DIGITAL MEDICINE SOCIETY

V3 in Action:

How organizations are systematically embedding V3 in their digital measures strategy

November 3, 2022 11 AM ET

Ariel Dowling
Head of Sensing and Measurement, Takeda

Elena Izmailova
Chief Scientific Officer, Koneksa

Moderator: Jen Goldsack
CEO, Digital Medicine Society

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

We deliver clinical quality work on a tech timeline

New knowledge & capabilities in the field spark new collaboration opportunities

Communication & education

Resources & publications generated by DiMe & thought leaders in the field are exchanged between various stakeholders & across the many disciplines in the field.

Community

DiMe members, partners, & experts from across tech & healthcare unite to collaborate & identify ways to overcome barriers to success.

Actionable, evidence-based resources

Greatest challenges & opportunities to advancing the field

Research

Experts from across all disciplines address shared challenges through deep inquiry & data generation, creating actionable, evidence-based resources.

Source: https://www.dimesociety.org/index.php/knowledge-center/dime-generated-content

But first, housekeeping

- Please note: **today's session is being recorded**
    - Slides and recording will be available on DiMe's webinar page after the session
- To ask a question for discussion during live Q&A, please either:
    - **'Raise your hand'** in the Reactions and the moderator will unmute you to ask your question live, or
    - **Type your question** into the chat box

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V3 is a modular evaluation process

Design Specifications & Modular Prototyping

Verification

Evaluates and demonstrates the performance of a sensor technology within a **BioMeT** , and the sample-level data it generates, against a pre-specified set of criteria.

Analytical validation

Evaluates the performance of algorithm, and the ability of this component of the **BioMeT** to measure, detect, or predict physiological or behavioral metrics

Clinical validation

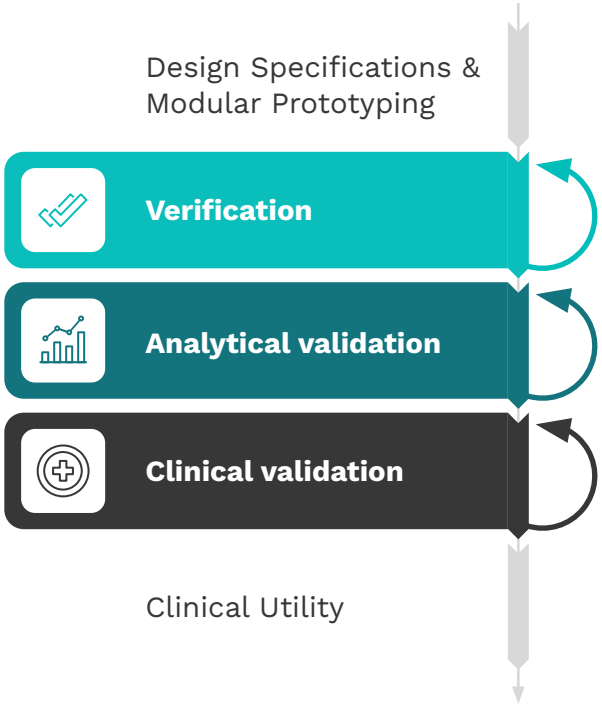
Evaluates whether a **BioMeT** acceptably identifies, measure, or predicts a meaningful clinical, biological, physical, functional state, or experience, in the states context of use (which includes a specified population).

