ActiGraph™

DIGITAL HEALTH MONTHLY

SCIENTIFIC WEBINAR SERIES

Modernizing Clinical Research with AI and Digital Data: ActiGraph's Acquisition of Biofourmis Connect

February 20, 2025

NEXT MONTH Digital Health Monthly topic:

Combining Active and Passive DHT Monitoring to Accelerate Neurology Drug Development Through Functional Biomarkers: A Scientific Partnership Between ActiGraph and Indivi

Agenda

- **The "Why" Behind the Biofourmis Connect Acquisition**

Jeremy Wyatt

Chief Executive Officer, ActiGraph

- **Sensor-Derived and AI-Driven Insights Generation**

Christine Guo, PhD

Chief Scientific Officer, ActiGraph

- **Digital Clinical Trial Platform and Integration Roadmap**

Kim Rejndrup

Chief Product Officer, ActiGraph

The "Why" Behind the Biofourmis Connect Acquisition

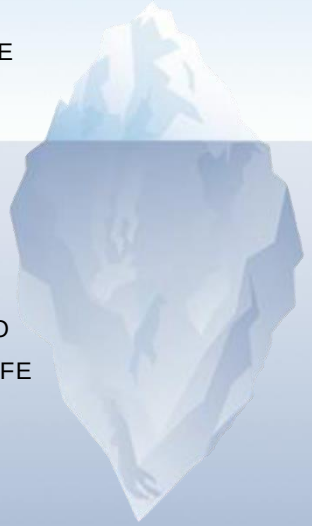
Jeremy Wyatt

Chief Executive Officer, ActiGraph

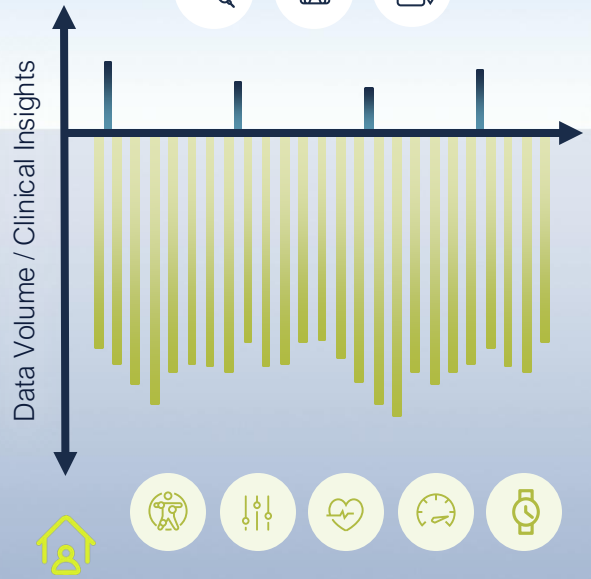
Modernize Clinical Research with Continuous Digital Data

WHAT WE SEE IN CLINIC

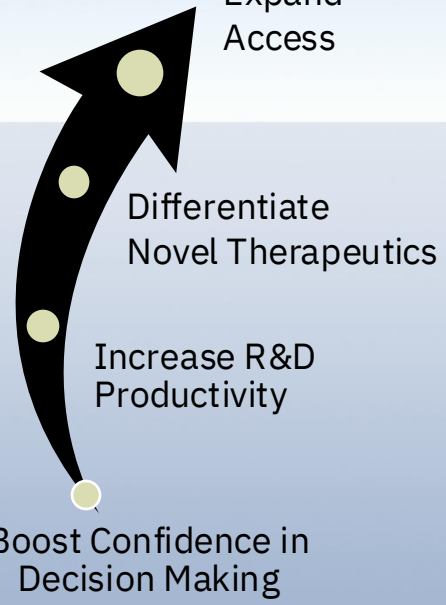
WHAT PATIENTS DO IN THE REAL LIFE



EPISODIC, SUBJECTIVE



CONTINUOUS, OBJECTIVE, PRECISE



Aligns with FDA Decision Making based on PDUFA VII

ActiGraph

ActiGraph BiofourmisConnect

Data sciences

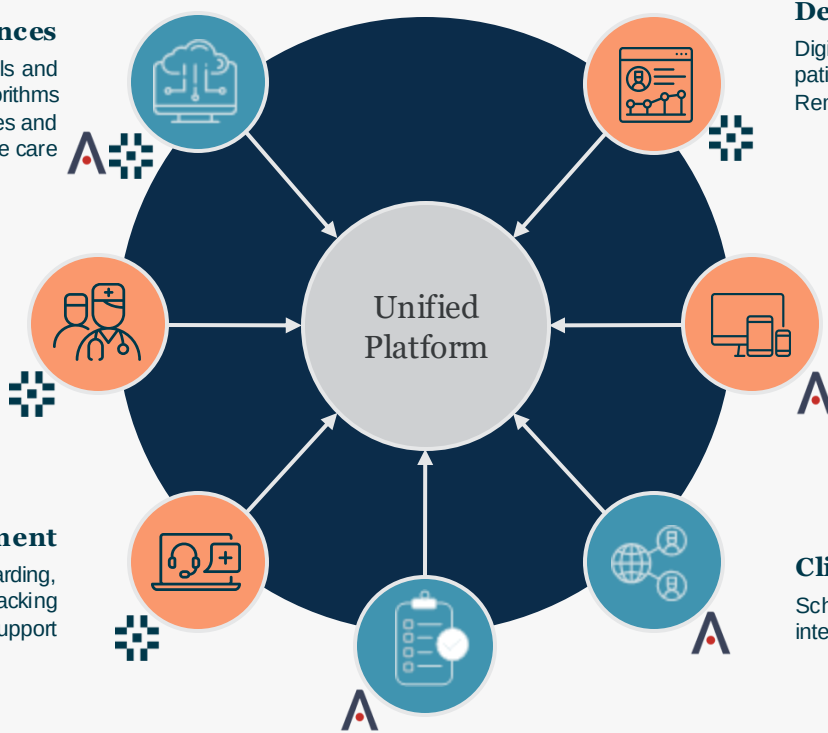
Harness physiologic data into digital vitals and digital biomarkers, and implement algorithms that can help enhance therapies and personalize care

Clinical Command Center

Tools to enhance clinical operations and study management for both sites and sponsors

Patient support & engagement

Virtual team to assist with onboarding, patient engagement, adherence tracking and 24/7 technical support



Regulatory & Compliance

Scalable product development services and workflows to enhance privacy and security needs

Decentralized technologies

Digital tools for remote management of patients including eConsent, ePRO, Remote Data Capture, and Virtual Visits

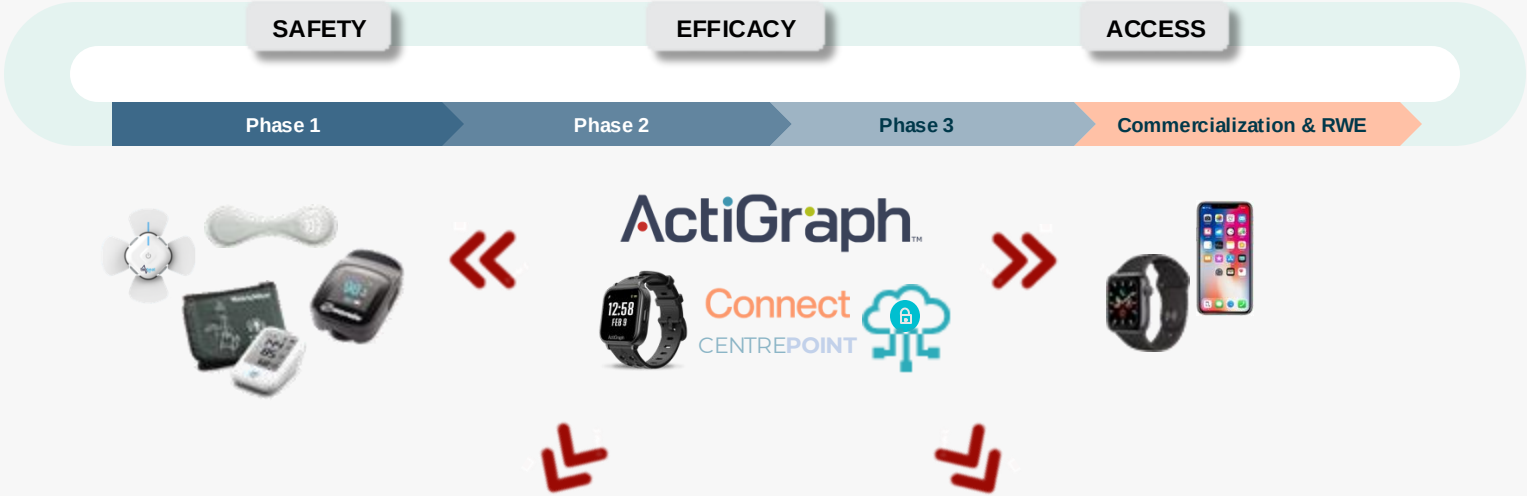
Integrations with multiple devices and sensors

