FONDAZIONE
PER LA RICERCA FARMACOLOGICA
GIANNI BENZI
ONLUS

Machine Learning Systems applied to health data and systems

An overview on technological development, regulatory challenges and ethical issues

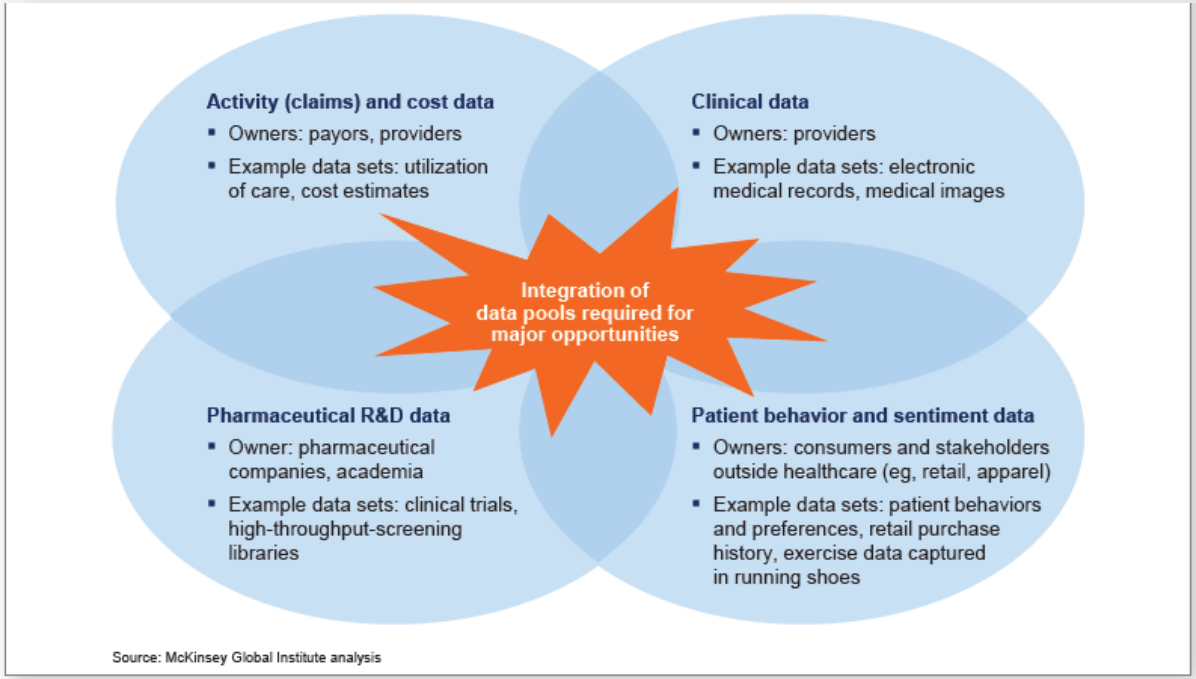
Fedele Bonifazi
Elisabetta Volpe
Giuseppe Digregorio

Fondazione per la Ricerca Farmacologica Gianni Benzi onlus

Via Abate Eustasio, 30 – 70010 Valenzano (BA) Tel.: +39 080 2052499
www.benzifoundation.org

FONDAZIONE
PER LA RICERCA FARMACOLOGICA
GIANNI BENZI
ONLUS

*The importance of **health data**, a potential **treasure** trove for medicine and pharmacology*



It's a capital mistake to theorise before one has data

[Sherlock Holmes, A Study in Scarlett (A. C. Doyle)
suggested by Leveraging Data in Healthcare, R.M.S. Busch CRC Press]

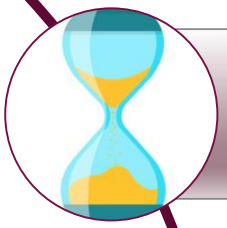
FONDAZIONE
PER LA RICERCA FARMACOLOGICA
GIANNI BENZI
ONLUS

Sources for Health Data

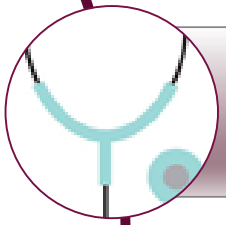
- Clinical Records
- Laboratory
- Imaging data
- Medical Device
- Claims data
- Pharmacies
- Survey
- Clinical trials
- Social Data
- "Omics" data (genome, transcriptome, metabolome, proteome, exposome, methylome and microbiome)
- Internet of things (IoT)
- *Social networks and apps*

FONDAZIONE
PER LA RICERCA FARMACOLOGICA
GIANNI BENZI
ONLUS

The Health Data Challenge

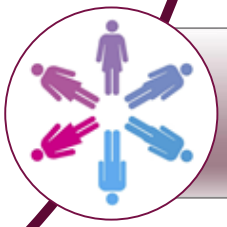


For the first time in history a large amount of data is available.



All this data cannot be used by individual physician.

