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Training on the Use of Technology to Collect Patient-Reported Outcome Data Electronically in Clinical Trials: Best Practice Recommendations from the ePRO Consortium

Moderated by: Susan Dallabrida
Presented by: Jenny Ly
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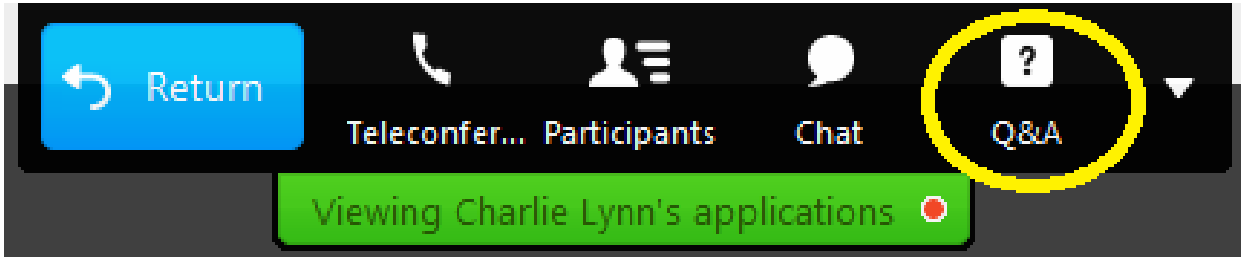

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Biographies

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Mr. **Serge Bodart** is currently Senior Adviser for Outcomes Science at BracketGlobal, a clinical trial technology and specialty services provider based in Wayne, PA. He is Bracket representative in the ePRO Consortium. He has been immersed in the ePRO industry for the past 18 years. With his associate, Dr. Pornel, Serge founded SYMFO, a European based ePRO provider. As the Co-founder and Chief Executive Officer of Symfo, Serge has been involved in all aspects of the eCOA life cycle from concept to commercialization. Prior to his ePRO career, he served as Major and helicopter pilot for over 20 years in the Belgian Army Aviation. Serge is currently based in Montreal, Canada and holds a master's degree of Science in Telecommunications from the Polytechnic Division of the Royal Military Academy in Brussels, Belgium.

Dr. **Jenny Ly** is currently a Clinical Science Advisor at ERT. She is a neuropsychologist with over 10 years of experience in the management and design of clinical trials. She has extensive experience developing training content for site staff, study participants, and caregivers that align with eCOA implementation and workflow for trials in a number of therapeutic areas including Alzheimer's disease, migraine, epilepsy, asthma, COPD, and IBS. She is experienced in cognitive debriefing, usability testing, and COA/eCOA instrument validation. She authored over 10 manuscripts and taught statistical methods courses. She obtained her Ph.D. in Clinical Psychology from The Graduate Center-City University of New York.

Dr. **Susan Dallabrida** is the eCOA Vice President of Clinical Science and Consulting at ERT. She has over 22 years of experience leading clinical research, trial design and strategy, and product development. She is expert in instrument development and psychometric validation and conceptual equivalence/ content validity studies for eCOA/COA. She interacts with regulatory agencies such as the FDA to support development and use of PRO's for labeling claims. She is expert in eCOA/COA design for clinical trials and optimizing data quality via incorporation of outcomes reliability training for site raters, subjects and caregivers, clinical data surveillance and clinical data validation. She earned a B.A. in Chemistry and a B.S. in Biology, both cum laude, from Bloomsburg University; and a Ph.D. in Biochemistry and Molecular Biology from Pennsylvania State University.

About Critical Path Institute (C-Path)

- 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

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.

Membership


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Upcoming publication of ePRO Consortium

Ly JJ, Crescioni M, Eremenco S, Bodart S, Donoso M, Butler AJ, Dallabrida SM. Training on the use of technology to collect patient-reported outcome data electronically in clinical trials: best practice recommendations from the ePRO Consortium. *Ther Innov Regul Sci*. Recommended for publication.

Agenda

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1. Introduction
2. Investigative Site Personnel Training
3. Participant Training
4. Conclusion

Introduction

Importance of electronic data capture in clinical trials

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- Different ePRO technology
  - Smartphones
  - Tablets
  - Interactive voice response (IVR) system
  - Internet/web-based system

- Evidence suggests ePRO is preferred by the majority of study participants
- Recommended by regulatory agencies

Elash et al. Value Health 2015; 18:A342
Ring et al. Patient 2008; 1: 105
Salaffi et al. Clin Exp Rheumatol 2009; 27: 459

Advantages of ePRO vs. paper

- Reduce missing data
- Time-stamped records
- Increase actual compliance
- Reduce site and participant burden
- Reduce data entry errors

Importance of training

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Regulatory guidelines on training

FDA
21 CFR Part 11

(i) Determination that persons who develop, maintain, or use electronic record/electronic signature systems have the education, training, and experience to perform their assigned tasks.

