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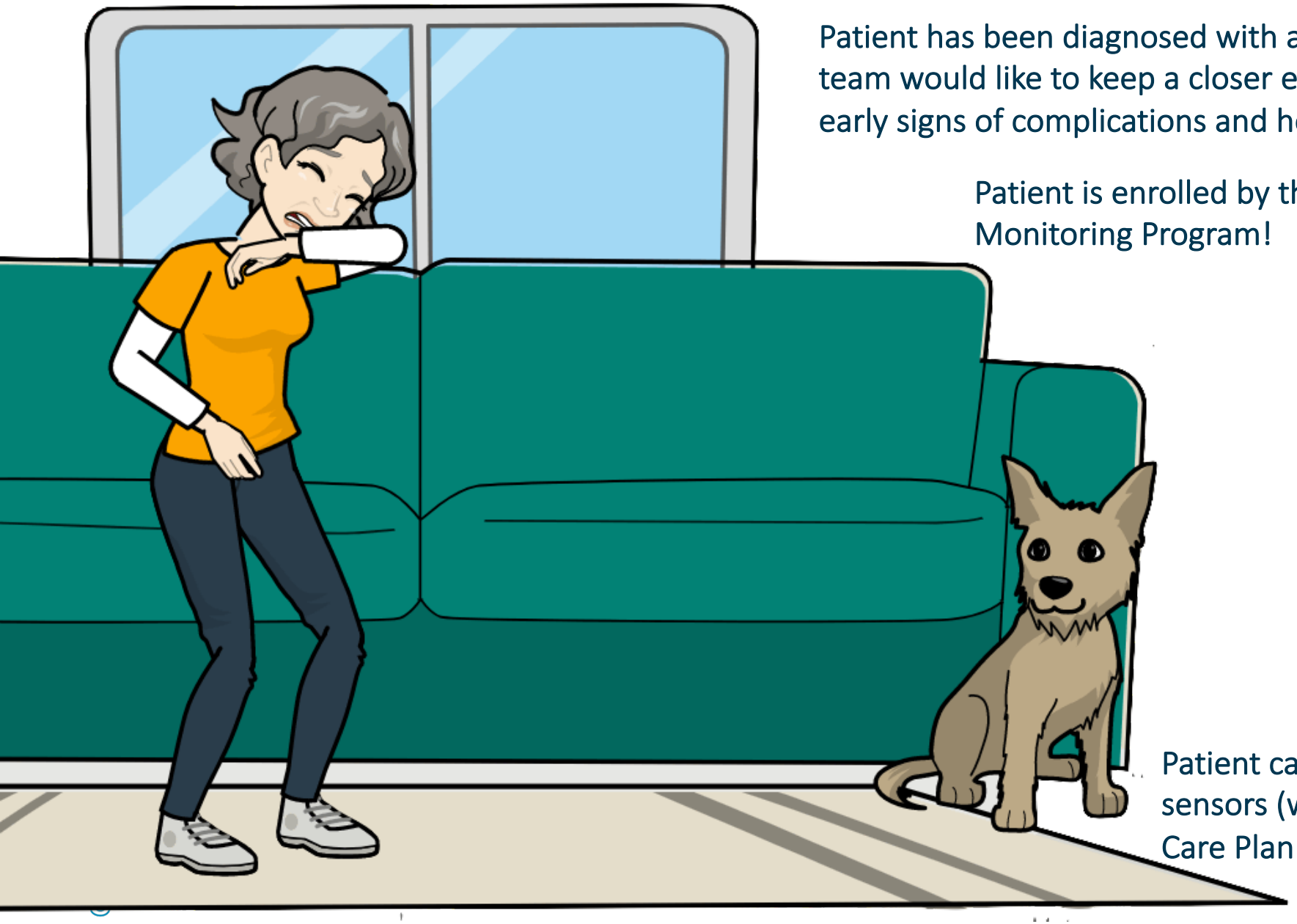
Powering Personalized Predictive Care

Healthcare is Bringing Hospital to Home - Is Pharma's R&D Ready?

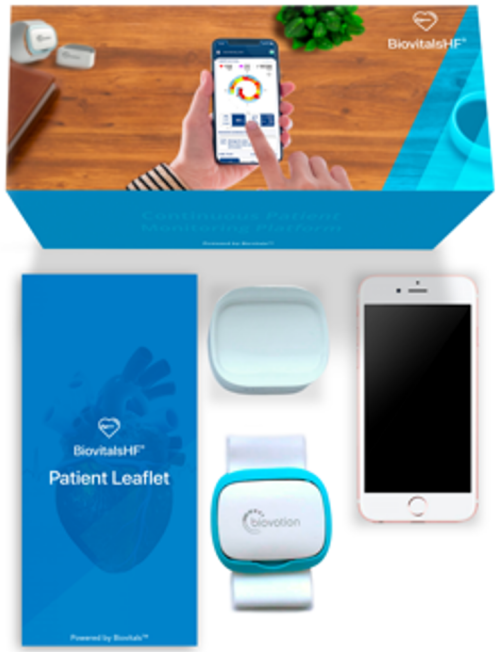
November 2020

Bloomberg CNBC Forbes Pink Sheet Informa Pharma Intelligence mobihealthnews MedCity News FierceBiotech TechCrunch BUSINESS INSIDER The Boston Globe NIKKEI ASIAN REVIEW

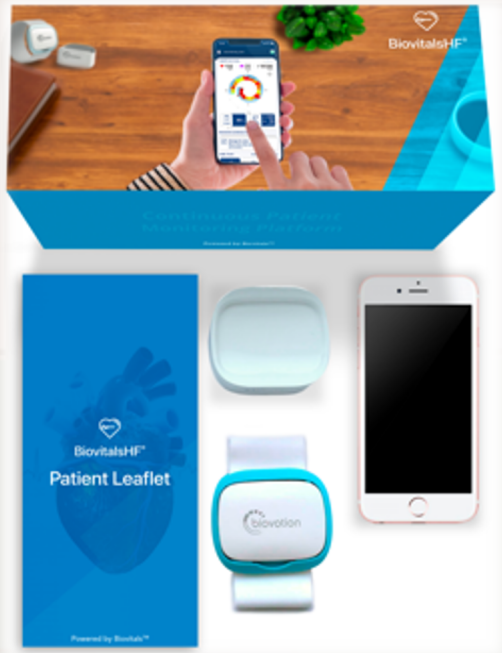


Patient has been diagnosed with a chronic condition and her medical team would like to keep a closer eye on her at home so they can detect early signs of complications and help her lead a healthier life.