Explosion in knowledge is beyond use for any capacity.



It would be helpful to use the latest techniques in managing data.

FONDAZIONE
PER LA RICERCA FARMACOLOGICA
GIANNI BENZI
ONLUS

Processing all the available data to **unlock** their full potential in current clinical practice.

The **amount** and **heterogeneity** of Health data require new and powerful tools.

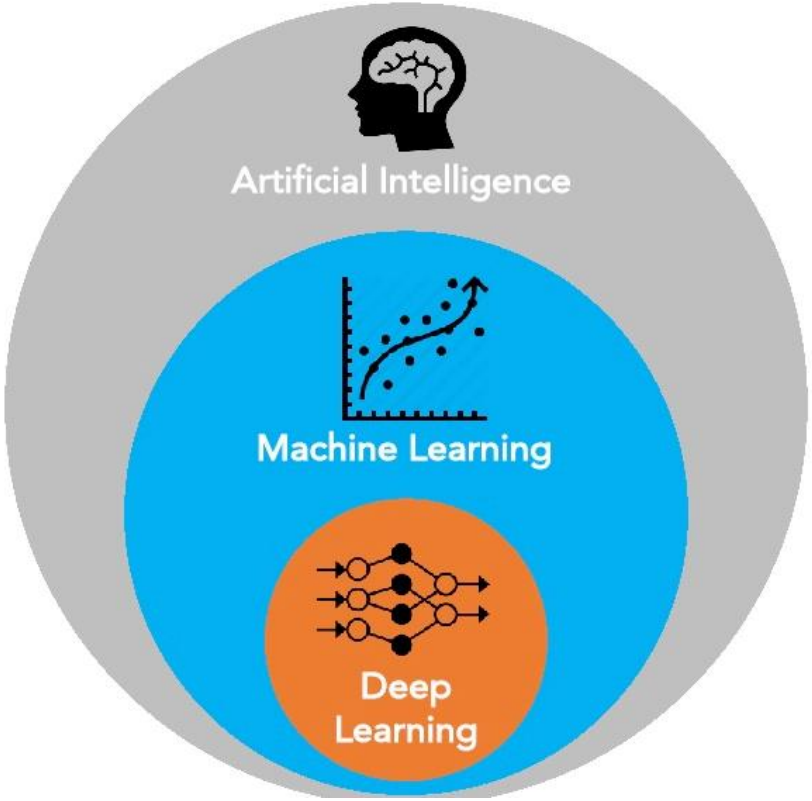
FONDAZIONE
PER LA RICERCA FARMACOLOGICA
GIANNI BENZI
ONLUS

What tools does technology offer us to manipulate data and extract information?

Artificial Intelligence is a a branch of computer science dealing with the simulation of human intelligence processes. These processes include learning, recognizing and self-correction.

Machine Learning is a field of Artificial Intelligence, focused on getting machines to act without being programmed to do so.

Deep Learning is a class of machine learning algorithms that uses artificial neural networks (ANNs) with many layers of nonlinear processing units for learning data representations.

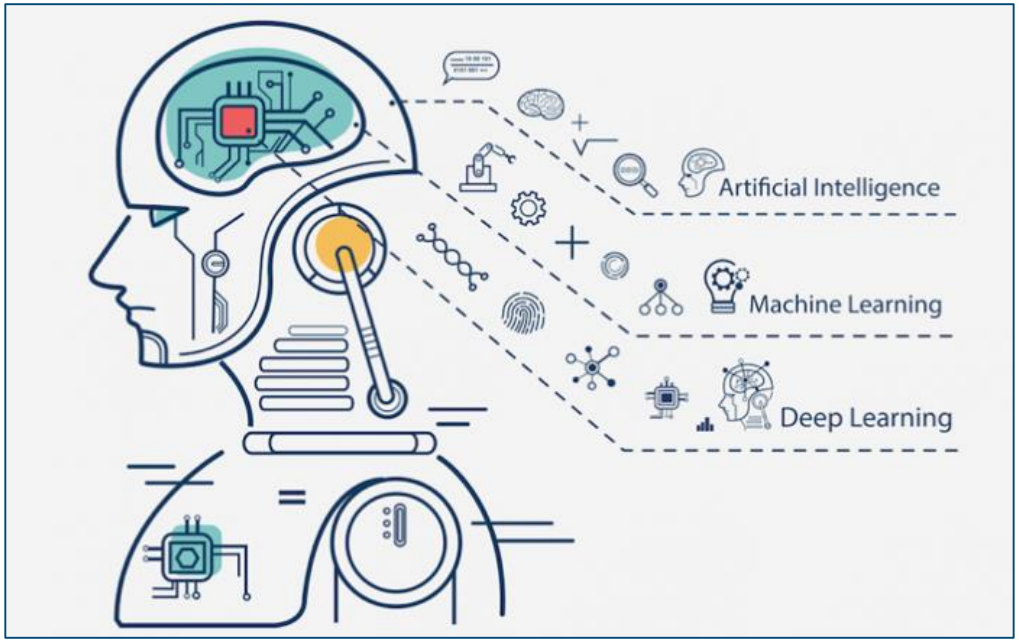


FONDAZIONE
PER LA RICERCA FARMACOLOGICA
GIANNI BENZI
ONLUS

Why using AI techniques ?

