GDSD 2025

DATA-DRIVEN MEDICINE

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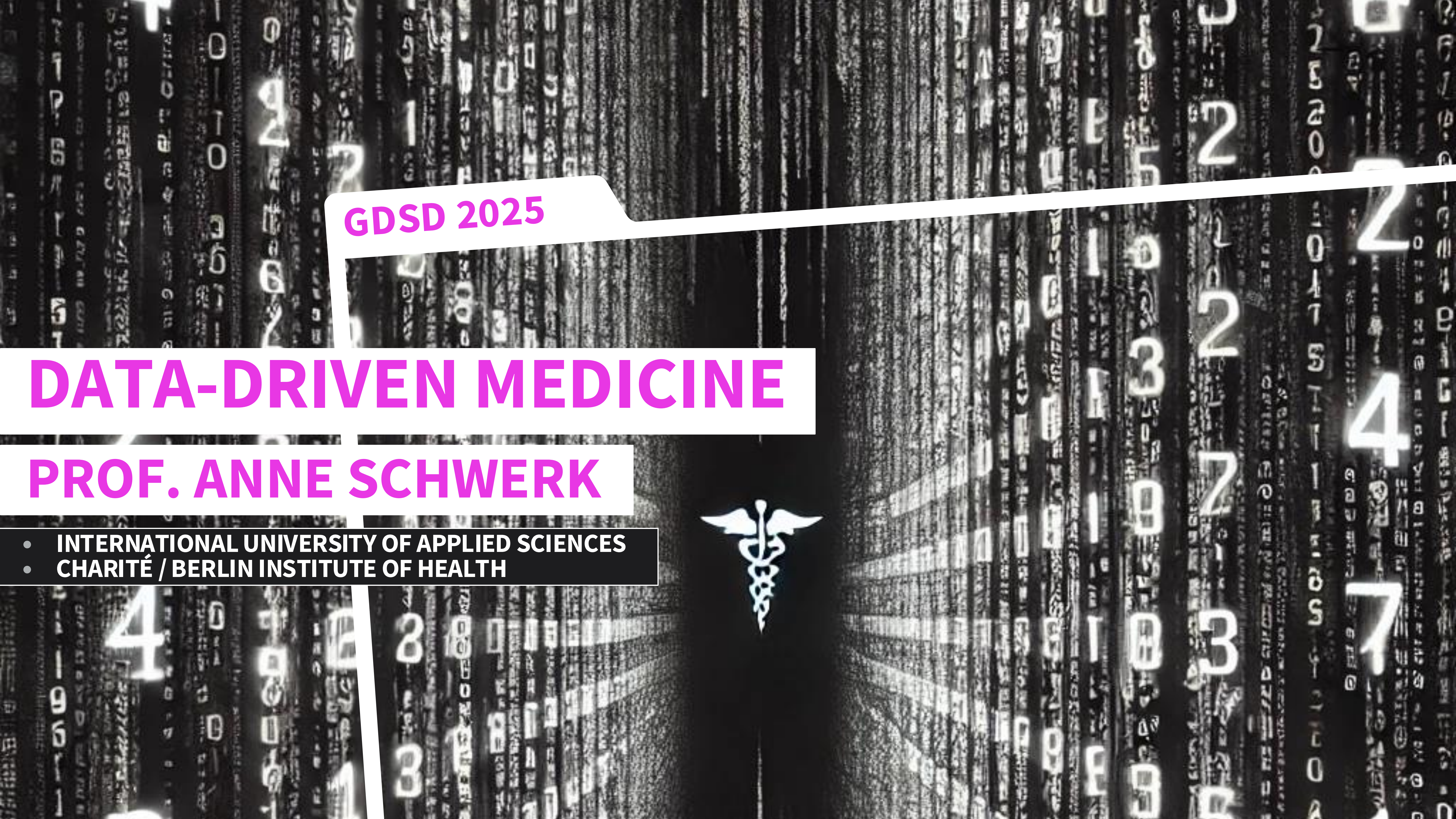


