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What Do You Do with Your Clinical Outcome Assessments (COAs) in a Pandemic?

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Conflict of Interest and Disclosures

- **Jason Randall** and **Tara Symonds** are employees of **Clinical Outcomes Solutions (COS)**
- **Selena Daniels** is an employee of the **Food and Drug Administration**
- **Elizabeth (Nicki) Bush** is an employee and shareholder of **Eli Lilly and Company**

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What Do You Do with Your Clinical Outcome Assessments (COAs) in a Pandemic?

Instructors

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Tara Symonds, PhD

ISPOR Workshop
17th May 2021

Purpose

- Goal: to discuss ideas and best practices regarding Clinical Outcome Assessment (COA) development, validation, and implementation in a clinical trial during a pandemic

What is a COA?

- There are different types of COA measures:
  - Patient-reported outcomes (PRO)
  - Clinician-reported outcomes (ClinRO)
  - Observer-reported outcomes (ObsRO)
  - Performance outcomes (PerfO)

What Do You Do with Your Clinical Outcome Assessments (COAs) in a Pandemic? Regulatory Perspective

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17th May 2021

Disclaimer

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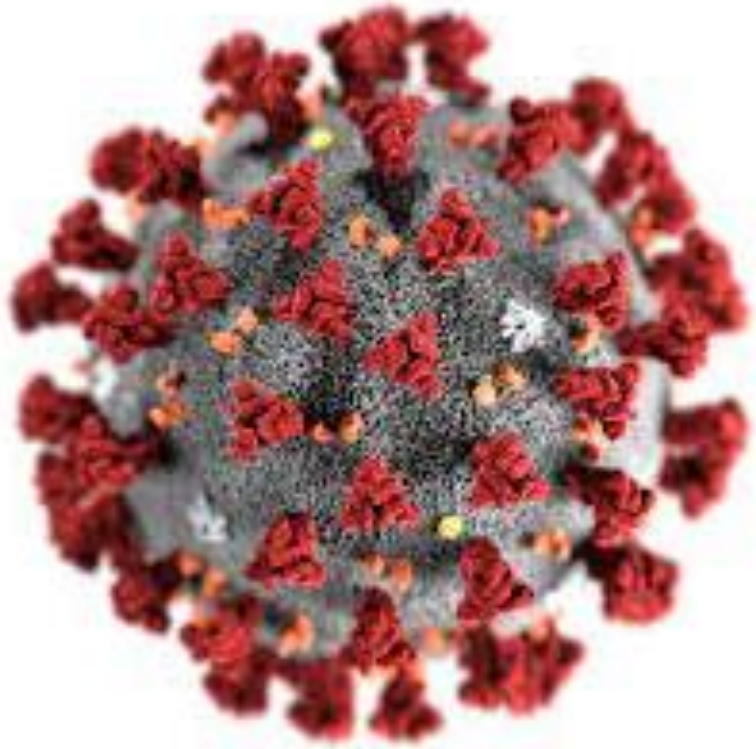
Challenges of COVID-19 Pandemic to Clinical Trials

Social distancing and quarantine→

- Study participants' inaccessibility
  - —Lack of in-person data collection



Contains Nonbinding Recommendations

Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency

Guidance for Industry, Investigators, and Institutional Review Boards

March 2020

Updated on January 27, 2021

General Considerations for Use of Remote COAs

Increased variability in data

Feasibility of the Assessment Method Within the Context of Use

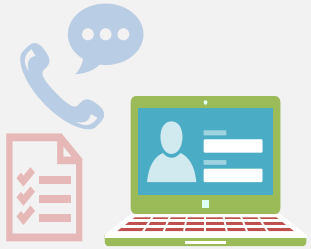
Documentation and Audit trails

Availability of technology and technical support

Specific Considerations for use of remote COAs:

Patient-reported and Observer-reported outcomes

Potential for missing data



Potential for bias of scores when switching modes of administration

Verbal administration is not a substitute for safety monitoring

Specific Considerations for use of remote COAs:

Performance and Interview-based Clinician-reported outcomes

- Appropriateness of remote assessment
- Special investigator training for assessment administration
- Adequate procedures for assessing and confirming the safety of trial participants, their privacy, and appropriate setting and resources

Other Considerations:

COA Measurement Strategy

Summary

Trial participant safety is priority

Determine whether endpoint is measurable during pandemic

Select an appropriate and feasible assessment method

Provide adequate training and support for remote assessments

Polling Question

What is the priority when conducting clinical trials during the COVID-19 pandemic?

