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Recruitment and Retention During a Pandemic: The experiences of the CTN0080 MOMs study

Friday, June 4th, 2021

Learning Objectives:

1) Assess the aims and objectives of the CTN0080 MOMs study
2) Describe the impact of the COVID-19 pandemic on study recruitment and retention
3) Explain specific protocol changes used to address COVID-related issues impacting the CTN0080 MOMs study
4) Identify at methods used to increase recruitment and retention in the CTN0080 MOMs study

Target Audience:

Clinical Research Professionals (CRPs) at UC/H and Cincinnati Children's Hospital Medical Center (CCHMC): including Principal Investigators (PIs), Research Nurses (RNs), Critical Care Unit Nurses (RNs), Pharmacy Technicians and Regulatory Specialists.

Off-Label Disclosure Statement:

Faculty members are required to inform the audience when they are discussing off-label, unapproved uses of devices and drugs. Physicians should consult full prescribing information before using any product mentioned during this educational activity.

Learner Assurance Statement

The University of Cincinnati is committed to resolving all conflicts of interest issues that could arise as a result of prospective faculty members' significant relationships with drug or device manufacturer(s). The University of Cincinnati is committed to retaining only those speakers with financial interests that can be reconciled with the goals and educational integrity of the CME activity.

Accreditation Statement for Directly Sponsored Activity

The University of Cincinnati is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

The University of Cincinnati designates this live activity for a maximum of 1 *AMA PRA Category 1 Credit*™. Participants should claim only the credit commensurate with the extent of their participation in the activity.

CRPs, NPs, PAs, and RNs can count activities certified for *AMA PRA Category 1 credit*™ for professional credit reporting purposes. Other healthcare professionals should inquire with their certifying or licensing boards.

Disclaimer Statement

The opinions expressed during the live activity are those of the faculty and do not necessarily represent the views of the University of Cincinnati. The information is presented for the purpose of advancing the attendees' professional development.

Speaker Disclosure:

In accordance with the ACCME Standards for Commercial Support of CME, the speakers for this course have been asked to disclose to participants the existence of any financial interest and/or relationship(s) (e.g., paid speaker, employee, paid consultant on a board and/or committee for a commercial company) that would potentially affect the objectivity of his/her presentation or whose products or services may be mentioned during their presentation. The following disclosures were made:

Planning Committee Members:

- Brett Kissela, MD, Course Director – No Relevant Relationships
- Maria Stivers, MS – No Relevant Relationships
- Zachary Johnson, BS – No Relevant Relationships
- Nate Harris, BS, Course Coordinator – No Relevant Relationships
- Brandon Armstrong, CME Program Coordinator – No Relevant Relationships

