Intro to ePRO – Part II

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Objectives

- ✓ Recap: Intro to ePRO – Part I
- ✓ Describe current ePRO data collection modes
- ✓ Strengths and limitations of each ePRO mode
- ✓ Discuss the ePRO mode selection process
- ✓ Introduce key considerations for selecting the most appropriate mode for a study
- ✓ Overview of the considerations for migrating an existing PRO instrument to an electronic mode

ePRO Consortium

The Critical Path Institute established the ePRO Consortium on April 1, 2011

Mission: To advance the quality, practicality, and acceptability of electronic data capture (EDC) methods used in clinical trials for PRO endpoint assessment

ePRO Consortium Member Firms

Benefits of Collaboration

A coordinated approach to gathering evidence supporting the measurement equivalence of the various ePRO modes

Collective development of ePRO migration best practices

- Methodological guidance on ePRO implementation in clinical trials (e.g., mixing modes within a trial)
- Development of publicly available specification documents for migrating specific PRO instruments to available ePRO platforms

Definitions/Abbreviations

eCOAs – electronic Clinical Outcome Assessments

- ePRO - electronic Patient-Reported Outcomes
- eClinRO - electronic Clinician-Reported Outcomes
- eObsRO - electronic Observer-Reported Outcomes
- ePerfO - electronic Performance Outcomes

A patient-reported outcome (PRO) is any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else.[1]

A PRO instrument is used to measure ***treatment benefit*** or risk in medical product clinical trials.

[1] Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims, FDA, December 2009

Current ePRO Data Collection Modes

Voice, Web, Smartphone, Tablet/Laptop/PC, BYOD

Tablets (site-based)

