Machine Learning in Cardiovascular Disease: From Diagnostics to Prediction

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JOHNS HOPKINS
MEDICINE

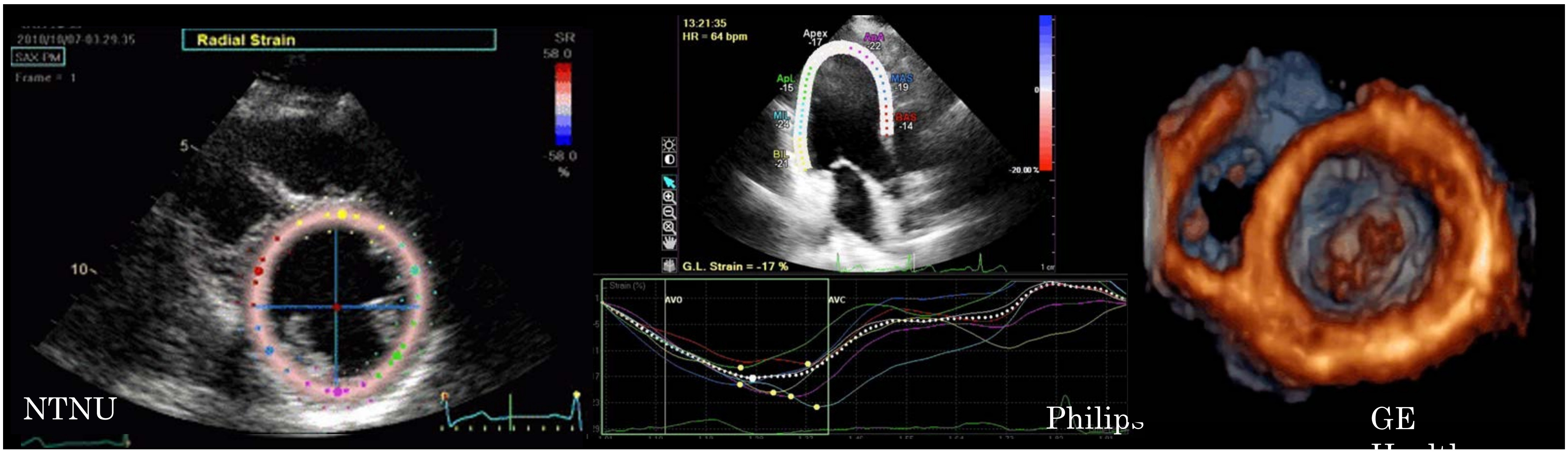
OUTLINE

- BIG DATA
- MACHINE INTELLIGENCE IN IMAGING
- IMAGES TO DIAGNOSIS
- DIAGNOSIS TO PREDICTION
- CHALLENGES FOR THE FUTURE
- EXPECTATIONS

Big Data

Big Data Definitions

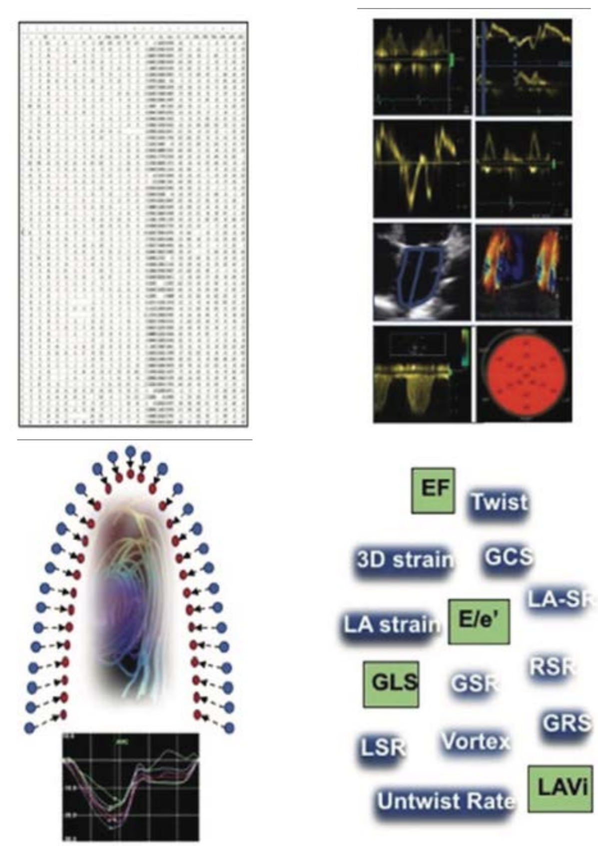
Big Data - “the information asset characterized by such a high volume, velocity and variety to require specific technology and analytical methods for its transformation into value”



The Echocardiogram – Is it Big Data?

4 V's of the Echocardiogram

- **Volume** – so many pixels
- **Velocity** – so little time
- **Variety** – structure and function and flow (oh, my!)
- **Value** – not fully tapped



Kutty S. The 21st Annual Feigenbaum Lecture: J Am Soc Echocardiogr 2020

Machine Intelligence – Terms to Know

artificial intelligence

[ahr-t*uh*-**fish**-*uh*l in-**tel**-i-j*uh*ns]

machine learning

[m*uh*-**sheen**-lur-ning]

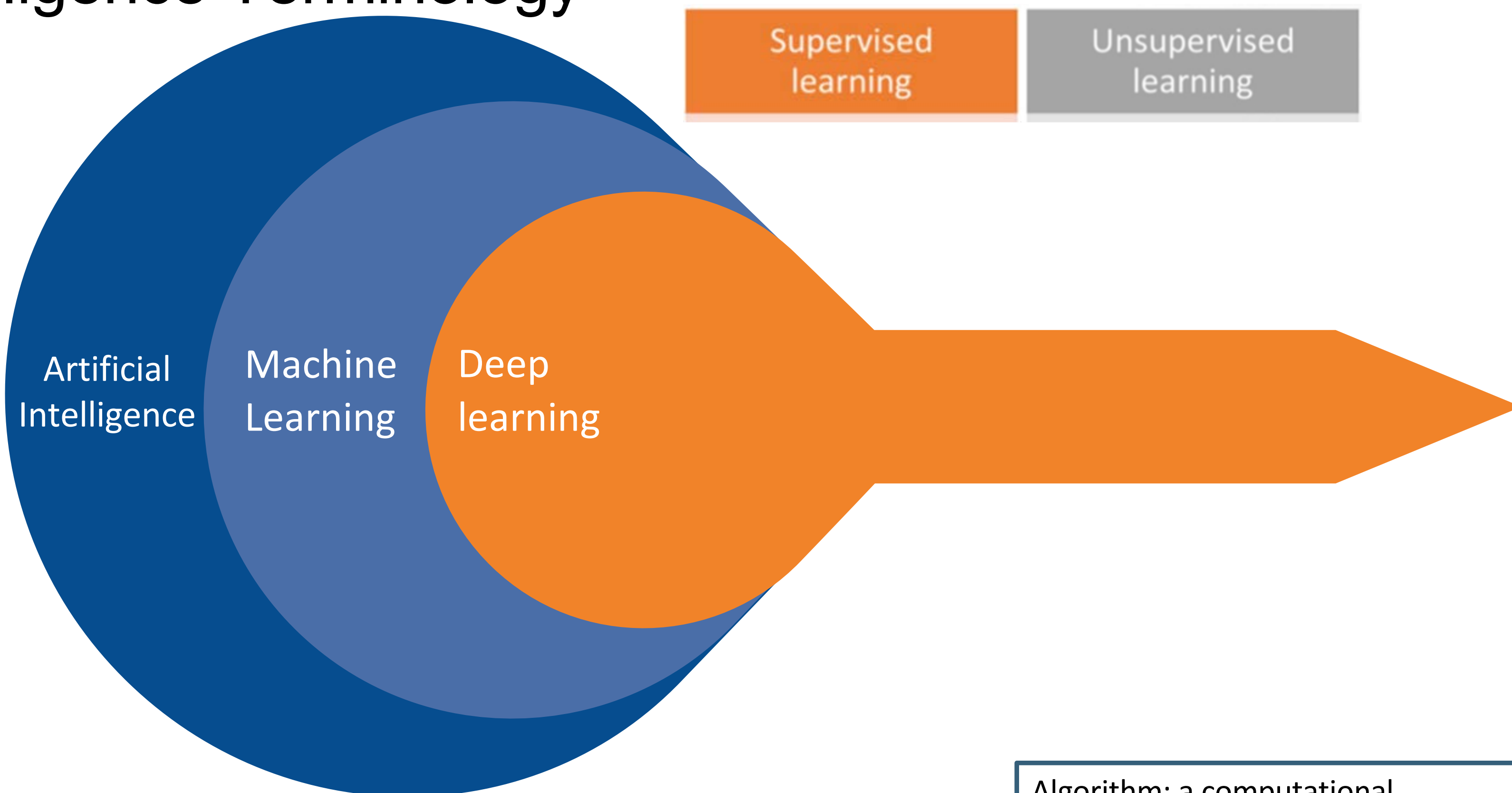
deep learning

[**deep** lur-ning]

algorithm

[**al**-g*uh*-ri*th*-*uh*m]

Artificial Intelligence Terminology



AI: Any technique that enables computers to mimic human intelligence

ML: Statistical techniques that enable machines to improve at tasks with experience

