THE PROGRESSION OF DIGITAL BIOMARKERS IN CLINICAL TRIALS AND BEYOND
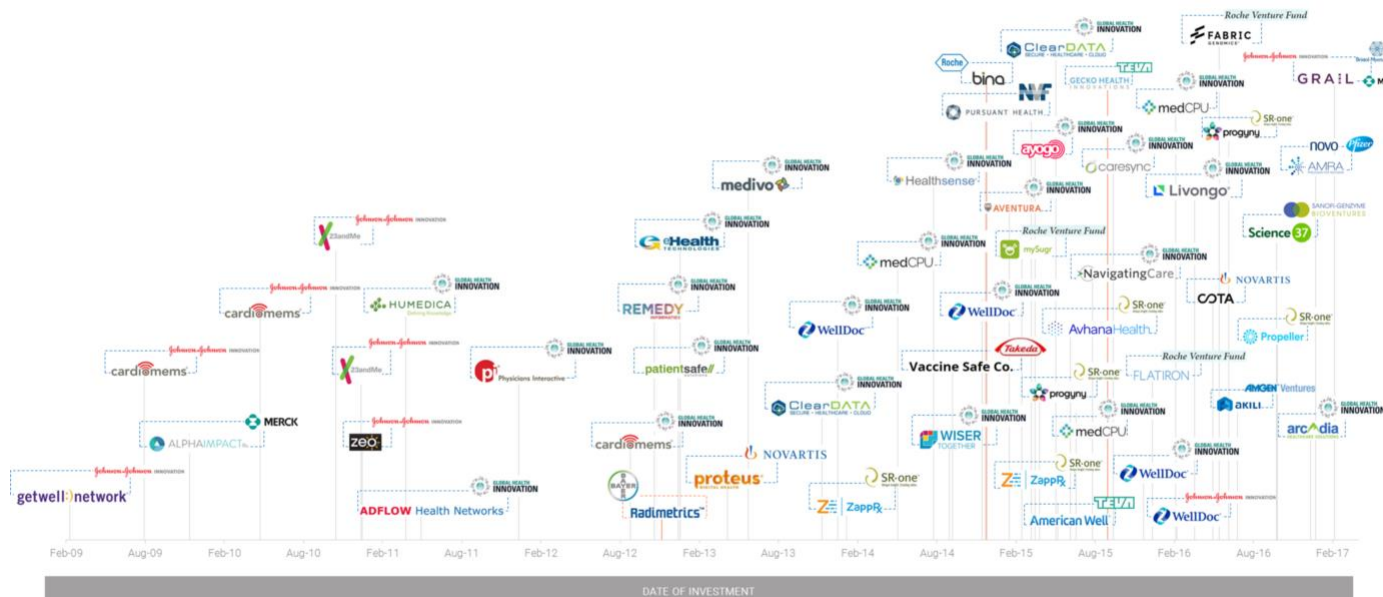
IPAC-RS Digital Devices Roundtable Series

Joe Corrigan, James Blakemore

The Rapid Growth of Digital Health

The adoption of connected healthcare

DIGITAL HEALTH STARTUPS
A TIMELINE OF PHARMA EQUITY INVESTMENTS & ACQUISITIONS IN DIGITAL HEALTH COMPANIES
2009-2017 (4/06/17)

Sources: CB insights, CapGemini Research, Fierce Pharma

The adoption of connected healthcare

Digital healthcare funding: $5.6bn in Q2 2020 to $14.5bn Q2 2021

Deal sizes have increased: Many Start-ups exceeding $100m rounds

Digital health market is expected to exceed $425bn by 2027[1,2]

