Patient-centricity in digital evidence generation

HealthXL Masterclass

May 2023

Ieuan Clay & Robert Wright

VivoSense

Agenda

Each section consists of:

- Brief overview (5’)
- Discussion (10’)

Introduction

- Does evidence generation in clinical development need shaking up?
- What is driving growth in DHT usage in clinical trials?

Patient-centricity in evidence generation

- Why is patient-centricity so important?
- What are the benefits of co-creation?

Setting the stage

- What tools do we have for including patient input into evidence selection?
- Strategic considerations - How do we identify opportunities? What are our requirements?

Putting it into practice

- Robust methodologies for involving the patient voice

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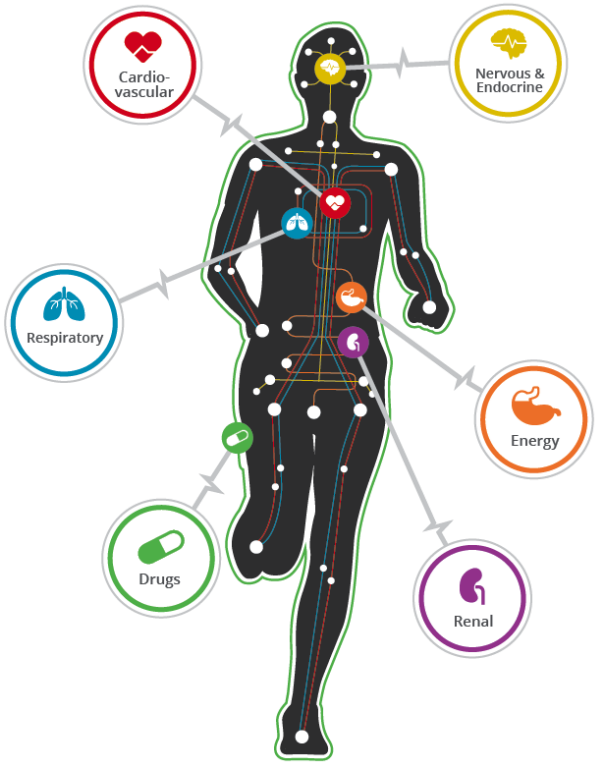
Introduction

- Does evidence generation in clinical development need shaking up?
- What is driving growth in DHT usage in clinical trials?

Chain of evidence

What is drug development trying to achieve?

Physiology



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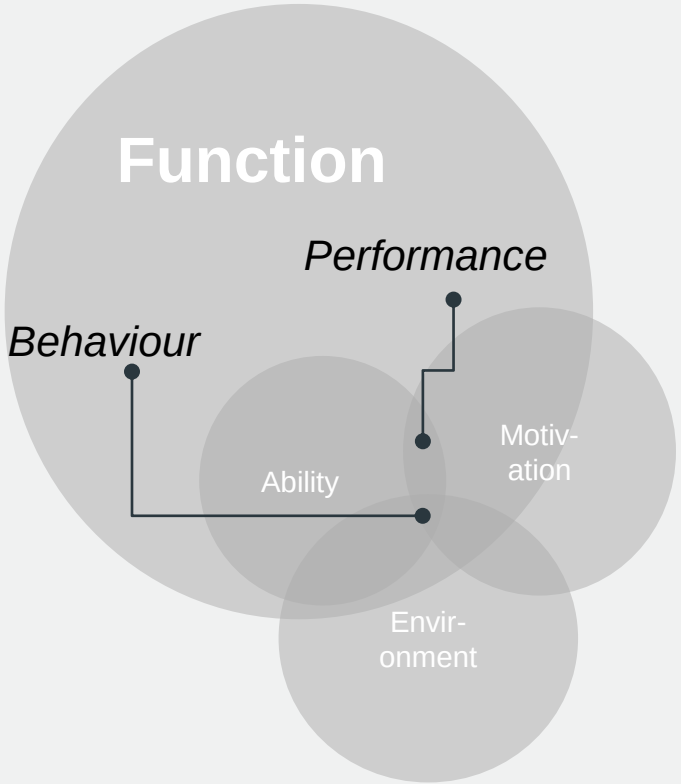
Function



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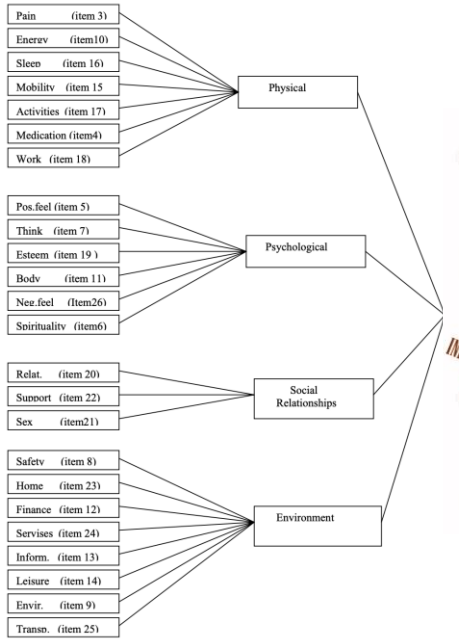
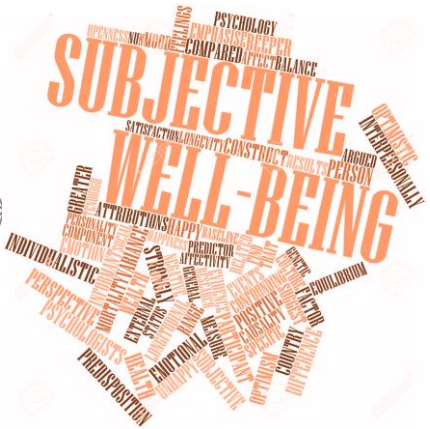
Perception





