



Partnerships for developing patient- centric, digital clinical measures

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About VivoSense

VivoSense has a 13-year history of developing, validating and deploying novel digital endpoints for their delivery in regulated clinical trials.

Development of novel endpoints

- Meaningful aspects of health identification
- Data strategy by therapeutic area and pipeline
- Algorithm development strategy

Portfolio analysis & DHT strategy

- Asset and protocol analysis and review
- Sensor review
- Measure review
- Data storage and analysis plan
- Team education
- Regulatory strategy

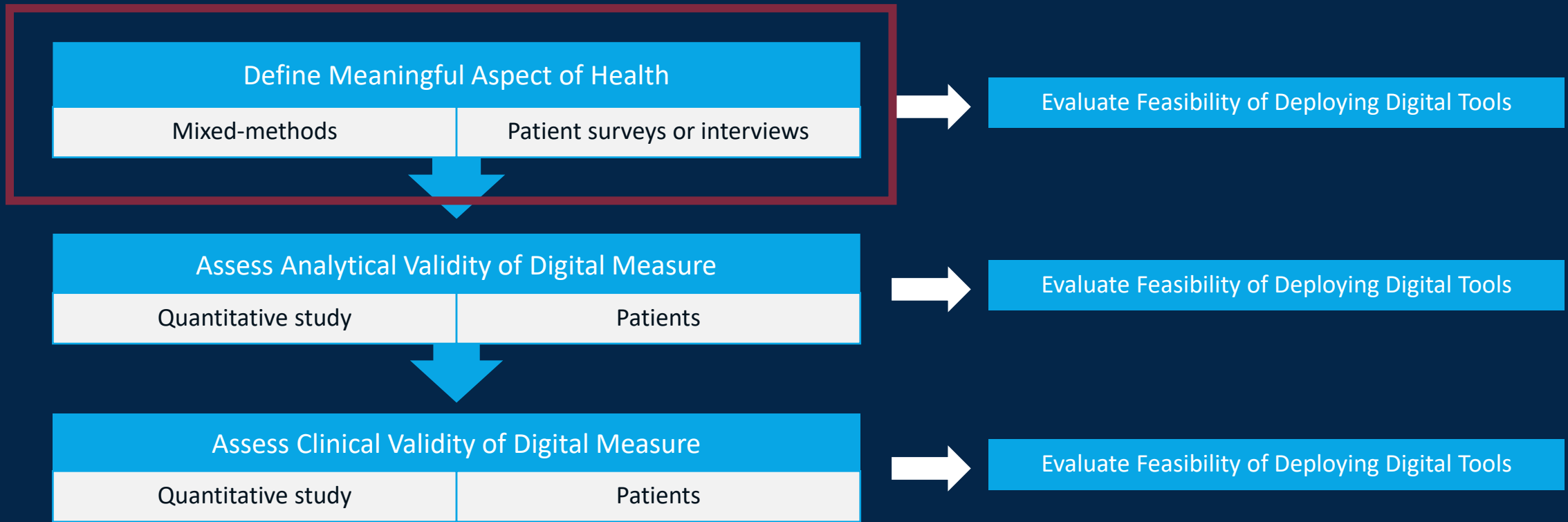
Prospective study design and analysis

- Sensor selection
- Measure selection
- Protocol design
- Data analysis and interpretation
- Regulatory strategy

Retrospective analysis

- Data cleaning
- Data analysis
- Data harmonization
- Data interpretation

VivoSense's Approach to Digital Measure Development



Continuous patient engagement key element of our process.

Digital Measures that Matter Framework

Meaningful Aspect of Health

Aspect of a disease that a patient a) does not want to become worse, b) wants to improve or c) wants to prevent

- *May be shared across some conditions and diseases*



CRITICAL PATIENT INPUT:

What do you wish that you could do, but your condition prevents you from doing it?

What part of your life is most frustratingly impacted by **your** condition?

Concept of Interest

Simplified or narrowed element that can be practically measured

- *Patients may have different symptoms*
- *Symptoms may vary over time*
- *Symptom relevance may vary over time*

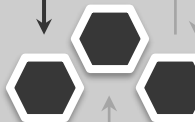


What are the symptoms that most impact your ability to do these activities?

Outcome to be measured

Specific measurable characteristics

- *Measures may be relevant to multiple symptoms*
- *Assess technical specifications of sensor and whether it is suitable for measuring this outcome in this population*

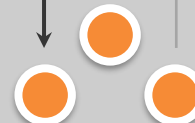


Do these measures make sense to you?

Endpoint

Health research only; Precisely defined, statistically analyzed variables

- *Sensors may support multiple measures & endpoints*



How much change do we need to see in this symptom before it really starts to make a positive difference in your life?

VivoSense's Approach to Systematically Determine MAH and Select Endpoint(s) across Patient Populations



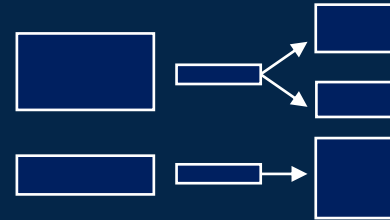
Evaluate existing evidence and identify gaps

- Literature review
- Patient advocacy groups
- [FDA-led PFDD Public Meetings](#)
- Large, multistakeholder, formal meetings



Design optimal study to fill gaps

- Qualitative research
 - 1 x 1 semi-structured interviews
 - Focus groups
- Quantitative survey
 - Population specific
- Mixed methods
 - Combined qualitative and quantitative insights



Develop conceptual framework

- **Conceptual Model**
 - Thematic analysis to identify common health experiences
 - Identify narrowed COIs
- **Measurement Model**
 - Identify candidate outcome measures
 - Identify candidate DHTs



Select endpoint(s)

- Prioritize endpoints based on
 - Degree of importance to patients
 - Is it a hallmark of the condition or a downstream effect?
 - Degree of importance to other stakeholders
 - Target of the drug
 - Sensitivity to change

Practical Example: Patient-informed digital endpoint selection

Results from VivoSense led **qualitative study**. The most burdensome symptoms spontaneously reported and probed through structured interviews are shown with supporting quotations from patients with declines in cognitive and physical functioning.