AI-DRIVEN MEDICINE

INTERNATIONALE HOCHSCHULE

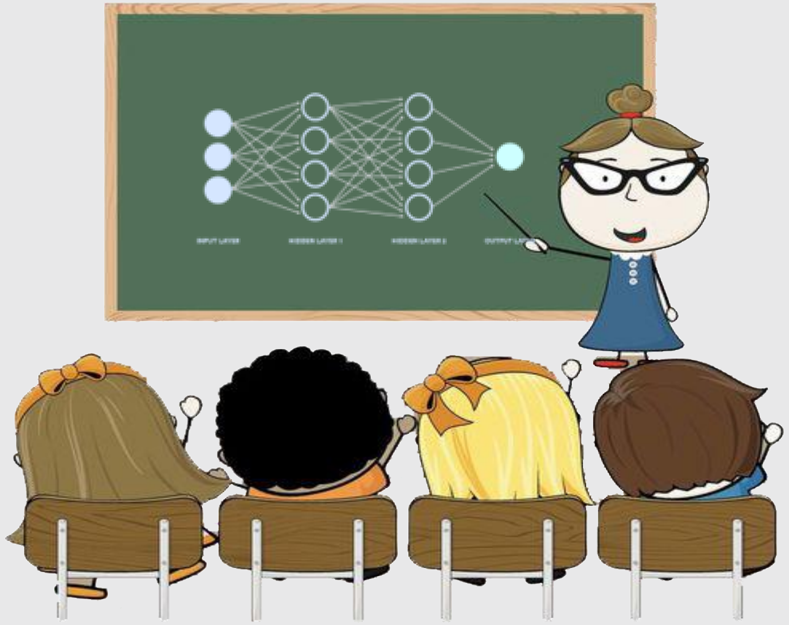
Overview: AI and Healthcare Data 1

Examples 2

Take-Home-Message 3

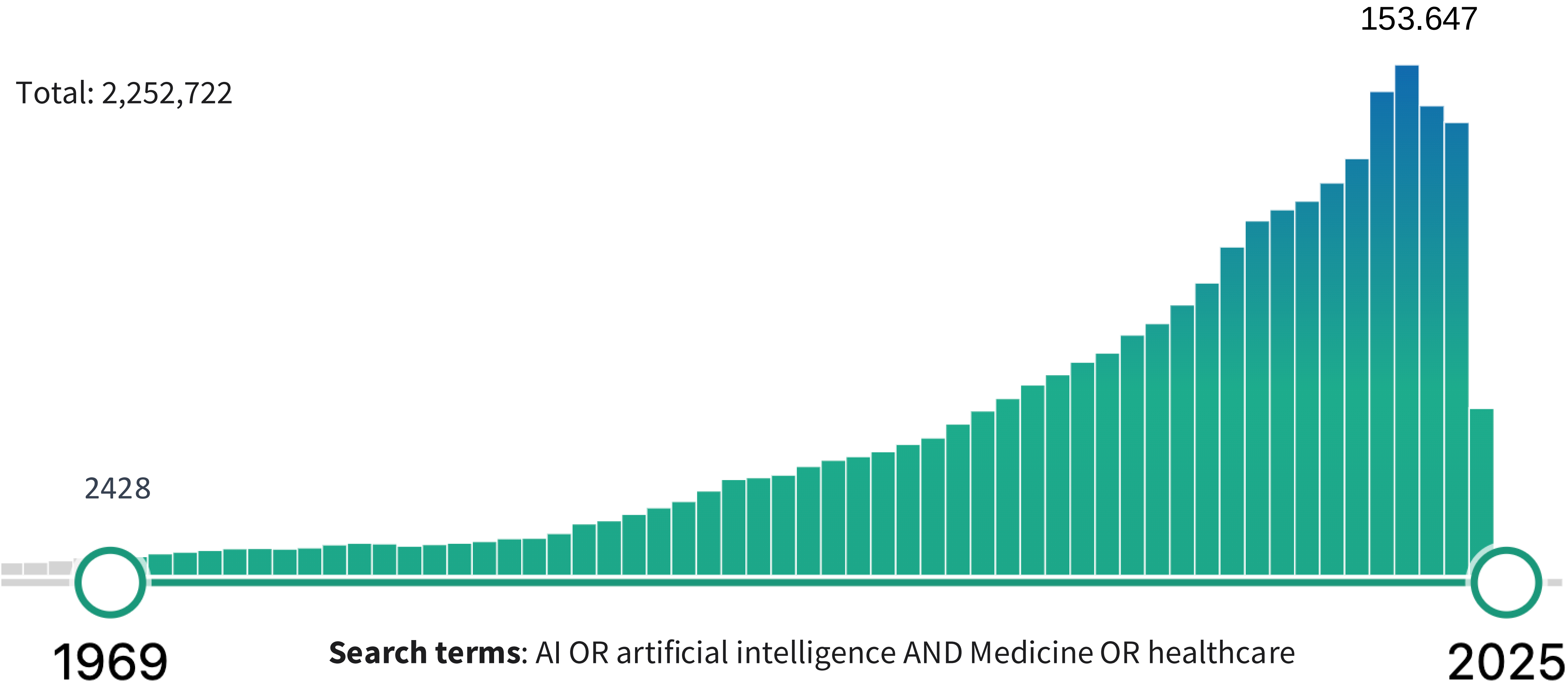
#1

Overview: AI and Healthcare Data



INCREASED RELEVANCE OF MEDICAL AI

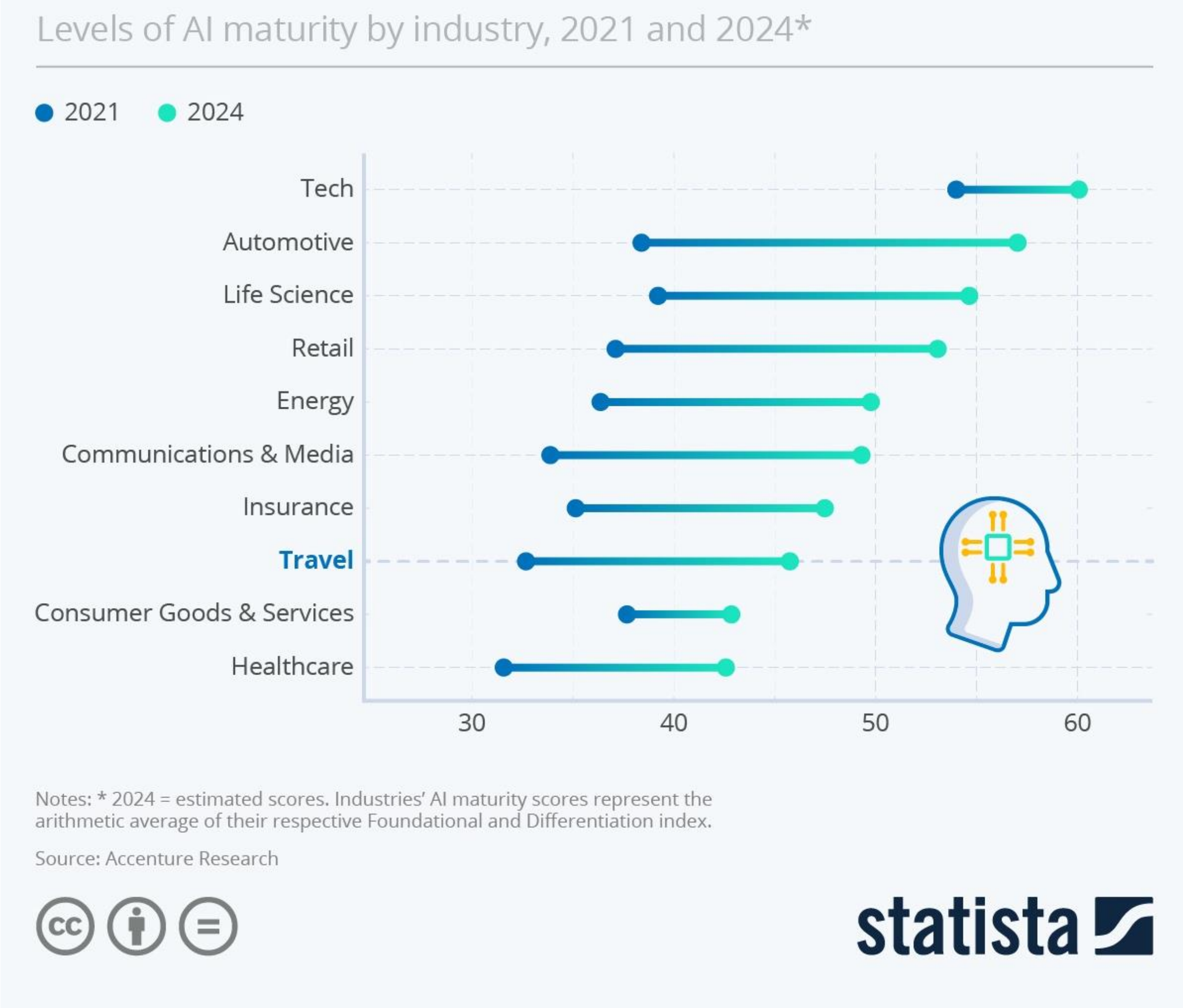
PUBLICATIONS



Search terms: AI OR artificial intelligence AND Medicine OR healthcare

Source of the image: PubMed

ADOPTION OF AI PER INDUSTRY



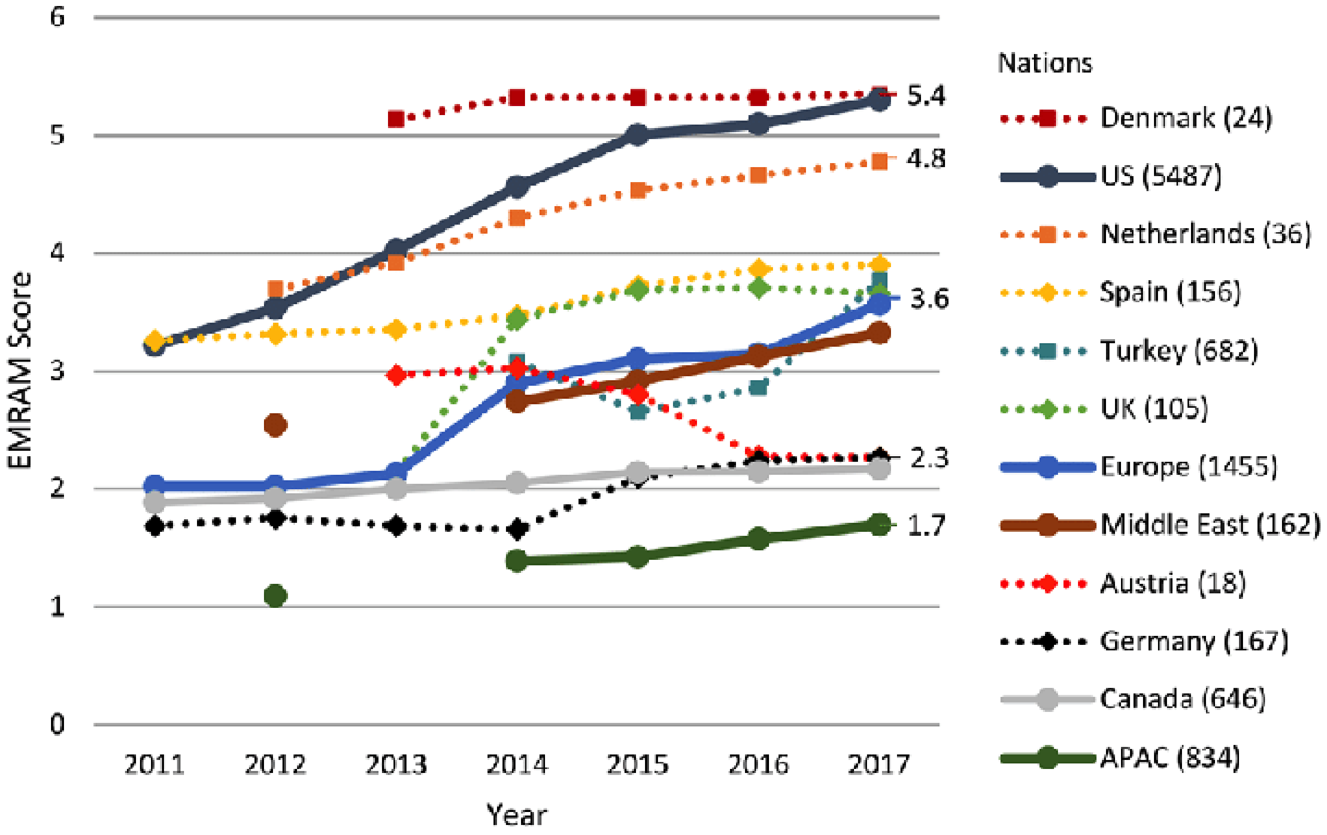
Levels of AI maturity by industry, 2021 and 2024*

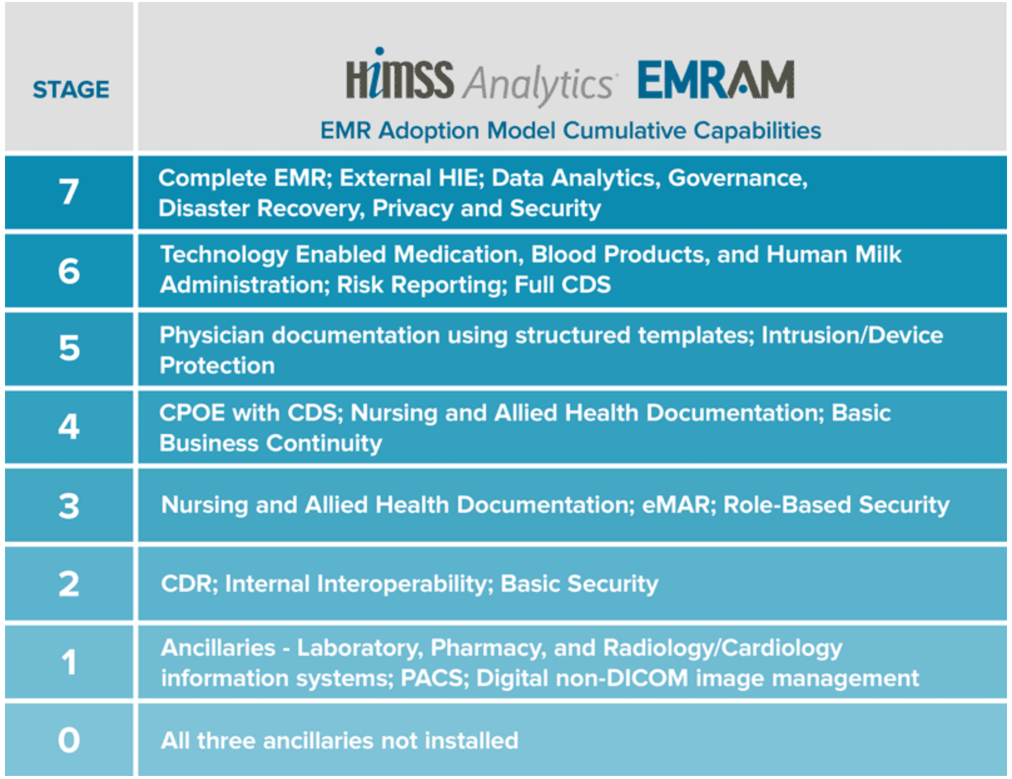
Notes: * 2024 = estimated scores. Industries' AI maturity scores represent the arithmetic average of their respective Foundational and Differentiation index.

Source: Accenture Research

– Source: https://indatalabs.com/blog/ai-adoption-by-industry

LACK OF DIGITALISATION



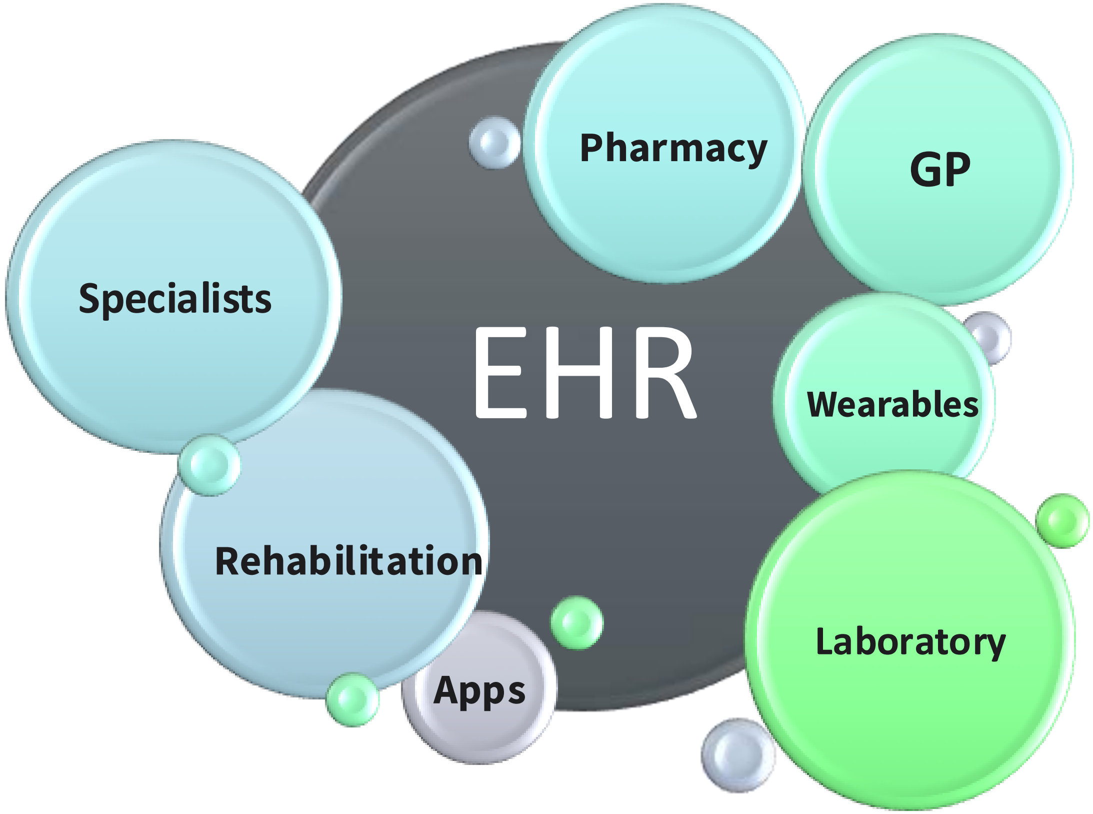


STAGE	HIMSS Analytics EMRAM EMR Adoption Model Cumulative Capabilities
7	Complete EMR; External HIE; Data Analytics, Governance, Disaster Recovery, Privacy and Security
6	Technology Enabled Medication, Blood Products, and Human Milk Administration; Risk Reporting; Full CDS
5	Physician documentation using structured templates; Intrusion/Device Protection
4	CPOE with CDS; Nursing and Allied Health Documentation; Basic Business Continuity
3	Nursing and Allied Health Documentation; eMAR; Role-Based Security
2	CDR; Internal Interoperability; Basic Security
1	Ancillaries - Laboratory, Pharmacy, and Radiology/Cardiology information systems; PACS; Digital non-DICOM image management
0	All three ancillaries not installed

Bukowski et al. (2020); https://www.nexus-marabu.de/nachricht/neue-himss-emram-kriterien