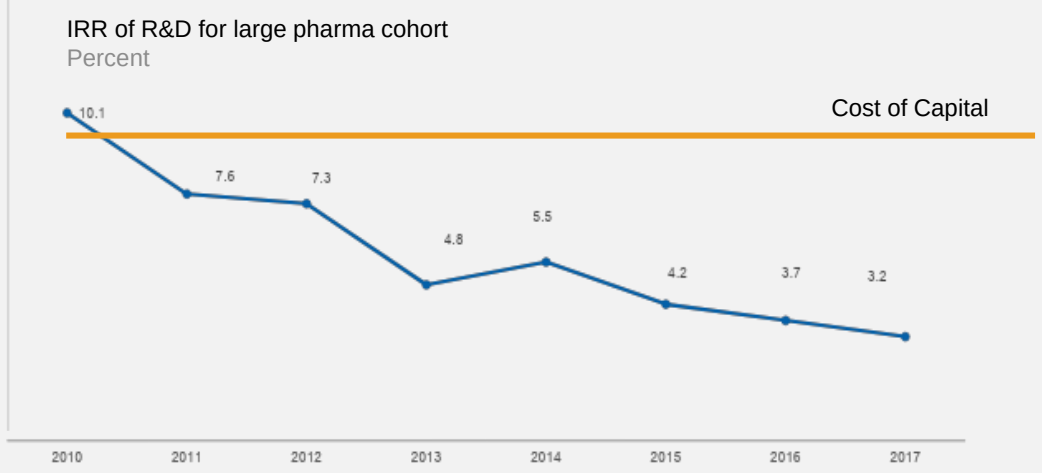
*Source: WHOQOL

See also: Sensors in clinical trials: Leveraging digital technology to improve testing of tomorrow's medicines – YouTube

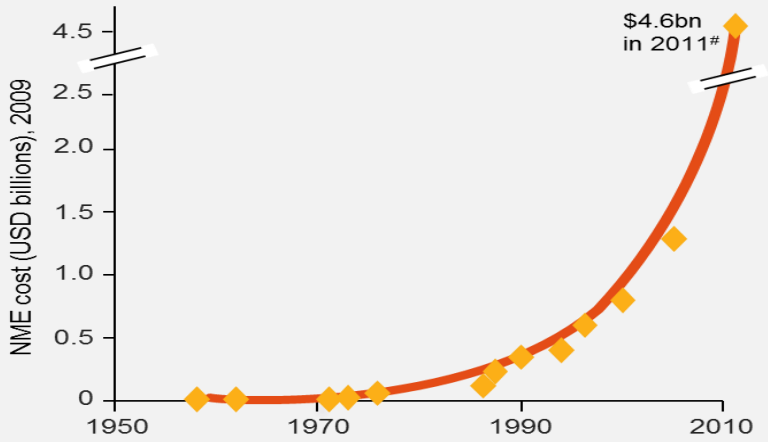
Why is clinical development in need of disruptive innovation?

Costs and complexity rising, ROI and motivation falling

ROI of R&D continues to fall ...[1]



... while costs of development continues to rise[2]



Over the past decade, clinical trial protocols have become increasingly complex and costly, especially in Phase III [3]

25% Number of planned study volunteer visits

34% Average cost per study volunteer per visit

70% Total number of procedures per protocol

When deciding to join a trial, aspects participants found very important are negatively impacted [4]

73% Types of medical procedures required

60% Physical location of study center

56% Length of participation

Sources:

1. Business Monitor International, Harvard Business Review and CMS (Centers for Medicare and Medicaid Services); Deloitte 2017 Status of Pharma R&D report
2. Adapted from: Munos, B. Nature Reviews Drug Discovery, 8:959, 2009
3. Getz, K. A. & Campo, R. A. New Benchmarks Characterizing Growth in Protocol Design Complexity. Ther. Innov. Regul. Sci. 52, 22–28 (2018)
4. Report from CISCRP. Perceptions & Insights Study Report on The Participation Decision-Making Process, (2017).

Concept

“I can get on with my own activities, I can easily forget I’m in a clinical trial”

Reality

“It’s quite lonely waiting for different medical workers to give me different tests, and take all these samples from me”

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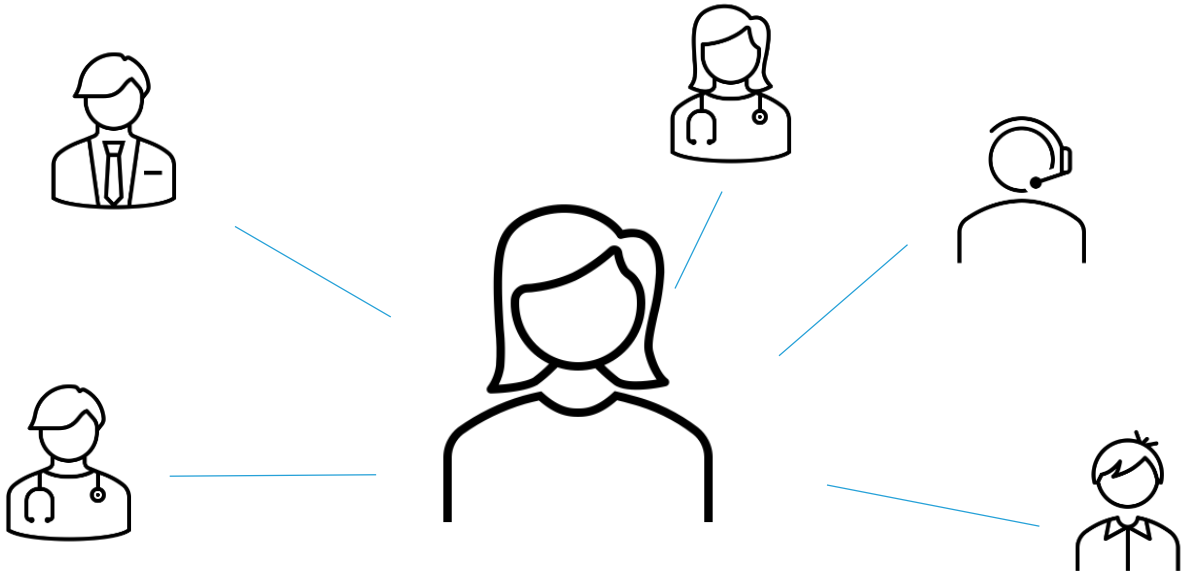
The patient at the centre



