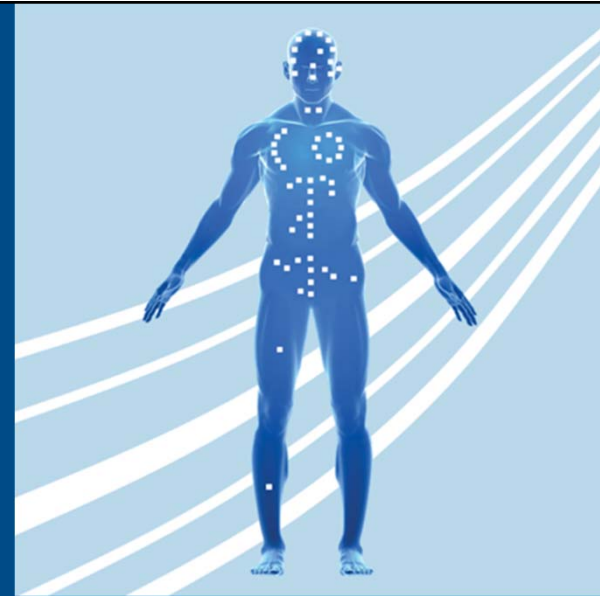


THE POTENTIAL OF THE DIGITAL TWIN AS A DISRUPTOR OF HEALTHCARE: PERSPECTIVE FROM MEDICAL DEVICES

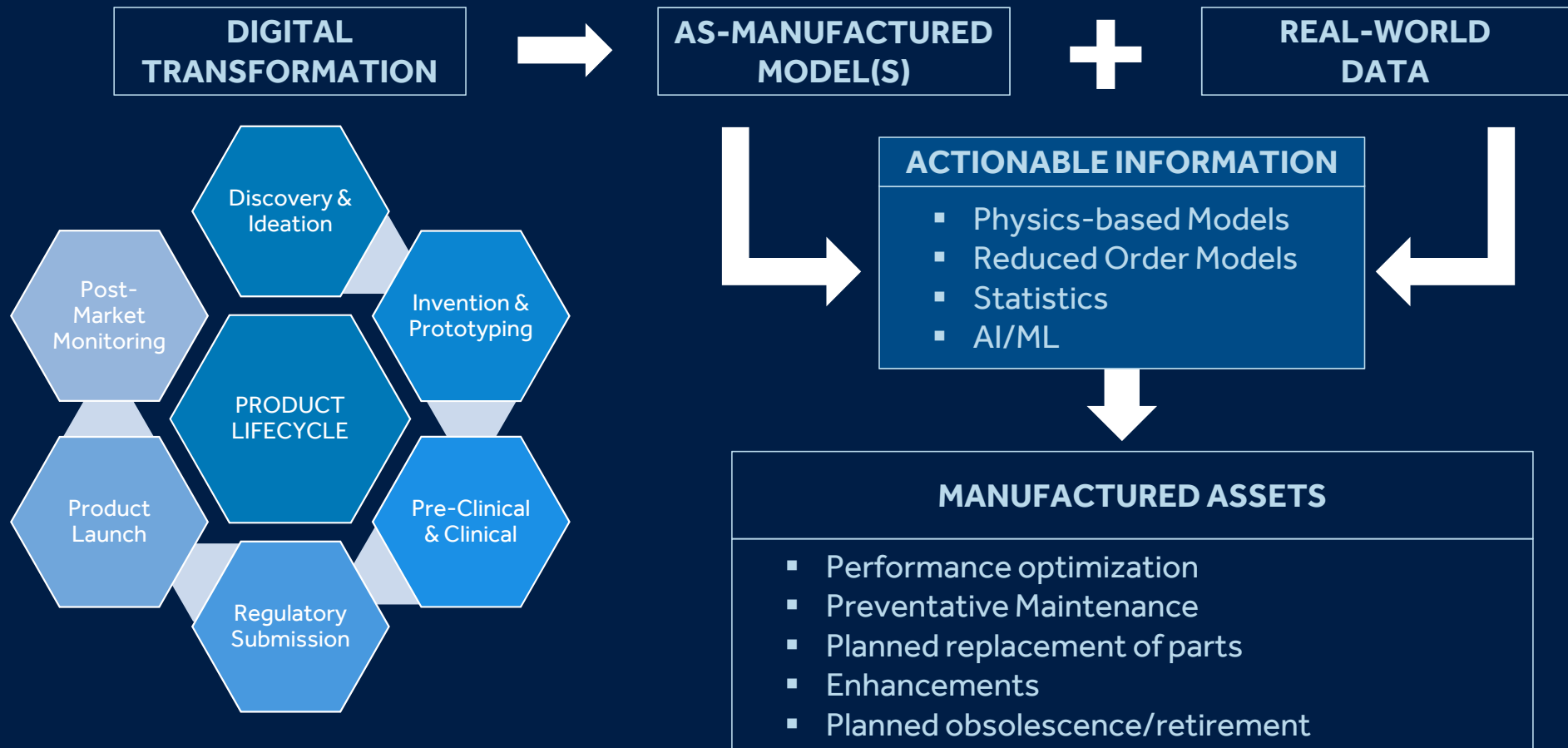
MARK PALMER, MD, PHD
DISTINGUISHED SCIENTIST
