Landscape Analysis of Biometric Monitoring Devices (BMDs) utilized in assessing Cognition, Sleep and Mobility in Alzheimer disease and other age-related Neurological Diseases.

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Background

The general public and collective biomedical research enterprise are increasingly embracing local and remote monitoring technologies, mobile smartphone apps, and portable/wearable devices into their activities of daily living. Many view these devices as future path to provide a deeper understanding of disease processes, patients' cognitive and functional status, and quality-of-life assessments. Biometric Monitoring Devices (BMDs) refer to the use of a biosensor(s) to continuously collect objective data on a biological recognition element (glucose, hormone levels, etc.), or integrated physiological parameters (blood pressure, mobility/motor, memory/processing, speech/sleep patterns, social engagement, etc.). BMDs utilize algorithms to transform data into a format that is interpretable as a specific measure, or, an aggregate functional outcome. Health platforms using BMDs are providing clinicians real-time evidence that allows efficient and continuous collection of data and assessments to monitor clinically meaningful parameters.

The lack of clarity regarding the appropriate use of BMDs as Drug Development Tools to support drug registration trials was recently underscored by the newly appointed Commissioner of the FDA, Dr. Scott Gottlieb's June 15, 2017, blog: "Fostering Medical Innovation: A Plan for Digital Health Devices" (Ref. 1).

Methods

The Coalition Against Major Diseases (CAMD) is a non-profit consortium at the Critical Path Institute. In the rapidly-evolving space of BMD utilization (Figure 1), CAMD convened diverse stakeholders from industry, academia, advocacy groups, and regulatory agencies to create new Drug Development Tools (DDTs) that can accelerate the drug development process. CAMD conducted a landscape analysis of BMDs utilized in assessing cognition, sleep, and mobility in Alzheimer disease (AD) and other age-related neurological diseases (Figure 2).

Figure 1 Examples of Efforts in the Rapidly-Evolving Digital Space

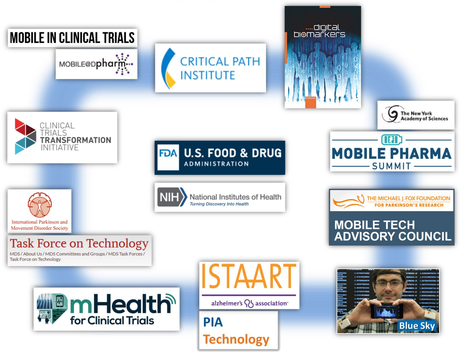
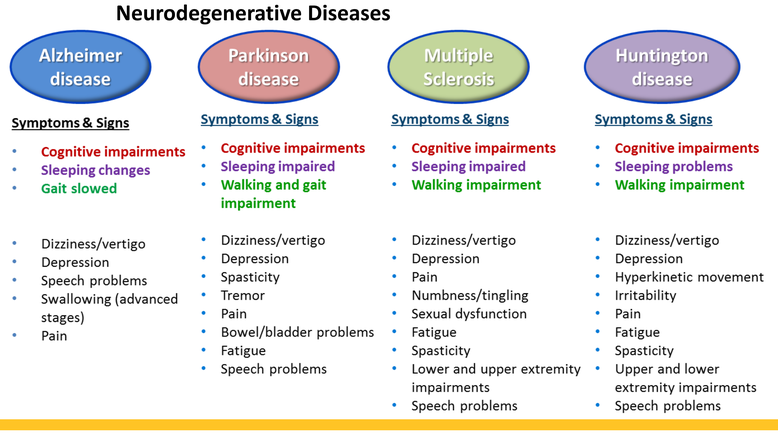


Figure 2 Impaired Cognition, Sleep and Mobility are Prominent across Neurodegenerative Diseases

