ePRO CONSORTIUM
CRITICAL PATH INSTITUTE

Webinar Series

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Best Practices for Avoiding Paper Backup When Implementing Electronic Approaches to Patient-Reported Outcome Data Collection in Clinical Trials

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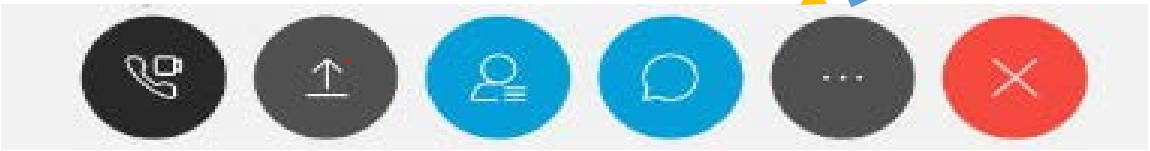

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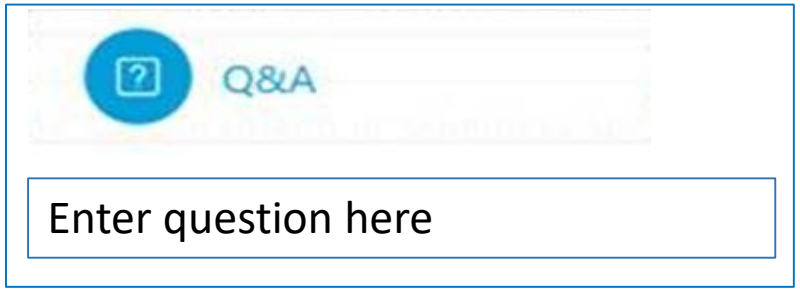

Q&A Feature

Q&A

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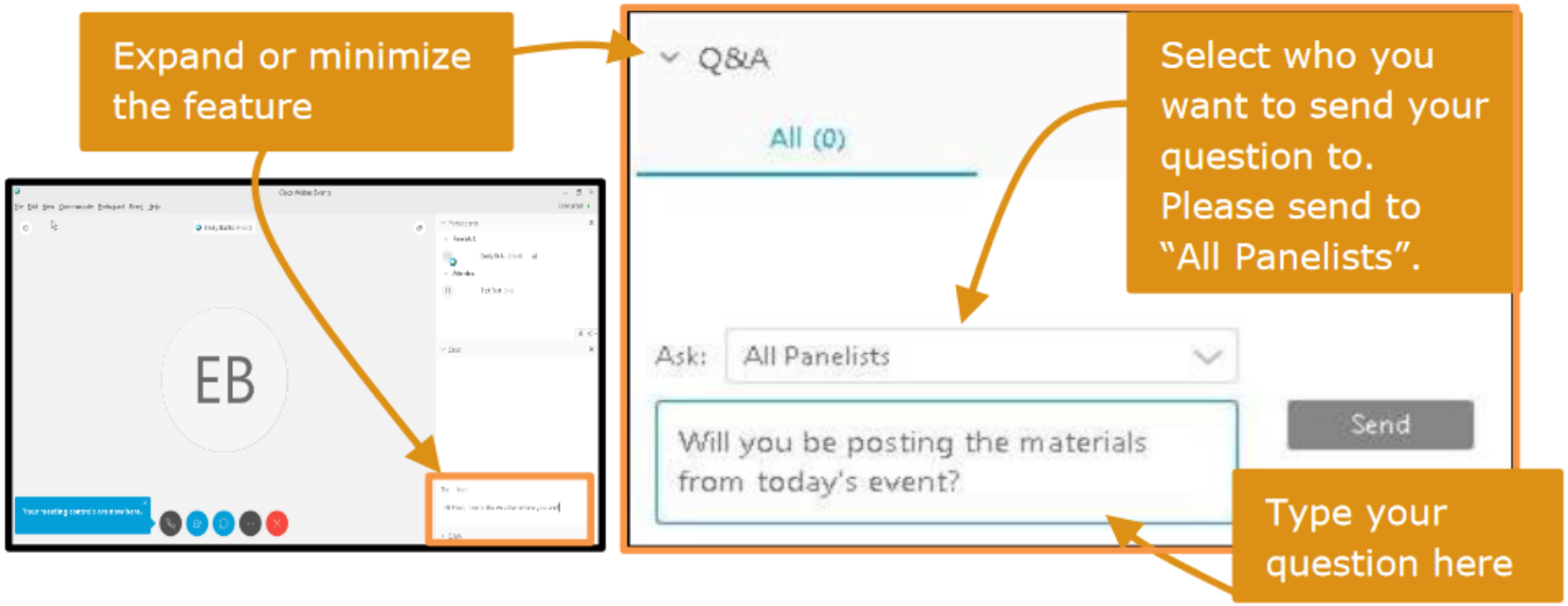

