HHS Public Access

Author manuscript

Vaccine. Author manuscript; available in PMC 2016 April 06.

Published in final edited form as:

Vaccine. 2015 December 8; 33(49): 6970–6976. doi:10.1016/j.vaccine.2015.09.115.

Risk factors for severe outcomes among members of the United States military hospitalized with pneumonia and influenza, 2000–2012

Maria D Van Kerkhove[1,2], **Michael J. Cooper**[3], **Angelia A. Eick-Cost**[3,4], **Jose L. Sanchez**[4], and **Steven Riley**[1]

[1]MRC Centre for Outbreak Analysis and Modelling, Department of Infectious Disease Epidemiology, Imperial College London, London UK W2 1PG

[2]Center for Global Health, Institut Pasteur, Paris France 75015

[3]Armed Forces Health Surveillance Center, 11800 Tech Road, Suite 220, Silver Spring, MD, 20904 USA

[4]Cherokee Nation Technology Solutions, in support of the Armed Forces Health Surveillance Center, 11800 Tech Road, Suite 220, Silver Spring, MD 20904 USA

Abstract

Background—The progression from hospitalization for a respiratory infection to requiring substantial supportive therapy is a key stage of the influenza severity pyramid. Respiratory infections are responsible for 300,000 to 400,000 medical encounters each year among US military personnel, some of which progress to severe acute respiratory infections.

Methods—We obtained data on 11,086 hospitalizations for pneumonia and influenza (P&I) among non-recruit US military service members during the period of 1 January 2000 through 31 December 2012. From these, we identified 512 P&I hospitalizations that progressed to severe episodes using standard case definitions. We evaluated the effect of demographic and occupational characteristics, comorbid conditions, and history of influenza vaccination on the risk of a hospitalized P&I case becoming a severe case. We also evaluated the risk of a severe outcome and the length of time since influenza vaccination (within 180, 60 and 30 days).

Results—The median age of subjects at the time of the P&I episode was 32 years (range, 28–40) and subjects were predominantly male (89.5%). In a univariate analysis, demographic risk factors for a severe episode included service in the US Air Force (RR=1.6 relative to US Army, 95%CI 1.3-2.1), US Coast Guard (RR=2.1, 1.2-3.7) or US Navy (RR=1.4, 1.1-1.8). Being born in the US and recent influenza vaccination (within 180 days of episode) were protective against developing severe disease. Among comorbid conditions, univariate risk factors for severe disease included chronic renal or liver disease (RR=4.98, 95%CI 4.1-6.1), diseases of the circulatory system (RR=3.1, 95%CI 2.6-3.7), diabetes mellitus (RR=2.3, 95%CI 1.5-3.6), obesity (RR=1.6, 95%CI

Corresponding author: Head, Outbreak Investigation Task Force, Center for Global Health, Institut Pasteur, Paris France, maria.van-kerkhove@pasteur.fr, Phone: + 33 6 77 94 83 56.

Conflict of Interest Statement

The authors report no conflicts of interest.

1.2-2.1), cancer (RR=1.6, 95%CI 1.3-2.0) and chronic obstructive pulmonary disease (RR=1.4, 95%CI 1.1-1.7). Although many of the risk factors found to be significant in univariate analysis were no longer significant under a multivariate analysis, receipt of any influenza vaccine within 180 days of episode remained protective (RR=0.81, 95%CI 0.67-0.99), while serving in the US Coast Guard (RR=1.9, 95%CI 1.1-3.4) or US Air Force (RR=1. 5, 95%CI 1.2-2.0), presence of renal or liver disease (RR=3.6, 95%CI 2.9-4.6) and diseases of the circulatory system (RR=2.2, 95%CI 1.8-2.8), remained significantly associated with a higher risk of developing severe disease.

Conclusions—In a large cohort, after adjusting for many possible risk factors, influenza vaccination was protective against severe episodes among P&I hospitalizations. The service-specific (US Coast Guard or US Air Force) increased risk may represent some differences in data (e.g., coding or reporting practices) as opposed to genuine differences in physiological outcome. Our findings suggest that renal and liver disease as well as diseases of the circulatory system may contribute to influenza severity in this population independently of age and other potential comorbidities. These findings provide additional evidence for the prioritization of specific risk groups within the US military for influenza vaccination.