“Nothing about us, without us”

See also:

Nothing about us without us – Wikipedia; Patient centricity: 4 reasons why it's not just a buzz word (clinfo.eu); JMIR Human Factors - From Testers to Cocreators—the Value of and Approaches to Successful Patient Engagement in the Development of eHealth Solutions: Qualitative Expert Interview Study

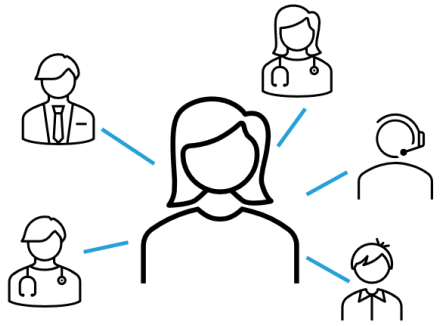
Discussion

- How do you see these trends affecting your company?
- What is driving growth in DHT usage in clinical trials?

Patient-centricity in evidence generation

- Why is patient-centricity so important?
- What are the benefits of co-creation?

Patient centricity is not just about ethics

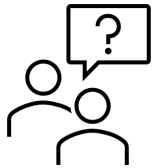


Helps structure and design trials in a way that is **mutually beneficial**

Co-creation means:

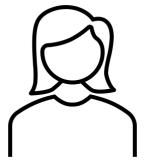
- **Bi-directionality** (not transactionality)
- **Clarity and trust**
- **Value for all stakeholders**

Demonstrating value to different stakeholders



…why should internal resource be invested into implementing this evidence tool?

…why should patients care if a new evidence tool shows that a drug “works”?



…why should a regulator (or anyone) care about this evidence tool?

Regulators and patient centricity: DHT Passive Monitoring COAs

8 DHT Passive Monitoring COAs submitted to FDA

Chronic Heart Failure (CHF)	DDT COA #000114: Chronic Heart Failure-Activity Monitor-Based Endpoint Measure	Daily physical activity	Patients with CHF	Letter of Intent-Accepted
Sarcopenia	DDT COA #000105: Actibelt® in Sarcopenia	Change in real-world walking speed	Patients with sarcopenia in recovery after surgical treatment of hip fracture	Letter of Intent-Accepted
Duchenne Muscular Dystrophy (DMD)	DDT COA #000103: ActiMyo®	Daily activity monitor	Children, adolescent, and adult patients (> 5 years old) with DMD	Letter of Intent-Accepted
Huntington's Disease	DDT COA #000129: Advanced Gait Analysis	Passive gait abnormality	Ambulatory adults with pathogenic genetic mutation and CAG expansion indicative of HD	**Letter of Intent-Not Accepted**
Parkinson's Disease	DDT COA #000142: Virtual Motor Exam for Parkinson's Disease, Part III Estimator (VME Part III)	Motor symptom severity	Adults diagnosed with Parkinson's Disease	**Letter of Intent-Not Accepted**
Musculoskeletal Pain	DDT COA #000102: Physical Activity Accelerometry Assessment for Analgesic Clinical Trials (PAACT)	Physical activity	Non-cognitively impaired adults with a diagnosis of osteoarthritis of the knee	Letter of Intent-Accepted
Multiple Sclerosis	DDT COA #000106: Actibelt® in MS	Change in real-world walking speed	Patients with MS	Letter of Intent-Accepted
Atopic dermatitis	DDT COA #000120: Scratch Sensor	Itch intensity and persistence	Patients > 2 years with atopic dermatitis	Letter of Intent-Accepted

