

Survey-based Patient Reported Outcomes Measure (FLU-PRO® Plus) Discriminates Between COVID-19 and Influenza Like Illness.

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Background

- The FLU-PRO© instrument is a self-administered, online, patient reported outcome (PRO) survey tool
- Captures the presence and severity of influenza/influenza-like symptoms across body systems
 - Rate the intensity and/or frequency of 32 symptoms in the past 24 hours on a five-point scale
 - Scored into six domains developed using a two-stage qualitative approach
 - **FLU-PRO© Plus** has two additional items (34 total) and domain to capture loss of smell/taste
- Additional Patient Global Assessments (PGA) to assess global health status and general quality of life (QoL) in relation to symptom presentation

Introduction

- Pilot feasibility study evaluating routine surveillance of respiratory viral syndromes using the FLU-PRO© Plus in clinical practice
 - Response and adherence rate of patients asked to respond to FLU-PRO Plus for a 14-days
 - Supported by Arnold Ventures Foundation
 - Active during 2020/2021 influenza season



Three study sites – HealthPartners (MN), Kaiser Permanente (GA, MA)

Specific Aims

Aim 1: To evaluate if symptom clusters derived from the factor structure of the FLU-PRO© Plus discriminate adult COVID-19 cases from non-COVID cases for those with influenza like illness

Aim 2: To assess the correlation between global health status, quality of life, and symptom burden

Methods

- Patients with a diagnosis or positive lab test of either COVID-19 or influenza like illness (ILI) were recruited to complete FLU-PRO© Plus
 - Two diagnostic groups: COVID-19 positive and non-COVID-19 ILI
 - Symptomatic participants that completed the first survey were included in the analytic sample
- Exploratory factor analysis (EFA) was used to reduce 34 items to 3 factors expressed as “symptom clusters”
 - Varimax rotated, standardized item distributions $\sim N(0, 1)$
 - To determine diagnosis discrimination, cluster scores were used as independent variables for logistic regression predicting COVID-19 diagnosis
 - Concurrent validity of the clusters was evaluated with simultaneously collected PGA measures

