

## Machine Learning for Healthcare 6.7930, HST.956

### Lecture 6: Risk stratification (cont'd) & Physiological time-series Feb 28, 2023 Peter Szolovits (with many slides from David Sontag)





# Outline for today's class

- 1. Using ML for risk stratification (continued)
  - Alternative framing: survival modeling
  - Evaluation: metrics, interpretability
- 2. Physiological time-series: application to detecting irregular heart arrythmias
  - Small data approach
  - Big data approach
  - Current research

# Reminder: (One) framing for ML as binary classification



#### Exclusion criteria:

- Diabetes diagnosis (according to our rule) observed prior to January 1, 2009
- Less than 6 months of enrollment in feature construction window
- Member left health insurance prior to Jan. 1, 2011

[Razavian, Blecker, Schmidt, Smith-McLallen, Nigam, Sontag. Big Data. '16]

# Alternative framing: ML with survival models

 Regression (i.e., predict time to event) with <u>right-</u> <u>censored</u> data



<sup>[</sup>Wang, Li, Reddy. Machine Learning for Survival Analysis: A Survey. 2017]

# Alternative framing: ML with survival models

- Advantages over window-based classification
  - More data for training (fewer exclusions)
  - Allows for more fine-grained metrics in evaluation
- Why not just minimize mean-squared error with observed events using least squares linear regression?
  - Time-to-event is non-negative (and non-Gaussian)
  - Naively removed censored events could introduce substantial bias



# ML with survival models (more on this later in the semester)

• f(t) = P(t) be the probability of death at time t



Fig. 2: Relationship among different entities f(t), F(t) and S(t).

[Wang, Li, Reddy. Machine Learning for Survival Analysis: A Survey. 2017] [Ha, Jeong, Lee. Statistical Modeling of Survival Data with Random Effects. Springer 2017]

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## "Table 1" – who did this study include?

| Table 1. Subjects' characteristics of the cohort included in training and validation |                  |                          |  |
|--|------------------|--------------------------|--|
| Characteristic   | Total population | Population with diabetes |  |
| Average age (SD)   | 47.69 (17.1)     | 58.57 (13.3)             |  |
| Female ratio   | 55%              | 51%                      |  |
| Average length of data in years (SD)   | 3.3 (1.0)        | 3.4 (1.0)                |  |
| Hypertension (ICD9 401)  | 30.2%            | 62%                      |  |
| Hypercholesterolemia (ICD9 272.0)  | 18.7%            | 33.6%                    |  |
| SD, standard deviation.  |                  |                          |  |

## But what about... Past hospitalizations? Race/ethnicity? Lab values? Radiology results?

[Razavian, Blecker, Schmidt, Smith-McLallen, Nigam, Sontag. Big Data. '16]

## "Table 1", better example

| Table 1. Characteristics of 47 119 Hospitalized | Patients      | Blood pressure, mean (SE), mm Hg           |                        |
|---|---------------|--|------------------------|
| Characteristic                                  | Finding       | Systolic                                   | 123.3 (18.             |
| Age, mean (SE), y                               | 60.9 (18.15)  | Diastolic                                  | 67.8 (12.              |
| Female  | 23 952 (50.8) | Creatinine, mean (SE), mg/dL               | 1.01 (1.               |
| Black/African American race                     | 5258 (11.2)   | Sodium, mean (SE), mEq/L                   | 138.4 (3.7             |
| Hispanic/Latino ethnicity                       | 3667 (7.8)    | BNP, pg/mL                                 |                        |
| Medicaid  | 8303 (17.6)   | <500                                       | 1721 (23.4)            |
| Heart failure in problem list                   | 3630 (7.7)    | 500-999                                    | 878 (12.0)             |
| Prior diagnosis of any heart failure            | 2985 (6.3)    | 1000-4999                                  | 2498 (34.0)            |
| Prior diagnosis of primary heart failure        | 615 (1.3)     | 5000-9999                                  | 931 (12.7)             |
| Prior echocardiography                          | 15 938 (33.8) | 10 000-19 999<br>≥20 000                   | 652 (8.9)<br>667 (9.1) |
| Loop diuretics                                  |               | Blood pressure                             | 007 (9.1)              |
| Inpatient                                       | 6837 (14.5)   | Any systolic                               | 46 982 (99.7)          |
| Outpatient                                      | 6427 (13.6)   | Any diastolic                              | 46 982 (99.7)          |
| ACE inhibitors or ARB                           |               | Any creatinine                             | 46 598 (98.9)          |
| Inpatient                                       | 13 166 (27.9) | Any sodium                                 | 46 613 (98.9)          |
| Outpatient                                      | 14797 (31.4)  | Any BNP                                    | 7347 (15.6)            |
| β-Blockers                                      |               | Problem list                               |                        |
| Inpatient                                       | 19748 (41.9)  | Acute MI                                   | 952 (2.0)              |
| Outpatient                                      | 14870 (31.6)  | Atherosclerosis                            | 6147 (13.0)            |
| Heart failure with β-blockers                   |               | Final discharge diagnosis of heart failure |                        |
| Inpatient                                       | 6310 (13.4)   | Any diagnosis                              | 6549 (13.9)            |
| Outpatient                                      | 8644 (18.4)   | Principal diagnosis                        | 1214 (2.6)             |

