NIH StrokeNet

PREVENTION | TREATMENT | RECOVERY

# Biweekly Update
# 10-April 2020

**StrokeNet Enrollment Update**

| | | | |
|---|---|---|---|
| ARCADIA | 440/1100 | CREST 2 | 1653/2480 |
| Sleep SMART | 253/3062 | CREST H | 139/500 |
| TRANSPORT2 | 11/129 | MOST | 33/1200 |
| I-ACQUIRE | 22/240 | ARCADIA-CSI | 52/500 |
| ASPIRE | 0/700 | SATURN | 0/1480 |

## StrokeNet COVID-19 Updates

Effective Tuesday, 24-March, 2020 **ALL** StrokeNet trials have suspended enrollments/randomizations. This move has been reported to the CIRB as a study-wide event by the Project Manager of each StrokeNet trial; individual sites **DO NOT** need to report this event.

For subjects who have already been randomized, please continue to perform follow-up visits, but *do so remotely*. This will also be reported to the CIRB as a study-wide event by the trial Project Managers.

We want you to know that the StrokeNet NCC and NDMC are still open for business. We would like to encourage all that have not yet been released to enroll, to continue to work toward site activation.

Should your institutional guidelines allow, please proceed with startup activities:

- CIRB submission
- Finalizing the Clinical Trial Agreement
- Uploading startup documents to WebDCU™
- Remote training
- Completing readiness calls

In addition, please think creatively about how you and we can improve StrokeNet activities locally (example working on remote consenting process for acute trials) or nationally.

Regardless, the health and safety of our patients and colleagues is our top priority. If you have any questions, please reach out to us.

# FDA/NIH/NINDS Updates

FDA is actively continuing its efforts to provide the clarity needed to help ensure the safety of clinical trial participants, maintain compliance with good clinical practice (GCP), and minimize risks to trial integrity during the **COVID-19** pandemic by providing our stakeholders a single place to obtain guidance. For more information, please visit:

https://www.fda.gov/drugs/coronavirus-covid-19-drugs/clinical-trial-conduct-during-covid-19-pandemic

### eRA Moving to the Cloud

Just a reminder that eRA is planning a major undertaking this month, to migrate its modules and data to the Amazon Web Services (AWS) cloud April 17-20 (Fri-Mon).

During this cloud migration, from 8 a.m. ET on Friday, April 17 to 8 p.m. ET on Monday, April 20, all eRA modules (eRA Commons, ASSIST, IAR, iEdison, etc.) and all informational websites (era.nih.gov, etc.) will be unavailable.

Any affected due dates will be covered under NIH's late application policy due to **COVID-19**, which allows all applications submitted late for due dates between March 9, 2020, and May 1, 2020, to be accepted through May 1, 2020.

Grants.gov will continue processing applications during the migration window. Applications received via Grants.gov will be put in a queue, and then eRA will process them on Monday night, April 20. The standard 2-day viewing window for successfully submitted applications will be applied.

Note that eRA will be closely monitoring the availability of staff needed to do the migration; please check the eRA Cloud Migration webpage of the eRA website for confirmation of its plans late next week.

Cloud computing provides us with a number of advantages. These include improved security, reliability, and scalability of the system.

### 2-Factor Authentication for eRA Modules

eRA is moving to two-factor authentication via login.gov, meaning that log-in will require something you know (password) and something you have (a phone or other device). This new log-in method, optional at first but which may be required later, will be available Wednesday, April 8, 2020 for users of eRA Commons, Commons Mobile, IAR and ASSIST.

This change, part of HHS's Reinvent Grants Management initiative, will help reduce the burden on principal investigators and research administrators by providing them the ability to log in to four different grants systems (eRA, Grants.gov, GrantSolutions and Payment Management System) using the same username and password via login.gov. Two-factor authentication will help ensure the security of your personal information.

To help you take advantage of this new option, they have compiled a number of resources:

Accessing eRA Modules via login.gov Webpage
- https://era.nih.gov/register-accounts/access-era-modules-via-login-gov.htm

Three video tutorials
- https://era.nih.gov/era-training/era-videos.htm#2FA

Accessing eRA Modules via login.gov FAQs
- https://era.nih.gov/faqs.htm#XXIV

eRA Commons online help
- https://era.nih.gov/erahelp/Commons/default.htm#cshid=12

ASSIST Online Help
- https://era.nih.gov/erahelp/assist/default.htm#cshid=100

# Clinical Research Training Opportunities

**Research Coordinator Training Opportunities**

Below are links below to several recorded clinical research lectures from the University of Cincinnati. It is suggested that they be viewed in the order posted below, as the material builds in these first 3 webinars. Future lectures will be recorded and posted in the Biweekly Update.