DL: Multilayered neural networks which can train themselves to perform tasks on vast amounts of data

Algorithm: a computational technique that accepts input variables, or features, and from this produces the output(s) needed to solve a problem

Manlhiot C, Kutty S et al. Can J Cardiol 2022. Van den Eynde J, Kutty S et al. Current Opin Cardiol 2022

Supervised ML Algorithms Commonly Used in Medicine

- Regression
  - Linear
  - Logistic
- Support Vector Machines
- Decision Trees and their Ensembles
  - Gradient Boost
  - Random Forest
- Neural Networks

Support Vector Machine: Outcome Prediction

OBJECTIVE

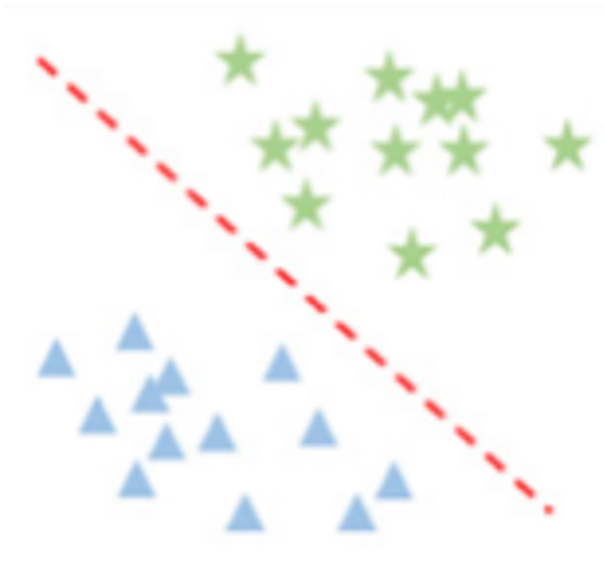
Find a classifier that distinguishes blue triangles from green stars using features x1 and x2

UNDERSTAND

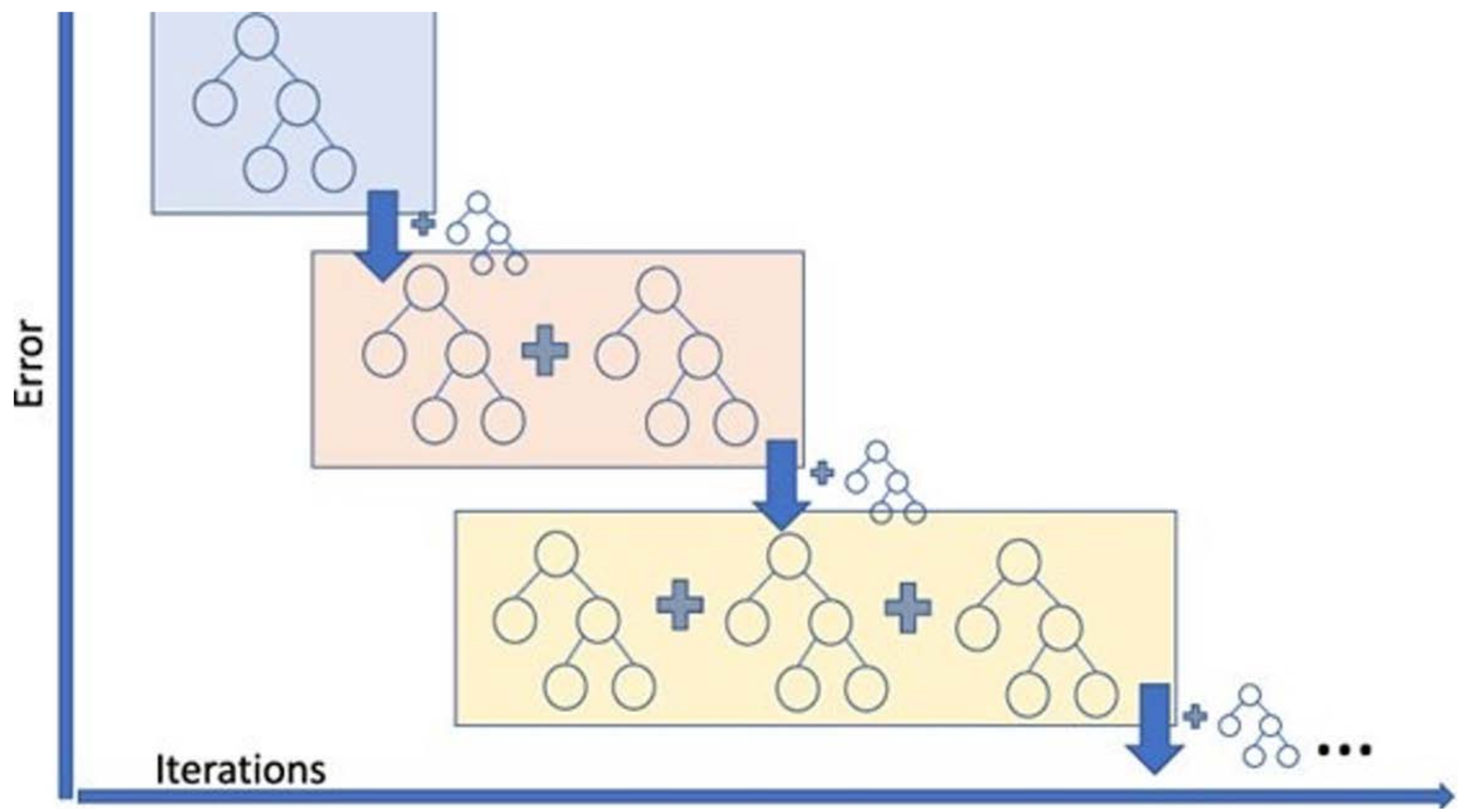
The solution is a line (2D), plane (3D), or hyperplane (nD)

LEARNING ALGORITHM

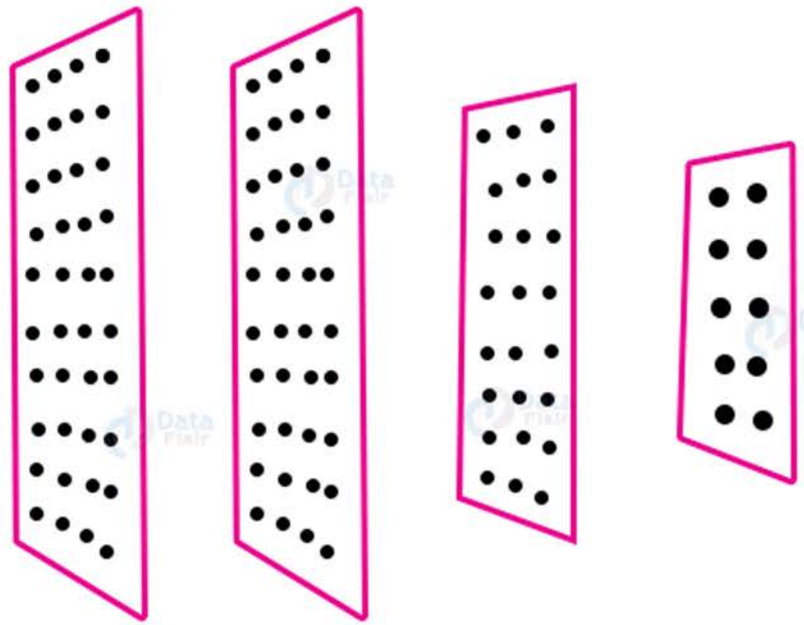
Initialization → Loss (Cost)
Minimization and Marginalization



