

Staying Alert to Data Quality: A Shiny App to Visualise the Electronic Patient Reported Outcome (ePRO) Data

Wenyi Liu

Principal Data Scientist
Hoffmann-La Roche

First and Foremost

- The data used in the demo were randomly selected from an Influenza study and data were de-identified.
- The shiny app was created based on the Roche-developed TEAL package
 - The teal package is a framework that leverages the R Shiny package to scale development of shiny apps.
 - More details available at <https://insightsengineering.github.io/teal/main/>



Overview

- What is PRO and ePRO data
- Increased recognition of PROs in clinical trials
- Advantages and challenges of using ePRO data
- The Shiny app
 - Data collection tracking
 - Body temperature tracking
 - Endpoint tracking
 - Rebounds
- Discussions and Conclusions

What is electronic Patient-Reported Outcome (ePRO) data

- The U.S. Food and Drug Administration (FDA) defines a patient-reported outcome (PRO) as

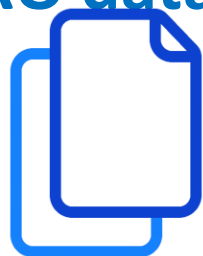
“Any report of the status of a patient’s health condition that comes directly from the patient, without interpretation of the patient’s response by a clinician or anyone else.”



What is electronic Patient-Reported Outcome (ePRO) data

- Measures subjective or objective symptoms or health outcomes, i.e.
 - Feeling better?
 - Be able to drive?
 - Pain level comparing to yesterday

PRO data can be collected in multiple ways



- ePRO data are PRO data collected via electronic methods, such as an electronic device, or mobile app
- Sometimes be used interchangeably with the term **eDiary**

Increased recognition of PROs in clinical trials

- Patients' perspectives

I'm COVID tested negative

vs.

I'm COVID symptom-free

- Cost vs. Benefit of treatment
- Support the decision of health authorities, public policies
- The use of PRO endpoints has increased over time

The increasing recognition of PROs in clinical trials

Example 1: Influenza

- To evaluate time to alleviation of influenza signs and symptoms, maintained for 24 hours

Item	No Problem	Minor Problem	Moderate Problem	Major Problem	Don't Know/Not Applicable
1. Poor appetite	☐	☐	☐	☐	☐
2. Not sleeping well	☐	☐	☐	☐	☐
3. Irritable, cranky, fussy	☐	☐	☐	☐	☐
4. Feels unwell	☐	☐	☐	☐	☐
5. Low energy, tired	☐	☐	☐	☐	☐
6. Not playing well	☐	☐	☐	☐	☐
7. Crying more than usual	☐	☐	☐	☐	☐
8. Needing extra care	☐	☐	☐	☐	☐
9. Clinginess	☐	☐	☐	☐	☐
10. Headache	☐	☐	☐	☐	☐
11. Sore throat	☐	☐	☐	☐	☐
12. Muscle aches or pains	☐	☐	☐	☐	☐
13. Fever	☐	☐	☐	☐	☐
14. Cough	☐	☐	☐	☐	☐
15. Nasal congestion, runny nose	☐	☐	☐	☐	☐
16. Vomiting	☐	☐	☐	☐	☐
17. Not interested in what's going on	☐	☐	☐	☐	☐
18. Unable to get out of bed	☐	☐	☐	☐	☐

Since the last assessment has the subject been able to return to day care/school, or resume their normal daily activity in the same way as performed prior to developing the flu? ☐ Yes ☐ No

This form was filled out by:

- ☐ Parent
☐ Carer
☐ Other

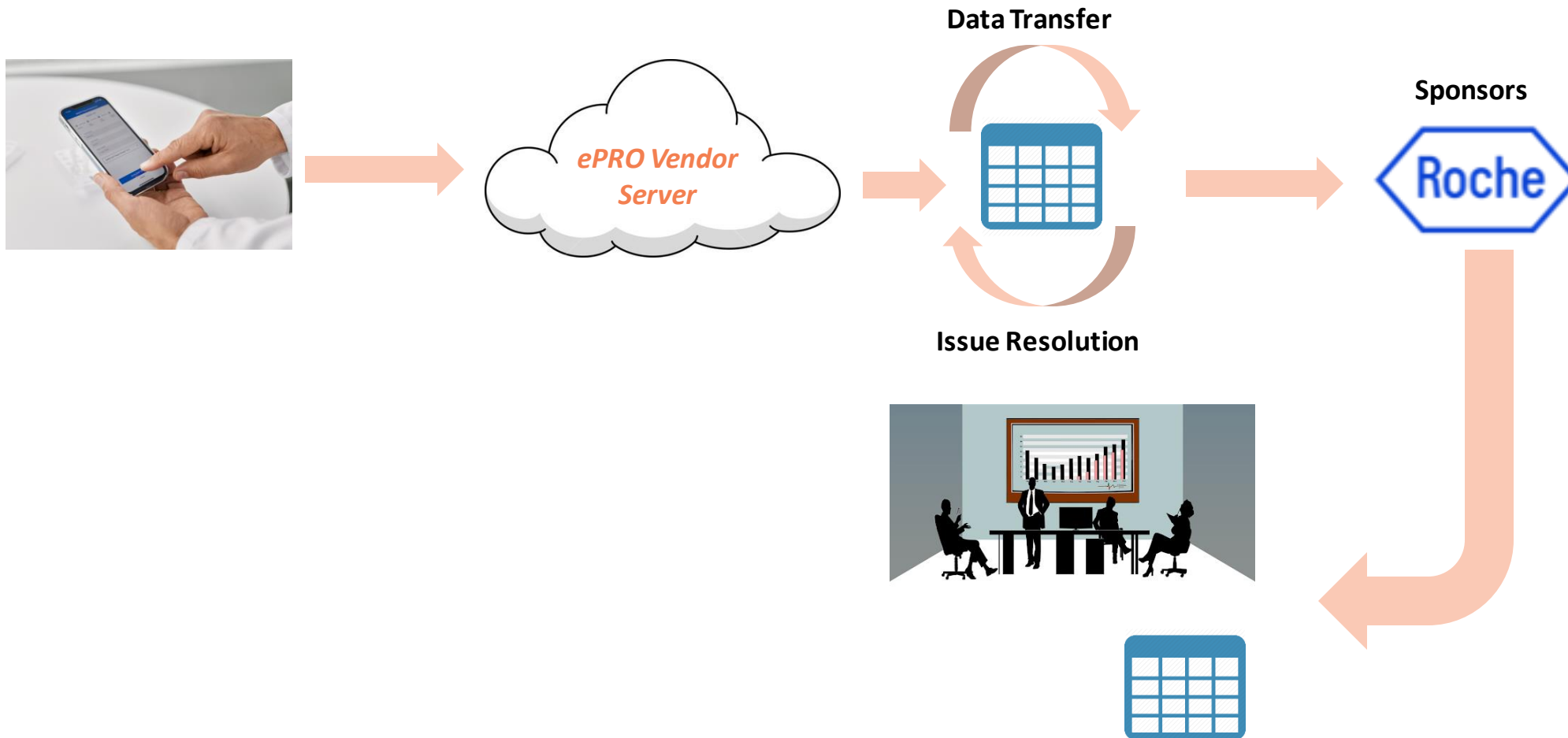
The increasing recognition of PROs in clinical trials