Device agnostic platform connects medical-grade clinical devices and sensors for physiology monitoring and data collection

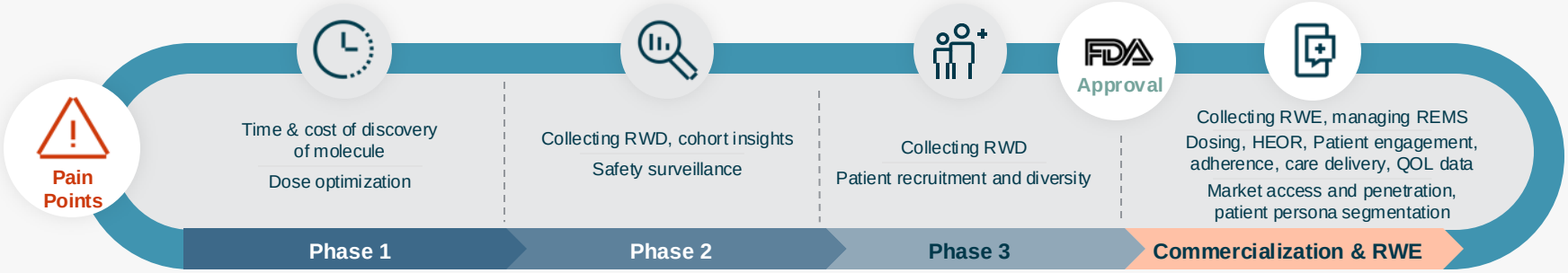
Clinical Operations

Scheduling, documentation, and EDC integration, logistics, virtual support

Expansion of ActiGraph Capabilities



Opportunity to Optimize Drug Lifecycle Value



Co Development → Digital Biomarkers | SaMD | Digital Companions

Clinical Development and Digital Trials

Commercial Validation & Market Access

Early-stage Candidates

- **Early evidence** to advance promising candidates, or "fail fast" unsuitable ones
- **Differentiation through SaMD** development

Mid/Late-stage Candidates

- Remote/decentralized monitoring for enhanced patient experience and **access to diverse population**
- Biosensor data for **improved assessment of efficiency, side effects, and outcomes**

Marketed Drugs

- Observational data and surveillance to inform **FDA post-market drug safety monitoring**
- Outcomes data so reimbursement can be informed by the **outcomes of real-world patients**

Algorithm Innovation & Integration

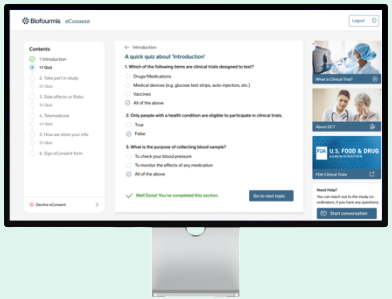
Learn about DECODE Partnerships

Algorithms obtained through proprietary development, acquisition, and in-licensing partnerships

...and more

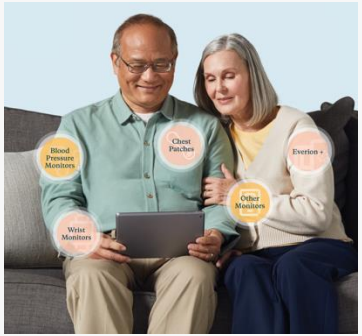
Solutions for patient centered clinical trials

Virtual Enrollment and eConsent



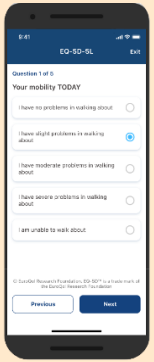
Streamline enrolment workflows and onboarding

Connected Sensors



Enable continuous participant monitoring

ePRO



Collect participant assessments and outcomes

Virtual Visits

Empower participant engagement and support

Sensor-Derived and AI-driven Insights Generation

Christine Guo, PhD

Chief Scientific Officer, ActiGraph

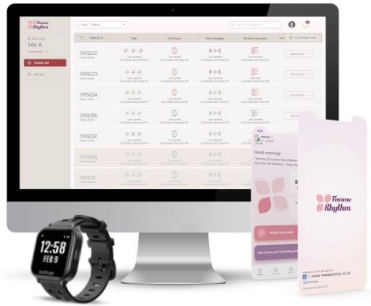
Sensor-derived and AI-driven Insights Generation

Comprehensive Tracking of Efficacy and Safety in Clinical Research

DHTs for Efficacy Measures

Pain Assessment

Objective Pain Measurement Using a Wearable Biosensor and a Mobile Platform in Patients With Endometriosis (NCT04318275)



DHTs for Safety Monitoring

Smart and Predictive Alert

Immunotherapy in the Outpatient Setting with continuous safety monitoring – case study with Yescarta (NCT05108805)

Day -5 to -3	Day 0	Day 1-14
Outpatient clinic: 1. Education about vital sign collection at home/ telemedicine 2. Pre-Yescarta® Chemotherapy	**Outpatient clinic:** Before 12:00 – Yescarta® premeds and infusion **At Home:** 16:30–RN visits subject at home 22:00–telemedicine call with NP	**Outpatient clinic:** Subject reports daily at 8:00 after checking vital signs at home **At home:** Subject returns home by 10:00 and checks vital signs at 12:00 16:30–RN visits subject at home 20:00–vital signs checked by subject 22:00–telemedicine call with NP

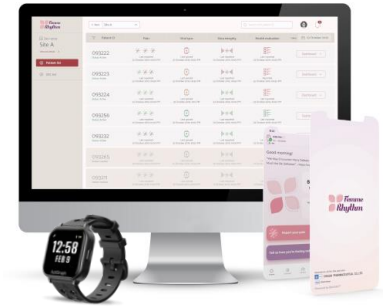
Sensor-derived and AI-driven Insights Generation

Comprehensive Tracking of Efficacy and Safety in Clinical Research

DHTs for Efficacy Measures

Pain Assessment

Objective Pain Measurement Using a Wearable Biosensor and a Mobile Platform in Patients With Endometriosis (NCT04318275)



DHTs for Safety Monitoring

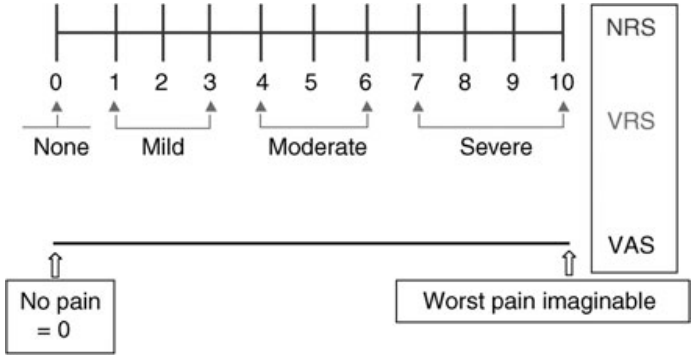
Smart and Predictive Alert

Immunotherapy in the Outpatient Setting with continuous safety monitoring – case study with Yescarta (NCT05108805)

Day -5 to -3	Day 0	Day 1-14
Outpatient clinic: 1. Education about vital sign collection at home/ telemedicine 2. Pre-Yescarta® Chemotherapy	**Outpatient clinic:** Before 12:00 – Yescarta® premeds and infusion **At Home:** 16:30–RN visits subject at home 22:00–telemedicine call with NP	**Outpatient clinic:** Subject reports daily at 8:00 after checking vital signs at home **At home:** Subject returns home by 10:00 and checks vital signs at 12:00 16:30–RN visits subject at home 20:00–vital signs checked by subject 22:00–telemedicine call with NP

Pain Digital Biomarker

- PAIN: “an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage”
- Persistence of pain is a serious health condition
- Sub-optimal or non-treatment of pain has profound physical, emotional and societal costs.
- Chronic pain affects approximately 20% of the population worldwide and costs between $560–635 billion in the United States alone
- Current ‘gold-standard’ pain assessment tools
  - Numeric rating scales (NRS)
  - Visual analogue scale (VAS)



