# Putting the PASC Score to the Test: Clinical vs. Statistical Accuracy in Long COVID Diagnosis

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## ABSTRACT

***OBJECTIVE:*** To validate the RECOVER Post-Acute Sequelae of SARS-CoV-2 infection (PASC) score in a cohort of patients who develop long COVID (LC) or fully recover while iteratively improving the tool's sensitivity and specificity.

***METHODS:*** A cross-sectional study in 130 LC patients followed at LC clinics in Baltimore, MD, USA, who met the National Academies of Sciences, Engineering, and Medicine (NASEM) 2024 LC definition, and 60 SARS-CoV-2 exposed but fully recovered individuals. LC participants were required to have at least one neuropsychiatric symptom. Participants completed comprehensive surveys and questionnaires assessing symptoms based on published methods to determine PASC score. Using the NASEM 2024 LC definition as the "true" condition, we compared evaluation metrics for the RECOVER PASC score cutoff (*PASC*>12) and the presence of individual/multiple symptoms. Evaluation metrics (e.g., sensitivity, specificity, F1) were calculated based on these classifications for the overall PASC score and symptom combinations.

***RESULTS:*** The LC cohort ($n$=130) had a mean age of 47.2 years and was predominantly female (72%), White (79%), and well-educated (77%>16 years). Controls ($n$=60) were similar demographically. LC diagnosis and PASC scores were significantly associated ($\chi^2$=102.99, $P$<0.001). The PASC score showed excellent specificity (100%) and positive predictive value (PPV; 100%) albeit limited sensitivity (80%), missing 20% of participants with LC. We found that loss of smell/taste, post-exertional malaise, or lack of sexual desire or capacity demonstrated 94% sensitivity, 92% specificity, and 96% PPV, 87% NPV, and an F1 score of 0.949.

***CONCLUSION:*** Validation of the RECOVER PASC supports its utility and highlights the need for ongoing refinement of the LC definition. We call for national efforts to develop readily implementable clinical tools for LC diagnosis.

*KEY WORDS:* COVID-19; PASC score; long COVID; long COVID diagnosis

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## INTRODUCTION

In the wake of the COVID-19 pandemic, 1 in 10 people with SARS-CoV-2 infection will develop a condition known as long COVID (LC). An estimated 26.4% of adults with LC in the USA have symptoms leading to impairments in performing basic activities of daily living,[1] which has led experts to call LC a mass-disabling event. The CDC estimates that 6.9% of US adults have had long COVID, which translates into more than 22 million individuals.[2] In 2024, the National Academies of Sciences, Engineering, and Medicine (NASEM) defined LC as an infection-associated chronic condition (IACC), characterized by symptoms present for at least 3 months, as a continuous, relapsing, and remitting disease state that affects multiple organ systems.[3] Currently, no standardized diagnostic criteria confirm the diagnosis of LC. Given the condition's heterogeneous phenotypes and the limited scientific understanding of postinfectious fatiguing illnesses, many LC patients face skepticism and dismissal from the medical community.[4]

The most frequent symptoms of LC include post-exertional malaise (PEM), fatigue, dizziness, brain fog, and gastrointestinal (GI) symptoms.[4] The National Institutes of Health's Researching COVID to Enhance Recovery (RECOVER) Initiative published their findings on their large national cohort that included individuals infected or uninfected with SARS-CoV-2, before the development of the NASEM LC definition. They developed a symptom-based case definition that could be used to identify cases of Post-Acute Sequelae of SARS-CoV-2 infection (PASC).[1] In the absence of a gold standard diagnostic test, and with broad multisystemic involvement of the condition, the focus was to identify the symptoms that differentiated the infected versus uninfected individuals. A total of 44 symptoms were assessed, of which 12 differentiated SARS-CoV-2 infected from uninfected patients. The PASC score symptoms in order of highest to lowest scoring included loss of or change in smell or taste, PEM, chronic cough, brain fog, thirst, palpitations, chest pain, fatigue, sexual desire or capacity, dizziness, gastrointestinal symptoms, abnormal movements, and hair loss. A score greater than or equal to 12 was the

cut point determined to distinguish PASC+ versus PASC-intermediate individuals.

