

Notice of Intent to Publish Research Opportunity Announcements for the NIH Post-Acute Sequelae of SARS-CoV-2 Infection Initiative: PASC Data Repositories and Mobile Health Platform

Related Announcements

In February 2021, NIH published the first two Research Opportunity Announcements (ROAs) in support of its Post-Acute Sequelae of SARS-CoV-2 Infection (PASC) Initiative: [OTA-21-015A](#) for the Clinical Science Core, Data Resource Core, and PASC Biorepository Core, and [OTA-21-015B](#) on SARS-CoV-2 Recovery Cohort Studies. Potential applicants are encouraged to review these ROAs to understand the role and function of these key elements of the PASC Initiative.

Purpose

This Notice is to alert the community that NIH plans to publish two additional ROAs in support of the PASC Initiative, one on PASC Data Repositories and one on a Mobile Health Platform. The solicited research will improve understanding of and develop strategies to prevent and treat post-acute manifestations of SARS-CoV-2 infection across the lifespan. Publication of the ROAs is expected in May 2021. Funding of the projects will utilize NIH's Other Transaction Authority (OTA), which offers flexibility and the ability to engage partners in collaborative innovation and problem solving. Initial awards are anticipated to be made in June 2021.

This Notice is being provided for informational purposes to allow potential applicants additional time to develop responsive applications. NIH reserves the right to modify the scope and objectives as described in this Notice. Final scope, objectives, and requirements will be set forth in the published ROAs.

Background: PASC Initiative

Recovery from SARS-CoV-2 infection is extremely variable, with many recovering quickly while for other patients there are important post-acute sequelae. Reported symptoms among persons who have been infected with SARS-CoV-2 range from mild to incapacitating, may persist after recovery from acute disease, may involve multiple organs and systems, and can adversely affect overall quality of life. In some cases, new symptoms and findings are reported that appear linked to the timing of acute infection but emerge subsequently and evolve over time. The magnitude of the public health impact of these sequelae is currently unknown but potentially large given the numbers of individuals across the age spectrum who have been and will be infected with SARS-CoV-2. It is a public health priority that we better understand and develop strategies to prevent and treat PASC and that these strategies enable rapid innovation, evolution, and adaptation as more is learned about PASC and its potential impact on public health over time.

The goal of the trans-NIH PASC Initiative is to rapidly improve understanding of recovery after SARS-CoV-2 infection and to prevent and treat PASC. Toward these ends, the Initiative is designed to address these fundamental scientific questions:

- What is the clinical spectrum of and biology underlying recovery from acute SARS-CoV-2 infection over time?
- For those patients who do not fully recover, what is the incidence/prevalence, natural history, clinical spectrum, and underlying biology of this condition? Are there distinct phenotypes of patients who have prolonged symptoms or other sequelae?
- Does SARS-CoV-2 infection initiate or promote the pathogenesis of conditions or findings that evolve over time to cause organ dysfunction or increase the risk of developing other disorders?

The Initiative is designed to be a collaborative and inclusive approach for rapidly advancing our understanding of the recovery process and the epidemiology (including incidence/prevalence) and natural history (including duration) of PASC. Studies conducted will characterize: the clinical spectrum of recovery from SARS-CoV-2 infection across the lifespan, including the subset of patients who have symptoms of disease beyond the standard course; the individual, clinical, and contextual factors that contribute to the duration, types of symptoms, and severity of disease; phenotypes of patients who have prolonged symptoms or other sequelae; the impact of treatments for acute COVID-19 or for post-acute symptoms on the duration and severity of symptoms; and factors that impact the outcomes in patients infected by SARS-CoV-2.

Background: PASC Data Resource Core

In the hub-and-spoke model described below, the Data Repositories serve as the spokes surrounding the central coordinating hub, which is the PASC Data Resource Core (DRC). The DRC, which was described in a previous ROA (see [OTA-21-015A](#)), will play a critically important and central role in coordinating and integrating data from the PASC Data Repositories (described below) and will work collaboratively with the Mobile Health Platform (described below). To assist applicants for the Data Repositories and Mobile Health Platform in understanding the importance of coordination and integration of the data across the various repositories, we provide in the paragraphs below some additional details about the anticipated role of the DRC.

