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Long Covid Defined

E. Wesley Ely, M.D., M.P.H., Lisa M. Brown, M.P.H., and Harvey V. Fineberg, M.D., Ph.D.,
for the National Academies of Sciences, Engineering, and Medicine Committee on Examining
the Working Definition for Long Covid*

The Covid-19 pandemic has been perceived mainly as a dangerous acute outbreak of infection that killed more than a million people in the United States and 7 million worldwide.^{1,2} However, in the pandemic's wake, Covid-19 has left many millions more with a variety of chronic, systemic, and often disabling conditions collectively known as "long Covid." In the United States alone, survey data indicate that approximately 7% of adults and more than 1% of children — numbering 15 to 20 million Americans and more than 60 million globally — have had long Covid.^{3,4}

Because of the novelty and diverse expression of this condition, a variety of terms and definitions have been advanced for long Covid, although none have gained wide acceptance and support from patients, clinicians, researchers, and government agencies. In recognition of the shortcomings of the existing definitions, the Administration for Strategic Preparedness and Response and the Office of the Assistant Secretary of Health in the Department of Health and Human Services tasked the National Academies of Sciences, Engineering, and Medicine (NASEM) with developing an improved definition for long Covid that would take into account the needs of patients as well as the views and understanding of a range of experts.

Here, we describe the process and rationale for the resulting 2024 NASEM long Covid definition.⁵ As committee members and lead staff who produced the definition, we can attest that the process inspired discovery and deepening appreciation for the reality and severity of this condition. As a clinician, one of us (Dr. Ely) can admit to early skepticism. Having worked with severely ill patients in the intensive care unit and researched their survivorship trajectories for 25

years,⁶ we found that the myriad signs and symptoms reported by patients with long Covid seemed to mirror those described by patients after critical illness. At first, it appeared plausible to attribute these numerous adverse outcomes — including cognitive impairment, neuromuscular disease, depression, and severe fatigue — to the acquired chronic disease state called the post intensive care syndrome (PICS).⁷⁻⁹ This hypothesis faltered when symptoms similar to PICS began cropping up in tens of thousands of patients from the first wave of the pandemic, most of whom had never been admitted to a hospital during their acute SARS-CoV-2 infection and reported only mild initial symptoms. Patient advocacy groups marshalled social media and quickly established themselves as citizen scientists, coining the term long Covid.

Patients with long Covid join the ranks of millions before them with chronic conditions in which associations with infections have been found (e.g., myalgic encephalomyelitis–chronic fatigue syndrome, post-treatment Lyme disease, and multiple sclerosis, among others). These conditions had been identified during the preceding decades without a pandemic to garner concerted attention to their plight. Mindful of these patients, the committee set out to develop a definition for long Covid that offers legitimacy and a path toward therapeutic answers through future clinical trials.

PROCESS

The committee found no standardized guidelines for developing a disease definition, apart from a few cautions about things to avoid, such as stigmatizing a group or place. The committee

Box 1. 2024 NASEM Long Covid Definition*

Long Covid is an infection-associated chronic condition that occurs after SARS-CoV-2 infection and is present for at least 3 months as a continuous, relapsing and remitting, or progressive disease state that affects one or more organ systems.

Long Covid manifests in multiple ways. A complete enumeration of possible signs, symptoms, and diagnosable conditions of long Covid would have hundreds of entries. Any organ system can be involved, and patients can present with the following:

- **Single or multiple symptoms, such as** shortness of breath, cough, persistent fatigue, postexertional malaise, difficulty concentrating, memory changes, recurring headache, lightheadedness, fast heart rate, sleep disturbance, problems with taste or smell, bloating, constipation, and diarrhea.
- **Single or multiple diagnosable conditions, such as** interstitial lung disease and hypoxemia, cardiovascular disease and arrhythmias, cognitive impairment, mood disorders, anxiety, migraine, stroke, blood clots, chronic kidney disease, postural orthostatic tachycardia syndrome and other forms of dysautonomia, myalgic encephalomyelitis–chronic fatigue syndrome, mast-cell activation syndrome, fibromyalgia, connective-tissue diseases, hyperlipidemia, diabetes, and autoimmune disorders such as lupus, rheumatoid arthritis, and Sjögren's syndrome.

