Symptom Burden of Acute Influenza Infection Among US Adults: An Interim Analysis of a Nationwide Prospective Study

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INTRODUCTION

- Influenza infection is associated with substantial health care resource utilization and medical costs in the US [1].
- Many flu patients experience respiratory symptoms, which can negatively affect their quality of life and work productivity.
- CDC classifies flu severity as high for the 2024-2025 United States flu season based on influenza-like illness, flu-related hospitalizations, and flu-coded deaths [2].
- Literature examining the patient-reported burden of symptoms associated with influenza infections is limited [3-6].

OBJECTIVE

- This study characterized the frequency and severity of acute symptoms among outpatients with test-confirmed influenza in the US during the 2024/2025 season.

METHODS

- Symptomatic US adults with positive results from rapid influenza diagnostic tests or rapid molecular assays for influenza infection at CVS Health from 10/24/2024-4/15/2025 (recruitment ongoing) (CT.gov: NCT05160636) were included.
- Self-reported socio-demographics, clinical characteristics and vaccination status were collected via an online survey at enrollment (Day 1).
- Prevalence of 12 acute symptoms were self-reported by participants at enrollment and recalled prior to infection (pre-infection period). These 12 symptoms were selected based on CDC [7], and previous literature assessing the patient symptom burden associated with influenza infection [8].
- Symptom severity was measured by patients using an FDA-based 4-point scale (0=none, 1=mild, 2=moderate, 3=severe).
- Numbers of total acute symptoms and acute symptoms measured by patients using the FDA-based scale were summarized using descriptive statistics.
- Outcomes were compared between Day 1 and pre-infection baseline using paired t-tests.

RESULTS

- Of 720 participants in this interim analysis, mean age was 42.0 (SD: 13.0), 73.8% were female, 47.1% had ≥1 comorbidity, 48.8% received influenza vaccinations within the current respiratory season, and 84.4% had self-reported antiviral use. (**Table 1**)
- At enrollment, participants had a mean of 9.2 (SD: 1.7) acute symptoms, with cough (97.5%), stuffy or runny nose (97.4%), and fatigue or tiredness (96.8%) being the most frequent. (**Figure 1**)
- Relative to pre-infection baseline, there was a significant increase in the number of acute symptoms at enrollment (+8.1; p<0.001). (**Table 2**)
- The acute symptoms most often reported by patients as moderate/severe at enrollment were fatigue or tiredness (80.1%) and stuffy or runny nose (79.9%). (**Figure 1**)
- Participants reported a mean of 7.0 (SD: 2.3) acute symptoms as moderate/severe at enrollment, which was a statistically significant increase from the pre-infection baseline (+7.0; p<0.001). (**Table 2**)

Table 1. Patient Characteristics

	Statistics
Total n	720
Age, years, mean (SD)	42.0 (13.0)
Gender, n (%)	
Male	187 (26.0%)
Female	531 (73.7%)
Unknown	2 (0.3%)
Race / Ethnicity, n (%)	
White or Caucasian	583 (81.0%)
Black or African American	34 (4.7%)
Hispanic	53 (7.4%)
Other	50 (7.0%)
US Geographic Region, n (%)	
Northeast	128 (17.8%)
South	336 (46.7%)
Midwest	220 (30.6%)
West	32 (4.4%)
Other/Unknown	4 (0.6%)
Social Vulnerability Index [a], mean (SD)	0.32 (0.19)
≥1 comorbid condition [b], n (%)	339 (47.0%)
Receiving 2024-2025 Influenza Vaccination, n (%)	351 (48.8%)
Antiviral Use (baloxavir, oseltamivir and others), n (%)	608 (84.4%)

[a] Social Vulnerability Index is a score that ranges from 0 to 1. Higher values correspond to higher vulnerability. [9]
[b] Comorbid conditions include cancers or malignancies (other than skin cancer), cerebrovascular disease, chronic kidney disease, chronic lung conditions, chronic liver disease, endocrine disorders, heart conditions, mental health conditions, obesity (BMI >40), weakened immune system/ immunocompromised, blood disorders, smoker, or active tuberculosis

