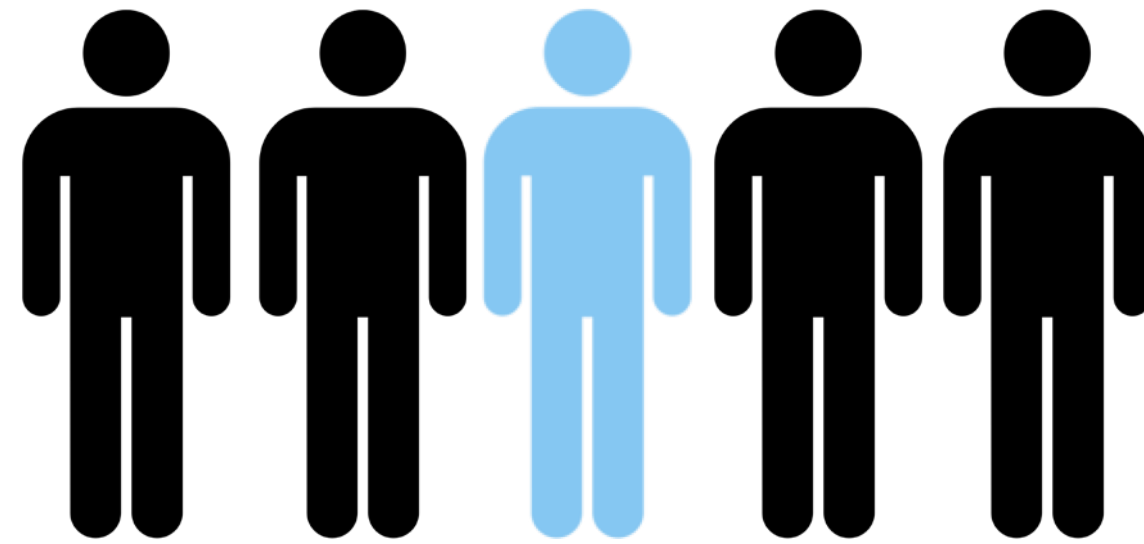


spring

personalized behavioral healthcare



1 of every 5 Americans

Costs **\$210 Billion** in U.S. every year

15% of severe depression ends in suicide

1 in 10

Americans take antidepressants

70%

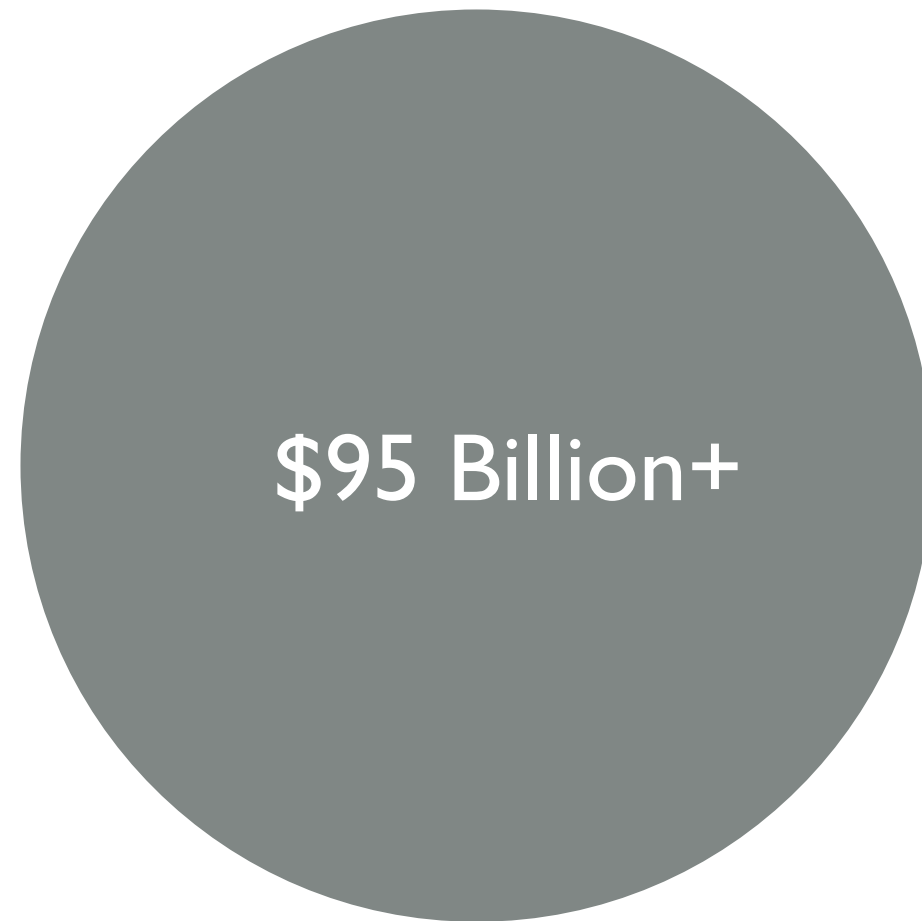
of patients
do not recover
from initial treatment



