PLACE

PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

ROMA
Centro Congressi
di Confindustria
Auditorium
della Tecnica

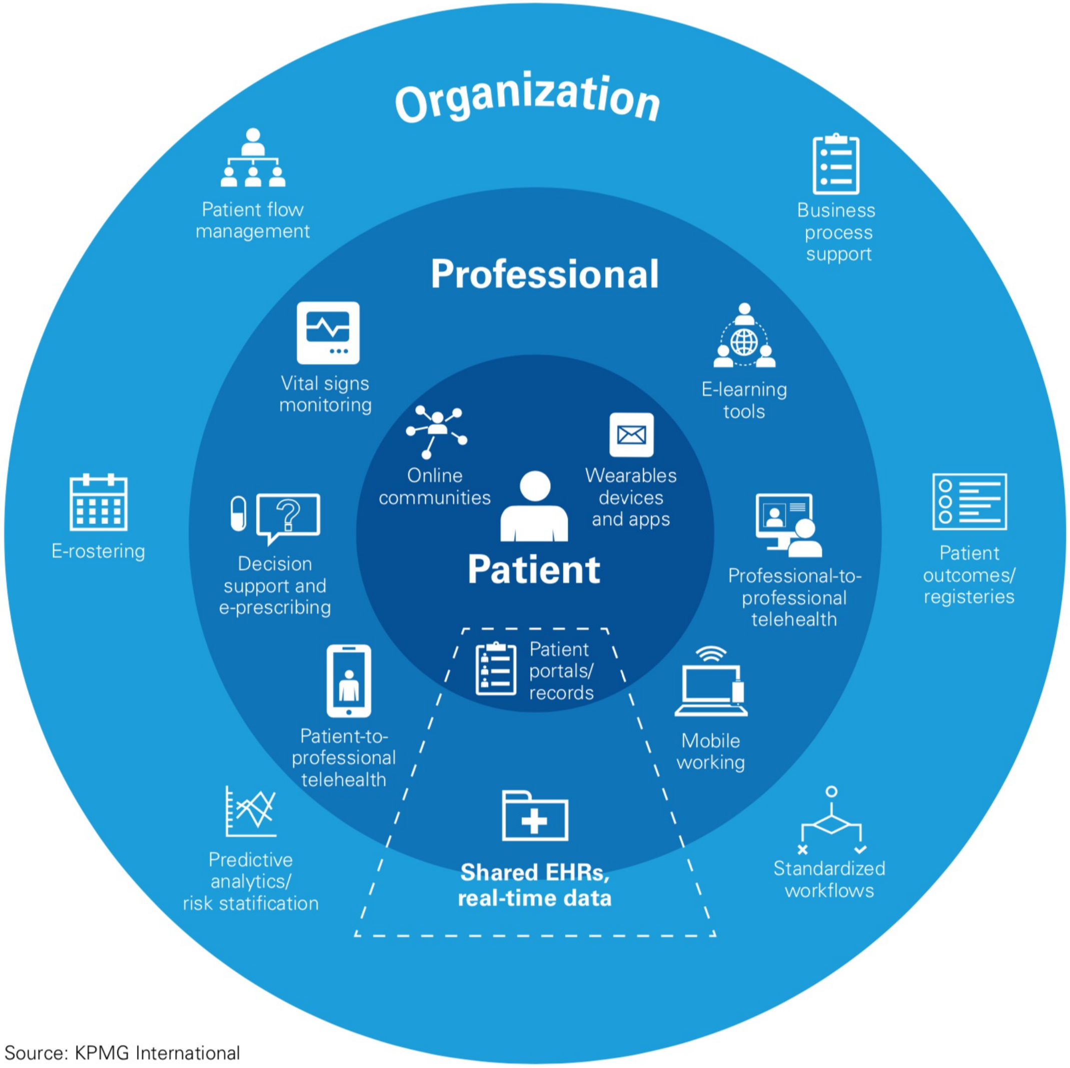
9ª Edizione

30 Settembre
1 Ottobre
2022

Tecnologia digitale e precision medicine

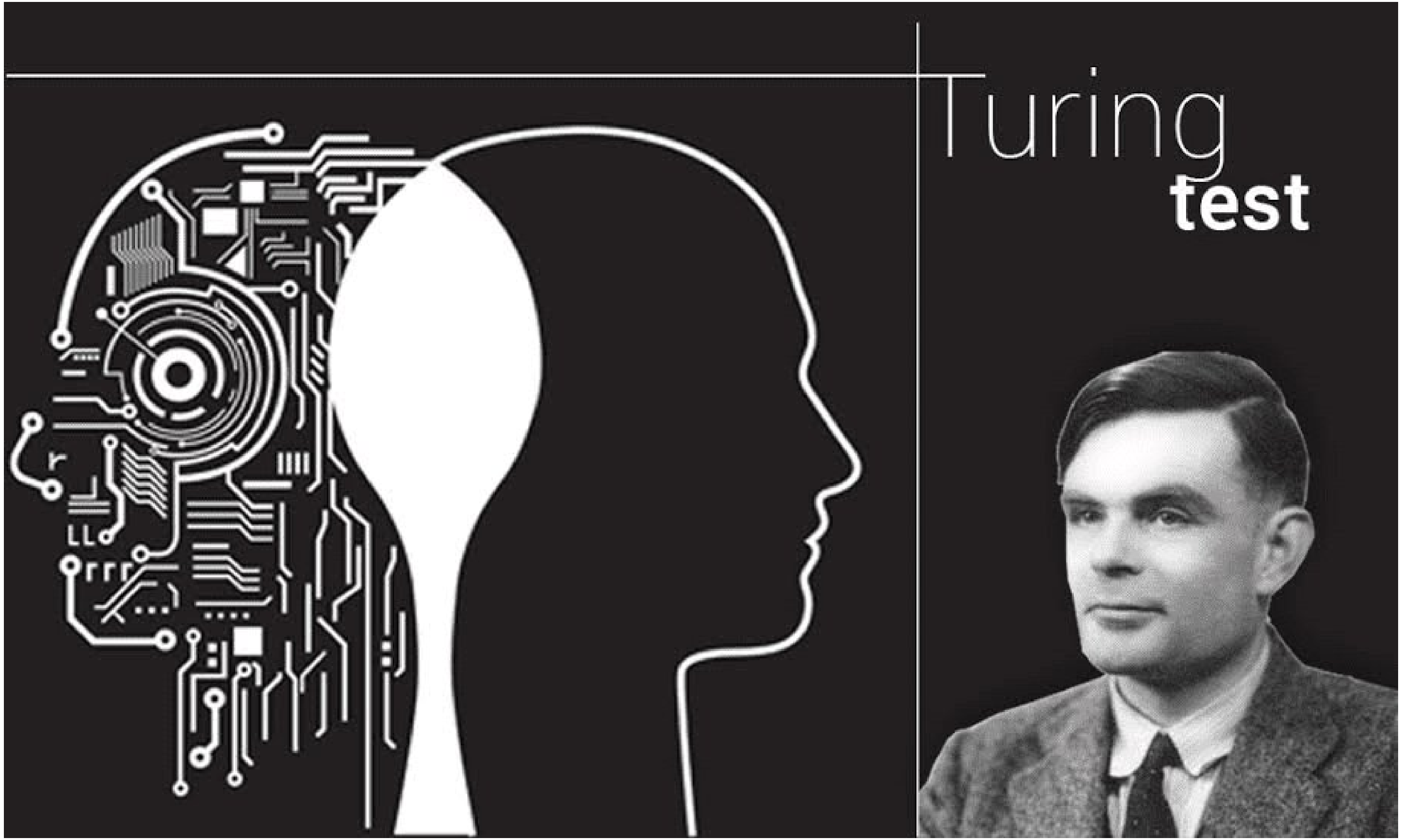
Molte possibili applicazioni dell’intelligenza artificiale in cardiologia