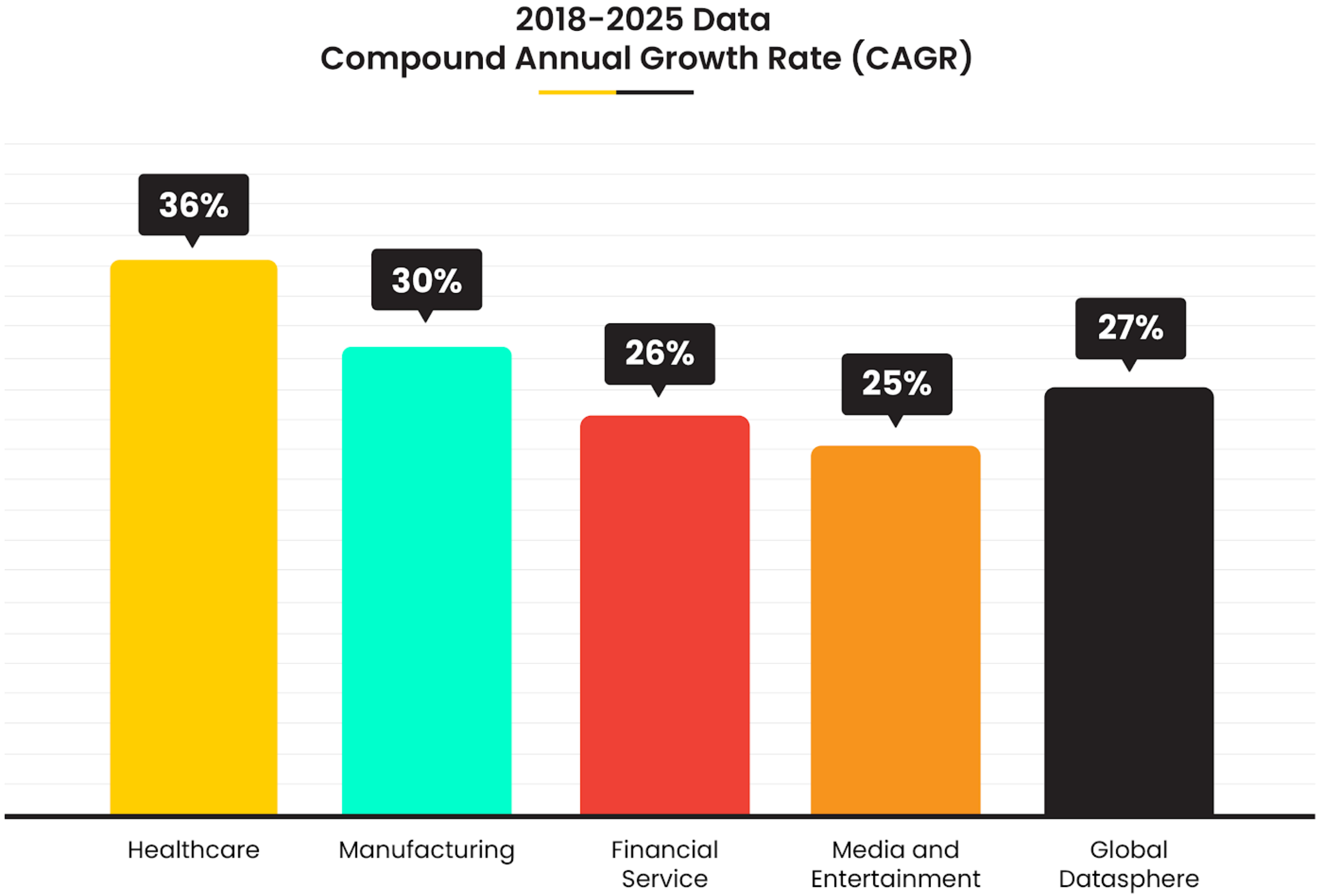
CHALLENGES: HEALTHCARE DATA

- Lack of data & inhibited sharing:
  - Labeled data
  - Benchmark data sets & open data
  - Data silos
  - Lack of cross-validation options
  - Lack of standardization/ interoperability
- Data quality:
  - Imbalanced data
  - Missing data
  - Incomplete data
  - Standardization



Source of the image: Schwerk (2023)

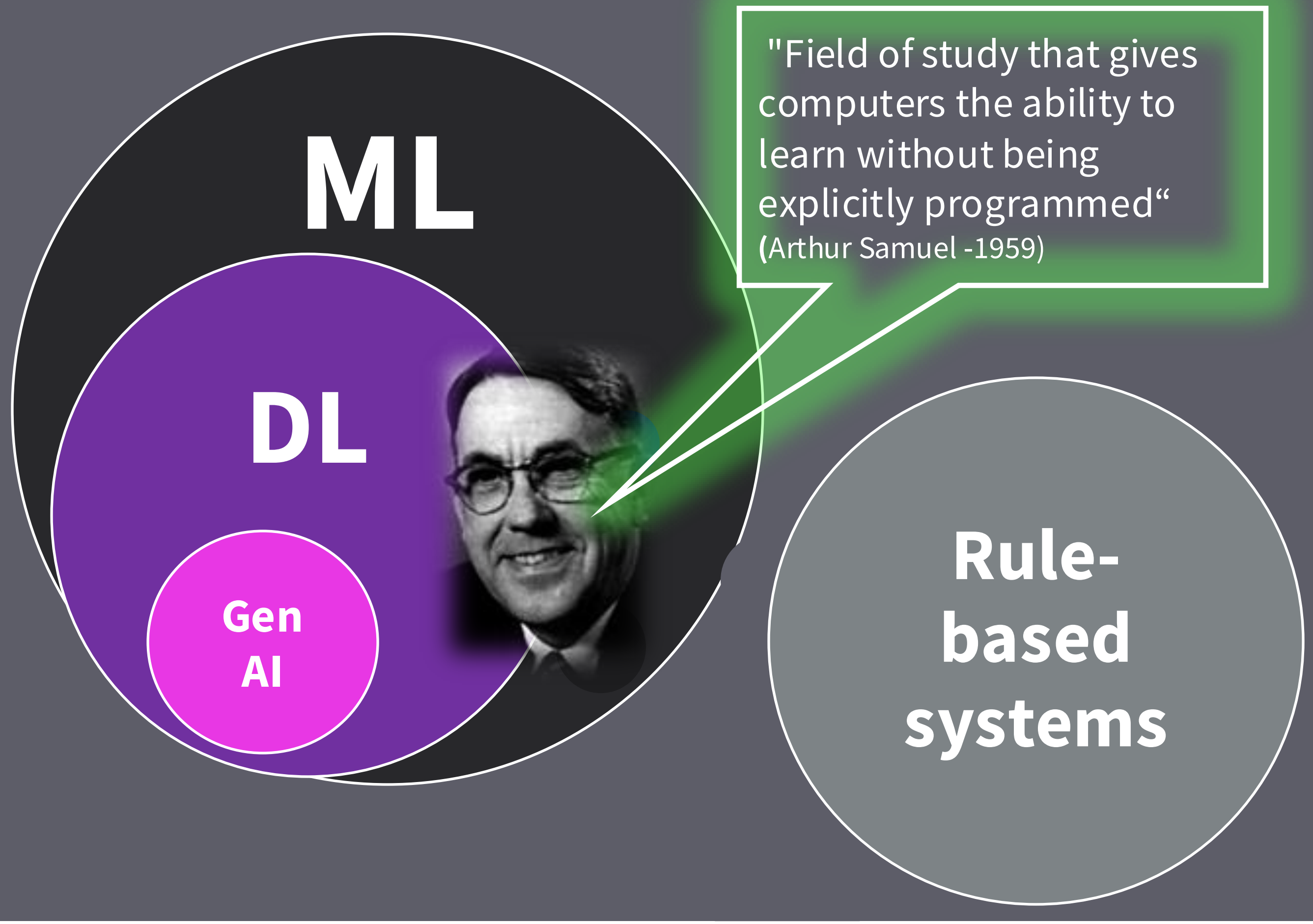
HEALTHCARE DATA INCREASE



Source: https://www.rbccm.com/en/gib/healthcare/episode/the_healthcare_data_explosion

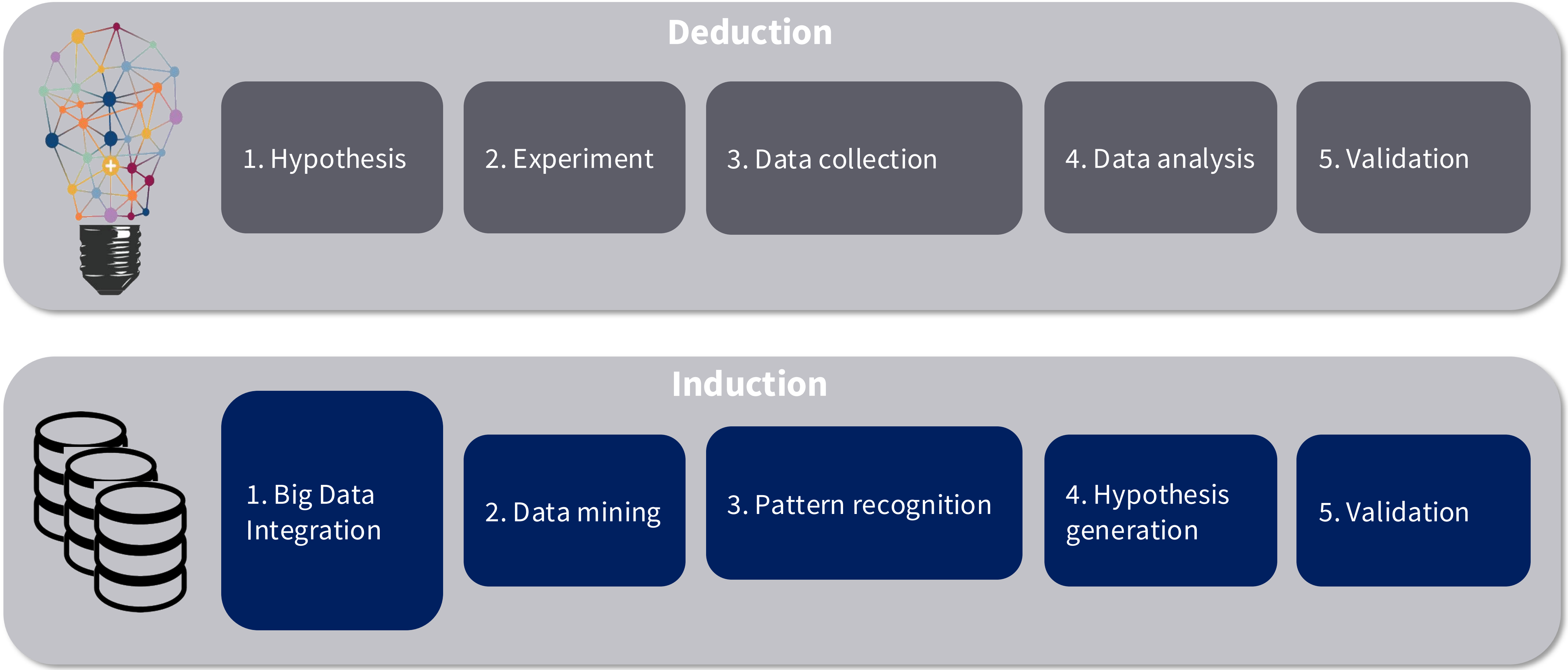
DEFINITION: AI

Artificial Intelligence: IT systems with human-like behavior – based on statistical & mathematical models



"Field of study that gives computers the ability to learn without being explicitly programmed“ (Arthur Samuel -1959)