Clinical Utility

BioMeT - Biometric Monitoring Technology

Source: https://www.nature.com/articles/s41746-020-0260-4

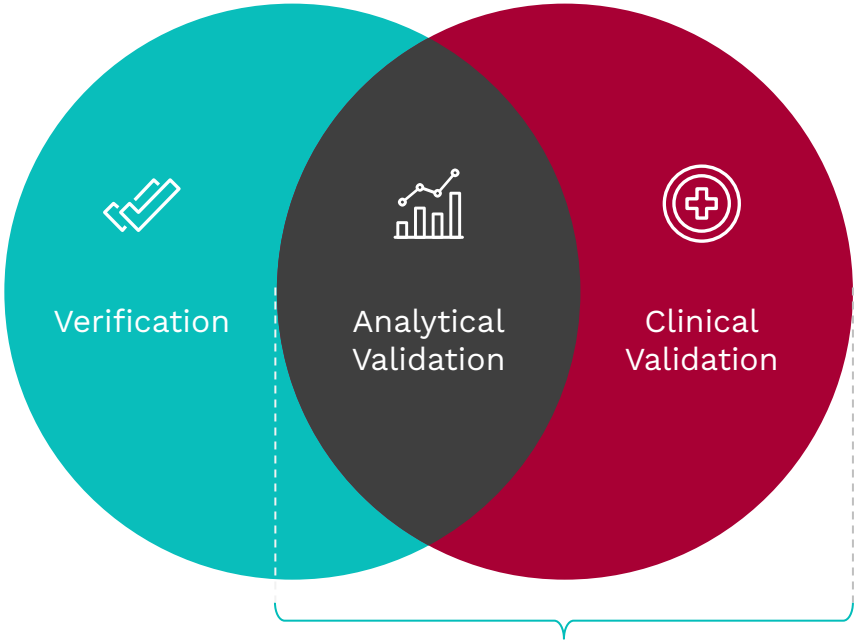
Modular evaluation of digital measures



Changes to hardware/firmware?	• Reverification, or • Documentation of back-compatibility
Changes to software that change algorithm?	• Repeat analytical validation, or • Documentation of back-compatibility
Expansion to a new patient population?	• Repeat clinical validation if analytical validation in new population is documented, or • Repeat analytical & clinical validation

Source: https://www.nature.com/articles/s41746-020-0260-4

V3 processes are typically conducted by experts across disciplines and domains



Activity performed by:

(non-clinical) engineers

Both engineers and clinically-trained professionals

Clinically-trained professionals

Source: https://www.nature.com/articles/s41746-020-0260-4

Adoption of the V3 framework

The V3 Framework is emerging as the industry standard for evaluating DHTs:

- **Cited over 120 times** in the scientific literature
- Foundational to **EMA** and **NIH** perspectives and recommendations
- Aligned with **FDA** guidance

Sources: https://www.nature.com/articles/d41573-020-00168-z, https://content.iospress.com/articles/journal-of-parkinsons-disease/jpd202416, https://www.commondataelements.ninds.nih.gov/sites/nindscde/files/Doc/PD/F3012_Best_Practices_for_Digital_Health_Outcomes.pdf

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Determine Fit for Purpose: V3 Framework

Verification → Sensor performance verification against a reference shake table

Analytical Validation → Algorithm performance versus a benchmark, human rater to measure time and number of steps

Clinical Validation → Relationship with conventional outcomes and assessment properties

Case study

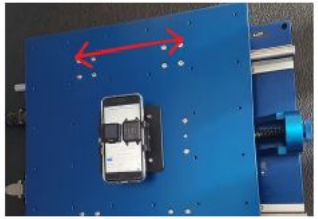
- walk duration
- walking distance
- number of steps
- walking speed
- stride period

Adopted from: npj Digital Medicine (2020) 3:55 ; https://doi.org/10.1038/s41746-020-0260-4