Regulators and patient centricity: DHT Passive Monitoring COAs

8 DHT Passive Monitoring COAs submitted to FDA (likely already out of date!)

Chronic Heart Failure (CHF)	DDT COA #000114: Chronic Heart Failure-Activity Monitor-Based Endpoint Measure	Daily physical activity	Patients with CHF	Letter of Intent-Accepted
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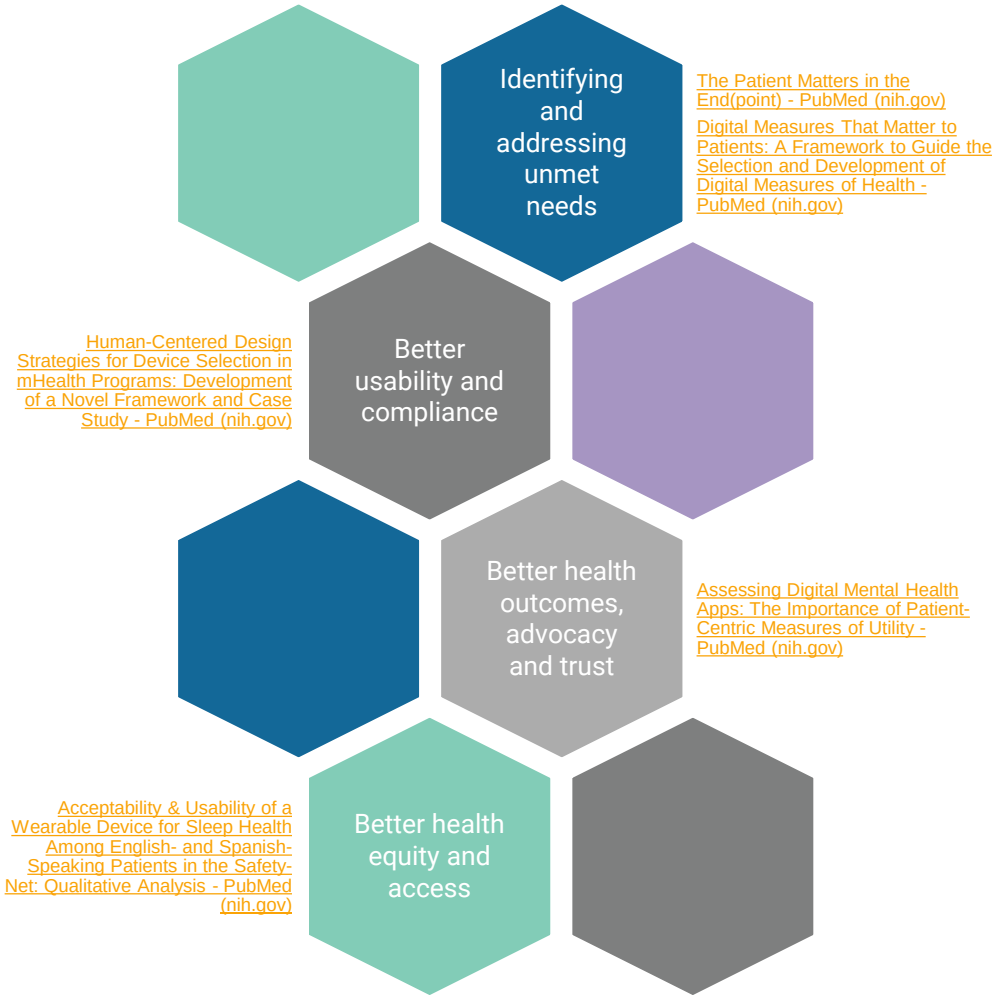
Multiple Sclerosis	DDT COA #000106: Actibelt® in MS	Change in rea walking speed		
Atopic dermatitis	DDT COA #000120: Scratch Sensor	Itch intensity and persistence	Patients > 2 years wit	-

2 Rejected at LOI Stage due to lack of data to support meaningfulness to patients

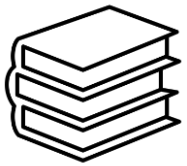
Further benefits to co-creation in evidence generation

Value throughout the evidence generation process



Adapted from: JMIR Human Factors - From Testers to Cocreators—the Value of and Approaches to Successful Patient Engagement in the Development of eHealth Solutions: Qualitative Expert Interview Study

Other relevant literature



- The Patient Matters in the End(point) - PubMed (nih.gov)
- Patient and public involvement in research: from tokenistic box ticking to valued team members - PubMed (nih.gov)
- Digital approaches to enhancing community engagement in clinical trials | npj Digital Medicine (nature.com)
- “Nothing about us without us”—patient partnership in medical conferences | The BMJ
- JMIR Human Factors - From Testers to Cocreators—the Value of and Approaches to Successful Patient Engagement in the Development of eHealth Solutions: Qualitative Expert Interview Study
- Accelerating Adoption of Patient-Facing Technologies in Clinical Trials: A Pharmaceutical Industry Perspective on Opportunities and Challenges - PubMed (nih.gov)

Discussion

- Do you see other benefits?

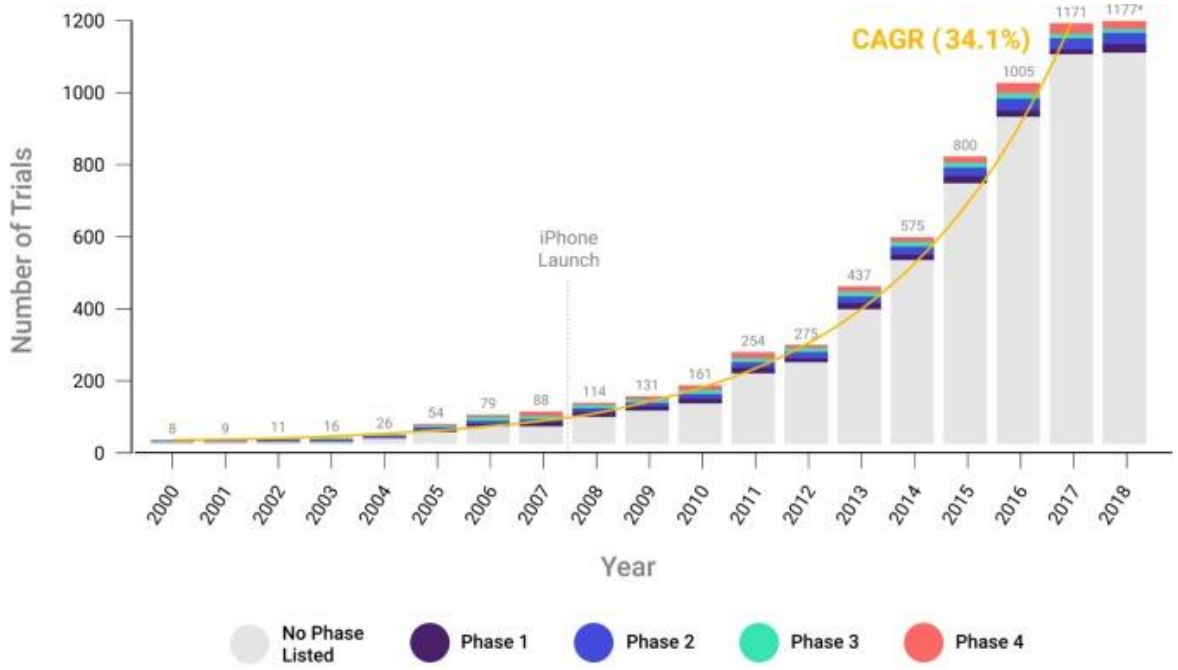
Setting the stage

What frameworks do we have for including patient input into evidence selection?