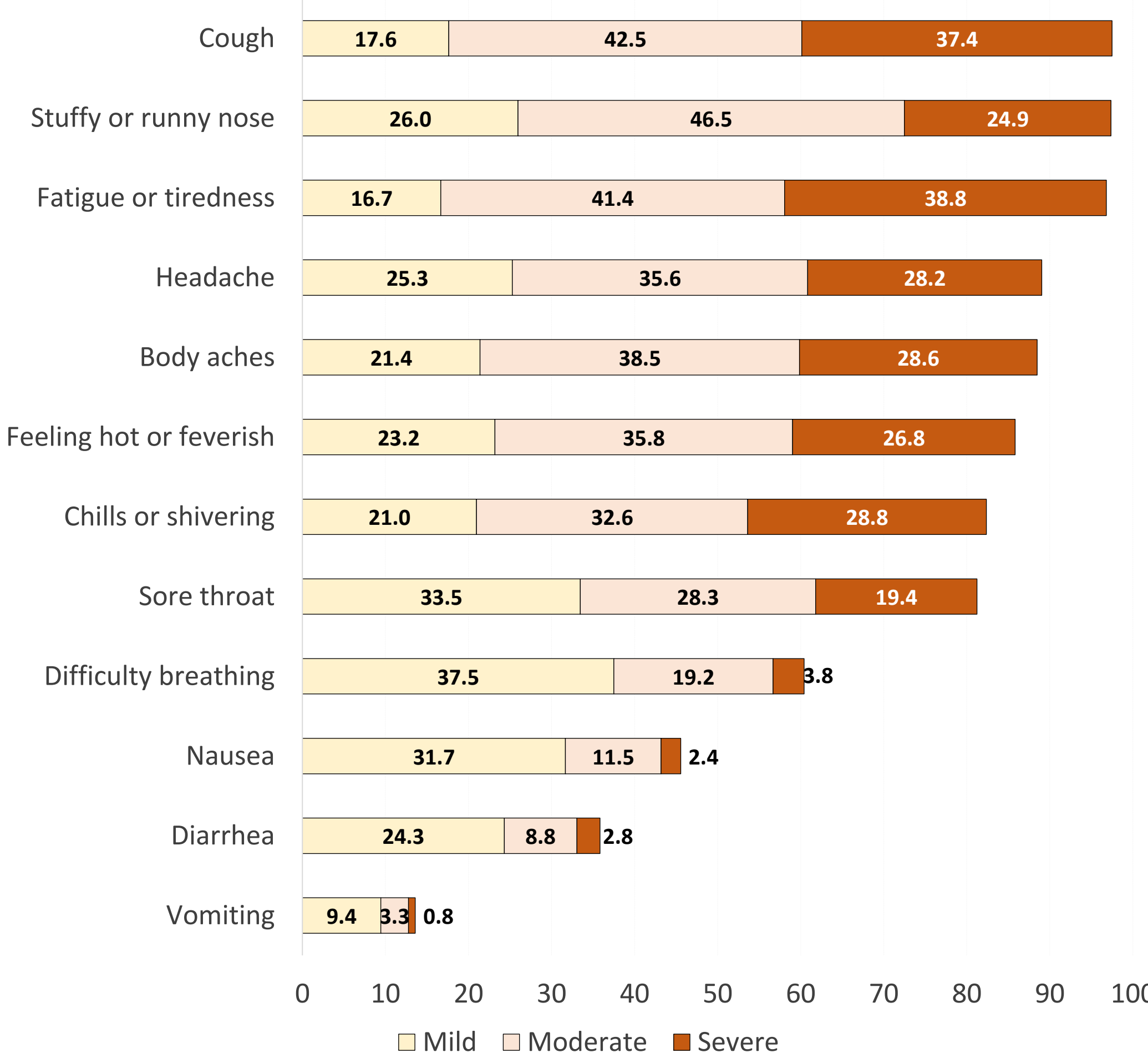### Figure 1. Acute Respiratory Infection Symptoms at Enrollment, %

Symptom	Mild	Moderate	Severe
Cough	17.6	42.5	37.4
Stuffy or runny nose	26.0	46.5	24.9
Fatigue or tiredness	16.7	41.4	38.8
Headache	25.3	35.6	28.2
Body aches	21.4	38.5	28.6
Feeling hot or feverish	23.2	35.8	26.8
Chills or shivering	21.0	32.6	28.8
Sore throat	33.5	28.3	19.4
Difficulty breathing	37.5	19.2	3.8
Nausea	31.7	11.5	2.4
Diarrhea	24.3	8.8	2.8
Vomiting	9.4	3.3	0.8

Table 2. ARI Symptom Summary Pre-Infection and at Enrollment, mean (SD)

	Pre-infection	Day 1	Change [a]
Number of symptoms of any severity	1.1 (1.4)	9.2 (1.7)	+8.1 (2.0)
Number of symptoms measured as moderate or severe	0.1 (0.3)	7.0 (2.3)	+7.0 (2.3)
Number of symptoms measured as severe	0.0 (0.1)	3.7 (2.6)	+3.7 (2.6)

[a] All P values of paired t-test less than 0.001.

CONCLUSIONS & DISCUSSIONS

- **The interim data of this study show that the burden of influenza-related respiratory symptoms is sizable and persists in the 2024/25 season in the US, with most symptoms self-reported as moderate or severe.**
- **Prevalence and severity of symptoms are similar to previous literature [6] for overlapping symptoms, with our study examining more symptoms comprehensively in the most current respiratory season.**
- **Key limitations: all data collected were self-reported and subject to missingness, errors, recall bias, and selection bias associated with survey drop-off. Findings may not be generalizable to a different season, or a different care setting.**
- **These findings underscore the need for continued monitoring and evaluation of symptom progression.**
- **The data raise awareness of patient burden and the importance of preventive measures such as influenza vaccination.**

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