5–33.0)	1.1 (0.5–2.6)	44.6 (35.0–54.2)	1.4 (0.7–2.8)	51.3 (40.9–61.7)	1.7 (0.8–3.8)	38.4 (34.9–41.8)	1.1 (0.8–1.4)
30–39	45.1 (30.9–59.2)	1.9 (0.8–4.5)	67.7 (50.5–85.0)	2.1 (1.0–4.3)	66.2 (49.0–83.34)	2.3 (1.0–5.0)	58.4 (52.2–64.6)	1.7 (1.3–2.1)
40+	94.7 (61.4–128.1)	4.0 (1.7–9.6)	138.1 (98.2–178.0)	4.7 (2.2–9.8)	152.7 (110.8–194.6)	5.2 (2.4–11.4)	130.1 (115.0–145.3)	3.7 (2.8–4.8)
Sex								
Female	64.2 (41.6–86.9)	2.0 (1.3–2.9)	62.2 (40.0–84.5)	1.1 (0.7–1.6)	95.6 (67.7–123.5)	1.6 (1.2–2.3)	74.0 (64.6–83.4)	1.5 (1.3–1.8)
Male	32.9 (26.2–39.5)	Ref	58.7 (49.8–67.6)	Ref	58.7 (49.7–67.7)	Ref	48.7 (45.5–51.2)	Ref
Race/ethnicity								
Black, non-Hispanic	18.5 (7.6–29.5)	0.4 (0.2–0.8)	28.9 (15.1–42.6)	0.4 (0.3–0.7)	45.2 (27.8–62.6)	0.6 (0.4–1.0)	26.9 (21.8–32.0)	0.4 (0.4–0.5)
Other	38.9 (22.6–55.1)	0.9 (0.6–1.5)	52.0 (33.4–70.6)	0.8 (0.5–1.1)	58.5 (38.9–78.2)	0.8 (0.6–1.2)	39.5 (33.2–45.9)	0.6 (0.5–0.8)
White, non-Hispanic	42.3 (33.9–50.9)	Ref	69.5 (58.4–80.7)	Ref	70.8 (59.4–82.2)	Ref	62.9 (58.8–67.0)	Ref
Service								
Army	29.2 (21.8–36.5)	Ref	53.9 (43.9–63.9)	Ref	54.7 (44.4–65.0)	Ref	46.8 (43.1–50.4)	Ref
Navy/ Coast Guard	74.2 (45.7–102.7)	2.5 (1.6–4.0)	78.8 (50.1–107.4)	1.5 (1.0–2.2)	132.7 (95.2–170.26)	2.4 (1.7–3.4)	78.4 (67.4–89.5)	1.7 (1.4–2.0)
Air Force	51.8 (30.2–73.5)	1.8 (1.1–2.9)	79.9 (53.1–106.8)	1.5 (1.0–2.2)	63.1 (39.33–87.0)	1.2 (0.8–1.8)	62.7 (53.8–71.7)	1.3 (1.1–1.6)
Marine Corps	33.3 (17.0–49.6)	1.5 (0.9–2.5)	47.9 (27.4–68.3)	0.9 (0.6–1.4)	51.6 (31.0–72.3)	0.9 (0.6–1.5)	45.9 (38.2–53.6)	1.0 (0.8–1.2)
Military occupation								
Combat-specific	31.6 (18.9–44.2)	Ref	53.9 (37.4–70.3)	Ref	69.8 (50.8–88.8)	Ref	50.6 (44.4–56.8)	Ref
Health care	50.8 (25.9–75.7)	1.6 (0.9–3.0)	61.6 (33.9–89.3)	1.1 (0.7–2.0)	69.0 (39.5–98.5)	1.0 (0.6–1.6)	62.2 (51.5–72.9)	1.2 (1.0–1.5)
Other	37.5 (29.5–45.6)	1.9 (1.3–3.0)	60.7 (50.5–70.9)	1.1 (0.8–1.6)	61.4 (51.1–71.8)	0.9 (0.6–1.2)	51.6 (48.0–55.2)	1.0 (0.9–1.2)
Rank								
Enlisted	28.9 (22.6–35.3)	Ref	49.4 (41.1–57.7)	Ref	53.3 (44.6–62.1)	Ref	41.8 (38.8–44.7)	Ref
Officer	80.5 (56.7–104.3)	2.8 (1.9–4.0)	105.8 (79.3–132.4)	2.1 (1.6–2.9)	113.0 (85.7–140.2)	2.1 (1.6–2.8)	105.1 (94.7–115.5)	2.5 (2.2–2.8)