Example 2: Ulcerative Colitis

UC-PRO/SS Domain	Question	Response to Question
Bowel Movement Signs and Symptoms	In the past 24 hours, how many bowel movements did you have?	0=0, 1=1-2, 2=3-4, 3=5-6, 4=7-9, 5=10-12, 6=13-17, 7=18 or more
	In the past 24 hours, how often were your bowel movements mostly or completely liquid?	0=Never 1=Rarely 2=Sometimes 3=Often 4=Always
	In the past 24 hours, did you have blood in your bowel movements?	0=No 1=Rarely 2=Sometimes 3=Often 4=Always
	In the past 24 hours, did you have mucus (white material) in your bowel movements?	0=No 1=Rarely 2=Sometimes 3=Often 4=Always
	In the past 24 hours, did stool, blood, or liquid leak out before you reached a toilet?	0=No 1=Rarely 2=Sometimes 3=Often 4=Always
	In the past 24 hours, did you feel the need to have a bowel movement right away?	0=No 1=Mild 2=Moderate 3=Severe 4=Very Severe

- To evaluate the efficacy of treatment for UC bowel movement signs and symptoms at Week 10 as assessed by the Ulcerative Colitis Patient-Reported Outcome Signs and Symptoms (UC-PRO/SS) measure

Using electronic methods to collect PROs



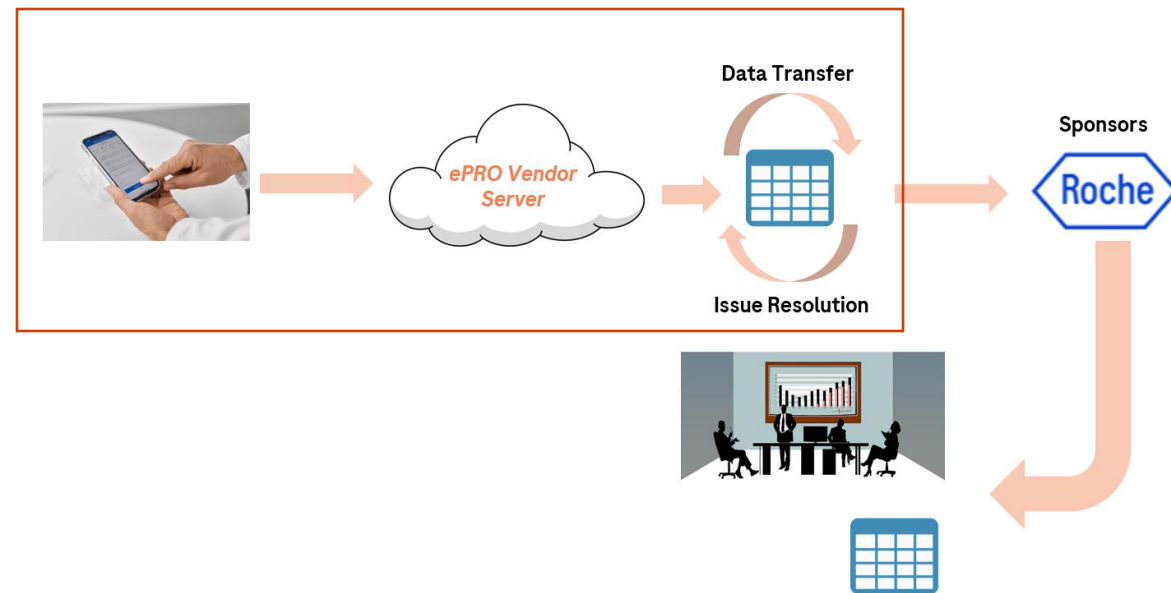
Using electronic methods to collect PROs

■ Advantages

- Fast and real-time measurement
- Resources and cost-saving
- Reduce patients' burden of visiting doctor's office
- Enable more data collection

■ Challenges

- Patients lacking medical knowledge
- Missing data, due to
 - Miss the time window
 - Technical problems
- Unable to fix the data issues



The Shiny App to track and detect data issues

Demo

[Data Table](#)
[Diary Tracking](#)
[Time-to-Event Tracking](#)
[Body Temperature](#)
[Time-to-Event Rebound](#)

☐ unfiltered data
 ☒ filtered data
 ☐ Show only distinct rows:

[ADSL](#)
[ADTTE](#)
[QS](#)
[DS](#)
[EX](#)
[SV](#)

Select variables:

USUBJID, SEX, RACE, ETHNIC

Show 30 entries

	USUBJID	SEX	RACE	ETHNIC
1	S88	F	WHITE	Hispanic or Latino
2	S12	F	WHITE	Hispanic or Latino
3	S67	M	WHITE	Hispanic or Latino
4	S58	F	MULTIPLE	Not Hispanic or Latino
5	S05	F	WHITE	Not Hispanic or Latino
6	S77	F	WHITE	Not Hispanic or Latino
7	S29	F	WHITE	Hispanic or Latino
8	S09	F	WHITE	Hispanic or Latino
9	S45	M	WHITE	Hispanic or Latino
10	S63	F	WHITE	Hispanic or Latino
11	S42	M	WHITE	Hispanic or Latino
12	S36	F	UNKNOWN	Hispanic or Latino
13	S71	F	UNKNOWN	Hispanic or Latino
14	S67	M	WHITE	Hispanic or Latino
15	S76	M	WHITE	Hispanic or Latino

Active Filter Summary

	Obs	Subjects
ADSL	88/88	88/88
ADTTE	1297/1297	88/88
QS	36309/36309	90/90
DS	616/616	88/88
EX	968/968	88/88
SV	1601/1601	90/90

Active Filter Variables

ADSL
 ADTTE
 QS
 DS
 EX
 SV

Add Filter Variables

Add ADSL filter

■ completed ■ missing ■ not expected ■ NA



complete: diaries are completed at scheduled timepoints
missing component(s): diaries are completed but ≥ 1 questions were not answered
missing: diary data are not available
not expected: diary data are not expected but was collected
not yet: patients haven't reached that study day yet
NA: symptom diary data are NA if they are after patients early withdrawal date

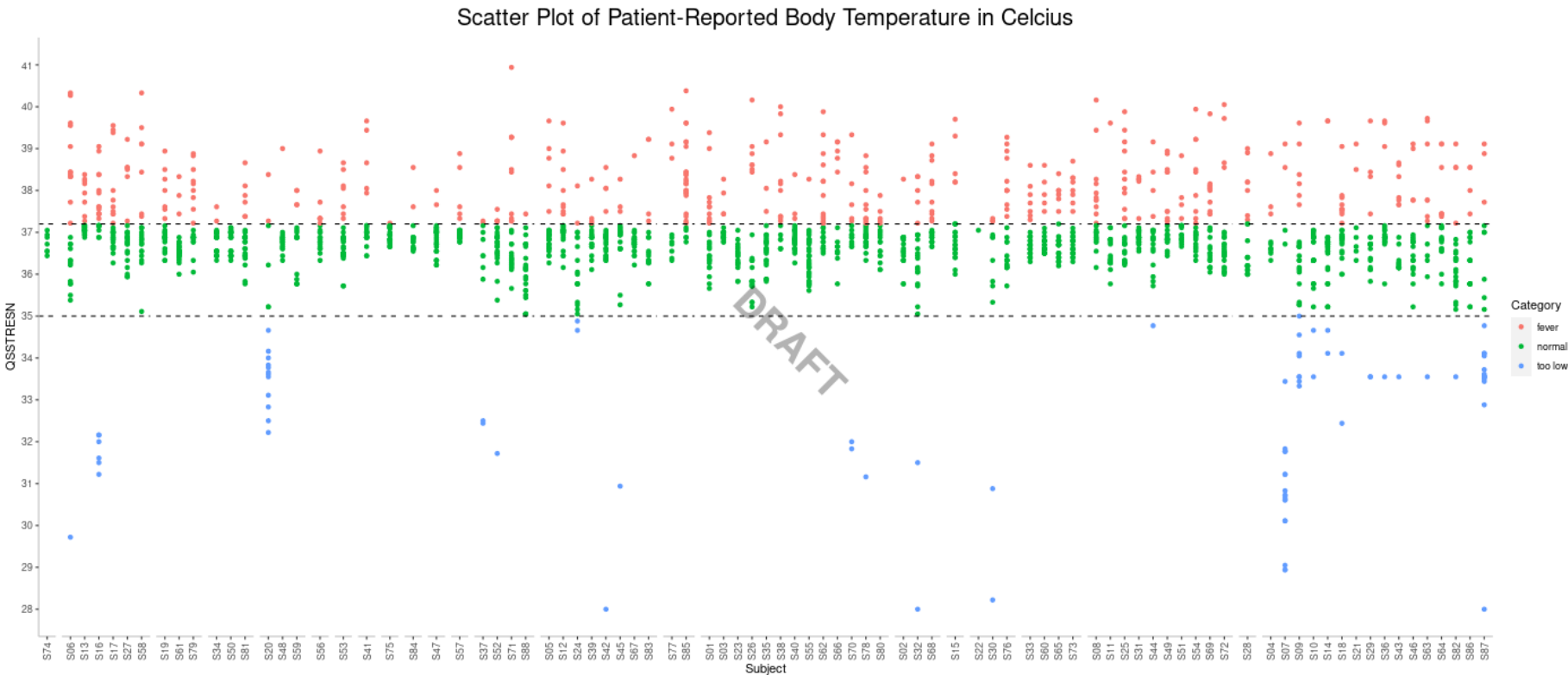
- Overall picture of missing data
- Consecutive missing for certain patients
- Systematic missing for certain sites
- “Not expected” entries could be device setup issue or system issue
- During study, check whether data were transferred on time