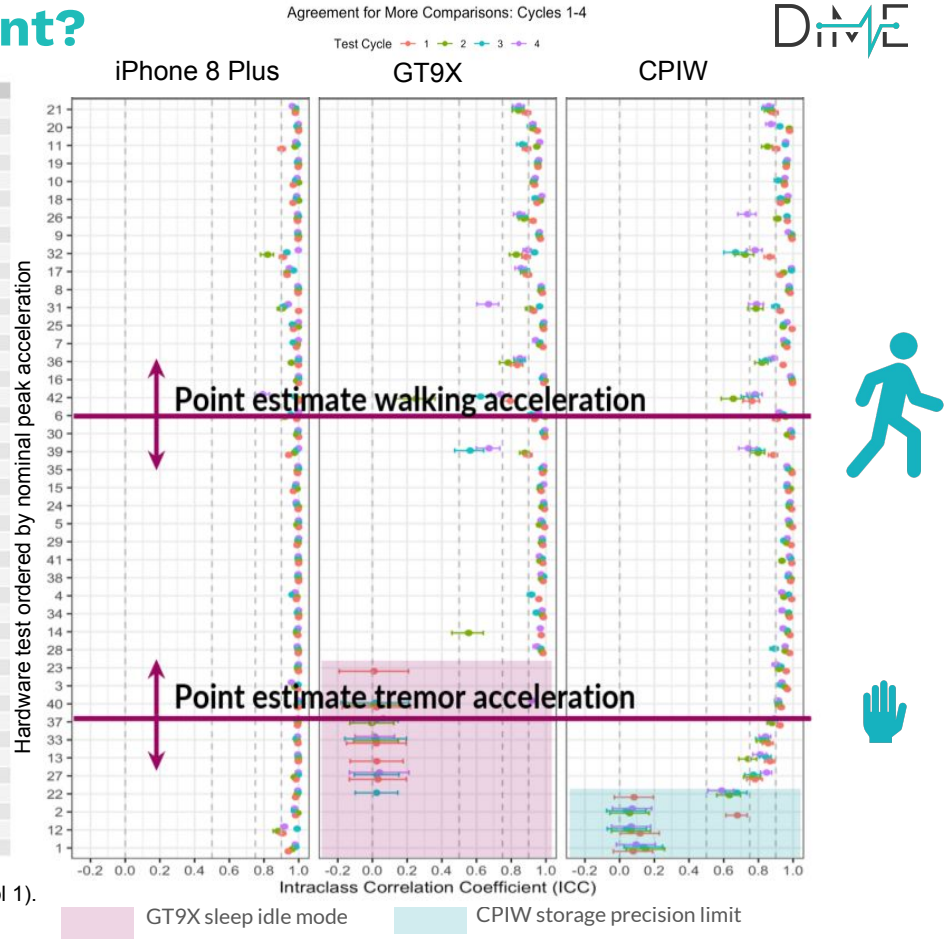
Why Sensor Verification Is Important?

Sensor Verification

- Fit for purpose principle is always context of use dependent
- Context of use is often different than original intended use of a selected technology/ device
- Needs to be established regardless of regulatory status of a technology/ device
- Access to sample level data is critical



A	F	accel
10	9	3.261
10	8	2.577
5	10	2.013
10	7	1.973
5	9	1.631
10	6	1.449
5	8	1.288
20	4	1.288
30	3	1.087
10	5	1.006
5	7	0.986
30	2.5	0.755
5	6	0.725
20	3	0.725
10	4	0.644
40	2	0.644
60	1.5	0.544
5	5	0.503
30	2	0.483
50	1.5	0.453
10	3	0.362
40	1.5	0.362
5	4	0.322
20	2	0.322
30	1.5	0.272
60	1	0.242
50	1	0.201
5	3	0.181
10	2	0.161
40	1	0.161
30	1	0.121
5	2	0.081
20	1	0.081
60	0.5	0.06
50	0.5	0.05
10	1	0.04
40	0.5	0.04
30	0.5	0.03
5	1	0.02
20	0.5	0.02
10	0.5	0.01
5	0.5	0.005

