PRISM Prevalence Assessment™

Prevalence Reconstruction & Integrated Systems Modeling

Illustrative Research Assessment: ME/CFS in the United States

Research Execution: Insights of CYNAERA Institute
Proprietary Methodology Owner: Cynthia Adinig
Report Date: November 17, 2026
Geographic Scope: United States
Population: U.S. adults
Research Category: Infection-Associated Chronic Conditions

Public demonstration based on previously published research by Cynthia Adinig. The quantitative findings originate from the 2026 ME/CFS prevalence modeling study and are not presented as a new or independently validated PRISM-CC analysis.

Executive Summary

Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a complex, multisystem neuroimmune condition characterized by substantial limitations in physical and cognitive function, post-exertional malaise, and fluctuating clinical presentation. Historically, prevalence estimates have been constrained by inconsistent diagnostic recognition, limited specialist access, differences in case definitions, and incomplete population identification (Institute of Medicine, 2015; Nacul et al., 2011; Vahratian et al., 2023).

The emergence of Long COVID has increased the importance of reassessing ME/CFS prevalence. Research from the NIH RECOVER-Adult cohort identified individuals meeting established ME/CFS diagnostic criteria following SARS-CoV-2 infection, demonstrating a significant infection-associated pathway that must be considered when evaluating contemporary population estimates (Vernon et al., 2025).

Adinig (2026) applied the US-CCUC™ framework to existing epidemiological evidence, diagnostic recognition limitations, infection-associated trajectories, and population overlap. The resulting conservative modeled estimate identified approximately **18–26 million U.S. adults** with ME/CFS or ME/CFS-consistent illness patterns, with a central planning estimate of approximately **22 million**.

The assessment identifies a substantial difference between conventional surveillance-based estimates and the broader modeled population. These measurements reflect different definitions and methods and should not be interpreted as equivalent counts of clinically confirmed cases.

1. National Prevalence Assessment

2026 U.S. Modeled Population Estimate

22 million adults

Modeled planning range: 18–26 million U.S. adults

Assessment Measure	Finding
Conservative modeled range	18–26 million adults
Central planning estimate	Approximately 22 million
Broader modeled classification population	27.5–34.65 million
CDC NHIS 2021–2022 reference	Approximately 3.3 million adults
Estimate category	Research-based population model
Principal research source	Adinig (2026)

The conservative range is taken from Adinig's previously published US-CCUC™ analysis. The broader classification population represents a separate modeling category encompassing ME/CFS-consistent illness trajectories before the full conservative reporting adjustments are applied.

The 18–26 million estimate is a modeled projection, not a measured clinical registry count or a validated national census of ME/CFS cases.

2. Transparent Quantitative Analysis

2.1 Central Estimate

The central planning estimate is the midpoint of the published conservative range.

(18,000,000 + 26,000,000) ÷ 2 = 22,000,000 adults

The full modeled interval spans eight million individuals.

26,000,000 − 18,000,000 = 8,000,000 adults

The midpoint provides a practical reference for scenario-based planning. It does not represent a statistically estimated mean, and the range is not a 95% confidence interval.

2.2 Comparison With CDC Surveillance

The CDC's National Health Interview Survey reported that 1.3% of U.S. adults had ME/CFS in 2021–2022, representing approximately 3.3 million adults (Vahratian et al., 2023).

A numerical comparison with the conservative modeled range produces the following ratios.

Modeled Population	Ratio to 3.3 Million CDC Reference
18 million	5.45 times
22 million	6.67 times
26 million	7.88 times

For example:

22,000,000 ÷ 3,300,000 = 6.67

The central modeled population is therefore approximately 6.7 times the historical CDC survey estimate.

This ratio describes the difference between two published estimates using different approaches. It does not establish that the CDC missed exactly 18.7 million clinically confirmed cases.

2.3 Classification Versus Conservative Reporting

Adinig (2026) also identified a broader modeled classification population of approximately 27.5–34.65 million adults exhibiting ME/CFS-consistent trajectories.