Biographies

Celeste Elash: Celeste A. Elash, MS, is the Director of eCOA Sciences for YPrime. Throughout her 25-year industry career, Celeste has served as a clinical research scientist, with a variety of contributions for the advancement of patient-focused drug development and eCOA adoption. Prior to joining YPrime, Celeste served as an independent consultant to biopharmaceutical companies and clinical science advisor for two eCOA providers. She has also done clinical research for Purdue University, The University of Pittsburgh and Western Psychiatric Institute and Clinic. Her experience spans more than 150 domestic and global clinical trials, academic research projects, and qualitative research projects.

Cindy Howry: Cindy Howry, MS, is CEO of .assisTek, an eSource company providing solutions used to collect data, electronically, from patients and clinicians in clinical trials and disease management. Ms. Howry has more than 35 years of experience in management and leadership, including 18 years in the eCOA/ePRO industry. Previously, she served three years as Industry Vice-Director for the ePRO Consortium. She has been instrumental in developing solutions for implementing electronic clinical outcome assessments in clinical trials while providing recommendations and best practices for designing new strategies and solutions.

Paul O'Donohoe: Paul O'Donohoe, MSc, is Scientific Lead, eCOA and Mobile Health at Medidata Solutions, a clinical software platform provider. He is responsible for developing the company's scientific expertise for electronic clinical outcome assessments and mobile health in clinical trials, and supports internal teams and Sponsors around the implementation of industry and regulatory best practices in studies using eCOA. He is passionate about developing the field of mobile health through research and active involvement in industry consortia, and is currently the Industry Vice-Director of the ePRO Consortium.

About Critical Path Institute

- Established in 2005 by the University of Arizona and the U.S. Food and Drug Administration (FDA)
- An independent, non-profit organization
  - Dedicated to implementing FDA's Critical Path Initiative
  - Enables pre-competitive collaboration that includes regulatory input/expertise
- Critical Path Institute is supported, in part, by Critical Path Public-Private Partnerships Grant Number U18 FD005320 (effective 2015-2020) from FDA.
- Support for the ePRO Consortium comes from membership fees paid by members of the ePRO Consortium (https://c-path.org/programs/epro/).

ePRO Consortium

- The Electronic Patient-Reported Outcome (ePRO) Consortium was established by the Critical Path Institute (C-Path) in 2010. Along with C-Path, the members of the ePRO Consortium are firms that provide electronic data collection technologies and services for capturing patient-reported outcome (PRO) and other clinical outcome assessment (COA) data in clinical trials.

- The mission of the ePRO Consortium is to advance the science of clinical trial endpoint assessment by collaboratively supporting and conducting research, designing and delivering educational opportunities, and developing and disseminating best practice recommendations for electronic collection of clinical outcome data.

