

Medical Digital Twins

Opportunities and Hurdles

Webinar, April 16th 2020

Frank E. Rademakers

Emeritus professor Medicine

Agenda

- Some concepts
- Opportunities
- Hurdles
- Regulatory environment
- Conclusion

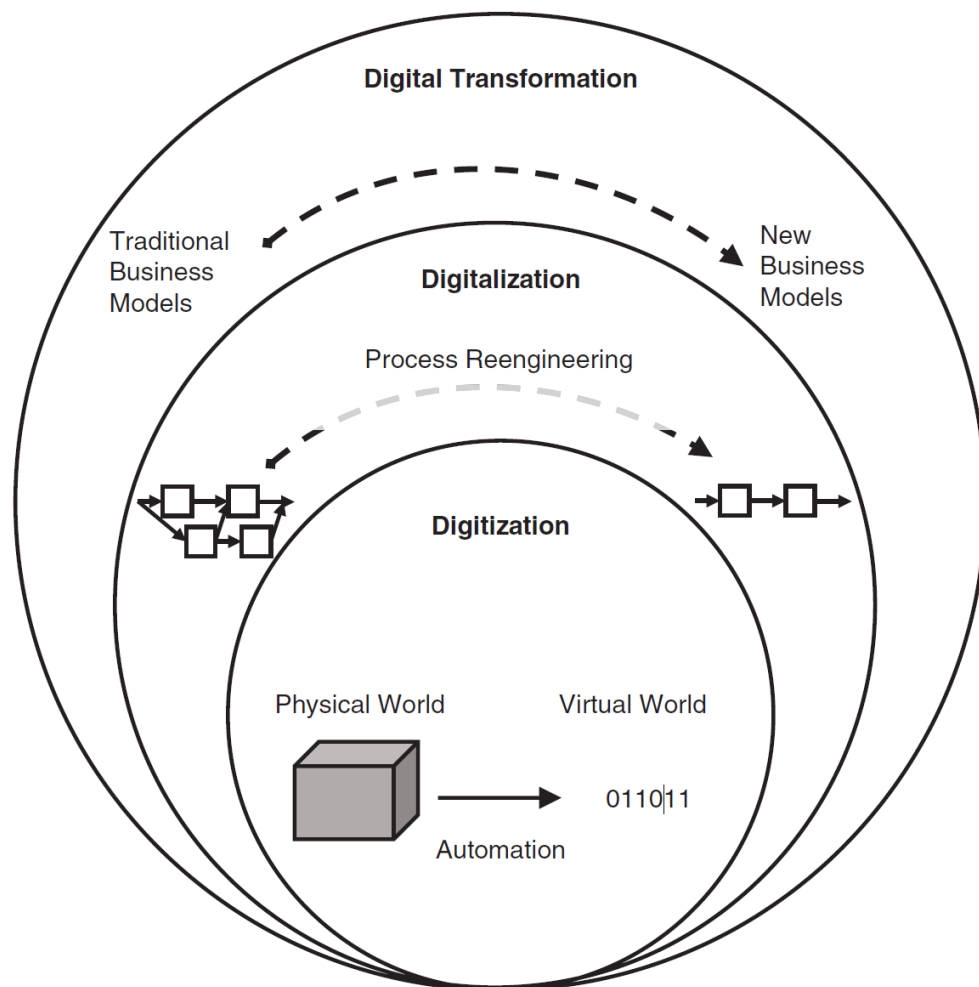


FIGURE 1. The three steps toward Digital Transformation.

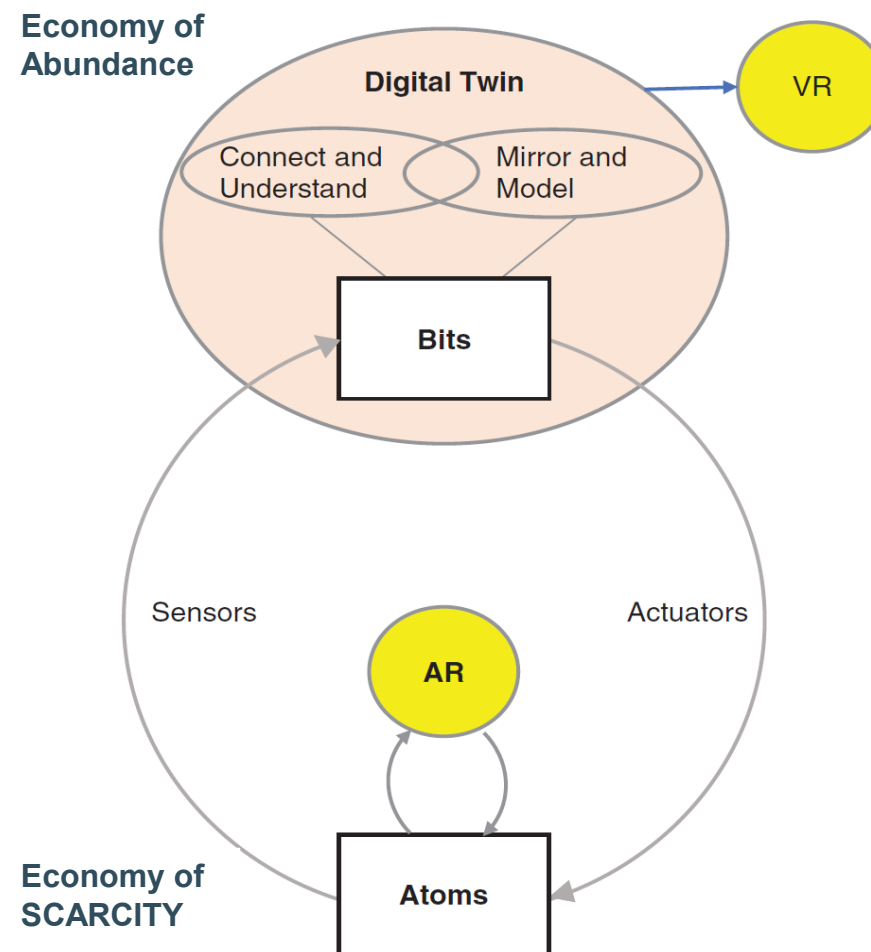


FIGURE 2. The underpinning of the Digital Transformation.

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

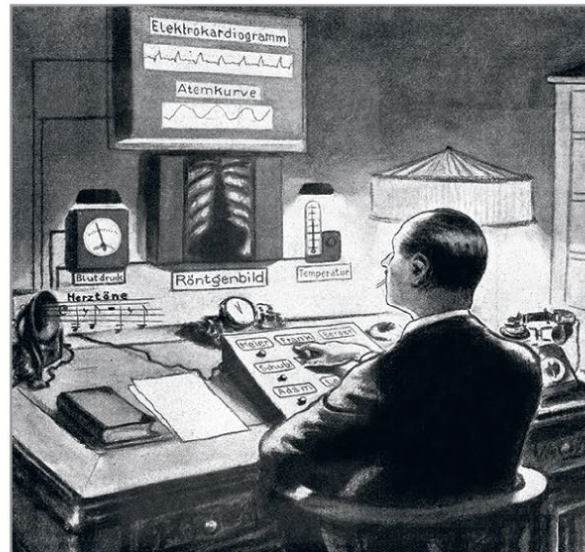
From: Fritz Kahn and the Centenary of The Doctor of the Future

