Challenges in Obtaining Estimates of the Risk of Tuberculosis Infection during Overseas Deployment

James D. Mancuso* and Mia Geurts

Division of Tropical Public Health, Department of Preventive Medicine and Biostatistics, Uniformed Services University of the Health Sciences, Bethesda, Maryland; Office of Student Affairs, Harvard Medical School, Boston, Massachusetts

Abstract. Estimates of the risk of tuberculosis (TB) infection resulting from overseas deployment among U.S. military service members have varied widely, and have been plagued by methodological problems. The purpose of this study was to estimate the incidence of TB infection in the U.S. military resulting from deployment. Three populations were examined: 1) a unit of 2,228 soldiers redeploying from Iraq in 2008, 2) a cohort of 1,978 soldiers followed up over 5 years after basic training at Fort Jackson in 2009, and 3) 6,062 participants in the 2011–2012 National Health and Nutrition Examination Survey (NHANES). The risk of TB infection in the deployed population was low—0.6% (95% confidence interval [CI]: 0.1–2.3%)—and was similar to the non-deployed population. The prevalence of latent TB infection (LTBI) in the U.S. population was not significantly different among deployed and non-deployed veterans and those with no military service. The limitations of these retrospective studies highlight the challenge in obtaining valid estimates of risk using retrospective data and the need for a more definitive study. Similar to civilian long-term travelers, risks for TB infection during deployment are focal in nature, and testing should be targeted to only those at increased risk.

BACKGROUND

The risk of tuberculosis (TB) disease in the U.S. military is about eight times lower—0.4 per 100,000 in 2012—than in the age-adjusted general U.S. population.¹ This is largely due to moderately restrictive standards for induction into military service, such as exclusions for human immunodeficiency virus and other immunocompromising conditions.² Nevertheless, the military has unique potential risks for TB exposure, including deployment to TB-endemic areas and exposures in congregate settings such as basic training³ and naval vessels.^{4,5} More than 1 million service members have deployed to TB-endemic areas since 2001. Although the potential for exposure during these deployments is unquestioned, demonstrating the actual risk of infection has been difficult. For example, a prior study showed no association between the occurrence of active TB disease and military deployment.⁶ Still, surveillance data showed that nine (24%) of the 38 cases of TB in the U.S. military between 2008 and 2012 were temporally associated with deployment or other overseas military service.¹ Although this is a substantial proportion of the total burden of disease, the actual rates are still very low.

Perhaps, however, these service members truly are being infected during deployment but the infection remains latent, since the service members have intact immune systems and are otherwise healthy. Are these deployments creating a reservoir of latent TB infection (LTBI) that will reactivate into TB disease as these service members' age, potentially plaguing the Veterans Administration and U.S. health-care system for years to come? Previously published data suggest that this is a concern. The risk of LTBI in long-term civilian travelers has been estimated at 4.2 per 100 person-years⁷ or 2.3% per episode of travel,⁸ and previous military studies have suggested an overall risk of 2.0% per deployment. However, these estimates conceal a great deal of uncertainty and heterogeneity. For example, during one deployment to Afghanistan, a unit

reported tuberculin skin test (TST) conversions in 15% of their soldiers,⁹ and other units have reported a risk of up to 10%. In addition, many of these estimates have been found to contain a large proportion of false positives, in large part due to prior TST positives. These pseudoepidemics of TST conversions were also associated with exposure to non-tuberculous mycobacteria (NTM); Aplisol[®] brand TST (JHP Pharmaceuticals, Rochester, MI); and errors in TST administration, reading, and documentation.⁹

Because of these limitations, there has been no valid estimate of the risk of LTBI resulting from overseas military deployment. Estimates of this risk are important in informing U.S. military force health protection policy during deployment, as well as informing health-care policies for LTBI testing and treatment of returning service members and veterans. The purpose of this study was therefore to provide an estimate of the incidence of TB infection in U.S. military service members resulting from overseas military deployment and other military service. Of particular interest was the comparison of the risk of LTBI between deployed and non-deployed service members. Ideally, this estimate would be obtained in a prospective cohort study in which testing is performed both before and after deployment. In the absence of such a study, we had to rely on less valid estimates from retrospective cohort and prevalence studies.

METHODS

Three complementary populations were used to assess LTBI resulting from military deployment in this study.

