

# Artificial Intelligence in Health Care

**Atul Butte, MD, PhD**

Chief Data Scientist, University of California Health (UC Health)

Priscilla Chan and Mark Zuckerberg Distinguished Professor

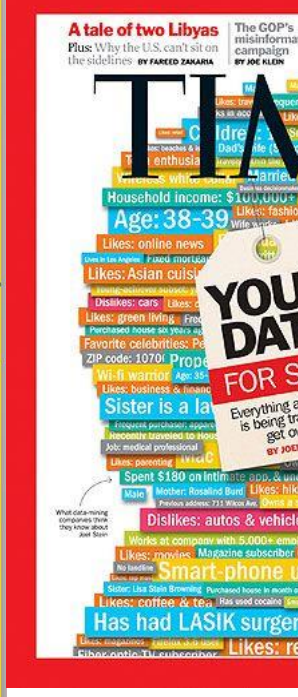
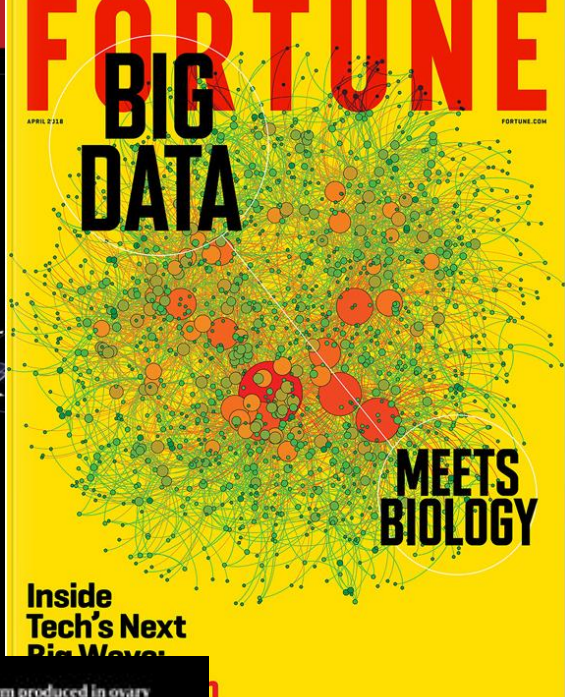
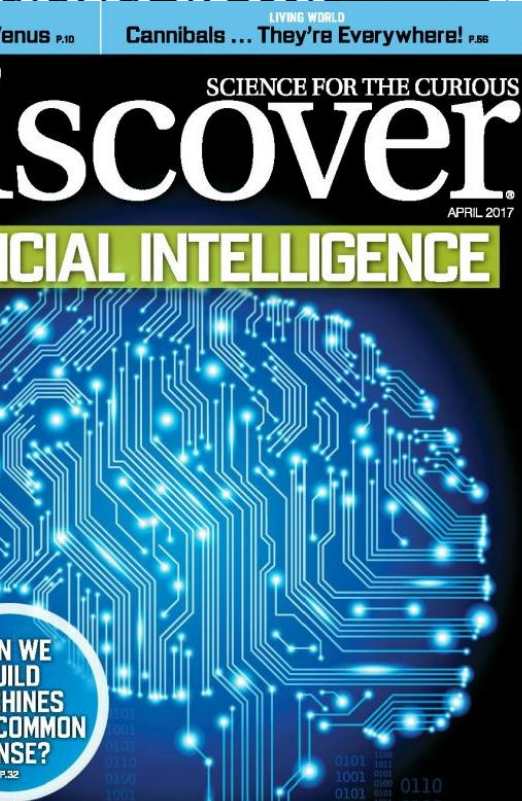
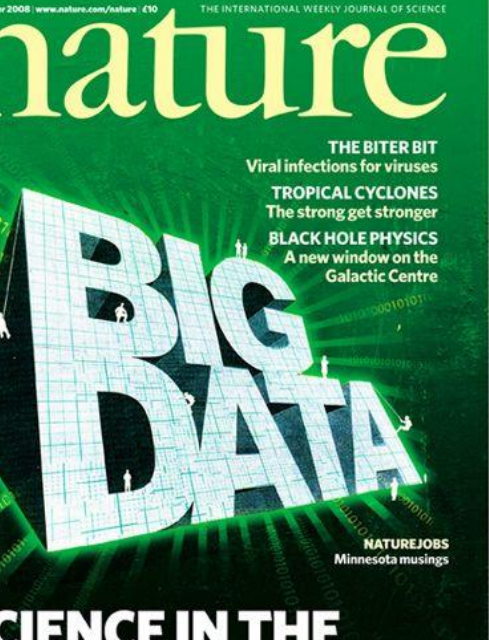
Director, Bakar Computational Health Sciences Institute, UCSF

atul.butte@ucsf.edu ▪ @atulbutte

# Conflicts of Interest

- Scientific founder
  - Personalis
  - NuMedii
  - Carmenta (Progenity)
  - Genstruct
- Honoraria for talks
  - Lilly
  - Pfizer
  - Siemens
  - Bristol Myers Squibb
  - AstraZeneca
  - Roche
  - Genentech
  - Warburg Pincus
  - CRG
  - AbbVie
  - Westat
- Past or present consultancy
  - Personalis
  - NuMedii
  - Lilly
  - Johnson and Johnson
  - Roche
- Other corporate relationships
  - Genstruct
  - Tercica
  - Ecoeos
  - Helix
  - Ansh Labs
  - uBiome
  - Prevendia
  - Samsung
  - Assay Depot
  - Regeneron
  - Verinata (Illumina)
  - Pathway Diagnostics
  - Geisinger Health
  - Covance
  - Wilson Sonsini Goodrich & Rosati
  - Orrick
  - 10X Genomics
  - GNS Healthcare
  - Gerson Lehman Group
  - Coatue Management
- Shares or Ownership
  - Johnson and Johnson
  - Optum
  - NuMedii (major)
  - Personalis (major)
  - Apple
  - Facebook
  - Alphabet (Google)
  - Microsoft
  - Amazon
  - Snap
  - 10x Genomics
  - Illumina
  - Nuna Health
  - Assay Depot (Scientist.com)
  - Vet24seven
  - Regeneron
  - Sanofi
  - Royalty Pharma
  - AstraZeneca
  - Moderna
  - Biogen
  - Paraxel
  - Sutro
- Speakers' bureau
  - None
- Companies started by students
  - Carmenta
  - Serendipity
  - Stimulomics
  - NunaHealth
  - Praedicat
  - MyTime
  - Flipora
  - Tumbl.in
  - Polyglot
  - Iota Health
  - Ongevity Health







# Artificial Intelligence and Machine Learning

- **Artificial Intelligence:** aspects of human intelligence modeled by computers
- **Machine Learning:** implementing aspects of AI through processing data
  - Supervised or unsupervised learning
- **Deep Learning:** one type of ML, modeling brain architecture with layers of individual classifiers, adding non-linearity

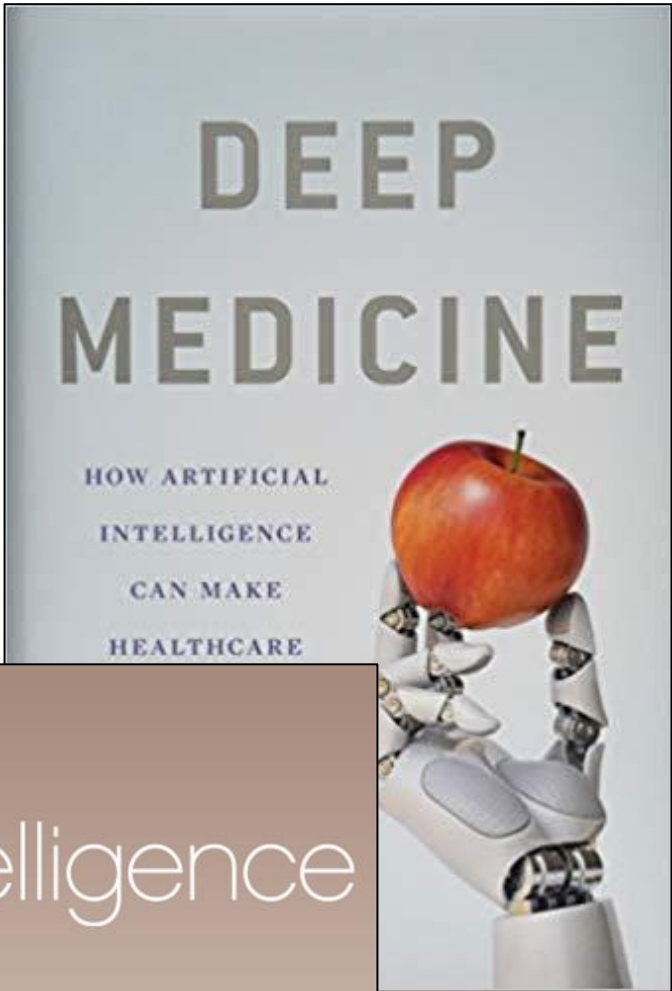
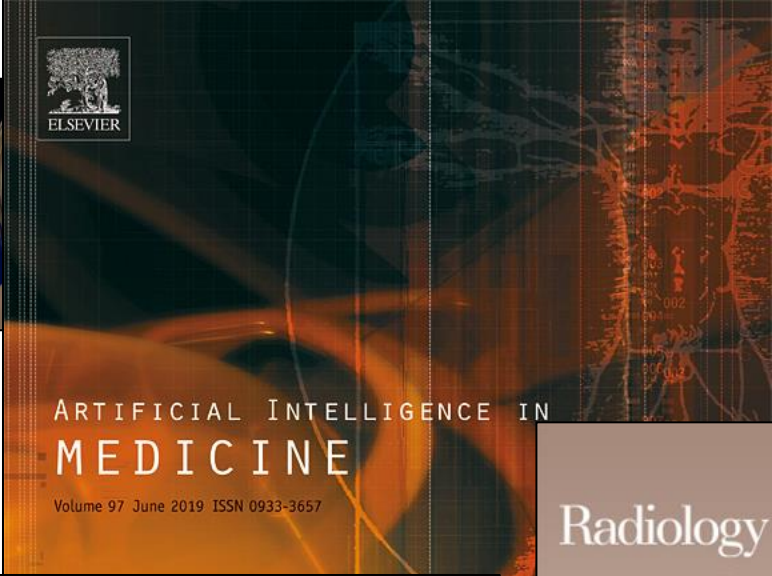
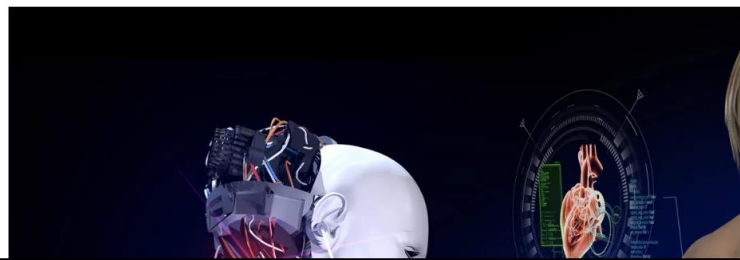


# 3 ways AI is already changing medicine

They might surprise you.

By Julia Belluz | @juliaoftoronto | julia.belluz@voxmedia.com | Mar 15, 2019, 12:40pm EDT

f       SHARE



JAMA Network

Open

Editorial

Advancing Health and Health Care Using Machine Learning

JAMA Network Open Call for Papers

Frederick P. Rivara, MD, MPH; Stephan D. Fihn, MD, MPH; Roy H. Perlis, MD, MSc

The promise of machine learning to transform all aspects of medicine and health care has been celebrated, but to date this transformation remains largely aspirational.<sup>1-5</sup> Medicine poses unique challenges compared with areas like recognizing images, driving autonomous vehicles, or gaming, which machine learning has had remarkable success. Obstacles to successful application of machine learning in medicine include availability of large, high-quality databases to derive prediction models that are accurate and interpretable and deployment of these models in ways that improve, rather than simply complicate, medical practice.

JAMA Network Open, a fully open access journal in the JAMA Network of journals with an international audience of health care clinicians and policy makers, is pleased to announce a call for papers on "advancing health and health care using machine learning." We are interested in reporting original research that describes ways in which validated applications of machine learning, artificial intelligence, and data science can be used to improve patient care, reduce costs, and advance medical research.

PERSPECTIVE | FOCUS

<https://doi.org/10.1038/s41591-018-0316-z>

nature medicine

A guide to deep learning in healthcare

Andre Esteva<sup>1,3\*</sup>, Alexandre Robicquet<sup>1,3</sup>, Bharath Ramsundar<sup>1</sup>, Volodymyr Kuleshov<sup>1</sup>, Mark DePristo<sup>2</sup>, Katherine Chou<sup>2</sup>, Claire Cui<sup>2</sup>, Greg Corrado<sup>2</sup>, Sebastian Thrun<sup>1</sup> and Jeff Dean<sup>2</sup>

Here we present deep-learning techniques for healthcare, centering our discussion on deep learning in computer vision, natural language processing, reinforcement learning, and generalized methods. We describe how these computational techniques can

## An Artificial Intelligence Program to Advise Physicians Regarding Antimicrobial Therapy\*

EDWARD H. SHORTLIFFE†, STANTON G. AXLINE, BRUCE G. BUCHANAN,  
THOMAS C. MERIGAN, AND STANLEY N. COHEN

Stanford University, Stanford, California 94305

### ANTIMICROBIAL THERAPY CONSULTATION SYSTEM

551

)  
INSTRUCTIONS? (Y OR N)  
\*\*yes

I AM HERE TO ADVISE YOU REGARDING AN APPROPRIATE CHOICE OF INFECTIOUS DISEASE THERAPY. I UNDERSTAND THAT YOU HAVE A PATIENT FROM WHOM A POSSIBLY POSITIVE CULTURE (CALLED 'CULTURE-1') HAS BEEN OBTAINED. PLEASE ANSWER THE FOLLOWING QUESTIONS, TERMINATING EACH RESPONSE WITH 'RETURN'.

IF YOU ARE NOT CERTAIN OF YOUR ANSWER, YOU MAY MODIFY THE RESPONSE BY INSERTING A CERTAINTY FACTOR (A NUMBER FROM 1 TO 10) IN PARENTHESES AFTER YOUR RESPONSE. ABSOLUTE CERTAINTY (10) IS ASSUMED FOR EVERY UNMODIFIED ANSWER. NOTE THAT YOU MAY ALSO ENTER '?' IF YOU DO NOT KNOW THE ANSWER TO A QUESTION, '??' IF YOU WOULD LIKE TO SEE A LIST OF RECOGNIZED RESPONSES, THE WORD 'WHY' IF YOU WOULD LIKE TO SEE THE DECISION RULE WHICH HAS GENERATED THE QUESTION, OR THE WORD 'HELP' IF YOU ARE CONFUSED BY A QUESTION AND WOULD LIKE IT REPHRASED. TOGETHER WE WILL TRY TO DETERMINE APPROPRIATE THERAPY FOR THIS PATIENT.

#### SUMMARY:

'??' - ANSWER NOT KNOWN  
'???' - REQUEST FOR RECOGNIZED RESPONSES  
'WHY' - REQUEST FOR CURRENT DECISION RULE  
'HELP' - REQUEST FOR RESTATEMENT OF QUESTION

#### SAMPLE RESPONSE:

DID ORGANISM-1 GROW IN CLUMPS, CHAINS, OR PAIRS?  
\*\*CHAINS (7) PAIRS (3)

" 2-MAY-73 14:42:55"

PATIENT'S NAME:

\*\*J. Wilson

-----PATIENT-1-----

9. Beutler E, Dern RJ, Alving AS: The hemolytic effect of primaquine. VI. An in vitro test for sensitivity of erythrocytes to primaquine. *J Lab Clin Med* 45:40-50, 1955
10. Beutler E: A series of new screening procedures for pyruvate kinase deficiency, glucose-6-phosphate dehydrogenase deficiency, and glutathione reductase deficiency. *Blood* 28:553-562, 1966
11. Beutler E, Duro O, Kelly BM: Improved method for the determination of blood glutathione. *J Lab Clin Med* 61:882-888, 1963
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16. Carson PE, Flanagan CL, Ickes CE, et al: Enzymatic deficiency in primaquine-sensitive erythrocytes. *Science* 124:484-485, 1956
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## SPECIAL ARTICLE

### MEDICINE AND THE COMPUTER

#### The Promise and Problems of Change

WILLIAM B. SCHWARTZ, M.D.\*

**Abstract** Rapid advances in the information sciences, coupled with the political commitment to broad extensions of health care, promise to bring about basic changes in the structure of medical practice. Computing science will probably exert its major effects by augmenting and, in some cases, largely replacing the physician. As influences in of both physi-

care, it will also inevitably exact important social costs — psychologic, organizational, legal, economic and technical. Only through consideration of such potential costs will it be possible to introduce the new technology in an effective and acceptable manner. To accomplish this goal will require new

MANY doctors consider to medicine. The possibility that computers can reshape the medical profession fundamentally and profoundly change recruitment and the possibility that 2000 will be a day. This article, in some ways, is acted by such a role of the computer in the health-care system. The health-care system envisions a new type of function, admissions, the operation of the system, and the offer of consideration.