Patient is enrolled by the care team into a Remote Monitoring Program!



Patient can either go home with the wearable sensors (with cellular connectivity), smartphone & Care Plan / or kit can be sent direct to her home.



Remote Care team remotely onboards patient via Video Chat…

…they also track patient's compliance to the Remote Patient Monitoring (RPM), and assist with troubleshooting any technical difficulties the patient might be facing

- Passive monitoring using a wearable to capture multiple vitals signs
- Dynamic survey questions to gauge patient health
- Guideline Direct Medical Therapy (GDMT) to improve compliance and optimal dose

Patient starts using the companion app...

...helps capture vital signs passively, report symptoms, monitors compliance to GDMT / advises clinician on optimal dose (HF), and remotely communicate via text/video with the care team

The app also measures, displays and reports the patient's compliance to the requests.

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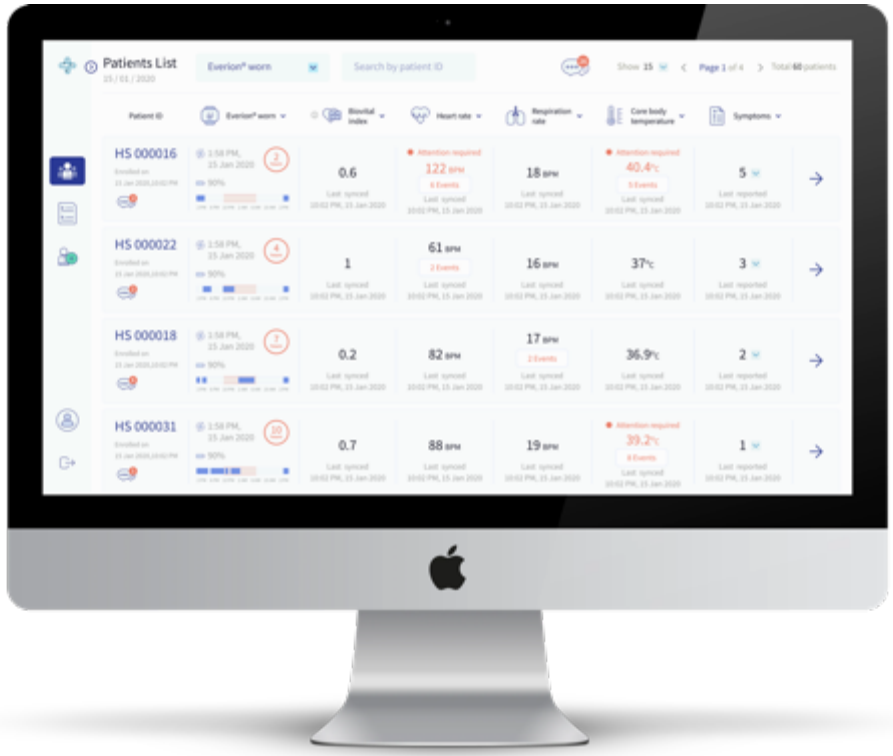
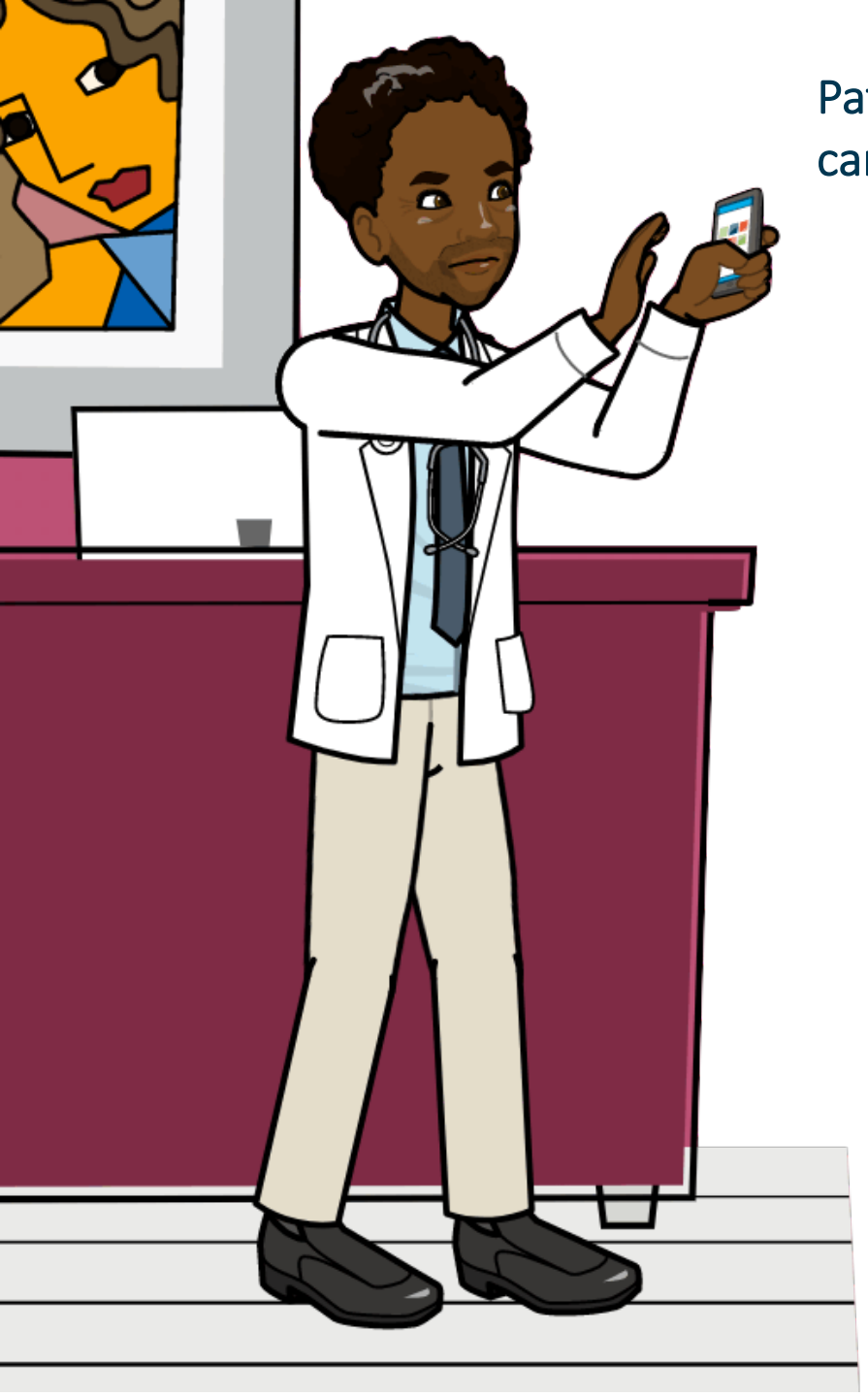
While at home…

