V3 in Action:
How organizations are systematically embedding V3 in their digital measures strategy

November 3, 2022 11 AM ET
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.

Introducing the Digital Medicine Society (DiMe)

We launched in May 2019...

Introducing the Digital Medicine Society (DiMe)

... and sit at the intersection of two communities

Source: https://www.dimesociety.org/index.php/about-us-main
Introducing the Digital Medicine Society (DiMe)

We deliver clinical quality work on a tech timeline

**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.

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

New knowledge & capabilities in the field spark new collaboration opportunities

Greatest challenges & opportunities to advancing the field

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).

**BioMeT** - Biometric Monitoring Technology

Source: [https://www.nature.com/articles/s41746-020-0260-4](https://www.nature.com/articles/s41746-020-0260-4)
Modular evaluation of digital measures

- **Design Specifications & Modular Prototyping**
- **Verification**
  - Changes to hardware/firmware?
    - Reverification, or
    - Documentation of back-compatibility
- **Analytical validation**
  - Changes to software that change algorithm?
    - Repeat analytical validation, or
    - Documentation of back-compatibility
- **Clinical validation**
  - 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](https://www.nature.com/articles/s41746-020-0260-4)
V3 processes are typically conducted by experts across disciplines and domains

Activity performed by:

- Verification
- Analytical Validation
- Clinical Validation

Stage involves human subjects

- (non-clinical) engineers
- Both engineers and clinically-trained professionals
- Clinically-trained professionals

Source: [https://www.nature.com/articles/s41746-020-0260-4](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://www.nature.com/articles/d41573-020-00168-z)
- [https://content.iospress.com/articles/journal-of-parkinsons-disease/jpd202416](https://content.iospress.com/articles/journal-of-parkinsons-disease/jpd202416)
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Head of Sensing and Measurement, Takeda

Elena Izmailova
Chief Scientific Officer, Koneksa

Moderator: Jen Goldsack
CEO, Digital Medicine Society
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?

- 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

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Analytical Validation of Algorithm in Human Subjects

- 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

**Table: Analytical Validation**

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

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
Clinical Validation Is Not the Whole Story

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?
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

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
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
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!

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/1FAIpQLSdv8VWdAnLinGjk73PJDxR9exPyKpeSdmlxGud5ANYl-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)

Del Smith
Co-founder and CEO
Acclinate

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

Ingrid Oakley-Girvan
SVP of Research and Strategy
Medable

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

Ricki Fairley
CEO
Touch, The Black Breast Cancer Alliance

Sam Eells
Co-founder
Lightship

Shivani Mehta
Head Marketing and Sponsorship
Johnson and Johnson

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
Virtual Journal club

The Patient Matters in the Endpoint

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)
CEO
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THANK YOU

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