Predictive Analytics and machine learning in clinical decision systems: simplified medical management decision making for health practitioners

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Artificial Intelligence. From Hype to reality

A convergence of **algorithmic advances**, **data proliferation** and **tremendous increase in computing power and storage** has propelled Artificial Intelligence (AI) from hype to reality.

- **1805** – Mathematician Legendre - foundation for machine learning
- **1818** – Mary Shelley – Frankenstein, the AI Monster
- **1958** – First Self-learning Algorithms (Artificial Neural Networks)
- **1965** – Birth of deep learning algorithms
- **1965** – Exponential growth in chip power
- **1991** – Opening of the World Wide Web to the public
- **2004** – Web 2.0 launching the era of user-generated data
- **2005** – Storage cost drop to $0.79 from $277 10 years earlier
- **2014** – Number of mobile devices exceeds the number of humans

Algorithmic Advancements | Exponential Increase in Computing Power and Storage | Explosion of Data

Artificial Intelligence. Today in Healthcare

AI is **revolutionizing** the **healthcare industry in many areas**. Hence, it is not only rising to be a **top priority** for the majority of **pharmaceutical companies**, but also increasing the **attractiveness** of the healthcare industry to the **government** and to **non-pharma firms.**

2016 2017 2018

UCB is implementing AI in settings across **research & early development**, **regulatory and safety**, **manufacturing / supply chain**, and enabling functions (i.e., **Purchasing & Finance**)

France puts **healthcare** at the heart of $1.8B **AI strategy** with the commitment to open access to the **French patient data**. French President Emmanuel Macron recognizes the **potential of AI** in making **medical care** more **predictive** and **personalized**.

Apple has added a new **'Movement Disorder API'** to its open-source Research Kit framework that will allow Apple Watch to continuously **monitor Parkinson's disease symptoms- tremors and dyskinesia.**

In addition to the PillPack acquisition for drug delivery and the joint healthcare venture with JP Morgan and Berkshire Hathaway, Amazon is focusing on growing **Alexa's healthcare skills** to improve the patient experience and helping users manage a **chronic illness or helping the elderly** (e.g.: remind people to take their medication).

The 4 Types of Machine Learning

SUPERVISED

SEMI-SUPERVISED

UN-SUPERVISED

REINFORCEMENT

Nevala K. The Machine Learning Primer. SAS Institute Inc. 2017. https://www.sas.com/content/dam/SAS/en_us/doc/whitepaper1/machine-learning-primer-108796.pdf. Accessed September 26, 2018.

The 4 Types of Machine Learning

SUPERVISED

- Machine is taught by example
  - Examples of desired inputs / outputs are provided; machine then solves similar problems
  - “Machine” (aka algorithm) uses input to determine correlations and logic that can predict the answer
- Practical Application
  - Customer Segmentation, Fraud detection, Risk assessment
    - Based on history, behavior, intent
    - Identify most valuable and most at-risk cohorts

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The 4 Types of Machine Learning

SEMI-SUPERVISED

- Machine is taught by example
  - Similar to “Supervised” Learning
  - Exception: Some of the input data provided is tagged with the desired output (answer) while the reminder is untagged
- Practical Application
  - Web page classification, image recognition/ classification
    - Based on a variety of criteria
    - Identify potentially offensive content or web pages

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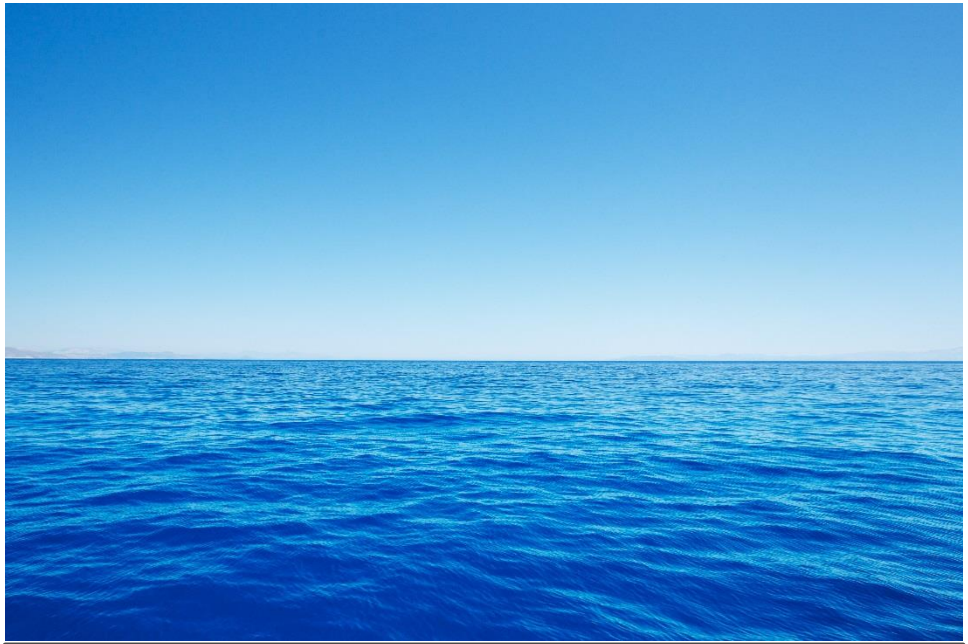
The 4 Types of Machine Learning