That figure is distinct from the conservative 18–26 million reporting range. The original analysis accounts for population overlap, uncertainty in diagnostic classification, and other considerations before selecting the lower public-facing estimate.

These two outputs should not be added together. They describe related categories within the same modeling framework and may contain overlapping individuals.

This distinction is particularly important when population estimates are used in research investment proposals, clinical workforce planning, and institutional communications.

3. Epidemiological Evidence and Diagnostic Recognition

The CDC's survey findings provide an important contemporary baseline. However, NHIS results depend on survey responses concerning prior diagnosis and current status. They are not equivalent to a comprehensive clinical examination of the entire U.S. adult population (Vahratian et al., 2023).

The National Academies' 2015 report documented widespread underdiagnosis and substantial variation in clinician familiarity with ME/CFS. The report estimated that approximately 84%–91% of individuals with the condition had not received a diagnosis, indicating that recorded clinical identification could substantially underrepresent affected populations (Institute of Medicine, 2015).

Community-based epidemiological research has also demonstrated sensitivity to diagnostic criteria, ascertainment procedures, and population selection. Nacul et al. (2011) found that prevalence estimates varied according to case definition in a repeated cross-sectional primary care study.

These findings support a distinction between measured diagnostic recognition and potential underlying prevalence.

The existence of underdiagnosis does not independently prove any particular adjusted population estimate. However, it establishes a scientifically relevant limitation that must be incorporated into the interpretation of surveillance-based results.

4. Long COVID and Infection-Associated Population Expansion

NIH RECOVER-Adult research identified ME/CFS following SARS-CoV-2 infection, providing important evidence of overlap between Long COVID and established ME/CFS diagnostic presentations.

The study reported that 4.5% of infected participants met 2015 Institute of Medicine ME/CFS criteria at least six months after infection, compared with 0.6% of uninfected participants. It also reported that 88.7% of participants with post-COVID ME/CFS met criteria for Long COVID (Vernon et al., 2025).

These findings demonstrate the importance of accounting for overlapping classifications rather than treating Long COVID and ME/CFS as entirely separate populations.

Longitudinal research has documented persistent fatigue, cognitive dysfunction, post-exertional symptom worsening, and other multisystem manifestations following infection (Davis et al., 2021; Peter et al., 2025).

Adinig (2026) incorporates infection-associated trajectories into the broader US-CCUC™ prevalence framework while accounting for overlapping populations and uncertainty in classification.

Assessment interpretation: Long COVID research provides a substantial epidemiological basis for reevaluating ME/CFS prevalence, but diagnostic overlap and differences in research definitions must be addressed to avoid duplicate counting.

5. Demographic and Special Population Considerations

The interpretation of ME/CFS prevalence may be influenced by demographic differences, healthcare access, occupational characteristics, diagnostic recognition, and the representation of special populations.

Historical surveillance and clinical datasets may not fully capture individuals who lack access to appropriate evaluation or whose symptoms are assigned to overlapping diagnostic categories.

In addition, working-age adults, individuals with fluctuating function, people unable to attend repeated clinical appointments, and populations with limited specialist access may be underrepresented in some healthcare-derived datasets.

These considerations are relevant when interpreting national estimates and identifying research populations requiring additional attention.

They do not justify applying an arbitrary demographic adjustment. Population-specific corrections should be based on relevant source evidence and defensible analytical assumptions.

6. Remission, Relapse, and Population Identification

ME/CFS commonly involves fluctuating symptoms and post-exertional worsening, which complicate interpretation of point-in-time measures.

RECOVER findings describe variability in ME/CFS symptom expression following infection (Vernon et al., 2025). Longitudinal Long COVID research similarly documents persistent and changing symptom patterns over extended periods (Davis et al., 2021; Peter et al., 2025).

An individual experiencing a period of reduced symptoms may not necessarily have achieved sustained recovery. Differences between symptom improvement, functional stability, and resolution of illness are therefore relevant to population classification.