Patient undergoing treatment for cancer

“And now, I’m good for about two hours, and then I have to lay down. I’m tired. I cannot help you do anything else. I can’t do any dishes. I can’t watch the kids. I have to lay down. That’s just how it is.

Caregiver: "If she does a lot of things during the day and does not take **extended breaks, her mental fatigue impacts her physical ability to do things.**"

Patient and caregiver reports change in activity levels/resting patterns

What about activity/inactivity has changed or is difficult?

- Frequency
- Duration
- Intensity
- Definition of meaningful change

What symptoms impact activity/rest?

Practical Example: Patient-informed digital endpoint selection

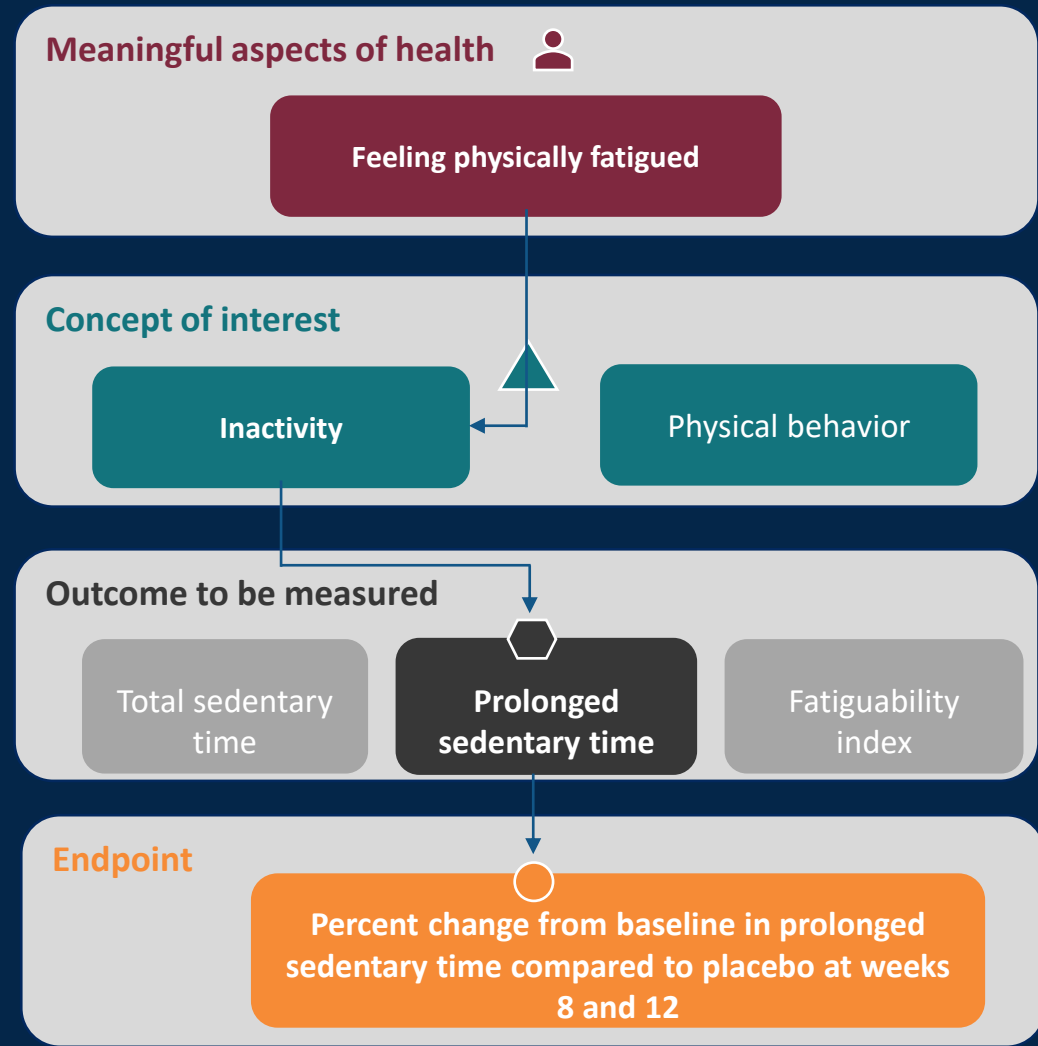
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Patient Centric - Meaningfulness

VOICE OF THE PATIENT REPORT

Rett Syndrome Externally-Led Patient-Focused Drug Development Meeting

Meeting Date: March 11, 2022



Breathing Irregularities are Meaningful to Parents

- Explore meaningful aspects of health as defined by caregivers of individuals with Rett syndrome
- - 13 Semi-structured in-depth interviews with caregivers



Meaningfulness

- “It's painful to watch her hold her breath involuntarily so long that she absolutely has a panicked look on her face. It's so difficult. It affects so much.”
- “She has indicated to us that she, you know through her communication devices, that it's hard for her to breathe and that she wishes breathing was more easy.”