THE END OF THEORY - DEDUCTION VERSUS INDUCTION



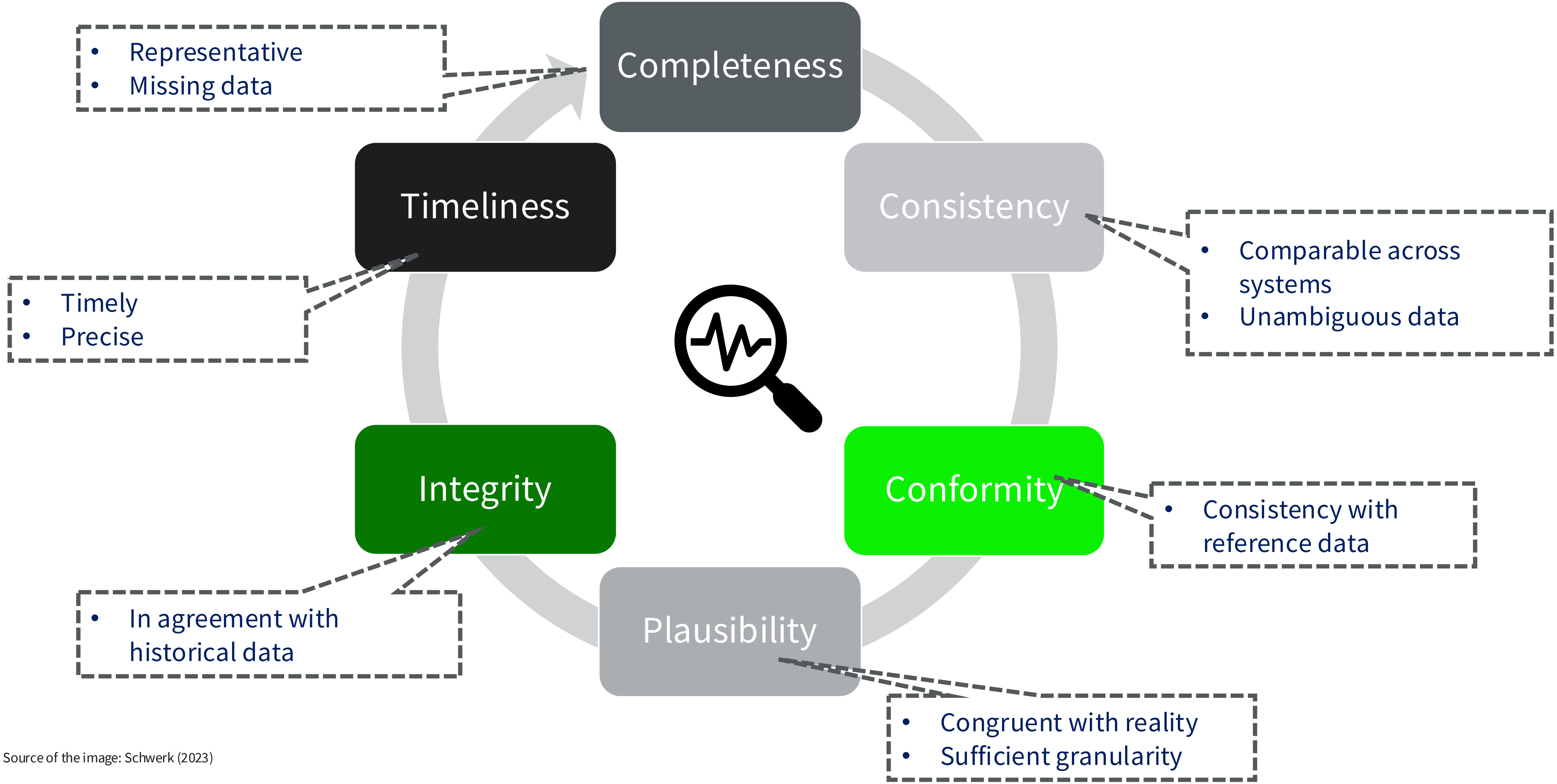
Deduction

1. Hypothesis
2. Experiment
3. Data collection
4. Data analysis
5. Validation

Induction

1. Big Data Integration
2. Data mining
3. Pattern recognition
4. Hypothesis generation
5. Validation

IMPORTANCE OF DATA: DATA QUALITY



Completeness
- Representative
- Missing data

Consistency
- Comparable across systems
- Unambiguous data

Conformity
- Consistency with reference data

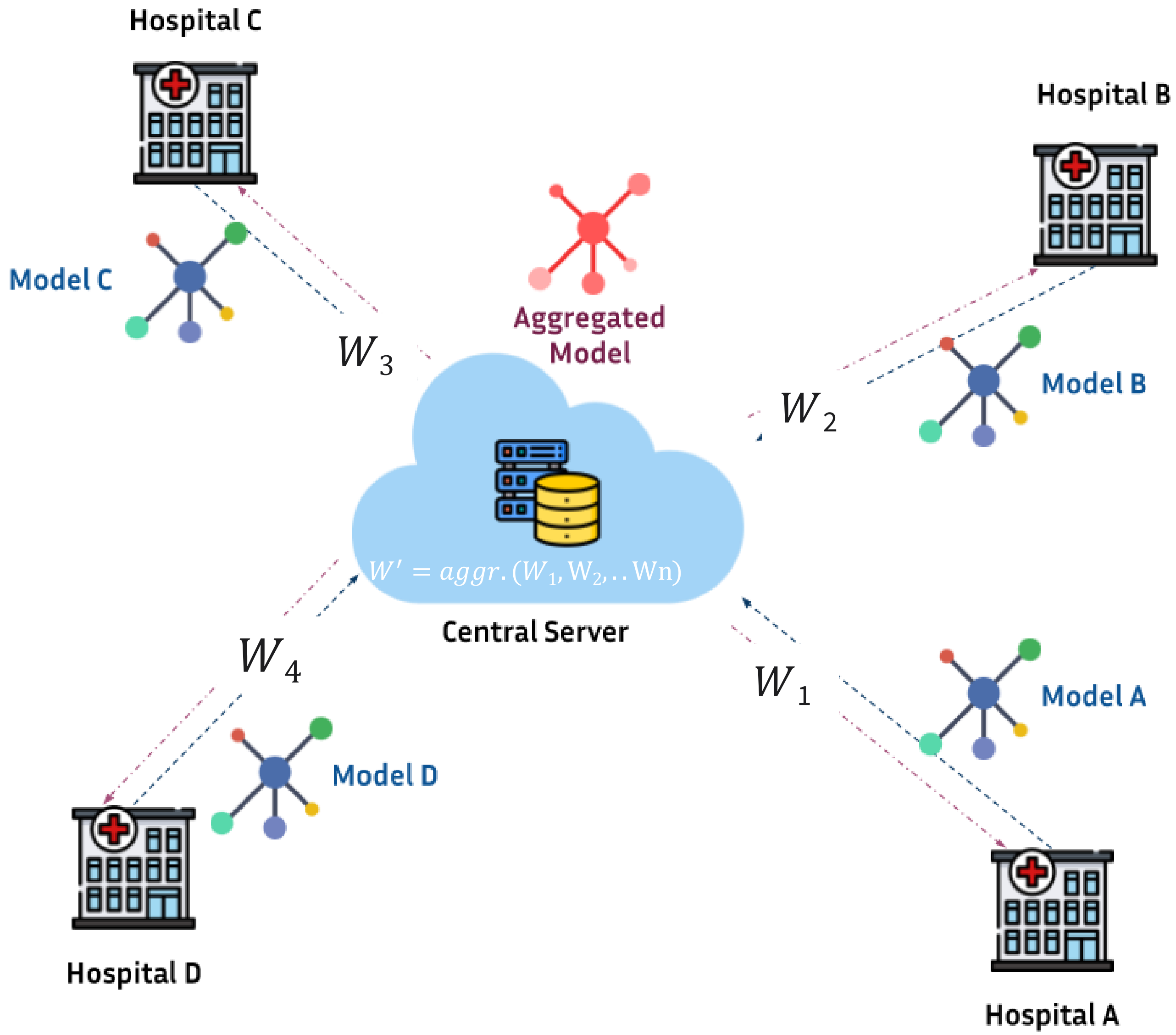
Plausibility
- Congruent with reality
- Sufficient granularity

Integrity
- In agreement with historical data

Timeliness
- Timely
- Precise

Source of the image: Schwerk (2023)

IMPROVED DATA QUALITY: FEDERATED ML

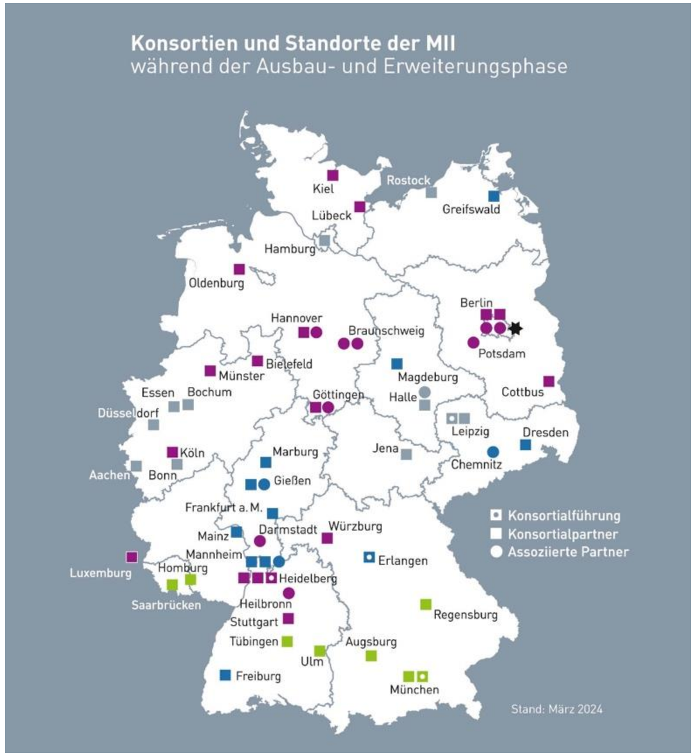


Source: https://fedbiomed.org/

- **Data protection:** Data remains at the original location - only model parameters are shared
- **Decentralization:** Hospitals train local models and send encrypted parameters to central coordinators
- **Iterative process:** The coordinator aggregates local models into a global model and shares it. The process is repeated until the model converges

RESEARCH DATA PORTAL FOR HEALTH (FDPG)

- Initiated by the Medical Informatics Initiative (MII) launched in 2016 by the BMBF
- A federated network for centralized and decentralized data access
- Core data set from primary IT systems of the universities →local data integration centers
- Standardization to MII format
- Depending on the basis of use:
  - Distributed evaluations
  - Central evaluations (with broad consent)



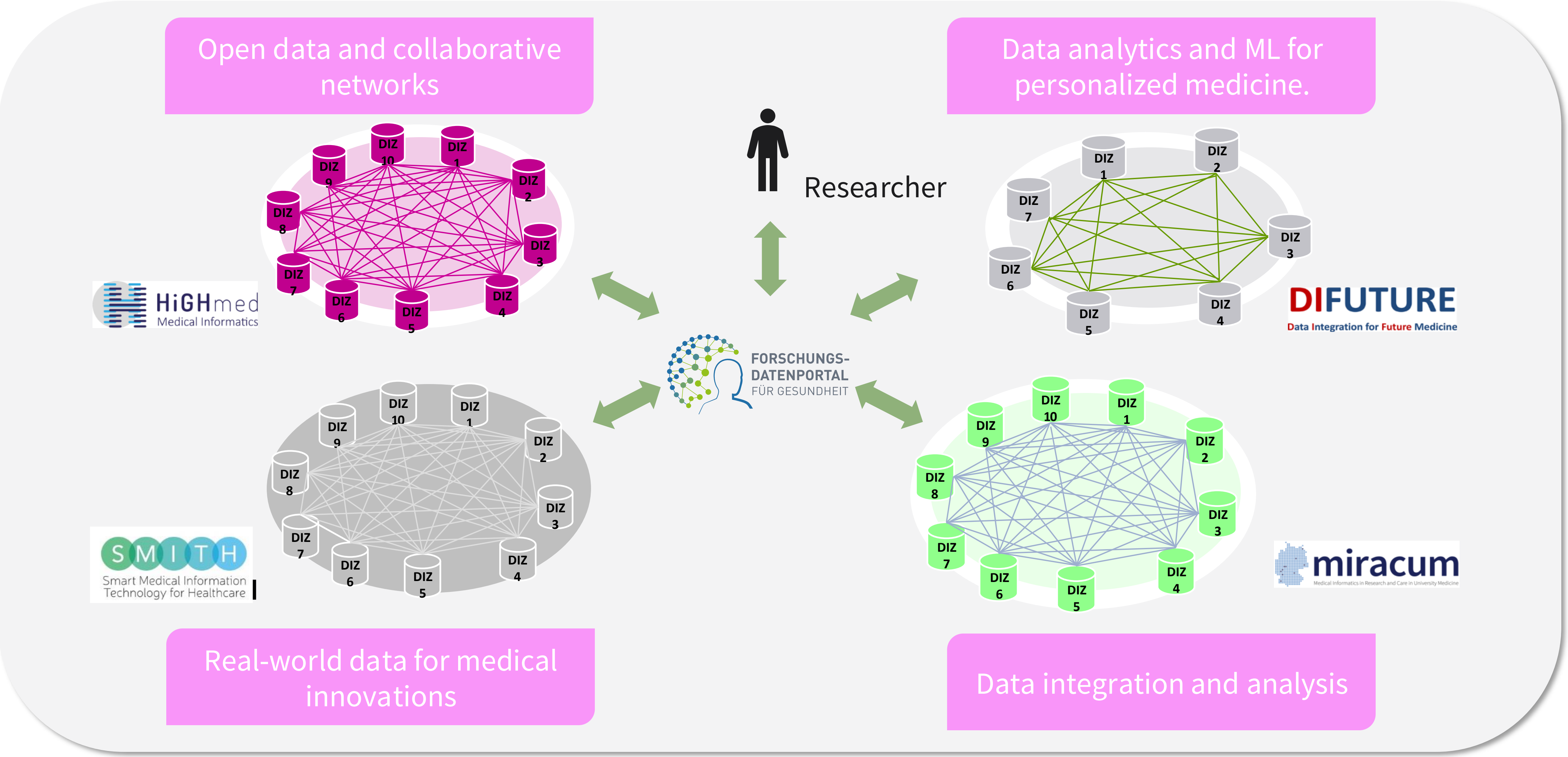
Konsortien und Standorte der MII
während der Ausbau- und Erweiterungsphase

Stand: März 2024

- 15 M EHRs
- 160 M Diagnoses
- 1.5 Billion Lab values

→ **2-3 M uncoded rare diseases**

THE FDPG



Open data and collaborative networks

Data analytics and ML for personalized medicine.

