



# Characterization of human metapneumovirus (hMPV) infection among adults with influenza-like illness

Michelnde Ridoré MS<sup>2,9</sup>, Wei-Ju Chen PhD<sup>2,9</sup>, Mary P. Fairchok MD<sup>2,3,9</sup>, Christina Schofield MD<sup>3</sup>, Kristina St. Clair DO MTM&H<sup>4</sup>, Patrick J. Danaher MD<sup>5</sup>, Michael Rajnik MD<sup>6</sup>, Erin McDonough BS<sup>7</sup>, Leslie Malone MS, MB(ASCP)CM<sup>8</sup>, Elena Grigorenko PhD<sup>8</sup>, Donald Stalons PhD<sup>8</sup>, Deepika Mor MS<sup>2,9</sup>, Timothy H. Burgess MD MPH<sup>6</sup>, John C. Arnold MD<sup>1</sup>, Eugene V. Millar PhD<sup>2,9</sup>



Correspondence: emillar@idcrp.org

1 Naval Medical Center San Diego CA; 2 Infectious Disease Clinical Research Program, Bethesda MD; 3 Madigan Army Medical Center, Tacoma WA; 4 Naval Medical Center Portsmouth VA; 5 San Antonio Military Health System, San Antonio TX; 6 Walter Reed National Military Medical Center, Washington DC; 7 Naval Health Research Center, San Diego CA; 8 Diatherix Laboratories, LLC., Huntsville, AL; 9Henry M. Jackson Foundation for the Advancement of Military Medicine, Bethesda MD

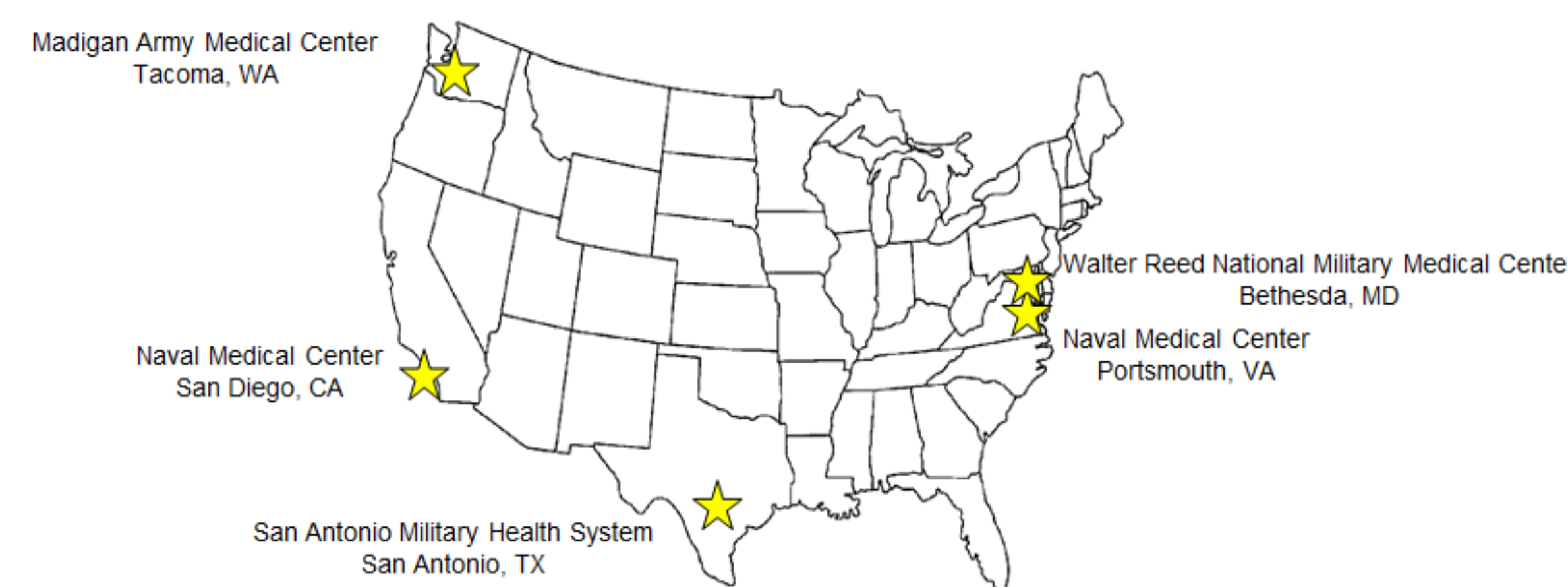
## Introduction

- Human metapneumovirus (hMPV) is a known cause of influenza-like illness (ILI). Much of what is known regarding the epidemiology and clinical characteristics of hMPV stems from studies of children and individuals with underlying medical conditions.
- Evaluations of the burden and characteristics of hMPV infection among otherwise healthy adults are warranted.