The DRC will serve as the data hub for the PASC Initiative. It will lead PASC-related data management and cross-initiative harmonization, integration, and sharing by coordinating activities of the Data Repositories and fostering relationships and synergy between various repositories and other elements of the Consortium. The DRC will lead assessments and decision-making processes regarding adoption and implementation of data collection standards, a core set of PASC common data elements (CDEs) and tools, and harmonization procedures including mapping to common data models (e.g., OMOP) in collaboration with the NIH, the Data Repositories, the Clinical Science Core, and PASC Investigator Consortium to maximize comparability across the program and measurement modes (e.g., web, mobile app, in-person) for longitudinal research and evaluation of program impact.

In addition, the DRC will assist research projects with linking these data across Data Repositories and with stored biospecimens and data from other sources and providing data informatics tools to monitor program consortium progress and performance. It will also coordinate and facilitate the necessary data harmonization, mapping to common data models (e.g., OMOP), quality control, data curation, and analyses to prepare necessary data across all sites for ingestion and integration into the PASC Data Repositories. Lastly, the DRC will work with the PASC Data Repositories to ensure all PASC data is indexed and findable across the landscape of repositories. To this end the DRC will provide a master index of all data across the PASC repository landscape and maintain clear provenance of the data. Data will be made available in the appropriate data repository. In addition, the DRC will provide an easy-to-use front-end portal with capabilities to find and aggregate data across the repositories and will work with NIH to ensure researchers can use repositories' analytical workbenches for analysis of these data in a secure cloud environment.

The DRC will also collaborate with the Mobile Health Platform and Digital Health Data Repository to make mobile health and related digital data generated by the PASC Initiative Clinical Recovery Cohort studies rapidly available to the PASC Investigator Consortium and to the greater research community.

Research Opportunity Details

ROA #1: PASC Data Repositories

NIH intends to solicit applications for the following: a **Digital Health Data Repository, Imaging Data Repository, Pathology Data Repository, Electronic Health Records (EHR) and Other Real-World Data (RWD) Repository**, and **Clinical and Observational Data Repository** to support data archiving and sharing for the PASC Initiative. NIH's vision for these data repositories is that they work collaboratively with the DRC to ensure integration of data across the repositories and with the PASC Investigator Consortium to rapidly and flexibly deploy, manage, and grow a robust, secure digital infrastructure that can meet the near-term and long-term needs of the program. In this vision, the PASC data repositories are the spokes in a hub-and-spoke model, with the PASC DRC serving as the coordination hub. The data repositories are expected to be capable of handling, deidentifying, and harmonizing data and information, making data and its derivatives readily available to researchers, and having the appropriate security and controls procedures for secure data access and analysis within and across their platforms.

The PASC Data Repositories are envisioned to serve as spokes and will work with PASC study awardees and the DRC (hub) to develop (and revise as necessary) standards, metadata, and common data elements that apply to the types of data collected by the respective Initiative awardees. It is anticipated that the PASC Data Repositories may be required to handle most of the data harmonization, deidentification, and curation of awardee data. The PASC Data Repositories will work with the DRC to enable facile data integration and sharing within their platform and to enable data discoverability from the DRC's data portal. In addition, it is anticipated that the PASC Data Repositories will enable their analytics platforms or workbenches to allow for federated analysis through a secure workbench managed by the DRC, with NIH partnership. In this way, data generated through the PASC Initiative will be made FAIR and will be easily integrated together regardless of where the data resides across PASC repositories. It is therefore important for awardees to nimbly adapt to the changing landscape of studies, measures, and needs of the Initiative. The PASC Data Repositories should be able to effectively collaborate and integrate with the various relevant data repositories and infrastructure that NIH and others have established (e.g., the National COVID Cohort Consortium (N3C), Rapid Acceleration of Diagnostics (RADx), All of Us, BioData Catalyst, the Gabriella Miller Kids First Data Resource, etc.).

