DC CTSA Spring Regulatory Update & Hot Topics in Clinical and Translational Research

Moving Swiftly to Combat the COVID-19 Global Health Crisis

Regulatory Issues Related to Human Subject COVID-19 Research

Moderator: Mary Schmiedel, J.D.

Senior Director, Office of Research Oversight
Georgetown University

11:40 - 12:25 AM EST

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GHUCCTS
Georgetown-Howard Universities Center for Clinical and Translational Science

CTSI Clinical and Translational Science Institute at Children's National
A PARTNERSHIP WITH THE GEORGE WASHINGTON UNIVERSITY

DC CTSA Spring Regulatory Update & Hot Topics in Clinical and Translational Research

Moving Swiftly to Combat the COVID-19 Global Health Crisis

Regulatory Issues Related to Human Subject COVID-19 Research

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Department of Health and Human Services

COVID-19 and a Year of Opportunity

CTSA Conference

April 23, 2021

Heidi W Maloni PhD NP

Administrative Research Hold

- The Office of Research and Development (ORD) placed a hold on all ORD funded non-critical, in-person human research subject interactions to include:
  - In-person recruitment/enrollment. Including screening visits
  - In-person interactions and interventions
  - In-person follow-up (except in studies with participants already enrolled, can continue for safety)
- The DC VA Medical Center Director and R&D program issued a broader hold on all in-person research activities

- R&D program at DC VA placed research hold on non-COVID in-person research studies on March 11.2020
- Exceptions for critical safety visits for participants enrolled in ongoing clinical trials

Resuming research

- Consider local and site-based factors
  - DC orders lifts restrictions for nonessential businesses
  - DCVA has resumed in-person patient visits for nonessential procedures and services
  - University affiliates allow research resumption
  - Ability to combine research visits with clinical visits
  - Ability for ancillary services such as lab and radiology
  - Necessity of in-person vs remote study visits
  - Availability of testing for symptomatic personnel

- Required steps to resume research
  - Facility sign-off to resume research from "Incidence response group and/or Chief of Staff
  - The signed form is sent to ORD and titled "Resume Research "
  - Risk Assessment
  - Plan for mitigating risk

Risk Assessment

- Determine the impact of re-opening research on the medical center
  - No private sponsors of funded studies offered to pay for or reimburse the hospital for supplies. At least two Central IRB approved study sponsors offered to reimburse for PPE supplies.
- Protocols are categorized as low, medium, or high

- Phased opening
  - Phase one:
    - low impact studies
    - August 30,2020 start date
  - Phase two:
    - Medium impact studies
    - Coordinate with DC VA opening 50%
  - Phase three:
    - Multiple research only visits in clinical areas
    - Hospital open to 60%

- Precautions with phased opening
  - Telehealth tools encouraged for group research
  - Centrifuged blood and body fluid criteria
  - Aerosol generating procedures criteria
  - PIs to assure safety procedures
  - Training staff on proper don/doff of PPE and cleaning per CDC guidelines
  - Telephone COVID screening
  - Encourage HIPAA compliant telehealth tools

Risk mitigation strategies

- Ability to provide
  - PPE for participants and staff
  - Physical distancing
  - Proper cleaning of spaces where visits occur
  - Limit unnecessary exposure from the hospital
- PI plan for communication of risk and mitigation strategies
- Submit plan to ORD and DCVA

PI Creativity

- Amendments to existing protocols to allow for remote study visits
- Amendments to existing protocols to allow for remote consenting
- Amendments to existing protocols to allow for remote collection of data
- Protocols aimed to understand acceptability, utility and effectiveness of remote research

