KU LEUVEN

Virtual Human Digital Twins

A Key Tool for New Patterns for Prediction and Prevention

The Clinician Viewpoint

Tuesday, October 22th 2024

Frank E. Rademakers

Emeritus Professor KU Leuven

TwinHealth

Maximize the Health Potential of Every Person from before Birth until Death

Delivering Informed, Personalised Co-Decision Making for every circumstance and context

Why do we need to create TwinHealth?

- What are problems in the present Health Care Systems?
  - Prevention underused
    - Not starting from unmet needs
    - Risk factors undetermined or not taken into account
    - Late/wrong diagnoses
  - Data Overload
  - Standardized treatment schemes/ guidelines: average patient
    - Need for personalization
  - Limited resources
    - Health Care Providers
    - Budget
  - Human Fallibility: Fast & Slow Thinking, Bias & Noise
  - Information from daily life missing
    - Decisions made on sparse information
  - Social and environmental context missing

Challenges for current healthcare system

- **Prevention underused**
  - **Not starting from unmet needs**
  - **Risk factors undetermined or not taken into account**
  - **Late/wrong diagnoses**

- Human Fallibility: Fast & Slow Thinking, Bias & Noise
- Social and environmental context missing
- Information from daily life missing
  - Decisions made on sparse snapshot information about individual patients

NEEDS EXAMINATION, EVALUATION AND DISSEMINATION (NEED): ASSESSMENT FRAMEWORK

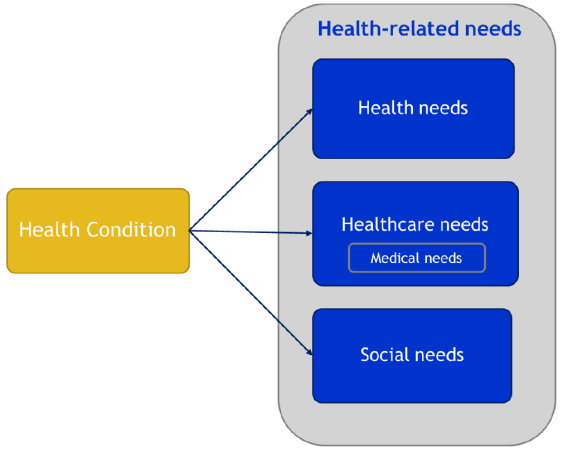
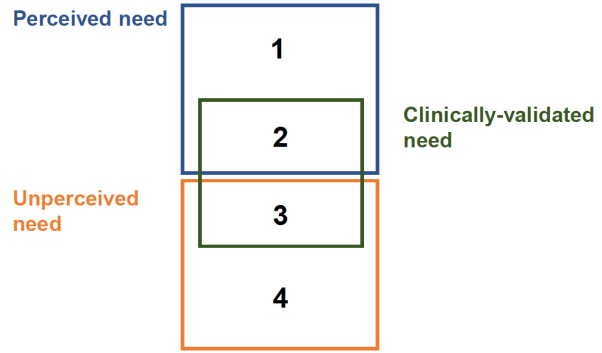
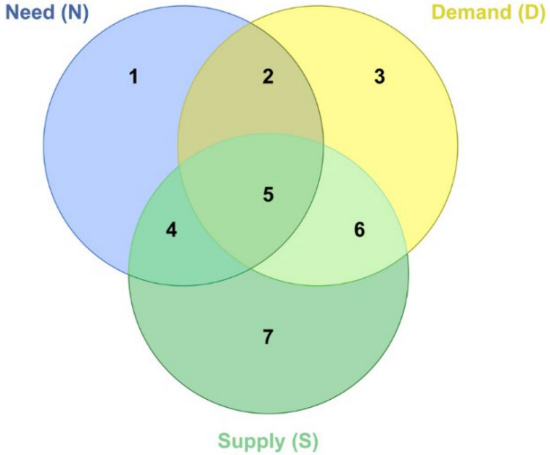


Figure 5 – Relation between perceived, unperceived, and clinically-validated need



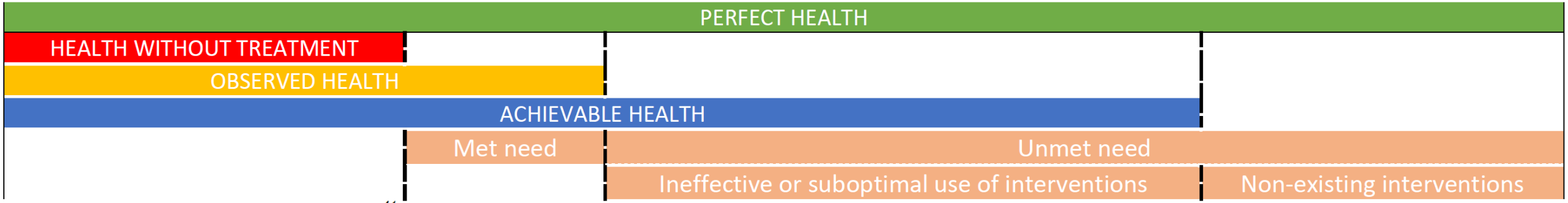
Source: KCE, inspired by Allin et al. (2010) [39]

Figure 6 – Interactions between Need, Demand and Supply in healthcare

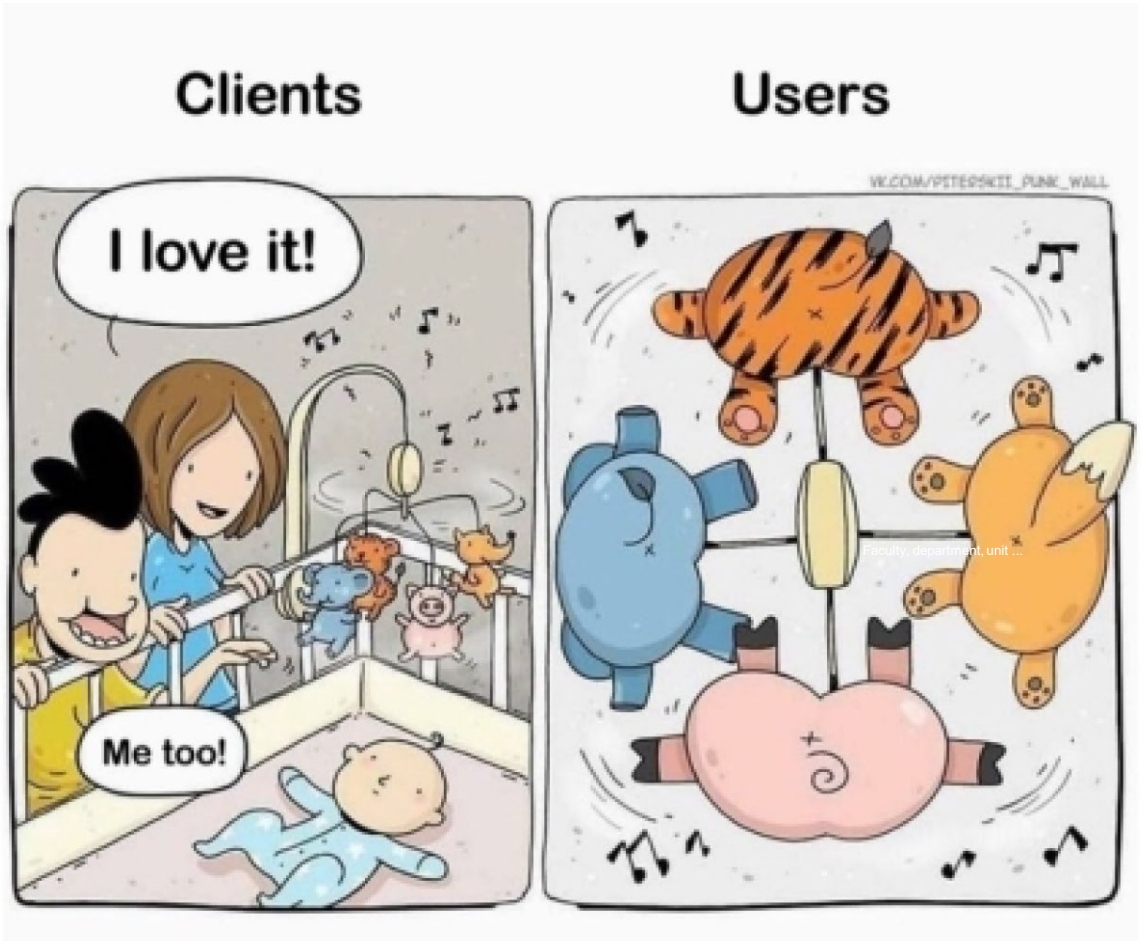


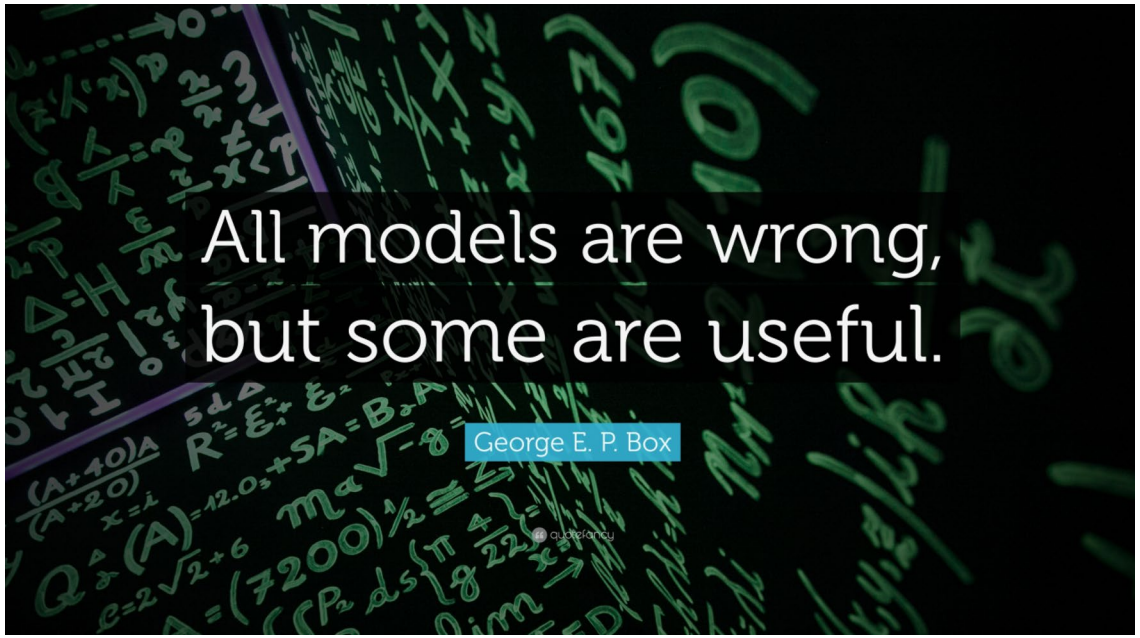
Source: Santana et al. (2023) [40]

Figure 7 – Identifying unmet need using an adaptation of Incerti et al.'s approach



Source: adapted from Incerti et al. (2019) [41] Note: This figure represents the conceptual approach to disaggregating need for a population with a specific health issue, assuming that, ceteris paribus, disease burden increases with age.