## Methods

- Since 2009, we enrolled otherwise healthy military personnel and beneficiaries into an observational, longitudinal study of influenza-like illness (ILI) at five military treatment facilities across the continental United States (**Figure 1**).

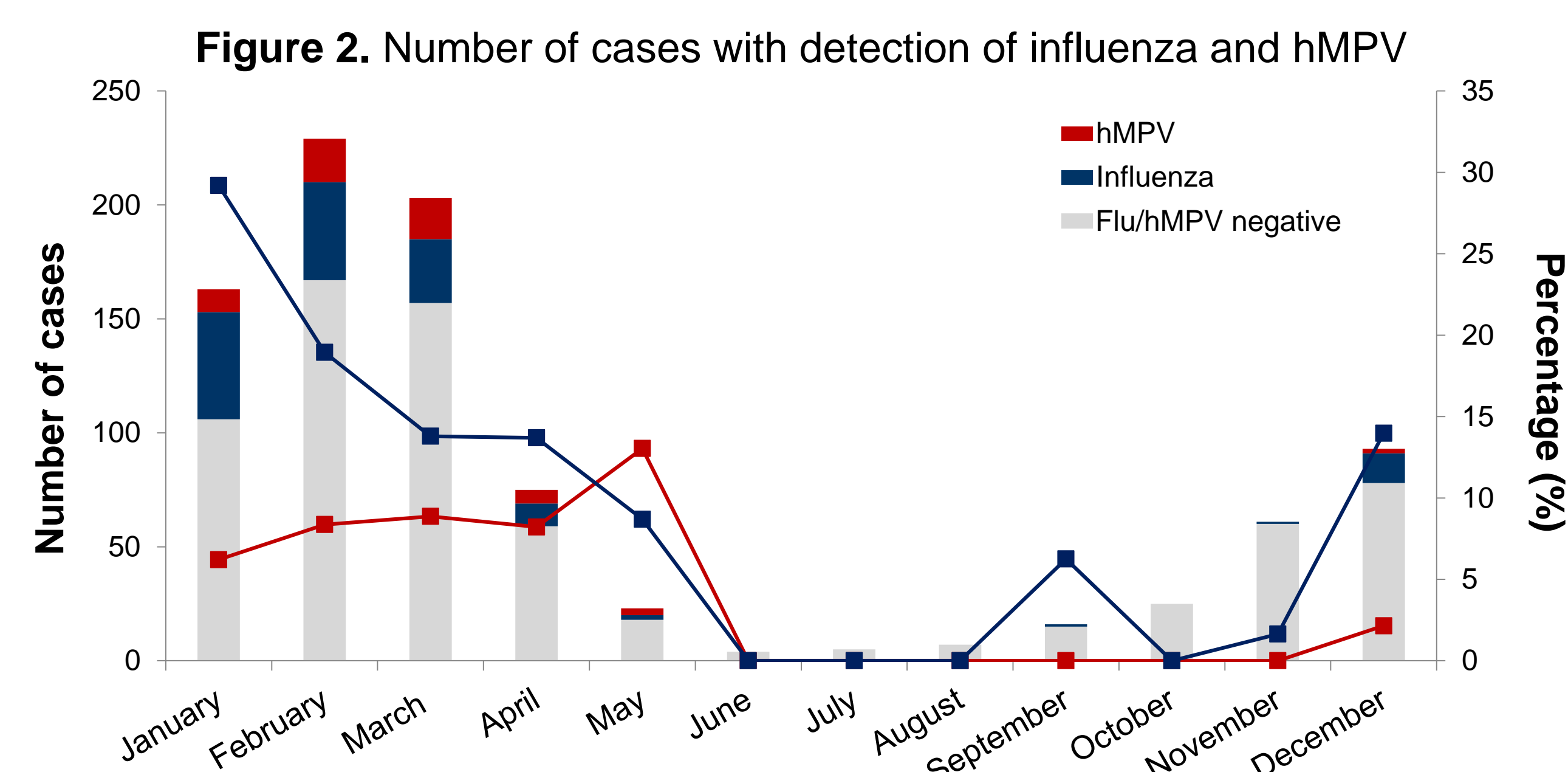
**Figure 1.** Clinical sites participating in the ARIC Natural History Study