Clinical Need for Objective Pain Assessment Tool

Self-reports are susceptible to inter-individual variabilities

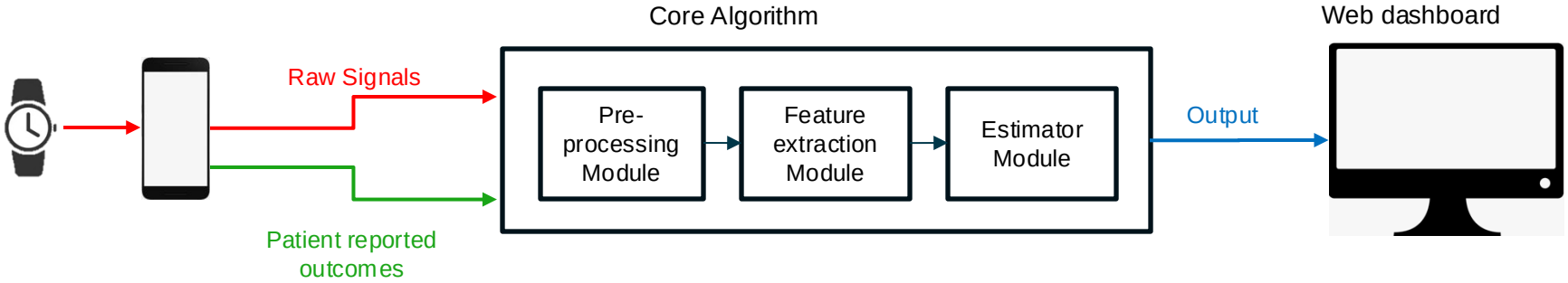
Accurate assessment of pain trends in highly critical for effective Pain Management

These pain scales could generate recall-bias

No objective tools to support clinicians in assessing:

- Whether someone is in pain
- The intensity of pain
- How pain impacts the patient's daily activities
- Whether an interventional procedure or a medication, provides a meaningful reduction of pain.

Pain Estimation ML Model



Multimodal Raw Signals

- PPG/BVP
- ACC
- Skin temperature
- etc

Patient reported outcomes

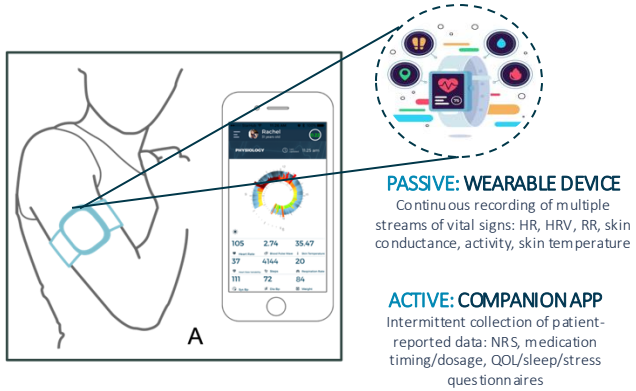
1. NRS
2. Disease-specific info
3. Medication timing, dosage
4. Pain trigger/location

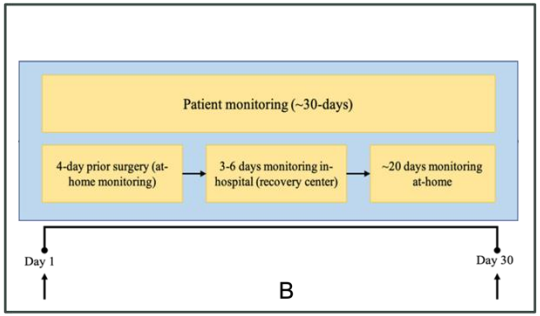
Output

Pain Index

Acute Pain Assessments: Post-surgical Pain (ObservePAIN)

Collaborator	Mundipharma Pharmaceuticals
Number of subjects	55 patients between 21 and 80 who have undergone knee replacement, Anterior Cruciate Ligament (ACL), Knee Arthroscopy and Foot & Ankle related surgery.
Duration	30 days
Data Collection	Pain reporting through mobile app and physiological data capture through wearable device over 30 days. Patients are monitored 4 days prior to surgery, followed by 3-6 days in-hospital monitoring and then subsequently 20 days at-home monitoring post-surgery.
Primary Endpoints	Agreement between patient-reported NRS pain (classified into None-Mild and Moderate-Severe) and BiovitalsPain™ Index, measured
Secondary /Exploratory Endpoints	Agreement between patient-reported NRS pain categories (classified into None-Mild, Moderate and Severe) and the BiovitalsPainTM Index. Agreement between patient-reported binary NRS pain categories (classified into None-Mild and Moderate-Severe) and the BiovitalsPain™ Index in patients using opioid medication for postsurgical pain relief.



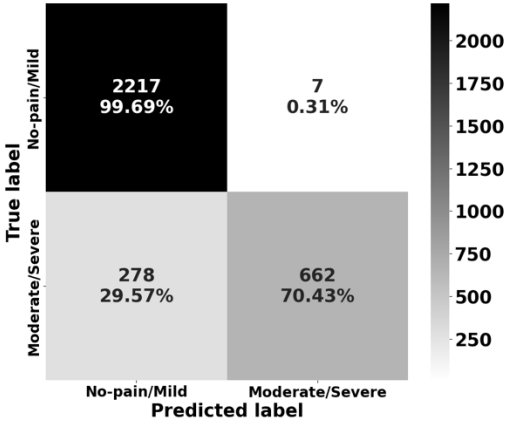


Results: Binary Classification

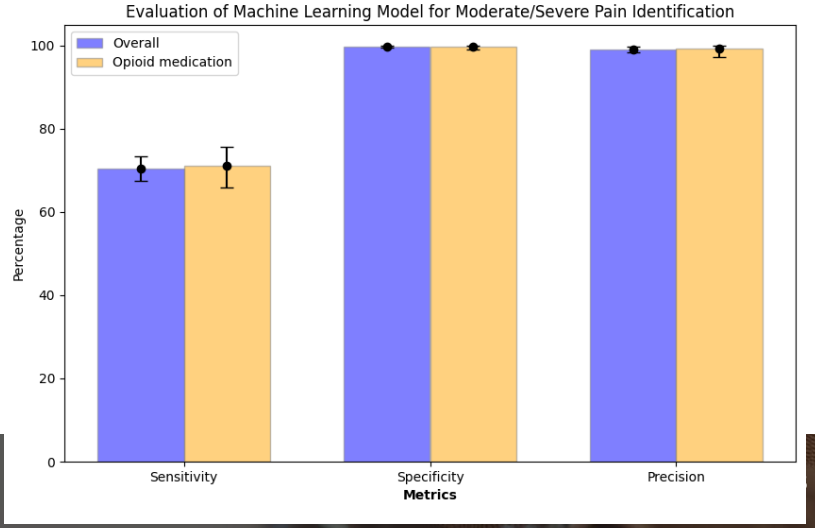
Primary objective: Pain identification for opioid prescription

- Pain Index Model structured towards high specificity to minimize false positives
- Likely reduce the chance of overmedication in patients, leading to lower rates of opioid prescription.

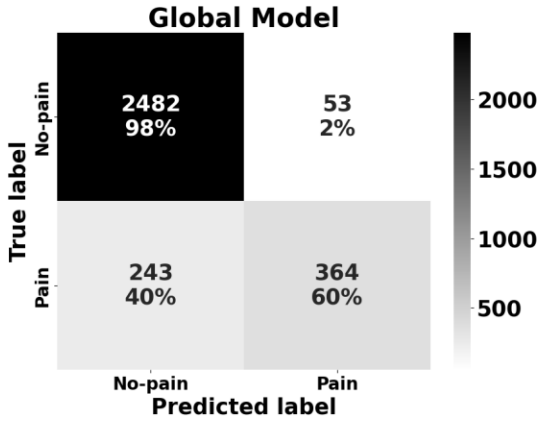
Metrics	Pain Index Model
Sensitivity	70.4% (67.5% - 73.3%)
Specificity	99.7% (99.5%-99.8%)
Precision	99.0% (98.2%-99.7%)

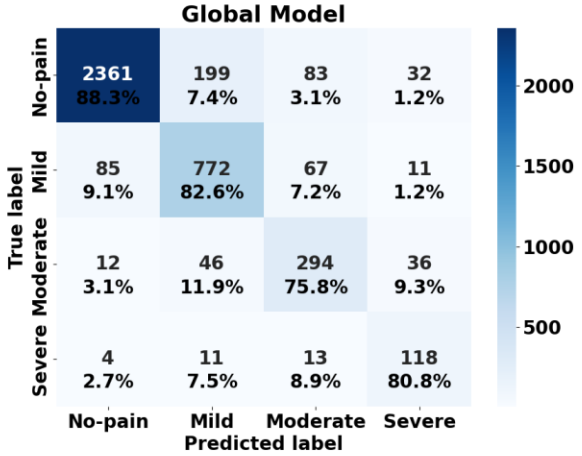


- Pain Index has comparable performance even in the patients using opioid medication for pain relief subgroup
- These patients are likely to have a different pain trajectory over time due to the influence of opioid medication.



