Data science supporting medicines and healthcare development

Industry perspective and Novartis experience

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Pavia
26th October 2018

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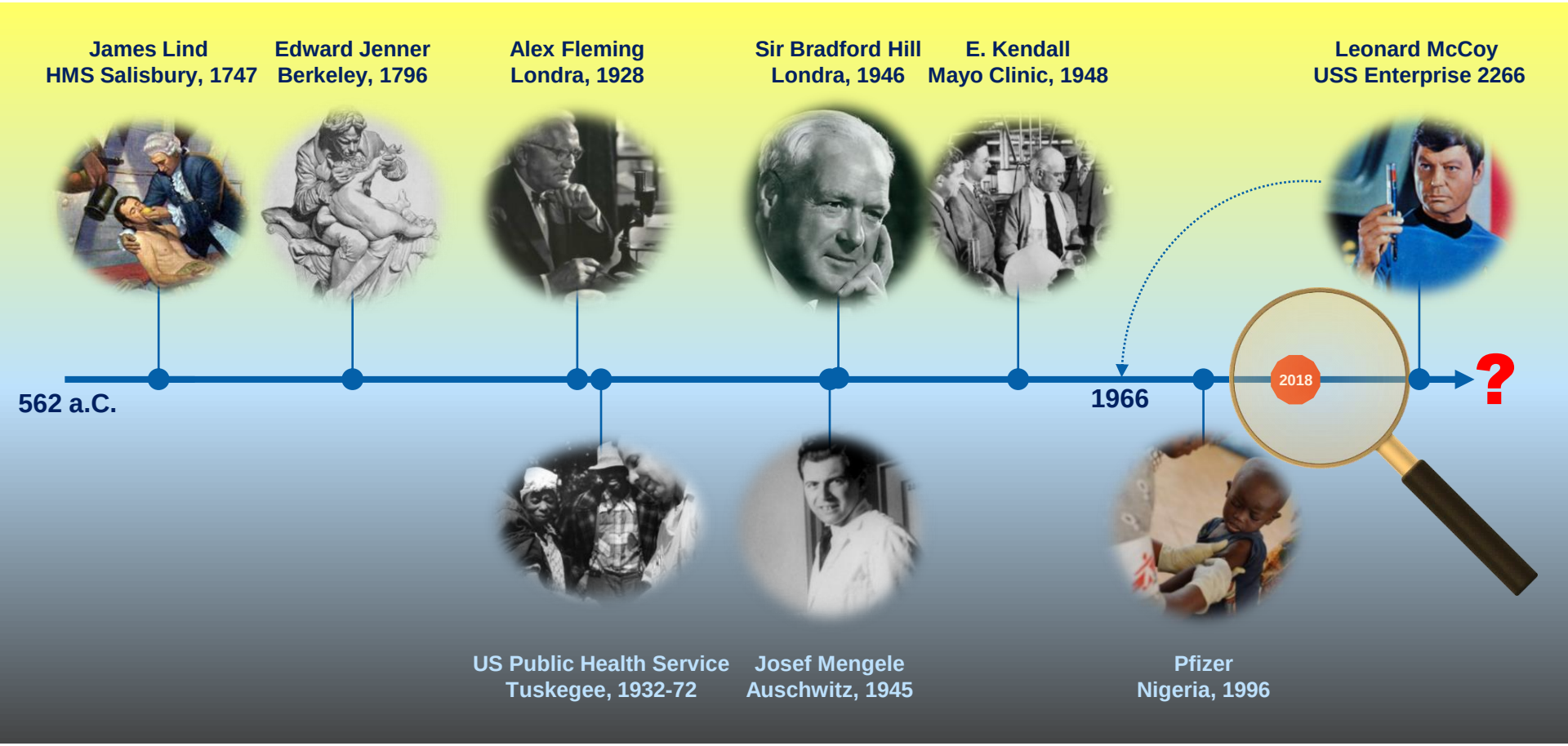
The history of Clinical Research is studded with lights and shadows…



"The charm of history and its enigmatic lesson consist in the fact that, from age to age, nothing changes and yet everything is completely different."
Aldous Huxley

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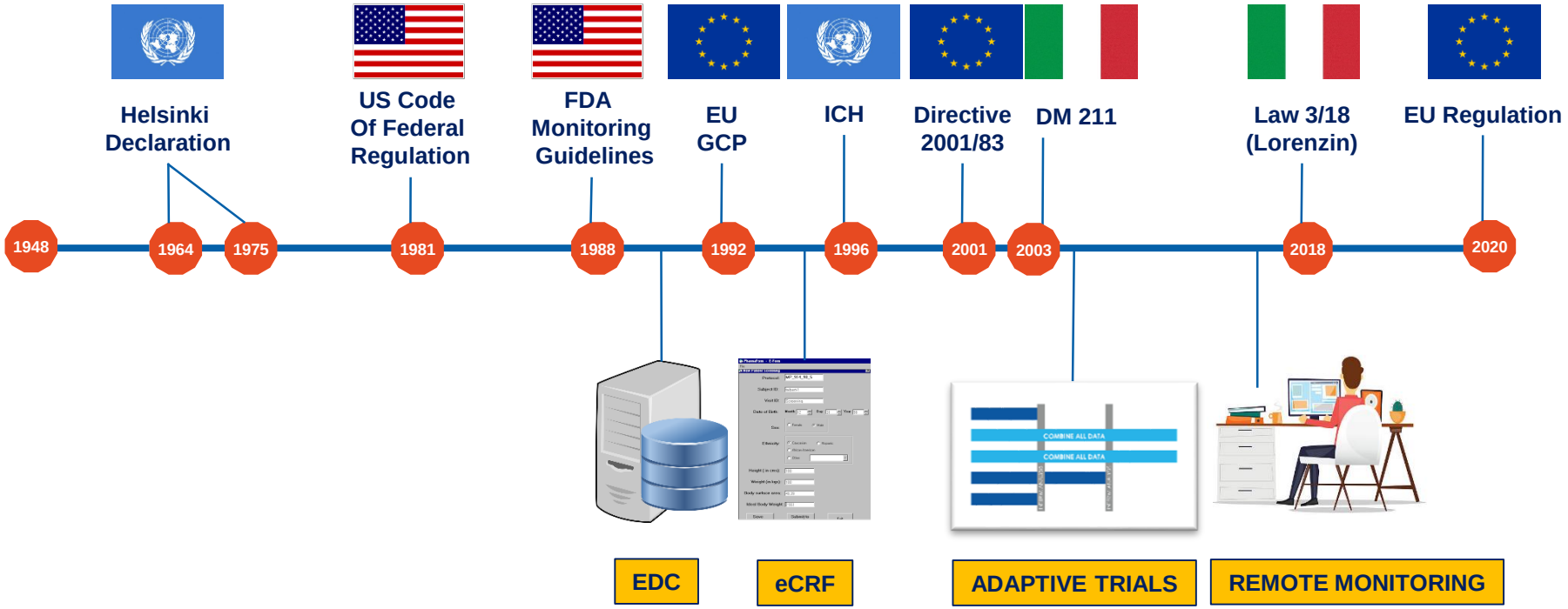
Since 1948 the way of doing clinical research has undergone few changes (although substantial)

FUNDAMENTAL STAGES OF THE EVOLUTION OF THE MODALITIES FOR THE CONDUCT OF CLINICAL RESEARCH IN THE LAST 70 YEARS



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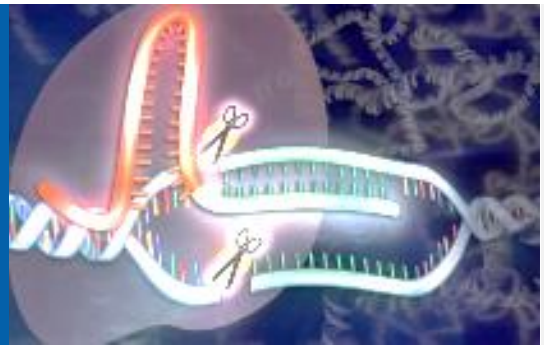
Looking to the future, the external context appears dynamic but complex