Sources: CB insights, CapGemini Research, Fierce Pharma
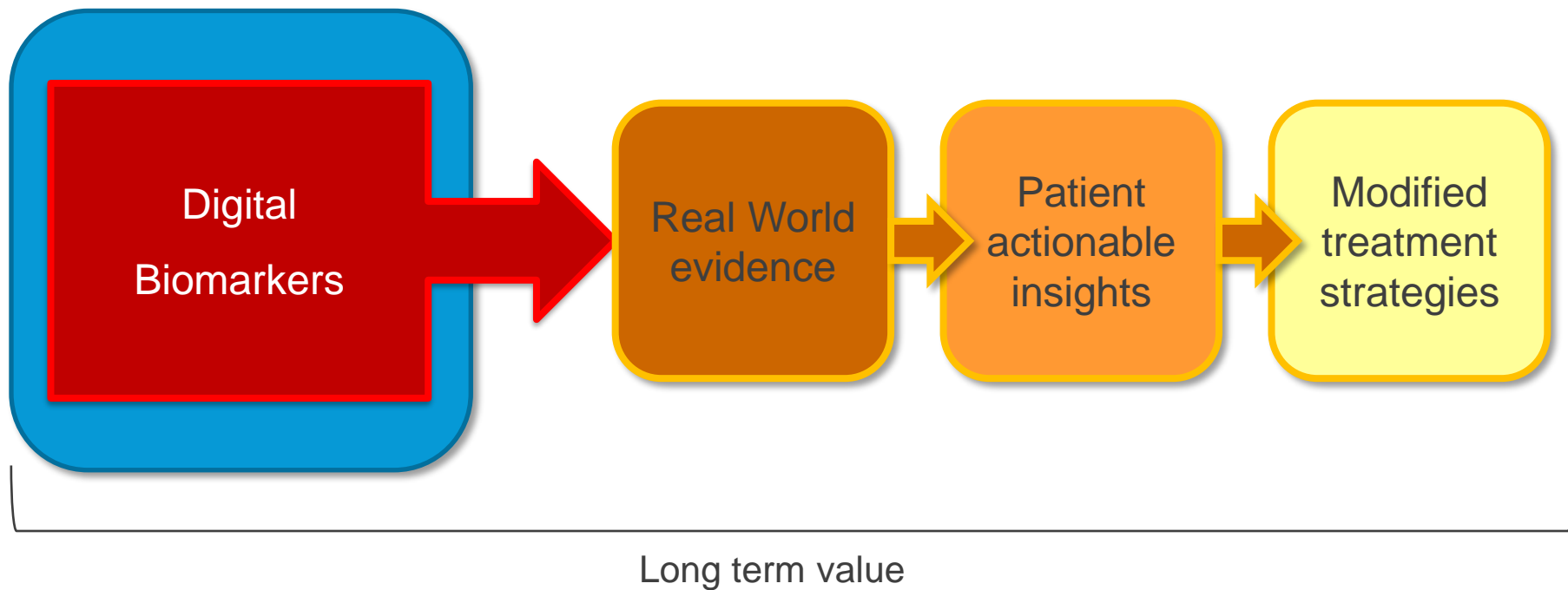
The adoption of connected healthcare

"

Everyone is after this space, but it's the ability to make a single use case work that drives success

"

- Director of Digital Medicines, Global Medical Device Company

The progression of Digital Biomarkers in clinical trials and beyond

Digital Biomarkers → Real World evidence → Patient actionable insights → Modified treatment strategies

