



Etiology and clinical characteristics of influenza-like illness in healthy adults by hospitalization status

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Background

- Viral respiratory infections are a common cause of hospitalization for younger, otherwise-healthy populations.
- In this study, we describe the epidemiology of influenza-like illness in non-elderly adults within the U.S. Military Health System (MHS) by pathogen and hospitalization status.

Methods

- The Acute Respiratory Infection Consortium (ARIC) is a prospective cohort of patients with influenza-like illness within the MHS (see figure 1 for clinical sites).
- Participants between 18 and 65 years of age were identified in outpatient settings between 2012 and 2017
- Inclusion criteria:**
 - Measured temperature of $\geq 38^{\circ}\text{C}$, OR subjective fevers OR chills and nightsweats.
 - Cough, dyspnea, or sore throat
 - Onset within 7 days of presentation
- Exclusion criteria:**
 - Pregnancy
 - Cardiac, respiratory, renal, or neurologic disease or immunocompromising condition (including HIV infection)
 - Long-term aspirin therapy
- Demographics, nasopharyngeal swabs and symptom data were collected; swabs were tested for viral pathogens using a target-enriched multiplex PCR panel (TEM-PCR™, Diatherix LLC).
- Symptom presence and severity were recorded as: 0 (none); 1 (mild); 2 (moderate); and 3 (severe). Participants were trained by research personnel on the definitions of each score.
- Data were analyzed to compare clinical features and risks for hospitalization.
- Statistical significance determined by exact or chi-square test, as appropriate for the tested variables.

Results

- 397 participants met inclusion criteria,
 - 34 participants required hospitalization
 - 363 participants remained as outpatients.
- Median length of hospitalization was 2 days.
- A virus was identified in 58.4% of outpatients (OP) and 55.9% of inpatients (IP)
 - Coronaviruses (63/363), enteroviruses (50/363), and influenza A (73/363) predominated in OP
 - Influenza A predominated among IP (35.3%, 12/34, $p=0.039$).**
- There were no significant differences between OP and IP in terms of age, gender, ethnicity, or tobacco use.
- IP were **more likely to be obese** (BMI ≥ 30 , 43.3% vs. 20.5%, $p=0.004$).
- IP were **less likely to have received influenza vaccination** (84.0% vs. 55.9%, $p<0.001$) and **more likely to receive treatment with a neuraminidase inhibitor** (45.5% vs. 16.9%, $p<0.001$).
- IP with influenza did not report more severe symptoms (chills, cough, sore throat, diarrhea, myalgia, or headache) on enrollment but were **more likely to have fever** (temperature $\geq 38.0^{\circ}\text{C}$) than OP (92.9% vs. 57.1%, $p=0.014$).