De Biase Luciano



Source: KPMG International

A. M. Turing (1950) Computing Machinery and Intelligence. Mind 49: 433-460.

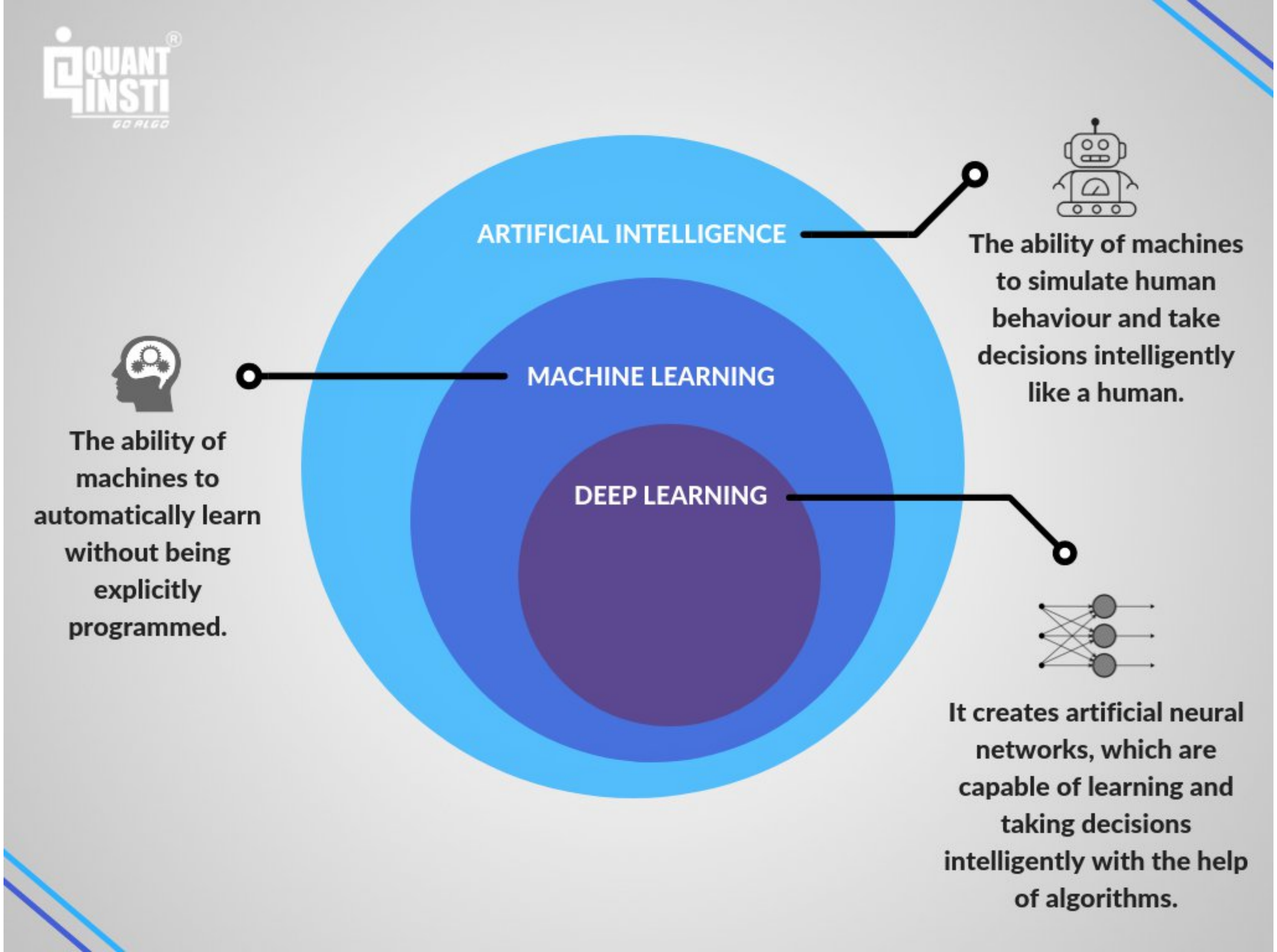


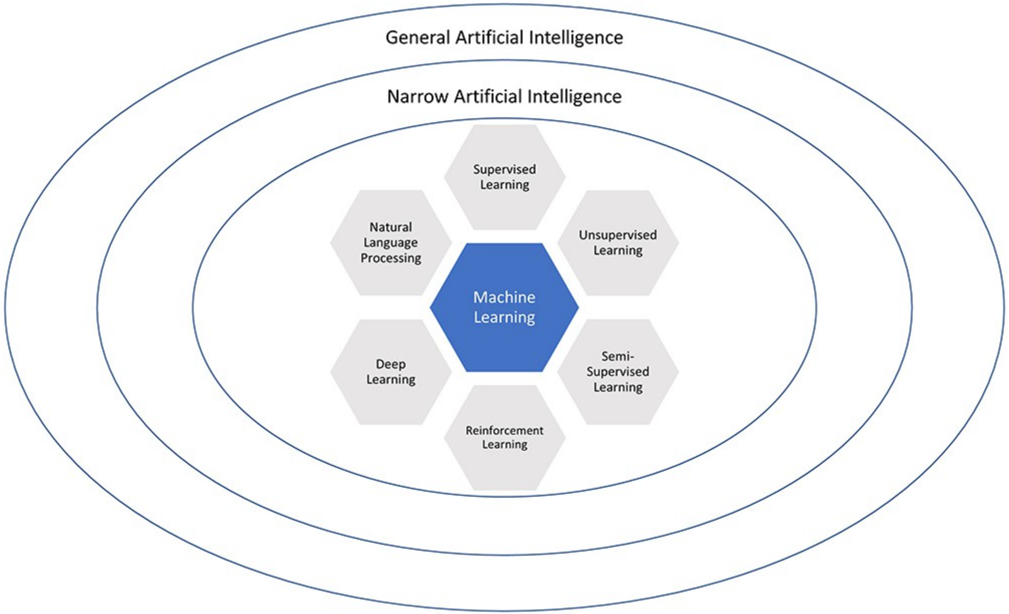
John McCarthy 2004
AI definition

- It is the science and engineering of making intelligent machines, especially intelligent computer programs.
- It is related to the similar task of using computers to understand human intelligence, but AI does not have to confine itself to methods that are biologically observable."

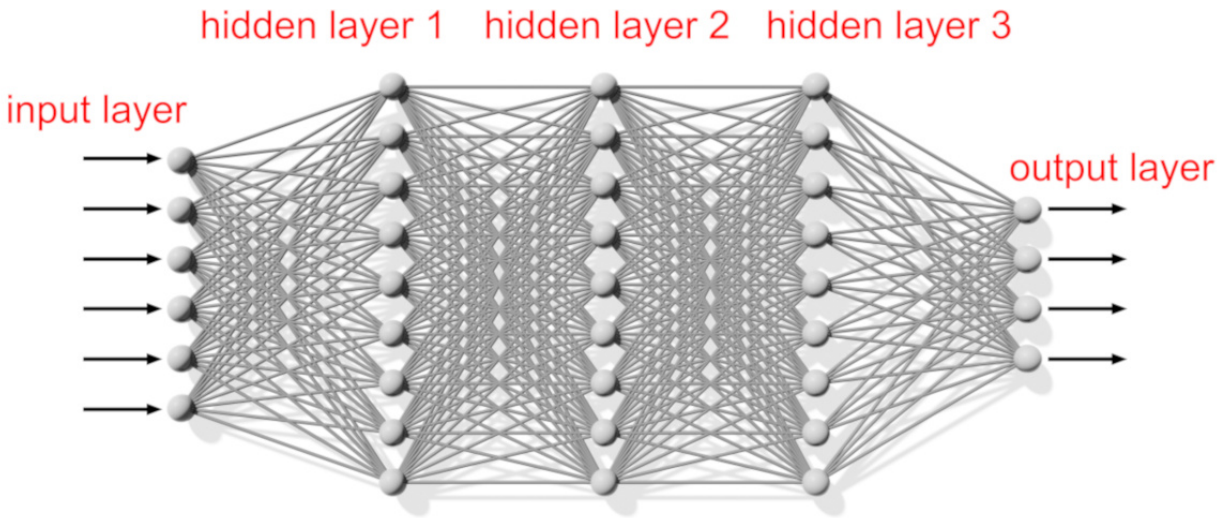
Computer systems

- **Human approach:**
- Systems that think like humans
- Systems that act like humans
- **Ideal approach:**
- Systems that think rationally
- Systems that act rationally