1. Research Coordinator Neuroanatomy Lecture-20200331 1404-1
https://ucincinnati.webex.com/recordingservice/sites/ucincinnati/recording/playback/8a08ba4ddc14462097f664a597a09b38

2. Research Coordinator Vascular Imaging - CTA Review!-20200402 1400-1
https://ucincinnati.webex.com/recordingservice/sites/ucincinnati/recording/playback/4e557ae36b084568add1bcbf3c3c614f

3. Research Coordinator Stroke Localization Lecture-20200403 1408-1
https://ucincinnati.webex.com/recordingservice/sites/ucincinnati/recording/playback/1eb5c7d8c9e847409f2db9bd6c23f630

**NINDS Training Opportunities**

In addition, here are a few (free) self-directed training opportunities for NIH StrokeNet Program Managers, Coordinators & Trainees:

1. The Introduction to the Principles and Practice of Clinical Research (IPPCR) course focuses on the spectrum of clinical research and the research process by highlighting biostatistical and epidemiologic methods, study design, protocol preparation, patient monitoring, quality assurance, ethical and legal issues, and much more. Individuals internal and external to NIH are able to register for the course.
https://ocr.od.nih.gov/courses/ippcr.html

2. Ethical & Regulatory Aspects of Clinical Research course is offered to anyone interested or involved in the ethics of clinical research with human subjects. Participants represent multiple disciplines including research teams, IRB members, physicians, psychologists, nurses, social workers, administrative staff, students, and others.

https://bioethics.nih.gov/courses/ethical-regulatory-aspects.shtml

https://videocast.nih.gov/PastEvents?c=22

3. Principals of Clinical Pharmacology is an online lecture series covering the fundamentals of clinical pharmacology as a translational scientific discipline focused on rational drug development and utilization in therapeutics. The course focuses on the following core principles of pharmacology: pharmacokinetics; drug metabolism and transport; drug therapy in special populations; assessment of drug effects; drug discovery and development; pharmacogenomics and pharmacotherapy. Individuals internal and external to NIH will be able to register for the course.

https://ocr.od.nih.gov/courses/principles-clinical-pharmacology.html

# StrokeNet Trial Updates

ARCADIA•CSI
Cognition & Silent Infarcts

The ARCADIA-CSI Study Team is wishing all of our sites the best during this challenging time. We are thinking of all of you and hoping you and your families are staying safe and healthy.

As of March 17, 2020, ARCADIA-CSI has suspended enrollment. This information was submitted to the cIRB. The acknowledgment letter can be found in WebDCU in the Toolbox -> Project Documents.

SRU testers who conduct the neurocognitive assessment will be administering exams remotely from private rooms at home, using an encrypted system to access firewalled-protected UAB servers where all reservation information, PHI and test data are stored. No data of any kind will be stored remotely.

For already-enrolled CSI patients, who have not had their neurocognitive assessment, the SRU will resume follow-up telephone exams to patient homes using the existing protocol for reservations and calls

We continue to have site readiness calls and our newest sites are:

University of Nebraska

OSF St. Francis

Please contact Tashia Harris, herndotl@ucmail.uc.edu or Stephanie Kemp, skemp@standford.edu with any questions.

ARCADIA

**Thank you to all on the frontlines – stay safe and healthy!**

As you all know, enrollment and randomizations are suspended until further notice due to COVID-19.

As of the pause, our enrollment numbers have not changed. We have 1709 participants consented and 440 participants randomized at 101 sites. Our enrollment was paused at 40% of the overall goal. We have now released to enroll a total of 144 sites, 134 of which were active prior to the pause. During the pause, we plan to continue working on adding other qualified sites to the ARCADIA roster. Please let us know of any excellent stroke sites that are interested in participating in this important trial.

During the pause, we're working on various protocol amendments and additional financial support to address the research challenges caused by this pandemic. More information to come once these changes are CIRB/funding approved. In the meantime, we are asking that you not close out subjects that surpass the 120-day randomization window in the expectation that we will be able to re-consent and randomize them once the amendment is approved and the enrollment/randomization pause is lifted for the trial.