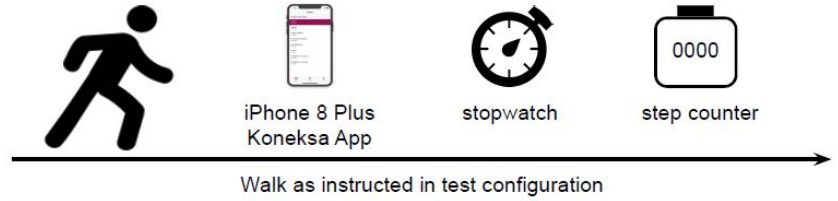


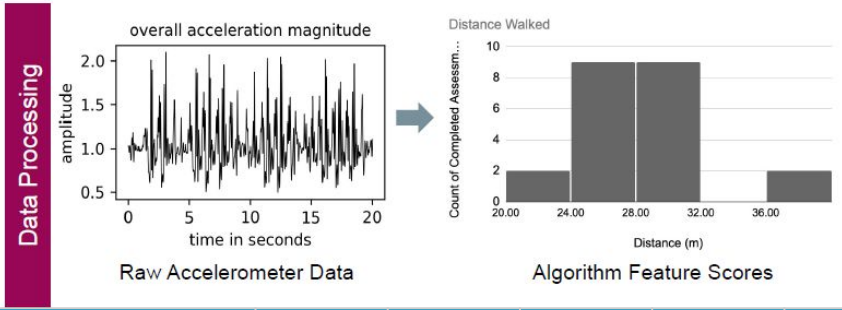
Peter Kelly, Chengrui Huang, Robert Ellis. Comparison of Accelerometers Used for Measurement of Upper Body Postural Tremor, and Gait and Balance. Movement Disorder Society 2020; 35 (suppl 1). MDS Virtual Congress 2020. Abstract # 1415.

Analytical Validation of Algorithm in Human Subjects

Analytical Validation

- Can be performed in healthy population
- Benchmark can include a human rater or a device
- May require multiple iterations for algorithm optimization
- Testing for operational tolerance may be required
- Publicly available algorithms need to undergo the same procedure



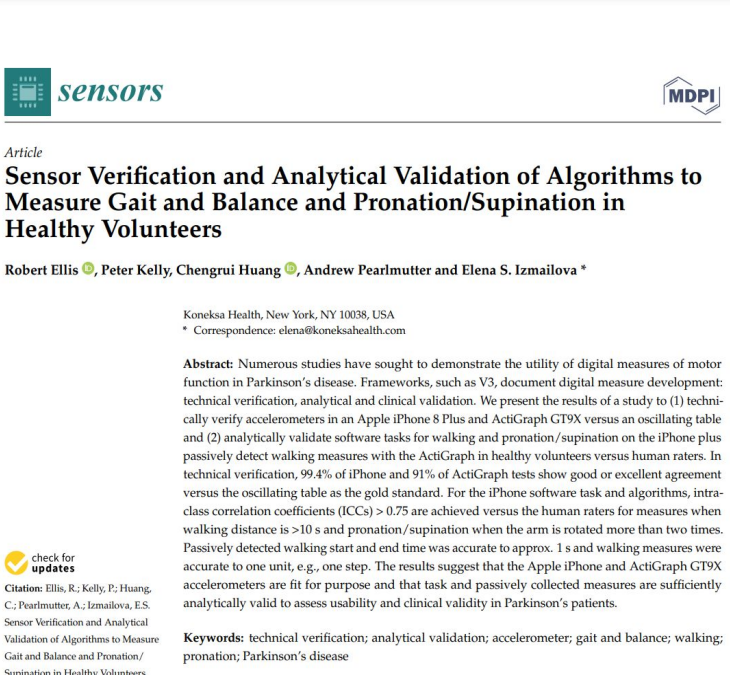


Assessment	Duration (s)	Distance (m)	Steps (count)	Speed (m/s)	Stride Period (s)
Analytical Validity (combined results for 5s, 10s, 15s, 20s walk)	0.989	0.987	0.992	0.764	0.593
Operational Variation (Loose Pocket)	N/A 20s walk of fixed duration	0.850	0.868	0.741	0.850
Operational Variation (Shoulder Bag)		0.932	0.858	0.837	0.798

Development of an Algorithm for the Evaluation of Gait and Balance Impairments in CNS Disorders.
Robert Ellis, Peter Kelly, Chengrui Huang. International Society for CNS Trials Methodology Autumn Meeting (Virtual), September 2020.