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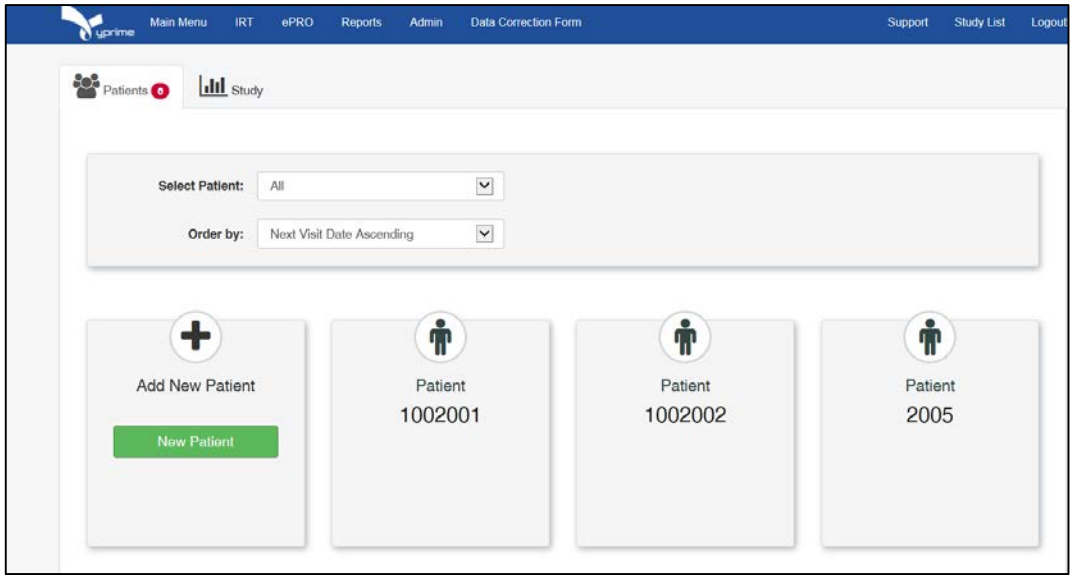
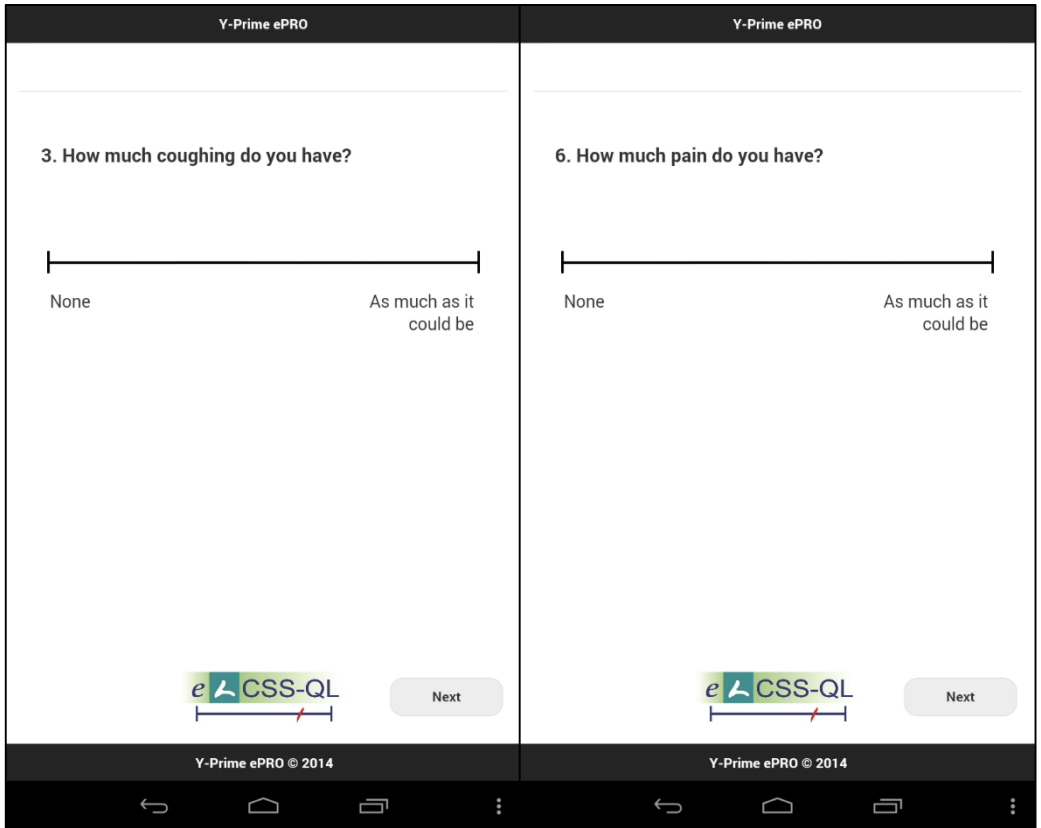
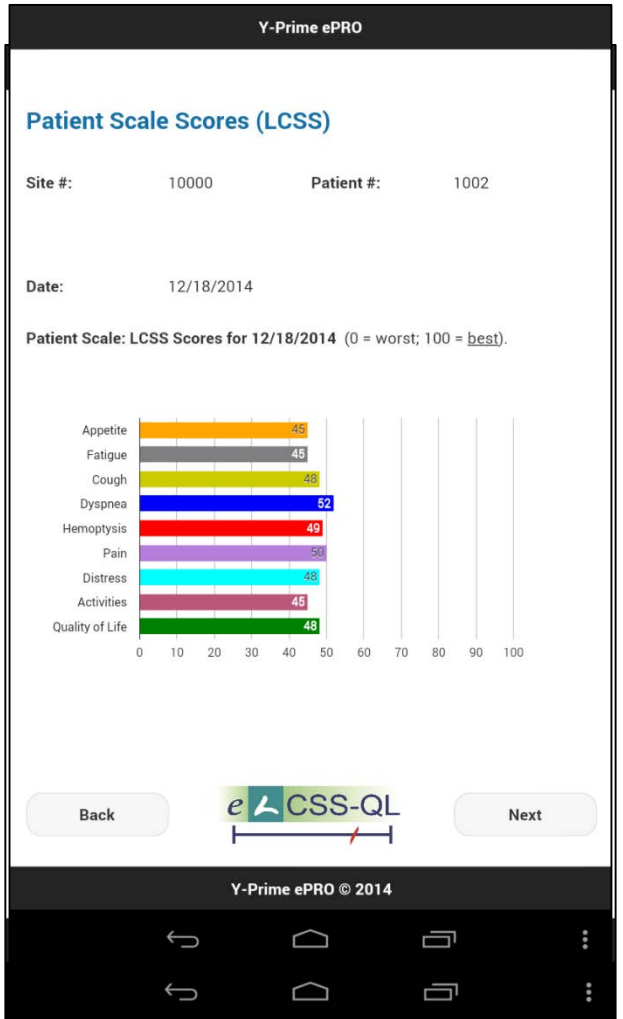
- Patients, doctors, and clinicians complete at site
- One device with multiple user
- Laptop or mini-tablet