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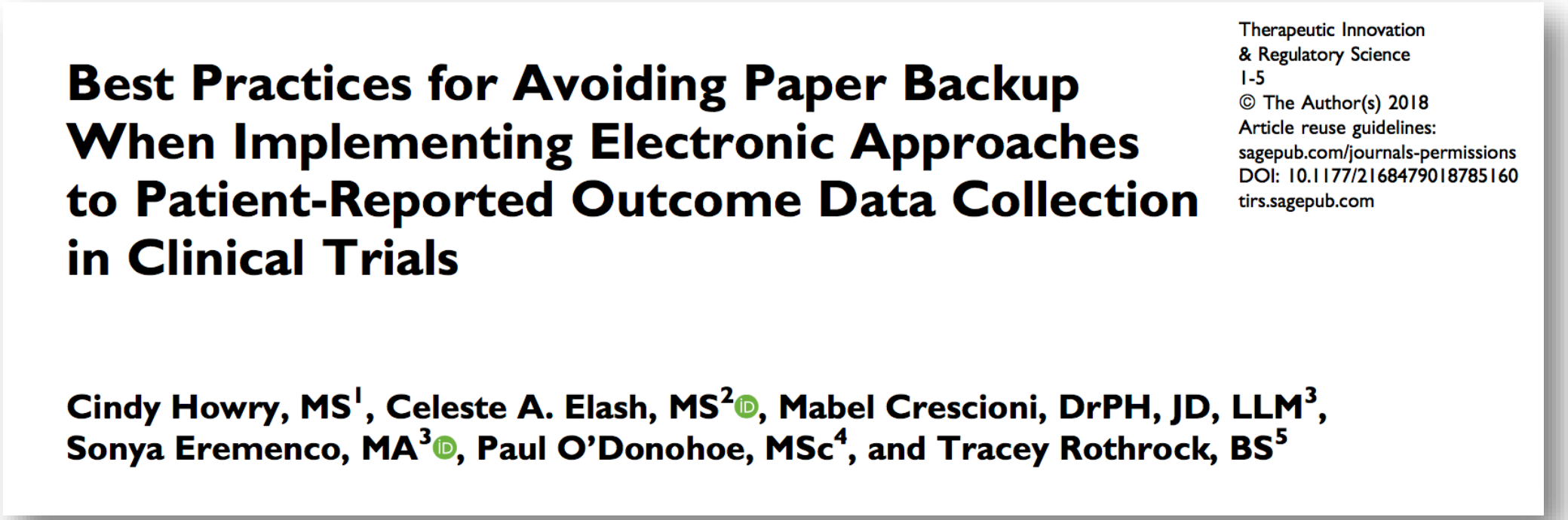

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Best Practices for Avoiding Paper Backup When Implementing Electronic Approaches to Patient-Reported Outcome Data Collection in Clinical Trials

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https://www.ncbi.nlm.nih.gov/pubmed/30244593

Agenda

1. Introduction
2. Challenges to ePRO Data Collection
3. Alternatives to Paper Backup
4. Problems with Paper Backup
5. Conclusion

Introduction

- Electronic data collection is the new gold standard for capturing PRO data
- It can enhance data quality and accuracy of responses
- Regulators encourage its use instead of paper-based data collection

Industry Landscape

- Estimated $500M was spent on eCOA in clinical trials in 2018
- Approximately 1,000 - 1,500 studies used electronic collection for COA in 2018
- The annual growth rate is 16% - very high for technology sector
- Yet, less than 25% of clinical trials using COAs are capturing these data electronically
- The rapid growth has brought significant opportunities and challenges for us as an industry

Background: Electronic Collection of PRO Data

What is electronic data collection?

Using a computerized system to collect data electronically rather than on a paper-based format in a clinical trial.