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09 June 2010
EMA/INS/GCP/454280/2010
GCP Inspectors Working Group (GCP IWG)

Reflection paper on expectations for electronic source data and data transcribed to electronic data collection tools in clinical trials

Studies on importance of training

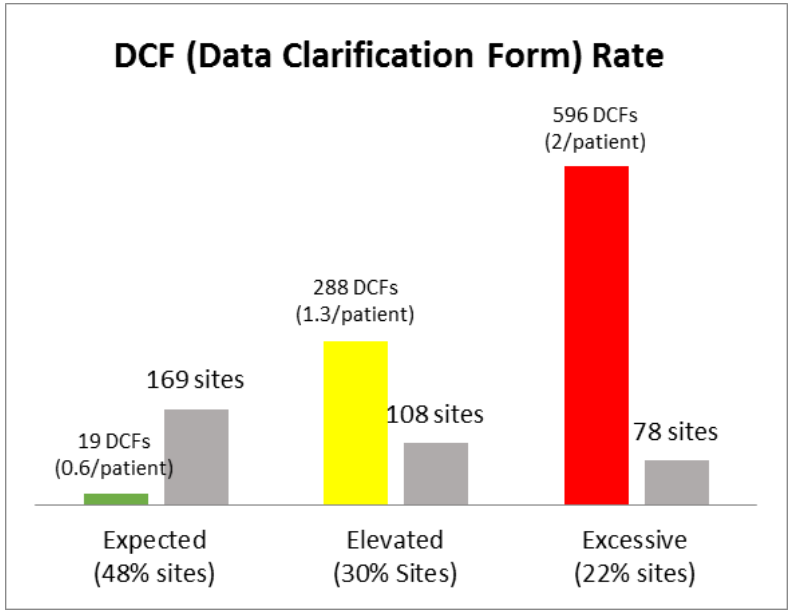
- Comprehensive and role-specific training for clinicians, staff, and patients using the ePRO system
- Staff train patients to use ePRO system

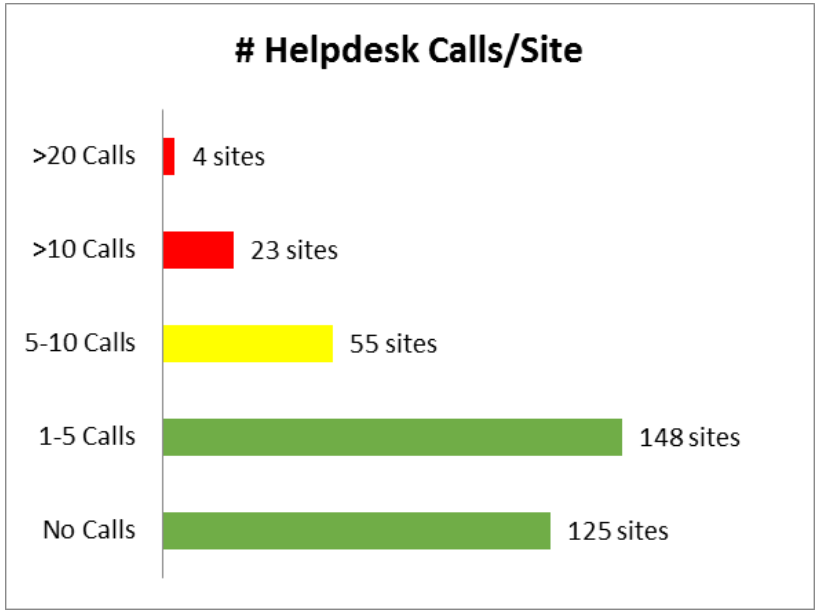
Bennet et al. CA Cancer J Clin 2012; 62:336

Case study

Phase III Program, 355 Sites, 18 months into 4-year study.

- Site Training was not well controlled, and many eLearning quizzes were never completed.
- 48% of sites had expected Data Clarification Form (DCF) rates; 77% had low helpdesk call volumes and were performing very well with the system.
- Problem sites were targeted for re-training.
- Lesson learned: timely, mandatory training requirements DURING LAUNCH to avoid this situation in future studies.