Strategic considerations - How do we identify opportunities? What are our requirements?

Pharmaceutical companies investing into connected digital products and digital measures

The **use of connected digital products in clinical trials has grown exponentially** in recent years (see figure), powered by combining the skills and experience of healthtech vendors and pharmaceutical companies.



Clinical trials using connected sensor products by study start year and phase. Each bar represents the total number of clinical trials started annually that include a connected digital product, segmented by phase.

Source: [Quantifying the use of connected digital products in clinical research | npj Digital Medicine (nature.com)]

Measures that Matter

Involving patients in selecting evidence generation tools

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Viewpoint - Review Article

Digital Measures That Matter to Patients: A Framework to Guide the Selection and Development of Digital Measures of Health

Manta C.[a,b] · Patrick-Lake B.[a,c] · Goldsack J.C.[a]

Author affiliations

Corresponding Author

Keywords: Digital medicine Patient engagement Digital measures

Digit Biomark 2020;4:69–77

https://doi.org/10.1159/000509725

How do we ensure that selected tools or newly developed tools provide meaningful insights and create value for all stakeholders?

- Does the evidence have face validity for patients?
- Do all stakeholder agree that this would be a good basis for defining success?
- Are regulators convinced that your decision criteria provide value?
- Etc.

“Measures that Matter to patients” ensures that specific measurement concepts are rooted in meaningful aspects of health

Digital Measures That Matter to Patients: A Framework to Guide the Selection and Development of Digital Measures of Health - FullText - Digital Biomarkers 2020, Vol. 4, No. 3 - Karger Publishers

Measuring what matters

CRITICAL PATIENT INPUT:

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*

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*

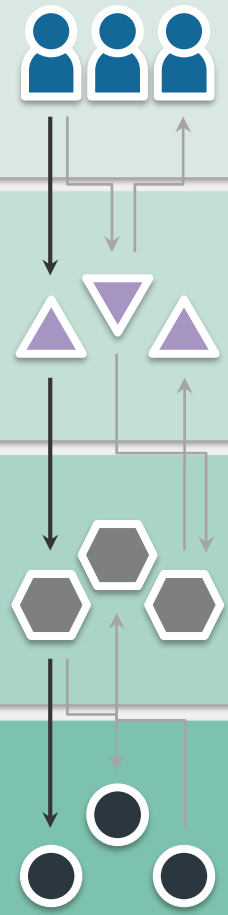
Do these measures make sense to you?

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?



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Measuring what matters: worked example

Meaningful Aspect of Health

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?

Ability to Perform Ambulatory Activities

Concept of Interest

Critical Patient Input:

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

Walking Capacity

Lower Extremity Balance

Lower Extremity Strength

Outcome to be measured

Critical Patient Input:

- Do these measures make sense to you?

Steps per day

- Rheumatoid Arthritis[29]

Duration of walking bouts per day

- Parkinson's Disease[30]
- Huntington Disease[30]

Frequency of walking bouts per week

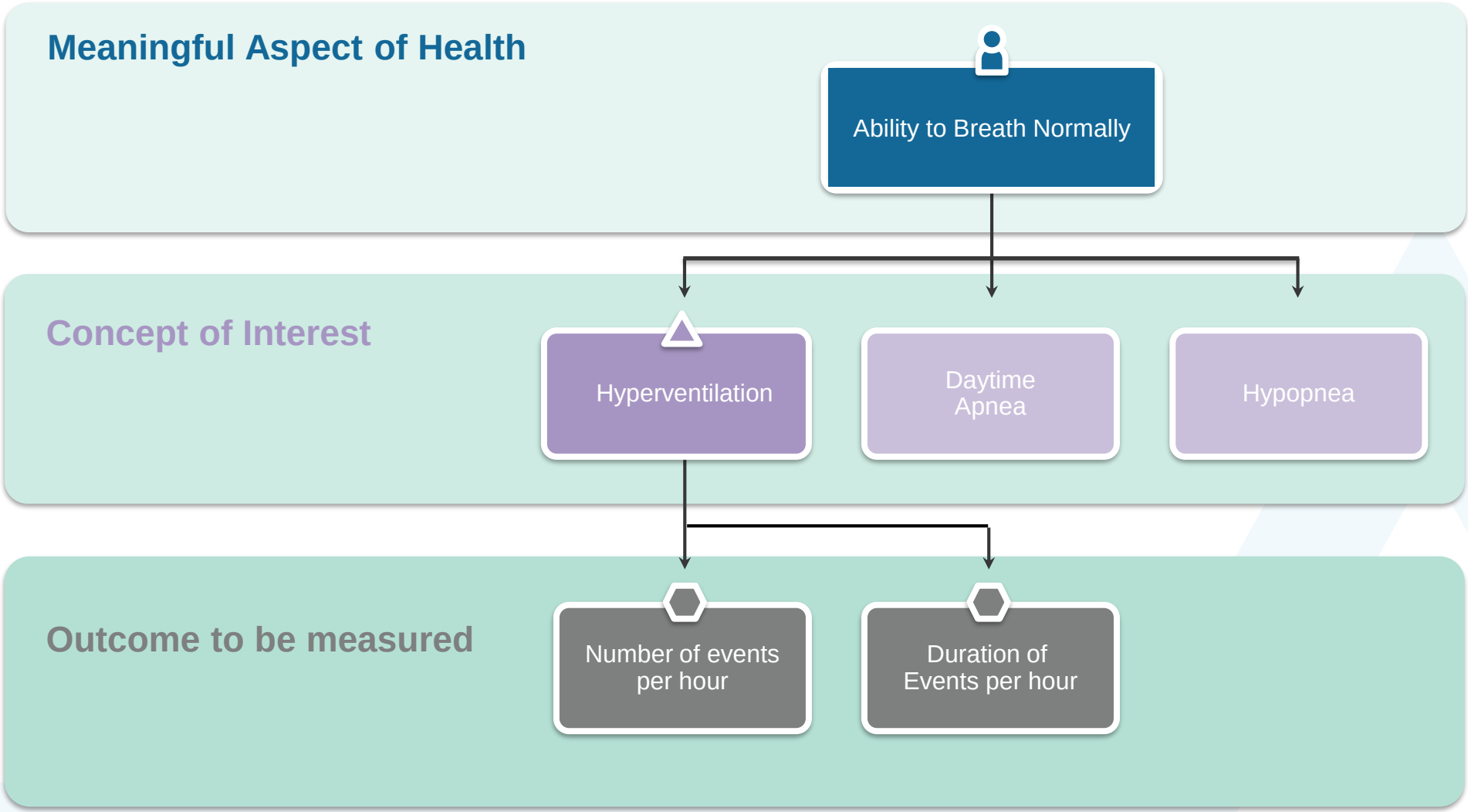
- Huntington Disease[32]