Opportunities



- High medical needs
- New pharmacological sciences
- Demand for curative therapies and improvement of quality of life
- Digital revolution and big data

Challenges

- Increase of competitiveness
- Increasing standard of care
- Pressure on price and access
- Reputation of the industry

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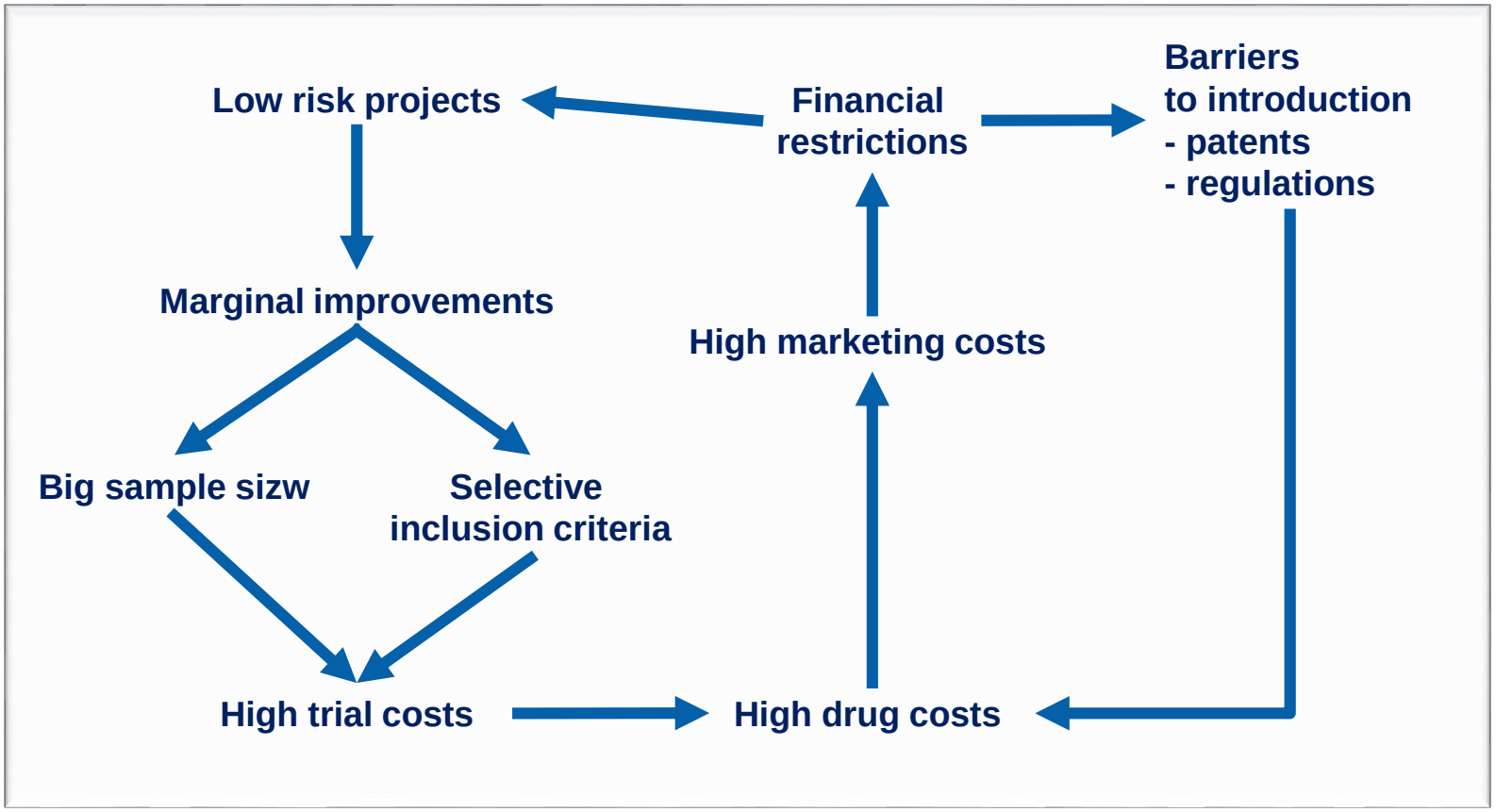
Much greater efforts are needed to achieve small improvements in selected populations

A VICIOUS CIRCLE WITH LARGE REPLACEMENTS ON THE COSTS OF RESEARCH



Global pharmaceutical development and access: critical issues of ethics and equity, MEDICC Review 2011

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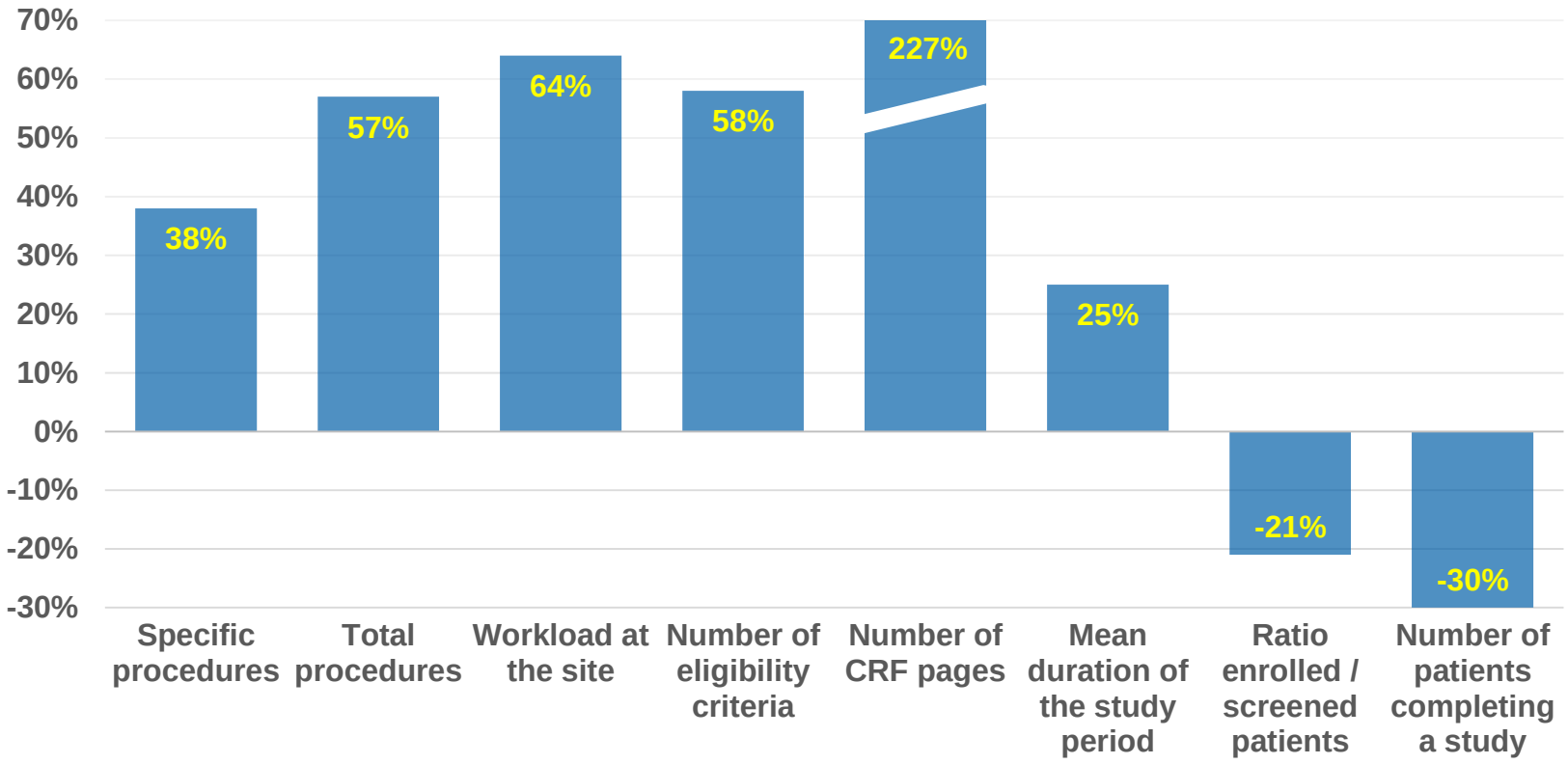
The complexity of clinical research is therefore constantly increasing …