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

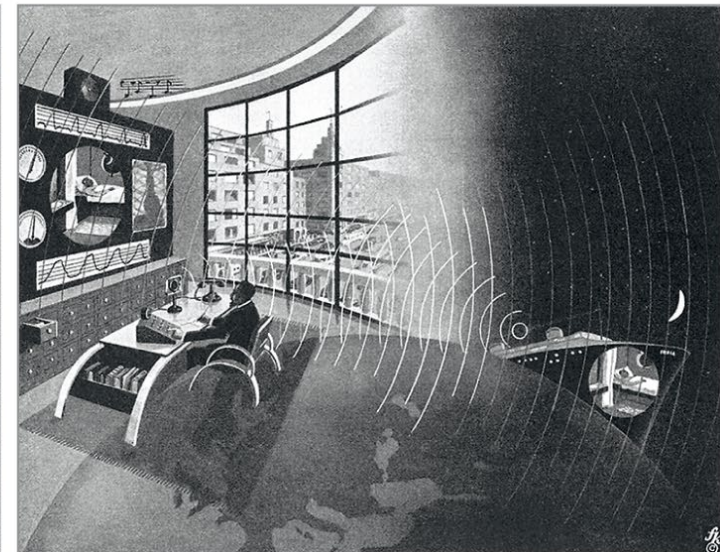
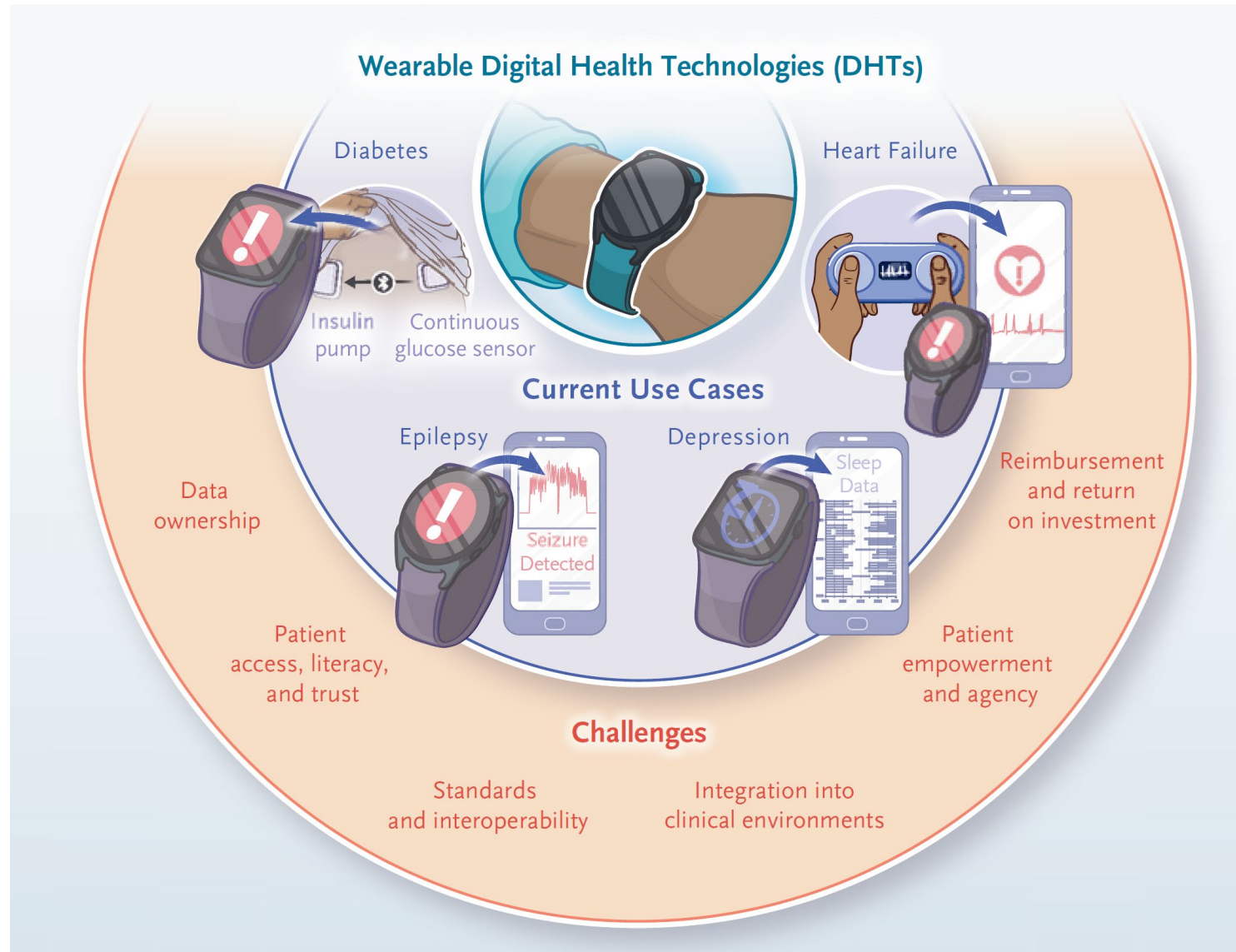


Figure Legend:

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



N Engl J Med 2024;390:1118-27.
DOI: 10.1056/NEJMr2307160

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

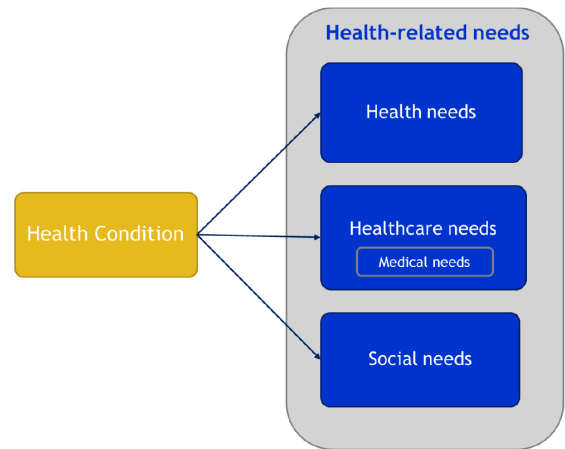
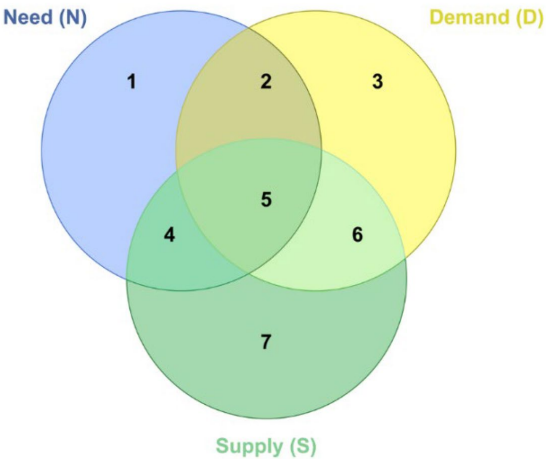


Figure 5 – Relation between perceived, unperceived, and clinically-validated need



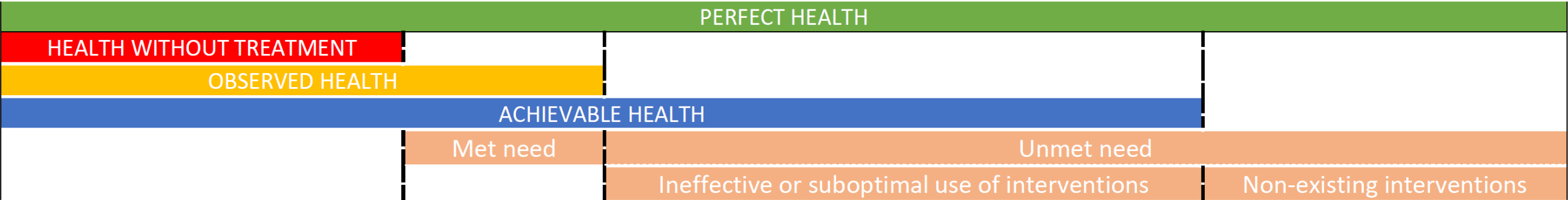
Source: KCE, inspired by Allin et al. (2010) ³⁹

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



Source: Santana et al. (2023) ⁴⁰

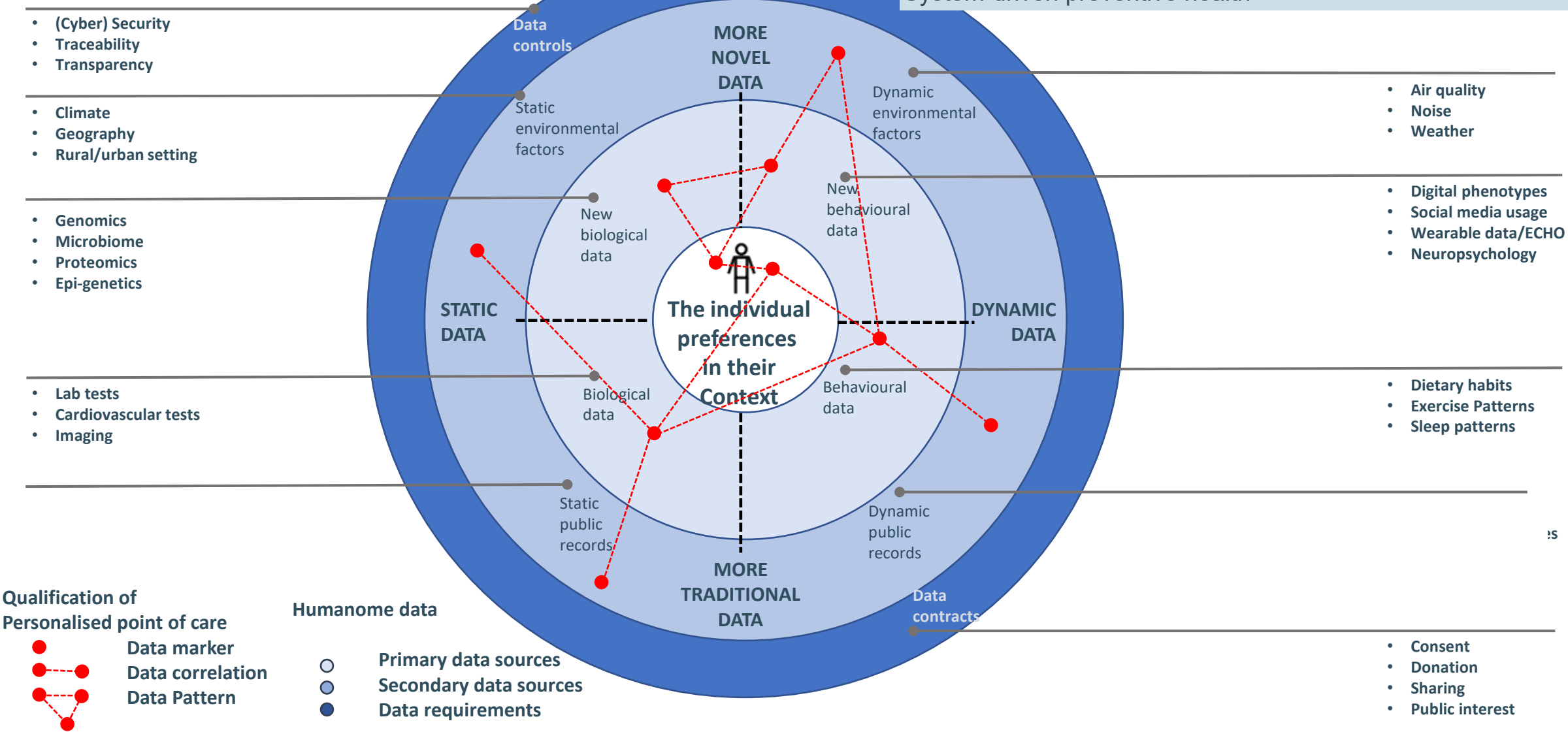
Figure 7 – Identifying unmet need using an adaptation of Incerti et al.’s approach



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.