[a]Incidence rate per 100,000 person-years
IRR=incidence rate ratio; CI=confidence interval

TABLE 3. Relationship between tick submission rates and Lyme disease incidence rates, all military treatment facility (MTF) clusters, 2006–2012

Independent variable[a]	n	Pearson correlation		Linear regression	
		Coefficient	p-value[b]	R^2	p-value
Log_{10} tick submission rate	14	0.75	<.001	0.63	<.001
Log_{10} non-vector submission rate	14	0.69	0.003	0.46	0.007
Log_{10} vector submission rate	14	0.68	0.004	0.49	0.008
Log_{10} infected vector submission rate	9[c]	0.18	0.644	-	-

[a]Rates were calculated as number of ticks submitted per 100,000 active component person-years.
[b]Two-tailed Pearson correlation
[c]Five MTF clusters did not submit any *B. burgdorferi*–infected *I. scapularis* ticks over the surveillance period.

cases but did not submit any *I. scapularis* ticks (n=18). In these areas, LD incidence appears to be independent of the rate of tick submissions.

EDITORIAL COMMENT

The mean annual LD incidence rate of 52.2 per 100,000 person-years in this study is high compared to an earlier estimate of

TABLE 4. Relationship between military treatment facility (MTF) cluster correlation - annual tick submission and annual Lyme disease incidence, 2006–2012

Independent variable[a]	n	Linear regression		Repeated sampling adjustment		
		R^2	p-value	R	R^2	p-value
Log$_{10}$ all tick rate	98	0.56	<.01	0.51	0.326	<.01
Log$_{10}$ non-vector tick rate	98	0.45	<.01	0.55	0.286	<.01
Log$_{10}$ vector tick rate	80[b]	0.23	<.01	0.41	0.238	0.09
Log$_{10}$ infected vector tick rate	53[c]	0.14	0.48	0.04	0.001	0.99

[a]Rates were calculated as number of ticks submitted per 100,000 active component person-years.
[b]18 MTF clusters did not submit an *I. scapularis* tick during the surveillance period.
[c]35 MTF clusters did not submit a *B. burgdorferi*–infected *I. scapularis* tick during the surveillance period.

TABLE 5. Subgroup analyses of the relationships between tick submission rates and Lyme disease (LD) incidence rates, 2006–2012

Independent variable[a]	n	Linear regression		Repeat sampling adjusted		
		R^2	p-value	R	R^2	p-value
Subgroup 1: MTF clusters with submitting vector ticks with EIP[b] ≥ 20% (IDSA empiric Rx threshold)						
Log$_{10}$ tick rate	39	0.568	<.01	0.733	0.537	0.01
Log$_{10}$ non-LD vector rate	39	0.192	0.04	0.641	0.41	0.13
Log$_{10}$ LD vector rate	39	0.155	0.04	0.48	0.23	0.33
Log$_{10}$ infected LD vector rate	39	0.161	0.04	0.178	0.032	0.89
Subgroup 2: MTF clusters submitting *I. scapularis* ticks with an EIP[b]=0% (vector present, agent [*B. burgdorferi*] is not)						
Log$_{10}$ tick rate	26	0.549	<.01	0.249	0.062	0.81
Log$_{10}$ non-LD vector rate	26	0.499	<.01	0.282	0.08	0.76
Log$_{10}$ LD vector rate	26	0.666	<.01	0.416	0.173	0.51
Subgroup 3: MTF clusters reporting incident LD but did not submit *I. scapularis* (LD vector) ticks						
Log$_{10}$ non-LD vector rate	18	0.415	<.01	0.535	0.286	0.18

