Symptom Criteria for COVID-19 Testing of Heath Care Workers

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ABSTRACT

Background: Symptom criteria for COVID-19 testing of heath care workers (HCWs) limitations on testing availability have been challenging during the COVID-19 pandemic. An evidence-based symptom criteria for identifying HCWs for testing, based on the probability of positive COVID-19 test results, would allow for a more appropriate use of testing resources.

Methods: This was an observational study of outpatient COVID-19 testing of HCWs. Prior to testing, HCWs were asked about the presence of 10 symptoms. Their responses were then compared to their subsequent pharyngeal swab COVID-19 polymerase chain reaction test results. These data were used to derive and evaluate a symptom-based testing criteria.

Results: A total of 961 HCWs were included in the analysis, of whom 225 (23%) had positive test results. Loss of taste or smell was the symptom with the largest positive likelihood ratio (3.33). Dry cough, regardless of the presence or absence of other symptoms, was the most sensitive (74%) and the least specific (32%) symptom. The existing testing criteria consisting of any combination of one or more of three symptoms (fever, shortness of breath, dry cough) was 93% sensitive and 9% specific (area unce the curve [AUC] = 0.63, 95% confidence interval [CI] = 0.59 to 0.67). The derived testing criteria consisting of any combination of one or more of two symptoms (fever, loss of taste or smell) was 89% sensitive and 48% specific (AUC = 0.75, 95% CI = 0.71 to 0.78). The hybrid testing criteria consisting of any combination of one or more of four symptoms (fever, shortness of breath, dry cough, loss of taste or smell) was 98% sensitive and 8% specific (AUC = 0.77, 95% CI = 0.73 to 0.80).

Conclusion: An evidence-based approach to COVID-19 testing that at least includes fever and loss of taste or smell should be utilized when determining which HCWs should be tested.

The 2019-novel coronavirus (COVID-19) pandemic has placed unique stressors on health care systems.[1] The burden of caring for the volume and complexity of patients during the pandemic is further complicated by strains on the health care workforce. Throughout the United States, countless health care workers (HCWs) who have suspected or confirmed COVID-19 have been kept out of work. Initial efforts centered around quarantining HCW with potential epidemiologic links such as travel history or exposure to a confirmed case without personal protective equipment. As the prevalence of disease in the United States increased, the practice of quarantining asymptomatic HCWs was abandoned by most health care systems.

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While regional and organizational variation exists, most HCWs today are isolated and excluded from work only if they have symptoms of potential COVID-19 infection such as fever, cough, or shortness of breath.[2] These symptoms are consistent with, but may not be adequately sensitive or specific for, the diagnosis of COVID-19. Preexisting medical conditions, other more benign viral illnesses, bacterial infections, and allergies[3] may also produce similar symptoms. Many HCWs with these symptoms are willing and able to perform their work functions, but are kept out of work for fear they may transmit COVID-19 to others. The limitations on testing resource availability and the paucity of evidence to inform test utilization have compounded these challenges.

An evidence-based symptom criteria for identifying HCWs for testing, based on the likelihood of a positive polymerase chain reaction (PCR) result for COVID-19 would allow for a more appropriate use of testing resources.

METHODS

This was an observational study of HCW tested for COVID-19. This study was approved by the University at Buffalo Institutional Review Board.

Setting

During a period of limited testing resources, a health system created a program for outpatient testing of HCW for COVID-19. HCW with symptoms concerning for COVID-19 infection were evaluated for potential testing through a centralized nurse call center. HCWs were eligible to return to work after a single negative test.

Data were collected from a health care system in western New York from March 26, 2020, to April 16, 2020. On the first day of data collection, the county had 166 (18 per 100,000) laboratory-confirmed cases of COVID and 2 (<1 per 100,000) confirmed COVID deaths. On the last day of data collection, the county had 1,951 (212 per 100,000) laboratory-confirmed cases of COVID and 115 (13 per 100,000) confirmed COVID deaths (source: Erie County Department of Health).