THE HUMANOME – A PERSONALISED POINT OF CARE DATA CONCEPT

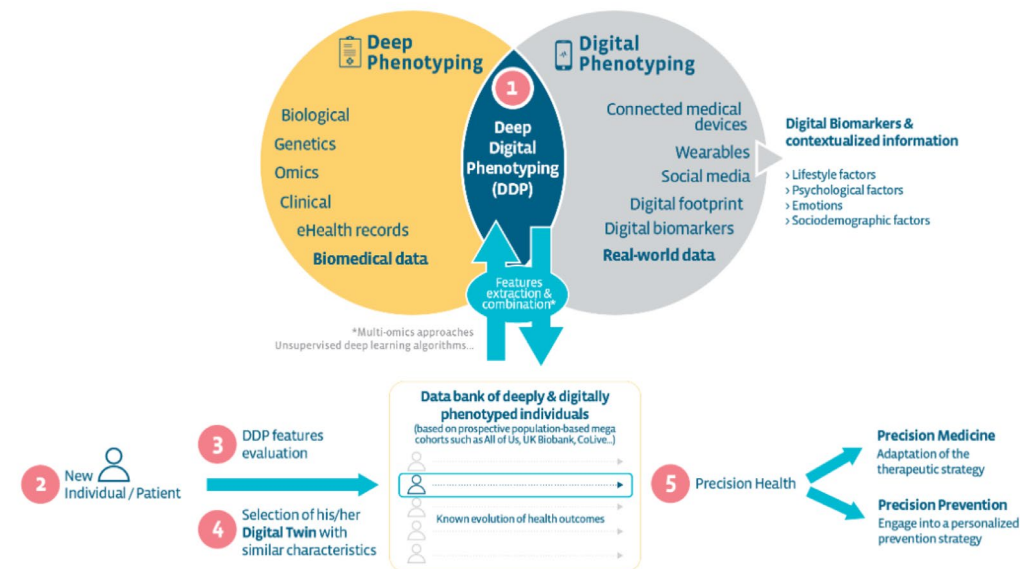
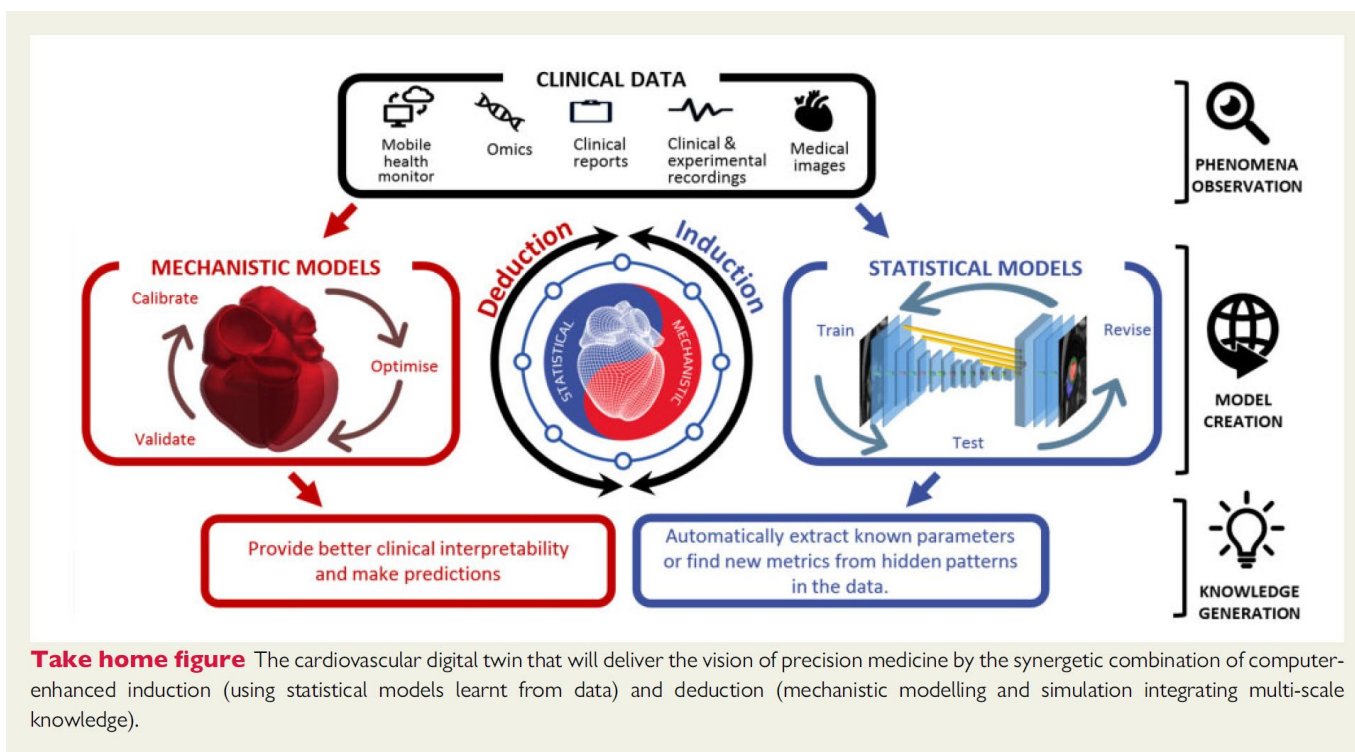
Individual-driven preventive health
Individual-driven preventive health, motivating the system
System-driven preventive health, motivating the individual
System-driven preventive health



Ocean of data, desert of interpretation and use



MDT based on statistical and mechanistic modeling



[doi:10.1093/eurheartj/ehaa159](https://doi.org/10.1093/eurheartj/ehaa159)

From Data to Wisdom and Impact

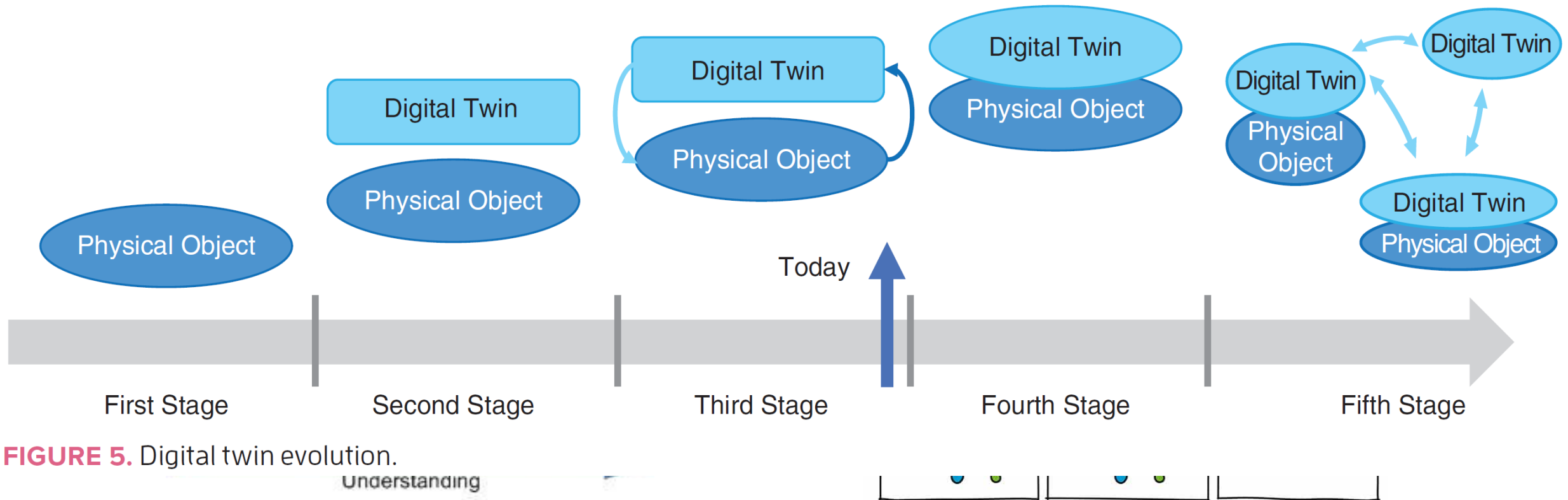
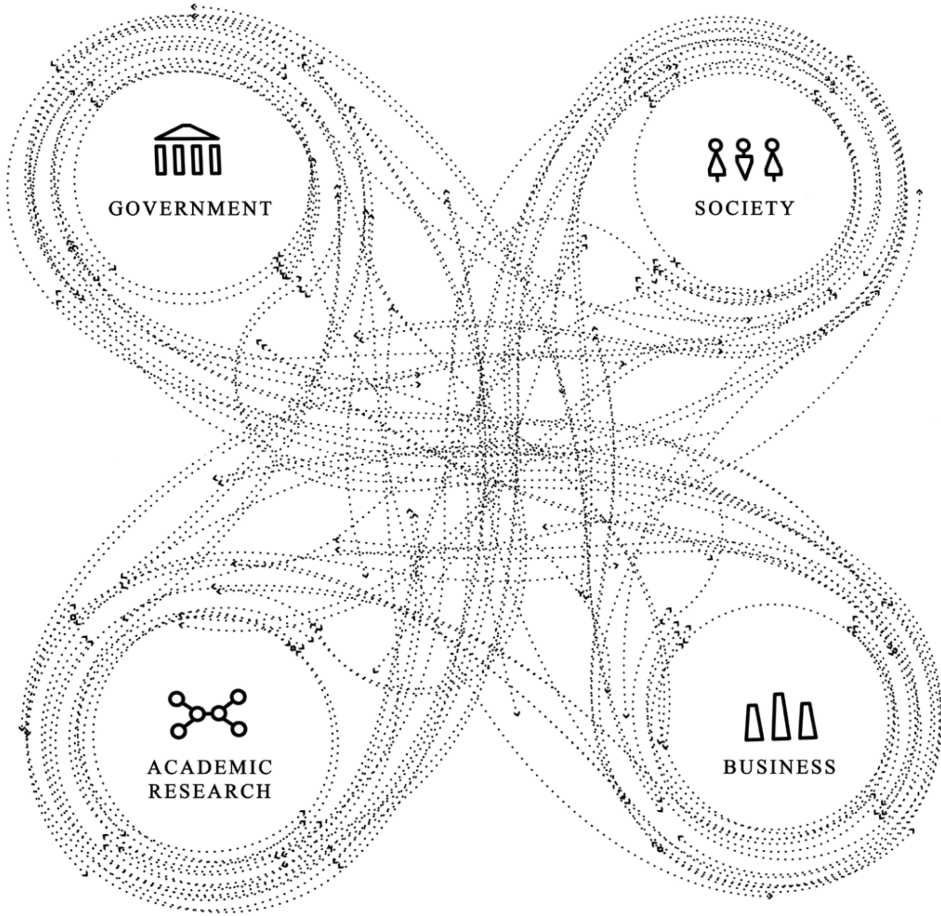
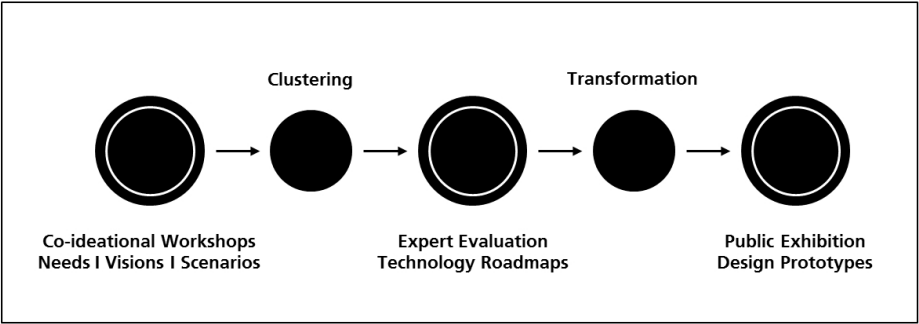