Keywords

pneumonia; influenza; vaccination; risk factors; military

Introduction

The burden of influenza in the United States (US) is significant, typically affecting the very young and old, those with chronic health conditions and pregnant women. Among the general population, many aspects of respiratory diseases, particularly influenza, are well studied and monitored through the US Centers for Disease Control and Prevention surveillance systems[1]. Historically, military populations have been at high risk of acute influenza-related respiratory illnesses, especially among recruits and during fall-winter months [2, 3]. The living, environmental, and physical conditions of US military personnel have been shown to compromise the immune systems of recruits leading to higher levels of respiratory disease when compared to non-military recruits [2, 4, 5]. The burden of severe illness due to influenza in the US military population as a whole, however, is largely unknown.

During the 1918 influenza pandemic, the US military experienced attack rates as high as 25% and case fatality rates averaging 5% (ranging from 1–8%)[6]. During the 2009 pandemic, attack rates among military personnel measured during clusters of infection among specific military units ranged from as low as 3% [7] and as high as 70% [8]. In confined settings, such as aboard navy ships, serologic attack rates of influenza among US and foreign military crew have been estimated to be between 30–50% [9, 10]. Estimates of the proportion of the US military infected with influenza, risk factors for severe outcomes among those infected with influenza, and trends in incidence and cross-protective immunity are important for understanding the burden of influenza in this unique cohort.

The US military has played a key role in the development, deployment, and management of influenza vaccines for the US population at-large. For example, the US military led the

development of influenza vaccines in the late 1930's when Drs Salk and Francis developed the first inactivated vaccines which were used to protect US military personnel during the World War II [11]. The US military was also the first institution which established a universal influenza vaccination policy in the early 1940's, many decades before widespread immunization of healthy young people was recommended by the CDC and other international health officials[12].

The Global Emerging Infections Surveillance and Response System (GEIS), now part of the Armed Forces Health Surveillance Center (AFHSC), of the US Department of Defense was established in 1997 to provide surveillance for respiratory infections and other global emerging infections among US military personnel. Respiratory infections and illnesses remain one of the leading causes of medical encounters and lost work time of service members [13–15]. Incidence of pneumonia and influenza (P&I) typically follow a seasonal pattern with the highest incidence in the winter months of the northern hemisphere [16]. An exception was during the 2009 pandemic when there were peaks in the spring as well as autumn months of 2009, followed by a winter peak in 2009–2010 [16]. The AFHSC has found that respiratory infections account for between 300,000 and 400,000 medical encounters annually among Service Members[17, 18].

The principal objective of this study was to evaluate and quantify demographic, immunologic, occupational and medical risk factors associated with severe P&I outcomes among non-recruit US military personnel who were hospitalized anytime between 1 January 2000 and 31 December 2012.

Methods

Data analyses

We obtained data on the active component US military personnel who had an inpatient diagnosis of P&I between 1 January 2000 and 31 December 2012. We further classified the P&I episodes as severe or non-severe using the criteria and ICD-9 codes presented in Table 1. We excluded individuals who were classified as a recruit at the time of the episode. Data on potentially important demographic (e.g., country of origin, race-ethnicity, age, sex) and occupational (e.g., occupation, service, rank) characteristics that may influence the risk of a hospitalized P&I episode becoming a severe episode were obtained for each subject.

In addition to standard demographic and occupational variables, we also investigated the potential role of other health-related comorbidities and the risk of a P&I becoming severe including pregnancy, asthma, chronic obstructive pulmonary disease (COPD), disease of the circulatory system, diabetes mellitus (DM), sickle cell disease, chronic kidney and liver disorders, cancer, and chronic immunosuppressive conditions or human immunodeficiency virus (HIV) infection. For example, we considered the presence of an encounter for asthma or DM at any time prior to an admission for P&I as a potential risk factor for a severe outcome as a result of hospitalization. Additionally, we evaluated whether prior influenza vaccination (e.g., prior vaccination [Yes/No]) and vaccination within 180 days, 60 days and 30 days of the P&I episode influenced the risk of severe P&I. The type of vaccination including inactivated split virus vaccine (CVX code 15), inactivated whole virus Influenza

virus vaccine for intramuscular or jet injection use (CVX code 16), live attenuated influenza virus vaccine (LAIV) for intranasal use (CVX code 111), and unspecified influenza virus vaccine (CVX code 88) was also evaluated for their potentially protective effects.

