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Characterization of the long-term health effects of Legionnaires' Disease among U.S. Veterans

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# Characterization of the long-term health effects of Legionnaires' Disease among U.S. Veterans

By

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Bachelor of Science in Nursing
Baker University
2013

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An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
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in Epidemiology
2018

# Abstract

Characterization of the long-term health effects of Legionnaires' Disease among U.S. Veterans

By Natasha Ross

Background: Legionnaires' Disease (LD) is responsible for 2-9% of community-acquired pneumonias in the U.S. (7). Previous research suggests there may be long-term health complications, but data is limited and no research extends beyond 2 years after post-LD infection. Our study characterizes the health effects of LD up to 5 years post-LD diagnosis and investigates whether an association exists between ICU admission during acute LD infection and negative health outcomes in 5-year follow-up. Methods: In this retrospective cohort study of 292 Veterans' Health Administration patients hospitalized between 2005 and 2010 with laboratory-confirmed LD, we collected data from electronic medical records on health history, LD severity (including ICU admission during LD hospitalization) and ICD-9 discharge diagnoses codes for 5 years post-LD or until death. Ordinal logistic regression was used to explore associations between ICU admission and risk of hospitalization after the incident LD admission. Results: Among the 161 veterans with at least one hospitalization within 5 years of their LD admission, among the most frequently observed discharge diagnoses for acute conditions were acute renal failure (n=49, 2.8%) and unspecified pneumonia (n=47, 2.7%). Patients admitted to the ICU during their qualifying LD visit were more likely to have a greater number of hospitalizations within 5 years compared to non-ICU patients ($OR_{Hosp}$ 1.92 $CI_{95\%}$ 1.25, 2.95). Conclusions: In addition to chronic conditions prevalent in this population, we found acute diagnoses that may warrant further research regarding their associations with LD. Findings also indicate that LD requiring ICU admission may be associated with more subsequent hospitalizations. Further research is needed regarding the prevalence of pre-existing conditions and their effects on hospital course for LD and other pneumonias, differences in health outcomes after pneumonias of different etiologies, and associations between the severity of incident pneumonias and adverse health outcomes.

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## Introduction

Legionnaires' Disease (LD), an acute pneumonia caused by bacteria in the genus *Legionella*, is estimated to be the cause of 2-9% of all community-acquired pneumonias in the U.S. (1). Unlike LD cases associated with widely publicized outbreaks, sporadic cases (i.e., cases never definitively associated with an outbreak) are likely under-recognized since non-specific pneumonia is often treated empirically with antibiotics. Because it is estimated that less than 5% of actual LD cases are ever identified and reported (2), the potential burden of disease caused by *Legionella* is likely much larger than currently estimated. Concomitantly, this under-recognition of acute LD cases precludes the ability to study long-term health outcomes associated with LD.

Current research on health outcomes following an LD diagnosis is limited, with most studies following LD cases for less than two years. In a 2008 Dutch cross-sectional study of health outcomes after Q-fever and LD, the 190 LD patients more frequently reported fatigue and poorer quality of life one year after their infection (3). Another study sampled 122 individuals who contracted LD during an outbreak in 1999 in the Netherlands and found that 64% had not attained their pre-illness quality of life 2 years following their LD episode (2002). Many also reported fatigue (75%), dyspnea (17%), memory loss and/or loss of concentration (66%); there was also evidence of neuromuscular dysfunction on account of reports of muscle ache and/or weakness (63%) (4). A smaller cross-sectional study conducted among 86 LD patients from the Netherlands in 2004 reported 24% of patients had pulmonary abnormalities in follow-up radiology exams at 18 months after acute infection, resulting in a 20% mean reduction in gas transport capabilities (3). While these studies followed LD cases for longer durations

than most, no studies to our knowledge have followed subjects beyond 2 years after LD diagnosis, and none have explored whether LD requiring ICU admission is associated with worse long-term health outcomes compared to non-ICU care for LD.

To help address these knowledge gaps in understanding the long-term health consequences of LD, our study leveraged the national electronic health record (EHR) system of the Veterans Health Administration (VHA) in the Department of Veterans Affairs (VA) to 1) characterize the health effects of LD up to 5 years post-LD diagnosis, and 2) investigate whether LD requiring ICU admission is associated with adverse long-term health outcomes, including the number and causes of subsequent hospitalizations within 5-years post-LD diagnosis.