Digital Measures That Matter to Patients: A Framework to Guide the Selection and Development of Digital Measures of Health - FullText - Digital Biomarkers 2020, Vol. 4, No. 3 - Karger Publishers

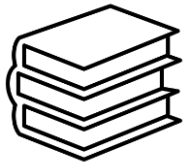
Unmet need in Rett syndrome

Rett Syndrome Patient-Focused Drug Development Meeting (rettpfdd.org)
About Rett Syndrome, Symptoms, Causes, Diagnosis and Treatments (reverserett.org)
VivoSense Announces Expanded Collaboration with RSRT

Measures that Matter in Rett Syndrome



Other frameworks and relevant literature



- It's not about the capture, it's about what we can learn": a qualitative study of experts' opinions and experiences regarding the use of wearable sensors to measure gait and physical activity - PubMed (nih.gov)
- Digital approaches to enhancing community engagement in clinical trials | npj Digital Medicine (nature.com)
- JMIR Human Factors - A Human-Centered Design Methodology to Enhance the Usability, Human Factors, and User Experience of Connected Health Systems: A Three-Phase Methodology
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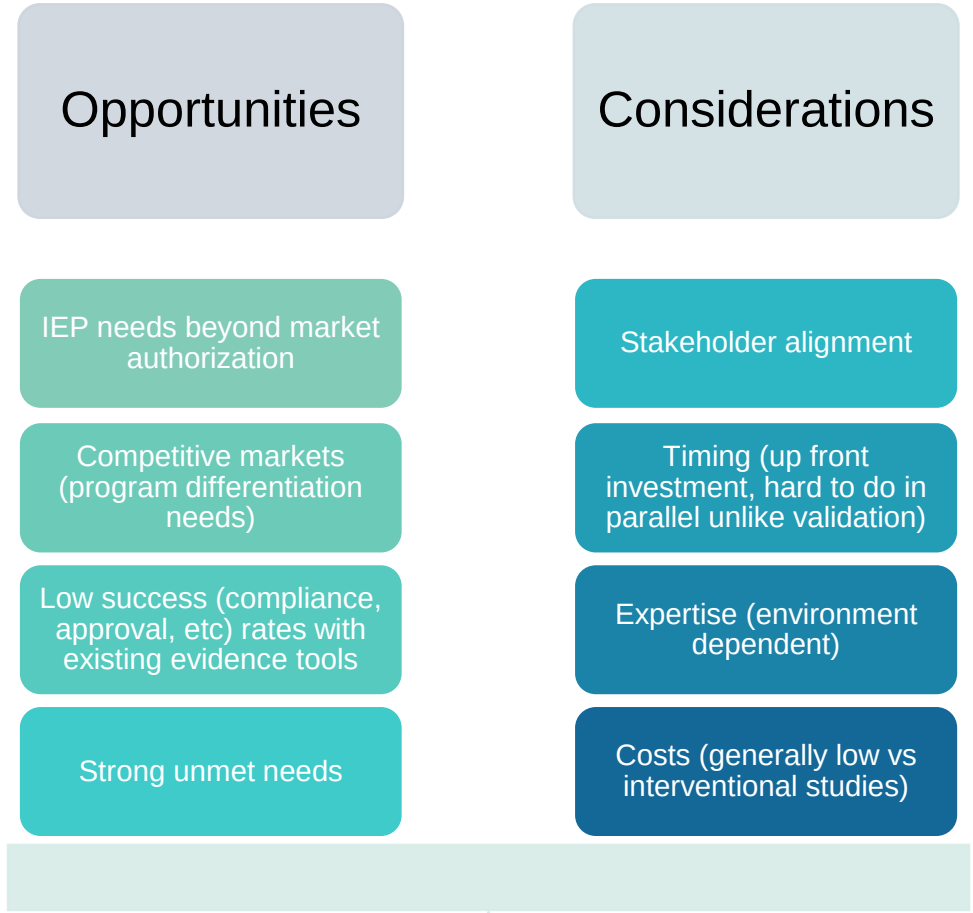
- JMIR Human Factors - Understanding the Subjective Experience of Long-term Remote Measurement Technology Use for Symptom Tracking in People With Depression: Multisite Longitudinal Qualitative Analysis

Strategic considerations



Worked example

Atopic dermatitis (Eczema)

&

Discussion

Strategic considerations:
How do we identify opportunities?
What are our requirements?

Patients working with government and regulatory authorities - The ‘more than skin deep’ initiative

The Challenge:

More than 33 million Americans of all ages experience **eczema**, an inflammatory skin disease that results in rashes and patches of itchy, red skin, often leading to diminished quality of life and significant emotional burden in addition to pain, physical discomfort, and sleep disturbance for affected individuals. Despite the high prevalence of this condition, there are **limited** topical and systemic FDA-approved **therapies** for eczema.

