Enrollment Trends at Stanford University: A Closer Look at RECOVER Long COVID Study Data

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BACKGROUND

- COVID-19 emerged in late 2019, infecting 177 million people and causing 3.8 million deaths worldwide.
- Acute symptoms include fever, cough, shortness of breath, and loss of taste or smell.
- Over 70% of those infected experience persistent symptoms, ranging from fatigue to severe conditions like stroke and kidney failure, known as post-acute sequelae of SARS-CoV-2 (PASC).
- Causes of PASC remain unclear but may involve viral persistence, severe illness complications, and pandemic-related health impacts.
- Healthcare systems needed to define Long COVID and its impact on the human body.
- To understand Long COVID, NYU Langone Health and the National Heart, Lung, and Blood Institute launched the RECOVER trial.
- The RECOVER trial includes observational studies of Adult, Pediatric, and Pregnancy cohorts.
- Stanford University (Hub-site) and Stanford Tri-Valley (Sub-site) are two of 86 Adult study sites.
- Hub site enrollment began in late 2021, sub-site enrollment in Fall 2022.
- 12,561 participants have been enrolled in the Adult cohort nationwide since the study's launch.
- The Sub-Site at SHC Tri-Valley expands participant access, diversifying the study population while serving the East Bay and Central Valley communities.

PURPOSE

Identify, evaluate and characterize the heterogeneity in the pace and extent of recovery after acute COVID-19 infection, the clinical course of PASC symptoms in subjects who have recovered from acute infection, and the risk factors associated with the severity of the clinical course of PASC.

METHODS

Design: This is a longitudinal meta-cohort study combining retrospective and prospective elements to evaluate the clinical spectrum, progression, prevalence, and mechanisms of Post-Acute Sequelae of SARS-CoV-2 (PASC). It includes both infected and uninfected adults at various stages during and after infection.

Participants: 12,561 adults (10,434 infected, 2,127 uninfected) across diverse demographics and clinical settings. Recruitment is stratified by sex, race/ethnicity, and illness severity. Participants are categorized into four groups:

- **Acutely Infected:** Positive within 30 days.
- **Acutely Uninfected:** Negative within 30 days.
- **Post-Acute Infected:** Positive more than 30 days ago.
- **Post-Acute Uninfected:** Negative more than 30 days ago.

Recruitment Strategies: Sponsor-provided RECOVER recruitment Portal, community outreach (flyers), and internal referrals from healthcare providers.

Duration: Participants are followed for up to four years, with periodic reassessments to track symptoms and recovery trajectories.

Data Collection: Managed by REDCap electronic data capture (EDC) system

- **Surveys:** Surveys administered every 3 months on demographics, social determinants of health, medical/vaccination history, acute COVID-19 course, and current symptoms.
- **Tiered Testing**
  - **Tier 1:** Physical exams, bloodwork, and optional biospecimen collection based on infection status and time since infection. Visits at baseline, 3 months, 6 months, 1 year after testing depending on enrollment group, and annually thereafter.
    - **Optional Biospecimen Collection:** Blood, urine, stool, and other samples stored at MAYO Clinic.
  - **Tier 2 and 3 Testing – Optional Additional Assessments:** Advanced clinical and biological assessments to explore PASC mechanisms. and confirmed by the clinical team. Safety is prioritized with physician review of participant readiness.
    - **Tier 2 Tests:** Moderately invasive assessments, including home sleep studies, 6-minute walk tests, neurological and psychiatric evaluations, autoantibody panels, glucose tolerance testing, and advanced imaging like chest CT and echocardiography. Annual reassessments for most tests, with some repeated based on clinical need.
    - **Tier 3 Tests:** Invasive procedures like biopsies, brain and cardiac MRIs, or autonomic function tests, invasive cardiopulmonary exercise testing (iCPET), and lumbar punctures. Most are completed once per participant for the duration of the study. Some low-burden assessments may be repeated annually

Adaptive Design: Testing assignments and relevant symptom lists are updated periodically to incorporate emerging PASC knowledge. Proportions of participants undergoing testing adjust dynamically to maintain statistical validity and minimize risks.

Analysis: Data from surveys, biospecimens, and advanced testing are compared between infected and uninfected cohorts to identify PASC prevalence, risk factors, and biological mechanisms.