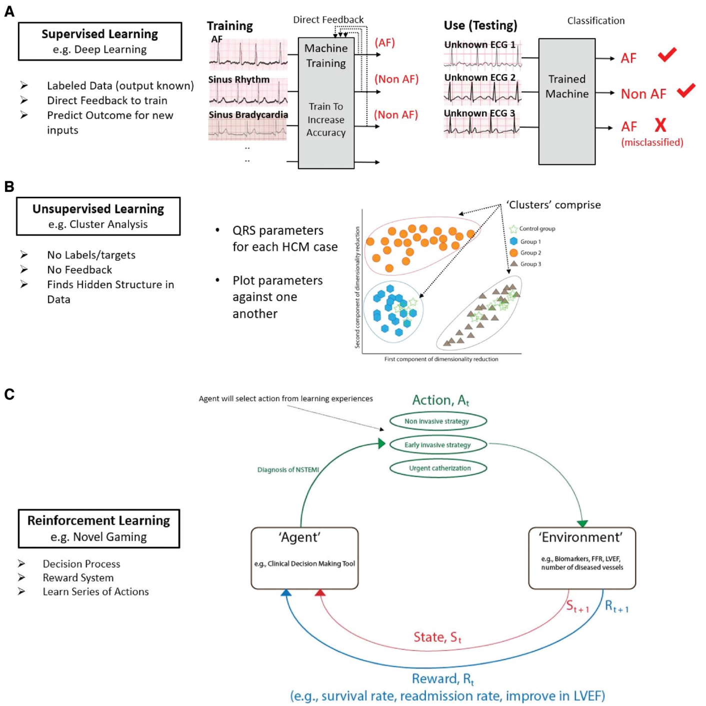

QUANT INSTI
GO ALGO
ARTIFICIAL INTELLIGENCE
MACHINE LEARNING
DEEP LEARNING
The ability of machines to simulate human behaviour and take decisions intelligently like a human.
The ability of machines to automatically learn without being explicitly programmed.
It creates artificial neural networks, which are capable of learning and taking decisions intelligently with the help of algorithms.


General Artificial Intelligence
Narrow Artificial Intelligence
Supervised Learning
Natural Language Processing
Unsupervised Learning
Machine Learning
Deep Learning
Semi-Supervised Learning
Reinforcement Learning

Reti neurali
un modello di calcolo la cui struttura assomiglia alla rete dei neuroni



Types of machine learning in cardiovascular science



Eur Heart J, Volume 40, Issue 25, 1 July 2019, Pages 2058–2073, https://doi.org/10.1093/eurheartj/ehz056

Type of Learning	Machine Learning Algorithm	Outcomes	Strengths	Weaknesses
Supervised *Labeled data with defined outputs*	Classification	Categorical	Training data set is reusable if features do not change	Large, accurately labelled training data sets are required. Can be costly and time-consuming At risk of overfitting and does not generalize well if the training data set is heterogenous
	Regression	Continuous		
Unsupervised *Unlabeled data with unknown outputs*	Clustering	Similarity of Inputs	No previous knowledge of the data set is required and hence the scope of human error is reduced. Faster to perform.	The spectral classes do not necessarily represent features on the ground and can take time to interpret
	Dimensionality Reduction	Extract Relevant Features		
	Association	Co-occurrence Likelihood		
	Anomaly Reduction	Outliers		
Semi-Supervised	Generative	Combination of supervised and unsupervised outcomes	Stable algorithm which reduces the time needed to annotate date	Iteration results are not stable and can hence have a low accuracy
Reinforcement	Reward based	Sequential decision making	Can self-correct inherent errors introduced during programming	Requires a lot of data and computational power

La qualità dei dati che analizziamo è fondamentale

- Controllo della qualità
- Validazione esterna
- Sicurezza dei dati
- Dimostrazione della superiorità dell’approccio con IA

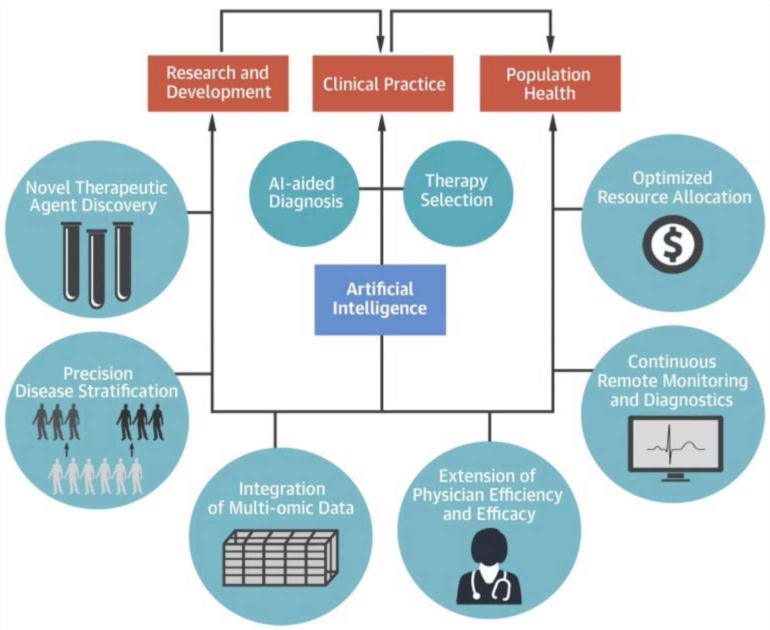
La forza del Deep Learning

- Identificare relazioni fra i dati indipendentemente da relazioni che il medico ha individuato in anticipo
- Migliorare l’analisi dei dati rispetto alla statistica tradizionale

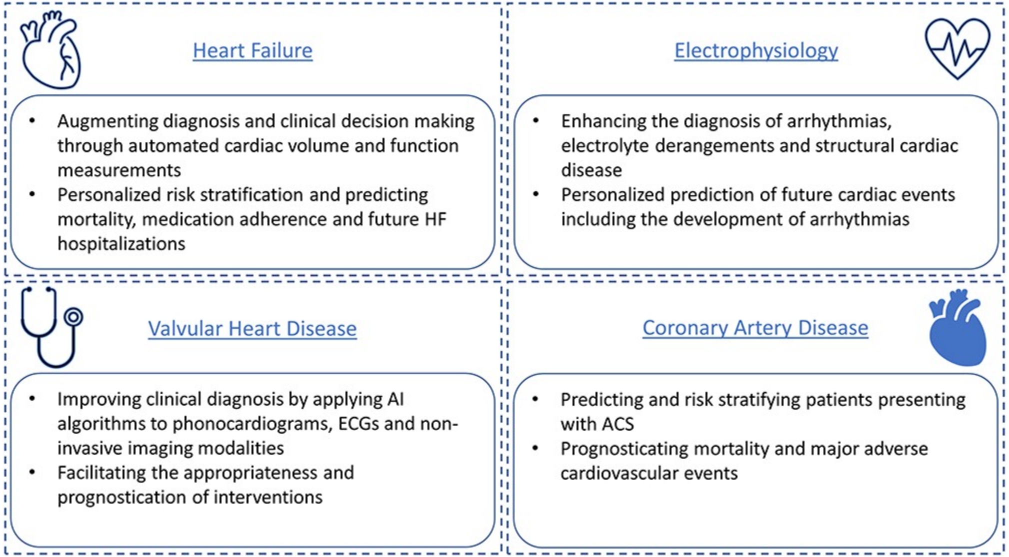
Troppo complicato?
Beh si, ma le usiamo tutti i giorni

- Riconoscimento vocale (Alexa, Siri)
- Riconoscimento immagini (smart phone, programmi di immagazzinamento e trattamento immagini)
- Previsioni del tempo
- Bancomat

CENTRAL ILLUSTRATION: Role of Artificial Intelligence in Cardiovascular Medicine



Johnson, K.W. et al. J Am Coll Cardiol. 2018;71(23):2668-79.



Heart Failure
Augmenting diagnosis and clinical decision making through automated cardiac volume and function measurements
Personalized risk stratification and predicting mortality, medication adherence and future HF hospitalizations
Electrophysiology
Enhancing the diagnosis of arrhythmias, electrolyte derangements and structural cardiac disease
Personalized prediction of future cardiac events including the development of arrhythmias
Valvular Heart Disease
Improving clinical diagnosis by applying AI algorithms to phonocardiograms, ECGs and non-invasive imaging modalities
Facilitating the appropriateness and prognostication of interventions
Coronary Artery Disease
Predicting and risk stratifying patients presenting with ACS
Prognosticating mortality and major adverse cardiovascular events

Elettrocardiografia

- Previsioni cardiotossicità da antracicline
- Stima frazione di eiezione
- Previsione FA dopo crioablazione
- Mortalità post infarto
- Diagnosi e previsione di valvulopatie
- Diagnosi fibrillazione atriale
- Ecc…

Neural network design to classify atrial fibrillation from the electrocardiogram.

