Clinical Research Coordinators' Workshop: Study Implementation, Documentation, and Regulations

Application of Remote Technology in Research

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The Evolution of Telehealth Technology

- Limitations to in-person research was recognized in **2010** with solution guidance on remote clinical trial monitoring for VA
- The COVID pandemic changed everything
- In VA, COVID-19 required an immediate administrative hold on funded studies (BLRD, HSRD,RRD,QUERI,CSP, or MVP) for non-critical interaction.
- Teletechnologies became essential to support research

Adaptation

- Hence, the birth of online, telehealth, telephone recruitment, enrollment and follow-up visit
- Today the use of telehealth technologies has transformed research meeting needs of both participants and the PIs
- Allowing for the birth of completely remote studies or decentralized clinical trials

Research Mechanics -Remote

- To Recruit
- To Inform
- To Collect
- To Share
- To Analyze
- To Monitor

The Tools for Remote Access

A telehealth program, conducting a remote study, requires supportive tools of communication

To Recruit

- Recruitment flyers and letters remain the mainstay
- Differences are the How and the Where
- Encrypted email is permissible for recruitment

Opt-out letter as seen from a DC Metro Bus

"We've come a long way, baby"
Approved Video Communication Technologies

- Via VA Video Connect (VVC)- preferential method for conducting video encounters
- Apple FaceTime
- Facebook Messenger Video Chat
- Google Hangouts video
- Skype
- WhatsApp

To Inform

Electronic Methods to Securely Obtain Informed Consent

- Use of eConsent is approved by ISSO, local IRB and R&DC
- Obtaining wet, electronic, or digital signatures from VA research participants or a LAR is approved via specific means.
- The informed consent form may be combined with the HIPAA Authorization form if the study does not involve optional banking of identifiable private information or identifiable biospecimens.

Wet signature- marking a document

May be obtain remotely by signing at home and sending via VA fax or digital imaging to MyHealtheVet secure messaging.
Mailing not recommended
IRB may approve to waive the HIPAA authorization

Rights Management Services (RMS): Secure Transmission Using Encrypted Email with Return of Wet Signatures

- The Azure Rights Management (Azure RMS) VA cloud-based protection service to securely transmit IRB-approved informed-consent forms to VA research participants.
- Research subjects can open and view RMS encrypted email from any compatible web browser or email account, such as Google mail (Gmail), Yahoo or, Microsoft Outlook.
- Participants or a LAR can be instructed to use their personal cell phones to take a picture of the signed informed consent form containing a wet signature, upload the image file using their personal email account (e.g., Gmail, Yahoo, or Microsoft Outlook), and send it back to the VA research team.

Other approved platforms

- **MyHealtheVet**: Secure Transmission Using Encrypted Email with Return of Wet Signatures
  - Not OK for recruitment
  - OK for ICF transmission and return of wet signature ICF and PHI
  - the MyHealtheVet enrollment process supports verifying a subject's identity before allowing access to the application for increased authentication.
  - OK for other study methodologies
- **DocuSign:** Transmitting Informed Consent Forms and Obtaining Digital Signatures
  - Request envelopes from ORD (https://dvagov.sharepoint.com/sites/VHAORPPE/DocuSign)
  - FDA regulated study of drug, supplement, or device requires two- factor authentication (2FA) of e-signature per code of federal regulations, 21 CFR part 11
- **iMedConsent:** Internal to VA only
- **Secure Multi-Functional Device (MFD) Printer**: to scan ICF into electronic medical record

To Collect

Conducting your Study Video platforms

- Microsoft TEAMS platform is approved and secure
- VA Video Connect platform encouraged
- Non-public facing remote audio or video communication technology include: Apple FaceTime, Facebook Messenger video chat, Google Hangouts video, Skype or WhatsApp.
- ZOOM is not secure