We still need to continue to follow our already randomized subjects and send those still taking study drug their medication. IF you are shipping study drug and not handing it directly to the participants, then please remember to add the date they received the study drug to the corresponding CRF (F513) and not the date it was dispensed by your institution, while noting in the comments the date the study drug was dispensed by the pharmacy and shipped. Also, don't forget that Pam sent out a NTF on March 30th which lets your pharmacies know that we allow them to ship study drug to the participants if that is allowed at your sites. Please note that although we had originally recommended signatures required for delivery, we have since rescinded this to maintain physical distancing requirements in a subsequent email sent by Rebeca on 4/1.

We will continue to send site-wide emails to make sure your sites are kept informed. As personnel change and new staff comes onboard often, we ask that you distribute these emails to all of your team members and let us know if anyone has been missed.

Please see our recent ARCADIA newsletter for March to see additional details and suggestions related to COVID-19. The slides from the recent webinars (ARCADIA & StrokeNet) also include useful information about COVID-19 and will be available in WebDCU.

Our thoughts and prayers are with all of you on the frontlines and our participants. Please keep safe!

**Webinar**: Our next PI and coordinator webinar will be April 28th at 2 PM Eastern--save the date! We're asking that at least 1 person from each site attend the monthly webinar and pass the information along to their team. Also, please send suggestions for topics you'd like discussed.

If you miss out on a webinar, you will soon be able to find the slides on the StrokeNet website (https://nihstrokenet.org/intranet/minutes/trial-webinars).

- Enrollment and randomization activities were suspended on March 20, 2020
- Screening activities are continuing as permitted by local institutional policies
- Our protocol allows consent via telephone/telehealth contact. Methods to implement remote consent and randomization are being developed for consideration by the cIRB.
- We would like to encourage all sites that have not been released to enroll to continue to work on startup activities:
    - cIRB submission
    - Finalizing clinical trial agreement
    - Uploading startup documents to WebDCU
    - Receiving study drug and lab kits
    - Completing readiness calls
    - Sites with CTA & cIRB can schedule a readiness call https://doodle.com/poll/rnnu37hfvmca36z9
- 89 executed CTAs and 83 sites with cIRB approval
- 33 sites released to enroll
- ASPIRE Webinar #1 is April 22, 2020 3:00p-4:00p EDT https://nihstrokenet.adobeconnect.com/trials/ To take part in the conversation dial 1 (877) 621-0220 Pass Code: 745694

**From the CREST-2 Clinical Coordinating Center:**

| | CREST-2 | CREST-2 StrokeNet |
|---|---|---|
| CEA | 870 | 378 (44% of total) |
| CAS | 783 | 133 (17% of total) |
| **Total** | **1653** | **511 (31% of total)** |

## COVID-19 Updates & CREST-2

**CREST-2 Will Be Stopping Enrollment:** The COVID-19 pandemic has already led to suspension of elective surgery and elective procedures at many if not most major medical centers. Accordingly, because of patient and health personnel safety, we have concluded that suspension of all CREST-2 enrollments should be instituted immediately. The CREST-2 Low Enrollment Policy has also been suspended. In the meantime, we would encourage you and your team members to continue your screening efforts and log them in the event that the patient may be eligible at a later time. We will let you know when enrollment may re-start.

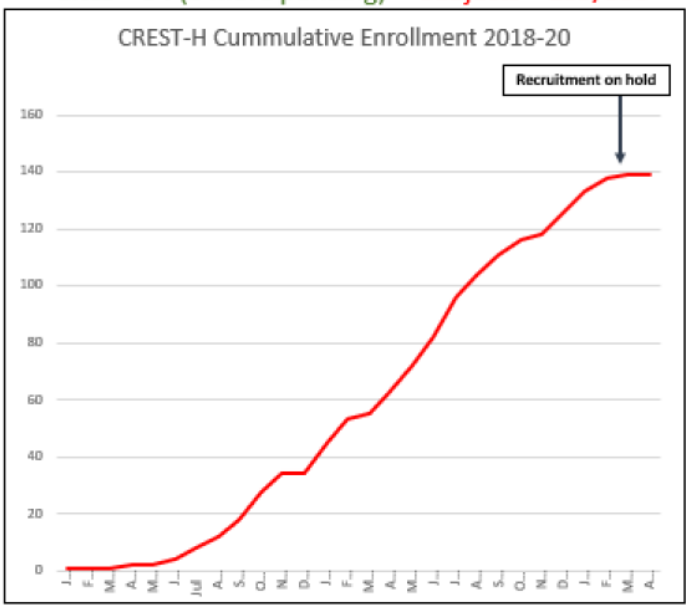
**COVID-19 Survey:** The Clinical Coordinating Center sent a survey to all greenlighted principal investigators and coordinators on COVID-19 policies at their institution on March 17th. We received 158 responses from 110 sites – if you participated in the survey, thank you! This information was extremely helpful in understanding how your institution has responded to COVID-19.