Important Features of Long Covid

- It can follow asymptomatic, mild, or severe SARS-CoV-2 infection. Previous infections may have been recognized or unrecognized.
- It can be continuous from the time of acute SARS-CoV-2 infection or have a delayed onset for weeks or months after what had appeared to be full recovery from acute infection.
- It can affect children and adults, regardless of health, disability, or socioeconomic status, age, sex, sexual orientation, race, ethnic group, or geographic location.
- It can exacerbate preexisting health conditions or present as new conditions.
- It can range from mild to severe and can resolve over a period of months or can persist for months or years.
- It can be diagnosed on clinical grounds; no biomarker that is currently available conclusively determines the presence of this condition.
- It can impair patients' ability to work, attend school, take care of family, and care for themselves, resulting in profound emotional and physical effects on the patients, their families, and caregivers.

* This definition has been slightly edited from the original report⁵ with no intended change in meaning.

identified five criteria for such a definition: accuracy and precision, feasibility in application, acceptability to affected parties, accessibility and understandability, and balancing benefits and harms, including the potential effect on health equity and unintended consequences. The committee determined at the outset that engagement with patients who were affected by long Covid and interdisciplinary dialogue were critical to achieving the desired transparency, accuracy, relevance, usefulness, and acceptability of the definition.

The committee used a multiphase process of systematic engagement and information gathering. This process included the use of focus groups, a questionnaire, a public comment portal, and several public meetings, including a 2-day symposium. More than 1300 people participated in these activities, including patients and caregivers, public health and health care professionals, researchers, policy and advocacy professionals, payers, health care business professionals, and members of the public. In this outreach, the committee members sought input from persons who represented the full spectrum of interested and affected patients, geographic areas, and demographic groups. The detailed findings from the

engagement process have been published in a publicly available report, *What We Heard: Engagement Report on the Working Definition for Long Covid*.¹⁰ The committee also scrutinized existing definitions for long Covid and assembled and analyzed primary literature and reviews related to this condition.

DEFINITION

Recognizing the limitations of existing knowledge while taking full advantage of accumulating clinical and scientific data, the committee crafted a three-part definition of long Covid. The 2024 NASEM definition⁵ includes a core description, a list of characteristic symptoms and associated diagnosable conditions, and seven important features (Box 1). The essential elements of the definition are shown in Figure 1.

TERMINOLOGY

To create a consistent definition, we needed to develop consistent terminology. Three notable aspects of terminology were adopted by the committee. First, the committee adopted the