[Blecker et al., Comparison of Approaches for Heart Failure Case Identification From Electronic Health Record Data, JAMA Cardiology 2016]

## Logistic regression with L1 regularization

 Penalizing the L1 norm of the weight vector leads to *sparse* (read: many 0's) solutions for *w*.

$$\begin{split} \min_{w} \sum_{i} \ell(x_{i}, y_{i}; w) + \lambda ||w||_{1} & ||\vec{w}||_{1} = \sum_{d} |w_{d}| \\ \text{instead of} \\ \min_{w} \sum_{i} \ell(x_{i}, y_{i}; w) + \lambda ||w||_{2}^{2} & ||\vec{w}||_{2}^{2} = \sum_{d} w_{d}^{2} \end{split}$$

Let's understand why...

## Logistic regression with L1 regularization

• Penalizing the L1 norm of the weight vector leads to *sparse* (read: many 0's) solutions for *w*.



## Logistic regression with L1 regularization

- <u>769</u> variables have non-zero weight, of >42K. Look at most positive & most negative
- Positively weighted diagnosis codes include

Pituitary dwarfism (253.3), Hepatomegaly(789.1), Chronic Hepatitis C (070.54), Hepatitis (573.3), Calcaneal Spur(726.73), Thyrotoxicosis without mention of goiter(242.90), Sinoatrial Node dysfunction(427.81), Acute frontal sinusitis (461.1), Hypertrophic and atrophic conditions of skin(701.9), Irregular menstruation(626.4), ...

• Positively weighted laboratory features include

Albumin/Globulin (Increasing -Entire history), Urea nitrogen/Creatinine -(high - Entire History), Specific gravity (Increasing, Past 2 years), Bilirubin (high -Past 2 years), ...

[Razavian, Blecker, Schmidt, Smith-McLallen, Nigam, Sontag. Big Data. '16]

## Interpreting high-dimensional linear models

- How do we interpret such high dimensional models...?
- A useful trick to build intuition: use higher value of  $\lambda$  (i.e., more regularization) than needed

$$\min_{w} \sum_{i} \ell(x_i, y_i; w) + \lambda ||w||_1$$

- What will the effect be?
- Intuition: often many predictive yet highly correlated features. Selects a representative set which still performs well



• Choice of  $\lambda$  depends on application: how much performance are you willing to give up for a simpler (more explainable) model?

# Features selected using model learned with more L1 regularization

#### History of Disease

Impaired (elevated) Fasting Glucose (Code 790.21)

Abnormal Glucose NEC (790.29)

Hypertension (401)

Obstructive Sleep Apnea (327.23)

Obesity (278)

Abnormal Blood Chemistry (790.6)

Hyperlipidemia (272.4)

Shortness Of Breath (786.05)

Esophageal Reflux (530.81)

#### **Top Lab Factors**

Hemoglobin A1c /Hemoglobin.Total (High - past 2 years)

Glucose (High-Past 6 months)

Cholesterol.In VLDL (Increasing - Past 2 years)

Potassium (Low - Entire History)

Cholesterol.Total/Cholesterol.In HDL (High - Entire History)

Erythrocyte mean corpuscular hemoglobin concentration -(Low - Entire History)

Eosinophils (High - Entire History)

Glomerular filtration rate/1.73 sq M.Predicted (Low -Entire History)

Alanine aminotransferase (High Entire History)

[Razavian, Blecker, Schmidt, Smith-McLallen, Nigam, Sontag. Big Data. '16]