VARIATIONS OBSERVED IN CLINICAL RESEARCH 2008-2010 VS 2000-2003



K.A. Getz, R.A. Campo, and K.I. Kaitin. "Variability in Protocol Design Complexity by Phase and Therapeutic Area." Drug Information Journal 2011; 45(4): 413-420.

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.....the R&D costs are constantly increasing

Table 8. Mean Cost per Study Volunteer per Visit.

All Therapeutic Areas	2001-2005, $	2006-2010, $	2011-2015, $	Change Between 2001-2005 and 2011-2015, %
Phase I protocols	1259	1547	1873	49
Phase II protocols	862	1185	1386	61
Phase III protocols	728	949	978	34
Phase IV protocols	617	878	758	23
Mean overall cost	747	1016	1065	43
CoV	.98	.62	.68	

Therapeutic Innovation & Regulatory Science 2018, Vol. 52(1) 22-28

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Technologies drive changes…

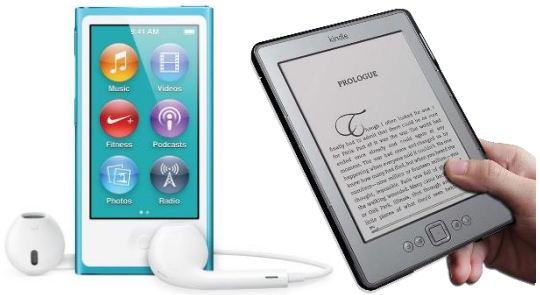
20 YEARS AGO…

TO BUY MUSIC OR BOOKS

- Provider-centric
- Not so convenient
- Expensive

- Internet
- New devices
- Digitalization
- Access to data
- New competitors

TODAY



- Consumer-centric
- Convenient
- Cheap

CONDUCT A CLINICAL TRIAL

- Internet
- New devices
- Digitalization
- Access to data
- New competitors

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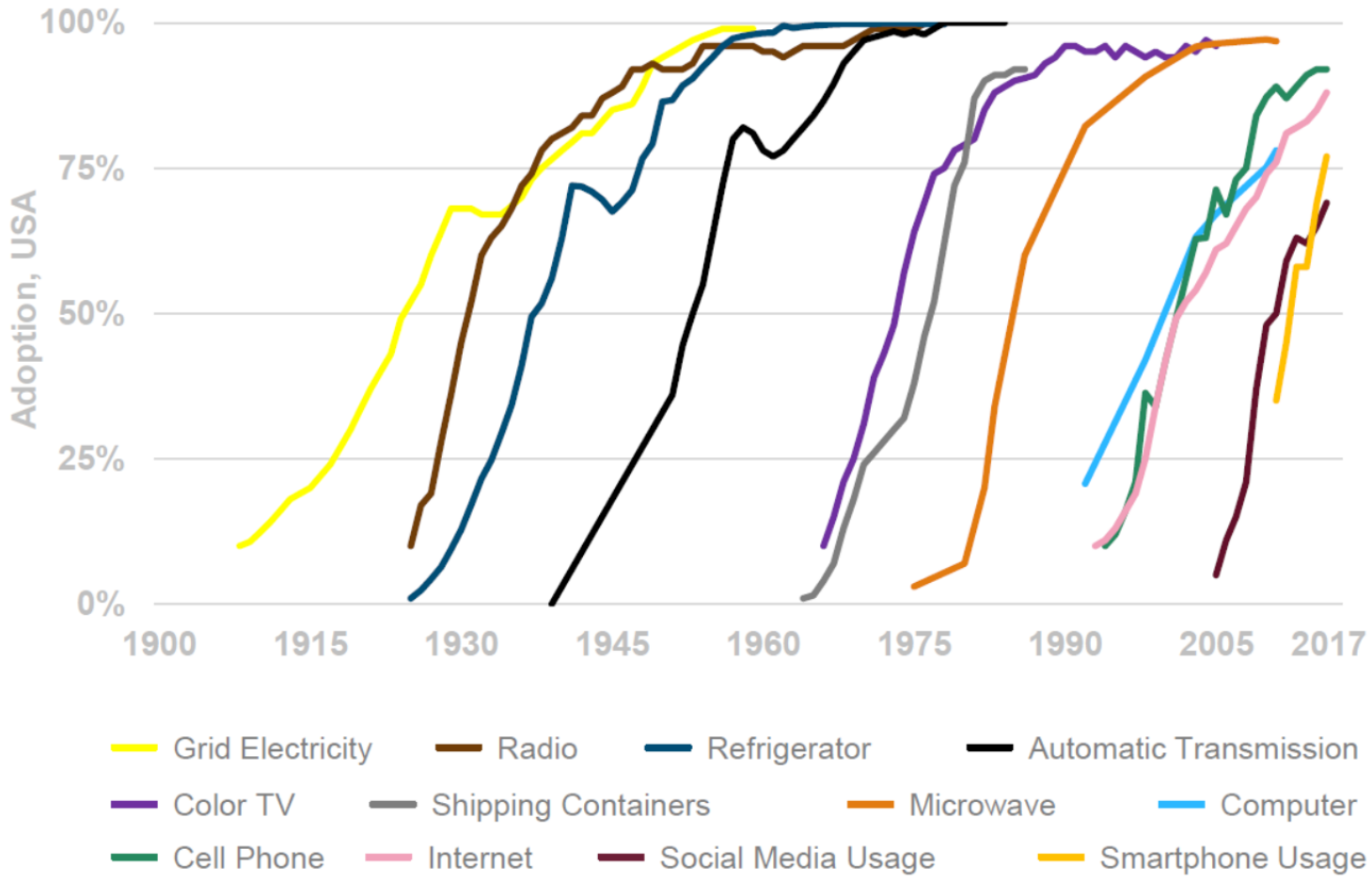
The adoption curves of new technologies are increasingly steep



Fonte: «Internet Trends 2018». Mary Meeker. Kleiner Perkins

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Digital technology innovation will change the clinical development of drugs

Digital technologies will redesign development by accelerating innovation and involving the entire health ecosystem in new ways of collaboration. We will focus on technologies that are likely to have the greatest impact:

Advanced Analytics
AA will be used to acquire knowledge and to demonstrate value and achieve better results, such as new treatments and technologies

Automation

RPA (Robotic Process Automation) is the next-generation solution for automating repetitive jobs

Augmented / Virtual Reality

AR and VR will blur the boundaries between the digital and the physical world.