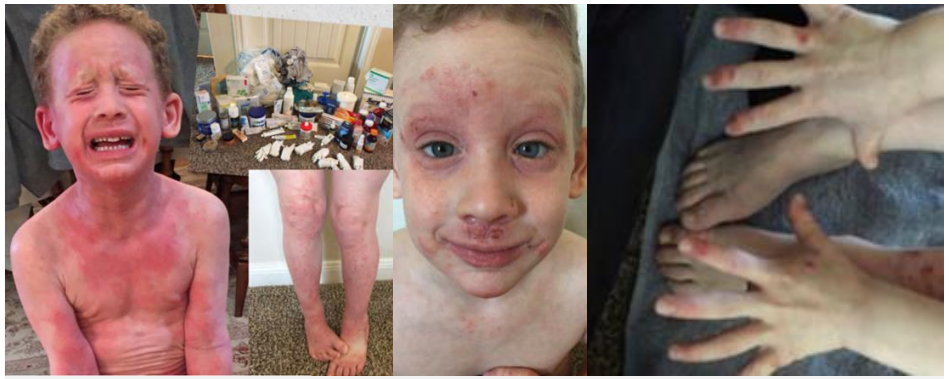
The Approach:

The Patient-focused drug discovery **(PFDD) initiative** is part of **FDA’s commitments** to hear directly from patients and caregivers about burdens of their condition and its treatment. This includes helping to define unmet need, trial design, measurement selection and more.

The Result:

Key learnings:

- Patients with **chronic** and other serious **diseases** are experts on what it’s like to live with their condition
- Patients’ “chief complaints” may not be factored explicitly into drug development plans, including measures of drug benefit planned in trials



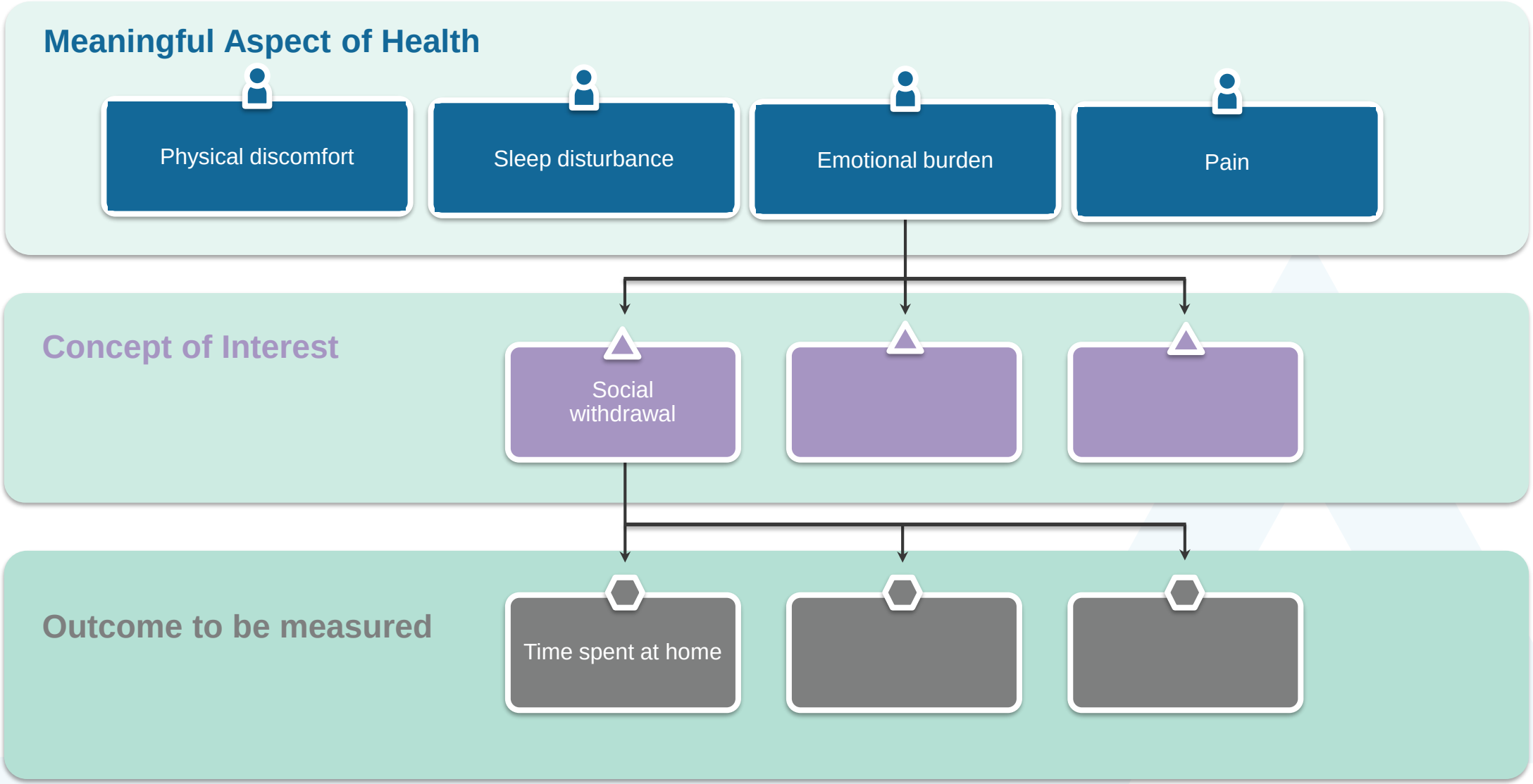
“Throughout his short life, Cooper has been on 10 topical steroids, 2 topical antibiotics, 2 nonsteroidal creams, 10 different allergy and asthma medications, multiple eye creams and drops, allergy immunotherapy via shots and drops, oral steroids, multiple oral antibiotics, several bath additives, multiple rounds of allergy testing, and various creams, supplements, probiotics, and vitamins. And that is just what we can remember. He has seen numerous dermatologists, allergists, immunologists, pediatricians, and alternative medicine doctors.”

