

# **Searching for the Truth: Behavioral Assessments in MTN-017**

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# **The behavioral truths that concern us in microbicide trials are...**

- To what extent participants use products as indicated (adherence)**
- What factors or events may affect product use**

# Measuring adherence

## □ Direct methods

biological assays of active drug, metabolite or other markers in blood, urine, other bodily fluids or hair confirm active drug ingestion

## □ Indirect methods

pill count, pharmacy refill records, electronic drug monitoring (MEM's caps), therapeutic impact (e.g., VL or CD4 count), clinician assessment, medical chart review, and self-reports (quantitative and qualitative).



# Limitations of direct methods

- PK testing depends of what matrix (plasma, hair, PBMC, or dried blood spot is used).
- Each represents a trade-off of recent behavior with increasingly averaged distant behaviors.
- In the case of plasma TFV,
  - it can only detect recently drug use.
  - It may tell us lack or recent use (no drug detected)
  - It may be imprecise to tell the number of doses taken (single dose or multiple doses can give detectable levels)



# Limitations of indirect methods

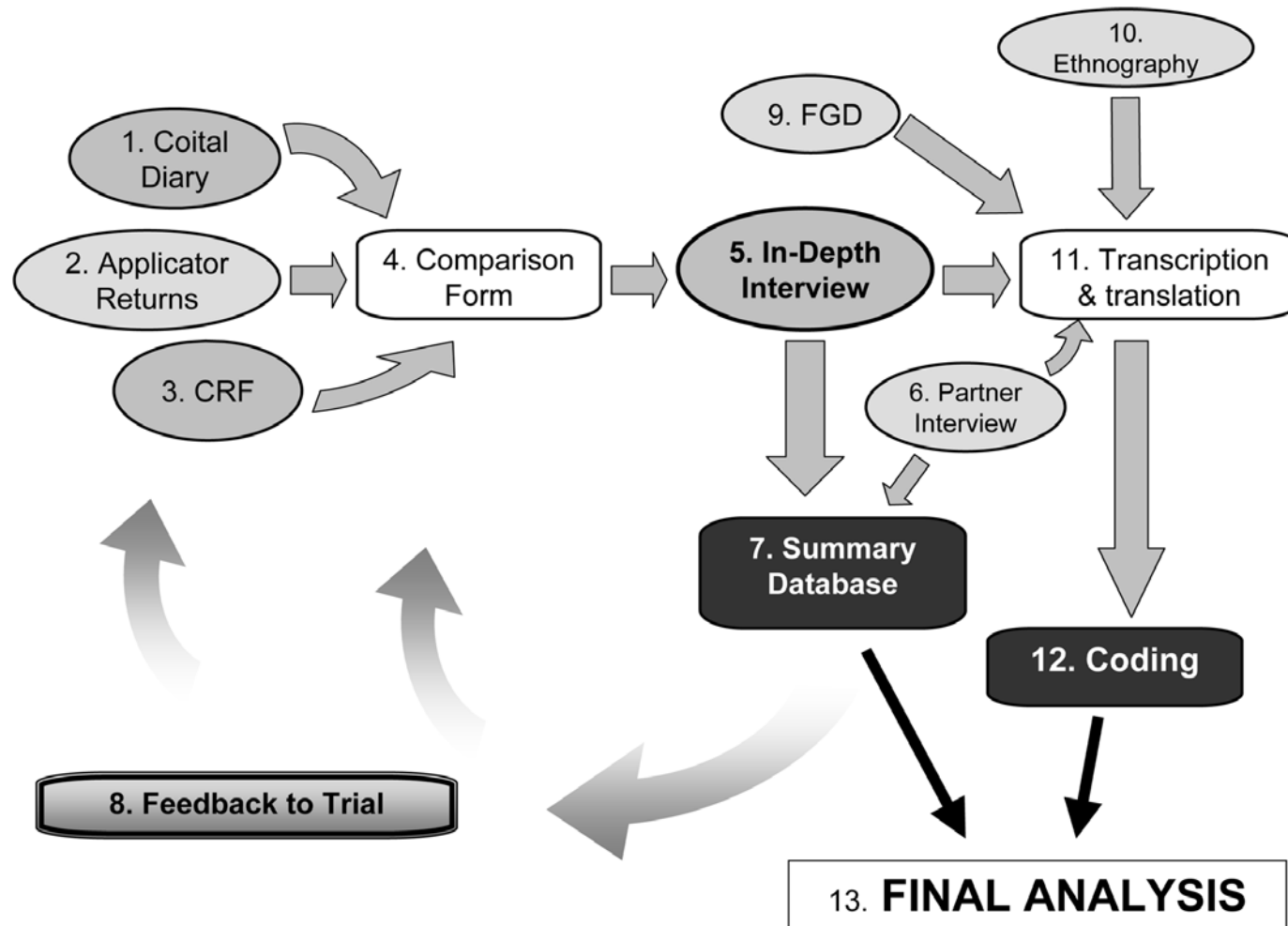
- **Pill or applicator counts**
  - **Forgetting to bring to the clinic**
  - **Dumping**
- **Self reports**
  - **Recall bias, especially with habitual behaviors**
  - **Social desirability**
  - **Deceit**
  - **Qualitative data have little generalizability**