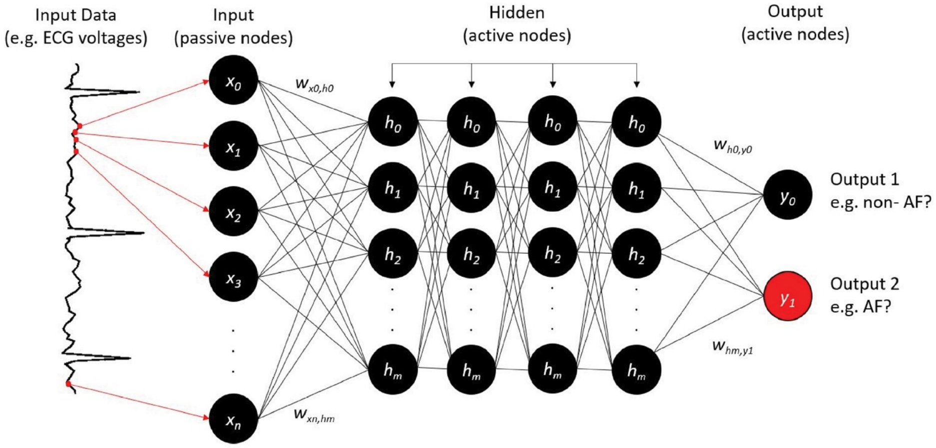


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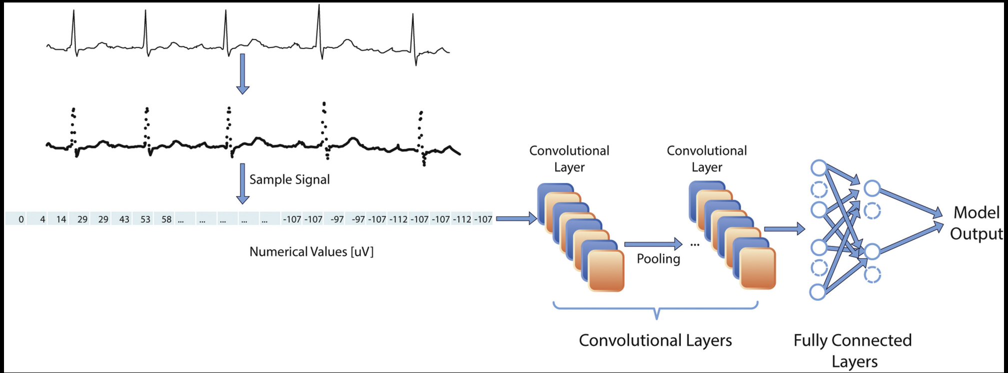
Figure1



Mayo Clinic Proceedings 2020 951015-1039DOI: (10.1016/j.mayocp.2020.01.038)

Apple Heart Study

- Quanto è precisa la diagnosi di ritmo tramite fotopletismografia in questa fase dello sviluppo tecnico?
- Nel mondo reale gli utilizzatori di smart watch sono giovani a basso rischio di FA

Previsione di eventi basata su analisi ecg.

Attia et al EHJ 2021

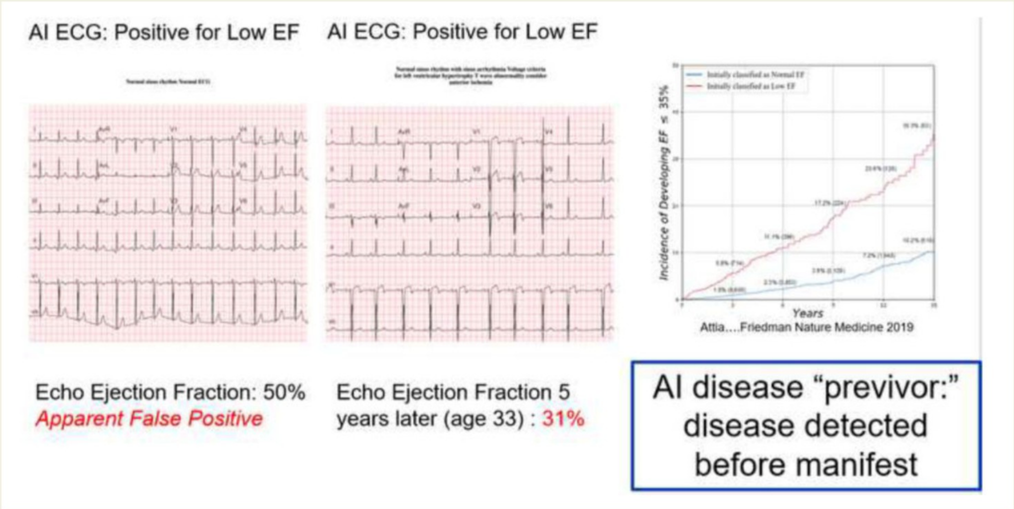


Figure 5 Artificial intelligence disease previvor. Left panel—an apparently normal electrocardiogram is identified by artificial intelligence as being associated with a low ejection fraction. A contemporaneous echocardiogram depicts normal ventricular function (ejection fraction 50%). Middle panel—5 years later, at age 33, additional electrocardiograms changes are now visible to the human eye, and repeat echocardiography shows depressed ventricular function (ejection fraction 31%). Right panel—risk of developing ejection fraction <35% with a positive artificial intelligence electrocardiogram (red line) vs. with a negative artificial intelligence electrocardiogram for low ejection fraction (blue line). Further details in the text. AI, artificial intelligence; ECG, electrocardiogram; EF, ejection fraction.

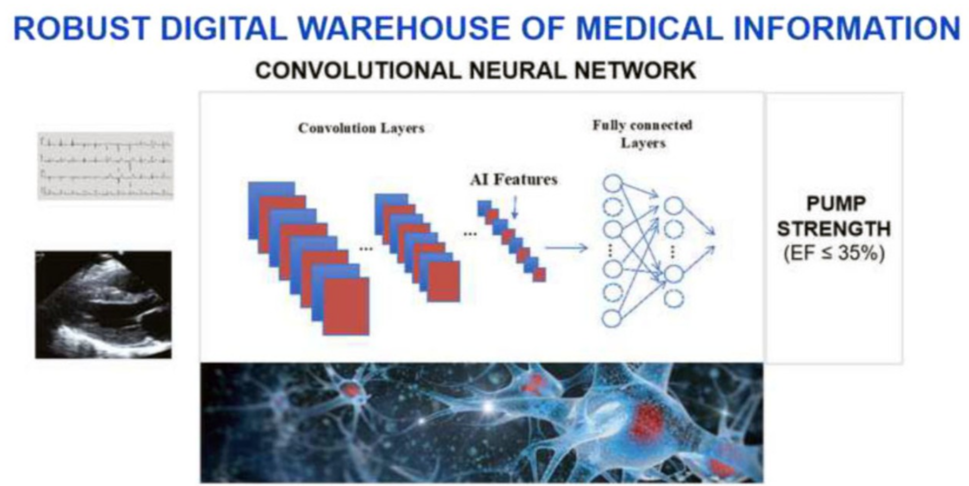


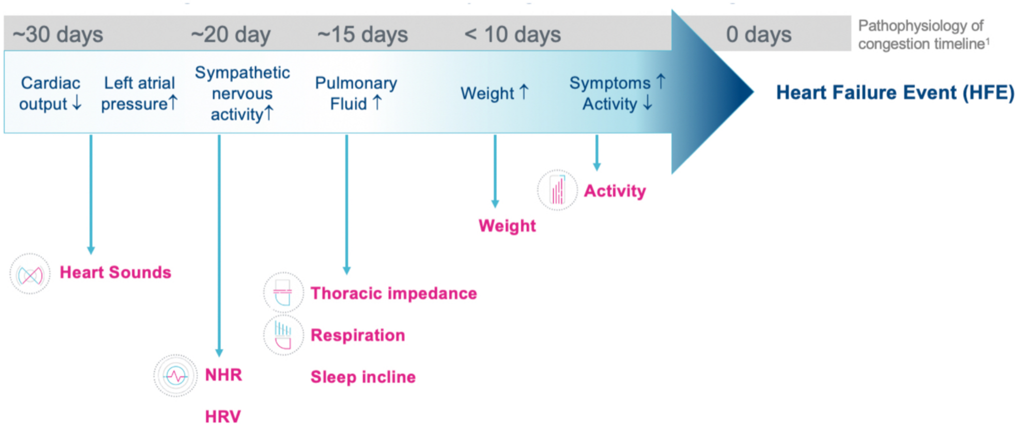
Figure 2 A convolutional neural network is trained by feeding in labelled data (in this case voltage time waveforms), and through repetition it identifies the patterns in the data that are associated with the data labels (in this example, heart pump strength, or ejection fraction). The network has two components, convolution layers that extract image components to create the artificial intelligence features, and the fully connected layers that comprise the model, that leads to the network output. While large data sets and robust computing are required to train networks, once trained, the computation requirements are substantially reduced, permitting smartphone application. AI, artificial intelligence; EF, ejection fraction.