Results: Pain Index Estimation

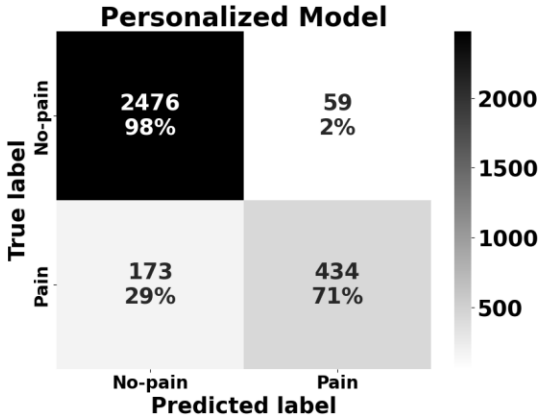




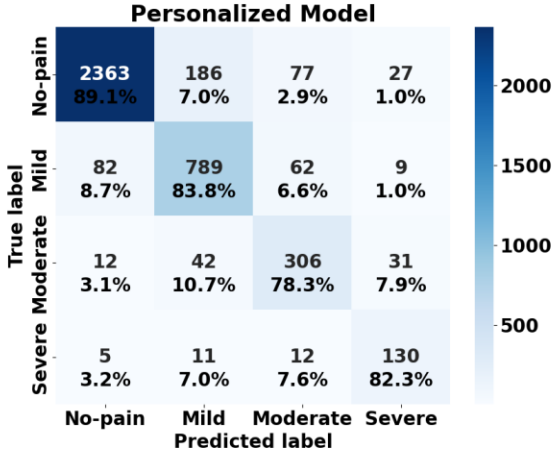
Agreement = 85.5%:
Cohen's Kappa = 0.73

	No Pain (0)	Mild (1-3)	Moderate (4-6)	Severe (7-10)
Sensitivity	88.3%	82.6%	75.8%	80.8%
Specificity	93.1%	92.0%	95.7%	98.0%
Precision	95.9%	75.1%	64.3%	59.9%

Results: Pain Index Estimation – Personalized Model



Metrics	Global Model	Personalized Model
Sensitivity	0.6	0.71
Precision	0.87	0.88
Specificity	0.97	0.97



Agreement = 86.6%:
Cohen's Kappa = 0.75

	No Pain (0)	Mild (1-3)	Moderate (4-6)	Severe (7-10)
Sensitivity	89.1%	83.8%	78.3%	82.3%
Specificity	93.4%	92.5%	96.0%	98.3%
Precision	96.0%	76.8%	67.0%	66.0%

Sensor-derived and AI-driven Insights Generation

Comprehensive Tracking of Efficacy and Safety in Clinical Research

DHTs for Efficacy Measures

Pain Assessment

Objective Pain Measurement Using a Wearable Biosensor and a Mobile Platform in Patients With Endometriosis (NCT04318275)

DHTs for Safety Monitoring

Smart and Predictive Alert

Immunotherapy in the Outpatient Setting with continuous safety monitoring – case study with Yescarta (NCT05108805)

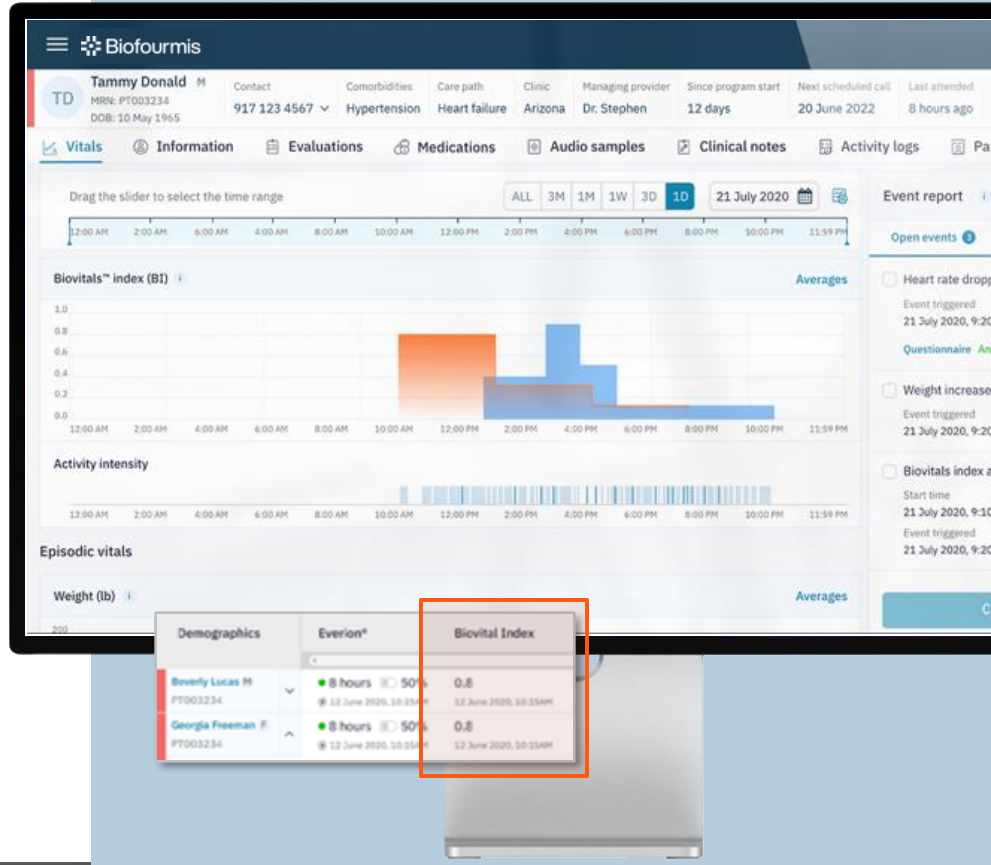
Day -5 to -3	Day 0	Day 1-14
Outpatient clinic: 1. Education about vital sign collection at home/ telemedicine 2. Pre-Yescarta® Chemotherapy	**Outpatient clinic:** Before 12:00 – Yescarta® premeds and infusion **At Home:** 16:30–RN visits subject at home 22:00–telemedicine call with NP	**Outpatient clinic:** Subject reports daily at 8:00 after checking vital signs at home **At home:** Subject returns home by 10:00 and checks vital signs at 12:00 16:30–RN visits subject at home 20:00–vital signs checked by subject 22:00–telemedicine call with NP

Biovitals® Index

Personalized baselines driving notifications of clinically-significant deviations

Personalized & Predictive

- FDA-cleared, machine learning algorithm that models vital baseline personalized to each subject
- Biovitals® Index (BI) is a scalar index between 0 and 1 that measures deviations in a subject's vital signs from his/her own baseline
- If BI is above 0.7 for a defined time period, a notification will be triggered, indicating the subject has significant deviation from their baseline and may be at increased risk for clinically significant deviations
- A foundation for disease-specific tailoring to fit a variety of clinical use cases



Biovitals Index -- Performance in COVID RPM:

Correlation with Biovitals Index, NEWS2 and COVID Viral Load

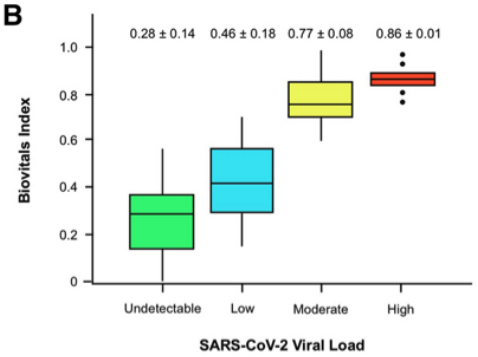
Study population: Thirty-four patient with mild COVID-19 at Queen Mary Hospital, HK