Adinig (2026) discusses these considerations through the CYNAERA Remission Standard™, which distinguishes temporary improvements in function from sustained resolution.

For prevalence assessment, this creates a need to specify whether the estimate concerns current symptom expression, a defined clinical diagnosis, or a modeled population with continuing vulnerability.

7. Related Clinical Populations

ME/CFS frequently overlaps clinically with other infection-associated and multisystem conditions, including dysautonomia, postural orthostatic tachycardia syndrome, and orthostatic intolerance.

Research has described autonomic dysfunction in Long COVID and the possible involvement of overlapping physiological mechanisms (Chadda et al., 2022; Raj et al., 2021).

Additional clinical research has investigated associations among Long COVID, generalized joint hypermobility, orthostatic intolerance, and ME/CFS presentations (Grach et al., 2024).

These findings inform clinical classification and research design but do not establish that everyone with an overlapping condition meets ME/CFS diagnostic criteria.

Assessment interpretation: Population estimates must preserve distinctions between comorbidity, overlapping symptoms, and confirmed diagnostic classification. Individuals represented in multiple clinical categories should not automatically be counted as unique additional cases.

8. Research Findings and Confidence

Finding 1: Contemporary modeled prevalence substantially exceeds historical surveillance estimates.

Adinig (2026) reports a conservative range of 18–26 million U.S. adults. This estimate is considerably higher than the CDC's NHIS estimate of approximately 3.3 million adults, although the two sources use different methods and definitions.

Finding 2: Diagnostic underrecognition is a documented epidemiological concern.

Federal reports and clinical research establish substantial historical diagnostic limitations, supporting the need to distinguish diagnostic identification from underlying population prevalence (Institute of Medicine, 2015; Vahratian et al., 2023).

Finding 3: Infection-associated onset materially affects contemporary research questions.

NIH RECOVER-Adult findings demonstrate that a measurable subset of individuals following SARS-CoV-2 infection meets established ME/CFS criteria (Vernon et al., 2025).

Finding 4: Population overlap must be addressed.

ME/CFS, Long COVID, and related conditions cannot be treated as mutually exclusive categories. Any national reconstruction must account for overlapping classifications.

Finding 5: Temporal variability complicates measurement.

Fluctuating symptoms, post-exertional worsening, and periods of improved function may influence point-in-time classification and survey responses.

Evidence confidence: Strong support exists for historical underdiagnosis, infection-associated ME/CFS, and overlapping clinical populations. The specific 18–26 million national estimate remains a model-derived projection requiring continued evaluation and independent validation.

9. Institutional Research Applications

The modeled population range has implications for national research planning, clinical education, diagnostic access, therapeutic development, and institutional funding priorities.

Organizations can use the findings as a clearly attributed research scenario when evaluating the potential scale of unmet research needs. The estimate may also inform discussions about clinical trial recruitment, specialist training, and the geographic distribution of services.

The distinction between the central estimate, conservative range, and broader classification population is essential when communicating findings to policymakers, funders, and research institutions.

The analysis does not independently establish a specific federal funding amount. Funding recommendations should be developed from documented scientific priorities, proposed program activities, and appropriate cost assessments.

10. Final Assessment

Modeled U.S. adult prevalence range: 18–26 million

Central planning estimate: Approximately 22 million

Broader modeled classification population: 27.5–34.65 million

Existing epidemiological research documents substantial historical underdiagnosis of ME/CFS, while NIH RECOVER findings provide additional evidence of infection-associated ME/CFS following SARS-CoV-2 infection.

Adinig's 2026 prevalence modeling work integrates these considerations into a broader population reconstruction, producing a conservative planning range substantially above traditional surveillance references.

The assessment supports the use of approximately 22 million as a clearly labeled modeled planning midpoint, accompanied by the full 18–26 million range, source attribution, and appropriate methodological qualifications.

These findings provide a quantitative foundation for research planning and institutional discussions without representing the modeled population as an independently verified count of clinically confirmed diagnoses.

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