\*From the Department of Medicine, and the Center for Hospital Administration, Stanford University School of Medicine.

Table 1. Example of an Actual Consultation in Which the Computer Assists the Physician in the Evaluation of a Complex Acid-Base Disturbance.\*

COMPUTER: WHAT IS THE PLASMA CO <sub>2</sub> CONTENT, PLEASE?	1. WHEN THE DISSOCIATED PRODUCTS OF THE ACID ARE H <sup>+</sup> AND AN ANION OTHER THAN CHLORIDE AS IN THE CASE OF:
Physician: 15 mmoles/L	A. — KETOACIDS (DIABETIC KETOACIDOSIS)
COMPUTER: AND THE PLASMA pH, PLEASE?	B. — LACTIC ACID (LACTIC ACIDOSIS)
Physician: 7.14	C. — UNKNOWN ORGANIC ACIDS (AS SEEN IN SALICYLATE INTOXICATION OR POISONING WITH METHYL ALCOHOL, ETHYLENE GLYCOL, PARALDEHYDE).
COMPUTER: THE FINDING OF A LOW CO <sub>2</sub> CONTENT, LOW pH AND NORMAL Pco <sub>2</sub> (CALCULATED TO BE 42 mmHg) INDICATES THE PRESENCE OF A MIXED RESPIRATORY AND METABOLIC ACIDOSIS, AND THE PATIENT SHOULD THEREFORE BE CHECKED FOR ANY SOURCE OF IMPAIRED VENTILATION. I WILL NOW BE GLAD TO ASSIST WITH THE DIAGNOSIS OF THE METABOLIC COMPONENT OF THIS PATIENT'S DISORDER. WHAT IS THE SERUM SODIUM CONCENTRATION, PLEASE?	2. WHEN (AS IN RENAL INSUFFICIENCY) THE REDUCTION IN PLASMA HCO <sub>3</sub> CONCENTRATION IS INDUCED BY DEFECTIVE EXCRETION OF HYDROGEN ION AND IS NOT ACCOMPANIED BY AN INCREASE IN CHLORIDE REABSORPTION.
Physician: 240 mEq/liter	COMPUTER: IF YOU WOULD LIKE A MORE COMPLETE DISCUSSION OF THIS PROBLEM PLEASE SO INDICATE (BY TYPING YES) AND I CAN SUGGEST SEVERAL REFERENCES. [When requested, references are provided here.]
COMPUTER: IMPOSSIBLE VALUE! PLEASE CHECK AND RE-ENTER THE CORRECT SODIUM CONCENTRATION.	COMPUTER: I AM NOW READY TO ASSIST IN NARROWING THE LIST OF POSSIBLE DIAGNOSES. WHAT IS THE BLOOD SUGAR, PLEASE?
Physician: 140 mEq/liter	Physician: 135 mg/100 ml
COMPUTER: WHAT IS THE CHLORIDE CONCENTRATION?	COMPUTER: AND THE SERUM KETONE LEVEL, EXPRESSED IN TERMS OF DILUTED PLASMA?
Physician: 103 mEq/liter	Physician: 1 to 2
COMPUTER: THE CALCULATED "ANION GAP" IS 22 mEq/liter. METABOLIC ACIDOSIS WITH AN INCREASED "ANION GAP" IS SEEN IN	COMPUTER: AND THE CREATININE CONCENTRATION?
1. DIABETIC KETOACIDOSIS	Physician: 2.1 mg per 100 ml
2. SALICYLATE POISONING	COMPUTER: AND THE SALICYLATE CONCENTRATION, PLEASE?
3. ETHYLENE GLYCOL POISONING	Physician: 0
4. METHYL ALCOHOL POISONING	
5. PARALDEHYDE INGESTION (RARELY)	
6. LACTIC ACIDOSIS	

# First FDA Approval For Clinical Cloud-Based Deep Learning In Healthcare



Be  
FUL  
Opin

The first FDA  
clinical setti  
and industry

Arterys's me  
help doctors  
network wh  
improve its  
new case it e

## Viz.ai Granted De Novo FDA Clearance for First Artificial Intelligence Triage Software

A new era of intelligent stroke care begins as regulatory approval is granted for the Viz.ai LVO Stroke Platform

The platform  
Occlusion (I  
access to lif

NEWS PROVID  
Viz.ai, Inc. →  
Feb 15, 2018, 09



## FDA permits marketing of AI software autonomously detects diabetic retinop

By **Dave Muoio** | April 12, 2018

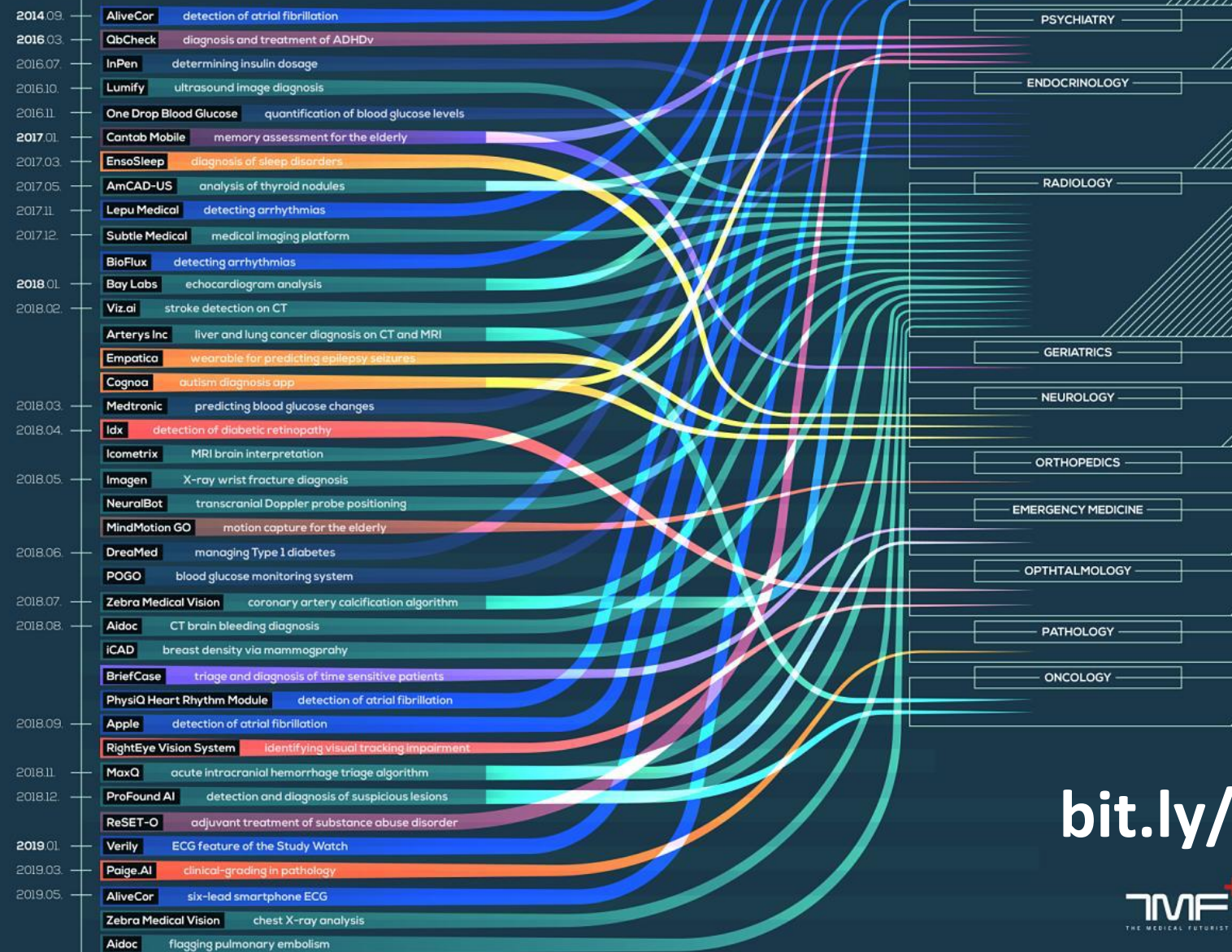
The FDA has granted diagnostics company IDx's De Novo request



SH



# FDA APPROVALS FOR ARTIFICIAL INTELLIGENCE-BASED ALGORITHMS IN MEDICINE



[bit.ly/tmfFDA19](https://bit.ly/tmfFDA19)

# Over 100 now approved just counting radiology!

Our list of FDA cleared AI algorithms provides valuable details on each model, bringing all of the relevant information together for easy access. Convenient summaries for each algorithm include model manufacturer, FDA product code, body area, modality, predicate devices, evaluation related to product performance, and clinical validation. Our Define-AI use cases match many of the models and those are listed under Related Use Cases. For other details, clicking on the model will take you directly to the FDA summary.

Check back regularly to see which new algorithms are available and have been added to the list. Send information on AI algorithms that are not listed and report missing information to [DSI@acr.org](mailto:DSI@acr.org).

Search	Company	Subspecialty	Body Area	Modality	Date Cleared
Product	Company	Subspecialty	Body Area	Modality	Date Cleared
<a href="#">qp-Prostate</a>	Quibim	Abdominal Imaging	Prostate	MR	02/04/2021
<a href="#">Visage Breast Density</a>	Visage Imaging GmbH	Women's Imaging	Breast	MAM	01/29/2021
<a href="#">uAI EasyTriage-Rib</a>	Shanghai United Imaging Intelligence Co., Ltd.	Chest Imaging	Chest	CT	01/15/2021
<a href="#">BrainInsight</a>	Hyperfine Research, Inc.	Neuroradiology	Brain	MR	01/07/2021
<a href="#">SQuEEZ Software</a>	Cardiowise, Inc.	Cardiac Imaging	Heart	CT	12/18/2020
<a href="#">EchoGo Pro</a>	Ultromics Ltd.	Cardiac Imaging	Heart	US	12/18/2020
<a href="#">HepaFat-AI</a>	Resonance Health Analysis Service Pty Ltd.	Abdominal Imaging	Liver	MR	12/07/2020
<a href="#">HealthJOINT</a>	Zebra Medical Vision Ltd.	Musculoskeletal Imaging	Knee	XRAY	12/04/2020
<a href="#">HALO</a>	NiCo-Lab B.V.	Neuroradiology	Brain	CT	11/20/2020
<a href="#">Genius AI Detection</a>	Hologic, Inc.	Women's Imaging	Breast	XRAY	11/18/2020
<a href="#">PROView</a>	GE Medical Systems	Abdominal Imaging	Prostate	MR	11/17/2020
<a href="#">FastStroke, CT Perfusion 4D</a>	GE Medical Systems	Neuroradiology	Brain	CT	11/12/2020
<a href="#">Neuro.AI Algorithm</a>	TeraRecon, Inc.	Neuroradiology	Brain	CT,MR	11/06/2020
<a href="#">WRDensity</a>	Whiterabbit.ai Inc.	Women's Imaging	Breast	MAM	10/30/2020
<a href="#">LSN</a>	Imaging Biometrics, LLC	Abdominal Imaging	Liver	CT	10/29/2020
<a href="#">AVIEW LCS</a>	Coreline Soft Co., Ltd	Chest Imaging	Lung	CT	10/16/2020
<a href="#">Syngo.CT Neuro Perfusion</a>	Siemens Healthineers	Neuroradiology	Brain	CT	10/11/2020
<a href="#">Quantib Prostate</a>	Quantib BV	Abdominal Imaging	Prostate	MR	10/11/2020
<a href="#">Cleerly Labs V2.0</a>	Cleerly, Inc.	Cardiac Imaging	Coronary Arteries	CT,CTA	10/02/2020

[http://bit.ly/acr\\_ai](http://bit.ly/acr_ai)





U.S. FOOD & DRUG  
ADMINISTRATION

## Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD)

*Discussion Paper and Request for Comments*



PATTERN  
RECOGNITION



AUTOMATION



NEURAL  
NETWORKS



ALGORITHMS



U.S. FOOD & DRUG  
ADMINISTRATION

FRAMEWORK FOR FDA'S

## REAL-WORLD EVIDENCE PROGRAM



U.S. FOOD & DRUG  
ADMINISTRATION



U.S. FOOD & DRUG  
ADMINISTRATION

CENTER FOR DEVICES & RADIOLOGICAL HEALTH  
DIGITAL HEALTH PROGRAM

## DIGITAL HEALTH INNOVATION ACTION PLAN



# Why is AI back in biomedicine?

- Great hardware from video gamers
- Software libraries with novel machine learning methods
- More big data sets to train with
  - Molecular data, genomics on more people, more cases
  - Electronic health records
- Hard unsolved questions need answers
  - Patient predictions
  - Efficient drug discovery
  - Population modeling

National Cancer Institute

# The Cancer Genome Atlas

Understanding genomics to improve cancer care



NIH HUMAN MICROBIOME PROJECT

CCLE Cancer Cell Line Encyclopedia

HOME BROWSE ANALYSIS TOOLS

Broad-M

Food and Drug Administration

**MEDWATCH**

fitbit

BROAD INSTITUTE

# All of US

## RESEARCH PROGRAM

NIH LINCS PROGRAM

HOME ABOUT CENTERS DATA ASSAYS

Connectivity Map

This research effort aims to generate a detailed map that links gene patterns associated with drug candidates and a variety of genetic manipulations. The Connectivity Map is the most comprehensive effort yet for using genomics in a drug-discovery framework, involving biologists, genomics specialists, and computational biologists, as well as expertise from the pharmaceutical industry.

Connectivity Map Project Website

HEP

Human Epigenome Project

UK 10K

National Cancer Institute

Surveillance Epidemiology and End Results

providing information on cancer statistics to help reduce the burden of these diseases on the U.S. population

Home About SEER Cancer Statistics Datasets & Software Publications

LINCS  
of biology by  
and other cell  
exposed to a

dbGaP

GENOTYPE and PHENOTYPE

PGKB

# PharmGKB

GO Advanced search

# The United States is spending \$billions on electronic health records, and too few are using any of this data

## Sutter's \$1 Billion Boondoggle-New Electronic Records System Goes Dark

California Nurses Association Press Release, 8/27/13

[Contact Information](#) | [Media Center](#)

### Yet Another Risk

A controversial e...  
billion went comp...  
additional risk be...

For several mont...  
care delivery tha...  
over 100 reports...  
Oakland, docum...

Sutter managem...

## Partners' \$1.2b patient data system seen as key to future

Aims for one file per person, fewer errors



## How Kaiser bet \$4 billion on electronic health records -- and won

Kaiser Permanente CIO Philip Fasano explains how electronic records have paid off and the health care giant's embrace of mobile technology

