A Diagnostic Survey for Screening Patients for Post-Covid Conditions

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Introduction
Post-Covid conditions1 may afflict 10–30% of individuals following infection with SARS-CoV-2 and have been defined as symptoms present or persisting ≥3 months after infection, and continue for ≥2 months, without an alternative diagnosis.2 They have been characterized by the array of patient reported symptoms across organ system domains, with fatigue, breathlessness, and confusion commonly described.3 Despite numerous reports, no consensus has been reached regarding the diagnostic symptoms of post-Covid conditions. This cross-sectional study evaluates the use of a standardized symptom survey as a diagnostic screening test for post-Covid conditions.

Materials and Methods
No extramural funding supported this work. This work was done in accord with the Declaration of Helsinki and received Institutional Review Board approval at Hackensack Meridian Health. Participants were anonymously recruited from electronic medical record data of patients who had a positive COVID-19 PCR test between July 1, 2020 and August 30, 2021, and those who were subsequently evaluated for post-Covid conditions at a Covid Recovery Clinic. Patients were evaluated 3–12 months following their infection. In December 2021, using REDCap,4 participants were contacted by email, provided informed consent, completed the survey online.

The survey rated the intensity or impact of 25 common symptoms associated with post-covid conditions which occurred “during the past week” and “prior to COVID infection”, using a 5-point scale (0=not present; 1=mild, does not interfere with daily activities; 2=moderate, sometimes interferes; 3=severe, always interferes; 4=very severe, I am disabled by this symptom). Symptom scores, 0 to 4 for each symptom, produced a composite score (0 to 100) for each time point. A change in the composite score between the two time points was calculated for each participant (potential range −100 to +100).

Receiver operating characteristic (ROC) curve analyses were used to identify an ideal cut point in the change composite scores for grouping the patients into the two groups - those who had been evaluated for post-Covid conditions in the Clinic and those who had not. The ideal cut point from ROC analysis would be used to recategorize the patients into new groups of participants with post-Covid conditions (> cut point) versus those who had recovered from their Covid infection (≤ cut point). A change score of 11 points was identified as the ideal cut point.

Results
Responses were obtained from 19.2% (144/750) of patients who had been evaluated in Clinic for post-Covid conditions, and 6.5% (97/1500) who were not. The ROC curve analysis identified an ideal cut point of 11 for the change in the composite score from pre-infection to the present, as the ideal cut point separating participants who recovered after infection from those who presented with post-COVID conditions. Demographics and comorbid conditions were similar.
(Table 1), with the greatest change in symptom ratings for post-exertional weakness or exhaustion, excessive fatigue, confusion, memory problems and dyspnea (Table 2).

For the Clinic participants, 107 of the 144 had a change in symptom score of >11, indicating a sensitivity for this scale and cut point to identify post-COVID condition patients of 74%; 25 of the 97 Positive PCR participants had a score of <11, with a specificity of 74%.