# Debugging ML setup through model interpretation

- Suppose a highly weighted positive feature is for "injection of aflibercept", a treatment for diabetic macular edema. What could we infer?
- Suppose we see many features for flu vaccines with high positive and negative weights. Looking up the NDC code for one of them, we see it is "influenza A virus A/Hong Kong/ 4801/2014 (H3N2) antigen 0.03 MG". What could we infer?
- Note, these would have been much harder to diagnose using the deep model

## Receiver-operator characteristic curve



### Comparison with the deep models

We consider three prediction tasks. Over a horizon of 3 to 9 months into the future, predict:



Evaluate using de-identified dataset of ~120K Medicare Advantage members

Kodialam et al., Deep Contextual Clinical Prediction with Reverse Distillation, AAAI '21

ML methods that we compare

- **SARD** (Kodialam et al. 2021)
- **BEHRT** (Li et al. 2020): another transformer-based neural network for claims data
- **RETAIN** (Choi et al. 2016): a recurrent neural network designed with interpretability in mind
- Windowed linear model (Razavian et al. 2015)

Kodialam et al., Deep Contextual Clinical Prediction with Reverse Distillation, AAAI '21

### Results on the 3 prediction tasks

#### AUC-ROC scores on test set

| Task Name<br>Model   | EoL  | Surgery | LoH  |
|--|------|---------|------|
| <i>L</i> <sub>1</sub> -reg. logistic regression [Razavian et al. 2015] | 83.4 | 79.2    | 73.1 |
| RETAIN [Choi et al. 2016]  | 82.2 | 79.8    | 72.5 |
| BEHRT [Li et al. 2020]   | 83.1 | 80.3    | 71.2 |

| SARD | 85.6 | 83.1 | 74.3 |
|------|------|------|------|

SARD uses "reverse distillation" (RD) for pre-training (see Kodialam et al. '21)

Kodialam et al., Deep Contextual Clinical Prediction with Reverse Distillation, AAAI '21

## Closing reflections for risk stratification

- How can we build models that work with multimodal data?
  - Multiple choices for neural network architectures
  - Will often be missing one or more modalities
- How do we choose which target to predict? Has implications for health equity
- What is a "good" result? Depends on the use case high PPV for targeting interventions, high NPV (negative predictive value) for screening

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## **Detecting atrial fibrillation**





### AliveCore ECG device

ECG = electrocardiogram

## **Detecting atrial fibrillation**



### Apple Watch





[Clifford, Liu, Moody, Mark. PhysioNet Computing in Cardiology Challenge 2017]



## Traditional approach



2. Common structure of the QRS detectors.

[Kohler, Hennig, Orglmeister. The Principles of Software QRS Detection, IEEE Engineering in Medicine & Biology, 2002]



#### 3. Peak detector proposed in [41].

[Kohler, Hennig, Orglmeister. The Principles of Software QRS Detection, IEEE Engineering in Medicine & Biology, 2002]



Fig. 1 Time series showing RR intervals from subject 202 from MIT-BIH arrhythmia database. (-----) Assessment of atrial fibrillation (AF) or non-atrial fibrillation (N) as reported in database

[Tateno & Glass, Automatic detection of atrial fibrillation using the coefficient of variation and density histograms of RR and ΔRR intervals. MBEC, 2001]

#### Cardiac Arrhythmia Classification:

A Heart-Beat Interval-Markov Chain Approach \*

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Received March 2, 1970

A sequence of heart-beat intervals (R-R wave intervals) is automatically transformed into a three-symbol Markov chain sequence. For convenience the symbols used may be thought of as S-R-L for short, regular, and long heart-beat intervals, respectively. The **probability** that the observed sequence was generated by each of a set of prototype models characteristic of different cardiac disorders is computed. That prototype corresponding to the largest probability of observed sequence generation is designated as the disorder. This procedure is the equivalent of **Kullback's** classification by the minimization of directed divergence procedure.

In a **preliminary** experiment **primarily** using data sequences of 100 heart-beat intervals, 35 different known cases were automatically classified into six cardiac disorders without error. The disorders considered were **atrial fibrillation**, **APC** and VPC, bigeminy, sinus tachycardia with occasional bigeminy. sinus tachycardia, and ventricular tachycardia.

