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# TITLE: Continuing Clinical Research During Shelter-in-Place

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## INTRODUCTION

In order to control the spread of the SARS-CoV2 virus, many hospitals have prohibited or limited the scope of in-person clinical research assessments in accordance with regional restrictions. In this webinar, the American Neurological Association (ANA) interviewed Drs. Devin Brown, a stroke neurologist at University of Michigan; Jeffrey Cohen, a multiple sclerosis (MS) neurologist at Cleveland Clinic; and Lesli Skolarus, a stroke neurologist at University of Michigan. These physician scientists are conducting multicenter clinical trials and they discussed how they are adjusting their ongoing studies to follow current guidelines and assure participant and staff safety. Plans for future clinical trial modifications were also discussed.

## SAFETY CONCERNS AND OTHER CHALLENGES FACED WHILE CONDUCTING CLINICAL RESEARCH DURING THE COVID-19 OUTBREAK

The panelists identified many universal challenges while conducting clinical research during the COVID-19 outbreak, including: restrictions on in-person recruitment and outcome assessments, restrictions on specimen processing, strains on Institutional Review Boards to review protocol changes, and reluctance of study participants to come to medical facilities for research-related activities. The panelists acknowledged that sites across the United States are differentially impacted by COVID-19, resulting in different accommodations for each site in a multicenter trial.

The panelists also discussed specific challenges encountered in their clinical trials. Dr. Skolarus is currently conducting a community-based mobile health technology intervention to reduce blood pressure (Reach Out)[1]. Because her trial recruits from the emergency department, Dr. Skolarus' team faces recruitment challenges in a population with an undifferentiated risk of SARS-CoV2 exposure. In-person outcome assessments were not possible during Michigan's Stay-at-Home order. In order to fulfill their commitment to enrolled participants, they transitioned to remote outcomes assessment via telephone. In addition, Reach Out is transitioning to virtual screening and enrollment to avoid unnecessary study staff and participant exposure. Dr. Cohen's study compares hematopoietic stem cell transplantation (HSCT) to highly effective disease modifying therapies in people with relapsing multiple sclerosis (MS) (BEAT-MS)[2]. This trial includes collaborations with multiple departments, including interventional radiology for lumbar punctures and the transplant team for HSCT. These departments have their own regulations during the current outbreak, which have limited necessary testing and treatment administration. Dr. Cohen faces additional challenges as HSCT, and possibly highly effective disease modifying therapies, increase infection risk. In addition to instituting screening procedures and contact precautions for participants and staff, he has revised all consent forms to reflect potential COVID-19 risks. Dr. Brown codirects a clinical trial to determine whether treatment of obstructive sleep apnea (OSA) with continuous positive airway

pressure (CPAP) in patients with stroke improves stroke recurrence or recovery (Sleep SMART)[3]. With the COVID-19 outbreak, Dr. Brown's team paused in-person interactions including enrollments study-wide for a period of time, and has provided guidance to mitigate the risk of potential viral transmission to household members of participants using CPAP.

## HOW TO DETERMINE WHICH ASPECTS OF A TRIAL CAN BE TRANSITIONED TO A VIRTUAL PLATFORM

The panelists highlighted the need for validated, widely accepted virtual outcome measures to help maintain safety in clinical trials. They discussed their own strategies to modify ongoing and future clinical trials in detail. Sleep SMART already utilized a telemedicine platform for care management and could continue to collect outcome measures via telephone (such as the modified Rankin Scale-9Q)[4]. In contrast, Dr. Skolarus has adapted her study and highlighted a novel use of participants' smart devices to assist with data collection. A primary outcome of Reach Out includes blood pressure readings at six and twelve months; to improve the validity of these assessments, the study team requests participants to text a non-identifiable picture of the blood pressure cuff on their arm. Finally, the Mellen Center for MS Treatment and Research has developed self-administered versions of MS outcomes that can be administered on a tablet or smart phone[5]. Validated telemedicine outcomes could be helpful in future clinical trials and present new opportunities to researchers. However, the panelists agreed that mixing validated in-person outcomes with unvalidated virtual outcomes could affect clinical trial interpretation and should be avoided, if possible.

## IMPACT OF COVID-19 ON FUTURE CLINICAL RESEARCH

The COVID-19 pandemic will undoubtedly leave a lasting impact on clinical research. The panelists anticipated that future studies might include screening through electronic medical record-based algorithms and remote recruitment facilitated by e-consenting. In addition, study visits may transition to virtual assessments to maintain safety of participants and research staff. The panelists also expected newer technologies, like wearable devices, to be utilized more often for remote data collection. However, virtual outcomes introduce a risk of selection bias. The panelists noted that patients have unequal access to and familiarity with technology, including smart phones and computers. Therefore, researchers must exercise additional caution to ensure their studies prioritize inclusion of underserved populations.

Scientists and physicians must also consider the impact of COVID-19 on current research. Dr. Cohen highlighted that physicians will have to grapple with unanticipated direct and indirect consequences of COVID-19 when interpreting trial results. For example, many neurologists may adjust their prescribing patterns to treat MS based on individual patient characteristics, the specific immunomodulatory effects of disease modifying therapies, and their need for infusion in a medical facility. In addition, the economic and mental health consequences of COVID-19 may affect demographic and quality of life outcomes . Several groups have outlined the impact of COVID-19 on research networks and ongoing clinical trials with blueprints for reinstitution of clinical trial enrollment[6,7].

Overall, the panelists remained optimistic that aspects of future clinical research may benefit from the challenges faced during the current pandemic. New clinical trials that take advantage of the tools discussed above can address novel questions and reach a larger patient base. Although the reasons behind the shift are multifactorial, Dr. Skolarus noted increased participant retention after transitioning to virtual study visits. The panelists agreed that the scientific community needs to validate and reach consensus on preferred virtual outcome measures to power new trials. Dr. Skolarus reminds our audience that, while adjusting research trials can be challenging, adapting to our new research environment will be critical to ensuring the success of future studies.

**Suggested Supplemental Material**

The full-length version of the webinar can be reached at https://myana.org/education/ana-webinars or via the QR code

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