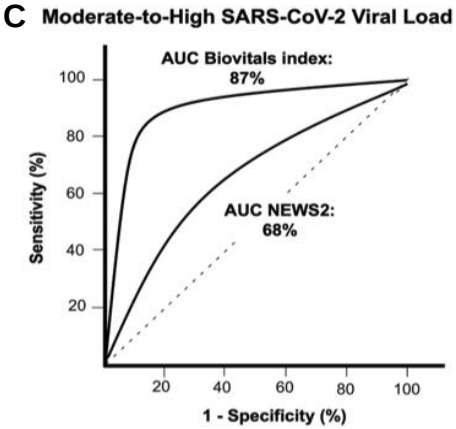
Methodology:

- Patient was wearing Everion during the study.
- Biovitals Index (BI) was generated autonomously, independent of symptoms and other medical data

Conclusion:

- BI was linearly positively associated with NEWS2 ($p<0.001$) (Fig A) and SARS-CoV-2 Viral Load ($p<0.0001$) (Fig B)
- Performance of BI was better (AUC = 87%) than that of NEWS2 (AUC = 68%) to identify moderate/high viral load (Fig C)
- BI was observed to be higher in the presence of clinical worsening events and lower in their absence. (Fig D)

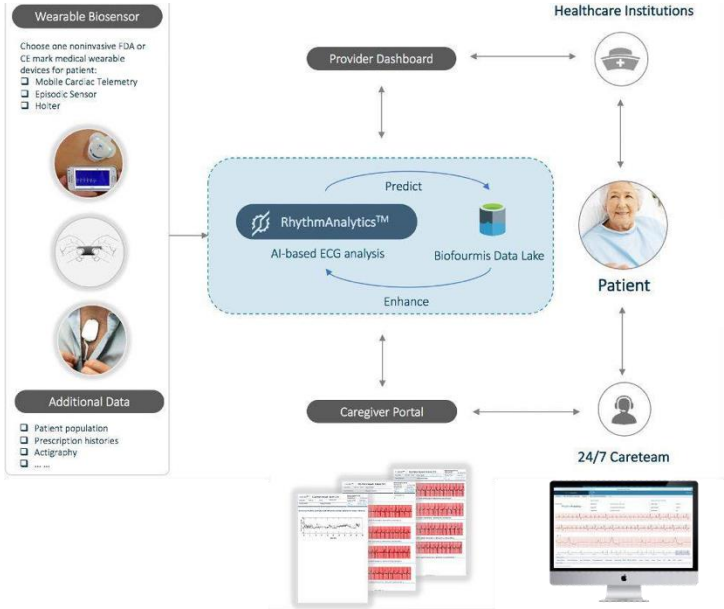




*[1] *UN, Ka-Chun, et al. Observational study on wearable biosensors and machine learning-based remote monitoring of COVID-19 patients. Scientific reports, 2021, 11.1: 1-9.*

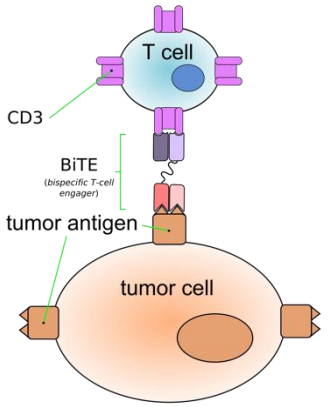
RhythmAnalytics™ for Arrhythmia Real Time Detection

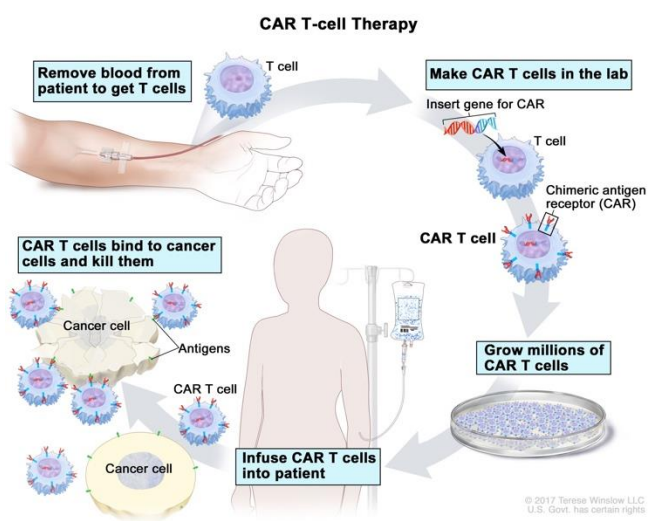
- Real-time detect beats/arrhythmias, morphology and heart rate measurement with high accuracy (real-world performance 95%+)
- Powerful 510(k) algorithm and easy to use cloud-based scalable API to be integrated by the client.
- Device agnostic.



% (95% CI)	Accuracy	F_1	FNR	FPR	NPV	PPV	Sensitivity	Specificity
Atrial fibrillation	98.4 (97.88-98.79)	97.5 (96.92-98.04)	0.0 (0.00-0.13)	2.4 (1.86-2.95)	100.0 (99.87-100.00)	95.2 (94.38-95.91)	100.0 (99.87-100.00)	97.7 (97.05-98.14)
Pause	99.7 (99.46-99.87)	99.5 (99.14-99.70)	0.0 (0.00-0.14)	0.4 (0.19-0.65)	100.0 (99.86-100.00)	99.0 (98.52-99.29)	100.0 (99.86-100.00)	99.7 (99.35-99.81)
PSVT	94.8 (93.98-95.57)	91.6 (90.55-92.54)	0.0 (0.00-0.13)	7.2 (6.32-8.17)	100.0 (99.87-100.00)	84.5 (83.16-85.75)	100.0 (99.87-100.00)	92.8 (91.83-93.68)
PVC	95.7 (94.94-96.39)	93.4 (92.46-94.24)	3.6 (3.01-4.35)	4.6 (3.89-5.39)	98.3 (97.76-98.70)	90.6 (89.50-91.59)	96.4 (95.65-96.99)	95.4 (94.61-96.11)
Sinus bradycardia	98.9 (98.42-99.19)	98.3 (97.74-98.68)	0.0 (0.00-0.13)	1.7 (1.27-2.20)	100.0 (99.87-100.00)	96.6 (95.89-97.19)	100.0 (99.87-100.00)	98.3 (97.80-98.73)
Sinus tachycardia	99.4 (99.05-99.62)	99.1 (98.68-99.37)	0.0 (0.00-0.13)	0.9 (0.61-1.30)	100.0 (99.87-100.00)	98.2 (97.66-98.62)	100.0 (99.87-100.00)	99.1 (98.70-99.39)
Ventricular bigeminy	98.5 (98.00-98.88)	97.7 (97.10-98.18)	0.0 (0.00-0.13)	2.2 (1.73-2.79)	100.0 (99.87-100.00)	95.5 (94.70-96.19)	100.0 (99.87-100.00)	97.8 (97.21-98.27)
Ventricular trigeminy	97.6 (96.95-98.06)	96.2 (95.47-96.84)	0.0 (0.00-0.13)	3.5 (2.92-4.24)	100.0 (99.87-100.00)	92.7 (91.71-93.58)	100.0 (99.87-100.00)	96.5 (95.76-97.08)
Any arrhythmia	98.4 (98.15-98.66)	99.0 (98.78-99.19)	1.9 (1.66-2.22)	0.2 (0.14-0.33)	93.0 (92.43-93.48)	99.9 (99.87-99.98)	98.1 (97.78-98.34)	99.8 (99.67-99.86)
Mean of specific arrhythmias	97.9 (97.55-98.21)	96.7 (96.46-97.27)	0.6 (0.51-0.84)	2.6 (2.24-2.99)	99.8 (98.81-99.13)	94.0 (94.11-95.16)	99.5 (99.16-99.49)	97.2 (97.02-97.76)

Immunotherapies and their Challenges





Goal

- Immune System Kills Tumor Cells

Current Issues

- Efficacy
- Recruitment
- Cost
- **Side Effects/Toxicities**
  - Sepsis
  - Cytokine Release Syndrome
  - Neurotoxicity

https://en.wikipedia.org/wiki/Blinatumomab#/media/File:BiTE_antibody_en.svg

https://www.cancer.gov/publications/dictionaries/cancer-terms/def/car-t-cell-therapy

Hegde, P.S. and Chen, D.S., 2020. Top 10 challenges in cancer immunotherapy. *Immunity*, *52*(1), pp.17-35.