Clients
Users
I love it!
Me too!


All models are wrong,
but some are useful.
George E. P. Box

Challenges for current healthcare system

- **Handling Data Overload**

Challenges for current healthcare system

- Handling Data Overload
- **Need for personalization**
  - **Standardised treatment schemes/guidelines: treating the average patient**

Challenges for current healthcare system

- Handling Data Overload
- Need for personalization
  - Standardised treatment
- **Limited resources**
  - **Health Care Providers**
  - **Budget**
- Human Fallibility: Fast &
- Social and environmenta
- Prevention underused
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- Information from daily life missing
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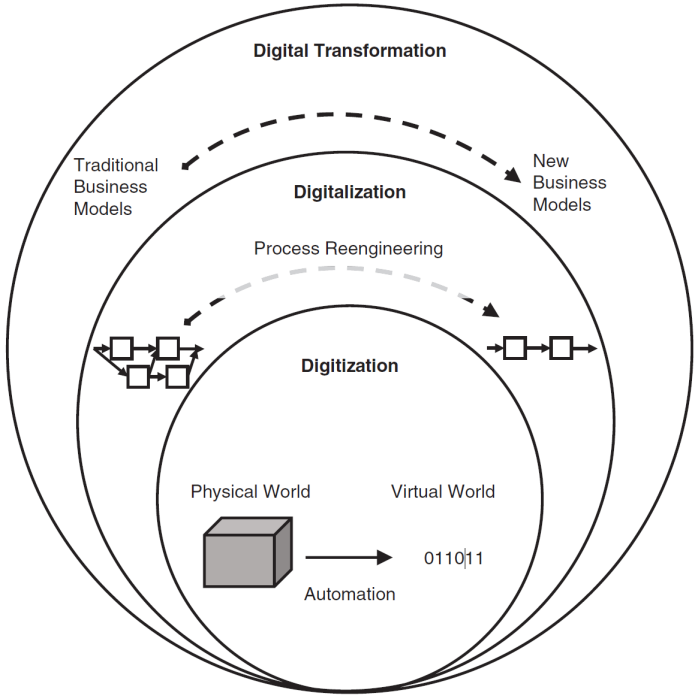

FIGURE 1. The three steps toward Digital Transformation.

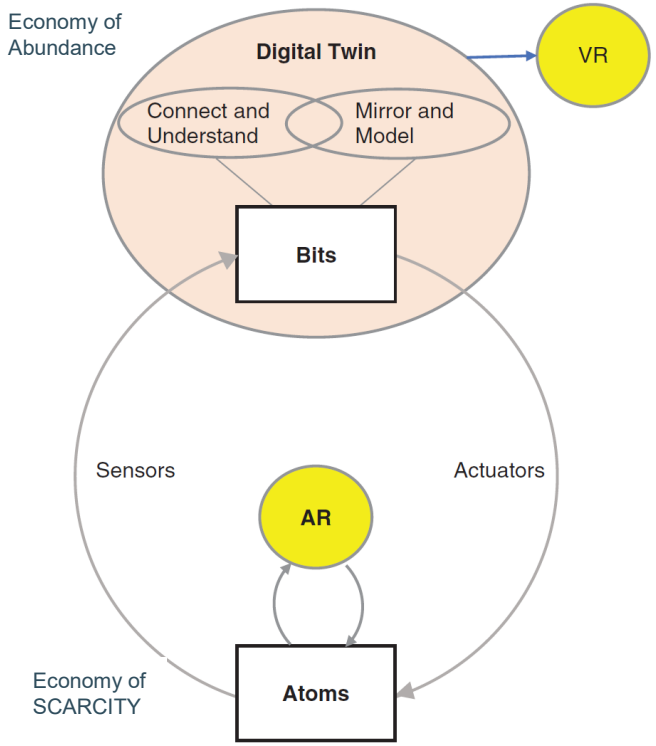

FIGURE 2. The underpinning of the Digital Transformation.

Challenges for current healthcare system

- verload
- alization
- reatment schemes: average patient/guidelines
- es
- roviders
- **Human Fallibility: Fast & Slow Thinking, Bias & Noise**
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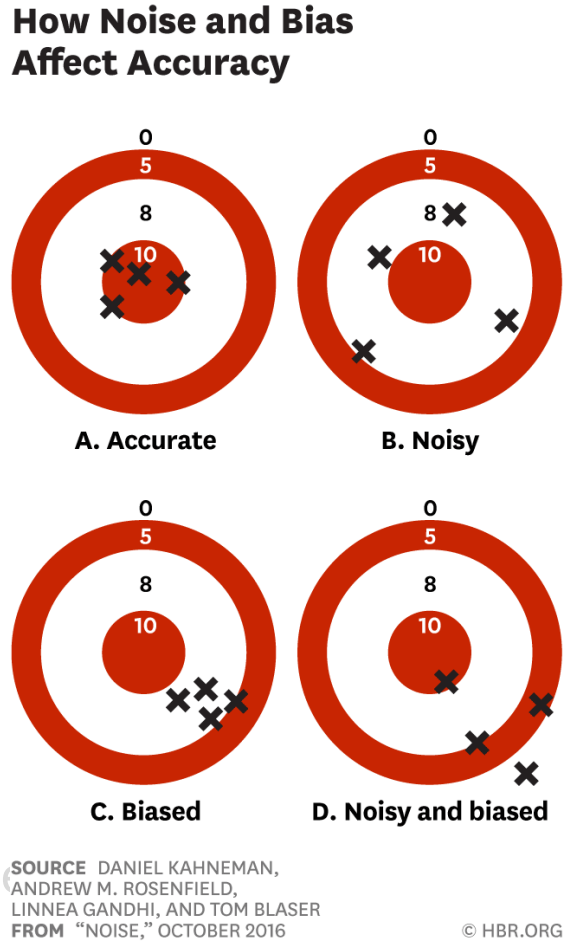

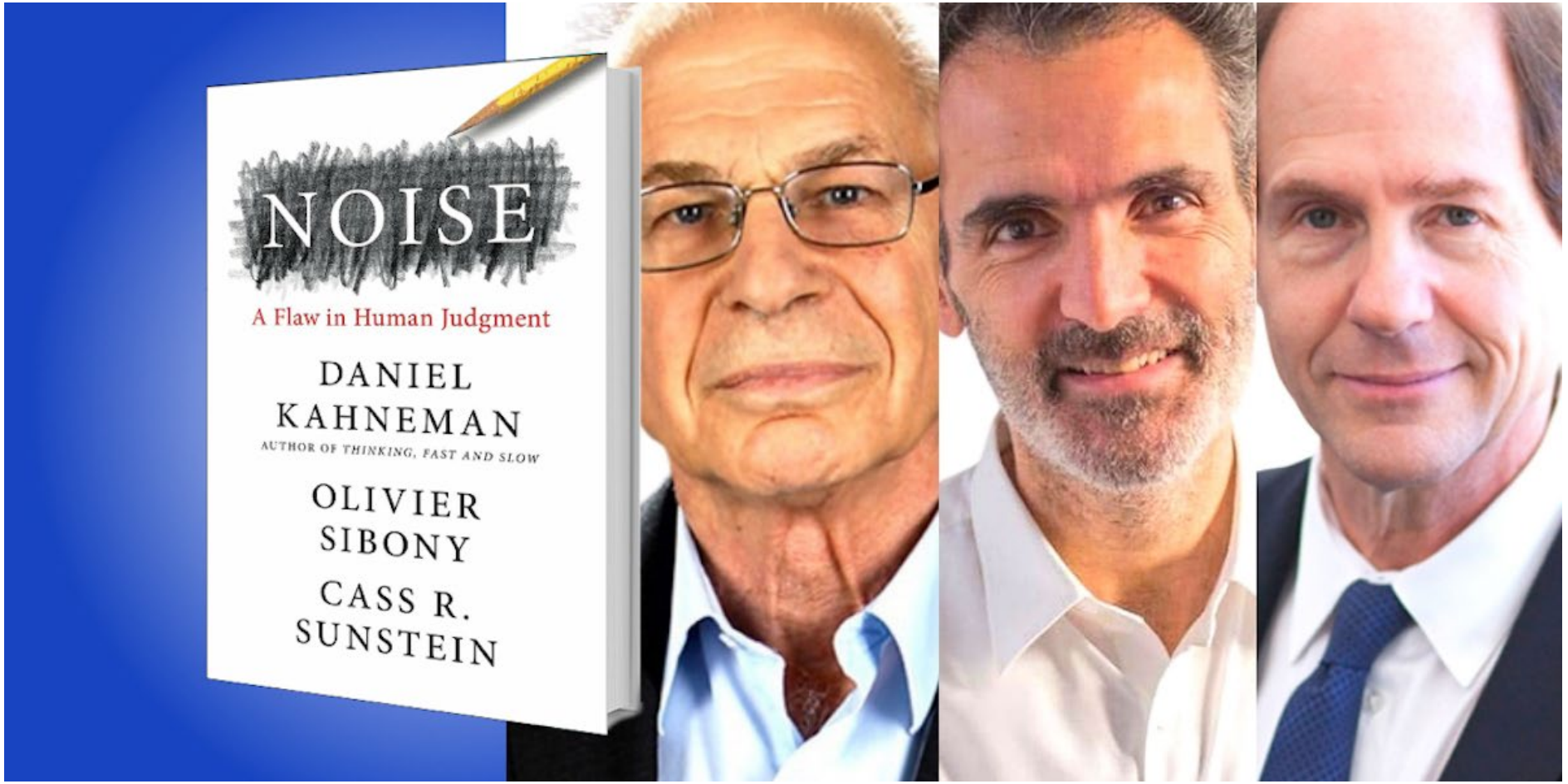
NOISE
A Flaw in Human Judgment
DANIEL KAHNEMAN
AUTHOR OF THINKING, FAST AND SLOW
OLIVIER SIBONY
CASS R. SUNSTEIN