# Currently...

- **No gold standard to measure adherence**
- **No perfect assessment method**

# Mixed methods and triangulation



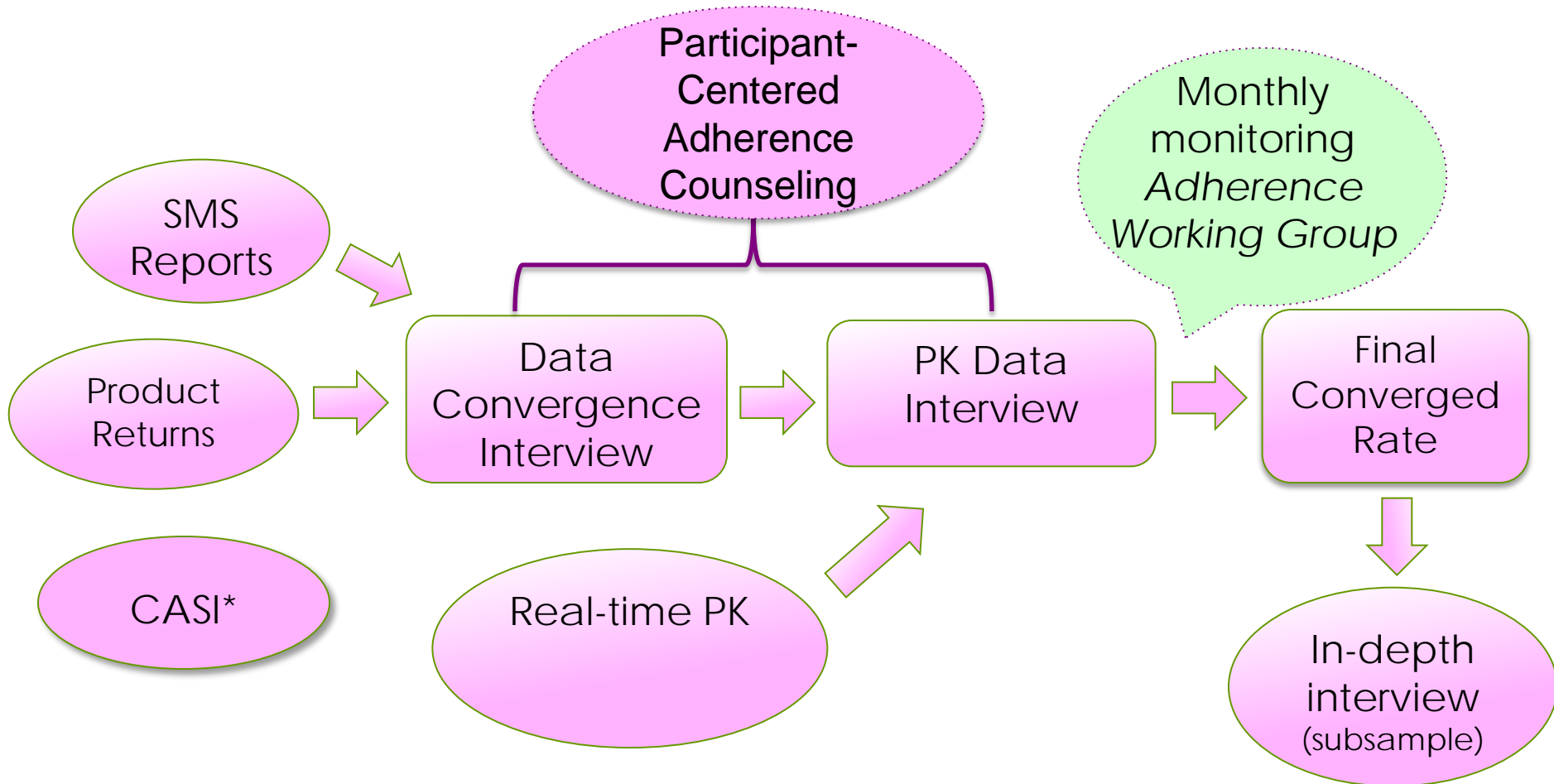


# **Assessments in MTN 004, 006, 007, 012 and Project Gel**

- Phone reporting system**
- CASI**
- Remote video or phone interviewing**
- Return of used and unused applicators**



# MTN 017 Adherence Measurement and support



\*CASI data reviewed at end of study

Adapted from Pool et al. (2010) *PLoS One*

# SMS

- Daily reminder at time of the day chosen by participant
- Inquires about product use since last report
- Offers compensation for each completed session, and bonus if a certain number of sessions per week are completed
- Allows for daily collection of event-level data
- Thorough daily data monitoring and cleaning
- Allows BRWG to alert site staff if a participant becomes unresponsive (i.e., no message received in the past 48 hours)