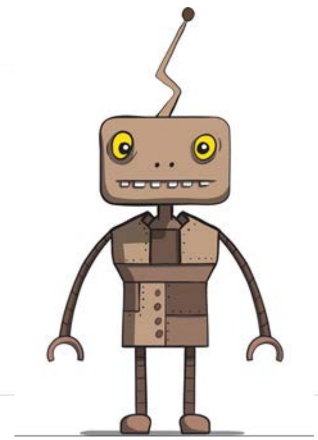
Gradient Boosting and Random Forest

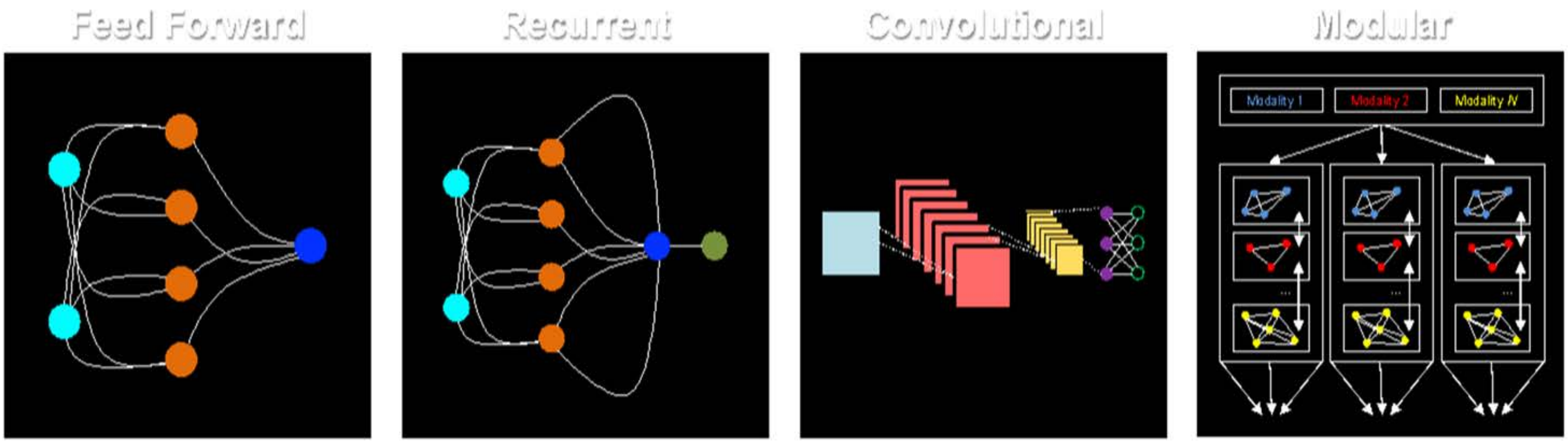


Components of Neural Networks



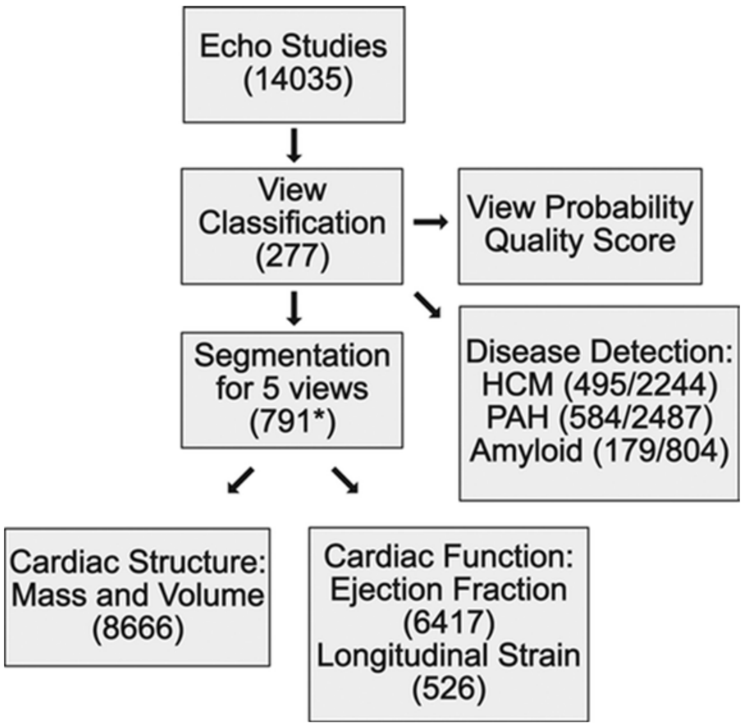
That's a bicuspid aortic valve!

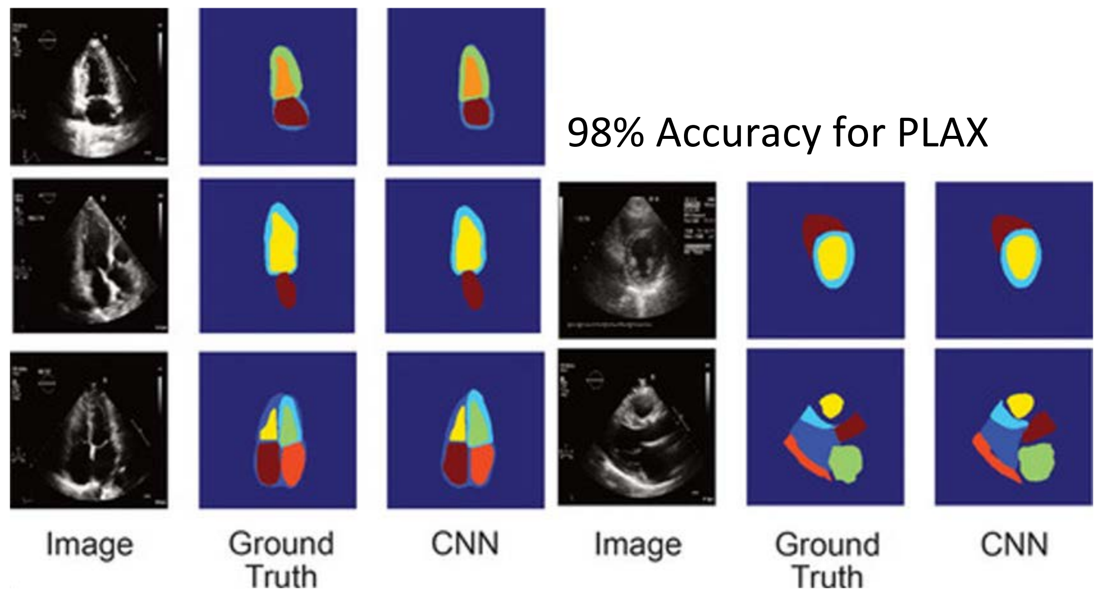



Feed Forward
Recurrent
Convolutional
Modular
Modality 1
Modality 2
Modality N

Big Data and Cardiac Imaging: Image Management

ML and Cardiac Imaging:
Image Segmentation, Functional Information, Diagnosis



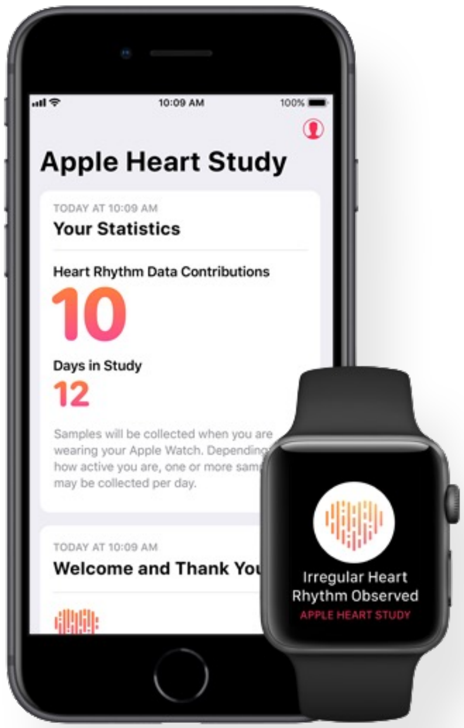


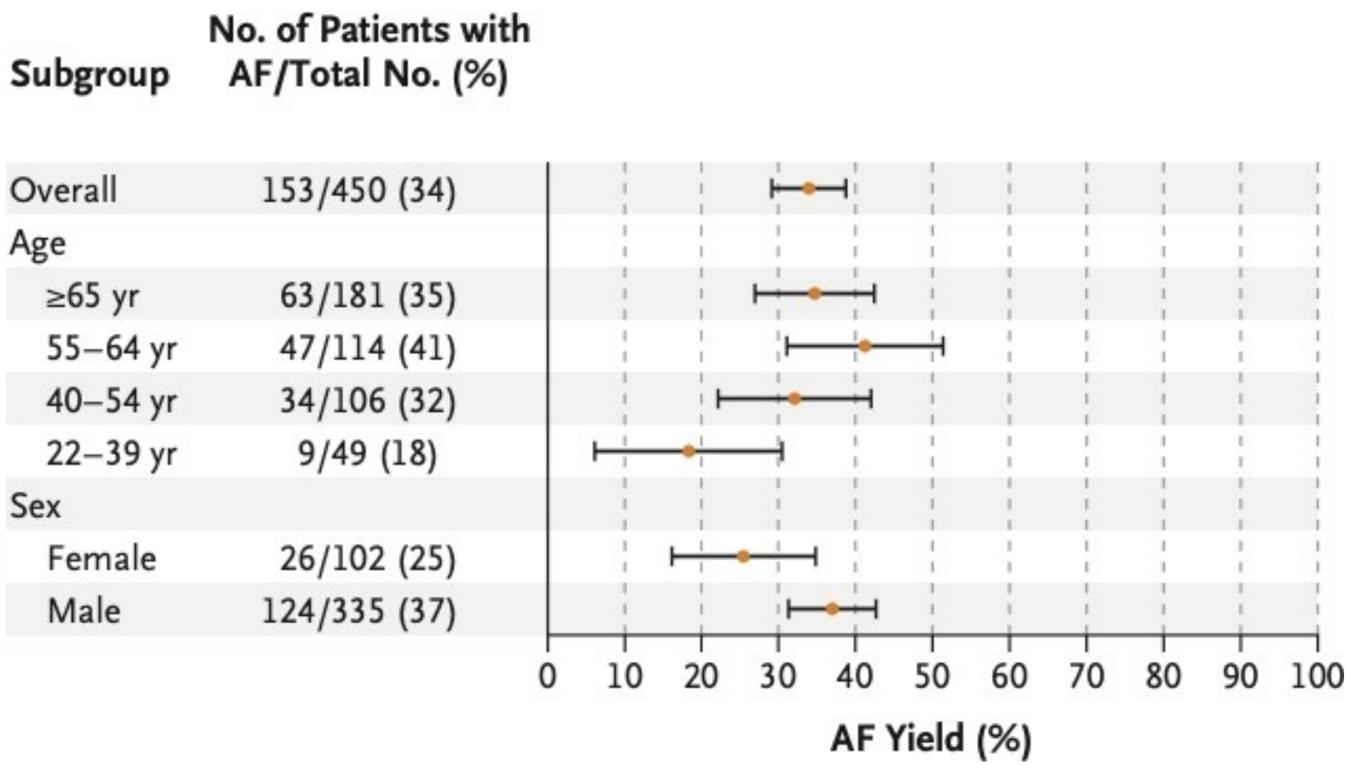
98% Accuracy for PLAX

Zhang et al., Circulation., 2018 Ouyang D et al., Nature, 2020 Duffy et. al, JAMA Cardiol, 2022