Ubiquitousness

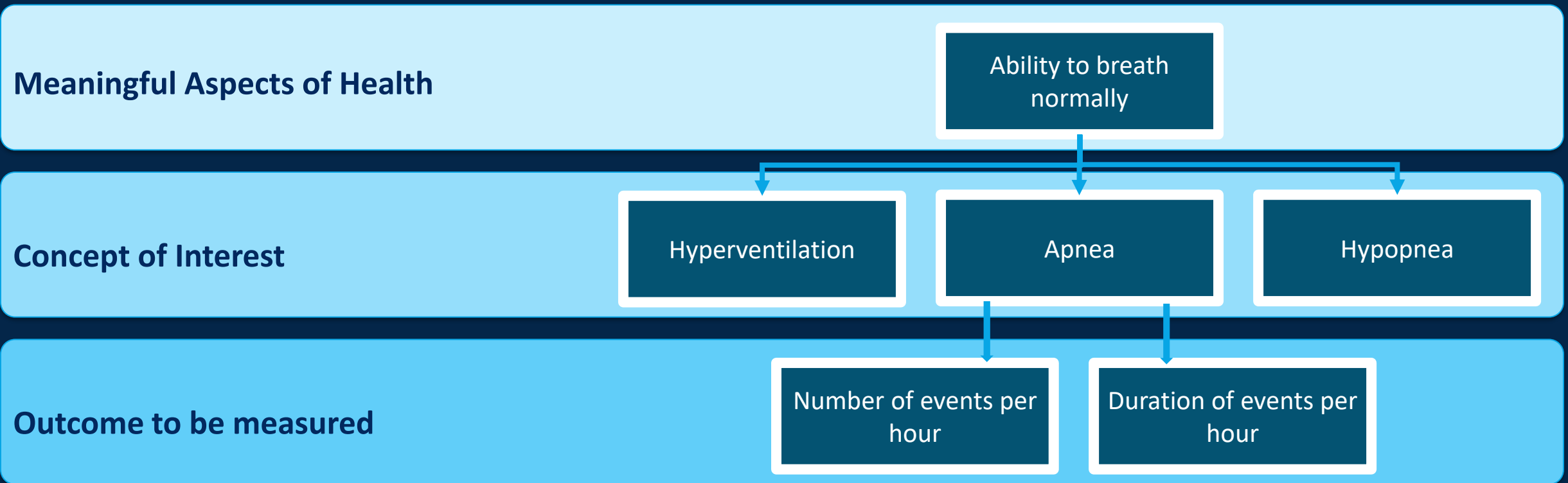
- “That's like [breathing problems], to me that's just her.”
- “I think she has to really focus on breathing. Can you imagine having to focus on your breathing? It doesn't just happen. You have to think about it. Like you have to think to do something that you don't do on an every-day basis.”

Emotional Relevance

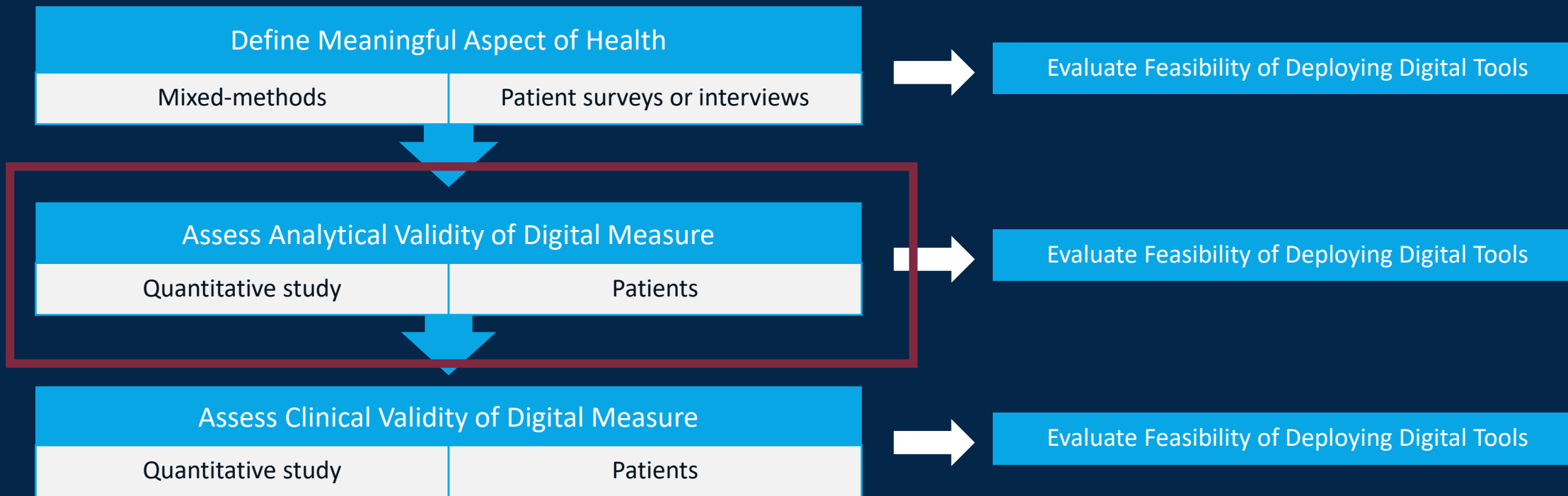
- “I think it scares her. I know that it **scares** her. Those breathing episodes really **scare** her. Can't imagine”
- “Sometimes its **scary** to watch because you see her lips turning a little darker purple and then she starts breathing again”