Symptoms

A standardized list of symptoms was developed and utilized as part of usual care by the health system's COVID-19 call center. Prior to scheduling COVID-19 testing, call center nurses were instructed to ask HCWs about the presence or absence of the following symptoms: fever (measured or subjective), fatigue, dry cough, loss of appetite (anorexia), pain in your muscles (myalgia), difficulty breathing (dyspnea), coughing up phlegm (expectoration), sore throat (pharyngalgia), diarrhea, and loss of taste or smell. The first eight symptoms were chosen because they were the most common symptoms described by Wang et al.[4] The latter two symptoms were chosen because more recent literature suggests they may play an important diagnostic role.[5,6] HCW responses were documented using electronic fixed-text fields that populated a Microsoft SharePoint 2013 database. Symptom data were extracted from the database by the primary investigator (BMC).

Testing

Nasopharyngeal or oropharyngeal swabs were performed at drive through testing sites as part of usual care. Samples were tested using real-time PCR diagnostic panels. Test results were reported as qualitatively positive or negative for the presence of nucleic acid from COVID-19. For the purposes of this study, the result of the single COVID-19 PCR test was considered diagnostic for presence or absence of the disease.

Data Analysis

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and positive likelihood ratio (PLR) were calculated for each symptom. In a stepwise fashion, the symptoms were selected for inclusion in the derived symptom criteria for testing. The symptom with the largest PLR was selected and included in the criteria. HCWs with that symptom were then excluded and the analysis was rerun with the remaining cases to determine the next symptom with the largest PLR. These steps were repeated until no new symptoms had significant PLR. PLR was chosen to balance the competing goals of disease identification and resource utilization.

The new derived symptoms criteria were then compared to existing criteria of fever, dry cough, or difficulty breathing and a hybrid of the two criteria. The sensitivity, specificity, PPV, NPV, and PLR were calculated for each criteria. Logistic regressions were performed to create receiver operator curves. The area under the curve (AUC) was determined for the various criteria. These data were analyzed using SAS version 9.4.

Sample Size

The original power analysis for this study was designed to ensure that the least common symptom had at least 20 occurrences with positive tests in the data set.[7] The model was based on the assumption that diarrhea would be the least common symptom and would be present in 7.8% of patients.[4] Based on that assumption, it was anticipated that 256 COVID-19–positive patients would have to be included in the data set. Data collection was stopped early after the health care system modified its screening methods in a manner that would have biased further observational data collection. At that point, there were already at least 35 occurrences of each of the 10 symptoms with a positive test result in the data set.

RESULTS

The health system's COVID-19 call center data set contained records from 1,114 HCWs. This included 141 records without documented symptoms and 12 records with documented symptoms but without documented laboratory results that were excluded from the analysis. Records from the remaining 961 HCWs were included in the analysis, of which 225 (23%) had positive test results.

Dry cough, regardless of the presence or absence of other symptoms, was reported by 666 (69%) HCW. It was the most sensitive (74%) and the least specific (32%) symptom. The characteristics of the 10 symptoms to predict a positive COVID-19 PCR are demonstrated in Table 1.

A single symptom only from the list was reported by 84 (9%) HCWs prior to testing. This included 28 (3%) HCWs who reported a dry cough only, none (0%) of which had subsequent positive COVID tests. In addition, 25 (3%) HCWs had a subjective or measured fever only, four (16%) of which had subsequent positive COVID tests. The testing results for HCWs with single symptoms are demonstrated in Table 2.

Loss of taste or smell was the symptom with the largest PLR (3.33, 95% confidence interval [CI = 2.60 to 4.06) and was the first symptom chosen for the testing criteria derivation. Once the 218 (23%) HCWs with loss of taste or smell had been removed from the data set, the second step of the analysis was run with the remaining 743 HCWs, 115 (15%) of which had positive test results. In the second step of the analysis, fever was the symptom with the largest PLR (1.79, 95% CI = 1.56 to 2.03)) and was the next symptom chosen for the testing criteria derivation. Fever was present in 364 (49%) HCWs in the second step of the analysis, 90 (25%) of which had positive test results. Once all HCWs with loss of taste or smell and/or fever had been removed from the data set, the third step of the analysis was run with the remaining 379 HCWs, 25 (7%) of which had positive test results (Table 3). In the third step of the analysis, no remaining symptoms had significant PLR (range = 0.70, 95% CI = 0.29 to 1.11 to 1.04, 95% CI = 0.70 to 1.39).