We examined the concordance of the PASC score in a cohort of patients followed by a specialized LC clinic at a large tertiary referral medical center. The present study aimed to validate the RECOVER PASC score and contribute to the iterative process for ongoing refinement of the definition of LC. External validation of diagnostic and screening instruments across diverse populations is critical to establishing their reliability, accuracy, and external validity. Tools derived from large, heterogeneous datasets must be examined in rigorously phenotyped clinical cohorts to assess their discriminative performance and ensure that predictive accuracy is maintained across varying case mixes and settings. Without such validation, their clinical and research applications remain uncertain.

## MATERIALS AND METHODS

### Human Participants

The study protocol was approved by the Johns Hopkins Institutional Review Board. Participants provided written informed consent and were recruited from the Johns Hopkins Post-Acute COVID-19 Team (PACT) and the LC Myalgic Encephalomyelitis Chronic Fatigue Clinics in Baltimore, MD, USA. Individuals were included if they had been enrolled in the JH COVID-BRAIN study between July 2023 and June 2025 and met the NASEM 2024 published definition of LC, presented with at least one neuropsychiatric symptom (i.e., brain fog or headaches)[3] and were between the ages of 18 and 80. Exclusion criteria consisted of the following: (1) Lack of English proficiency, (2) active or recent (within 3 months) substance misuse assessed by clinical interview and toxicology (nicotine/cannabis allowed), (3) history of psychosis, and (4) MRI contraindications. Control participants are group-matched by age, biological sex, and SARS-CoV-2 infection status. The control participants were screened for LC symptoms through questionnaires and a clinical provider-directed interview.

### Clinical Assessments During Study Enrollment

RADx® Underserved Populations (RADx-UP) Tier 1 and 2 assessments and the Yale COVID-19 Review of Systems (Yale CRS)-version 10 were collected in order to characterize participants in terms of preexisting conditions, acute and LC symptomatology, vaccination status, COVID variant (based on the date of initial infection) and complications, and self-reported disability. In order to compute the PASC score and determine PASC categorization (PASC+ or PASC intermediate), we collected the following questionnaires and items: Neuro-QoL SF v2.0 Short Form,[5] Seattle Angina Questionnaire (SAQ-7),[6] and PROMIS SF v1.0-Fatigue 13a (FACIT-Fatigue).[7] Additionally, participants were asked the following questions to assess the other symptoms based on the methods of the PASC score publication: (1) loss of/change in smell or taste; (2) PEM/worsening of symptoms after even minor physical or mental effort; (3) persistent chronic cough; (4) excessive thirst; (5) palpitations, racing heart, arrhythmia, and skipped beats; (6) changes in desire for/comfort with/capacity for sex; (7) gastrointestinal (GI) symptoms (feeling full, vomiting after eating, diarrhea, constipation); (8) abnormal movements; (9) hair loss; and (10) felt faint, dizzy, "goofy," or had difficulty thinking soon after standing up from a sitting or lying position.

### Data Analysis and Statistics

Using the NASEM 2024 LC definition as the "true" condition, we compared evaluation metrics for the RECOVER PASC score cutoff (PASC total $\geq 12$) as well as comparing the presence of individual, pairs of, and triplets of symptoms. For symptom combinations, participants were categorized as having LC if they reported *any* of the symptoms in the combination. Evaluation metrics such as sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and F1 score were calculated based on these classifications for both the overall PASC score and for individual symptoms, as well as combinations. Given this, the dataset was imbalanced due to more true LC participants than controls, and thus, traditional evaluation metrics, such as accuracy, may not provide the most meaningful interpretation. Therefore, we calculated evaluation metrics including sensitivity, specificity, and F1 score not only for the PASC score cutoff but also for reported symptoms and symptom combinations. All analyses were conducted in IBM SPSS software version 31 and R version 3.3.3.