# SMS Reports and Calendars

SMS reports updated daily and posted on Atlas for sites to access

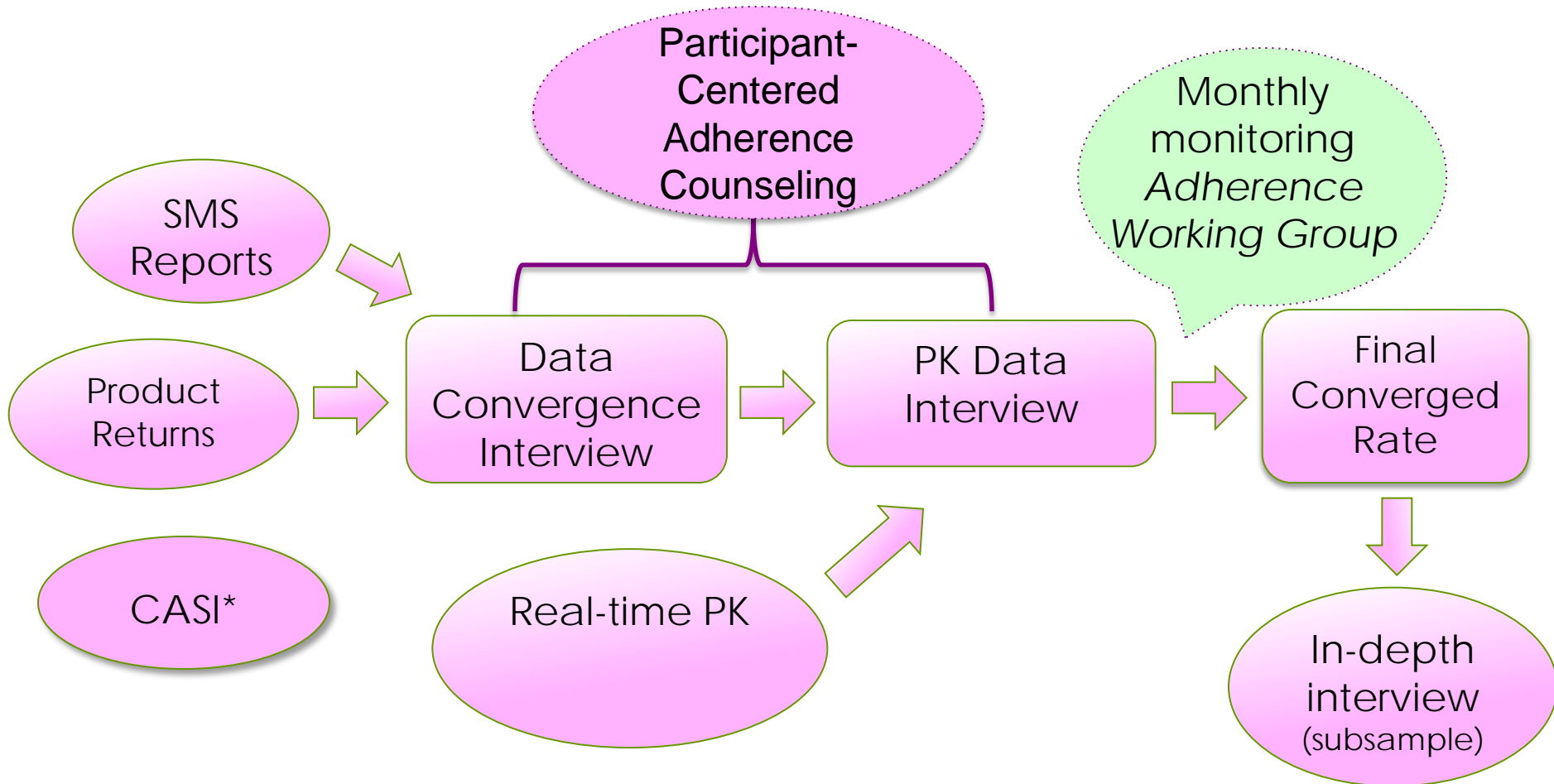
Password	PTID	PERIOD 1, MID-PERIOD				
		# Times Product Used	# Reports Completed	Start Date/End Date	# Reminders Sent	Bonus
		34	25	09/17/14-10/15/14	26	Y
		25	29	10/09/14-11/06/14	29	Y
		25	27	11/06/14-12/02/14	27	Y
		24	24	11/10/14-12/02/14	24	Y
		10	24			
		22	23			

## October-November 2014

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
			Nov 5 1	6 1	7 1	8 1
9 1	10 No report	11 1	12 1	13 1	14 1	15 1
16 1	17 1	18 1	19 1	20 1	21 1	22 No report
23 1	24 1	25 1	26 1	27 1	28 1	29 1
30 1	Dec 1 1	2	3 Visit 10			

Calendars prepared in advance of visits for discussion during Data Convergence Interviews

# MTN 017 Adherence Measurement



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# Participant-Centered Adherence Counseling

