Understanding Priorities for the Use of Digital Health Technologies to Support Clinical Trials for Drug Development and Review

Duke-Margolis Center for Health Policy | Virtual Public Meeting

March 28-29, 2023

Duke | MARGOLIS CENTER *for* Health Policy

Welcome and Overview | Day 1

Mark McClellan

Director, Duke-Margolis Center for Health Policy

Statement of Independence

The Robert J. Margolis, MD, Center for Health Policy is part of Duke University, and as such it honors the tradition of academic independence on the part of its faculty and scholars. Neither Duke nor the Margolis Center take partisan positions, but the individual members are free to speak their minds and express their opinions regarding important issues.

For more details on relevant institutional policies, please refer to the Duke Faculty Handbook, including the Code of Conduct and other policies and procedures. In addition, regarding positions on legislation and advocacy, Duke University policies are available at http://publicaffairs.duke.edu/government.

Disclaimer

Funding for this workshop was made possible in part by a cooperative agreement from the U.S. Food and Drug Administration. The views expressed in written workshop materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services nor does mention of trade names, commercial practices, or organizations imply endorsements by the U.S. Government.

Meeting Agenda (Day 1)

1:00 pm Welcome and Opening Remarks

1:15 pm Session 1: Perspectives on Use of DHTs in Clinical Trials

2:50 pm Break

3:00 pm Session 2: Impact of DHTs on Clinical Trial Accessibility and Diversity

4:05 pm Concluding Remarks

4:15 pm Adjournment

All times listed in ET

Meeting Agenda (Day 2)

1:00 pm Welcome and Overview

1:10 pm Session 3: Actigraphy in Clinical Trials to Support Drug Development

2:30 pm Break

2:40 pm Session 4: Use of Other Sensor-Based DHTs in Clinical Trials for Drug Development

3:40 pm Break

3:50 pm Session 5: Key Priorities for the Advancement and Integration of DHTs into Clinical Trials for Drug Development

4:35 pm Closing Remarks

4:45 pm Adjournment

Opening Remarks from FDA

Jacqueline Corrigan-Curay

Center for Drug Evaluation and Research

U.S. Food and Drug Administration

Session 1: Perspectives on Use of DHTs in Clinical Trials

1:15 pm – 2:50 pm EST

Leonard Sacks

Associate Director of Clinical Methodology

Office of Medical Policy, Center for Drug Evaluation and Research

US Food and Drug Administration

Use of Digital Health Technologies in Clinical Trials

Leonard Sacks
Office of Medical Policy
CDER
FDA

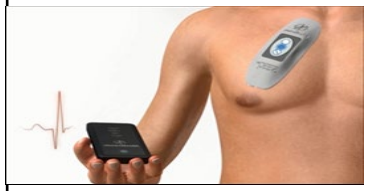
New technologies, new capabilities

- We all recognize the profound impact that new technologies have on our ability to gather clinical data
- Computers that formerly occupied entire buildings are now condensed into our cellphones with extraordinary capacities for data storage and analysis
- DHTs provide opportunities to quantify clinical features more precisely
- To transmit data from patients wherever they are

What are DHTs?

A digital health technology (DHT) is a system that uses computing platforms, connectivity, software, and/or sensors, for healthcare and related uses. Examples include but are not limited to portable sensors and/or mobile applications (mobile apps) such as activity trackers and smart watches.

- Our focus today is on a subset of these which are portable instruments that can be worn by patients or placed in their environments
- More specifically we will be discussing those that involve the use of sensors to measure clinical features

Transducer	Output	Clinical feature to be measured	Data processing	Clinical DHT
Galvanometer	voltage/ current/ impedance	Heart rhythm	Algorithm	
Accelerometer	Voltage/ current/ impedance	Walking, Scratching Sleep Tremor	Algorithm	
Photoelectric sensor	Voltage/ current/ impedance	Blood oxygen saturation	Algorithm	
Electrochemical sensor	Voltage/ current/ impedance	Blood glucose	Algorithm/ Calibration Curves	
Thermocouple	Voltage/ current/ impedance	Temperature	Algorithm	

As far as biosensors go, they measure clinical features

Discrete events

- Steps
- Breaths
- Coughs
- Heart beats
- Seizures
- Tremor
- FEV1

Continuous/frequent readings

- Glucose
- pO_2
- Temperature
- ECG
- Blood pressure

Importance in clinical management

- DHTs are already in widespread clinical use e.g., continuous glucose monitors, ambulatory blood pressure monitors, mobile cardiac monitors
- Their clinical value is appreciated in making more comprehensive clinical assessments, and allowing us to monitor patients from their homes rather than at clinic visits

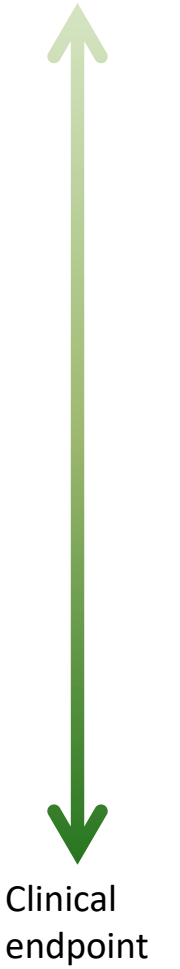
Importance in drug development

- Clearly these advantages can also be applied to clinical trials
- DHTs may allow us to modernize the performance of trials, improve trial efficiencies
- Measurement in challenging populations e.g., neonates, patients with dementia
- Measure new clinical characteristics such as stamina, gait stability, tremor
- They may provide more convenient and/or precise ways to measure existing features e.g., sleep, exercise, blood pressure
- They may allow measurement of rare events which were difficult to capture e.g., arrhythmias, seizures, apneic spells

Novel types of data that continuous recording by biosensors can provide

Opportunities	Examples
Richer data instead of snapshots	- average steps per day v.s. 6MWD, - continuous glucose monitoring v.s. HBA1C
Ability to detect rare events	- arrhythmias, seizures, apneic spells
Data from patients who cannot report	- scratching in infants with atopic dermatitis, sleep in patients with dementia
Dose response information	- on/off effects in Parkinson's
New types of measurement	- Accelerometer measurements of gait stability that may predict falls - Measurements of coughing, sneezing, tremor - Behavior patterns in dementia or depression

Summary of endpoints in registrational trials 2015-2020



Type of endpoint	NDAs N=218	Examples of endpoints measured
Chemistry	30%	HBA1c, pregnancy test, GFR
Hematology		Severe neutropenia
Pathology		Increase/decrease of parabasal cells; biopsy proven acute rejection, clearing of anterior chamber cells
Microbiology		Sustained virological response, plasma viral load, conversion to negative sputum
Imaging +/- (survival, clinical signs)	22%	Bone mineral density; vertebral fractures, spleen volume, progression free survival
Physiological/ functional measurement	7%	6 minute walk, normal sinus rhythm, FEV1, sleep studies
Clinical event /clinical sign	22%	Death, hospitalization, MACE, MS relapse
CRO/PRO	32%	Toronto western spasmodic torticollis rating scale, Hamilton depression rating scale, Rheumatology scale ankylosing spondylitis scale, psoriasis severity index, seizures, sleep, prostate symptom score

Types of endpoints where DHTs may play a role

- Clinical laboratory measurements
  - Continuous glucose monitoring, pulse oximetry
- Physiological measurements
  - Heart rate and rhythm, breathing and lung function, seizures, syncope, temperature, weight
- Performance assays
  - Stamina, strength, coordination, abnormal movements, sleep, cognition

Challenges in replacing tried and tested methods with new methods

- Why has the uptake of DHTs in trials lagged behind?
- A world of uncharted territory
- Reluctance to move from tried and tested measures to those with potential advantages and potential risks and uncertainties- applies to regulators and to industry
- How to recognize improvements on existing “gold standards”
- How to recognize disadvantages

Scientific data

- Scientific data are key to confidence in new measurements
- How do new measurements stack up against existing benchmarks of drug activity?
- How robust are they in measuring known drug effects?
- What other approaches should we be taking to bolster our confidence in DHTs?