Wearables & Machine Learning in Clinical Trials

Apple heart study and Fitbit heart study

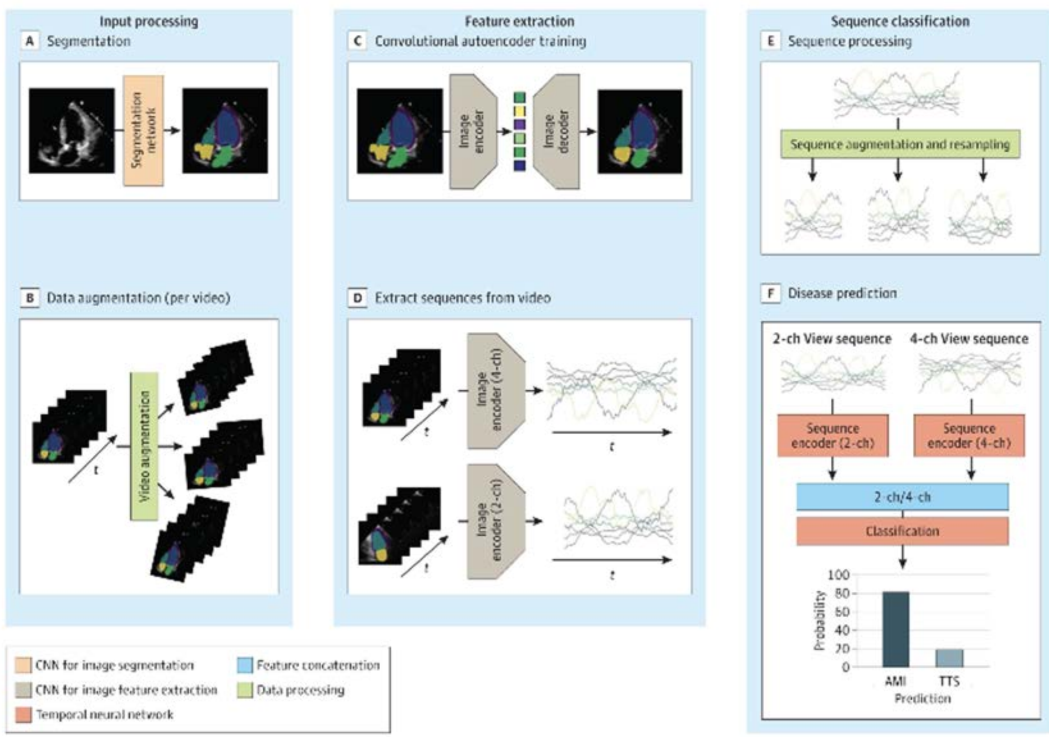




Perez et. al 2019. NEJM

Lubitz SA, et al. Circulation. 2022

ML and Cardiac Imaging - Distinguishing between Diagnoses

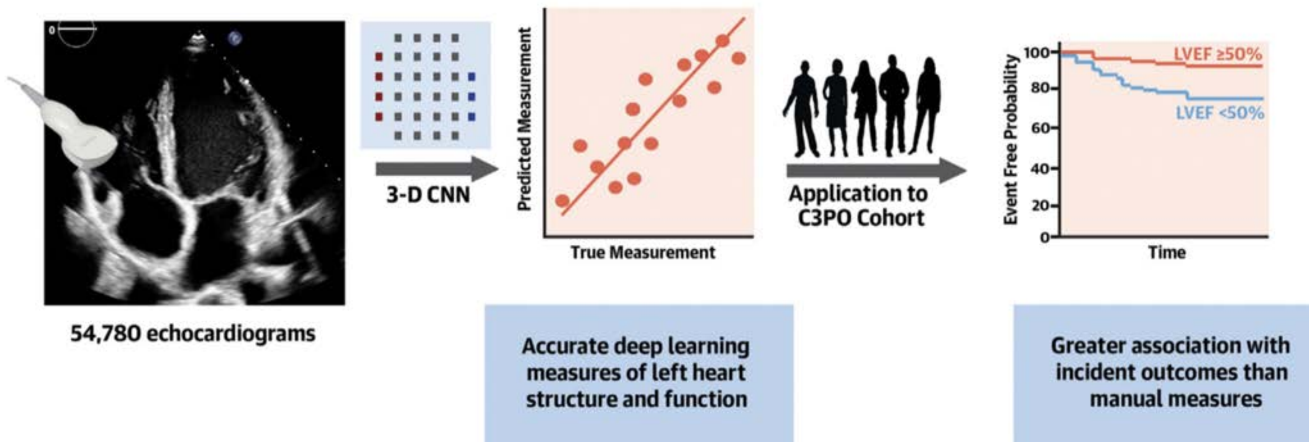


- **Multicenter study of Takotsubo Registry and Zurich Acute Coronary Registry**
- **448 pts (228 for model training, 220 for testing) in cohort**
- **Fully automated system**
  - Convolutional neural network
  - Echo feature extraction
  - Autoencoder
- **Algorithm vs 4 expert practicing cardiologists**
- **ML more accurate that cardiologists**
  - Model AUC 0.79, accuracy 0.748
  - Cardiologist AUC 0.71, accuracy 0.644

Laumer F, et al: JAMA Cardiol. 2022 May

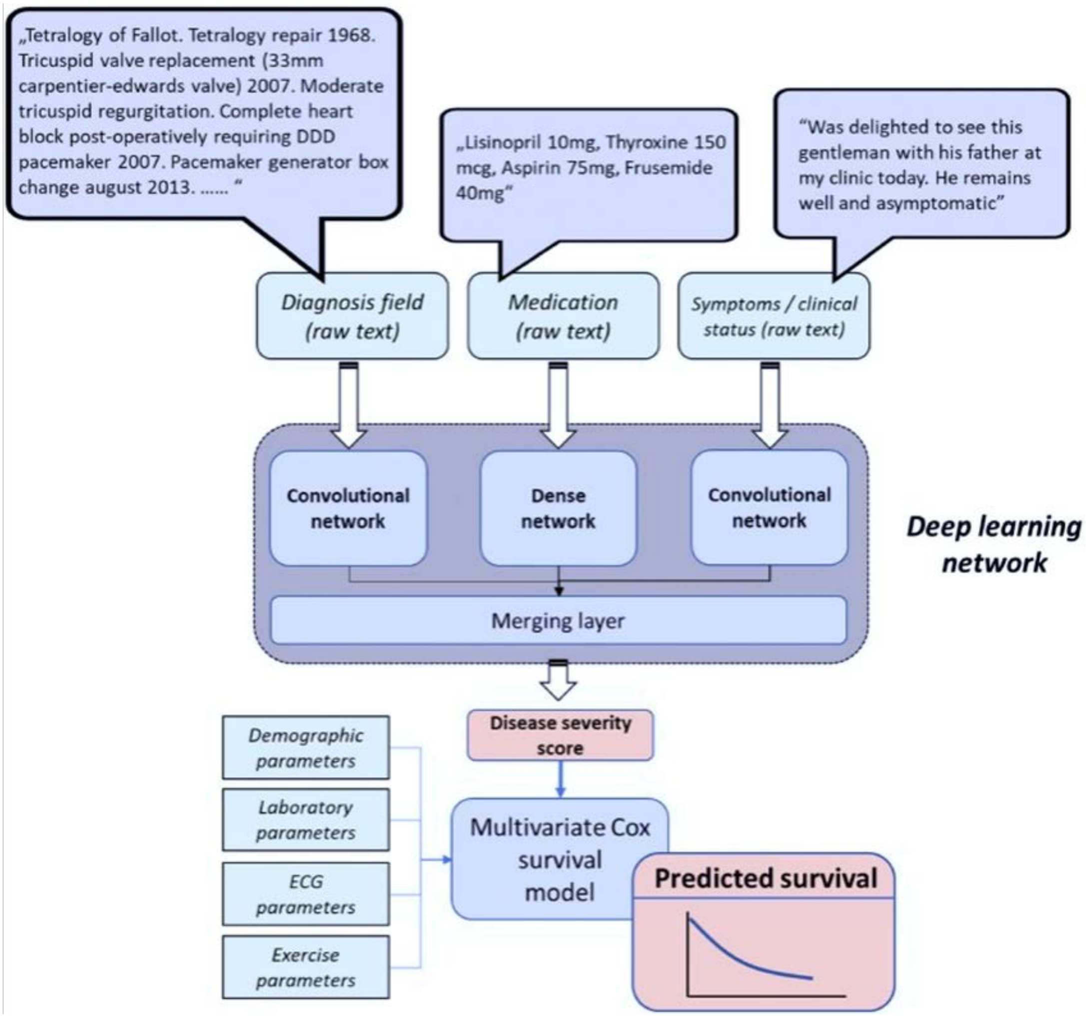
ML and Echo Prediction - Primary Cardiology