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

Qualitative study

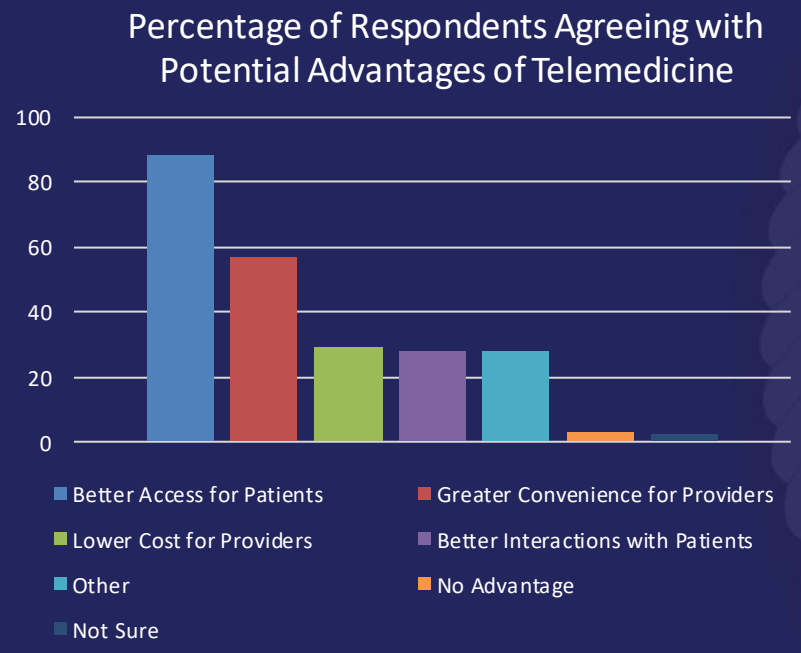
- Conducted 9/2020 and 1/2021
- Aims: Understand perceptions and experience…
- Amended protocol to allow for verbal consent
- Participants- PwMS, providers, payers
- 30-60 min semi-structured interviews via ZOOM
- Interviews were audio recorded and transcribed
- Inductive analysis for themes

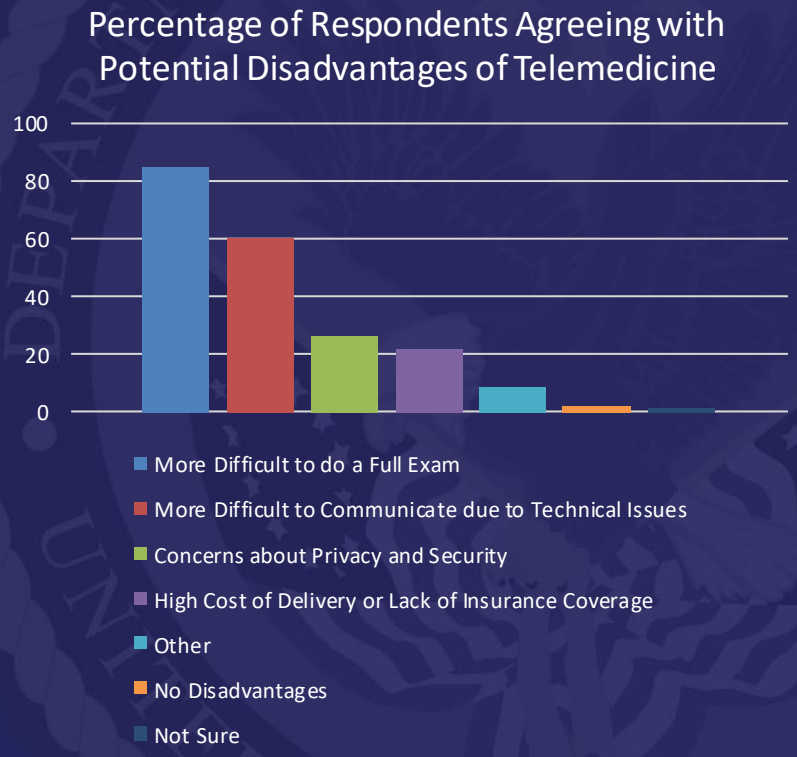
Themes….COVID

- 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

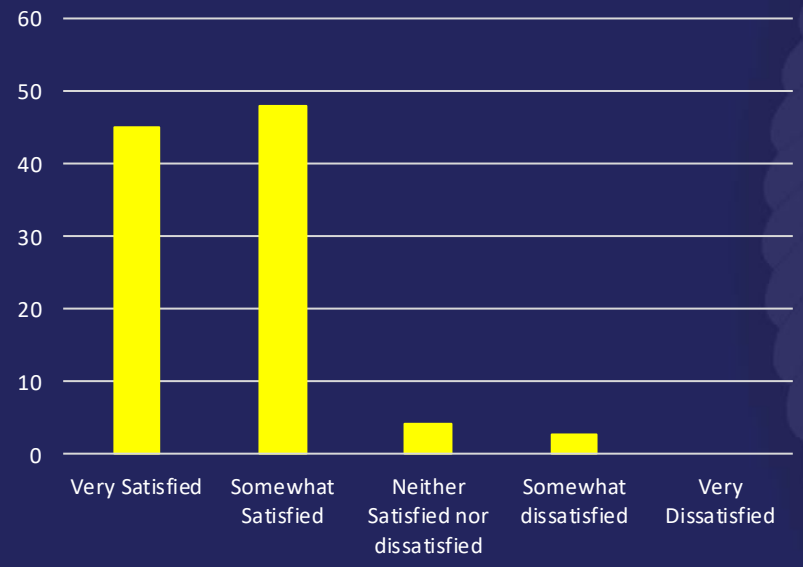
Results: Benefits and Drawbacks of Telemedicine for MS Care