- Provisioned device-based systems (e.g., handheld devices, smartphones, and/or tablets)
- Bring Your Own Device (BYOD) (e.g., smartphones, tablets)
- Web-based
- Interactive voice response systems (IVRS) and voice-driven solutions

Current Electronic Approaches

Provisioned device-based system:

- Subjects enter data on study-assigned devices
- Modes:
  - Smartphone – Android or iOS (Apple)
  - Tablet – Android or iOS (Apple)

BYOD (Bring Your Own Device) system:

- Subjects use their own personal smartphone or tablet to collect field-based PRO assessments, electronically
- Application is installed on subject's device

Web-based

- Subjects use web/internet to enter data for field- and site-based PRO assessments, electronically

IVRS (Interactive Voice Response System):

- Subjects use touch-tone keypad to provide response on telephone-based system

Data Collection Environments

Site-based

- Subject enters PRO data during a clinic visit with supervision by site staff
- Typically, data are collected on a mini-tablet or tablet device

Field-based

- Subject enters PRO data outside of the clinic environment
- Subjects uses the device to enter data at home, school, workplace or anywhere outside the clinic without clinic supervision

Benefits of ePRO Data Collection

- Allows for more accurate and complete data with an electronic audit trail with date- and time-stamping
- Improved protocol compliance
- Avoidance of secondary data entry errors
- Easier implementation of skip logic and branching in measurements
- Less missing or skipped data
- Real-time access to data
- Potential cost savings
- Regulatory acceptance
- Subject preference – Users, subjects and clinic staff, generally prefer electronic data collection to paper after using an electronic solution

Challenges to ePRO Data Collection

Provisioned Devices:

- Technology failures of device hardware/software
- Loss of device
- Damage to device
- Cellular or Wi-Fi network connection issues

Challenges to ePRO Data Collection - Continued

BYOD

- Dependent on user being able to access app store
- Potential for user to delete app
- Potential for user to turn off notifications and reminders
- Dependent on active Wi-Fi or internet connection during setup and transmission of data
- Potential for user to lose app among all the apps already on the device
- Loss or damage of device
- Potential distraction when using other apps on phone

Resistance to ePRO Data Collection

There can be resistance to the use of ePRO systems in clinical trials from the following stakeholders for a number of reasons:

- Sponsors
- Sites
- Subjects

Resistance to ePRO Data Collection

Sponsors

- Can be driven by a previous negative history – hardware, software, operational issues
- Key challenges to the success of eCOA studies have been identified and a new initiative led by C-Path is under way to address them
  - Misalignment of expectations
  - Clear identification of critical issues vs. concerns
  - Better collaboration between eCOA providers, contract research organizations (CROs), and sponsors is essential
  - Using technology is never guaranteed to be error free

Resistance to ePRO Data Collection

Sites

- Absolutely vital for the success of the study to have site staff buy-in to the electronic solution
  - Sites negatively disposed to technology can pass this feeling onto subjects
- Resistance can be driven by a previous negative experience with technology
- There can also be a perception of additional burden having to use electronic systems
  - Have to recognise that there is some merit to this and provide appropriate support
  - Training, both before the study and available throughout, is key
  - Technical support (e.g., helpdesk) should be provided as standard
  - Ensuring minimum technical requirements are assessed during feasibility, e.g., internet connection to which external devices can connect

Resistance to ePRO Data Collection

Subjects

- May be worried about using a device for something perceived to be so important for a significant period of time
  - May be worried they "won't be able to do it"
- Perception of burden – however goes beyond technology to the study design
- If the technology doesn't work well, there will be obvious push-back
- Populations often thought to be resistant to new technology (e.g., older adults or the technology-naive) generally prefer electronic data collection to paper after using it
  - Systems need to be as simple and user-friendly as possible
  - Training, both before the study and available throughout, key
  - Customer support should be available 24/7 for subjects, parents, and caregivers when completing PRO measures outside of the clinic (field-based)

Addressing Challenges to ePRO Data Collection

- Resistance from sites and subjects can be overcome with training and experience with electronic data collection
- Sponsors still need to be prepared to address technology and user error challenges that prevent sites and subjects from entering data per protocol
- Possible options
  - Wait until new device becomes available to continue entering data
  - Consider other backup solutions
    - Feedback from regulators encouraging paper backup solutions

Recommendation

Recommendation of ePRO Consortium that paper backups not be used in studies planning to collect PRO data electronically.