William Osler

- *Medicine is a science of uncertainty and an art of probability.*

- ***It is much more important to know what sort of a patient has a disease than what sort of a disease a patient has.***
- *The good physician treats the disease; the great physician treats the patient who has the disease.*
- ***We are constantly misled by the ease with which our minds fall into the ruts of one or two experiences***
- *Look wise, say nothing, and grunt. Speech was given to conceal thought.*
- *To confess ignorance is often wiser than to beat about the bush with a hypothetical diagnosis.*

William Osler. Counsels and ideals. 1921:214

Challenges for current healthcare system

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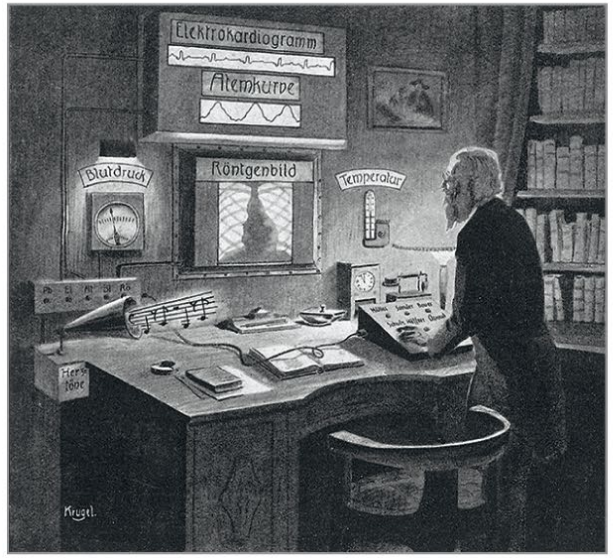
- Need for personalization
  - Standardised treatment schemes: average patient/guidelines
- Limited resources
  - Health Care Providers
  - Budget
- Human Fallibility: Fast & Slow Thinking, Bias & Noise
- Social and environmental context missing
- Prevention underused
  - Risk factors undetermined or not taken into account
  - Late/wrong diagnoses
- **Information from daily life missing**
  - **Decisions made on sparse snapshot information about individual patients,**
  - **Mainly from in-hospital encounters and testing**

JAMA Network™

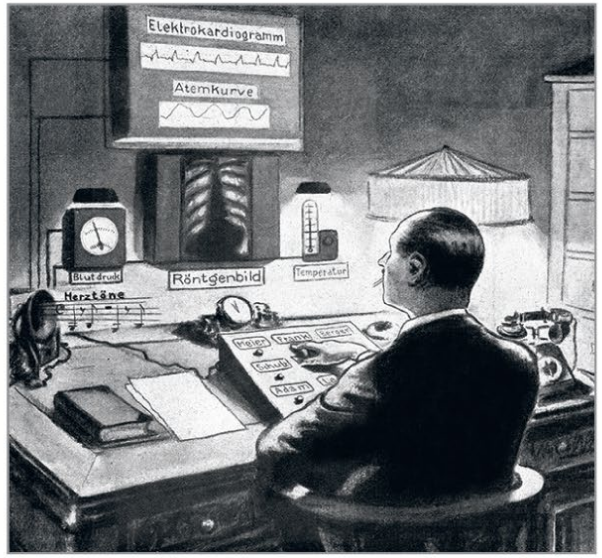
From: **Fritz Kahn and the Centenary of The Doctor of the Future**

JAMA. Published online May 06, 2024. doi:10.1001/jama.2024.6041

A Initial portrayal of *The Doctor of the Future*, 1924



B Modern Technology Expanding the Doctor's Scope, 1925



C The Doctor Is Connected to His Patients Throughout the World, 1939

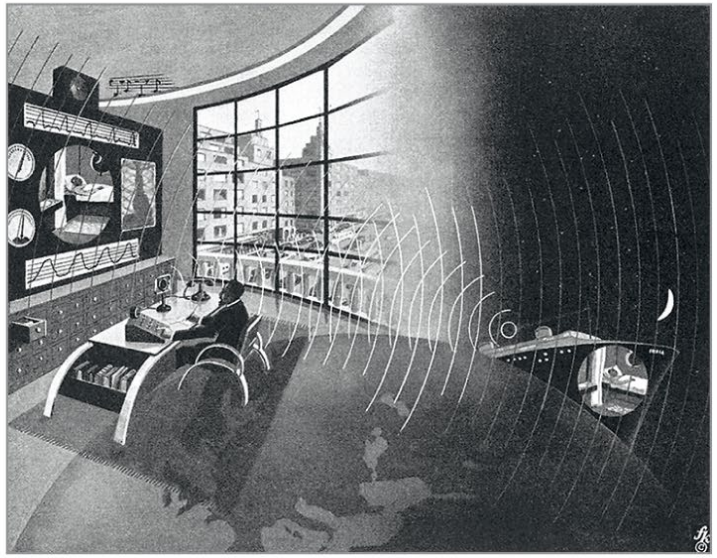
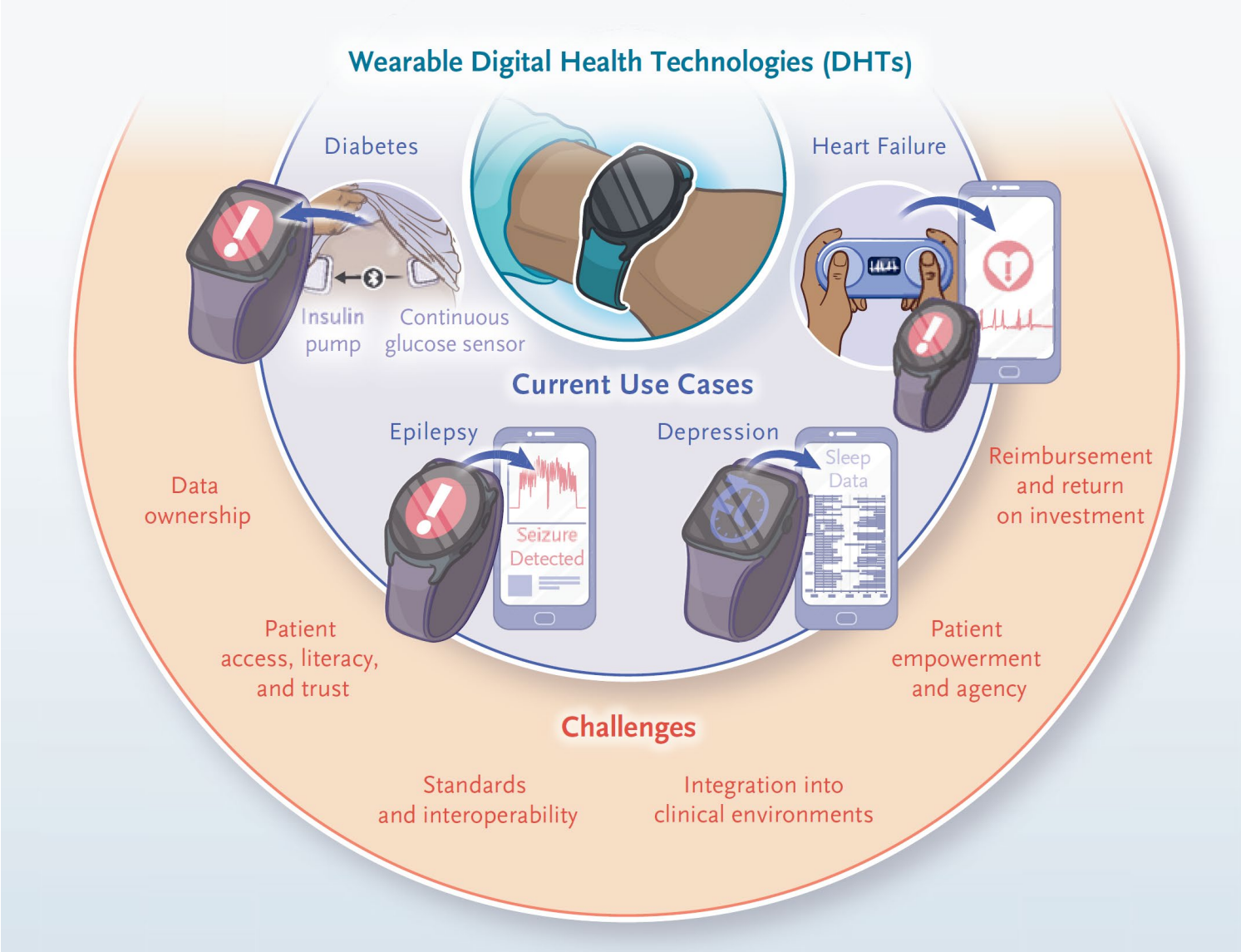


Figure Legend:

The Doctor of the Future A, Artist: Arno Krugel. Copyright: Kosmos/von Debschitz. B, Artist: unknown (attr. Fritz Schüler). Copyright: Ullstein/von Debschitz. C, Artist: unknown (attr. Fritz Schüler). Copyright: Fritz Kahn/von Debschitz.