NIH anticipates that overall governance of the PASC Initiative including the DRC, Clinical Science Core, Data Repositories and other awardees will be managed through a steering committee structure. A steering committee would be responsible for ensuring that the DRC and Data Repositories are meeting the needs of the consortium and the greater research community.

Toward these ends, NIH plans to publish a ROA to solicit applications for the following repositories:

Digital Health Data Repository, for which applicants will be expected to:

- Curate, perform quality assurance and quality control (QA/QC), aggregate, and store the digital health data being collected by the SARS-CoV-2 Recovery Cohort studies via the **Mobile Health Platform** (see **ROA #2: Mobile Health Platform** section below) and other PASC-related digital platforms, as appropriate.
- Facilitate the linkages of the digital health data from the Mobile Health Platform to the other data collected by relevant Recovery Cohort studies.
- Enable the PASC Consortium and greater research community to access the data through a portal and workbench managed by the DRC, including capabilities for data analytics, as appropriate.

- Ensure that digital health data are standardized so that comparisons can be made between different forms of sensor data (e.g. sampling rates, units of measure, binary characteristics such as active vs. sedentary, etc.).
- Facilitate the standardization and/or harmonization (i.e., mapping to common data elements) of PASC Initiative digital health data, including mobile technologies, wearable devices, sensors and internet technology for health, healthcare and clinical research, and others, as needed.
- Support the PASC Clinical Science Core and the PASC Consortium in developing and validating a standardized and/or harmonized set of digital health measures for assessing the trajectory of acute SARS-CoV-2 infection and PASC over time – including the data elements, temporality of assessment, and on-screen display of questions. These measures are likely to evolve as more is learned about recovery from SARS-CoV-2 infection and PASC. The measures should include:
 - Core questions about the symptoms experienced by patients to chart recovery or worsening over time of symptoms and quality of life.
 - Sensor data from consumer wearable devices that can capture data and specific symptoms or clusters of symptoms that patients are experiencing (e.g. heart rate, respiration rate, blood oxygen, activity levels, cough, sleep patterns, actigraphy, temperature, etc.).
 - Serial at-home COVID-19 antigen testing to monitor possible reinfection.

Imaging Data Repository, for which applicants will be expected to:

- Provide for image deidentification, adhering to community standards and practices.
- Curate, perform QA/QC, aggregate, and store the digital images (including but not limited to neuroimaging, physiological, computed tomography and radiographic) being collected by the SARS-CoV-2 Recovery Cohort studies and other PASC-related activities as appropriate.
- Employ an imaging data dictionary consistent with standards and practices in the scientific community.
- Provide a means to link (e.g., privacy preserving record linkage) the imaging data to the other data collected by the clinical cohort studies. Enable the PASC Consortium and greater research community to access the data through the DRC’s portal, including capabilities for data analytics that can be securely deployed in or federated with the DRC’s workbench.
- Facilitate the standardization and/or harmonization (i.e., mapping to common data elements) of PASC Initiative imaging health data, consistent with standards and practices in the scientific community.
- Provide imaging-specific tools such as DICOM viewers, tools for annotating images, imaging analysis workflows, as well as well-developed data science, AI, and ML methods.
- Provide for the development and implementation of innovative imaging tools.

Pathology Data Repository, for which applicants will be expected to:

- Curate, perform QA/QC, aggregate, and store the digital pathology images (including but not limited to histopathology, whole slide imaging) being collected by the SARS-CoV-2 Autopsy Cohort studies and other PASC-related activities as appropriate.
- Employ a data dictionary consistent with standards and practices in the scientific community.
- Provide a means to link the pathology data to the other data collected by the clinical cohort studies. Enable the PASC Consortium and greater research community to access the data through the DRC’s portal, including capabilities for data analytics that can be securely deployed in or federated with the DRC’s workbench.