## Methods

*Study populatio*n

The population in this study included individuals discharged from a VA medical facility in the U.S. or territories between federal fiscal year (FY) 2005 and FY 2010 with an International Classification of Diseases, 9$^{th}$ revision, Clinical Modification, (ICD-9-CM) diagnosis code for LD (482.84).

This study was conducted in conjunction with the VHA National Infectious Diseases Service located in Cincinnati, Ohio. The study protocol was reviewed by the Cincinnati VA Medical Center Research Service for adherence to VA patient privacy policy and approved by the University of Cincinnati Institutional Review Board (IRB), the IRB of record for the Cincinnati VA Medical Center (IRB#2017-3328).

*Data Collection*

To identify patients at VA medical facilities with an inpatient LD diagnosis between FY 2005 and FY 2010, the VHA Patient Treatment Files (PTF) were queried for the ICD-9-CM discharge diagnosis code for LD (482.84). Patients suspected of having LD via this initial ICD-9-CM search were then confirmed through medical chart review using the VHA EHR system for evidence of laboratory verification via urine antigen test (UAT) or respiratory culture. Discharge date of this "qualifying LD visit" was recorded from the medical record database search to calculate length of stay, and death dates were pulled from a search of the same national VA medical record database.

For all patients whose records indicated laboratory-confirmed LD, medical records were examined further for details on clinical course of the admission. Doctors' admission history and physical notes provided pertinent respiratory and immune history, including chronic obstructive pulmonary disease (COPD), emphysema, asthma, cancer, smoking and human immunodeficiency virus (HIV) status. Intensive care unit (ICU) admission data, including information on mechanical ventilation and sepsis diagnoses during the qualifying LD visit, were collected from doctors' and nurses' notes. ICU admission was considered a surrogate of LD case severity, as compared to cases not considered severe enough by clinicians to warrant ICU admission. Data on radiology studies, including x-ray and Computed Tomography (CT) scan results, were collected through radiology reports.

To collect data on long term health outcomes, LD case patients' social security numbers were used to search the PTF for all subsequent inpatient hospitalizations within the 5-year period after the LD qualifying visit. All ICD-9-CM discharge codes associated

with any hospitalization during this follow-up period were recorded to investigate associations between incident LD case severity and reasons for subsequent hospitalizations. Social security numbers, and other personal identifiers were removed prior to analysis.

*Statistical Analysis*

Differences in demographic characteristics, pre-existing conditions and indicators of disease severity between ICU-admitted and non-ICU-admitted patients were assessed using two-sided t-tests for continuous variables and Fisher's exact tests for categorical variables. Length of stay for the qualifying visit was calculated from admission and discharge dates, and differences were assessed with a two-sided t-test. Frequency counts were used to identify the primary ICD-9-CM codes most often observed at the first hospitalization after the qualifying LD visit; differences in frequencies of codes at subsequent hospitalizations between ICU and non-ICU LD cases were assessed using two-sided t-tests. Frequency counts were also used to find the ICD-9-CMcodes most often observed in the hospitalizations in the 5-year follow-up.

Ordinal logistic regression and unconditional logistic regression were used to assess the association between ICU admission and hospitalizations in the 5-year follow-up period. For the ordinal regression analyses, the outcome variable was defined by three groups: 0-1 subsequent hospitalizations, 2 subsequent hospitalizations, and 3 or more subsequent hospitalizations, according to the sample's hospitalization tertiles. The proportional odds assumption was assessed using log-log survival curves and goodness of fit tests. To assess confounding, any diagnosis of emphysema, asthma, and COPD were

condensed into one dichotomous chronic respiratory history variable to avoid over stratification of our limited sample. Similarly, any diagnosis of HIV and current or past history of cancer were also condensed into one dichotomous immunocompromised status variable. In the fully adjusted models, variables for age, respiratory history, smoking, immunocompromised status, and race were included. ICU was jointly tested with chronic respiratory history, age, and immunocompromised status, followed by backwards elimination for confounding assessment. A separate model using only respiratory history as a confounder was also used to assess the odds ratio for subsequent hospitalizations in ICU versus non-ICU LD patients.