UN-SUPERVISED

- Machine studies data to identify patterns
  - There is no answer key
  - Machine determines correlations and relationships by parsing the available data
- Practical Application
  - Anomaly/ Intrusion detection, identify like things
    - Identify potential "hot spots" for disease outbreak
    - Which customers similar behaviors

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The 4 Types of Machine Learning

REINFORCEMENT

- Machine is provided a set of allowed actions, rules, and potential end states (rules defined)
  - Machine applies rules, explores different actions / results → learns to use rules to create a desired outcome
- Practical Application
  - Navigation, gaming and robotics
    - Identify best route from A to B based on current traffic, weather, etc.
    - Optimize resource deployment and routing to maximize efficiency and minimize cost across a fleet

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AI Enables Prediction Models and CDS Innovations, Which May Enhance Patient Care & Outcomes

Enable earlier patient identification and diagnosis

Reduce total cost of care

Enhance patient outcomes/ adherence

Improve workflow efficiency and referral optimization

Allow for adoption of appropriate treatment/ care pathways

Increase performance metrics

While many companies are pursuing machine learning approaches, clinical expertise in the disease area and deep knowledge of the market dynamics are required to contextualize the data, bring appropriate resources together, and fit solutions along the clinical workflow

Artificial Intelligence: is the Buzz Real?

Computer models might be able to help HCPs choose seizure medications with a greater chance for positive outcomes - "Personalized Medicine"

Unmet Patient Needs:

(Optimizing AED choice)

- Seizures in ~ 60% of patients respond to their first AED
- 15% spend 2 - 5 years finding an effective AED regimen
- 25 - 30% are treatment resistant

***Drug is not necessarily a UCB drug**

Leveraging Machine Learning To Improve Patient Outcomes in Epilepsy

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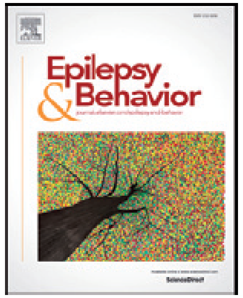

Changing the approach to treatment choice in epilepsy using big data

CrossMark

Orrin Devinsky [a,*], Cynthia Dilley [b], Michal Ozery-Flato [c], Ranit Aharonov [c], Ya'ara Goldschmidt [c], Michal Rosen-Zvi [c], Chris Clark [b], Patty Fritz [b]

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[c] IBM Research, University of Haifa Campus, Mount Carmel, Haifa 3498825, Israel

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Changing the Approach to Treatment Choice in Epilepsy using Big Data

UCB - IBM collaboration to retrospectively estimate the effectiveness of different treatment approaches using cognitive computing to analyze data from a large claims database

Machine-learning methods used to create a predictive algorithm estimating the success probability for a given patient and specific treatment regimen