Artificial Intelligence

AI and Machine Learning will have a huge impact on R & D, e.g. identifying biomarkers and treatments

Blockchain

Blockchain is a technology that creates trust in the digital world based on cryptography and distributed register

Internet of Things / Sensors

The Internet of Things connects objects to communicate, perceive, or interact with the object's state or environment

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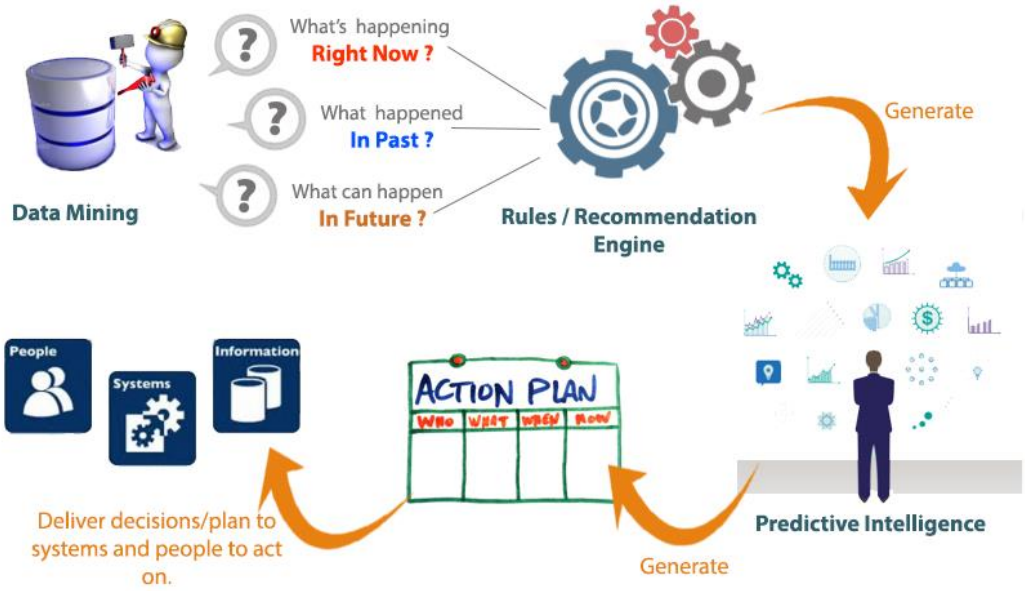
Advanced Analytics in Drugs R&D



In **pipeline management**, insights from simulations and competitive intelligence analysis can help optimize the portfolio and prioritize projects.

In **asset management**, analysis based on different scenarios and workload prediction can help optimize processes and resource utilization.

In **early development,** AA methods can help discover genotype / phenotype links to accelerate translational medicine, or develop criteria (biomarkers) for development strategies.

In **development**, AA can help optimize study design, patient recruitment and trial execution

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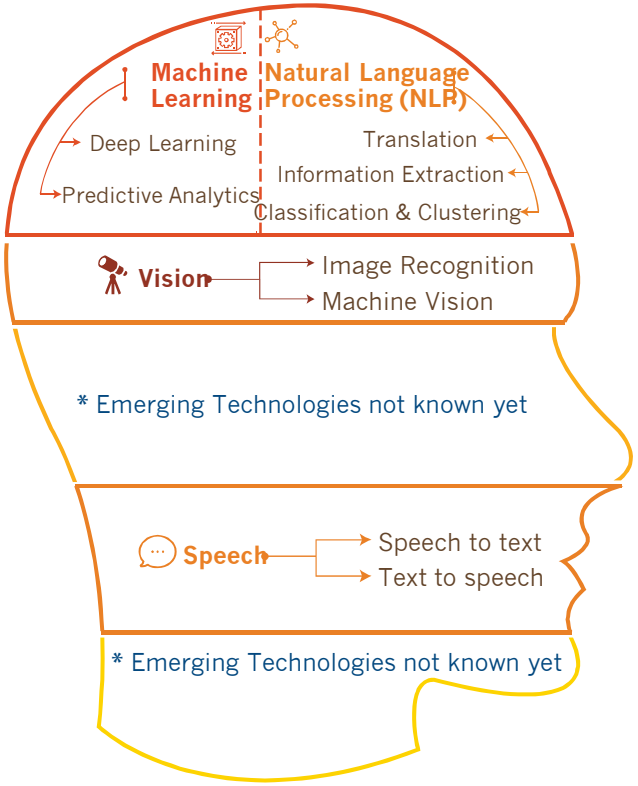
Artificial Intelligence can support decision making in the discovery and development phases



In the **discovery of new drugs**, to speed up the selection phases through in silico modeling of existing molecular and clinical data and the screening of literature and public data to identify new candidate molecules and predict the probability of success.

In **clinical development**, to facilitate communication with experimenters and patients by means of voice assistance services (chat bots) to answer questions, provide ad hoc support and remember medication intake; to interpret and react automatically to emotional states of patients through emotional detection.

In **pharmacovigilance**, to allow the automation of the identification of adverse events by analyzing and detecting the signals coming from all the collected data.

On **real-world data**, to analyze the impact of treatments, extract patient biological data to determine drug response or disease evolution.

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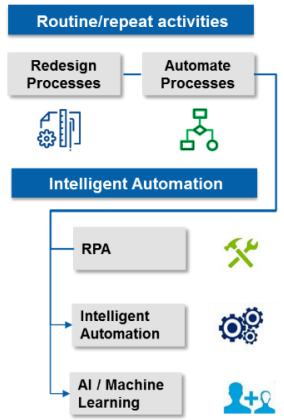
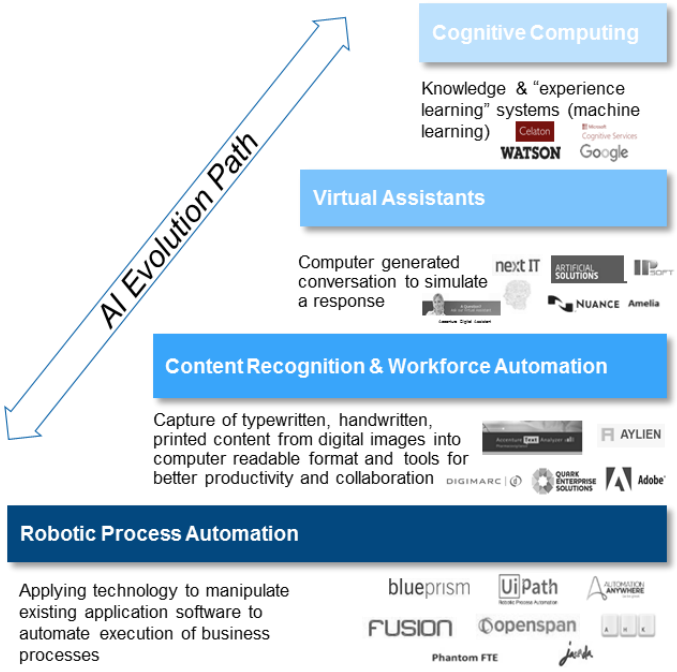
Automation can be used in development to increase productivity and reduce costs





Intelligent automation in laboratories, particularly in routine diagnostic tasks, can increase efficiency, eliminate errors and reduce costs.

Electronic data acquisition for clinical trials can be supported by collection, cleaning and processing of automated data. Automating digital archiving of documents and electronic signatures can reduce costs.

Intelligent automation of processing and reporting of adverse events can increase the efficiency and transparency of Pharmacovigilance.

The automation of regulatory processes can support the compilation of information necessary for submission and accelerate and harmonize workflows

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eSource/ePRO: data collection, transmission and visualization technologies

How would it be if...

- ... the investigator could copy all the visits from the beginning of the study, or specific parts, on his tablet, just before the patient shows up for the next visit?
- ... could the centers enter the data only once, and not transcribe them from the medical records (paper or electronic) in the EDC systems?
- ... could we see the data within a few hours of their collection by the center or by the patient?
- ... could the number of monitoring visits at the center be reduced through the use of remote monitoring and risk-based visits algorithms?

