



# Using Machine Learning to Optimize Recruitment for Clinical Trials

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# Disclosures

- **Grants/research support:** Boston Scientific, Medtronic, Abbott, Servier, Novartis, Bayer, BMS/Pfizer, ARCA Biopharm
- **Consulting fees:** Boston Scientific, Medtronic
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# Artificial Intelligence in Research



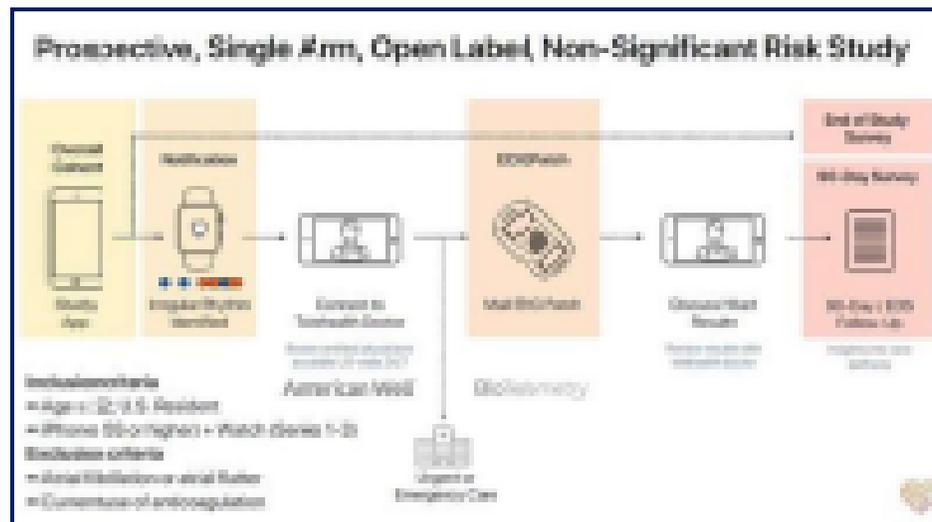
- Big data; artificial intelligence
- Pros
  - Broadly applicable
  - Reach into general population
  - Large statistical power
  - Cost-effective research
  - No need for patient contact
- Cons
  - “Opaque”
  - Clinical translation
  - Potential for errors

# Machine-learning to predict AF

- Attia ZI, et al. Lancet 2019
- 650,000 sinus rhythm ECGs from Mayo Clinic
- Training/validation datasets
- Examined prediction of AF on any other ECG from same patient
- AUC 0.87;
- AUC increased to 0.90 if including all NSR ECGs during first month
- Sensitivity 79%, specificity 80%

# Apple Heart Study

- The Apple Heart Study used a novel study design of self-enrollment.
- 419,297 people self-enrolled in the study within an 8-month enrollment period.



- Apple Watch had moderate accuracy in AF detection.

Turakhia et al. Presented at ACC 2019

## CORRESPONDENCE RETRACTION

Retraction: Cardiovascular Disease, Drug Therapy, and Mortality in Covid-19. N Engl J Med. DOI: 10.1056/NEJMoa2007621



### Retraction—Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis

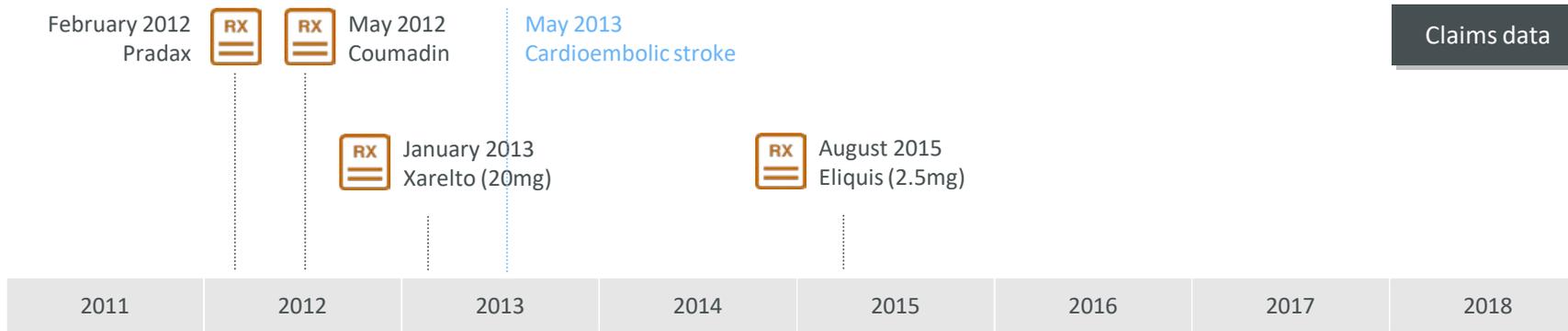
Published Online  
June 4, 2020  
[https://doi.org/10.1016/S0140-6736\(20\)31324-6](https://doi.org/10.1016/S0140-6736(20)31324-6)

