



IDENTIFYING SYMPTOM PHENOTYPES AND THEIR ASSOCIATION WITH RESPIRATORY PATHOGENS USING LATENT CLASS MODELLING: IMPLICATION FOR EARLY SYSTEM WARNING IN GHANA

Eric Behene¹, Selassie Kumordjie¹, Kevin Nii Yartey Yartey¹, Bright Asare¹, Helena Dela¹, Emefa Korkor Narh¹, Harriet Manu², Eric Appiah², William Asiedu², Victor Asoala³, Joseph Alale Aweeya³, Joseph Humphrey Kofi Bonney⁴, Naiki Attram⁵, Anne T. Fox⁶, Shirley Nimo-Paintsil⁵

¹Noguchi Memorial Institute for Medical Research (NMIMR), Contracted Support to U.S. Naval Medical Research Unit - EURAFCENT, Ghana Detachment, Accra, Ghana; ²Ghana Armed Forces, Accra, Ghana; ³Navrongo Health Research Center, Upper East Region, Ghana; ⁴Virology Department, Noguchi Memorial Institute for Medical Research, University of Ghana, Legon, Ghana; ⁵U.S. Naval Medical Research Unit - EURAFCENT, Ghana Detachment, Accra, Ghana; ⁶Goldbelt Apex Inc., Contracted Support to U.S. Naval Medical Research Unit - EURAFCENT, Ghana Detachment, Accra, Ghana



Introduction

Respiratory infections remain one of the major contributors to morbidity and mortality in low- and middle-income countries (LMICs), largely owing to inadequate laboratory infrastructure that limits timely and accurate diagnosis, thereby hindering appropriate clinical management and treatment.

An essential component of managing patients with respiratory infections is the classification of clinical phenotypes at hospital presentation to distinguish disease severity, identify emergency cases, and guide timely clinical decision-making and appropriate treatment.

Study Objective

To use latent class analysis to identify distinct clinical phenotypes of respiratory infections that may improve public health surveillance and support early detection of respiratory pathogens.