Long term value

Three key factors

Digital Biomarkers
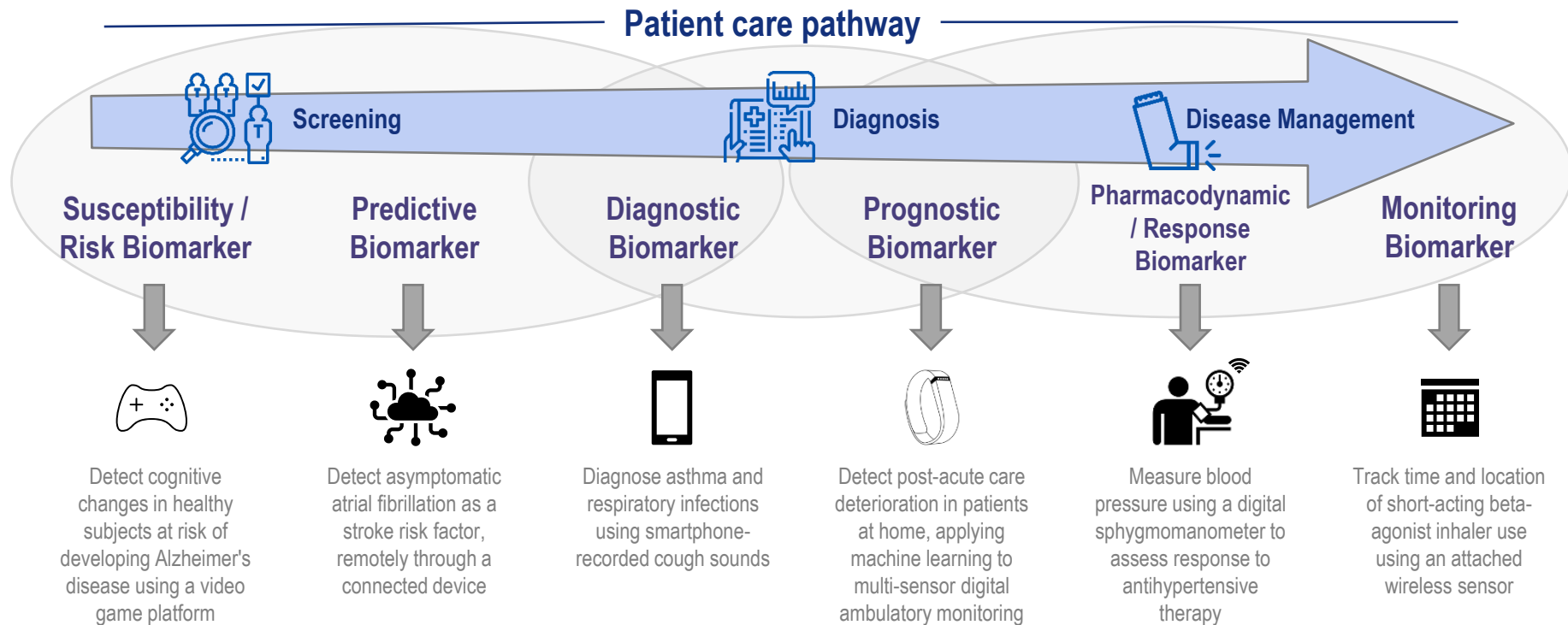
Machine Learning & AI

Network effects

Digital Biomarkers

What is a digital biomarker?

- We tend to think a biomarker: "*is a biological molecule found in body fluids or tissues that is a sign of a normal or abnormal process*"
  National Cancer Institute

- Digital biomarkers are *"…objective quantifiable physiological and behavioural data collected by digital devices"*
  Digital Biomarkers Journal, Karger Publishers

- But there is confusion here – digital biomarkers are also any data collected by digital devices, including portables, implantables, digestibles and drug delivery devices