Clinicians resort to a **long process of trial-and-error** when prescribing antidepressants

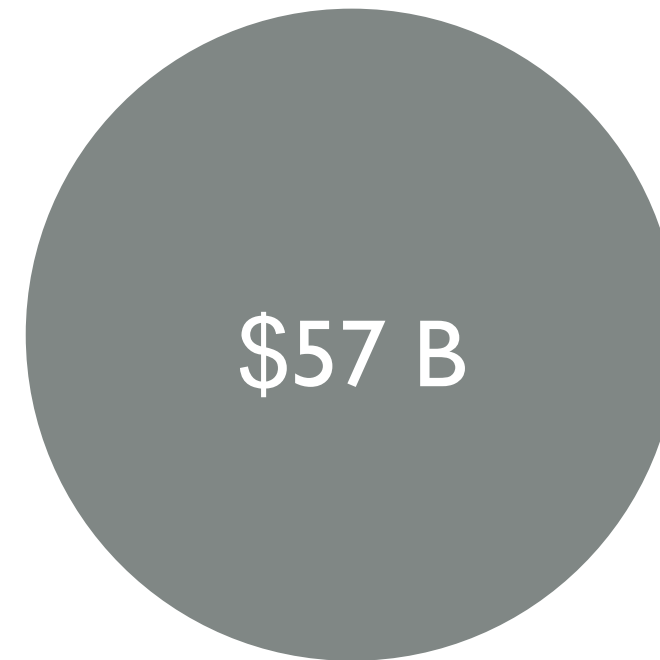


TRIAL-AND-ERROR IS EXPENSIVE



\$95 Billion+

Annual Direct
Medical Costs of
Depression in US



\$57 B

Preventable
Costs



\$27 B+

Costs Preventable
By Spring

Machine-learning
can predict treatment outcomes in depression.

Machine-learning is a method of data analysis that automates
analytical model building.

Feature

**Predicting antidepressant response**

Can a machine learning approach help clinicians identify which patients will, or will not, respond to antidepressants?



*Research peer-reviewed and published in the Lancet: Chekroud, Adam Mourad, et al. "Cross-trial prediction of treatment outcome in depression: a machine learning approach." The Lancet Psychiatry (2016).

*Provisional patent on IP
*Exclusive license from Yale

ARTS & HUMANITIES

BUSINESS, LAW, SOCIETY

CAMPUS & COMMUNITY

SCIENCE & HEALTH

Yale's depression model outperforms psychiatrists

By Bill Hathaway

January 20, 2016

Cross-trial prediction of treatment outcome in depression: a machine learning approach

Adam Mourad Chekroud, Ryan Joseph Zotti, Zarrar Shehzad, Ralitza Gueorguieva, Marcia K Johnson, Madhukar H Trivedi, Tyrone D Cannon, John Harrison Krystal, Philip Robert Corlett

Summary

Background Antidepressant treatment efficacy is low, but might be improved by matching patients to interventions. At present, clinicians have no empirically validated mechanisms to assess whether a patient with depression will respond to a specific antidepressant. We aimed to develop an algorithm to assess whether patients will achieve symptomatic remission from a 12-week course of citalopram.