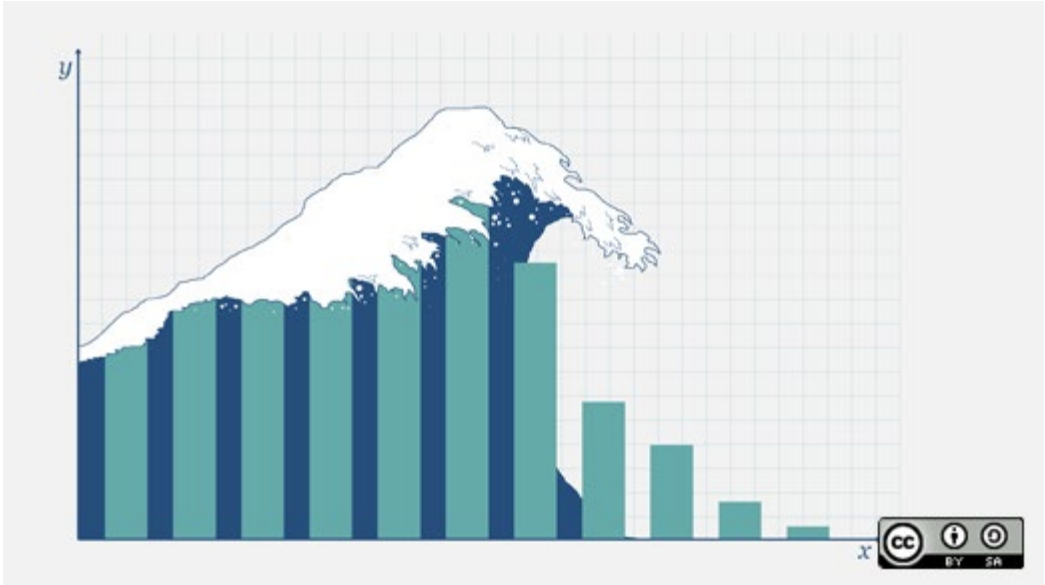
Collecting data--web-based surveys

- Approved commercial systems for survey/questionnaire data
- Frameworks for data collection and analysis
  - **WESTAT**
  - **Qualtrics** VHA ORD QualtricsPortal - Home (sharepoint.com)
  - **REDCap** (**R**esearch **E**lectronic **D**ata **C**apture) *https://vaww.virec.research.va.gov/REDCap/Overview.htm*
    - REDCap is a free, secure Web application that facilitates the collection and entry of research data. Tools enable users to quickly develop surveys and databases from conception to production on the Web without additional software requirements. This tool helps researchers enter, store, and manage their project data in a systematic manner.

In Home Devices for Collecting Data

- **Remote EEG:** EEG is an important marker of brain function. Since advanced EEG machines are large and difficult to use, low-density portable EEG monitors collect EEG in home using the Muse 2 portable EEG device.
- **Ballistocardiography:** measure of ballistic forces generated by the heart through contraction. A technique for producing graphic representation of repetitive motion of the body
- **Actigraphy:** measure of sleep parameters (sleep/wake cycles); worn on wrist
- **Remote labs:** Nurses making house calls…such cutting edge technology; use of neighborhood labs
- **Remote Vital sign monitoring**

To Share
To Analyze
To Monitor



To Share

- **VA Box:** similar to commercially available Dropbox but offers secure data storage

  Specifically for larger data.

  VABox.com does external sharing.

  Can upload files as large as 150 GB.

  Files in VABox will be retained for seven years after use.

  Home - VA Box.com Requests (sharepoint.com)

- **National Research Dashboard** Dashboards (va.gov)
  - The VA Innovation and Research Review System (VAIRRS)
  - Visual tool to search the national VAIRRS dataset for active research projects and to help connect researchers working on similar topics.
  - Facility-level dashboard and analysis to support management and understanding of local research programs and to help providers identify studies for their patients

Virtual Data Monitoring

- Remote monitoring supported in VA since 2010
- **Webex** is used to conduct remote monitoring for clinical trial monitoring by external monitors (non-VA employees) who require access to protected health information and the Electronic Health Record (EHR) using a VA employee as the driver of the documents.
- Either CPRS/VISTA or JLV can be used for remote monitoring visits.
- Both privacy and informed consent regulatory requirements must be verified prior to scheduling the remote monitoring visit.
- The VA research team member must ensure that the signed HIPAA authorizations specifies the disclosure of protected health information (PHI) to clinical trial monitors for those subjects whose records are to be monitored permitting access to the records.