FIGURE 5. Digital twin evolution.

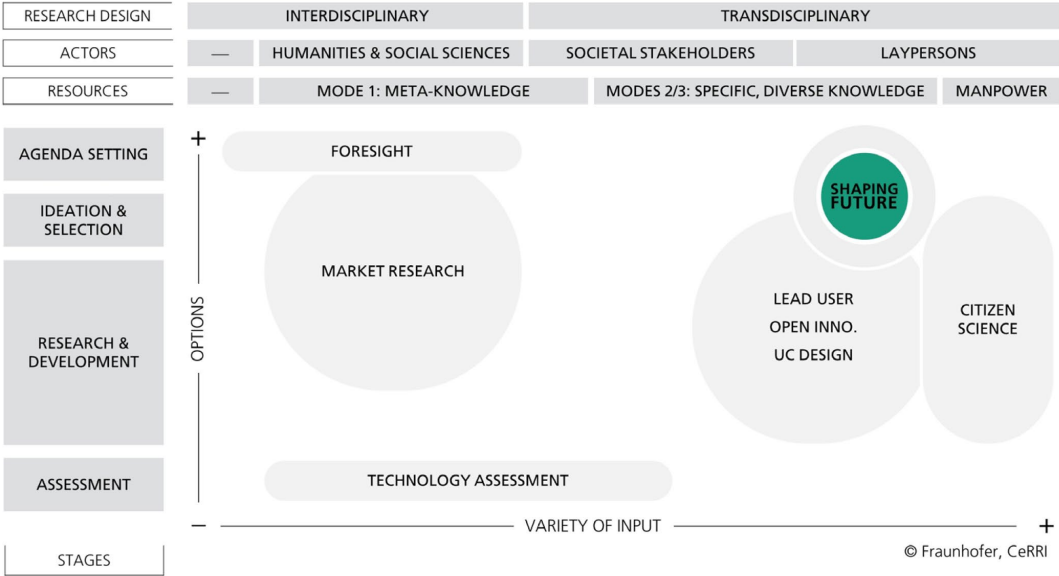
Co-shaping the Future in Quadruple Helix Innovation Systems: Uncovering Public Preferences toward Participatory Research and Innovation



The Quadruple Helix Model adapted by Fraunhofer (2016), originally developed by Carayannis and Campbell (2009). Copyright © 2015 Fraunhofer.



ROLE OF SOCIETY IN RESEARCH AND INNOVATION



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

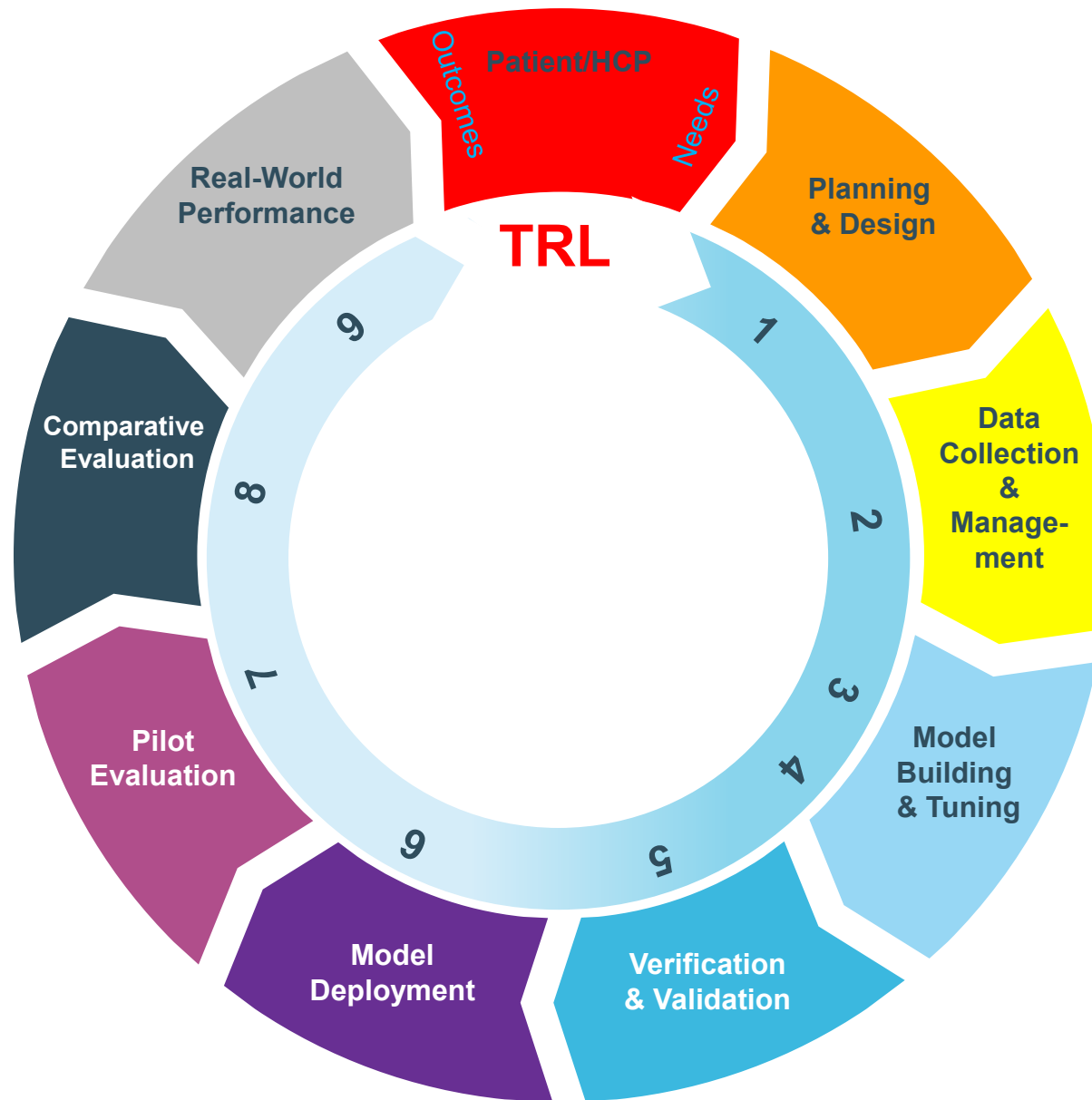
Value Creation Through Artificial Intelligence