STRATEGIC SCIENTIFIC OPERATIONS



Medtronic
Further, Together

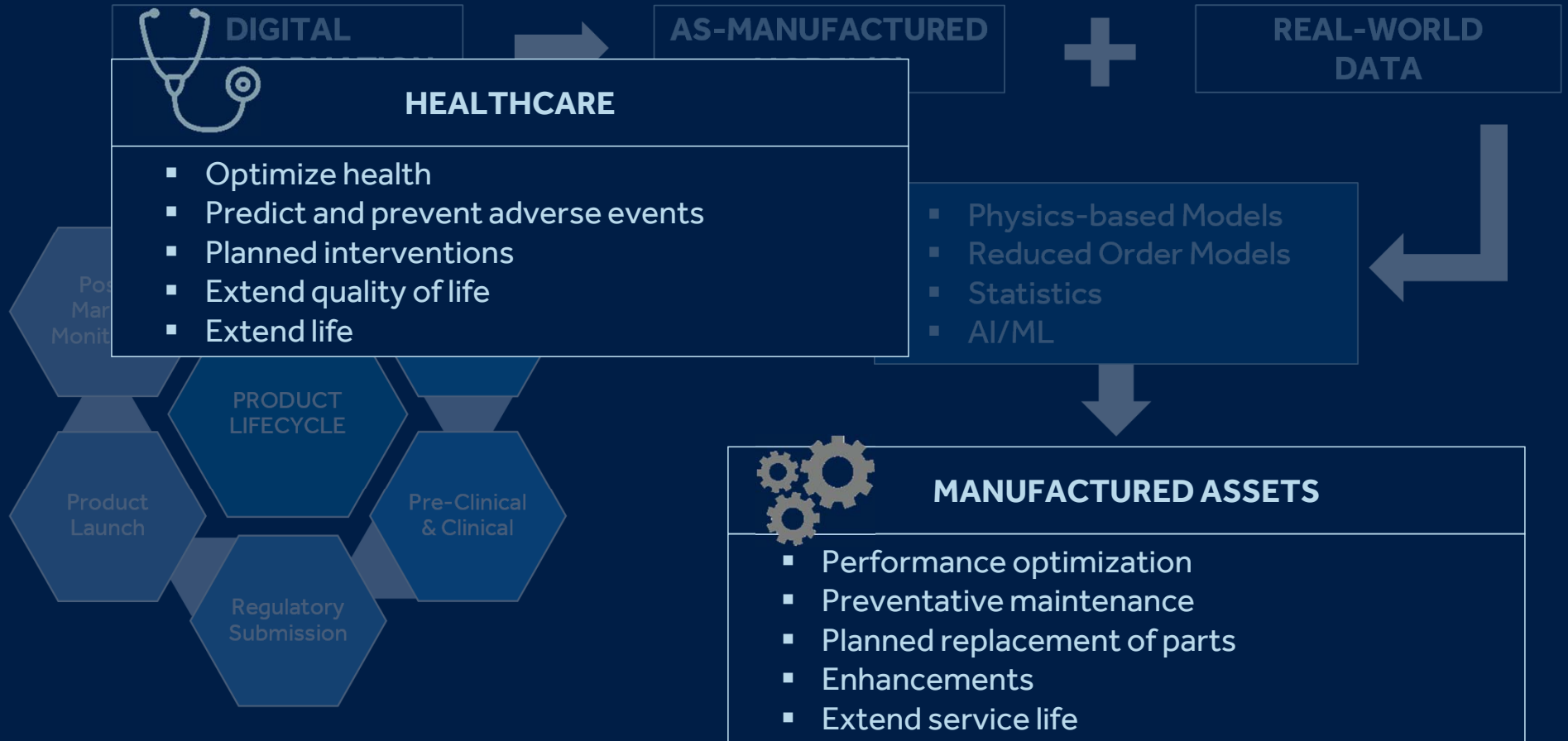
DIGITAL TWINS

DEFINITION



DIGITAL TWINS

DEFINITION



DIGITAL TWINS IN HEALTHCARE

"HOLY GRAIL"