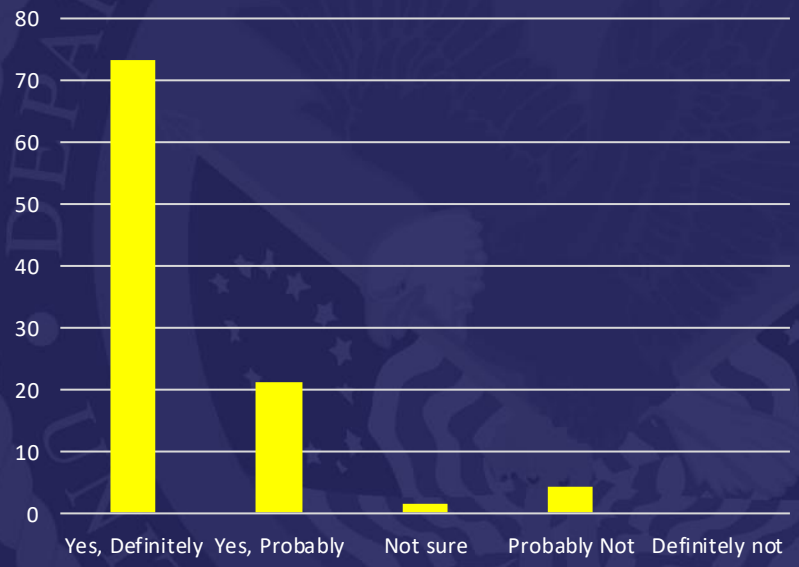


Results: Satisfaction with Telemedicine

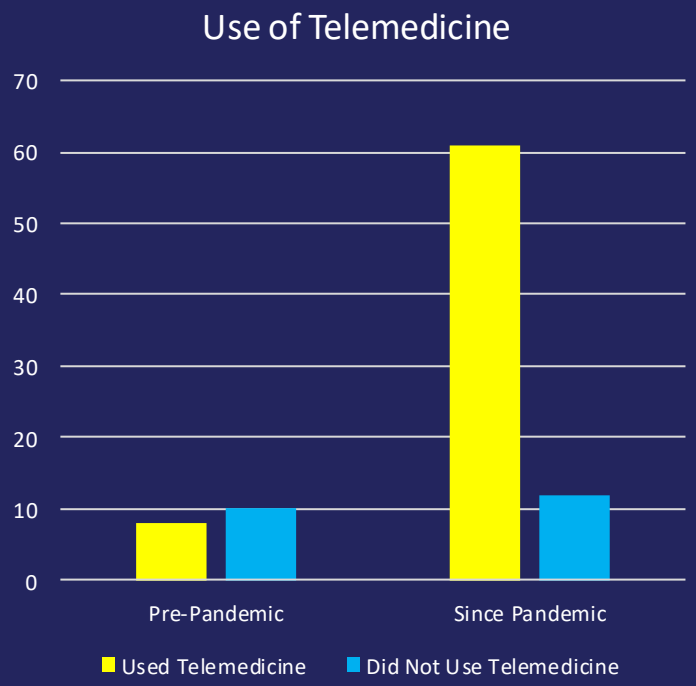
How Satisfied were Respondents with their last Telemedicine Visit