## RESULTS

### Study Population

The LC cohort ($n=130$) had a mean age of 47.2 years and was predominantly female (76%), and the majority had a level of education equivalent to a bachelor's degree or higher (77%) (Table 1). The healthy controls ($n=60$) were similar demographically. Among LC patients, common preexisting conditions included depression (51%) and other mental health disorders (41%), asthma (32%), hypertension (32%), and autoimmune disease (26%) (Table 2). On the Yale CRS, the most common symptoms experienced during acute COVID-19 included upper respiratory symptoms, headaches, cough or shortness of breath, and fever followed by loss or worsened sense of taste and/or smell. The most common LC symptoms included PEM, gastrointestinal, fatigue, palpitations, chest pain, and cognitive symptoms. On the RADx-UP, 52% of LC patients reported experiencing disability, mostly involving difficulty with concentration and memory (75%), walking or climbing stairs (71.9%), doing errands alone (63.2%), and dressing or bathing (46.4%). The common SARS-CoV-2 strains that preceded LC symptoms were pre-Delta (36%), Omicron (28%), and Delta (28%).

**Table 1 Characteristics of Patients with Long COVID (LC, NASEM 2024) Versus Controls (SARS CoV 2 Infected, Fully Recovered)**

| | LC ($n=130$) $n$ (%) | Controls ($n=60$) $n$ (%) | $p$-value |
|---|---|---|---|
| Age, M (SD) | 47.2 (13.3) | 45.7 (16.4) | 0.49 |
| Biological sex | 99 (76.2) | 40 (65.6) | 0.16 |
| Gender identity | | | 0.60 |
| Female | 94 (72.3) | 40 (65.6) | |
| Male | 30 (23.1) | 20 (32.8) | |
| Female to male transgender | 1 (0.8) | 0 (0.0) | |
| Male to female transgender | 2 (1.5) | 0 (0.0) | |
| Other | 2 (1.5) | 1 (1.6) | |
| Missing | 1 (0.8) | 0 (0) | |
| Sexual identity | | | 0.70 |
| Only straight or heterosexual | 92 (70.8) | 44 (72.1) | |
| Mostly straight or heterosexual | 12 (9.2) | 3 (4.9) | |
| Only lesbian or gay | 8 (6.1) | 3 (4.9) | |
| Mostly lesbian or gay | 3 (2.3) | 1 (1.6) | |
| Bisexual | 11 (8.5) | 6 (9.8) | |
| Other | 3 (2.3) | 4 (6.6) | |
| Missing | 0 (0.8) | 0 (0.0) | |
| Race | | | 0.49 |
| White | 103 (79.2) | 43 (70.5) | |
| Black | 15 (11.5) | 8 (13.1) | |
| Asian | 6 (4.6) | 6 (9.8) | |
| Other | 5 (3.8) | 4 (6.6) | |
| Unkown or not reported | 1 (0.8) | 0 (0) | |
| Ethnicity | | | 0.99 |
| Hispanic or Latino | 9 (6.9) | 4 (6.6) | |
| Not Hispanic or Latino | 119 (91.5) | 56 (91.8) | |
| Unknown or not reported | 2 (1.5) | 1 (1.6) | |
| Education | | | 0.19 |
| High school graduate/GED | 5 (3.8) | 0 (0.0) | |
| Some college | 25 (19.2) | 7 (11.5) | |
| College graduate | 45 (34.6) | 22 (36.1) | |
| Graduate/Professional | 55 (42.3) | 32 (52.5) | |

## Frequency of LC Diagnosis Using the RECOVER PASC Score

Table 3 shows the concordance of LC diagnosis via NASEM 2024 and the PASC score screenings. LC diagnosis and PASC score were significantly associated, $\chi^2=102.99$ and $P<0.001$. Overall, 80% of the cases were classified consistently. The percent of false negatives, where a positive LC diagnosis was missed due to the PASC score falling < 12, was 20%. The specificity of the PASC score was 100%, as all individuals without LC were correctly identified as negative. The PPV was 100%, indicating that 100% of individuals who tested PASC+ had LC. However, the NPV was 69.76%, indicating that 30% of those who tested negative for LC were false negatives. Given the imbalance in the dataset, this resulted in an F1 score of 0.889. The cases with PASC scores < 12 and the individual symptoms endorsed are in Supplemental Table 1.