Patient's symptoms start worsening…



- Care team has overview of her compliance, continuous vitals signs, personalized alerts (PROs / patient symptoms), and ability to chat/video call patient
- Admin screen will show all details relative to on-board,, off-board, and consults for effective & optimal billing to CMS etc



Patient is eligible for an up titration of his HF medication! His treating cardiologist receives an alert on his smartphone app…

Solution enables remote titration and dose optimization of HF medication using an easy to use smartphone app for the clinician…

Biofourmis overview

We're powering **Personalized Predictive Care**

Global **tech-enabled Healthcare company** – with a new organization model (Pharma + Technology company)

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- **biofourmis Health**
  Virtual Care Models to manage patients remotely: Acute -> Post-Acute
- **biofourmis Therapeutics**
  Software-based therapeutics for treatment & management of patients

What Do We Do?

We use our proprietary data platform, *Biovitals®* to build **software-as-treatment** to treat and manage patients with **unmet clinical needs**

We improve **patient outcomes** while **minimizing the cost and burden** of care by delivering more **precise intervention** at the right time

NOVARTIS · AstraZeneca · mundipharma · CHUGAI (A member of the Roche group) · MAYO CLINIC · BRIGHAM HEALTH BRIGHAM AND WOMEN'S HOSPITAL · MASSACHUSETTS GENERAL HOSPITAL · Duke Clinical Research Institute · NHS · MINISTRY OF HEALTH SINGAPORE · Australian Government Department of Health · 醫院管理局 HOSPITAL AUTHORITY

Facts about Biofourmis

>200	Employees across 4 offices Boston, Singapore, India, Zurich
$145M	Capital raised $100m Series C led by SoftBank Vision Fund
>4.5M	Patients Real World Data 75% Cardiometabolic; 25% Oncology
>70	Global Patents granted >15 pending and in-preparation
>25	Multi-year partnerships Pharmaceuticals, Health Systems & Payers
15	Regulatory authorizations U.S. FDA, and 6 other countries FDA Pre-Cert Program, ISO13485, ISO27001, SOC2 (ongoing), FDA CFR Part 11 compliant
3	Strategic acquisitions Biovotion AG, Gaido Health, & Hashtaag

Executive Summary

- Health care is shifting to
  1. At home care (from Clinic, Hospital, Nursing home, Assisted living)
  2. Remote continuous monitoring (from episodic)
  3. Personalized (Digital) Biomarkers (from one size fits all)
  4. Value based care (from Fee-for-service)
  5. Non-physicians (e.g. Nurses, PAs) playing a bigger role (from physicians centered care)
- Will the changes stick post-Covid?
  - COVID-19 has been a catalyst, but many other drivers should make it stick
  - Unsustainable per capita healthcare costs
  - Changing payment structures, incentives, and reimbursement for remote care
  - Maturing IoT for health (wearables and sensors) - Clinical grade, patient friendly
    - Form factor, battery life and connectivity (cellular)
  - Rise of AI/ML tools and CDS (Clinical Decision Support) systems
- Pharma can leverage these changes for positive impacts!

Shift #1 - At home care (from Clinic, Hospital, Nursing home, Assisted living)

- Safer
- On demand/need
- Convenient
- Cheaper ?
  - Maybe not as compared to out-patient visit vs telemedicine
  - Far cheaper compared to hospital stay

UNINTENDED CLINICAL CONSEQUENCES

Hospital Acquired Conditions (HACs), Fall, etc.

Functional status never regained

20% suffer delirium

POOR INPATIENT ACCESS

~12 hours Emergency Room (ER) wait

Often >100% capacity

EXPENSIVE

Often negative margin for Internal Medicine (IM) admissions

Problems with hospital-based care

Hospital@Home Program – Economic benefits

Demonstrated significant **reduced cost, health care use, and readmissions while increasing physical activity** compared to hospital care.