To **support** the decision-making process

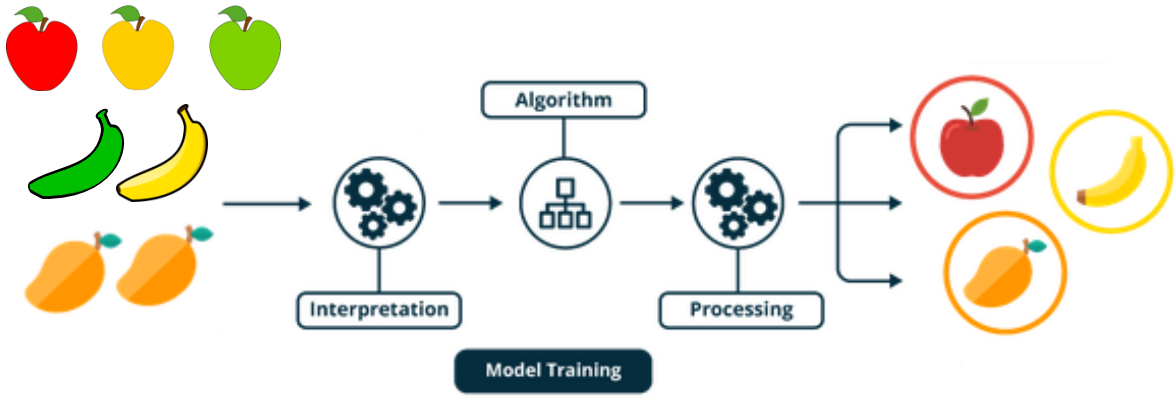
- ✓ better decisions
- ✓ in less time
- ✓ reducing human medical errors



…These processes include learning, recognizing and self-correction

FONDAZIONE
PER LA RICERCA FARMACOLOGICA
GIANNI BENZI
ONLUS

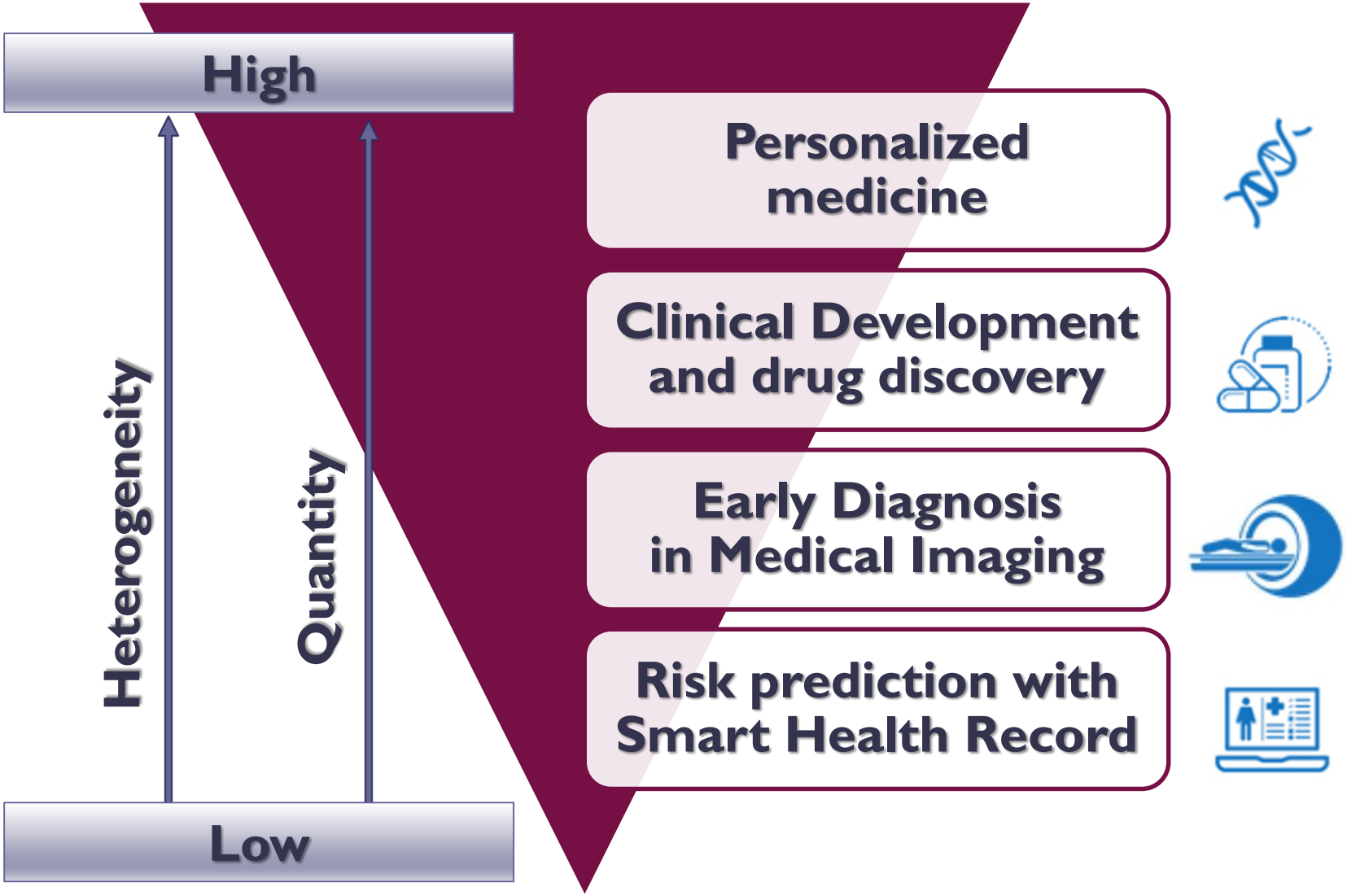
What is Machine Learning?