N Engl J Med 2024;390:1118-27.
DOI: 10.1056/NEJMra2307160

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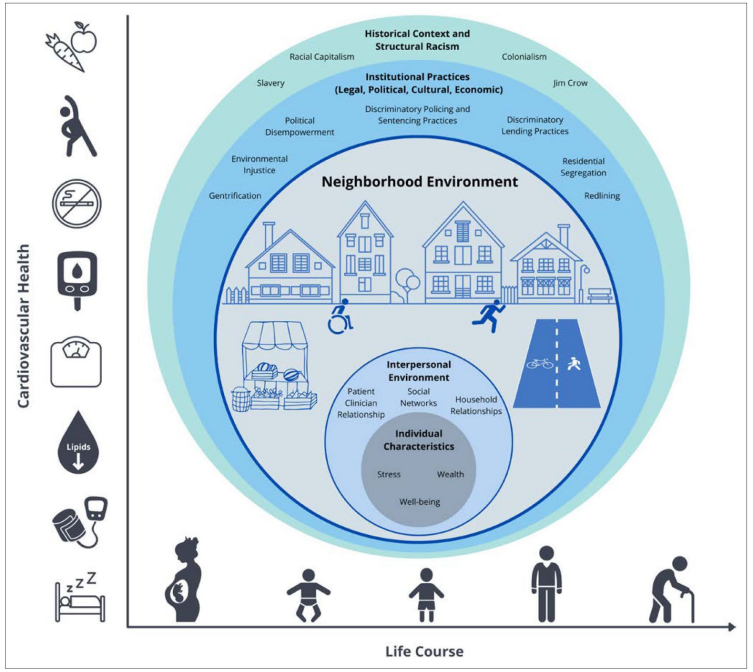


Figure 1. **The multilevel and interacting factors that determine and shape the relation of the neighborhood with cardiovascular health and outcomes.**

How can TwinHealth address these gaps?

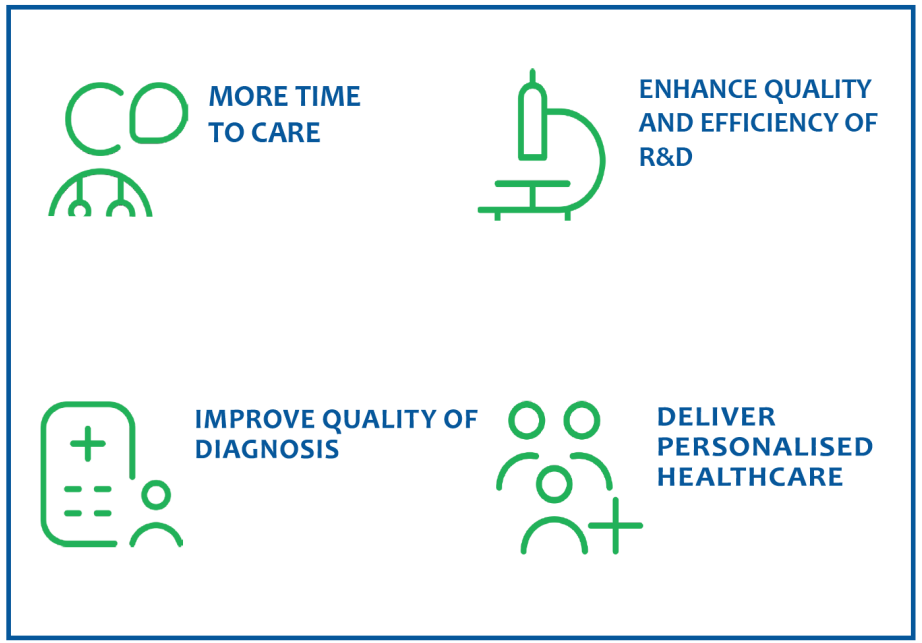
- Start from the needs of patients and HCP's
- Gather the relevant information
- Interpret that information
- Put it at the fingertips of patients and HCP's
- Help making the right decisions about prevention, diagnosis, treatment and follow-up
- Keep improving the system with the input from every interaction

Provide a clinical decision support tool based on Medical Digital Twins

How can TwinHealth address these gaps?

- Start from the needs of patients and HCP's

2023 Survey Results: What can AI do for patients?



9 Principles to Regulate AI in Healthcare

1. RESPECT HUMAN DIGNITY
2. ADDRESS DATA QUALITY AND INTEGRITY
3. ENGAGE PATIENTS AND HEALTHCARE PROFESSIONALS
4. ENSURE ACCESSIBILITY AND INCLUSIVITY
5. KEEP HUMANS IN CONTROL
6. PROTECT HEALTH DATA AND PATIENT CONFIDENTIALITY
7. FOSTER RESPONSIBILITY AND ACCOUNTABILITY
8. ENHANCE TRANSPARENCY
9. PRIORITISE EDUCATION, TRAINING, AND DIGITAL LITERACY

EPF European Patients Forum

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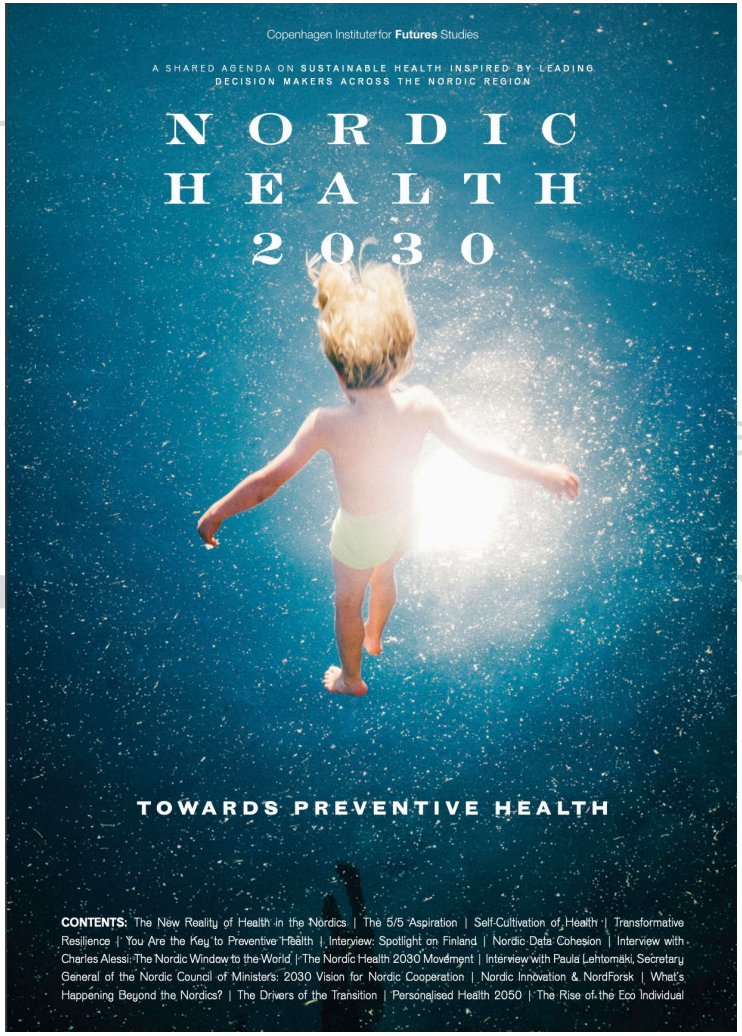
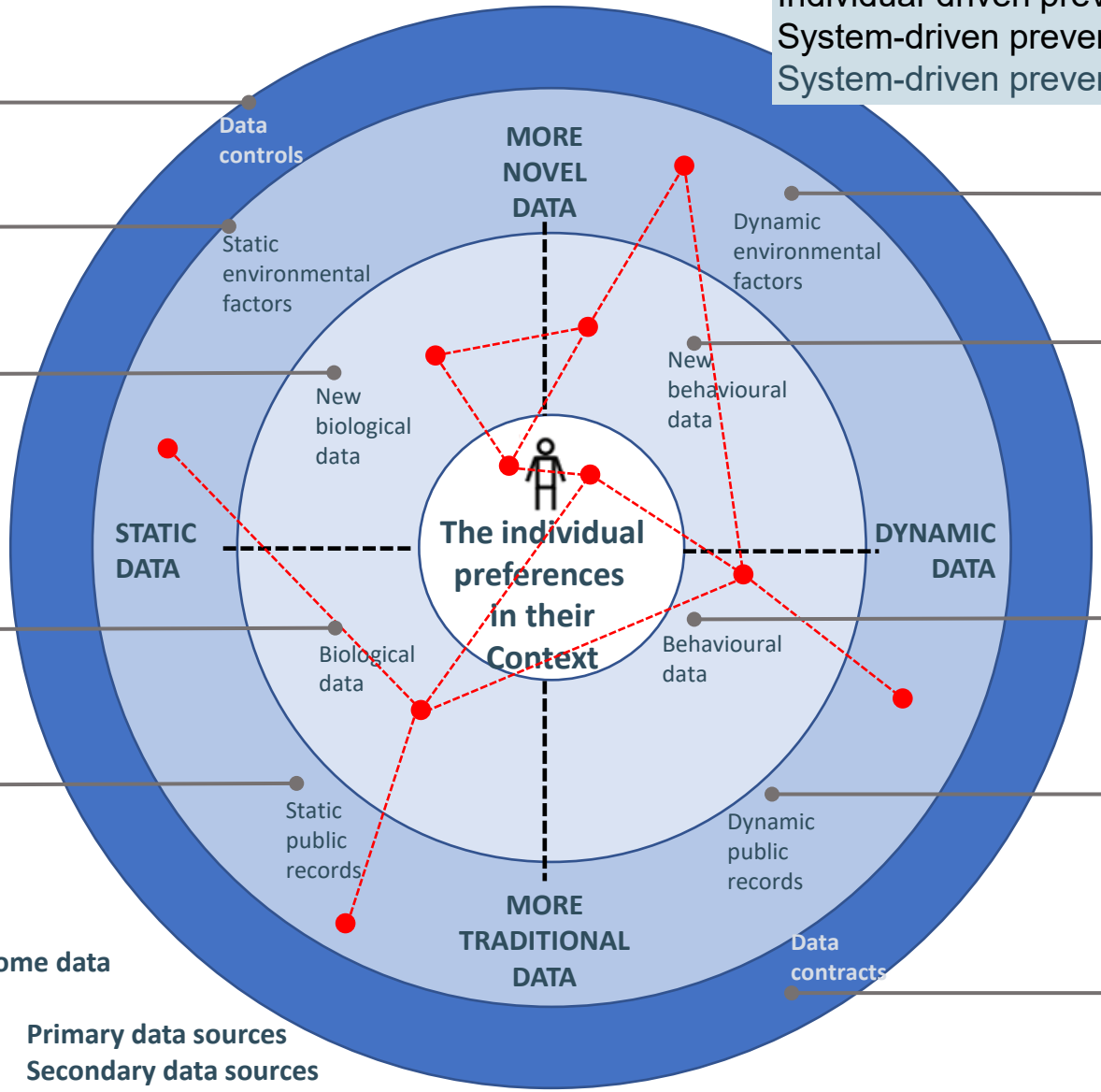