Working towards a common goal

- FDAs commitment to modernize clinical trials, incorporate technological and scientific advances and potentially address the enormous costs and burden of drug development
- Interest from Congress, industry and others in the community to enhance efficiencies in drug development
- Interests of new stakeholders, engineers, and DHT manufacturers in supporting clinical trials
- Patients seeking more convenient ways to participate in the research enterprise

PDUFA VII DHT Commitments

IV.C. ENHANCING USE OF DIGITAL HEALTH TECHNOLOGIES TO SUPPORT DRUG DEVELOPMENT AND REVIEW

- C.1 Develop Framework
- C.2 Establish Committee
- C.3 Convene 5 public meetings
- C.4 Identify 3 demonstration projects
- C.5 Develop Guidance
- C.6 Develop Prescription Drug User-Related Software (PDURS) Guidance
- C.7 Expand review capabilities
- C.8 Enhance IT capabilities to review DHT-generated data

https://www.fda.gov/media/151712/download


Framework for the Use of Digital Health Technologies in Drug and Biological Product Development
INNOVATION PREDICTABILITY ACCESS

Electronic Systems, Electronic Records, and Electronic Signatures in Clinical Investigations Questions and Answers

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Published March 16, 2023

Submit Comments by 05/15/2023

DHTs for Drug Development Webpage

FDA U.S. FOOD & DRUG ADMINISTRATION

← Home / Science & Research / Science and Research Special Topics / Digital Health Technologies (DHTs) for Drug Development

Digital Health Technologies (DHTs) for Drug Development

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Science and Research Special Topics

- Digital Health Technologies (DHTs) for Drug Development
- Advancing Regulatory Science
- Clinical Trials and Human Subject Protection
- Critical Path Initiative
- Minority Health and Health Equity Research and Collaboration
- Nanotechnology Programs at FDA

Digital health technologies (DHTs) offer many potential benefits in the development of medical products, including drugs. Advances in DHTs, including electronic sensors, computing platforms and information technology, provide new opportunities to obtain clinical trial data directly from patients. Portable DHTs that may be worn, implanted, ingested, or placed in the environment allow real-time collection of data from trial participants in their homes or at locations remote from clinical trial sites. Potential advantages of these DHTs include the ability to:

- make continuous or frequent measurements of clinical features
- record or measure novel clinical features that could not be captured during traditional study visits
- decentralize clinical trial activities by obtaining clinical data from study participants remotely

FDA is committed to supporting the use of DHTs in clinical drug development and has developed a comprehensive program to engage with stakeholders in this important scientific area.

The Prescription Drug User Fee Act VII has outlined several activities related to DHTs for drug development and review, which FDA has committed to undertake. These activities include:

Content current as of:
03/15/2023

Regulated Product(s)
Drugs

www.fda.gov/digitalhealth

Tracking Submissions Containing DHT Data
Form 1571 and Form 356H

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

INVESTIGATIONAL NEW DRUG APPLICATION (IND)
(Title 21, Code of Federal Regulations (CFR) Part 312)

12B. Does the submission contain: Digital Health Technology (DHT) data or a proposal to collect DHT data?

☐ Yes ☐ No

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

APPLICATION TO MARKET A NEW OR ABBREVIATED NEW DRUG OR BIOLOGIC FOR HUMAN USE
(Title 21, Code of Federal Regulatio

25. Does the submission contain:

Only Pediatric data?	Digital Health Technology (DHT) data?
☐ Yes ☐ No	☐ Yes ☐ No

Digital Health Technologies for Remote Data Acquisition in Clinical Investigations

Guidance for Industry, Investigators, and Other Stakeholders

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Published Dec 2021

Method of measurement versus Endpoints

- Validation and verification are technological assessments. They address how well the **technology** measures the clinical feature of interest.

- Justification of an endpoint (or a clinical outcome assessment) is a clinical issue. It addresses how well the **clinical feature** of interest represents a meaningful response to treatment (nothing to do with the DHT).

Formulating a meaningful clinical endpoint

What is being measured?	Steps
What is the time window of observation?	4 weeks
What is the formula for the response in each patient?	Change from week 1 to week 4 in average daily step count

Is the DHT suitable for use in the trial?

(Operational issues)

- Ugly or elegant?
- Easy to put on ?
- Easy to operate?
- Comfortable to wear for the required time period?
- Battery life?
- Syncing data?
- “Bring your own” approach?

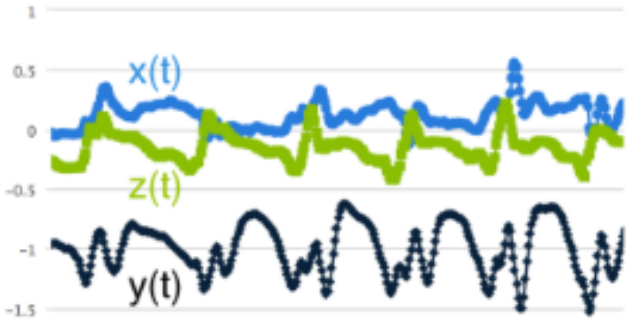
Uses for DHTs

- Enrollment screening and enrichment
  - Help us quantify disease severity, functional status at enrollment
- Safety monitoring
  - Identification of rare AEs, real time access to safety data
- Dose effect
  - Visualize response over dosing interval
- Endpoints
  - Most compelling in superiority studies. Non-inferiority studies may be challenging to interpret

Actigraphy

total acceleration
measured by the phone

(x(t), y(t), z(t))



Actigraphy

- We are generally not aware of how much we exercise, sleep or sit, which is one of the reasons actigraphy apps are so popular
- These data may be equally informative for clinical trials in a number of neuromuscular, cardiorespiratory and rheumatologic diseases where we rely on assessments of patient functionality
- For some of these diseases, such as heart failure, pulmonary hypertension, muscular dystrophy, we have relied on the 6 minute walk distance (6MWD) to measure the effects of treatment
  - This is a clumsy test confounded by performance anxiety, levels of enthusiasm, pain or discomfort to name a few

Actigraphy

- Actigraphy offers many potential advantages over the 6MWD
  - Provides data over long periods of time rather than just at study visits
  - Allows data to be obtained from patients in their homes, performing activities of daily living without the need to travel to trial sites
  - Seems to be a more natural way to measure functionality
- Actigraphy may also be tailored to measure other specific activities such as tremor, scratching, coughing
- Accelerometers are in widespread use in cellphones, smartwatches and a plethora of wellness and fitness devices so the technology is already fairly well understood.
- For these reasons, actigraphy is the technology that has received the most attention from industry and regulators
- We have an entire session on actigraphy hoping to address challenges and identify opportunities in order to support its use in clinical trials

Other Sensors

- Actigraphy is clearly not the only technology of interest.
- Medical devices may also play a significant role in evaluating the effects of treatment.
- Continuous glucose monitoring has had a major impact on the clinical management of diabetes. Small wearable sampling devices allow easy access to glucose levels as they change over the day. The value of these is probably under-utilized in clinical research.
- Small wearable monitors that can measure cardiac rate and rhythm, record ECGs, measure blood oxygen saturation and more, are widely available. We look forward to hearing how these may play a role in clinical trials.
- Another promising area involves sensors that are not worn but are placed in the patient's environment. These are versatile in measuring patient movement, activities, and many physiological or pathological events. They may also simplify the demand on patients that wearables present.

The list goes on…

- Microphones that analyze voiceprints
- Cameras for visible lesions
- Electrodes to monitor muscles, nerves and brains
- Undoubtably plenty that we have not thought about

Patients

- A fundamental consideration regarding DHTs is the people who will use them.
- On one hand DHTs offer opportunities to gather data from patients wherever they are. This may appeal to patients who have difficulty traveling to clinical sites such as those with socio-economic challenges. This promises to make trials more inclusive.
- On the other hand there are individuals who are unable or unwilling to use electronic technology.
- How do we strike the right balance to make trials more inclusive?
- Could the use of DHTs provide biased data? For example, sicker patients not using their DHTs, resulting in a selective loss of data on poor outcomes.
- Perhaps a neglected, but foundational question is whether patients believe that DHTS reflect their experience.
- Our session on diversity and inclusion will address this.

Ultimate public health goals

- Shouldn’t lose sight of goal for patients, and diseases
- More drugs for areas of medical need
- Better characterization of drug effect in clinical trials

Aims of the Meeting

- Understand the landscape of available technologies and their uses:
  - Actigraphy
  - Other sensors
- Identify areas of opportunity, new technologies for measurement, diseases that can be studied in new ways
- Identify ways to gain confidence in the use of DHTs for drug development
- Identify gaps – Scientific and regulatory gaps to support use of these technologies
- Identify usability issues that may either promote or discourage engagement of diverse populations

Matthew Diamond

Chief Medical Officer

Digital Health Center of Excellence

US Food and Drug Administration

Permission to include slides pending.

Lucy Cesnakova

Program Lead

Digital Medicine Society

DIGITAL MEDICINE SOCIETY

The role of DHTs in advancing drug development

Workshop: Understanding Priorities for the Use of Digital Health Technologies to Support Clinical Trials for Drug Development and Review

Mar 28-29, 2023 | Virtual

Lucy Cesnakova, MS
Program Lead
(DiMe)

Our purpose

DiMe is a global non-profit dedicated to advancing the **ethical**, **effective**, **equitable**, and **safe** use of digital medicine to redefine healthcare and improve lives.