RANDOMIZED CONTROL TRIAL OVERVIEW

- **91 adults** (43 home and 48 control) admitted via the emergency department with selected acute conditions (**heart failure, COPD/Asthma, Infection**)

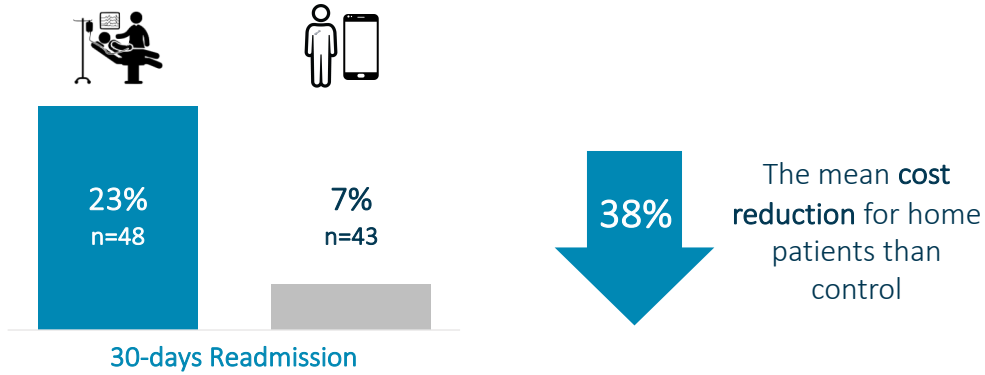
Control: Monitoring and treatment as usual, in-hospital setting

Home: Monitoring and treatment, at-home setting

- **Patients monitored at home using VitalPatch** (continuous monitoring of temperature, heart, rate, respiratory rate, telemetry, movement, and falls)
- **Monitoring was done through machine-based algorithms**, which produced alarms for review by both nurse and physician
- **Primary outcome:**
  - total direct cost of the acute care episode (sum of costs for non-physician labor, supplies, medications, and diagnostic tests)
- **Secondary outcome**
  - Healthcare use and,
  - Physical activity during the acute care episode and at 30-days

STUDY RESULTS[1]

Annals of Internal Medicine



COST	Relative Reduction %	P Value
Acute Care Episode		
Unadjusted cost	41	<0.001
Adjusted Mean cost (95% CI)	38	<0.001
Acute Care Episode & 30 days after acute care episode		
Unadjusted cost	41	<0.001
Adjusted Mean cost (95% CI)	36	<0.001

1 Levine, David M., et al. "Hospital-Level Care at Home for Acutely Ill Adults: A Randomized Controlled Trial." *Annals of Internal Medicine* (2019).

Shift #2 - Remote Continuous Monitoring (from Episodic)

CONTINUOUS MONITORING

Using wearable biosensors to capture continuous physiology data and easy to use UI/UX to drive patient engagement

ACTIVE DATA

EARLY DETECTION

Personalized physiology analytics to detect physiology changes precursor to decompensation

OPTIMIZE THERAPY

Treatment algorithm and care pathway to improve guideline-directed use of medication

CLINICAL AND ECONOMIC OUTCOMES

Clinical outcomes: Quality of Life, Hospitalization & Mortality
Economic outcomes: 30-days hospitalization, Annual healthcare spend

e.g. AI/ML driven Software to enable early detection of HF exacerbation and augment guideline directed use of heart failure therapies