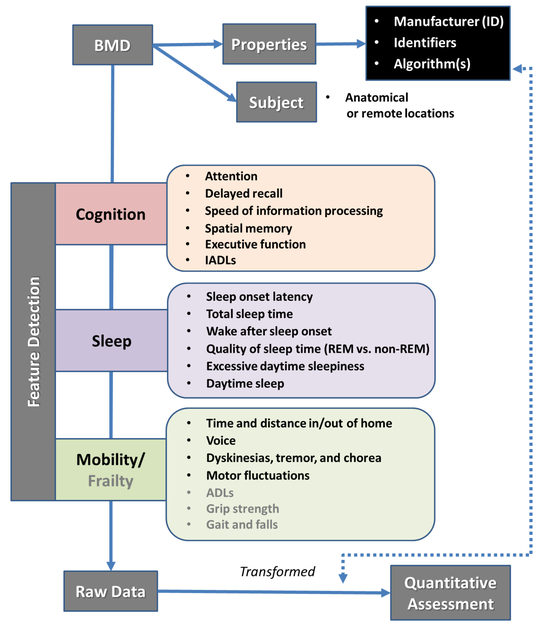


Results

- CAMD convened workshops to gather and unify the research community, subject-matter experts, device developers, standard development organizations, and regulators around the identification of existing gaps and challenges.
- CAMD performed a landscape assessment of the evolving digital space (Table 1), with focus on:
  - Pre-competitive coordination/collaboration with key organizations;
  - Creation of a common lexicon and information dissemination (Ref. 2);
  - Assessments of existing devices in use;
  - Regulatory-science-based planning of use-cases for potential integration into clinical trial tools and a regulatory pathway across neurological diseases.

Figure 3 Data flow from Biometric Monitoring Devices (BMDs) assessing specific Measures for each Concept-of-Interest: High-level Information Capture

- BMDs represent a paradigm shift in developing evidence of biomarker changes or clinical endpoints for clinical trials.
- An innovative approach to data standardization across concepts-of-interest in neurodegenerative diseases (Figure 3), data integration, data analytics, and result validation is required.



Conclusion

- BMDs are promising, but as yet unproven, DDTs to advance innovative treatments for various stages of AD and other neurodegenerative diseases. A limitation of this initial survey is that it does not contain all the evolving technologies and approaches. This will be the focus of a future review.
- The volume and quality of studies of BMD data generation/validation/ interpretation, the comparability among studies, and the pathway to overcome the challenges confronting the successful use and acceptance of BMDs for clinical research in CNS diseases will be improved with pre-competitive sharing of study results to insure comparability of assessments.
- For additional FDA guidance on this topic see Ref. 3.

References

1. Gottlieb, S. Fostering Medical Innovation: A Plan for Digital Health Devices. FDA Voice, June 15, 2017 (see QR code)
2. Dorsey, E.,R. A digital journal for a digital era. Digital Biomarkers (2017) DOI: 10.1159/000458512
3. FDA – Digital Health (see QR code)

Table 1 Preliminary Landscape Survey of FDA-Cleared Devices and Devices Seeking FDA Approval