https://www.hopkinsmedicine.org/inhealth/about-us/immunotherapy-precision-medicine-action-policy-brief

Sepsis – Assessment of risk

Sepsis/Severe Infection are major SAE common in immunotherapy populations

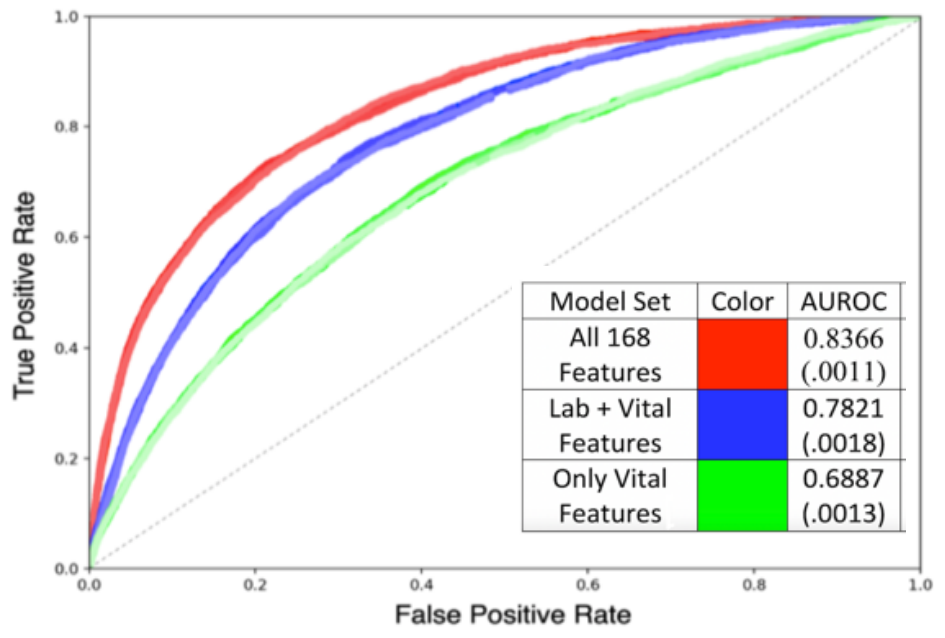
- CRS symptoms are like those of sepsis/infection

Evaluated the ML-based warning tool for sepsis around the time of clinical onset using 2019 PhysioNet Computing in Cardiology Competition dataset

- 4,000 developed/admitted with sepsis out of 40,000 patients evaluated

Vital sign features able to be monitored in remote settings: RR, SpO2, Temp, HR, BP are predictors of sepsis in advance of clinical onset

Continuous remote patient monitoring enhances the probability of early detection of infection & sepsis onset[1]



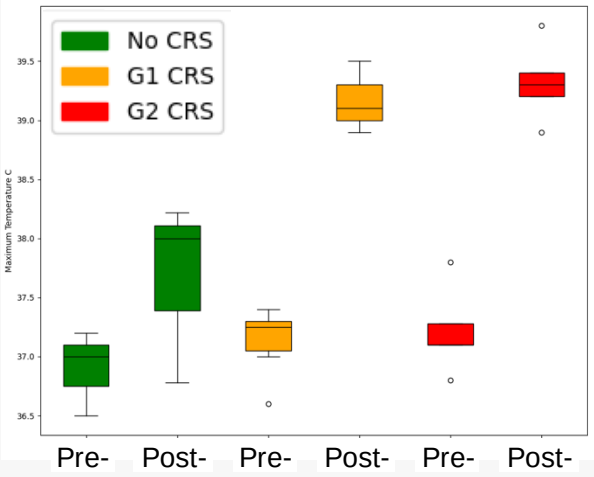
1) M. J. Pettinati, G. Chen, K. S. Rajput and N. Selvaraj, "Practical Machine Learning-Based Sepsis Prediction," 2020 42nd Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC), 2020, pp. 4986-4991, doi: 10.1109/EMBC44109.2020.9176323.

Cytokine Release Syndrome (CRS)

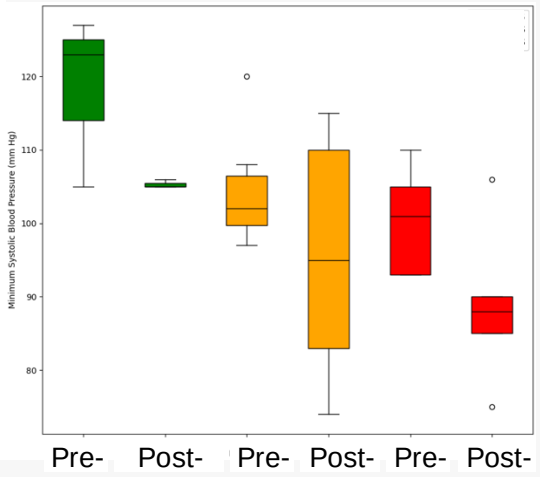
- **Challenges**
  - Patient Safety
  - Require Inpatient Treatment / Limit Access
  - Subjectivity in Adjudication based on episodic data
  - Potential for Treatment Variability
- **Opportunities with continuous monitoring**
  - Precise characterization of CRS
  - Enhance safety in outpatient setting
  - Increased Access to Treatments

CRS Parameter	Grade 1	Grade 2
Fever*	Temperature ≥38°C	Temperature ≥38°C
Hypotension	None	Not requiring vasopressors
Hypoxia	None	Requiring low-flow nasal cannula‡ or blow-by

Maximum Temperature

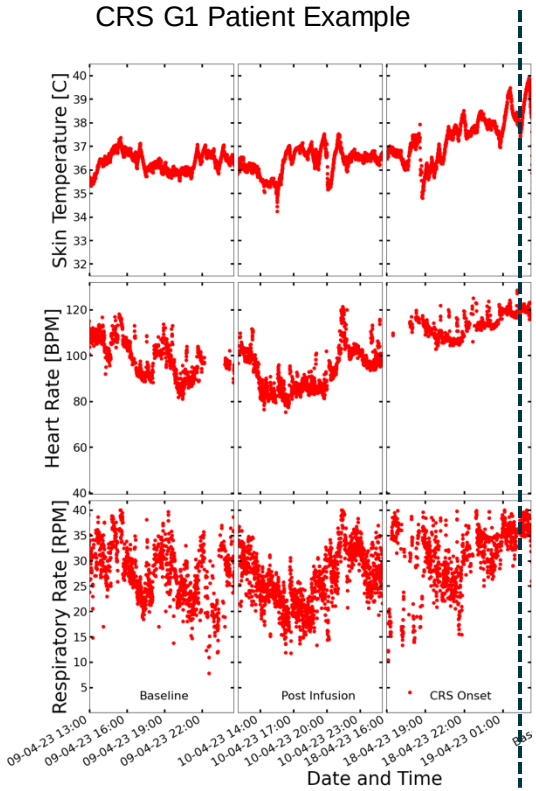


Minimum Systolic Blood Pressure



CAR-T Patient-level Case Studies: Continuous Data

- Multivariate continuous monitoring can be powerful to address inter-individual and intra-day variations
- Continuous vital monitoring is superior to the current episodic approach.
- The collection of CRS events needs to be standardized
- Preliminary analysis showed multivariate AI-driven approach hold potential to provide early warning of severe CRS (G>2)