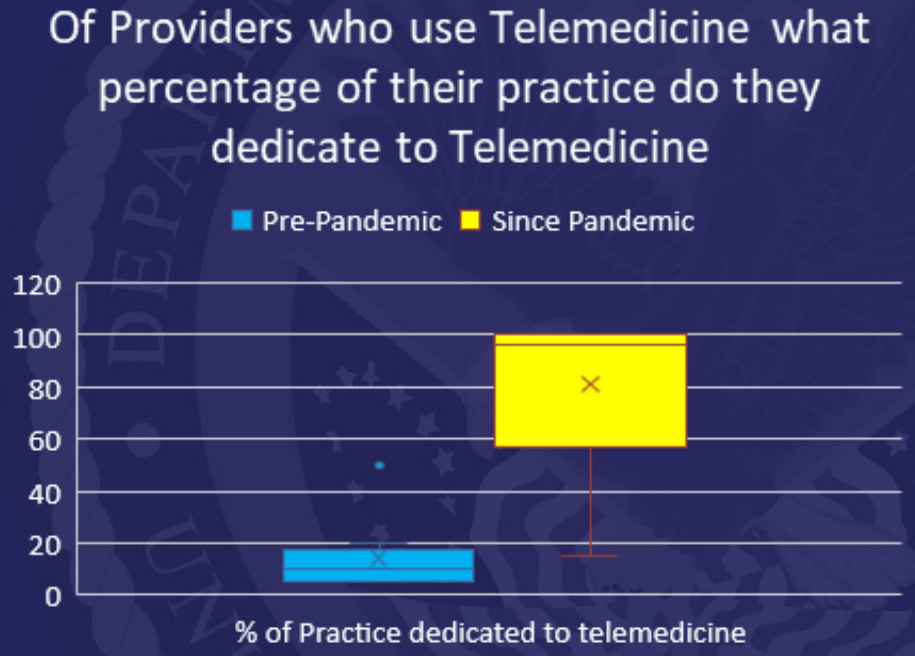


How likely were Respondents to want to continue using Telemedicine



Results: Telemedicine Pre-COVID19 vs. During COVID19 Pandemic





Results

- 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.

- Conclusions
  - The COVID-19 pandemic forced widespread utilization and reimbursement for telemedicine and relaxed legal policies that made it possible to implement.
  - Telemedicine is an efficient, convenient platform for many aspects of MS care and is supported by the majority of PwMS and providers.

Implications for the Future and Discussion

Is remote/virtual research here to stay?

What are the disadvantages?

What are the advantages?

MedStar Health

It's how we treat people.

April 23, 2021

Working with you is… Not Killing Me

Collaboration with Institutions and Investigators

James H. Boscoe, Director, Office of Research Integrity

MedStar Health Research Institute

Agenda

1. MedStar / Georgetown relationship
2. Joint Guidance for response to COVID –19
3. Adjustments to an existing study
4. Start up of Multi-Site COVID –19 study
5. Considerations for the Future

Working Together
MedStar Health and Georgetown University

Institutional Collaboration
MedStar / Georgetown

- MedStar Georgetown University Hospital
  - Unique relationship
  - Catholic Directive
- Separate IRBs
  - Georgetown University IRB
  - MedStar Health Research Institute IRB
- Investigator's perspective
  - Opportunities and Challenges
  - IRBs working to harmonize policy and procedure

Working Through COVID:
MedStar Health and Georgetown University

MedStar Health

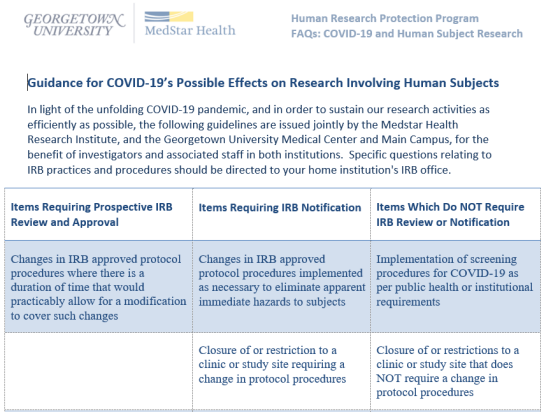
Rapid Changes

- COVID-19 Restrictions
- Finding allowable flexibility in the regulations
- Guidance from Regulatory Agencies
- General recommendations
  - Don’t panic
  - Be flexible
  - Maintain compliance

Coordinated Communication:
MedStar Health and Georgetown University

Communication:
Joint Guidance to Investigators

- Input from both MHRI and GU
- Single Guidance document
- General guidance
- Specific guidance
  - Follow Institutional and Public Health guidance / mandates
  - IRBs are fully functional
  - Changes to protocol or operations (study visits, temporary closure)
  - Recommendations for in person monitoring
  - Screening for COVID-19
  - What if staff or participant test positive



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Human Research Protection Program
FAQs: COVID-19 and Human Subject Research

Guidance for COVID-19's Possible Effects on Research Involving Human Subjects

In light of the unfolding COVID-19 pandemic, and in order to sustain our research activities as efficiently as possible, the following guidelines are issued jointly by the Medstar Health Research Institute, and the Georgetown University Medical Center and Main Campus, for the benefit of investigators and associated staff in both institutions. Specific questions relating to IRB practices and procedures should be directed to your home institution's IRB office.