Results

Figure 1 – ARIC participating clinical sites, 2012-2017

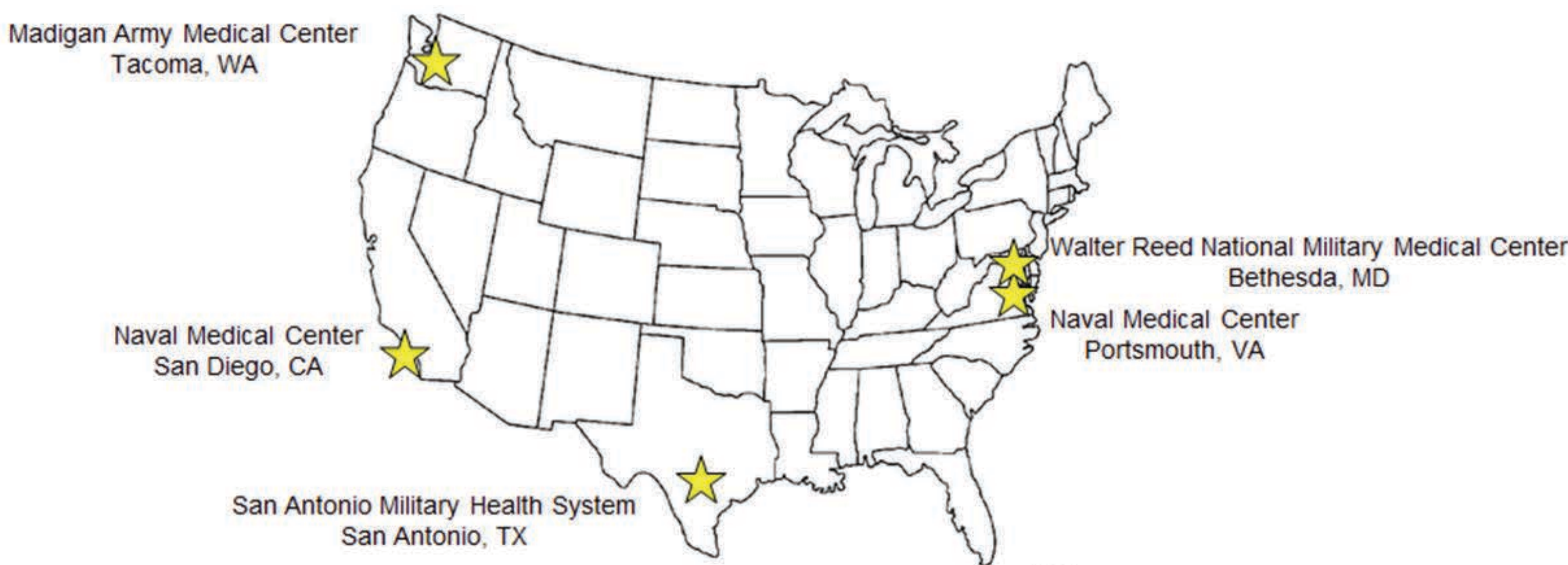


Table 1 - Characteristics of ARIC inpatients and outpatients from 2012-2017

	Hospitalization status				P-value
	Outpatient (N=363)		Inpatient (N=34)		
	Median	(Range)	Median	(Range)	
Days of hospitalization	NA	NA	2	(1-19)	NA
	N	(%)	N	(%)	
Age (year)					
1 18-25	145	(39.9)	11	(32.4)	0.199
2 25-30	73	(20.1)	6	(17.6)	
3 30-45	112	(30.9)	10	(29.4)	
4 45-65	33	(9.1)	7	(20.6)	
Sex					
Male	212	(58.4)	15	(44.1)	0.107
Female	151	(41.6)	19	(55.9)	
Ethnicity					
White	244	(67.4)	22	(64.7)	0.271
African American	53	(14.6)	9	(26.5)	
Asian	22	(6.1)	1	(2.9)	
Others	43	(11.9)	2	(5.9)	
Missing	1		0		
Obesity					
No	275	(79.5)	17	(56.7)	0.004
Yes	71	(20.5)	13	(43.3)	
Missing	17		4		
Smoking status					
Current	54	(14.9)	5	(14.7)	0.927
Former	55	(15.2)	6	(17.6)	
Never	254	(70.0)	23	(67.6)	
Child <5 yrs in household					
No	286	(78.8)	27	(79.4)	0.932
Yes	77	(21.2)	7	(20.6)	
Influenza vaccination in the current season					
No	58	(16.0)	15	(44.1)	<0.0001
Yes	304	(84.0)	19	(55.9)	
Missing	1		0		
Receiving neuraminidase inhibitor					
No	301	(83.1)	18	(54.5)	<0.0001
Yes	61	(16.9)	15	(45.5)	
Missing	1		1		