Post-deployment testing of a unit returning from Iraq, 2008. The first population studied was an Army infantry brigade, which performed routine TB testing after returning from a 12-month deployment to Iraq in 2008. Army policy at the time was still in transition from a policy of testing all soldiers after deployment¹⁰ to that of targeted testing based on the amount of indoor exposure to local nationals,¹¹ so the unit performed testing on all soldiers. No known exposures to cases of TB disease occurred during the deployment. The unit kept records of all TST results in a spreadsheet. Demographics and some limited TB exposure

*Address correspondence to James D. Mancuso, Division of Tropical Public Health, Department of Preventive Medicine and Biostatistics, Uniformed Services University of the Health Sciences, 4301 Jones Bridge Road, Bethesda, MD 20814. E-mail: james.mancuso@usuhs.edu

TABLE 1
Association of tuberculin skin test results with self-reported exposure and provider assessment in a unit returning from Iraq, 2008

Factor	TST ≥ 10 mm	TST < 10 mm	Prevalence ratio	95% CL
Indoor exposure to local and third-country nationals				
None	5	200	1 (Reference)	–
Minimal	3	269	0.45	0.1, 1.9
Moderate (at least 1 hour per week)	8	693	0.47	0.2, 1.4
Extensive	15	1,022	0.59	0.2, 1.6
Provider TB assessment				
Minimal	9	720	1 (Reference)	–
Increased	22	1,471	1.2	0.6, 2.6
Foreign birth				
Yes	13	156	10.4	5.0, 21.8
No	14	1,883	1 (Reference)	–
Race				
Not Caucasian	16	600	2.8	1.4, 5.6
Caucasian	15	1,597	1 (Reference)	–
Age				
30 or older	12	479	2.2	1.1, 4.6
Under 30	19	1,718	1 (Reference)	–
Rank				
Officer	6	198	2.5	1.0, 5.9
Enlisted	24	1,971	1 (Reference)	–

CL = confidence limit; TB = tuberculosis; TST = tuberculin skin test.
Some categories do not add up to 2,228 due to missing data.

and assessment data were available from the post-deployment health assessment Form DD2796. The unit checked each soldier's TB test registry records (i.e., the Medical Protection System [MEDPROS]) for prior positive test results at time of redeployment, suggesting that this cohort could provide a good estimate of LTBI incidence.

Follow-up of a 2009 Fort Jackson study of recruits. The second population was a group of 1,978 participants assembled during a 2009 study of Army recruits at Fort Jackson, in which the prevalence of and risk factors for LTBI were assessed.^{3,12} All uninfected soldiers were assessed retrospectively in 2014 for incidence of LTBI (i.e., had a newly positive TB test) from their times of entry into military service (between April and June 2009) up to the end of the follow-up period in May 2014. Demographic and TB exposure history before military service were available from the 2009 study. TSTs performed after basic training and records of deployments during military service were obtained from the Army's TB test registry (MEDPROS). Only those with at least one

TST result available in MEDPROS after basic training were included in the analysis. In addition, the complete military electronic medical record was reviewed for all participants who had a positive test during military service.

The 2011–2012 National Health and Nutrition Examination Survey. The third population was obtained from the 2011–2012 National Health and Nutrition Examination Survey (NHANES). We used the same methods in this analysis as those described in previous reports.¹³ In brief, NHANES is a cross-sectional, nationally representative health examination survey that provides prevalence estimates and trends over time. In 2011–2012, TB testing with both a TST and an interferon gamma release assay (IGRA) were performed in addition to the usual demographics and health status information. We used the 6,062 participants who completed the demographic questionnaire, had a valid TST result, and had a valid, non-indeterminate IGRA result. Of note, the NHANES also included two questions about military service. The first asked whether the subject had served previously in the military and

FIGURE 1. Flow of participants, follow-up of 2009 Fort Jackson study population. BCT = basic combat training; TST = tuberculin skin test.

TABLE 2
Characteristics of the study participants, Fort Jackson follow-up study

Characteristic	Deployed (N = 309)	Non-deployed (N = 524)
Age	21.6 (SD 4.2)	21.7 (SD 4.1)
Female*	63 (20%)	156 (30%)
No. of TSTs after basic training*	2.1 (SD 0.9)	1.4 (SD 0.7)
History of BCG vaccine	4 (1%)	15 (3%)
Race/ethnicity		
White	218 (71%)	339 (65%)
Black	61 (20%)	106 (20%)
Hispanic	23 (7%)	77 (15%)
Asian	9 (3%)	23 (3%)
Other	18 (6%)	38 (7%)
TB prevalence in country of birth		
< 20	297 (96%)	489 (93%)
20–100	5 (2%)	13 (2%)
> 100	7 (2%)	22 (4%)

BCG = Bacille Calmette-Guérin; TB = tuberculosis; SD = standard deviation; TST = tuberculin skin test.