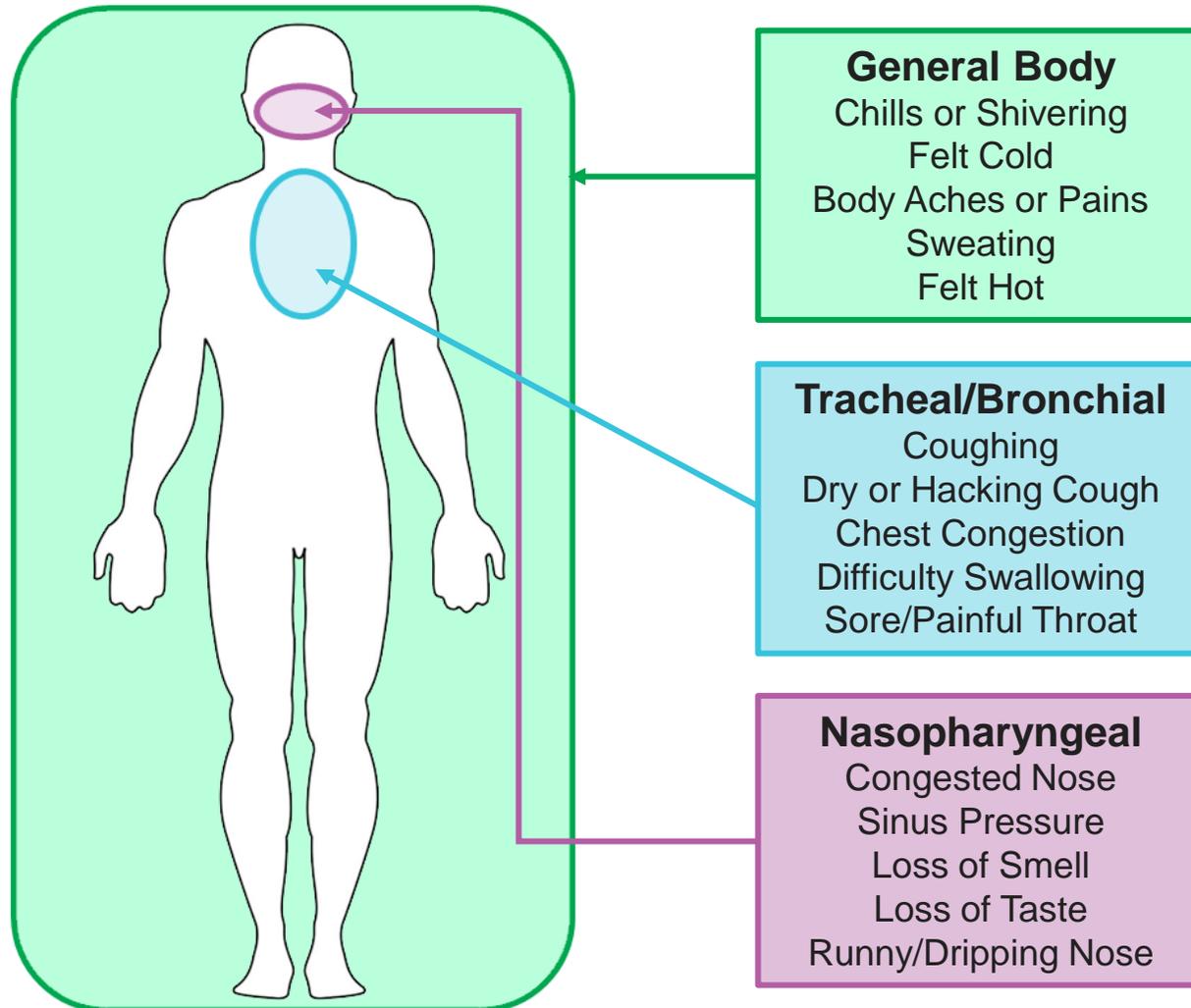
Results – Analytic Sample

- A total of 317 responded to the Day 1 FLU-PRO© Plus survey
 - 205 (65%) with COVID-19
 - 112 (35%) with non-COVID ILI
- Patients in the COVID-19 group more likely to be younger, non-White, and Hispanic
- Difference between patient groups viewed as a product of enrollment process and recruitment site location versus pathogen specific
 - Example: HP recruited bulk of ILI group from a less racially diverse population as compared to KPGA

	COVID-19 N = 205	Non-COVID ILI N = 112
Age*, Mean ± SD	47 ± 16	52 ± 15
Sex, Female	67%	73%
Race*		
White	63%	87%
Black or African American	24%	9%
Asian	3%	2%
Hispanic	2%	0
American Indian	<1%	0
Multiple	2%	1%
Unknown	5%	2%
Ethnicity*, Hispanic	6%	1%
Language, English	99%	100%

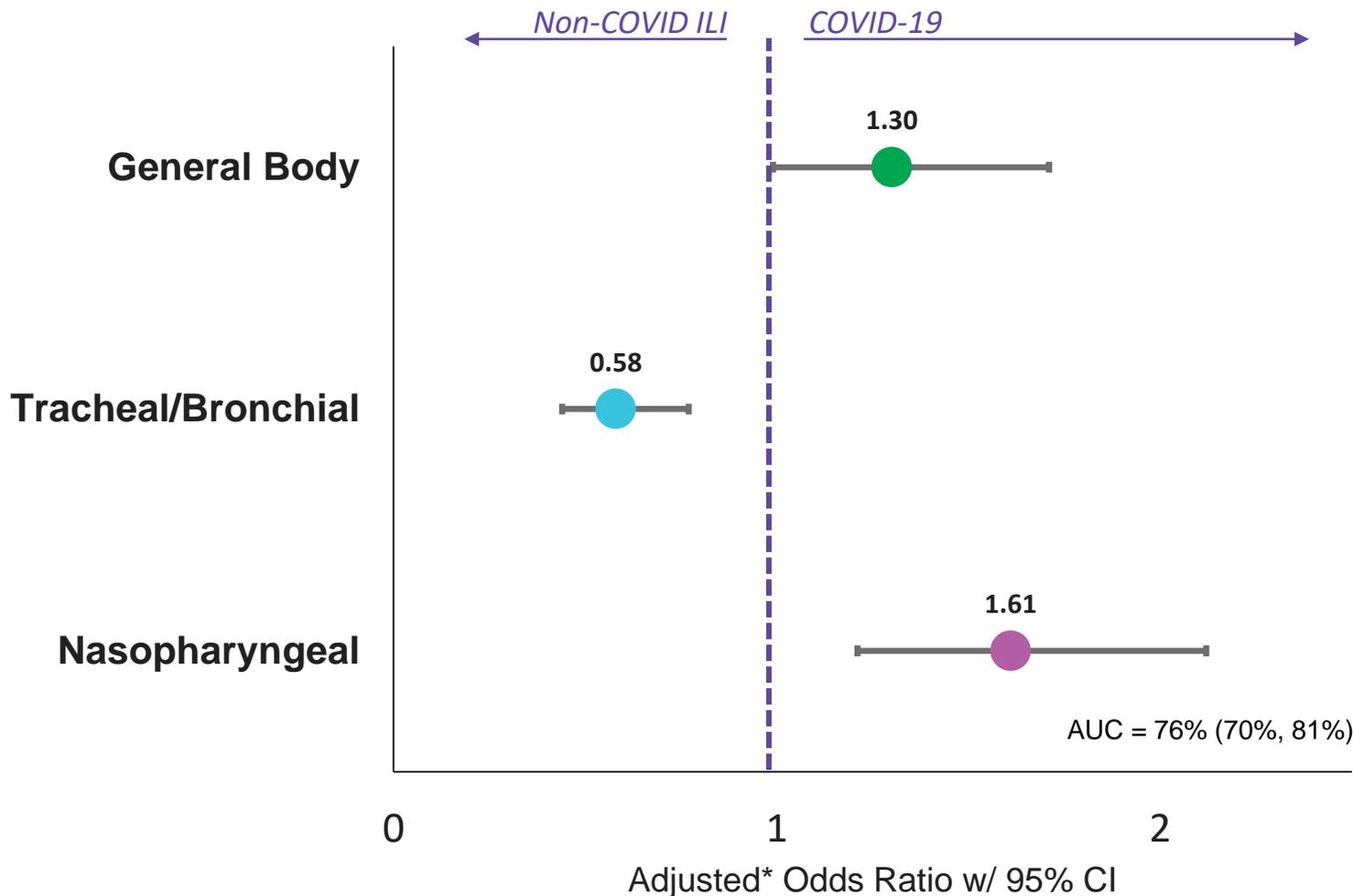
* p<.05 when compared between groups using Fisher's exact/t-test