[a]Rates were calculated as number of ticks submitted per 100,000 active component person-years.
[b]Entomological infection prevalence (EIP) was calculated as number of *B. burgdorferi* PCR (+) vector ticks per total number of vector ticks submitted.
MTF=military treatment facility; IDSA=Infectious Disease Society of America

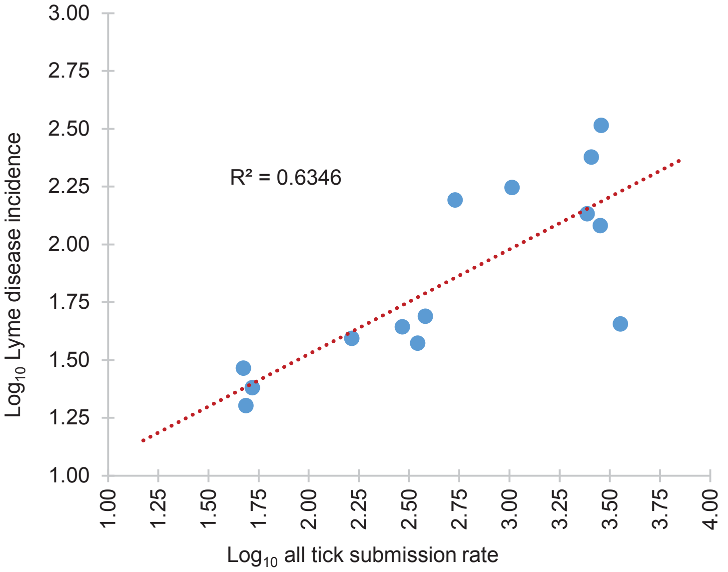
LD incidence in service members. A previously published *MSMR* report estimated that the annual rate of LD in active component service members was, at most, 16 cases per 100,000 person-years.[1] Notable differences in case definitions may explain this difference. In the *MSMR* report, two outpatient visits for LD were required within 60 days to qualify as an incident case. This case definition was more specific than the definition used in this analysis (which required only a single outpatient visit for LD to define a case). Conversely, the AFHSC definition may have missed cases that were clinically diagnosed and who either did not require or did not attend a follow-up visit. Furthermore, the AFHSC report included all active component person-time in their rate calculations, while this analysis restricted the denominator to person-time from MTFs that both diagnosed LD and submitted ticks to the HTTKP. Despite the effects of an arguably aggressive case-finding strategy and a restricted denominator, annual LD incidence rates in this study remain comfortably within the expected range of LD incidence as reported by the CDC.[18]

There was a trend toward increased LD rates with increasing age and increasing rank. From an occupational exposure perspective, this trend appeared unexpected. Greater tick exposures were predicted for younger and junior enlisted service members who were perhaps more likely to encounter ticks as a function of their occupation than their more senior colleagues. However, the peak in incidence with increasing age is consistent with the distribution of LD by age group in the civilian population.[19,20] A bimodal distribution (first peak in early adolescence) generally seen in civilian populations may not have been detected in this analysis because of the study population demographics.

The available data suggest that rates of tick submissions to the HTTKP can explain a significant amount of the annual variation in LD incidence. Notably, tick submission rates are better able to account for annual variation in disease incidence in those areas where the baseline risk of LD acquisition is greatest (EIP of 20% or greater).