*P < 0.05.

Some participants entered more than one race/ethnic group.

TABLE 3

Naive analysis of association of LTBI with selected characteristics, Fort Jackson follow-up study

Characteristic	LTBI	No. of LTBI	Prevalence ratio (95% CL)
Age at accession			
≥ 30 years	3	52	2.5 (0.8, 8.2)
< 30 years	17	759	1 (Reference)
Birth country			
TB prevalence ≥ 20 per 100,000	8	39	11.1 (4.8, 25.9)
TB prevalence < 20 per 100,000	12	774	1 (Reference)
Asian race			
Yes	3	29	4.4 (1.4, 14.3)
No	17	784	1 (Reference)
BCG vaccinated			
Yes	5	14	14.2 (5.8, 35.3)
No	15	799	1 (Reference)
Positive TST at accession			
Yes	6	5	32.0 (15.1, 67.7)
No	14	808	1 (Reference)

BCG = Bacille Calmette-Guerin; CL = confidence limit; LTBI = latent TB infection; TB = tuberculosis; TST = tuberculin skin test.

the second asked whether the subject had served overseas while in military service. The responses to these questions were combined into a composite military exposure variable.

Outcome measurement and statistical methods. The primary criterion for a positive TST was an induration of 10 mm or larger, consistent with previous recommendations for long-term civilian travelers.⁷ IGRA testing was also occasionally performed at provider discretion in the Fort Jackson follow-up study, and it was performed on all participants in the NHANES study. TSTs were performed according to Centers for Disease Control and Prevention guidelines,¹⁴ as were IGRA tests.¹⁵ SAS version 9.3 (SAS Institute Inc., Cary, NC) was used for all analyses. The risk of LTBI was expressed as a proportion. Exact binomial confidence limits were used for all proportions with less than five positive tests. Bivariate and multivariate odds ratios (ORs) and 95% confidence limits were calculated using logistic regression. Analysis of NHANES data used complex survey analysis methods. Weighted estimates of prevalence, ORs, and 95% confidence limits were based on standard errors incorporating the complex sample design. As in previous studies,¹³ additional weights were calculated to account for nonparticipation in TB testing, and these weights were used to adjust the estimates.

RESULTS

Post-deployment testing of a unit returning from Iraq, 2008. The association of a positive TST with reported TB

exposure among the first population of 2,228 soldiers tested from a unit returning from Iraq in 2008 is shown in Table 1. Although we generated an initial estimate of an incidence of 31 out of the 2,228 tested (1.4%), we immediately became suspicious that this was not a valid estimate. First, neither subject reporting nor provider assessment of TB exposure was significantly associated with a positive TST. Army policy transitioned in 2008 to targeted testing after deployment, which involved testing all soldiers who had 1 hour per week of indoor exposure to local or third-country nationals.¹¹ However, Table 1 suggests that this question was not a good predictor of TB infection, because neither self-reported exposure nor provider assessment was associated with a positive TST. Because the exposure variables were not associated with a positive TST, we looked at other established risk factors, some of which are also shown in Table 1. Foreign birth had the strongest association, although race, age, and rank also had significant effects. The strong association of a positive TST with risk factors existing before entry into military service suggested to us that these were actually prevalent, rather than incident, cases of LTBI.

Follow-up of a 2009 Fort Jackson study of recruits. The flow of study participants for the second population, the Fort Jackson follow-up study, is shown in Figure 1. Of the 1,978 enrolled, 157 (7.9%) were not found in the MEDPROS TB registry, likely due to discharge from military service. An additional 988 (49.9%) had no further TSTs recorded after basic training, so they were not eligible for inclusion in the follow-up study. This left 833 (42.1% of the original study population) remaining for analysis, 309 (37.1%) of whom had a reported history of deployment over the 5-year interval. Characteristics of deployed soldiers were similar to the non-deployed except for having a greater proportion of males and greater average number of TSTs performed (Table 2). Twenty (2.4%) of these soldiers had a positive TST documented after basic training. A naive analysis of risk factors for having a positive TST after basic training is shown in Table 3. Similar to Table 1, it showed that LTBI was associated with established risk factors such as foreign birth and race, again suggesting that the TB test registry captured prevalent, rather than incident, cases. After comparison with data from the original 2009 study,³ we found that 10 of the 20 positives (50%) during military service had a history of a prior positive test (Table 4). An additional five (25%) had repeat testing ordered by the treating health-care provider, which was negative using either a TST or an IGRA. This left five cases of incident LTBI among the remaining at-risk population of 823 (0.6%) over the 5-year interval. All five of these