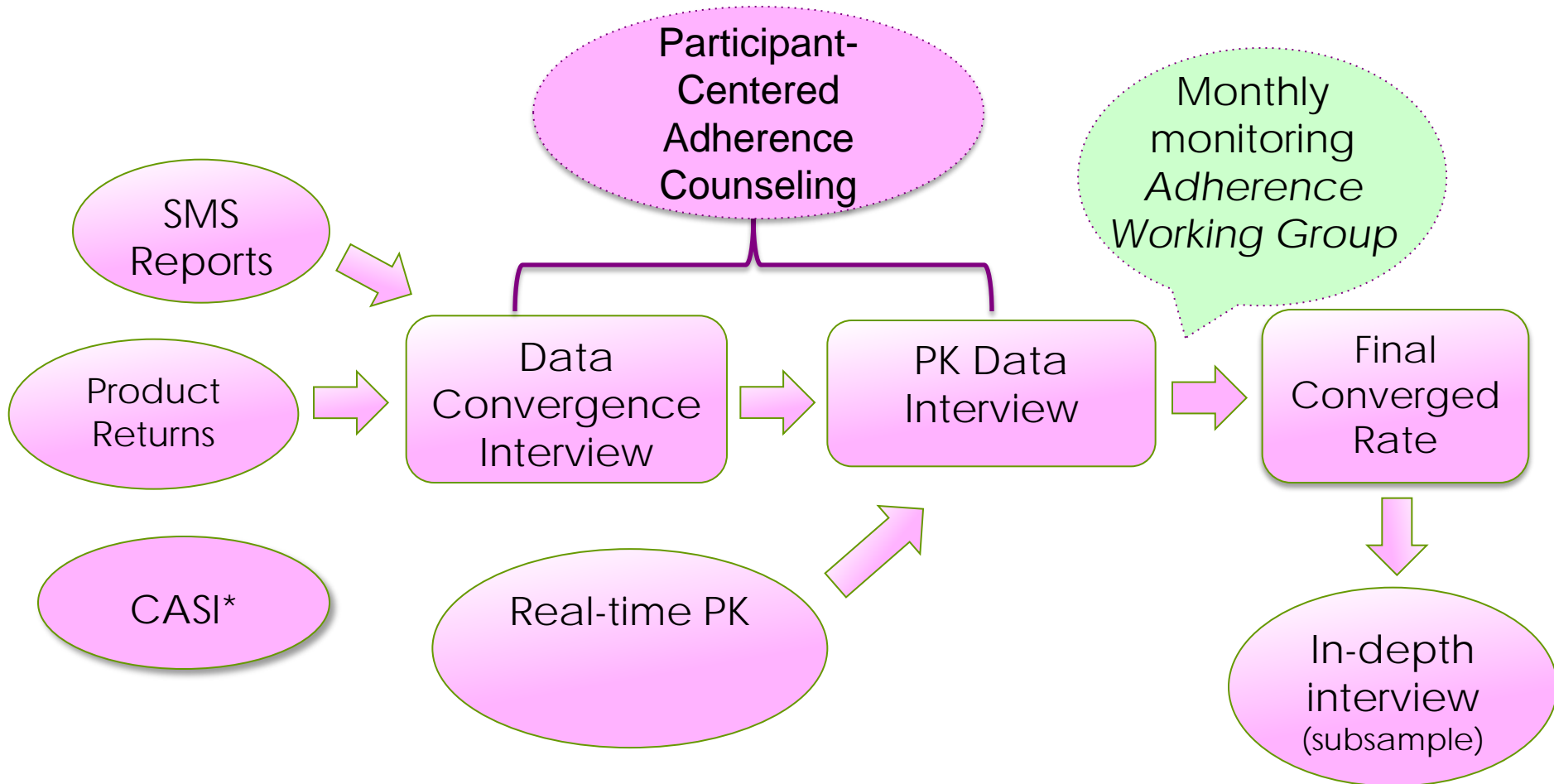
## Review and converge adherence data

- *Help us figure out the most accurate estimate of how many times you used the product. Which of these (i.e., SMS, returned product count) do you think best represents the actual number of times you used the product. Why?*
- *Is this number completely accurate, or do we need to adjust it up or down?*

## Explore adherence to product use

- *It's great that you were able to use the product over the past four weeks! What helped you use it on those occasions?*
- *What are some of the obstacles that came up that kept you from using the product more regularly?*
- *What might you do to overcome this obstacle? What else?*