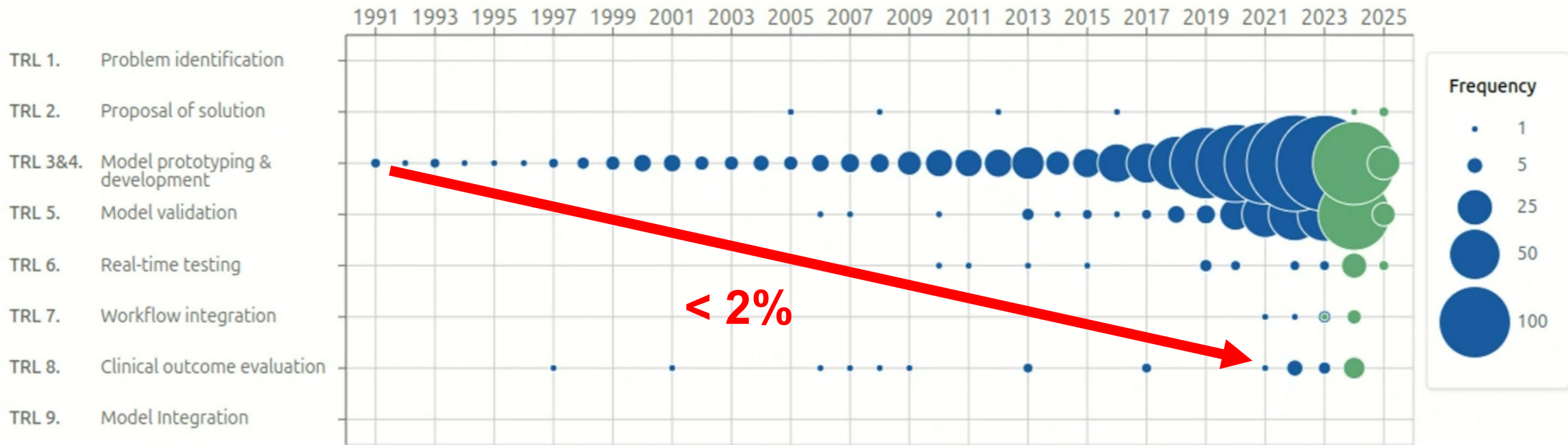
Value Equations

$$\begin{array}{lcl} \text{Societal} & \begin{array}{c} \text{Icon of three people} \\ \text{Value} \end{array} & V = \frac{E}{C} \\ & & \begin{array}{c} E \\ \text{Effectiveness} \\ C \\ \text{Costs} \end{array} \\ \\ \text{Clinician} & \begin{array}{c} \text{Icon of a doctor} \\ \text{Value} \end{array} & V = Q = \frac{A \cdot (O + S)}{W} \\ & & \begin{array}{c} Q \\ \text{Quality} \\ A \\ \text{Appropriateness} \\ O \\ \text{Outcome} \\ S \\ \text{Service} \\ W \\ \text{Waste} \end{array} \\ \\ \text{Financial} & \begin{array}{c} \text{Icon of a dollar bill} \\ \text{Value} \end{array} & V = \pi = \frac{R}{C} \\ & & \begin{array}{c} \pi \\ \text{Net Profit Margin} \\ R \\ \text{Revenue} \\ C \\ \text{Costs} \end{array} \end{array}$$

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



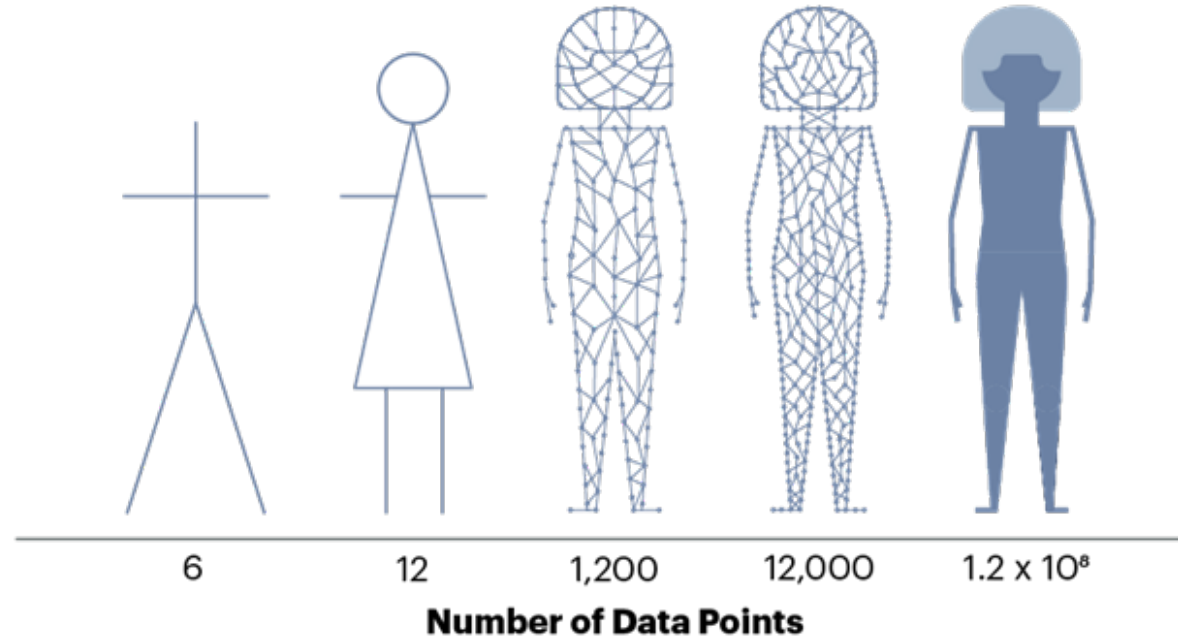


Number of studies published according to their level of readiness and year of publication

Digital Twin data quality

Digital Twins Are Only as Good as Their Data Source

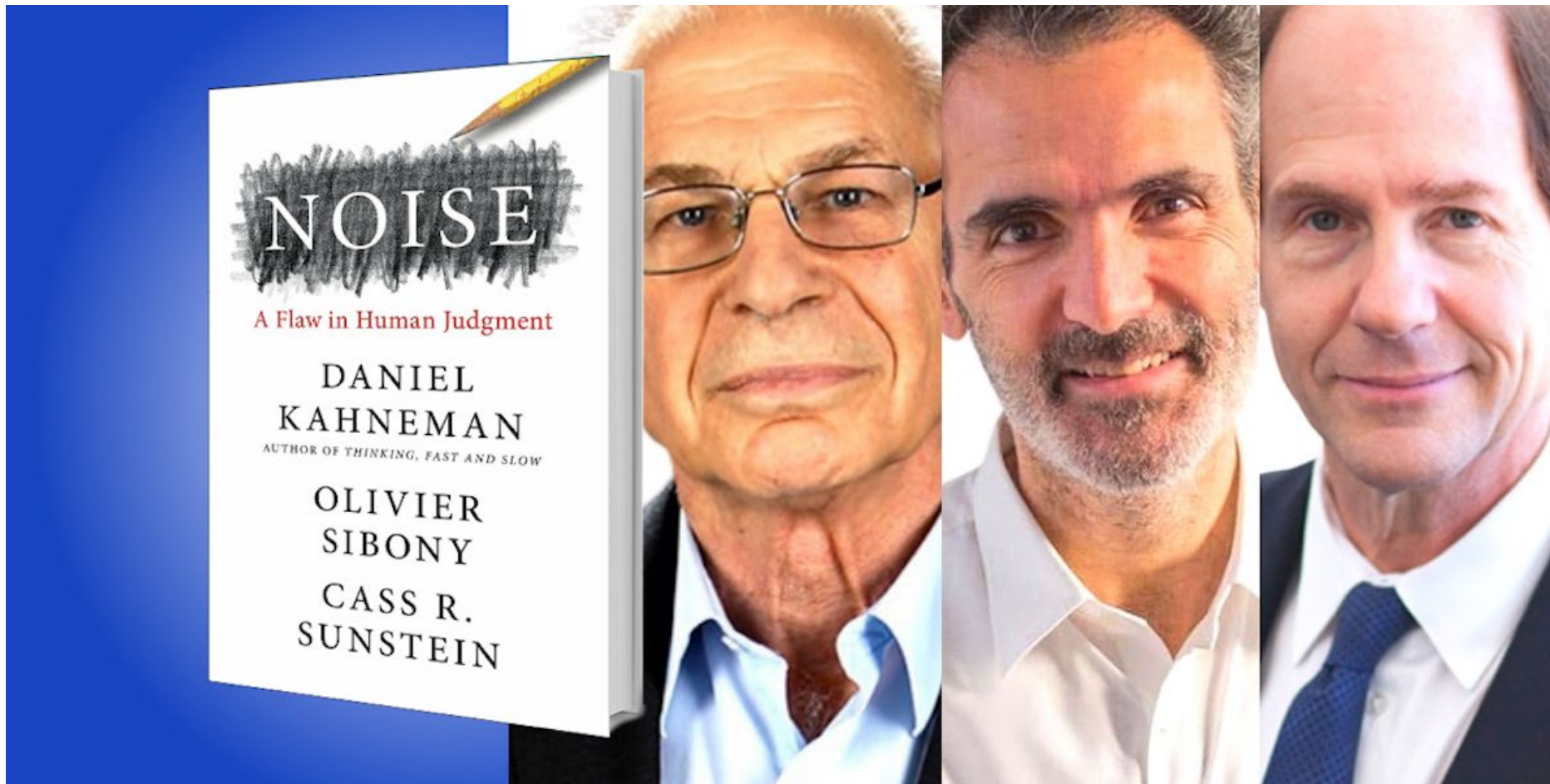
Evolution of Digital Twins — Better Data Enables Better Twins