De-identified data was obtained from the Defence Medical Surveillance System, AFHSC, Silver Spring, Maryland [data from 2000–2012; released on 14 August 2013]. We conducted univariate analyses using generalized linear models and estimated the relative risk (RR) of a severe episode among all hospitalized P&I episodes. Variables that were statistically significant ($p<0.05$) in the univariate model were included in a multivariate model. Analyses were conducted in Stata and R. These analysis build on previous studies [15–16] by testing specific hypotheses about the factors that cause hospitalized P&I to become SARI within a multivariate statistical model. The earlier work focussed on describing the unadjusted trends in these outcomes.

IRB Approval

IRB approval was sought and granted by the Imperial College Ethics Committee and the project was deemed public health surveillance by the US Army Public Health Command Human Protections Administrator and the Naval Medical Research Center, Office of Research Administration.

Results

We identified 11,053 hospitalized P&I inpatient clinical episodes that occurred among 10,384 unique individuals during the 12-year study period. There were a total of 10,541 non-severe and 512 severe P&I inpatient encounters among the study population meeting the case definitions shown in Table 1. The proportion of P&I episodes by northern hemisphere influenza season are shown in Figure 1A (primary axis). The largest proportion of severe P&I episodes over the 12-year study period was during the 2009–2010 northern hemisphere influenza season.

Demographic, occupational and underlying conditions

Overall, the median age of subjects experiencing an inpatient P&I episode during the study period was 32 years (range 19–72) at the time of event and our study cohort was predominantly male (92.8%; n= 9,638/10,384) and Caucasian (64.8%). Approximately one-half (53.2%) were serving in the US Army at the time of the P&I episode (Table 1; Figure 2). The majority of these subjects were serving in the US Army at the time of the P&I episode (Table 2, Figure 2).

The demographic and occupational characteristics of the severe (n=512) and non-severe (n=10,541) patients at the time of hospitalization episode are shown in Table 2. The median age of patients at the time of the hospitalization was similar between patients who experienced severe P&I and patients hospitalised for non-severe P&I episode (33 vs. 32 years old, p=0.08). The majority of subjects were serving in the US at the time of their episode (85.4%), and were born in the US (76.7%).

Univariate analysis

Univariate risk factors for severe P&I include service in the US Air Force (RR=1.6, 95% CI 1.2-3.7), US Coast Guard (RR=2.1, 95% CI 1.2-3.7) or US Navy (RR=1.4, 95% CI 1.1-1.8) relative to the risk in the US Army (Table 2). Birth in the US (compared to outside the US) was protective against severe P&I episodes (RR=0.80, 95% CI 0.65-0.98). There were no differences in country of service (US vs. non-US) or ethnicity among subjects experiencing a severe vs. non-severe P&I episode.

The proportion of underlying medical conditions diagnosed before the P&I episode among the included subjects is shown in Table 2. Among severe P&I episodes, diseases of the circulatory system (51.4%) were most often detected, followed by chronic renal or liver diseases (31.6%), cancer (26.8%), COPD (21.7%), asthma (14.3%) and obesity (13.7%). In univariate analyses, risk factors for severe P&I include chronic or liver disease (RR=4.98, 95% CI 4.1-6.1), DM (RR=2.3, 95% CI 1.5-3.6), obesity (RR=1.6, 95% CI 1.2-2.1), cancer (RR=1.6, 95% CI 1.3-2.0), asthma (RR=1.3, 95% CI 1.0-1.7), diseases of the circulatory system (RR=3.1, 95% CI 2.6-3.7), and COPD (RR=1.4, 95% CI 1.1-1.7).