To further evaluate the performance of the PASC score, we examined combinations of symptoms. In addition to calculating evaluation metrics for the overall PASC score, we computed sensitivity, specificity, PPV, NPV, and F1 score for individual symptoms, pairs of symptoms, and triplets of symptoms. Participants were categorized as having LC if they endorsed any of the symptoms within the combination. The combination of loss of smell/taste, PEM, and lack of sexual desire or capacity yielded the highest performance metrics (94% sensitivity, 92% specificity, $F1=0.949$) (Supplemental Table 2), indicating these symptoms may be key contributors to LC identification.

## Differences Between LC Patients with a PASC+ versus PASC-Intermediate Score

Although the majority of sociodemographic factors were similar between patients with an LC diagnosis who tested PASC+ and those who tested PASC intermediate, the PASC+ group was slightly younger and more likely to report having asthma, other mental health or chronic conditions, and self-reported disability. The PASC-intermediate group was more likely to have a cancer diagnosis in the past 12 months (Table 2). Additionally, the PASC+ group was more frequently associated with the pre-Delta or Delta variant than the PASC-intermediate group. During acute SARS-CoV-2 infection, the PASC+ group was more likely to report nausea or vomiting and a loss or worsened sense of taste compared to the PASC-intermediate group. With respect to the PASC score symptoms, the PASC+ group was more likely to report differences in smell/taste, PEM, chronic cough, brain fog, thirst, palpitations, chest pain, fatigue, GI symptoms, and abnormal movements compared to the PASC-intermediate group.

## DISCUSSION

This study is the first attempt at validating the PASC score in a cohort of clinically diagnosed LC patients receiving care at a specialized clinic. Based on the PASC score, 80% of our LC patients would be qualified as PASC+, missing 20% of patients with LC. These PASC-intermediate patients had severe enough symptoms to seek out medical care; nevertheless, they had a lower self-reported disability, suggesting a lower symptom burden than the PASC+ group. This finding is consistent with the original PASC score publication demonstrating that higher scores were associated with lower quality of life based on the PROMIS Global 10 scores.[1] Failing to identify 20% of people with LC has significant implications for developing a long COVID definition and understanding this disease state's clinical and population impact. In the absence of an established biomarker to diagnose LC, the need for the development of a clinical tool to assist in the identification of LC patients is crucial. Refining the PASC score by ongoing validation in multiple settings has the potential of developing an implementable screening tool for the clinical and research setting.

Using statistical metrics of classifier performance analysis, we identified three hallmark symptoms: PEM, altered or absent smell and taste, and lack of sexual desire or capacity.

**Table 2 Characteristics of 130 Patients with Long COVID (LC) According to NASEM 2024 and by the RECOVER Postacute Sequela of SARS-CoV-2 Infection (PASC) Score Cutoff (≥ 12)**