Advantages and Disadvantages

Facilitates representation

Decreases discomfort

Reduces barriers

Allows for social distancing

For the participant: reduction in barriers to participation

- Decreases burden: Convenience
- Less stress; no travel; participation from the comfort of home

For the research team:

- Do you have the infrastructure
- What education is required for the team and the participant
- May be some extra initial work and organization
- Ease in recruitment
- ICF must be explicit and contain information about PHII and remote study monitoring
- May require extra effort to engage

Let's Operationalize Teletechnology

Nurse Practitioners' Lived Experience of Opioid Prescribing Practices for Chronic Pain in Veterans

PI: Heidi Maloni and Angela Cooper

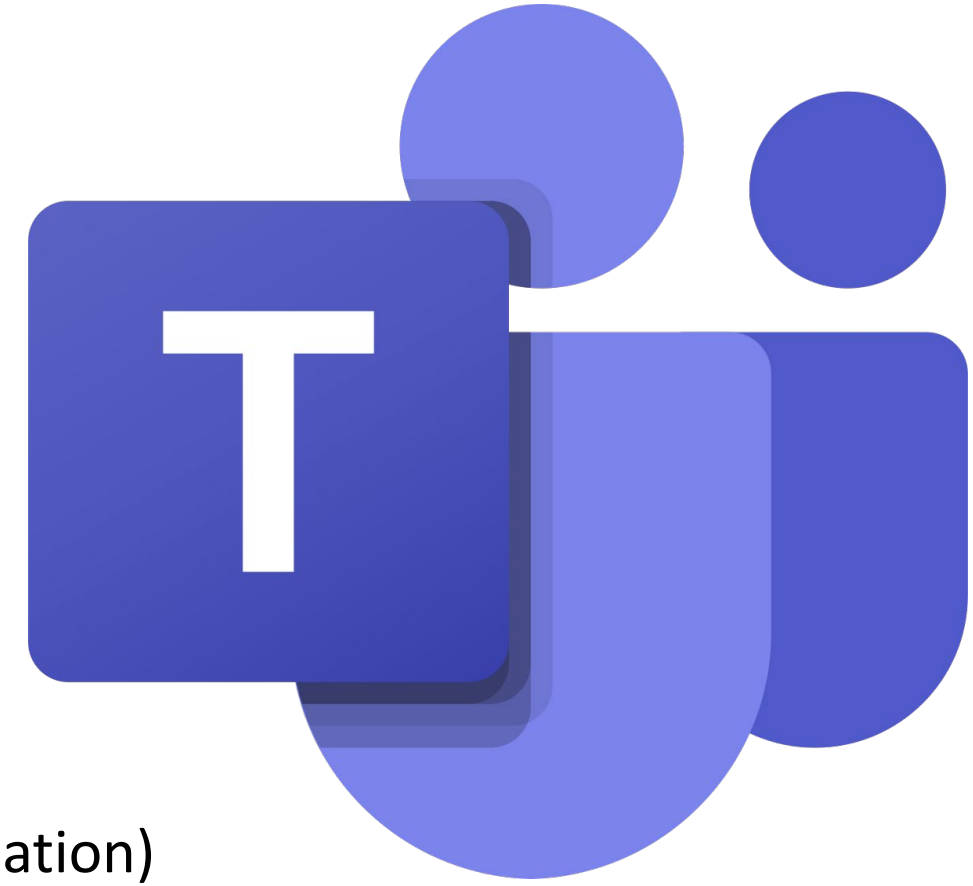
- Fully remote qualitative interview research
- Aim is to describe the lived experience of NPs prescribing opioids in veterans diagnosed with chronic pain.