The characteristics of three possible testing criteria are demonstrated in Table 4. The existing testing criteria consisting of any combination of one or more of three symptoms (fever, shortness of breath, dry cough) had the smallest AUC. The derived testing criteria consisting of any combination of one or more of two symptoms (fever, loss of taste or smell) had the greatest PLR of the three criteria, but also the lowest sensitivity.

Table 1
Statistics for Presence of Each of the 10 Symptoms From the Data Set (n = 961)

Symptoms	TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV	PLR
Fever	143	413	323	82	0.64 (0.57–0.70)	0.56 (0.53–0.60)	0.31 (0.26–0.35)	0.83 (0.80–0.87)	1.45 (1.26–1.63)
Fatigue	150	289	447	75	0.67 (0.61–0.73)	0.39 (0.36–0.43)	0.25 (0.22–0.29)	0.79 (0.75–0.84)	1.10 (0.98–1.22)
Dry cough	166	236	500	59	0.74 (0.68–0.80)	0.32 (0.29–0.35)	0.25 (0.22–0.28)	0.80 (0.75–0.85)	1.09 (0.99–1.19)
Loss of appetite	90	542	194	135	0.40 (0.34–0.46)	0.74 (0.70–0.77)	0.32 (0.26–0.37)	0.80 (0.77–0.83)	1.52 (1.21–1.82)
Pain in your muscles	128	389	347	97	0.57 (0.50–0.63)	0.53 (0.49–0.56)	0.27 (0.23–0.31)	0.80 (0.76–0.84)	1.21 (1.04–1.37)
Difficulty breathing	83	418	318	142	0.37 (0.31–0.43)	0.57 (0.53–0.60)	0.21 (0.17–0.25)	0.75 (0.71–0.78)	0.85 (0.69–1.02)
Coughing up phlegm	35	625	111	190	0.16 (0.11–0.20)	0.85 (0.82–0.88)	0.24 (0.17–0.31)	0.77 (0.74–0.80)	1.03 (0.67–1.39
Sore throat	83	392	344	142	0.37 (0.31–0.43)	0.53 (0.50–0.57)	0.19 (0.16–0.23)	0.73 (0.70–0.77)	0.79 (0.64–0.94)
Diarrhea	57	544	192	168	0.25 (0.20–0.31)	0.74 (0.71–0.77)	0.23 (0.18–0.28)	0.76 (0.73–0.80)	0.97 (0.72–1.22)
Loss of taste or smell	110	628	108	115	0.49 (0.42–0.55)	0.85 (0.83–0.88)	0.50 (0.44–0.57)	0.85 (0.82–0.87)	3.33 (2.60–4.06)

For TP, TN, FP, and FN value is number of case. For sensitivity, specificity, PPV, NPV, and PLR value is shown with 95% CI.
TP = true positive; TN = true negative; FP = false positive; FN = false negative; PPV = positive predictive value; NPV = negative predictive value; PLR = positive likelihood ratio.

Table 2
Statistics for Presence of Each of the 10 Symptoms When Only One Symptom Was Present (n = 84)

Symptom	TP	FP	PPV
Fever	4	21	0.16
Fatigue	1	5	0.17
Dry cough	0	28	N/A
Loss of appetite	0	0	N/A
Pain in your muscles	0	2	N/A
Difficulty breathing	0	4	N/A
Coughing up phlegm	0	2	N/A
Sore throat	1	7	0.13
Diarrhea	0	2	0.00
Loss of taste or smell	3	4	0.43

For TP and FP value is number of case. For specificity, value is shown.
TP = true positive; FP = false positive; PPV = positive predictive value.

The hybrid testing criteria consisting of any combination of one or more of four symptoms (fever, shortness of breath, dry cough, loss of taste or smell) had the greatest sensitivity.