Items Requiring Prospective IRB Review and Approval	Items Requiring IRB Notification	Items Which Do NOT Require IRB Review or Notification
Changes in IRB approved protocol procedures where there is a duration of time that would practicably allow for a modification to cover such changes	Changes in IRB approved protocol procedures implemented as necessary to eliminate apparent immediate hazards to subjects	Implementation of screening procedures for COVID-19 as per public health or institutional requirements
	Closure of or restriction to a clinic or study site requiring a change in protocol procedures	Closure of or restrictions to a clinic or study site that does NOT require a change in protocol procedures

Guidance in Action:
Limit Non-Research Risk

Diabetes Research: Change in Study Visit Location

- Participants with Diabetes
  - Interventional study
  - Long-term (7 years)
- Visits typically in Primary Care office
  - March 2020 conducting COVID testing
  - Need to limit potential exposure
- Plan to change location temporarily
  - Report to the IRB with no protocol modification
  - Included plan for communication with participants

Mayo Clinic
Expanded Access: Convalescent Plasma

Working with Mayo Clinic

- Started with Mayo Clinic and FDA
- Mayo Clinic as Coordinating center and sIRB
- Eventually included more than 2800 sites
- Rapid start up

Working with MedStar / Georgetown Investigators

- Special provision approved by FDA
  - Atypical documentation of reliance
  - Limited role of local IRB
  - Mandated acceptance of protocol and consent language
- Communication in real time locally
  - Assist MedStar investigators with startup
  - Set and communicate local requirements
  - Facilitate communication with Mayo as needed

Considerations for the Future

Considerations for the Future

- Clear and Open Communication is Critical
- Investigators
- IRBs need to work together
- Frequent collaborators
  - Harmonize when possible
  - Clearly communicate different requirements

Thank you

It's how we treat people.

MedStar Health

Moving Swiftly to Combat COVID-19: Leveraging Regulatory Flexibilities in the Common Rule

Dr. Yvonne Lau, MBBS, MBHL, PhD

Director, Division of Education and Development (DED)
HHS Office for Human Research Protections (OHRP)

April 23, 2021

OASH | Office for Human Research Protections

Disclaimer

The opinions expressed are those of the presenter and do not necessarily reflect the policy of the U.S. Department of Health and Human Services

Reminder! How the Common Rule Works

- The Common Rule regulatory requirements apply to ***nonexempt human subjects research*** funded by HHS and the other Common Rule agencies and departments
  - Regulatory requirements stipulate, amongst others, the operation of the IRB, informed consent requirements, etc.
- When these regulatory requirements do NOT apply, it means that

Investigators/Institutions have **Flexibility** (for review and consent) outside the regulations!

(Should still pay attention to participants' rights & welfare)

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When Do Regulatory Requirements NOT Apply (1)

- When the research does **not** receive federal funding from a Common Rule agency or department, it may not need to comply with any Common Rule requirements
  - While institutions are still allowed to "check the box" to comply with the Common Rule when they file their FWA, this is done voluntarily and OHRP does not encourage institutions to do so
  - Institutions can "uncheck" the box anytime

When Do Regulatory Requirements NOT Apply (2)

When:

- The entire human research study fits the conditions of one or more ***Exemptions*** at 46.104(d), e.g., the study only involves volunteers completing an online survey about their mental health during the COVID pandemic; **OR**
- The research is **not** ***Human Subjects Research***, e.g., secondary research using only nonidentifiable data or nonidentifiable biospecimens collected from clinical care; **OR**
- The study is **not** ***Research***, e.g., when the study belongs to activities deemed not be research under the Public Health Surveillance exclusion

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Excluded Public Health Surveillance Activities

- These activities must be conducted, supported, requested, ordered, or authorized by a ***Public Health Authority*** (as defined in the Common Rule);