Methods

- Recruitment flyer distributed in three VA Medical Centers
- Encrypted email link to schedule a virtual interview
- Pseudonym assigned the day of the study
- Interviews are audio-recorded on a secure VA platform (Microsoft Teams) for later transcription; participants are informed notes are recorded during the interview.
- A demographic questionnaire is requested and sent to the PI via encrypted email
- Participants are employees
- A copy of Notice of Privacy (NoPP) given to all non-Veterans enrolled

Tele-technology at work

- Informed Consent via DocuSign
- Study interview via Microsoft Team



(An incidental occurrence when
participant photos appeared requiring
an ICF/HIPAA amendment to allow for
both voice and photo capture -of course
this constituted and was reported as a study deviation)

- Analysis using NVIVO qualitative software

Confirmatory Trial for Alleviating FatiguE in Multiple Sclerosis- CAFÉ MS

- A fully **Decentralized Trial** with the aim of testing two different experimental online programs as potential treatments for fatigue in individuals diagnosed with multiple sclerosis
- DOD funded; FDA regulated; multisite trial (5 VAMC and one nonVA MS conglomerate) seeking to enroll 2000 participants
- All recruitment, consenting and study activities are via a remote portal utilizing all the modalities previously presented
- Trial success is optimized by its decentralized design

The Gurus of teletechnology research over 5 years!

Studies with:

- Remote eligibility screening
- DocuSign ICF with electronic documentation
- Mobile health apps
- Remote monitoring devices
- Wearable devices
- Use of telemedicine and video connect
- Data collection through REDCap formally Qualtrics

Investigators

Matthew Reinhard PsyD and Michelle Costanzo PsyD

War Related Illness and Injury Study Center (WRIISC) and the Complex Exposures Threats Center of Excellence (CETCE)

WRIISC
War Related Illness & Injury Study Center

CETCE
Complex Exposure Threats Center of Excellence

Veteran occupational and deployment related Exposure Evaluation and Risk Stratification (Veteran Exposu-ERS)