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eSource will bring clear benefits to data collection and management

Traditional approach to data collection and management in clinical trials


PATIENT VISIT


DATA ENTRY
IN THE CLINICAL FOLDER


DATA ENTRY
IN CRF / eCRF


MONITORING
DATA SOURCE
VERIFICATION


DATA CLEANING

QUERIES


DATA ANALYSIS

MONITORING / SDV

Mobile digital platforms for collecting clinical data


PATIENT VISIT


DATA ENTRY
IN DIGITAL DEVICE


SIGN OFF
DATA IN EDC


DATA CLEANING


DATA ANALYSIS

REMOTE MONITORING

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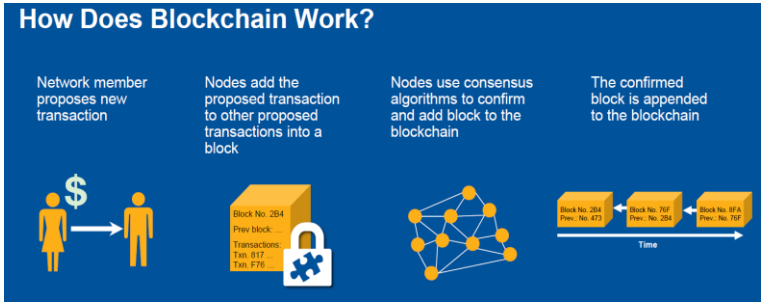
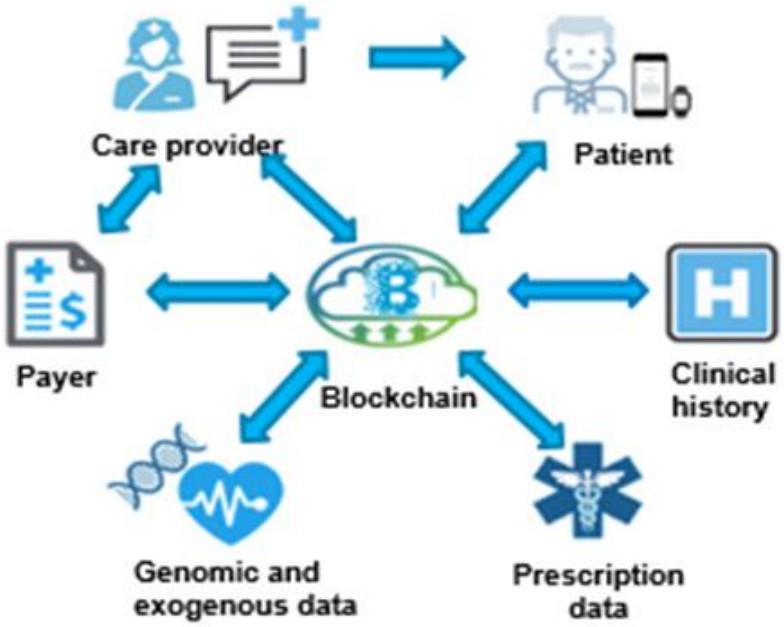
Blockchain in Development: possible multiple applications





- As proof of the integrity and traceability (audit-trail) of data collected in clinical trials from data collection to statistics produced.
- To provide the patient with the opportunity to share their health data with researchers in a controlled manner. In the coming years there will be an increasing number of blockchain applications on EHR data.
- To share clinical trial data with research organizations and healthcare organizations, or to share adverse events and supply chain tracking with regulatory bodies.

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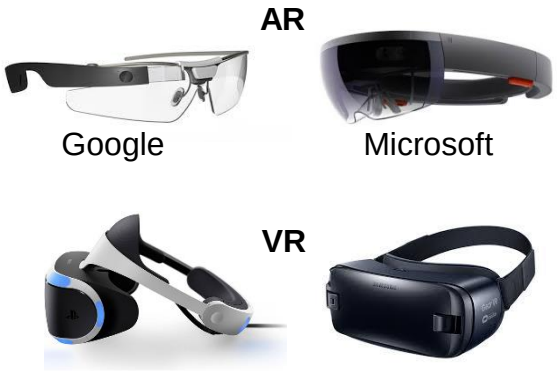
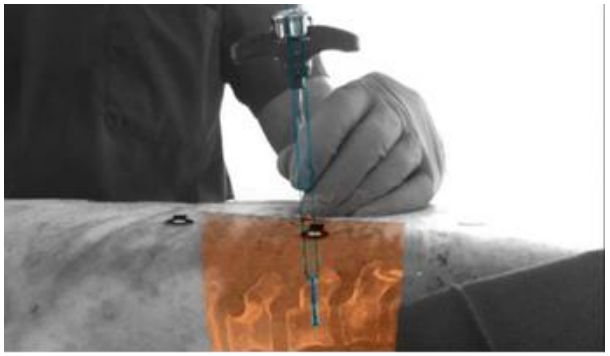
Virtual and augmented reality will fade the boundaries between the digital and the physical world





How would be if...

... through augmented reality a nurse who has to do a withdrawal could visualize the patient's veins projected directly on the arm? Or could a doctor performing a medical procedure see "through" the skin of his patients as if he had X-ray vision?

... use virtual reality for the digital training of investigators or patients on how to follow study protocols? Or to simulate "a patient's day in life" with researchers or patients to improve the design of the trial? Or to enable virtual collaboration between centers of a study or decentralized (site-less) trials?

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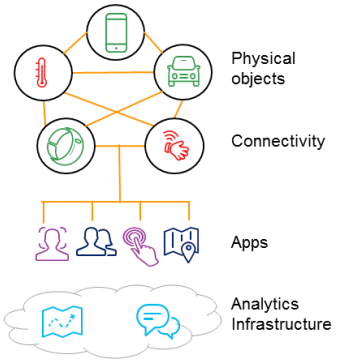
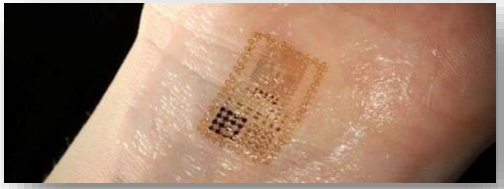
Internet of Things and Sensors - for patient monitoring, drug delivery, diagnostics …



How would be if...

... could we use wearable or implantable devices that allow continuous monitoring of vital signs / clinical data, and help understand the patient's condition and activate an action if necessary, reducing the need for medical examinations during the study?



... could we replace long center infusions with wearable devices or patches that administer the drug slowly at home, also allowing to measure if and how much drug was taken, absorbed and at what time, and potentially how the patient responds to the drug?

... could we replace invasive procedures with self-tests that can be used when it is more convenient and wherever you are?

... could we measure PK levels or liver function at home, at work, or in the nearest pharmacy, using a drop of blood on a piece of paper?

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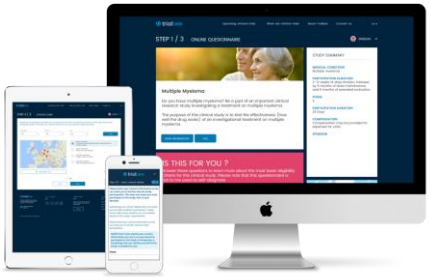
The patient is the protagonist of clinical research

How would be if...

... it was much easier and more convenient to participate in a clinical study, and was therefore accessible to many more people to contribute to the development of new treatments?

... could you participate in a clinical study from your home, or from your workplace, or going to the nearest and convenient locations such as the municipal pharmacy, or even a shopping center?



... the smartphone, iPad, or internet browser was the "companion" for the study, help to understand what to do and when, and explain the effects of the treatment whenever you need it?

... during the study, all the data collected - at home, at work, at the municipal pharmacy - were constantly monitored to ensure greater safety and effectiveness of the treatment?