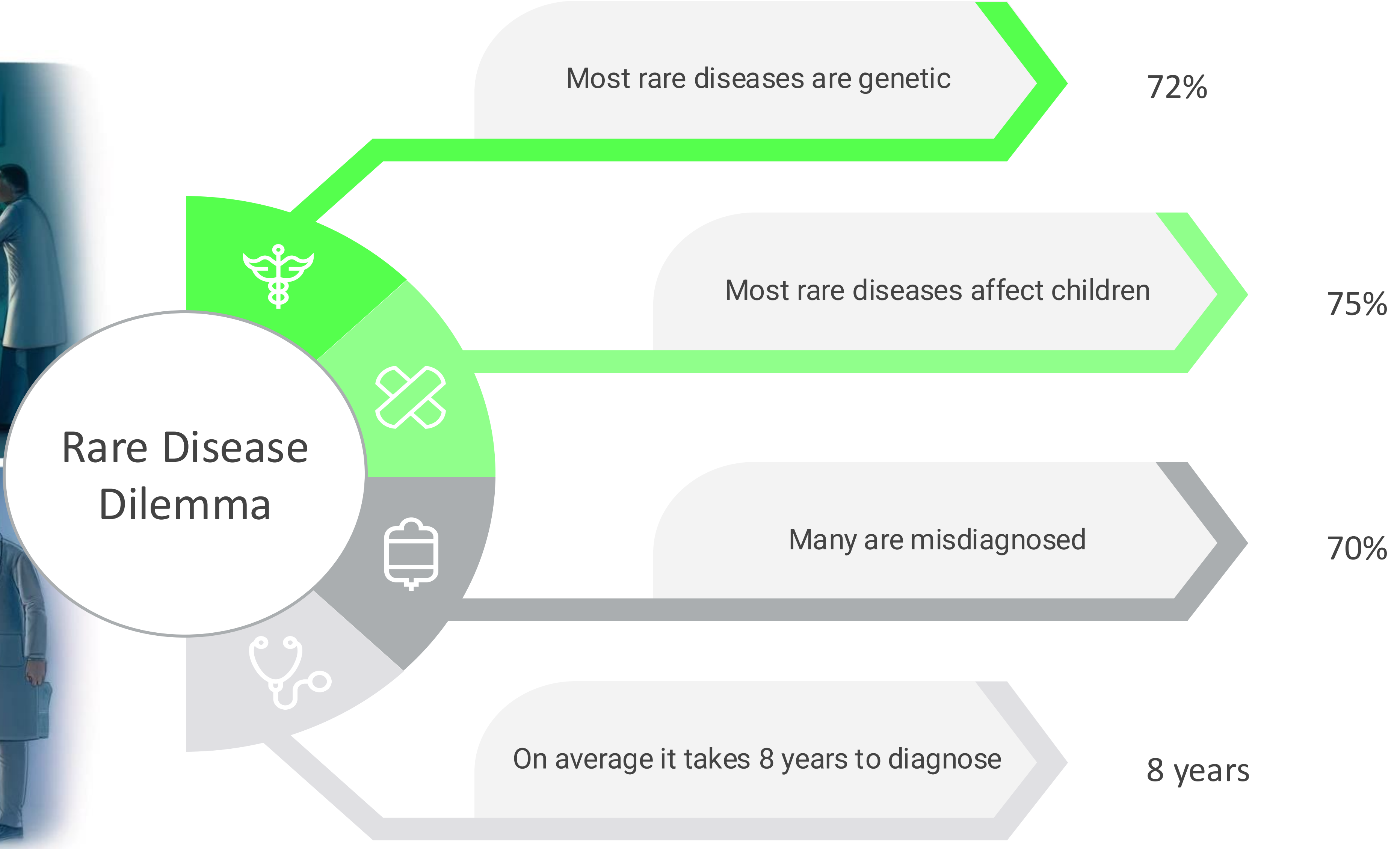
Real-world data for medical innovations

Data integration and analysis

#2

Examples

RARE DISEASES: DIAGNOSTIC ODYSSEY



Rare Disease Dilemma

Most rare diseases are genetic 72%

Most rare diseases affect children 75%

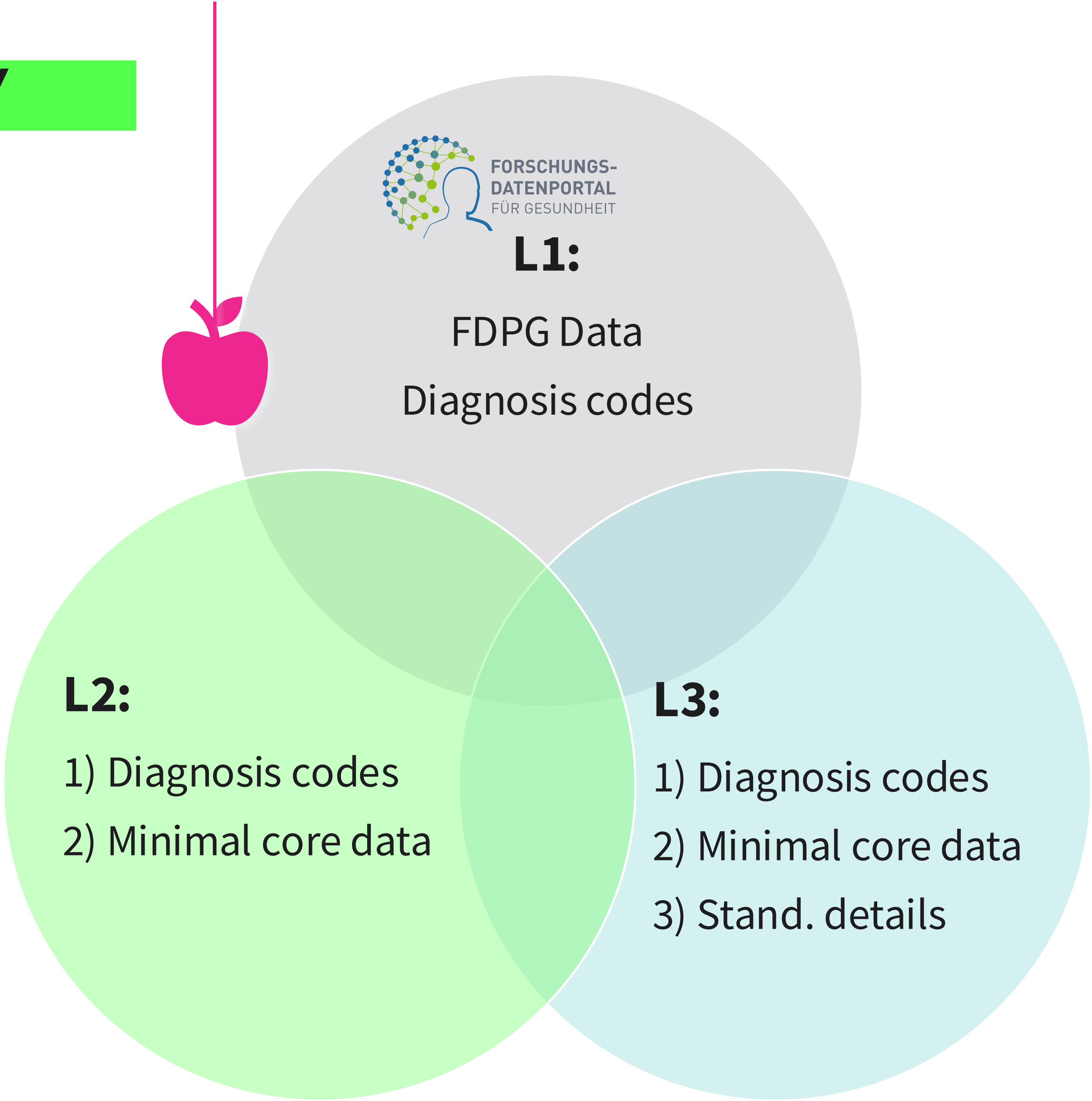
Many are misdiagnosed 70%

On average it takes 8 years to diagnose 8 years

— Source: www.Eurordis.org

DATA AVAILABILITY

- FDPG Data
- Orpha / ICD Codes



L1:

FDPG Data

Diagnosis codes

L2:

1) Diagnosis codes

2) Minimal core data

L3:

1) Diagnosis codes

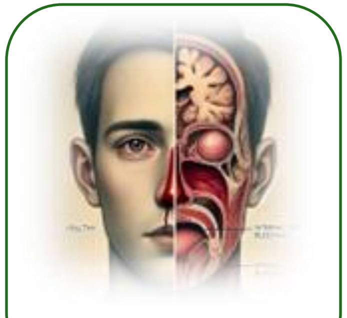
2) Minimal core data

3) Stand. details

- Addition through clinics
- **Goal**: Europe-wide analysis

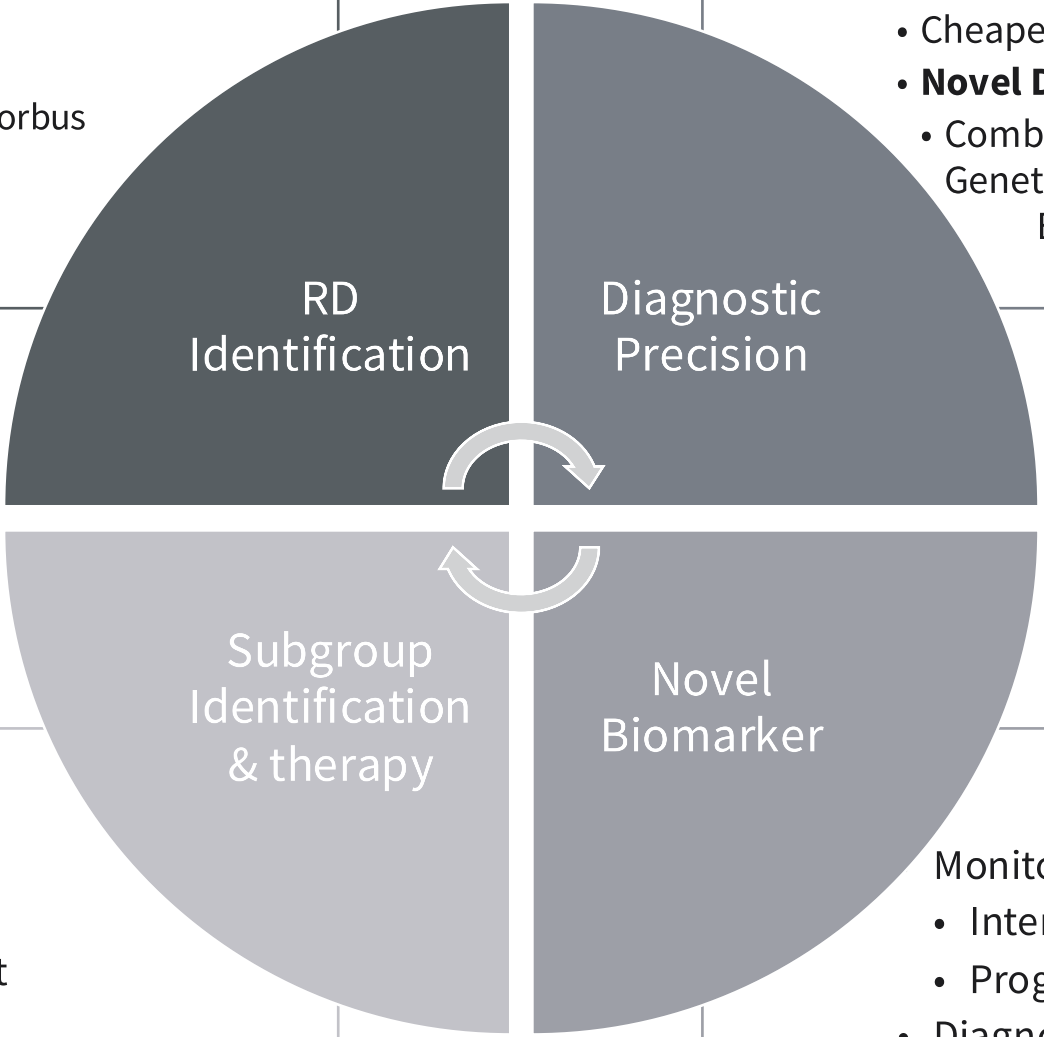
- Special data:
  - Progress data
  - Intervention data
  - PROMs
  - Omics
- European Registers