DISCUSSION

This study examined the association between clinical symptoms and COVID-19 PCR pharyngeal swab test results within the context of a derivation of an evidence-based testing criteria. When adequate testing resources are available, testing criteria based on fever, cough, difficulty breathing, and/or loss of taste or smell is a reasonable approach and is superior to testing criteria based on only fever, cough, and/or difficulty breathing. When testing resources are limited, a strategy of testing based on fever and/or loss of taste or smell should be considered.

A major finding of this study is the role of anosmia and ageusia in the diagnosis of COVID-19. Respiratory tract infections can cause direct damage to neurons in the olfactory epithelium. Postinfectious olfactory dysfunction is seen frequently after a respiratory tract infection and accounts for 18% to 45% of all cases of anosmia.[8] Recent reports have suggested that anosmia and ageusia could be potential symptoms of COVID-19.[5,9,10] During the pandemic, COVID-19

Table 3
Statistics for Presence of Each of the Eight Symptoms, After All HCWs With Fever and/or Loss of Taste or Smell Were Removed From the Data Set (n = 379)

Symptoms	TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV	PLR
Fatigue	15	150	204	10	0.60 (0.41–0.79)	0.42 (0.37–0.48)	0.07 (0.04–0.10)	0.94 (0.90–0.98)	1.04 (0.70–1.39)
Dry cough	18	94	260	7	0.72 (0.54–0.90)	0.27 (0.22–0.31)	0.06 (0.04–0.09)	0.93 (0.88–0.98)	0.98 (0.73–1.23)
Loss of appetite	4	287	67	21	0.16 (0.02–0.30)	0.81 (0.77–0.85)	0.06 (0.00–0.11)	0.93 (0.90–0.96)	0.85 (0.06–1.63)
Pain in your muscles	8	224	130	17	0.32 (0.14–0.50)	0.63 (0.58–0.68)	0.06 (0.02–0.10)	0.93 (0.90–0.96)	0.87 (0.36–1.38)
Difficulty breathing	8	192	162	17	0.32 (0.14–0.50)	0.54 (0.49–0.59)	0.05 (0.02–0.08)	0.92 (0.88–0.96)	0.70 (0.29–1.11)
Coughing up phlegm	4	299	55	21	0.16 (0.02–0.30)	0.84 (0.81–0.88)	0.07 (0.00–0.13)	0.93 (0.91–0.96)	1.03 (0.07–1.99)
Sore throat	8	197	157	17	0.32 (0.14–0.50)	0.56 (0.50–0.61)	0.05 (0.02–0.08)	0.92 (0.88–0.96)	0.72 (0.30–1.14)
Diarrhea	4	278	76	21	0.16 (0.02–0.30)	0.79 (0.74–0.83)	0.05 (0.00–0.10)	0.93 (0.90–0.96)	0.75 (0.06–1.43)

For TP, TN, FP, and FN value is number of case. For sensitivity, specificity, PPV, NPV, and PLR value is shown with 95% CI.
TP = true positive; TN = true negative; FP = false positive; FN = false negative; PPV = positive predictive value; NPV = negative predictive value; PLR = positive likelihood ratio.

Table 4
Statistics for Performance of the Three Criteria Applied to the Data Set (n = 961)

Symptoms	TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV	PLR	AUC
Fever, loss of taste or smell	200	354	382	25	0.89 (0.85–0.93)	0.48 (0.44–0.52)	0.34 (0.31–0.38)	0.93 (0.91–0.96)	1.71 (1.57–1.86)	0.75 (0.71–0.78)
Fever, difficulty breathing or dry cough	210	66	670	15	0.93 (0.90–0.97)	0.09 (0.07–0.11)	0.24 (0.21–0.27)	0.81 (0.73–0.90)	1.03 (0.98–1.07)	0.63 (0.59–0.67)
Fever, difficulty breathing, dry cough, loss of taste or smell	220	58	678	5	0.98 (0.96–1.00)	0.08 (0.06–0.10)	0.24 (0.22–0.27)	0.92(0.85–0.99)	1.06 (1.03–1.09)	0.77 (0.73–0.80)

For TP, TN, FP, and FN value is number of case. For sensitivity, specificity, PPV, NPV, PLR, and AUC value is shown with 95% CI.
TP = true positive; TN = true negative; FP = false positive; FN = false negative; PPV = positive predictive value; NPV = negative predictive value; PLR = positive likelihood ratio; AUC = area under the curve.

testing should be considered for patients with isolated anosmia and/or ageusia.