To assess differences in time to hospitalization or death between ICU and non-ICU groups, Cox proportional hazard models were fit to calculate hazard ratios. Age, respiratory history, smoking, and immunocompromised status were considered confounders in these models.

## Results

The initial search of the national VA EHR for the ICD-9-CM diagnosis code for LD yielded 332 possible cases between FY 2005 – FY 2010. Twenty-two patients (6.6%) were excluded due to no evidence of confirmatory LD laboratory testing in their medical record [Figure 1]. Eighteen patients (5.8%) died during their qualifying LD visit; these individuals were also excluded from the study sample, leaving a cohort of 292 LD cases for analyses of long term health outcomes.

Demographic, select medical history, and LD severity indicators are presented in Table 1. The median age of study subjects was 61 years, and the cohort was primarily male (97.3%), white (73.3%), and a reported smoker (65.8%). While the proportions of patients presenting with asthma, emphysema, cancer and HIV at their qualifying LD visit were comparable between those admitted to the ICU and those not admitted to the ICU, the prevalence of COPD was significantly higher among the ICU group compared to the non-ICU group (36.2% vs. 21.0%; $p < 0.01$). Compared to the non-ICU group, ICU patients were also more frequently diagnosed with sepsis during admission (31.5% vs. 4.9%; $p < 0.01$), intubated (27.7% vs. 0.0%; $p < 0.01$), and had a longer length of stay (16.8 days vs. 6.1 days; $p < 0.01$).

Of the 292 patients in the study sample, 131 (45%) had no subsequent hospitalization recorded in the VA EHR in the 5 years following their incident LD hospitalization, with 34 dying without a subsequent hospitalization. For the remaining 161 patients with record of at least one subsequent hospitalization, the most common ICD-9-CM discharge diagnosis observed for the first hospitalization after incident LD admission was unspecified pneumonia (n=14, 8.7%) [Table 2]. This was substantially more than the next most frequent diagnoses of Coronary Atherosclerosis of Coronary Artery (n=6, 3.7%). When 26 hospitalizations occurring within 30 days of discharge for LD visit were excluded, pneumonia still occurred twice as frequently as the next most diagnosed condition (n=12) [Table 3]. Excluding 43 hospitalizations occurring within 60 days of discharge for LD visit, pneumonia was still more frequent than any other diagnosis (n=11) [Table 4]. While more diagnoses of respiratory illness including pneumonia were observed at first hospitalization post-LD among ICU cases (15) than

non-ICU cases (10), association between ICU admission and respiratory illness at first hospitalization did not reach statistical significance and was attenuated further upon adjustment for the aforementioned pre-existing conditions [Table 6].

For the entire 5-year follow-up period, the most common ICD-9-CM discharge diagnosis for subsequent hospital admissions was unspecified hypertension (n=79, 4.5%) [Table 5]. Included within the most frequently observed discharge diagnoses found in LD patients during 5-year follow-up were the following acute diagnoses: acute renal failure (n=49, 2.8%), and unspecified pneumonia (n=47, 2.7%), as well as the following chronic diagnoses: chronic airway obstruction (n=38, 2.2%) and end-stage renal disease (n=20, 1.1%).

In regards to the number of hospitalizations within 5 years following the qualifying LD visit, cases admitted to the ICU during their qualifying visit were more likely to have a greater number of hospitalizations within 5 years compared to non-ICU cases ($OR_{Hosp}$ 1.92 $CI_{95\%}$ 1.25, 2.95). [Table 6] This association remained statistically significant after adjusting for age, immunocompromised status, smoking, and respiratory history ($OR_{HospAdj}$ 1.93 $CI_{95\%Adj}$ 1.25, 3.00).