| | **LC (*n* = 130) N/%** | **PASC + (*n* = 104) n (%)** | **PASC-intermediate (*n* = 26) n (%)** | ***p*-value** |
|---|---|---|---|---|
| ***Demographics*** | | | | |
| Age, M (SD) | 47.2 (13.3) | 46.0 (13.0) | 52.2 (13.5) | 0.03 |
| Biological sex | 99 (76.2) | 83 (79.8) | 16 (61.5) | 0.07 |
| White | 103 (79.2) | 84 (80.8) | 19 (73.1) | 0.42 |
| Not Hispanic or Latino | 119 (91.5) | 94 (90.4) | 25 (96.2) | 0.69 |
| College graduate or higher | 100 (76.9) | 77 (74.0) | 23 (88.5) | 0.19 |
| ***RADx® Underserved Populations (RADx-UP)*** | | | | |
| **Pre-existing conditions** | | | | |
| Immunocompromised condition | 27 (20.8) | 22 (21.2) | 5 (19.2) | 0.857 |
| Autoimmune disease | 34 (26.2) | 31 (29.8) | 3 (11.5) | 0.138 |
| Hypertension | 42 (32.3) | 36 (34.6) | 6 (23.1) | 0.451 |
| Diabetes | 12 (9.2) | 9 (8.7) | 3 (11.5) | 0.649 |
| Chronic kidney disease | 7 (5.4) | 4 (3.8) | 3 (11.5) | 0.143 |
| Cancer diagnosis and/or treatment in the past 12 months | 4 (3.1) | 1 (1.0) | 3 (11.5) | 0.026 |
| Cardiovascular disease | 5 (3.8) | 4 (3.9) | 1 (3.8) | 1.000 |
| Asthma | 42 (32.3) | 39 (37.5) | 3 (11.5) | 0.011 |
| Chronic obstructive pulmonary disease | 4 (3.1) | 4 (3.8) | 0 (0) | 0.583 |
| Other chronic lung disease | 6 (4.6) | 5 (4.8) | 1 (3.8) | 1.000 |
| Sickle cell anemia | 0 (0) | 0 (0) | 0 (0) | - |
| Depression | 67 (51.5) | 57 (44.8) | 10 (38.5) | 0.268 |
| Alcohol or substance use disorder | 0 (0) | 0 (0) | 0 (0) | - |
| Other mental health disorders | 54 (41.5) | 48 (46.2) | 6 (23.1) | 0.018 |
| Other chronic condition | 56 (43.1) | 52 (50.0) | 4 (15.4) | 0.005 |
| **Self-reported disability and of those with disability,** | 67 (52.3) | 56 (54.4) | 2 (8.0) | < 0.001 |
| Difficulty hearing | 4 (7.0) | 3 (5.5) | 1 (50.0) | 0.137 |
| Vision difficulty even with glasses | 2 (3.6) | 2 (3.7) | 0 (0) | 0.943 |
| Difficulty concentrating, remembering, or making decisions | 42 (75.0) | 41 (75.9) | 1 (50.0) | 0.441 |
| Serious difficulty walking or climbing stairs | 41 (71.9) | 40 (72.7) | 1 (50.0) | 0.735 |
| Difficulty dressing or bathing | 26 (46.4) | 26 (48.1) | 0 (0) | 0.494 |
| Difficulty doing errands alone (i.e., shopping) | 36 (63.2) | 36 (65.5) | 0 (0) | 0.147 |
| **Ever received a COVID-19 vaccine** | 122 (93.8) | 98 (94.2) | 24 (92.3) | 0.748 |
| **Current non-smoker** | 119 (93.0) | 94 (91.3) | 25 (100.0) | 0.672 |
| **Marijuana use in the past 12 months** | 29 (23.8) | 22 (22.2) | 7 (30.4) | 0.580 |
| **COVID-19 variant** | | | | < 0.001 |
| Pre-delta | 47 (36.2) | 44 (42.3) | 3 (11.5) | |
| Delta | 36 (27.7) | 33 (31.7) | 3 (11.5) | |
| Omicron | 37 (28.5) | 23 (22.1) | 14 (53.8) | |
| Post-omicron | 9 (6.9) | 4 (3.8) | 5 (19.2) | |
| Unknown | 1 (0.8) | 0 (0) | 1 (3.8) | |
| **Hospitalization from COVID-19 (ICU or inpatient)** | 20 (15.4) | 17 (16.7) | 3 (12.0) | 0.566 |
| ***Yale COVID-19 Review of Symptoms-version 10*** | | | | |
| **Symptoms during acute COVID-19** | | | | |
| Fever | 96 (73.8) | 75 (72.1) | 21 (80.8) | 0.369 |
| Cough or shortness of breath | 106 (81.5) | 87 (83.7) | 19 (73.1) | 0.214 |
| Upper respiratory (sore throat, congestion) | 108 (83.1) | 85 (81.7) | 23 (88.5) | 0.413 |
| Nausea or vomiting | 47 (36.2) | 45 (43.3) | 2 (7.7) | < 0.001 |
| Diarrhea | 41 (31.5) | 34 (32.7) | 7 (26.9) | 0.571 |
| Loss or worsened sense of smell | 57 (43.8) | 49 (47.1) | 8 (30.8) | 0.133 |
| Loss or worsened sense of taste | 62 (47.7) | 54 (51.9) | 8 (30.8) | 0.053 |
| Seizure | 2 (1.5) | 1 (1.0) | 1 (3.8) | 0.361 |
| Headache | 108 (83.1) | 89 (85.6) | 19 (73.1) | 0.128 |
| Confusion | 57 (43.8) | 48 (46.2) | 9 (34.6) | 0.289 |
| **Any COVID-19 complications** | | | | |
| Required NC 02 | 8 (6.2) | 8 (7.9) | 0 (0) | 0.205 |
| Required NIV | 3 (2.3) | 3 (3.0) | 0 (0) | 1.000 |
| Required intubation | 4 (3.1) | 3 (3.0) | 1 (3.8) | 1.000 |
| Co-morbid infection | 5 (3.8) | 5 (5.0) | 0 (0) | 0.582 |
| Thrombosis | 4 (3.1) | 4 (4.0) | 0 (0) | 0.581 |
| Bleeding | 4 (3.1) | 3 (3.0) | 1 (3.8) | 1.000 |
| Stroke | 2 (1.5) | 2 (2.0) | 0 (0) | 1.000 |
| Extracorporeal Membrane Oxygenation (ECMO) | 2 (1.5) | 1 (1.0) | 1 (3.8) | 0.369 |
| ***PASC score items*** | | | | |
| Smell/taste | 44 (33.8) | 40 (38.5) | 4 (15.4) | 0.026 |
| Postexertional malaise | 110 (84.6) | 100 (96.2) | 10 (38.5) | < 0.001 |
| Chronic cough | 27 (20.8) | 26 (25.0) | 1 (3.8) | 0.017 |