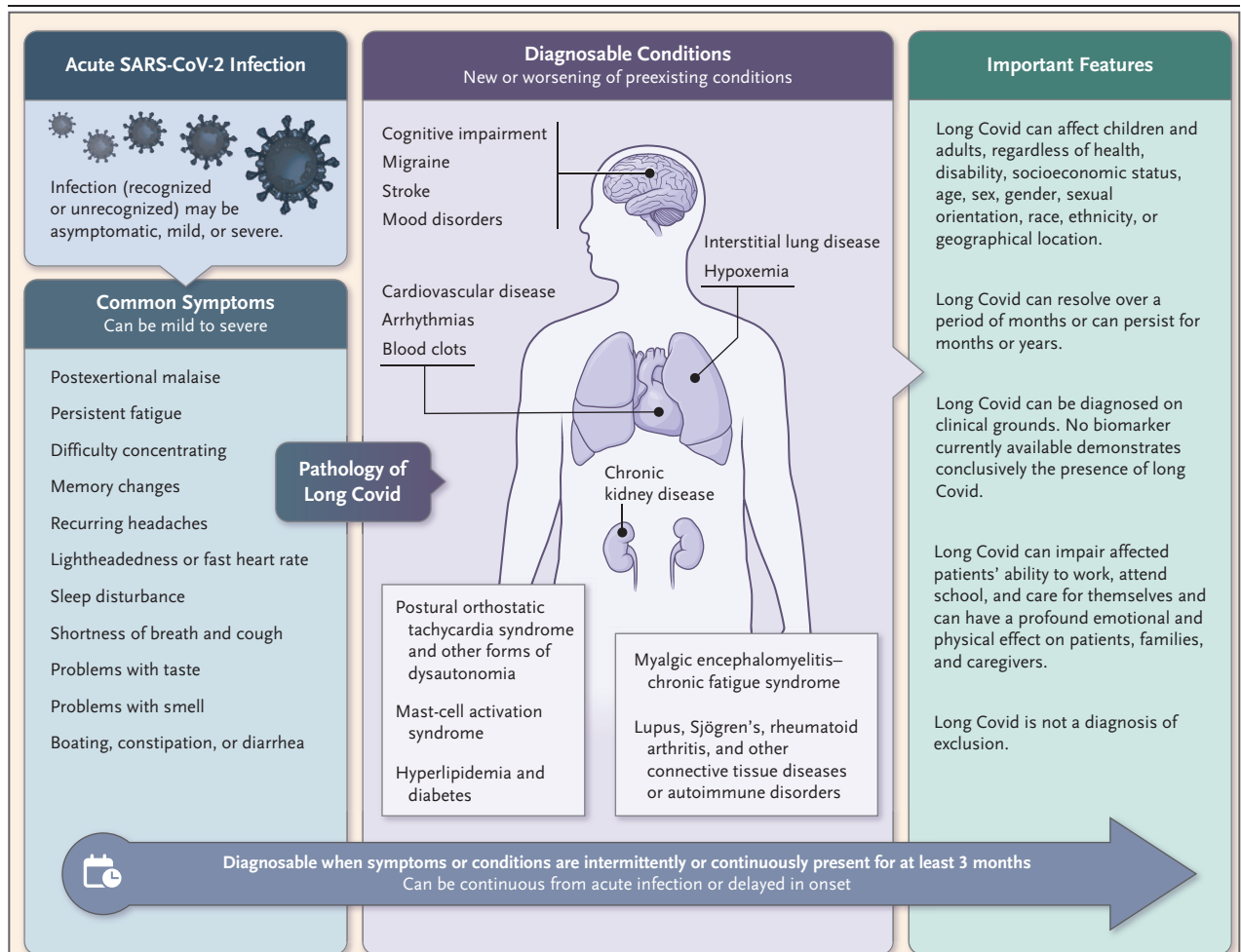


Figure 1. Disease State of Long Covid.

Shown is the disease state of a patient with long Covid, starting with symptoms of acute infection by SARS-CoV-2, diagnosable conditions lasting 3 months or longer, and important features of this condition. Single or multiple organ systems may be involved. Important features that are outlined on the far right relate to the diversity, duration, diagnosis, and disability of this infection-associated chronic condition. (Adapted with permission from the National Academies Press.⁵)

patient-coined term “long Covid” as a simple, well understood, and readily communicated label for this condition and urged its uniform use. Fancier or technical terms, such as postacute sequelae of Covid (PASC), lend a patina of arcanity while adding nothing to the meaning. Second, the definition situates long Covid among the larger class of infection-associated chronic conditions. The family of such conditions shares an association with acute infection by viruses, bacteria, fungi, or parasites, with long Covid representing only the most recent and prominent example. Third, the committee applied the term “disease state” to emphasize the reality and potential se-

verity of the condition. We learned from patients’ reported interactions with physicians and other health care professionals that such terms as “syndrome” may connote an amorphous ailment that will be dismissed as not having a physical basis.

COMPARISONS

Table 1¹¹⁻¹⁶ compares the 2024 NASEM long Covid definition with six previous definitions of long Covid. Among the key components are attribution to acute infection, duration of symptoms, time course, clinical features, attention to equity, emphasis on functional impairment, relation to

Table 1. Components of Long Covid Definitions.*

Elements of Disease Definition	U.S. CDC, 2020 ¹¹	U.K. NICE, 2020 ¹²	U.S. OASH, 2022 ¹³	WHO Adults, 2022 ¹⁴	WHO Children, 2022 ¹⁵	U.S. RECOVER, 2023 ¹⁶	NASEM, 2024 [‡]
Classification							
Uses the term “long Covid”	Yes	No	Yes	No	No	No	Yes
Describes long Covid as a disease state	No	No	No	No	No	No	Yes
Places long Covid among infection-associated chronic conditions	No	No	No	No	No	No	Yes
Attribution to infection							
Allows inclusion of asymptomatic, mild, or severe acute SARS-CoV-2	Yes	No	No	No	No	Yes	Yes
Requires proof of confirmed or probable infection or requirement of SARS-CoV-2 test	No	No	No	Yes	Yes	No	No
Timing							
States symptoms or conditions present for at least 3 mo	No	Yes	No	No	No	Yes	Yes
Indicates continuous or delayed onset of symptoms or conditions	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Clinical features							
Indicates long Covid is a single or multiple organ disease state	No	Yes	Yes	No	No	Yes	Yes
Includes new clinical features or exacerbation of preexisting features	No	No	No	Yes	Yes	No	Yes
Mentions severity of symptoms	No	No	Yes	No	No	Yes	Yes
Describes continuous, relapsing–remitting, or progressive nature of symptoms	No	Yes	Yes	Yes	Yes	Yes	Yes
Includes language on recovery timeline (can resolve or persist for months to years)	No	No	No	No	No	Yes	Yes
Patient-oriented features							
Includes equity language	No	Yes	No	No	No	No	Yes
Highlights effect on daily functioning	No	No	No	Yes	Yes	Yes	Yes
Incorporates alternative diagnoses	No	No	No	No	Yes	No	Yes
Indicates that diagnosis is a clinical judgment due to absence of proven biomarkers	No	No	Yes	No	No	No	Yes
Includes risk factors	No	No	Yes	No	No	No	No†