- **Multi-institutional sample ambulatory care database**
  - 63,028 echos, 27,135 pts
- **Automated echo measurements**
  - Convolutional NN to measure LVEDD, LVESD, LVEF, IVS, LA dimension
  - Predictions of time-to-event
- **Best Predictor (Hazard Ratio: ML vs. Standard)**
  - Heart failure (2.27, 1.78)
  - Atrial fibrillation (2.23, 1.66)
  - Myocardial infarction (1.74, 1.39)
  - Mortality (1.89, 1.65)



Lau ES, et al. J Am Coll Cardiol. 2023

Using a personalized AI-generated care plan

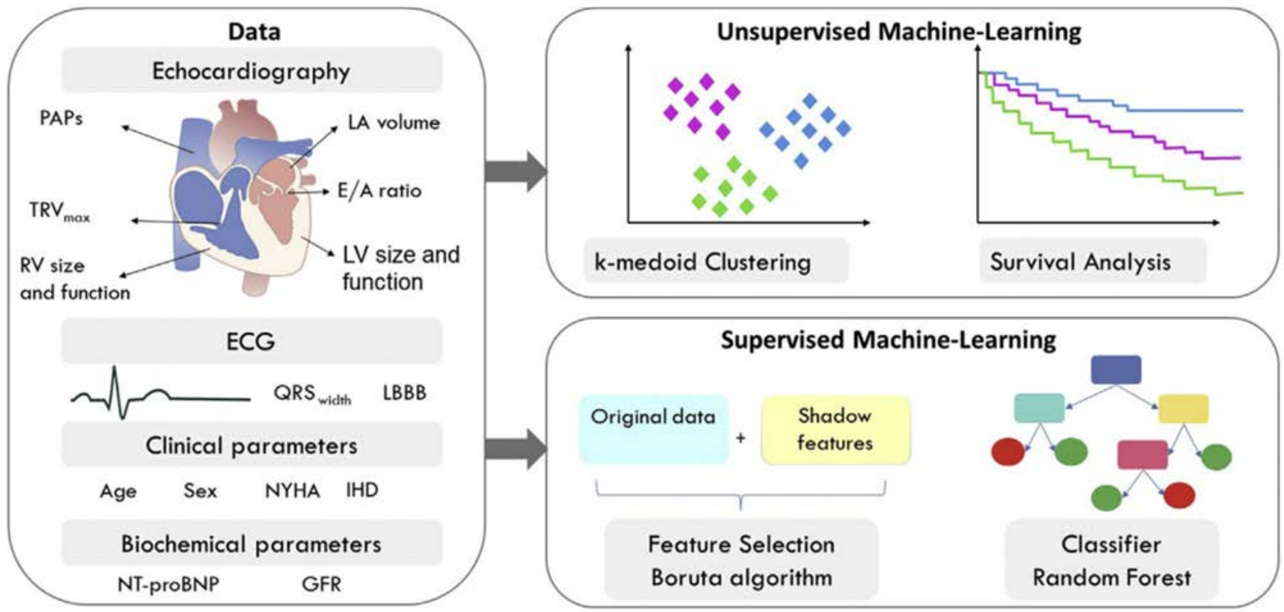


Machine learning algorithms estimating prognosis and guiding therapy in adult congenital heart disease: data including 10019 patients

Diller et al. European Heart Journal. 2019

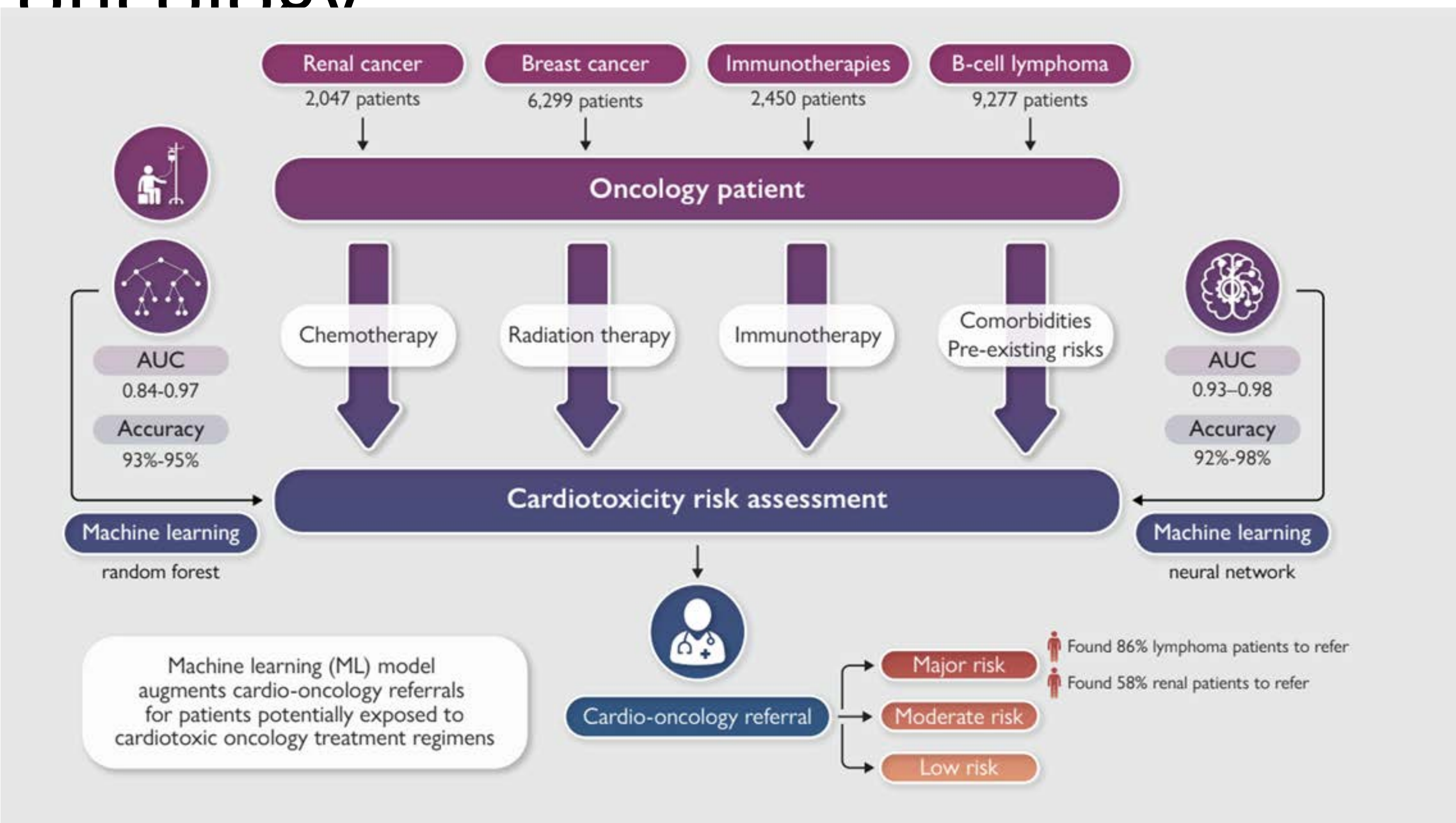
Diagnosis to Prediction – CRT in Heart Failure

- **Multicenter study: 193 pts with systolic heart failure and criteria for CRT**
  - 28 clinical, echocardiographic, and EKG features
- **Unsupervised learning**
  - 2 phenogroups w/ significantly different prognosis
- **Supervised learning (random forest)**
  - 16 features predictive of CRT response
  - 11 features predictive of prognosis
- **ML reliably identified clinical and echo features associated with outcomes**
  - AUC 0.81 for CRT response, 0.84 for prognosis



Galli E, et al: J Am Soc Echocardiogr. 2021

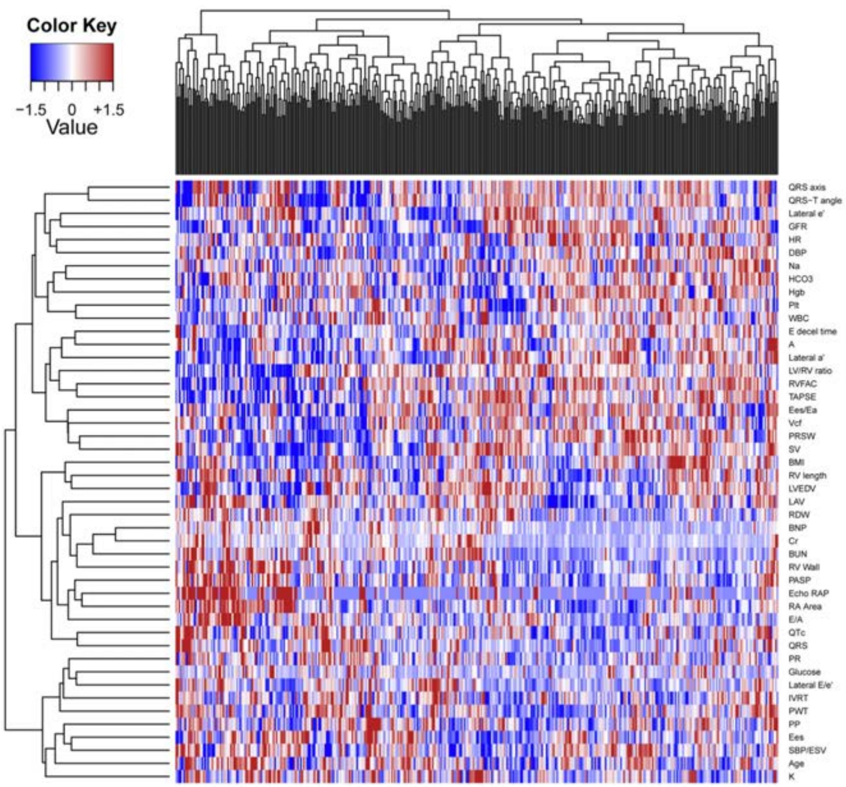
ML and Cardiac Imaging Prediction - Cardio-oncology