- Eligibility.** Patients presenting for care <72h after the onset of ILI, defined as fever (temperature of 100.4° F or greater at the time of evaluation, or by self-report) and sore throat or one of the following respiratory symptoms: cough, sputum production, shortness of breath, or chest pain. Patients with underlying medical conditions were excluded.
- Clinical and demographic information,** and a nasopharyngeal swab was collected at baseline (day 0). Participants returned on days 3±1, 7±2 and 28±7; a daily symptom diary was completed for the first seven days following ILI onset. Symptom presence and severity was recorded either by self-report (diary) or interview as: 0 (none); 1 (mild: not changing activity or requiring treatment); 2 (moderate: requiring some modification in activity and/or medication); and 3 (severe: incapacitating, unable to perform normal activities, requiring bed rest and/or medication). Participants were trained by research personnel on the definitions of each score. Swabs were tested for influenza by real-time reverse transcription polymerase chain reaction (rtRT-PCR) at the Naval Health Research Center (San Diego, CA).
- A target-enriched multiplex PCR (TEM-PCR) panel for 13 bacterial and 10 viral respiratory pathogens was developed by Diatherix Laboratories, LLC. (Huntsville, AL). The platform relies upon nested multiplex PCR to provide the initial target enrichment and super primers to amplify and label the PCR products. The viral respiratory pathogens on the panel include: adenovirus, coxsackievirus/echovirus, bocavirus, coronavirus, human metapneumovirus, rhinovirus, influenza A/B, parainfluenza and respiratory syncytial virus.
- We measured presence of a symptom at any severity level (mild, moderate and severe); further stratified comparisons were based on moderate/severe versus none/mild, and severe versus mild/moderate/none. Composite measures were the sum of individual symptom scores in the following categories: (1) lower respiratory symptoms: cough, breathing difficulty, hoarseness and chest pain, (2) upper respiratory symptoms: earache, runny nose, sore throat and sneezing; (3) systemic symptoms: chills, muscle ache, headache and fatigue; (4) total symptoms: sum of the above three categories.
- Statistical analyses were performed using SAS (Version 9.3; SAS Institute, Cary, NC). The study was approved by the Infectious Disease Institutional Review Board of the Uniformed Services University of the Health Sciences (IDCRP-045).

## Results

- From 2009-2014, a sample of 898 cases with ILI were tested for viral respiratory pathogens using Diatherix TEM-PCR panel. Of these, 58 (7%; 11% children, 4% adults) had detection of human metapneumovirus (hMPV). hMPV was detected between December and May. (**Figure 2**)



- Twenty-eight (48%) cases were ≥18y. Of the 28 adult cases, 6 (21%) had co-detection of other viral pathogens (**Table 1**), including three with influenza. These three cases were excluded from subsequent comparisons of clinical characteristics.

**Table 1.** Viral respiratory pathogens detected among hMPV-positive adult ILI patients

	Pathogen 1	Pathogen 2	Pathogen 3	Pathogen 4	Pathogen 5
Case 1	BOCV	Coxsackievirus/ Echovirus			
Case 2	Coxsackievirus/ Echovirus				
Case 3	HRV				
Case 4	INFA	HRV	RSVA	RSVB	
Case 5	INFA	INFB	HRV	RSVA	RSVB
Case 6	INFA	INFB	HRV	RSVB	