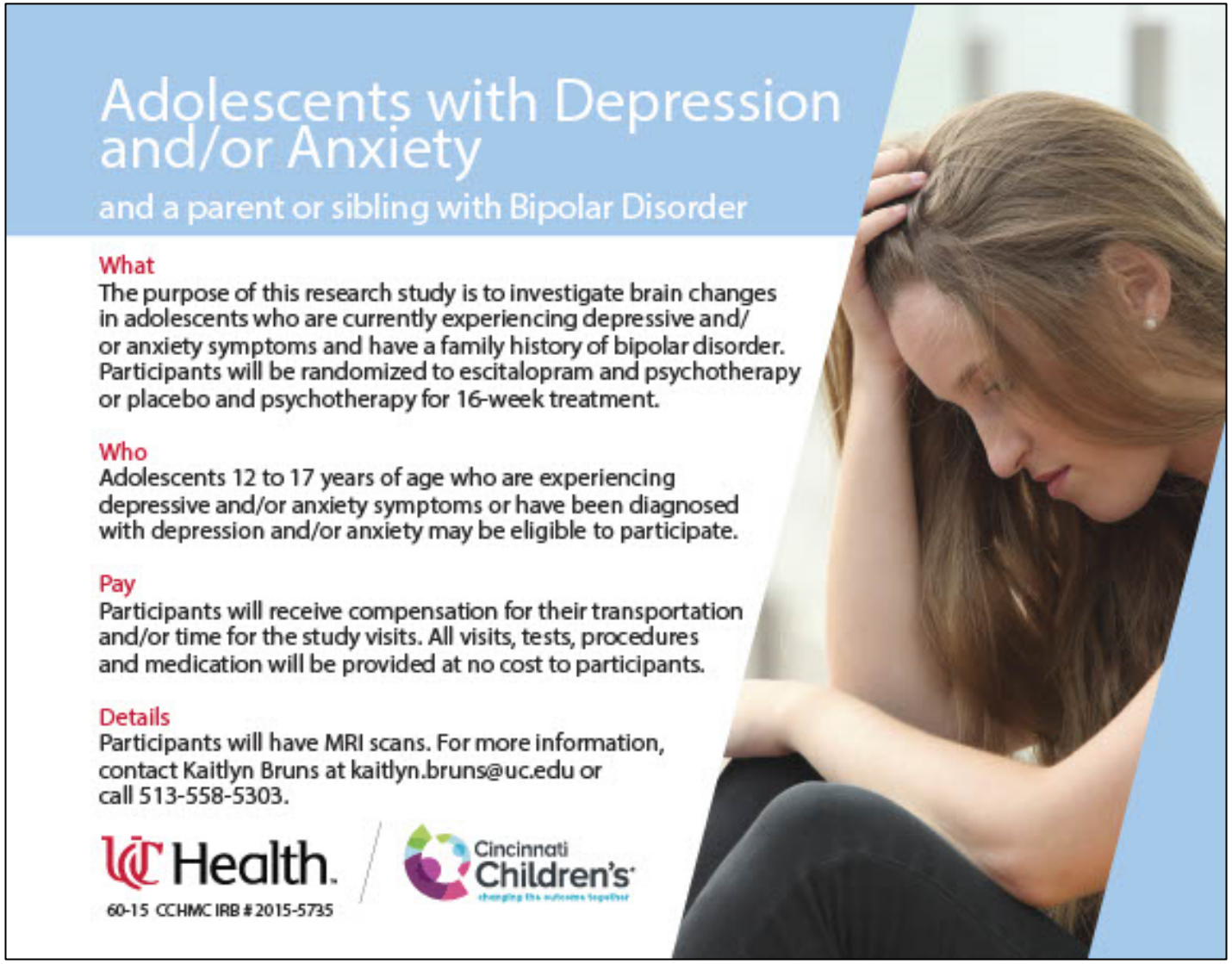
Speakers:

Frankie B. Kropp, MS, LICDC-CS
University of Cincinnati College of Medicine
NIDA CTN Ohio Valley Node
Department of Psychiatry and Behavioral Neuroscience
Addiction Sciences Division

No Relevant Relationships

OCR Announcements:

June 2021 Study of the Month



OCR Announcements:

UC Health

SOP Update:

Greenphire ClinCard System:

The method of requesting Greenphire Clincards has been updated to an online submission platform.
The older method involved completing a study action form and a study information sheet and forwarding the request by email.

This has all been updated to an online electronic request and submission method, eliminating the need to submit the request by email, further streamlining the process.
The link to the online Greenphire request Form: Greenphire Request Form

For detailed information on this update to the Greenphire Clincard request method and the online request form link, please see the recently updated SOP :
UCH-OCR-OPS-SOP-005-02:
Greenphire ClinCard Participant Compensation and Reimbursement System

All OCR SOPs are accessible from the UC Health intranet home page utilizing the Compliance 360 policy search function or reach out to the Office of Clinical Research with any questions or concerns.

OCR Announcements:

Thursday, June 17th, 2021, 12:00noon - 1:00pm
Virtual Presentation

UC Health Investigational Pharmacy (IDS): Overview, Updates, Best Practices and FAQs

Please join us for an overview of best practices and frequently asked questions when it comes to engaging Investigational Pharmacy (IDS) for your studies. This IDS refresher presentation will also include any updates to IDS procedures, as well as a refresher/overview of Beacon Builds.

Lisa Altenau, PharmD, RPh
Mary Burns, PharmD, RPh
University of Cincinnati Medical Center
UC Health Office of Clinical Research
Investigational Pharmacy

UC Health Clinical Research Orientation and Training (CRO&T)

Thursday, June 10th, 2021
9:00 am - 3:00 pm
Virtual presentation

The last day of registration is EOB Friday, June 4th, 2021

Please contact Nate Harris
Nate.Harris@UCHealth.com
for information and registration

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Today's Presentation:

Recruitment and Retention During a Pandemic: The experiences of the CTN0080 MOMs study