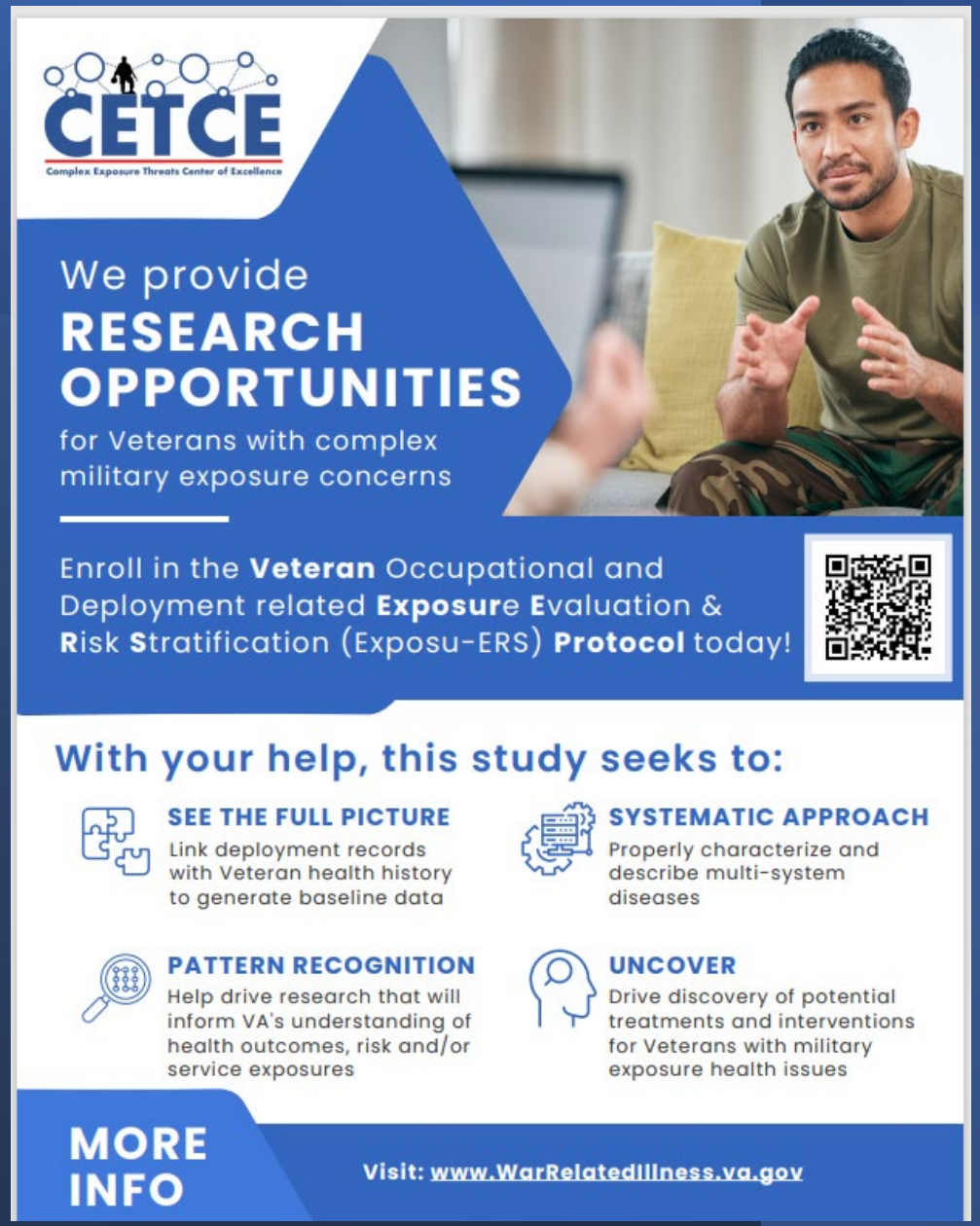
PI: Michelle Costanzo, PhD

- to assess chronic health outcomes in Veterans with a history of complex military environmental and occupational exposures to better understand the links between military environmental exposures and the risks of developing chronic diseases later in life.

Remote Activities

- A virtual eligibility session
- A virtual neuropsychological and cognitive testing session
- 7 days of at-home assessments with devices to assess sleep behavior, brain function, and daily activity
- Wearing a portable EEG device which looks like a head band for few minutes during the day
- ,Physical activity and sleep will be evaluated using an Actigraph, a compact wrist-worn device.

Remote recruitment and eligibility screen



QR code for Qualtrics recruitment

You are interested in participating in the Veteran occupational and deployment related Exposure Evaluation and Risk Stratification (Veteran Exposu-ERS) conducted by the Complex Exposure Threats Center of Excellence (CETCE).

The purpose of this study is to assemble data on Veterans with complex military environmental and occupational exposures.
This study will serve as an active surveillance that can yield generalizable knowledge of Veteran's military exposure history and emerging exposures of interest.
This study will help the VHA's medical recognition and diagnosis of diseases states by identifying defining characteristics and symptom profiles.
Do you wish to proceed to answer basic contact questions for the study team to reach out to you to discuss in more detail of the study procedures and conduct a pre-screening survey for study enrollment?
Yes / No
Qualtrics recruitment questions:

- What is your name _____?
- Are you a Veteran Yes / No?
- What is the best number to contact you _____?
- What are the best times for the study team members to reach out to you?

WRIISC
War Related Illness & Injury Study Center

An exercise program guided by heart rate variability in Veterans with chronic multi-symptom illness

- a home-based exercise intervention that leverages remote technology to collect data from participants (e.g., activity monitoring device and heart rate monitor).
- New tools required a protocol amendment
  - Consumer activity monitor and HR monitor
    - Emfit QS (thin strip with biosensors placed under mattress to collect HR, breathing, movement during sleep).
  - Add instruction manual to be sent to participants.
  - Questionnaire: remote collection via Qualtrics survey platform or paper copies per participant preference.
  - Virtual delivery of psychometric questionnaires (Qualtrics)
  - Update security plan for use of additional computers in data analysis
  - Modify the ICF and HIPAA authorization
  - Modify recruitment letter

WRIISC
War Related Illness & Injury Study Center

Multimodal observational study of veterans with TBI with varying symptoms

- **Aims** to understand the physical and psychological consequences of TBI using a multi-modal observational inventory
- Remote Consent
- Remote data acquisition (devises mailed to participants
  - (1) psychological assessments -Qualtrics
  - (2) neuro-cognitive activity measured using electroencephalography (EEG) and eye-tracking (portable electroencephalography (Muse 2; measures brain activity)
  - (3) neural structure and functional organization
  - (4) sleep using actigraphy and ballistocardiography (Emfit; measures sleep and autonomic measures), and actigraphy (measures sleep and activity)
  - (5) self-report questionnaires via Qualtrics