- ✓ Let's pretend to create a **system** that answers the question of whether a fruit is an apple, a banana or an apricot.
- ✓ This question is called "**model**" and the model is created via a process called **training**.
- ✓ After data training, the model is able to recognize a **new item** submitted to the system.

FONDAZIONE
PER LA RICERCA FARMACOLOGICA
GIANNI BENZI
ONLUS

Current and future Machine Learning Health data applications



FONDAZIONE PER LA RICERCA FARMACOLOGICA GIANNI BENZI ONLUS

PLOS ONE

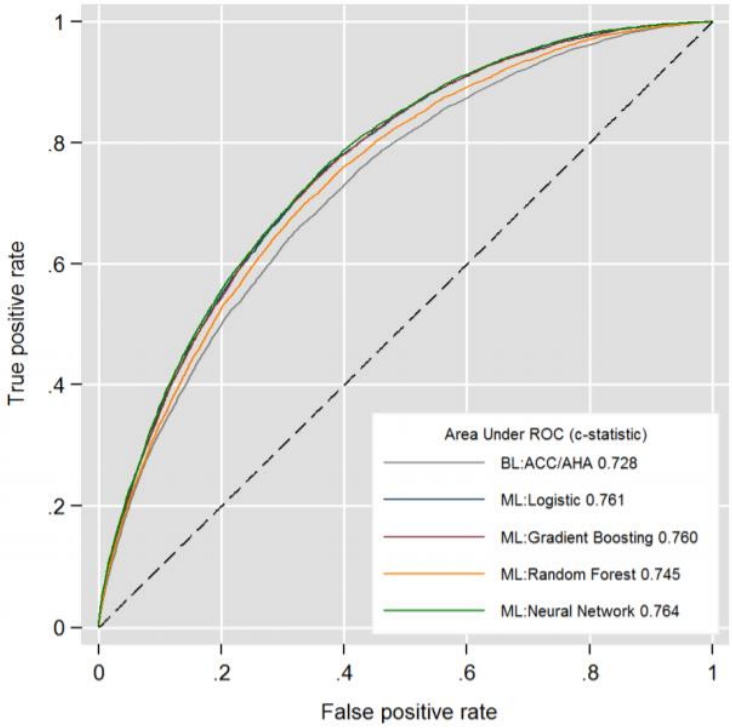
Risk prediction

Machine Leaning offers opportunity to improve accuracy by exploiting complex interactions between risk factors.
Can it improve cardiovascular risk prediction?

RESEARCH ARTICLE

Can machine-learning improve cardiovascular risk prediction using routine clinical data?

Stephen F. Weng[1,2☯]*, Jenna Reps[3,4☯], Joe Kai[1,2‡], Jonathan M. Garibaldi[3,4‡], Nadeem Qureshi[1,2‡]



Machine-learning Algorithms			
ML: Logistic Regression	**ML: Random Forest**	**ML: Gradient Boosting Machines**	**ML: Neural Networks**
Ethnicity	Age	Age	Atrial Fibrillation
Age	Gender	Gender	Ethnicity
SES: Townsend Deprivation Index	Ethnicity	Ethnicity	Oral Corticosteroid Prescribed
Gender	Smoking	Smoking	Age
Smoking	*HDL cholesterol*	*HDL cholesterol*	Severe Mental Illness
Atrial Fibrillation	HbA1c	Triglycerides	SES: Townsend Deprivation Index
Chronic Kidney Disease	Triglycerides	Total Cholesterol	Chronic Kidney Disease
Rheumatoid Arthritis	SES: Townsend Deprivation Index	HbA1c	*BMI missing*
Family history of premature CHD	BMI	Systolic Blood Pressure	Smoking
COPD	Total Cholesterol	SES: Townsend Deprivation Index	Gender