RESULTS

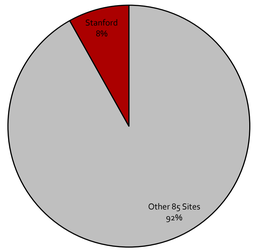

Figure 1. NIH RECOVER Total Enrollment and Stanford Enrollment

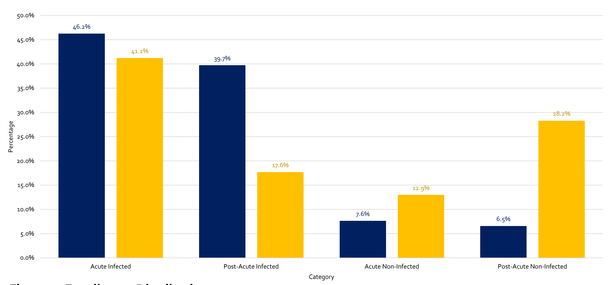

Figure 2. Enrollment Distribution

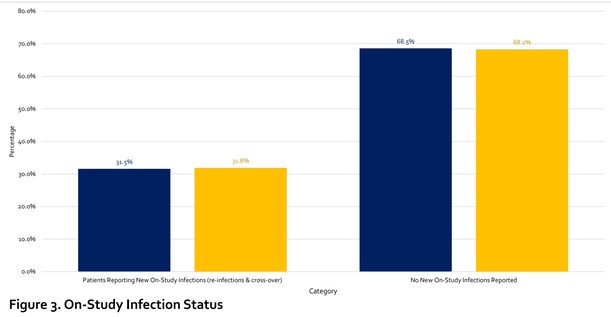

Figure 3. On-Study Infection Status

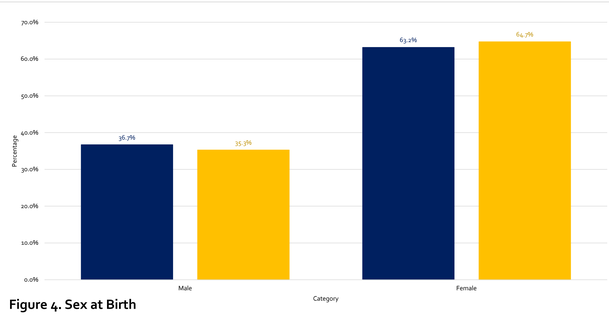

Figure 4. Sex at Birth

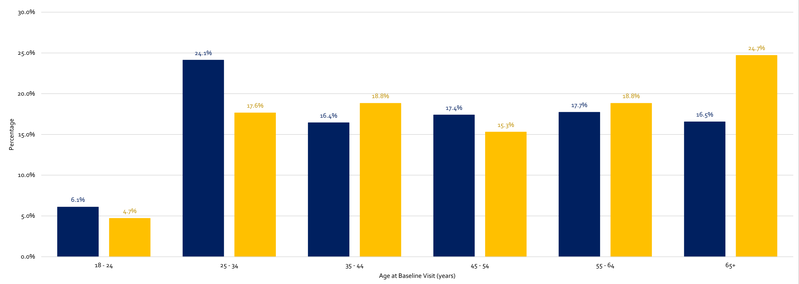

Figure 5. Age Distribution

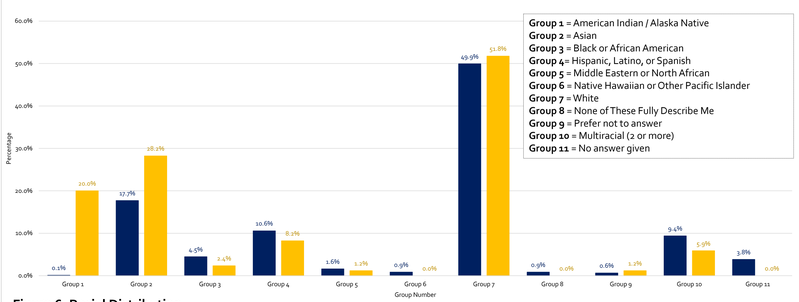

Figure 6. Racial Distribution

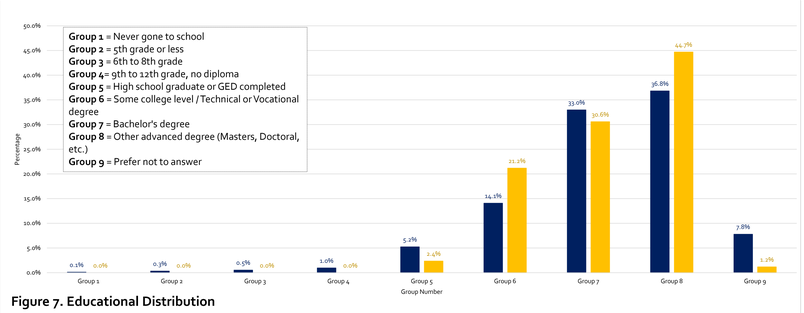

Figure 7. Educational Distribution

Legend

- 11601 (Stanford Hub Site)
- 11602 (Stanford Sub Site)

Figure 1

NIH RECOVER has 86 sites and a total of 12,561 Adult participants. Stanford Hub Site and Sub Site have 1022 participants, constituting 8% of the entire RECOVER study enrollment.

Figure 2

Hub Site
- Acute Infected: 46.2%
- Post-Acute Infected: 39.7%
- Acute Non-Infected: 7.6%
- Post-Acute Non-Infected: 6.5%

Sub Site
- Acute Infected: 41.2%
- Post-Acute Infected: 17.6%
- Acute Non-Infected: 12.9%
- Post-Acute Non-Infected: 28.2%

Figure 3

Hub Site
- New On-Study Infections: 31.5%
- No New On-Study Infections Reported: 68.5%

Sub Site
- New On-Study Infections: 31.8%
- No New On-Study Infections Reported

Figure 4

Both sites have a majority of female participants.

Figure 5

Hub Site
- Age 18-24: 6.1%
- Age 25-34: 24.1%
- Age 35-44: 16.4%
- Age 45-54: 17.4%
- Age 55-64: 17.7%
- Age 65+: 16.5%

Sub Site
- Age 18-24: 4.7%
- Age 25-34: 2%
- Age 35-44: 18.8%
- Age 45-54: 15.3%
- Age 55-64: 18.8%
- Age 65+: 24.7%

Figure 6

The largest racial group enrolled at both the Hub and Sub sites is White. The Hub Site's second largest enrollment group are people who reported their race as Asian. The Sub site's next largest racial group is those that reported being American Indian or Alaskan Native.

Figure 7

Most participants at both the Hub and Sub sites have advanced degrees. The second largest educational level group is individuals with Bachelor's degrees.