CLINICAL OBJECTIVES

- Optimize health
- Predict and prevent adverse events
- Planned interventions
- Extend quality of life
- Extend life

MODIFIABLE FACTORS

- Diet
- Exercise
- Sleep
- Environment
- *Medication*
- *Therapy*
- *Surgery*
- *Implantables*



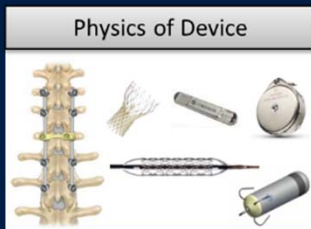
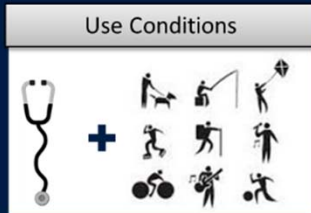
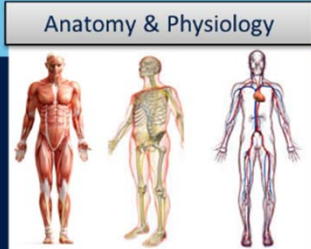
PREDICT IMPACT ON PHYSIOME



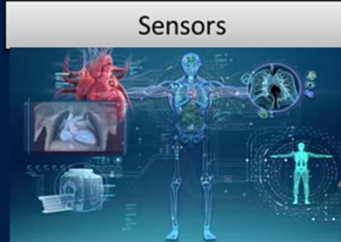
DIGITAL TWINS IN HEALTHCARE

CURRENT PERSPECTIVES

PHYSICAL SCIENCE



DIGITAL THREAD



DATA SCIENCE



DIGITAL TWIN



Digital twins exist at the nexus of physical engineering, data science, and machine learning, and their value translates directly to measurable business outcomes.*

DIGITAL TWINS IN HEALTHCARE

CURRENT PERSPECTIVES

PHYSICAL SCIENCE

DIGITAL THREAD

Anatomy & Physiology



Use Conditions



Physics of Device



Electronic Health Record



Sensors



Internet of Things



HEALTHCARE

- Optimize health
- Predict and prevent adverse events
- Planned interventions
- Extend quality of life
- Extend life

**IF THIS IS WHAT IS OUR
FOUNDATION, HAVE WE
ALREADY FAILED?**

DIGITAL TWIN IN HEALTHCARE: CHALLENGES

1. DEFINING THE REFERENCE STATE

PHYSIOME

- Genome
- Transcriptome
- Proteome
- Metabolome
- Morphome
- *Individuals differ at every level of their physiome*
- *Differences impact how they respond to modifiable factors*
- *Changes over lifetime*

EVIDENCE BASED MEDICINE

- Roots in clinical education
- Goal: reduce variability in resources and outcomes
- Ideally generated from Randomized Control Trials
- Analysis assumes "statistical homogeneity"
- Trials do not map well to real world (bias, tails)

MODIFIABLE FACTORS

- Diet
- Exercise
- Sleep
- Environment
- *Medications*
- *Therapy*
- *Surgery*
- *Implantables*



PERSONALIZED MEDICINE

- Roots in pharmacology
- Goal: Pharmacogenetics for tailoring of drugs
- Function of ~ 33% of genome still unknown
- Role of gene-gene interactions uncertain
- Assumes "statistical heterogeneity"
- Designing and funding RCT is challenging

DIGITAL TWIN IN HEALTHCARE: CHALLENGES

2. THE DATA (MINIMIZE INTERACTION WITH HEALTH SYSTEM)



CLINICAL ANALOG

- Optimize health
- Predict and prevent adverse events
- Planned interventions
- Extend quality of life
- Extend life



DATA STREAMS

- Diet
 - Location/GPS
 - Activity monitors
 - Some vitals
 - Sleep monitors
 - Biomarkers
- *Medications*
 - *EHR*
 - *Vitals*
 - *Labs*
 - *Imaging*
 - *Biomarkers*
 - *Genetic analysis*

MODIFIABLE FACTORS

- Diet
 - Exercise
 - Sleep
 - Environment
- *Medications*
 - *Therapy*
 - *Surgery*
 - *Implantables*

- Are the existing clinical measurements optimal for predicting health?
- How do we generate accessible and affordable streams of data?
- How to ensure data quality? (eg: bad sensor placement)
- Majority of variables that define physiome are inaccessible
- Reliance on longitudinal "health record"