**Update on CREST-2 Calls:**

- CREST-2 Coordinators' Calls will go from a monthly to a **weekly basis on Tuesday's at 4pm EST**
- CREST-2 PI Calls will go from a quarterly to a **monthly basis on Thursday's at 5pm EST**

# CREST-H

Sites = 54 (6 more pending)  Subjects = 139/350




- New subject recruitment is on hold
- Follow ups (for CREST-2) by telephone
- Most critical is the 1-year cognitive exam
  - Primary endpoint for CREST-H
  - done by telephone through CREST-2
- 1-year follow up perfusion scans may be done at a delayed time point after 1-3 months
- Once enrollment resumes, we need about 1 of 3 CREST-2 patients to meet our target, so let's hit the ground running!

# MOST

Multi-Arm Optimization of Stroke Thrombolysis

- Thank you to the following two sites that completed Site Readiness Calls!
  - **Akron General Medical Center, Akron, OH-** Dr. James Gebel and Debra Hudock
  - **Community Regional Medical Center of Fresno, Fresno, CA-** Dr. Alan Long and Rebekah Garcia
- As of 10-Apr-2020, there are **33 subjects** randomized and **54 sites** released to enroll, **17** of which have enrolled at least one subject.
- During the trial-wide enrollment suspension due to the COVID-19 pandemic, we will focus efforts on processing a protocol amendment. Changes include allowing 90-day visits for enrolled subjects to occur remotely (phone, telemedicine, video call) and allowing study drug administration to occur up to 75 minutes after tPA administration.
- Once CIRB approval is granted, the amendment will be disseminated to all sites for processing. **Please review the remote work capability of your regulatory team and your local IRB to manage the protocol amendment.** We will discuss the protocol amendment in more detail on the Investigator Call on Monday, April 20, 2020 at 2 PM ET.
- For sites are released to enroll please continue to complete screening logs in WebDCU™.
- **For sites not yet activated, please note we will continue the site activation process including completion of regulatory documents, delivery of study drug and releasing sites to enroll. Our goal is to have as many sites ready as possible once we are able to return to usual procedures.**
- Thank you all for your efforts!
- **The PI hotline is available 24/7 for any questions: 1-833-229-MOST**

SATURN

We hope that everyone is safe and well!

During this time please continue to complete trial start-up activities and paperwork to continue to work to complete the following items to be ready for activation once enrollment resumes:

- cIRB Submission – reminder to please send your documents to Emily or Jen at the NCC who will submit to the cIRB on your behalf
- Clinical Trial Agreement Execution – please follow-up with your institution to move this process along
- Protocol Training is available in WebDCU toolbox and on WebDCU Training Campus https://webdcu.musc.edu/campus/
- Study documents are available in WebDCU toolbox – including regulatory documents, regulatory parameters document, training materials, DRAFT CRFs, protocol appendices, Provider Information Sheets, Participant Information Sheets and MOP
- Reminder to **enter site address** into WebDCU for supplies – under Site Management>Clinical Site>click on your site to edit and enter address
- Reminder to acknowledge receipt of lab kits in WebDCU once received at your site
- Reminder to complete and submit site DOA in WebDCU
- Reminder to upload approved Regulatory documents into WebDCU
- Reminder to participate in the Doodle Poll once you receive the Readiness Call Scheduling email with the link

If you have any questions regarding start-up please reach out to these contacts at the NCC:
Kimberlee Bernstein Project Manager gammk@ucmail.uc.edu
Wren Hanson Contracts hansonwm@ucmail.uc.edu
Emily Stinson Regulatory stinsoey@ucmail.uc.edu
Jen Golan Regulatory golanjl@ucmail.uc.edu

TRANSPORT2

Our next PI and Coordinator call that was scheduled for **Monday, April 13th at 11am ET**, has been **CANCELED** due to sites being on hold for research activities. We will resume the site call on **Monday, April 27th at 11am.** If anyone has topics they would like to discuss during the call, please send them to Julia Gonzalez, (Julia.jackson@duke.edu).

Please make sure you have completed your BlueCloud recertification training by logging into the website: http://duke-transport2.trainingcampus.net. Individuals who have expired or about to expire training have been sent reminder emails. Note this is for the scoring of the Fugl Meyer, not the video training.