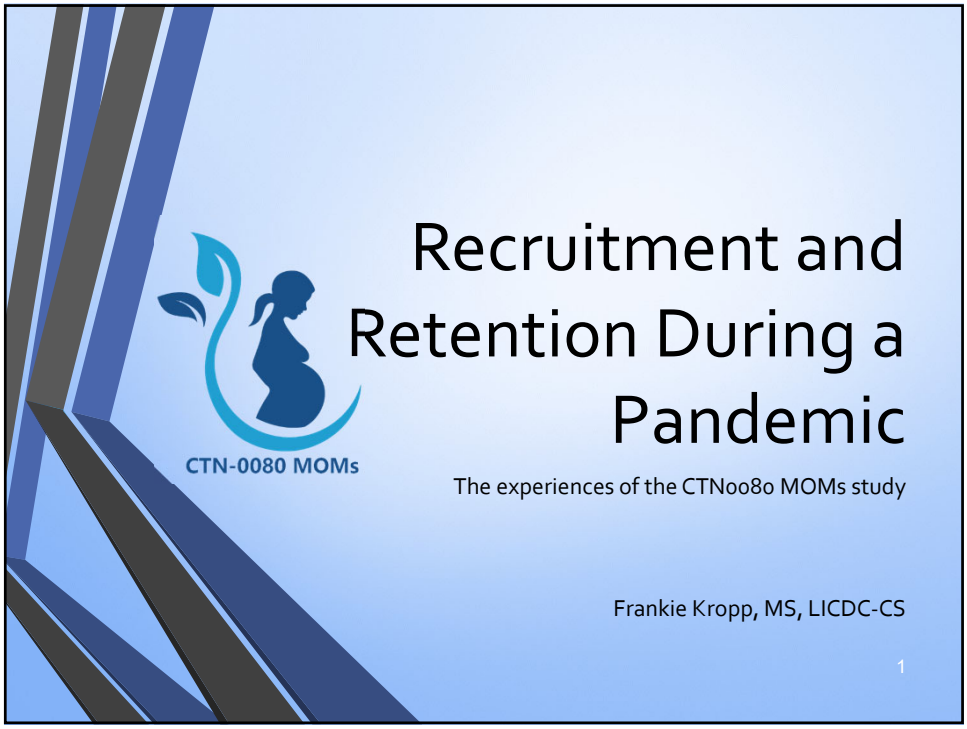
Frankie B. Kropp, MS, LICDC-CS

University of Cincinnati College of Medicine

NIDA CTN Ohio Valley Node

Department of Psychiatry and Behavioral Neuroscience

Addiction Sciences Division



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Background and Rationale

- US opioid-use epidemic associated with a significant increase in the prevalence of:
  - pregnant women with opioid use disorder (OUD)
  - infants with neonatal opioid withdrawal syndrome (NOWS)

Rates of opioid use and opioid overdose have increased during COVID

- NOWS is associated with adverse health effects for the infant and with costly hospitalizations
- Methadone- or buprenorphine (BUP)-maintenance treatment recommended for pregnant women with OUD

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Treatment of Opioid Use Disorder

- Methadone – full agonist

- Naltrexone – full antagonist

- Buprenorphine – partial agonist

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Sublingual Buprenorphine (BUP-SL)

- Advantages of BUP-SL, relative to methadone:
  - Greater convenience for pregnant women
  - Lower NOWS severity in their infants
- BUP-SL disadvantages:
  - Poorer treatment retention rates relative to methadone
  - Potential for misuse and diversion
  - Daily peak/trough cycle
    - For the fetus, the BUP peak is associated with adverse effects, including decreased fetal heart rate variability
    - BUP trough may be associated with plasma levels insufficient for suppressing opioid withdrawal symptoms and producing adequate opioid blockade

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Extended-Release Buprenorphine (BUP-XR)

Advantages relative to BUP-SL:

- Avoids daily peak/trough cycle
- Eliminates potential for misuse and diversion

Potential disadvantages relative to BUP-SL:

- Medication cost; however may have cost offsets
- Fetal exposure to BUP-XR solvents
  - Monthly formulations (CAM2038 and Sublocade®) utilize N-methyl-2-pyrrolidone (NMP)
  - Weekly CAM2038 (Braeburn) does not use NMP

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Study Objectives

Primary: To evaluate the impact of treating OUD in pregnant women with BUP-XR, compared to BUP-SL, on mother-infant outcomes

Secondary: To test conceptual models of the mechanisms by which BUP-XR may improve mother-infant outcomes, relative to BUP-SL

Tertiary: To determine the economic value of BUP-XR, compared to BUP-SL, to treat OUD in pregnant women