Recommendations

It is the recommendation of the Critical Path Institute's ePRO Consortium that paper backups not be used in studies planning to collect PRO data electronically, particularly not in clinical trials for registration purposes, given the significant drawbacks of paper-based data collection. Paper backups are also not ideal in the site-based setting due to the challenges of setting up a parallel data entry system and are best avoided in these settings as well.

Possible Alternatives to Paper Backups

1. Backup devices at site
2. Web- or app-based solutions to capture data in the interim
3. Telephone/IVRS to capture data in the interim

Backup Devices

- Site-based data collection - backup device per site
- Field-based data collection - subjects instructed to contact their site or the helpdesk to troubleshoot
  - If issue persists, a replacement device should be shipped locally

- *Considerations:*
  - Increased hardware cost and risk of missing data
  - Reduced cost compared to alternative backup systems

Web- or App-based Solutions

- A version of the instrument accessible via a browser or app installed on the sites' or subjects' own device
- Reduces risk of missing data while replacement device is being delivered

- *Considerations:*
  - Requires suitable device (increasingly not an issue)
  - Additional cost to build the instruments on a website or app
  - Access rights need to be managed to ensure sites and subjects cannot access website or app before (or after) they have a justifiable reason to
  - Raises question of "mixed modes"

Telephone/IVRS solutions

- Telephone /IVRS solutions where sites and subjects can access audio versions of questionnaires and select a response on the telephone keypad

- *Considerations:*
  - Relatively low-cost, low friction way of capturing date and time-stamped data
  - Can only support certain type of relatively simple questionnaires
  - Raises question of “mixed modes,” might need to consider a quantitative or qualitative sub-study to ensure equivalence of the data

Problems with Paper Backups

1. Access to paper versions of PRO instruments
2. Challenges of reverting back to electronic data collection
3. Logistics and costs of dealing with paper in an electronic study
4. “Mixed modes”

Access to paper versions of PRO instruments

- Many instrument owners require separate licensing for paper and electronic versions of the instrument
- Just because one has a license for using an instrument electronically does not mean one has permission to use it on paper
- Official versions of paper instruments need to be provided to sites or subjects, either hardcopies or files for printing when needed
  - However, access should be controlled

Reverting Back to Electronic Data Collection

- If paper formats of instruments are made available, sites may be more likely to use them and reluctant to go back to electronic data collection
- Particularly a challenge at sites with a negative attitude toward the electronic system to begin with
- There needs to be a clear process for sites and subjects to raise technology issues so they can be remediated and/or a replacement device can be provided rather than reverting to paper

Logistics and Cost of Paper

- Paper-based data need to be entered into the study database
  - Requires a separate data entry system to be developed - increased cost
  - Requires additional site time for double data entry and reconciliation
- Data queries delay database lock
- Paper-based data are now “source” and need to be stored and Source Data Verified (SDV) as per regulations

Mixed Modes

- Data captured on different modes introduces an additional potential source of variance
- May need to explore equivalence quantitatively or qualitatively before the study kicks-off, or with a post hoc analysis once the data are collected
- “Spectrum” of concern – electronic to paper; country to individual
- Less of concern as the evidence for comparability across modes of data collection grow

Eremenco S, Coons SJ, Paty J, Coyne K, Bennett AV, McEntegart D, et al. PRO data collection in clinical trials using mixed modes: report of the ISPOR PRO mixed modes good research practices task force. Value Health. 2014;17:501–16.