Source: Gartner

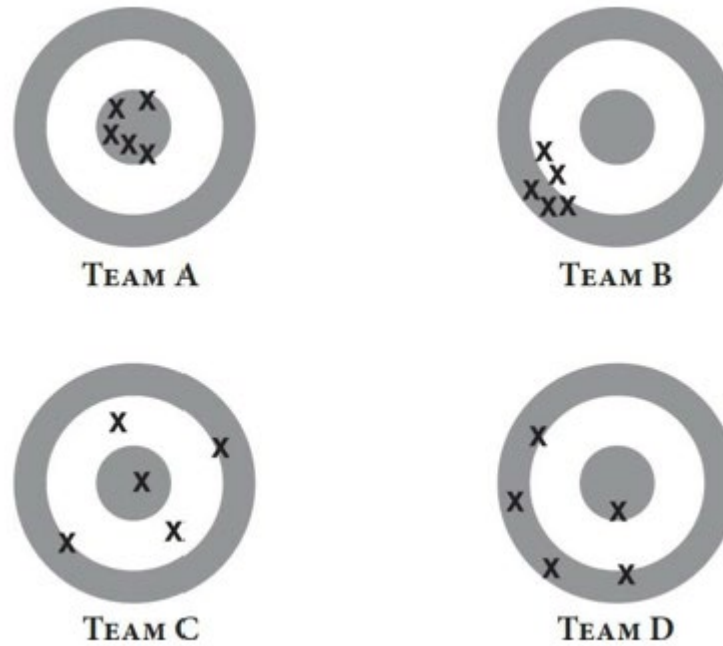
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Gartner.

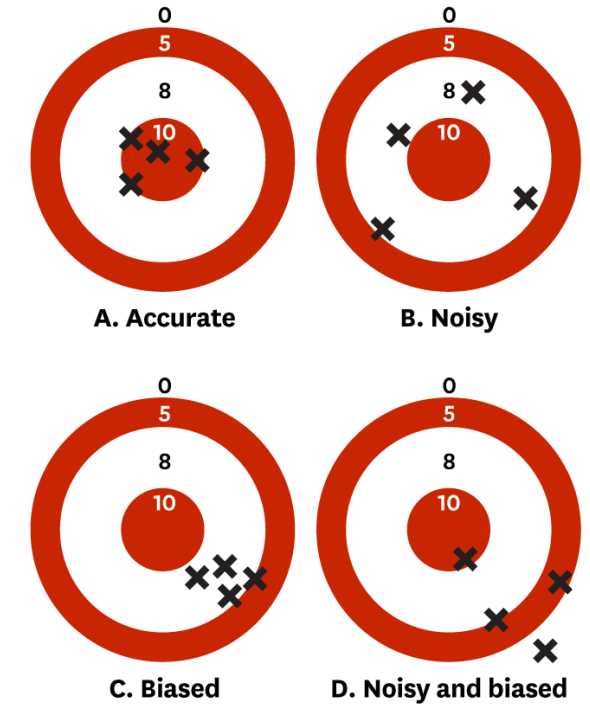


Man is a Deterministic Device thrown into a Probabilistic Universe.

Amos Tversky



How Noise and Bias Affect Accuracy



SOURCE DANIEL KAHNEMAN,
ANDREW M. ROSENFELD,
LINNEA GANDHI, AND TOM BLASER
FROM "NOISE," OCTOBER 2016

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$$\text{Overall Error (MSE)} = \text{Bias}^2 + \text{Noise}^2$$

Risk–benefit assessment: factors to consider

1. Medical purpose
2. The intended medical conditions
3. The intended population
4. The AI tool's operation
 1. Inputs: data
 2. Algorithm
 3. Outputs
 4. Presentation of results
 5. Integration in workflow
 6. Outcomes impacted by AI tool
5. The intended user in their respective environment and scope
6. The potential for shift/drift ('off-label use')