Tablets (site-based)





Clinician



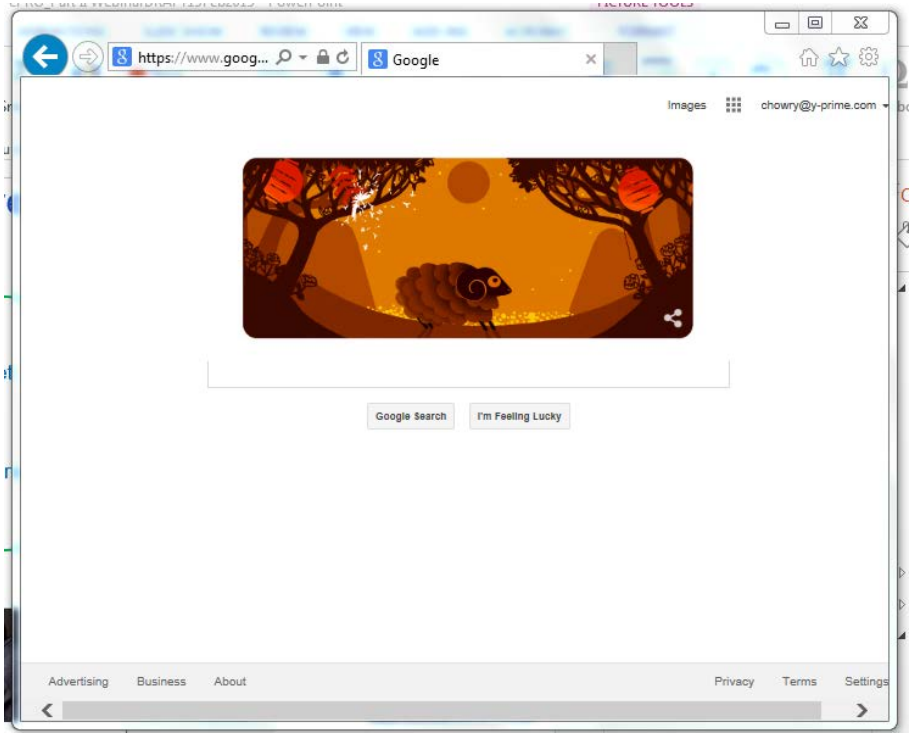
Smartphones (field-based)

Other References:

- At home (home-based)
- Medication diary
- eDiary
- Diary log
- Event-based
- One device per patient

Interactive Web Response (IWR)

- Site-based
- Designated PC, laptop, or tablet
- Internet connection
- No built-in camera



Interactive Voice Response (IVR)