Results – Exploratory Factor Analysis



- Three symptom clusters of five items each were identified:
 - General Body (27% of item variance)
 - Tracheal/Bronchial (8% of item variance)
 - Nasopharyngeal (7% of item variance)
- Positive factor scores
 - Presence/severity symptoms contributes to higher scores on the respective cluster
- Two EFA clusters are hybrids of original FLU-PRO domains
 - Tracheal/Bronchial – Chest x Throat
 - Nasopharyngeal – Nose x Head x Sense
 - Different factor structure than identified in homogenous ILI sample

Results – Logistic Regression



*Adjusted for age, gender, race (white/non-white)

- Higher Nasopharyngeal cluster scores → Increased odds of COVID-19 diagnosis
 - aOR: 1.61 [1.21, 2.11]
- Lower Tracheal/Bronchial cluster scores → Decreased odds of COVID-19 diagnosis
 - aOR: 0.58 [0.45, 0.76]
- General Body, $p = .056$
 - aOR: 1.30 [1.00, 1.71]

Results – Health Status, Quality of Life, and Symptom Burden

PGA Item	Pearson Correlation (r)		
	General Body	Tracheal / Bronchial	Naso-pharyngea I
Severity of symptoms today	+0.49	+0.34	
Symptoms interfered with usual activities	+0.56	+0.14	+0.16
Returned to usual activities today	-0.33		-0.15
Physical health today	-0.40	-0.30	
Returned to usual health today	-0.15		

- General Body cluster scores associated with all five PGA items
 - Tracheal/Bronchial: 3/5
 - Nasopharyngeal: 2/5
- More extreme symptom presentations correlated with:
 - Increased reports of symptom burden interfering with usual activities
 - Lower reports of return to usual health/activities
 - Lower ratings of global physical health

Note: Only includes Pearson correlation coefficients (r) where $p < .05$

FLU-PRO© Plus captured distinct symptom patterns for viral respiratory illnesses

- The levels of the symptom clusters presentations are correlated with health status and QoL
- Limitations
 - Study pre-dated delta/omicron variants and wide-spread vaccination
 - Diagnosis categorization method – Could be minor overlap
 - Low prevalence of influenza during 2020/2021 influenza season
 - Excludes hospitalized and asymptomatic patients
- Future work
 - Evaluate whether clusters of symptoms carry prognostic information
 - Collect responses for a larger, more diagnostically diverse sample
 - Include more robust diagnostic information, data on comorbidities, and vaccination status

Discussion – How can we use FLU-PRO® Plus in practice?

- Clinical
 - Help triage work-flow and direct treatment
 - Standardized symptom reports for clinicians to direct patient care
 - Excellent tool for telemedicine
- Societal
 - Inform screening questions for public health initiatives
 - Set expectations for return to usual health to lessen burden on care systems
 - Viral surveillance
- Research
 - Standardized, real time documentation of symptom expression
 - Captures variation in symptom presentation