Figure 2 – Percentage of outpatient and inpatient ILI cases by pathogen

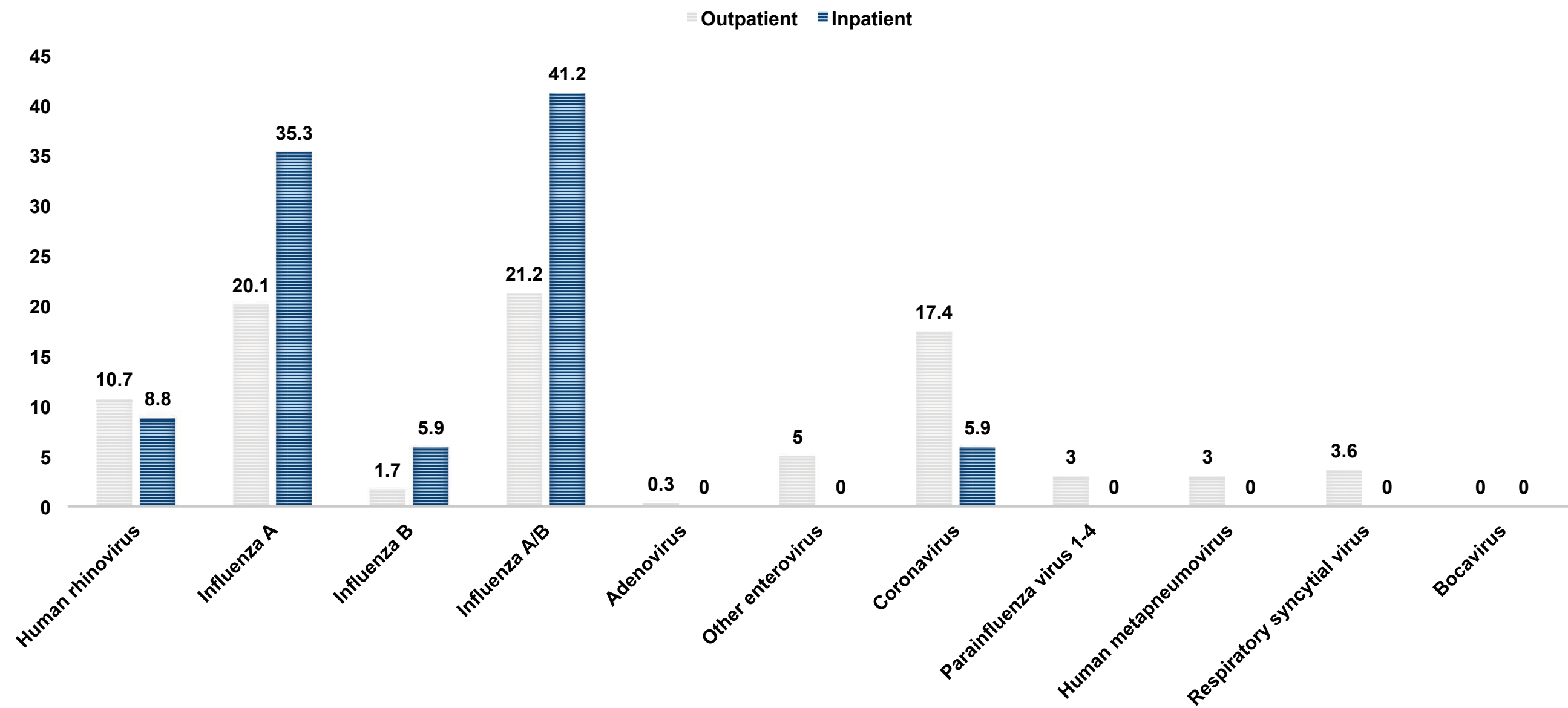


Table 2 – Symptoms and fever in outpatients and inpatients with influenza

	Hospitalization status among subjects with influenza (N=91)				
Reported symptoms at enrollment (by severity score)	Outpatient (N=77)		Inpatient (N=14)		
	Med.	(IQR)	Med.	(IQR)	P-value
Chills	2	(1, 3)	1	(0, 2)	0.157
Cough	2	(2, 3)	2	(2, 3)	0.851
Sore throat	2	(1, 2)	1	(1, 2)	0.601
Diarrhea	0	(0, 0)	0	(0, 0)	0.540
Muscle aches	2	(1, 3)	1	(0, 2)	0.105
Headache	2	(1, 3)	2.5	(0, 3)	0.869
Reported fever	N	(%)	N	(%)	
Temperature ≥38.0° C	44	(57.1)	13	(92.9)	0.034
Reported chills without fever	27	(35.1)	1	(7.1)	
No fever and no chills	6	(7.8)	0	(0.0)	
Documented fever (≥38.0° C)					
Yes	44	(57.1)	13	(92.9)	0.014
No	33	(42.9)	1	(7.1)	

Conclusions

- In a cohort of healthy adults with ILI, hospitalized patients were less likely to have received influenza vaccination and more likely to receive treatment with a neuraminidase inhibitor.
- Obesity and influenza A infection are associated with increased risks for hospitalization.
- Patients with influenza requiring hospitalization were more likely to be febrile but otherwise presented with similar symptoms as outpatients.

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