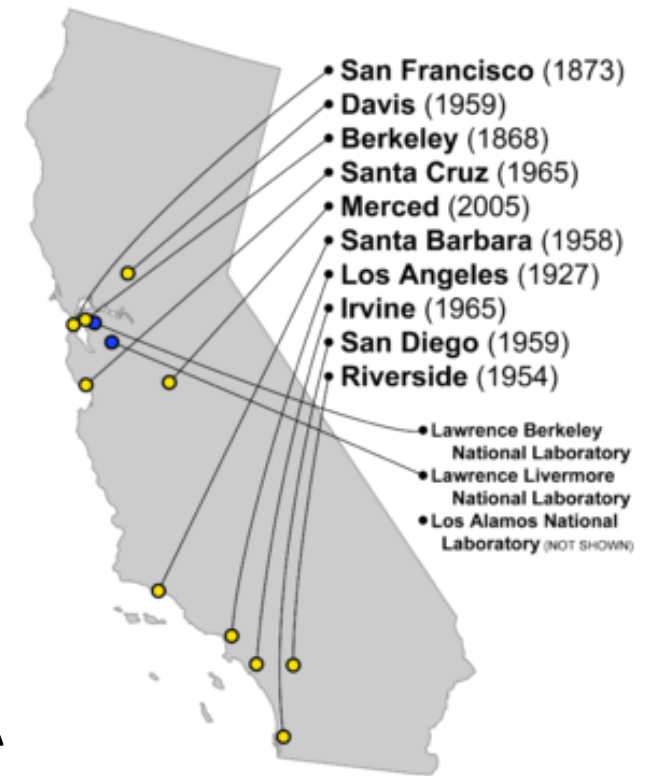


# University of California

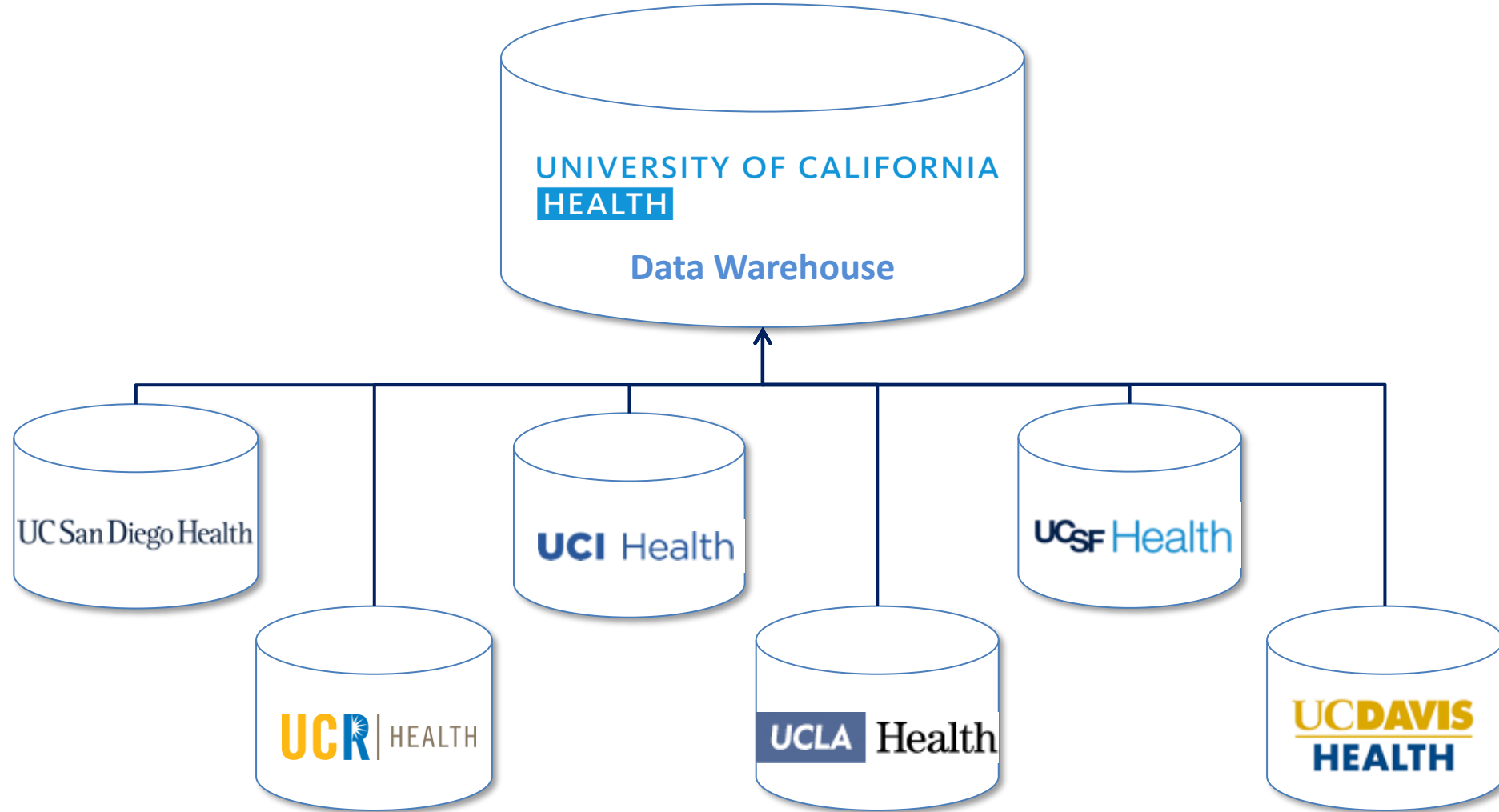
- 10 campuses and 3 national labs
- ~200,000 employees, ~250,000 students/yr

## UC Health

- 20 health professional schools (6 med schools)
- Train half the medical students and residents in California
- ~\$2 billion NIH funding
- \$13+ billion clinical operating revenue
- 5000 faculty physicians, 12000 nurses
- UCSF and UCLA are in US News top 10
- 5 NCI Comprehensive Cancer Centers, 5 NIH CTSA
- IRB reliance, centralized contracting



# *Combining healthcare data from across the six University of California medical schools and systems*

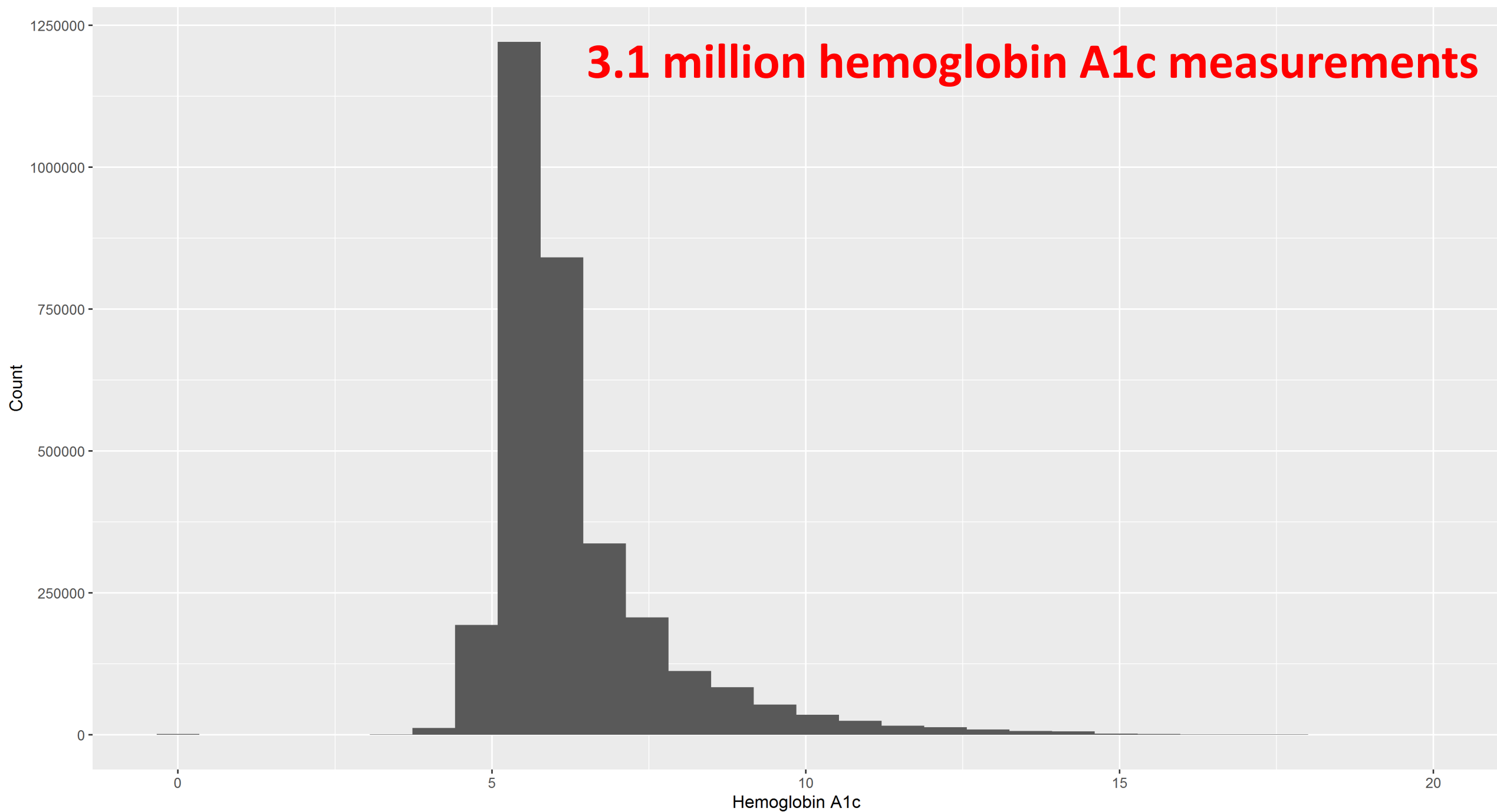


# The University of California has an incredible view of the medical system

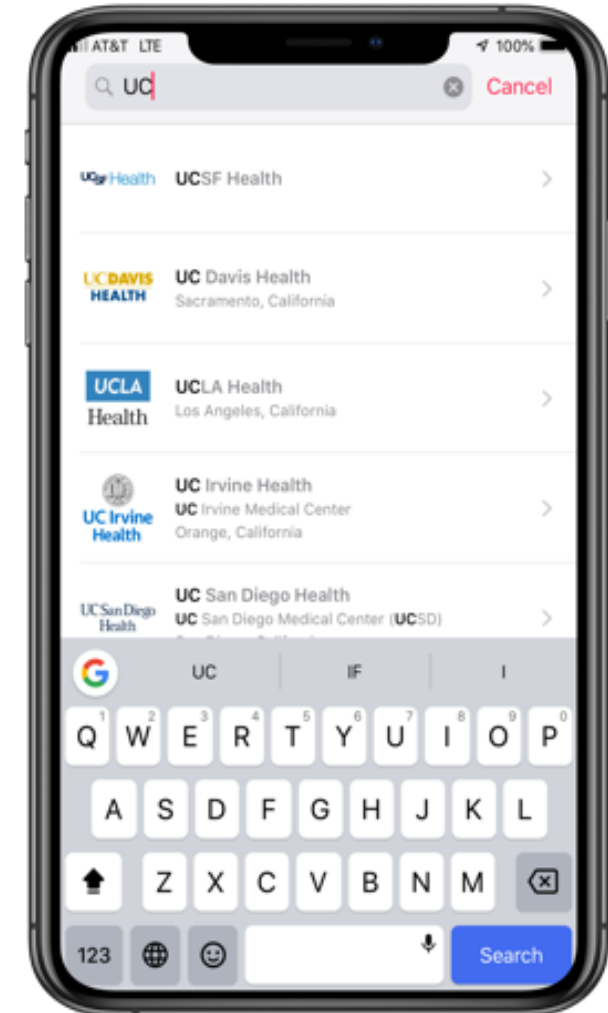
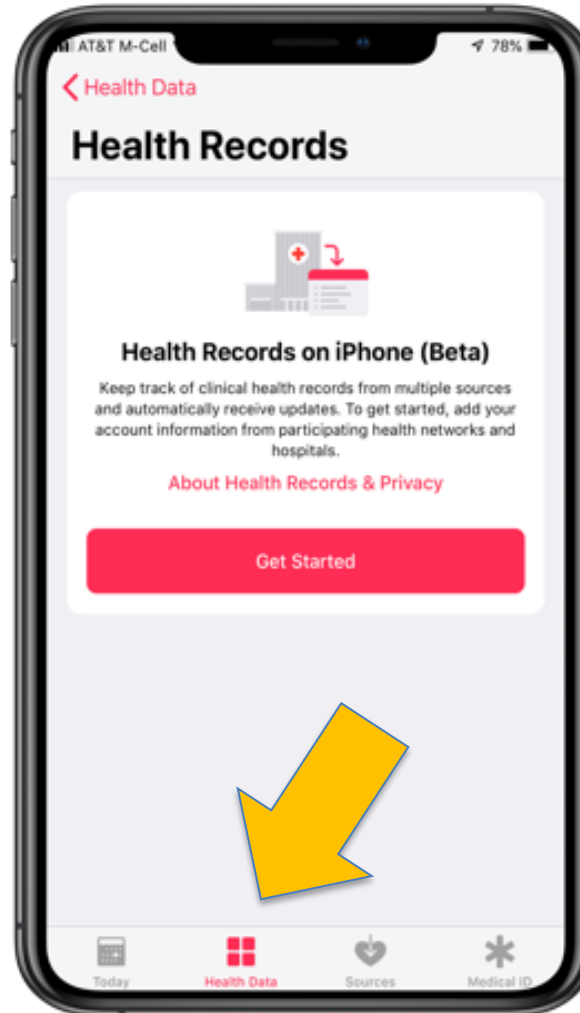
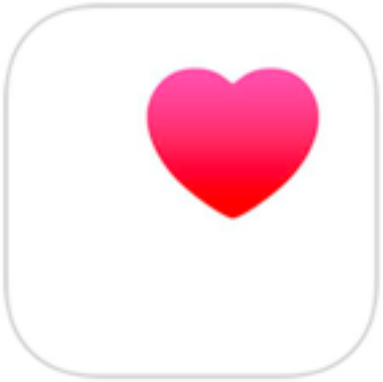
- Combined EHR data from UCSF, UCLA, UC Irvine, UC Davis, UC San Diego, and UC Riverside
- Central database built using OMOP (not Epic) as a data backend
  - First Epic installation was January 2012
  - Structured data from 2012 to the present day
  - **7.0 million patients with “modern” data**
  - 220M encounters, 560M procedures, 798M med orders, 722M diagnosis codes, 2.1B lab tests and vital signs
  - “From Tylenol to CAR-T cells...”
  - California OSHPD data, pathology and radiology text elements, death index
  - Claims data from our self-funded plans now included
  - Continually harmonizing elements
- Quality and performance dashboards



3.1 million hemoglobin A1c measurements across University of California Health



# *All University of California academic medical centers provide health data to patients through FHIR (and Apple Health)*



[bit.ly/ucappleh](https://bit.ly/ucappleh)

# UC Health Patients (since January 2012)

Gender All

ADI All

Race All

Age All

Active? All

PCP? All

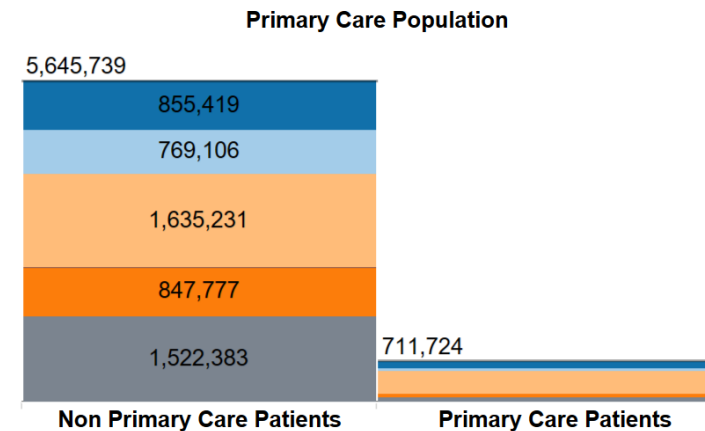
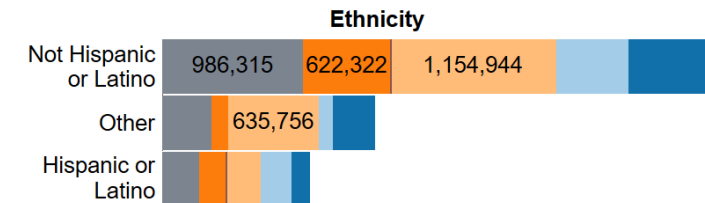
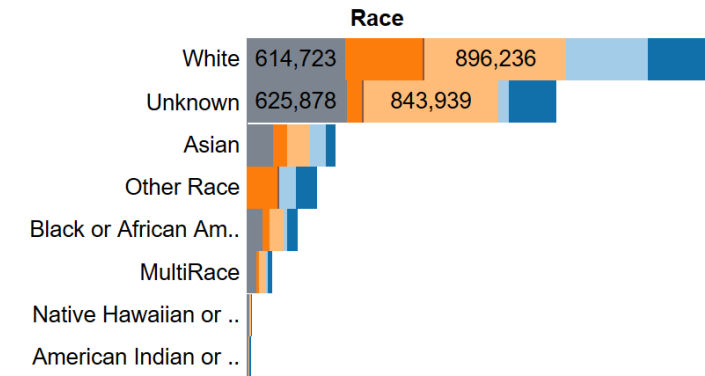
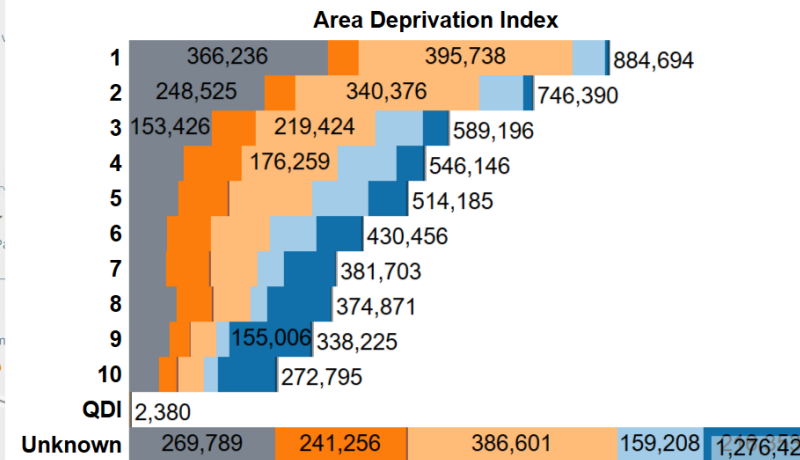
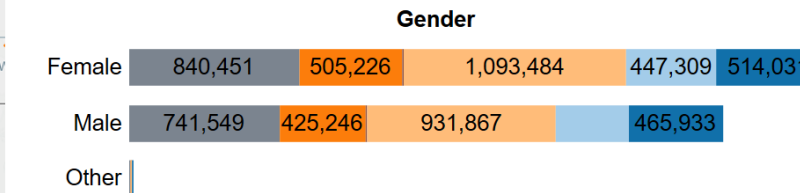
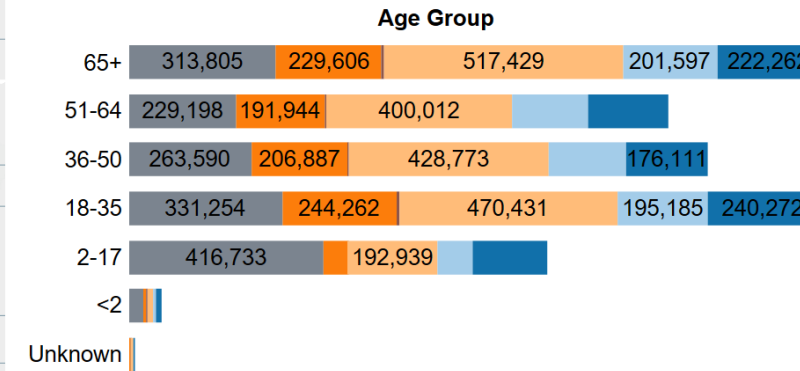
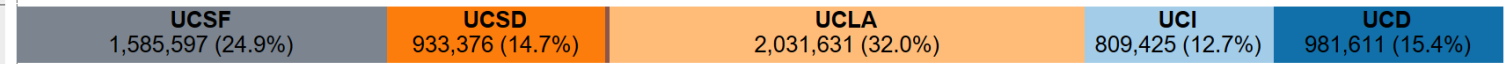
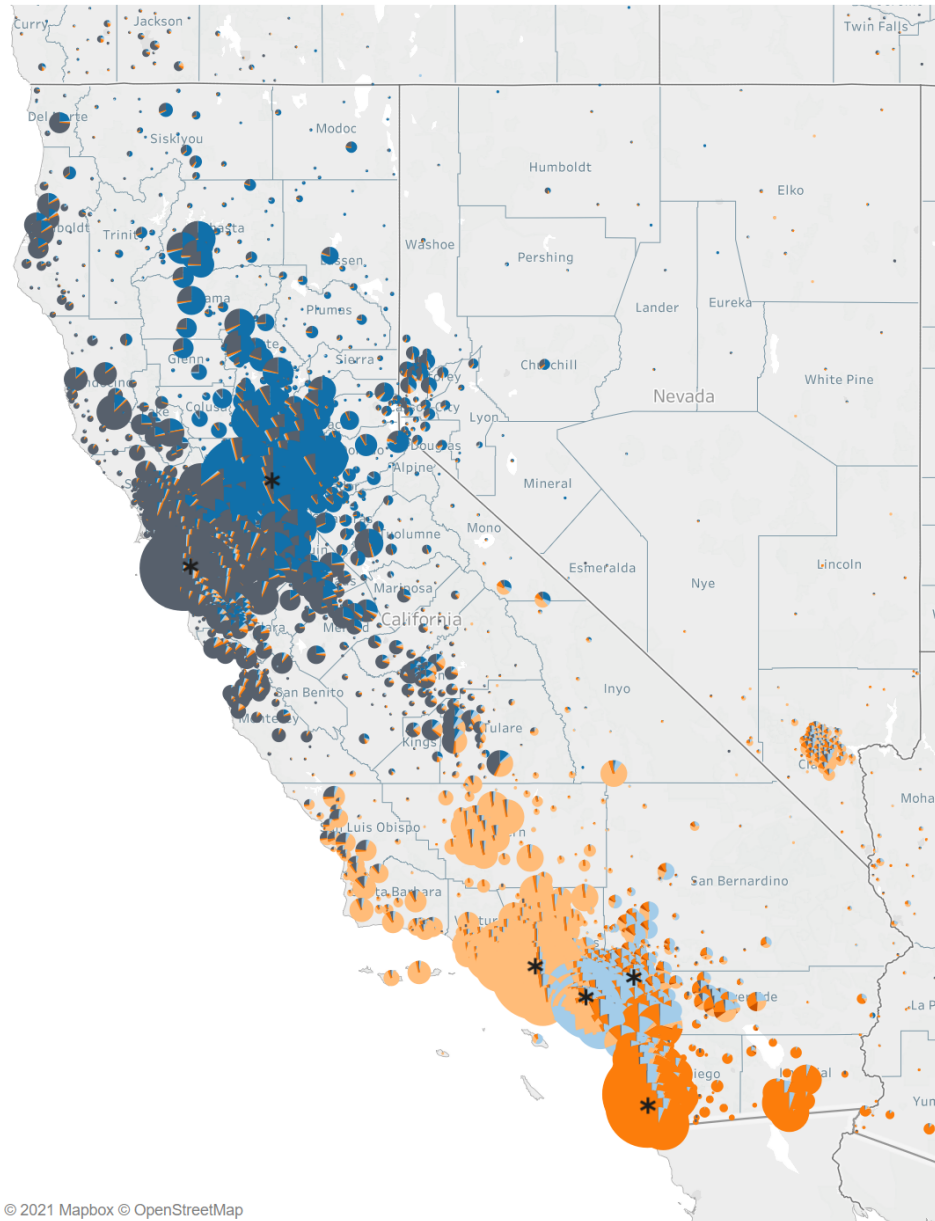
Ethnicity All