Methods

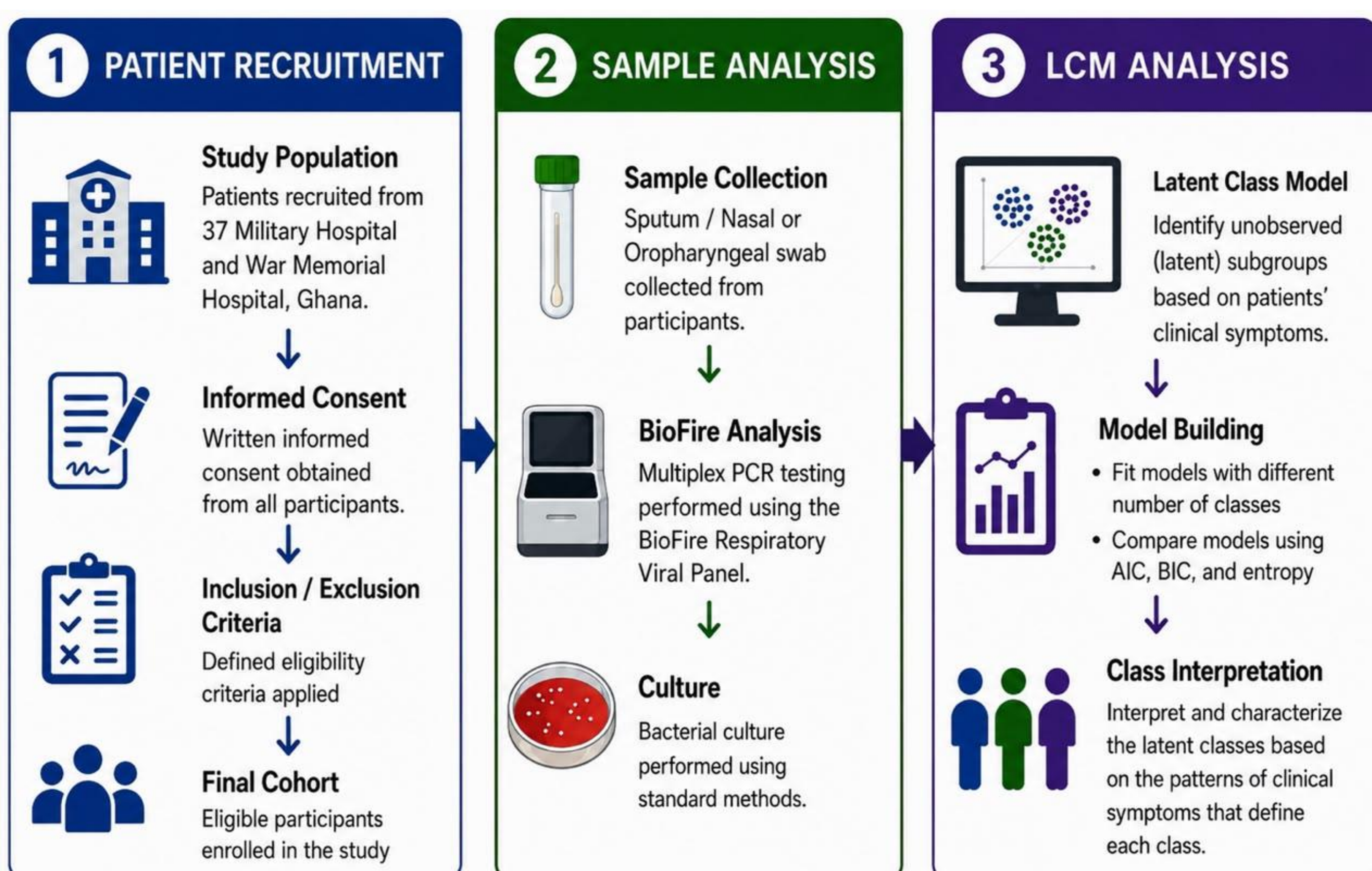


Figure 1: Sampling process, laboratory analysis and Latent Class Model (LCM)

Results

A total of 390 febrile patients were enrolled, of which 42% (165) were suspected to have respiratory infections. Respiratory samples were obtained from 59% males, 79% civilians and 84% adults (≥ 18 years).

- The clinical symptom phenotypes distribution did not differ significantly between males and females (p -value=0.661).
- High percentage of adult patients (≥ 18 years) presented with respiratory systemic phenotypes compared to children (< 18 years) (p -value=0.0148). *Figure 2*
- High proportion of military personnel presented with respiratory systemic phenotypes compared to civilians; however, population type did not significantly associate with clinical symptom phenotype (p -value=0.055).