The proportions of subjects experiencing a hospitalized P&I episode who were vaccinated for influenza are shown by influenza season are shown in Figure 1A (secondary axis). Over the course of the 12-year study period, 42.9% of subjects experiencing a hospitalized P&I episode were vaccinated for influenza in the six months prior to the episode. However, vaccination coverage varied by year, with the highest vaccination coverage occurring during the H1N1 pandemic between 2009 and 2011 (Figure 1A secondary axis). The type of influenza vaccine used varied by influenza season (Figure 1B). Intranasal vaccine was introduced during the 2004–2005 influenza season and was the most frequently used vaccine from 2007 onward.

In univariate analyses, vaccination for influenza of any type administered in the six months prior to the P&I episode had a protective effect against developing severe disease (RR=0.74, 95% CI 0.62-0.89). Slightly different protective effects were observed for various vaccine types, including LAIV (CVX code 111) introduced during the 2004–2005 influenza season (RR=0.70, 95% CI 0.54-0.91) and the inactivated split influenza virus vaccine (CVX code 15) used throughout the entire study period (RR=0.76, 95% CI 0.60-0.97; Table 2).

Multivariate Analyses

Variables included in the multivariate model included age group, sex, birth country (US/non-US), branch of military service, the presence of asthma, COPD, DM, chronic renal or liver failure, cancer, diseases of the circulatory system, and obesity diagnosed before the P&I event, and any influenza vaccination in 180 days prior to P&I event. In the multivariate model, any vaccination in the six months prior to the episode was protective against severe P&I disease, while the diagnosis of chronic renal or liver failure (RR=3.6, 95% CI 2.9-4.6), disease of the circulatory system (RR=2.2 95% CI 1.8-2.8), serving in the US Air Force (RR=1.5, 95% CI 1.2-2.0) or US Coast Guard (RR=1.9, 95% CI 1.1-3.4) were associated with an elevated risk of developing severe P&I disease (Table 2).

Sensitivity analyses for vaccination

We also conducted a subgroup analysis of those episodes in which the individual had received an influenza vaccine in the 6 months prior to the P&I episode. In addition to evaluating whether any vaccination within 180 days of the P&I episode reduced the risk of a severe P&I event, we ran separate multivariate models looking at vaccination within 60 days and 30 days of the P&I event. In these univariate models, vaccination within 60 days was non-significant, but suggested protection (RR=0.91, 95%CI 0.71-1.2) against developing severe P&I and vaccination within 30 days of the episode suggested an even stronger effect (RR=0.71, 95%CI 0.47-1.1), but was also non-significant.

Discussion

Our results demonstrate an elevated risk of severe outcomes for P&I hospitalization among non-recruit, US military personnel diagnosed with asthma, chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM), chronic renal or liver disease, cancer, diseases of the circulatory system, or for those who were obese. These are common risk factors for severe outcomes among the general civilian population [19, 20]. However, only the presence of renal or liver disease and diseases of the circulatory system remained significantly associated with severe outcomes in the multivariate model, suggesting that the other comorbidities may be less causal.

We also found elevated risks for military personnel who served in the US Air Force or the US Coast Guard. While the number of subjects in the US Air Force (n= 1,767) or US Coast Guard (n=180) at the time of the P&I episode were much smaller than for the US Army (n=5,878), vaccination rates in our hospitalized cohort were similar across all branches of service. There were too few severe P&I episodes for military members serving in the US Coast Guard (n=14) to evaluate underlying medical conditions in this subgroup; however, amongst the US Air Force personnel, the presence of COPD, chronic renal or liver disease, cancer and obesity were risk factors for severe outcomes. It is possible that the overall population of the different branches of the military had differing rates of medical comorbidities, which we were not able to describe with the data available to this study. However, given that our results are restricted to the risk of hospitalized cases becoming severe cases, such differences in the overall population are unlikely to explain the observed patterns.

The reasons for service-specific (e.g., US Coast Guard and US Air Force) increased risk are unclear and may represent preferential reporting (e.g., better and more complete assessment of severe P&I outcomes), different times from symptom onset to seeking treatment, or different coding practises between the services and not a real difference in risk. Additional studies are needed to explain this finding, to include prospective follow-up of influenza-infected patients in the military.