- In other words *a **digital biomarker is any physiological or biological signal that is digitally captured.***
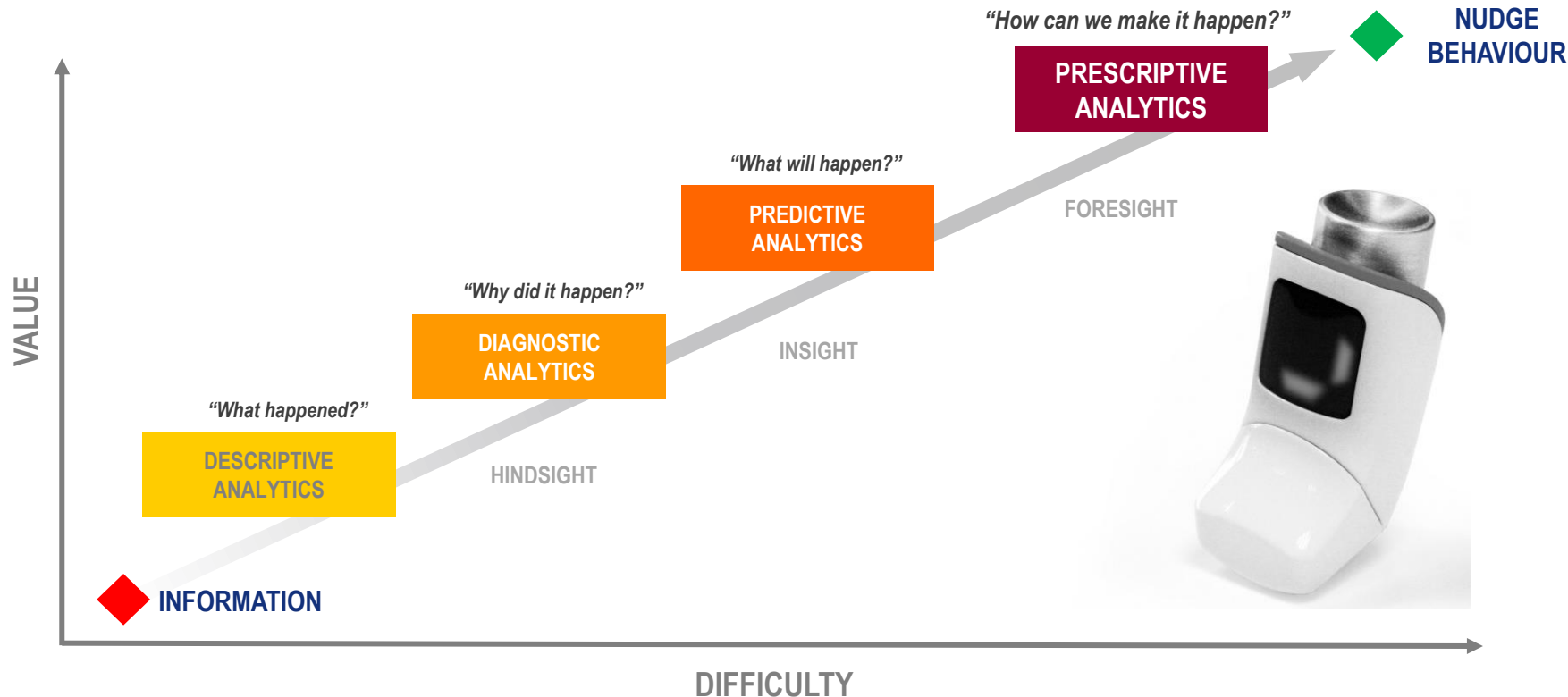
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Clinical application of digital biomarkers

Patient care pathway

Screening   **Diagnosis**   **Disease Management**

Susceptibility / Risk Biomarker

Predictive Biomarker

Diagnostic Biomarker

Prognostic Biomarker

Pharmacodynamic / Response Biomarker

Monitoring Biomarker

Detect cognitive changes in healthy subjects at risk of developing Alzheimer's disease using a video game platform

Detect asymptomatic atrial fibrillation as a stroke risk factor, remotely through a connected device

Diagnose asthma and respiratory infections using smartphone-recorded cough sounds

Detect post-acute care deterioration in patients at home, applying machine learning to multi-sensor digital ambulatory monitoring

Measure blood pressure using a digital sphygmomanometer to assess response to antihypertensive therapy

Track time and location of short-acting beta-agonist inhaler use using an attached wireless sensor