a) Selecting measurable endpoints

b) Trial participant safety

c) Using appropriate remote assessments

What Do You Do with Your Clinical Outcome Assessments (COAs) in a Pandemic? Considerations from a Qualitative and Developmental Perspective

Jason A Randall PhD

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17th May 2021

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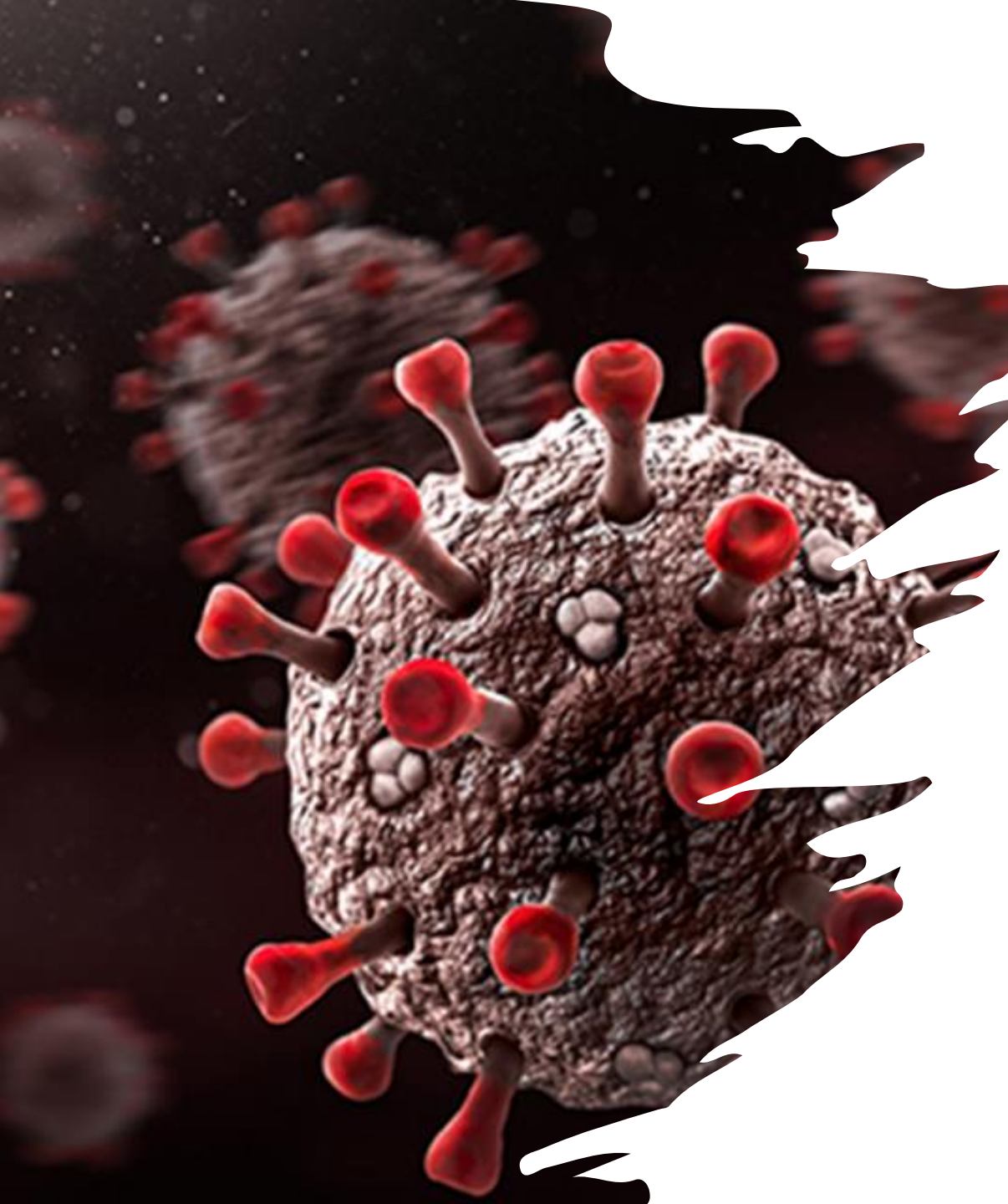


The Impact of COVID 19

- COVID-19 restrictions have prevention of in-person data collection,
  - A key part of COA measure development and administration.
- Some COA measures may be administered virtually with little modification.
- Other ClinRO and PerfO measures may be more difficult to administer remotely.