THE HUMANOME – A PERSONALISED POINT OF CARE DATA CONCEPT

Individual-driven preventive health
Individual-driven preventive health, motivating the system
System-driven preventive health, motivating the individual
System-driven preventive health



- (Cyber) Security
- Traceability
- Transparency

Data controls

Using public data

Using location Information

Apps & Wearables

Linking medical records

Existing & Novel

Linking personal data

Social Media

Data contracts

- Consent
- Donation
- Sharing
- Public interest

Qualification of Personalised point of care

- Data marker
- Data correlation
- Data Pattern

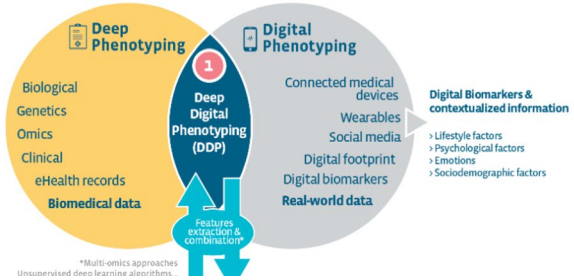
Humanome data

- Primary data sources
- Secondary data sources
- Data requirements

Ocean of data, desert of interpretation and use

How can TwinHealth address these gaps?

- Start from the needs of patients and HCP
- Gather the relevant information
- **Interpret that information**



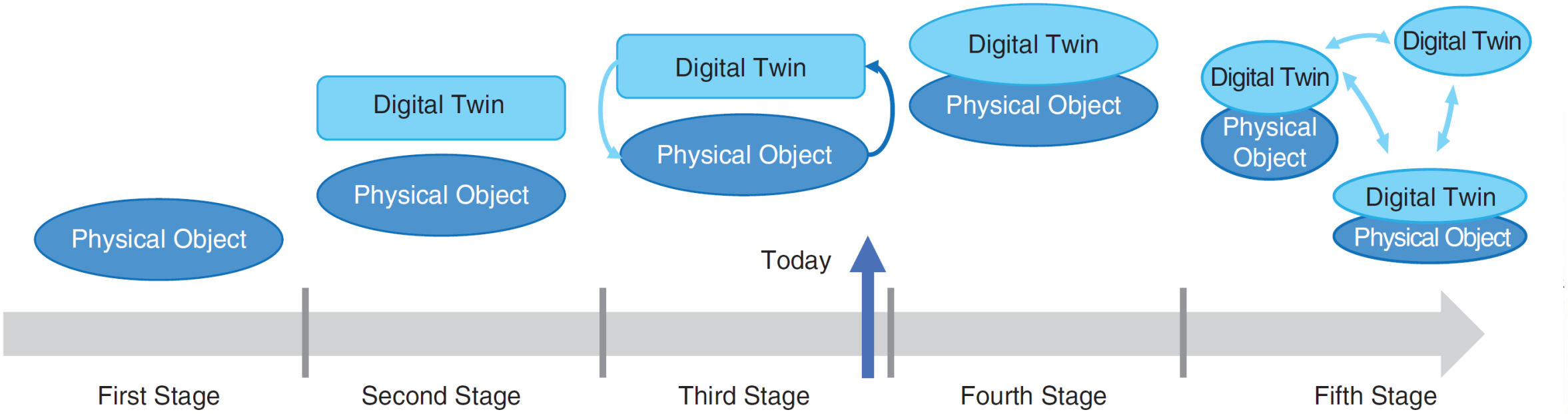
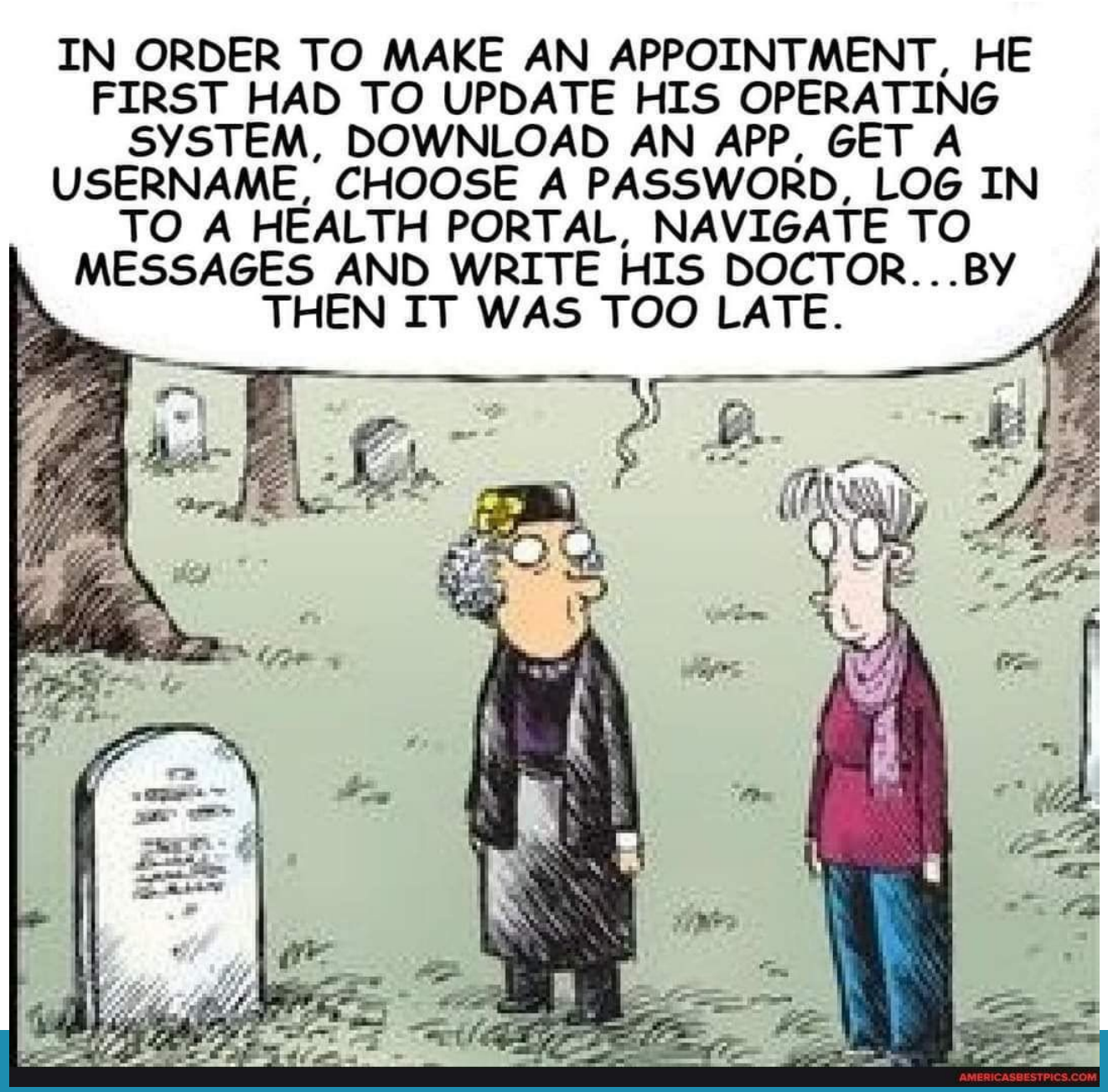


FIGURE 5. Digital twin evolution.

How can TwinHealth address these gaps?

- Start from the needs of patients and HCP's
- Gather the relevant information
- Interpret that information
- **Put it at the fingertips of patients and HCP's**
- **At the Point-of-Care**
- Help making the right decisions about preventio and follow-up
- Keep improving the system with the input from


IN ORDER TO MAKE AN APPOINTMENT, HE FIRST HAD TO UPDATE HIS OPERATING SYSTEM, DOWNLOAD AN APP, GET A USERNAME, CHOOSE A PASSWORD, LOG IN TO A HEALTH PORTAL, NAVIGATE TO MESSAGES AND WRITE HIS DOCTOR...BY THEN IT WAS TOO LATE.
AMERICASBESTPICS.COM

How can TwinHealth address these gaps?