* CDC denotes Centers for Disease Control and Prevention, NASEM National Academies of Sciences, Engineering, and Medicine, NICE National Institute for Health and Care Excellence, OASH Office of the Assistant Secretary for Health, RECOVER Researching Covid to Enhance Recovery (National Institutes of Health), and WHO World Health Organization.
 † Risk factors are described in the NASEM report that contains the definition but are not specifically included in the definition.

other diagnosable conditions, biomarkers, and risk factors.

The 2024 NASEM definition was crafted to be intentionally inclusive and readily communicated among patients, family members, caregivers, and others. Because patients with acute SARS-CoV-2 infection may have residual symptoms for a couple months before recovery, the committee adopted the requirement that symptoms must have been present for at least 3 months to fulfill the definition. This 3-month period may begin after an interval of apparent recovery after acute infection. The definition incorporates an explicit statement on equity, highlights the potential severity and duration of long Covid, and does not require proof of previous acute symptomatic or asymptomatic SARS-CoV-2 infection. By now, most persons worldwide have had at least one episode of acute SARS-CoV-2 infection. A requirement for proof of diagnosis could wrongly exclude many patients, because early antigen tests had many false negatives and patients who have performed home tests typically discard test strips. Furthermore, although antibody testing can sometimes indicate a past SARS-CoV-2 infection, there are notable limitations, including fluctuation or waning of antibody levels over time and across different assays, complications in antibody test results owing to vaccination against Covid-19, and the effects of sex and age on the sensitivity of antibody testing.¹⁷⁻²²

Few other definitions list characteristic symptoms or associated diagnosable conditions. Rather than regarding long Covid as a diagnosis of exclusion, the NASEM definition expressly notes that such other diagnosable conditions can be part of the picture of long Covid.

Expert history taking and clinical judgment are required to assess patients who may have either exacerbation of baseline coexisting illnesses or de novo diseases. For example, in the case of neurologic disease,^{23,24} a 62-year-old man who has preexisting mild cognitive impairment may have accelerated brain atrophy on magnetic resonance imaging (MRI) with clinical progression to moderate dementia with long Covid. Likewise, 8 months after having SARS-CoV-2 infection, a cognitively and physically healthy 46-year-old woman may receive a diagnosis of mild neuropsychological impairment (i.e., “brain fog”) and postexertional malaise that progresses over the next 2 years into mild dementia with disabling fatigue. Box 2 presents

three case vignettes involving patients with long Covid. The first vignette provides an example of why the diagnosis allows for a presumed asymptomatic previous infection, without confirmatory testing, and why the definition does not require that long Covid be a diagnosis of exclusion.

In a longitudinal Covid-19 cohort study in Arizona, investigators found that underlying autoimmune diseases were associated with an increased risk of long Covid (adjusted odds ratio, 3.78; 95% confidence interval, -1.31 to 10.91).²⁵ In addition, new-onset immune dysregulation can also occur as part of long Covid. In three large cohort studies performed in Germany, Taiwan, and the United Kingdom, investigators who compared 2 million patients with Covid-19 with 6.8 million controls found that autoimmune diseases including rheumatoid arthritis, Sjögren’s syndrome, systemic lupus erythematosus, inflammatory bowel disease, and diabetes mellitus were more likely to develop in the patients who had Covid-19 than in controls, with adjusted hazard ratios of approximately 1.5 to 3.0.²⁶⁻²⁸

LIMITATIONS

Many limitations in the 2024 NASEM definition — for example, the absence of definitive biomarkers — reflect the limitations in current scientific knowledge. There is an inescapable circularity in relying on symptoms to define long Covid and using the definition to indicate what symptoms may be attributable to this condition. Notably, the 3-month disease threshold should not be taken as a reason to ignore symptoms at an earlier stage, since patients with earlier symptoms warrant careful assessment and treatment.