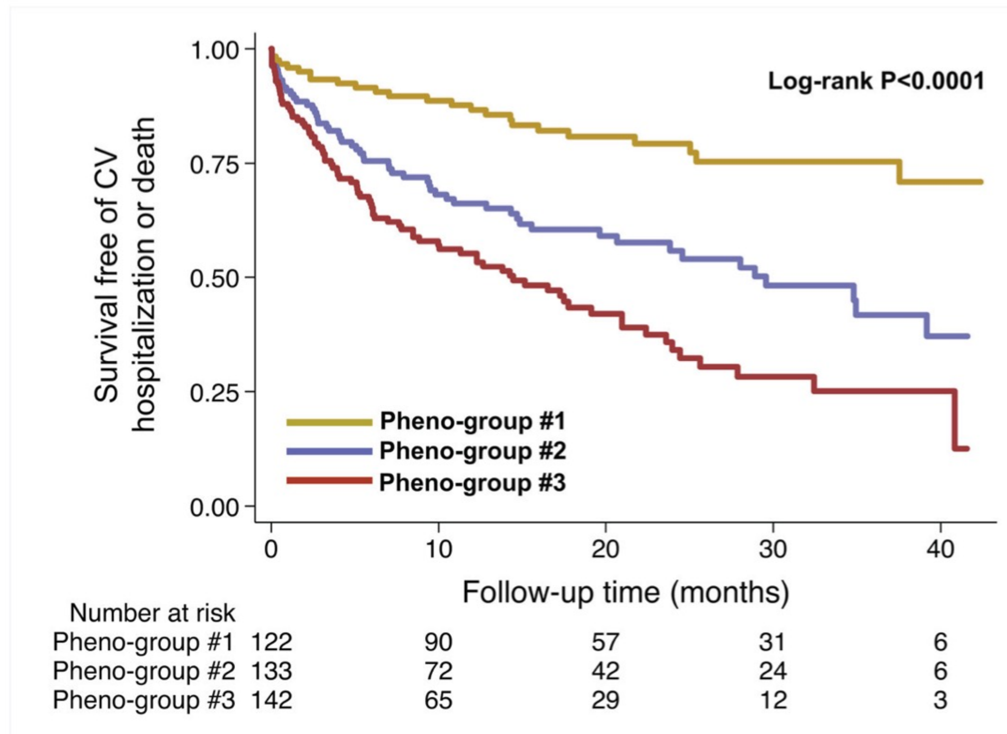


- **Single center study**
- **20,023 pts (80% for model training, 20% for testing)**
  - Clinical, echo, and EKG features
- **ML methods**
  - Neural network
  - Random forest
- **Risk assessment for cardiotoxicity**
  - Model AUC > 0.90
- **System being integrated into EMR to guide cardio-oncology referral**

Al-Droubi SS, et al. Eur Heart J Digit Health. 202

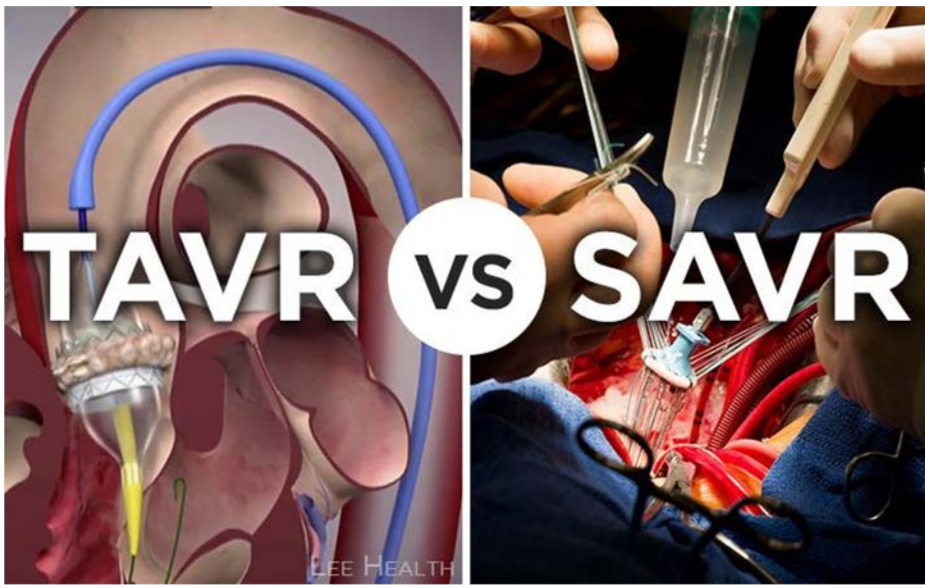
Echocardiography and Phenomapping for Outcomes Prediction





Shah et. Al, Circulation, 2015

We are doing it in Interventional Cardiology



To select surgical replacement or TAVR for severe aortic stenosis

Develop a machine learning predictive model

Validated vs actual choices made in independent sample—98% accuracy

Results serve as an assistance tool to guide clinicians

Clinical trials

- Show better outcomes when using the predictive model in practice

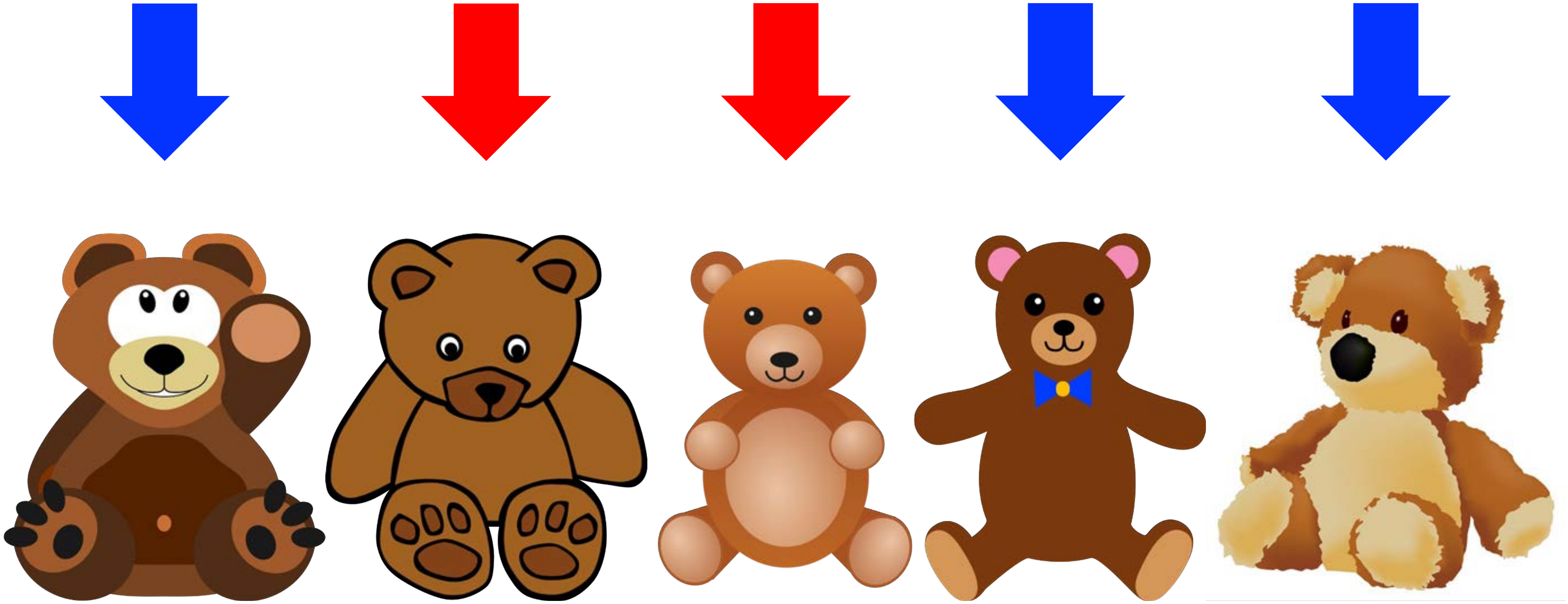
Chokesuwattanaskul R, et al: Machine Learning-Based Predictive Model of Aortic Valve Replacement Modality Selection in Severe Aortic Stenosis Patients. Med Sci (Basel). 2023


Data is often kept in 'silos'
- Isolated from other critical patient information
- Not as useful as it could be
Silo demolition is required to connect everything we know