V3 Framework

- Transformational for educating the scientific community
- Building a tribal language
- Bringing everyone on the same page how to validate technologies for use in clinical trials



sensors

MDPI

Article

Sensor Verification and Analytical Validation of Algorithms to Measure Gait and Balance and Pronation/Supination in Healthy Volunteers

Robert Ellis, Peter Kelly, Chengrui Huang, Andrew Pearlmutter and Elena S. Izmailova *

Koneksa Health, New York, NY 10038, USA
* Correspondence: elena@koneksahealth.com

Abstract: Numerous studies have sought to demonstrate the utility of digital measures of motor function in Parkinson's disease. Frameworks, such as V3, document digital measure development: technical verification, analytical and clinical validation. We present the results of a study to (1) technically verify accelerometers in an Apple iPhone 8 Plus and ActiGraph GT9X versus an oscillating table and (2) analytically validate software tasks for walking and pronation/supination on the iPhone plus passively detect walking measures with the ActiGraph in healthy volunteers versus human raters. In technical verification, 99.4% of iPhone and 91% of ActiGraph tests show good or excellent agreement versus the oscillating table as the gold standard. For the iPhone software task and algorithms, intra-class correlation coefficients (ICCs) > 0.75 are achieved versus the human raters for measures when walking distance is >10 s and pronation/supination when the arm is rotated more than two times. Passively detected walking start and end time was accurate to approx. 1 s and walking measures were accurate to one unit, e.g., one step. The results suggest that the Apple iPhone and ActiGraph GT9X accelerometers are fit for purpose and that task and passively collected measures are sufficiently analytically valid to assess usability and clinical validity in Parkinson's patients.

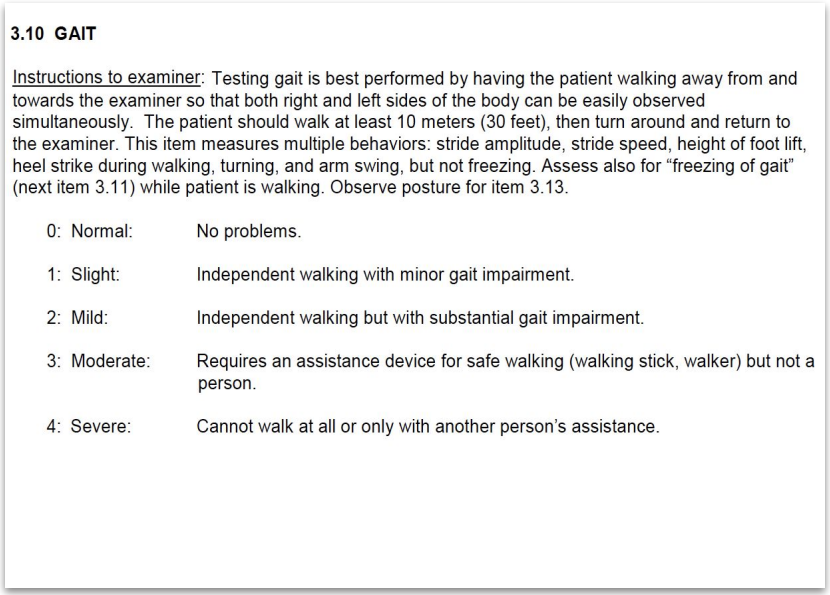
Keywords: technical verification; analytical validation; accelerometer; gait and balance; walking; pronation; Parkinson's disease

check for updates

Citation: Ellis, R.; Kelly, P.; Huang, C.; Pearlmutter, A.; Izmailova, E.S. Sensor Verification and Analytical Validation of Algorithms to Measure Gait and Balance and Pronation/Supination in Healthy Volunteers

Clinical Validation Is Not the Whole Story

Clinical Validation



3.10 GAIT

Instructions to examiner: Testing gait is best performed by having the patient walking away from and towards the examiner so that both right and left sides of the body can be easily observed simultaneously. The patient should walk at least 10 meters (30 feet), then turn around and return to the examiner. This item measures multiple behaviors: stride amplitude, stride speed, height of foot lift, heel strike during walking, turning, and arm swing, but not freezing. Assess also for "freezing of gait" (next item 3.11) while patient is walking. Observe posture for item 3.13.

0:	Normal:	No problems.
1:	Slight:	Independent walking with minor gait impairment.
2:	Mild:	Independent walking but with substantial gait impairment.
3:	Moderate:	Requires an assistance device for safe walking (walking stick, walker) but not a person.
4:	Severe:	Cannot walk at all or only with another person's assistance.