Because of its intentional inclusivity, the definition can lead to high diagnostic sensitivity (few false negatives) and low diagnostic specificity (more false positives). For this reason, the report⁵ stresses that applying the definition in clinical care depends on the experience and judgment of the clinician and careful consideration of alternative causes of a patient’s presentation. For many research purposes, additional eligibility criteria — such as specific age, other demographic features, presence of a specified set of symptoms, or documentation of previous SARS-CoV-2 infection — may be useful to test hypotheses regarding treatment or mechanisms of disease. In such a trial, all research partici-

Box 2. Case Vignettes: Representative Examples of Long Covid

These case vignettes involve 3 patients who have received a diagnosis of long Covid. Each gave explicit written permission to share their personal clinical experiences and reflections in the hope that others will learn about the disease state.

Patient 1:

"To be honest, long Covid has made me feel like I'm not me anymore. I've had to adjust what I eat, where I go. I lost my identity as a hairdresser and cook. I was the active parent of a total of 17 children and godchildren, even though I only birthed three. I can't even pick them up anymore because my hands are ruined...the only thing I feel in my hands is pain. I can't trust myself to hold the children or to console them physically, and that is devastating to me. It's a double-edged sword because if I don't do it, I feel worthless, and if I try, I fail in being the superwoman they used to see."

Patient 1 is a 38-year-old woman of color who was previously healthy, receiving no medications, and working two jobs as a cook and hair stylist. In the fall of 2020, she was caring for two family members with acute Covid-19 and did not get sick herself at that time, although several months later she noticed that her hands had changed color and hurt a great deal when she was in the freezer at work, a condition that was later diagnosed as Raynaud's phenomenon. She is now 41 years old and has received a diagnosis of Sjögren's syndrome and scleroderma. She has lost 2 fingertips and half of her thumb on one hand and has limited range of motion from scarring due to previously gangrenous digits on her other hand and both feet. Her current medications include hydroxychloroquine, nifedipine, sildenafil, aspirin, apixaban, ibuprofen, and acetaminophen. She lost private insurance, was taken off Medicare and Medicaid, and is now pursuing insurance in the marketplace. She finds herself in severe financial straits.

Regarding rejected disability claims, she explains: *"I have been rejected from Social Security disability income 4 times because I'm judged to be able bodied. How can I be able bodied if I'm not able to control my body? What further destruction of my hands and feet needs to occur for me to qualify for our government's disability benefits when I've been forced to retire as a cook and hair stylist at 41 years young?"*

Patient 2:

"My long Covid life remains terrifying. Last weekend I washed my car, dried it, put it back in the garage. Then I got violently sick and could hardly get up to get food. I was unable to read or even call my mom. I'm a shell of myself. But my physical issues aren't half as bad as my brain problems. It's hard to describe. You can say brain fog, but that doesn't come close to doing it justice."

Patient 2 is a 28-year-old man who was previously a mechanical engineer at an electrical car company and now designs surgical devices. He was previously vaccinated without incident. After initially recovering at home from a mildly symptomatic bout with acute SARS-CoV-2 in April 2022, he reported having severe postexertional malaise and memory difficulties and has been diagnosed with long Covid. He used to bike up 3500 feet into the Santa Ana Mountains and is now unable to bike at all. He receives medical care at a leading clinic for patients with long Covid and sees a health coach, psychologist, and "extensivist" physician. His current medication list includes metoprolol, midodrine, fludrocortisone, and a transdermal patch containing nicotinamide adenine dinucleotide (NAD) for the treatment of postural orthostatic tachycardia syndrome, hypotension, and fatigue. His condition is worsening. His difficulty concentrating, memory deficits, and mental fatigue eclipse his physical disabilities. He has a younger sibling with Down syndrome and is afraid that his previous goal of becoming the full-time caregiver for his brother (when his parents are unable) will not be possible.