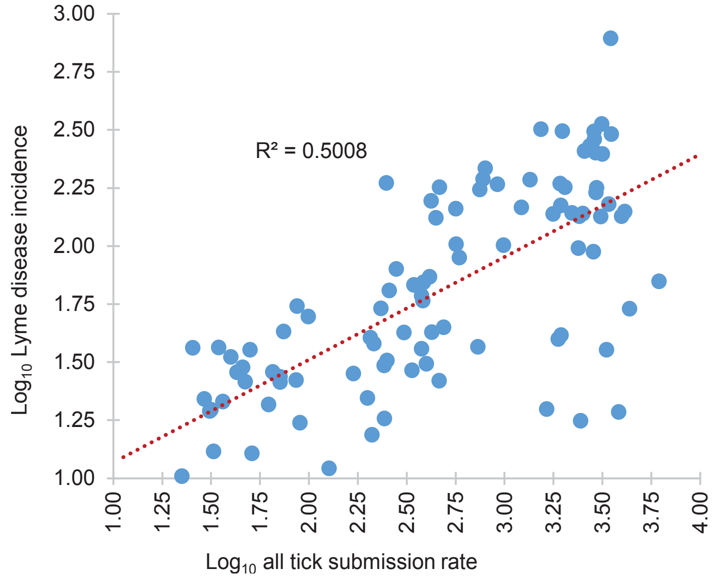
Unexpectedly, the rates of *I. scapularis*– and more specifically, *B. burgdorferi*–infected *I. scapularis* (confirmed infected vectors) were not found to be associated with LD incidence. Several potential hypotheses may explain this lack of association. First, providers may have viewed any tick bite (independent of species) as a potential vector for LD rather than risk misidentifying a tick and delaying treatment. Second, because the HTTKP is voluntary, ticks may be undersubmitted in endemic regions (providers no longer perceive a benefit to submitting them). Third, some ticks will fall off or be actively removed by patients before they seek medical care. Thus, the ticks removed from patients at a clinical encounter represent only a point-in-time (cross-sectional) sample of actual human–tick interaction. A patient may present with symptoms of LD but have only a non-LD vector attached at that particular point in time (*I. scapularis* tick may have fallen off).

FIGURE 5. Relationship between aggregated tick submission rates by military treatment facility cluster and Lyme disease incidence, active component, U.S. Armed Forces, 2006–2012



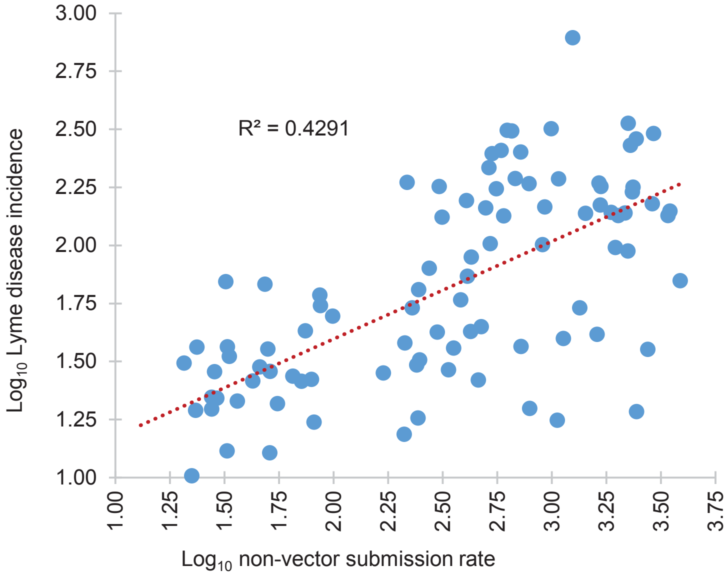
R^2 adjusted for repeated measures at individual military treatment facility clusters

FIGURE 6. Relationship between annual tick submission rates and Lyme disease incidence, active component, U.S. Armed Forces, 2006–2012



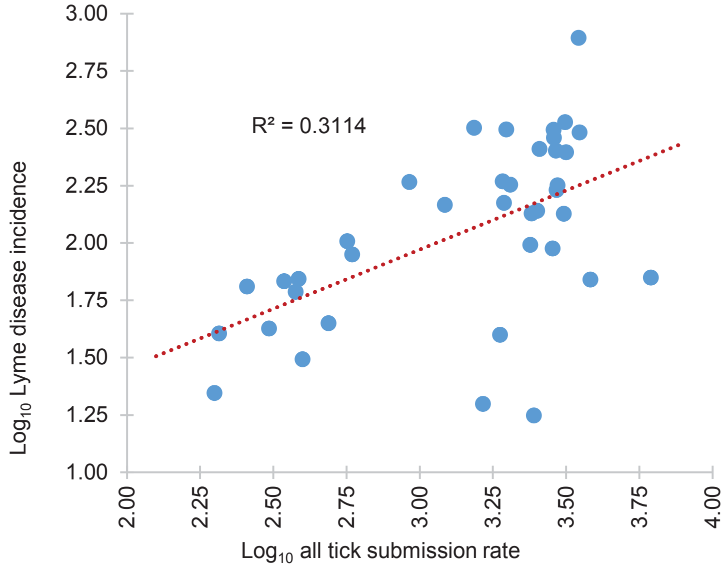
R^2 adjusted for repeated measures at individual military treatment facility clusters