DIGITAL TWIN IN HEALTHCARE: CHALLENGES

3. DEFINING THE DISEASE OR ABNORMAL STATE

PHYSIOME

- Genome
 - Transcriptome
 - Proteome
 - Metabolome
 - Morphome
- *Individuals differ at every level of their physiome*
 - *Differences impact how they respond to modifiable factors*
 - *Changes over lifetime*



MODIFIABLE FACTORS

- Diet
 - Exercise
 - Sleep
 - Environment
- *Medications*
 - *Therapy*
 - *Surgery*
 - *Implantables*

- How to manage genotypic expression of disease risk?
- How to manage genotypic expression of disease in absence of phenotype?
- Normal range for one individual may be pathological for another
- Time scale of onset of disease
- Time course of the disease

CHRONIC DISEASE

DIGITAL TWINS IN CHRONIC DISEASE

A NEAR-REAL-TIME LINKAGE BETWEEN PHYSICAL AND DIGITAL WORLDS

PHYSICAL SCIENCE

Anatomy & Physiology



Use Conditions



Physics of Device



DIGITAL THREAD

Electronic Health Record



Sensors



Internet of Things



DATA SCIENCE

Machine Learning



Statistical Analysis



Big Data Analytics



DIGITAL TWIN

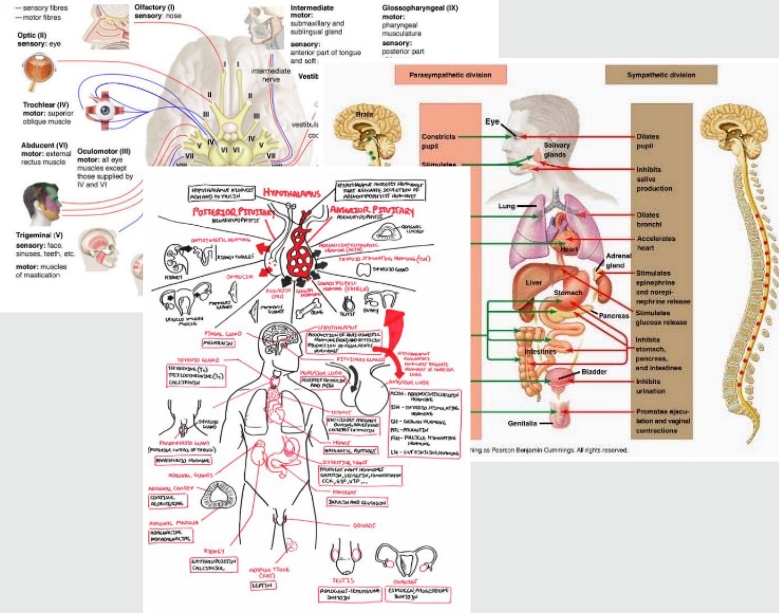


Digital twins exist at the nexus of physical engineering, data science, and machine learning, and their value translates directly to measurable business outcomes.*

DIGITAL TWINS IN CHRONIC DISEASE DEVICES & HUMANS

PHYSIOLOGY

The Peripheral Nervous System Cranial Nerves



HEALTHY



- complex milieu of overlapping control systems
- Multiple pathways influencing parameter of interest
- Coupled PDE's

CHRONIC DISEASE

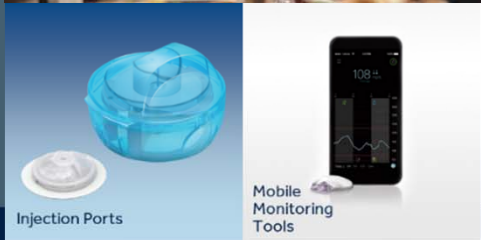


- Control systems are saturated
- Deviation from reference is clear
- Measurements well defined
- Axes of intervention well defined
- Coupled ODE's

DIGITAL TWINS IN CHRONIC DISEASE

SENSOR ENABLED DEVICES & HUMANS

PHYSICAL PRODUCTS IN THE REAL WORLD



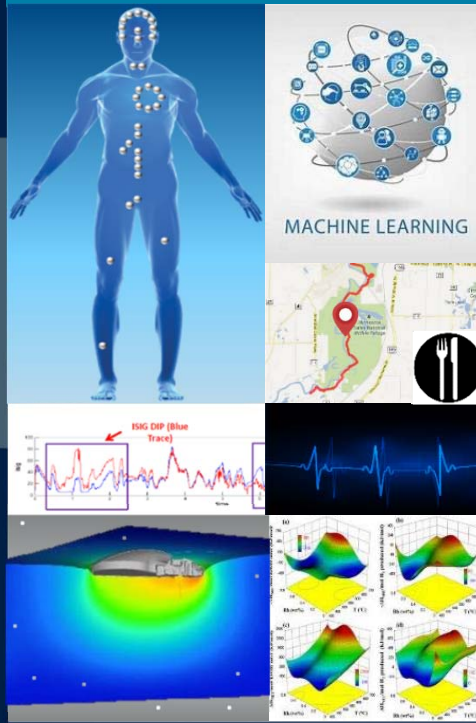
Injection Ports

Mobile Monitoring Tools



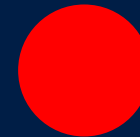
Insulin Pumps with built-in Continuous Glucose Monitoring