Remote Monitoring on Starship Enterprise

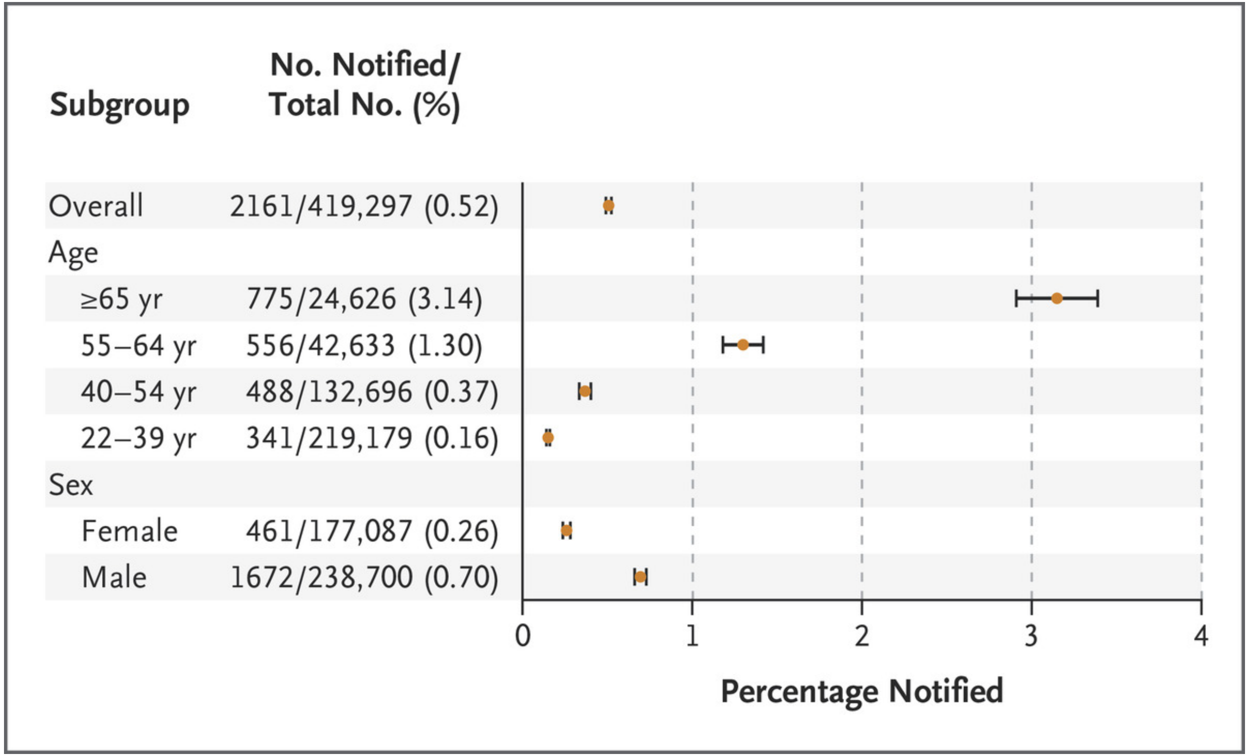
Telemedicina

- Segnalazioni per assunzioni farmaci
- Follow up dei pazienti
- Individuazione cluster di fattori di rischio
- Consigli medici tempestivi
- Individuazione precoce di sintomi
- Connessione con cartelle cliniche elettroniche

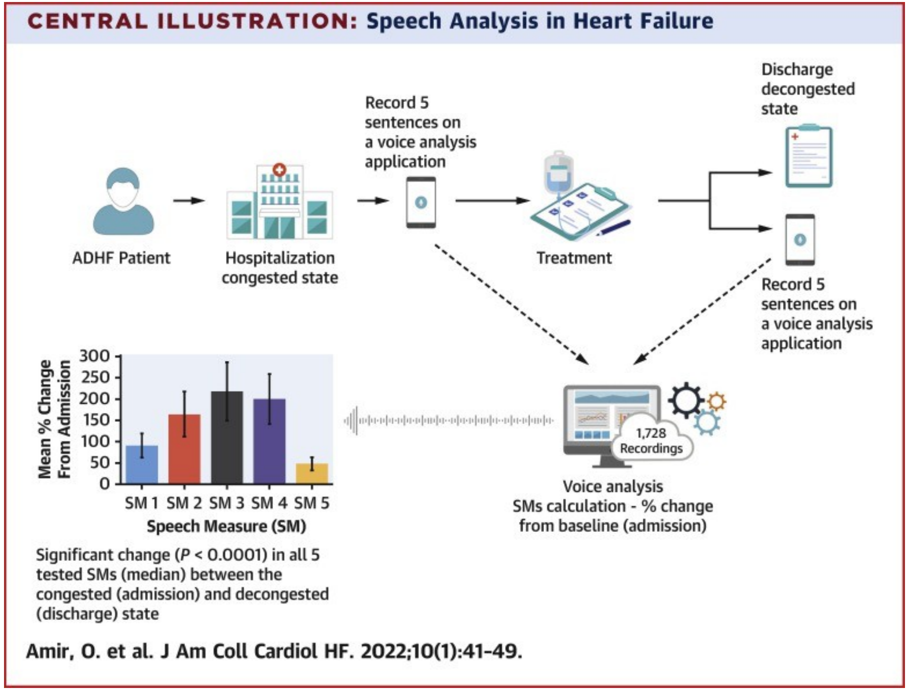
Previsione multiparametrica degli eventi: HeartLogic



Note: There is a large individual variability in presentation and time course, even for the same patient. Thus, several patterns may precede a decompensation.


Subgroup
No. Notified/ Total No. (%)
Overall
2161/419,297 (0.52)
Age
≥65 yr
775/24,626 (3.14)
55–64 yr
556/42,633 (1.30)
40–54 yr
488/132,696 (0.37)
22–39 yr
341/219,179 (0.16)
Sex
Female
461/177,087 (0.26)
Male
1672/238,700 (0.70)
0
1
2
3
4
Percentage Notified

Speech analysis and worsening heart failure



Published in final edited form as:
J Vasc Surg. 2017 June ; 65(6): 1753–1761. doi:10.1016/j.jvs.2016.11.031.

Mining Peripheral Arterial Disease Cases from Narrative Clinical Notes Using Natural Language Processing

Naveed Afzal, Ph.D.[a], **Sunghwan Sohn, Ph.D.**[a], **Sara Abram, M.D.**[b], **Christopher G. Scott, M.S.**[a], **Rajeev Chaudhry, M.B.B.S., MPH**[c], **Hongfang Liu, Ph.D.**[a], **Iftikhar J. Kullo, M.D.**[b], and **Adelaide M. Arruda-Olson, M.D., Ph.D.**[b]