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THE DIGITAL REVOLUTION IS HERE

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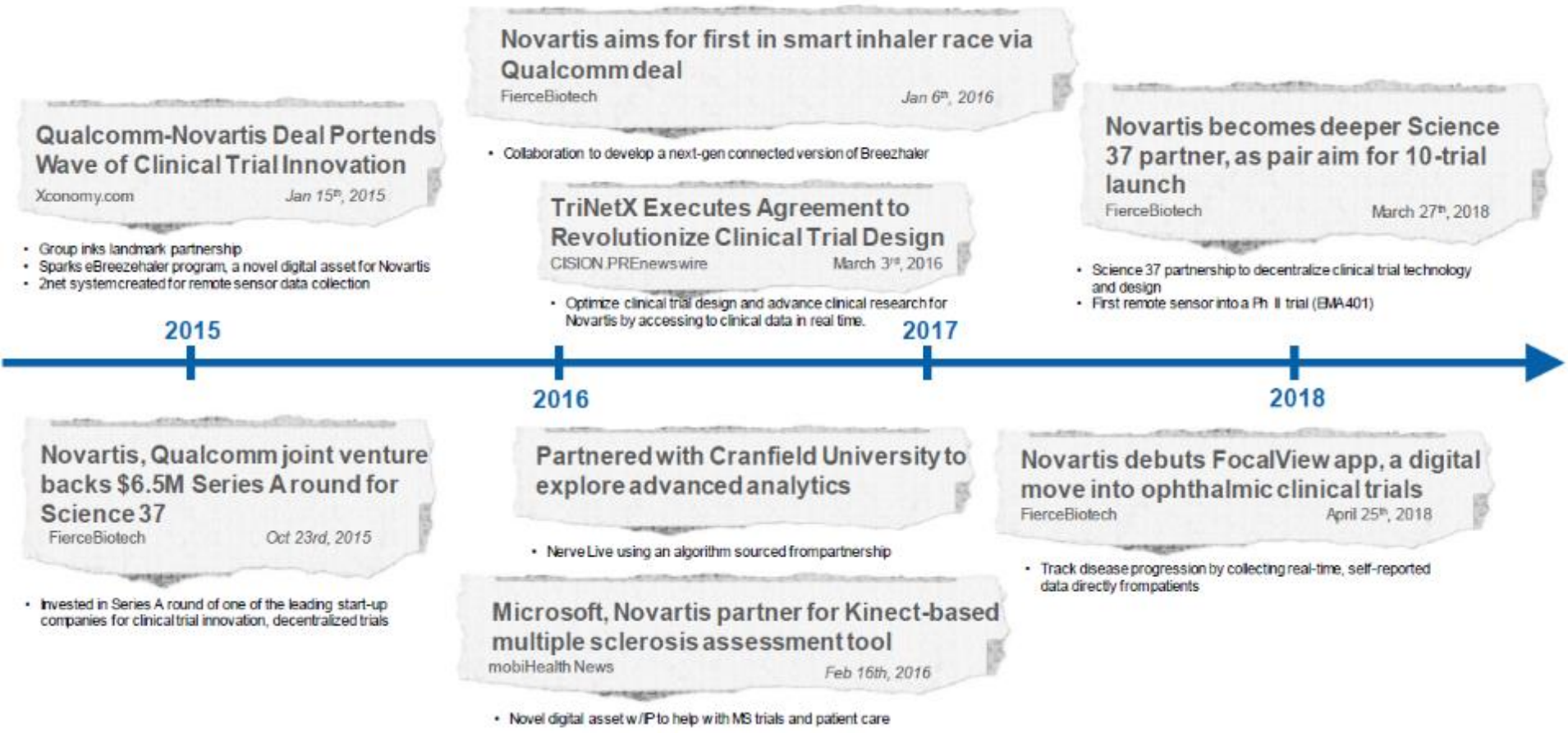
Novartis has signed numerous high tech collaborations in the last years



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We are reshaping the science of innovation

Drug Discovery → **Clinical Trials** → **Late Stage**

AI target identification
Partnership with Pear Therapeutics

In-silico disease modelling

Bringing clinical trial to the patient
Alliance with Science 37

Data science revolution
Nerve Live

Impactful Real World Evidence
Real world real time data

Integrated Healthcare for a value-based system

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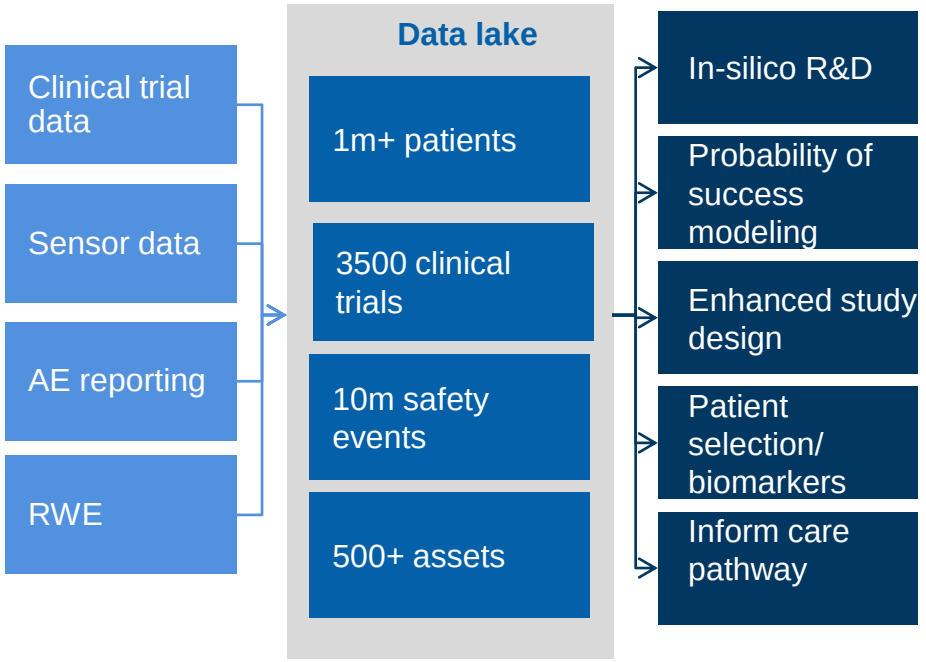
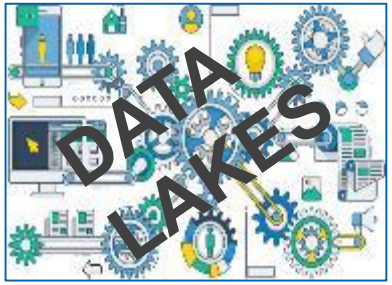
Data lakes are created through new generation scientific data platforms that allow the use of innovative applications





Pooling our vast repositories of data, applying machine learning and predictive analytics to gain insights and optimize all elements of clinical development