Average time to first hospitalization after incident LD admission was 29.5 months in ICU-admitted LD patients and 36.1 months in non-ICU-admitted LD patients. Time to first hospitalization was significantly shorter in ICU patients compared with non-ICU patients ($HR_{Crude}$ 1.46, 95% CI: 1.06, 2.02), an association which became non-significant after adjustment for respiratory history alone ($HR_{RespAj}$ 1.37, 95% CI: 0.98, 1.90) and remained significant after full adjustment for age, smoking, respiratory history, and immunocompromised status ($HR_{Adj}$ 1.46 $CI_{95\%Adj}$ 1.05, 2.04). Age, respiratory history,

smoking, immunocompromised status, and ICU admission were assessed for proportional hazards, and found to have no significant violations in graphical log-log survival curves, goodness of fit testing, and time-dependent variable testing.

## Discussion

As the first study to explore health-related outcomes of Legionnaires' disease patients beyond 2 years post-LD diagnosis, this work begins to offer insights into the longer-term health outcomes and consequences of LD. We found unspecified pneumonia to be the most frequently cited discharge diagnosis code for a first hospitalization after an admission for LD, occurring more than twice as frequently than the next most diagnosed condition (n=14). When discharge diagnosis codes from first hospitalizations within 30 or 60 days of the incident LD admission were excluded, unspecified pneumonia remained the most frequent diagnosis, thus supporting the hypothesis that these pneumonias were likely not continuations of the incident LD episode. During the entire 5-year follow-up period, unspecified pneumonia was also frequently observed, as were chronic respiratory disorders, chronic and acute kidney disorders, and chronic cardiac disorders. We also found that admission to an ICU during an LD hospitalization significantly increased the likelihood of subsequent hospitalization compared to non-ICU LD cases, a finding that suggests that LD infections resulting in an ICU admission may play a role in increased morbidity after the LD episode.

With so little known on the long-term health consequences of LD, especially among cases never linked to an LD outbreak, this largely descriptive study generates numerous hypotheses worthy of further exploration. Our study also begins to examine whether LD resulting in an ICU admission impacts long term health. In our analysis, LD

requiring ICU admission was associated with a higher average number of hospitalizations in the 5-year follow-up period and a shorter time to first subsequent hospitalization than non-ICU LD cases. This included a non-significant but increased likelihood of subsequent hospitalizations for pneumonia. With further study, we may be able to discern if this finding is unique to LD, or if similar frequencies of pneumonia are observed following hospitalization for pneumonias of other etiologies.

Chronic and acute kidney disorders were also frequently observed in follow-up. Because ICU can be used as a surrogate for severity, and admission to the ICU for any reason is known to be associated with subsequent morbidity, especially in elderly populations, further research is needed to determine whether the increased risk for subsequent hospitalizations observed here is different from the risk for rehospitalization following ICU admission for other reasons (6). Furthermore, it will be imperative within said studies to rigorously control for preexisting conditions that would precipitate ICU admission and contribute to adverse health outcomes regardless of the disease exposure of interest. Additional research into the outcomes of severe LD compared to less severe LD would be well served by including comparisons to ambulatory or non-hospitalized cases. Comparing LD cases to patients diagnosed with pneumonia of other etiologies will also be prudent and shed light onto whether LD pneumonia has a different morbidity or mortality profile over time compared to pneumonias caused by other pathogens.

Because the intent of this study was to identify and characterize all hospitalized cases of LD in the VA medical system from FY 2005 to FY 2010, we did not identify a comparison group, nor did we explore outpatient records related to non-hospitalized cases. A particular strength of this study however was the availability and accessibility

of LD patients' medical records in the national VA EHR system, allowing for long-term follow-up of a large cohort of patients. A comparable dataset is not as readily available from private sector healthcare records.

The limited number of studies that have examined health outcomes after LD have found decreases in reported quality of life, with reports of fatigue, dyspnea, muscle aches, and weakness being common (4). Many of the most frequently observed ICD-9-CM discharge codes observed within the 5-year follow-up period of our study would likely be associated with these same symptoms in clinical presentation; pneumonia, acute kidney failure, and chronic airway obstruction can all contribute to the aforementioned symptoms. Moreover, our findings align with the observation from a study which found that nearly a quarter of 122 LD patients from a March 1999 LD outbreak in the Netherlands still had pulmonary abnormalities 16 months after their acute LD infection (3). It is possible these abnormalities could contribute to discharge codes of unspecified pneumonia, unspecified atrial fibrillation, and chronic airway obstruction.