Results Cont'd

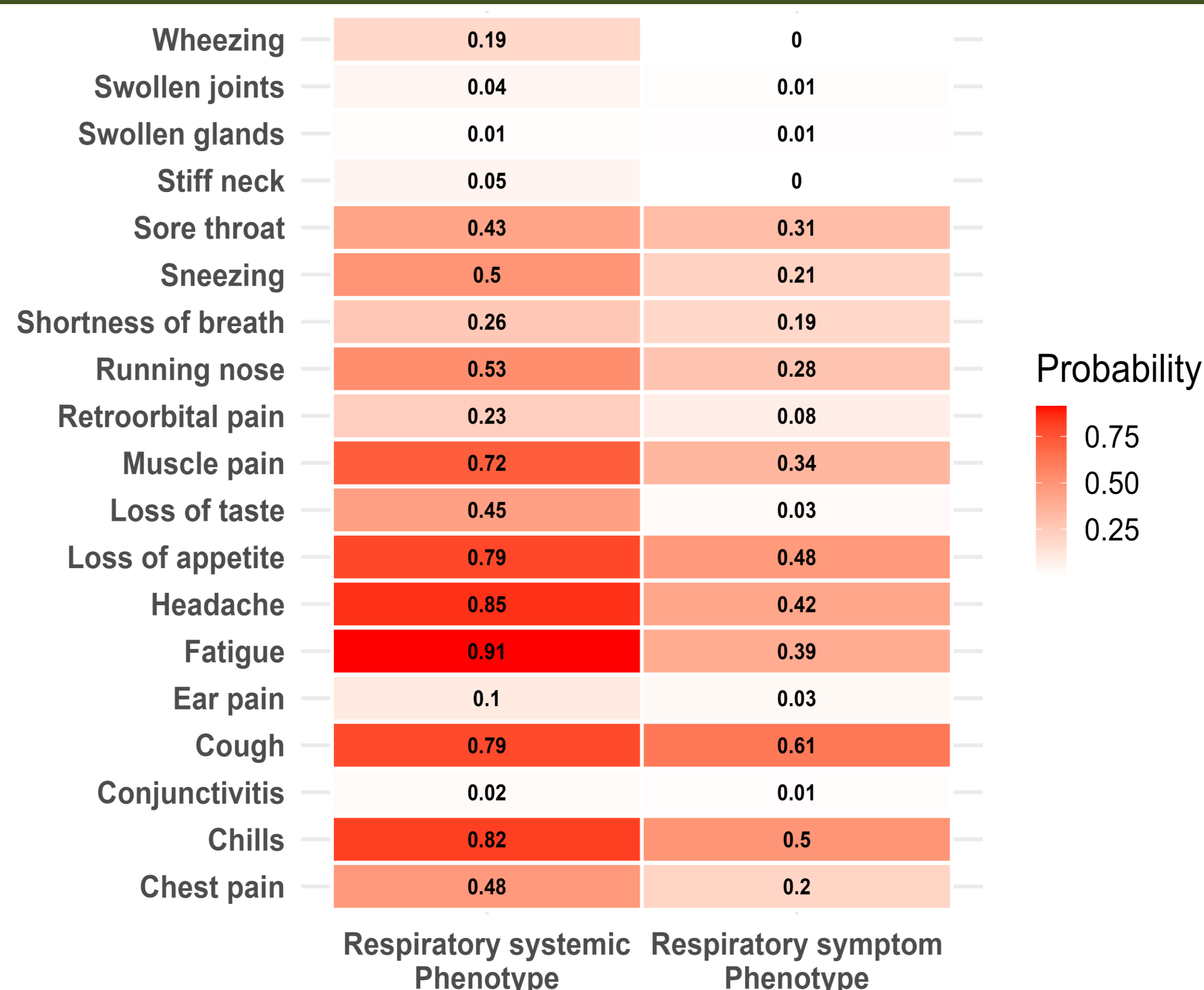


Figure 2: Clinical phenotypes identified by LCM, showing the probability of occurrence of each symptom within the identified phenotypes.

Note: Respiratory systemic phenotype - High probability of both respiratory (particularly cough) and systemic symptoms (fatigue, headache, chills, muscle pain and loss of appetite).

Respiratory symptom phenotype - Predominantly respiratory symptom (particularly cough) and low probabilities of systemic symptoms.