TABLE 4
Estimated incidence of LTBI using the electronic TB registry, Fort Jackson follow-up study

Assessment	Deployed		Non-deployed		Total	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
Positive TSTs after BCT	4/309	1.3 (0.4–3.3%)	16/524	3.1 (1.8–4.9%)	20/833	2.4 (1.5–3.7%)
Non-incident cases	4		11		15	
Had a prior positive TST	2		8		10	
Negative on retest	2		3		5	
Incidence of TB infection from the electronic TB registry	0/307	0 (0–1.2%)	5/516	1.0 (0.3–2.2%)	5/823	0.6 (0.2–1.4%)
Estimated incidence of TB infection updated after medical record review	2/309	0.6 (0.1–2.3%)	3/514	0.6 (0.1–1.7%)	5/823	0.6 (0.2–1.4%)

BCT = basic combat training; CI = confidence interval; TB = tuberculosis; TST = tuberculin skin test.

TABLE 5
Line listing of the five incidence cases of LTBI, Fort Jackson follow-up study

Reason tested	Age (at entry into service)	Sex	Component	Birth country	Previously deployed?	TST 1* (date)	TST 2 (date)	TST 3 (date)	Assessment
Post-deployment	19	M	Active	United States	Yes	0 mm (May 9, 2009)	10 mm (September 10, 2010)		Deployment related
Post-deployment	23	M	Active	United States	Yes	3 mm (May 15, 2009)	0 mm (January 25, 2011)	12 mm (March 16, 2012)	Deployment related
Pre-deployment	23	M	Guard	United States	No	0 mm (May 2, 2009)	12 mm (July 15, 2013)		Not deployment related
Pre-deployment	18	M	Active	United States	No	6 mm (May 23, 2009)	12 mm (3 September 13)		Not deployment related
Unknown	34	M	Guard	United Kingdom	No	0 mm (Jun 8, 2009)	11 mm (June 15, 2010)		Not deployment related

M = male; TST = tuberculin skin test.

*Test performed in basic training.

cases occurred among the non-deployed population according to the MEDPROS TB test registry data. However, additional review of the electronic medical record revealed that two of these cases were misclassified as non-deployed (Table 5). The resulting estimate of TB incidence occurring after deployment was 0.6% (95% confidence interval [CI]: 0.1–2.3%), which was similar to the incidence among the non-deployed of 0.6% (95% CI: 0.1–1.7%).

The 2011–2012 NHANES. The characteristics of the third study population (NHANES 2011–2012) are shown in Table 6, stratified by category of military service: civilian, non-deployed military veterans, and deployed veterans. Military participants were more likely to be male, adult, U.S. born, and Caucasian. Associations between LTBI and age, foreign birth and race were seen for both TST and IGRA in Table 7. These were similar to those demonstrated in the previous two populations in this report. The prevalence of LTBI among deployment and non-deployed veteran participants in the NHANES was not significantly different from those with no history of military service using either a positive TST or IGRA as the outcome. Although the unadjusted and adjusted prevalence was consistently slightly higher among the deployed compared with the non-deployed military, none of these differences were statistically significant. In a separate domain analysis analyzing only the subpopulation of those serving in the military (data not shown), the adjusted ORs again failed to reach significance: the adjusted OR for deployed veterans compared with non-deployed veterans using TST was 1.9 (95% CI: 0.78–4.76), whereas with IGRA the adjusted OR was 1.71 (95% CI: 0.74–3.94).

DISCUSSION

The risk of new TB infection among soldiers deployed overseas in recent conflicts was low (0.6%) and was similar to that found among non-deployed soldiers. The prevalence of LTBI in the 2011–2012 NHANES was not significantly different among deployed veterans, non-deployed veterans, and those with no history of military service. Administrative databases poorly reflected the true incidence of LTBI, largely due to including many prevalent cases that existed before entry into military service—50% of those testing positive after basic training had evidence of prior infection. The strong association of these cases with foreign birth, race, and other factors unrelated to military service also suggested that these were prevalent, rather than incident, cases. Previously used screening tools for targeted TB testing were found to be poor predictors of LTBI, whether using self-reported exposures or provider assessment.