Patient Volume by Home Zip Code

Most Recent Visit Date Range

January 2012 to July 2021  
and Null values

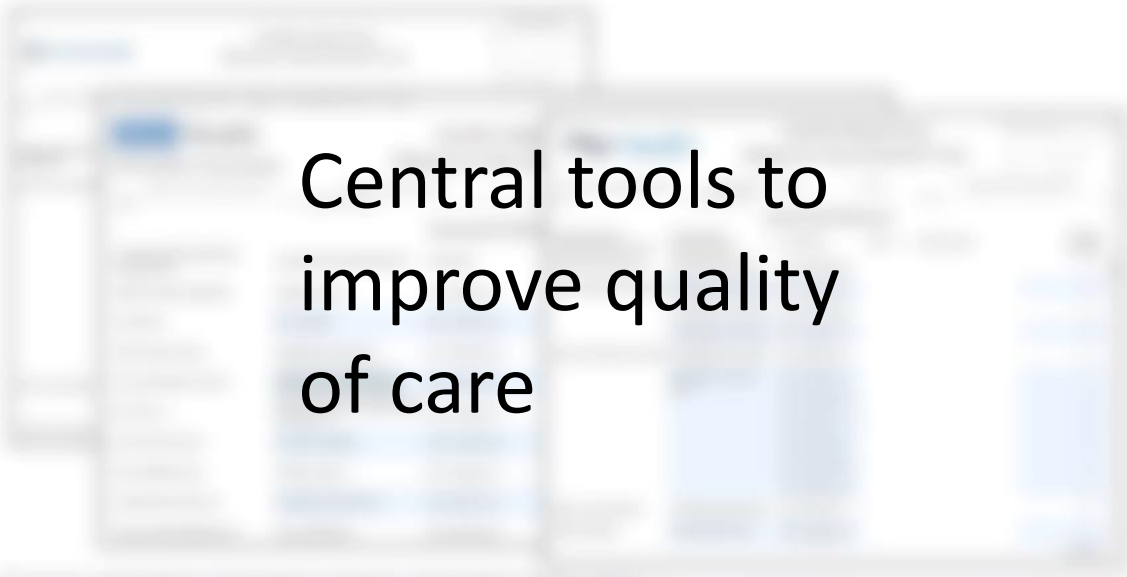
6,357,463 Total UC Health Patients




Non Primary Care Patients

Primary Care Patients

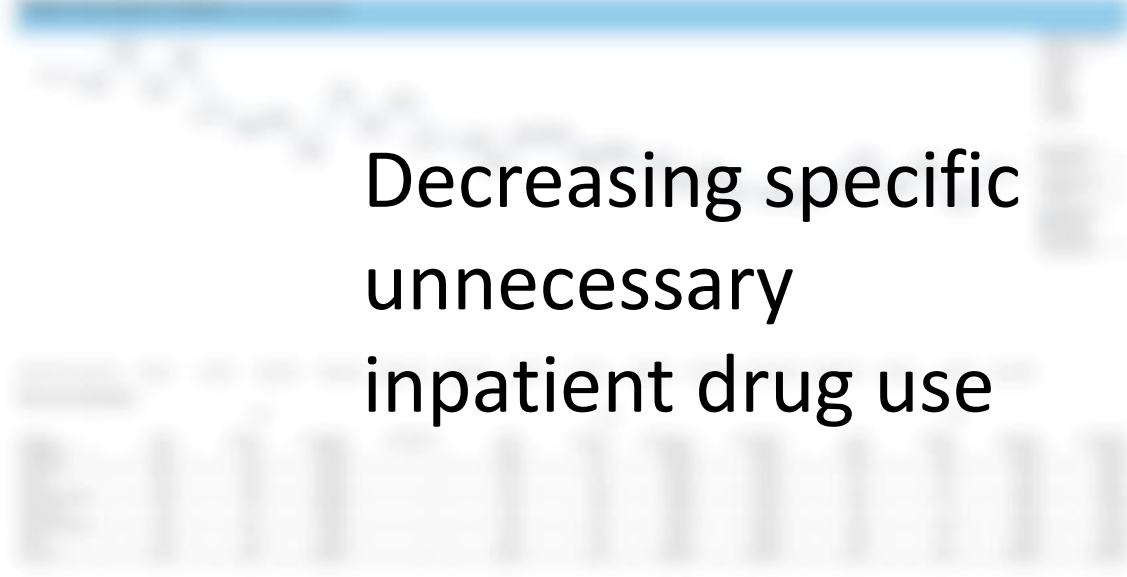
# Many operational teams within UC Health now using and benefitting from the UC Health Data Warehouse, saving \$millions



Central tools to  
improve quality  
of care



Managing costs  
in our self-  
funded health  
plans



Decreasing specific  
unnecessary  
inpatient drug use



Centralized  
population health  
management



# One dashboard for primary care and specialists covers all 46+ thousand UC Health patients with type 2 diabetes

UC Health Diabetes Patient Profile (Data through July 2021)

UCSF

UCLA

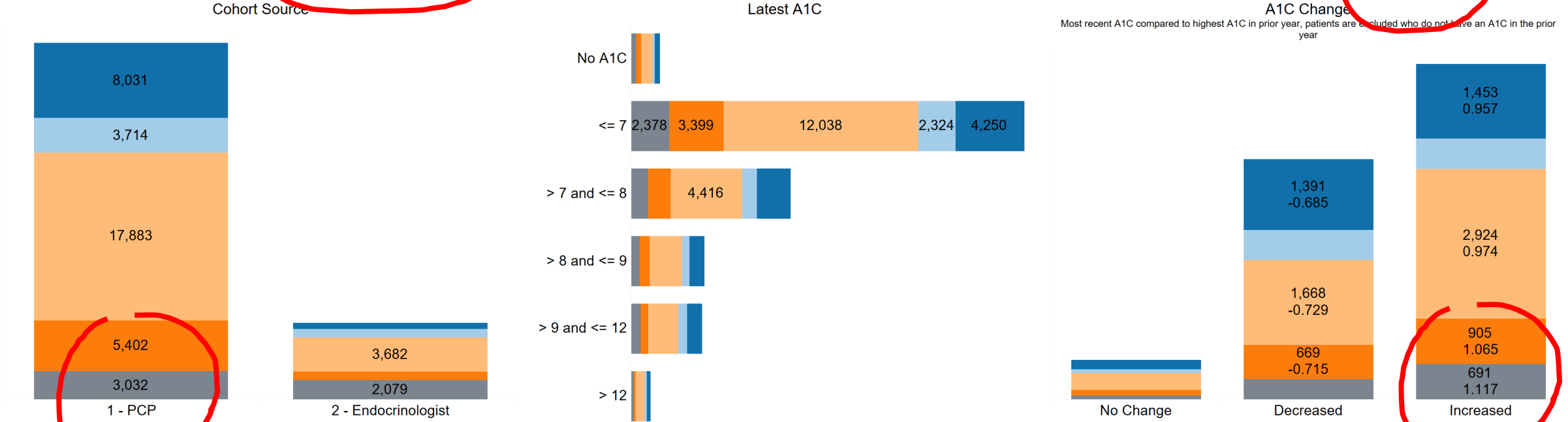
UCD

UCSD

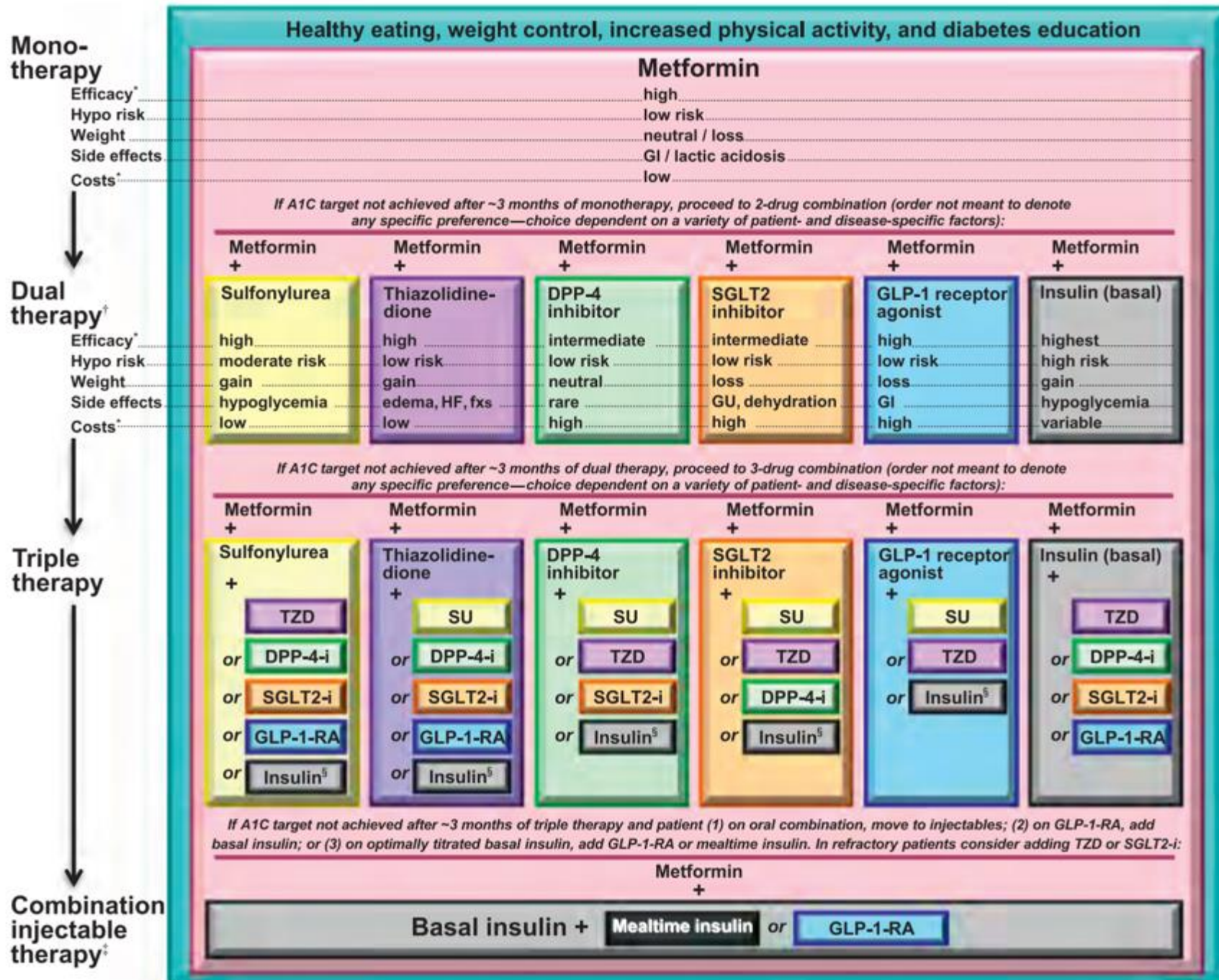
UCI

Cohort Source Fil..  
All

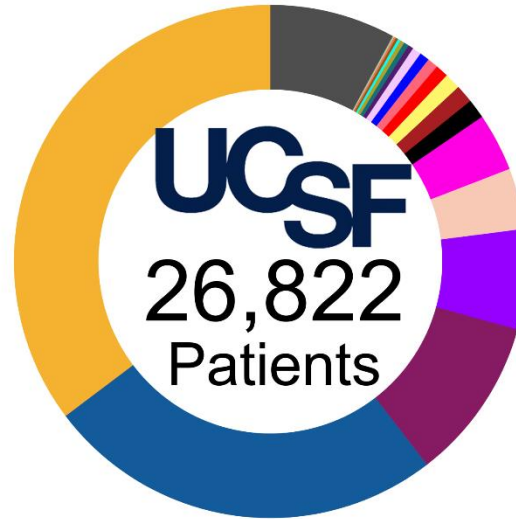
Total Patients:  
46,208



Measure Name	50% IHA Benchmark	UCD		UCI		UCLA		UCSD		UCSF	
		1 - PCP	2 - Endocrinol..	1 - PCP	2 - Endocrinol..	1 - PCP	2 - Endocrinol..	1 - PCP	2 - Endocrinol..	1 - PCP	2 - Endocrinol..
Optimal Diabetes Care (A1C control, BP control, Eye Exam, Nephropathy Attention)	18.02%	40.76%	11.74%	26.46%	9.61%	19.91%	8.16%	29.79%	11.64%	19.75%	6.04%
A1C Control (A1C < 8.0%)	61.07%	66.57%	31.14%	63.61%	53.18%	66.77%	58.32%	67.66%	42.11%	59.92%	44.96%
Blood Pressure Control (<140/90)	56.86%	73.25%	73.35%	65.31%	57.18%	63.34%	60.27%	66.65%	46.98%	57.07%	36.94%
Eye Exam	46.52%	73.39%	34.03%	50.20%	24.47%	37.21%	19.28%	53.19%	32.95%	43.86%	17.01%
Medical Attention for Nephropathy	90.97%	89.48%	78.62%	90.01%	87.02%	86.57%	81.16%	88.80%	72.41%	83.59%	66.93%
Poor A1C Control (A1C > 9.0%)	27.83%	18.71%	55.01%	22.48%	32.44%	18.09%	29.89%	17.27%	48.27%	24.75%	42.93%