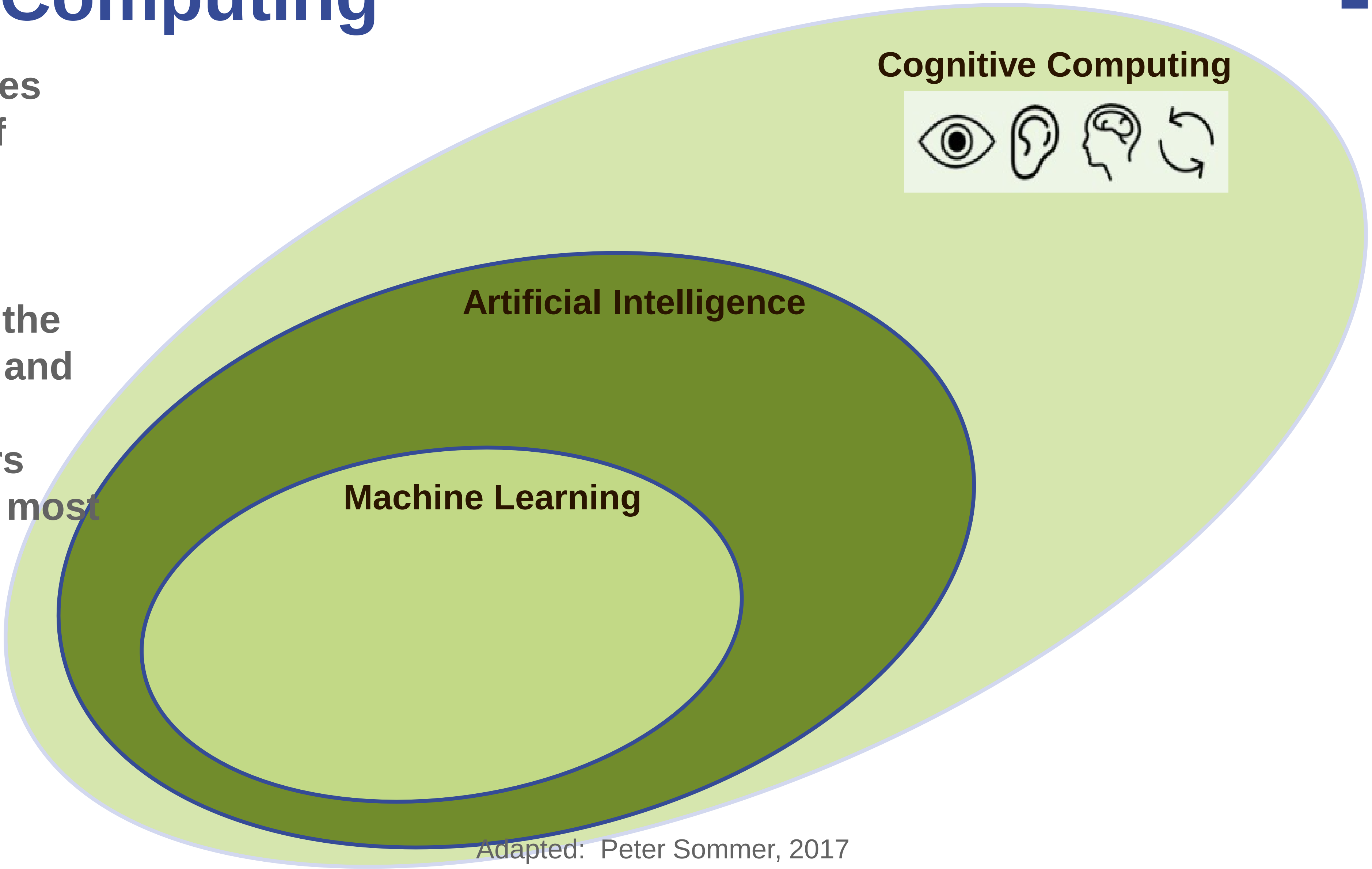
Model then used to predict the treatment regimen with the highest success probability (e.g., lowest chance of being changed later) for each patient (aka model-predicted AED regimen)

Analysis of health-care service utilization performed to investigate resource utilization (e.g., hospitalizations, physician visits, AED use)

Devinsky O, Dilley C, Ozery-Flato M, et al. Changing the approach to treatment choice in epilepsy using big data. *Epilepsy & Behavior*. 2016;56:32-37.