An automatic procedure to classify cardiac arrhythmias using a Markov chain interpretation of heart-beat interval **data** is reported. A sequence of heart-beat

#### Detection of Atrial Fibrillation Using Artificial Neural Networks

SG Artis, RG Mark, GB Moody

Harvard-MIT Division of Health Sciences and Technology, Cambridge, MA

#### Abstract

Artificial neural networks (ANNs) were used as pattern detectors to detect atrial fibrillation (AF) in the MIT-BIH Arrhythmia Database. ECG data was represented using generalized interval transition matrices, as in Markov model AF detectors[1]. A training file was developed, using these transition matrices, for a backpropagation ANN. This file consisted of approximately 15 minutes each of AF and non-AF data. The ANN was succesfully trained using this data. Three standard databases were used to test network performance. Postprocessing of the ANN output yielded an AF sensitivity of 92.86% and an AF positive predictive accuracy of 92.34%.

#### 1 Introduction

A 12 - - 1 - 4 - 2 - - - - 1 - 1 - 24 - 1 - - 1 - 4 - -

on R-R interval sequences using a variety of statistical methods [1] but there is room for improvement in these techniques.

Pattern classifiers exist in many forms, and artificial neural networks (ANNs) represent an important subset of these classifiers. ANNs are attractive for solving pattern recognition problems because few assumptions about the underlying data need to be made. The task of the operator of an ANN is to separate the data into subsets. The network will be able classify these subsets according to type as long as they are distinct. Neural network training requires appropriate training data, pre-processing and post-processing algorithms, an appropriate network topology, and a training algorithm, as well as evaluation databases. This document will present the design and evaluation of a technique which detects AF in the presence of other cardiac arrhythmias using a backpropagation artificial neural network.

# Winning approach in 2017 Physionet challenge

- Training data: ~8500 ECGs
- Best algorithms use a combination of expert-derived features and machine learning



[Teijeiro, Garcia, Castro, Felix. arXiv:1802.05998, 2018]

| tSR: Proportion of the record length interpreted as<br>a regular rhythm (Normal rhythm, tachycardia or<br>bradycardia). | t1b: Number of milliseconds from the beginning of the<br>record to the first interpreted heartbeat.                  |
|---|--|
| tOR: Number of milliseconds interpreted as a non-regular<br>rhythm.   | <pre>longTch: Longest period of time with heart rate over<br/>100bpm.</pre>  |
| RR: Median RR interval of regular rhythms.  | RRd_std: Standard deviation of the instant RR variation.   |
| RRd: Median Absolute Deviation (MAD) of the RR<br>interval in regular rhythms.  | MRRd: Max. absolute variation of the RR interval in regular rhythms.   |
| RR_MIrr: Max. RR irregularity measure.  | RR_Irr: Median RR irregularity measure.  |
| PNN{10,50,100}: Global PNNx measures.   | o_PNN50: PNN50 of non-regular rhythms.   |
| mRR: Min. RR interval of regular rhythms.   | o_mRR: Min. RR interval of non-regular rhythms.  |
| n_nP: Proportion of heartbeats with detected P-wave<br>inside regular rhythms.  | n_aT: Median of the amplitude of the T waves inside<br>regular rhythms.  |
| n_PR: Median PR duration inside regular rhythms.  | <b>Psmooth:</b> Median of the ratio between the standard deviation and the mean value of P-waves' derivative signal. |
| Pdistd: MAD of the measure given by the P wave<br>delineation method.   | MPdist: Max. of the measure given by the P wave delineation method.  |
| prof: Profile of the full signal.   | pw_profd: MAD of pw_prof.  |
| xcorr: Median of the maximum cross-correlation<br>between QRS complexes interpreted in regular rhythms.                 | o_xcorr: Median of the maximum cross-correlation<br>between QRS complexes interpreted in non-regular<br>rhythms.     |
| PRd: Global MAD of the PR durations.  | QT: Median of the corrected QT measure.  |
| TP: Median of the prevailing frequency in the TP<br>intervals.  | TPfreq: Median of the frequency entropy in the TP intervals.   |
| pw_prof: Profile measure of the signal in the P-wave area.  | nT: Proportion of QRS complexes with detected T waves.   |
| n_Txcorr: Median of the maximum cross-correlation<br>between T-waves inside regular rhythms.                            | n_Pxcorr: Median of the maximum cross-correlation<br>between P-waves inside regular rhythms.                         |
| baseline: Profile of the baseline in regular rhythms.   | o_baseline: Profile of the baseline in non-regular rhythms.  |
| wQRS: Proportion of wide QRS complexes (duration<br>longer than 110ms).   | wQRS_xc: Median of the maximum cross-correlation<br>between wide QRS complexes.                                      |
| wQRS_prof: Median of the signal profile in the 300ms<br>before each wide QRS complex.                                   | <pre>w_PR: Proportion of heartbeats with long PR interval<br/>(longer than 210 ms).</pre>                            |
| $x_xc$ : Median of the maximum cross-correlation between ectopic beats.   | <pre>x_rrel: Median of the ratio between the previous and<br/>next RR intervals for each ectopic beat.</pre>         |