Patient Centric – Digital Measures that Matter

Breathing Irregularities

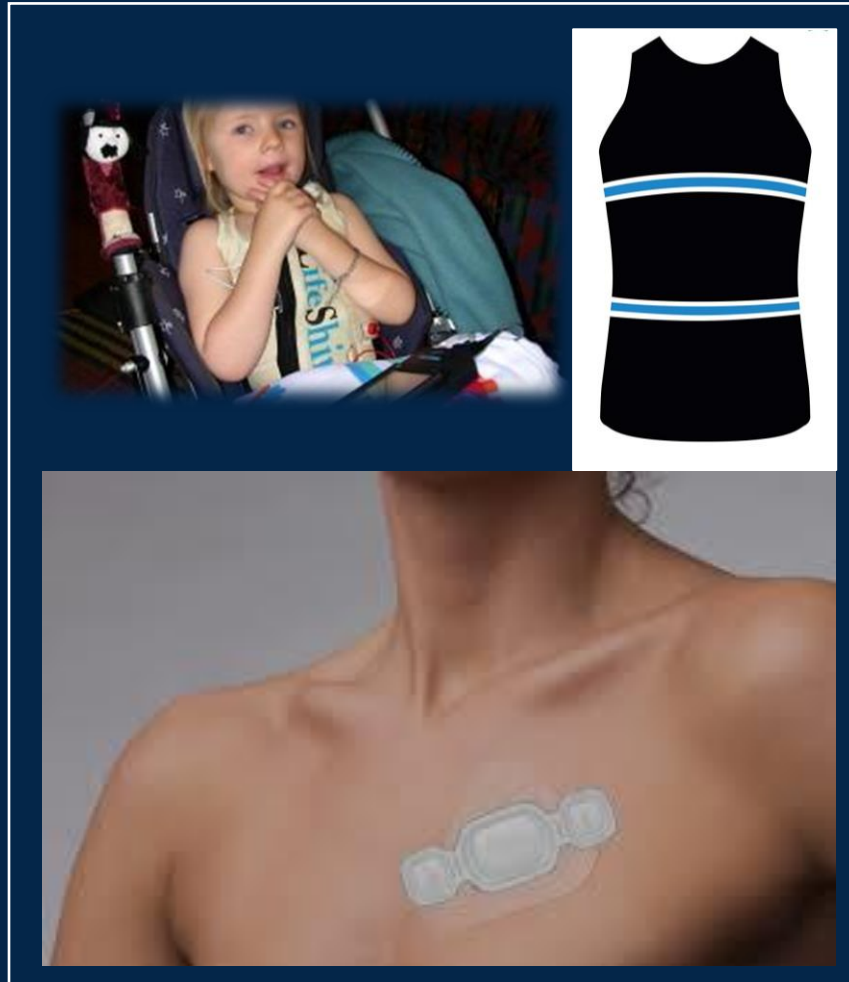


VivoSense's Approach to Digital Measure Development



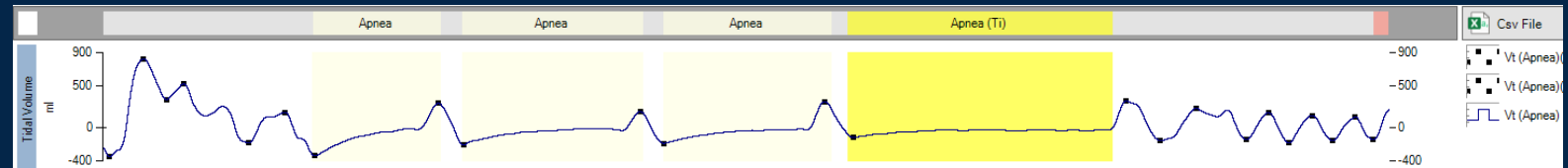
Continuous patient engagement key element of our process.

Measuring Breathing Irregularities in Rett Syndrome

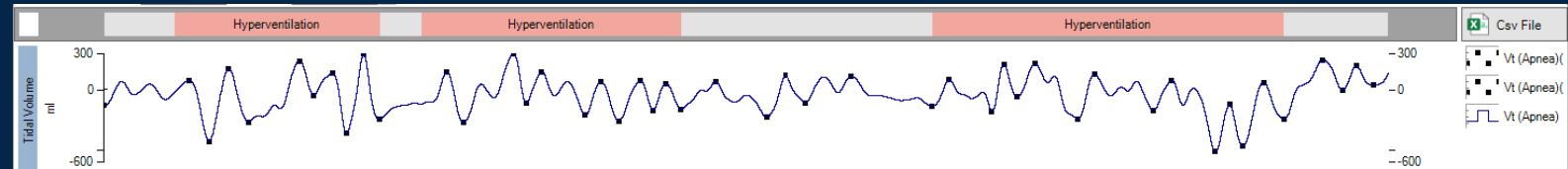


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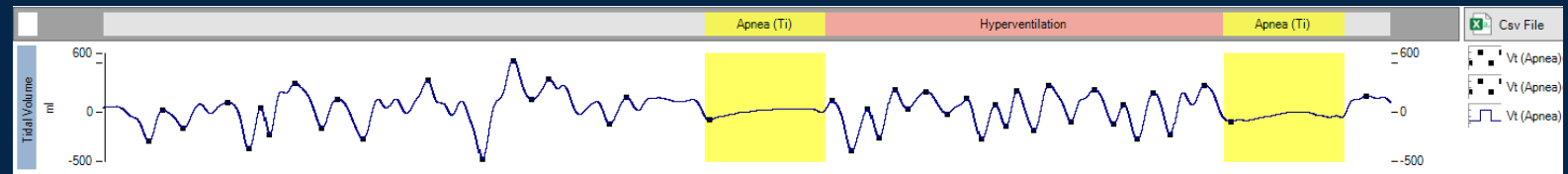
Apnea / breath holds