- Listen to voice
- Enter response on keypad

Enrollment by

Study Site

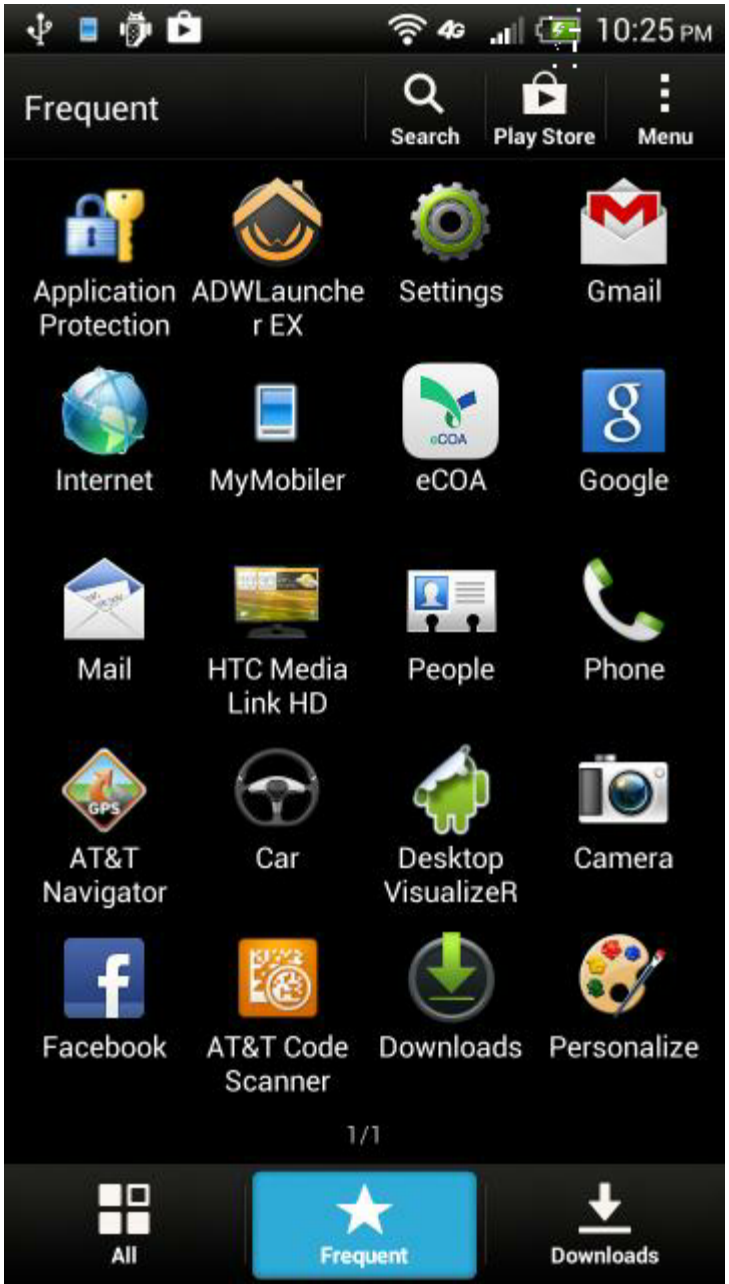
Patient call or receive call at interval appropriate for session

Patient – System Interaction

Call results in real-time via web service

BYOD (Bring Your Own Device)

- Use personal smartphone
- iOS and Android



Strengths/Limitations of each Mode

- Strengths/limitations given context of use
- Appropriateness/feasibility of mode given study factors
- In certain study scenarios – one mode may be more appropriate than others, where other mode(s) may be limited/non-feasible

Smartphone/Handhelds

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Strengths include:

- Usable by most populations
- Ideal for mobility
- Ideal for consistency
- Familiarity of device
- Large numbers of items
- Visual components (pictures/diagrams)

Limitations include:

- Populations with:
  - Visual impairment
  - Severe
  - Severe migraine episodes
- Costs of provisioning devices

Tablets

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Strengths include:

- Usable by most populations
- Ideal for consistency and mobility purposes
- Large numbers of items/responses
- Visual components (pictures/diagrams)

Limitations include:

- Cost of provisioning devices
- Populations with:
  - Visual impairment
  - Severe arthritis
  - Dexterity issues
  - Severe migraine episodes

Interactive Web Response (IWR)

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Strengths include:

- Usable by most populations
- Wide availability of the Internet
- Large numbers of items/response options
- Visual components (pictures/diagrams)

Limitations include:

- Active connection to Internet
- Populations with:
  - Visual impairment
  - Paralysis
  - Dexterity issues
  - Severe migraine episodes
- Screen size variability

Interactive Voice Response (IVR)

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Strengths include:

- Usable by most populations
- Familiarity with phone
- Most have access to landline or cell phone
- Wide availability phone service

Limitations include:

- Populations with:
  - Hearing impairment
  - Short-term memory issues
- Long-length instruments
- Visual instruments (e.g. body diagram, VAS)
- No camera capability

ePRO Mode Selection Process

ePRO Mode Selection Process

Appropriate ePRO mode selection should be based on different considerations:

- √ Patient characteristics
- √ Study design (diary)
- √ Study logistics
- √ Instrument characteristics

Patient Characteristics

Patient population/ therapeutic area

- Functional conditions of target population that may impact the way a diary can be administered:
  - Diabetes-related vision deterioration
  - Dry eye
  - Hearing loss
  - Parkinson's disease-related tremors
  - Stroke-related physical or cognitive impairment

Patient burden

- Time required
- Convenience
- Mode's ease of use for target population
- Cognitive burden

Study Design (Diary)

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Diary setting	• Field-based (home-based) • Study site-based
Diary frequency	• Episodically (when symptom/episode occurs) • 4x per day • 1x per day • 2x per week, etc.
Diary duration	• 2 weeks • 1 month • 1 year, etc.
Time per diary entry	• 5-10 minutes per entry • 20-30 minutes per entry • >30 minutes per entry, etc. • Time is important to consider along with frequency

Study Logistics

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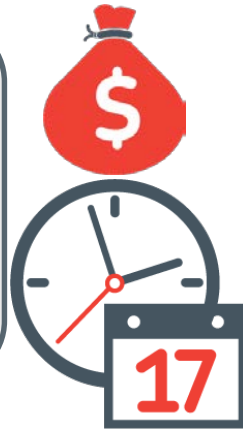
Study factors

- Sample size
- Costs/budget
- Timelines
- Diary mode access (phone, Internet, computer, etc. or sponsor provisioned devices)
- Site capacity (patient training, support, storage, etc.)



Participating regions

- Electronic infrastructure (Internet connectivity variation, phone service)
- Shipping requirements (if supplying diary mode)
- Required languages

Intended use of PRO data

- Label claim, primary/secondary/exploratory endpoint
- Study phase
- Regulatory acceptability of mode given intended use

Instrument Characteristics

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Diary length

- Number of items
- Number of words per item
- Number of response options
- Item branching

Structure of response options

- Complexity
- Response scale: visual analog scale (VAS); numeric rating scale (NRS) verbal rating scale (VRS)
- Visual elements (e.g., body diagram)

Instrument author restrictions

- Does author have restrictions on allowed modes of administration?

Mode Selection Process: Example 1

Factor	Study Characteristic
Location	• Global (US, Europe, Asia)
Therapeutic area	• Flu vaccine
Target enrollment	• 10,000 patients
Diary design	• 8 items measuring severity of symptoms • 7 response options (verbal response scale)
Diary setting	• Field-based
Diary frequency/duration	• Once daily for 1 week
Other study factors	• Fast start-up for each country - system needs to be ready when the flu epidemic reaches each country • Study budget

Example 1: Mode Evaluation

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IVR:	Smartphone/ Handheld Device:	IWR:
• **# of response options** – patients may have trouble remembering 7 response options with waiting for all responses to be read out	• **Costs** – costs of provisioning 10,000 devices • **Timelines** – time to ship (customs regulations) • **# of response options** – 7 response options may be difficult to fit on small screen in certain languages	• **Logistics** – feasible in large scale study; majority eligible patients will have Web access • **# of response options** – 7 response options fit well with IWR since due to capability of using larger screen size

Example 1:
Most Appropriate Mode Choice

IWR:

- ✓ Quick implementation – meets timelines
- ✓ Logistically feasible
- ✓ Meets study budget needs
- ✓ Easy for patients to visually see items/responses (due to being able to use larger screen size)