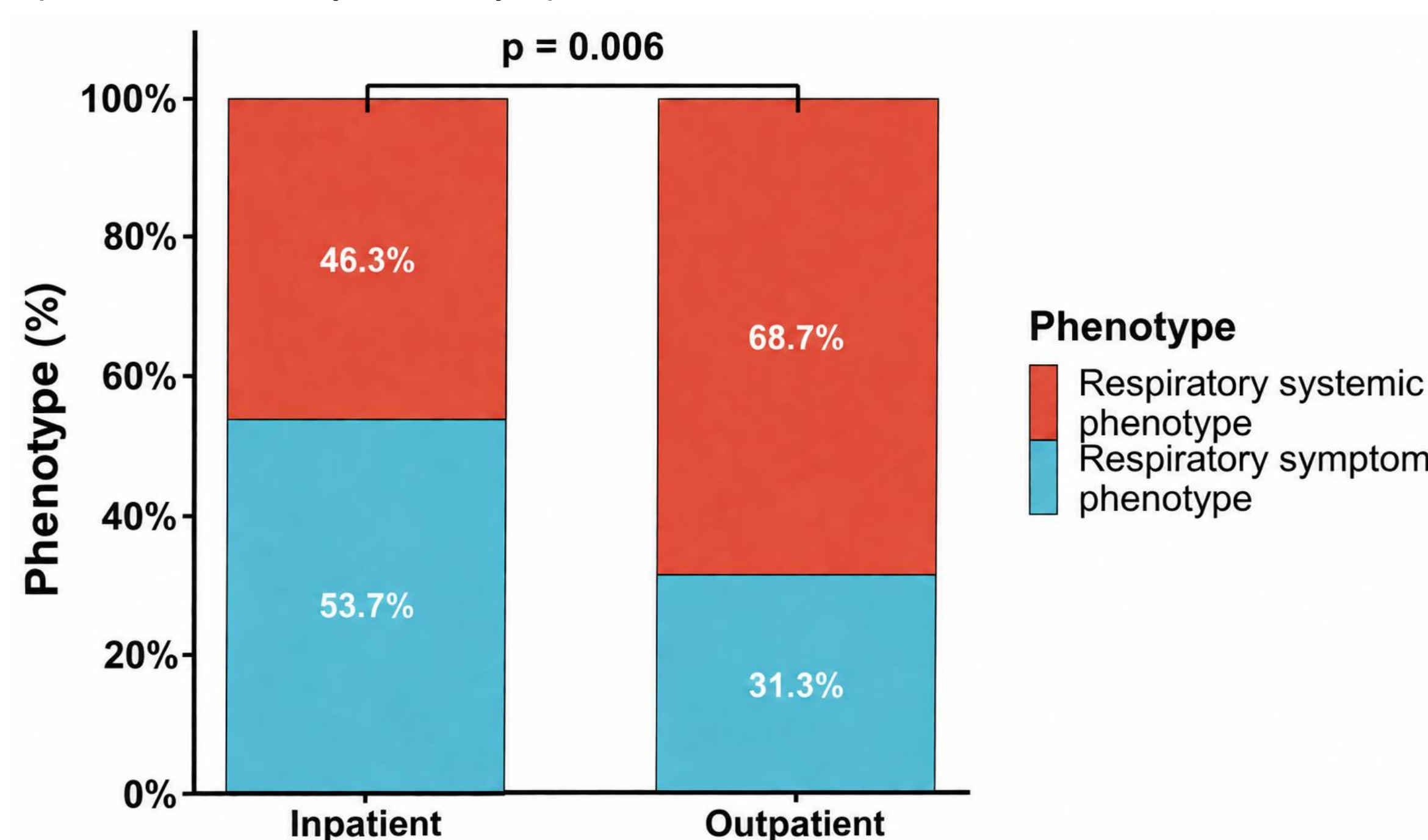


Figure 3: Association between clinical phenotypes and type of encounter.