Clinical Validation
Relationship with conventional **clinical outcomes** in addition to:
Construct Validity convergent and known group validity of new measures versus existing validated measures
Responsiveness: sensitivity to change and responder analysis over relevant timescales
Reliability: test-retest reliability of measures, reliability of devices

+

Usability, Safety and Face Validity
Usability: can patients perform data collection procedures independently and navigate technology-related apps?
Safety: can patients safely use the digital instrument?
Multi site operational tolerance: can site staff and patients operate the instrument successfully and routinely with high compliance in a clinical study setting?
Face validity: how the data behaves overall and whether it can be interpreted in the context of a chosen indication?

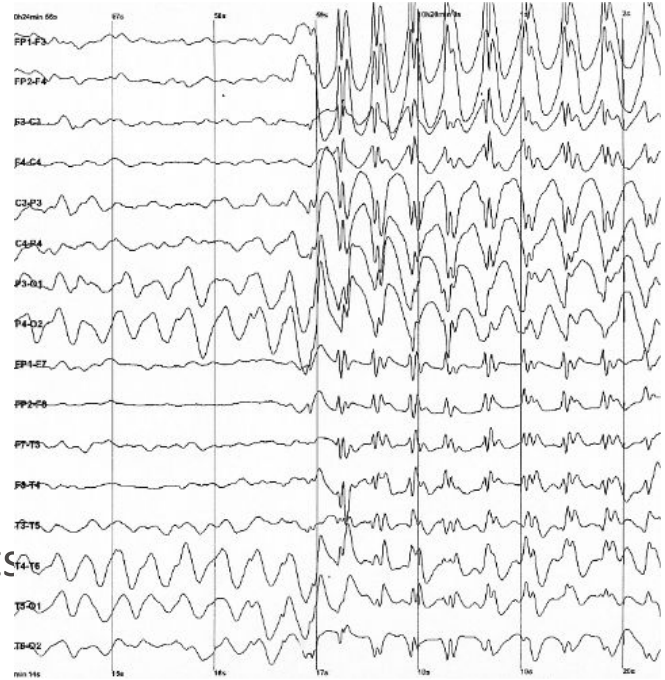
koneksa

Case Study 2: Clinical Validation of a Digital Health Technology

Clinical Validation of Portable EEG

Study: Wake and Sleep State Transitions on a Portable Electroencephalogram (EEG) Device in Narcolepsy Patients and Healthy Participants

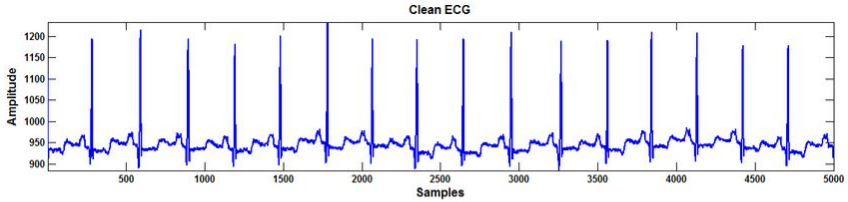
- Validation
  - Concordance of sleep state scoring
  - Correlation of sleep transitions
  - *In-clinic comparison to gold standard PSG*
- Digital Biomarker
  - Night to night variability in sleep patterns
    - Sleep transitions
    - Healthy vs Narcolepsy
  - *At-home data (portable EEG only)*
- Patient population: Healthy and Narcolepsy patients



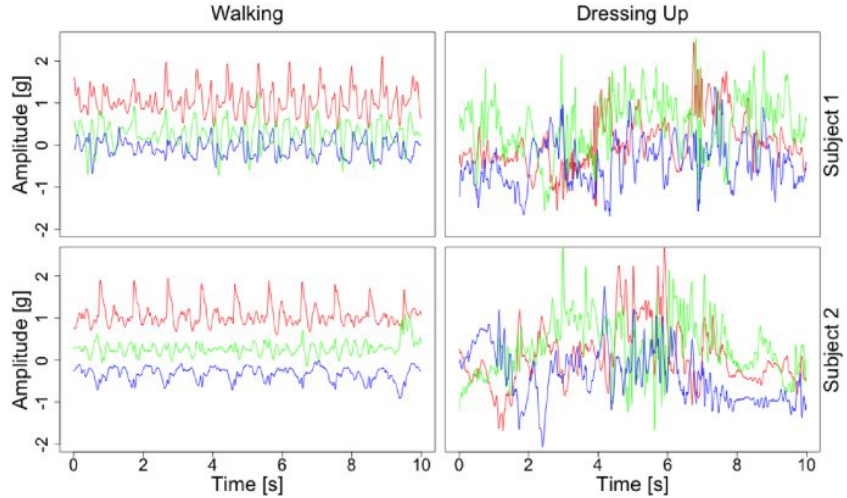
https://en.wikipedia.org/wiki/Epilepsy#/media/File:Spike-waves.png