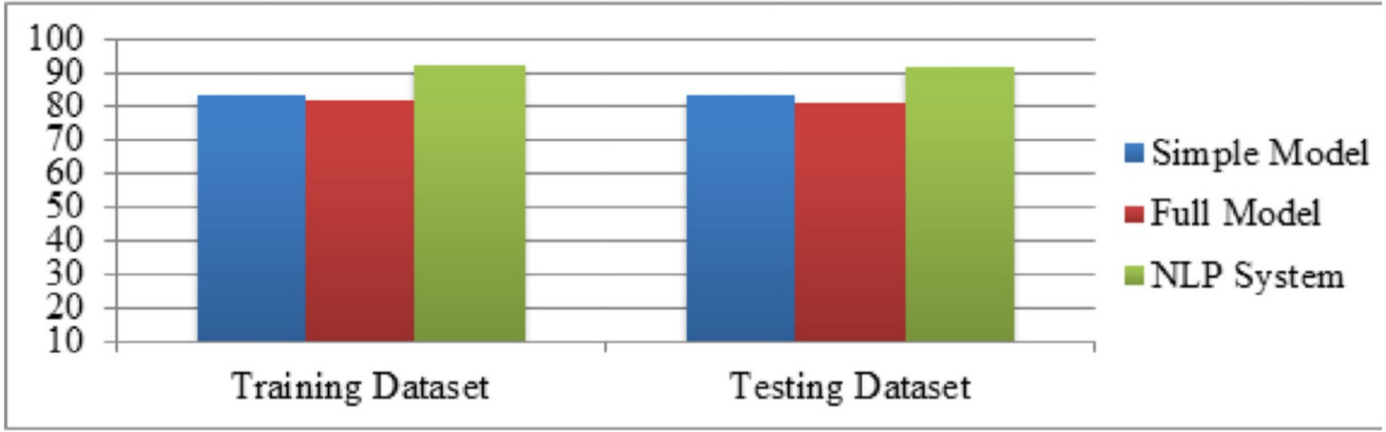


Figure 4. Accuracy of NLP algorithm compared with billing code algorithms (simple model and full model) for ascertainment of PAD status

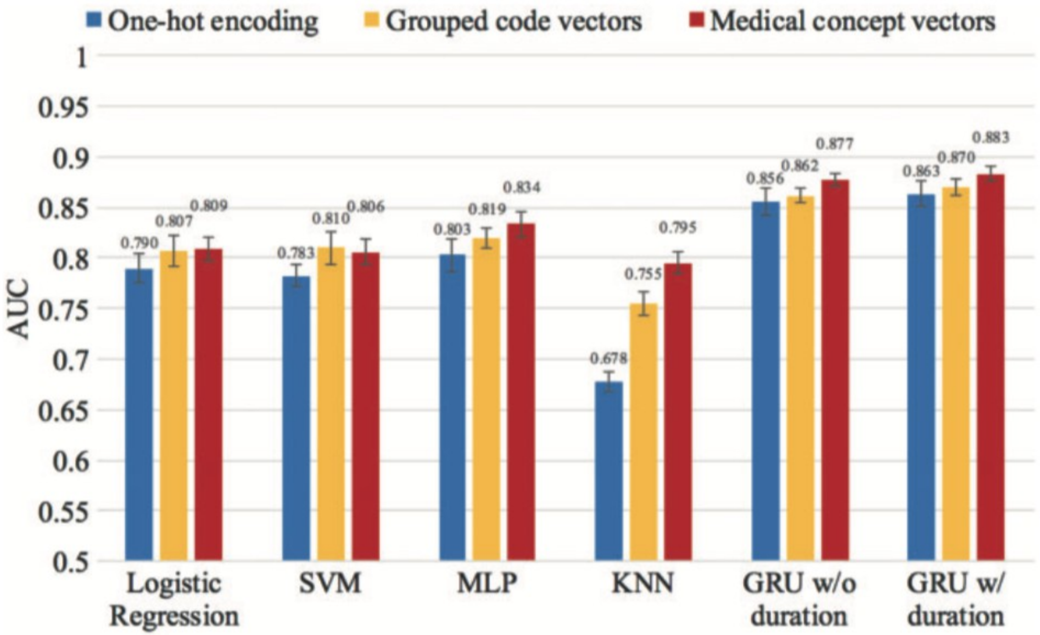
Speech analysis and smart phone

- 20 donne e 20 uomini, età media 75 anni, NT proBNP 7002
- Speech analysis
  - Ripetizione di 5 frasi 3-4 volte all'ingresso in ospedale e alla dimissione

Using recurrent neural network models for early detection of heart failure onset

Edward Choi, 1 Andy Schuetz,2 Walter F Stewart, 2 and Jimeng Sun1

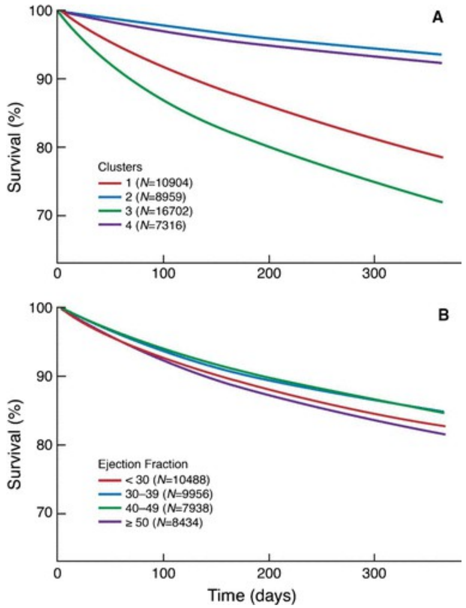
Journal of the American Medical Informatics Association, 24(2), 2017, 361–370



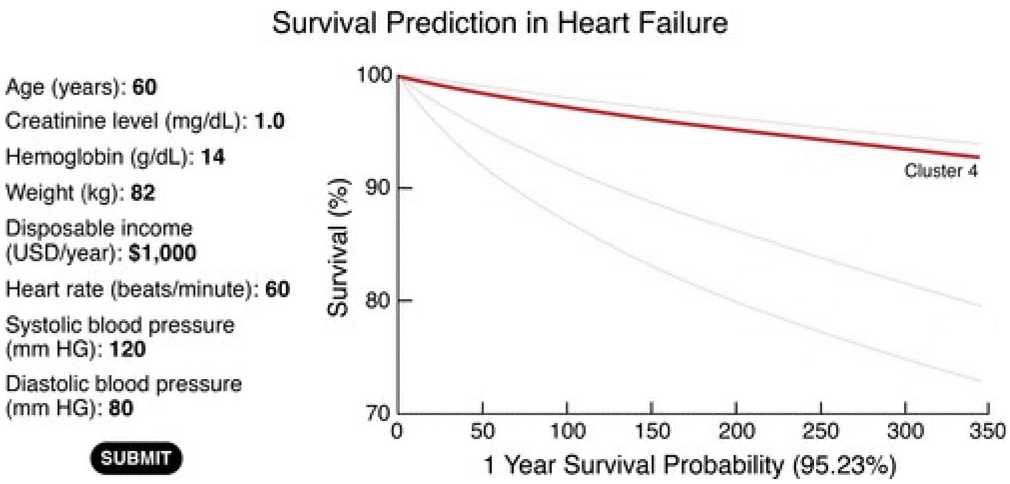
Machine Learning Methods Improve Prognostication, Identify Clinically Distinct Phenotypes, and Detect Heterogeneity in Response to Therapy in a Large Cohort of Heart Failure Patients

Tariq Ahmad, et al JAHA 2018

- We applied machine learning methodologies to a large clinical data set (>40 000 heart failure patients) and demonstrated that these methods can predict outcomes in a highly accurate manner as well as identify clinically distinct subgroups that have differential responses to commonly used therapies
- Clusters variables: age, creatinine, hemoglobin, weight, heart rate, systolic blood pressure, mean arterial, pressure, and income



Nihar R. Desai. Journal of the American Heart Association. Machine Learning Methods Improve Prognostication, Identify Clinically Distinct Phenotypes, and Detect Heterogeneity in Response to Therapy in a Large Cohort of Heart Failure Patients, Volume: 7, Issue: 8, DOI: (10.1161/JAHA.117.008081)