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- Interpret that information
- Put it at the fingertips of patients and HCP's
- Help making the right decisions about prevention, diagnosis, treatment and follow-up
- Keep improvin

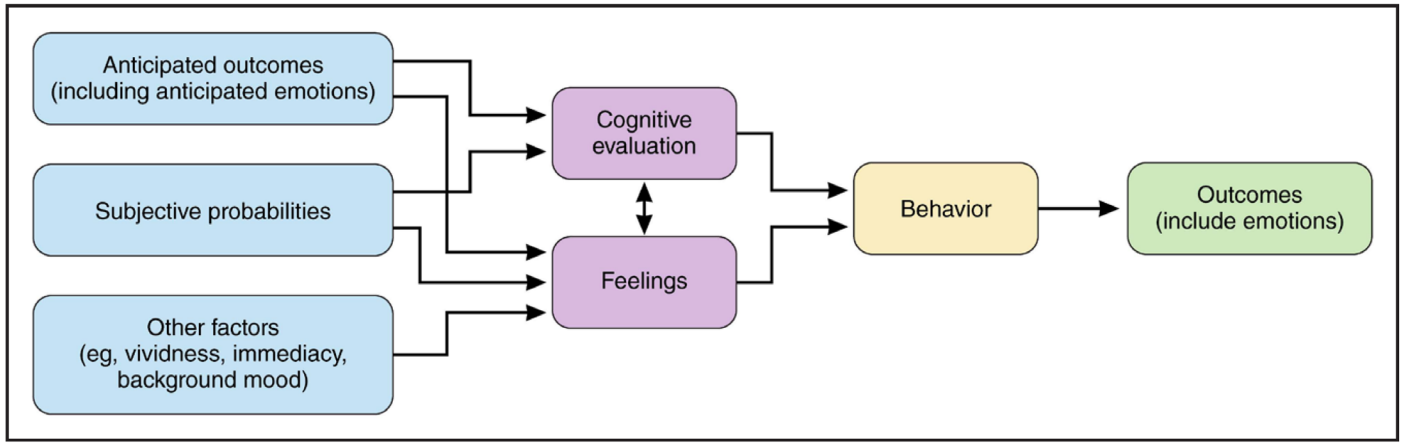


Figure 1. Cognitive/consequentialist vs risk-as-feelings perspectives.
Choice under risk and uncertainty are typically viewed through a cognitive and consequentialist framework. However, affect experienced at the moment of decision-making can diverge from cognitive assessments. When this happens in risky situations, emotion often drives behavior. Adapted with permission from Loewenstein et al.[24] Copyright © 2001 The American Psychological Association.

How can TwinHealth address these gaps?

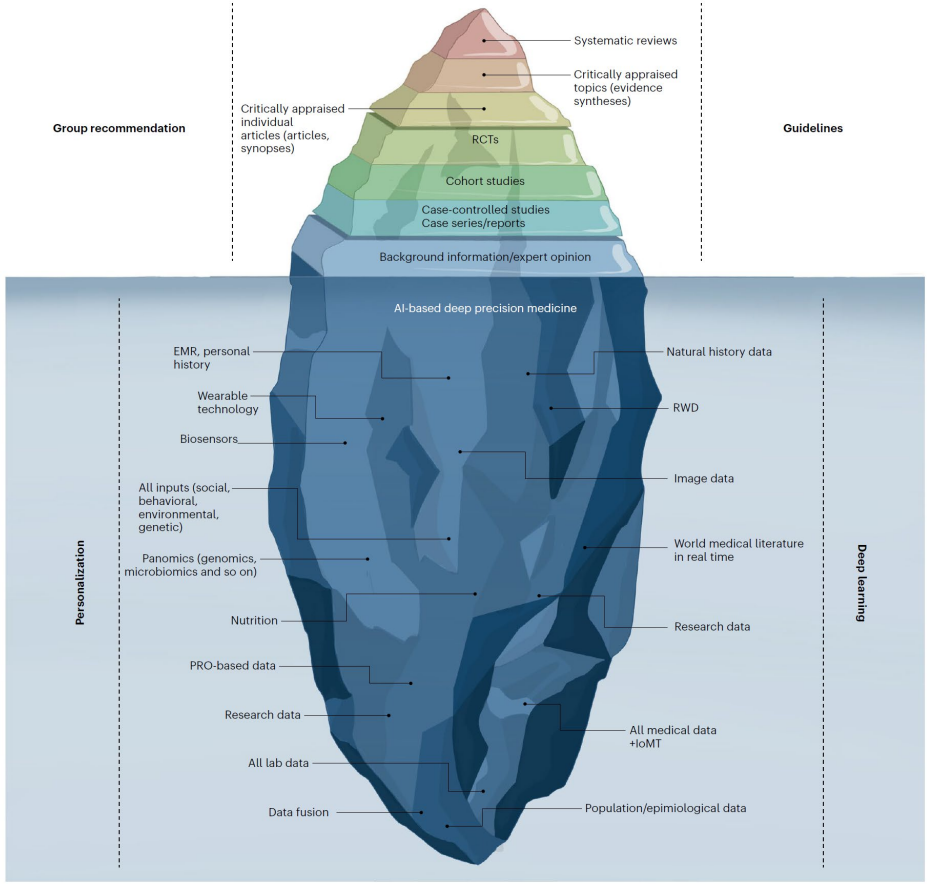
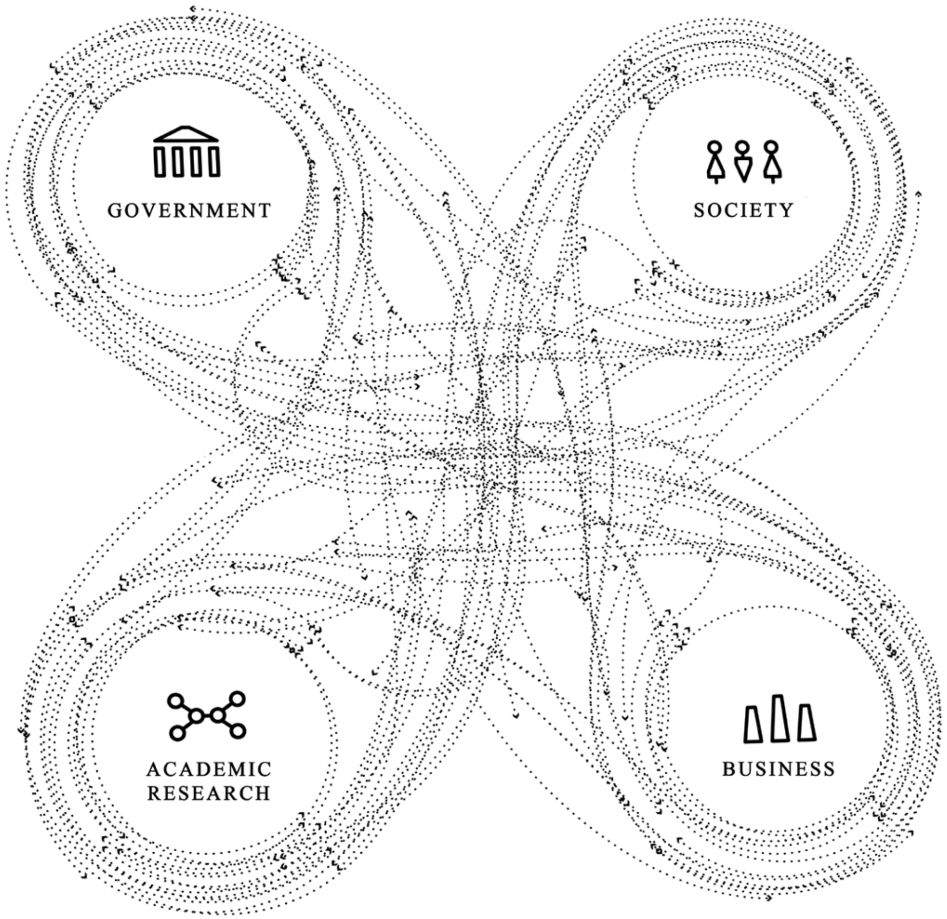


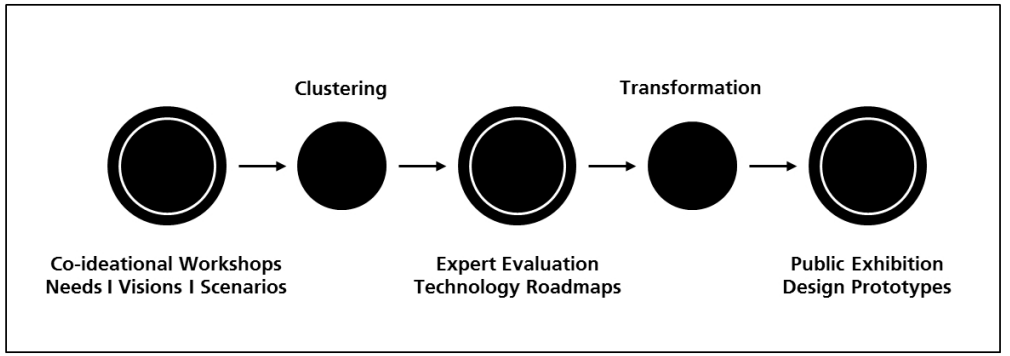
Fig. 4 | Evidence-based deep medicine iceberg.