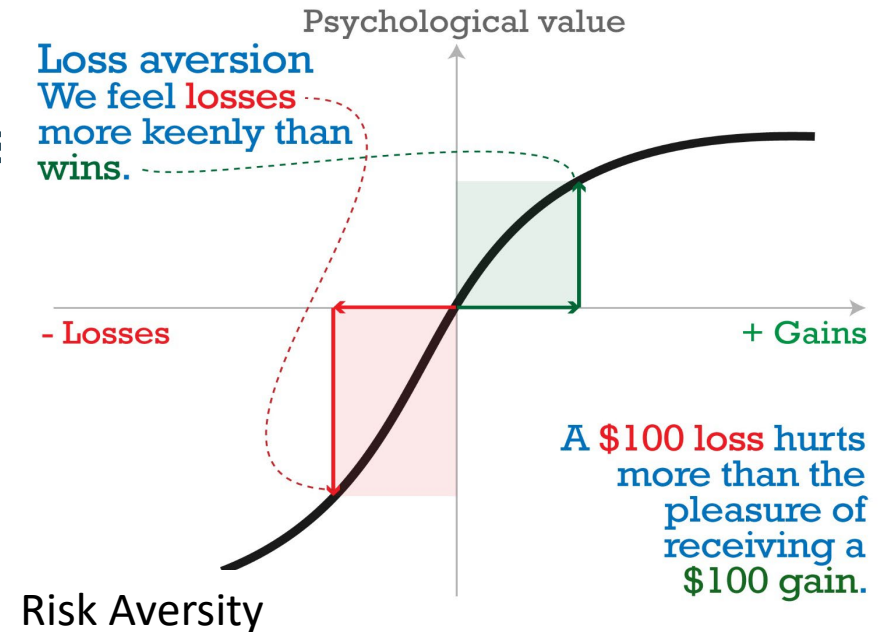


Table 1: Overview of EU Legislations in the Digital Sector

Research & Innovation	Industrial Policy	Connectivity	Data & Privacy	IPR	Cybersecurity	Law Enforcement	Trust & Safety	E-commerce & Consumer Protection	Competition	Media	Finance
Digital Europe Programme Regulation, (EU 2021/1594)	Recovery and Resilience Facility Regulation, (EU 2021/241)	Frequency Bands Directive, (EU 2019/172)	ePrivacy Directive, (EU 2002/95), (EU 2009/136)	Database Directive, (EC 1996/9)	Regulation for a Cybersecurity Act, (EU 2019/881), (2023/0108C.OO)	Law Enforcement Directive, (EU 2019/890)	Product Liability Directive (PLD), (EC 1985/274), (2023/0302C.OO)	Unfair Contract Terms Directive (UCTD), (EC 1993/13)	EC Merger regulation, (EC 2004/139)	Satellite and Cable Directive, (EC 1993/93)	Common VAT system, (EC 2006/112), (2023/0912C.OO)
Horizon Europe Regulation, (EU 2021/695), (EU 2021/784)	InvestEU Programme Regulation, (EU 2021/623)	Radio Spectrum Directive, (EU 2002/97)	European Statistics, (2023/0237C.OO)	Community Design Directive, (EC 2009/25), (2022/0531C.OO)	Regulation to establish a European Cybersecurity Competence Centre, (EU 2021/687)	Directive on combating fraud and counterfeiting of non-cash means of payment, (EU 2019/713)	Toys Regulation, (EC 2009/18), (2023/0290C.OO)	Price Indication Directive, (EC 1999/6)	Technology Transfer Block Exemption Regulation, (EU 2014/916)	Information Society Directive, (EC 2001/29)	Administrative cooperation in the field of taxation, (EU 2011/116)
Regulation on a pilot regime for distributed ledger technology, (EU 2022/698)	Connecting Europe Facility Regulation, (EU 2021/1153)	Open Internet Access Regulation, (EU 2015/2120)	General Data Protection Regulation (GDPR), (EU 2016/679)	Enforcement Directive (IPR), (EC 2004/48)	NIS 2 Directive, (EU 2022/2555)	Regulation on interoperability between EU information systems in the field of borders and visa, (EU 2019/817)	European Standardization Regulation, (EU 2017/1025)	E-commerce Directive, (EC 2000/31)	Company Law Directive, (EU 2017/1132), (2023/0089C.OO)	Audio-visual Media Services Directive (AVMSD), (EU 2010/13)	Payment Service Directive 2 (PSD2), (EU 2015/2366), (2023/0290C.OO)
Regulation on High Performance Computing Joint Undertakings, (EU 2021/1173), (2024/0011C.OO)	European Electronic Communications Code Directive (EECC), (EU 2018/1972)	Regulation on the free flow of non-personal data, (EU 2019/1302)	Directive on the protection of personal data processed by EU institutions, bodies, offices and agencies, (EU 2018/1725)	Directive on the protection of trade secrets, (EU 2019/643)	Cybersecurity Regulation, (EU 2019/281)	Regulation on terrorist content online, (EU 2017/186)	Radio Equipment Directive (RED), (EU 2014/53)	Unfair Commercial Practices Directive (UCPD), (EC 2005/29)	Market Surveillance Regulation, (EU 2017/1020)	Portability Regulation, (EU 2017/1128)	Digital Operational Resilience Act (DORA Regulation), (EU 2022/2554)
Regulation on Joint Undertakings under Horizon Europe, (EU 2021/2088), (2022/0030C.OO)	Regulation on top-level domain Regulations, (EU 2019/517)	Open Data Directive (PSD), (EU 2019/1024)	Regulation on the free flow of non-personal data, (EU 2019/1302)	Design Directive, (2022/0048C.OO)	Information Security Regulation, (EU 2017/1232), (2022/0150C.OO)	Temporary CSAM Regulation, (EU 2021/1232), (2022/0150C.OO)	eIDAS Regulation (European Digital Identity Framework), (EU 2014/910)	Directive on Consumer Rights (CRD), (EU 2011/83)	PSR Regulation, (EU 2019/1150)	Satellite and Cable II Directive, (EU 2019/789)	Crypto-assets Regulation (MCA), (EU 2023/1114)
Decision on a path to the Digital Decade, (EU 2022/2481)	Roaming Regulation, (EU 2022/612)										
European Chips Act (Regulation), (EU 2023/1781)	Union Secure Connectivity Programme, (EU 2023/598)										
Establishing the Strategic Technologies for Europe Platform (STEP), (EU 2024/799)	Global Infrastructure for Europe Platform Act, (EU 2024/1309)	European Data Act (Regulation), (EU 2024/2854)	Standard essential patents, (2023/01338C.OO)	Cyber Solidarity Act (Regulation), (2023/01098C.OO)	Digitalisation of cross-border judicial cooperation, (EU 2023/2844)	General Product Safety Regulation, (EU 2023/988)	Regulation on cooperation for the enforcement of consumer protection laws, (EU 2017/2394)	Vertical Block Exemption Regulation (VBER), (EU 2022/720)	European Media Freedom Act, (EU 2024/1083)	Copyright Directive, (EU 2019/790)	Financial Data Access Regulation, (2023/0205C.OO)
European critical raw materials act (Regulation), (EU 2024/1292)	New radio spectrum policy programme (RSPP), (EU 2024/1292)										
Net Zero Industry Act, (2023/0081C.OO)	Digital Networks Act										
EU Space Law	European Health Data Space (Regulation), (2022/0140C.OO)	Interoperable Europe Act, (EU 2019/1000)	Directive on combating violence against women, (2023/0068C.OO)	Machinery Regulation, (EU 2021/1230)	Geo-Blocking Regulation, (EU 2016/202)	Digital Market Act (DMA Regulation), (EU 2022/1925)	Remuneration of musicians from third countries for recorded music played in the EU, (EU 2022/2554)	Digital content Directive, (EU 2019/770)	Regulation on distortive foreign subsidies, (EU 2022/2550)	Horizontal Block Exemption Regulations (HBER), (EU 2023/1056), (EU 2023/1067)	Digital euro, (2023/0212C.OO)
EU Space Law	Harmonisation of GDPR enforcement procedures, (2023/0290C.OO)	Access to vehicle data, functions and resources	GreenData4all	AI Act (Regulation), (2021/0108C.OO)	Digital content Directive, (EU 2019/770)	Regulation on certain aspects concerning contracts for the sale of goods, (EU 2019/771)	Horizontal Block Exemption Regulations (HBER), (EU 2023/1056), (EU 2023/1067)	Political Advertising Regulation, (EU 2024/950)	Single Market Emergency Instrument (SMEI), (2022/0278C.OO)	Platform Work Directive, (2021/0414C.OO)	Right to repair Directive, (2023/0830C.OO)
EU Space Law	Consumer protection: strengthened enforcement cooperation	AI Liability Directive, (2023/0530C.OO)	Digital Services Act (DSA Regulation), (EU 2022/2065)	Platform Work Directive, (2021/0414C.OO)	Political Advertising Regulation, (EU 2024/950)	Single Market Emergency Instrument (SMEI), (2022/0278C.OO)	Right to repair Directive, (2023/0830C.OO)	Consumer protection: strengthened enforcement cooperation	Platform Work Directive, (2021/0414C.OO)	Right to repair Directive, (2023/0830C.OO)	Consumer protection: strengthened enforcement cooperation

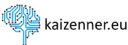


Table 2: Overview of EU governance Mechanisms and Agencies in the Digital sector

Research & Innovation	Industrial Policy	Connectivity	Data & Privacy	IPR	Cybersecurity	Law Enforcement	Trust & Safety	E-Commerce & Consumer Protection	Competition	Media	Finance
1 European Commission (DG CNCT) Unit B.1 (EU 2021/693)	4 Governing Board of European High-Performance Computing Joint Undertaking (EuroHPC-JU) (EU 2021/1173)	1 European Commission (DG DEFS) Unit B.1 (EU 2023/588)	2 European Health and Digital Executive Agency (HaDEA), (EU 2021/173)	1 European Union Intellectual Property Office (EUIPO) (EU 2012/288), (EU 2017/11001)	1 CERT-EU (EU 2004/681)	2 European Anti-Fraud Office (OLAF) (EC 1999/352)	2 European Commission (DG CNCT) Unit B.3 (Consumer Enforcement and Redress)	1 European Commission (DG JUST) Unit B.3 (Consumer Enforcement and Redress)	1 European Commission (DG CNCT) Unit F.2 & F.3 (EU 2022/1355), (EU 2022/2053)	1 European Board for Media Services (EBM) (EU 2024/1083)	1 European Central Bank (ECB) (EU 2013/256), (2023/0212C.OO)
2 European Research Council (ERC) (EU 2012/1173)	4 Governing Board of Chips Joint Undertaking (Chips JU) (2022/0033NLEJ)	2 Body of European Regulators for Electronic Communications (BEREC) (EU 2012/216), (EU 2022/612)	4 European Data Protection Board (EDPB) (EU 2016/679)	2 European Patent Organisation (EPO) (EU 2012/257)	2 European Cybersecurity Competence Centre (ECCC) (EU 2017/687)	1 EU Fundamental Rights Agency (FRA) (EC 2007/168)	4 Gateway coordination group (EU 2018/1724)	6 European Board for Digital Services (EBDS) (2022/2063)	1 European Commission (DG COMP, Antitrust)		2 European Securities and Markets Authority (ESMA) (EU 2009/65), (EU 2023/1114)
3 European Innovation Council & SMEs Executive Agency (EISMEA) (EU 2021/1173), (EU 2021/694), (EU 2021/695)	4 European Digital Infrastructure Consortium (EDIC) (EU 2022/2481)	3 European Union Agency for the Space Programme (EUSPA) (EU 2019/789)	4 European Data Protection Supervisor (EDPS) (EU 2018/1725)	4 European Observatory on Infringements of IP Rights (EUIPR) (EU 2012/288)	2 European Defence Agency (EDA) (ECFSP 2015/1833)	1 Europol (EU 2016/794)	4 European Artificial Intelligence Board (2021/0106C.OO)	7 Consumer Protection Cooperation Network (CPC) (EU 2017/2394)	1 European Commission (DG GROW) Unit A.4 (EU 2022/2781C.OO)		3 European Banking Authority (EBA) (EU 2013/256), (EU 2022/2554), (EU 2023/1114), (2023/0205C.OO)
2 European Research Executive Agency (REA) (EU 2021/1173), (EU 2021/694), (EU 2021/695)	4 European Chips Infrastructure Consortium (ECIC) (EU 2023/731)	4 Governing Board of Smart Networks and Services Joint Undertaking (SNS JU) (EU 2021/2085)	3 European Statistical System Committee (ESSC) (2009/223)	3 Compulsory licences advisory body (2023/0205C.OO)	2 EU Agency for Cybersecurity (ENISA) (EU 2013/881)	1 European Public Prosecutor's Office (EPPO) (EU 2017/1939)	3 European Committee for Electrotechnical Standardization (CENELEC) (EU 2012/1025)	7 European Consumer Centres Network (EU 2012/690)	5 Advisory Committee on Restrictive Practices and Dominant Positions (EC 2003/1)		3 European Insurance and Occupational Pensions Authority (EIOPA) (EU 2022/2554), (2023/0505C.OO)
4 European Institute of Innovation & Technology (EIT) (EU 2007/1173), (EU 2021/694), (EU 2021/695)	3 European Semiconductor Board (ESB) (EU 2023/1781)	3 European Space Agency (ESA) (EU 2023/588)	4 European Data Innovation Board (EDIB) (EU 2022/856), (EU 2023/2554)	3 European Agency for Cybersecurity (ENISA) (EU 2013/881)	2 EU Agency for Cybersecurity (ENISA) (EU 2013/881)	1 Europol (EU 2016/794)	3 European Committee for Standardization (CEN) (EU 2012/1025)	7 Consumer Safety Network (EU 2023/988)	1 Advisory Committee on Concentrations (EC 2004/139)		1 Committee on Administrative Cooperation for Taxation (EU 2011/116)
7 European Digital Innovation Hubs Network (EDIH) (EU 2021/694)	3 European Critical Raw Materials Board (ECRM) (EU 2024/1252)	4 Communications Committee (COCOM) (EU 2018/1572), (EU 2015/211), (EU 2023/612)	1 Interoperable Europe Board (IEB) (EU 2024/500)	3 European Cybersecurity Certification Group (ECCG) (EU 2018/681)	3 Eurojust (EU 2016/172)	3 Eurojust (EU 2016/172)	3 European Telecommunications Standards Institute (ETSI) (EU 2012/1025)		6 Contact Committee (EU 2017/1132)		1 VAT Committee (EC 2006/112), (CN 2022/20507)
	5 Net-Zero Europe Board (2023/0081C.OO)	5 .eu Multi-stakeholder Advisory Group (EU 2019/511)	5 European Health Data Space Board (EHDS) (2023/0140C.OO)		3 Interinstitutional Cybersecurity Board (ICBS) (EU 2023/2063)	3 Frontex (EU 2019/1995)			5 High-Level Group on DMA (EU 2022/1925)		3 The Standing Committee on Administrative Cooperation (CN 2022/20507)
	2 European network of competence centers in semiconductors (EU 2023/1781)	4 Interoperable Europe Board (EU 2024/500)			1 NIS cooperation group (EU 2022/2550)	3 Interoperability Advisory Group (EU 2019/117)			7 European Competition Network (ECN) (EC 2003/1)		
					3 Interinstitutional Information Security Coordination group (2022/0084C.OO)	7 European Judicial Network in criminal matters (2022/0066C.OO)			7 Union Product Compliance Network (EU 2019/1020)		
					3 Network of National Coordination Centres (EU 2012/1687)						
					3 CSIRTs network (EU 2022/2550)						
					7 EU CyCLoHe (EU 2022/2555)						