FIGURE 7. Relationship between annual "non-vector" tick submission rates and Lyme disease incidence, active component, U.S. Armed Forces, 2006–2012



R^2 adjusted for repeated measures at individual military treatment facility clusters

FIGURE 8. Relationship between annual tick submission rates from military treatment facility clusters with entomological infection prevalence greater than 20% and Lyme disease incidence, active component, U.S. Armed Forces, 2006–2012



R^2 adjusted for repeated measures at individual military treatment facility clusters

It was also interesting that, in some MTF clusters, LD cases were diagnosed in the absence of *I. scapularis* ticks being submitted. Potential explanations for this include 1) ticks fall off or are removed; 2) late, chronic, or atypical LD may present months to years after an initial tick bite; and 3) an acute infection acquired in one location may have been diagnosed at a distant MTF. In fact, the probability of imported cases may be higher in a military population—whose members may train in an endemic area, but return for treatment to a non-endemic area—than in a comparable civilian cohort. It is possible that some encounters for tick bite may be coded as LD encounters.

This study has a number of significant limitations. First, this was an ecological study; the available tick data were not directly linked to individual patients. Second, the case definition favored enhanced case finding at the cost of higher false positive rates (sensitivity over specificity). Third, data on the precise location of tick acquisition were not available; they were assumed to have been acquired within the boundaries of an MTF's host state, and were usually aggregated into MTF clusters. This geographic aggregation is particularly problematic for those ticks submitted from MTFs located in close geographic proximity to state boundaries or to multiple MTFs, and should be acknowledged. Finally, the use of DMSS data for surveillance purposes involves accepting both under- and overreporting of cases as case detection depends on provider ICD-9-CM coding. The strengths of this analysis are as follows: 1) large numbers of both LD cases and submitted ticks; 2) expert tick identification; 3) robust testing of ticks for human pathogens; and 4) accurate mid-year location data for an otherwise highly mobile population.

LD incidence in active component service members correlates strongly with the submission rate of ticks removed from active component service members. Incorporating tick removal rates and other entomological data into existing passive surveillance systems for LD may improve the quality of these systems—particularly in areas where LD is known to be endemic. Beyond enhancing passive surveillance, disseminating the tick data already being collected by the HTTKP may have additional benefits.

First, from a direct patient care perspective, reporting regional EIP data for *I. scapularis* ticks may allow healthcare providers to more confidently follow IDSA guidelines for LD prophylaxis. Second, from a preventive medicine standpoint, informing providers in areas of potential emerging infection threat where the EIP=0% (*I. scapularis* are being found feeding on humans but have not yet tested positive for *B. burgdorferi* infection) may provide added justification for strengthening exposure prevention programs before LD becomes endemic. Third, from a public health perspective, HTTKP data may help appropriately target LD resources to MTFs where *I. scapularis* ticks are being encountered. Conversely, at locations where LD vectors are not found but ticks continue to bite service members, continuing medical education programs might reinforce that appropriate diagnostic testing for tick-borne diseases other than LD may be indicated.[21]

The lack of association between *I. scapularis* ticks and LD supports a need for improved visual tick identification guides in the ambulatory care setting. The strong association demonstrated between tick bites and LD incidence, independent of tick species, suggests that there may be uncertainty in a provider's self-assessed proficiency to correctly identify the species of ticks found biting their patients. The provision of an updated visual identification guide that includes photos of engorged female ticks (in addition to the traditional unfed female tick images) as well as up-to-date information for local resources (including local/state health departments and the HTTKP) may help address this concern.

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