Typical Qualitative Process for COA measure development

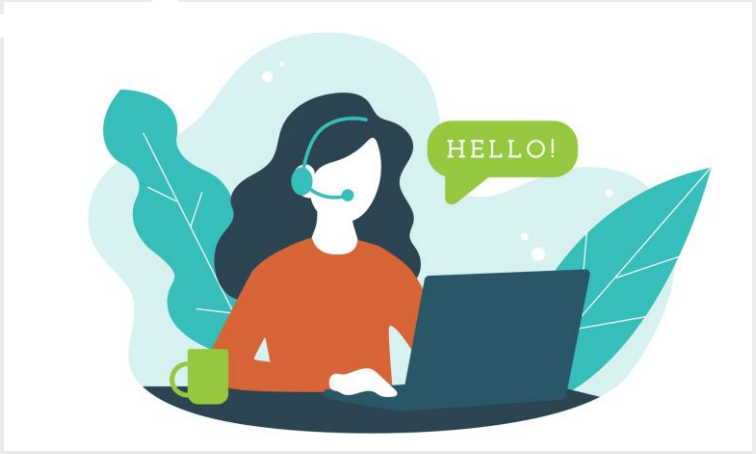
- Development and validation of a COA measure typically involves a qualitative component.

- Face-to-face interviews have typically been seen as the gold standard of interviewing.
  - This creates a problem in a global pandemic when face-to-face interactions are minimized or not possible.

What Can be Done?

- Interviews can be moved to other platforms such as:
  - Telephone (direct or virtual services), video calls, and other online platforms

- However, other factors need to be considered when altering the platform:
  - Patient demographics
  - Access to devices
  - Cognitive ability
  - Type of interview



Data collection: Moving from Face-to-Face to Virtual Administration

- Most COA measures are developed for face-to-face data collection which is not ideal in a pandemic.
  - Also, can lead to change in how the measure is administered from one visit to the next
- Some COA measures may be administered virtually with little modification.
  - PRO and ObsRO measures can often be moved to electronic administration with only minor changes.
- ClinRO and PerfO measures may be more difficult to administer remotely.
  - These might involve a patient activity or clinician assessments.
  - More consideration is needed for these COA measures.

Changing the Mode of Administration When a Trial is On-Going

It is not as easy as just changing the mode of administration

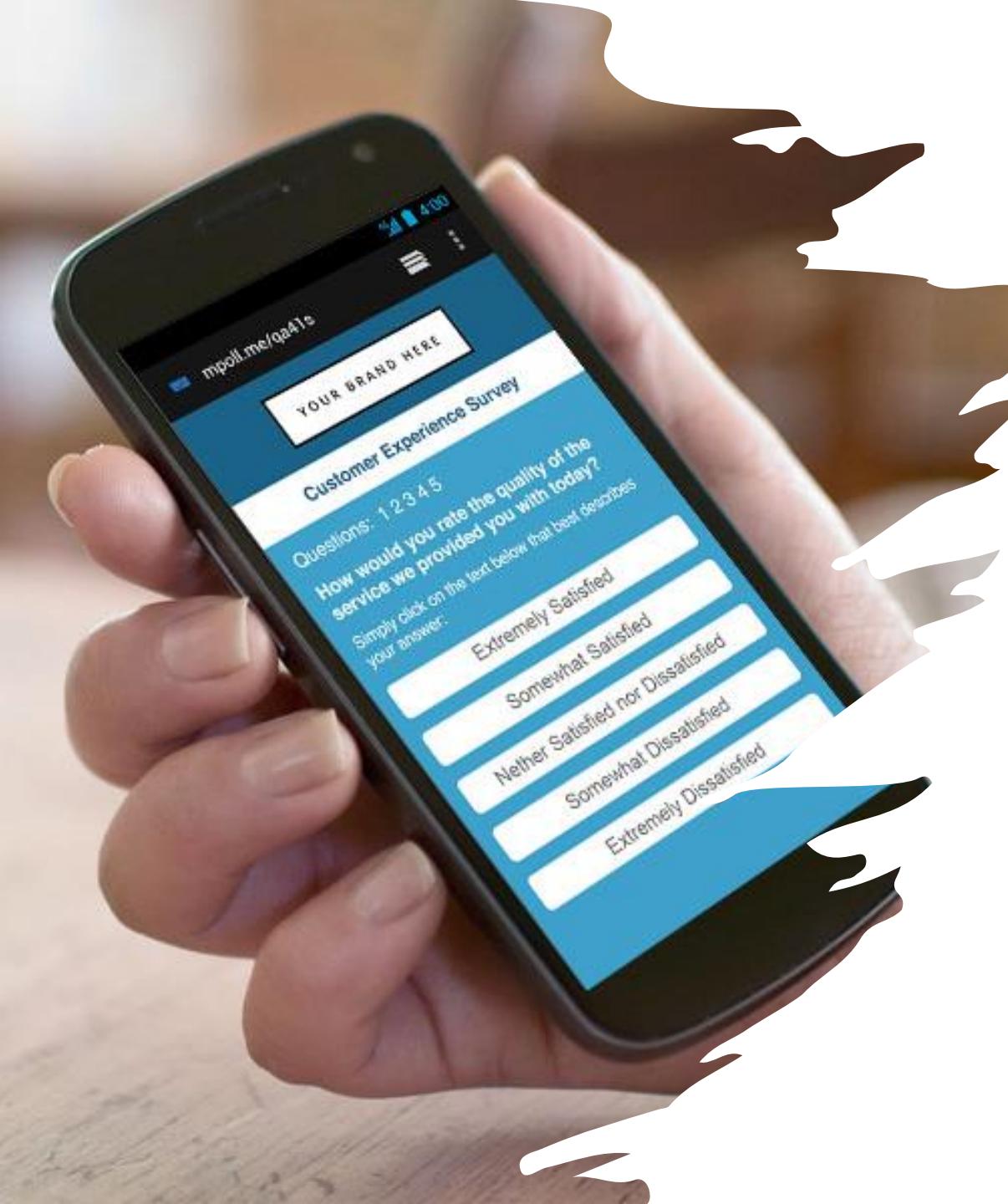
Changing the administration method has implications which need to be addressed:

- Is the new mode of administration suitable and appropriate for the COA and measurement objectives.
- Do we need to consider any other factors such as response and scoring options
- Is there equivalence between the different modes of administration?

Polling question

After changing the mode of administration for a COA measure, when would you consider exploring equivalence in your studies?

A. For all COA measures when the mode of administration is changed.
B. Only for PRO and ObsRO measures.
C. Only for PerfO and ClinRO measures.
D. Only if there is a substantial change in the COA (i.e., not pen and paper to electronic).



Confirming Equivalence

- When changing mode of administration confirming equivalence is a key part for ClinRO/PerfO.
  - Is data collected virtually the same as face-to-face?

How can I confirm Equivalence

- Equivalence should be explored either in a stand alone study or by leveraging clinical trial data
- If stand alone:
  - Utilise patients with the condition of interest
  - Patients should complete/be scored using the COA measure as originally intended and then again using the new mode of administration.
  - A suitable time should have passed between ratings to minimise learning effects but short enough that the patient remains stable.
    - 2 weeks may be a suitable time frame depending on the measure and population
- Correlations between assessments should be explored, typically using intraclass correlation coefficient (ICC).
  - ICC scores above 0.7 demonstrate a good correlation that would demonstrate equivalence.

How do you explore the impact of a Pandemic on clinical trial data ?

- Exit interviews can be a great way to talk to patients about how the pandemic impacted their experience of a clinical trial.

- This can help provide meaningful patient data to explore/support clinical trial findings.

Closing Remarks

Virtual interviews should be considered when appropriate for development and validation of COA measures.

Moving ClinRO/PerfO measure from face-to-face to virtual data collection, requires equivalence testing.

Consider using exit interviews to explore the impact of the pandemic on their data and experiences.