After publication of our *Lancet* Article,<sup>1</sup> several concerns were raised with respect to the veracity of the data and analyses conducted by Surgisphere Corporation and its founder and our co-author, Sapan Desai, in our publication. We launched an independent third-party peer review of Surgisphere with the consent of

We all entered this collaboration to contribute in good faith and at a time of great need during the COVID-19 pandemic. We deeply apologise to you, the editors, and the journal readership for any embarrassment or inconvenience that this may have caused.

# Ensho vs Big Data: Case study, 67 year-old female

- We have focused on developing machine learning techniques that excel at extracting rich insights from nuanced data, rather than identifying patterns in large volumes of data
- "Big Data" approaches assume reliable insights can be generated by aggregating large amounts of structured data but structured data, like claims, are often incomplete and mask underlying issues



Claims data

CT scan showed evidence of a small left posterior parietal infarct... Interestingly, this woman was previously diagnosed with atrial fibrillation in addition to congestive heart failure and she was previously put on anticoagulation. She has tried different medications including Coumadin, Dabigatran and went back on Coumadin and finally she was on Xarelto but just 5 days prior to her event she decided to discontinue Xarelto and go on a natural blood thinner of Japanese origin to avoid being on prescription medication for anticoagulation. She reports not being on anticoagulation for 5 days and currently since her admission she was put back on Xarelto again.

I have calculated Mrs. [REDACTED]'s GFR. Although the laboratory report would suggest her GFR is 57; it is in fact, 31 ml/min. The eGFR is inaccurate in elderly women with low body mass. Given this GFR, I have discontinued Xarelto and I have replaced it with Eliquis 2.5-mg bid.

Ensho data



## Unlocking data: Encounter notes

- Rich information relevant to patient identification is typically locked away in encounter notes and can only be queried using natural language processing techniques

Mr. [REDACTED] was seen in follow-up today in our [REDACTED] office on January 30, 2019 for reassessment of his **paroxysmal atrial flutter** and coronary artery disease. To review this very pleasant 58 year old gentleman has **hypertension** and previous smoking. He has obstructive sleep apnea on CPAP. He has **end-stage renal failure due to FSGS and is on hemodialysis**. He had a history of alcohol excess. In 2016, he had a grade 2 LV and had cardiac catheterization. This showed a normal left main. The first diagonal had a 40% ostial stenosis, LAD was normal. Circumflex had mild disease. The RCA had a 30% proximal, 50% mid and 40% at the acute marginal. Medical therapy was continued. Post-procedure he had a transient episode of confusion. He was subsequently found to have a **right pontine stroke**. **This was felt to be possibly secondary to the procedure.**

In August 2017 he had acute renal failure and was severely anemic. He subsequently was instituted on dialysis. He was incidentally found to be in atrial flutter with an atrial rate of about 250 beats per minute. Since he was to going to be on dialysis anticoagulation was not recommended.

He has been and remains active. He has had no chest pain. He remains free of palpitations or presyncope. He denies orthopnea or PND. He has had no bleeding complications.

He was seen by the renal transplant team in [REDACTED] and was seen by [REDACTED] from cardiology. There were no concerns.

Medications include ECASA 81 mg OD, Amlodipine 10 mg OD, Atorvastatin 20 mg OD, Eprex 4000 units a week, Labetalol 200 mg OD, and Replavite.

Blood pressure was 128/80, heart rate was 78 beats per minute and irregular. He had a variable S1. He had no ankle edema.