Adapted from Coravos, A., Khozin, S. & Mandl, K.D. (2019) Developing and adopting safe and effective digital biomarkers to improve patient outcomes. npj Digit. Med. 2, 14
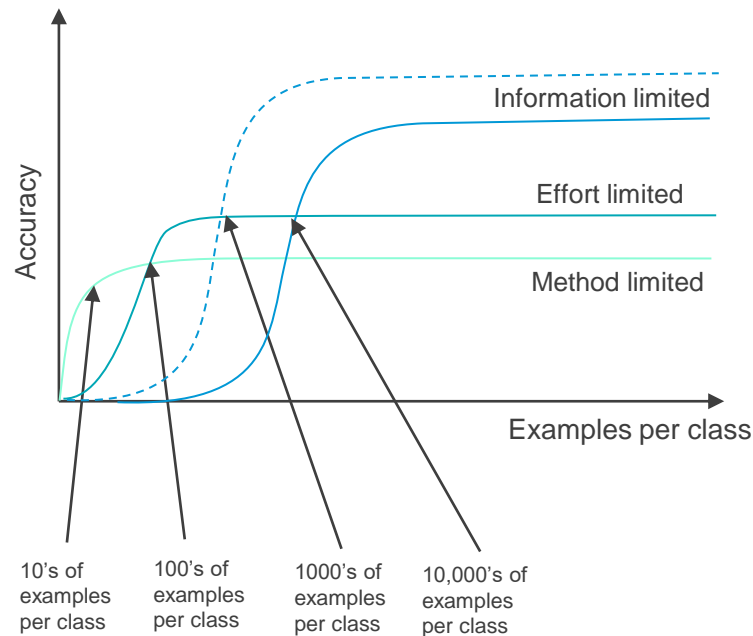
The goal for digital biomarkers: enabling analytics – information versus actionable insights

"How can we make it happen?"

NUDGE BEHAVIOUR

PRESCRIPTIVE ANALYTICS

FORESIGHT

"What will happen?"

PREDICTIVE ANALYTICS

INSIGHT

"Why did it happen?"

DIAGNOSTIC ANALYTICS

"What happened?"

DESCRIPTIVE ANALYTICS

HINDSIGHT

INFORMATION

VALUE

DIFFICULTY

Machine Learning (ML) & Artificial Intelligence (AI)

AI and machine learning allow better use data, but human insight is essential

- Statistical methods are the most effective way of determining effects in small studies

- Statistical Machine learning methods (e.g. SVM, Random forests) can do better but **leverage domain expertise** to describe features in the data e.g.

  – Characteristic waveforms, keywords in text

- Deep learning methods self generate these features so:

  – We can use previously "intractable" data,

  – We can discover more from more data, but they are limited by the information content of the signal

- Domain expertise is essential:

  – Data curation (90% of human effort)

  – There is an information limit with all data sources

  – Asking the right question (deep understanding of value)

Accuracy vs Examples per class chart with curves labelled "Information limited", "Effort limited", and "Method limited". Arrows point to "10's of examples per class", "100's of examples per class", "1000's of examples per class", "10,000's of examples per class".

Novartis's eBreezehaler

- Novartis developed the eBreezehaler to monitor patient usage

- The device uses an algorithm to determine an inhalation event from its sound signature

- Novartis subsequently showed that the integrated sensor technology could also provide an indication of inhalation technique[1]

(1) Adding Electronics to the Breezhaler(R): Satisfying the Needs of Patients and Regulators, Colthorpe P, Pavkov R, Rozenman Y, Humby C, Respiratory Drug Delivery 2018. Volume 1, 2018: 71-80