Source: https://www.dimesociety.org/index.php/about-us-main

We launched in May 2019...

CISION
PR Newswire

Digital Medicine Society Now Accepting Members

New nonprofit aims to advance digital medicine to optimize human health

DIGITAL MEDICINE SOCIETY

NEWS PROVIDED BY
Digital Medicine Society (DiMe) →
May 14, 2019, 01:53 ET

BOSTON, May 14, 2019 /PRNewswire/ -- The Digital Medicine Society (DiMe), a Massachusetts nonprofit corporation with 501(c)(3) application pending, has launched.

STAT Topics Opinion Podcast Video Newsletters Events Log I

FIRST OPINION

DiMe: Calling all who serve in digital medicine

By JEN GOLDSACK, BEAU WOODS, *and* ERIC PERAKSLIS / JUNE 5, 2019

Source:https://www.prnewswire.com/news-releases/digital-medicine-society-now-accepting-members-300848402.html and https://www.statnews.com/2019/06/05/new-digital-medicine-society/

… and sit at the intersection of two communities

Source: https://www.dimesociety.org/index.php/about-us-main

Despite hundreds of diseases having no cure, today's clinical trials industry is characterized by…

Protracted timelines

It takes, on average, **10-15 years** to bring a new drug to market.

Recruitment challenges

One in five trials is terminated with no answer about drug efficacy due to failure to recruit.

Low rates of technical success

The likelihood of successfully bringing a new molecule to market is **just 5%**.

Equity & access challenges

There remain populations that are still and repeatedly **underrepresented** in clinical trials.

104 Sponsors have collected digital endpoints

Primary, Secondary or Label Claim

Abbott, abbvie, ABIDE THERAPEUTICS, ACTELION, addex Therapeutics, ALKAHEST, ALTAVANT SCIENCES, Altec, ALTOIDA, ANATARA LIFESCIENCES, aspen, AstraZeneca, AVAZIA, BAYER, BEATS MEDICAL, Bellerophon THERAPEUTICS, BIOAGE, Biogen, Bright Cloud International Corp, Bruyère, Cavion, CEREGATE, Cereno Scientific, CFDRC, CuraSen, Daiichi-Sankyo, DANONE ONE PLANET. ONE HEALTH, dexcom, Diurnal, dm, DSM, EDIFICE HEALTH, Eisai, ESTRA, FIBRONOSTICS, Forest Laboratories, Inc., FrieslandCampina, gbt, Genentech, General Mills, GILEAD Creating Possible, gsk, Hamad, INmuneBio INNATE IMMUNITY, Insulet, janssen, JCHR, LALLEMAND, Lilly, LMC, Lycored, LV, MARREK, MEDICIS, Medtronic, MERCK, MGH 1811, mizkan, NANTCELL, Neurolixis, NOEMA PHARMA, NHS Northern Care Alliance NHS Foundation Trust, NOVARTIS, novo nordisk, ObvioHealth, OLATEC, ottobock., Pfizer, PHARMANEX, PRAXIS, PrecisionBiotics, proteus DIGITAL HEALTH, RedHill Biopharma, REGENERON, Renovia, ResMed, Sage Therapeutics, SANSUM DIABETES RESEARCH INSTITUTE, SANOFI, SAREPTA THERAPEUTICS, SENSIMED, SLEEPSPACE, SoniVie, SzeleSTIM, Takeda, TANDEM DIABETES CARE, ucb, VANDA PHARMACEUTICALS INC., VB, VERTEX, ViiV Healthcare, virta, ZOLL

Exploratory Only

CORTEXYME, Roche, sonova HEAR THE WORLD, sunovion, teva

Is your company's work missing?
Submit it to DiMe:
https://bit.ly/DiMe-Endpoints

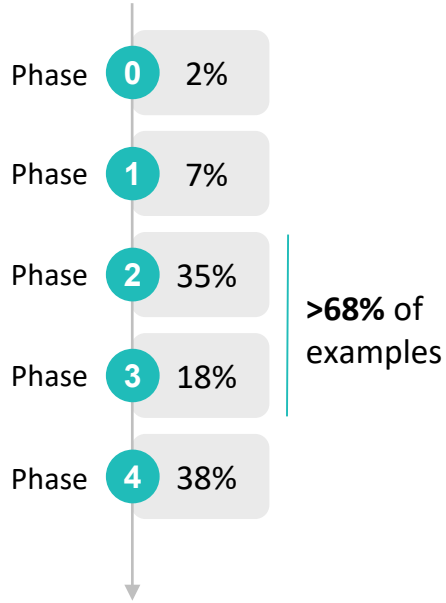
Source: https://www.dimesociety.org/index.php/knowledge-center/library-of-digital-endpoints

Last updated January 31, 2023

104 Sponsors have collected digital endpoints…

Sponsors start digital endpoint development early

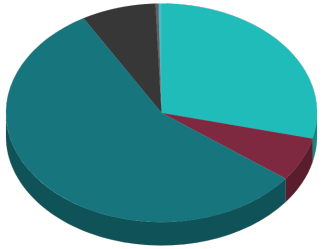
Digital Endpoints



**Only drug trials with reported phases are included*

Digital endpoints are being used across drug, device, biologic, and genetic product development

Investigational Product



Drug	51.2%
Device	34.1%
Biologic	8.3%
Other	6.1%
Genetic	0.3%

Pharma trusts digital products, primary/ secondary endpoints

Endpoint Positioning

116	Primary endpoints
206	Secondary endpoints
20	Label Claim
6	Exploratory
26	Other

378 UNIQUE ENDPOINTS

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Source: https://www.dimesociety.org/index.php/knowledge-center/library-of-digital-endpoints

Last updated January 31, 2023

FDA Launched new draft guidance in Dec 2021

Clarifies that DHTs need not necessarily be medical devices

Supports BYOD approaches

Source: https://journals.sagepub.com/doi/pdf/10.1177/1073110520917047, Playbook team analysis | Available at playbook.dimesociety.org

EMA Guidance and Qualified Digital Endpoints

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

26 April 2019
EMA/CHMP/SAWP/178058/2019
Committee for Medicinal Products for Human Use (CHMP)

Qualification opinion on stride velocity 95th centile as a secondary endpoint in Duchenne Muscular Dystrophy measured by a valid and suitable wearable device*

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

1 June 2020
EMA/219860/2020
Human Medicines Division

Questions and answers: Qualification of digital technology-based methodologies to support approval of medicinal products

Status as of June 2020

Source:https://www.ema.europa.eu/en/documents/scientific-guideline/qualification-opinion-stride-velocity-95th-centile-secondary-endpoint-duchenne-muscular-dystrophy_en.pdf and https://www.ema.europa.eu/en/documents/other/questions-answers-qualification-digital-technology-based-methodologies-support-approval-medicinal_en.pdf

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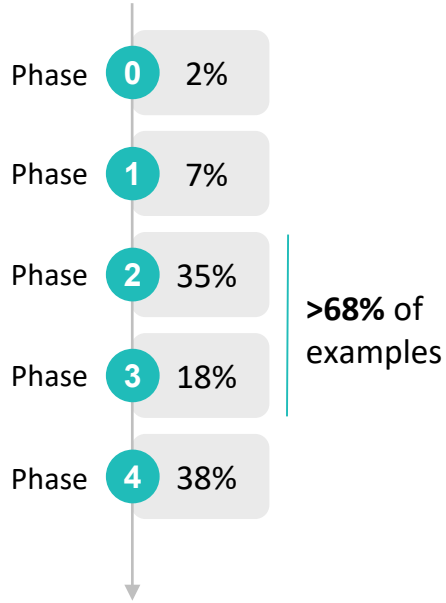

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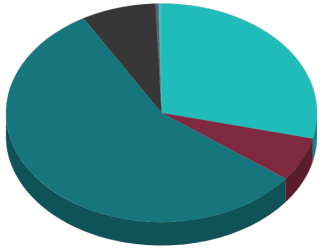

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Source: https://www.dimesociety.org/index.php/knowledge-center/library-of-digital-endpoints

Last updated January 31, 2023

The Rapid Evolution of Digital Endpoints: Are We Headed in the Right Direction?

The number of unique digital endpoints being used in industry-sponsored trials of new medical products is skyrocketing, but is more always better?