Methods We used patient-reported data from patients with depression (n=4041, with 1949 completers) from level 1 of the Sequenced Treatment Alternatives to Relieve Depression (STAR*D; ClinicalTrials.gov, number NCT00021528) to identify variables that were most predictive of treatment outcome, and used these variables to train a machine-learning model to predict clinical remission. We externally validated the model in the escitalopram treatment group (n=151) of an independent clinical trial (Combining Medications to Enhance Depression Outcomes [COMED]; ClinicalTrials.gov, number NCT00590863).

Findings We identified 25 variables that were most predictive of treatment outcome from 164 patient-reportable variables, and used these to train the model. The model was internally cross-validated, and predicted outcomes in the STAR*D cohort with accuracy significantly above chance (64.6% [SD 3.2]; p<0.0001). The model was externally validated in the escitalopram treatment group (N=151) of COMED (accuracy 59.6%, p=0.043). The model also performed significantly above chance in a combined escitalopram-bupropion treatment group in COMED (n=134; accuracy 59.3%, p=0.033), but not in a combined week-forcing mistreatment group (n=140; accuracy 51.4%, p=0.52).

Lancet Psychiatry 2016; 3: 243-50

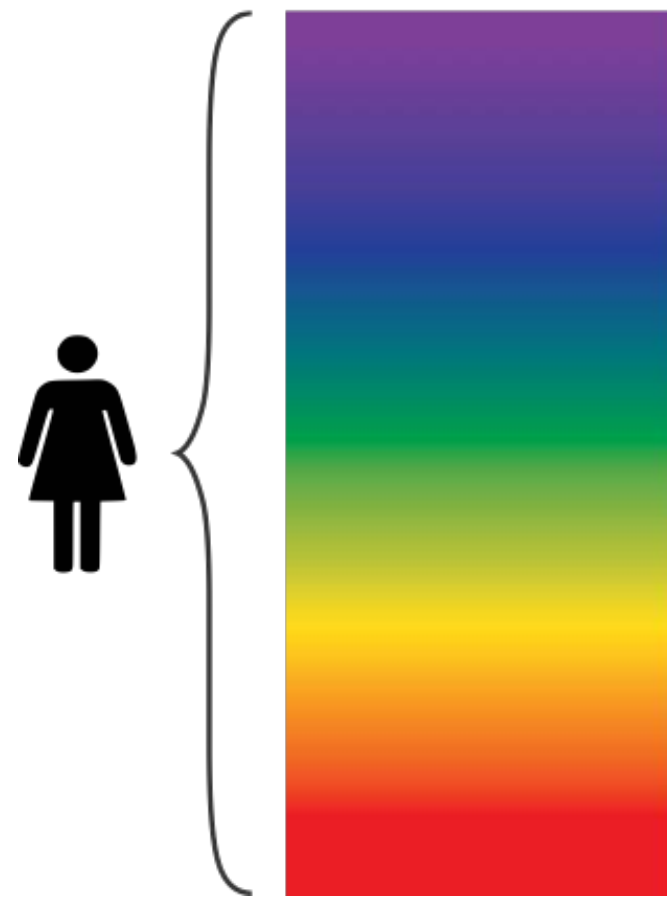
Published Online
January 20, 2016
[http://dx.doi.org/10.1016/S2215-0366\(16\)00471-X](http://dx.doi.org/10.1016/S2215-0366(16)00471-X)

See [Comment](#) page 192

Department of Psychology
(A M Chekroud MSc,
Z Shehzad MSc,
M K Johnson PhD,
T D Cannon PhD),
Department of Biostatistics
(R Gueorguieva PhD), and
Department of Psychiatry
(T D Cannon, J H Krystal MD,
P R Corlett PhD), Yale University,
New Haven, CT, USA; Capital
One, Midland, VA, USA
(R) Zotti BS; Department of
Psychiatry, UT Southwestern,

OUR APPROACH

- I. Took the largest ever clinical trial on depression (STAR*D, n~6000) and pulled all patient information available before patient started treatment.