Source: American Diabetes Association Standards of Medical Care in Diabetes (2016)



#### Monotherapies:

- Metformin (Met)
- Insulin
- Sulfonylurea (SU)
- Meglitinides
- DPP-4 Inhibitor (DPP-4)
- Thiazolidinedione (TZD)
- SGLT-2 Inhibitor (SGLT-2I)
- GLP-1 Agonist
- Alpha Glucosidase Inhibitor

Other Combinations

#### Dual therapies:

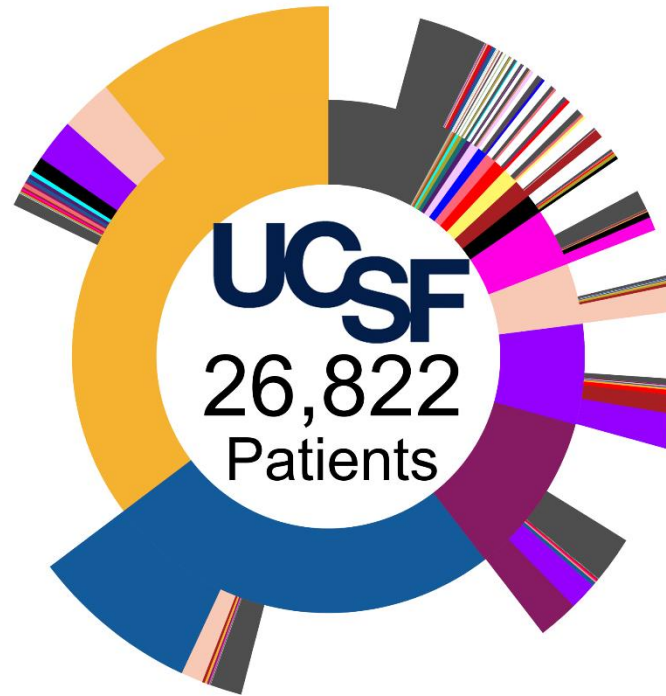
- Met & SU
- Met & DPP-4
- Met & Insulin
- Met & GLP-1 Agonist
- Met & Meglitinides
- Met & TZD
- Met & SGLT-2I
- Met & Alpha Glucosidase Inhibitor

#### Triple therapies:

- Met, SU, & DPP-4
- Met, SU, & Insulin
- Met, DPP-4, & Insulin
- Met, SGLT-2I, & Insulin

26,822 Type 2 Diabetes  
Patients at UCSF since EHR  
Adoption in 2012

**Tom Peterson**  
**[bit.ly/uc\\_dc\\_5](https://bit.ly/uc_dc_5)**



#### Monotherapies:

- Metformin (Met)
- Insulin
- Sulfonylurea (SU)
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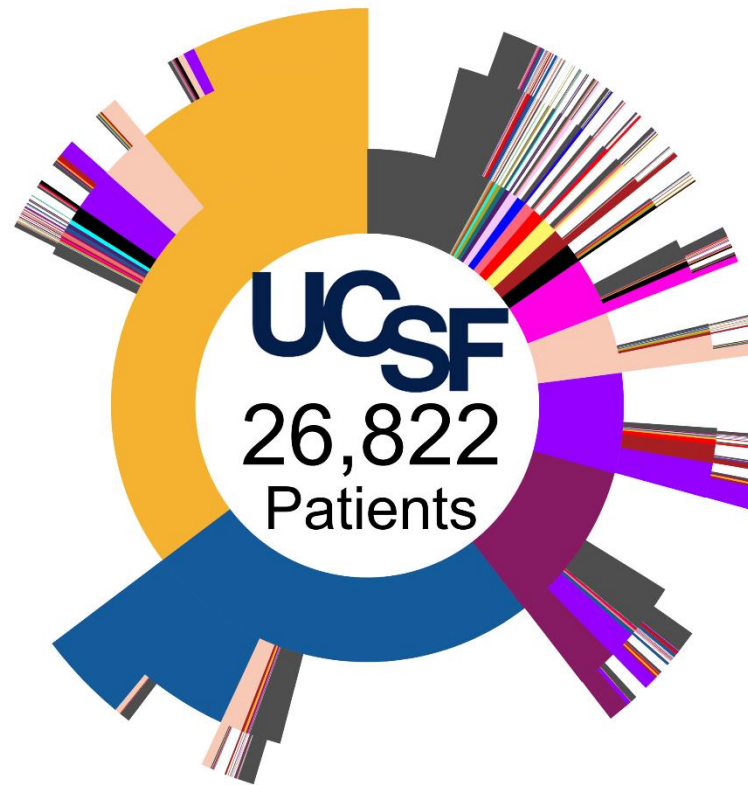
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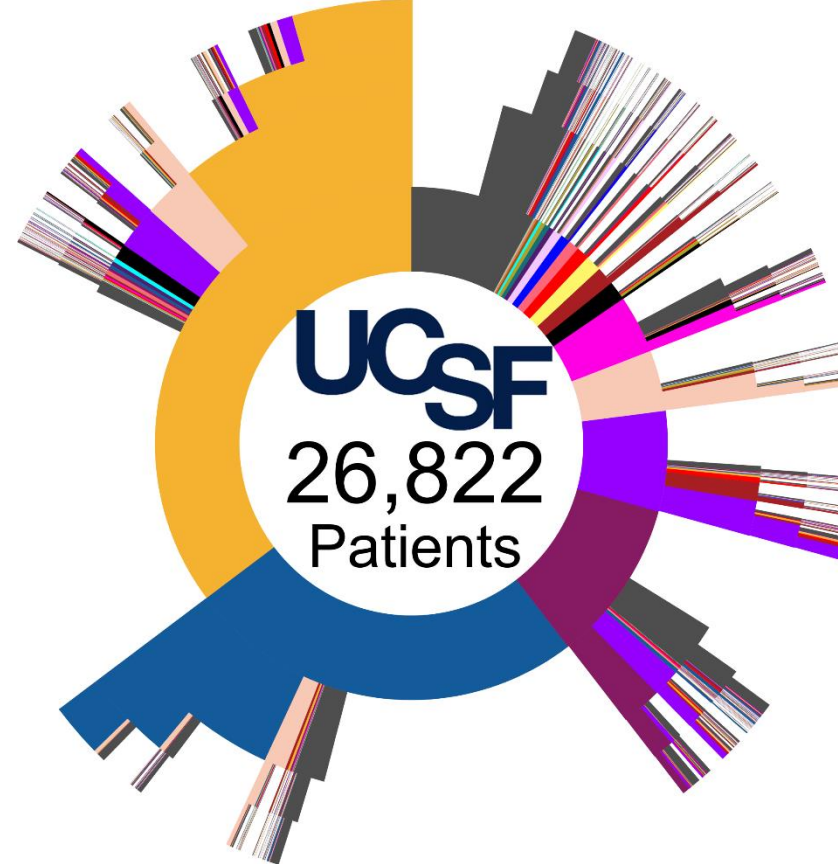
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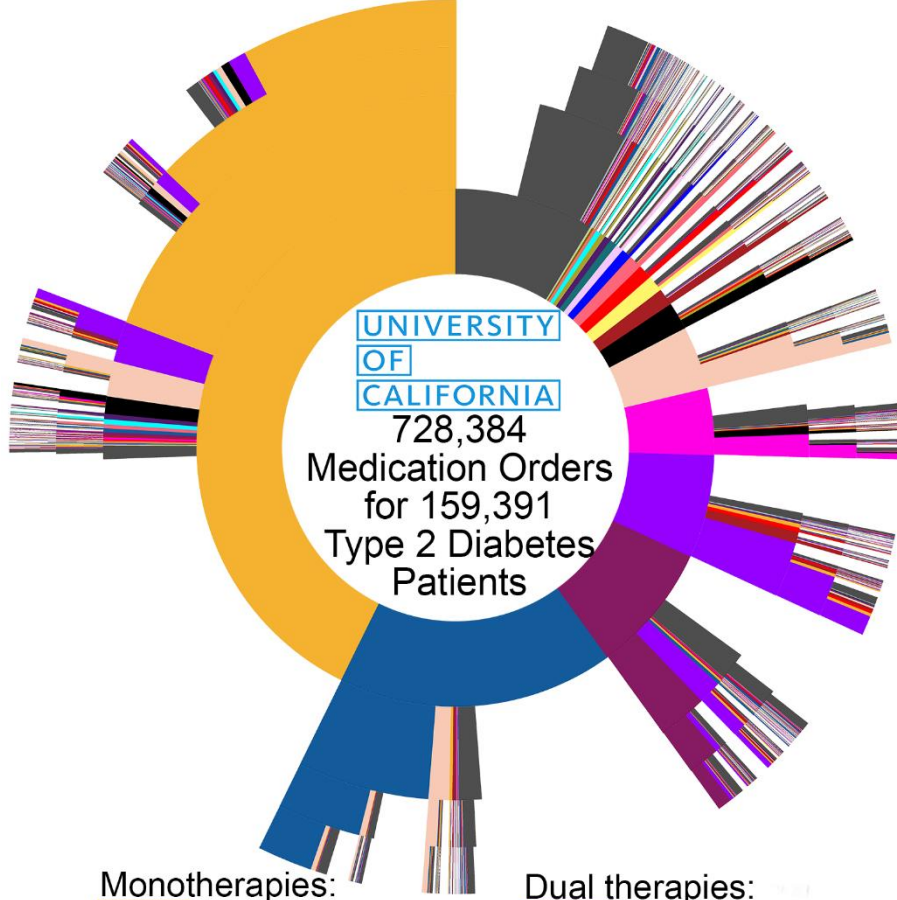
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26,822 Type 2 Diabetes  
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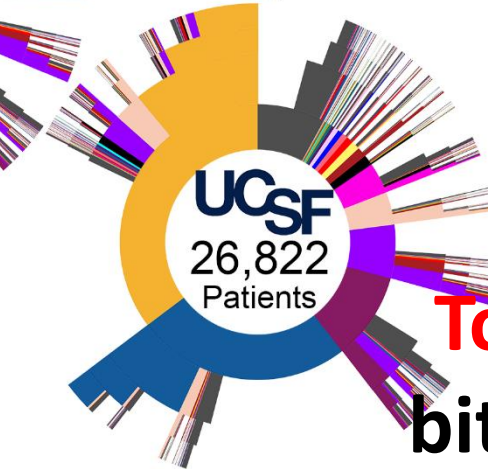
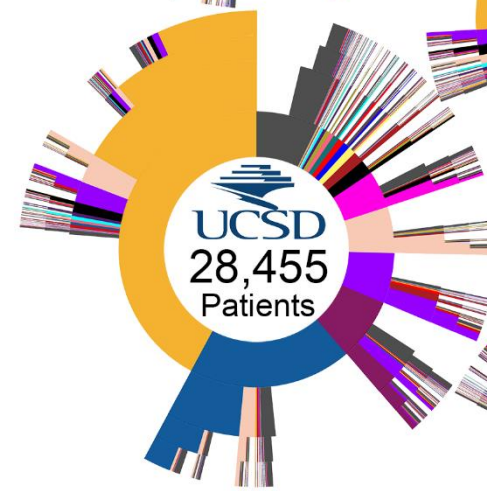
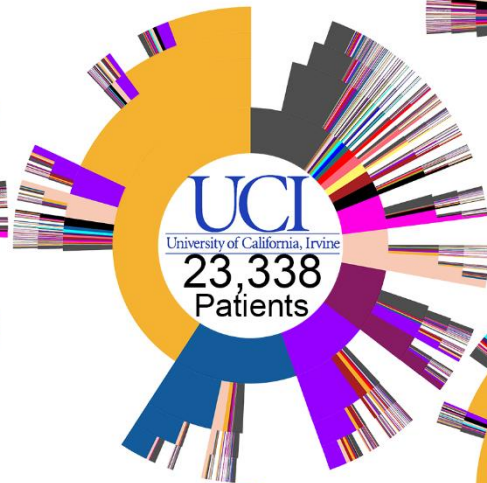
Other Combinations

**Dual therapies:**

- Met & SU
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**Triple therapies:**

- Met, SU, & DPP-4
- Met, SU, & Insulin
- Met, DPP-4, & Insulin
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**Tom Peterson**