Angela Fox, Cooper’s mom shares her son’s struggle about the burden of Eczema and lack of patient driven development of novel medicine

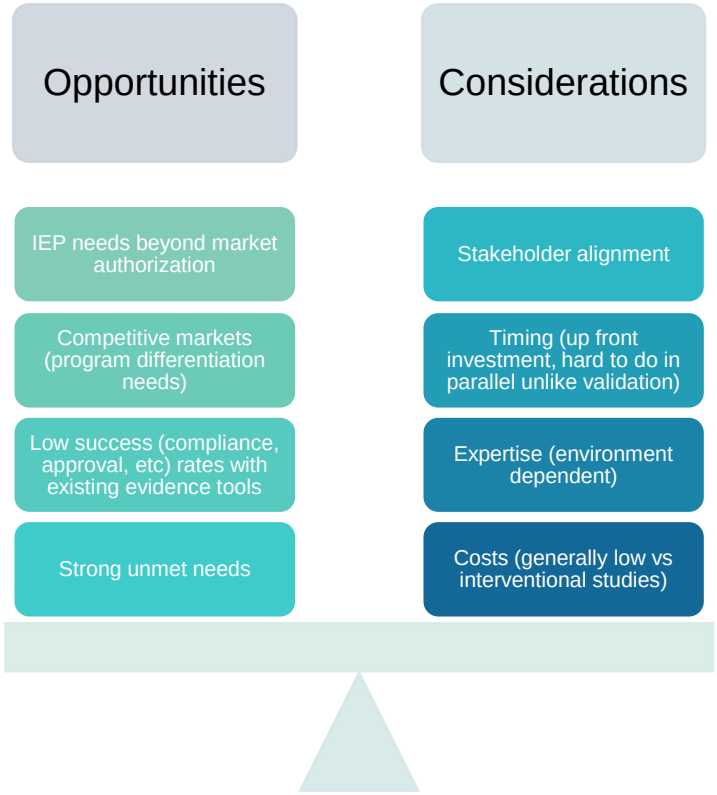
A total of 60 PFDD meetings have been held on a wide range of rare and prevalent medical conditions along with FDA now has a variety of patient-focused programs that **inform decision-making** across the agency

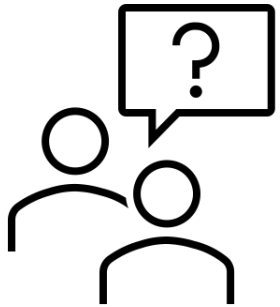
Source: http://www.morethanskindeep-eczema.org/ https://playbook.dimesociety.org/tools/glossary/#patient-engagement
Learn more about FDA’s goals for PFDD: https://www.fda.gov/drugs/development-approval-process-drugs/cder-patient-focused-drug-development

Worked example in Atopic Dermatitis: group exercise



Strategic considerations





Can you think of anything else?
What are opportunities or hurdles that you see?

Putting it into practice

Robust methodologies for involving the patient voice

(Formal) Methods for gaining patient input

PFDD workshops

FDA-led Patient-Focused Drug Development (PFDD) Public Meetings | FDA

Large, multistakeholder, formal meetings

Used to listen to patient (and caregiver) experience, **understand the lived experience, define needs and provide direction** to the research community

Qualitative

JMIR Human Factors - Understanding the Subjective Experience of Long-term Remote Measurement Technology Use for Symptom Tracking in People With Depression: Multisite Longitudinal Qualitative Analysis

IRB-approved interview-based studies, with individual or group input

Researchers use a guided interview to **gain insights into defined topics**

Input continues until “concept saturation” is reached

Quantitative

Chapter 13 Methods for Survey Studies - Handbook of eHealth Evaluation: An Evidence-based Approach - NCBI Bookshelf (nih.gov)

IRB-approved, large(r) scale, survey-based

Used to **determine generalizability** of qualitative results (e.g. 25% of all patients reported XYZ, which rose to 80% when only low SES patients were considered)

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Key terms

Formative

- Qualitative, Quantitative and mixed methods
  Employed **before or during** research programs **to refine** and improve that program
  Usage in evidence generation: understanding needs, acceptance, accessibility, etc
  See: Formative research: What, why, and how (gfmer.ch) / JMIR Formative Research

Summative

- Qualitative, Quantitative and mixed methods
  Employed **after** a research program is complete to **rigorously assess** conclusions
  Usage in evidence generation: demonstrating equitability, efficacy, etc
  See: Formative vs. summative research. Quick and dirty versus slow and… | by Nick Dauchot | UX Collective (uxdesign.cc)

Informal (ok… less formal) methods

Advocacy

- Parent Project Muscular Dystrophy (PPMD) | Fighting to End Duchenne (parentprojectmd.org)
- Rett Syndrome Research Trust: Singularly focused on a cure for Rett syndrome (reverserett.org)
- DBSA - Depression and Bipolar Support Alliance (dbsalliance.org)
- About Us | Cancer Support Community

Patient committees

Mobilise-D

- Information on the Patient and Public Involvement and Engagement Structures within Mobilise-D – Mobilise-D

Patient representation

Diane Stephenson

- The Qualification of an Enrichment Biomarker for Clinical Trials Targeting Early Stages of Parkinson's Disease - PubMed (nih.gov)

Steve Bourke

- From Testers to Cocreators-the Value of and Approaches to Successful Patient Engagement in the Development of eHealth Solutions: Qualitative Expert Interview Study - PubMed (nih.gov)

Discussion

- How are you implementing this in your company?
- Do you have examples from your work?

Ieuan Clay, Director Science
ieuan.clay@vivosense.com

Robert Wright, Senior Research Scientist
robert.wright@vivosense.com

Please reach out if you have any questions

Thank you

linkedin.com/company/vivosense
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