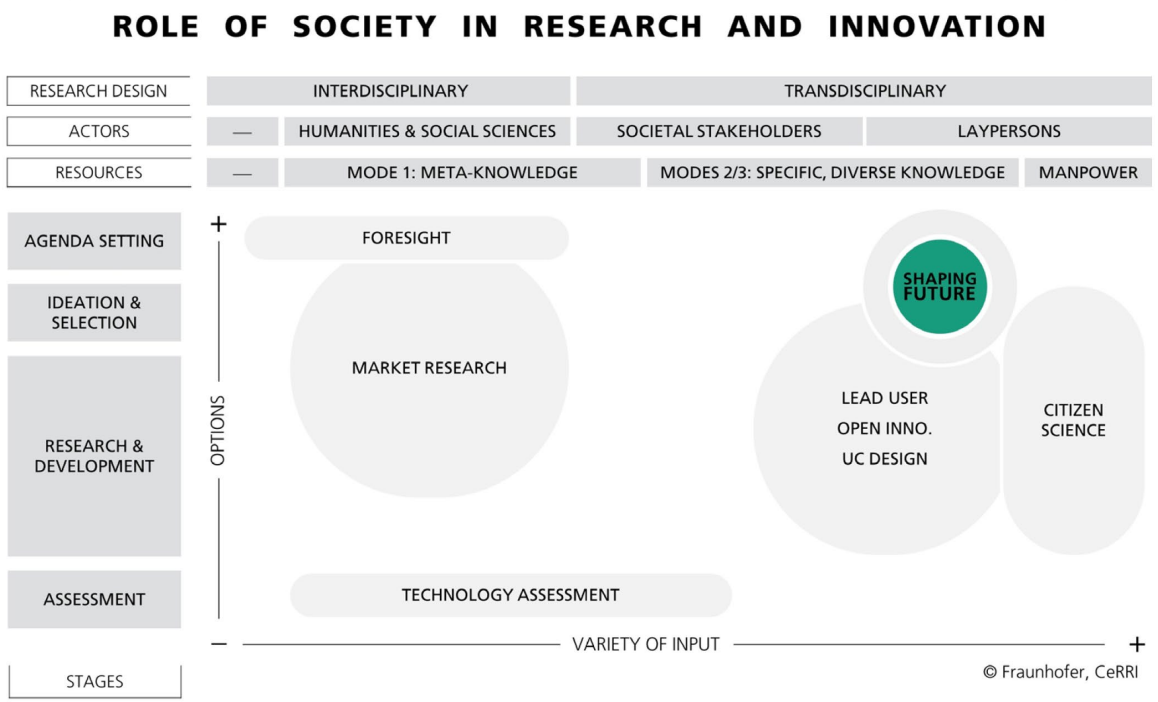
- Start from th
- Gather the
- Interpret tha
- Put it at the
- Help making ion, diagnosis, treatment and follow-u
- **Keep improving the system with the input from every interaction**

Co-shaping the Future in Quadruple Helix Innovation Systems: Uncovering Public Preferences toward Participatory Research and Innovation



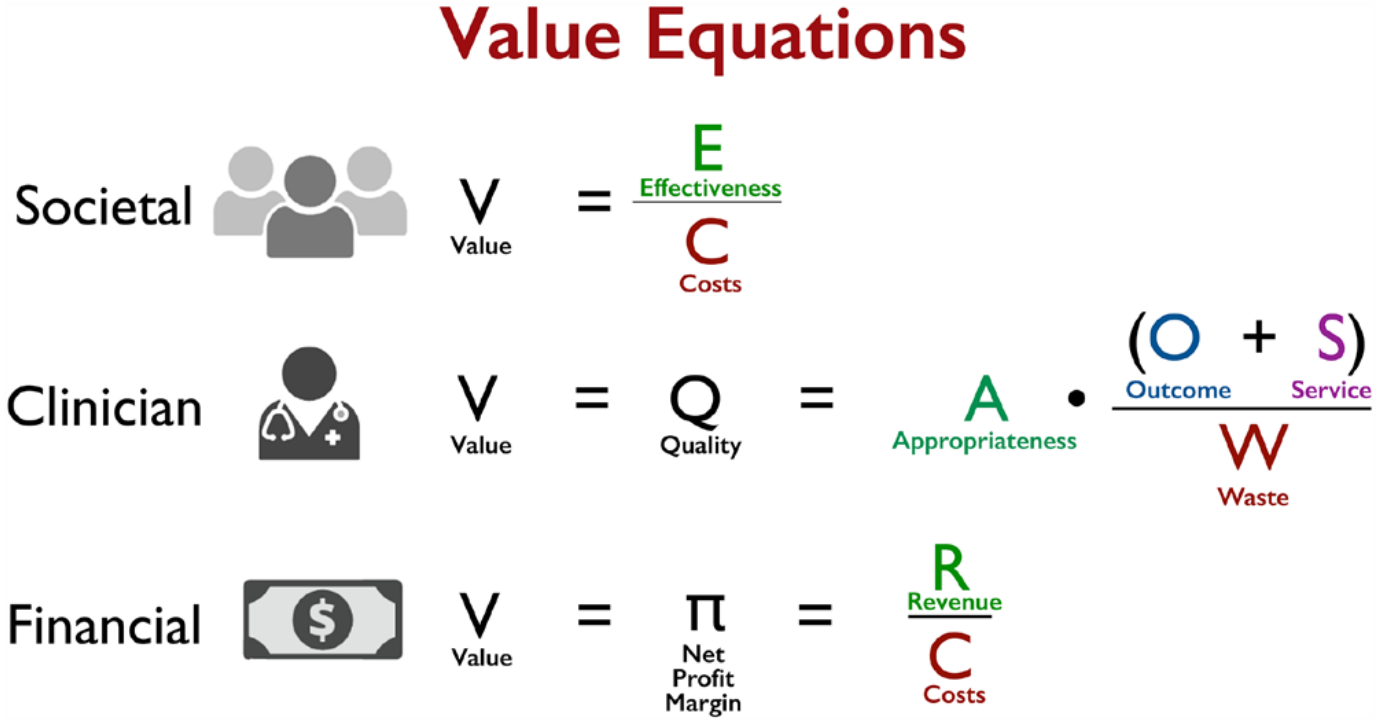
The Quadruple Helix Model adapted by Fraunhofer (2016), originally developed by Carayannis and Campbell (2009).





she ji The Journal of Design, Economics, and Innovation Volume 5, Number 2, Summer 2019.
doi.org/10.1016/j.sheji.2019.04.002

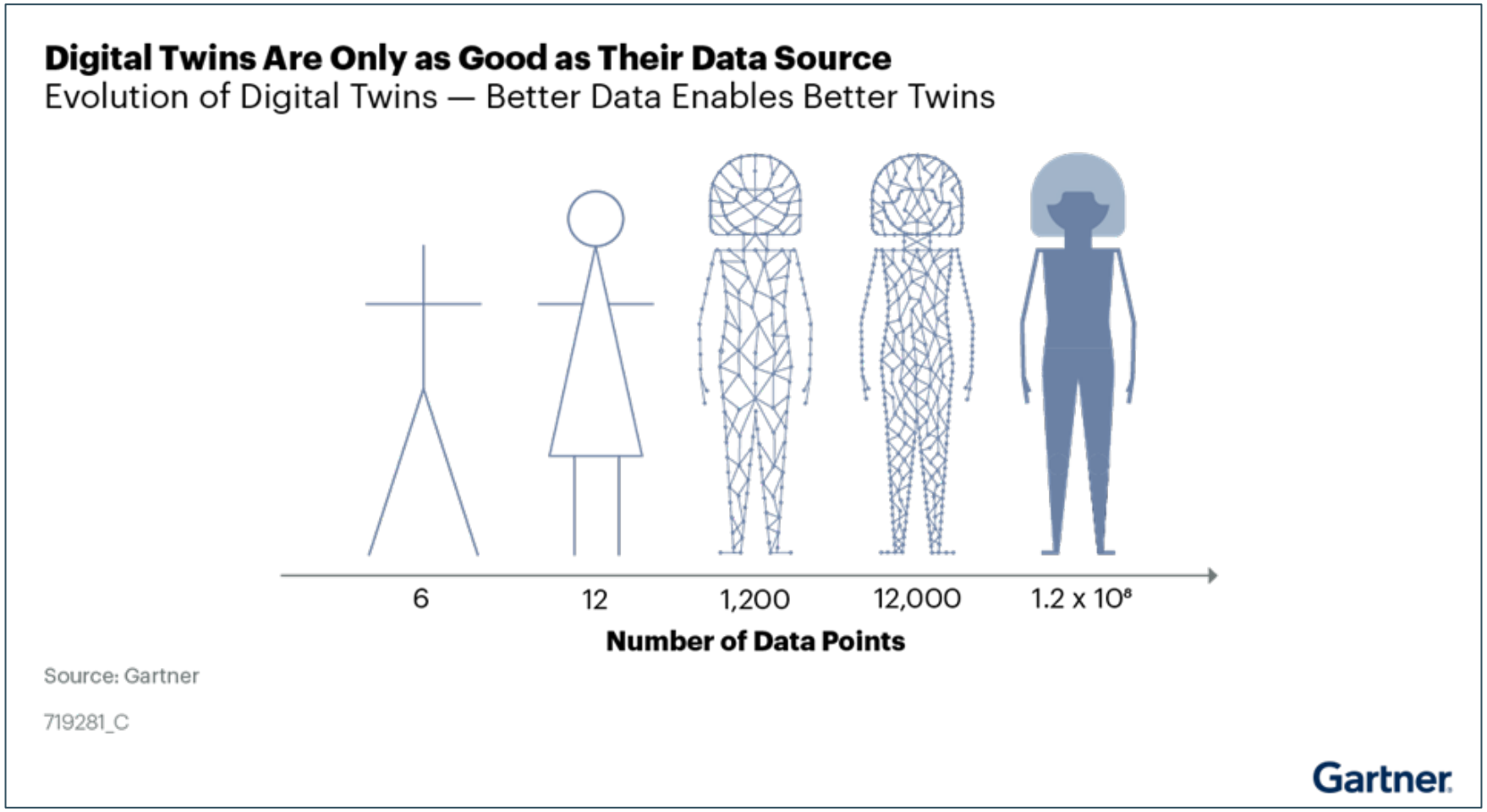
Value Creation Through Artificial Intelligence and Cardiovascular Imaging: A Scientific Statement From the American Heart Association



Deriving value: 3 widely referenced value equations representing (1) societal, (2) clinician, and (3) finance perspectives. The third expression of net profit margin is an explicit mathematical expression used in accounting; the first 2 expressions are conceptual. Understanding varying stakeholder perspectives for resource allocation to acquire, implement, and maintain artificial intelligence (AI) solutions is fundamental to selecting AI tools within a health care environment.