It must be kept in mind that this study only addresses the risk of becoming a severe acute respiratory infection case conditional on being admitted to a hospital. We describe only the tip of the severity pyramid. It is possible, but not necessarily the case, that the same risk factors we describe here may act less differently at other levels of the severity pyramid.

However, in this relatively healthy cohort, we suggest that risk factors operating at the severe end of disease progression merit further consideration as these factors must be much closer to drivers of mortality and, if modifiable, have much greater potential impact on morbidity than do risk factors for mild illness.

The US Department of Defence (DoD) requires that all service personnel be vaccinated against influenza, with priority given to military units who are or will be deployed on ships and other critical missions, to Community of Operations and Continuity of government personnel [21, 22]. DoD and service immunization policies have required 90% influenza vaccination coverage of service members by the end of December [22]. Actual influenza coverage was historically less than 90%, but has been increasing over the past decade and has been at or above 90% for several current influenza seasons [23]. Since this study dates back 15 years, this may partially explain why we found vaccination levels among our study population of subjects hospitalized for P&I ranging between 14%–55% depending on the northern hemisphere influenza season. Although vaccination coverage among this cohort increased over time, the coverage was still lower than expected for all active military personnel and therefore needs to be explored. This finding itself may be associated with risk of P&I hospitalizations in general and should be explored in a comparison study with ambulatory P&I episodes and healthy control subjects.

Our results are limited by the fact that outcomes were identified by diagnostic ICD-9 codes, rather than an actual review of each subjects' medical records and laboratory data. Without laboratory confirmation, a diagnosis of P&I could have been caused by pathogens other than influenza. In addition, these findings may not be generalizable to the US population at-large, since the military population is a very unique cohort of largely healthy young males. Nonetheless, our study population is unique in size and comprehensiveness and provides a rich source of data for which to study. In addition, the risk factors identified in this study are well known risk factors for severe influenza outcomes in other populations and are among the recommended priority groups for vaccination in the United States [20]. The high rate of renal and liver diseases in the personnel who experienced severe P&I during the 12-year study period needs to be further explored.

Previous studies of US military populations found that those who received trivalent inactivated vaccine were less likely to visit medical facilities for respiratory illness than those who received live attenuated influenza vaccine[23]. Our study found that the type of vaccine used varied by influenza season and that while any vaccination for influenza was protective against developing severe P&I hospitalization, certain vaccines, specifically split virus vaccine and the intranasal vaccine vaccines, were effective against severe P&I hospitalization as well.

Routine, compulsory influenza vaccination constitutes the single most important and relevant control measure available to the military today. The low vaccination coverage of service members who experienced a hospitalized P&I episode may indicate a sub-population with the military that is not receiving the required annual influenza vaccination. The military should particularly emphasize vaccination of service members with co-morbid conditions to hopefully alleviate this increased risk of severe outcomes. Additional studies that compare

the risk of influenza hospitalizations to influenza ambulatory visits or healthy individuals are warranted and would help identify risk factors for the full spectrum of influenza severity for the US military.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We would like to thank Ms. Michelle Hiser for her assistance in collating and providing influenza-related reports as part of background information provided in this manuscript. We would also like to thank Dr. Lee Hurt and Ms. Kathleen Shannon at the AFHSC for their assistance in providing influenza surveillance data and files for analysis.

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Highlights

- Influenza vaccination is protective against severe P&I hospitalizations
- In this cohort, renal/liver or circulator diseases contribute to influenza severity independent of age
- Our results provide evidence for the prioritization for flu vaccination of specific risk groups