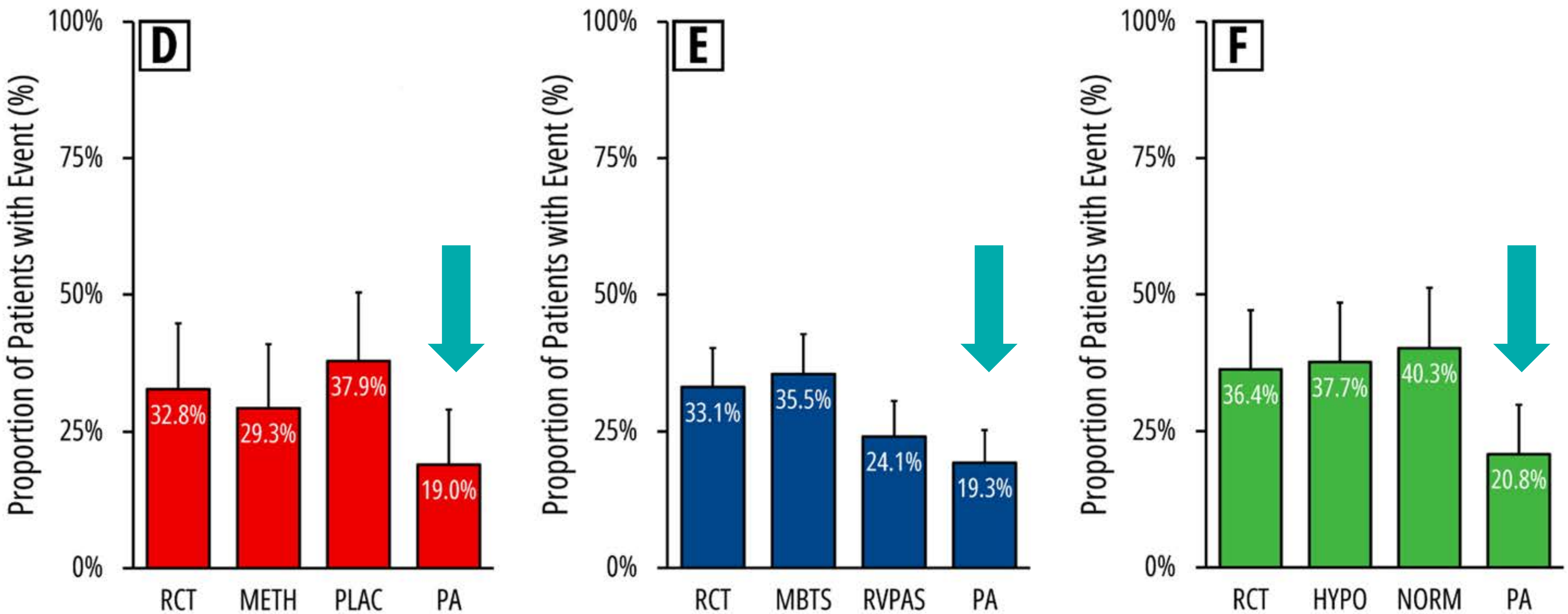
Do you know about any RCTs that provide evidence that we should

The Concept of the Heterogenous Treatment Effect

The research question: If we develop a predictive model to distinguish red arrow bears from blue arrow bears, and allocate treatment accordingly, would our bears do better overall?