Circulation. 2024;149:e296–e311.
DOI: 10.1161/CIR.0000000000001202

Digital Twin data quality



The next generation of evidence-based medicine

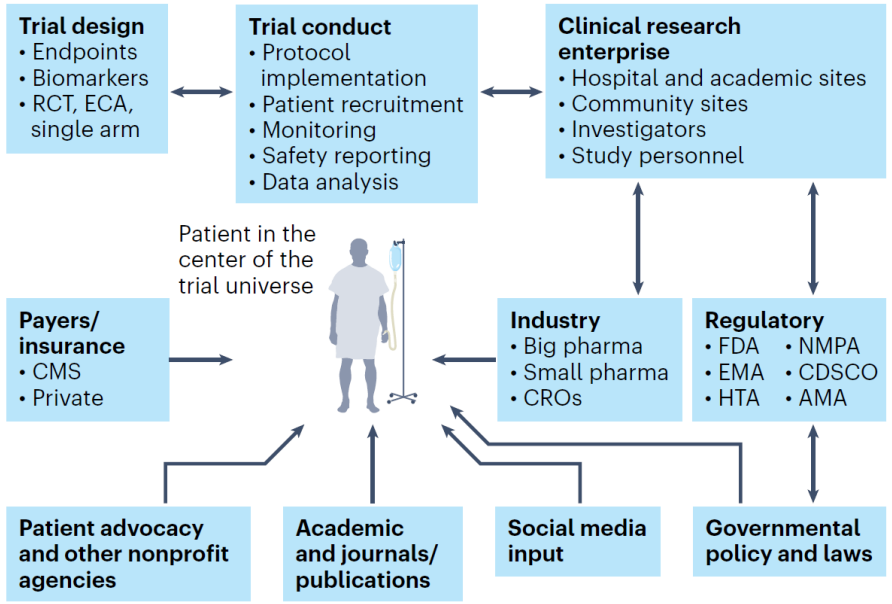
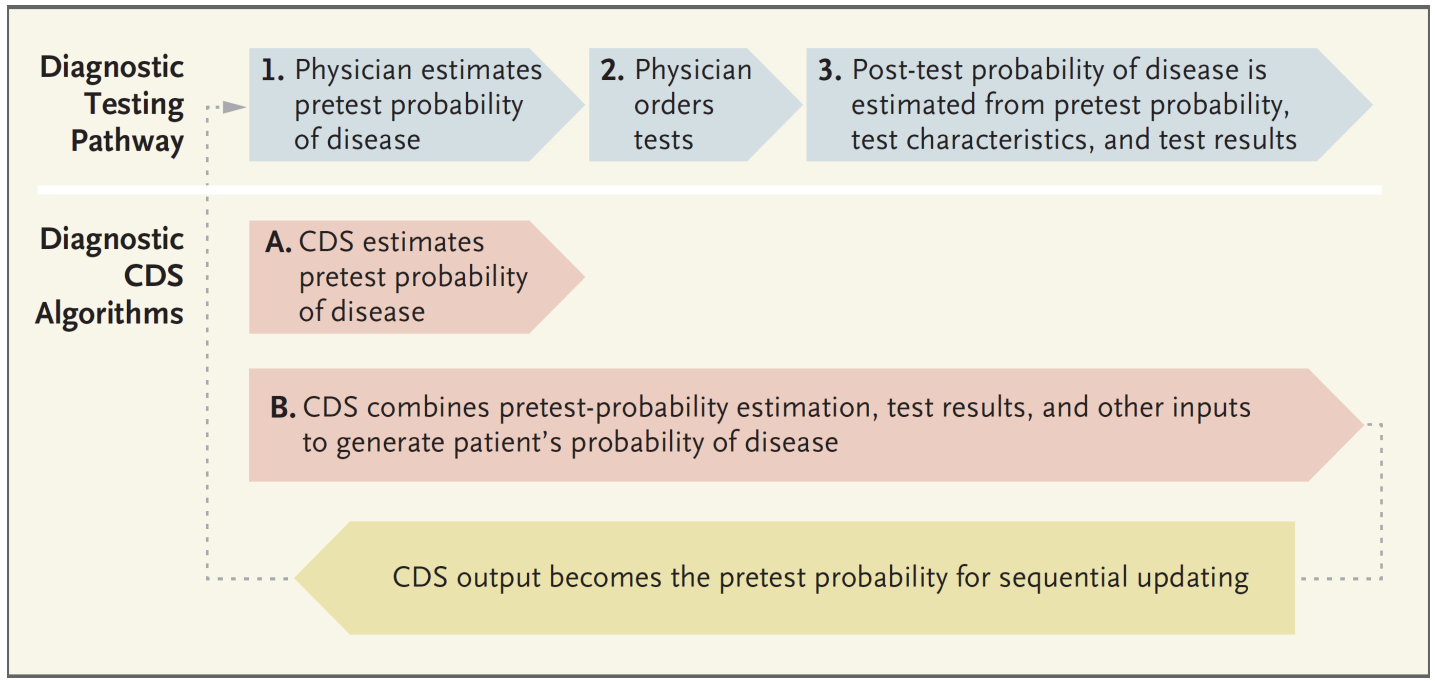


Fig. 3 | The patient as the center of the clinical trial universe in the clinical research enterprise. The main constituents of the clinical trial enterprise—patients, academic centers, industry sponsors (big and small pharma), government/cooperative group sponsors, regulatory agencies, patient advocacy organizations and CROs—need to work together, with the patient as the center of this clinical trial universe. AMA, African Medicines Agency; CDSCO, Central Drugs Standard Control Organization (India); CMS, Centers for Medicare and Medicaid Services; ECA, external control arm; EMA, European Medicines Agency; HTA, Health Technology Assessment; NMPA, National Medical Products Administration (China).

Nature Medicine | Volume 29 | January 2023 | 49–58.
doi.org/10.1038/s41591-022-02160-z

Preparing Physicians for the Clinical Algorithm Era



Diagnostic Testing Pathway and CDS Algorithms.
Diagnosis requires Bayesian reasoning, which involves estimating the patient's pretest probability of disease, ordering diagnostic tests, and estimating the post-test probability of disease on the basis of the pretest probability, test performance characteristics, and test results. Example A describes diagnostic clinical decision support (CDS) algorithms that operate only at the first step of this process to estimate the pretest probability of disease and guide diagnostic testing decisions (e.g., Wells' criteria for pulmonary embolism), whereas example B describes diagnostic CDS algorithms that operate at all three steps, combining pretest-probability estimation and some test results to estimate a patient's probability of disease (e.g., sepsis warning systems). The latter algorithms generally "fire" in the electronic medical record without intentional engagement from the physician and guide treatment decisions or subsequent testing.

Recommended Changes to Medical Education and Training to Improve Probabilistic Reasoning and Support Effective Use of CDS Algorithms.*

Recommendation	Approaches to Implementation
Preclinical medical education	
Teach probability in medical school using intuitive, modern approaches	• Create new curricula or access online curricula that use natural frequency trees and icon arrays to visualize probability of disease and to convey the concept that probability is fundamental to clinical medicine. • Integrate instruction in probability and probabilistic reasoning throughout medical school curricula, beyond diagnosis courses.
Teach probabilistic clinical reasoning	• Emphasize practical examples of probabilistic reasoning in both CDS use and traditional evidence-based diagnosis. • Encourage the use of gamified training for honing probabilistic reasoning skills.
Assess probability and probabilistic reasoning skills	• Include clinically relevant questions of probabilistic interpretation of CDS on USMLE board and shelf exams (instead of questions on definitions).
Teach core, foundational working knowledge of CDS and EHR implementation, relevant to clinical use	• Integrate the basics of machine learning into the curriculum, including discussions about biases and equity. • Make explicit the human–technology interaction that often determines whether a CDS is adopted. • Discuss principles of user-centered design of CDS that affect whether an algorithm is accepted and how it is used. • Provide a simplified overview of how CDS works in the clinical EHR.
Practice interpreting CDS output in applied learning	• Develop and use CDS-specific problem-based learning scenarios that emphasize core concepts: — Applying CDS algorithms to individual patients. — Examining how different inputs affect prediction. — Discussing potential sources of bias in algorithms. — Interpreting basic model performance concepts. — Communicating with patients about CDS-guided decision making.
Clinical training	
Reinforce probabilistic training and application	• Provide resources for incorporating probability into case discussions.
Build CDS interpretation into curricula	• Develop longitudinal curricula on the variety and use of CDS.
Reinforce working knowledge of CDS and EHR implementation, relevant to clinical use	• Incorporate basic algorithmic CDS principles (e.g., accuracy and bias) into clinical discussions and real-world case studies to elucidate how CDS accuracy or bias may affect clinical decision making. • Incorporate technical CDS knowledge and assessments (e.g., how CDS operates in the EHR and where to find more information regarding CDS alerts) into clinical orientations for new physicians.
Include working knowledge of CDS in ACGME core competencies	• The ACGME requires evidence-based medicine–related skills as part of its core competency in practice-based learning and improvement; these should be updated to explicitly include CDS interpretation.

n engl j med 389;6.
DOI: 10.1056/NEJMp2304839

Thank you for your attention