Our study has some other important strengths and limitations. First, this is the first study to attempt to examine health outcomes of LD cases regardless of their connection to an identified outbreak. The VA has had long-standing policy for preventing LD, including policy initiated in 2008 encouraging routine testing of pneumonia patients for LD. While the extent of this testing is not known, the policy likely promoted the diagnosis and therefore availability of a sizable number of LD cases for this analysis (n=292) regardless of their association, or lack thereof, to an outbreak. By not being limited to outbreak-associated cases and by being able to rely entirely on medical records

to examine case histories (as opposed to patient self-report), this study may have reduced reporting bias.

Utilization of data in medical records, including administrative discharge coding, has limitations. First, we were limited in our ability to distinguish chronic ICD-9-CM discharge codes (as evidence of pre-existing conditions) from new conditions diagnosed after the incident LD admission. This limited our ability to identify trends in development of chronic conditions after LD admission in our 5-year follow-up. Since we did not collect complete health histories on each case, it is possible that the incident and follow-up hospitalizations observed were simply a reflection of pre-existing conditions leading to poor overall health status. Even if the conditions were pre-existing, our conclusions would suggest that, for patients with pre-existing conditions, a severe LD infection resulting in an ICU stay may increase their risk of hospitalization in the following years. For these patients especially, our findings emphasize the necessity of definitive diagnostic testing and expedient delivery of appropriate antibiotics after identifying pneumonia. Second, while working with the VA EHR records afforded us the ability to track patients longitudinally regardless of which VA facility they visited, it is well known that patients served by the VA health system are not representative of the general U.S. population; they are disproportionately male, more sick and poorer (6). They may also receive care outside the VA healthcare system, and we did not attempt to obtain data from external healthcare providers to supplement our analyses. Despite these challenges, when adjusted for indicators of poor health status (e.g., respiratory history and immunocompromised status), the trend of increased hospitalizations after LD admission remained significant.

This study offers unique insight to differences between ICU-admitted and non-ICU admitted patients with LD, and provides a basis for understanding long term health effects of this disease. The availability of the VA EHR data used in this study demonstrates opportunities to evaluate and compare outcomes from different admission diagnoses and the health conditions found long after those admission. Further research regarding the prevalence of pre-existing conditions and their effect on hospital course for LD and other pneumonias, the differences in health outcomes after pneumonias of different etiologies, and the associations between those outcomes and the severity of incident pneumonia will add to our understanding of the impact of LD on health.