As a reminder, subject randomization is currently on hold, but please continue to pre-screen patients in a remote setting. Subjects who are in the 45 and 105 day follow-up assessment stage, please contact Wayne Feng (wayne.feng@duke.edu) and Gottfried Schlaug (Gottfried.schlaug@baystatehealh.org) for subject retention and follow-up issues. We are exploring new alternative ways to complete patient assessment visits.

To date, Moss Rehab, University of Kentucky, University Southern California, Medstar, Emory University, and University of Cincinnati continue to enroll. MUSC, Barnes Jewish, Burke, University of Texas, University Alabama, and Baystate are all open to enrollment! There are eleven subjects randomized in the trial. Five have completed the study, and six have completed the intervention phase and are in the follow-up period. Cleveland VA has a fully executed CTA and is working through their IRB submission. Duke has received CIRB approval, and is currently going through finance. UPMC is working through their IRB submission and has a signed CTA.

Thank you for your continued effort and flexibility during this time of uncertainty.

Sleep SMART

Thank you for your participation in Sleep SMART. We hope you are doing well, especially during this difficult time.

As of March 24, 2020, when Sleep SMART was suspended, 752 subjects were enrolled and 253 subjects were randomized.

Sites not yet released to enroll:

We want to encourage all sites that have not yet been released to enroll to continue to work toward site activation.

If your institutional guidelines allow, please proceed with start-up activities:

- CIRB submission
- Finalize the Clinical Trial Agreement and FusionHealth DUA and Consignment agreement
- Upload site and people documents to WebDCU
- Complete online training (https://webdcu.musc.edu/campus/)
- Complete readiness call
- Please review the site to-do checklist found in the WebDCU toolbox

Sites that have already enrolled:

In follow-up to our 3/30/20 email to sites about use of CPAP during the COVID-19 pandemic: please be sure you have spoken with each Sleep SMART subject who is randomized to use CPAP. The alternative, if it is hard to reach the subject, is to send the letter that was circulated.

**Don't forget these important reminders:**

1. Please continue to perform the 3- and 6-month follow-up visits by telephone, by a blinded study team member.
2. If the window for the 3-month visit ends and you have not been able to reach a subject, please continue to reach out to him/her until the 6-month window begins.
3. Please review the changes to the revised MOP, recently released.
4. Please check "Alerts" in WebDCU to find unresolved queries.
5. Visit our website: www.nihstrokenet.org/sleep-smart-trial/research-team to review helpful materials.
6. Please remember to report AEs. If you need guidance, please refer to the Sleep SMART MOP. Please recall that the only AEs that should be reported between consent and randomization are:
    - All SAEs (fatal and non-fatal) that are definitely related or stand a reasonable possibility to be related to the Nox T3 sleep apnea test or the aCPAP run-in night procedures (within 5 days of awareness of event for non-fatal; within 24 hours of awareness for fatal)
    - All non-serious AEs of special interest (see protocol 8.3.8) that are definitely related or stand a reasonable possibility to be related to the Nox T3 sleep apnea test or the aCPAP run-in night procedures (within 5 days of awareness of event)
    - Primary outcome events (ischemic stroke, ACS, and deaths) (within 5 days of awareness of event)
7. All responses to Data Clarification Requests (DCRs) must be submitted within 5 days of query generation, except those associated with Serious Adverse Events, which must be answered within 24 hours of query generation. Site payments are contingent upon the subject's data being entered, submitted, and all DCRs addressed.
8. For stroke outcome events, please be sure to upload documentation in the outcome packets that provides information about new stroke symptoms, including focal neurological symptoms and signs on exam, and associated dates.

**Save the date**-Our next PI and coordinator webinar will be Wednesday, April 29, 2020 from 1-2 EST. We will focus on the critical topic of CPAP adherence.

# Steering Committee Call

*Steering Committee Calls are a requirement for all NIH StrokeNet RCCs*
*(one representative per RCC required)*

The next Steering Committee call is scheduled for **Wednesday, 13-May, 2020, 12 noon ET.** Dial in: 513-621-0220; 1-877-621-0220; Passcode 434578.