ML FOR RARE DISEASE (RD) DIAGNOSTICS



Morbus Osler

- Undected RDs
- EHR-based Phenotypes
- **Example**: Morbus Osler



- Combined markers
- Cheaper Diagn.
- **Novel Diagnoses**:
  - Combined: Genetic (PRS) Epigenetic

Hypophosphatasia

Parkinson’s disease

- Precision medicine
- Treatment

Monitoring

- Interventions
- Progression

- Diagnostics

Gaucher disease

L1: ML FOR HYPOPHOSPHATASIA DIAGNOSIS

INTERNATIONALE HOCHSCHULE

- Hereditary disease: ALPL gene mutation
- 400 + disease-causing ALPL variants
- Symptoms:
  - **Severe**: Bone demineralization, respiratory failure, seizures
  - **Mild**: Tooth loss, periodontal disease
- Diagnosis: Ø 5.7 years delayed
  - Frequent misdiagnoses
  - ALP value + symptoms + genetics
  - Specific orpha code
- Incorrect treatment: bisphosphonates → Bone damage

→ Early diagnosis is crucial

L1 Analysis: Use ALP (+PLP) biomarkers + phenotypes to determine more specific biomarker thresholds → identify new patients and improve diagnostic precision

— Khan et al. 2024

L1: RBS FOR MORBUS OSLER DIAGNOSTIK

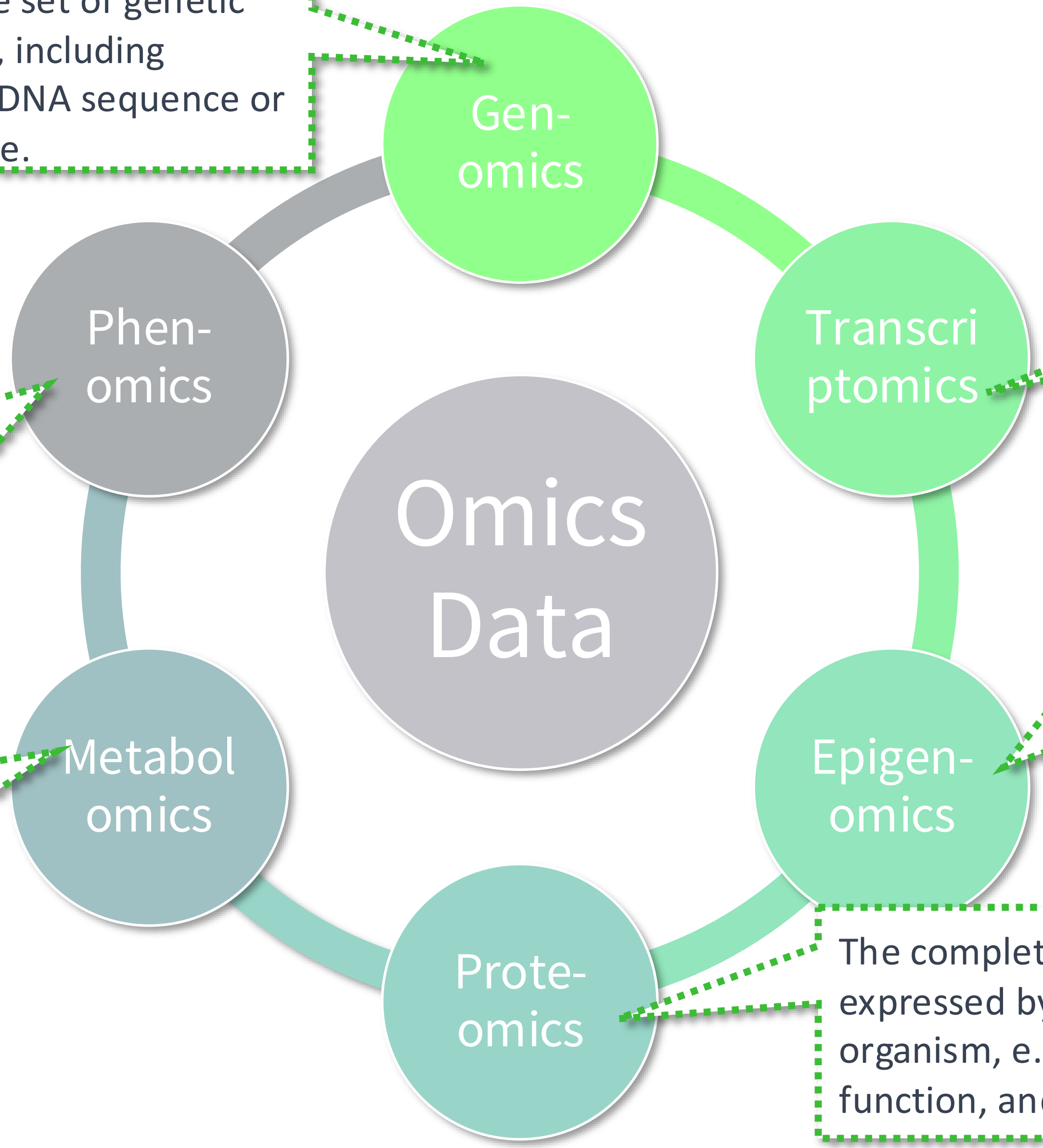
- Hereditary disease: : ENG, ACVRL1, or SMAD4 gene mutation
- 600 + disease-causing variants
- Symptoms:
    - **Severe:** Arteriovenous malformations → Bleeding, strokes, cardiac stress
    - **Mild:** Nosebleeds (epistaxis), telangiectasias on skin and mucous membranes
  - Diagnosis: Ø 26 years delayed
    - Frequent misdiagnoses
    - Curacao criteria + genetics
  - Incorrect treatment: anticoagulants → Bleeding

→ Early diagnosis is crucial

L1 Analysis: Using the ICD-10 code for identification & extended phenotyping
→ RBS on Curacao Criteria → New identifications

— Pierucci et al. 2012

L3 DATA: OMICS



Genomics: The complete set of genetic data of a cell, including variations in DNA sequence or DNA structure.

Transcriptomics: The complete set of RNA molecules transcribed from the DNA of an organism or a cell population, including messenger RNA (mRNA), and non-coding RNA

Epigenomics: The complete set of epigenetic changes, incl. changes in chromatin structure, DNA methylation, histone protein modifications, non-coding RNA

Proteomics: The complete set of proteins expressed by a cell, tissue, or organism, e.g. amount, identity, function, and interaction.

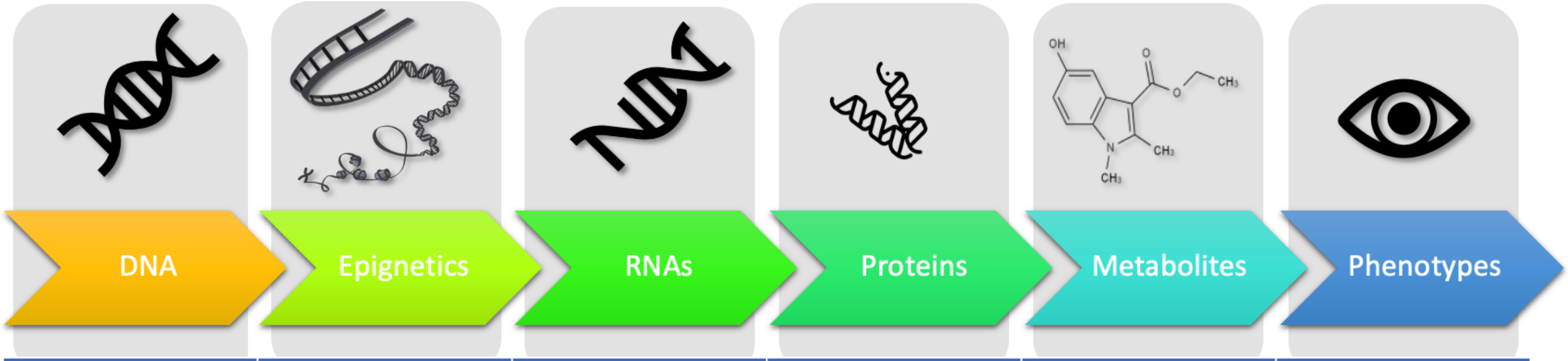
Metabolomics: The complete set of the small-molecule metabolites present in a cell, tissue, or organism

Phenomics: The complete set of physical and biochemical data sources, including images, blood tests, and data from EHRs

Source of the image: Schwerk (2023)

OMICS DATA AND ANALYSES

INTERNATIONALE HOCHSCHULE



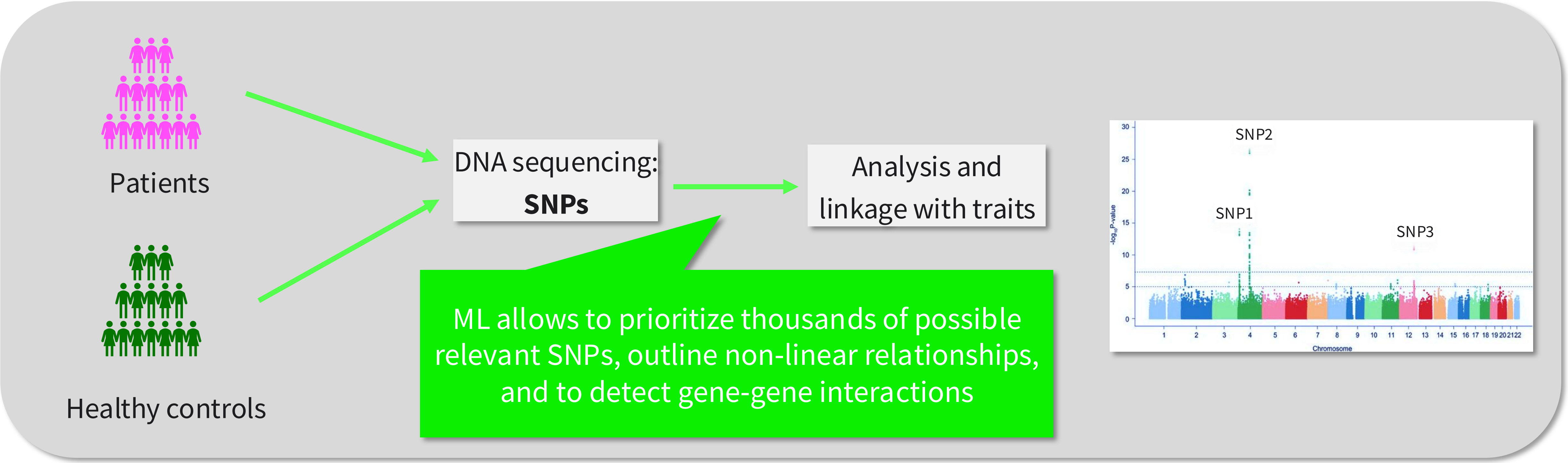
Omics	Genomics	Epigenomics	Transcriptomics	Proteomics	Metaolomics	Phenomics
Analysis	• eQTL • GWAS • PRS • Gene prioritization • Epistasis • Gene-based stratification	• Gene prioritization • Tumor heterogeneity • Drug Response Prediction	• Differential gene expression • Batch effect removal • Gene prioritization	• pQTL • Biomarker • Spatial proteomics: segmentation & protein mis-localizations	• Preprocessing • mQTL • Biomarker • Disease profiles • Metabolite identity/ pathway prediction	• PheWAS • Integrated omics • Image-based biomarker • EHR biomarker/ subgrouping