Digital Devices

- Portable EEG system
  - Lightweight and designed for nighttime use
- Portable ECG system (exploratory)
  - Chest patch for continuous at-home wear
- Accelerometry (exploratory)
  - Wrist-worn actigraphy for additional metrics
  - Activity level, intensity, rest, sleep
- ePRO
  - Sleep quality
  - Narcolepsy symptoms

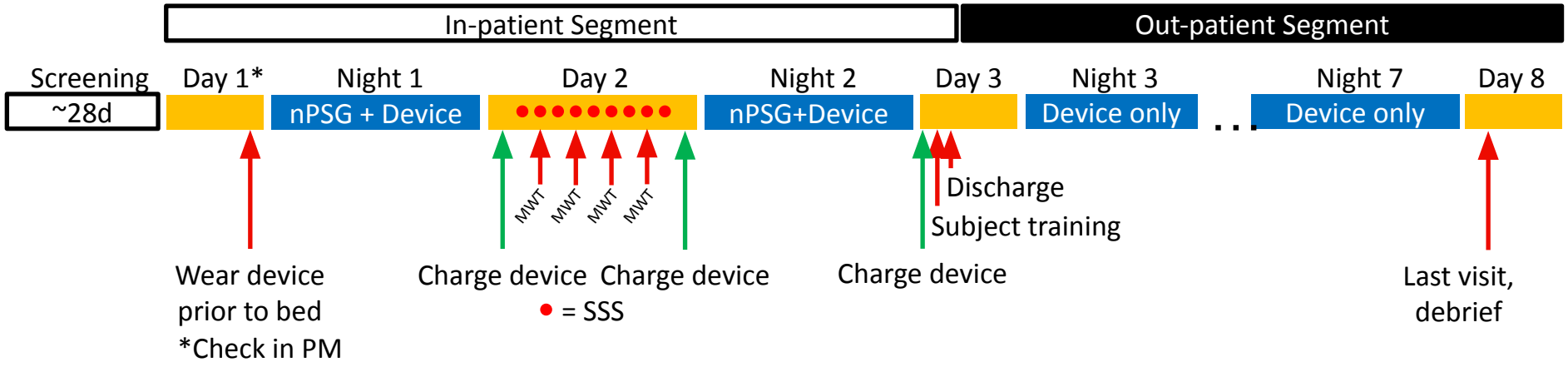


Mohan, N et al. (2016). Modified Variational Mode Decomposition for Power Line Interference Removal in ECG Signals. International Journal of Electrical and Computer Engineering (IJECE). 6. 151



Karas, M et al. (2018). Accelerometry Data in Health Research: Challenges and Opportunities: Review and Examples

Study Design



1. Study will include 16 people with narcolepsy and 16 age/gender matched healthy controls
2. Digital devices include night-time EEG, 24/7 accelerometry and ECG monitoring, and ePRO diary
3. 2 nights of in-patient testing to enable testing EEG device against gold-standard nPSG
4. 5 nights of out-patient testing for at-home use of digital devices
5. Subjects will keep an ePRO diary for sleep quality as well as narcolepsy symptoms