VIRTUAL PRODUCTS AND LIGHT WEIGHT MODELS



MACHINE LEARNING

ACTIONABLE PREDICTIONS



EMERGENCY PROTOCOL



WARNING PROTOCOL

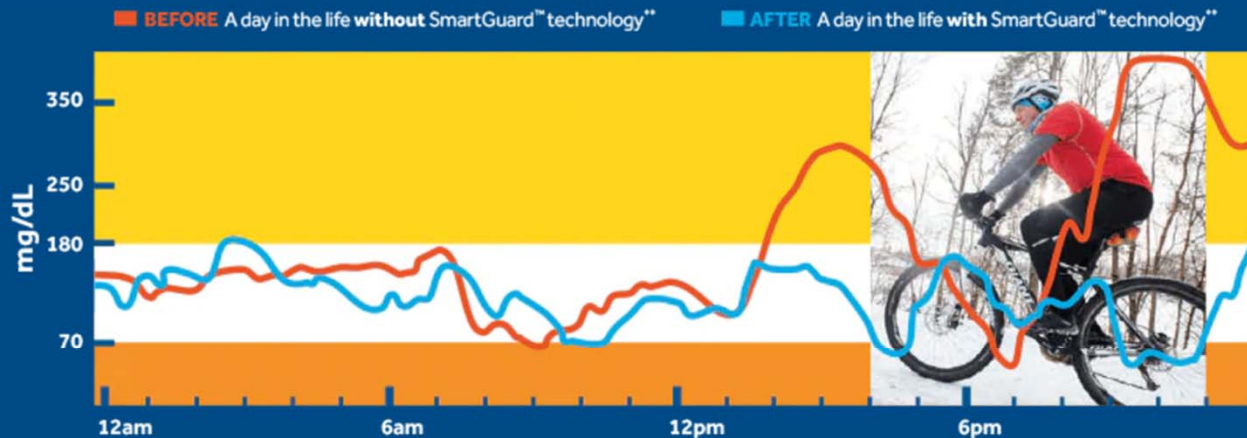


SYSTEMS NORMAL

DIGITAL TWINS IN CHRONIC DISEASE

CLOSED LOOP GLUCOSE MANAGEMENT SYSTEM

- Algorithm adapts to individual patient's glucose metabolism
- Automatically adjusts basal (background) insulin every five minutes based on CGM readings
- Patient administers bolus for meals
- Algorithm is resistant to over or underestimation of carb consumption
- Stops insulin up to 30 minutes before reaching preset low limits



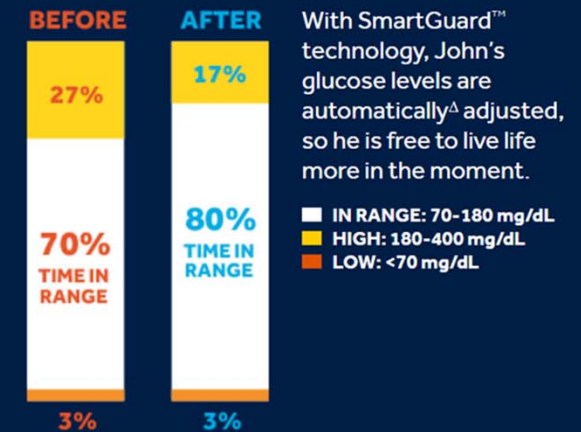
**JOHN'S
A1C.**

**BEFORE
8.1**

**AFTER
6.1**

**Representative of actual patient Carelink™ data. Individual results may vary.

HELPS IMPROVE TIME IN RANGE.



DIGITAL TWINS IN HEALTHCARE

OPTIMIZING MANAGEMENT OF INDIVIDUAL HEALTH



HEALTHCARE

- Optimize health
- Predict and prevent adverse events
- Planned interventions
- Extend quality of life
- Extend life



“Clinical medicine seems to consist of a few things we know, a few things we think we know (but probably don’t), and lots of things we don’t know at all.”

Naylor CD. “Grey zones of clinical practice: some limits to evidence-based medicine”. Lancet. 1995;345:840-842



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