**ECG showed atrial fibrillation** with ventricular rate of 78 bpm with poor R wave progression.



## Early outcomes

- Early outcomes data shows Ensho sites have identified greater numbers of patients than is typical
- No head-to-head data available yet comparing Ensho to manual processes

Program	Type	Representative Clinic	Patients identified
REFINE-ICD	Trial	4 cardiologists	758 Eligible + Potentially Eligible, subject to new data
BRAIN-AF	Trial	10 cardiologists	172
VESALIUS	Trial	10 cardiologists	67
COMPASS Risk Factors + CART	Knowledge Translation	11 cardiologists	1,674
Ivabradine Guideline	Knowledge Translation	10 cardiologists	226
hTTR Amyloidosis	Knowledge Translation	1 cardiologist	9 diagnosed 19 appropriate for workup
SGLT2i CVD Indication	Knowledge Translation	1 cardiologist	223



# Communicating results: lab-like reporting

- Subscribers receive lab-like reports that clearly explain eligibility in a transparent way

Easy-to-understand summary

Transparent and verifiable explanation for why patient was identified

Explanation of what eligibility requires

Ensho Health

### SGLT2i CVD Risk Optimization Program

RESULT: **ELIGIBLE**

NEXT VISIT: **January 16, 2020**      HCN: [REDACTED]      AGE: **69 years**  
 VISIT WITH: [REDACTED]      EID: **862374**      SEX: **Male**

**Summary**

Patient is eligible for optimization with an SGLT2i for CVD risk. Please note that:

- Most recent HbA1C = 7.4% (2018)
- Most recent eGFR = 71 (2018)

Eligibility requires:

1. Diagnosis of Type 2 Diabetes Mellitus
2. Established cardiovascular disease risk

**Criteria that have been satisfied:**

Inclusions satisfied:	From the record:	Source document:	Notes:
1 T2DM	1/2 tablet once a day and also high dose statin. He is also <b>diabetic</b> and on Metformin. Today, physical examination revealed a waist circumference of 104	Clinical Note Outgoing Consult Reply Apr 28, 2015	-
2 CVD risk	Recommendations / Clinical Findings Clinical Findings: J18 67 year old male with a past history of <b>M</b> , DM, HTN, FAXED OCT 3 1 2018 The patient complains of 2 day hx of "having to take a deep breath  unwell and asked the front desk for ASA as he felt he was having an MI. He went to the hospital and was treated. He was <b>stented</b> and the info is enclosed. There was no CHF arrhythmia and he talked and walked the staff's heart out on the wards. He h	Incoming Consult Request Nov 16, 2018  Incoming Consult Request Apr 21, 2015	-

**Other relevant information:**

Metrics:	From the record:	Source document:	Notes:
1 HbA1C	193 MPV= 10.0 Chl= 3.25 Tri= 1.78* HDL= 1.03 LDL= 1.41 Non-HDL= 2.22 Chl/HDL= 3.16 Creat= 96 eGFR= 71 Gluc= 8.6* <b>HbA1c= 7.4*</b> Your assessment and advice regarding the management of this patient	Incoming Consult Request Nov 16, 2018	-
2 GFR	193 MPV= 10.0 Chl= 3.25 Tri= 1.78* HDL= 1.03 LDL= 1.41 Non-HDL= 2.22 Chl/HDL= 3.16 Creat= 96 <b>eGFR= 71</b> Gluc= 8.6* HbA1c= 7.4* Your assessment and advice regarding the management of this patient	Incoming Consult Request Nov 16, 2018	-



# Machine learning of Predictors for Non-Obstructive Coronary Artery Disease

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JD Schwalm, Tej Sheth, Madhu K. Natarajan, Jeremy Petch, Peter Sztur, Shuang Di, Walter Nelson, Joel Kempainen

## Project Summary (continued):

**Methods:** Retrospective observational study of Hamilton Health Sciences and Niagara Health System's Corhealth cardiac registry (Includes demographics and angio results for > 10 years and > 20 000 patients). Predictive model developed using random forest and gradient boosting. Explanations for individual predictions created with LIME.

**Progress to Date:** Developed preliminary ML models using sample dataset. Transferring entire de-identified dataset for analysis. Predictive model expected by July.

**Next steps:** Seek funding for development of predictive model into an online clinical decision support tool and implementation evaluation in our region. Plans to expand with CorHealth at the provincial level.