Design with all stakeholders in mind

Patient

Clinician

Health system

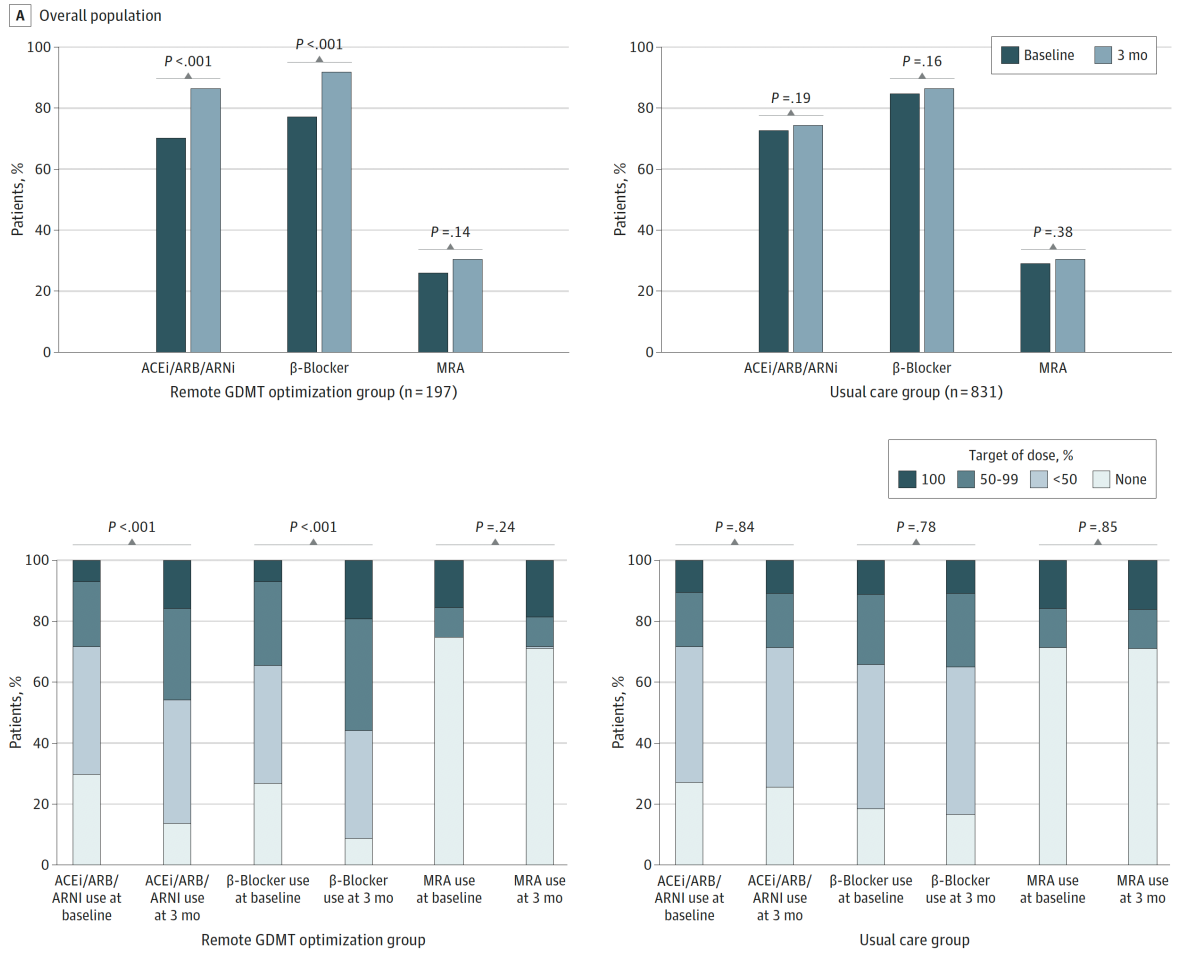
Proven clinical outcomes

Proven clinical evidence for Early detection and dose optimisation in patients with heart failure

- N=197 participated in medication optimization program & 831 continued with usual care
- Objective: To To determine whether a remote, algorithm-driven, navigator-administered medication optimization program could enhance implementation of GDMT in HFrEF.
- Patients were contacted via phone by a navigator who facilitated medication adjustment with surveillance of laboratories, physiology, and symptoms under supervision of a pharmacist, nurse practitioner, and HF cardiologist.
- Results[1]:
  - At 3 months, patients allocated to the remote intervention experienced greater increases from baseline in utilization of all categories of GDMT than those in the usual care group.
  - The proportion of patients advanced to target doses of GDMT was also higher in the intervention group at 3 months. (p<0.001)
  - Among the usual-care group, there were no changes from baseline in the proportion of patients receiving GDMT or the dose of GDMT in any category.

BRIGHAM HEALTH
BRIGHAM AND WOMEN'S HOSPITAL

JAMA Cardiology



1. Desai, Akshay S., et al. "Remote Optimization of Guideline-Directed Medical Therapy in Patients With Heart Failure With Reduced Ejection Fraction." *JAMA cardiology* (2020).

Shift # 3 Personalized Digital Biomarkers (from one size fits all)

Digital biomarkers are defined as OBJECTIVE, QUANTIFIABLE PHYSIOLOGICAL AND BEHAVIOURAL DATA that are collected and measured by means of DIGITAL DEVICES such as portables, wearables, implantable or digestible.

The data collected is typically used to EXPLAIN, INFLUENCE AND/OR PREDICT HEALTH-RELATED OUTCOMES.

Source: Digit Biomark e-ISSN: 2504-110X (Online) DOI: 10.1159/issn.2504-110X

Utility of digital biomarkers

Combat COVID-19 Pandemic

New Endpoints in Clinical Trials

Virtual Care/Monitoring

Utility of digital biomarkers

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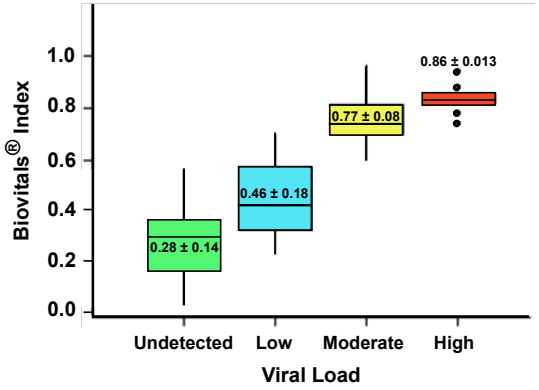
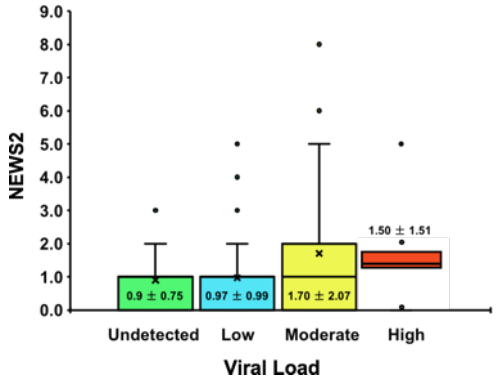
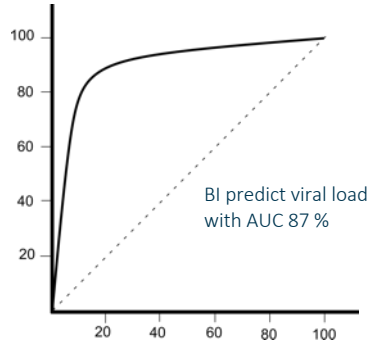
New Endpoints in Clinical Trials