- Re-iterate patient trainings
- Site communication
- ePRO device/app UI design improvement

Selected Clicking Data Points

	USUBJID	QSDY	QSTPT	VISIT	QSDTC	QSDY.SRC	
45	S02	10	MORNING Follow Up Visit 5 (Day 10)	2019-02-27T11:50:57	10		
	QSBFL	n_qs	n_nd	DSDECD	expected last day	status	query
45	<NA>	18	0	<NA>	<NA>	NA	COMPLETED not expected

Body Temperature Tracking



Issues to check:

- Messed up Celsius and Fahrenheit
- Invalid numbers (e.g. 28 Celsius)
- Outstanding sites

Actions to take:

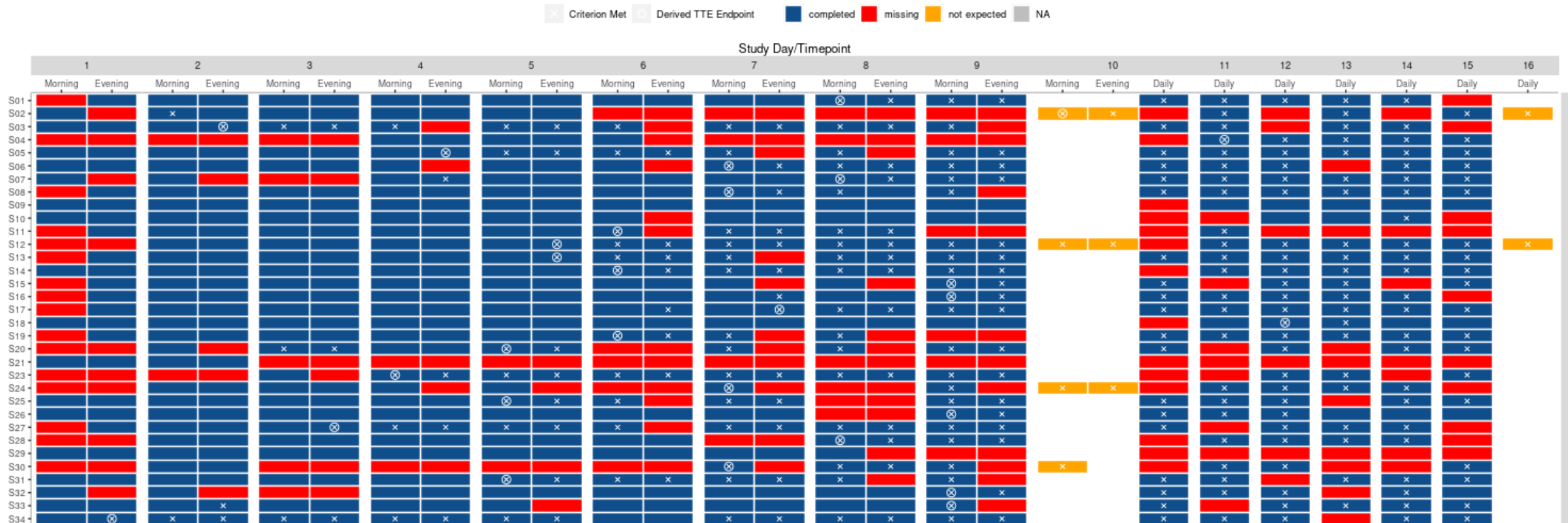
- Re-iterate patient trainings
- Site communication
- ePRO device/app UI design improvement