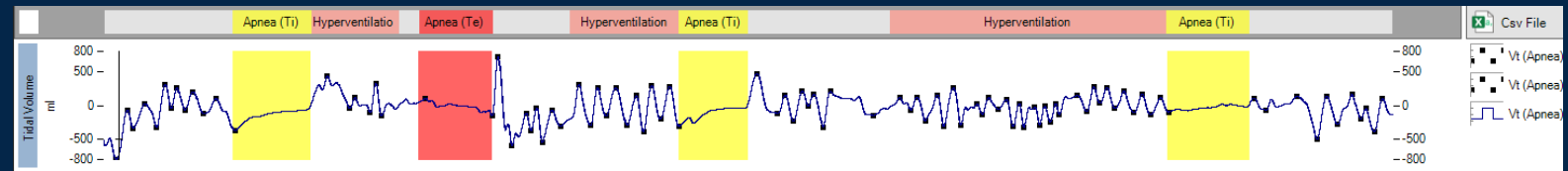
Hyperventilation



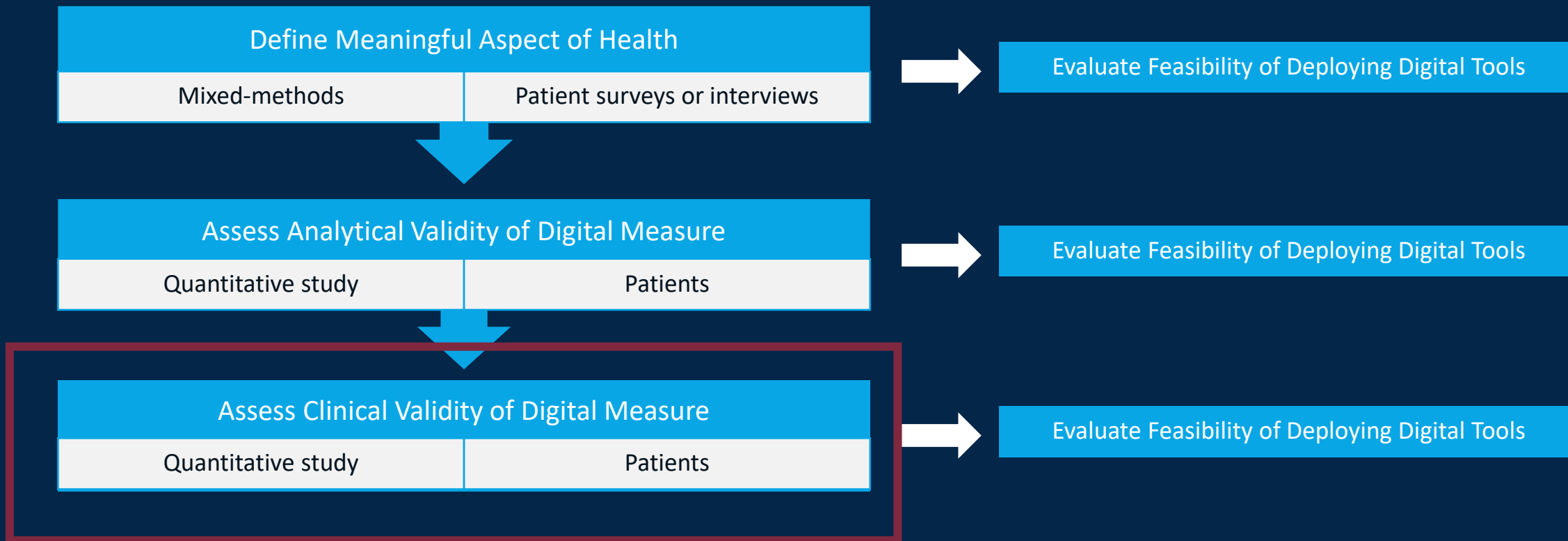
Hyperventilation & Apnea



Hyperventilation & Apnea



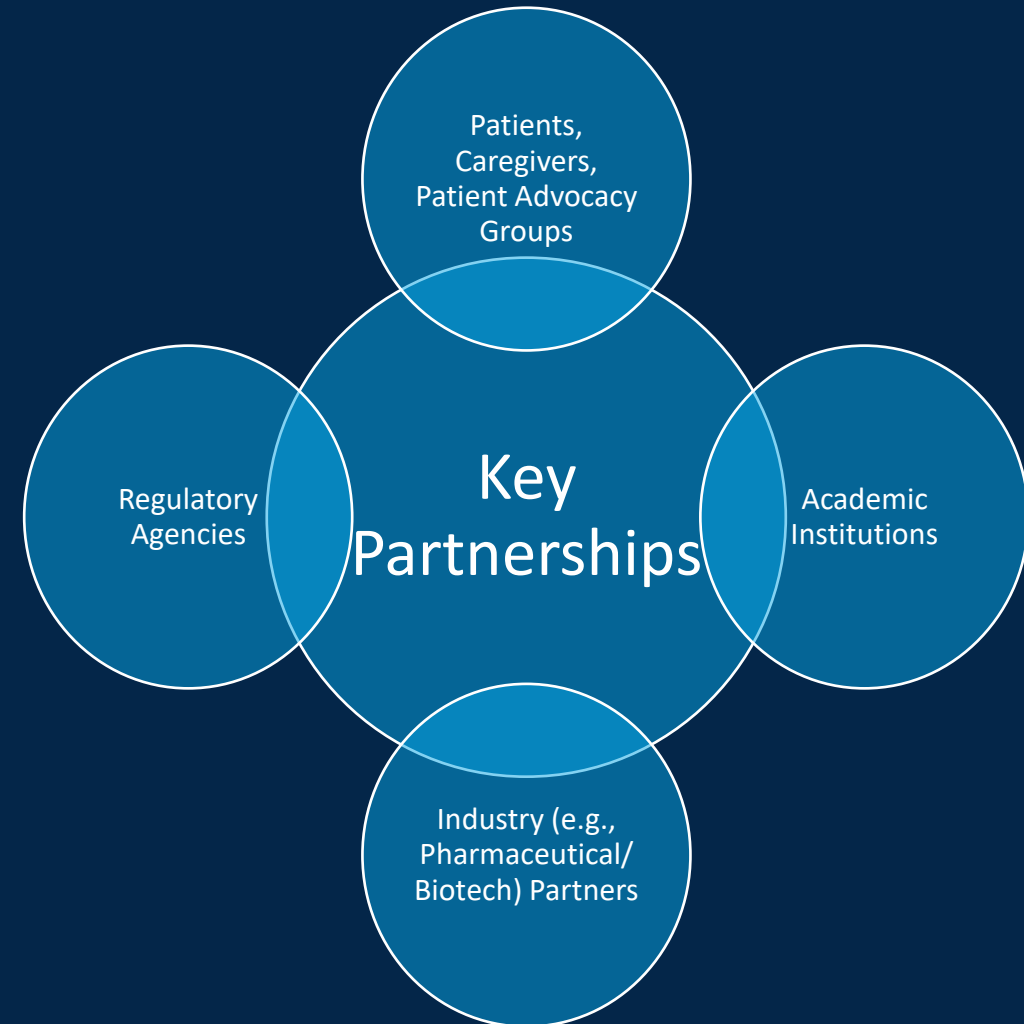