April 4, 2017 https://doi.org/10.1371/journal.pone.0174944

FONDAZIONE PER LA RICERCA FARMACOLOGICA GIANNI BENZI ONLUS

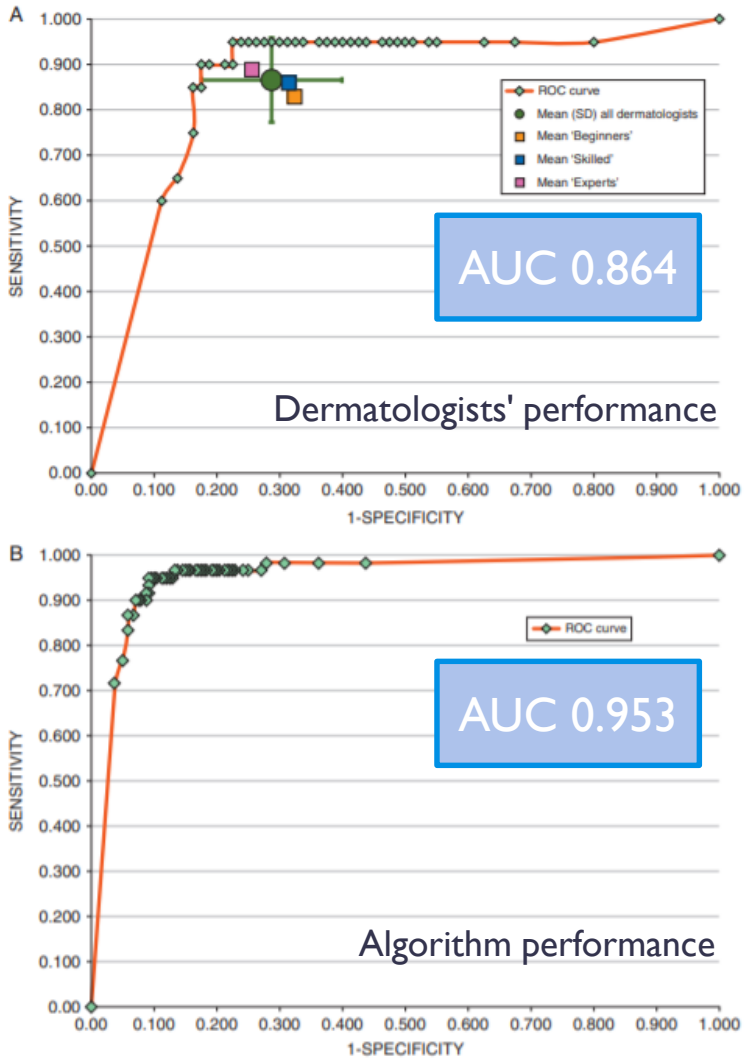
ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Early Diagnosis

ORIGINAL ARTICLE

Man against machine: diagnostic performance of a deep learning convolutional neural network for dermoscopic melanoma recognition in comparison to 58 dermatologists

H. A. Haenssle[1*,†], C. Fink[1†], R. Schneiderbauer[1], F. Toberer[1], T. Buhl[2], A. Blum[3], A. Kalloo[4], A. Ben Hadi Hassen[5], L. Thomas[6], A. Enk[1] & L. Uhlmann[7]



- ✓ The aim was to train, validate, and test a deep learning CNN for the diagnostic classification of dermoscopic images of lesions of melanocytic origin (melanoma, benign nevi) and to compare the results to an international group of 58 dermatologists (beginners, skilled and expert).
- ✓ A dataset of 100 images was collected created by the International Skin Imaging Collaboration (ISIC) melanoma project.

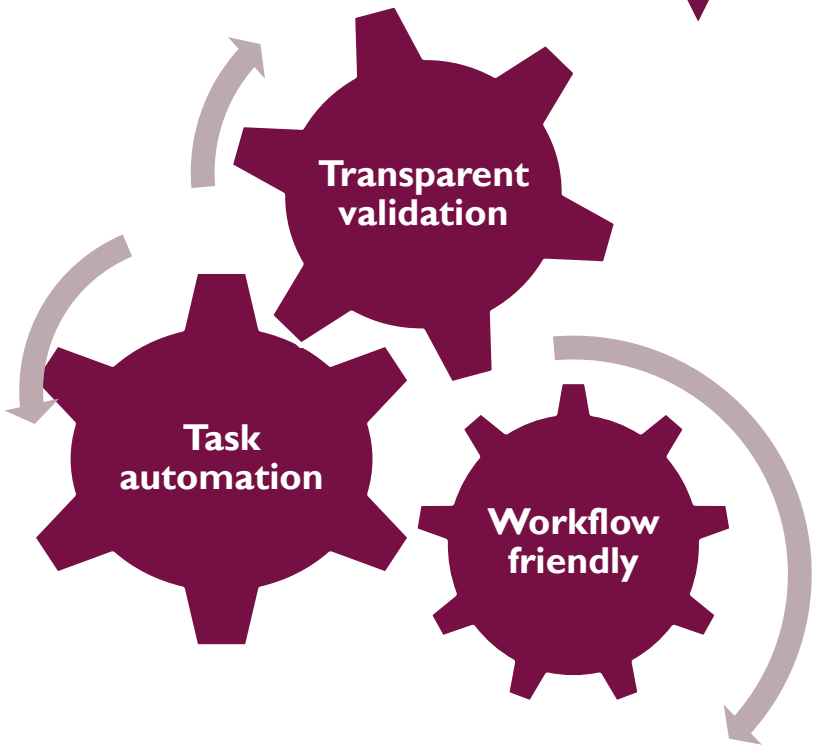
https://doi.org/10.1093/annonc/mdy166 Published online 28 May 2018