The incidence of LTBI associated with deployment found in this study (0.6%) was lower than that seen among long-term civilian travelers (~2%).^{7,8} The only prospective study among long-term travelers found an incidence of 1.8%,⁷ which was three times higher than that seen in our study. These differences are largely attributable to the heterogeneity between and within these populations. An example of this heterogeneity is demonstrated by a study of Peace Corps Volunteers (PCVs), whose overall risk of LTBI was estimated at 2.3% during their service (typically 2 years).¹⁶ However, this estimate also obscures the heterogeneity among the different countries, within each country, and according to the work and activities performed by each volunteer. The finding

TABLE 6

Characteristics of the study population stratified by category of military service, National Health and Nutrition Examination Survey, 2011–2012

Characteristic	No military service	Military service—never deployed	Military service—deployed overseas	Total	P value
	Weighted population (%)	Weighted population (%)	Weighted population (%)	Weighted population (%)	
Sex					
Male	117,168,000 (45)	10,354,000 (91)	9,006,000 (94)	136,528,000 (48)	< 0.0001
Female	144,180,000 (55)	1,108,000 (9)	608,000 (6)	145,846,000 (52)	–
Age group					
6–14	37,958,000 (15)	0	0	37,958,000 (13)	< 0.0001
15–24	42,716,000 (16)	260,000 (2)	38,000 (0)	43,014,000 (15)	–
25–44	75,943,000 (29)	1,571,000 (14)	2,143,000 (22)	79,657,000 (28)	–
45–64	74,005,000 (28)	5,902,000 (45)	3,141,000 (33)	82,238,000 (29)	–
65+	30,726,000 (12)	4,489,000 (39)	4,293,000 (45)	39,508,000 (14)	–
Birth country					
United States	216,384,000 (83)	10,989,000 (96)	9,294,000 (97)	236,667,000 (84)	< 0.0001
Foreign	44,963,000 (17)	424,000 (4)	321,000 (3)	45,798,000 (16)	–
Race/ethnic group					
Caucasian	163,286,000 (62)	8,914,000 (78)	7,377,000 (77)	179,578,000 (64)	< 0.0001
African–American	31,595,000 (12)	1,212,000 (11)	1,205,000 (13)	34,012,000 (12)	–
Hispanic	47,073,000 (18)	517,000 (5)	622,000 (6)	48,212,000 (17)	–
Asian	12,647,000 (5)	39,000 (0)	88,000 (1)	12,774,000 (5)	–
Other	6,746,000 (3)	730,000 (6)	324,000 (3)	7,800,000 (3)	–
TB test results					
TST positive (≥ 10 mm)	11,782,000 (4.5)	207,000 (1.8)	318,000 (3.3)	12,307,000 (4.4)	0.065
QFT positive	12,473,000 (4.8)	506,000 (4.4)	705,000 (7.3)	13,684,000 (4.8)	0.428

TST = tuberculin skin test; QFT = Quantiferon® Gold-in-tube test.

of a higher risk of infection among civilian travelers such as PCVs was expected due to their greater expected intensity, duration, and proximity of exposure to cases of TB disease compared with most service members. Similarly, many long-term civilian travelers work in medical or other humanitarian capacities, which may put them at greater risk for TB infection than military personnel.

The incidence of LTBI associated with deployment was also lower than that seen in previous military populations (up to 15%).^{9,17,18} However, many of these previous estimates of infection during deployment were not able to exclude prevalent cases, resulting in overestimates of incidence. The effect

of mixing incident and prevalent LTBI cases was clearly seen in the Fort Jackson follow-up population, in which the naive analysis showed strong associations with foreign birth and race due to the inclusion of prevalent cases. Previous studies also suffered from cross-reactivity to NTM, use of Aplisol, and errors in TST administration, reading, and documentation.⁹ None of the previous studies compared the risk of infection among deployed soldiers to the risk among non-deployed soldiers, as was done in this study. Our findings are also similar to those found in a previous study of active TB disease, which showed no association between TB and deployed service members compared with non-deployed members.⁶

TABLE 7

Association of LTBI prevalence with military service, National Health and Nutrition Examination Survey, 2011–2012