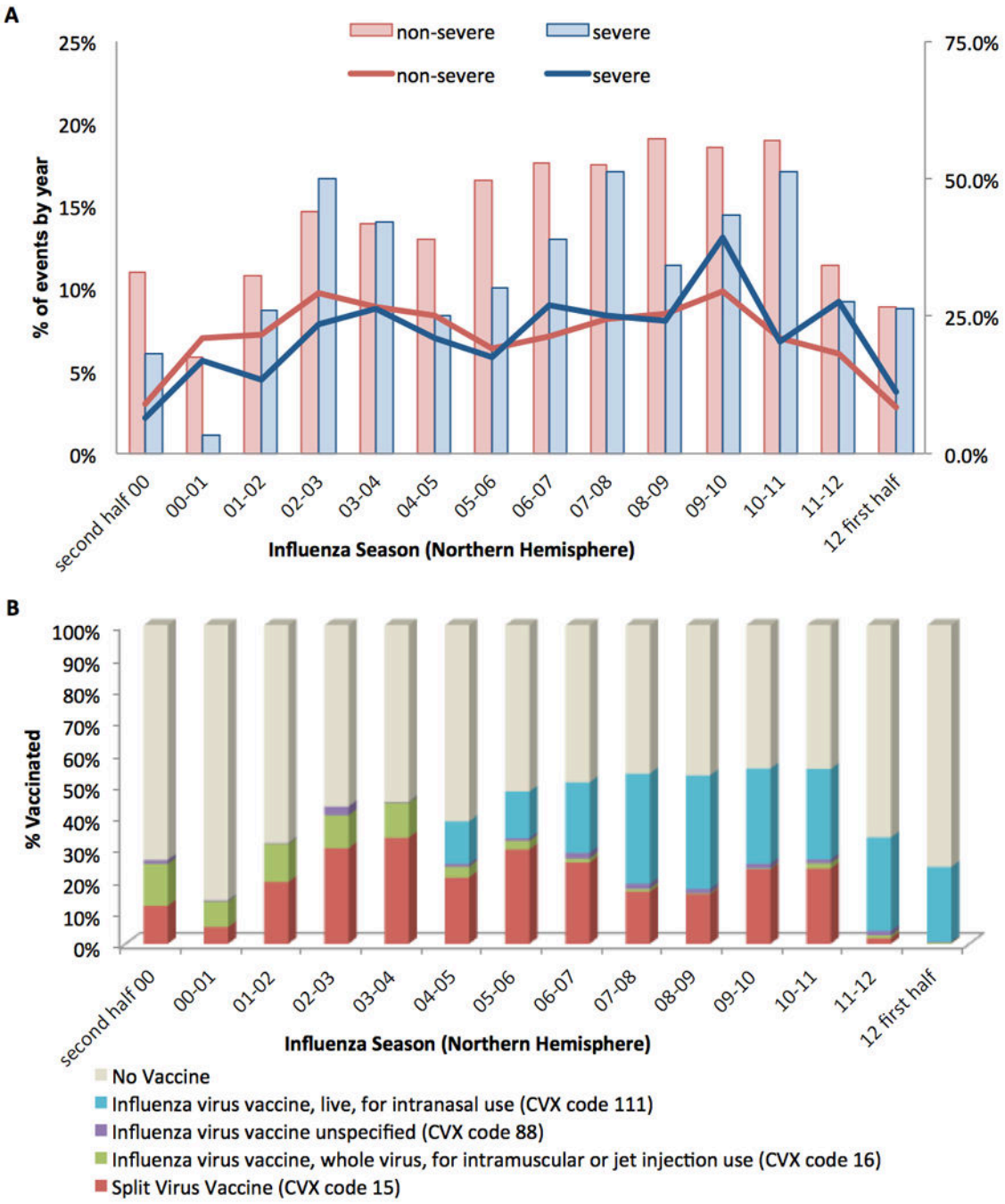

Figure 1.

A) Proportion of inpatient P&I episodes (primary axis) and proportion of subjects vaccination in the previous 180 days prior to P&I episode (secondary axis) by northern hemisphere influenza season; B) Influenza Vaccination used by Northern Hemisphere Influenza Season