- Facilitate the standardization and/or harmonization (i.e., mapping to common data elements) of PASC Initiative pathology data, consistent with standards and practices in the scientific community.

EHR/RWD Data Repository, for which applicants will be expected to:

- Curate, harmonize, perform QA/QC, aggregate, and store EHR and RWD being collected by the SARS-CoV-2 Recovery Cohort studies and other PASC-related activities as appropriate.
- Employ a data dictionary, and be able to map data to a common data model (OMOP) consistent with standards and practices in the scientific community.
- Be able to employ HL7 FHIR® (Fast Healthcare Interoperability Resources) standard to capture, integrate, and exchange clinical data for research purposes and to enhance capabilities to share research data ([NOT-OD-19-122](#)).
- Be able to appropriately anonymize and share EHR and RWD.
- Provide a means to link the EHR and RWD data, via privacy preserving record linkage (hash), to the other data collected by the SARS-CoV-2 Recovery Cohort studies. Enable the PASC Consortium and greater research community to access the data through the DRC's portal, including capabilities for data analytics that can be securely deployed in or federated with the DRC's workbench.
- Facilitate the standardization and/or harmonization (i.e., mapping to common data elements) of PASC Initiative EHR and RWD data, consistent with standards and practices in the scientific community.
- **Optional:** Establish and maintain an inventory of synthetic clinical data generation and verification/validation projects based upon the EHR and RWD being collected by the SARS-CoV-2 Recovery Cohort studies and other PASC-related activities as appropriate.

Clinical and Observational Data Repository, for which applicants will be expected to:

- Curate, harmonize, perform QA/QC, aggregate, and store clinical and observational data being collected by the SARS-CoV-2 Recovery Cohort studies and other PASC-related activities as appropriate.
- Employ a data dictionary, ability to work with consortium to develop and implement common data elements and ability to map data to a common data model (OMOP) consistent with standards and practices in the scientific community.
- Demonstrate capacity to employ HL7 FHIR® (Fast Healthcare Interoperability Resources) standard to capture, integrate, and exchange clinical data for research purposes and to enhance capabilities to share research data (NOT-OD-19-122).
- Be able to share appropriately anonymized clinical and related data with appropriate data control access procedures.
- Provide a means to link the EHR and RWD data to the other data collected by the SARS-CoV-2 Recovery Cohort studies. Enable the PASC Consortium and greater research community to access the data through the DRC's portal, including capabilities for data analytics that can be securely deployed in or federated with the DRC's workbench.
- Facilitate the standardization and/or harmonization (i.e., mapping to common data elements) of PASC Initiative clinical and observational data, consistent with standards and practices in the scientific community.

In addition to the above requirements, **all PASC Data Repository applicants** will be expected to:

- Enable researchers to bring their own data for analysis with the repository data.

- Support user authentication and authorization using the NIH Researcher Auth Service that ensure respect for patient consent as to data use related to Controlled Access data.
- Support the appropriate use of non-consented and de-identified data. Build a data management model that will link deidentified data (through a third party, via privacy-preserving record linkage) and coordinate linkage with the clinical and electronic health record-level data in the PASC DRC for inclusion in a larger NIH data integration model.
- Funded Data Repositories are expected to fully integrate, in a collaborative fashion, with the PASC DRC to support scientific collaboration, common data elements and data harmonization, data sharing, enabling cross-Consortium collaboration for easy access and findability and analysis of data and for rapid dissemination of findings.
- Maximize the value of the collective data sets and enable interoperability with other NIH COVID-19 research resources by supporting studies and working with the PASC DRC to make relevant data and analytical resources accessible through a cloud-based data workbench.
- Have the appropriate security protocols and processes including repository-managed systems that can obtain and maintain an Authority to Operate (ATO) compliant with applicable regulations and standards, including FISMA at the Moderate level and including cloud-specific controls where appropriate. Data Repositories will prepare all required Security Assessment and Authorization documentation based on NIST guidance and gain ATO approval from the appropriate Designated Authorizing Authority.