Jennifer Goldsack

Jan 26 · 6 min read

Source: https://medium.com/digital-medicine-society-dime/the-rapid-evolution-of-digital-endpoints-are-we-headed-in-the-right-direction-c25bbcb32eee

Ensure you identify measures that matter

Digital Biomarkers

Digit Biomark 2020;4:69-77

DOI: 10.1159/000509725
Received: May 9, 2020
Accepted: June 25, 2020
Published online: September 15,2020

Viewpoint **Review Article**

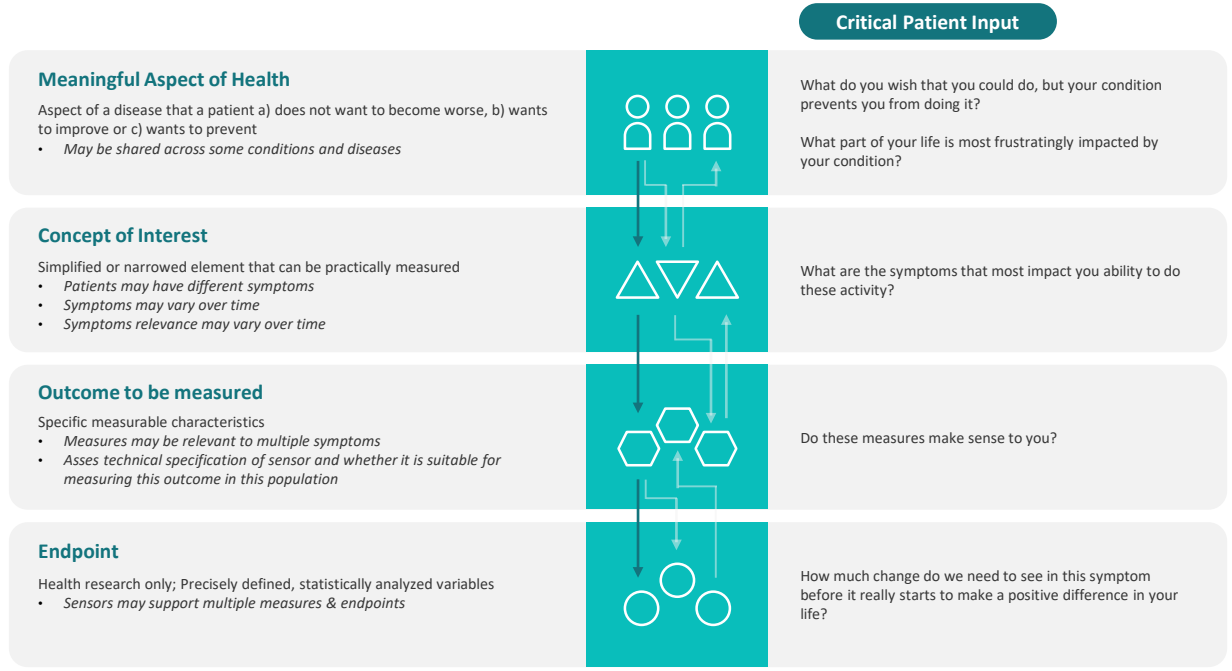
Digital Measures That Matter to Patients: A Framework to Guide the Selection and Development of Digital Measures of Health

Christine Manta [a,b] Bray Patrick – Lake [a,c] Jenifer C, Goldsack [a]

[a] Digital Medicine Society , Boston, MA, USA; [b]Elektra Labs, Boston, MA, USA; [c]Evidation Health, Inc., San Mateo, CA, USA

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

Digit Biomark 2020;4;69-77 = DOI:10.1159/00509725



This figure was adapted from original work by Evidation Health, with permission. This figure illustrates patient considerations that should drive digital measure selection and development, these should precede technical considerations [8]. Additional information on subsequent technical considerations are available at [36, 37, 38]

Source: https://www.karger.com/Article/Pdf/509725

DiME DIGITAL MEDICINE SOCIETY

NOCTURNAL SCRATCH

Digital Measures Development

Advancing nocturnal scratch as a digital endpoint for atopic dermatitis

Founding Project Partners

abbvie

Janssen | Pharmaceutical Companies of Johnson & Johnson

NOVARTIS

Pfizer

UCB

Project Collaborators

Advancing Innovation in Dermatology

almirall

gsk GlaxoSmithKline

LEO

Lilly

sanofi

Expert Partners:

National Eczema Association

GLOBAL PARENTS FOR ECZEMA RESEARCH
RESEARCH • SUPPORT • CHANGE

Duke University

Harvard Business School

Boston University

Health Outcomes Insights
Getting targeted answers to patient behaviour and outcomes

Source: https://dimesociety.org/access-resources/digital-measures-nocturnal-scratch/

NOCTURNAL SCRATCH

Digital Measures Development

LEARN MORE

Patient Research

- Data and evidence from mixed methods research
- Conceptual framework

Measures Terminology & Ontology

- Data and evidence supporting technical definition
- Evidence-based ontology

Deployment to Clinical Trials

- 10 tools supporting successful operational implementation
- Case studies

Payer Acceptance

- Translating patient value to commercial value
- Modeling potential increases in drug utilization
- Key insights & action items

DIGITAL MEDICINE SOCIETY

Source: https://dimesociety.org/access-resources/digital-measures-nocturnal-scratch/

DIGITAL MEDICINE SOCIETY

ALZHEIMER'S DISEASE & RELATED DEMENTIAS

Digital Measures Development

Identifying Patient Specified Digital Measures in Alzheimer's Disease and Related Dementias

Partners

abbvie

Alzheimer's Drug Discovery Foundation

Biogen

BOSTON UNIVERSITY

Cognito Therapeutics

Eisai

Lilly

MERCK

OREGON HEALTH & SCIENCE UNIVERSITY

Roche

Digital Solutions Collaborators

altoida

Aural Analytics

BioSensics™

CAMBRIDGE COGNITION

Cogniant

Cogstate

Cumulus

ki elements

koneksa

MEDIDATA

LINUS HEALTH

SageBionetworks

VivoSense

WINTERLIGHT

Source: https://dimesociety.org/access-resources/digital-measures-adrd/

DIGITAL MEDICINE SOCIETY

CORE MEASURES *of* PHYSICAL ACTIVITY

Digital Measures Development

Project Partners

ALEXION
ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY
COPD FOUNDATION
DEFENSE INNOVATION UNIT
Duke | BIG IDEAS LAB
MERCK
THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH
Nestlé
Open mHealth
Savvy COOPERATIVE

Digital Solutions Collaborators

Activinsights
ANALOG DEVICES AHEAD OF WHAT'S POSSIBLE™
empatica
evidation
fitbit
HumanFirst
IQVIA
koneksa
Medable
parexel
verily
VivoSense

Source: https://www.dimesociety.org/access-resources/digital-measures-physical-activity/