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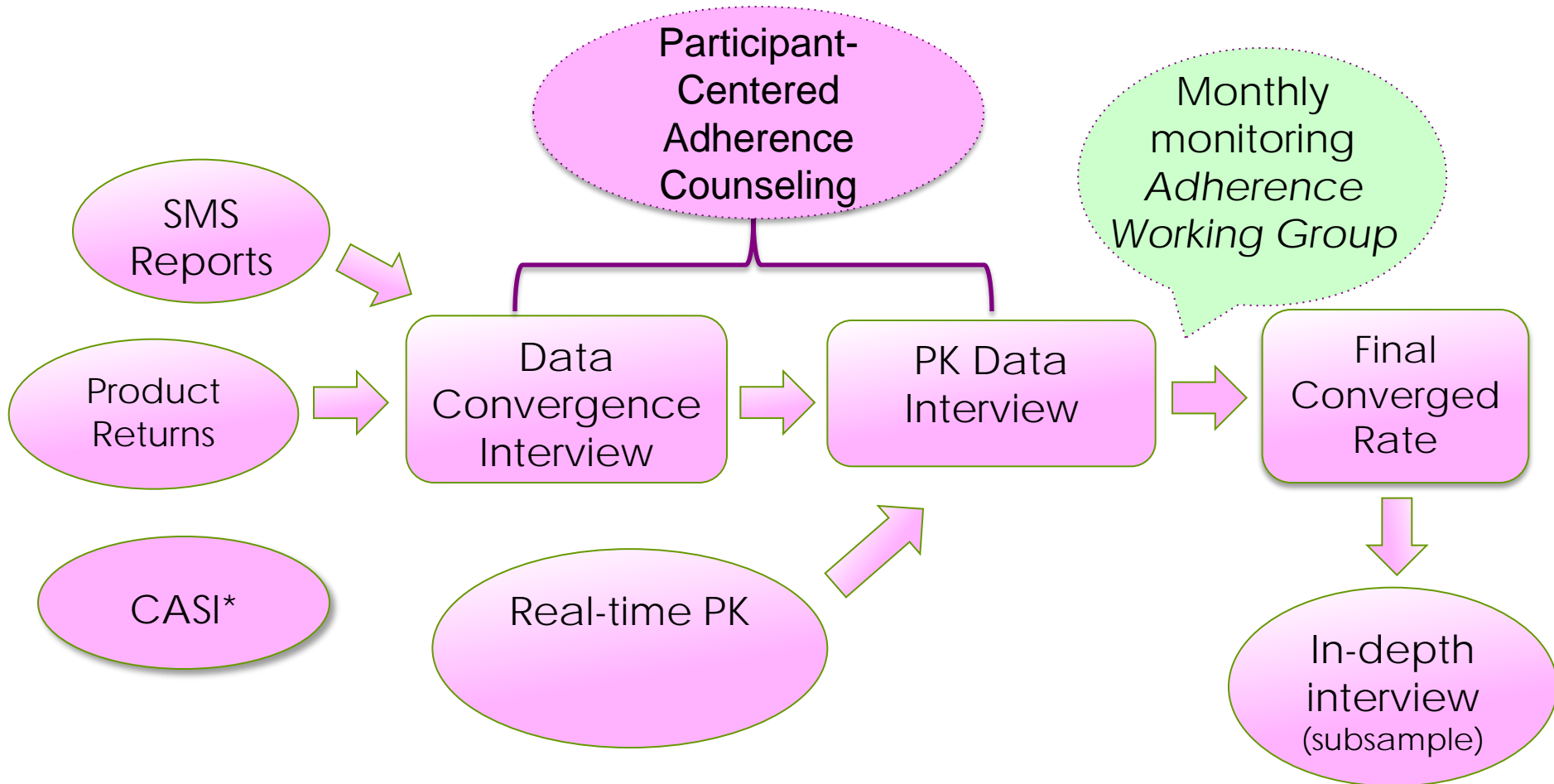
## Converge PK level with PRIOR product use reports

- *Last time, you reported using the product XX times. Now, the blood work does not show any product in your system. Why do you think that might be?*