ROA #2: PASC Mobile Health Platform

NIH intends to solicit research proposals to serve as the **Mobile Health Platform** for the PASC Initiative. Together with the **Digital Health Data Repository** (see **ROA #1: Data Repositories** section above), the Mobile Health Platform will facilitate the collection, annotation, harmonization, curation and sharing of digital health data collected via mobile apps and/or sensors by the PASC Investigator Consortium to augment and complement existing clinical, EHR, and other real-world data collection.

The Mobile Health Platform is expected to be capable of handling recruitment and engagement of participants, obtaining electronic consent, collecting standardized information from participants, and in collaboration with the Digital Health Data Repository, Data Resource Core, and Clinical Science Core, making data and its derivatives rapidly available to other members of the Consortium and to the greater research community.

Toward these ends, NIH plans to publish a ROA to solicit applications for a Mobile Health Platform, for which applicants will be expected to:

- Provide each SARS-CoV-2 Recovery Cohort study with a customized mobile app for enabling secure collection of a standardized set of digital health measures (defined below), as well as other standardized measures. Cohort studies that already employ their own apps will have the option to either adopt the Mobile Health Platform app or to modify their own apps to include the standardized measures. The Mobile Health Platform will need to support multiple, concurrent mobile-only and hybrid studies across the PASC Consortium, including multiple clinical study designs, with customized study deployments and study experience.
- Maintain integrity, confidentiality, privacy, and security of participant study data collected through the Mobile Health Platform. The Mobile Health Platform may require the creation and maintenance of System(s) of Record (SOR) to securely contain personally identifiable information (PII). The SORs will adhere to a Federal Information Security Management Act (FISMA)-moderate level of security controls. The Mobile Health Platform will be compliant with 21 CFR Part 11 (section D).

- Design and customize the Mobile Health Platform app in a manner that enables the data it collects to be combined with the clinical data collected by the Recovery Cohort studies (i.e., clinical cohort and EHR/RWD studies).
- For consortium studies that adopt the Mobile Health Platform, enable features that facilitate contacting/recontacting of participants in a secure manner.
- Provide eConsent capabilities as needed.
- Provide capabilities to share personalized results to participants, as appropriate.
- Support digital integration of serial at-home COVID-19 testing (e.g., reminders to test, testing instructions, sharing results with researchers, etc.).
- Procure consumer wearable devices and distribute them to subsets of participants in the Recovery Cohort. Provide training and support for device setup and troubleshooting.
- Share data collected through the Mobile Health Platform with the Digital Health Data Repository (see **ROA #1: Data Repositories** section above) using appropriate privacy and security safeguards and using appropriate standards for harmonization and interoperability.
- Support the PASC Clinical Science Core and the PASC Consortium in developing and validating a standardized and/or harmonized set of digital health measures for assessing the trajectory of acute SARS-CoV-2 infection and PASC over time – including the data elements, temporality of assessment, and on-screen display of questions. These measures are likely to evolve as more is learned about recovery from SARS-CoV-2 infection and PASC. The measures should include:
 - Core questions about the symptoms experienced by patients to chart recovery or worsening over time in symptoms and quality of life.
 - Sensor data from consumer wearable devices that can capture data and specific symptoms or clusters of symptoms that patients are experiencing (e.g. heart rate, respiration rate, blood oxygen, activity levels, cough, sleep patterns, actigraphy, temperature, etc.).
 - Data from serial at-home COVID-19 antigen testing to monitor possible reinfection.
- Facilitate the standardization and/or harmonization (i.e., usage of common data elements) of PASC Initiative digital health data, including mobile technologies, wearable devices, sensors and internet technology for health, healthcare, clinical research, and others as needed.

Additional ROAs may be issued in the future as needed.

Applicants are strongly encouraged to review in detail related PASC ROAs and be familiar with their contents: [OTA-21-015A](#) and [OTA-21-015B](#).

Inquiries

Please direct all inquiries to: NHLBI_OTA@mail.nih.gov