Considerations from a Clinical trial Perspective

Elizabeth (Nicki) Bush, MHS
Senior Advisor and Head, Patient-Focused Outcomes Center of Expertise
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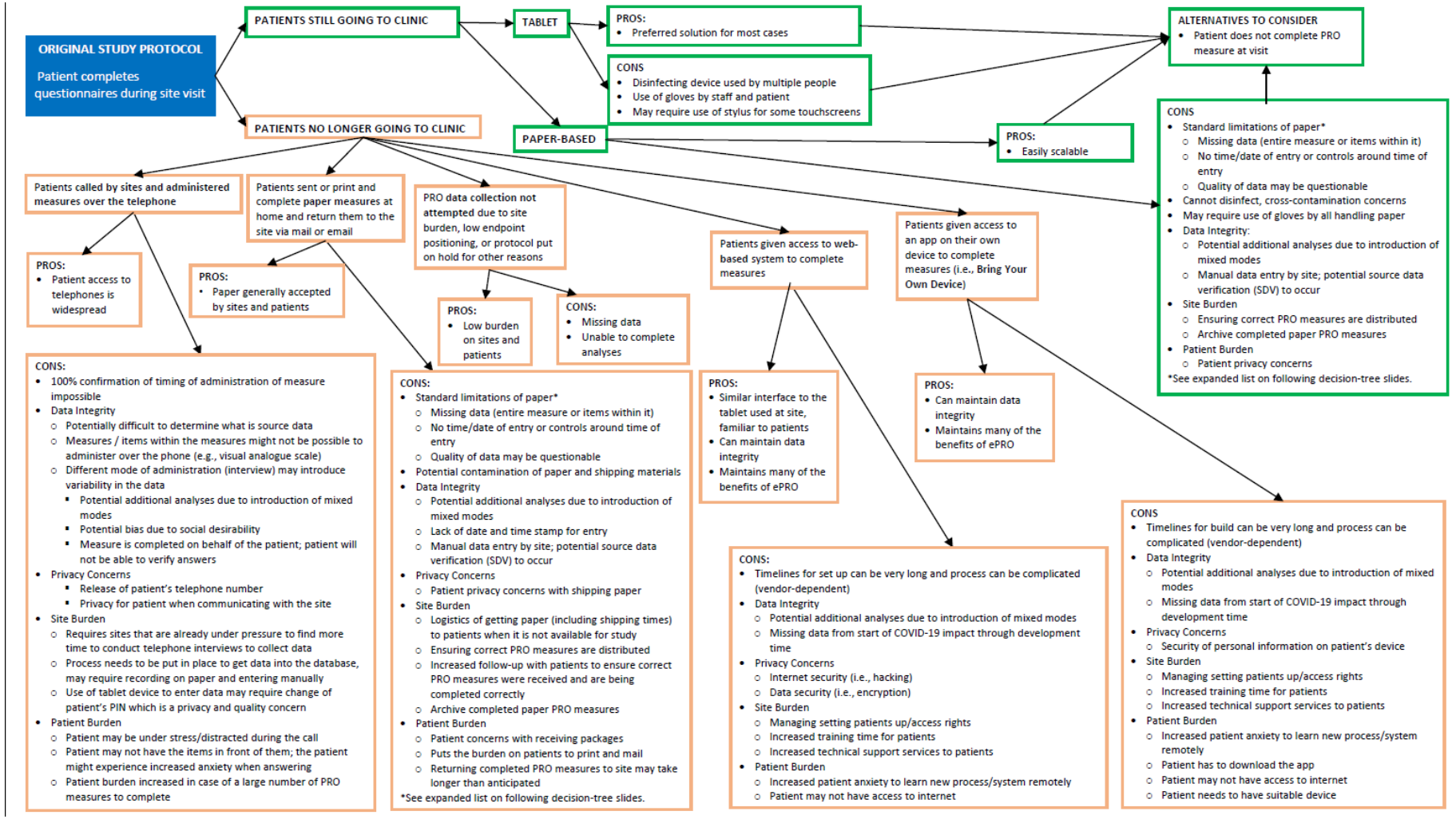
Mitigation – Data Collection

- Considerations
  - Safety
  - Burden
  - Data Integrity and Quality
  - Documentation
- Prioritization
- Consistency

Risk Assessment and Mitigation Strategies – PRO and ePRO Consortia



Source: https://c-path.org/wp-content/uploads/2020/06/COVID-19_CPath_v3.0_2020JUN5.pdf

Cross-functional Partnership

- Clinical Trial project management and operations
- eCOA implementation
- Copyright and Translations
- Statistics
- COA/Measurement

Design

- Recruitment methods
- Prioritize data needs
- Default to remote data collection

Data Analysis

- Intervention or Pandemic?
- Re-examine estimand attributes
- Pandemic-related intercurrent events
- Sensitivity, additional analyses

Resource: R. Daniel Meyer, Bohdana Ratitch, Marcel Wolbers, Olga Marchenko, Hui Quan, Daniel Li, Christine Fletcher, Xin Li, David Wright, Yue Shentu, Stefan Englert, Wei Shen, Jyotirmoy Dey, Thomas Liu, Ming Zhou, Norman Bohidar, Peng-Liang Zhao & Michael Hale (2020) Statistical Issues and Recommendations for Clinical Trials Conducted During the COVID-19 Pandemic, Statistics in Biopharmaceutical Research, 12:4, 399-411, DOI: 10.1080/19466315.2020.1779122

Thank you for listening. Any questions?

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