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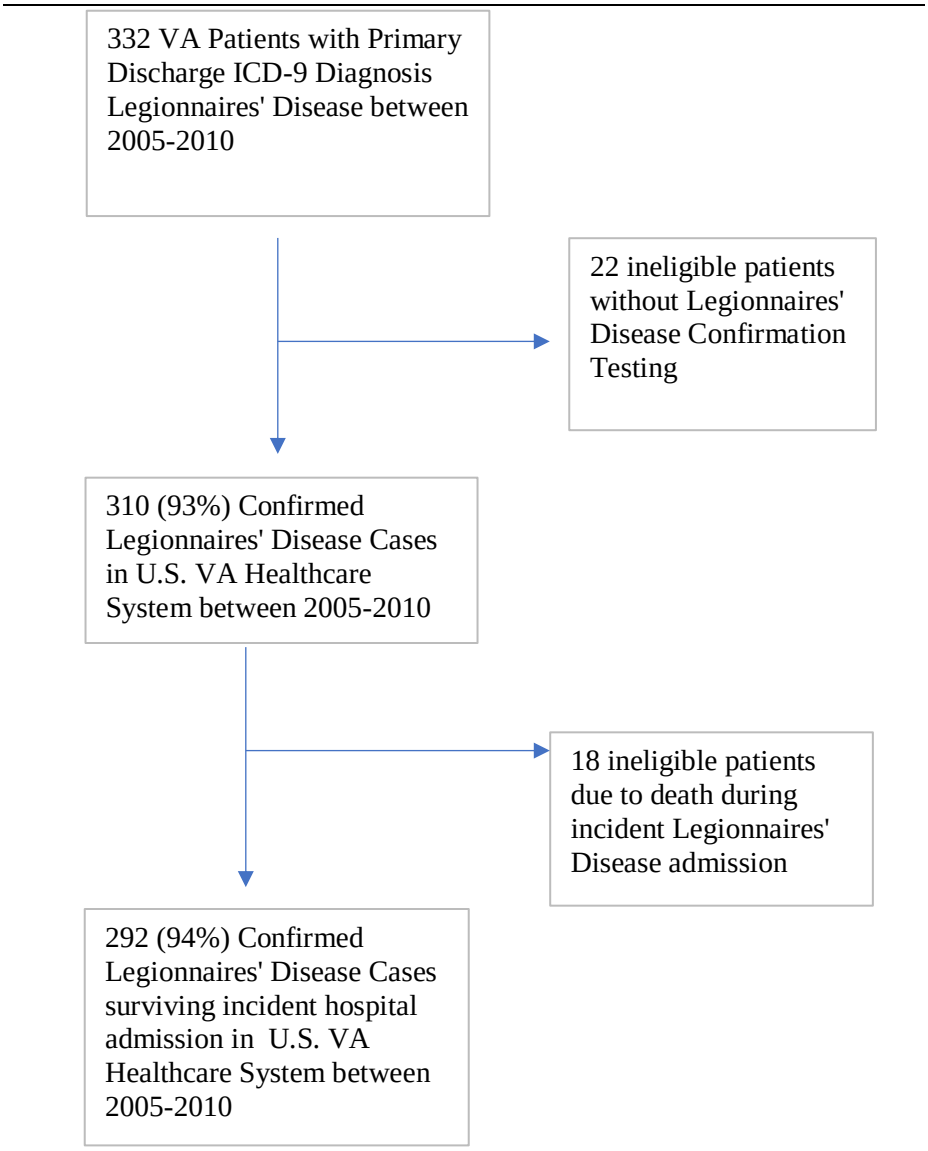
Figure 1. Study Population Selection from 332 VA Patients Discharged with Primary ICD-9 Diagnosis Legionnaires' Disease between 2005-2010




Abbreviations: VA Veteran's Affairs, ICD-9 International Classification of Diseases, 9th revision, Clinical Modification

Table 1. Demographics, Select Medical History, Legionnaires' Disease Severity Indicators, and Mortality of 292 Veterans Diagnosed with Legionnaires' Disease between 2005 - 2010 in any U.S. VA Hospital

| | | All Patients (n=292) | | ICU Admitted Patients (n=130) | | Non-ICU Admitted Patients (n=162) | | $p_a$ |
|---|---|---|---|---|---|---|---|---|
| Age at Admission | 25% | 56 | | 58 | | 56 | | 0.72 |
| | Median | 61 | | 61 | | 61.5 | | |
| | 75% | 71 | | 71 | | 71 | | |
| | 100% | 89 | | 89 | | 89 | | |
| | | n | % | n | % | n | % | |
| Men | | 284 | 97.3 | 125 | 96.1 | 159 | 98.1 | 0.47 |
| Women | | 8 | 2.7 | 5 | 3.9 | 3 | 1.9 | |
| White | | 214 | 73.3 | 96 | 73.9 | 118 | 72.8 | 0.73 |
| Black | | 69 | 23.6 | 31 | 23.9 | 38 | 23.5 | |
| Hispanic | | 2 | 0.7 | 0 | 0 | 2 | 1.2 | |
| Asian | | 2 | 0.7 | 1 | 0.8 | 1 | 0.6 | |
| Native American | | 5 | 1.7 | 2 | 1.5 | 3 | 1.9 | |
| Smoker at Incident Admission | | 192 | 65.8 | 89 | 68.5 | 103 | 63.6 | 0.39 |
| HIV Positive | | 10 | 3.4 | 4 | 3.1 | 6 | 5.5 | 0.77 |
| COPD | | 81 | 27.7 | 47 | 36.2 | 34 | 21 | <0.01 |
| Emphysema | | 2 | 0.7 | 1 | 0.8 | 1 | 0.1 | 0.88 |
| Asthma | | 11 | 3.8 | 5 | 3.9 | 6 | 3.7 | 0.95 |
| Cancer | | 66 | 22.6 | 24 | 18.5 | 42 | 25.9 | 0.13 |
| Diagnosed Septic at Admission | | 49 | 16.8 | 41 | 31.5 | 8 | 4.9 | <0.01 |
| Intubated during Admission | | 36 | 12.3 | 36 | 27.7 | 0 | 0 | <0.01 |
| Length of Stay (+ sd) | | 11.5 | (±19.45) | 16.8 | (± 34.5) | 6.1 | (± 4.4) | <0.01 |
| Mortality in Follow-up | | 90 | 30.8 | 41 | 31.5 | 49 | 30.3 | 0.81 |