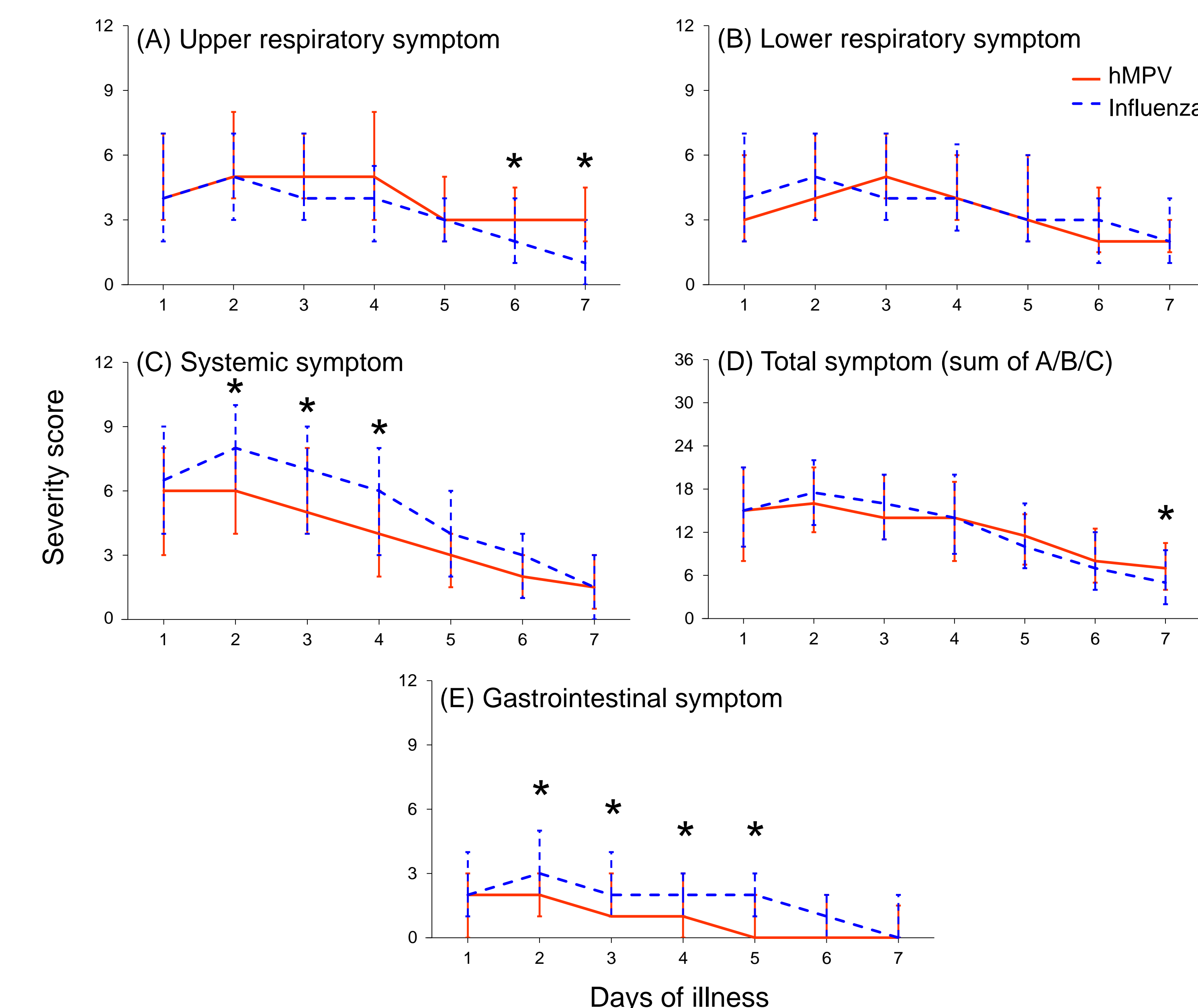
- Adult cases of hMPV were detected across multiple years and study sites. Cases with hMPV were more likely to be active duty members (88%) compared to influenza cases (66.4%, p=0.06) (**Table 2**).
- The prevalence of risk factors, including ethnicity, smoking status, obesity, contact to children under 5 yo in the household, and having any household member attending daycare, did not differ between cases of hMPV and influenza.

**Table 2.** Comparison of characteristics between ILI patients with hMPV and influenza virus

	hMPV (n=25)	Influenza (n=110)	P-value
	N(%)	N(%)	
Study site			
WRNMMC, MD	3(12.0)	2(1.8)	0.01
SAMMC, TX	6(24.0)	28(25.5)	
NMSD, CA	9(36.0)	50(45.5)	
NMCP, VA	7(28.0)	15(13.6)	
MAMC, WA	0(0.0)	15(13.6)	
Year of enrollment			
2010-2011	12(48.0)	16(14.5)	<0.01
2011-2012	6(24.0)	16(14.5)	
2012-2013	1(4.0)	40(36.4)	
2013-2014	6(24.0)	38(34.5)	
Military Status			
Active Duty	22(88.0)	73(66.4)	0.06
Retiree	2(8.0)	12(10.9)	
Beneficiaries	1(4.0)	25(22.7)	

- When compared to those with influenza, adults with hMPV reported more severe upper respiratory symptoms at days 5 and 6 of illness. By contrast, hMPV cases reported less severe systemic and gastrointestinal symptoms at 2 to 4 days of illness. (**Figure 3**)

**Figure 3.** Clinical severity of CVEV compared with influenza among adults (\*: p<0.05)



## Conclusions

- hMPV appears to be a relatively minor contributor to the burden of ILI among otherwise healthy adults.
- Approximately one quarter of hMPV adult cases had co-detection of other viral respiratory pathogens. Evaluations of hMPV clinical severity should assess the presence of co-infecting pathogens.
- hMPV-associated cases had more severe upper respiratory symptoms compared to influenza cases, while they had milder systemic and gastrointestinal symptoms.

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