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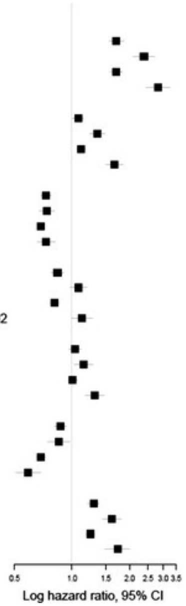
Cluster	Drug	Hazard ratio (95% CI)	p
	Diuretic		
Cluster 1	Interaction p < 0.001	1.71(1.56–1.87)	<0.001
Cluster 2		2.38(2.09–2.7)	<0.001
Cluster 3		1.7(1.58–1.83)	<0.001
Cluster 4		2.82(2.45–3.25)	<0.001
	Aldosterone antagonist		
Cluster 1	Interaction p = 0.6556	1.08(1.01–1.15)	0.03
Cluster 2		1.36(1.24–1.49)	<0.001
Cluster 3		1.11(1.06–1.17)	<0.001
Cluster 4		1.67(1.51–1.84)	<0.001
	ACE inhibitor		
Cluster 1	Interaction p < 0.001	7.31(6.89–7.76)	<0.001
Cluster 2		7.4(6.74–8.12)	<0.001
Cluster 3		6.87(6.58–7.18)	<0.001
Cluster 4		7.32(6.56–8.17)	<0.001
	ARB		
Cluster 1	Interaction p = 0.9868	8.4(7.78–9.07)	<0.001
Cluster 2		1.07(0.97–1.19)	0.16
Cluster 3		8.1(7.66–8.57)	<0.001
Cluster 4		1.13(1–1.28)	4.70E–02
	Digoxin		
Cluster 1	Interaction p = 0.7971	1.04(0.96–1.12)	0.29
Cluster 2		1.15(1.03–1.29)	0.01
Cluster 3		1.01(0.95–1.07)	0.71
Cluster 4		1.32(1.17–1.48)	<0.001
	Beta blocker		
Cluster 1	Interaction p < 0.001	8.7(8.07–9.38)	<0.001
Cluster 2		8.53(7.47–9.75)	<0.001
Cluster 3		6.85(6.49–7.23)	<0.001
Cluster 4		5.91(5.11–6.84)	<0.001
	Nitrates		
Cluster 1	Interaction p < 0.001	1.3(1.21–1.39)	<0.001
Cluster 2		1.62(1.44–2.01)	<0.001
Cluster 3		1.25(1.19–1.32)	<0.001
Cluster 4		1.73(1.49–2.01)	<0.001

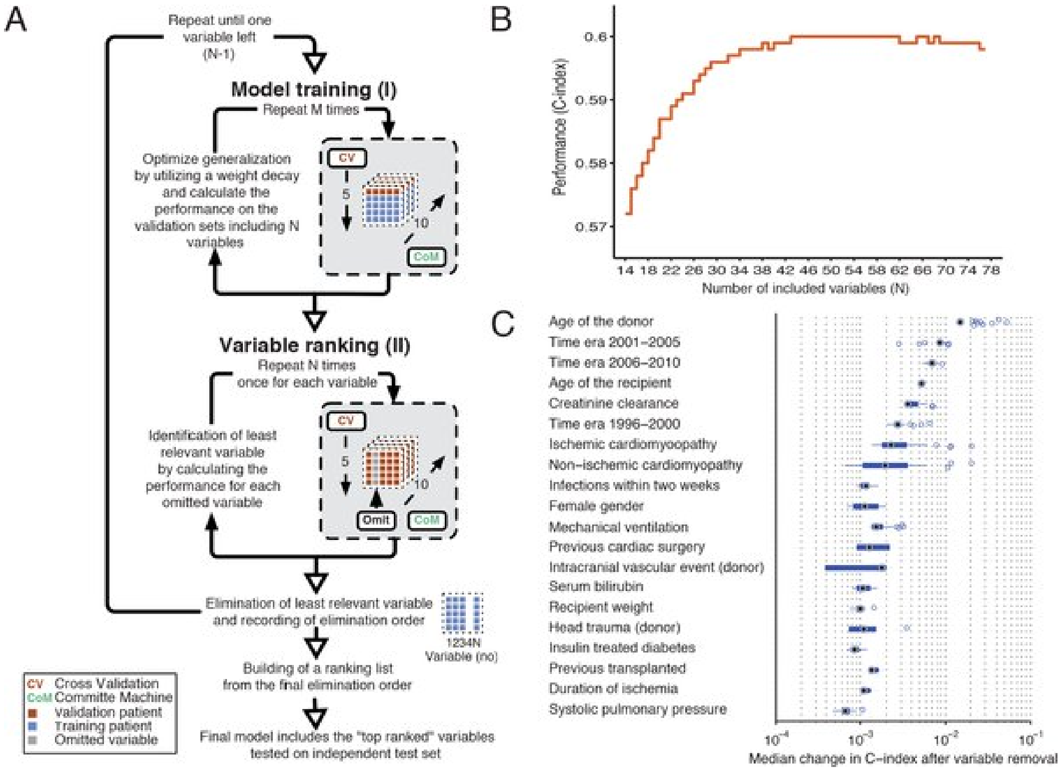


Nihar R. Desai. Journal of the American Heart Association. Machine Learning Methods Improve Prognostication, Identify Clinically Distinct Phenotypes, and Detect Heterogeneity in Response to Therapy in a Large Cohort of Heart Failure Patients, Volume: 7, Issue: 8, DOI: (10.1161/JAHA.117.008081)

The International Heart Transplant Survival Algorithm (IHTSA): A New Model to Improve Organ Sharing and Survival. PLOS ONE 10(3): e0118644.

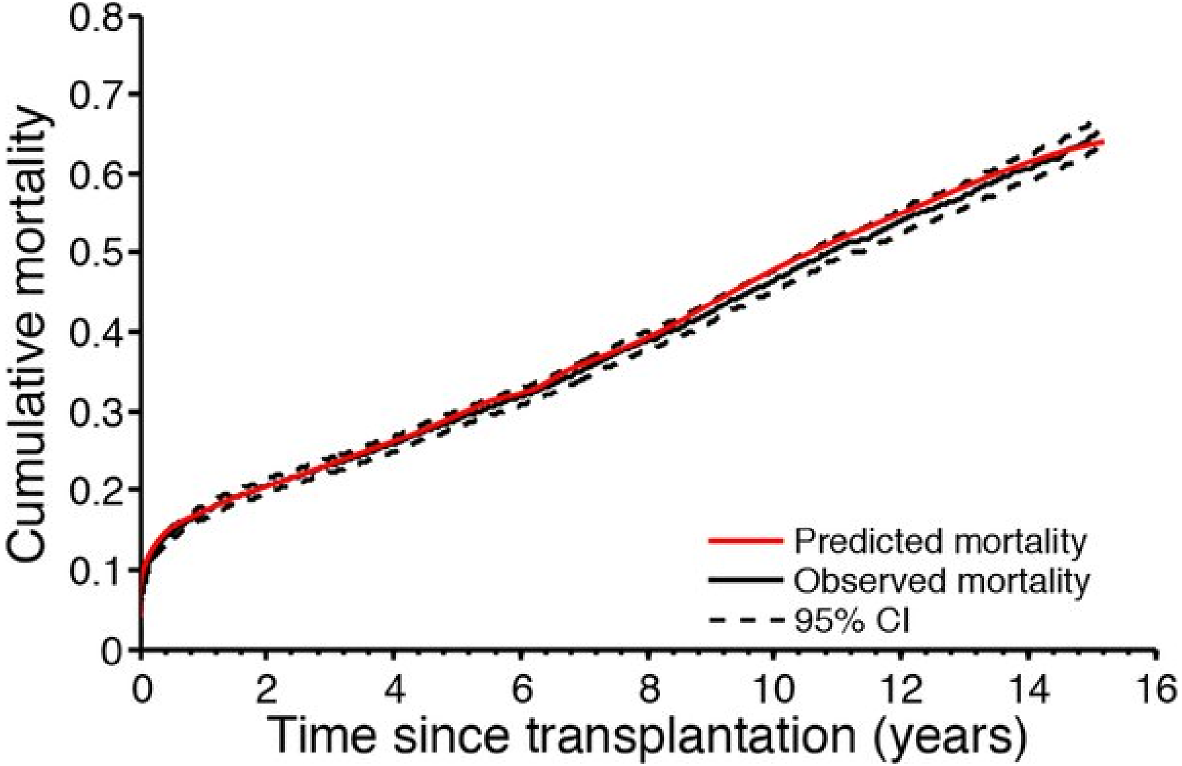
- The developed IHTSA model was deployed as a small web application (http://www.ihtsa.med.lu.se) where users can enter clinical data and get response in terms of estimated survival curves together with relevant survival and mortality numbers. The application was implemented as a simple CGI application using Perl (version 5.16.0) and Matlab (version 2010A) programs for running the survival models. Using a modular approach new survival models can easily be implemented and tested in the web application.

Fig 1. Schematic illustration of the variable-ranking process for the derivation cohort.



Nilsson J, Ohlsson M, Höglund P, Ekmehag B, Koul B, et al. (2015) The International Heart Transplant Survival Algorithm (IHTSA): A New Model to Improve Organ Sharing and Survival. PLOS ONE 10(3): e0118644. https://doi.org/10.1371/journal.pone.0118644
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0118644

Fig 2. Cumulative mortality for the internal validation cohort (IVC).