Abbreviations: V.A. Veterans Affairs, ICU Intensive Care Unit, HIV Human Immunodeficiency Virus, COPD Chronic Obstructive Pulmonary Disease, sd Standard Deviation

a p-values assessed with t-test of differences in means for continuous variables and Fisher's Exact Test for Dichotomous Variables

Table 2. Frequency of Primary ICD-9 Diagnosis Code for First Subsequent Hospitalization After Incident Legionnaires' Disease Hospitalization[a] among VA Patients to any US[b] VA Hospital Between 2005-2010

| Diagnosis | ICD-9 Code | Frequency (n=161) | Percentage |
|---|---|---|---|
| Pneumonia, unspecified | 486 | 14 | 8.7 |
| Coronary Atherosclerosis of Coronary Artery | 41401 | 6 | 3.7 |
| Obstructive Chronic Bronchitis with Acute Exacerbation | 49121 | 4 | 2.5 |
| Depressive Disorder | 311 | 4 | 2.5 |
| Hyperpotassemia | 2767 | 3 | 1.9 |
| Acute Pancreatitis | 5770 | 3 | 1.9 |
| Urinary Tract Infection | 5990 | 3 | 1.9 |
| Cellulitis of Leg | 6826 | 3 | 1.9 |
| Drug Induced Mood Disorder | 29284 | 3 | 1.9 |
| Cerebral Artery Occlusion with Cerebral Infarction | 43491 | 3 | 1.9 |
| Legionnaires' Disease Pneumonia | 48284 | 3 | 1.9 |
| Acute Respiratory Failure | 51881 | 3 | 1.9 |
| Chest Pain | 78659 | 3 | 1.9 |

Abbreviations: VA Veteran's Affairs', ICD-9 International Classification of Diseases, 9th revision, Clinical Modification

a Considered Legionnaires' Disease Diagnosis if Primary Discharge Code according to ICD-9 CM Discharge Diagnosis Code was 482.84 Legionnaire's Disease

b Hospitals in Puerto Rico were considered as U.S. VA Hospitals, as well as hospitals within all 50 U.S. states

Table 3. Frequency of Primary ICD-9 Diagnosis Code for First Subsequent Hospitalization After Incident Legionnaires' Disease Hospitalization among VA Patients to any US VA Hospital Between 2005-2010, Excluding Hospitalizations within 30 Days of Incident Legionnaires' Hospitalization Discharge

| **Diagnosis** | **ICD-9 Code** | **Frequency (n=135)** | **Percentage** |
|---|---|---|---|
| Pneumonia, unspecified | 486 | 12 | 8.9 |
| Coronary Atherosclerosis of Coronary Artery | 41401 | 6 | 4.4 |
| Obstructive Chronic Bronchitis with Acute Exacerbation | 49121 | 4 | 3.0 |
| Depressive Disorder | 311 | 4 | 3.0 |
| Acute Pancreatitis | 5770 | 3 | 2.2 |
| Urinary Tract Infection | 5990 | 3 | 2.2 |
| Cellulitis of Leg | 6826 | 3 | 2.2 |
| Drug Induced Mood Disorder | 29284 | 3 | 2.2 |
| Acute Respiratory Failure | 51881 | 3 | 2.2 |
| Congestive Heart Failure, Unspecified | 4280 | 3 | 2.2 |

Abbreviations: VA Veteran's Affairs', ICD-9 International Classification of Diseases, 9th revision, Clinical Modification