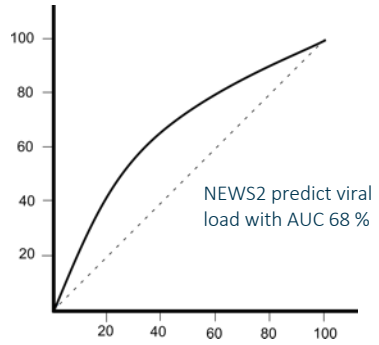
Virtual Care/Monitoring

Clinical performance of Biovitals® Index to detect Viral Load



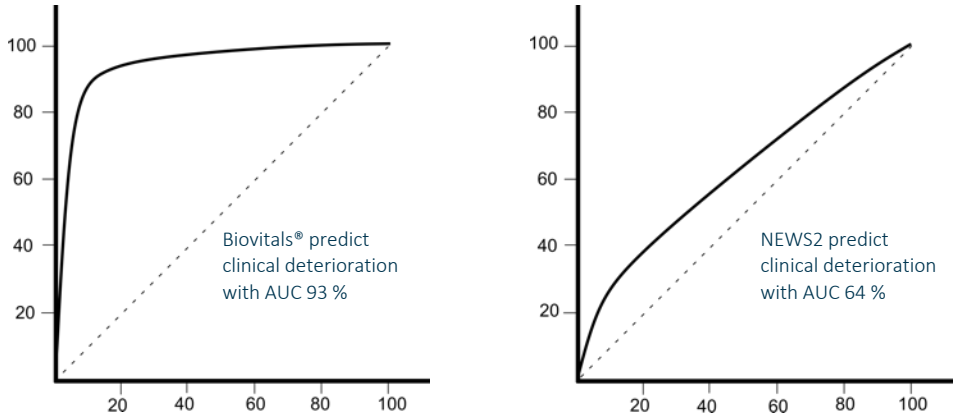


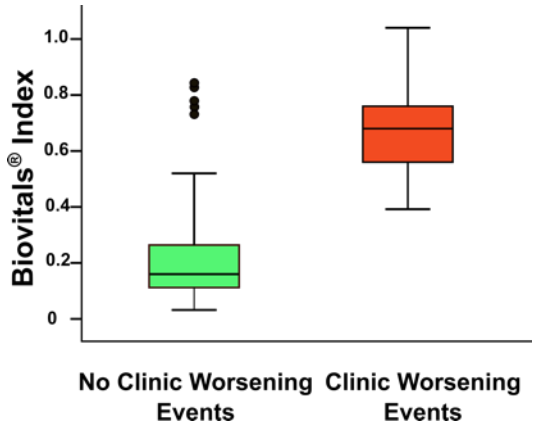




- The increase in viral load from respiratory samples as determined with RT-PCR Ct value for SARS-CoV-2 was associated with increasing 24-hour average Biovitals® Index (p<0.0001), but not the 24-hour NEWS2 (p=0.004, r=0.15).
- Furthermore, the diagnostic performance to identify moderate/high viral load in the respiratory samples was compared between the 24-hour average Biovitals® Index and the 24-hour NEWS2. The area under the curve of 24-hour average Biovitals® Index to identify moderate/high viral load was 0.87 (95% CI: 0.83-0.90), significantly larger than that of the 24-hour NEWS2 (0.68, 95% CI: 0.65-0.71).
- Specifically, the 24-hour average Biovitals® Index >0.5 correctly identified 100% moderate/high viral load with a false positive rate of 0.0% and a false negative rate of 11.9%. On the other hand, the 24-hour NEWS2 ≥5 identified 80% moderate/high viral load with a false positive rate of 0.4% and a false negative rate of 88.6%

Biovitals® predicts clinical deterioration in COVID-19 patients





- A total of 17 clinical worsening events occurred in these 34 COVID-19 patients during the hospitalization.
- Biovitals® Index alerts detected 16 out of 17 events (94.1%) prior to the actual occurrences with an AVERAGE PREDICTION TIME INTERVAL OF 21.0 HOURS, ranging from 6 to 39 hours. The area under the curve was 0.93 (95% CI: 0.89-0.95) with the optimal cutoff at sensitivity and specificity of 94.1% and 88.9% respectively.
- The performance of Biovitals® Index to predict clinical worsening events was then compared with the 24-hour NEWS2. The area under the curve for 24-hour NEWS2 to predict clinical worsening event was only 0.64 (95% CI: 0.61-0.67) with the optimal cutoff at sensitivity and specificity of 29.4% and 85.7% respectively.

Utility of digital biomarkers

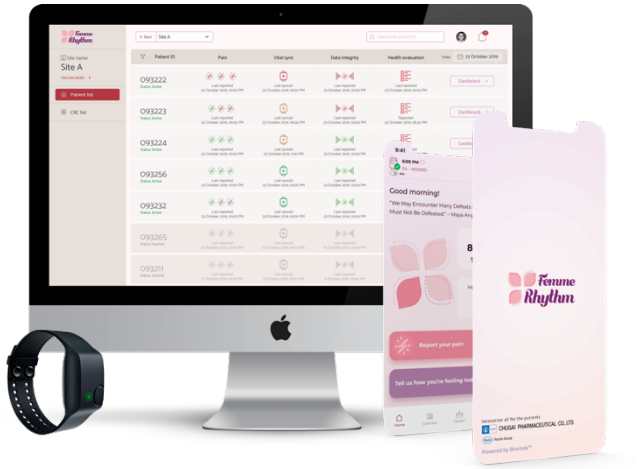
Combat COVID-19 Pandemic

New Endpoints in Clinical Trials

Virtual Care/Monitoring

Digital clinical trials

Biopharma companies have been working towards integrating digital measurements across the continuum of research and drug trials, ensuring connected devices can provide a holistic view of patient health and lead to new biomarker discovery



- **Chugai Pharmaceuticals** to co-develop a **companion therapeutics** (FemmeRhythm) with AMY109 for patients with **endometriosis**.
- Observational study **led by Mayo Clinic** (ClinicalTrials.gov Identifier: NCT04318275)

CHUGAI

Ongoing

- **FDA CDER funded study** to explore **novel patient-centric endpoints** in patients with **heart failure** – in order to leverage these surrogate endpoints to speed up drug trials
- Observational study ongoing **led by National Heart Center, Singapore & Mayo Clinic** (ClinicalTrials.gov Identifier: NCT04191356)

FDA U.S. FOOD & DRUG ADMINISTRATION

Ongoing

- **Mundipharma** to leverage algorithms for **objective assessment of pain**
- Observational study **led by Singapore General Hospital** (ClinicalTrials.gov Identifier: NCT03789630)

mundipharma

Complete

GUIDANCE DOCUMENT

Treatment for Heart Failure: Endpoints for Drug Development Guidance for Industry

JUNE 2019

Download the Draft Guidance Document | Read the Federal Register Notice

Draft | Level 1 Guidance

Not for implementation. Contains non-binding recommendations.