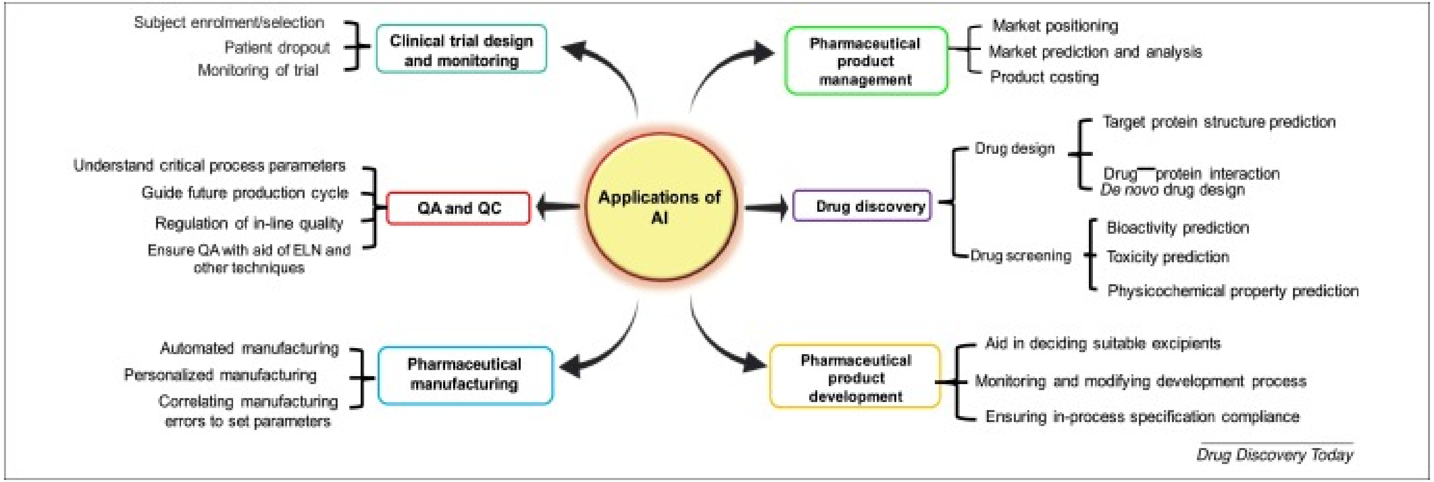
Nilsson J, Ohlsson M, Höglund P, Ekmehag B, Koul B, et al. (2015) The International Heart Transplant Survival Algorithm (IHTSA): A New Model to Improve Organ Sharing and Survival. PLOS ONE 10(3): e0118644. https://doi.org/10.1371/journal.pone.0118644
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0118644

Ricerca di nuovi farmaci

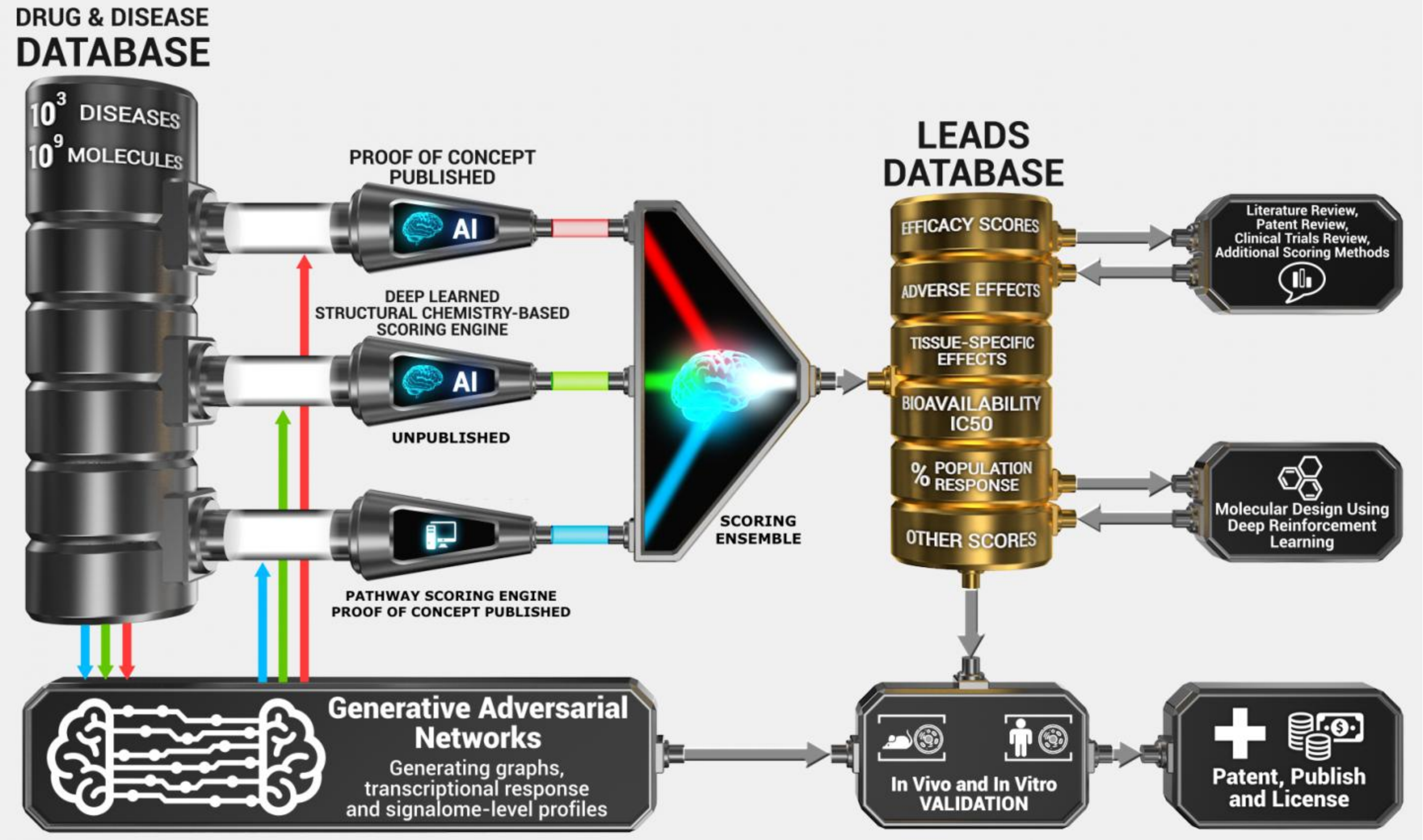
- Predicting the properties of a potential compound, meaning that only compounds with desired properties are chosen for synthesis – saving time and money by preventing work on compounds that are unlikely to be effective.
- Generating ideas for entirely novel compounds, where the ‘invented’ molecule is predicted to have all the desired properties required for success – which could hugely accelerate the discovery of effective new drugs.
- Alleviating the need for repetitive tasks, such as the analysis of thousands of histology images – saving hundreds of person-hours in the laboratory.

Applications of artificial intelligence (AI) in different subfields of the pharmaceutical industry, from drug discovery to pharmaceutical product management.
Drug Discovery Today 2021

Figure 2



pharmaceutical product management.



DRUG & DISEASE
DATABASE
10^3 DISEASES
10^9 MOLECULES
PROOF OF CONCEPT PUBLISHED
AI
DEEP LEARNED STRUCTURAL CHEMISTRY-BASED SCORING ENGINE
AI
UNPUBLISHED
PATHWAY SCORING ENGINE PROOF OF CONCEPT PUBLISHED
SCORING ENSEMBLE
LEADS DATABASE
EFFICACY SCORES
ADVERSE EFFECTS
TISSUE-SPECIFIC EFFECTS
BIOAVAILABILITY IC50
% POPULATION RESPONSE
OTHER SCORES
Literature Review, Patent Review, Clinical Trials Review, Additional Scoring Methods
Molecular Design Using Deep Reinforcement Learning
Generative Adversarial Networks
Generating graphs, transcriptional response and signalome-level profiles
In Vivo and In Vitro VALIDATION
Patent, Publish and License

Conclusioni

- Analisi di dati indipendenti da valutazioni umane può generare risultati inaspettati e utili
- La ricerca su grandi raccolte di dati può essere effettuata con l'approccio dell'IA
- Le applicazioni in cardiologia sono già presenti e sono in crescita