Objectives of webinar

- Recommend best practices for consistent and sufficient training of end users on ePRO devices and technology
  - Site staff
  - Study participants
- Promote training prior to initiating trial data collection
- Developed by consensus among members of Critical Path Institute's ePRO Consortium

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Investigative Site Personnel Training

Curriculum

1. Introduction to benefits of electronic data collection over paper
2. Study-specific training topics
3. Technology-specific training topics

Study-specific training topics

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- Study protocol assessment schedule
  - Assessment workflow
- PRO measure on technology system
  - Software structure and logic of ePRO implemented measures
  - Resolution of error messages
  - Integration of electronic systems (e.g., wearables)
- Participant compliance
  - Guidance to help participants understand importance of completing PRO measures on schedule
  - Regularly monitoring participant compliance

Technology-specific training topics

- Device and electronic system
  - Turning the device on and off
  - Charging the device
  - How to access the electronic system
  - Adding participants into the system
  - How to select responses in the system
- Data transmission troubleshooting
- Data and reports
  - Viewing and exporting data
  - Run reports on ePRO platform
  - Respond to alerts from ePRO platform
- Technical support

Training models

- Face-to-face Training
- Remote Training (Live Teleconference or Web Conference)
- Interactive Multimedia Electronic Training (on Device or via Web)

Best practices

Key learning principles

- Space training over time
- Combine graphics with verbal descriptions
- Administer quiz questions or knowledge checks
- Provide immediate feedback
- Optimal learning happens
  - Over time
  - Through repetition
  - Use of more than one delivery mode

Face-to-face training

- Delivery
  - Investigator's meetings (IMs)
  - Site initiation visits (SIVs)
  - Proxy training by clinical research associates (supplemental training)

- Recommendations
  - Conducted by subject matter experts
  - First exposure
  - Interactive element to increase engagement

- Things to consider
  - Cost
  - Retention of information
  - Site staff turnover

Remote Training

- Delivery
  - Live Teleconference
  - Web Conference

- Recommendations
  - Provide training devices or access to ePRO technology
  - Recorded to allow flexibility in schedule and review
  - Part of retaining process

- Things to consider
  - Difficulty troubleshooting problems
  - Not knowing if all trainees are engaged

Interactive Multimedia Training

- Delivery
  - Device
  - Web
- Recommendations
  - Use alone or in with other models
  - Didactic training with graphic and verbal description, software demonstration, troubleshoot instructions
  - Knowledge checks to engage trainees with immediate feedback
  - Self-paced, review info as needed
- Things to consider
  - Difficulty troubleshooting problems

Training materials

- Printed or PDF-style reference materials
  - Quick start guides
- eLearning or DVD copy of refresher training
- Training device or software emulator

Proficiency requirements

- Brief evaluation of understanding
- Competency or “passing” should be pre-defined
- Required minimum score defined on study-by-study basis
- Documentation and tracking of both training and competency exam

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Study Participant Training

Need for training

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- Participants are not or minimally familiar with:
  - Technology
  - Protocol
  - Patient-Reported Outcome Measures
  - Importance of compliance

- Keep participant engaged
- Reduce patient burden

Regulatory Requirements

- FDA PRO Guidance

Food and Drug Administration. Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. December 2009. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM193282.pdf. Accessed March 24, 2017.

2. Clinical Trial Quality Control

The quality of a clinical trial can be optimized at the design stage by specifying in the protocol procedures to minimize inconsistencies in trial conduct. We recommend a standardized order by which PRO and other clinical assessments are administered. Other examples of standardized instructions and processes that can appear in the protocol include:

- Training and instructions to patients for self-administered PRO instruments
- Interviewer training and interview format for PRO instruments administered in an interview format
- Instructions for the clinical investigators regarding patient supervision, timing and order of questionnaire administration during or outside the office visit, processes and rules for questionnaire review for completeness, and documentation of how and when data are filed, stored, and transmitted to or from the clinical trial site
- Plans for confirmation of the instrument's measurement properties using clinical trial data


Guidance for Industry
Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims

Regulatory Requirements

- FDA PRO Guidance

Food and Drug Administration. Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. December 2009. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM193282.pdf. Accessed March 24, 2017.