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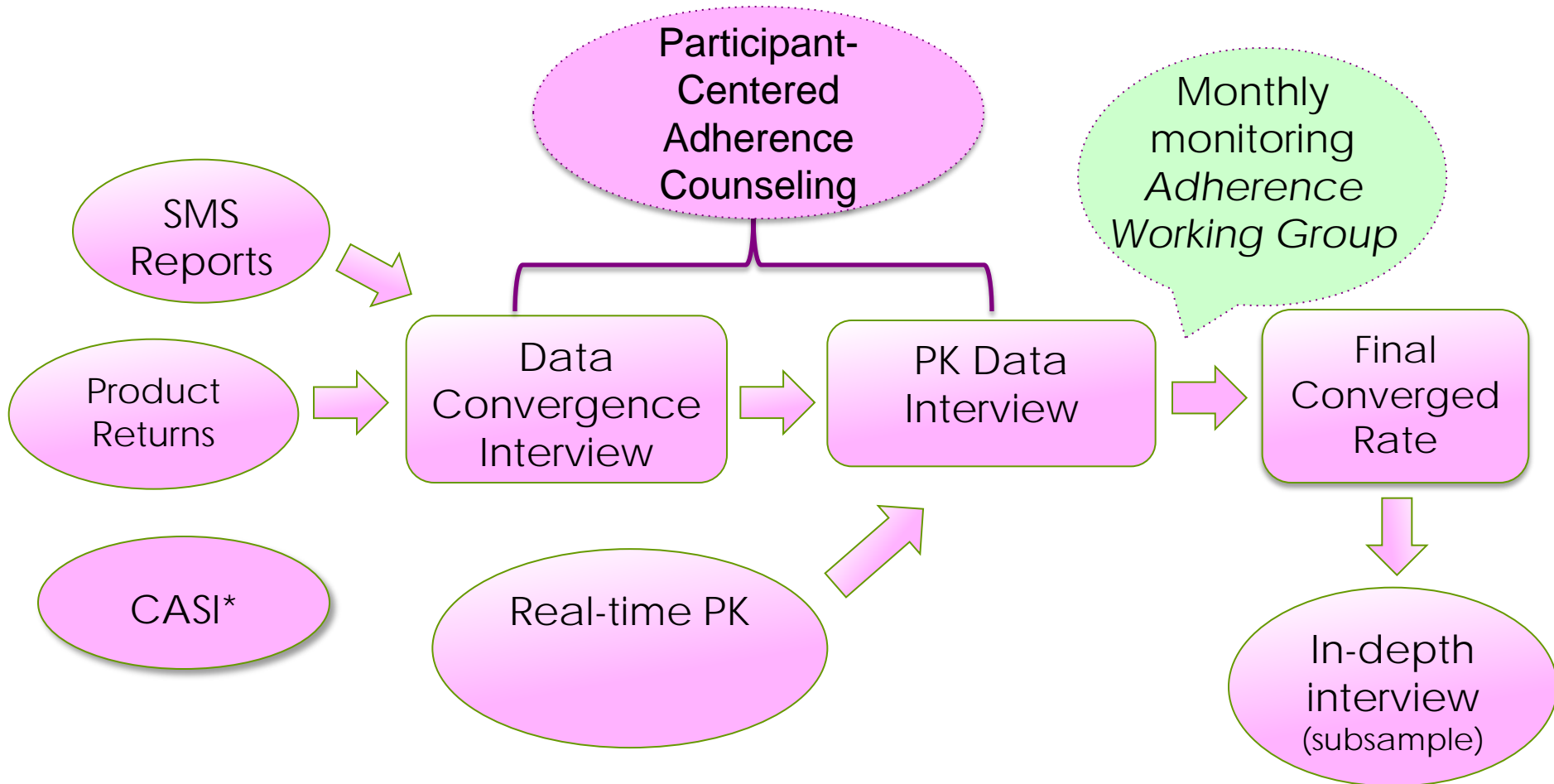
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# Adherence Counseling Monitoring

- 1426 sessions audio-recorded thus far
- 412 sessions reviewed thus far (4 different languages)
  - First 10 for each counselor
  - 1 out of 5 for sessions 11-25
  - 1 out of 10 for sessions 26+
- Session ratings
  - 1 (poor) to 7 (excellent) for session tasks
  - 1 (low) to 5 (high) for client-centeredness
  - “Passing” requires both
    - Avg of 5+ in session tasks
    - Avg of 4+ in client centeredness
- Phone conferences with site staff to review counseling procedures

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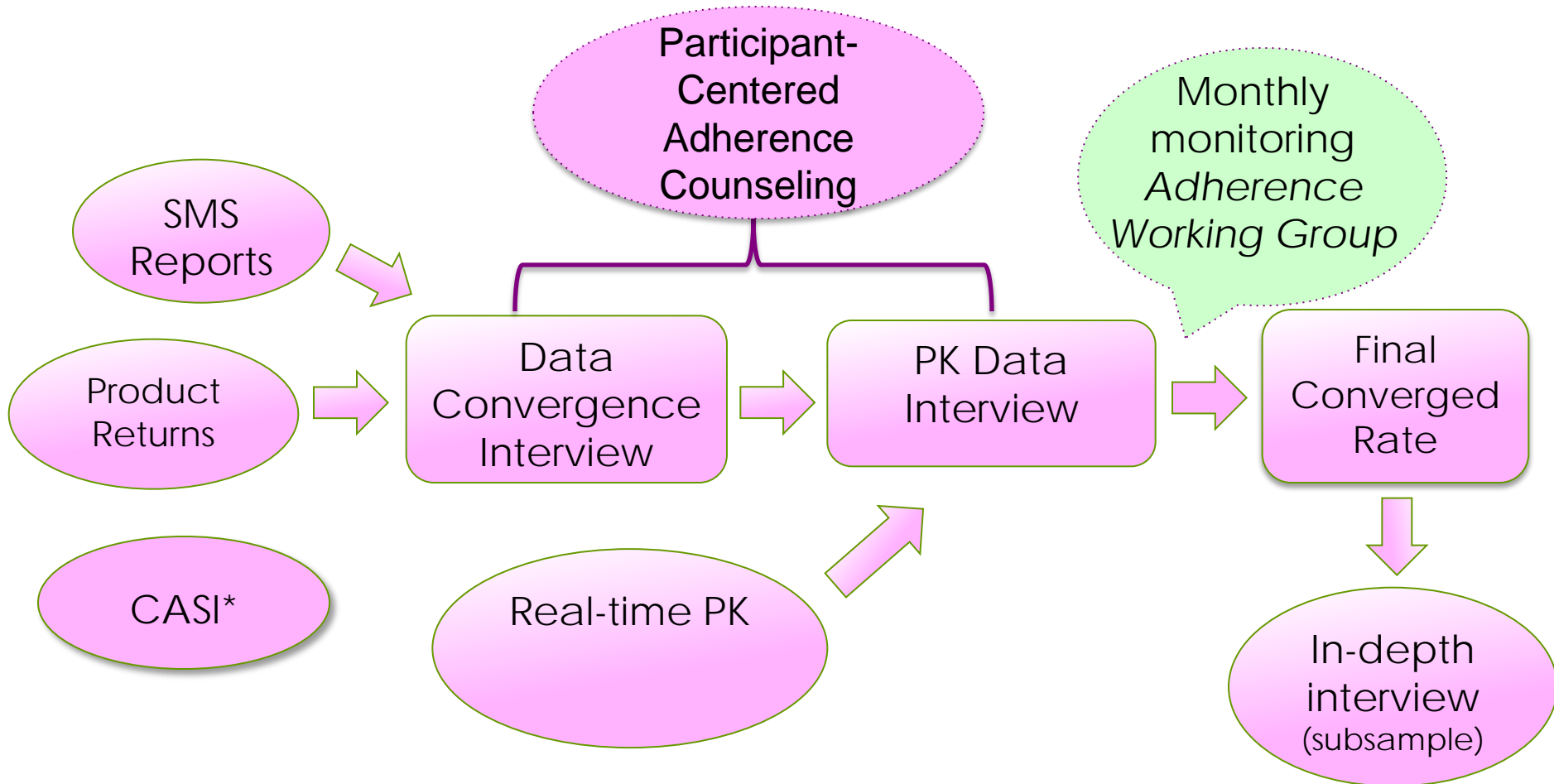
# On-going Monitoring with Adherence Working Group

