

## Analysis of Symptom Parameters in Relation to the Identification of Infectious Condition

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**Introduction:** A college campus presents a unique environment to study transmission of respiratory illness as well as the clinical progression of certain infections. The research team's overall goal is to characterize a contagious phenotype of someone recently infected with an acute respiratory illness and track the subsequent transmission of disease between college students living in close proximity. With that, this group sought out to determine if there is significance between self-assessed symptom scores and laboratory results from a participant's clinical samples. This relationship is crucial to define, as symptom scoring is utilized as a determinant of sickness, which dictates a participant's potential for further testing before laboratory results are processed. Clinical samples were collected from individuals with suspected acute respiratory infections from a cohort of living and learning program undergraduates during the Spring 2017 semester. Symptom scoring associated with the instances that the samples were collected at were analyzed, comparing 99 positive samples and 349 negative samples. A statistically significant difference was found between the median symptom score associated with positive and negative clinical samples for surveys on cough, upper respiratory composite and total symptom composite.

### Methods:

Participants visit clinic within 48 hours of symptom onset



Complete symptom survey, provide nose and throat swab samples, name close contacts for possible transmission



Samples analyzed for positive viral and bacterial targets using qPCR while symptom scoring evaluated with Mann-Whitney U Test

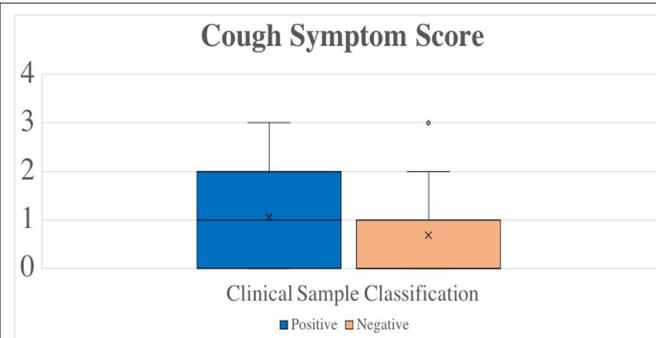


Fig. 1 shows the median, quartile spread, and extreme values for the cough score from the symptom survey. The symptom score is ranked on a 0 to 3 scale with increasing severity. The median for positive samples is 1 and for the negative samples it is 0. The difference in the means is statistically significant with Z Score -3.5459 and p-value 0.00038.

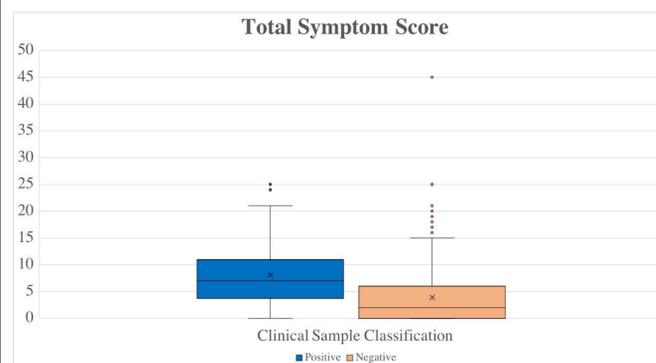


Fig.2 shows the spread for the total symptom score from the survey. This composite score is a sum of all 15 symptoms included on the survey ranked on the 0 to 3 scale with increasing severity. The median for positive samples is 7 and for negative samples it is 2, with this difference being statistically significant with Z Score -8.3609 and p-value <0.00001.

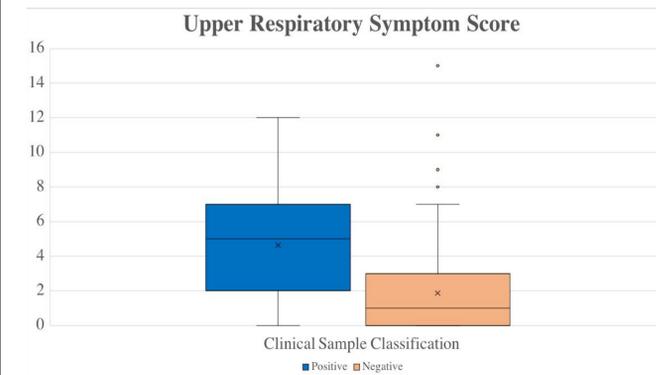


Fig. 3 shows the spread for the upper respiratory score from the symptom survey. This composite score is a sum of the following symptom scores each ranked on the 0 to 3 scale with increasing severity: "runny nose, stuffy nose, sneezing, sore throat, and earache." The median for positive samples is 5 and for negative samples it is 1, with this difference being statistically significant with Z Score -7.3906 and p-value <0.00001.

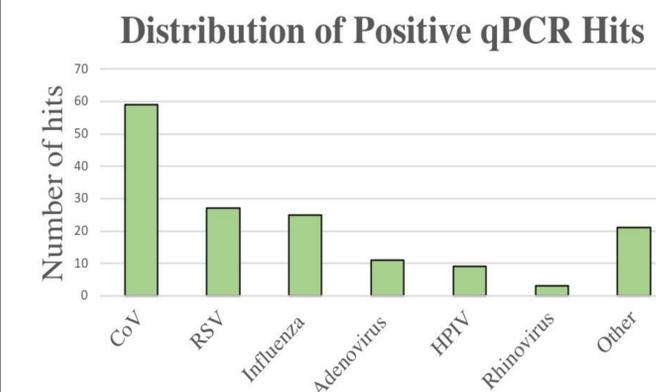


Fig.4 shows the distribution of all positive qPCR results (n=155) from combined nose and throat swabs in 99 positive samples. Results are counted for all possible hits for a given sample, as many individual samples had more than one positive hit stemming from either another strain of the same virus or a co-infection with another virus. "Other" classification is largely a collection of bacterial positives such as *Streptococcus pneumoniae*, *Streptococcus pyogenes*, and *Mycoplasma pneumoniae*.

### Discussion:

- Based on the Mann-Whitney U test, all of the differences in distribution between the positive and negative comparisons were found to be statistically significant, aiding in the validation of symptom scoring when comparing to lab standards for positive and negative disease state. As such, the graph data can be used to extrapolate some assumptions. For cough score, the median symptom score for the positive group was 1 and for the negative group it was 0. While there is obviously some range within the groups with the upper quartiles of negative cases reporting cough symptoms, the general expectation based on this data is that positive cases will present with cough while negative cases will present no cough. In instances where quick determinations are to be made, the presence or absence of cough could be seen as an indicator of the presence or absence of infection.
- Both the total symptom score and upper respiratory score were especially compelling since they include a more total picture of clinical presentation. The difference in medians of 5 and 4 respectively for total and upper respiratory allows for a practical separation of the positive and negative cases based on the associated clinical visit.
- While the difference in medians are significant, the group recognizes that this alone does not qualify the survey so additional statistical tests should be applied to evaluate the separation in scores and look for a possible trend in symptom scoring associated with differences in cycle threshold values of the qPCR testing. In relation to the standard composite scores focused on here, the group wants to further explore other possible combinations of symptoms that may be more indicative of a positive result.

### References:

Yan J, Grantham M, Pantelic J, et al. Infectious virus in exhaled breath of symptomatic seasonal influenza cases from a college community. *PNAS*. January 2018;201716561. doi:10.1073/pnas.1716561115

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