CONCLUSIONS

RECOVER COVID INITIATIVE: Efforts from RECOVER have assisted the National Academies of Sciences, Engineering, and Medicine (NASEM) to define Long-COVID

- Long-Covid: infection-associated chronic condition (IACC) that occurs after a 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.

ENROLLMENT TRENDS: Total enrollment : 1,022 (8% of RECOVER Adult cohort nationwide)

Similarities across both sites:
- Majority identify as white
- More females than males
- More likely to have pursued higher education (Bachelor's, Master's, Doctorate)
- Top enrolled cohort: Adult Infected

Differences across both sites:
- Stanford Hub Site (Main Campus):
  - Age group: 25-34 years old, likely due to proximity to Main Campus
  - Second largest enrolled cohort: Post-Acute Infected
- Stanford Sub Site (Tri-Valley):
  - Age group: 65 years and older, likely due to location and distance from Main Campus
  - Second largest enrolled cohort: Post-Acute Non-Infected, likely due to time of enrollment and sponsor standards

FUTURE STEPS: The RECOVER COVID Initiative is projected to complete data collection by the **end of 2025**

- NIH is launching sub-studies to further the goals of RECOVER
  - Ongoing:
    - **RECOVER-NEURO**: Investigating possible effective treatments for brain fog and memory, neurological symptoms of Long-Covid.
    - **RECOVER-VITAL:** Investigating the efficacy of Paxlovid as a Long-Covid intervention.
  - Upcoming:
    - **RECOVER-ENERGIZE:** To determine possible interventions for exercise intolerance and post-exertional malaise
    - **RECOVER-AUTONOMIC:** To investigate interventions for autonomic dysfunctions as a result of Long-Covid (tachycardia, dizziness, fatigue)

FUNDING

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Initiative: RESEARCHING COVID TO ENHANCE RECOVERY (RECOVER)
Protocol: NIH RECOVER: A Multi-site Observational Study of Post-Acute Sequelae of SARS-CoV-2 Infection in Adults

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