Fever has previously been identified as a common symptom of COVID-19 infection. Fever represents a systemic response to infection, but may not be present in early or mild cases.[4,11,12] While fever was commonly seen in patients with positive COVID-19 tests, most of these patients also had other symptoms suggestive of COVID-19.[4,11] Considerable efforts have been made to institute preshift temperature screening of HCW. The small number of positive tests in HCW with isolated fever, without any other symptoms, in this data set questions the utility of that practice. Myalgias have also classically been indicative of systemic viral infection.[13] However, myalgias in the absence of fever, anosmia, or ageusia did not play a significant role in our model.

Respiratory symptoms including cough, shortness of breath, and sore throat have been reported in the majority of patients with COVID-19.[4,11] COVID-19 is thought to be transmitted through large droplets. These droplets can be spread with activities such as coughing, sneezing, speaking, and even with breathing.[14] At this time, the literature is limited to reports that transmission is through large respiratory droplets and fomite transmission.[15] It is reasonable to infer that patients exhibiting respiratory symptoms would be among the most likely patients to transmit the COVID-19 to others via respiratory droplets.

There have also been reported cases of COVID-19 with primarily gastrointestinal (GI) symptoms such as nausea, vomiting, abdominal pain, diarrhea, or anorexia.[6] This includes cases of COVID-19 with GI symptoms in the absence of respiratory symptoms. However, these patients have typically presented with other constitutional symptoms such as fever. Patients presenting with GI symptoms are significantly more likely to have positive anal swabs in comparison to those who do not (73% vs. 14%, respectively).[13] While these findings cannot be used to rule out the presence of a COVID-19 infection in patients with isolated GI symptoms, it does suggest that patients with isolated GI symptoms are unlikely to have positive COVID-19 PCR testing from a pharyngeal swab. Fecal–oral transmission may also be possible, as is seen in common coronaviruses, although this has not yet been conclusively demonstrated.[16]

These testing criteria were judged based on the association between symptoms and subsequent pharyngeal swab test results. This should not be construed to necessarily predict the probability of antibody-proven acute illness or the risk of disease transmission. A case study, published by Bai et al.[17] described an asymptomatic carrier who transmitted COVID-19 to four individuals in China. Similarly, Mizumoto et al[18] reviewed the data from the Diamond Princess cruise ship where 17.9% of infected individuals had an asymptomatic course.

The study utilized PCR testing as the presumed standard for the presence or absence of COVID-19. Sensitivities for RT-PCR analysis of nasopharyngeal and oropharyngeal swabs have been shown to range widely.[19,20] Therefore, a single negative nasopharyngeal or oropharyngeal PCR test may be inadequate to rule out COVID-19. If testing criteria are based on and inform the usage of a laboratory test, its utility is only as good as the performance of that test. It is possible, though outside the scope of this study design, that certain constellations of symptoms in a patient with COVID-19 would have variable rates of detection using PCR testing of pharyngeal swabs.

This study featured HCWs who underwent outpatient COVID-19 testing during March and April 2020 in western New York. Changes to the underlying prevalence of disease would impact the PPV and NPV in similar populations. It is also unclear how these testing criteria would perform when utilized among other at-risk populations such as the lay public, patients requiring admission to the hospital, and nursing home residents. Further research is needed to validate these testing criteria for HCWs and other at-risk populations.

CONCLUSION

Limited testing resources have posed a significant challenged to health care systems' response to the COVID-19 pandemic. An evidence-based approach to COVID-19 testing that at least includes fever and loss of taste or smell should be utilized when determining which HCWs should be tested.

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