Characteristic	TST positive (≥ 10 mm)		QFT positive	
	Bivariate OR (95% CL)	Multivariate OR* (95% CL)	Bivariate OR (95% CL)	Multivariate OR* (95% CL)
History of military service				
None	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)
Military service, but not overseas	0.39 (0.23, 0.68)	0.75 (0.37, 1.51)	0.93 (0.37, 2.32)	0.82 (0.31, 2.22)
Military service, including overseas	0.72 (0.31, 1.71)	1.32 (0.53, 3.25)	1.58 (0.88, 2.84)	1.36 (0.66, 2.81)
Sex				
Male	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)
Female	0.86 (0.69, 1.07)	0.85 (0.64, 1.11)	0.70 (0.54, 0.90)	0.66 (0.52, 0.84)
Age group (years)				
6–14	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)
15–24	2.86 (1.46, 5.58)	2.14 (1.01, 4.51)	3.28 (1.48, 7.24)	2.75 (1.23, 6.15)
25–44	6.13 (3.02, 12.4)	3.67 (1.63, 8.28)	5.27 (2.16, 12.9)	3.73 (1.63, 8.54)
45–64	6.60 (3.68, 11.8)	5.91 (2.80, 12.5)	8.46 (3.64, 19.7)	8.16 (3.64, 18.3)
65+	4.17 (2.45, 7.09)	5.27 (2.59, 10.7)	10.5 (4.99, 22.2)	13.0 (5.73, 29.3)
Birth country				
United States	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)
Foreign	17.7 (10.2, 30.6)	7.99 (4.79, 13.3)	6.72 (4.29, 10.5)	4.05 (2.41, 6.80)
Race/ethnic group				
Caucasian	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)
African–American	7.84 (4.08, 15.1)	7.80 (4.52, 13.5)	2.03 (1.36, 3.04)	2.32 (1.49, 3.62)
Hispanic	15.3 (6.91, 33.7)	4.84 (2.18, 10.8)	4.08 (2.63, 6.32)	2.30 (1.46, 3.93)
Asian	31.2 (16.7, 58.3)	6.85 (3.43, 13.7)	7.61 (4.96, 11.7)	3.11 (1.90, 5.07)
Other	3.26 (0.96, 11.0)	2.73 (0.69, 10.8)	1.09 (0.37, 3.19)	1.12 (0.35, 3.65)

CL = confidence limit; LTBI = latent tuberculosis infection; OR = odds ratio; QFT = Quantiferon Gold-in-tube test; TST = tuberculin skin test.

*Adjusted for all the variables listed in the table.

Study strengths include consistency in the findings seen among the three study populations. The enumerated Fort Jackson follow-up population had known baseline TST prevalence, allowing more accurate differentiation between prevalent and incident cases. The NHANES study population is a nationally representative sample, which is generalizable to the U.S. population and uses a rigorous study methodology. The main limitation of this study is the difficulty in obtaining valid estimates of incidence using retrospectively collected data, particularly in identifying and excluding prevalent cases from risk estimates. Prevalence estimates by definition do not provide estimates of risk or incidence. Other major limitations include the small sample size of these studies and the potential for misclassification of both exposure and outcome status due to incomplete or erroneous information in the TB test registry (MEDPROS) or electronic medical records. Failure to have the TST read or documented, which is known to have occurred frequently in MEDPROS before 2010,¹⁹ may have resulted in underestimates of LTBI incidence. Duration of deployment is variable among both units and individuals, so incidence rates may be a better reflection of TB transmission, although this has not been the case in previous studies.⁸ On the other hand, the TST is known to have poor positive predictive value in low-risk populations like the U.S. Army,⁹ so many of the incident cases in both groups may have been false positives, resulting in non-differential misclassification and overestimates of incidence. Since two-step testing is not performed in basic training, subsequent testing may also have resulted in boosted reactions, which could overestimate the true incidence of infection.

Misclassification of exposure may also have occurred, particularly history of deployment during service. We were surprised that so few among the Fort Jackson cohort had a record of a deployment during the 5-year follow-up period, and we found evidence of misclassification from the administrative databases during our medical record review. However, the similarity in the estimates of deployed and non-deployed individuals suggests that this misclassification may not be clinically meaningful. Non-deployed soldiers may have had other exposures to TB, such as residence in Korea, health-care work, or other established risk factors, which could account for the similarity of non-deployed LTBI incidence to deployed incidence.^{3,9} Because the risk of LTBI among deployed service members is heterogeneous, the summary estimates of risk presented here may obscure very real differences within special risk groups such as prisoners of war,²⁰ medical personnel,¹⁷ or prison/detainee workers.²¹