TECH. ASSESS.	USE-CASE(S)	ATTRIBUTES	GAP	LINK
COGNITION				
Cognivue® (Cerebral Assessment Systems®)	• Computer-based platform designed expressly for primary-care physicians to measure and monitor brain health to detect the early signs of dementia	• 510K compliant • FDA cleared for specific use-case • Secure data transfer	Not validated for clinical trial assessments	
ImPACT® Applications, Inc. (Immediate Post-Concussion Assessment and Cognitive Testing)	• A clinician's computerized concussion testing of patients ages 12-59 • ImPACT is the most-widely used computerized neuro-cognitive test to help evaluate and manage concussions • Supported by a database of clinical research, including more than 250 peer-reviewed and 145 independent studies	• 510K compliant • FDA cleared for specific use-case • Secure data transfer • Extensive research • Pursuing additional uses	Not validated for clinical trial assessment of cognition, or use outside traumatic brain injury	
CANTAB® (Cambridge Cognition)	• CANTAB Recruit is an online trial recruitment platform helping pharmaceutical & biotechnology companies identify qualified clinical trial participants in high-need indications such as Alzheimer disease • CANTAB Connect offers precise, objective and reliable digital cognitive assessment solutions for pharmaceutical clinical trials in all therapeutic areas from phases I – IV • Wearable and smartphone apps for high frequency real-world data collection to improve the understanding of the real-world impact of clinical interventions • Assesses: Psychomotor speed, attention, memory, executive function and social function	• GCP Compliant • Analytically validated • Time-stamped • Assessments across various patient populations including: AD, Parkinson disease (PD), Epilepsy, Depression, Attention Deficit/ Hyperactivity Disorder (ADHD), Autism Spectrum Disorder, Down's Syndrome, Cognitive Safety, Mild Cognitive Impairment, Depression, Huntington disease, Multiple Sclerosis, Stroke, Schizophrenia, Traumatic Brain Injury	Currently undergoing clinical trial validation assessments for use-cases	
Cogstate	• Significant clinical trial experience across AD, PD, ADHD, Schizophrenia, Depression, Epilepsy	• Cleared in Canada • Secure data transfer • Culture and education-neutral • No learning effect	Not validated as COA in U.S. for AD	
Akili™ Interactive	• Measurements over time from tracking patients' conditions to understanding the effect of interventions on brain function • Screening and monitoring products for short measurements configurable to custom tracking needs (hourly, daily, weekly, etc.). • Each individual assessment utilizes the technology platform's proprietary measurement of cognitive control in a format that engages the patient	• High quality, ultra-frequent, more sensitive cognitive data for use in clinical decision making and clinical trials • GCP-compliant • Time-stamped • Active programs in ADHD, PD, AD, Depression, and others	Seeking: • 510K compliance • FDA clearance for specific use-cases • Large RCT in progress for ADHD therapy, smaller RCTs for other programs to confirm clinical validation	
SLEEP				
TECH. ASSESS.	**USE-CASE(S)**	**ATTRIBUTES**	**GAP**	**LINK**
Zmachine® Synergy (GENERAL sleep)	• General Sleep specializes in the design and development of medical devices which use electroencephalography (EEG) in a variety of clinical and research applications, such as anesthesiology, human performance, and sleep medicine	• FDA-cleared EEG-based sleep staging technology with traditional respiratory measures • Potential insurance reimbursement	Not validated for assessments in individuals with neurodegenerative diseases	
Actiwatch (Philips)	• Collects up to nine different parameters (depending on model) • Gathers important outcome measures for pharma, academic research, and clinical applications • Records valuable sleep and activity endpoints for studies in areas such as pain, fatigue, and depression • Off-wrist detection – indicates device not worn and audibly reminds to put device back on • Long-term recording – supports months of data recording • Advanced light sensing – records photopic, red, green, and blue light • Direct USB connectivity – enables rapid charging and data retrieval • Rechargeable battery – eliminates need for battery changes • Subjective scoring (Actiwatch Spectrum PRO only) – record two subjective scores manually/on a programmed schedule	• Validated against PSG gold standard for sleep measures • Used in hundreds of studies in a variety of environments • Used on infants through the elderly • FDA-cleared for specific use-case • Secure data transfer	Not validated for assessments in individuals with neurodegenerative diseases	
MOBILITY				
TECH. ASSESS.	**USE-CASE(S)**	**ATTRIBUTES**	**GAP**	**LINK**
MotionWatch 8® (CamNtech)	• Combining tri-axial accelerometer with built-in ambient light sensor and event marker, the MotionWatch 8 provides a solution for short-term or long-term activity and sleep recording with no interruptions for battery charging • Daytime Physical Activity Analysis • Detection of sleep disorders • Pediatric Sleep • Circadian Rhythm disorders • PLMS detection option	• 510K-compliant • FDA-cleared for specific use-cases • Secure data transfer • Event marker button • Light sensor • Up to 120 days recording time • Waterproof • Measures some sleep parameters	Not validated for clinical trial assessments for neurodegenerative diseases	
wGT3X-BT (ActiGraph™)	• Wearable activity monitors and cloud-based CentrePoint software platform deliver protocol-specific Daytime Physical Activity and sleep measures derived from high resolution accelerometer data and a selection of validated algorithms developed by members of the global academic research community • Daily activity profile - steps taken, kcals, and activity counts • Bouts of sustained physical activity • Intensity of physical activity (sedentary, MVPA, etc.) • Sleep score, including sleep time and efficiency • Patient wear time compliance • High resolution raw accelerometer data	• Cleared by FDA, EU, Canada, Australia/New Zealand • Class II medical device • USB and Bluetooth enabled smart technology • 25 day battery life • Waterproof • Measures some sleep parameters	Not validated for clinical trial assessments for neurodegenerative diseases	

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