Selected Clicking Data Points

USUBJID	SITEID	QSTEST	QSSSTRESN	QSSSTRESU	VISIT	QSTPT	QSDTC	QSDY	cat
145	S07 317919	ARFS1-Temperature (C)	28.94	C	Follow Up Visit 4 (Day 6)	EVENING	2019-01-27T15:50:48	6	too low
147	S07 317919	ARFS1-Temperature (C)	28.94	C	Day 7	EVENING	2019-01-28T15:20:55	7	too low
148	S07 317919	ARFS1-Temperature (C)	29.05	C	Day 8	MORNING	2019-01-29T07:08:26	8	too low

Endpoint Criteria Met Progress

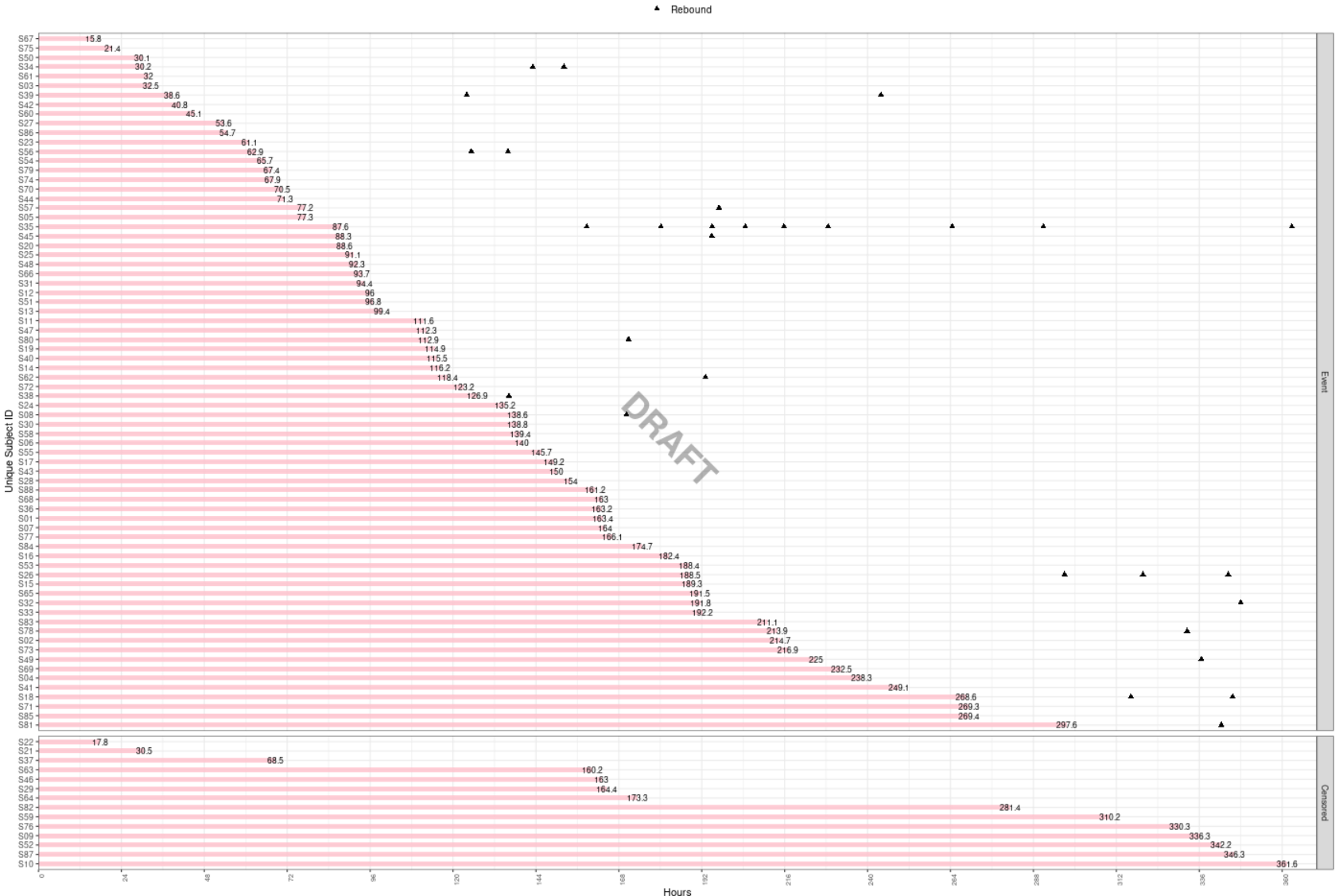
Diary Data Collection Status over Time



- Is missing data a roadblock for patients to achieve “endpoint”?
- Is it necessary to implement a more strict or relaxing missing data handling rule?

Symptoms Rebound

Swimmer Plot of Efficacy Endpoint and Rebounding Event
Time to Alleviation (TTA) of Influenza Signs and Symptoms (Hours)