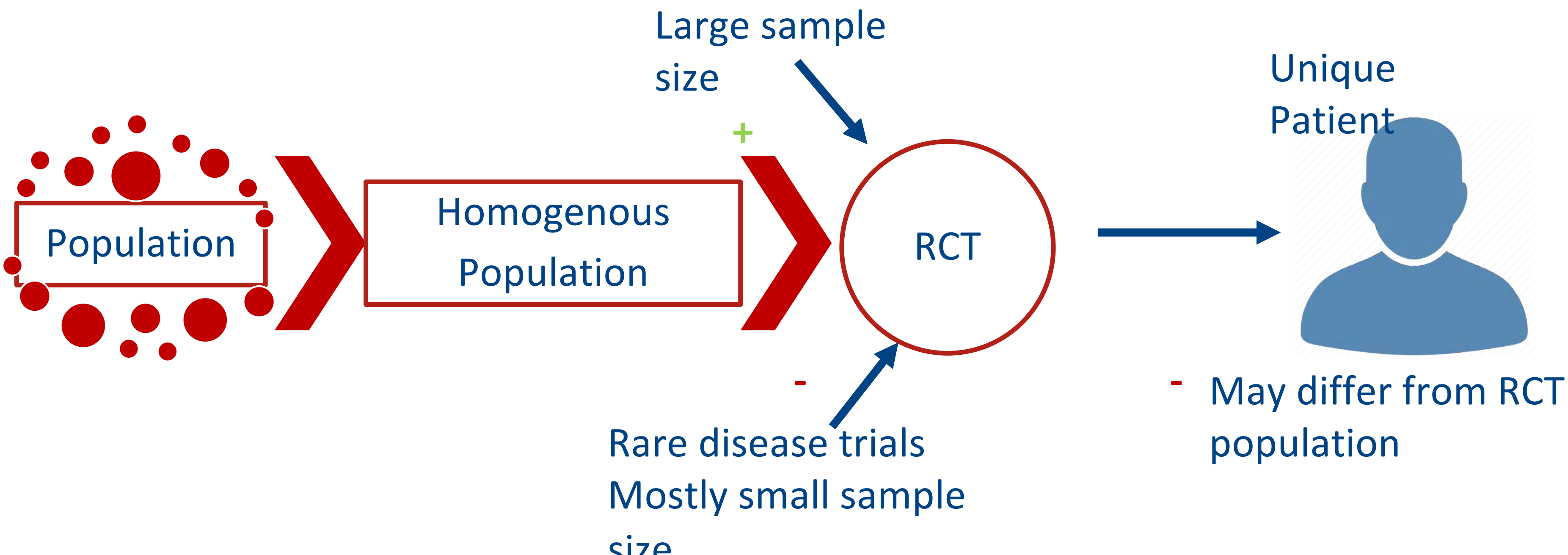


Simulated Results of Predictive Allocation

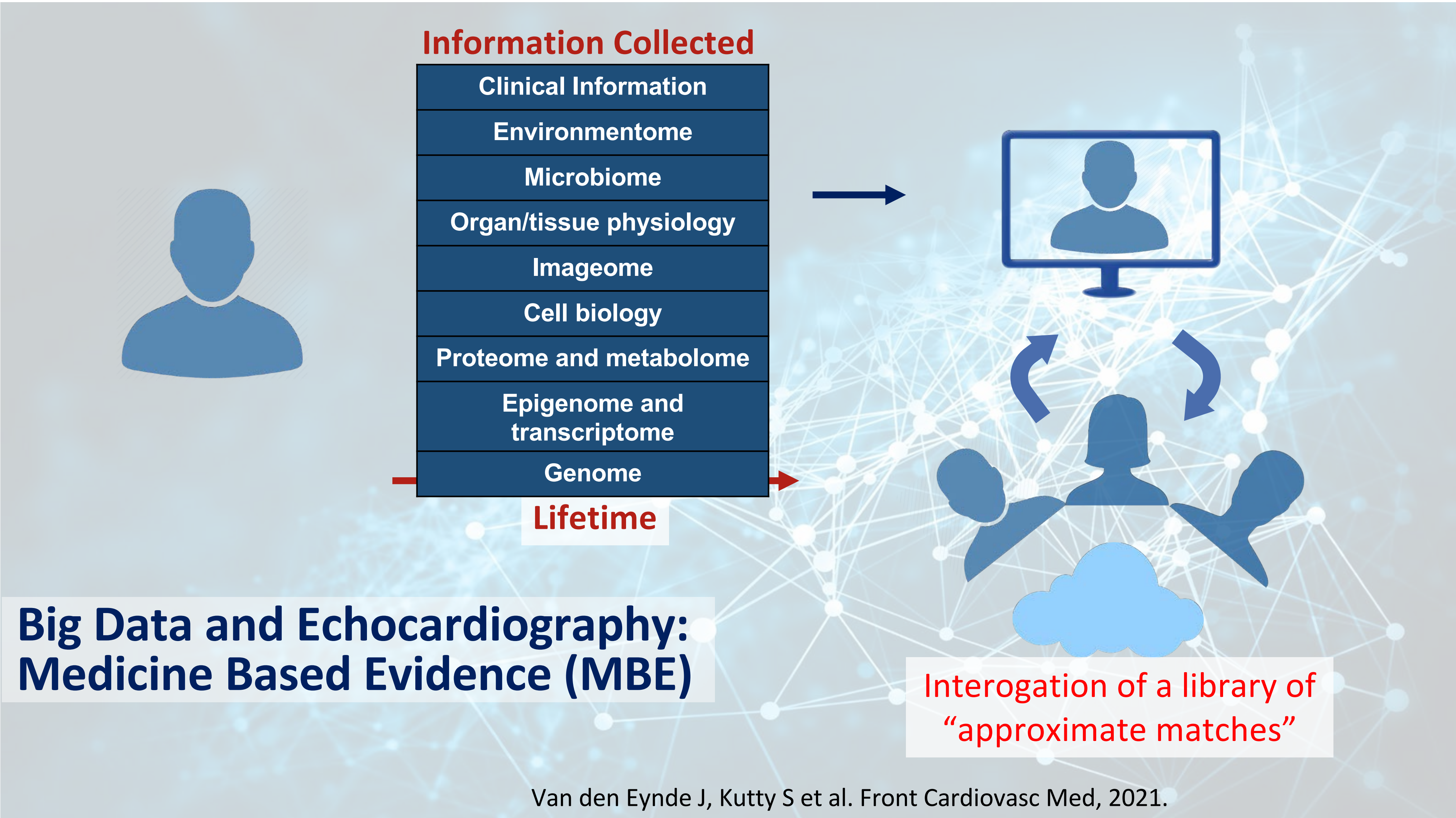


Jacquemyn X et al. J Am Med Inform Assoc. 2024

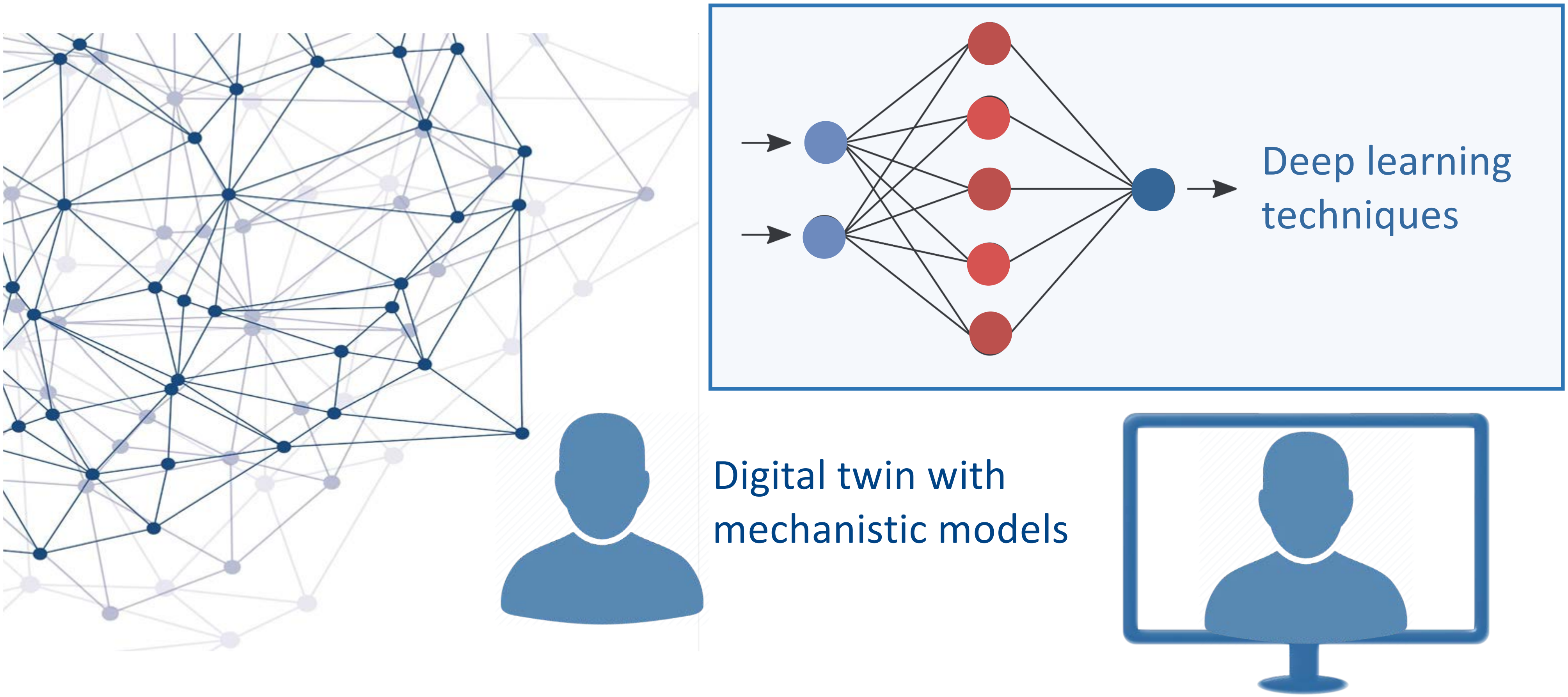
Big Data and Cardiac Imaging: Beyond the RCT and Evidence Based Medicine



Can deep learning help?


Information Collected
Clinical Information
Environmentome
Microbiome
Organ/tissue physiology
Imageome
Cell biology
Proteome and metabolome
Epigenome and transcriptome
Genome
Lifetime
Big Data and Echocardiography:
Medicine Based Evidence (MBE)
Interogation of a library of
“approximate matches”
Van den Eynde J, Kutty S et al. Front Cardiovasc Med, 2021.

Big Data and Imaging - Medicine Based Evidence



Hurdles for Machine Learning in Medicine

- Labor and Cost
  - Building databases
  - Writing algorithms
  - Maintenance
- Ethical
- Legal
- Acceptance
  - General public
  - Medical community

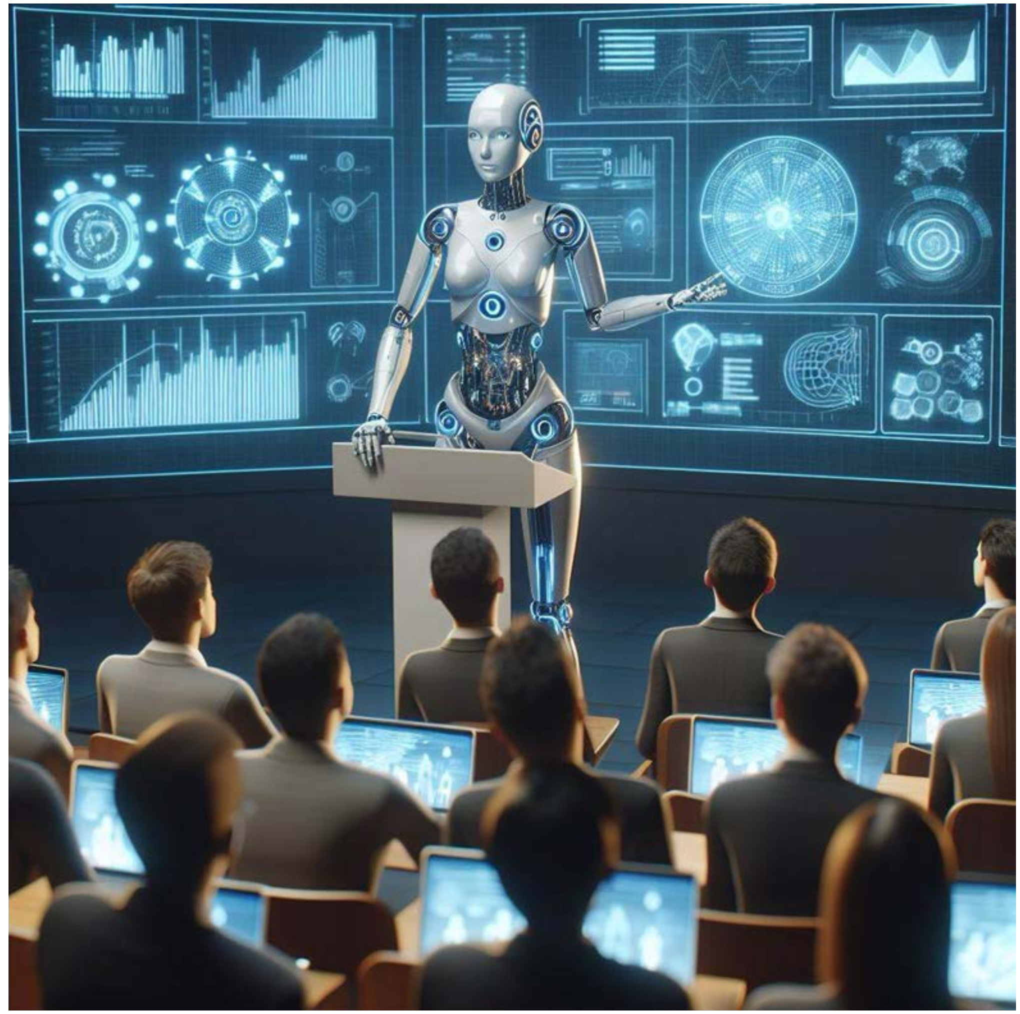
AI in healthcare presents specific challenges

ETHICA L		LEGA L	
Regulation Privacy Mitigation of Bias	Transparenc y Relevance	Governance Confidentialit y Liability	Accuracy Decision- making

Derived from Gerke S, et al. Academic Press, 2020 | Naik et. al, Frontiers in Surgery.2022

Summary and Conclusions

- Cardiac Imaging is big data
- Machine learning can apply
  - Image wrangling
  - Prediction
  - Clinical trials
- Examples
  - Cardiomyopathies
  - Ischemic heart disease
  - Congenital heart disease
  - Therapeutic outcomes
    - Adverse events
    - Resynchronization
- Barriers
- Potential
  - Better use of big data
  - Benefit of patients




MACHINE LEARNING IN CV DISEASE – FROM DIAGNOSTICS TO PREDICTION