This guidance is being distributed for comment purposes only.

Search for FDA Guidance Documents

Search for FDA Guidance Documents

Search General and Cross-Cutting Topics Guidance Documents

Docket Number: 2019-13800

Issued by: Center for Drug Evaluation and Research
Center for Biologics Evaluation and Research

This guidance has two purposes: 1) to make it clear that an effect on symptoms or physical function, without a favorable effect on survival or risk of hospitalization, can be a basis for approving drugs to treat heart failure; and 2) to provide recommendations to sponsors on the need to assess mortality effects of drugs under development to treat heart failure.

Content current as of:
06/27/2019

Regulated Product(s)
Biologics
Drugs
Clinical - Medical

Study design

Screening
Post-discharge

Day 0

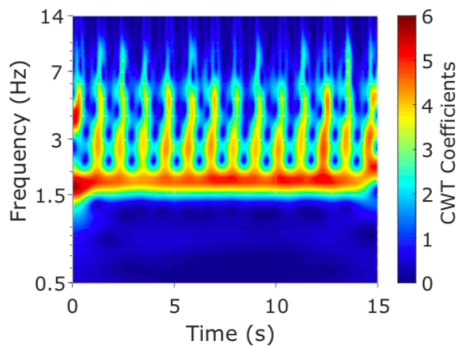
Day 30

Day 60

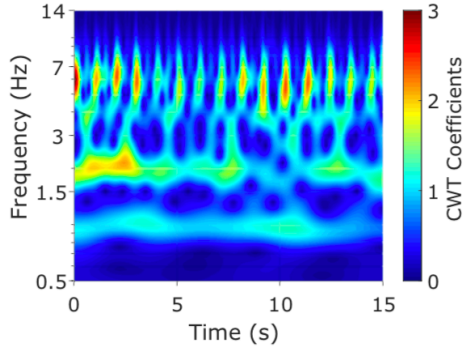
Remote home monitoring, N=150

Outcome Measurements

Primary	Correlation between physiology/actigraphy analysis with 6MWT, KCCQ, Labs
Secondary	(i) Compliance rate, (ii) Drop-out rate, (iii) mean time worn/day, and (iv) proportion of time worn that device produces reliable data.



Functional capacity at-baseline



Decline in functional capacity (Day 40)

Physiology and Actigraphy Biomarkers

Physiology (Raw Optical Signal & Accelerometer):

- Heart rate, HRV
- Accelerometer
- Respiration rate
- Inter-beat-Interval
- Blood Pulse Variation
- Skin temperature
- SpO2

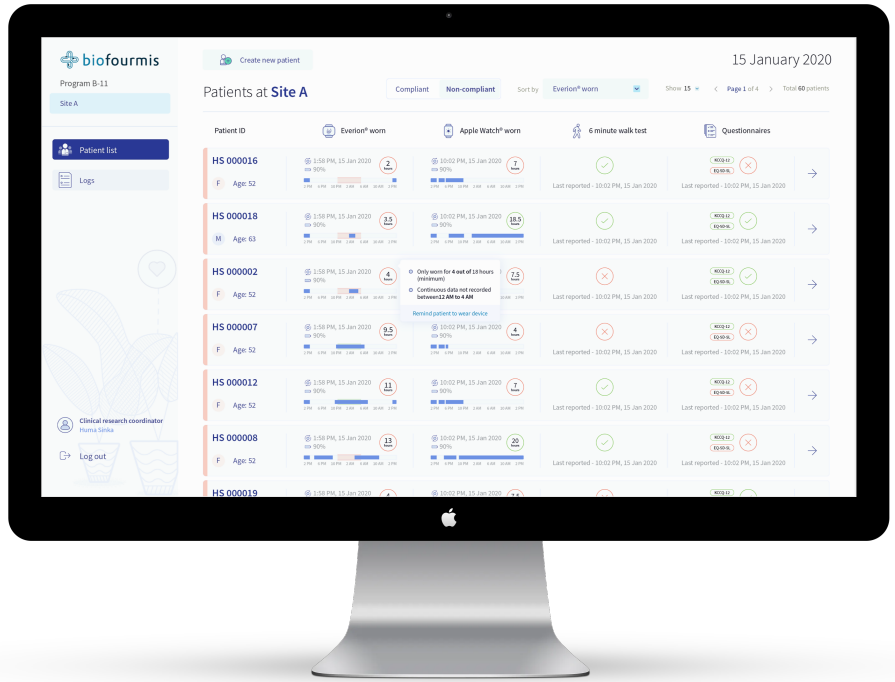
Actigraphy (Raw Accelerometer):

- Steps per day
- 6MST
- Peak 1-min cadence, Peak 30-min cadence and Max 5-min cadence
- Activity Intensity
- Time spent at stepping rate of >40 steps/min

Virtual study platform

Patient-facing companion Mobile App (iOS/Android)