DIGITAL MEDICINE SOCIETY

CORE MEASURES *of* SLEEP

Digital Measures Development

Partners

BAYER

BOSTON UNIVERSITY

DEFENSE INNOVATION UNIT

Duke

GSK

Jazz Pharmaceuticals

Lilly

National Sleep Foundation

NextSense
Revolutionizing Brain Health

Sage Therapeutics

Takeda

T.C. Demiroğlu Bilim University

UZ LEUVEN

VA U.S. Department of Veterans Affairs

Digital Solutions Collaborators

Activinsights

BEACONBIOSIGNALS

BIOSTRAP

Byteflies

dreem

Google

HumanFirst

ŌURA

Primasun

sleep number

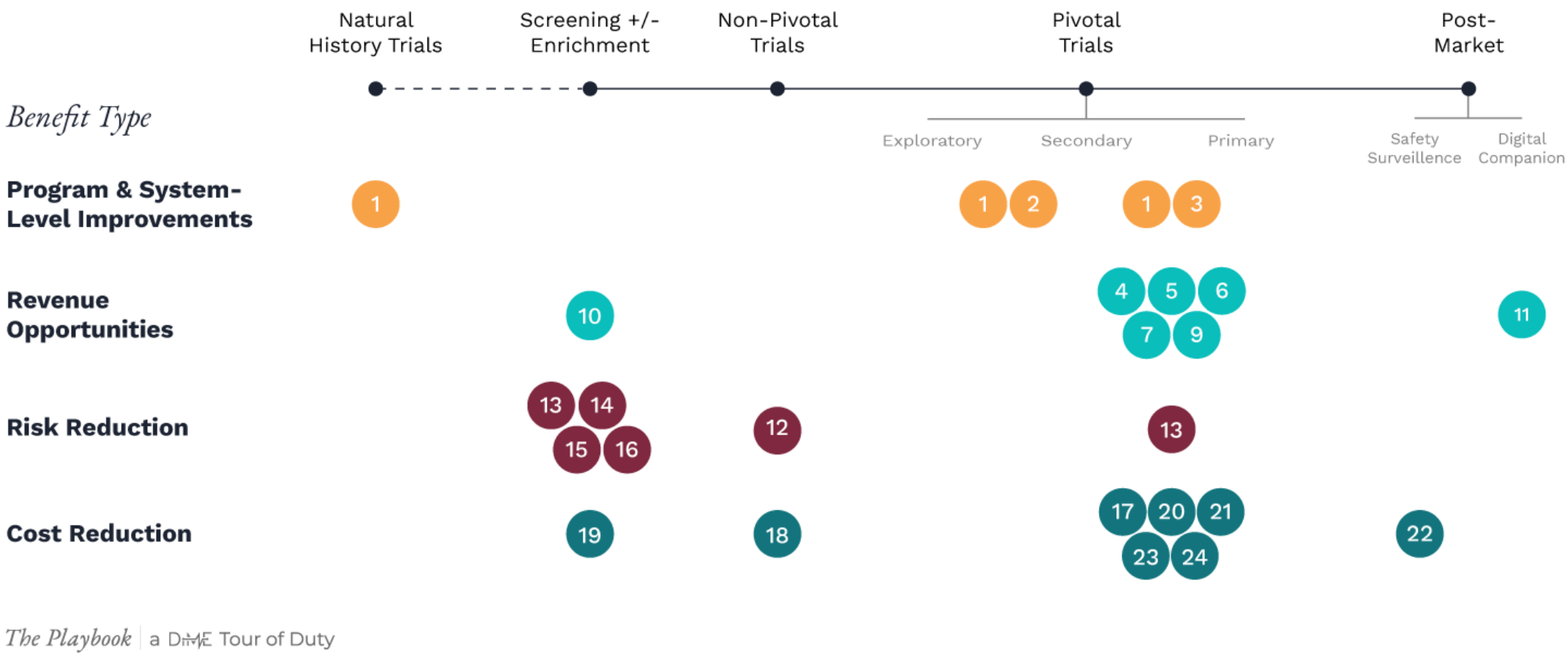
Softmatter

TNO innovation for life

VivoSense

Source: https://dimesociety.org/access-resources/core-measures-sleep/

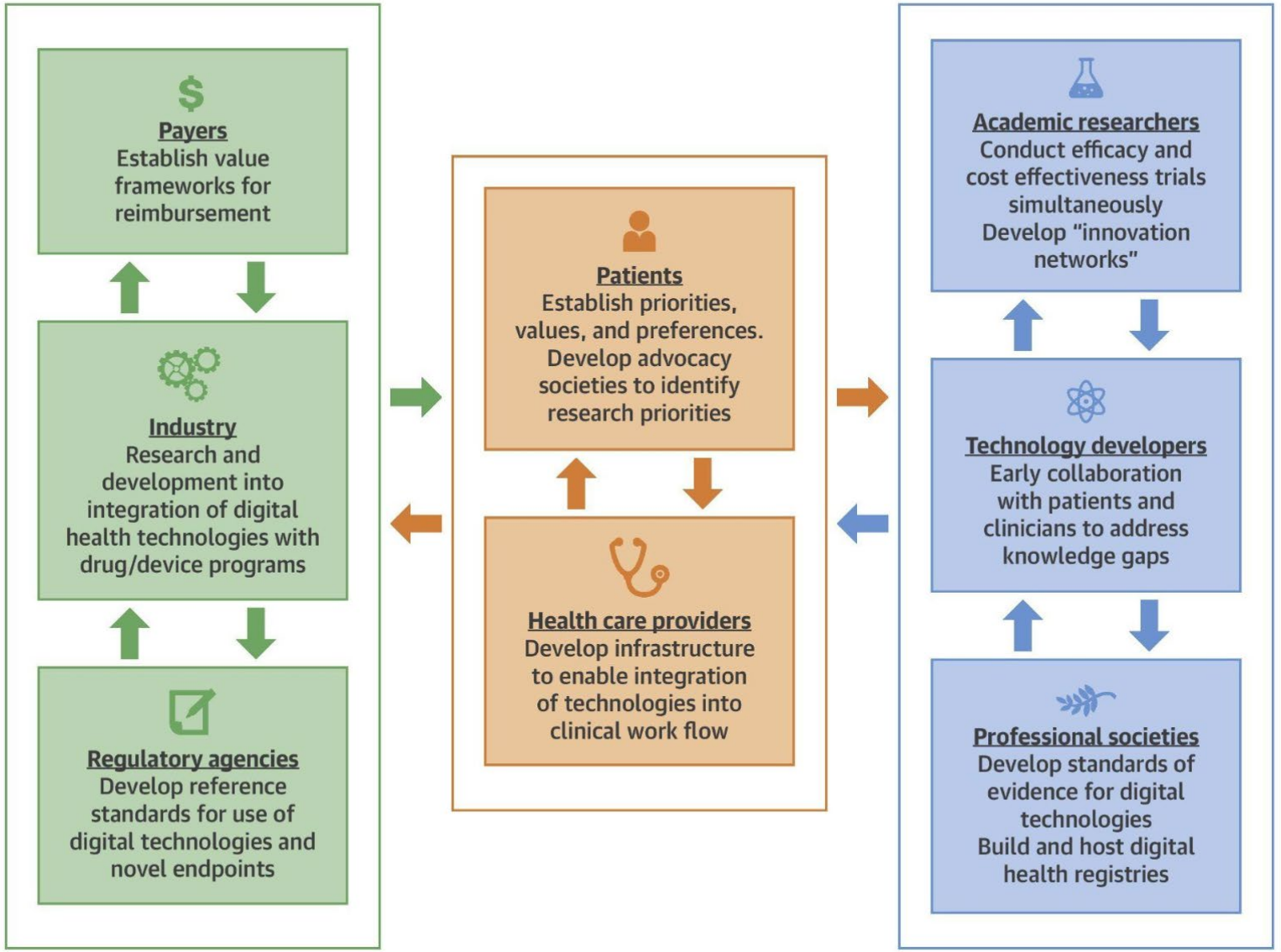
The *landscape of benefits* accompanying the use of digital clinical measures in medical product development



The Playbook | a DiME Tour of Duty

Source: https://playbook.dimesociety.org/dossiers/pharma-exec/

Multi-disciplinary efforts towards adoption and value capture



Source: Using Digital Health Technology to Better Generate Evidence and Deliver Evidence-Based Care