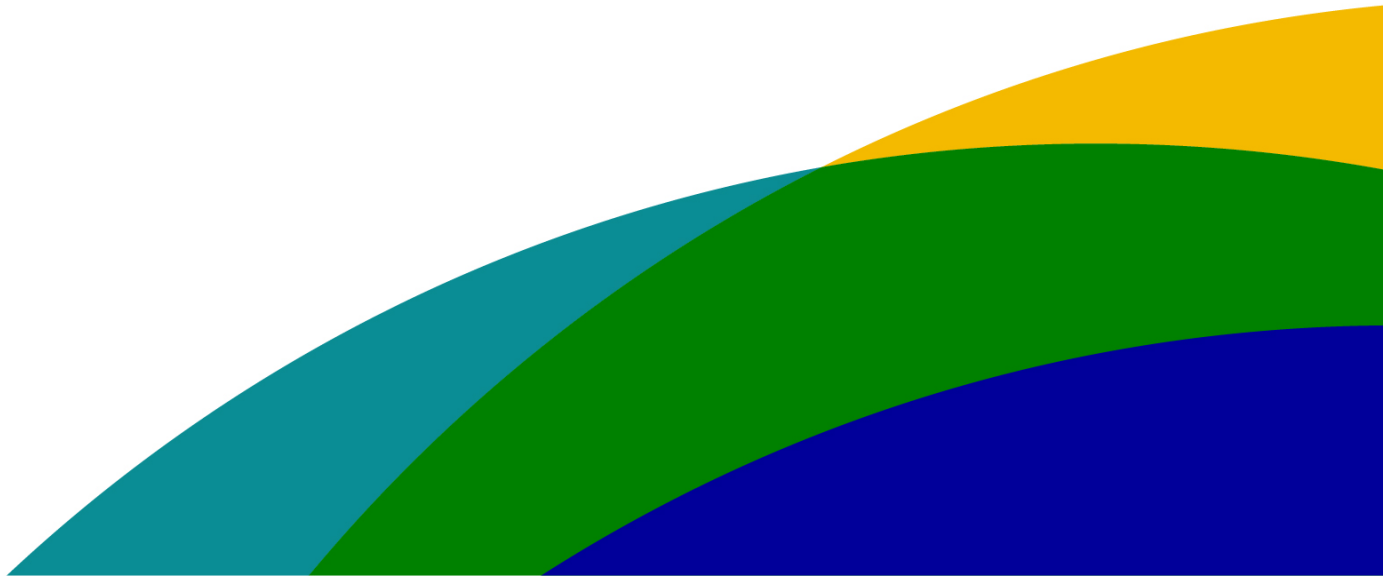
- The activities are **limited to those necessary to allow** a public health authority to identify, monitor, assess, or investigate **potential public health signals, onsets of disease outbreaks, or conditions of public health importance** (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products)...

Public Health Surveillance Exclusion: Example

If a public health authority authorizes general screening for COVID-19 for public health surveillance purposes, and requests that test results be shared as necessary to allow the public health authority to identify, monitor, assess or investigate the COVID-19 outbreak,

- an investigator may incorporate these activities into an existing research study visit without prior IRB review and approval

Tackling Special Challenges for Informed Consent During the COVID Pandemic



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Incapacitated Subjects

- Consider obtaining consent from the subject's legally authorized representative (LAR)
  - This is an individual … authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.
  - If there is no applicable law on LAR, this can be an individual **recognized by institutional policy** as acceptable for providing consent in the nonresearch context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research.

Consent Cannot Be Obtained in Person, Only Remotely

- Leverage the flexibilities available for studies that qualify for an exemption when applicable;
- Check if informed consent can be waived by meeting the conditions at §46.116(f)(3)(iii);
- Provide digital copy of consent form electronically, by phone, email, web link, or other methods. Make sure to include means for subjects to discuss the study.

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Consent Cannot Be Obtained in Person, Only Remotely (cont'd)

- Consider how to facilitate subjects signing and returning the form:
  - **Documentation (signing) can be waived** under §46.117(c)(1) if:
    - ✓ Consent form is the only document linking subject to research, and principal risk of harm results from a breach of confidentiality, **or**
    - ✓ Minimal risk research that only involves procedures that do not normally require written consent, **or**
    - ✓ Minimal risk research involving subjects who are members of a distinct community in which signing forms is not the norm, and an alternative mechanism for documentation is available
  - **Electronic signatures** (e.g. digital signatures, user name and password combinations, biometrics) **are permissible if** they are legally valid within the jurisdiction where the research is conducted (§46.117(a)). Check state & local laws

Don’t Forget …

- Whether consent is obtained in person or remotely, subjects or LAR must have sufficient opportunity to discuss and consider whether or not to participate in the research
- Unless waived, subjects or LAR must be provided with a copy (paper or electronic) of the consent document (with or without their signatures)

IRB Reviews for Changes to Studies

- Investigators may **submit** any proposed changes to previously approved research to the IRB **at any time**
- The IRB may use an **expedited review** procedure to review and approve those changes **if the changes are minor**
- Investigators may implement changes to approved research prior to IRB review and approval, if the changes are **necessary to eliminate apparent immediate hazards to the subject**