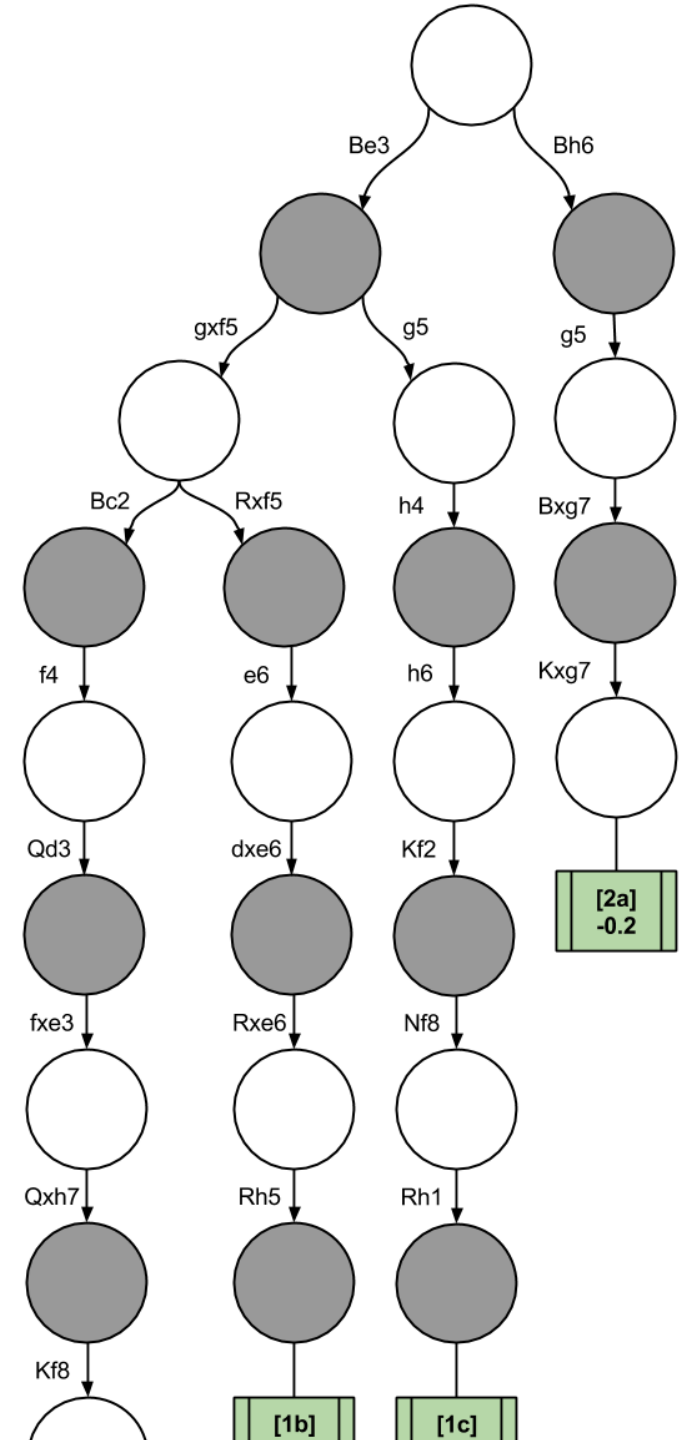
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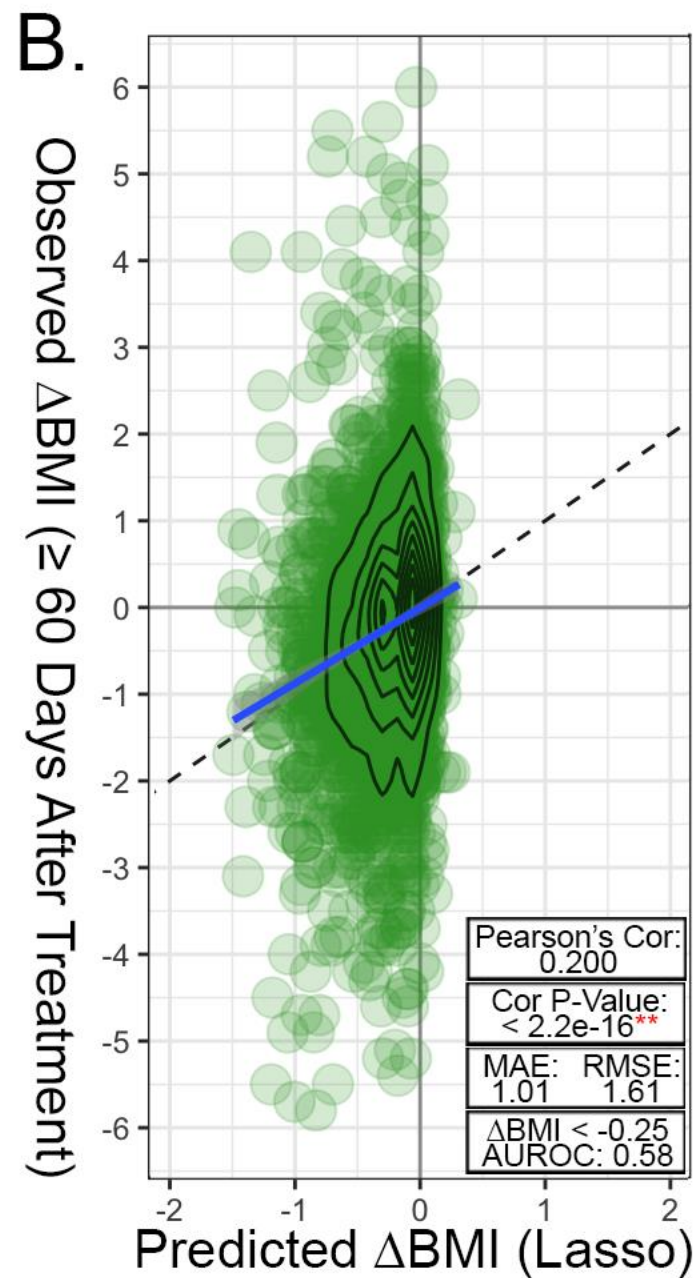
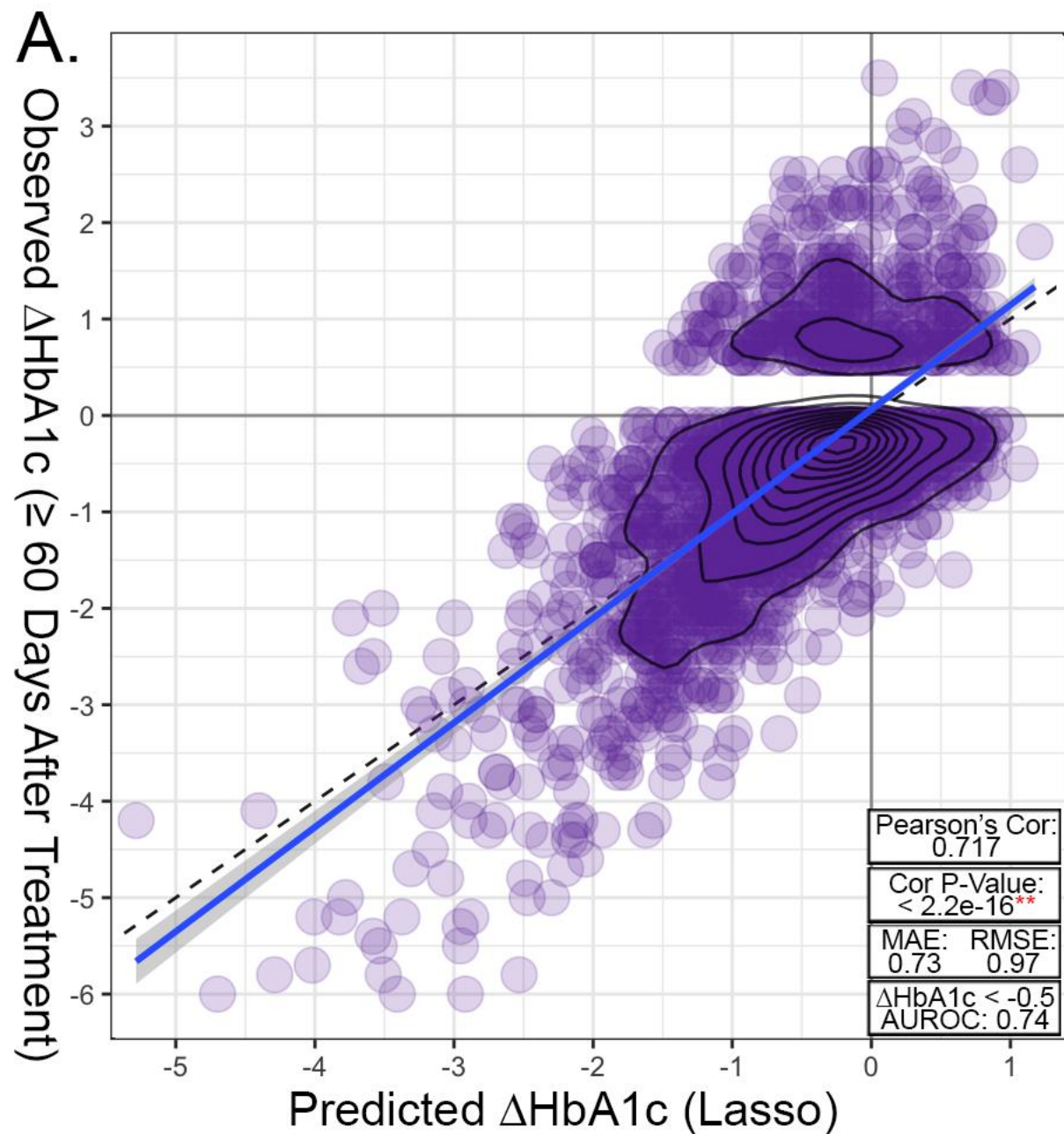




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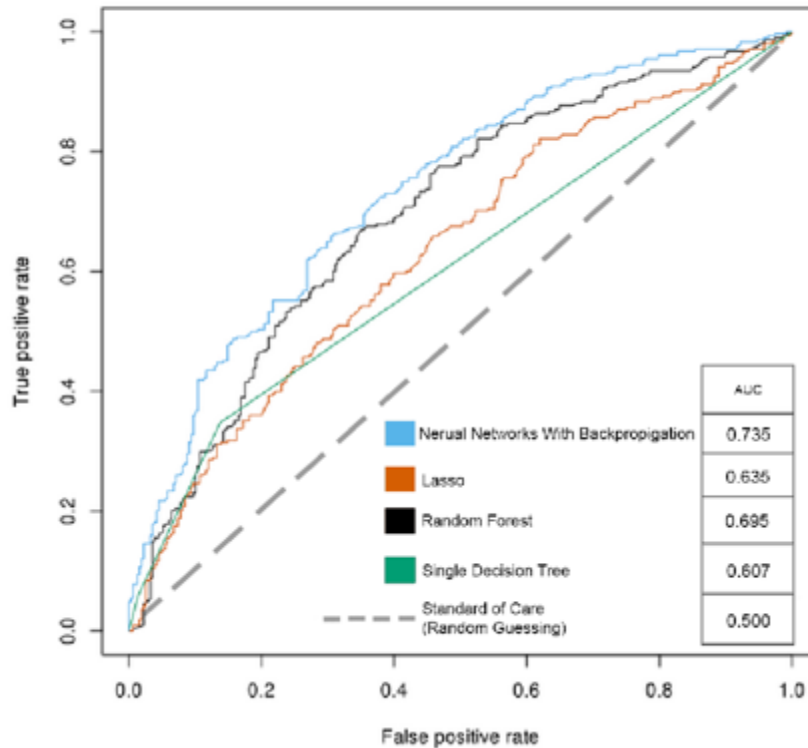




**Tom Peterson**

# Can we predict who will do well with metformin?

A. Model Comparison for Predicting Medication Class Increase Within 90 Days (Metformin Only)



B.

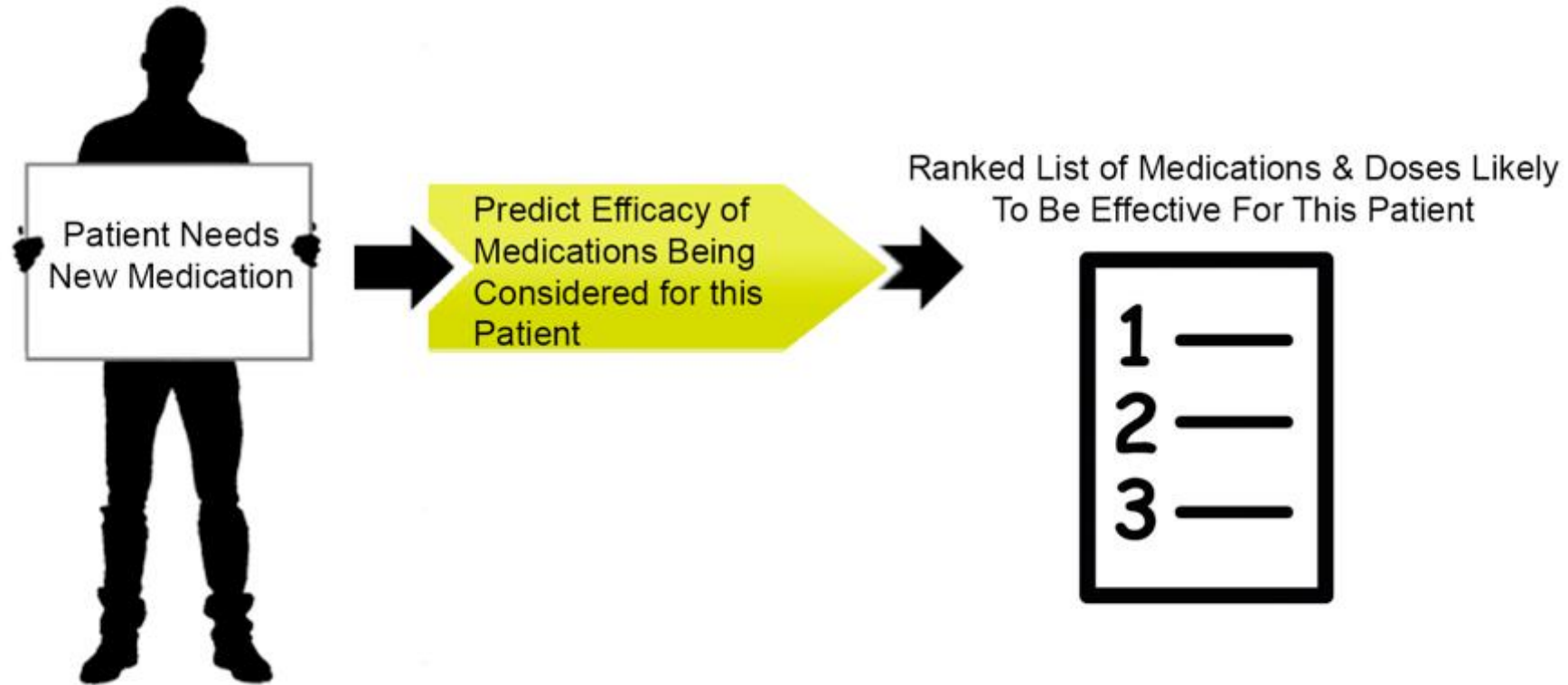
Decision Tree Used In Classification (AUC 0.607)



Tom Peterson



# Precision Medicine In Practice



# Predicting the future state of a patient with Rheumatoid Arthritis

JAMA  
Network | Open™



Original Investigation | Health Informatics

## Assessment of a Deep Learning Model Based on Electronic Health Record Data to Forecast Clinical Outcomes in Patients With Rheumatoid Arthritis

Beau Norgeot, MS; Benjamin S. Glicksberg, PhD; Laura Trupin, MPH; Dmytro Lituev, PhD; Milena Gianfrancesco, PhD, MPH; Boris Oskotsky, PhD; Gabriela Schmajuk, MD, MSc; Jinoos Yazdany, MD, MPH; Atul J. Butte, MD, PhD

### Abstract

**IMPORTANCE** Knowing the future condition of a patient would enable a physician to customize current therapeutic options to prevent disease worsening, but predicting that future condition requires sophisticated modeling and information. If artificial intelligence models were capable of forecasting future patient outcomes, they could be used to aid practitioners and patients in prognosticating outcomes or simulating potential outcomes under different treatment scenarios.

**OBJECTIVE** To assess the ability of an artificial intelligence system to prognosticate the state of disease activity of patients with rheumatoid arthritis (RA) at their next clinical visit.

**DESIGN, SETTING, AND PARTICIPANTS** This prognostic study included 820 patients with RA from rheumatology clinics at 2 distinct health care systems with different electronic health record platforms: a university hospital (UH) and a public safety-net hospital (SNH). The UH and SNH had substantially different patient populations and treatment patterns. The UH has records on approximately 1 million total patients starting in January 2012. The UH data for this study were accessed on July 1, 2017. The SNH has records on 65 000 unique individuals starting in January 2013. The SNH data for the study were collected on February 27, 2018.

**EXPOSURES** Structured data were extracted from the electronic health record, including exposures (medications), patient demographics, laboratories, and prior measures of disease activity. A longitudinal deep learning model was used to predict disease activity for patients with RA at their next rheumatology clinic visit and to evaluate interhospital performance and model interoperability strategies.

**MAIN OUTCOMES AND MEASURES** Model performance was quantified using the area under the

### Key Points

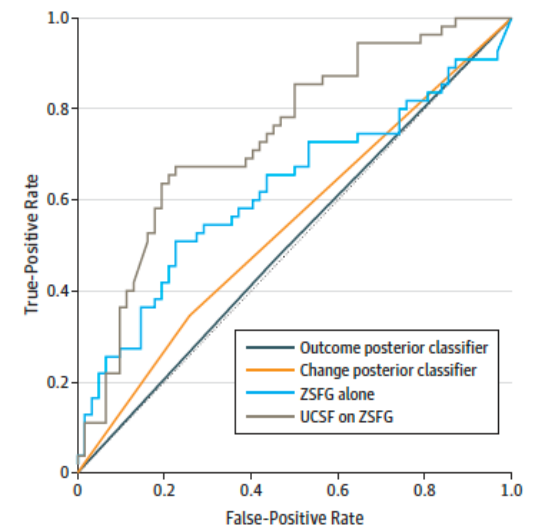
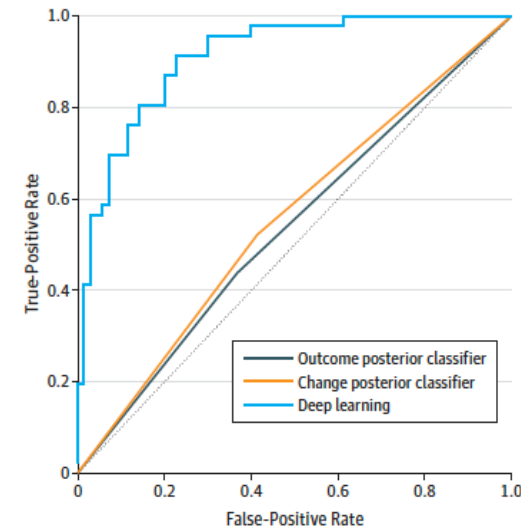
**Question** How accurately can artificial intelligence models prognosticate future patient outcomes for a complex disease, such as rheumatoid arthritis?

**Findings** In this prognostic study of 820 patients with rheumatoid arthritis, a longitudinal deep learning model had strong performance in a test cohort of 116 patients, whereas baselines that used each patient's most recent disease activity score had statistically random performance.

**Meaning** The findings suggest that building accurate models to forecast complex disease outcomes using electronic health records is possible.

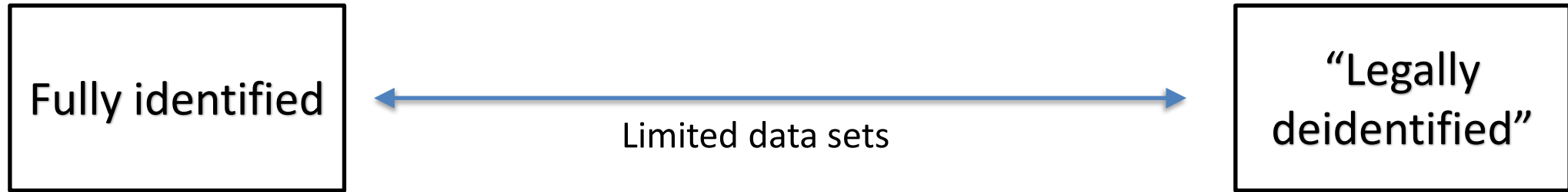
### + Supplemental content

Author affiliations and article information are listed at the end of this article.



**Beau Norgeot**  
**bit.ly/jamaRA**

# How will research access work?



- Researchers should first write and optimize OMOP SQL queries locally, on their own campuses
- When ready to scale (and authorized), we spin up a virtual machine for the researcher, populated with common tools
  - Electronically sign a UC Health data use agreement
  - R, Tableau, Jupyter Notebooks, Julia, SQL, Windows or Linux available
- Upload your scripts and run, but cannot download data
- Safe, respectful, regulated research use of clinical data



# Safe, Respectful access to Deidentified Data now available through Azure Databricks, single sign on

Microsoft Azure

PORTALatul.butte@ucsf.edu

Azure Databricks

Home

Workspace

Recents

Data

Clusters

Jobs

Models

Test 1 (SQL)

ucsf\_atul.butte\_user...