The 8-April Network Webinar was recorded, and it has been posted on the NIH StrokeNet website, along with the slide presentations. http://www.nihstrokenet.org/education/strokenet_meetings_presentations

# Coordinator Webinar

*Coordinator Webinars are a requirement for the NIH StrokeNet RCC Coordinators/Managers*

**Wednesday, April 22, 2020 - 1:30 PM ET**

Topic: Informed Consent and RPPR Review

Presenters: Aaron Perlmutter, NDMC; Joanna Vivalda, NINDS

Moderator: David Haney, RT, Case Western Reserve University

To join the meeting: ***https://nihstrokenet.adobeconnect.com/coordinator/***

Please enter as a guest, then your email address or your first and last name.
To take part in the conversation you MUST dial in. (877) 621-0220; Passcode: 434578

# Professional Development Webinar

*Professional Development Webinars are a requirement for the NIH StrokeNet Trainees*

**Thursday, April 23, 2020**

| | | |
|---|---|---|
| Presenters: | 1:00 | **James Giles, MD, PhD,** Washington University<br>Cost-Effectiveness Analysis of Transcarotid Artery Revascularization (TCAR) for Patients with Atherosclerotic Carotid Artery Stenosis |
| | 1:30 | **Jacqueline Hirsh Greer, MD,** Yale University<br>Obstructive Sleep Apnea as a Risk Factor for Intracerebral Hemorrhage |
| | 2:00 | **Maria Daniela Zambrano Espinoza, MD,** Columbia University<br>Effects of Clinically Meaningful Weight Changes on Premenopausal Women and Stroke Risk |

Moderator: **Farhaan Vahidy, MD, MBBS, MPH**

To join the meeting: *https://nihstrokenet.adobeconnect.com/pdw/.* Please enter as a guest, then your email address or your first and last name.

To take part in the conversation you MUST dial-in. (877) 621-0220 Passcode: 190825

# Grand Rounds

*Grand Rounds are a requirement for the NIH StrokeNet Trainees, however all are welcome to participate.*

**Thursday, April 30, 2020**

Topic: Feeding the Penumbra

Presenter: **Jeff Saver, MD,** UCLA

Moderator: **Randy Marshall, MD**

To join the meeting: *https://nihstrokenet.adobeconnect.com/grandrounds/.* Please enter as a guest, then your email address or your first and last name.

To take part in the conversation you MUST dial-in. (877) 621-0220 Passcode: 190825

# NIH StrokeNet Employment Opportunities

**University of Cincinnati Vascular Neurologist**

The Department of Neurology and Physical Medicine and Rehabilitation at the University of Cincinnati has new, exciting opportunities for **Vascular Neurologists** at Assistant, Associate, or Professor levels on both clinical and research career tracks.

The candidate will join an internationally renowned stroke program that includes:

- A highly collaborative, multidisciplinary team of 9 Vascular Neurologists, 7 Emergency Medicine Stroke Specialists, 9 Neurocritical Care Intensivists, 3 Interventionalists from Neurosurgery and Neurology, 2 Cerebrovascular Neurosurgeons, 6 Neuroradiologists, a large cohort of extremely experienced Research Coordinators, among others
- A JCAHO-Certified Comprehensive Stroke Center, including a 20-bed Neuroscience Intensive Care Unit and 10-bed variable acuity unit
- Multicenter, high-volume approach to acute stroke treatment and trial enrollment (550+ treated with reperfusion therapies in 2019), including a newly activated Mobile Stroke Unit
- A large, NIH-funded stroke research program, ranging from clinical trials in treatment, prevention, and rehabilitation/recovery, to epidemiology studies in health disparities and brain health, to molecular genetics
- A home to the National Coordinating Center (NCC) and a Regional Coordinating Center (RCC) of the NIH StrokeNet

The clinical practice would consist of a personally tailored combination of inpatient service, acute stroke call (including telemedicine), outpatient clinic, and teaching of residents and fellows from several different disciplines.

Exciting collaborative research opportunities are available for participation and growth, but not required.

**MINIMUM QUALIFICATIONS:** Must have an MD or DO, completed an ACGME-approved Vascular Neurology fellowship program, and be BE/BC.

**HOW TO APPLY**: Contact Pooja Khatri, MD, Director of the Vascular Neurology Division: pooja.khatri@uc.edu

*The University of Cincinnati, as a multi-national and culturally diverse university, is committed to providing an inclusive, equitable and diverse place of learning and employment.*

*For more information about StrokeNet employment opportunities, please visit*
*http://nihstrokenet.org/education/employment-opportunities*
*Contact: Jamey Frasure, PhD, RN, Director · NIH StrokeNet Coordinating Center · frasurjs@ucmail.uc.edu · 513-558 1742*
*https://www.nihstrokenet.org*