- ❑ For each negative PK result from daily regimens, BRWG prepares a report for the AWG with:
  - ❑ SMS Data
  - ❑ Comments from Data Convergence Interview CRF
  - ❑ Comments from PK Interview CRF
  - ❑ Comments from counseling session (Ivan & Titcha's review of audio recordings)
  
- ❑ Negative PK results for participants on oral or daily gel regimens are categorized as:
  - ❑ Expected (**Category 1**)
  - ❑ Unexpected (**Category 2**)

# Sample report to AWG

Regimen	Visit	DCI Results	Notes	Cat
Daily Gel	V9.0	15/28 (54%)	Participant reported intermittent product use via SMS. In the week prior to Visit 9, he reported 3 times of product use. This participant had a lot of difficulty with the product and incontinence using the product. He reported a very embarrassing experience with his partners and wound up reducing his use of the product significantly. In the PKI he attributes negative PK to bowel movements and incontinence shortly after product use which may have led to not enough product in his system.	1
Daily Gel	V10.	30/37 (81%)	37 days elapsed between visits 9 and 10. Participant used 30 gels but did not use any the week before his visit.	1
Daily Gel	V3.0	25/28 (89%)	SMS Report indicated product was used once per day, until the weekend before the visit. His visit was on 10/23, and he indicated no product use on 10/18, 10/19, and 10/20 and then product used once per day on 10/21 and 10/22. When participant was asked why he thought the test result was negative he stated that after using the product he would often go to the bathroom within 5-15 minutes of inserting it. When this occurred he would notice gel in his stool.	2
Daily Gel	V6.0	28/28 (100%)	SMS report indicates daily product use. During PK interview, participant stated that perhaps his PK was not detectable because he was taking medicine for gastritis. He could not think of any other reason why the result would be negative, and reassured the counselor that he had been taking the product.	2

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# IDI

- Subset of participants from each country/regimen
- Selected those with excellent or poor adherence during the first period