Physiology monitoring (Everion + Apple Watch), ePROs, Mobile-based 6MWT, Medication Management & Virtual Consultation



Investigator/Site Dashboard for monitoring

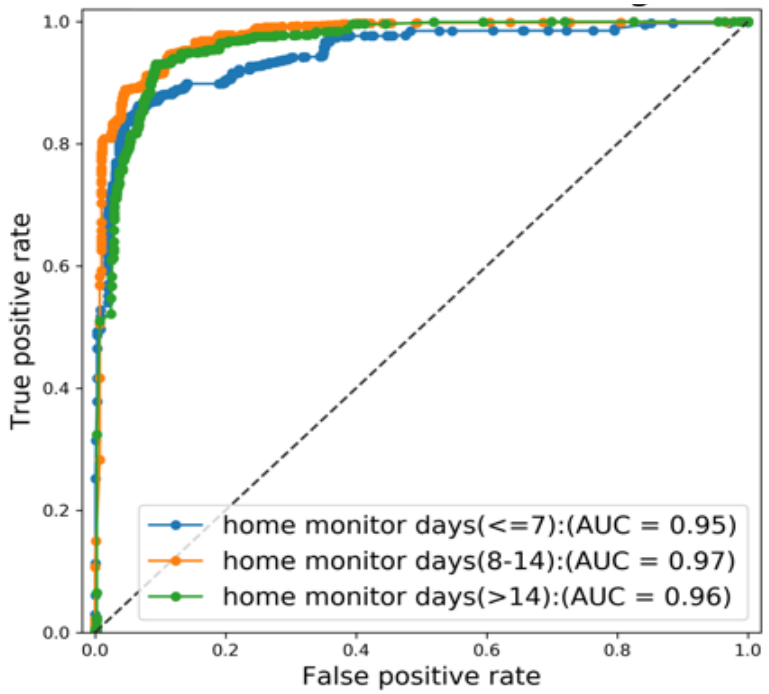
Track patient compliance, dynamically upload study tasks, and clinical intervention

Painfocus® - augmenting pain measurement

A holistic approach for objective assessment of pain levels in real-world setting to guide remote therapeutic decision making

OBSERVEPAIN STUDY ClinicalTrials.gov Identifier: NCT03789630

- 115 patients undergoing **Total Knee Replacement surgery**
- **Primary outcome:**
  - Objective qualification of Pain levels: Patient reported pain levels correlate with deviations in multivariate physiology biomarkers, which have shown to be associated with presence of pain.



MULTI-VARIATE ANALYSIS (ONLINE LEARNING) OF >20 DIGITAL BIOMARKERS

captured using raw sensor data: PPG, accelerometer, EDA, temperature, barometric pressure sensor

Shift #4 Value Based Care (from Fee for Service)

- Value based care (capitated/risk sharing models/ACOs)
- With COVID-19, Fee-for-service providers are getting killed - you can’t bill for services you’re not providing*
- Practices that had per capita contracts, and had guaranteed payment structures, they’re surviving and thriving
- Industry is learning that the risk factor that many were worried about goes both ways

* Source: Interview with Chris Jennings, policy consultant and former health care adviser to the Obama and Clinton administrations

Shift #5 Non-physicians (e.g. Nurses, PAs) to play bigger role

- Shortage of doctors, aggravated by COVID-19
- Cost pressures
- State laws giving more authority to non-physicians
- Clinical Decision Support Systems and AI/ML tools enabling non-physicians to do more

How can Pharma leverage these shifts? 1/3

1. Trial design - leverage sensors for continuous and at home data collection with an eye towards discovery of digital biomarkers

- Remote Patient visits (hybrid trials) and fully decentralized trials
- Future proofing - Should every molecule have at-least one study in the evidence generation plan where data is collected continuously?
- Enable retrospective analysis in future to deal with any safety signal that maybe discovered in later phases
- Build an internal or external capability for digital biomarker discovery

How can Pharma leverage these shifts? 2/3

2. Technology is evolving too fast, don't bet on a sensor/device, instead get a good partner (internal or external) that can:

- Provide a device agnostic platform that can collect data from multiple sensors
- Has workflows designed for patients, nurse/study coordinators, sponsor's study team
- Global scale
- Resources to invest in a long-term roadmap
- Has expertise in Pharma as much as healthcare to enable commercialization
- Can manage PHI (HIPAA, GDPR)

How can Pharma leverage these shifts? 3/3

3. Thinking beyond R&D

- Develop end-to-end digital strategy to go from early development to clinical development to commercialization phase
  - Have Digital innovation capability embedded in early development

- Consider opportunities across patient journey from diagnosis, acute care, post-acute/transitive care to chronic condition management
  - Early diagnosis and finding right patients
  - Treatment titration and triggers based on objective measurements (e.g. pain)
  - Virtual rehabs/digital companion care at home - Supporting patient through care pathway, enabling patient to transition from first line therapy to innovative therapy, increasing adherence

Emerging digital solution during COVID-19

	Patient-centric					Diagnostics-centric		R&D-centric	
HealthTech Clusters	Education	Triage	Telemedicine	Distribution	Chronic Disease Management	Point-of-Care Testing Diagnostics	Screening	Research	RCT
HealthTech Capabilities	• Health Information Platform • Consumer Education	• Medical Concierge • Chatbots • Track & Trace Apps	• Tele-consultation	• Consumer Market-places	• Digital Therapeutics • Disease Management	• On-Demand Lab Tests • Medical Diagnostics	• Medical Imaging • Teleradiology	• Drug Discovery	• Research Clinical Trials
Startup Load*	2	2	2	2	3	2	2	1	1
Patient Load**	3	3	3	2	1	2	1		1

Source: LEK

Q&A

thank you

For more information, contact Jaydev.Thakkar@biofourmis.com