Digital Clinical Trial Platform and Integration Roadmap

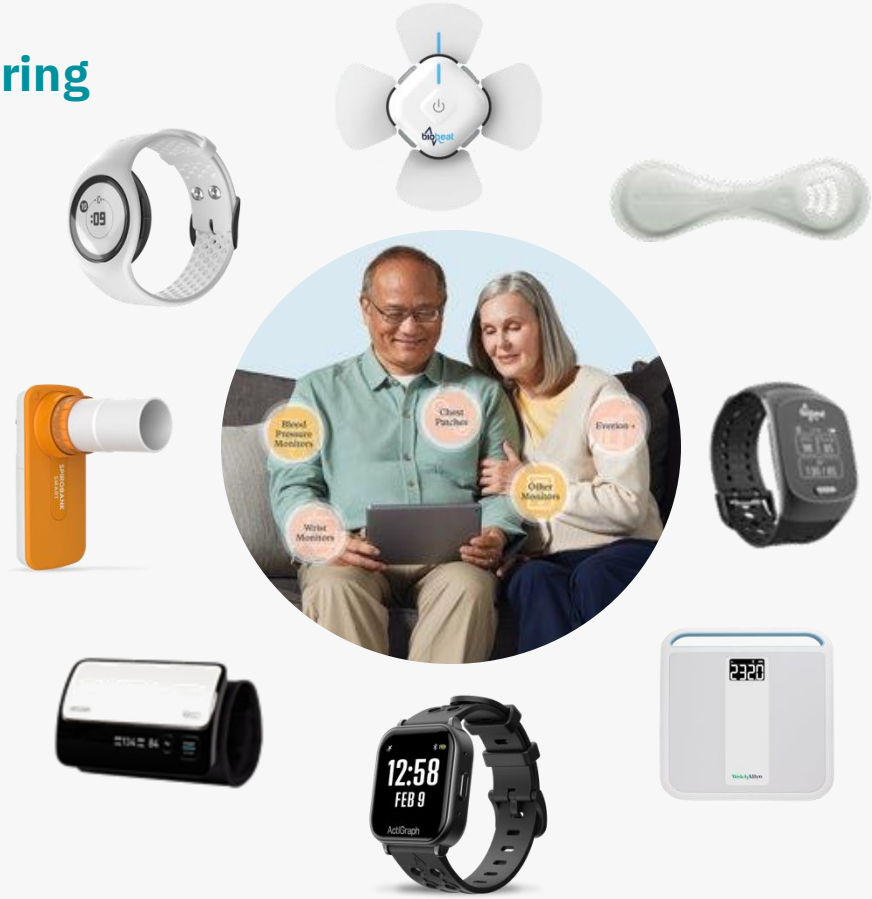
Kim Rejndrup

Chief Product Officer, ActiGraph

Device Agnostic Platform

Comprehensive connected device offering

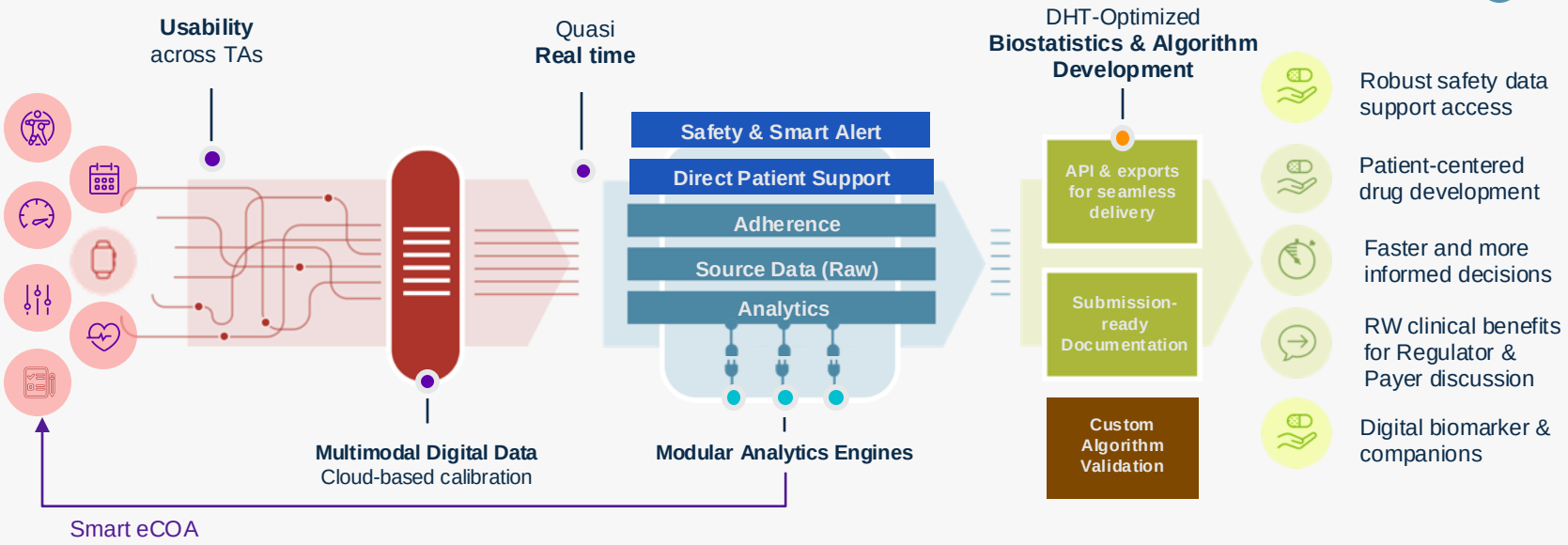
- ActiGraph Connect supports data collection from a suite of connected devices and sensors with multiple form factors – not just ActiGraph devices!
- New sensor solutions include ECG patch, pulse oximetry, spirometer, and blood pressure monitor
- Clients can capture a much wider variety of digital measures, expanding ActiGraph's capabilities to address areas of unmet need.



ActiGraph End-to-End DHT Ecosystem

Fully Integrated and Fit-For-Purpose Solutions

CENTREPOINT Connect



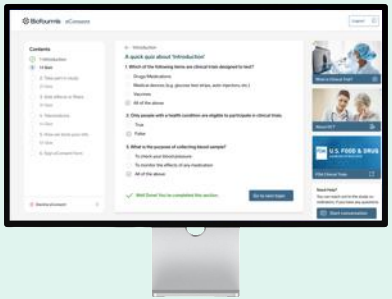
COLLECT THE RIGHT DATA

APPLY FIT-FOR-PURPOSE ALGORITHMS

GENERATE CLINICAL INSIGHTS

ActiGraph Connect Solutions for Digital Clinical Trials

eConsent

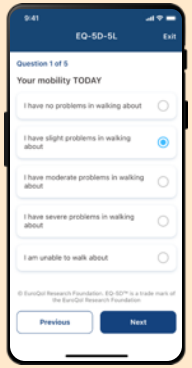


Streamline informed consent workflows and onboarding

Connected Sensors

Enable continuous participant data collection

ePRO



Collect participant assessments and outcomes

Virtual Visits

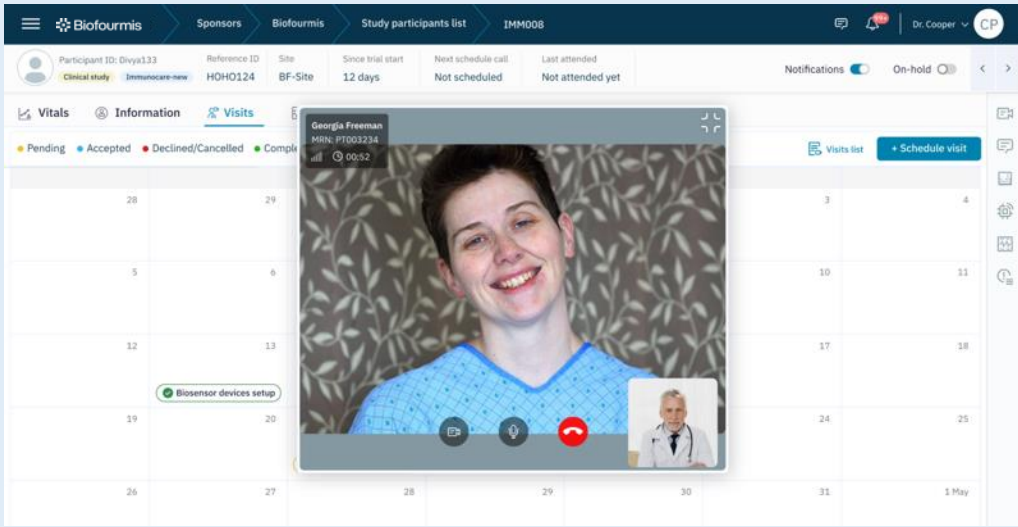
Empower participant engagement and support