# Machine-driven echocardiographic measurements

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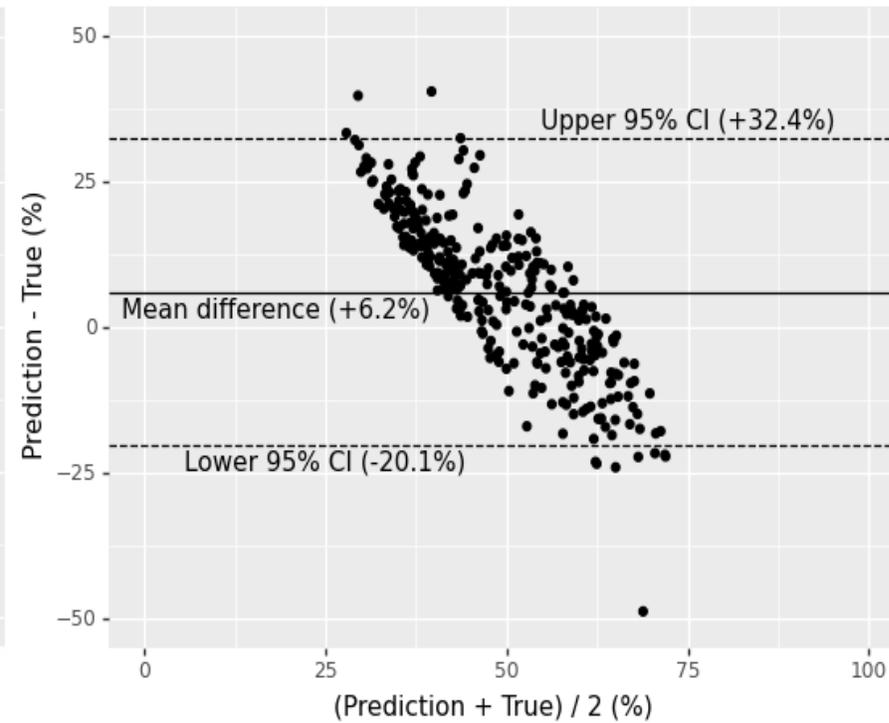
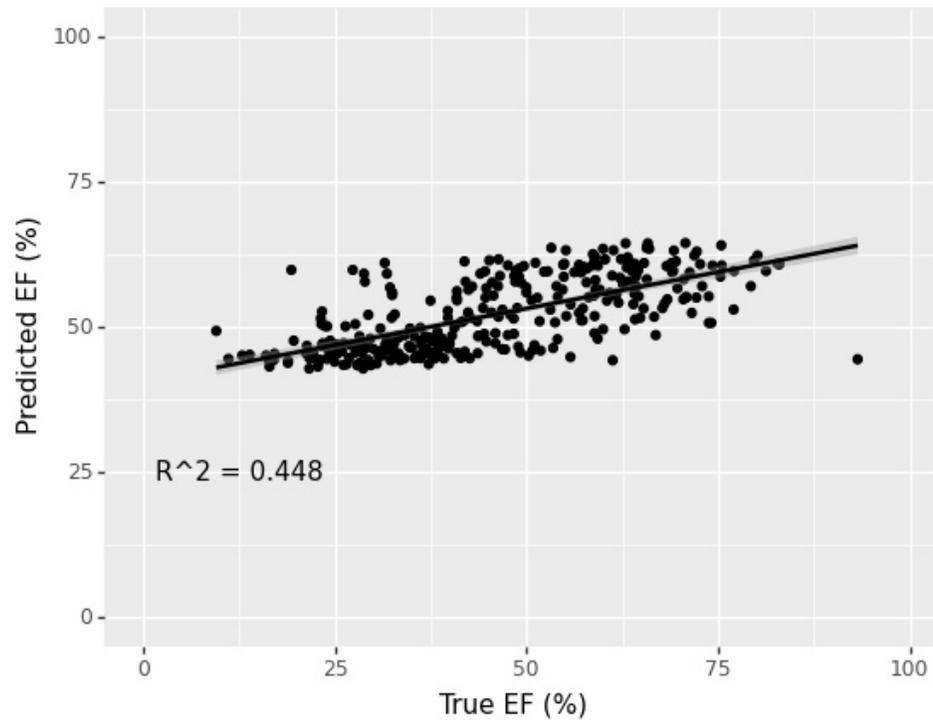
**Background**: machines may perform echocardiographic measurements more reproducibly and rapidly than humans

**Objective**: to develop a tool for the automated performance of several echocardiographic measurements

**Progress**: shared code has been adapted so that in a small sample of raw echo images, LV volumes can reproducibly be measured by machine in-house



# Echo



# Conclusions

- Artificial Intelligence will facilitate the design and conduct of clinical trials
- AI may replace conventional methods of observational trials
- However; like any research methodology, AI/Big Data approaches will need to evolve to address early shortcomings