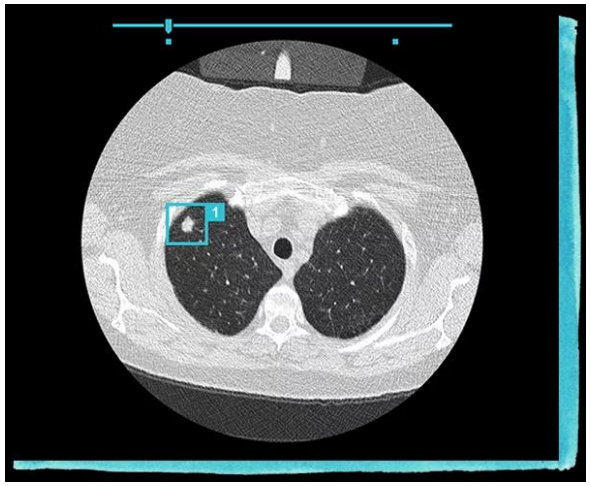
FONDAZIONE PER LA RICERCA FARMACOLOGICA GIANNI BENZI ONLUS

aidence
human sense in artificial intelligence

Early Diagnosis

- ✓ **Aidance** offers a software called **Veye Chest** which can help radiologists to detect, track and report on pulmonary nodules using machine learning.
- ✓ The pre-trained algorithm detects the presences or warning signs of pulmonary nodules within patient CT scans.





- ✓ **Veye Chest** has received the ***CE marking***, allowing its use in clinical practice across the EU.

An overview of Machine Learning in the European Pharmaceutical Industry

Tessella
·ALTRAN GROUP

Exscientia
DRIVEN BY KNOWLEDGE

healx

- ✓ **Algorithms for predicting which molecules would best bind to form stable compounds that can be applied to new drugs**
- ✓ **Software for discovering small molecules and compounds that could treat single and bispecific target diseases**
- ✓ **Drug discovery platform for developing rare disease treatments**