Explanation

1 EU Institution

2 Decentralised agency

3 Independent body

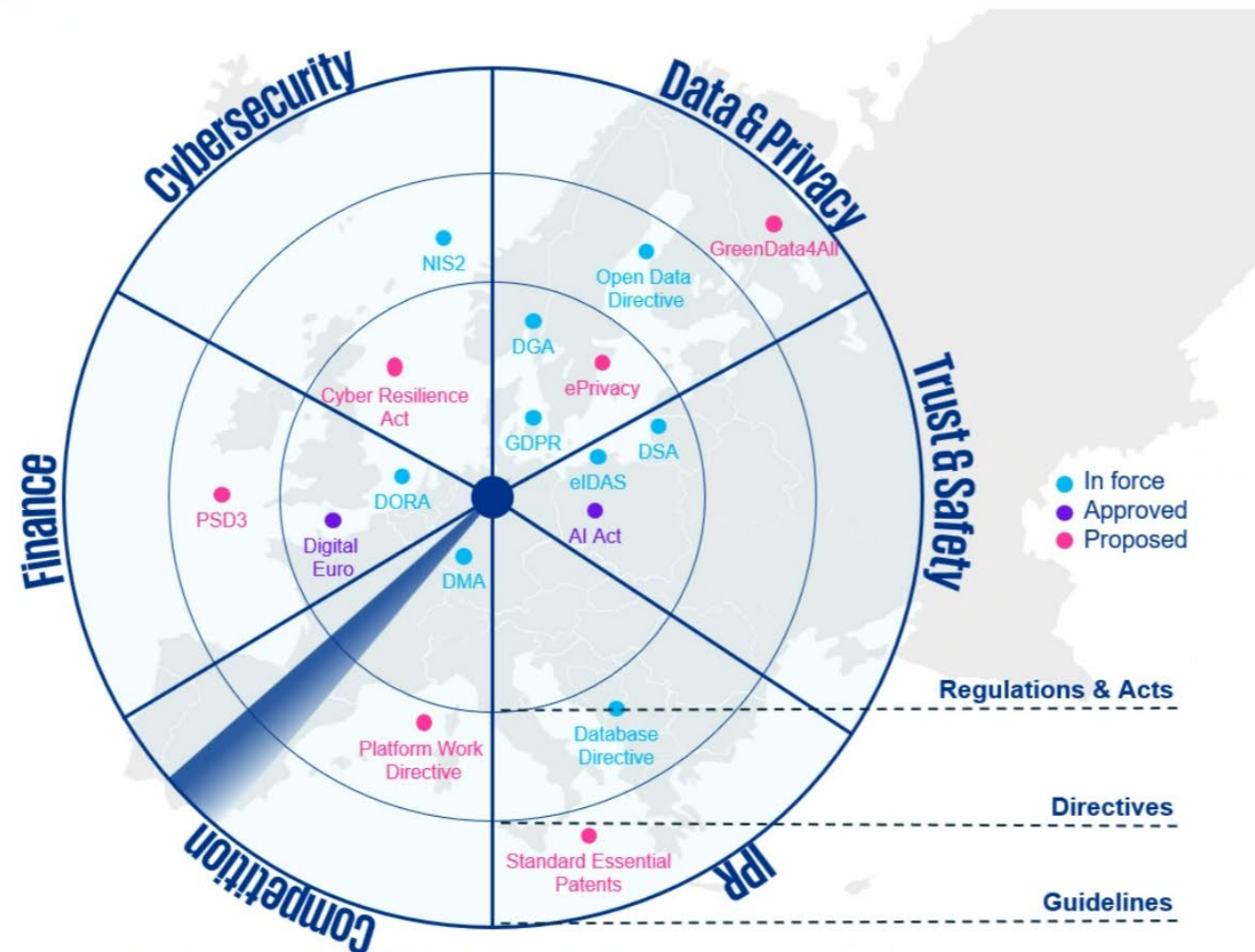
4 Network of Member States

5 Executive agency

6 Governing board

7 Advisory body

Regulatory Radar

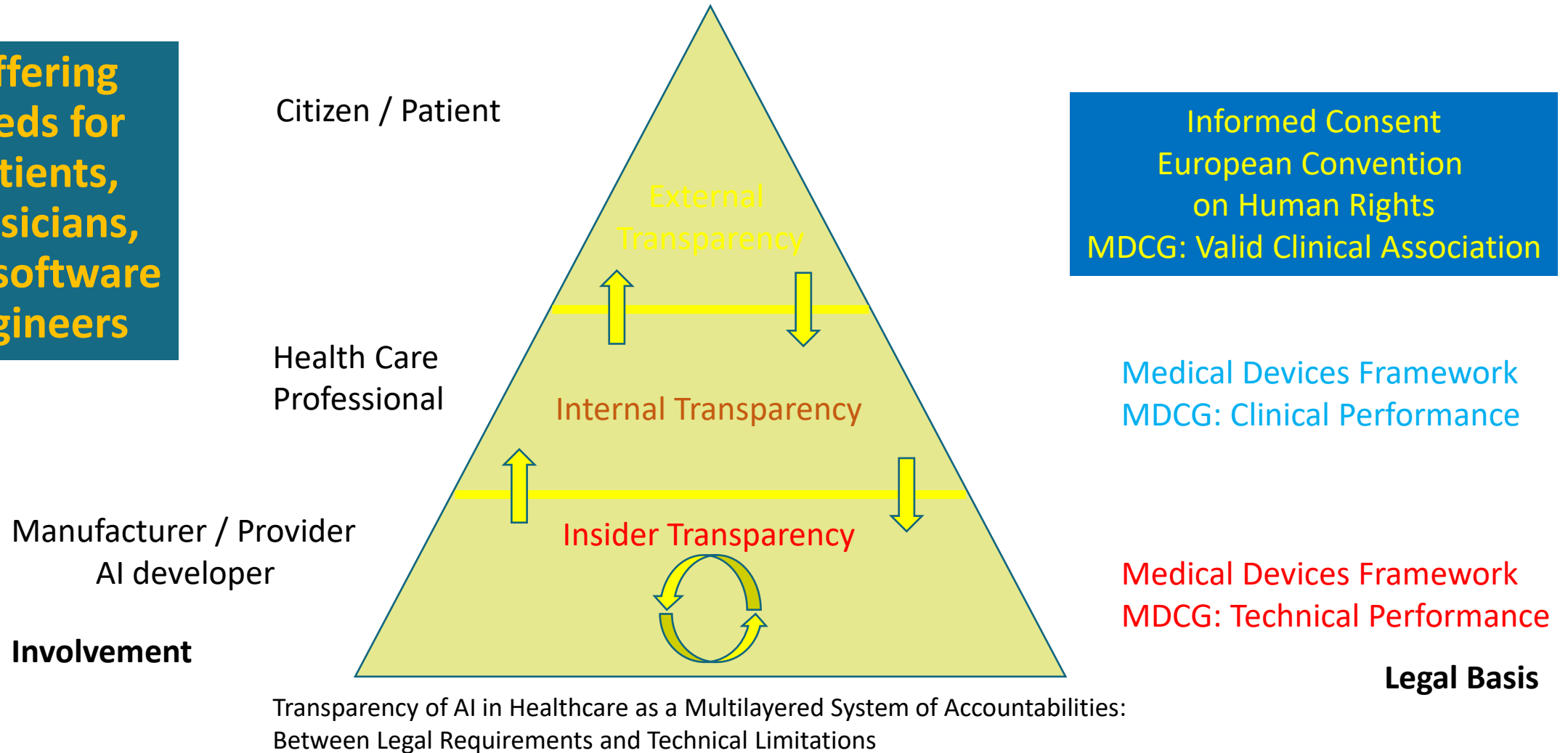


This image is indicative, it does not contain all EU legislation.

Source: 'A dataset on EU legislation for the digital world', Kai Zenner, J. Scott Marcus, Kamil Sekut and Hèctor Badenes Rodríguez published by Bruegel.

Transparency of artificial intelligence, machine learning medical device software and Digital Twins

Differing needs for patients, physicians, and software engineers



Transparency of AI in Healthcare as a Multilayered System of Accountabilities:
Between Legal Requirements and Technical Limitations

Anastasiya Kiseleva, Dimitris Kotzinos and Paul De Hert

Frontiers in Artificial Intelligence, 30.5.2022

Thank you for your attention