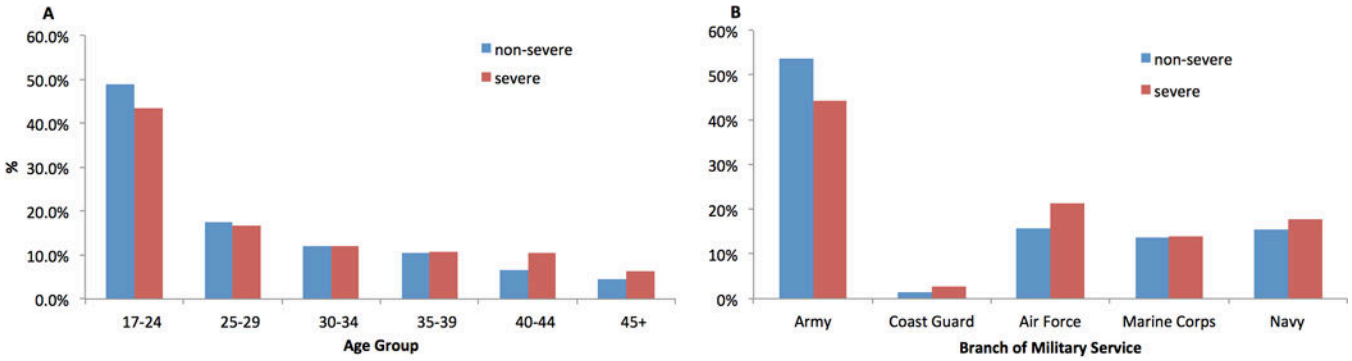

Figure 2.

Age-group and branch of military service of the subjects at the time of P&I inpatient episode during 1 January 2000 through 31 December 2012

Table 1

Case definitions and ICD-9 Codes for outcomes and potential risk factors

Variable	ICD-9 Code
Definition of condition	
Pneumonia & Influenza (P&I)	Hospitalization with a primary diagnosis of 480–488
	Severe P&I if any secondary diagnosis is 518.81 or 518.82, otherwise non-severe P&I
	Hospitalization with a primary diagnosis of 460–466 and any secondary diagnosis of 480–488
	Severe P&I if any secondary diagnosis is 518.81 or 518.82, otherwise non-severe P&I
	Hospitalization with a primary diagnosis of 518.81 or 518.82, with any secondary diagnosis of 460–466 or 480–488 (all episodes considered severe P&I)
ILI	79.99, 382.9, 460, 461.9, 465.8, 465.9, 466.0, 486, 487.0, 487.1, 487.8, 488, 490, 780.6, or 786.2
Underlying Condition	
Asthma	493
COPD	490, 491, 492, 494, 495, 496
DM	250
Chronic renal or liver disease	571.xx, 580–589
Cancer	140–239
Circulatory system	390–459
Pregnancy	V22, V23
Overweight/obesity	278.00–278.02, V85.2-V85.4
Sickle cell disease	282.6x
HIV infection	42
Immune disorder	279.xx
CVX codes for flu immunizations	111, 149, 150, 015, 016, 140, 141, 144, 088

Notes: P&I, pneumonia and influenza; ILI, influenza-like illness; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HIV, human immunodeficiency virus

Full listing of ICD9 codes provided as supplemental material

Table 2

Characteristics and vaccination history of US Military Personnel experiencing inpatient pneumonia and influenza (P&I) episodes during 1 January 2000 through 31 December 2012