Problem with Paper Backups - Conclusion

- Using paper backups obviously opens the door to all the risks paper introduces
  - Missing data
  - Out-of-range responses
  - Data not completed in a timely manner

- Need to balance “complete” data versus improved data quality

Backup Strategy

Technology will never be guaranteed to be issue free, but with appropriate planning the benefits far outweigh the possible risks

A Planned, Rather Than Ad Hoc, Approach to Alternate Options for ePRO Data Collection

Conclusion

- Realistically assess the risks to the data collection strategy for every study
  - Hardware and software can fail – however how likely is a failure?
- Balance “complete” data versus data quality – missing data may be easier to deal with than data you cannot trust
- Ensure the backup plan is absolutely clear to sites and patients and they have been trained on the process (e.g., requesting new devices)
- Training is absolutely key
  - Users that are comfortable with the electronic system will have fewer issues and will be less tempted to default to paper

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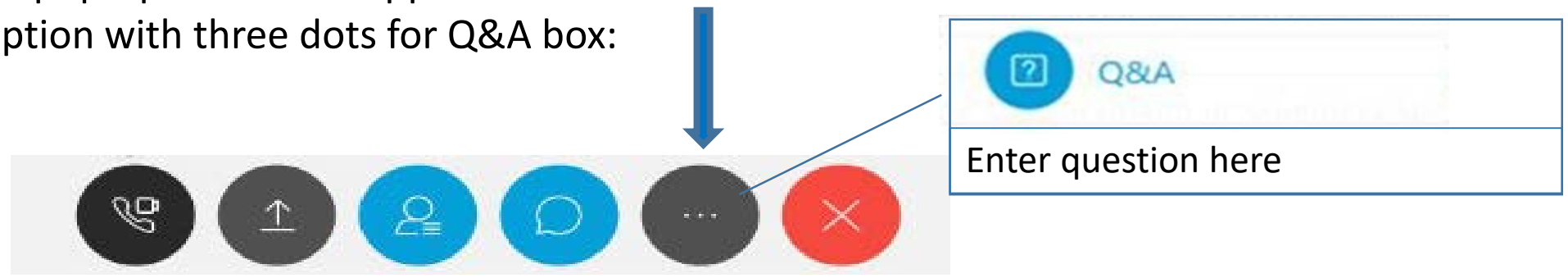

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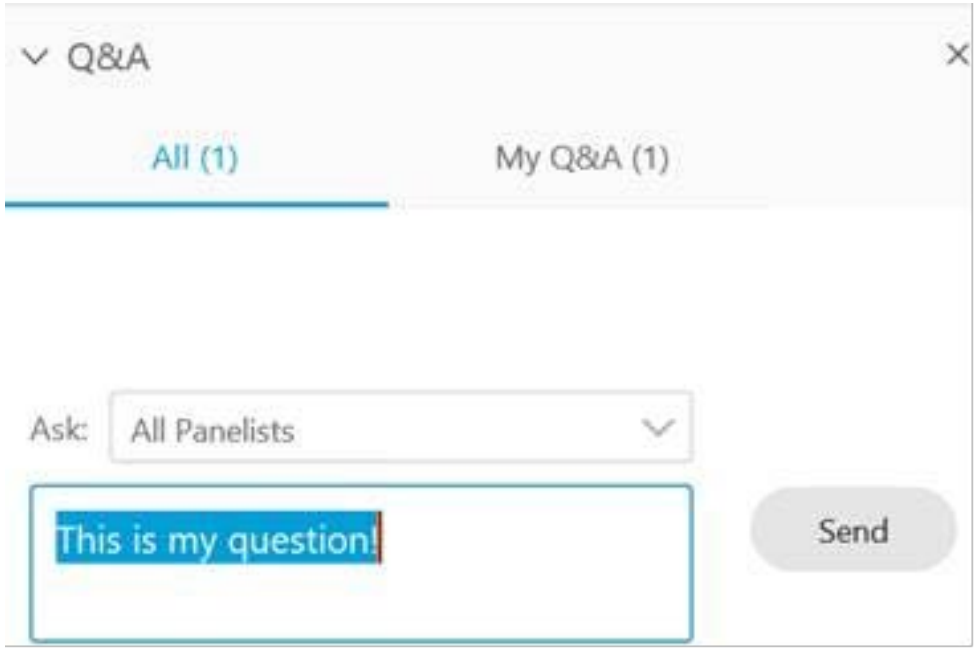

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