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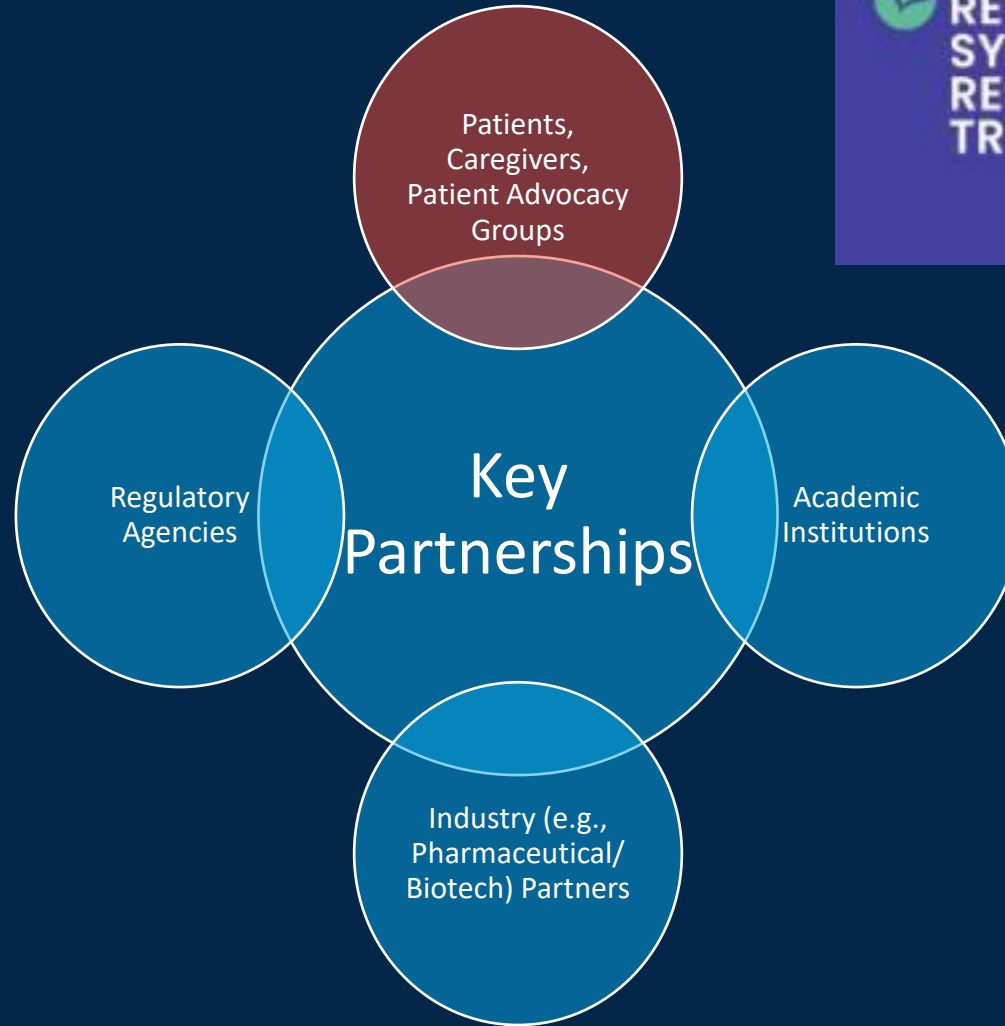
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Challenges Related to Establishing Evidence for Clinical Validity