Table 1 Participant Demographics and Comorbidities

|                         | Post-COVID Condition Subjects (Change Score >11) N=132 | Recovered Subjects (Change Score ≤11) N=109 | P-value |
|-------------------------|-------------------------------------------------------|-------------------------------------------|---------|
| **Participant Characteristics** |                                                       |                                           |         |
| Age: Mean ± SD           | 51.26 ± 13.37                                         | 49.37 ± 17.08                             | 0.3375  |
| Range                   | 22.00 to 81.00                                        | 20.00 to 99.00                           |         |
| Female Gender at birth  | 96/132 (72.7%)                                        | 67/109 (61.5%)                           | 0.0526  |
| **Race**                |                                                       |                                           |         |
| Asian                   | 4/125 (3.2%)                                          | 8/104 (7.7%)                             | 0.4288  |
| Black or African American | 8/125 (6.4%)                                      | 7/104 (6.7%)                             |         |
| Other                   | 9/125 (7.2%)                                          | 5/104 (4.8%)                             |         |
| Unknown                 | 0 (0.0%)                                              | 0 (0.0%)                                 |         |
| **Ethnicity**           |                                                       |                                           |         |
| White                   | 104/125 (83.2%)                                       | 84/104 (80.8%)                           |         |
| Hispanic                | 24/126 (19.0%)                                        | 8/107 (7.5%)                             | 0.0126  |
| Non-Hispanic            | 101/126 (80.2%)                                       | 99/107 (92.5%)                          |         |
| Unknown                 | 1/126 (0.8%)                                          | 0 (0.0%)                                 |         |
| **Comorbid Conditions** |                                                       |                                           |         |
| Hypertension            | 37/132 (28.0%)                                        | 27/109 (24.8%)                           | 0.5685  |
| Diabetes                | 12/132 (9.1%)                                         | 7/109 (6.4%)                             | 0.4441  |
| COPD                    | 1/132 (0.8%)                                          | 2/109 (1.8%)                             | 0.5910  |
| Asthma                  | 14/132 (10.6%)                                        | 10/109 (9.2%)                            | 0.7118  |
| Cardiac conditions      | 8/132 (6.1%)                                          | 10/109 (9.2%)                            | 0.3601  |
| Chronic kidney disease  | 3/132 (2.3%)                                          | 2/109 (1.8%)                             | 1.0000  |
| Stroke                  | 1/132 (0.8%)                                          | 1/109 (0.9%)                             | 1.0000  |
| Immunodeficiency (medical, drug) | 10/132 (7.6%)                                      | 3/109 (2.8%)                             | 0.0990  |
| Active cancer           | 12/132 (9.1%)                                         | 6/109 (5.5%)                             | 0.2919  |
| Hospitalized due to COVID-19 | 48/132 (36.4%)                                      | 32/109 (29.4%)                           | 0.2503  |

Notes: Chi-square test or Fisher’s exact test used for categorical variables, as appropriate. t-tests or Wilcoxon rank sum tests used for continuous variables, as appropriate.

Abbreviation: SD, standard deviation.
Table 2 Change in Symptom Scores (Pre-Covid-19 to ≥ 3 Months After Acute Covid-19 Infection)