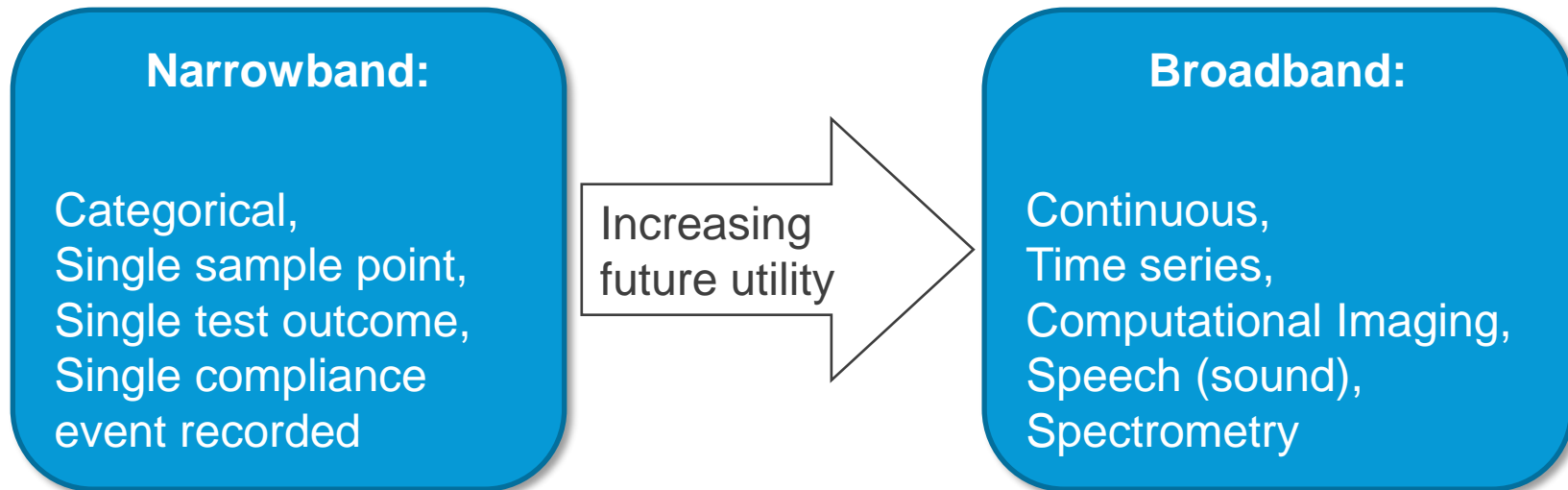# Teva is using continuous data for prediction

- Teva is running several studies in this space:

- Teva Asthma Predictive Analytics Study
  – Home spirometry to allow patients to self-assess their respiratory symptoms

- At digital health congress '21: Teva showed data from the ASTHMA study
  – Continuous data from the digihaler may be used to **predict exacerbations 5 days in advance**

*https://clinicaltrials.gov/ct2/show/NCT04997304*
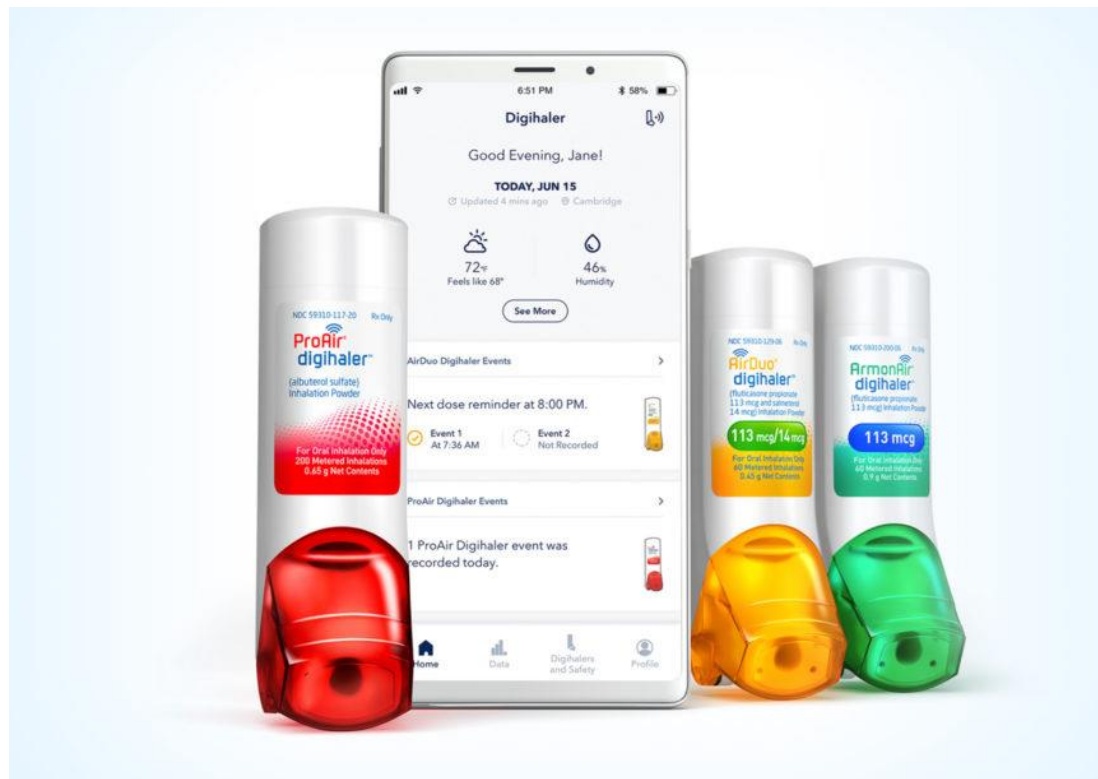
Outcome measures should be designed to support future product focus if possible