Variable*	Inpatient P&I episodes (n=11,053)		Univariate RR (95%CI)	Multivariate RR (95%CI)
	Non-Severe episodes n=10,541	Severe episodes n=512		
Sex (% male)[a]	9,201 (87.3)	437 (85.4)	0.85 (0.66–1.1)	0.87 (0.66–1.1)
Country of Birth				
US	8105 (76.9)	372 (72.7)	ref	
Non-US	1653 (15.7)	106 (20.7)	**0.80 (0.65–0.98)**	0.98 (0.75–1.3)
Unknown	783 (7.4)	34 (6.6)		
Median age (IQR)	32 (28–40)	33 (28–42)		
Age Groups N (%)				
17–24	1,054 (10.0)	57 (11.1)	ref	
25–29	2,396 (22.7)	108 (21.1)	0.83 (0.60–1.2)	0.80 (0.57–1.1)
30–34	2,829 (26.8)	120 (23.4)	0.78 (0.57–1.1)	0.72 (0.52–1.0)
35–39	1,490 (14.1)	66 (12.9)	0.82 (0.57–1.2)	**0.63 (0.43–0.93)**
40–44	1,116 (10.6)	54 (10.5)	0.90 (0.61–1.3)	**0.60 (0.40–0.90)**
45+	1,655 (15.7)	107 (20.9)	1.2 (0.86–1.7)	**0.65 (0.43–0.98)**
Branch of Service				
US Army	5651 (53.6)	227 (44.3)	ref	
US Coast Guard	166 (1.6)	14 (2.7)	**2.1 (1.2–3.7)**	**1.9 (1.1–3.4)**
US Air Force	1658 (15.7)	109 (21.3)	**1.6 (1.3–2.1)**	**1.5 (1.2–2.0)**
US Marine Corps	1432 (13.6)	71 (13.9)	1.2 (0.94–1.6)	1.3 (0.98–1.7)
US Navy	1634 (15.5)	91 (17.8	**1.4 (1.1–1.8)**	1.2 (0.90–1.5)
Underlying Medical Conditions[α]				
Asthma	1176 (11.2)	73 (14.3)	1.3 (1.0–1.7)	1.1 (0.87–1.5)
COPD	1732 (16.4)	111 (21.7)	**1.4 (1.1–1.7)**	1.1 (0.86–1.4)
DM	219 (2.1)	24 (4.7)	**2.3 (1.5–3.6)**	1.0 (0.65–1.6)
Chronic renal or liver disease	896 (8.5)	162 (31.6)	**4.98 (4.1–6.1)**	**3.6 (2.9–4.6)**
Cancer	1927 (18.3)	137 (26.8)	**1.6 (1.3–2.0)**	0.82 (0.65–1.0)
Diseases of the Circulatory System	2691 (25.5)	263 (51.4)	**3.1 (2.6–3.7)**	**2.2 (1.8–2.8)**
Obesity	949 (9.0)	70 (13.7)	**1.6 (1.2–2.1)**	1.1 (0.80–1.4)
Sickle cell disease	17 (0.16)	1 (0.20)	1.2 (0.2–9.1)	--
HIV infection	50 (0.47)	1 (0.20)	0.41 (0.06–3.0)	--
Immune disorder	69 (0.65)	6 (1.2)	1.8 (0.78–4.2)	--
Influenza Vaccination[β]				
Any vaccination (w/in 180d)	4554 (43.2)	185 (36.1)	**0.74 (0.62–0.89)**	**0.81 (0.67–0.99)**[γ]
Split virus vaccine (CVX code 15)	2137 (20.3)	89 (17.4)	**0.76 (0.60–0.97)**	0.87 (0.68–1.1)[±]

Variable*	Inpatient P&I episodes (n=11,053)		Univariate RR (95%CI)	Multivariate RR (95%CI)
	Non-Severe episodes n=10,541	Severe episodes n=512		
Influenza virus vaccine, whole virus, for intramuscular or jet injection use (CVX code 16)	487 (4.6)	23 (4.5)	0.87 (0.56–1.3)	0.863 (0.54–1.4) ±
Influenza virus vaccine unspecified (CVX code 88)	128 (1.2)	4 (0.78)	0.57 (0.21–1.6)	0.49 (0.18–1.4) ±
Influenza virus vaccine, live, for intranasal use (CVX code 111)	1802 (17.1)	69 (13.5)	**0.70 (0.54–0.91)**	0.76 (0.57–1.0) ±
Any vaccine within 60 days	709 (6.7)	25 (4.8)	0.91 (0.71–1.2)	1.0 (0.77–1.3)
Any vaccine within 30 days	1,579 (15.0)	71 (13.9)	0.71 (0.47–1.1)	0.81 (0.54–1.2)

Significant findings are in bold:

*at the time or diagnosed before the P&I event;

[a]among unique individuals, 92.8% (9638/10384) are male

†Multivariate model 1 including any vaccination within 180 days of event;

±multivariate model 2 including vaccine type and no vaccination within 180 days of event;

IQR= interquartile range; ref = reference group for RR calculations; IQR, inter-quartile range; αICD codes for each medical condition are shown in Table 1; P&I, pneumonia and influenza; RR, relative risk; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HIV, human immunodeficiency virus; βVaccination within 180 days of the P&I episode; --not included in the multivariate model; NS= not significant