***What was it like to use the product every day or before and after RAI during the past 8 weeks?***

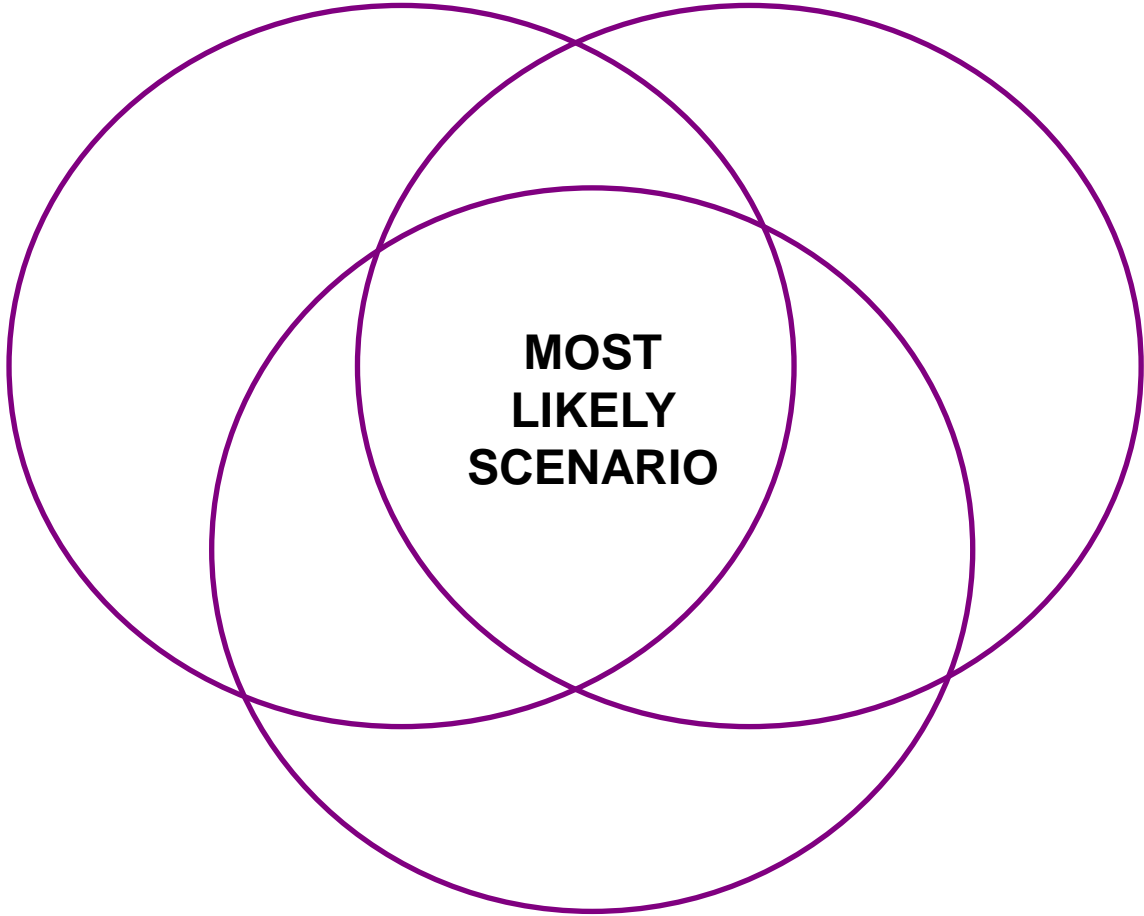
***What challenges did you encounter with using the product?***

***What helped you remember to use the product?***









**MOST  
LIKELY  
SCENARIO**

# What helps come closer to the truth?

- Deep respect for participants
- Making them feel like true partners in research
- Appreciation for what participants contribute to the study



# Data are being collected...

- Adherence to product use is good



- We had to raise the criterion of what was called poor adherence for IDI
- The proportion of PK discrepancies for daily product has been small, and only half of discrepancies were unexpected.



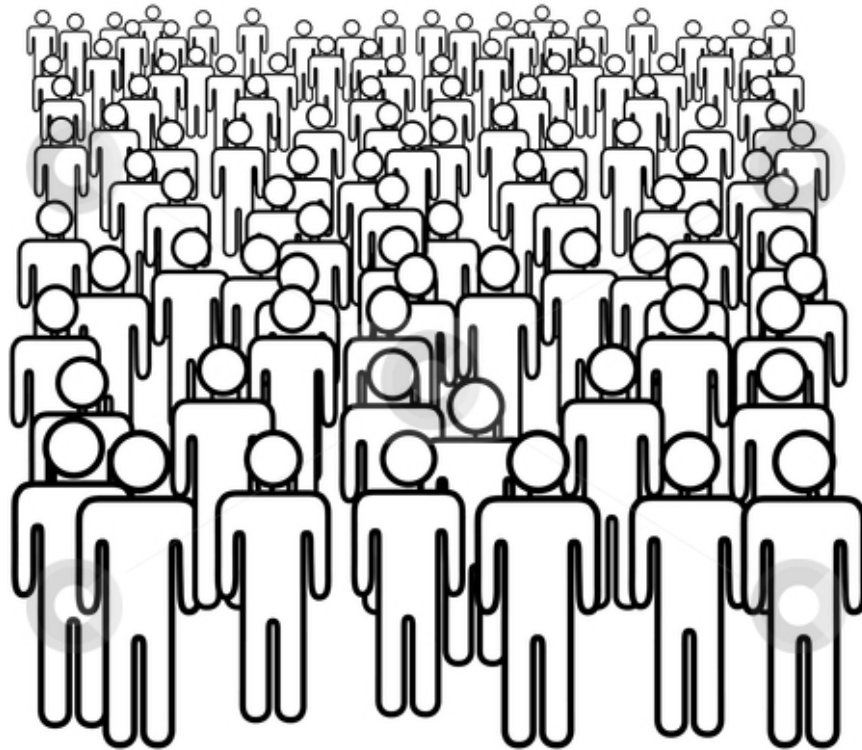
<b>Curtis Dolezal, Ph.D.</b>	<b>Ivan Balán, Ph.D.</b>	<b>Camagu Tuswa, PharmD</b>	<b>Rebecca Giguere, MPH</b>	<b>William Brown, III, Ph.D.</b>	<b>Titcha Ho, MA</b>	<b>Alex Carballo-Diéguez, Ph.D</b>
Data Analyst	Interventionist	RA/Xhosa Interviewer	Project Manager	Biomedical Informatician	RA/Thai Interviewer	Co-Investigator, Team Leader

Cheng-Shiun Leu, Ph.D. (Statistician); Alan Sheinfil, BA (RA)

**Thank you 017 team!**



**Thanks to the 195 men and  
transgender participants in 017**





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