Diversity

Individual or community identities

Equity

Justice, impartiality, fairness

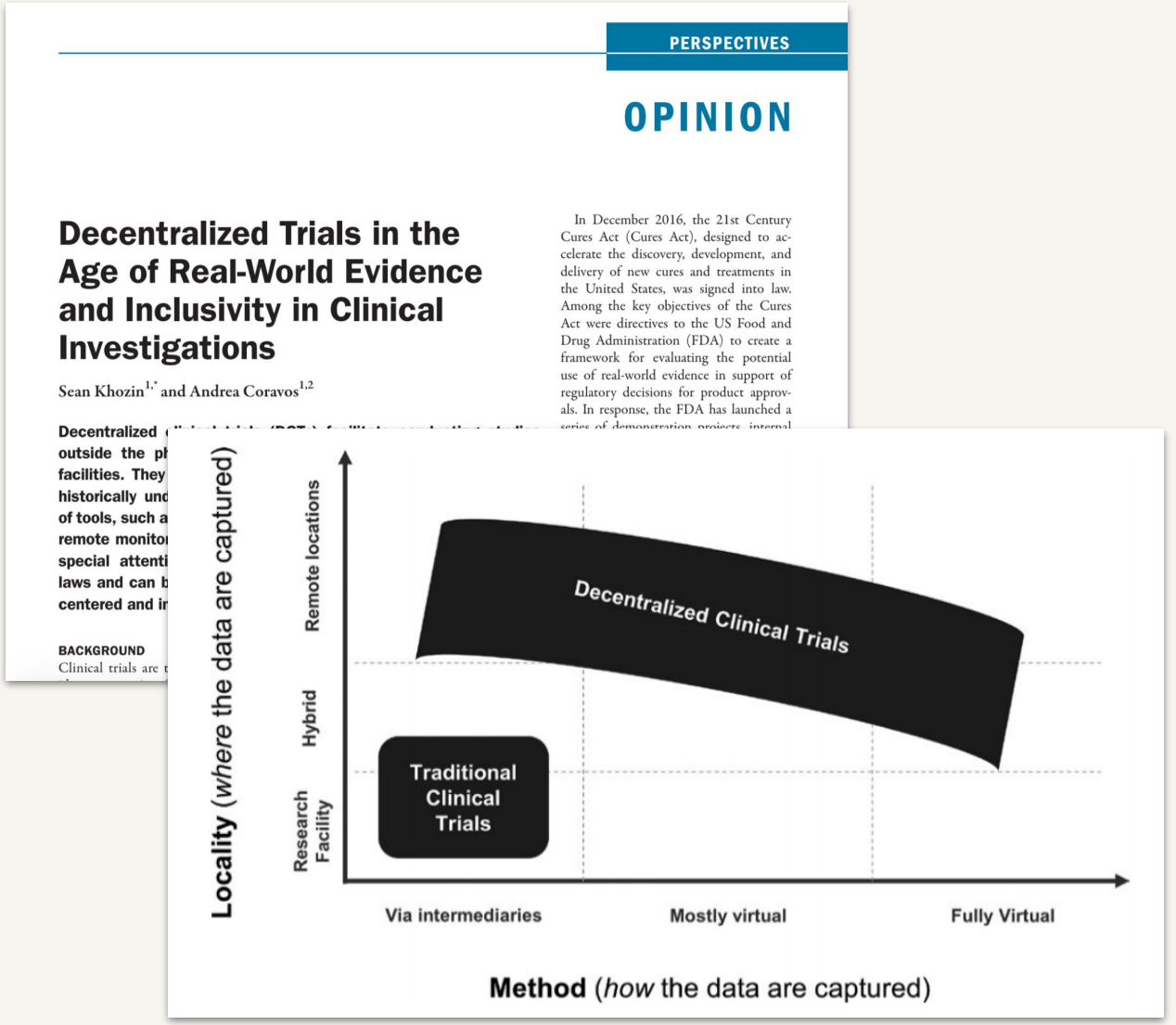
Inclusion

All welcomed, valued,
and can fully participate

SPOTLIGHT

Decentralized trials in the age of real-world evidence and inclusivity in clinical investigations

DCTs "...can **extend the reach** of clinical investigations ***to historically underserved populations*** while enabling incorporation of tools, such as digital health and telemedicine, for high-frequency remote monitoring of patients in **real-world settings**."



PERSPECTIVES

OPINION

Decentralized Trials in the Age of Real-World Evidence and Inclusivity in Clinical Investigations

Sean Khozin[1,*] and Andrea Coravos[1,2]

In December 2016, the 21st Century Cures Act (Cures Act), designed to accelerate the discovery, development, and delivery of new cures and treatments in the United States, was signed into law. Among the key objectives of the Cures Act were directives to the US Food and Drug Administration (FDA) to create a framework for evaluating the potential use of real-world evidence in support of regulatory decisions for product approvals. In response, the FDA has launched a

Source: https://ascpt.onlinelibrary.wiley.com/doi/10.1002/cpt.1441, Playbook team analysis | Access at playbook.dimesociety.org

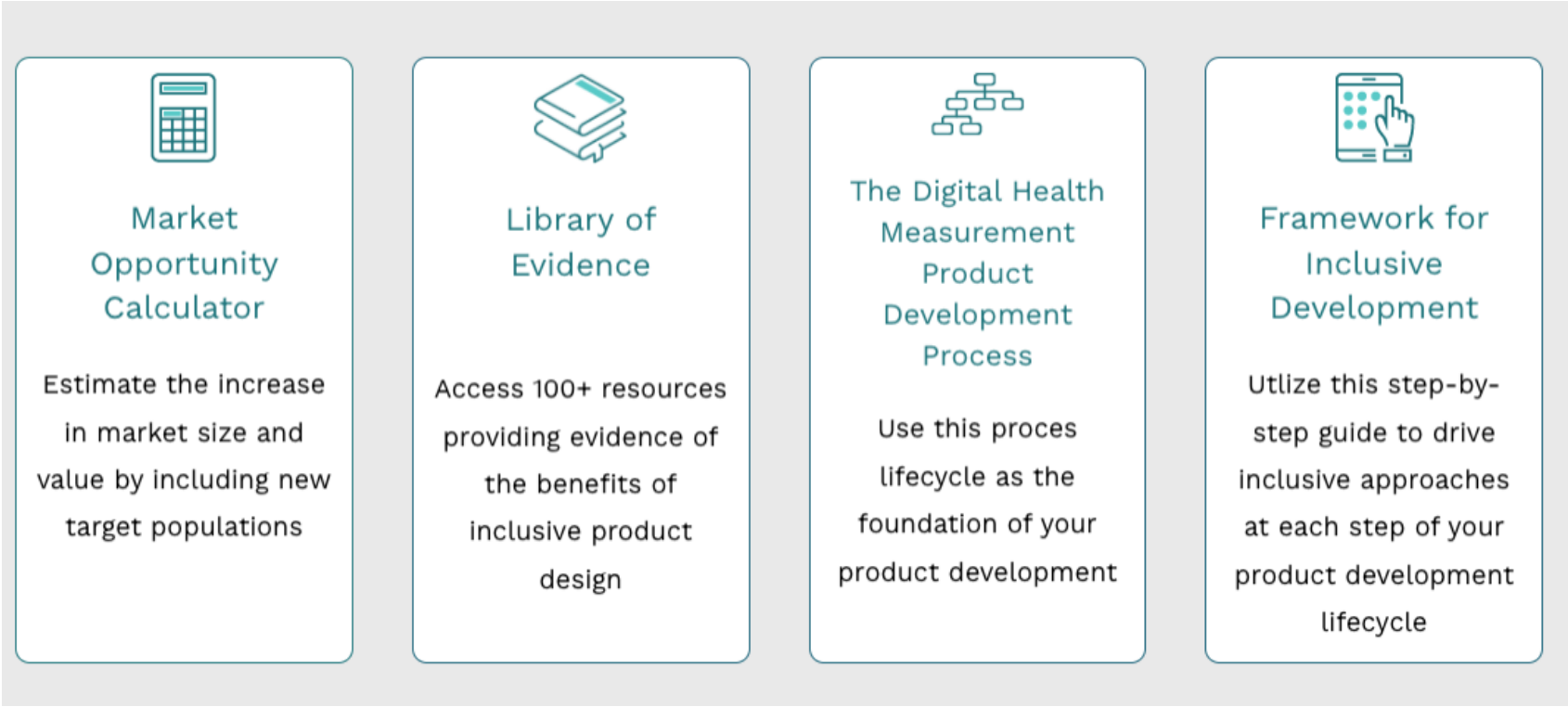
DATAcc Toolkit for Inclusive Development

for Digital Health Measurement Products

DATAcc

Digital Health Measurement Collaborative Community

This toolkit provides supporting tools and research that you need to take you from making the business case for an inclusive digital approach to success at every step of the process.



https://datacc.dimesociety.org/development/

DATAcc Toolkit for Inclusive Deployment
of Digital Health Measurement Products

DATAcc
Digital Health Measurement Collaborative Community

This toolkit is designed to help you ensure that, when digital health measurement is introduced to healthcare and research, all members of the community benefit.

The tools are organized by these three categories.

Source: https://datacc.dimesociety.org/deployment/

DIVERSITY, EQUITY & INCLUSION in Digitized Clinical Trials

Design a person-centered strategy with digital tools to increase diversity, equity, and inclusion in clinical trials

1 Assess

Assess opportunities for utilizing digital tools to be more diverse, equitable, and inclusive with your clinical trial design

2 Identify

Identify which digital tools are best suited to each step of your design process

3 Implement

Implement the person-centered principles as you put together a diversity plan

Source: https://dimesociety.org/access-resources/diversity-equity-inclusion/

Digital Medicine Fundamentals for Pharma

Join top ten pharma companies preparing their workforce for success in the digital era of clinical trials

1. **Module 1.** The first steps: What is digital medicine and why does it matter
2. **Module 2.** Digital landscape: The importance of digital, current landscape and trends shaping market
3. **Module 3.** A window of opportunity: Leveraging digital to accelerate and scale clinical trials
4. **Module 4.** The participant-first approach: Driving participant-centricity by integrating inclusivity and personalized development
5. **Module 5:** Managing Privacy, and Security: foundational elements of building trust
6. **Module 6.** Putting it into practice: Digitalization of clinical trials

Want to upskill your workforce for the digital era of clinical trials? Learn more: https://www.dimesociety.org/dime-academy/corporate-learning/

DIGITAL MEDICINE ACADEMY

Build a field of digital health that is worthy of trust. For everyone.

Applied Digital Health Ethics

DIGITAL MEDICINE ACADEMY

Learn about the latest and greatest in digital medicine ethics from the very best.

This new course will help you contribute to a new field: one that realizes the full potential of the digital era of healthcare while minimizing the risks of harm.