— Source of the image: Schwerk (2023)

SUBGROUP IDENTIFICATION: GENOME WIDE ASSOCIATION STUDIES

GWAS:

- Analyzes the genomes of large groups of people with and without a disease / trait
- Identifyies genomic variants (SNPs) - by assessing linkage disequilibrium



Patients

Healthy controls

DNA sequencing:
SNPs

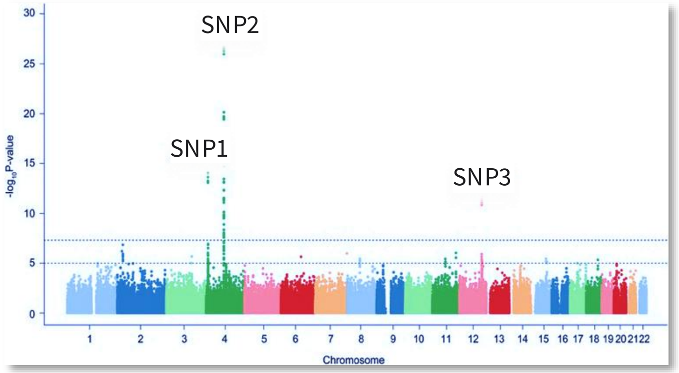
Analysis and
linkage with traits

ML allows to prioritize thousands of possible relevant SNPs, outline non-linear relationships, and to detect gene-gene interactions

— Source of the image : Schwerk (2023) and adapted from Matsuo et al. (2016;)

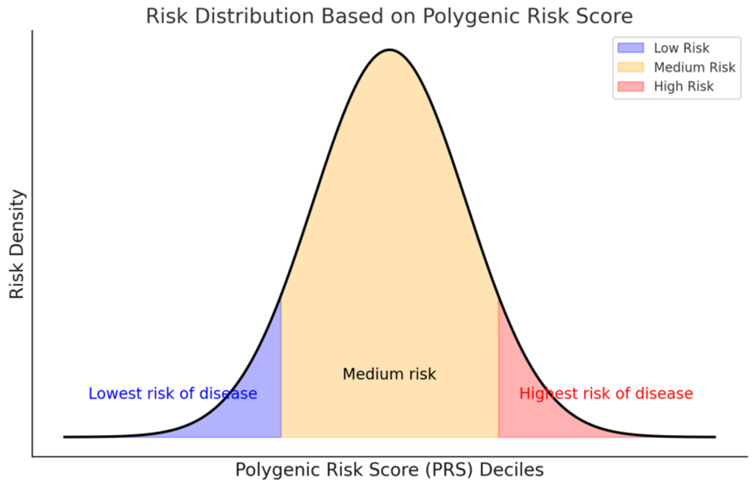
DIAGNOSTIC PRECISION: POLYGENIC RISK SCORE CALCULATION

- PRS sum weighted effect sizes of risk variants from GWAS to estimate disease susceptibility
- Linear approach: does not account for complex genetic interactions (e.g., epistasis)
- **ML helps to:**
  - Account for non-linear interactions
  - Combine multiple existing PRS



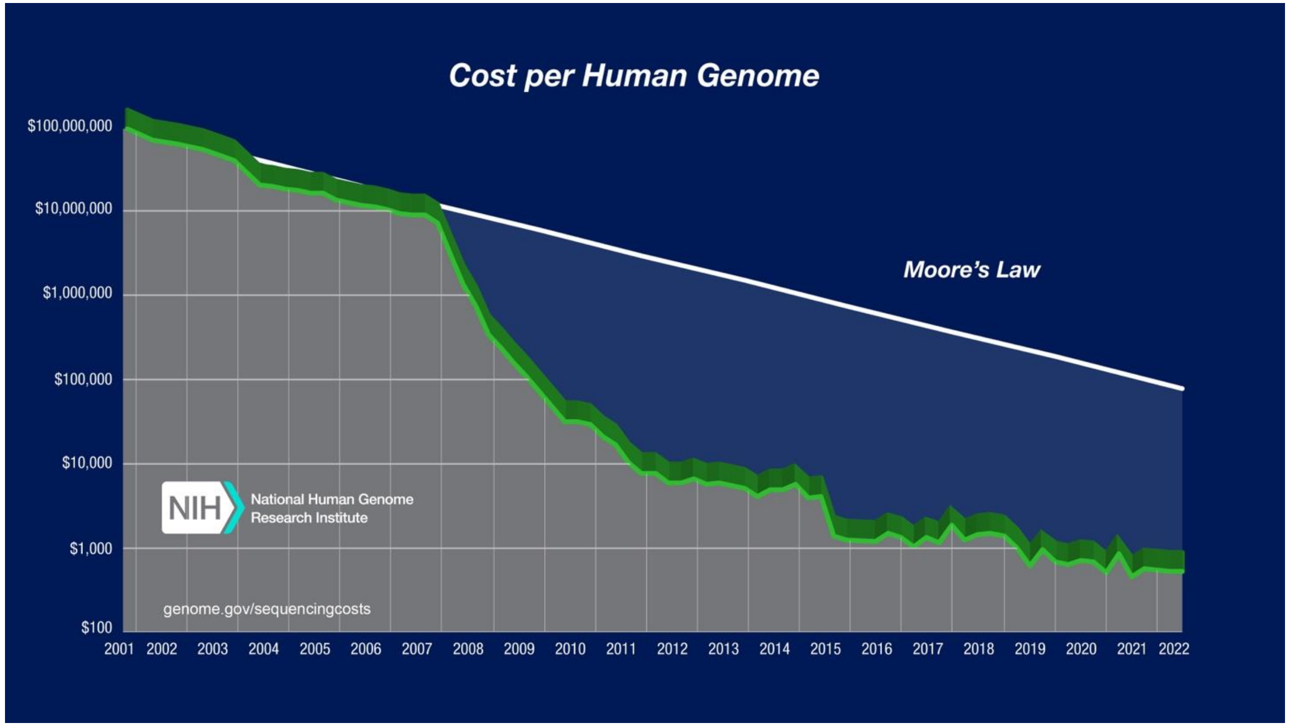
GWAS

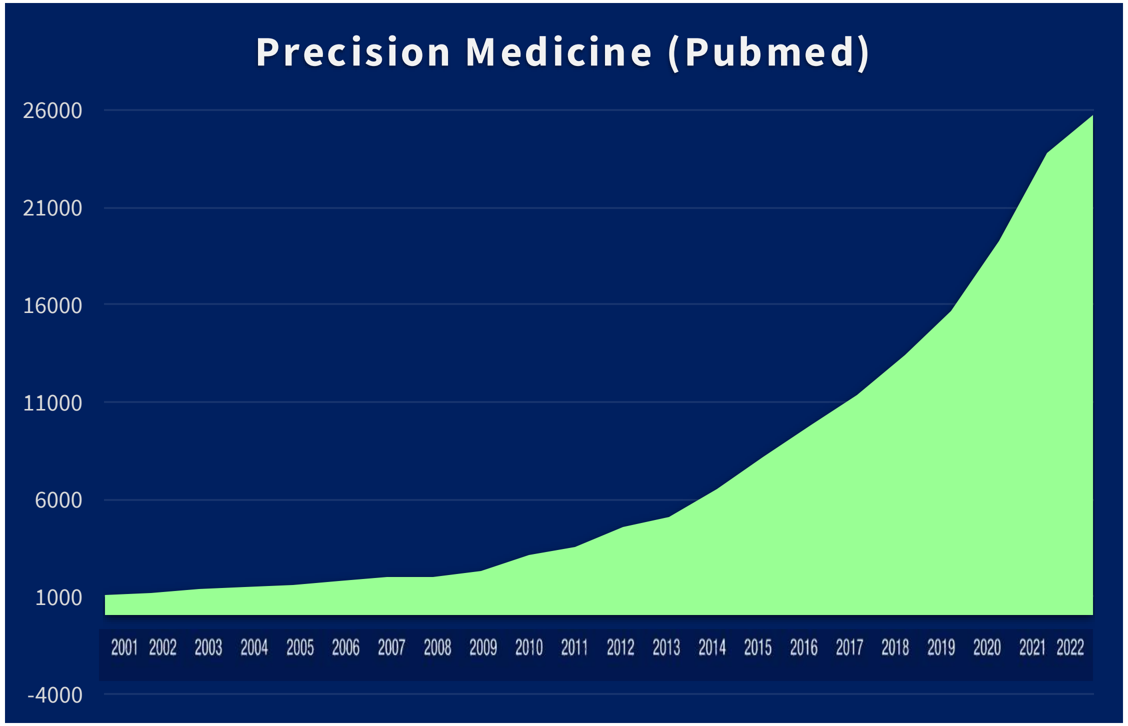
Top genetic variants
e.g. SNPs
(largest effect size)