WRIISC
War Related Illness & Injury Study Center

Multiple Sclerosis Telehealth Utilization Project

PI: Mitch Wallin MD and Heidi Maloni PhD, NP

- A study during the COVID pandemic to understand who uses telehealth and what are barriers through three aims 1) large database review; 2). MS database; 3). specific facilitators and barriers in qualitative study survey of patients, providers and payers
- Modifications
  - Verbal and witnessed informed consent for video individual and focus groups
  - Video interviews (both individual and groups)
- Publication:

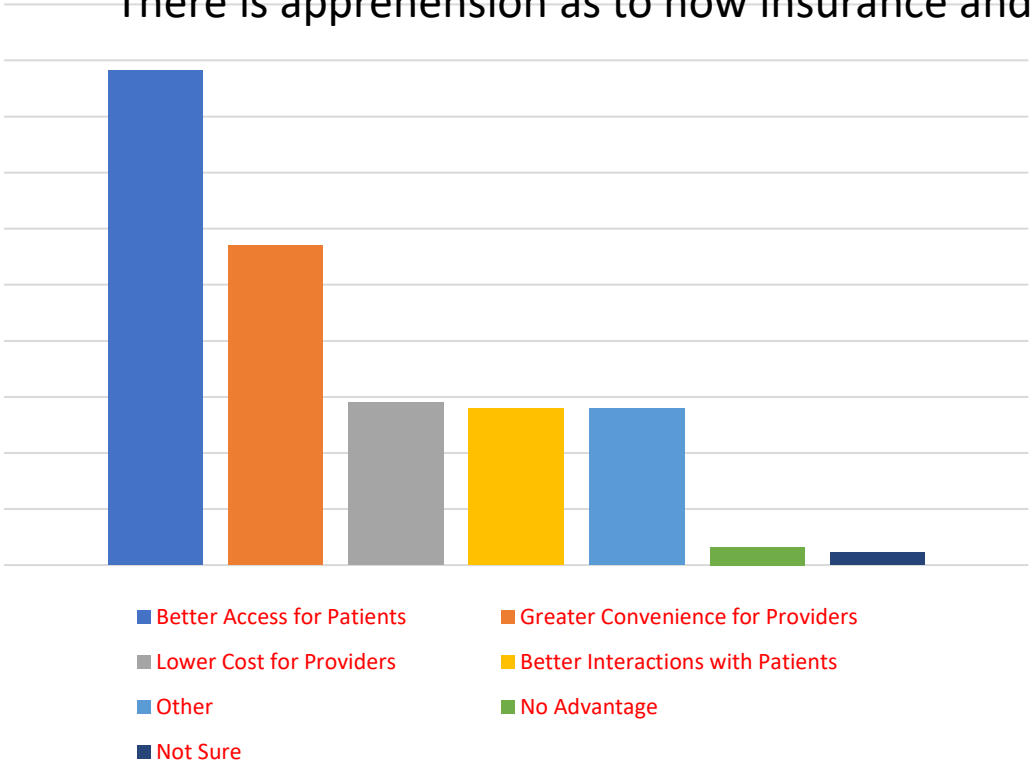
  Telemedicine and Multiple Sclerosis during the COVID-19 Pandemic: Perspectives from Patients, Healthcare Providers and Payers in the United States. Erin G. Roth, PhD, Heidi W. Maloni, PhD, ANP-BC, Sarah L. Minden, MD, Zipporah J. Miles, MPH, Mitchell T. Wallin, MD, MPH