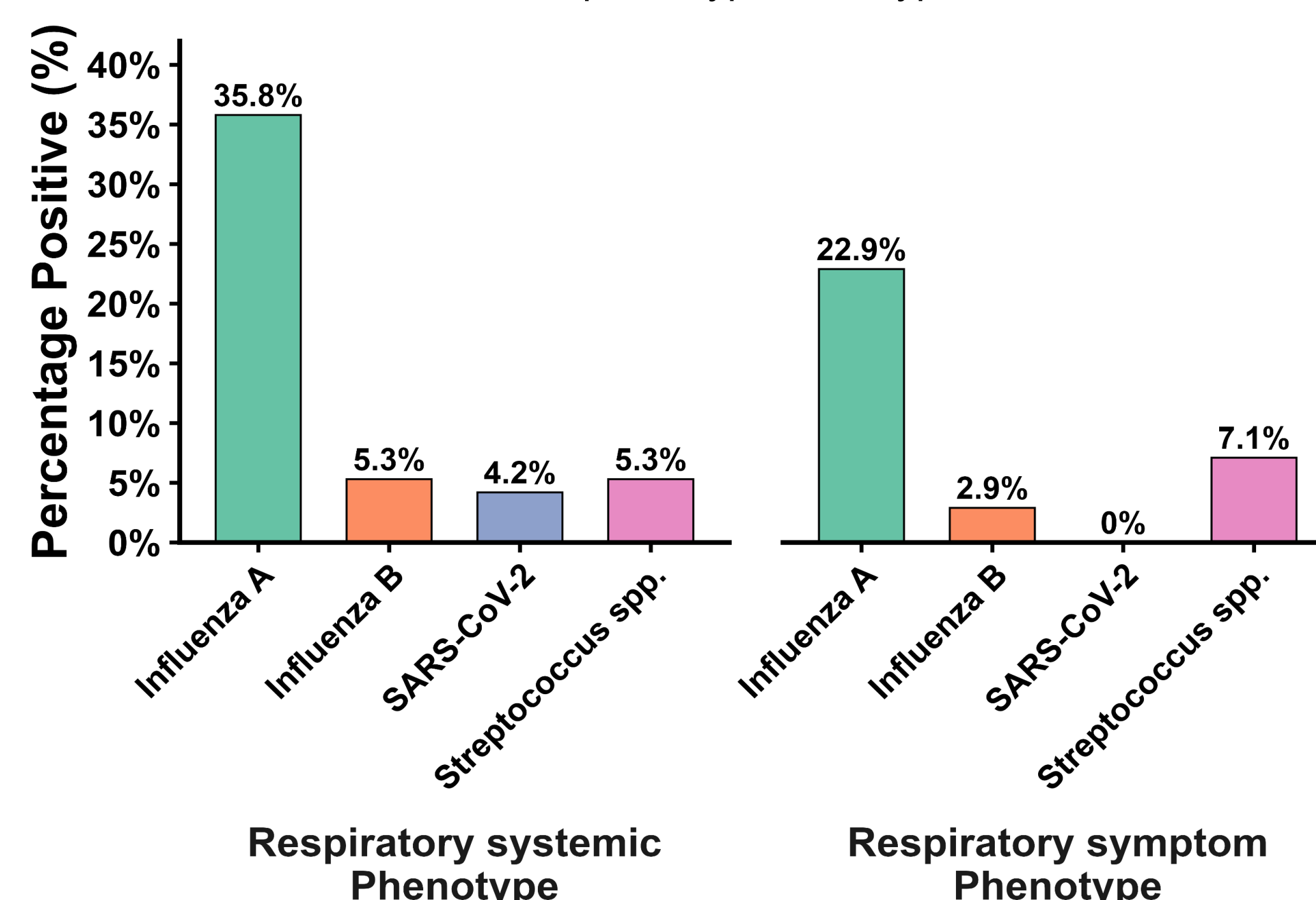


Figure 4: Distribution of identified respiratory pathogens by clinical phenotypes.