Source: https://www.dimesociety.org/dime-academy/for-individuals/#sign-up

NOCTURNAL SCRATCH

Digital Measures Development

LEARN MORE

Patient Research

Why patients want to reduce night-time scratching:

(excerpt from data collected from patients in interviews)

- It would mean fixing the whole disease, not just symptoms
- Improving the look of skin caused by night-time scratches
- Having better sleep
- Not to having the urge to scratch
- Fixing symptom that is hard to consciously control
- Having treatments with less side effects
- Improving quality of life

DIGITAL MEDICINE SOCIETY

Source: https://dimesociety.org/access-resources/digital-measures-nocturnal-scratch/

NOCTURNAL SCRATCH

Digital Measures Development

DIGITAL MEDICINE SOCIETY

THANK YOU

Lucy Cesnakova | lucy@dimesociety.org

@_DiMeSociety

linkedin.com/company/dime-society

Session 1: Perspectives on Use of DHTs in Clinical Trials

Moderator:

- Nancy Allen LaPointe, Duke-Margolis Center for Health Policy

Panelists:

- Leonard Sacks, US Food and Drug Administration
- Matthew Diamond, US Food and Drug Administration
- Lucy Cesnakova, Digital Medicine Society
- Cindy Geoghegan, Patient and Partners
- Carrie Northcott, Pfizer
- Alicia Staley, Medidata

Break

We will be back momentarily.

The next panel will begin at 3:00 p.m. (U.S. Eastern Time)

Session 2: Impact of DHTs on Clinical Trial Accessibility and Diversity

3:00 pm – 4:05 pm EST

Klaus Gottlieb

Vice President, Late Phase Immunology

Eli Lilly and Company

Digital Strategies for Improving Recruitment and Diversity in Clinical Trials

Klaus Gottlieb, MD, JD

Eli Lilly and Company

klaus.gottlieb@lilly.com

How can Digital Health Tools help?

- Overcoming geographical barriers
- Streamlining the recruitment process
- Enhancing patient engagement
- Improving data quality
- Addressing language and cultural barriers

Dermatology Trials Ideal for POC

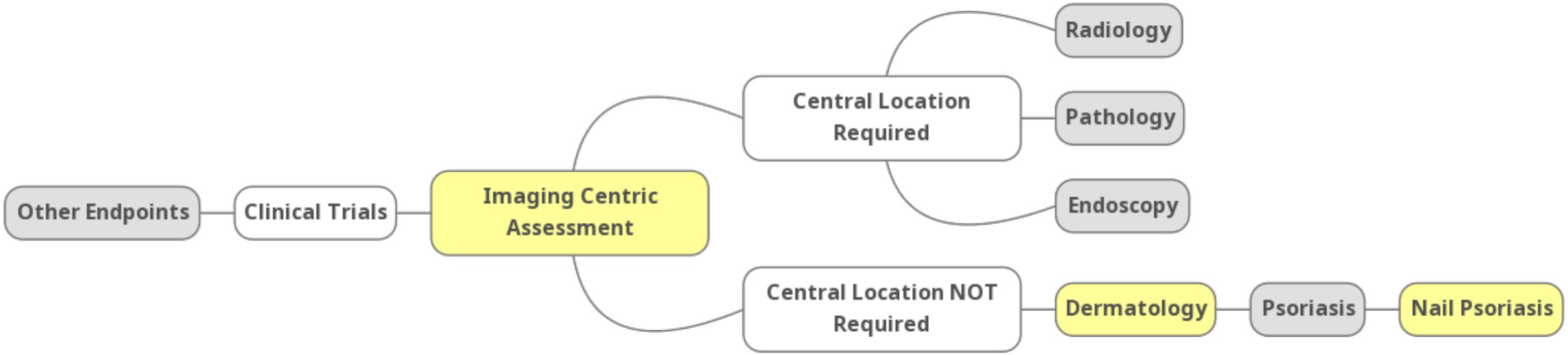
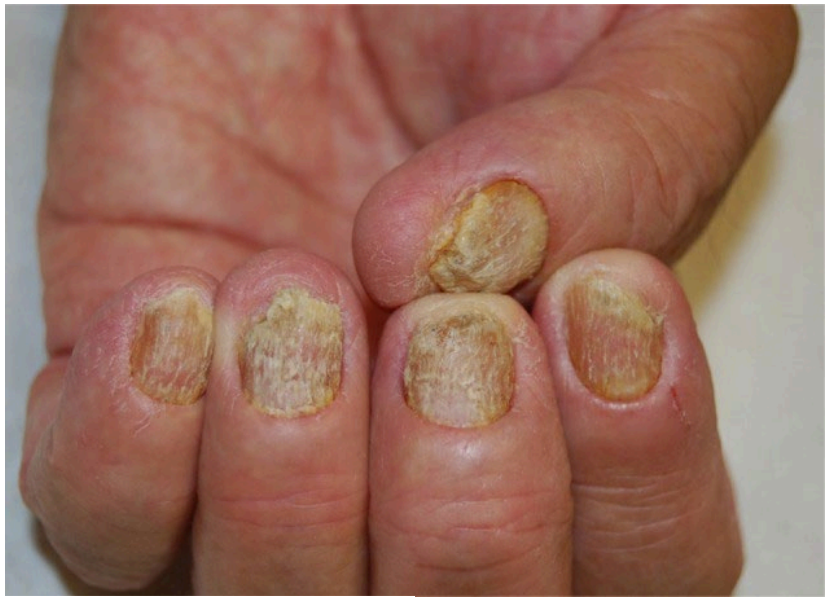


Image-based assessments that are location-independent are the most suitable for decentralization and automation, thanks to the wide availability of smartphone cameras and advancements in computer vision.

Nail Psoriasis – Remote Assessment

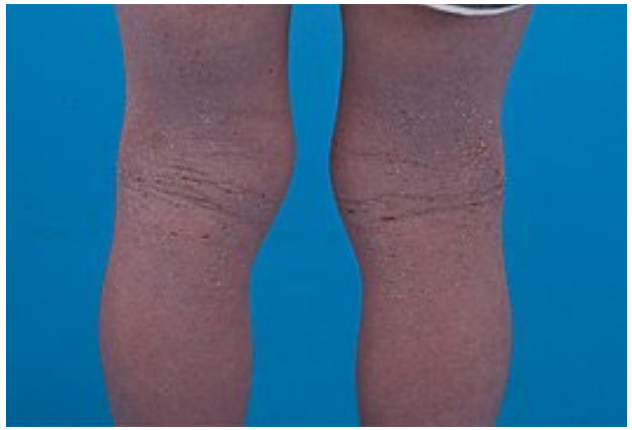
- **Nail psoriasis** is a common condition seen in about 10-78% of patients with psoriasis vulgaris and **70-80% of patients with psoriatic arthritis**. It is difficult to treat.
- Psoriasis is slightly less common in African-Americans but tends to be more severe.

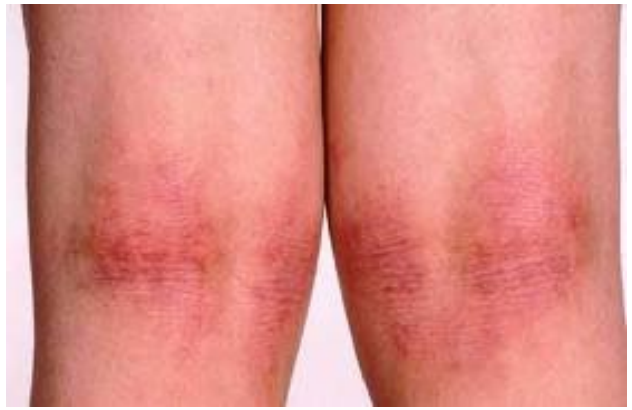


PSoSA (PSOriasis Special Areas) - a US-based, Single-Arm, Prospective, Multicenter, Observational Study of Nail and Scalp Psoriasis Improvement in Patients Treated with Ixekizumab (IXE)

Images obtained by physicians (office) and patients (smartphone app) are compared. Scoring is done by physicians and trained lay readers. An AI model will be developed.