Cognitive Computing

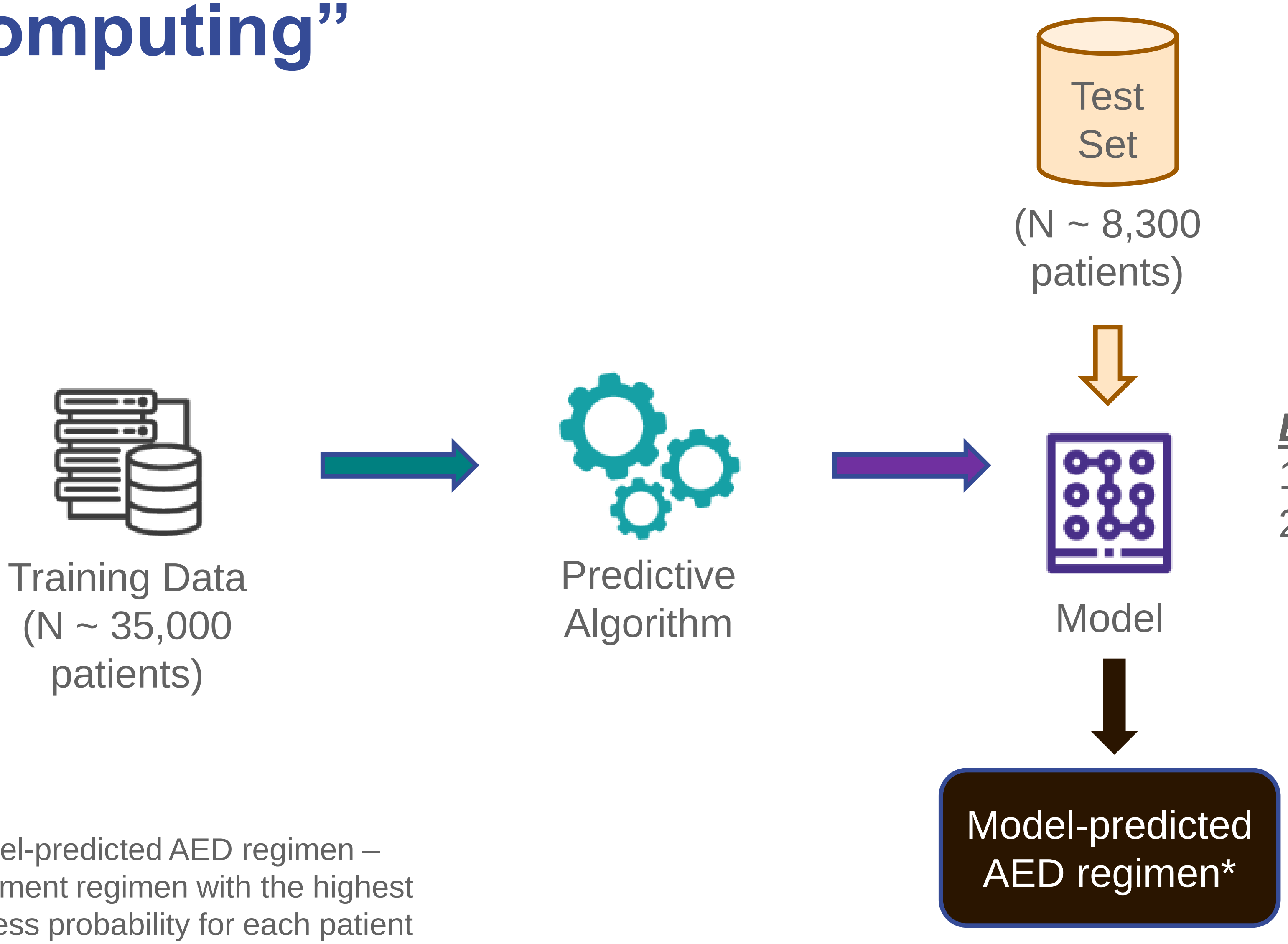
This approach takes mass quantities of structured and unstructured data from various sources and asks the computer to learn and return a set of structured answers based only on the most relevant data



Adapted: Peter Sommer, 2017

Sommer P. Artificial Intelligence, Machine Learning and Cognitive Computing. IBM Digital Nordic. 2017. https://www.ibm.com/blogs/nordic-msp/artificial-intelligence-machine-learning-cognitive-computing/. Accessed October 3, 2018.