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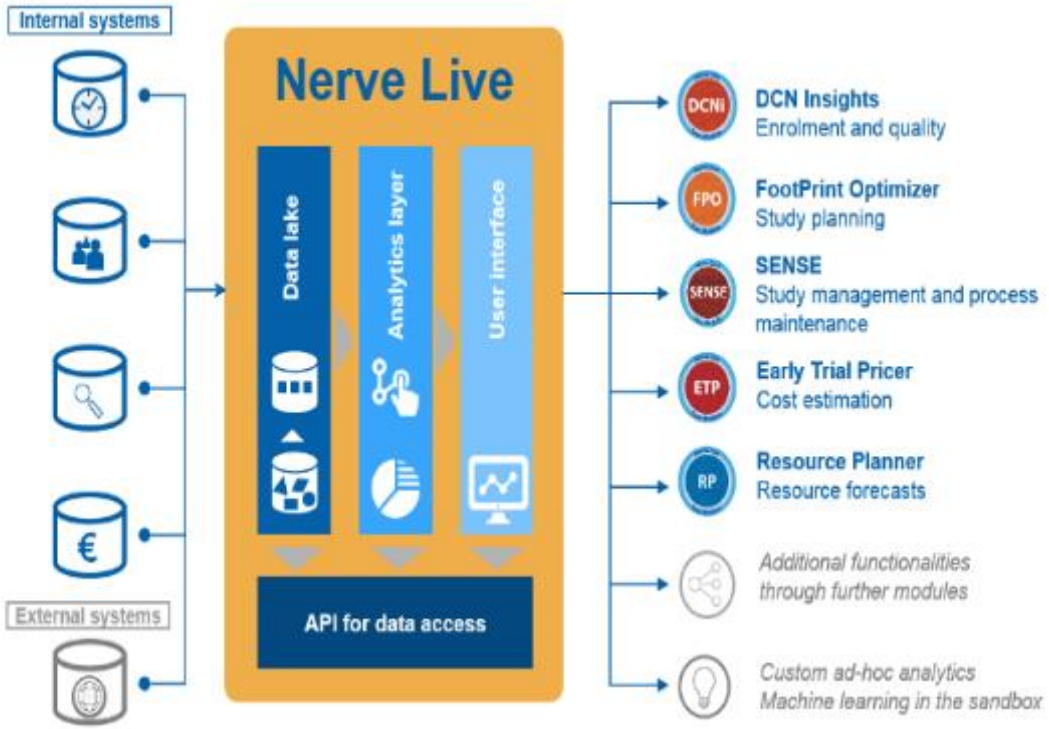
NERVE Live aims to transform performance by leveraging the ability of digital technology to optimize predictive analysis on available data



«...the brain of Nerve Live is an advanced analytics engine to process data and distll new, actionable insights from it»

«...with this system we can now apply algorithms that can use past and current data to make performance predictions that could enable to make better informed and faster decisions»

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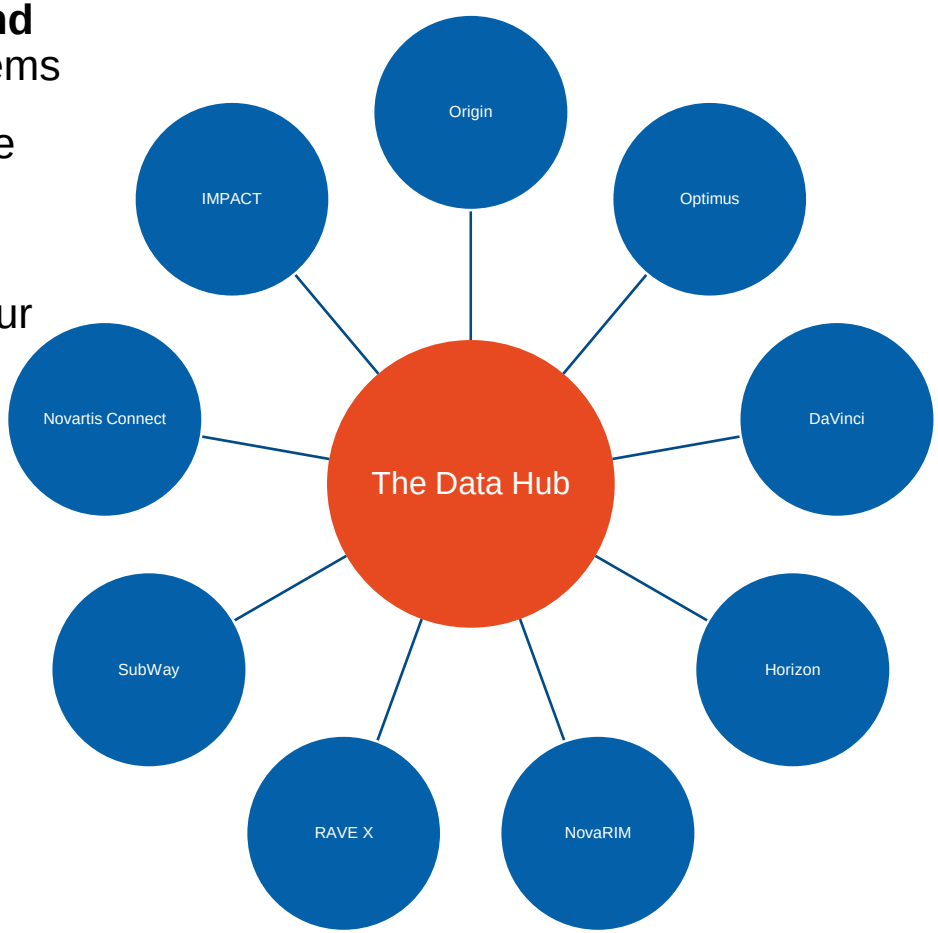
STRIDE is consolidating our base of connected and unified technological systems

- Long-term replacement, **alignment and enhancement** of our technology systems
- Through nine programs touching all we do across clinical trials
- Will deliver one connected, seamless, leading-edge system, as capable as our people



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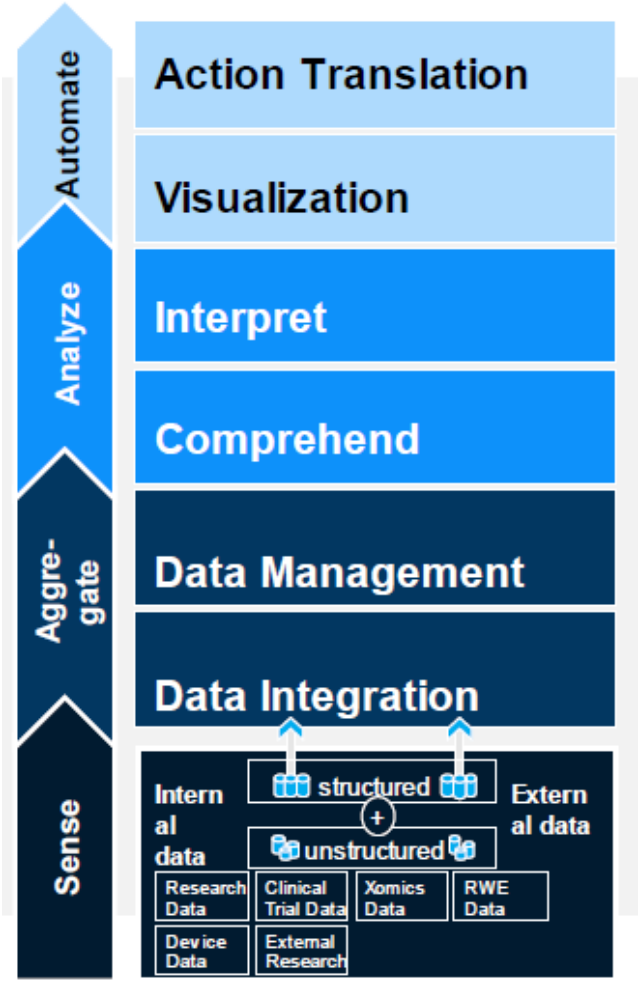
Data 42 integrates information from the research, development and RWE of more than 20 Novartis drugs



Data 42 will provide insights that will allow shorter studies tailored to the needs of the patient, which will allow the determination of the optimal dose and treatment regimes and will ultimately identify potential new applications for existing drugs.