About his severe neuropsychological dysfunction (early dementia), in his own words: *"At work my brain is just begging for rest. I struggle with finding words and completing tasks in a timely manner. ... I'll be in a meeting and know exactly what I want to say before I say it. ...I'll get to a word, and I just cannot think of the word. I'll just be like, 'Give me a moment,' and I'll go through my brain cycling through words. This week the word was "consistent." I couldn't think of the word consistent. I kept thinking it was coincident or concentric or constant. I used to build prototypes multiple days a week, and now if I do anything in the lab, I'm pretty much wiped out for a week. ...I mean, I've had to dig real deep. How much longer will I feel like this? I'm scared."*

Patient 3:

"Fundamentally, long Covid took away my life. I am unable to do the things that define me and that give me pleasure. I am unable to travel to see my family and friends. I feel imprisoned and in exile."

Patient 3 is a 75-year-old woman who is a retired professor of modern languages with a Ph.D. She was previously healthy with no comorbid disease. She took no medications before 2022 and had multiple Covid vaccine shots without incident. She was initially infected with SARS-CoV-2 in October of 2022, at which time she had fever, headache, and myalgias. She was never hospitalized, took Paxlovid at home, and felt better initially. Several weeks later, she had "severe rebound" of Covid and spent the next 4 months in bed. Before Covid, she was active with yoga, walking daily, traveling, and taking classes. In her long Covid disease state, she has limited physical activity, is unable to travel, and feels isolated. Her symptoms include unexpected episodes of severe tachycardia diagnosed as postural orthostatic tachycardia syndrome, fatigue, headache, body aches, neuropathy, weight loss, bloating, diarrhea, and insomnia. She is positive for microclots and has high titers for Epstein-Barr virus. She has been treated by two doctors, a cardiologist, a neurologist, functional medicine practitioners, and her primary care physician and is taking more than a dozen medications. She continues to have recurrent remissions and relapses of her long Covid symptoms.

She describes her plight as follows: *"Long Covid produces in me a state of hypervigilance that creates a feeling that the world is unsafe, that people and the environment are dangerous to me because they may expose me to a Covid reinfection or another risky infection. There is in me now a reluctance and an incapacity to reengage with life."*

pants will fit the 2024 NASEM definition, but not all patients who fit the definition will qualify as research participants. In general, erroneous classification of research participants with respect to the disease in question will reduce the statistical power of the trial to detect an effect.

The committee report discusses in greater detail clinical, research, and public health uses of the definition.²⁷ A separate NASEM report, sponsored by the Social Security Administration, deals in depth with issues related to long Covid and disability.³

One important feature in the definition states that long Covid can affect anyone. However, as the report also discusses, not everyone is at equal risk. Risk factors for long Covid include female sex, repeated infection, and more severe infection.^{29,30} As with any disease, clinicians should take account of risk factors in assessing the probability of disease in any patient.

It is possible that placing long Covid in the context of other infection-associated chronic conditions could dilute the focus on long Covid as a clinical entity. However, a consideration of the relationship between long Covid and other similar conditions could stimulate new lines of productive research on the cause and pathophysiological features of these complex conditions.

The report does not consider evidence about a possible association between immunization and the risk of long Covid. A recent large observational study³¹ showed that patients who had been vaccinated and then became infected with SARS-CoV-2 had a lower incidence and burden of long Covid than those who were unvaccinated and became infected.

CONCLUSIONS

The use of standard terminology and a standard definition can improve our understanding of the nature, scope, and burden of long Covid. On the basis of data from death certificates through 2023, the Centers for Disease Control and Prevention estimates that approximately 5000 patients in the United States have died from long Covid or from a condition in which long Covid was a contributing cause — a number that is almost certainly a dramatic undercount.³²

While we await the results of new studies of

long Covid, the 2024 NASEM definition takes advantage of the experience and views of patients with long Covid and input from scores of experts in a range of fields. In the committee report, we urge adoption of the 2024 NASEM definition in clinical practice. As in the report, we recommend revisiting the definition within 3 years on the basis of emerging scientific knowledge and understanding of long Covid.

We hope that the 2024 NASEM definition will facilitate communication among patients, such as those described in the clinical vignettes, and with family members and clinicians. A standard definition should enable better tracking of the burden of long Covid and facilitate the design and conduct of robust clinical trials that produce better treatments for this and other infection-associated chronic conditions. Above all, we hope that this definition contributes to compassionate and effective care for all patients in whom long Covid is diagnosed.

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*Members of the committee are listed in the Supplementary Appendix, available at NEJM.org.

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