| Symptom, Change in Score | Post-COVID Condition Subjects (Score >11) N=132 | Recovered Subjects (Score ≤11) N=109 | P-value |
|--------------------------|---------------------------------|----------------------------------|--------|
| Intermittent fever (N)   | 131                             | 107                              | <0.0001|
| Mean ± SD                | 0.62 ± 1.09                     | −0.12 ± 0.70                     |        |
| Excessive fatigue (N)    | 131                             | 106                              | <0.0001|
| Mean ± SD                | 2.11 ± 1.05                     | 0.33 ± 0.94                      |        |
| Excessive weakness or exhaustion after exertion (N) | 132 | 105 | <0.0001 |
| Mean ± SD                | 2.17 ± 1.11                     | 0.16 ± 0.93                      |        |
| Lightheadedness          | 130                             | 104                              | <0.0001|
| Mean ± SD                | 1.35 ± 1.15                     | 0.08 ± 0.72                      |        |
| Palpitations or a racing heart at rest | 132 | 104 | <0.0001 |
| Mean ± SD                | 1.36 ± 1.15                     | 0.06 ± 0.89                      | <0.0001|
| Shortness of breath      | 131                             | 103                              | <0.0001|
| Mean ± SD                | 1.85 ± 1.15                     | 0.17 ± 0.91                      | <0.0001|
| Cough                    | 124                             | 96                               | <0.0001|
| Mean ± SD                | 0.98 ± 1.10                     | 0.11 ± 0.60                      | <0.0001|
| Chest pain while taking a breath | 130 | 102 | <0.0001 |
| Mean ± SD                | 0.75 ± 1.09                     | −0.08 ± 0.61                     | <0.0001|
| Chest pain not associated with breathing | 127 | 97 | <0.0001 |
| Mean ± SD                | 1.27 ± 1.15                     | 0.07 ± 0.58                      | <0.0001|
| Diarrhea                 | 126                             | 97                               | <0.0001|
| Mean ± SD                | 0.56 ± 1.02                     | −0.07 ± 0.60                     | <0.0001|
| Nausea or vomiting       | 128                             | 103                              | <0.0001|
| Mean ± SD                | 0.50 ± 0.90                     | −0.07 ± 0.68                     | <0.0001|
| Hearing loss             | 127                             | 96                               | <0.0001|
| Mean ± SD                | 0.55 ± 0.98                     | 0.00 ± 0.15                      | <0.0001|
| Loss of ability to taste | 130                             | 105                              | <0.0001|
| Mean ± SD                | 0.94 ± 1.29                     | 0.08 ± 0.83                      | <0.0001|
| Loss of ability to smell | 130                             | 97                               | <0.0001|
| Mean ± SD                | 0.91 ± 1.20                     | 0.22 ± 0.83                      | <0.0001|
| Vision change or eye irritation | 129 | 99 | <0.0001 |
| Mean ± SD                | 0.91 ± 1.20                     | 0.22 ± 0.83                      | <0.0001|
| Headaches                | 130                             | 98                               | <0.0001|
| Mean ± SD                | 1.27 ± 1.17                     | 0.03 ± 0.67                      | <0.0001|
| Confusion or difficulty concentrating | 128 | 102 | <0.0001 |
| Mean ± SD                | 1.95 ± 1.19                     | 0.06 ± 0.56                      | <0.0001|
| Memory problems          | 129                             | 100                              | <0.0001|
| Mean ± SD                | 1.93 ± 1.19                     | 0.14 ± 0.45                      | <0.0001|
| Feeling of pins and needles and/or numbness in hands or feet | 127 | 96 | <0.0001 |
| Mean ± SD                | 1.22 ± 1.27                     | 0.16 ± 0.55                      |        |

(Continued)
Table 2 (Continued).

| Symptom, Change in Score | Post-COVID Condition Subjects (Score >11) N=132 | Recovered Subjects (Score ≤11) N=109 | P-value |
|--------------------------|-----------------------------------------------|--------------------------------------|---------|
| Generalized pain         | 129                                           | 100                                  | <0.0001 |
| Mean ± SD                | 1.26 ± 1.15                                   | 0.02 ± 0.43                          |         |
| Anxiety                  | 131                                           | 105                                  | <0.0001 |
| Mean ± SD                | 1.34 ± 1.15                                   | 0.05 ± 0.70                          |         |
| Depression               | 131                                           | 103                                  | <0.0001 |
| Mean ± SD                | 1.08 ± 1.07                                   | −0.01 ± 0.51                         |         |
| Insomnia                 | 127                                           | 103                                  | <0.0001 |
| Mean ± SD                | 1.32 ± 1.19                                   | −0.02 ± 0.70                         |         |

Notes: Chi-square test or Fisher’s exact test used for categorical variables, as appropriate. With bold all p-values <0.001.
Abbreviation: SD, standard deviation.

Discussion
Although this study represents a small sample size due to a low response rate, participant demographics and comorbidities were similar in both groups defined by the cut point of 11. The use of a value of change in composite symptom score for this 25-symptom survey accounts for pre-infection symptoms due to other conditions which may confound the diagnosis of post-Covid syndromes. It also quantifies and provides a comparison for the range, severity and functional impact of symptoms, while minimally limiting the number of symptoms considered to 25 for diagnostic purposes.

Conclusion
Given the prevalence of potential patients with post-COVID conditions, a clinical screening test to identify patients for care within specialized clinical programs and screen subjects for clinical trial enrollment, this survey performs well with 74% sensitivity and specificity in identifying participants with post-COVID conditions.

Disclosure
The authors report no conflicts of interest in this work.

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