TB is a unique communicable disease threat to military forces, but the risk of TB resulting from deployment remains uncertain. The limitations of these retrospective studies demonstrate the challenges in obtaining valid estimates of risk using retrospective data. We strongly feel that due to these limitations and the uncertainty in the resulting estimates, a more definitive, prospective cohort study should be undertaken. Our hope is that publication of these data might draw attention to this gap in the literature and could perhaps motivate interest in funding such a study. Despite these limitations, we were able to estimate that the risk for infection during these deployments is probably low—0.6% in this study. In addition, there was no difference seen in LTBI incidence in deployed compared with non-deployed service members. Furthermore, the prevalence of infection in the U.S. popu-

lation was not significantly different between those who had served in the military—deployed or non-deployed—and their nonmilitary counterparts. Because the positive predictive values of all commercially available TB tests are low in low-risk populations,³ universal testing of this population will result in a large proportion of false positives. Nevertheless, similar to civilian travelers, focal risks for TB infection during deployment may occur among groups such as health-care workers, those guarding detainees or prisoners, and other groups. Therefore, military TB testing programs should focus on these higher-risk groups, consistent with national and Department of Defense guidelines for targeted testing.^{22,23} These recommendations have already been incorporated into current Army regulations.²⁴

These data also suggest that military TB testing and data collection procedures can be improved. For example, 50% of those testing positive after basic training had evidence of prior infection, suggesting that those performing this testing are not accurately identifying those who should be excluded from testing, such as prior positives. Providers and public health personnel who care for military or veterans populations should be aware that patients referred for positive tests may have been infected before military service and should consider this when making treatment decisions. Finally, those supervising TB testing programs should be aware of these common issues and take measures to ensure that TB testing programs adhere to military policies,²⁴ guidelines for targeted testing,²² and quality assurance guidelines in the administration, reading, and documentation of TB testing.^{14,15,25–27}

Received July 23, 2015. Accepted for publication August 10, 2015.

Published online September 28, 2015.

Financial support: The Infectious Disease Clinical Research Program (IDCRP) funded the Fort Jackson portion of this project.

Disclaimer: The opinions or assertions contained herein are the private ones of the author and are not to be construed as official or reflecting the views of the Department of Defense, the United States Army, or the Uniformed Services University of the Health Sciences.

Authors' addresses: James D. Mancuso, Division of Tropical Public Health, Department of Preventive Medicine and Biostatistics, Uniformed Services University of the Health Sciences, Bethesda, MD, E-mail: james.mancuso@usuhs.edu. Mia Geurts, Office of Student Affairs, Harvard Medical School, Boston, MA, E-mail: mgeurts@harvard.edu.

REFERENCES

1. Mancuso JD, Aaron CL, 2013. Tuberculosis trends in the U.S. Armed Forces, active component, 1998–2012. *MSMR* 20: 4–8.
2. Office of the Under Secretary for Personnel and Readiness, 2010. *Department of Defense Instruction NUMBER 6130.03: Medical Standards for Appointment, Enlistment, or Induction in the Military Services*. Washington, DC: Department of Defense.
3. Mancuso JD, Tribble D, Mazurek GH, Li Y, Olsen C, Aronson NE, Geiter L, Goodwin D, Keep LW, 2011. Impact of targeted testing for latent tuberculosis infection using commercially available diagnostics. *Clin Infect Dis* 53: 234–244.
4. Houk VH, Kent DC, Baker JH, Sorensen K, Hanzel GD, 1968. The Byrd study. In-depth analysis of a micro-outbreak of tuberculosis in a closed environment. *Arch Environ Health* 16: 4–6.
5. Lamar JE 2nd, Malakooti MA, 2003. Tuberculosis outbreak investigation of a U.S. Navy amphibious ship crew and the Marine expeditionary unit aboard, 1998. *Mil Med* 168: 523–527.
6. Mancuso JD, Tobler SK, Eick AA, Keep LW, 2010. Active tuberculosis and recent overseas deployment in the U.S. military. *Am J Prev Med* 39: 157–163.