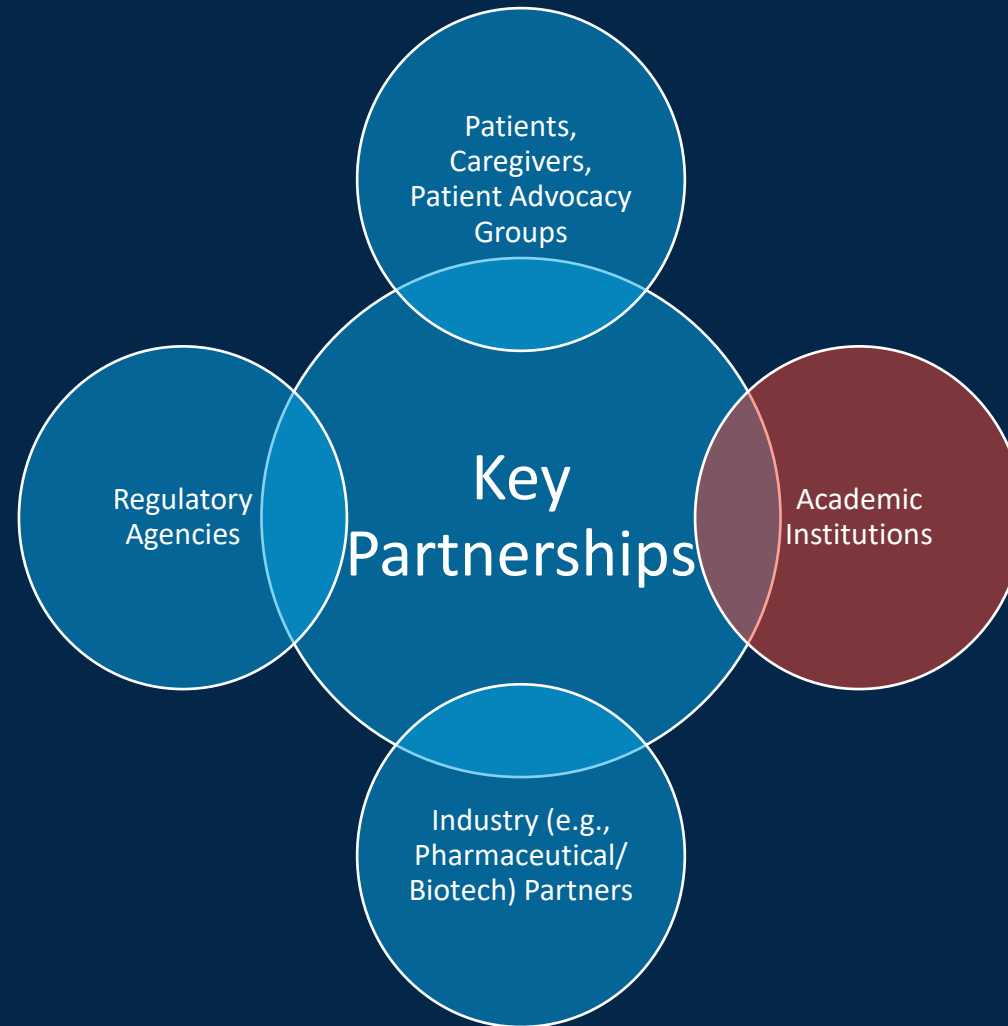
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2. Establishing clinical validity when incorporating outcome measures with known limitations
3. Recruitment, particularly in a rare disease population