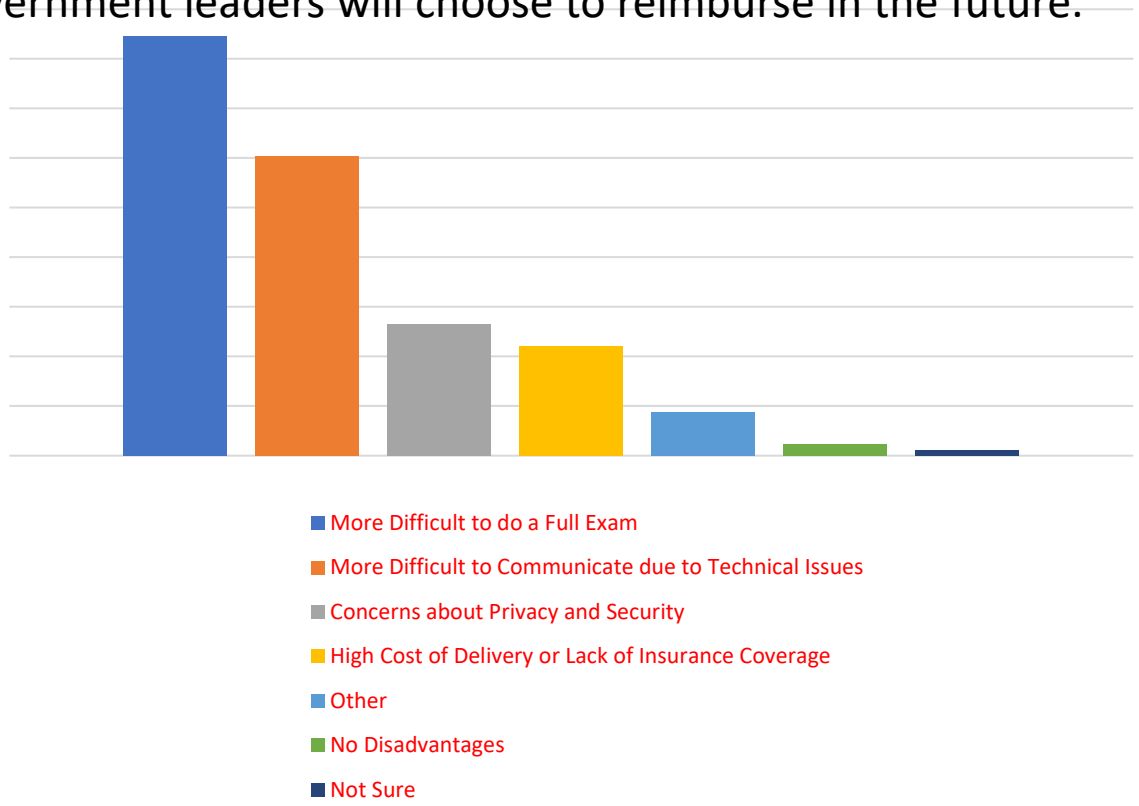
Themes emerged on the use of telehealth

- Convenience, improved access, technical challenges, perceptions of value
  - "…the single biggest transformation in healthcare delivery in fifty years; [and] it happened in four weeks"
  - "We can swim"
  - "Where's the play book"
  - "If he can't touch me, how does he know what's wrong"
  - "A visit should be more than just talk"
  - My provider looked at me the whole time and not her computer" "No interruptions, no pagers, no computers"
  - "There is benefit in 'seeing' the home environment"
  - "I saw the patient in his car as he was stopping for milk"
- Copays waived; licensing requirements relaxed across state lines

Results: Benefits and Drawbacks of Telemedicine for MS Care

The COVID-19 pandemic was the impetus for use of telemedicine.
Convenience and flexibility are valued despite technical challenges.
Payers uniformly covered telemedicine encounters during the pandemic
There is apprehension as to how insurance and government leaders will choose to reimburse in the future.





So when remote research and decentralized trials become "the way of the world"….

- **How is the study coordinator to prepare?**

  - a) become familiar with remote technology platforms
  - b) understand regulatory requirements for remote research
  - c) familiarize with DocuSign envelopes for ICF
  - e) familiarize with remote survey collection modalities
  - f) choose a secure platform to conduct study visits
  - g) educate the participant
  - h) recognize the How to remote study monitoring for your institution
  - i) Know the pitfalls