Table 1: Set of features used to train the global classifier

[Teijeiro, Garcia, Castro, Felix. arXiv:1802.05998, 2018]

## Not enough data for deep learning? Wrong architectures?

"However, the fact that a standard random forest with well chosen features performed as well as more complex approaches, indicates that perhaps a set of 8,528 training patterns was not enough to give the more complex approaches an advantage. With so many parameters and hyperparameters to tune, the search space can be enormous and significant overtraining was seen..."

[Clifford et al. AF Classification from a Short Single Lead ECG Recording: the PhysioNet/Computing in Cardiology Challenge, Computing in Cardiology 2017]

Stanford ML Group

### Cardiologist-Level Arrhythmia Detection With Convolutional Neural Networks

## Pranav Rajpurkar\*, Awni Hannun\*, Masoumeh Haghpanahi, Codie Bourn, and Andrew Ng

A collaboration between Stanford University and iRhythm Technologies

We develop a model which can diagnose irregular heart rhythms, also known as arrhythmias, from single-lead ECG signals better than a cardiologist.

Key to exceeding expert performance is a deep convolutional network which can map a sequence of ECG samples to a sequence of arrhythmia annotations along with a novel dataset two orders of magnitude larger than previous datasets of its kind.



[Rajpurkar et al., arXiv:1707.01836, 2017; Hannun et al. Nature Medicine '19]

## Differences with previous work

• Sensor is a Zio patch – conceivably much less noisy:



- ~90K ECG records annotated (from ~50K patients)
- Identify 12 heart arrhythmias, sinus rhythm and noise for a total of 14 output classes




### Deep convolutional network

- 1-D signal sampled at 200Hz, labeled at 1 sec intervals
- 34 layers
- Shortcut connections (ala residual networks) with maxpooling
- Subsampled every other layer (2<sup>8</sup> in total)

[Rajpurkar et al., arXiv:1707.01836, 2017; Nature Medicine '19]



## Example of 1D convolution







### Evaluation: beat-level ('Seq') vs. patient-level ('Set')

|                      | Seq   |          | Set   |         |
|----------------------|-------|----------|-------|---------|
|                      | Model | Cardiol. | Model | Cardiol |
| Class-level F1 Score |       |          |       |         |
| AFIB                 | 0.604 | 0.515    | 0.667 | 0.544   |
| AFL                  | 0.687 | 0.635    | 0.679 | 0.646   |
| AVB_TYPE2            | 0.689 | 0.535    | 0.656 | 0.529   |
| BIGEMINY             | 0.897 | 0.837    | 0.870 | 0.849   |
| CHB                  | 0.843 | 0.701    | 0.852 | 0.685   |
| EAR                  | 0.519 | 0.476    | 0.571 | 0.529   |
| IVR                  | 0.761 | 0.632    | 0.774 | 0.720   |
| JUNCTIONAL           | 0.670 | 0.684    | 0.783 | 0.674   |
| NOISE                | 0.823 | 0.768    | 0.704 | 0.689   |
| SINUS                | 0.879 | 0.847    | 0.939 | 0.907   |
| SVT                  | 0.477 | 0.449    | 0.658 | 0.556   |
| TRIGEMINY            | 0.908 | 0.843    | 0.870 | 0.816   |
| VT                   | 0.506 | 0.566    | 0.694 | 0.769   |
| WENCKEBACH           | 0.709 | 0.593    | 0.806 | 0.736   |

$$F_1 = rac{2}{ ext{recall}^{-1} + ext{precision}^{-1}} = 2 \cdot rac{ ext{precision} \cdot ext{recall}}{ ext{precision} + ext{recall}} = rac{ ext{tp}}{ ext{tp} + rac{1}{2}( ext{fp} + ext{fn})}$$
 Recall = sensitivity Precision = PPV

## **Evaluation: confusion matrix**



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### Predicting 1-year mortality using 12-lead ECGs