Cmd 1

```
1 %sql select visit_concept_id, concept_name, count(*) as cnt
2 from omop_deid.visit_occurrence as a join omop_deid.concept as b on b.concept_id = a.visit_concept_id
3 group by visit_concept_id, concept_name
4
```

▶ (6) Spark Jobs

visit_concept_id	concept_name	cnt
44818517	Visit derived from encounter on claim	126790
9202	Outpatient Visit	30726686
32024	Visit derived from encounter on medical professional claim	537158
600074748	Ambulatory Visit	165455361
32022	Visit derived from encounter on pharmacy claim	430137
9201	Inpatient Visit	1528859
32023	Visit derived from encounter on medical facility claim	108803
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Command took 19.43 seconds -- by atul.butte@ucsf.edu at 6/26/2020, 8:39:52 AM on ucsf\_atul.butte\_user\_cluster



- 500 registered attendees, 90 posters
- All UC Campuses represented, and two of our national labs
- Sessions rated highly across the board
- Leadership session outcome:
  - Planning for a Multi-campus Research Unit
  - Annual meeting





# Enabling UC researchers and patients to go beyond... machine learning in a safe, respectful, fair, equitable way in medicine

Alvin Rajkumar<sup>1,2</sup>, Eyal Oren<sup>1</sup>, Kai Chen<sup>1</sup>, Andrew M. Dai<sup>1</sup>, Nissan Hajaj<sup>1</sup>, Michaela Hardt<sup>1</sup>, Peter J. Liu<sup>1</sup>, Xiaobing Liu<sup>1</sup>, Jake Marcus<sup>1</sup>, Mimi Sun<sup>1</sup>, Patrik Sundberg<sup>1</sup>, Hector Yee<sup>1</sup>, Kun Zhang<sup>1</sup>, Yi Zhang<sup>1</sup>, Gerardo Flores<sup>1</sup>, Gavin E. Duggan<sup>1</sup>, Jamie Irvine<sup>1</sup>, Quoc Le<sup>1</sup>, Kurt Litsch<sup>1</sup>, Alexander Mossin<sup>1</sup>, Justin Tansuwan<sup>1</sup>, De Wang<sup>1</sup>, James Wexler<sup>1</sup>, Jimbo Wilson<sup>1</sup>, Dana Ludwig<sup>2</sup>, Samuel L. Volchenbourn<sup>1</sup>, Katherine Chou<sup>1</sup>, Michael Pearson<sup>1</sup>, Srinivasan Madabushi<sup>1</sup>, Nigam H. Shah<sup>4</sup>, Atul J. Butte<sup>2</sup>, Michael D. Howell<sup>1</sup>, Claire Cui<sup>1</sup>, Greg S. Corrado<sup>1</sup> and Jeffrey Dean<sup>1</sup>

Predictive modeling with electronic health record (EHR) data is anticipated to drive personalized medicine and improve healthcare quality. Constructing predictive statistical models typically requires extraction of curated predictor variables from normalized EHR data, a labor-intensive process that discards the vast majority of information in each patient's record. We propose a representation of patients' entire raw EHR records based on the Fast Healthcare Interoperability Resources (FHIR) format. We demonstrate that deep learning methods using this representation are capable of accurately predicting multiple medical events from multiple centers without site-specific data harmonization. We validated our approach using de-identified EHR data from two US academic medical centers with 216,221 adult patients hospitalized for at least 24 h. In the sequential format we propose, this volume of EHR data unrolled into a total of 46,864,534,945 data points, including clinical notes. Deep learning models achieved high accuracy for tasks such as predicting: in-hospital mortality (area under the receiver operator curve [AUROC] across sites 0.93–0.94), 30-day unplanned readmission (AUROC 0.75–0.76), prolonged length of stay (AUROC 0.85–0.86), and all of a patient's final discharge diagnoses (frequency-weighted AUROC 0.90). These models outperformed traditional, clinically-used predictive models in all cases. We believe that this approach can be used to create accurate and scalable predictions for a variety of clinical scenarios. In a case study of a particular prediction, we demonstrate that neural networks can be used to identify relevant information from the patient's chart.

npj Digital Medicine (2018)1:18 | doi:10.1038/s41746-018-0029-1

## INTRODUCTION

The promise of digital medicine stems in part from the hope that, by digitizing health data, we might more easily leverage computer information systems to understand and improve care. In fact, routinely collected patient healthcare data are now approaching the genomic scale in volume and complexity.<sup>1</sup> Unfortunately, most of this information is not yet used in the sorts of predictive statistical models clinicians might use to improve care delivery. It is widely suspected that use of such efforts, if successful, could provide major benefits not only for patient safety and quality but also in reducing healthcare costs.<sup>2–6</sup>

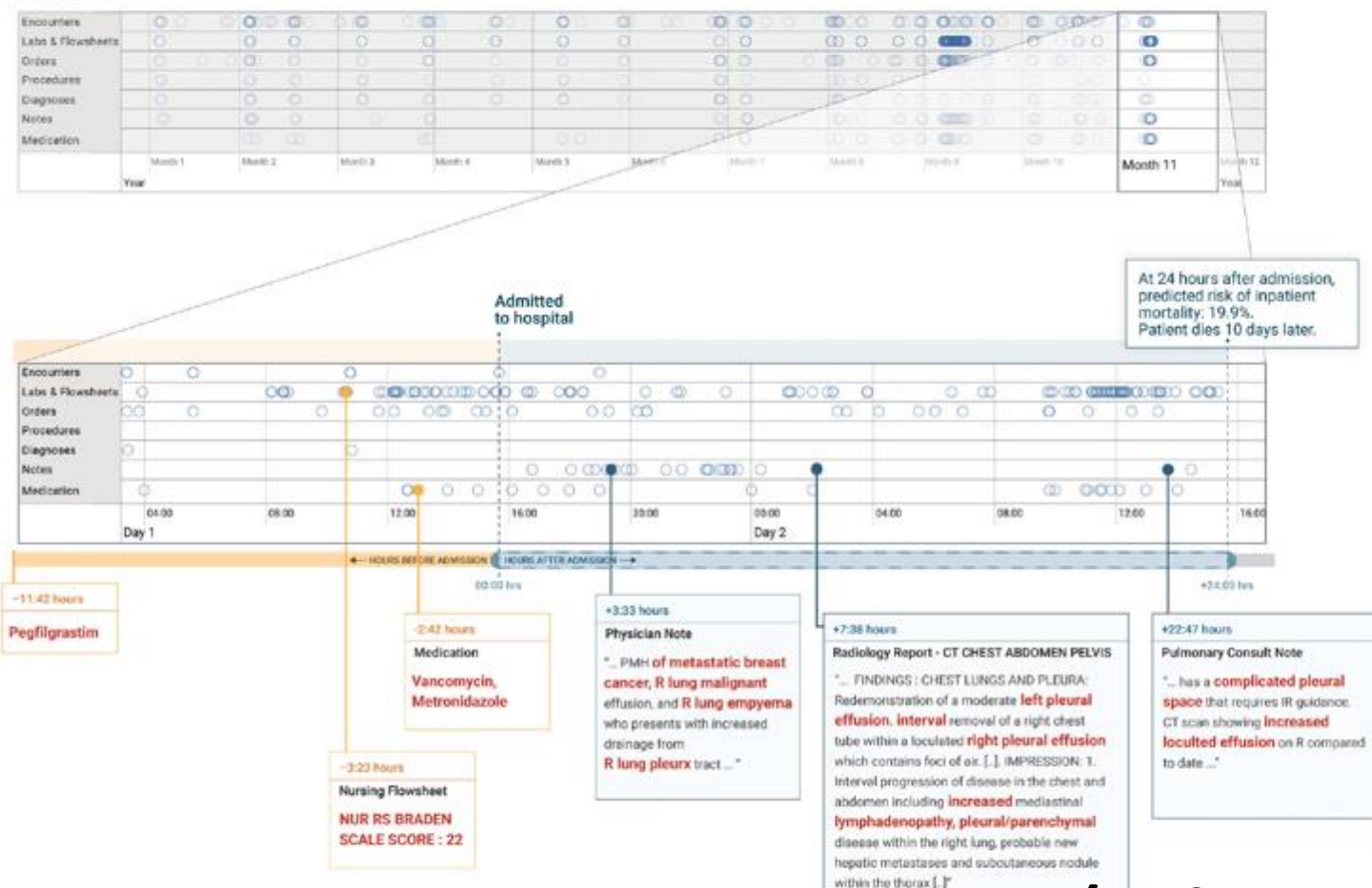
In spite of the richness and potential of available data, scaling the development of predictive models is difficult because, for traditional predictive modeling techniques, each outcome to be predicted requires the creation of a custom dataset with specific variables.<sup>7</sup> It is widely held that 80% of the effort in an analytic model is preprocessing, merging, customizing, and cleaning datasets,<sup>8,9</sup> not analyzing them for insights. This profoundly limits the scalability of predictive models.

Another challenge is that the number of potential predictor variables in the electronic health record (EHR) may easily number in the thousands, particularly if free-text notes from doctors,

nurses, and other providers are included. Traditional modeling approaches have dealt with this complexity simply by choosing very limited number of commonly collected variables to consider. This is problematic because the resulting models may produce imprecise predictions: false-positive predictions can overwhelm physicians, nurses, and other providers with false alarms and concomitant alert fatigue,<sup>10</sup> which the Joint Commission identifies as a national patient safety priority in 2014.<sup>11</sup> False-negative predictions can miss significant numbers of clinically important events, leading to poor clinical outcomes.<sup>11,12</sup> Incorporating the entire EHR, including clinicians' free-text notes, offers some hope of overcoming these shortcomings but is unwieldy for most predictive modeling techniques.

Recent developments in deep learning and artificial neural networks may allow us to address many of these challenges and unlock the information in the EHR. Deep learning emerged as the preferred machine learning approach in machine perceptual problems ranging from computer vision to speech recognition but has more recently proven useful in natural language processing, sequence prediction, and mixed modality data settings.<sup>13–17</sup> These systems are known for their ability to handle large volumes of relatively messy data, including errors in labels

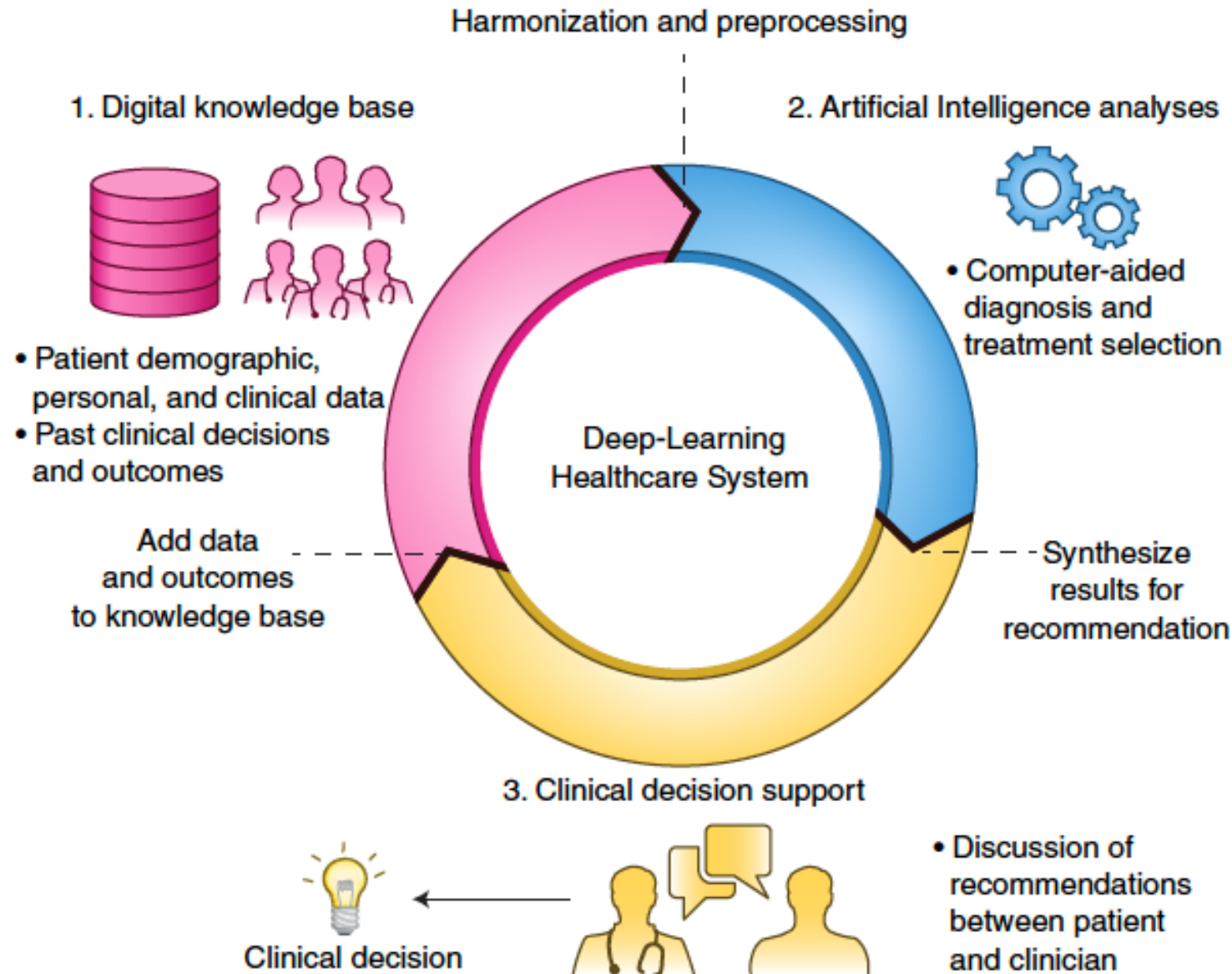
## Patient Timeline



<sup>1</sup>Google Inc, Mountain View, CA, USA; <sup>2</sup>University of California, San Francisco, San Francisco, CA, USA; <sup>3</sup>University of Chicago Medicine, Chicago, IL, USA and <sup>4</sup>Stanford University, Stanford, CA, USA  
Correspondence: Alvin Rajkumar (alvinrajkumar@google.com)  
These authors contributed equally: Alvin Rajkumar, Eyal Oren

Received: 26 January 2018 | Revised: 14 March 2018 | Accepted: 26 March 2018  
Published online: 08 May 2018

# A New Deep Learning Healthcare System



**Beau Norgeot**  
**[bit.ly/DLHCare](https://bit.ly/DLHCare)**



# Must be aware of biases in training data and methods

MIT  
Technology  
Review

Artificial intelligence Oct 25

## A biased medical algorithm favored people for health-care programs



A study has highlighted the risks inherent in using historical data to train machine learning algorithms to make predictions.

**The news:** An algorithm that many US health providers use to predict which patients will most need extra medical care privileged white patients over Black patients, according to researchers at UC Berkeley, whose study was published in the journal *Science*. Effectively, it bumped whites up the queue for special treatments for complex conditions like kidney problems or diabetes.

**The study:** The researchers dug through almost 50,000 records from a large, undisclosed academic hospital. They found that white patients were given higher priority for health-care programs than Black patients.

## How Biased is GPT-3?

Despite its impressive performance, the world's newest language model reflects societal biases in gender, race, and religion



Catherine Yeo Follow

Jun 3 · 4 min read ★



Last week, OpenAI released a new language model that has been known as the most powerful model to date, with 175 billion parameters.

GPT-3 is a language model that has been trained on a massive amount of data, and it has been shown to be able to generate text that is indistinguishable from human text. This article explores the biases that GPT-3 has inherited from its training data.

Its release was a major milestone for AI, but it also raised questions about the biases that GPT-3 has inherited from its training data. This article explores the broader societal implications of GPT-3's biases.

NEWS · 24 JANUARY 2020

## The battle for ethical AI at the world's biggest machine-learning conference

Bias and the prospect of societal harm increasingly plague artificial-intelligence research – but it's not clear who should be on the lookout for these problems.

Elizabeth Gibney



PDF version

### RELATED ARTICLES

How one conference embraced diversity



Can a major AI conference shed its reputation for hosting sexist behaviour?



Bias detectives: the researchers striving to make AI more ethical



# We need more transparency in developed and published models



## Minimum information about clinical artificial intelligence modeling: the MI-CLAIM checklist

Here we present the MI-CLAIM checklist, a tool intended to improve transparent reporting of AI algorithms in medicine.

Beau Norgeot, Giorgio Quer, Brett K. Beaulieu-Jones, Ali Torkamani, Raquel Dias, Milena Gianfrancesco, Rima Arnaout, Isaac S. Kohane, Suchi Saria, Eric Topol, Ziad Obermeyer, Bin Yu and Atul J. Butte

The application of artificial intelligence (AI) in medicine is an old idea<sup>1–3</sup>, but methods for this in the past involved programming computers with patterns or rules ascertained from human experts, which resulted in deterministic, rules-based systems. The study of AI in medicine has grown tremendously in the past few years

due to increasingly available datasets from medical practice, including clinical images, genetics, and electronic health records, as well as the maturity of methods that use data to teach computers<sup>4–6</sup>. The use of data labeled by clinical experts to train machine, probabilistic, and statistical models is called ‘supervised machine learning’. Successful

uses of these new machine-learning approaches include targeted real-time early-warning systems for adverse events<sup>7</sup>, the detection of diabetic retinopathy<sup>8</sup>, the classification of pathology and other images, the prediction of the near-term future state of patients with rheumatoid arthritis<sup>9</sup>, patient discharge disposition<sup>10</sup>, and more.