Atopic Dermatitis in Pigmented Skin

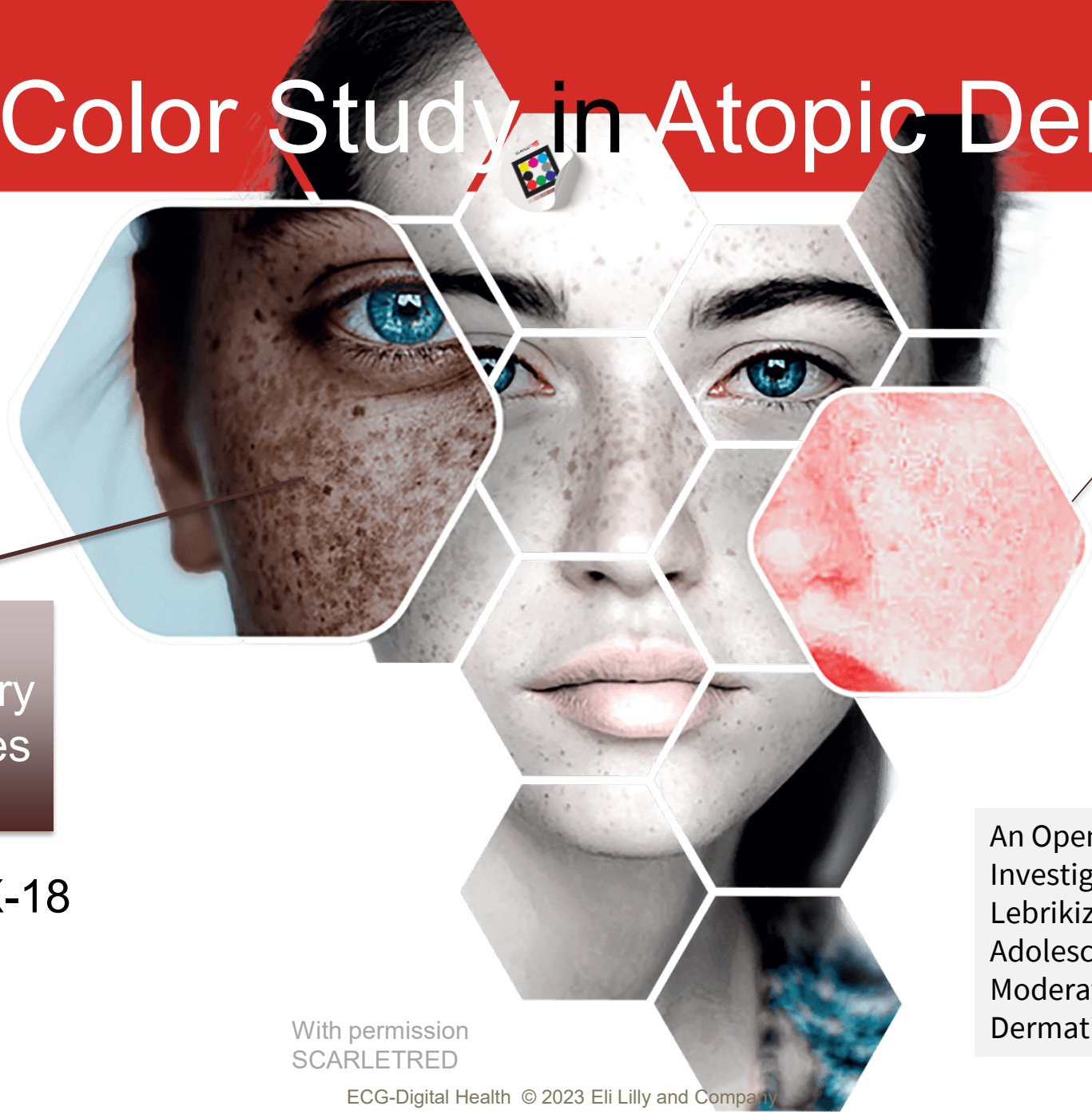




CC BY 2.0 NIAID

- Erythema is harder to see and evaluate (violaceous here)
- Inflammatory pigment changes are not part of the usual scoring
- Prurigo-like lesions are more common
- Patient perception different and self-examination more difficult

Skin of Color Study in Atopic Dermatitis



Post-Inflammatory Pigment Changes

Mexameter® MX-18

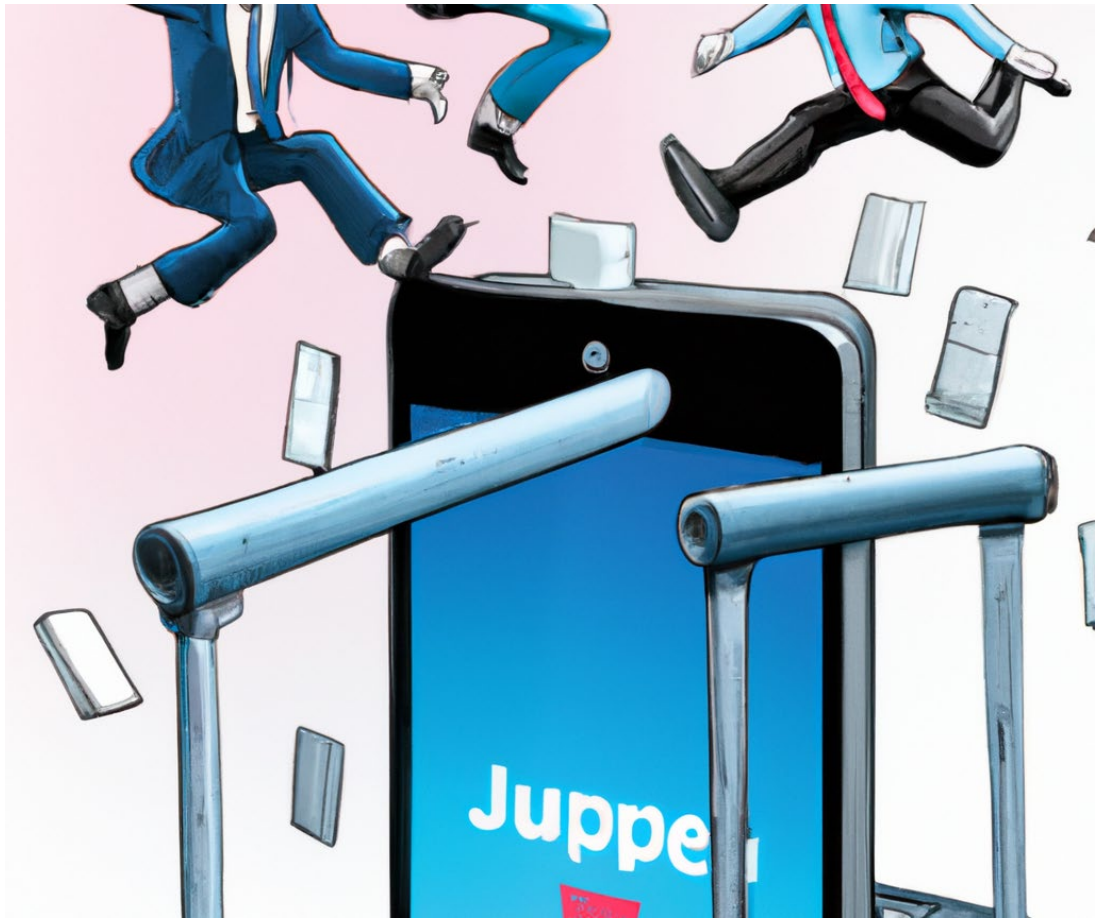
Erythema Scale

Scarletred® platform Mexameter® MX-18

An Open-Label, 24-Week Study to Investigate the Safety and Efficacy of Lebrikizumab in Adult and Adolescent Participants With Moderate-to-Severe Atopic Dermatitis and Skin of Color.

With permission SCARLETRED

Barriers to Using DHTs



Use of DHTs in clinical trials needs to be balanced with patient burden (additional wearables, multiple apps or iPhones, etc.) and with clinical utility.

Finding development partners is difficult

- Big Five Tech Companies show scant interest, the focus is instead on the consumer market
- Rigorous development in clinical trials could smooth conversion into consumer products

Regulatory Barriers

- Uncertainty of regulatory expectations for DHT verification and validation for a wide spectrum of uses in clinical studies, including:
  - Non-medical device to medical device
  - Exploratory endpoint to primary endpoint

- Uncertainty whether DHT developer evidence is sufficient to meet FDA expectations (if pharma can leverage)

- Update Clinical Imaging Guidance

Acknowledgments

- Derek Onken – Advanced Analytics and Data Sciences

- Sreekumar Pillai – Immunology Development

Patrick Gee

Founder and Chief Executive Hope Dealer

iAdvocate, Inc.

Session 2: Impact of DHTs on Clinical Trial Accessibility and Diversity

Moderator:

- ‘Lola Fashoyin-Aje, US Food and Drug Administration

Panelists:

- Patrick Gee, iAdvocate, Inc.
- Klaus Gottlieb, Eli Lilly and Company
- Wendy Camelo Castillo, University of Maryland, Baltimore
- Anne Peters, University of Southern California
- Reginald Swift, Rubix LS

Closing Remarks | Day 1

Mark McClellan

Director, Duke-Margolis Center for Health Policy

Thank You!

Contact Us

healthpolicy.duke.edu

Subscribe to our monthly newsletter at
dukemargolis@duke.edu

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