7. Cobelens FG, van Deutekom H, Draayer-Jansen IW, Schepp-Beelen AC, van Gerven PJ, van Kessel RP, Mensen ME, 2000. Risk of infection with *Mycobacterium tuberculosis* in travellers to areas of high tuberculosis endemicity. *Lancet* 356: 461–465.
8. Freeman RJ, Mancuso JD, Riddle MS, Keep LW, 2010. Systematic review and meta-analysis of TST conversion risk in deployed military and long-term civilian travelers. *J Travel Med* 17: 233–242.
9. Mancuso JD, Tobler SK, Keep LW, 2008. Pseudoepidemics of tuberculin skin test conversions in the U.S. Army after recent deployments. *Am J Respir Crit Care Med* 177: 1285–1289.
10. Office of the Surgeon General, 2003. *The Army Latent Tuberculosis Infection (LTBI) Surveillance and Control Program*. Falls Church, VA: Department of the Army.
11. Office of the Surgeon General, 2008. *Supplemental Guidance for the Army Latent Tuberculosis Infection (LTBI) Surveillance and Control Program*. Falls Church, VA: Department of the Army.
12. Mancuso JD, Mazurek GH, Tribble D, Olsen C, Arosen NE, Geiter L, Goodwin D, Keep LW, 2012. Discordance among commercially available diagnostics for latent tuberculosis infection. *Am J Respir Crit Care Med* 185: 427–434.
13. Bennett DE, Courval JM, Onorato I, Agerton T, Gibson JD, Lambert L, McQuillan GM, Lewis B, Navin TR, Castro KG, 2008. Prevalence of tuberculosis infection in the United States population: the national health and nutrition examination survey, 1999–2000. *Am J Respir Crit Care Med* 177: 348–355.
14. Diagnostic Standards and Classification of Tuberculosis in Adults and Children, 2000. This official statement of the American Thoracic Society and the Centers for Disease Control and Prevention was adopted by the ATS Board of Directors, July 1999. This statement was endorsed by the Council of the Infectious Disease Society of America, September 1999. *Am J Respir Crit Care Med* 161: 1376–1395.
15. Mazurek GH, Jereb J, Vernon A, LoBue P, Goldberg S, Castro K, 2010. Updated guidelines for using interferon gamma release assays to detect *Mycobacterium tuberculosis* infection—United States, 2010. *MMWR Recomm Rep* 59(RR-5): 1–25.
16. Jung P, Banks RH, 2008. Tuberculosis risk in US Peace Corps Volunteers, 1996 to 2005. *J Travel Med* 15: 87–94.
17. Kortepeter MG, Krauss MR, 2001. Tuberculosis infection after humanitarian assistance, Guantanamo Bay, 1995. *Mil Med* 166: 116–120.
18. Emmons EE, Ljaamo SK, 1999. Active tuberculosis in a deployed field hospital. *Mil Med* 164: 289–292.
19. Aaron CL, Mancuso JD, 2014. Development and implementation of a cohort review for latent tuberculosis infection. *MSMR* 21: 2–7.
20. Long E, 1955. *Tuberculosis in the Army of the United States in World War II; An Epidemiological Study with an Evaluation of X-ray Screening*. Washington, DC: U.S. Government Printing Office.
21. Centers for Disease Control and Prevention, 2006. Prevention and control of tuberculosis in correctional and detention facilities: recommendations from CDC. Endorsed by the Advisory Council for the Elimination of Tuberculosis, the National Commission on Correctional Health Care, and the American Correctional Association. *MMWR Recomm Rep* 55(RR-9): 1–44.
22. Centers for Disease Control and Prevention, 2000. Targeted tuberculin testing and treatment of latent tuberculosis infection. American Thoracic Society. *MMWR Recomm Rep* 49(RR-6): 1–51.
23. Assistant Secretary of Defense for Health Affairs, 2012. *Guideline for Tuberculosis Screening and Testing*. Washington, DC: Department of Defense.
24. United States Army Medical Command, 2013. *MEDCOM Regulation 40-64: The Tuberculosis Surveillance and Control Program*. Department of the Army. Joint Base San Antonio, Fort Sam Houston, TX. Available at: <http://www.pdhealth.mil/tuberculosis.asp>. Accessed September 8, 2015.
25. Centers for Disease Control and Prevention, 2012. *Mantoux Tuberculin Skin Testing Products*. Available at: <http://www.cdc.gov/TB/education/Mantoux/default.htm>. Accessed October 18, 2014.
26. Jensen PA, Lambert LA, Iademarco MF, Ridzon R, 2005. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR Recomm Rep* 54(RR-17): 1–141.
27. Division of Tuberculosis Elimination, 2013. *Core Curriculum on Tuberculosis*, 6th edition. Atlanta, GA: Centers for Disease Control and Prevention.