Quaternary: To evaluate the impact of BUP-XR, relative to BUP-SL, on neurodevelopment when the infant/child is approximately 12 and 24 months of age

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Study Design

Two-arm, open-label, non-inferiority, pragmatic randomized controlled trial

- N=300 (150 per treatment arm); 12 Sites
- BUP-XR (CAM2038) vs. BUP-SL
- Active treatment phase: pregnancy through 12 months postpartum
- Two optional sub-studies:
  - Conceptual Model Assessment (CMA)
  - Infant Neurodevelopmental Outcomes (INO)

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Inclusion/Exclusion Criteria

Inclusion

- Single fetus pregnancy 6-30 weeks EGA
- Moderate/severe opioid use disorder
- Already prescribed or good candidate for treatment with BUP
- Enrolled in outpatient OUD treatment at site
- Willing to be randomized
- Delivering at hospital with standardized care for NOWS

Exclusion

- Physiological dependence on alcohol or sedatives
- Medical or psychiatric condition that would make participation unsafe
- Prisoner status
- Receiving methadone or naltrexone
- In residential treatment beyond ASAM level 3.1
- Enrolled in similar research

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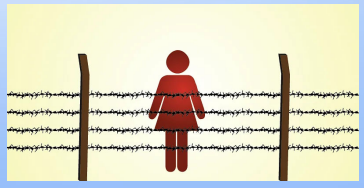
Barriers to Treatment

- Lack of specialized services
- Time consuming nature of treatment
- Responsibility for other children
- Greater social stigma
- Lack of support from family/partner
- Fear of losing custody
- Fear of prosecution



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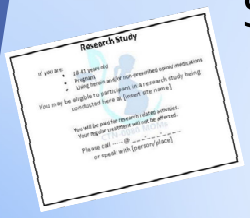
Site Recruitment



- All eligible sites selected based on their ability to recruit adequate numbers of the target population from within their clinic enrollment
- External recruitment allowable, but not anticipated

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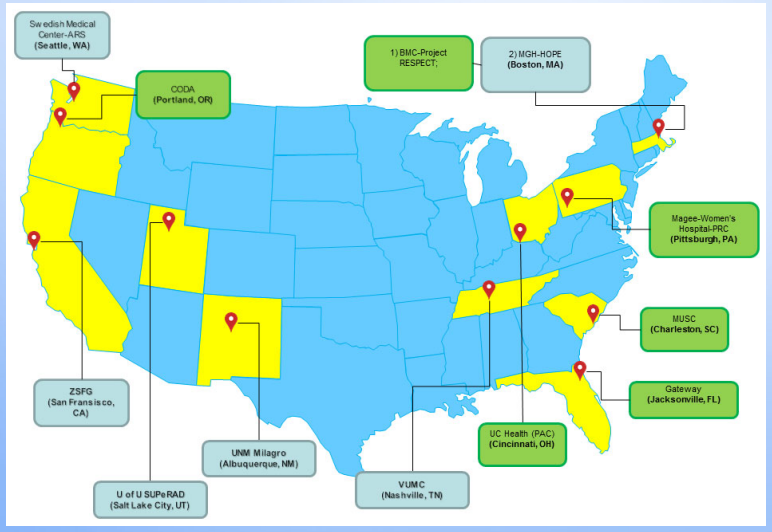
CTN-0080 Study Sites



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COVID-19 Impact

- Site initiations delayed
- Increase in use of telemedicine/decrease in face-to-face visits
- Overall decrease in clinic intakes in many sites
- Increase in late-EGA treatment entry

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Protocol Amendment

- Allowed for remote or off-site informed consent; electronic or wet signatures
- Allowed for remote or off-site data collection
- Phone or other telehealth methods for interviews
- Participants may access ePRO from personal devices for self-assessments
- Home visits, visits in associated community sites, visits in other non-associated community sites as appropriate
- Collecting urine and blood, and administering/dispensing medication off-site as permitted by policies and regulations
- Allowed participants to self-collect urine and ship back to site

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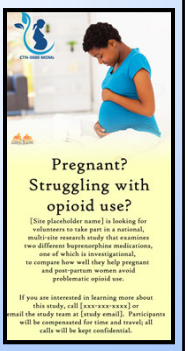
Lead Team Recruitment Materials

- Poster templates
- Flyer templates
- Rack/Post Card templates
- Tearpad-sized flyer templates
- Billboard-Bus-Bench templates
- Social media ad templates
- Web banner templates
- Press release/public service announcement templates