APPENDIX: INFORMATION ON A PRO INSTRUMENT REVIEWED BY THE FDA

The following topics represent areas that should be addressed in PRO documents provided to the FDA for review. The extent of background information provided in each section will vary depending upon the PRO instrument used. Some sections may be less relevant for a particular PRO instrument application than others, or may be less complete for discussions in early stages of medical product development. Refer to the content of this guidance for additional information concerning the types of evidence needed in each of the following areas.

If the PRO information is provided electronically, it should be placed in section 5.3.5.3 of the electronic common technical document.[11]

I. Instrument (review cannot begin without a copy of the proposed instrument):

A. Exact version of the instrument proposed or used in the clinical trial (protocol) under review and all instructions for use. Include screen shots or interviewer scripts, if relevant.

B. Prior versions, if relevant.

C. Instructions for use: An instrument user manual can be provided as Appendix A and referenced here.
1. Administration timing, method (e.g., paper or pencil, electronic), and mode (e.g., self-, clinician-, or interviewer-administered)
2. The scoring algorithm
3. Training method and materials used for questionnaire administration
   a. Patient training — summarize here and include a copy of all materials in Appendix A1
   b. Investigator training — summarize here and include a copy of all materials in Appendix A2
   c. Other training — summarize here and include a copy of all materials in Appendix A3

Regulatory Requirements

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- EMA Guideline (Oncology)

European Medicines Agency. The Use of Patient Reported Outcome (PRO) Measures in Oncology Studies: Appendix 2 to the Guideline on the Evaluation of Anticancer Medicinal Products in Man. November 2016. http://www.ema.europa.eu/docs/en_GB/document_library/Other/2016/04/WC500205159.pdf. Accessed March 24, 2017.

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- Education and training of patients before completion of the questionnaire, including that there is no incorrect answer and explaining the purpose of the assessment. If such education and training is

Regulatory Requirements

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- EMA Guideline (Asthma)

European Medicines Agency. Guideline on the Clinical Investigation of Medicinal Products for the Treatment of Asthma. May 2015. http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2015/12/WC500198877.pdf. Accessed March 24, 2017.

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Standardisation of clinical methodology is important. Patients should be adequately trained in respiratory function testing, inhaler technique, compliance and the use of patient diaries.

Regulatory Requirements

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- FDA Guidance (Ulcerative Colitis)

Food and Drug Administration. Ulcerative Colitis: Clinical Trial Endpoints Guidance for Industry. August 2016. https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM515143.pdf. Accessed March 24, 2017

FDA

Completion of Event Log or Diary*	• Patients should be trained on the completion of the event log or diary • The instructions for completion of the stool frequency and rectal bleeding assessments should be incorporated into the event log or diary for ready reference by the patient
Recording of Rectal Bleeding and Stool Frequency Assessments	• Patients should be directed to capture their rectal bleeding and stool frequency assessments in event logs or daily diaries* for 1 week before each visit

* Sponsors are encouraged to propose an electronic data collection method (e.g., voice response system, electronic diary, or Web-based system) as an alternative to pen and paper data collection. If an electronic data collection method is proposed, sponsors should provide instructions for training in electronic methods.

Training curriculum

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<u>Study-specific training topics</u>

- Patient-Reported Outcome Measure
  - Completion
  - Flow
- Use of rating scales (e.g. VAS, NRS)
- Navigation
- Error messages
- Study assessment schedule
- Participant responsibilities

Training curriculum

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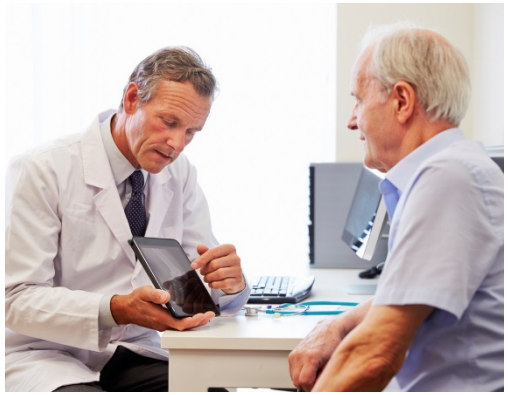
Technology-specific training topics

- Device specific aspects
  - On/Off
  - Charge device
  - Data transmission
  - Troubleshooting
- Security
  - Login procedure
  - Password protection
  - Attributability of data
  - Confidentiality
- Technical Support

Participant Training models

Individual training with site



Interactive multimedia electronic training

Participant Training models

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Individual training with site