Risk scoring

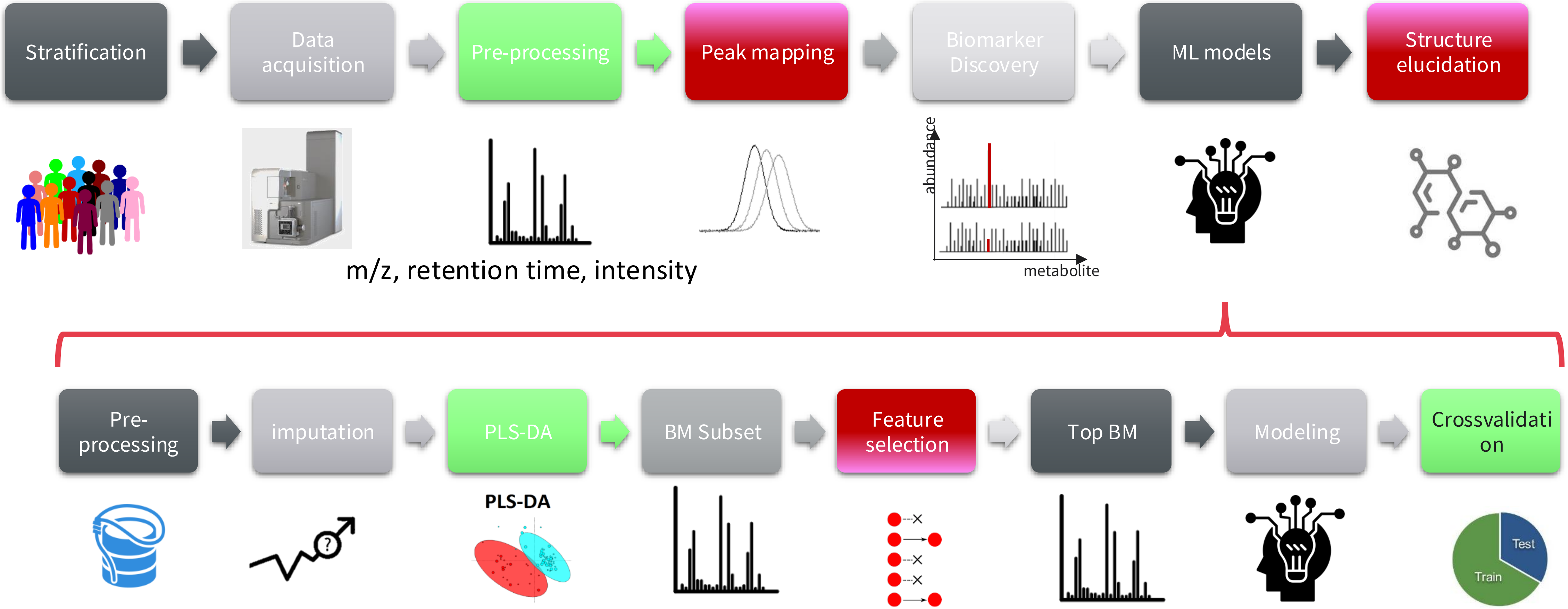
COST PER GENOME AND PRECISION MEDICINE PUBLICATIONS





Source of the image: NIH

UNTARGETED METABOLOMICS FOR FINDING NOVEL BIOMARKERS

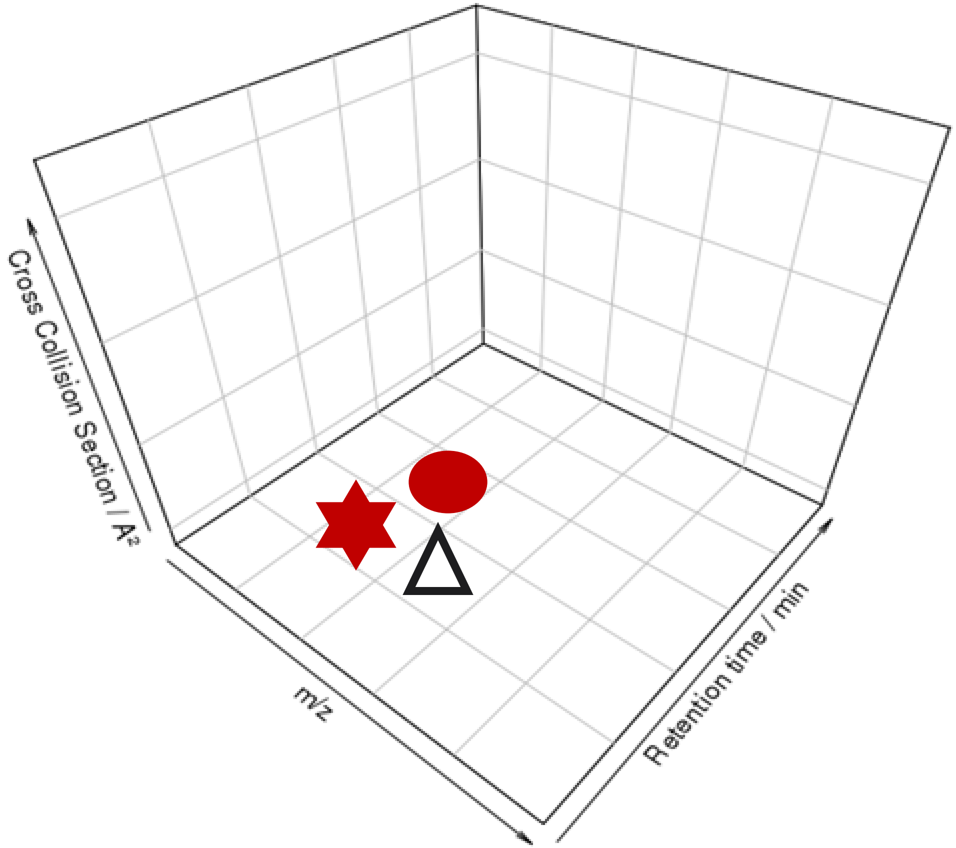


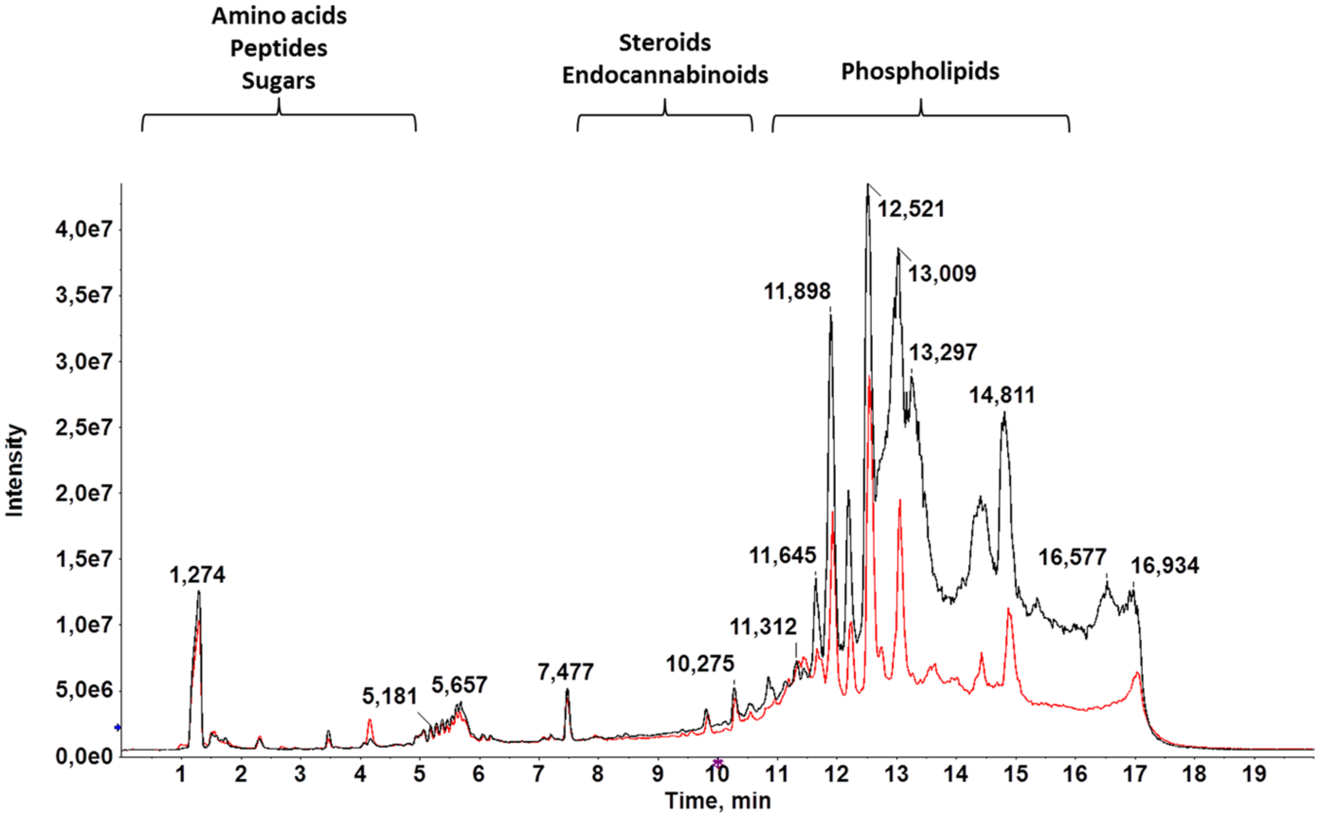
Stratification → Data acquisition → Pre-processing → Peak mapping → Biomarker Discovery → ML models → Structure elucidation

Pre-processing → imputation → PLS-DA → BM Subset → Feature selection → Top BM → Modeling → Crossvalidation

Source of the image: Schwerk (2023)

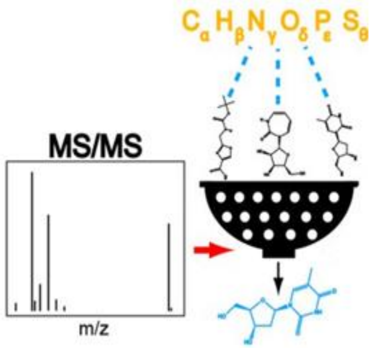
METABOLOMICS DATA: THREE DIMENSIONAL SPACE

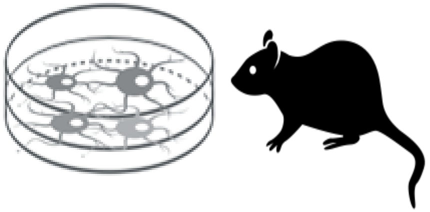


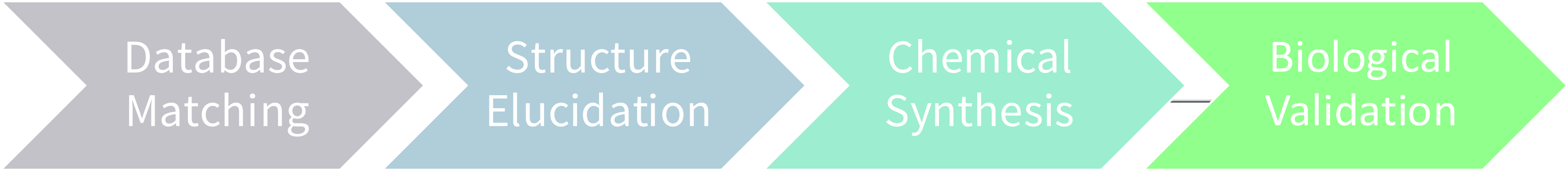


- **m/z (Mass-to-Charge Ratio):** the mass of a molecule divided by its charge
- **Retention Time:** the duration a metabolite takes to pass through the chromatography column before being detected
- **Intensity/ abundance:** concentration of metabolite in sample

EXPLAINING METABOLITES







MS FINDER
CFM-ID
CSI: FingerID
MetFrag

Database search
In silico fragmentation

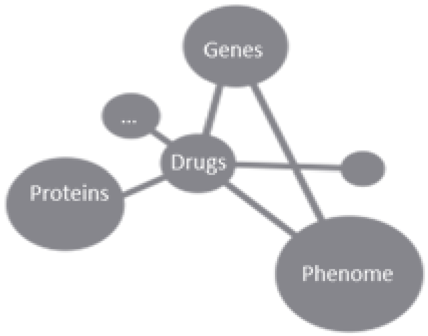
PRECISION DRUG DISCOVERY: PARKINSONS DISEASE

Cohorts

- GWAS
- Metabolome
- RNAseq
- Phenomics

✓**Big data**

Data



Intelligent Analysis

- Multi-omics
- AI + bioinformatics
- Medical experts
- Knowledge graph

✓**Actionable insights**

Disease Pathways

Target Discovery

- Genes
- Proteins
- RNAs
- Metabolites

✓**Druggable & novel**

Patient cell lines

Target Drug Screen

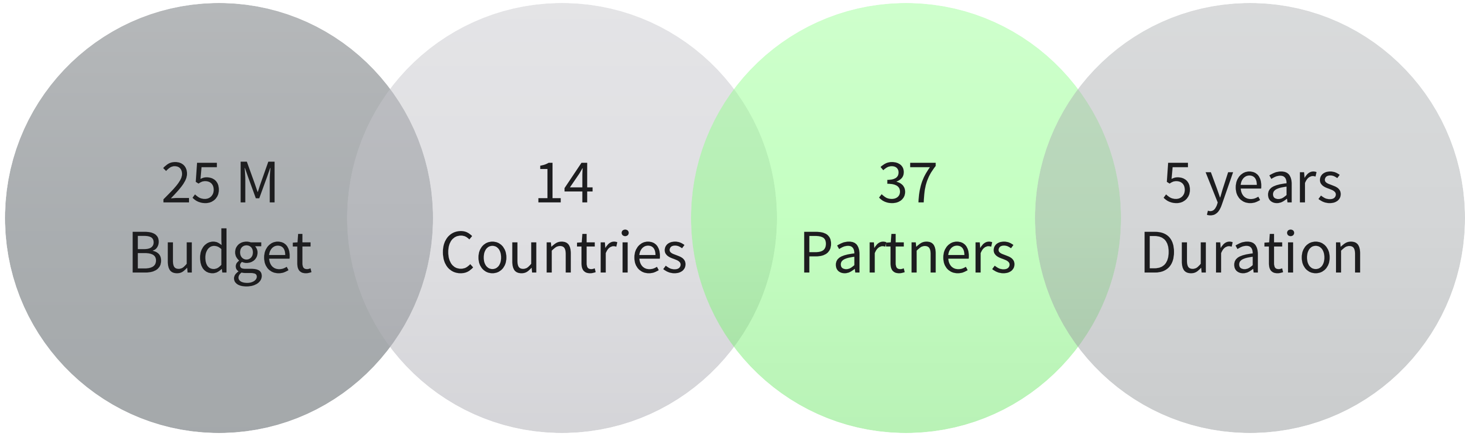
- Target validation
- Drug optimization
- High-throughput screening

✓**Precision treatment**

SCREEN4CARE

- **Genetic newborn screening:**
  - Early diagnosis of genetic RDs
- **Digital tools:**
  - Symptom checker
  - EHR algorithms
- **Infrastructure**:
  - Federated ML

SHORTENING THE PATH TO RARE DISEASE DIAGNOSIS BY USING NEWBORN GENETIC SCREENING AND DIGITAL TECHNOLOGIES



25 M Budget

14 Countries

37 Partners

5 years Duration

Improved the accuracy and speed of diagnosis

https://www.screen4care.eu/

#3

Take-Home-Message & Discussion

- **AI as a medical game changer:**
  - Access to digital data
  - High quality data

- **Expected AI revolution:**
  - Fastest growing healthcare data source
  - Text data and LLMs

THANK YOU

☎ Prof. Dr. Anne Schwerk

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