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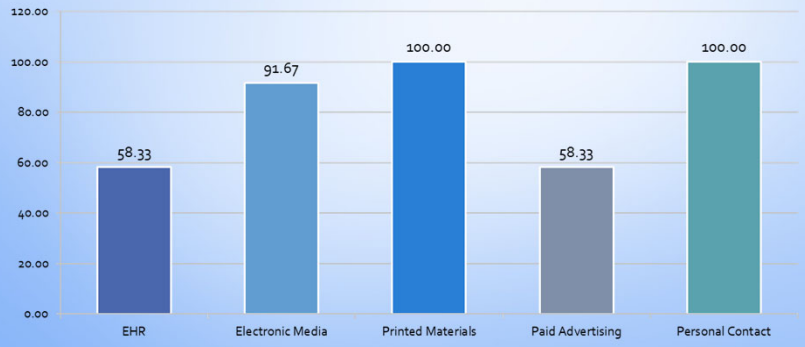
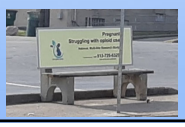
Expanded Recruitment Efforts

Methods
(% of sites utilizing)





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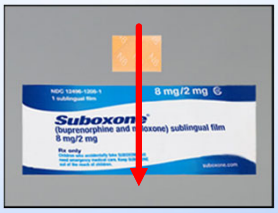
COVID-19
Another Surprise



Increase in methadone as the treatment of choice

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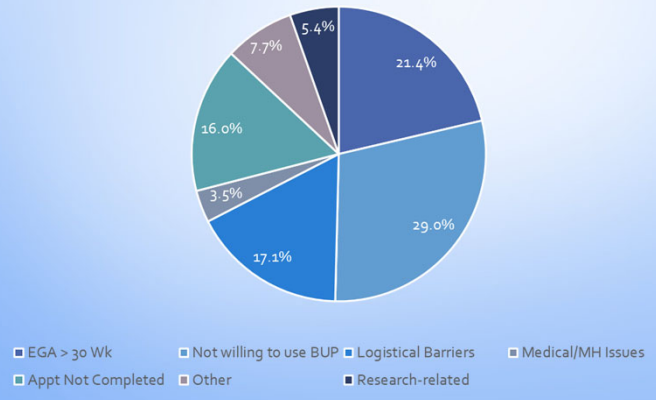
Reasons For Not Prescreening/Consenting



Note: individuals may be represented by multiple reasons

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More Adjustments

Recruitment is significantly below schedule (approximately 2 years), leading to:

- Site closures
- Reduction in target enrollment
- Loosening of exclusion criterion around residential treatment

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Retention

- Retention rates for BUP-maintained pregnant women estimated to be 57.7%
- Research on postpartum retention in MOUD indicates 36% dropout by 3 months and 62% by 6 months postpartum

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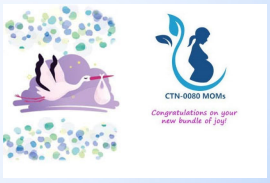
Lead Team Retention Materials



- Expanded Locator Form
- Appointment reminders
- Missed appointment letter/email/text/social media message
- Participant seasonal/occasion greeting cards
- Letters/info sheets to correctional facilities

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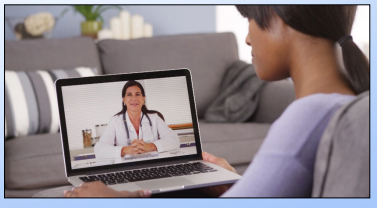
Retention Concerns Due To COVID

- Changes in clinical practice
- Fear of COVID exposure
- Loss of income/insurance
- Childcare issues



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Visit Locations

- Pregnancy Phase:
  - 90% in clinic
  - 15% via telemedicine
  - 6% offsite
- Postpartum Phase
  - 72% in clinic
  - 22% via telemedicine
  - 12% offsite

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Current Retention Rates

- Pregnancy phase medication visit completion – 96%
- Post partum phase medication visit completion – 88%
- Pregnancy phase research visit completion – 95%
- Post partum phase research visit completion – 98%
- Primary outcome collection – 84%

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Lessons Learned

- COVID-19 brought significant recruitment and retention challenges
- Sites may be unable to rely on "usual" recruitment methods
- Retention requires flexibility around how and where study procedures could be performed; this flexibility may benefit future studies even after the pandemic has subsided

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