**Table 2** (continued)

| | LC ($n=130$) N/% | PASC + ($n=104$) n (%) | PASC-intermediate ($n=26$) n (%) | *p*-value |
|---|---|---|---|---|
| Brain fog[a] | 80 (61.5) | 78 (75.0) | 2 (7.7) | < 0.001 |
| Thirst | 55 (42.3) | 53 (51.0) | 2 (7.7) | < 0.001 |
| Palpitations | 88 (67.7) | 83 (79.8) | 5 (19.2) | < 0.001 |
| Chest pain[a] | 81 (62.3) | 74 (71.2) | 7 (26.9) | < 0.001 |
| Fatigue[a] | 90 (69.2) | 84 (80.8) | 6 (23.1) | < 0.001 |
| Sexual desire or capacity | 58 (44.6) | 50 (48.1) | 8 (30.8) | 0.112 |
| Dizziness | 51 (39.2) | 40 (38.5) | 11 (42.3) | 0.719 |
| Gastrointestinal | 107 (82.3) | 92 (88.5) | 15 (57.7) | < 0.001 |
| Abnormal movements | 39 (30.0) | 38 (36.5) | 1 (3.8) | < 0.001 |
| Hair loss | 54 (41.5) | 46 (44.2) | 8 (30.8) | 0.213 |
| PASC total score, M (SD) | 17.8 (7.6) | 20.5 (5.8) | 7.1 (3.4) | < 0.001 |

PASC score is calculated by adding up the scores for each symptom an individual has (Table 2 in RECOVER[1]). Score < 12 = PASC-intermediate; ≥ 12 = PASC + ; [a] Additional severity criteria required (see eTables 1 and 2 in Supplemental 3 in RECOVER)

**Table 3 Sensitivity, Specificity, Positive and Negative Predictive Value of the RECOVER PASC Score**

| | | Long COVID (LC) NAM 2024 | | |
|---|---|---|---|---|
| | | **LC** | **Control** | **Total** |
| **RECOVER formula for defining PASC** | **PASC +** | **104** (A: True Positive) | **0** (B: False Positive) | **104** (Test Positive) |
| | **PASC-intermediate** | **26** (C: False Negative) | **60** (D: True Negative) | **86** (Test Negative) |
| | | **130** | **61** | **190** |

Sensitivity: A/(A + C) *100 = 104/(104 + 26)*100 = 80% RECOVER is able to detect 80% of the people with the disease. The test misses 20% of the people who have the disease. Specificity: D/(D + B) *100 = 60/(60 + 0)*100 = 100% RECOVER has 100% specificity. Out of the 60 people without PASC, 60 have true negative results while one individual tested positive for a disease that they do not have. Positive Predictive Value: A/(A + B)*100 = 104/(104 + 0)*100 = 100% Among those that test positive, 100% have the disease. Negative Predictive Value: D/(D + C)*100 = 60/(60 + 26)*100 = 69.76% Of those that test negative, 30% do have the disease, in other words, 30% were false negatives