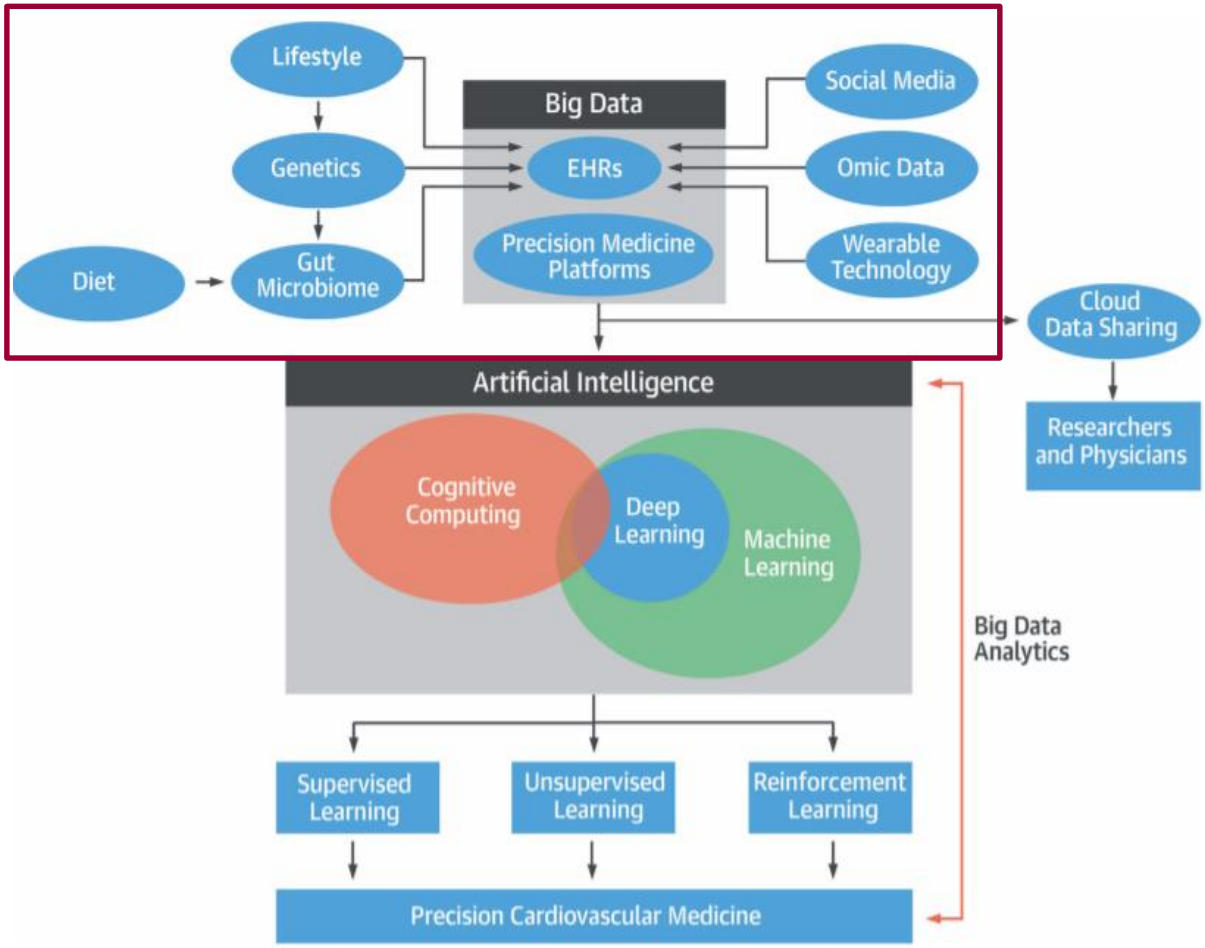
FONDAZIONE PER LA RICERCA FARMACOLOGICA GIANNI BENZI ONLUS

REVIEW TOPIC OF THE WEEK

Personalized Medicine

Artificial Intelligence in Precision Cardiovascular Medicine

Chayakrit Krittanawong, MD,[a,b] HongJu Zhang, PhD,[c] Zhen Wang, PhD,[d,e] Mehmet Aydar, PhD,[b,f] Takeshi Kitai, MD, PhD[b,g]



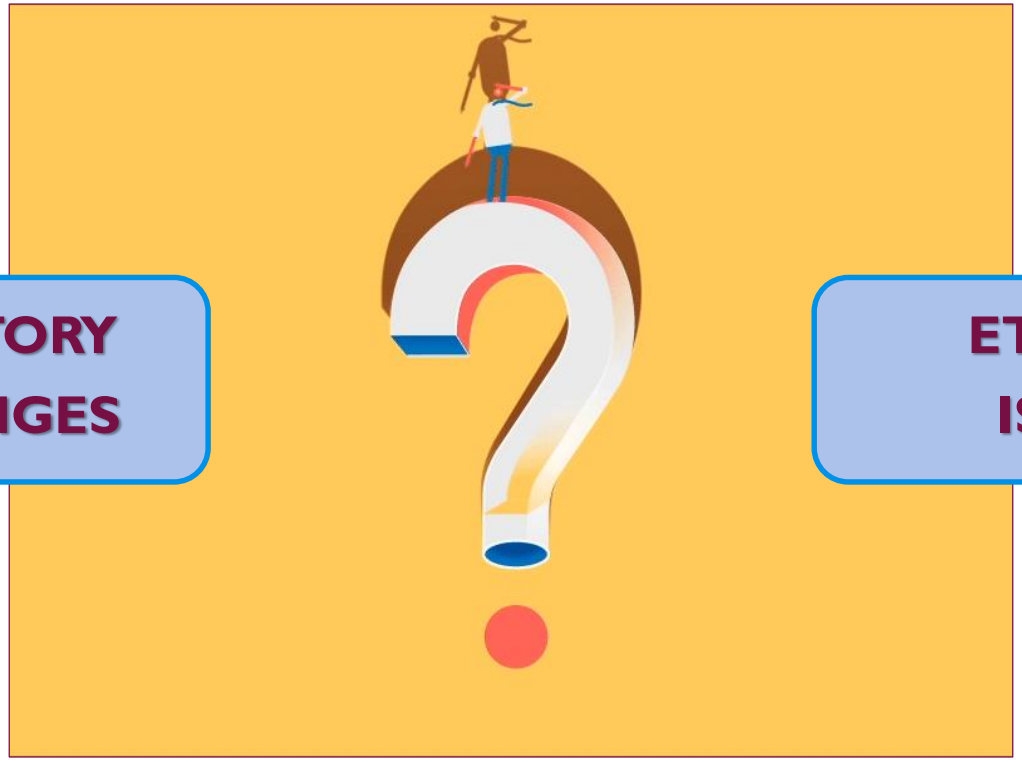
Big data can be stored through EHRs or precision medicine platforms and can be shared for data analysis with other physicians or researchers through secure cloud systems. Big data analytics using artificial intelligence (machine learning, deep learning, or cognitive computing) and 3 main types of learning algorithms will enable precision cardiovascular medicine.