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Convened Full Board IRB Reviews

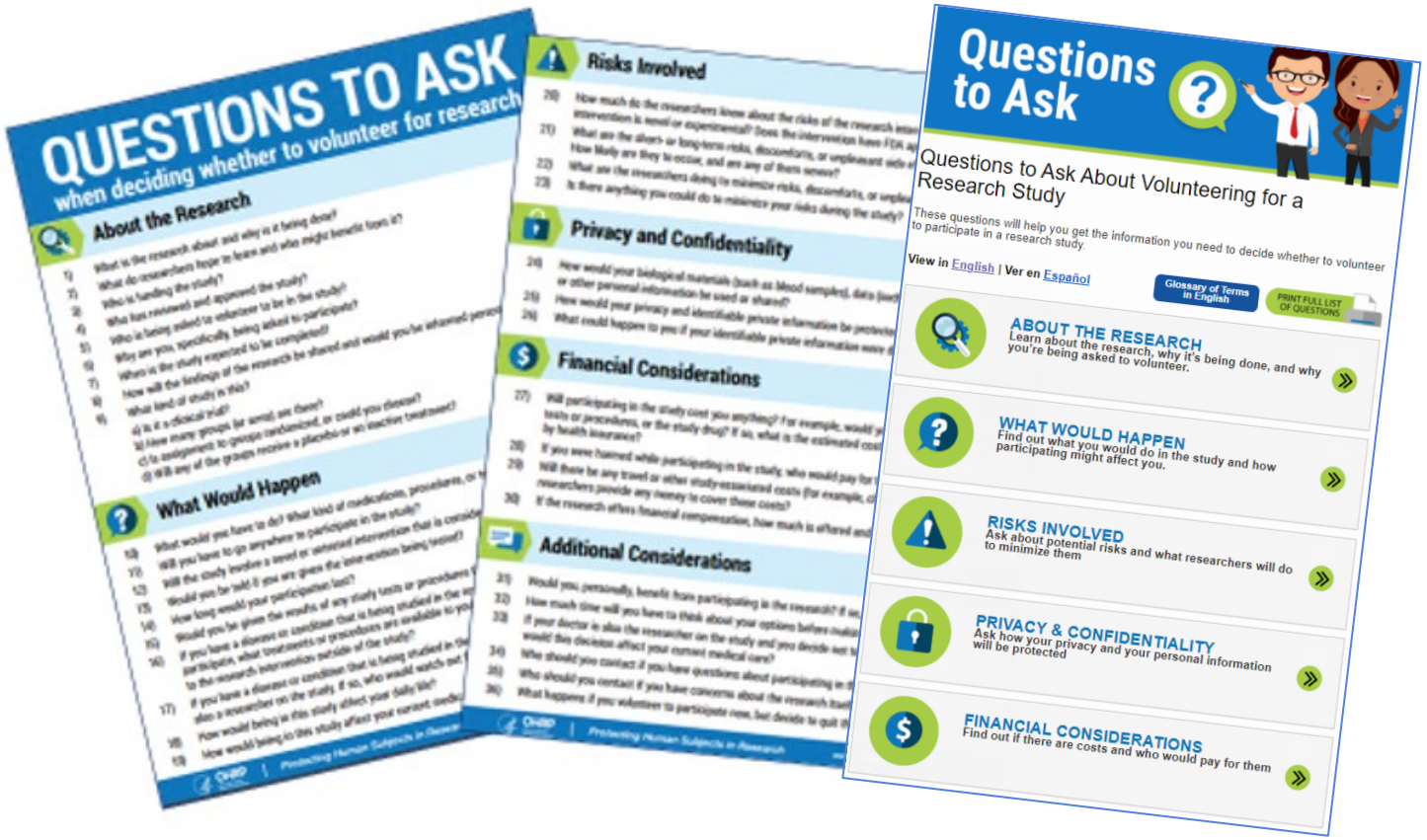
- Format of convened meetings
  - No requirement for in-person meetings. Can be done virtually, by phone or online.
    - ✓ Must ensure that quorum is maintained throughout. Quorum could be lost if members attending meeting become temporarily unavailable because of connection issues
- Eliminate the need for continuing reviews when:
  - Research can be approved by expedited review, **or**
  - Research has completed interventions and only involves:
    - ✓ Analyzing data, including analyzing identifiable private information or identifiable biospecimens
    - ✓ Accessing follow-up clinical data from clinical care procedures