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Science 37 helps to build the clinical study around the patient …

Traditional Site Based Approach

VS

Science 37 Patient-Centric Metasite™ Model

… moving the research center from the hospital to the patient's home

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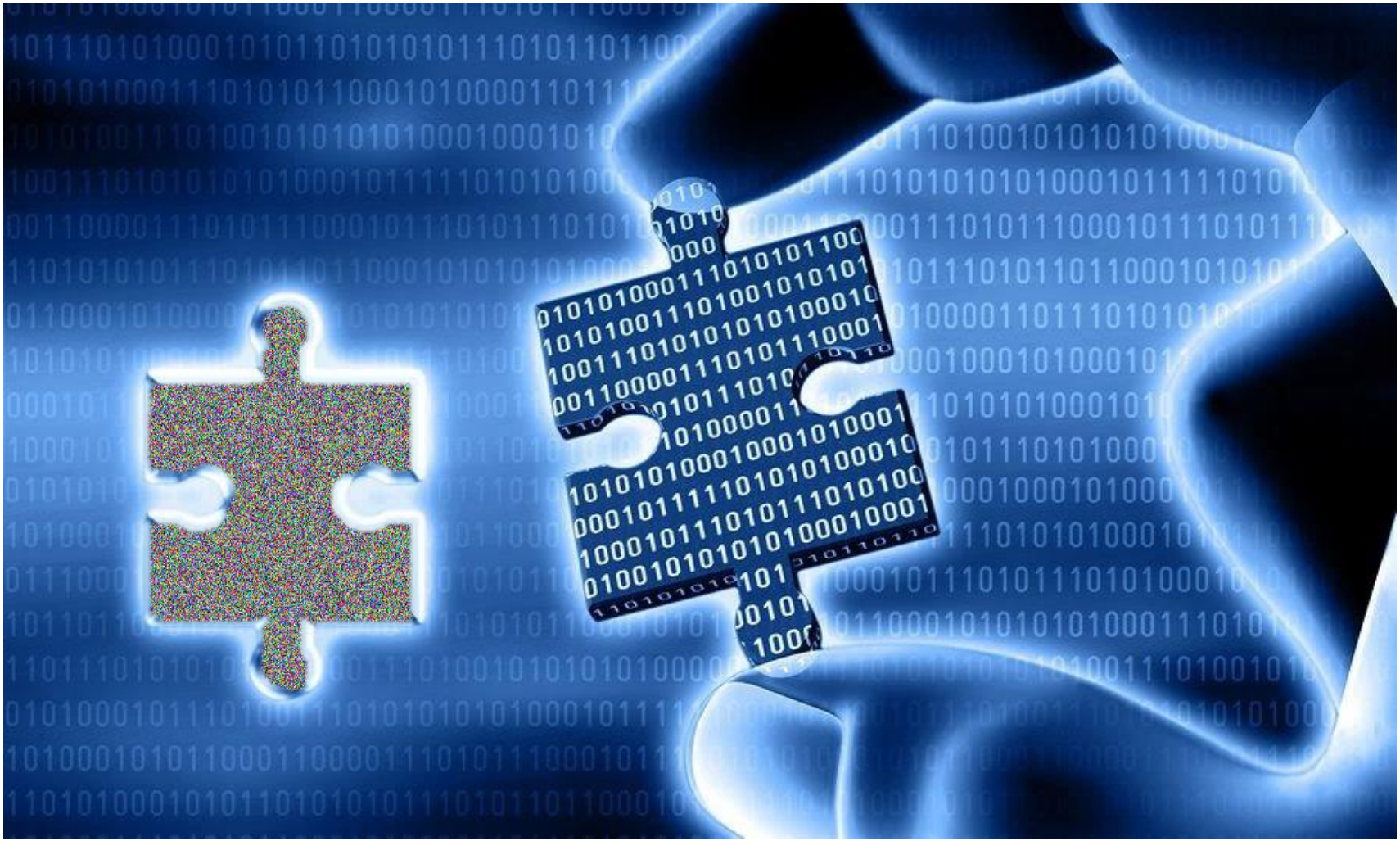
Can technology alone solve all problems or other challenges await us?



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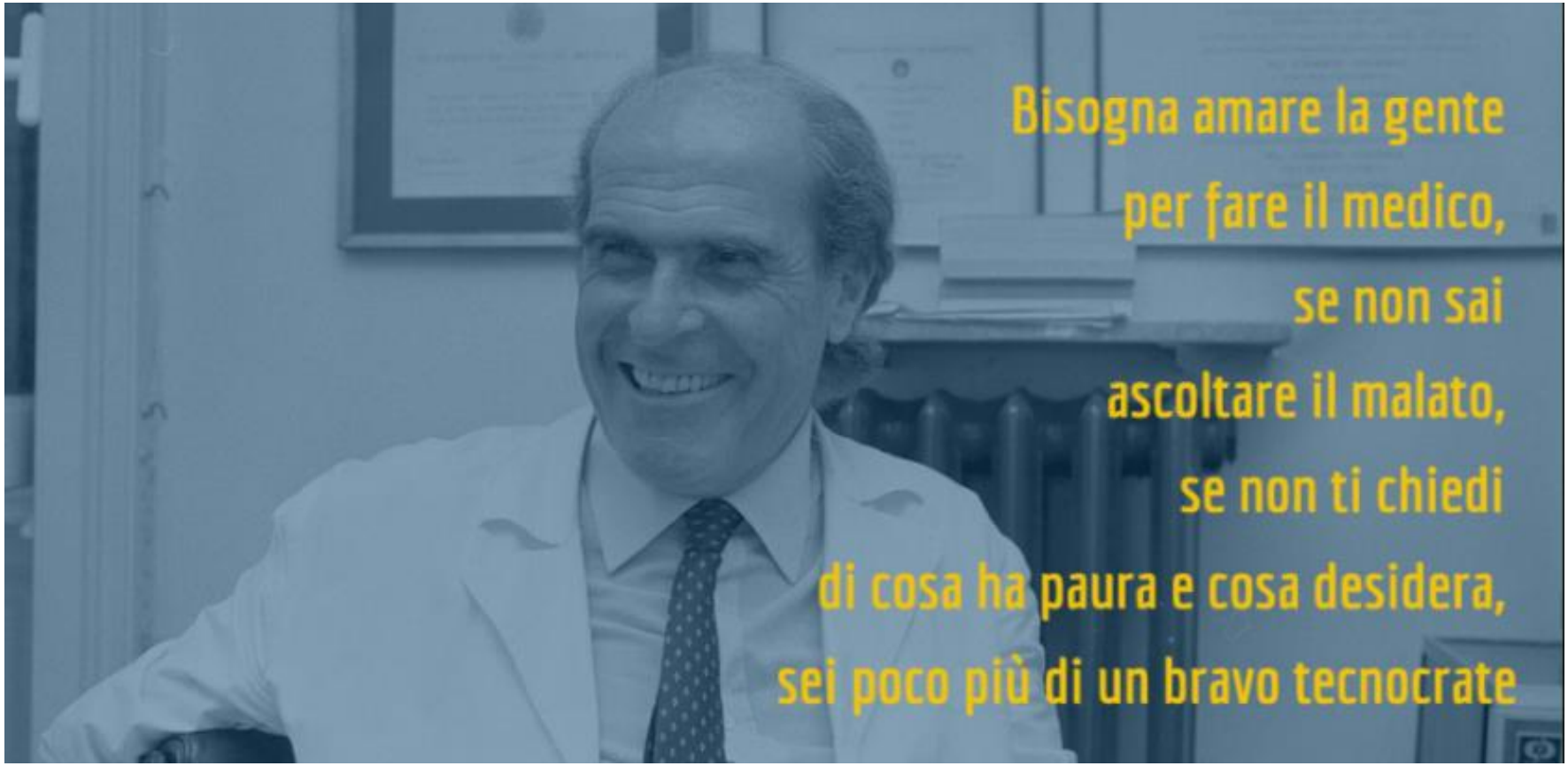

You have to love people to be a doctor, if you can not listen to the patient, if you do not ask what you're afraid of and what you want, you're little more than a good technocrat

Umberto Veronesi

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Thank you for your attention

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