- Measuring compliance is essential during the clinical trials phase – but we should aim to achieve these outcomes using data that could support future applications (even if we're unsure what they will be)

Narrowband:

Categorical,
Single sample point,
Single test outcome,
Single compliance
event recorded

Increasing
future utility

Broadband:

Continuous,
Time series,
Computational Imaging,
Speech (sound),
Spectrometry

Network Effects

The goal of digital platform adoption is stability via the "network effect"; where external participants contribute and add value
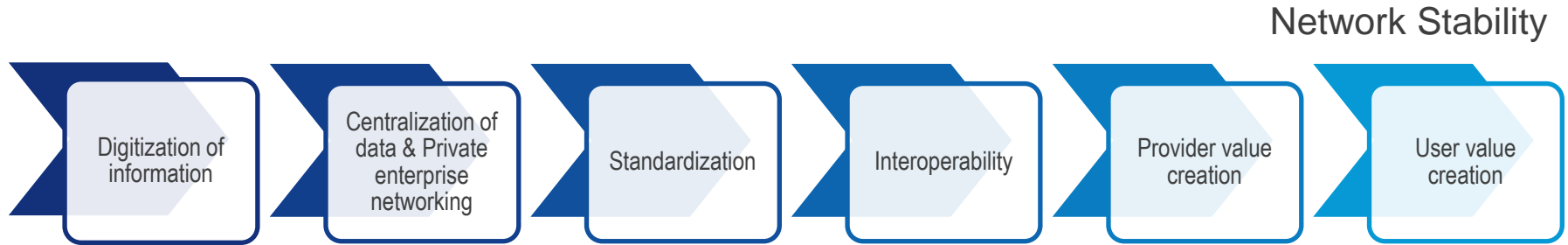
Once established, the network remains dominant.
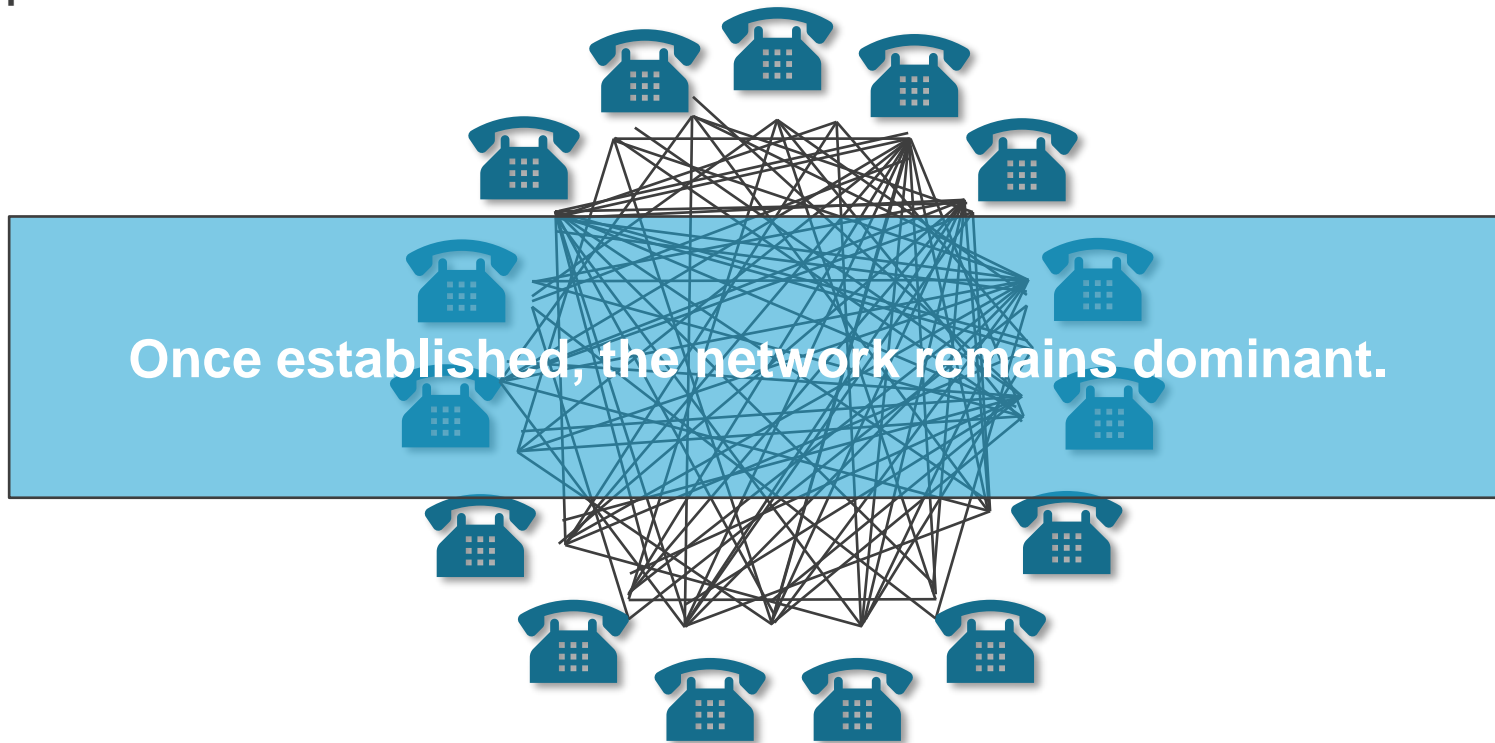
The goal of digital platform adoption is stability via the "network effect"; where external participants contribute and add value

- The network effect: as more people use a platform, the value of the service offered by the platform improves – which can lead to positive feedback of user growth.

- The value of the service is derived from use of the service, not provision

- The service is therefore context dependent (i.e. one network per patient / disease group)

- Where a single platform achieves positive feedback first, it tends to remain dominant.

- Network effects have become a strategic competitive advantage for digital businesses, where traditionally companies built and controlled assets, digital organisations aim to manage and build networks.

- **Being first to market with a product that delivers key user value is therefore essential**

Digital adoption enables translation of care from clinical to real-world environments

Network Stability

| Digitization of information | Centralization of data & Private enterprise networking | Standardization | Interoperability | Provider value creation | User value creation |

Digital adoption enables translation of care from clinical to real-world environments

Network Stability

Data Focus → **Product Focus** → **Platform Focus**

Bringing It All Together

Three key factors

Digital Biomarkers

Machine Learning & AI

Network effects

The progression of digital biomarkers in clinical trials and beyond

Long-term value in digital systems comes form the network effect

Personalised user value

Patient actionable insights

Real World evidence

Digital biomarkers (broadband data sources)

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