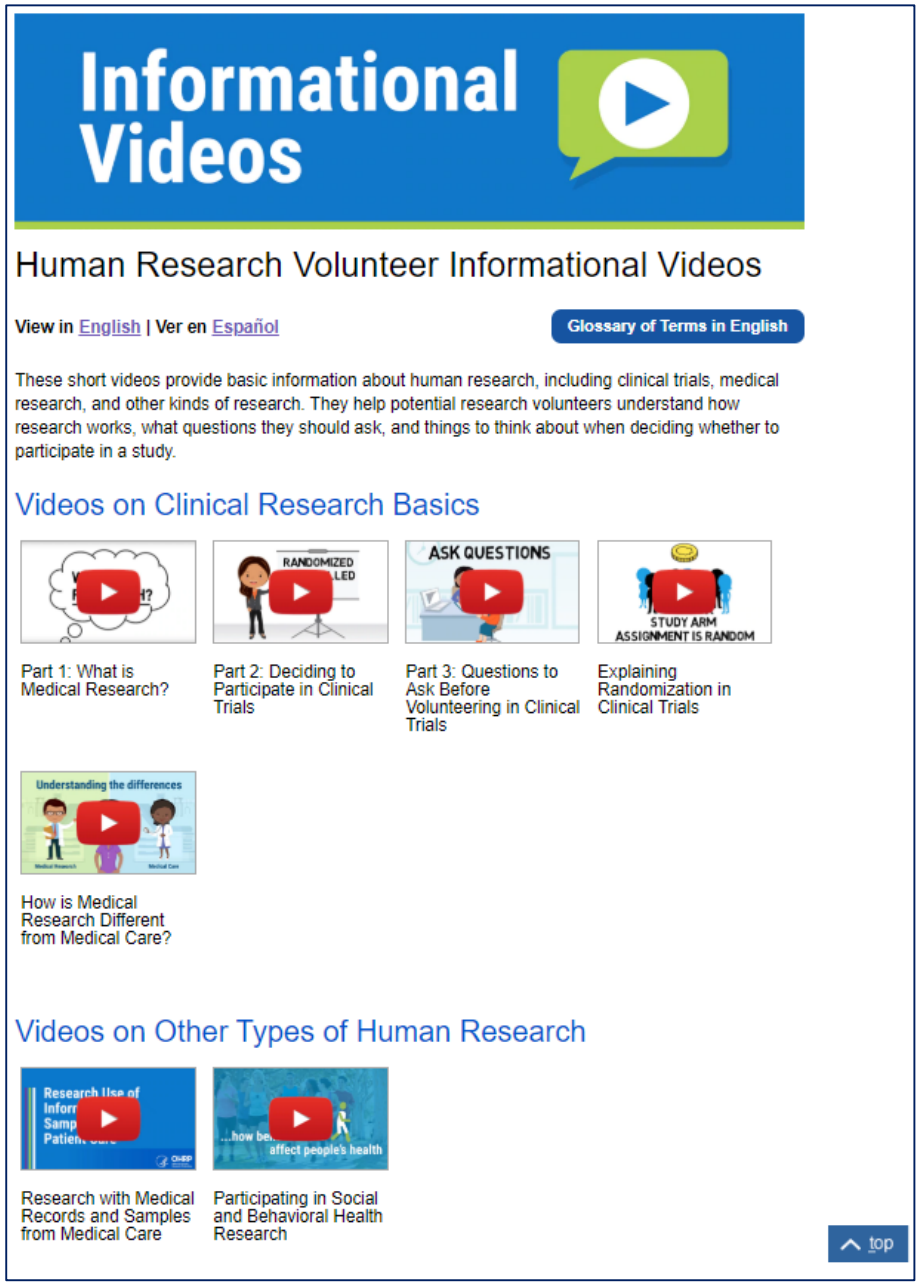
OHRP PUBLIC OUTREACH RESOURCES

www.hhs.gov/About-Research-Participation

Educate prospective participants!

Resources also in Spanish!





Contacts and Resources

- Contact us or submit your questions to OHRP@hhs.gov
- Visit OHRP website at www.hhs.gov/ohrp
- Review joint guidance between OHRP and FDA on Use of Electronic Informed Consent: Questions and Answers (2016)
- OHRP Resources for COVID-19 at https://www.hhs.gov/ohrp/education-and-outreach/online-education/hot-topics/index.html

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Please refer to the text of the revised Common Rule available on OHRP's website for a complete and accurate description of the regulatory requirements