-0.2

-0.4 -0.6

-0.8 -1.0

-1.2

- >2 million ECGs from 500k patients seen at Geisinger (in Pennsylvania) over 30 years
- Comparison of predictive performance (AUC):
  - .876 Deep model ECG + age, gender
  - .86 XGBoost using ECG measures + age, gender
  - \_ .816 Charlson comorbidity index

| [Figures from: Raghunath et al., Prediction of mortality from 12-lead electro-cardiogram voltage |
|--|
| data using a deep neural network, Nature Medicine 2020.  |

For related work, see also: Ribeiro et al., Automatic diagnosis of the 12-lead ECG using a deep neural network, Nature Communications 2020]

|                          | Holdout test dataset (total)             | Holdout test dataset |   |  |
|--------------------------|--|----------------------|---|--|
|                          |  | Predicted dead       | Predicted alive                                     |  |
| QRS duration (ms)        | 93±20                                    | 101±28               | 91±15   |  |
| QT (ms)                  | $393 \pm 44$                             | 388±60               | 395±38  |  |
| QTC (ms)                 | 436±34                                   | $458 \pm 42$         | 429±28  |  |
| PR interval (ms)         | 155±40                                   | $151 \pm 60$         | 156±31  |  |
| Ventricular rate (bpm)   | 77±19                                    | 88±23                | 73±16   |  |
| Average RR interval (ms) | 824±183                                  | 728±193              | 852±170   |  |
| Paxis                    | 47±25                                    | 48±31                | 47±23   |  |
| Raxis                    | 27±43                                    | 16±58                | 30±37   |  |
| T axis                   | 45±42                                    | 63±63                | 40±31   |  |
| Lead V2                  | 0.2<br>0<br>-0.2<br>-0.4<br>-0.6<br>-0.8 | Lead V3              | Patient<br>with<br>anterior<br>STEMI<br>who<br>died |  |
|                          |  |                      | within 1  |  |

year

Gradient-CAM (Selvaraju et al., IJCV '19)

#### "Table 1"

# Can we 'push' deep networks to discover new features?



[Beer, Eini-Porat, Goodfellow, Eytan, Shalit. Using deep networks for scientific discovery in physiological signals, Machine Learning in Healthcare 2020]

### Do models generalize across institutions?



[Alday et al., Classification of 12-lead ECGs: The PhysioNet/Computing in Cardiology Challenge 2020, Physiological Measurement, 2020]



Fig. 4: Effect of transfer learning from PTB-XL to ICBEB2018 upon varying the size of the ICBEB2018 training set.

[Strodthoff, Wagner, Schaeffter, Samek. Deep learning for ECG Analysis: Benchmarks and Insights from PTB-XL, IEEE Journal of Biomedical and Health Informatics, 2020]

# Obermeyer Talk last week



- "Machine Learning About Sudden Cardiac Death from ECG Waveforms"
  - 300K people/year (US) drop dead
  - Wearable monitors can detect arrhythmias
  - Fancy implantable cardioversion devices can shock heart to restore rhythm
  - False negatives: many don't get this treatment
  - False positives: 73% of these devices never fire
- Predict risk from waveform; stratify to high and low risk groups
  - Used best algorithms from Physionet Challenge
    - 64-layer ResNet, AUC>90%
- Will patient die? If so, from SCD?

### Predicting Risk of Cardiac Sudden Death

- Swedish Data (2014-18)
  - 401,765 ECGs from 119,724 patients
  - Every patient linked to EHR data, death certificates (if any)
- 0.7% have 1-yr SCD (14.8% of all deaths)
- Best current predictor: ejection fraction
  - 83.3% of SCD have EF≤35%
  - but, 75.2% of SCD have no EF recorded; so, only 20% of SCD appear high-risk
- Train: 30%, Validation: 30%, Test: 40%

- Beyond the AUC
  - High risk ≡ doctor inserts defibrillator (4.4%)
  - These account for ~24.5% of SCD
  - Is predictable risk preventable?
    - Proximal cause of SCD: VF/VT
- Happily, model worked well in Taiwan!
  - Despite different definition of SCD, different population
  - Matched case-control study, Swedish model can distinguish cases and controls, with AUC = 0.804 (vs. 0.846)
  - Adding clinical variables made transferred model AUC = 0.615 (!!!)
- How to incorporate into clinical workflow

https://www.broadinstitute.org/videos/ewsc-machine-learning-about-sudden-cardiac-deathecg-waveforms-ziad-obermeyer

# Closing reflections for ML on physiological data

- We are often in realm of "not enough data"
  - Modeling and incorporating prior knowledge can be critical to good performance
- Is machine learning actually picking up new features?
- How can we improve the interpretability and generalizability of the learned models?