Table 4. Frequency of Primary ICD-9 Diagnosis Code for First Rehospitalization After Incident Legionnaires' Disease Hospitalization among VA Patients to any US VA Hospital Between 2005-2010, Excluding Hospitalizations within 60 Days of Incident Legionnaires' Hospitalization Discharge

| Diagnosis | ICD-9 Code | Frequency (n=118) | Percentage |
|---|---|---|---|
| Pneumonia, unspecified | 486 | 11 | 9.3 |
| Coronary Atherosclerosis of Coronary Artery | 41401 | 6 | 5.1 |
| Obstructive Chronic Bronchitis with Acute Exacerbation | 49121 | 4 | 3.4 |
| Depressive Disorder | 311 | 3 | 2.5 |
| Acute Pancreatitis | 5770 | 3 | 2.5 |
| Cellulitis of Leg | 6826 | 3 | 2.5 |
| Drug Induced Mood Disorder | 29284 | 3 | 2.5 |
| Acute Respiratory Failure | 51881 | 3 | 2.5 |
| Congestive Heart Failure, Unspecified | 4280 | 3 | 2.5 |

Abbreviations: VA Veterans Affairs, ICD-9 International Classification of Diseases, 9th revision, Clinical Modification

Table 5. Most Frequent ICD-9 Discharge Diagnosis Codes in 5-year Follow-up after Incident Legionnaires' Disease in U.S. Veterans

| Diagnosis | ICD-9 Code | Frequency (n=1756) | Percentage |
|---|---|---|---|
| Unspecified Hypertension | 4019 | 79 | 4.5 |
| Diabetes Mellitus without Complication | 25000 | 64 | 3.6 |
| Acute Kidney Failure, Unspecified | 5849 | 49 | 2.8 |
| Unspecified Atrial Fibrillation | 42731 | 48 | 2.7 |
| Unspecified Pneumonia | 486 | 47 | 2.7 |
| Congestive Heart Failure, Unspecified | 4280 | 42 | 2.4 |
| Chronic Airway Obstruction, not elsewhere classified | 496 | 38 | 2.2 |
| Other and Unspecified Hyperlipidemia | 2724 | 36 | 2.0 |
| Coronary Atherosclerosis of Coronary Artery | 41401 | 36 | 2.0 |
| Obstructive Bronchitis with Acute Exacerbation | 49121 | 34 | 1.9 |
| Hypertensive Chronic Kidney Disease | 40390 | 26 | 1.5 |
| End Stage Renal Disease | 5856 | 20 | 1.1 |

Abbreviations: VA Veterans Affairs, ICD-9 International Classification of Diseases, 9th revision, Clinical Modification

Table 6. Crude and Adjusted Associations of Subsequent Hospitalizations in ICU versus Non-ICU Veterans in any U.S. VA Hospital Diagnosed with Legionnaires' Disease between 2005 - 2010

| | **OR** | **95% Confidence Interval** |
|---|---|---|
| Crude Hospitalization after Incident Admission in 5-year Follow-up[a] | 1.92 | (1.25, 2.95) |
| Hospitalization Fully Adjusted[a] | 1.93 | (1.25, 3.00) |
| Crude First Hospitalization for Respiratory Diagnosis after Incident LD Admission[bc] | 1.98 | (0.86, 4.57) |
| First Hospitalization for Respiratory Diagnosis Fully Adjusted[b] | 1.77 | (0.75, 4.18) |
| Crude First Hospitalization for Pneumonia Diagnosis after Incident LD Admission[b] | 2.05 | (0.77, 5.44) |
| First Hospitalization for Pneumonia Diagnosis Fully Adjusted[b] | 1.74 | (0.63, 4.80) |

Abbreviations: ICU Intensive Care Unit, V.A. Veterans Affairs, LD Legionnaires' Disease, OR Odds Ratio

a Found using ordinal logistic regression model, with fully adjusted models adjusting for age, respiratory history, immunocompromised history, and smoking at time of incident admission

b Found using logistic regression model with fully adjusted models adjusting for age, respiratory history, immunocompromised history, and smoking at time of incident admission

c Respiratory Diagnoses included Legionnaires' Disease, Unspecified Pneumonia, Acute Bronchitis, Klebsiealla Pneumonia, Pleural Effusion, Pneumothorax, Obstructive Chronic Bronchitis with Acute Exacerbation, Acute Respiratory Failure, and Tachypnea