Expected Outcome of Validation Study

- Determine if portable EEG is fit-for-purpose (clinical validation)
  - Narcolepsy patient population
- Digital Biomarker: sleep transitions
  - Can biomarker be measured at home
- Operational experience with digital devices
  - Build confidence across functional groups
- Results presented at Sleep 2022 conference in Charlotte, NC
  - Max Tolkoff, PhD

https://myfulfillmentcompany.com/operational-expertise/

Overall Message

- V3 framework: modular evaluation of digital measures
  - Verification
  - Analytical validation
  - Clinical validation
- Analytical validation: algorithmic performance against a gold standard
  - Takeda study: Withings ecosystem of devices
- Clinical Validation: does the DHT accurately measure a meaningful outcome metric for the specific patient population
  - Portable EEG system to measure sleep parameters remotely in patients with narcolepsy

Successful use of the V3 framework will demonstrate that your DHT is fit-for-purpose

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Resource in Action

Be a Part of the DiMe Community Resources in Action Hub

Tell us your DiMe “Resource in Action” story and we’ll feature it in our Resource in Action Hub!

DIGITAL MEDICINE SOCIETY

Submit to DiMe's Resource in Action Hub!

Source: https://www.dimesociety.org/community-building/case-study-hub/

The V3 Framework is the industry standard for evaluating DHTs:

- **Cited over 120 times** in the scientific literature
- Foundational to **EMA** and **NIH** perspectives and recommendations
- Aligned with **FDA** guidance

Share your interest in joining us:

Extending the V3 Framework to include principles of human factors, human-centered design and usability

Source: https://docs.google.com/forms/d/e/1FAIpQLSdv8VWdAnLinGjk73PJDxR9exPyKpeSdmxGud5ANYl-YgDS3g/viewform?usp=sf_link

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How Can We Be Accountable for D, Equity, and Inclusion in Digitized Clinical Trials?

Wednesday, November 30 at 12:00 PM (ET)

DIVERSITY, EQUITY, & INCLUSION in Digitized Clinical Trials

DIGITAL MEDICINE SOCIETY

Del Smith
Co-founder and CEO
Acclinate

Ingrid Oakley-Girvan
SVP of Research and Strategy
Medable

Ricki Fairley
CEO
Touch, The Black Breast Cancer Alliance

Shivani Mehta
Head Marketing and Sponsorship
Johnson and Johnson

Ed Ramos
Director, Digital Clinical Trials and Principal Science Officer at CareEvolution, Inc
Scripps Research

Michel Reid
Sr. Director and Head, Global Demographics & Diversity
GSK

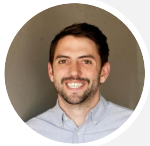
Sam Eells
Co-founder
Lightship

Yashoda Sharma (Moderator)
Program Director
Digital Medicine Society (DiMe)

The State of the Virtual Care Industry: Results from a New Benchmark Survey from Omada Health, DiMe & Rock Health

Thursday, December 1 at noon ET

Linette Demers (Moderator)
Director, IMPACT
Digital Medicine Society (DiMe)



Sean Duffy
CEO
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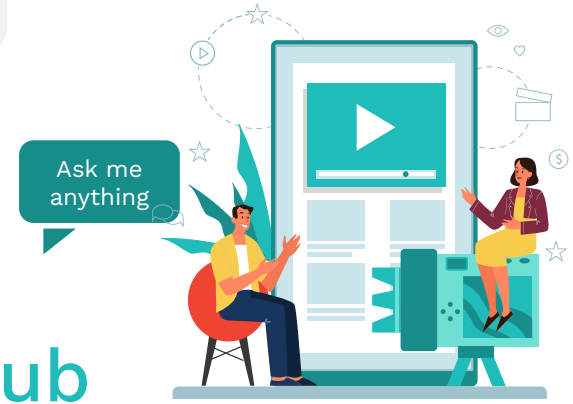
Meg Barron
VP, Digital Health Strategy
American Medical Association (AMA)

Kate Brown
Partner, Lead Center for Innovation
Mercer

Megan Zweig
COO
RockHealth

Virtual Journal club



The Patient Matters in the End(point)

December 7th, 2022 | 11am ET

Diana Rofail, PhD, MBA
Global Head and Senior Director, PCOR
Regeneron

Pip Griffiths, PhD
Program Lead
Digital Medicine Society (DiMe)

Jen Goldsack (Moderator)
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THANK YOU

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