A Machine-Learning Approach: Leveraging “Cognitive Computing”



Evaluation of Predictions:

1. Treatment change rates
2. Utilization of health-care services

*Model-predicted AED regimen – Treatment regimen with the highest success probability for each patient

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Patient Data Collection: 24 months

Pre-Index Period

- Patient & treatment features extracted (e.g., medication history, demographics, number and type of distinct drugs at index date, etc)

Outcomes

- **Success:** Longer-term stable treatment or complete withdrawal from AED treatment
- **Failure:** Any change (other than dose change or complete withdrawal of regimen)

MONTH

0 12 24

Index Date:
First date on which a treatment change occurred (switching, adding, or starting a new medicine)

Training Data: (N = ~ 35,000 patients)	Test set: (N= ~ 8,300 patients)	Patient features extracted: ~ 5,000 per patient

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Features of Clinical Interest with Strongest Correlation to Treatment Failure or Success

Correlation to Treatment FAILURE
No. of concomitant AEDs in ID treatment
No. of unique treatments 6 months prior to ID
No. of treatment change events 12 months prior to ID
ID treatment contains a first-generation AED
No. of AED dose increases 12 months prior to ID
ID treatment contains clonazepam
ID treatment has GABA-augmenting MOA
No. of GABA-augmenting AEDs 12 months prior to ID
No. of absence-activity AEDs 12 months prior to ID
No. of restarts 6 months prior to ID
No. of first-generation AEDs 12 months prior to ID
No. of discontinued treatment events 12 months prior to ID
No. of newer-generation AEDs 12 months prior to ID

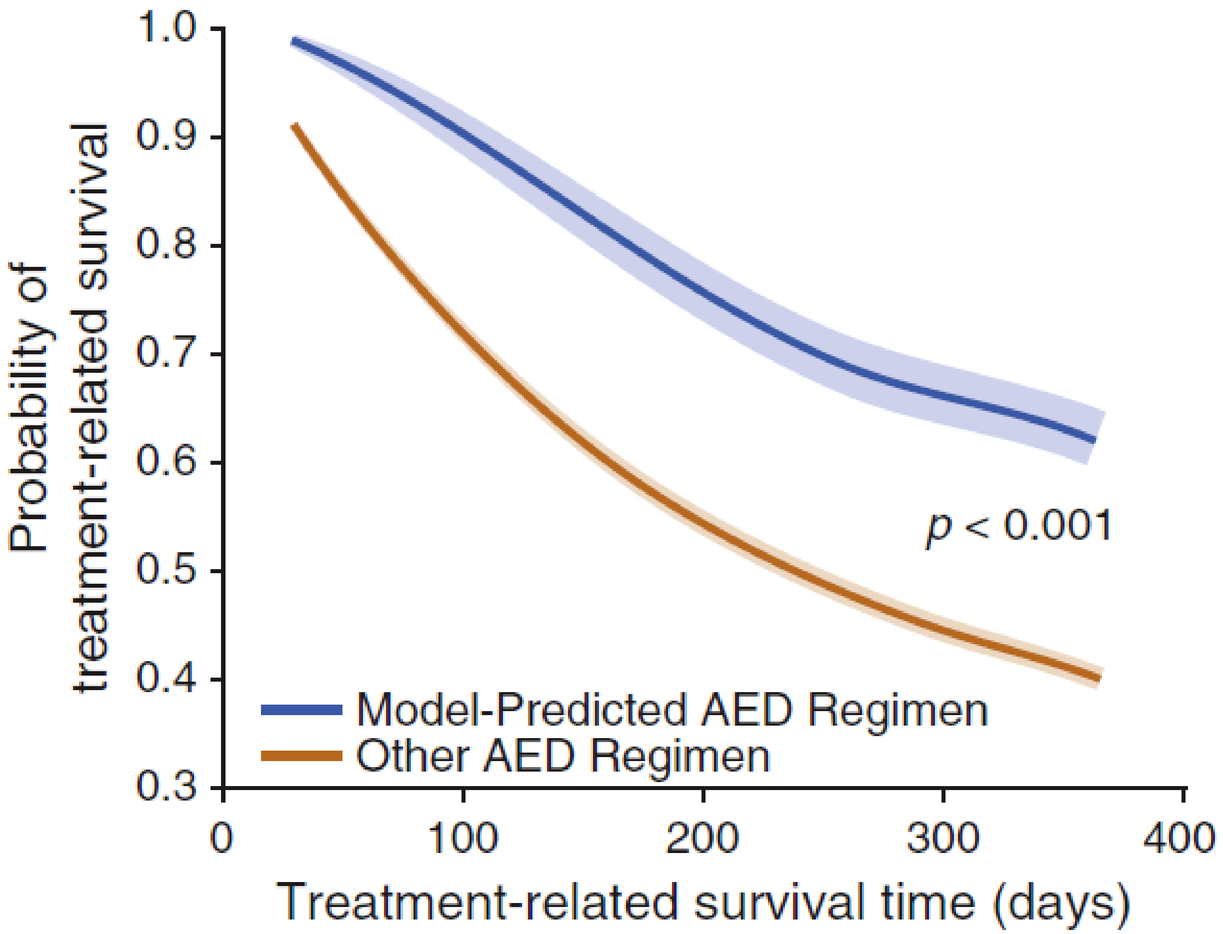
Correlation to Treatment SUCCESS
Age + Age
MPR of clonazepam 12 months prior to ID