Using the presence of these three symptoms yielded the highest sensitivity in identifying patients with LC, highlighting the importance of these hallmark symptoms in diagnosing LC. Even though these three symptoms are included in the PASC score, their weighted score is not high enough to reach the 12-point threshold for a PASC+ score. In 2024, an updated version of the RECOVER PASC score, renamed the *Adult Long COVID Research Index*, was published, incorporating a larger participant dataset and an expanded symptom list developed with input from the patient community.[8] In this 2024 iteration, the weighting for both *altered or absent smell or taste* and *post-exertional malaise (PEM)* was reduced by 1 point, while lack of sexual desire or capacity was removed from the index. Based on our findings, these modifications diminish the relative contribution of key long COVID symptoms that were most prominent in our cohort.

Smell and taste were assessed by asking participants about any loss or alteration in these senses. Altered smell or taste was reported by 33.4% of our long COVID cohort, less frequent than fatigue or post-exertional symptoms, but among the more specific manifestations of LC. Lack of sexual desire or capacity was evaluated by inquiring about changes in sexual desire, comfort, or ability. Sexual dysfunction may occur in long COVID, potentially related to autonomic, neuroendocrine dysregulation, or the broader physiological and psychosocial effects of chronic illness. PEM was described as an out-of-proportion flare in symptoms arising from previously well-tolerated activity. While the experience of PEM is variable in patients, there are three core components: exhaustion, cognitive difficulties, and neuromuscular complaints.[9]

The identification of these hallmark symptoms provides a potential pathway for the refinement of LC diagnostic tools. However, the paucity of education in the medical community at large, together with the historic skepticism of the medical establishment toward post-viral fatiguing illnesses,[10] means that many are not being diagnosed with LC. The lack of diagnosis of LC patients has significant implications for the allocation of funding for governmental research support and social security measures that this population needs. Furthermore, the existing socioeconomic barriers to accessing the healthcare system result in an underrepresentation of systemically marginalized populations, which have been disproportionately affected by the COVID-19 pandemic.[11]

Clinical scoring systems aid decision-making, manage clinical risk, and improve efficiency without replacing reasoning and judgment. The need to develop a LC clinical scoring system is

urgent. Due to the limited education of clinicians and the public on LC, as well as the lack of biomarker and diagnostic tools, many LC patients remain undiagnosed. Dissemination of clinical identification of hallmark symptoms along with an effective clinical prediction tool is the first step as we continue to work on understanding the biological mechanisms of LC.

The limitations of our study include a relatively small sample size and an imbalanced dataset with a limited number of controls, which likely contributes to the low NPV observed. Additionally, we understand the need to study other control groups of pre-pandemic post-viral syndromes that may shed light on the similarities and differences among IACC. Our study population is disproportionately white (79%), while our state's white population is estimated to be 47%.[12] This overrepresentation highlights systemic barriers in LC diagnosis and care, including differences in access to specialized clinics, awareness of research opportunities, and structural inequities in healthcare delivery. Future studies must prioritize inclusive recruitment strategies, including community partnerships and outreach to primary care, to ensure diagnostic tools like the PASC score are validated in and applicable to diverse populations.

We call for the development of NIH core outcome measures in LC research, including clinical scoring systems for defining diagnostic criteria for LC. The development of a scoring tool is urgently needed to improve the proper identification of LC cases, improve the quality of research, and provide care that meets the needs of LC patients.

## CONCLUSIONS

The validation of the RECOVER PASC score in our cohort provides insights for the iterative process needed for the ongoing refinement of the LC definition. Our analysis highlights the importance of symptom combinations, particularly PEM, altered smell/taste, and lack of sexual desire or capacity, in improving sensitivity for LC diagnosis. We call for national efforts to develop a readily implementable clinical tool for LC diagnosis.

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***Declarations***

***Ethics Approval and Consent to Participate*** *The study was reviewed and approved by the Institutional Review Board, Study Number IRB00375493. All the participants provided written informed consent to participate in this study.*

***Conflict of interest*** *All authors declare that they do not have a conflict of interest.*

***Data Sharing*** *Data for this study is being deposited to the NIMH Data Archive and will be accessible following the grant cycle ending.*



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