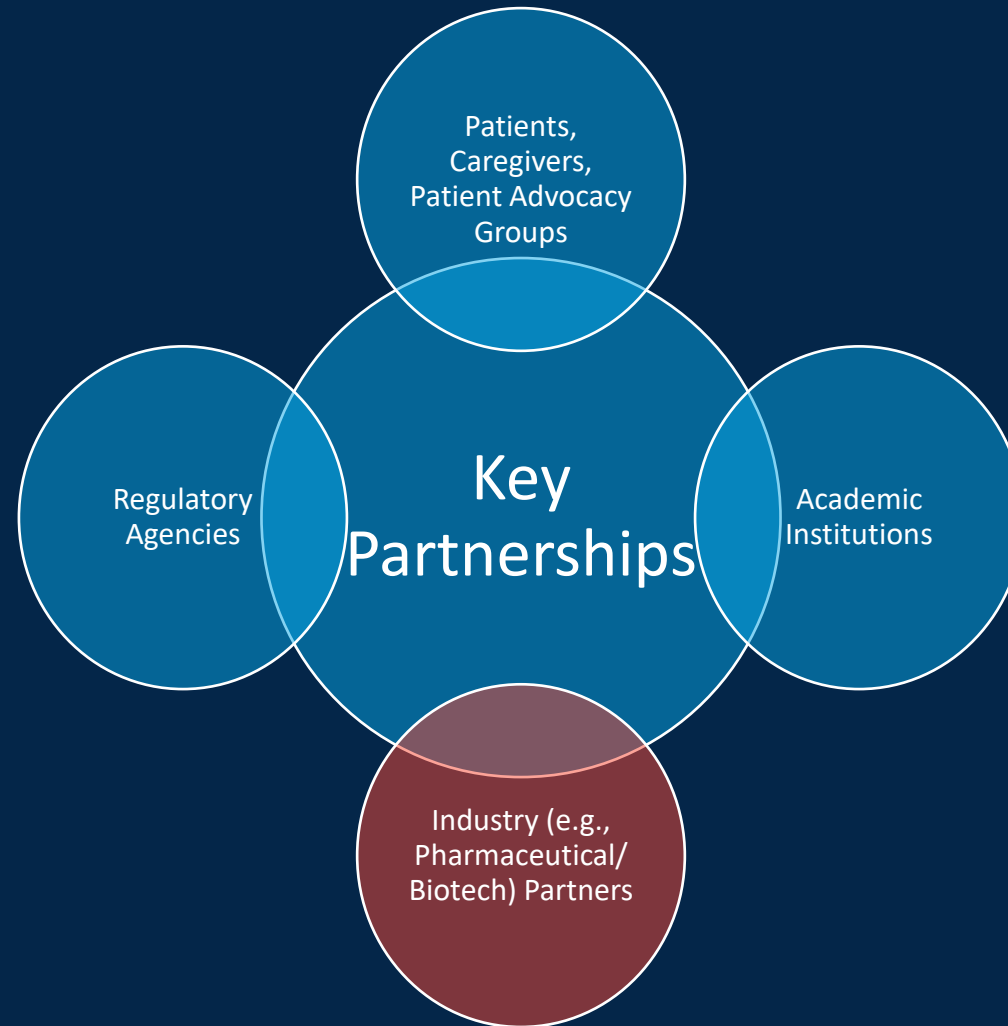
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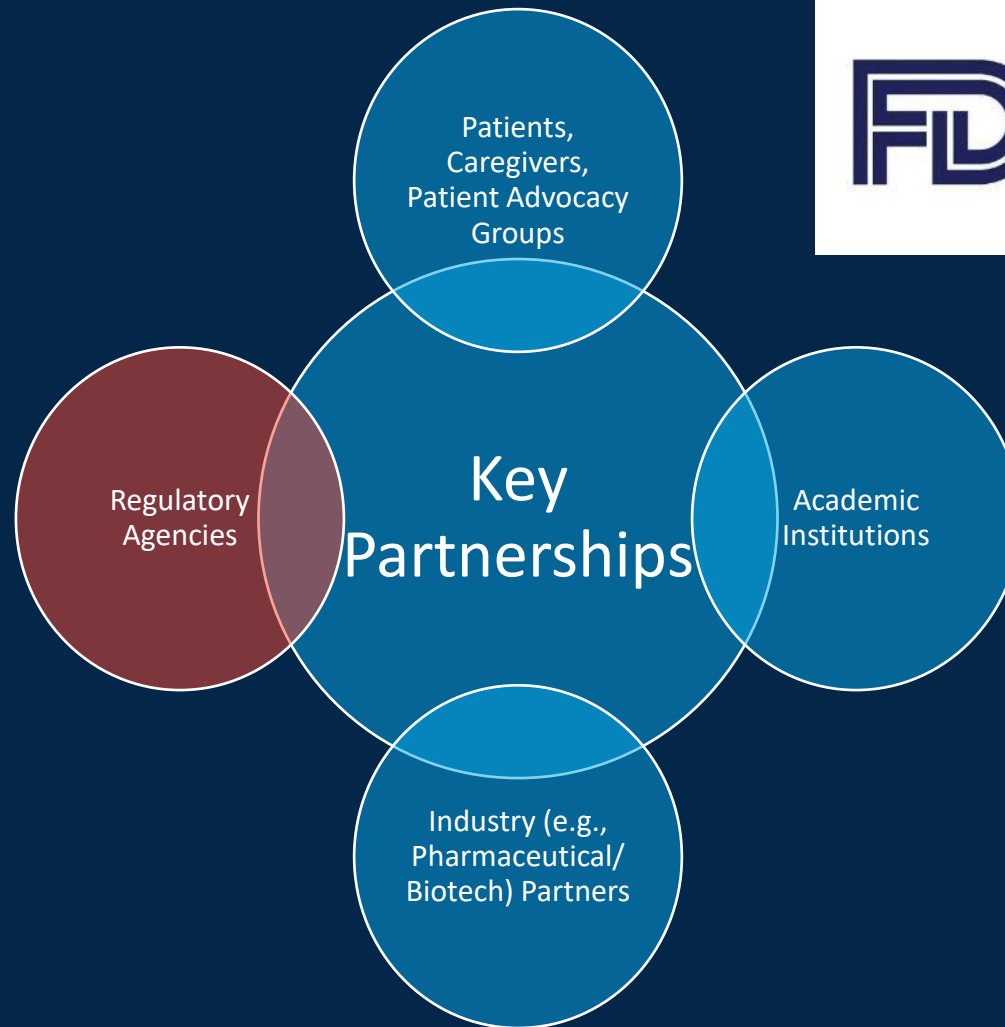
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Future Directions

- Partnerships between various stakeholders are essential for building evidence-base for clinical validity of digital health technologies
- Next step is to establish clinical validity
 - What is the next best step?

Thank you!
Questions?