Devinsky O, Dilley C, Ozery-Flato M, et al. Changing the approach to treatment choice in epilepsy using big data. *Epilepsy & Behavior*. 2016;56:32-37.

AED=antiepileptic drug, **ID**=index date, **MOA**=mechanism of action, **MPR**=mean possession ratio.

Results: Treatment Change Rates

Model-predicted AED regimen had **longer** median **survival rates** on average (e.g., longer time until a treatment change event) vs. patients receiving another AED regimen (median of >360 days vs. 239 days; *p<0.001*)



Note: Physician-chosen AED regimens matched in only 13% of cases

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Results: Utilization of Healthcare Resources

Model-predicted AED regimens produced better than expected outcomes for patients (e.g., longer time to subsequent treatment modification event and reductions in health-care resource utilization)

Predictions of Expected Yearly Health-care Utilization Savings in the Test Sample (N= ~8300 patients)

Feature	Observed utilization (U_{actual})[a]	Expected utilization on model-predicted AED (U_{model})	Delta ($U_{actual} - U_{model}$)	Yearly delta
No. of prescriptions for AED/SSRI/SNRI (30 days)	0.036049	0.035308	0.000741	73.73
No. of other prescriptions (30 days)[b]	0.162621	0.16142	0.001201	119.50
No. of days of epilepsy-related hospitalization	0.001802	0.00171	0.000093	281.47
No. of days of hospitalization[b]	0.008453	0.008271	0.000182	550.84
No. of physician visit/days				
Neurologist/specialist	0.018857	0.018599	0.000258	780.86
PCP/other	0.127702	0.126633	0.001069	3235.41
Emergency medicine	0.002736	0.002649	0.000088	266.34
No. of epilepsy-related procedures	0.000247	0.000238	0.000009	27.24
No. of other procedures[b]	0.060700	0.060058	0.000642	1943.06

AED, antiepileptic drug; PCP, primary care physician; SSRI, selective serotonin reuptake inhibitor; SNRI, serotonin–norepinephrine reuptake inhibitor.

[a] In training data set.

[b] Not related to epilepsy.

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AED=antiepileptic drug, **No.**=number, **PCP**=primary care physician, **SSRI**=selective serotonin reuptake inhibitor, **SNRI**=serotonin-norepinephrine reuptake inhibitor.

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Computer models might be able to help HCPs choose seizure medications with a greater chance for positive outcomes - "Personalized Medicine"

Unmet Patient Needs: ------------------------------ **Value Proposition:**

(Optimizing AED choice)

- Seizures in ~ 60% of patients respond to their first AED
- 15% spend 2 - 5 years finding an effective AED regimen
- 25 - 30% are treatment resistant

Providers	Evidence-based, real-time recommendation. Removal of "guessing game" in treatment decision.
Patients	Improved outcomes. Reduced utilization of healthcare resources. Precision and personalized access.
UCB	New source of patient value "The Right Patient gets the Right Drug at the Right Time*"

***Drug is not necessarily a UCB drug**

A Machine-Learning Approach: Potential Next Steps

Test Set

(N ~ 8,300)

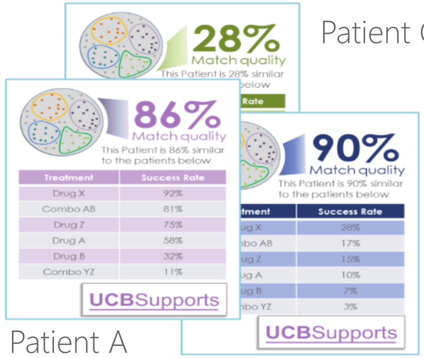
Training Data
(N ~ 35,000)

Predictive Algorithm

Model

Model-predicted AED regimen*

Patient C



Patient A

Patient B

Incorporating genomics as an additional data point enables for further personalizing clinical decision making

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