https://doi.org/10.1016/j.jacc.2017.03.571, 30 May 2017

FONDAZIONE
PER LA RICERCA FARMACOLOGICA
GIANNI BENZI
ONLUS

Questions for this new technological Era

REGULATORY CHALLENGES



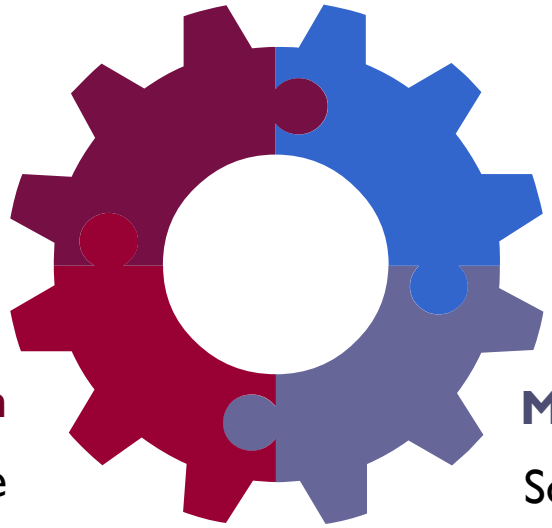
ETHICAL ISSUES

FONDAZIONE
PER LA RICERCA FARMACOLOGICA
GIANNI BENZI
ONLUS

Regulatory Challenges

Privacy

Some relevant EU provision, such as General Data Protection regulation, are applicable anyway even if GDPR could results in undesirable restrictions in the number and type of data to be accumulated.



Safety

What would be the right protocol to work out a quality assurance plan, a risk identification and management approach or how to prove safety and efficacy?

Standardization

Standards can be developed to align with and support existing regulatory frameworks, whilst keeping pace with evolving technologies.

Medical Device

Some of the previously mentioned concerns could be, at least partially, resolved in case the ML software is classified as a "Medical Device", a category covered by EU/national provisions.

FONDAZIONE PER LA RICERCA FARMACOLOGICA GIANNI BENZI ONLUS

REVIEW

CrossMark

Artificial intelligence as a medical device in radiology: ethical and regulatory issues in Europe and the United States

Filippo Pesapane[1] · Caterina Volonté[2] · Marina Codari[3] · Francesco Sardanelli[3,4]

The EU approach

- '**medical device**' means any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes:
  - diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease
  - … injury or disability
  - investigation, replacement or modification of the anatomy or of a physiological or pathological process or state
  - …

Table 1 Regulatory framework in the EU on medical devices

Directive 93/42/EEC	Directive on medical devices Will be replaced by MDR on 26 May 2020
MEDDEVS	Non-binding guidelines on legislation related to medical devices
MDR	Regulation on medical devices Applies from 26 May 2020 Repeals Directive 93/42/EEC
IVDR	Regulation on in vitro diagnostic medical devices Applies from 26 May 2022

MDR, Medical Device Regulation; IVDR, In Vitro *Diagnostic Medical Device Regulation; EEC, European Economic Community*

18 May 2018 https://doi.org/10.1007/s13244-018-0645-y

FONDAZIONE PER LA RICERCA FARMACOLOGICA GIANNI BENZI ONLUS

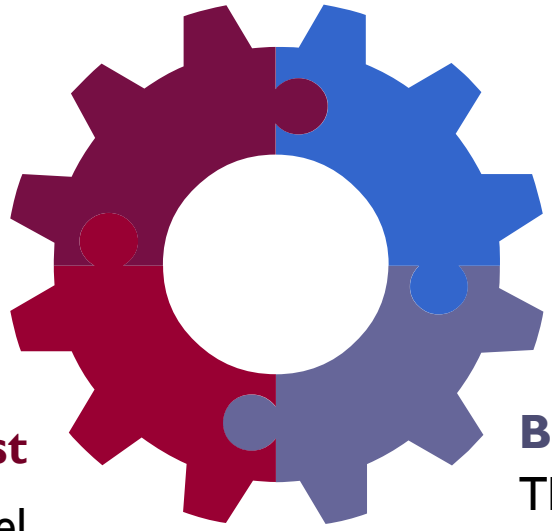
Ethical Issues

Black box negligence

Medical malpractice and product liability that arise with the use of "black-box" algorithms: users cannot provide a logical explanation of how the algorithm arrived at its given output

Self correction and automatic decision

The AI choice may not always correspond to the most ethical choice.



Trust

Many patients may not feel comfortable with a machine making potentially life and death decisions about Healthcare.

Bias

The implicit racial, gender or other biases of the humans that code the algorithms or the data that is fed into the algorithms can skew the results. Data may not be representative of the population.

FONDAZIONE
PER LA RICERCA FARMACOLOGICA
GIANNI BENZI
ONLUS