Before paper submission		
Study design (Part 1)	Completed: page number	Notes if not completed
The clinical problem in which the model will be employed is clearly detailed in the paper.	<input type="checkbox"/>	
The research question is clearly stated.	<input type="checkbox"/>	
The characteristics of the cohorts (training and test sets) are detailed in the text.	<input type="checkbox"/>	
The cohorts (training and test sets) are shown to be representative of real-world clinical settings.	<input type="checkbox"/>	
The state-of-the-art solution used as a baseline for comparison has been identified and detailed.	<input type="checkbox"/>	
Data and optimization (Parts 2, 3)	Completed: page number	Notes if not completed
The origin of the data is described and the original format is detailed in the paper.	<input type="checkbox"/>	
Transformations of the data before it is applied to the proposed model are described.	<input type="checkbox"/>	
The independence between training and test sets has been proven in the paper.	<input type="checkbox"/>	
Details on the models that were evaluated and the code developed to select the best model are provided.	<input type="checkbox"/>	
Is the input data type structured or unstructured?	<input type="checkbox"/> Structured <input type="checkbox"/> Unstructured	
Model performance (Part 4)	Completed: page number	Notes if not completed
The primary metric selected to evaluate algorithm performance (e.g., AUC, F-score, etc.), including the justification for selection, has been clearly stated.	<input type="checkbox"/>	
The primary metric selected to evaluate the clinical utility of the model (e.g., PPV, NNT, etc.), including the justification for selection, has been clearly stated.	<input type="checkbox"/>	
The performance comparison between baseline and proposed model is presented with the appropriate statistical significance.	<input type="checkbox"/>	
Model examination (Part 5)	Completed: page number	Notes if not completed
Examination technique 1 <sup>a</sup>	<input type="checkbox"/>	
Examination technique 2 <sup>a</sup>	<input type="checkbox"/>	
A discussion of the relevance of the examination results with respect to model/algorithm performance is presented.	<input type="checkbox"/>	
A discussion of the feasibility and significance of model interpretability at the case level if examination methods are uninterpretable is presented.	<input type="checkbox"/>	
A discussion of the reliability and robustness of the model as the underlying data distribution shifts is included.	<input type="checkbox"/>	
Reproducibility (Part 6): choose appropriate tier of transparency		Notes
Tier 1: complete sharing of the code	<input type="checkbox"/>	
Tier 2: allow a third party to evaluate the code for accuracy/fairness; share the results of this evaluation	<input type="checkbox"/>	
Tier 3: release of a virtual machine (binary) for running the code on new data without sharing its details	<input type="checkbox"/>	
Tier 4: no sharing	<input type="checkbox"/>	

PPV, positive predictive value; NNT, numbers needed to treat.

<sup>a</sup>Common examination approaches based on study type: for studies involving exclusively structured data, coefficients and sensitivity analysis are often appropriate; for studies involving unstructured data in the domains of image analysis or natural language processing, saliency maps (or equivalents) and sensitivity analyses are often appropriate.



## VIEWPOINT

# The Case for Algorithmic Stewardship for Artificial Intelligence and Machine Learning Technologies

**Stephanie Eaneff, MSP**  
Berkeley Institute for Data Science,  
University of California,  
Berkeley; and Bakar  
Computational Health  
Sciences Institute,  
University of California,  
San Francisco.

**Ziad Obermeyer, MD**  
University of California,  
Berkeley School of  
Public Health.

**Atul J. Butte, MD, PhD**  
Bakar Computational  
Health Sciences  
Institute, University of  
California, San  
Francisco; and Center  
for Data-Driven  
Insights and  
Innovation, University  
of California Health,  
Oakland.

**The first manual** on hospital administration, published in 1808, described a hospital steward as “an individual who [is] honest and above reproach,” with duties including the purchasing and management of hospital materials.<sup>1</sup> Today, a steward’s job can be seen as ensuring the safe and effective use of clinical resources. The Joint Commission, for instance, requires antimicrobial stewardship programs to support appropriate antimicrobial use, including by monitoring antibiotic prescribing and resistance patterns.

A similar approach to “algorithmic stewardship” is now warranted. Algorithms, or computer-implementable instructions to perform specific tasks, are available for clinical use, including complex artificial intelligence (AI) and machine learning (ML) algorithms and simple rule-based algorithms. More than 50 AI/ML algorithms have been cleared by the US Food and Drug Administration<sup>2</sup> for uses that include identifying intracranial hemorrhage from brain computed tomographic scans<sup>3</sup> and detecting seizures in real time.<sup>4</sup> Algorithms are also used to inform clinical operations, such as predicting which patients will

health systems must also develop oversight frameworks to ensure that algorithms are used safely, effectively, and fairly. Such efforts should focus particularly on complex and predictive algorithms that necessitate additional layers of quality control. Health systems that use predictive algorithms to provide clinical care or support operations should designate a person or group responsible for algorithmic stewardship. This group should be advised by clinicians who are familiar with the language of data, patients, bioethicists, scientists, and safety and regulatory organizations. In this Viewpoint, drawing from best practices from other areas of clinical practice, several key considerations for emerging algorithmic stewardship programs are identified.

## Create and Maintain an Algorithm Inventory

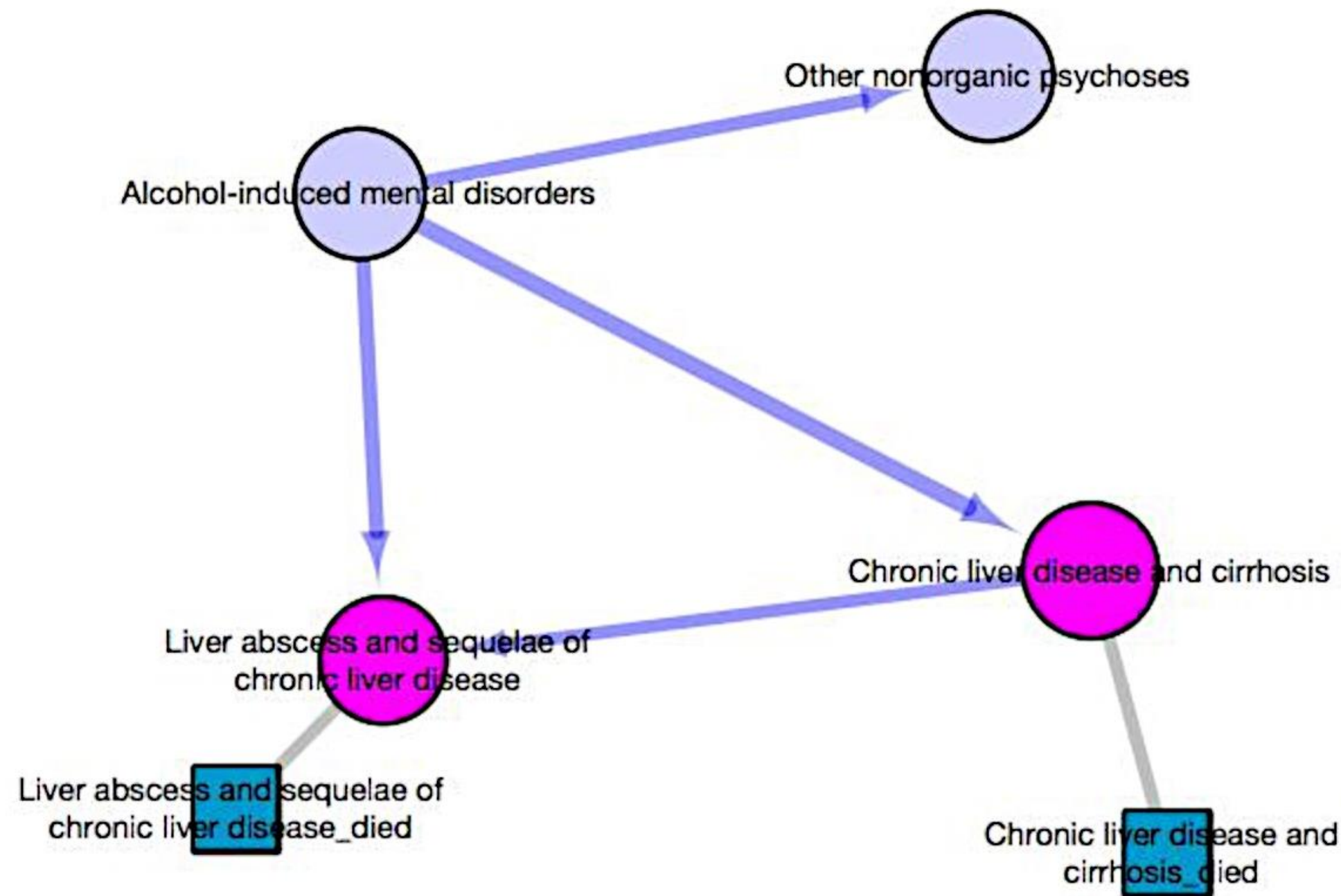
Health systems should inventory all predictive algorithms currently in use, with a particular emphasis on understanding the exact outcome being predicted and the decisions made on the basis of those predictions. This is particularly important because recent work has shown that algorithms can reach enormous scale

**Stephanie Eaneff**  
[bit.ly/algostew](https://bit.ly/algostew)



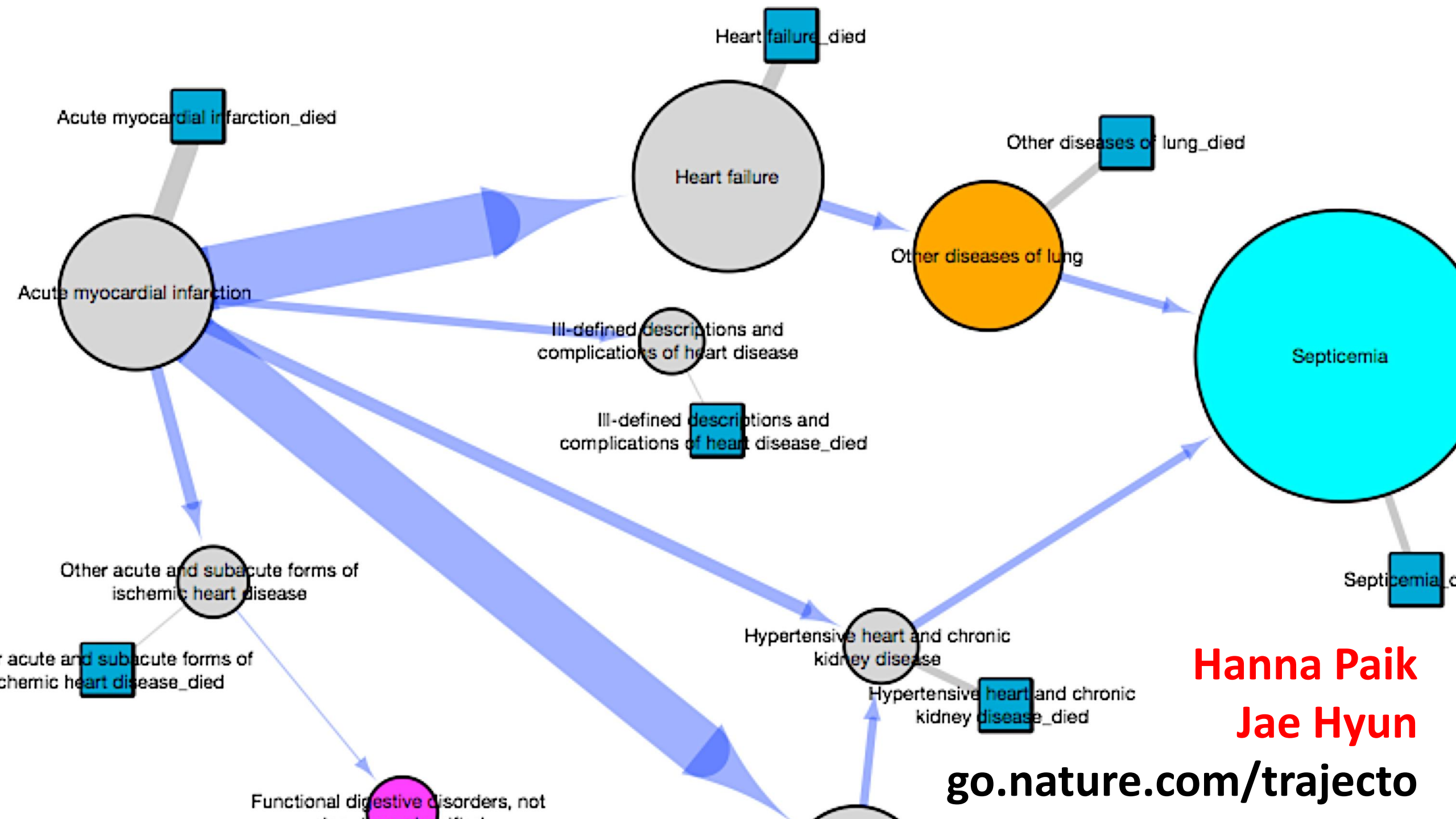
**Figure. Existing and Proposed Processes and Tools to Ensure Appropriate Use of Drugs for Algorithmic Stewardship Efforts**

	Existing processes and tools	Proposed processes and tools for algorithmic stewardship
① Clinical trials	Phase 1, 2, and 3 trials	Assess safety, efficacy, and fairness (potentially via clinical trials)
② Scale-up and early adoption	Hospital formulary	Algorithm inventory
③ Postmarket use and evaluation	Medication use evaluations	Algorithm use evaluations
④ Ongoing oversight	Antimicrobial steward role	Algorithmic steward role



**Hanna Paik**  
**Jae Hyun**

[go.nature.com/trajecto](https://go.nature.com/trajecto)



Hanna Paik  
Jae Hyun

[go.nature.com/trajecto](https://go.nature.com/trajecto)





# Collaborators

- Elizabeth Thomson, Patrick Dunn, Morgan Crafts / Northrop Grumman
- Quan Chen, Anupama Gururaj, Dawei Lin / NIAID
- Andrei Goga / UCSF Oncology
- Mallar Bhattacharya / UCSF Pulmonary
- Minnie Sarwal / UCSF Nephrology
- Geoffrey Gurtner / UCSF Surgery
- Roberta Diaz Brinton / Arizona
- Carol Bult / Jackson Labs
- Alejandro Sweet-Cordero, Julien Sage / Pediatric Oncology
- Takashi Kadowaki, Momoko Horikoshi, Kazuo Hara, Hiroshi Ohtsu / U Tokyo
- Kyoko Toda, Satoru Yamada, Junichiro Irie / Kitasato Univ and Hospital
- Shiro Maeda / RIKEN
- David Stevenson, Gary Shaw / Stanford Neonatology
- Mark Davis, C. Garrison Fathman / Stanford Immunology
- Russ Altman, Steve Quake / Stanford Bioengineering
- Euan Ashley, Joseph Wu / Stanford Cardiology
- Mike Snyder, Carlos Bustamante, Anne Brunet / Stanford Genetics
- Jay Pasricha / Stanford Gastroenterology
- Rob Tibshirani, Brad Efron / Stanford Statistics
- Hannah Valantine, Kiran Khush / Stanford Cardiology
- Mark Musen, Nigam Shah / National Center for Biomedical Ontology
- Sam So, Ken Weinberg, David Miklos / Stanford Oncology

## UCSF Health

Rick Larsen  
Nelson Lee  
Brian Chan  
Oksana Gologorskaya  
Sandy Stall  
Thomas Huray  
Jason Woll

## UC San Diego Health

Josh Glandorf  
Jennifer Holland  
Peter Ryan  
Andy Lucas  
Kirk Kurashige  
Calvin Fong

## UCI Health

David Merrill  
Dan Phillips  
Melody Hill  
Kathy Pickell  
Leanie Mayor  
Neaktisia Lee

## UNIVERSITY OF CALIFORNIA HEALTH

Atul Butte  
Carrie Byington  
Cora Han  
Pagan Morris  
Monte Ratzlaff  
Mike Kilpatrick  
Lisa Dahm  
Ayan Patel  
Aiden Barin  
Chaya Mohn  
Ray Pablo  
Tim Hayes  
David Gonzalez  
Rob Follett  
Teju Yardi  
Nadya Balabanova

## UCLA Health

Albert Duntugan  
Andrew Weaver  
Yael Berkovich  
Bill Lazarus  
Edgar Tijerino  
Jay Shah  
Vajra Kasturi  
Bill Cinnater  
Josh Pelino  
Shital Pandya  
Priya Sreedharan

## The Team

### The CIO Team

Ellen Pollack (UCLA)  
Chris Longhurst (UCSD)  
Scott Joslyn (UCI)  
Joe Bengfort (UCSF)  
Ashish Atreja (UCD)  
Tom Andriola (UCI)

## UCDAVIS HEALTH

Kent Anderson  
Steve Covington  
Hemanth Tatiparthi  
Ranjit Singh  
Jodi Nygaard  
Jeffrey Sterett  
Ralph Perrin  
Thomas Ami

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- Tarangini Deshpande
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## Admin and Tech Staff

- Andrew Jan
- Mounira Kenaani
- Kevin Kaier
- Boris Oskotsky
- Mae Moredo
- Ada Chen