Mode Selection Process: Example 2

Factor	Study Characteristic
Location	• United States
Therapeutic area	• Gastrointestinal
Target enrollment	• 50 patients
Diary design	• 20 episodic symptom items • Responses: 4 visual response options with pictures
Diary setting	• Field-based
Diary frequency/duration	• Required to respond once daily, and episodically (whenever symptoms are present) • 1 year
Other study factors	• Visual requirement for mode • Study budget • Timelines

Example 2: Mode Evaluation

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IVR:

- **Diary design** – visual requirement of response options not applicable for IVR

Smartphone/ Handheld Device:

- **Diary frequency/ duration** – convenient for patients for mobility purposes for episodic data entry
- **Diary design** – feasible for visual response options
- **Costs/timelines**– minimal concern with smaller sample size

IWR:

- **Diary frequency/ duration** – with episodic response, it may be challenging for the patient to find a computer during that episode
- **Diary design** – IWR would be feasible for visual response options

Example 2:
Most Appropriate Mode Choice

Smartphone/Handheld Device:

- ✓ Most convenient for patients since field-based with episodic response
- ✓ Allows delivery of visual nature of response options
- ✓ Costs of provisioning the smartphones/handheld devices are less of a concern with smaller sample size

Mode Selection

Mode selection:

- ✓ Begin as early as possible
- ✓ Should be based on considering all factors:
  - Patient characteristics & burden
  - Study design (diary)
  - Study logistics
  - Instrument characteristics

Appropriate ePRO mode selection results in:

- ✓ Higher data quality
- ✓ Enhanced patient's user experience (convenient & easy to use, minimized burden)
- ✓ Highest level of patient compliance with diary completion achieved
- ✓ Reduced sponsor burden

Migrating an Existing Instrument to an Electronic Mode: Introduction

Electronic Instrument Migration

- Migratibility assessment of the instrument

- √ Instructions
- √ Item stems
- √ Response options
- √ Languages

Instructions

Migratibility assessment

- Do the instructions make sense in the context of the mode?
- Instructions need to be appropriate to the actions of the mode.
- Use platform-neutral language in instructions where possible.

Example: original paper

Circle the response that best describes….

Example: platform neutral

Select the response that best describes….

Items

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Migratibility assessment

- Does instrument include split stems?
- Are items self-contained?
- Would the full item (stem and responses) be able to be fit on the screen?

Example of split stem (to be avoided):

During the past 4 weeks, how much has your pain interfered with:

1. Vigorous activities such as running or heavy lifting?

Not at all	Somewhat	Moderately	Extremely
○	○	○	○

2. Moderate activities such as climbing a flight of stairs?

Not at all	Somewhat	Moderately	Extremely
○	○	○	○

Example of complete item stems:

1. During the past 4 weeks, how much has your pain interfered with vigorous activities such as running or heavy lifting?

Not at all	Somewhat	Moderately	Extremely
○	○	○	○

2. During the past 4 weeks, how much has your pain interfered with moderate activities such as climbing a flight of stairs?

Not at all	Somewhat	Moderately	Extremely
○	○	○	○

Response Options & Languages

Response options: migratibility assessment

- Nature of response scale in appropriateness to mode (visual nature required?)
- Length & number of response options – may impact appropriateness to migrating to certain modes
- Implementation of edit checks (e.g. alerting patient of out-of range value, missing value)
- Branching logic

Languages: migratibility assessment

- Participating regions
- Space required for translated text
- Formatting associated with translated language

Migration

When modification is required consider:

- Does the content of the existing instrument change?
- What is the level of modification required?
- Does the level of modification require additional testing?

Attend C-Path 3rd webinar:

Migrating an existing PRO instrument

- Definition of faithful migration
- Process of conducting a faithful migration
- Mode-specific migration considerations
- Usability, feasibility, and user acceptance testing

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Q&A

Thank you for attending the ePRO Consortium Webinar

The Intro to ePRO – Part II presentation and audio will be available within two weeks on the c-path.org website