- Individual hands-on
- At trial initiation
- Use of practice mode
- Duration: 15 minutes
- Site can answer questions in real time
- Use of checklist to reduce variability

Practice Mode

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Use of a practice mode

- Items similar in format and structure
- Representative screens or menus
- Rating scales

Participant Training models

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Interactive multimedia electronic training

- Multimedia training module
  - Web Link
  - App on device
  - DVD
- At trial initiation
- Duration: 5 to 10 minutes
- Knowledge checks possible
- Available at all times
- Less variability

Participant Training Materials

- Reference materials needed
- Quick start guide and/or Participant user guide
  - Basic Instructions on technology
  - Instructions on pairing medical devices
  - Schedule of assessments
  - Participant roles and responsibilities
  - Support/Help desk

Proficiency requirements

- Brief competency test is recommended
  - All patients should complete training
  - Brief competency exam
  - No ‘passing’ score unless if used for cognitive capability
  - Document training and exam
  - Implementation of gating system can be useful
  - Remediated passing score is an alternative

Support

- What if I have questions?
  - Patients should first refer to site personnel
  - Sites are also responsible for study-specific, measure-related questions
  - Sometimes tech support is available
    - 24/7
    - Participant language
  - Support needs to be documented

In Conclusion

Conclusion

- Regulatory Authorities encourage
  - use of ePRO systems
  - site staff training
  - study participant training

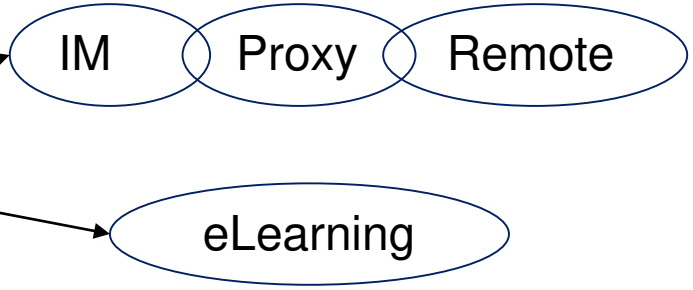
Conclusion

- Investigative Site Personnel Training Best Practices

Topics

- Benefits of electronic data collection
- Study specific topics (logic, schedule, etc.)
- Technology specific topics (set-up, use, repurposing devices, etc.)

Training models



Conclusion

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- Investigative Site Personnel Training Best Practices
  - Site staff need to complete training and competency exams
  - How to train patients (use checklist)
  - Hands-on training
  - Reference materials
  - Limit duration between site training and first patient in
  - Support

Conclusion

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- Participant training best practices

Curriculum

- Study specific topics (scales, navigation, schedule, etc.)
- Technology specific topics (login, passwords, data transmission, etc.)

Training models

- Individual training with site staff
- Interactive multimedia
- Hands-on
- Training/practice mode (with/without gating system)
- Reference materials
- Support

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Questions?

http://c-path.org/programs/epro

Upcoming publication of ePRO Consortium

Ly JJ, Crescioni M, Eremenco S, Bodart S, Donoso M, Butler AJ, Dallabrida SM. Training on the use of technology to collect patient-reported outcome data electronically in clinical trials: best practice recommendations from the ePRO Consortium. *Ther Innov Regul Sci*. Recommended for publication.

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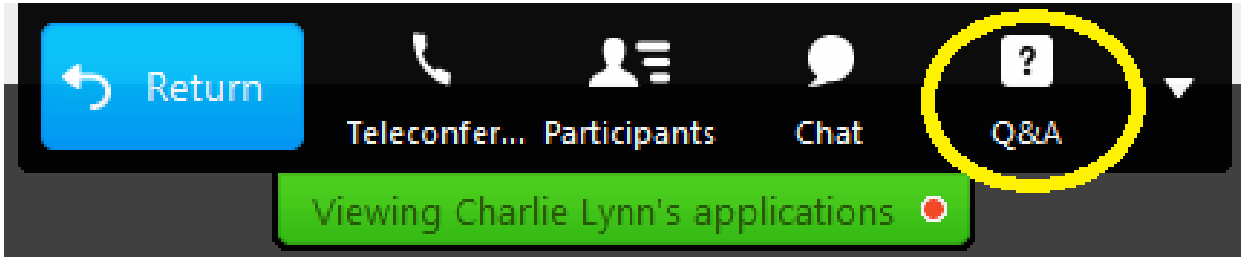

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