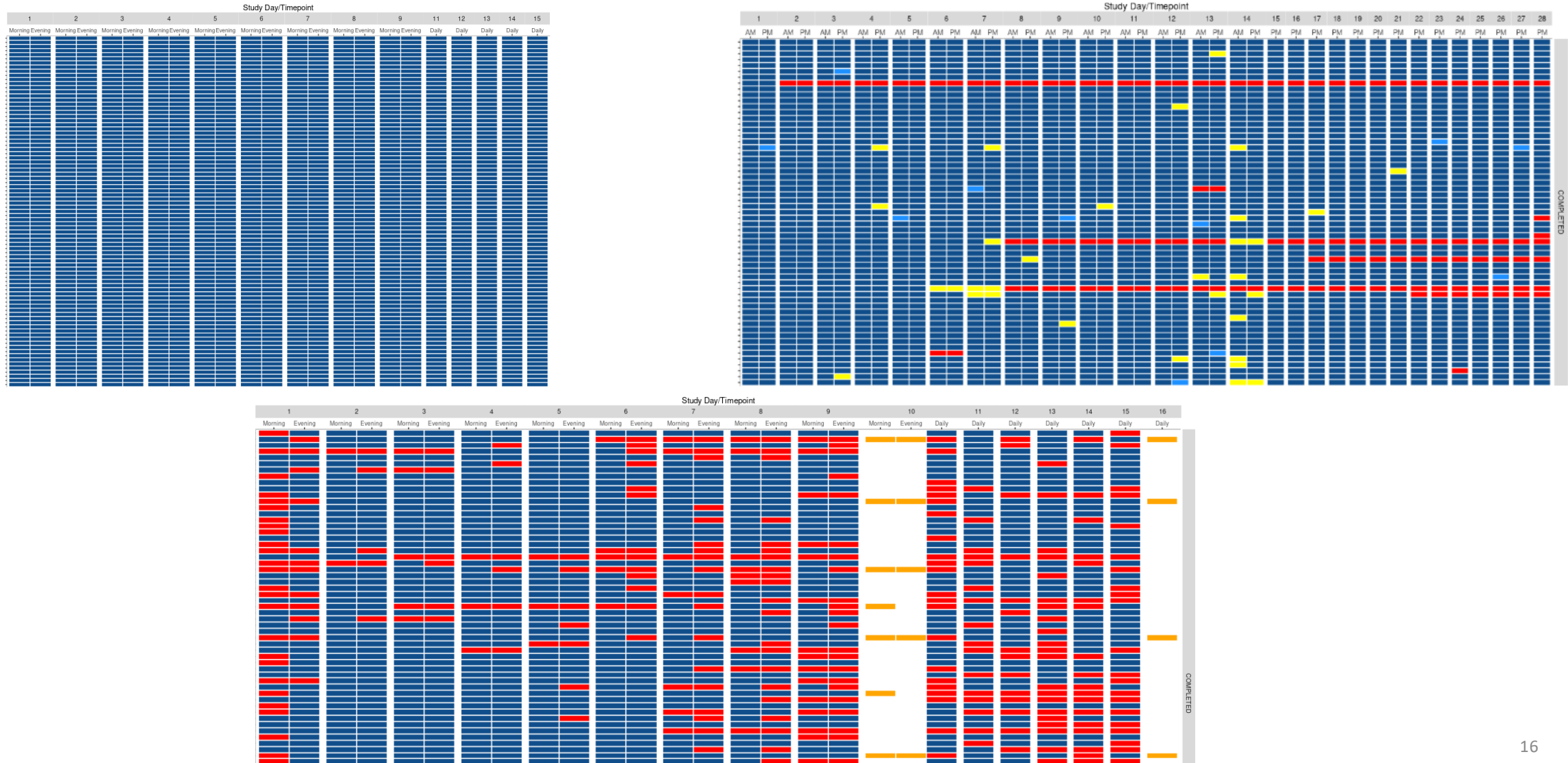
- Too many rebounds can impact the validity of drug effects

Selected Clicking Data Points

	USUBJID	AVAL	CNSR	VISIT	QSTPT	QSDY	Q17714
25	S26	188.5	Event	Day 13	DAILY	13	MODERATE PROBLEM
26	S26	188.5	Event	Day 14	DAILY	14	MODERATE PROBLEM
27	S26	188.5	Event	Optional Visit 2 (Day 15)	DAILY	15	MINOR PROBLEM
							Q17715 S00201 S00204 rebound.hour
25	MODERATE PROBLEM		N	38.61		297.0	
26	MODERATE PROBLEM		N	36.33		319.7	
27	MINOR PROBLEM		N	36.38		344.4	

Discussions

Evaluate the risk vs. benefit of using paper diaries or e-diaries



Discussions

The dilemma of collection more data vs. collection more accurate data

Scenario: ePRO data was collected twice a day: MORNING (8:00am – 10:59am) and EVENING (5:00pm – 7:59pm)

Method 1

ePRO system is open all day to allow patients to submit their entries any time during the day, but patients will get notified when it's time to submit data.

Pros: Allow the collection of more data

Cons: Unable to track timestamp automatically but need to rely on manual entries. Easy to get incorrect data.

Method 2

ePRO system is only open during the pre-defined time window and patients get notified when it's time to assess and submit data.

Pros: Automatically track the timestamp when data is collected. Patients can answer questions based on their real-time experience

Cons: Easy to miss out the time window

Conclusions

- PRO and ePRO is here!
- The demo is a shiny app, but there is no need to stick to one tool or software.
- The use of PRO and ePRO requires cross-functional collaboration

Questions

Doing now what patients need next