Visits – Participant experience

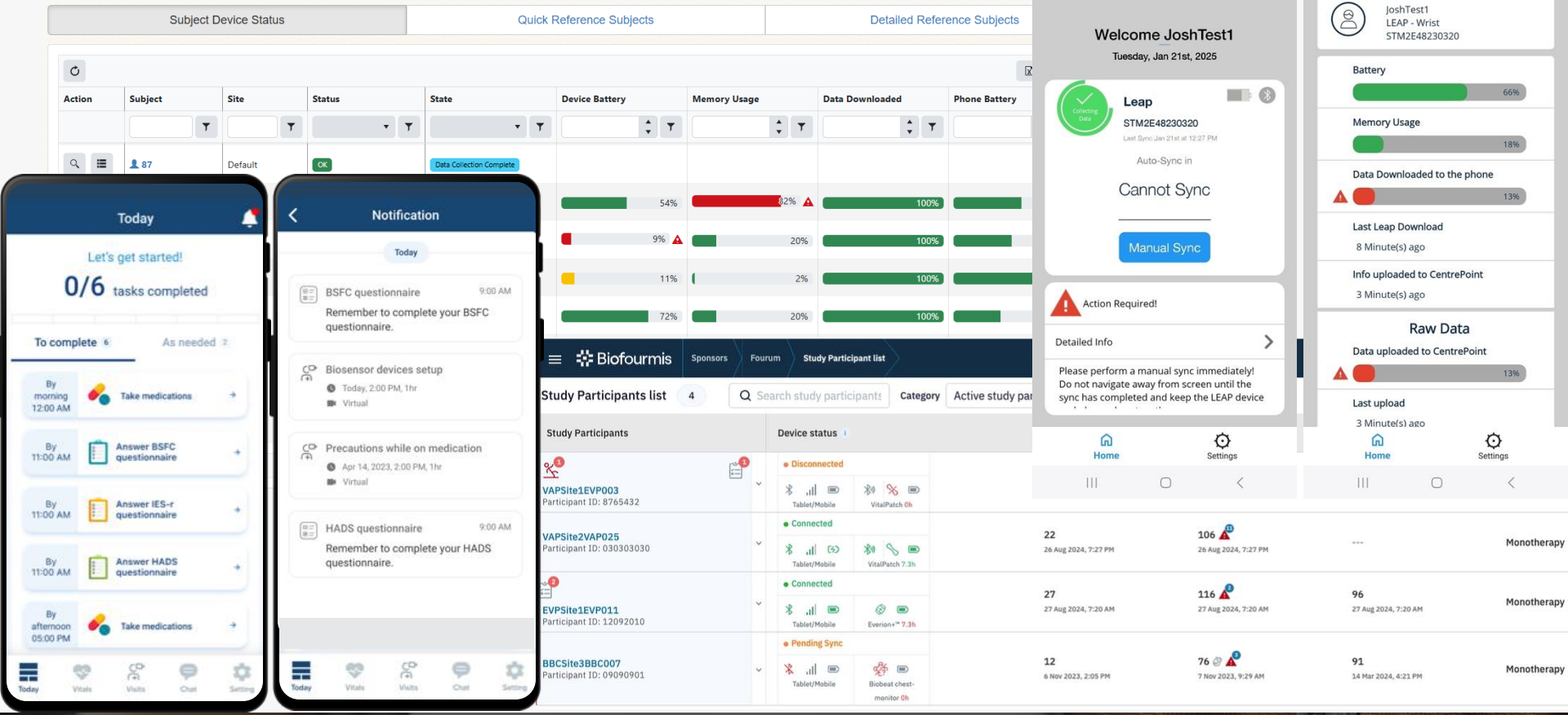
- **VIDEO CALL TO PARTICIPANT'S MOBILE DEVICE** – Empowers the participant to more easily advance the clinical research by completing their visits *at home.*
  - Virtual visits reduce the obstacles to clinical trial participants by removing the logistical challenges of their commute and waiting room times associated with in-person visits.
- **VISIT MANAGEMENT** – empowers the participant to manage complete their upcoming visits from the same mobile app they are already using to communicate with their study team and to complete study questionnaires.
- **VISIT REMINDERS** – Reminds the participant of any next-day or day-of appointments through push-reminders on their mobile device.

Visits – Site experience

- **SCHEDULE VISITS** – Easily schedule protocol-defined visits and ad-hoc calls with your study participants
- **TRACK AND MANAGE VISITS** – View each participant's series of upcoming and completed visits, receive notification reminders for upcoming appointments, and view "next schedule call" data across all site participants
- **EQUIP EACH VIRTUAL VISIT WITH PARTICIPANT DATA** – Connect to the participant with a video call, while also being able to reference their trial data including:
  - Recent vital trends
  - Recent questionnaire responses
  - Past communication logs and clinical notes
- **REDUCE THE BURDEN OF RESCHEDULING and MISSED VISITS** – Allowing study participants to complete their visits virtually and be reminded of them on their phones may help study compliance



Focus on Compliance



Adding more device integrations

- Continue to Identify Devices suitable for Clinical Trials
- Fit-for-purpose devices
- ActiGraph will integrate devices meeting our high-bar of quality



Closing Remarks

- ActiGraph now supports our customers with expanded technology and scientific products.
- The combined ActiGraph/Biofourmis platform services all trial phases, offering faster decisions and optimizing the drug development lifecycle in line with FDA's PDUFA VII initiatives
- We back up our new offerings with our technical, scientific, operational and regulatory expertise
- We can bring greater insights on both the efficacy and safety of novel therapeutics
- We are building the future of clinical trials with patient-focused digital data

ADDS 2025

ActiGraph Digital Data Summit 2025

Feb 10-12, 2025

Focused Sessions:

- Physical Activity
- AI in Digital Health
- ALS Workshop & Symposium
- Cohort Studies
- Multi-Stakeholder Collaborations

22 Speakers	**60** Attendees
9 Countries	**44** Organizations
12 Biopharma	**24** Universities

Thank you to our sponsor csem

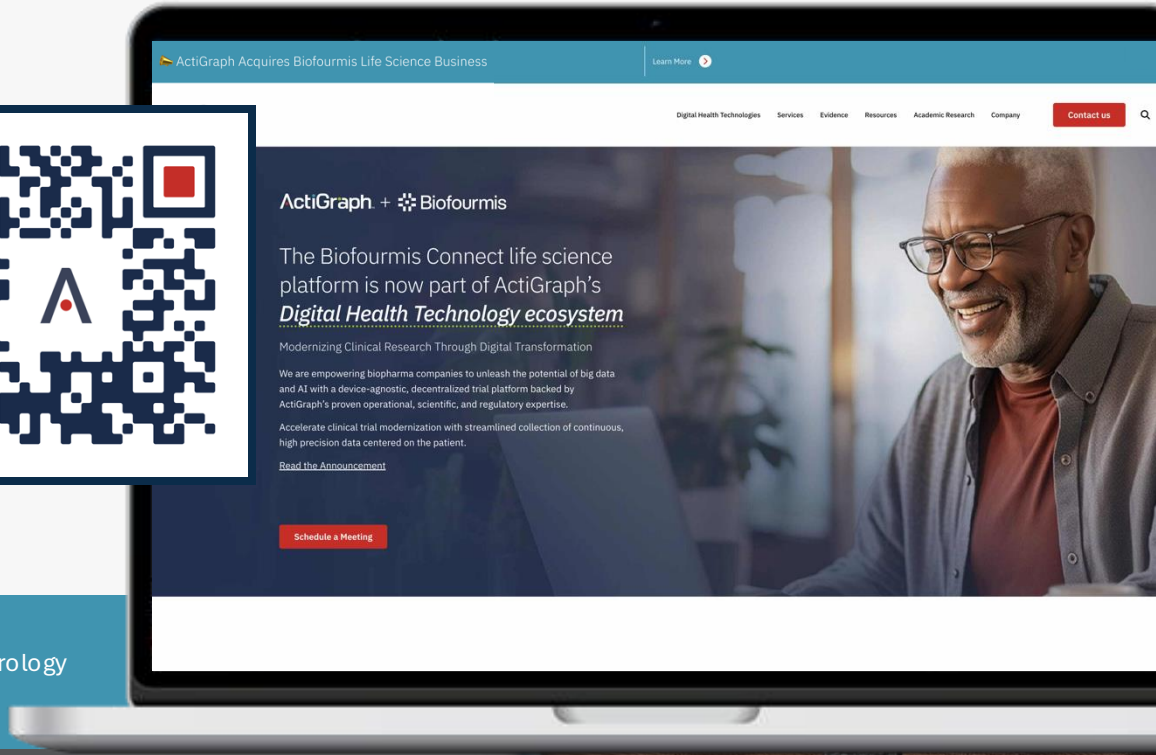
ADDS 2025


ADDS 2025
ADDS 2025
ADDS 2025


Acknowledgements
1495 ARC Study Participants with ALS
*473 Contributing Actigraphy

Modernizing Clinical Research with AI and Digital Data: ActiGraph's Acquisition of Biofourmis Connect

Scan to learn about Biofourmis Connect



Next Month Digital Health Monthly topic:
Combining Active and Passive DHT Monitoring to Accelerate Neurology Drug Development Through Functional Biomarkers: A Scientific Partnership Between ActiGraph and Indivi