Results Cont'd

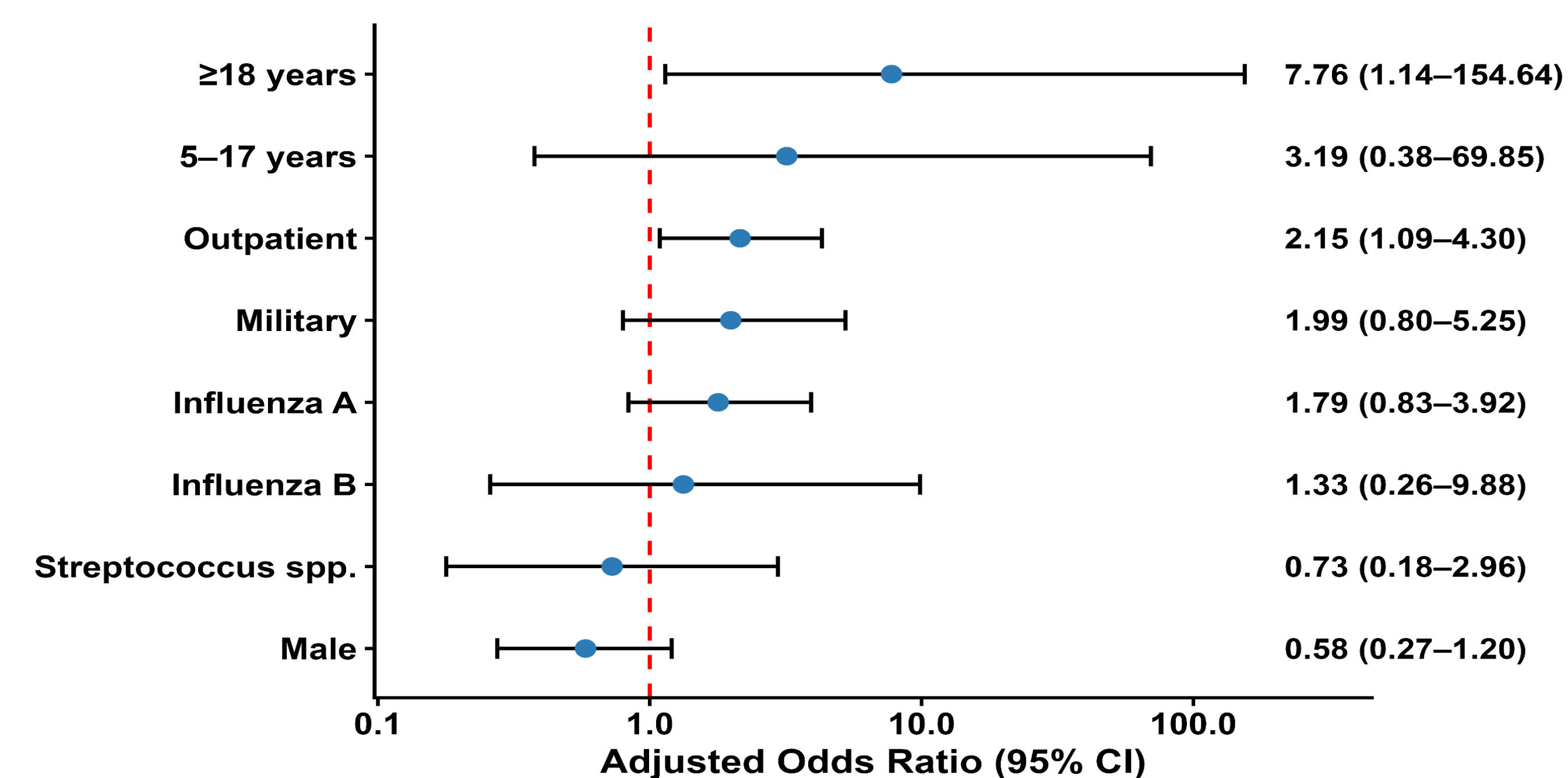


Figure 5: Forest plot showing the adjusted odds ratios (aORs) and 95% confidence intervals (CIs) for factors associated with the respiratory systemic phenotype.

Discussion

- Outpatients were more likely to belong to the respiratory–systemic phenotype, potentially due to earlier presentation with prominent systemic symptoms and a greater frequency of viral infections (Influenza and SARS-CoV-2). Inpatients were likely admitted based on respiratory deterioration and clinical severity rather than systemic symptom burden.
- Adults (≥ 18 years) had higher odds of belonging to the respiratory–systemic phenotype than children (< 5 years), potentially due to age-related differences in immune responses and greater ability to recognize and report subjective systemic symptoms.

Conclusion

Clinical phenotypes could support patient characterization and clinical decision-making by identifying distinct symptom patterns that complement respiratory infection surveillance efforts, particularly in settings with limited laboratory diagnostic capacity.

References

- Jackson, P., Muyanja, S. Z., & Siddharthan, T. (2023). Health equity and respiratory diseases in low-and middle-income countries. *Clinics in chest medicine*, 44(3), 623-634.
- Yamga, E., Mullie, L., Durand, M., Cadrin-Chenevert, A., Tang, A., Montagnon, E., Chartrand-Lefebvre, C., & Chassé, M. (2023). Interpretable clinical phenotypes among patients hospitalized with COVID-19 using cluster analysis. *Frontiers in Digital Health*, 5, 1142822. <https://doi.org/10.3389/fdgh.2023.1142822>

Acknowledgement

The authors would like to acknowledge the contribution of Staff of the Public Health Unit of the 37 Military Hospital, War Memorial Hospital, Navrongo Health Research Center, and study participants.

Partners/Collaborators