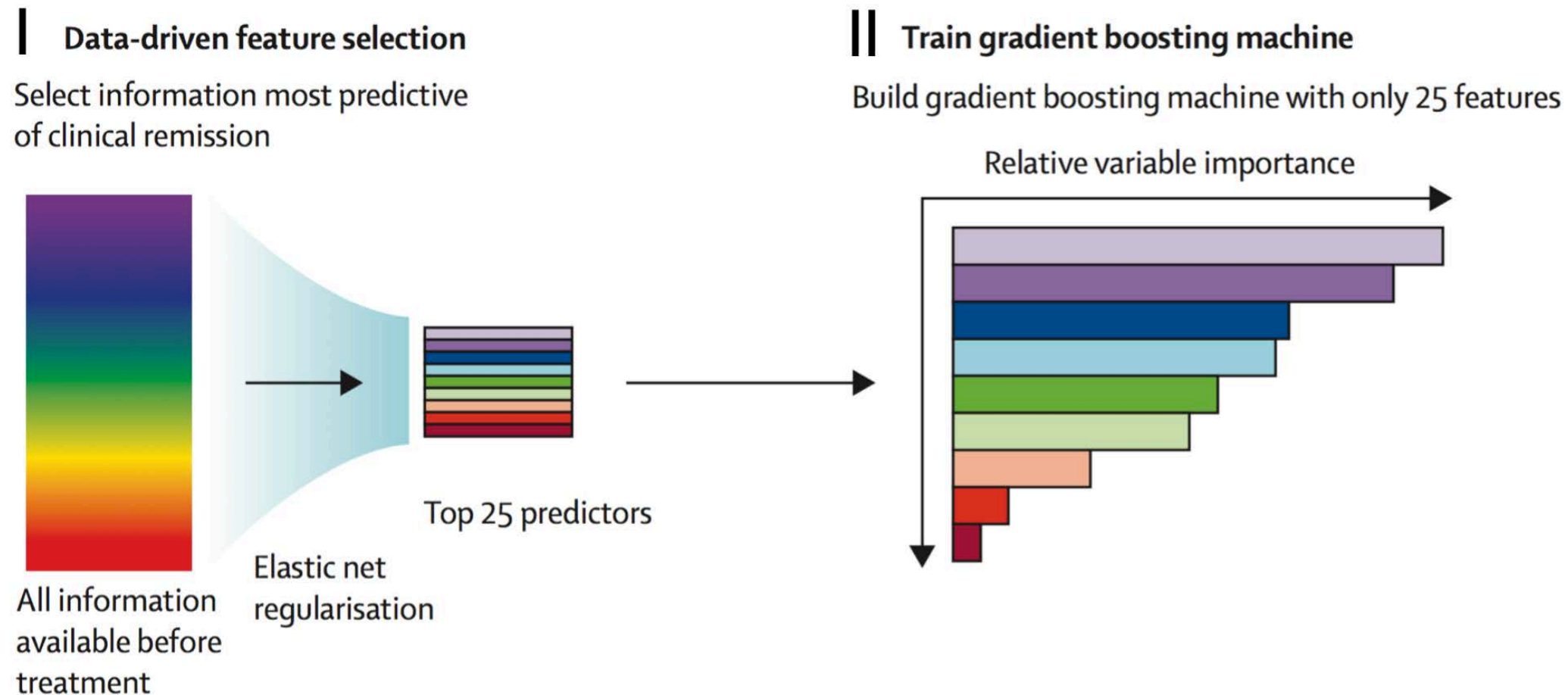


Include all readily-available data

- Demographic
- Diagnostic criteria (DSM-IV)
- Questionnaire responses about symptoms
- Psychiatric History
 - Family history

OUR APPROACH

Machine-learning model predicting antidepressant efficacy



- I. **Selected 25 strongest predictors of clinical remission** using *elastic net regularisation*
- II. **Determined relative variable importance** by training *gradient boosting machine*.
- III. **Validated the model** across two independent data sets:
(STAR*D ~ 4000, COMED ~ 300)

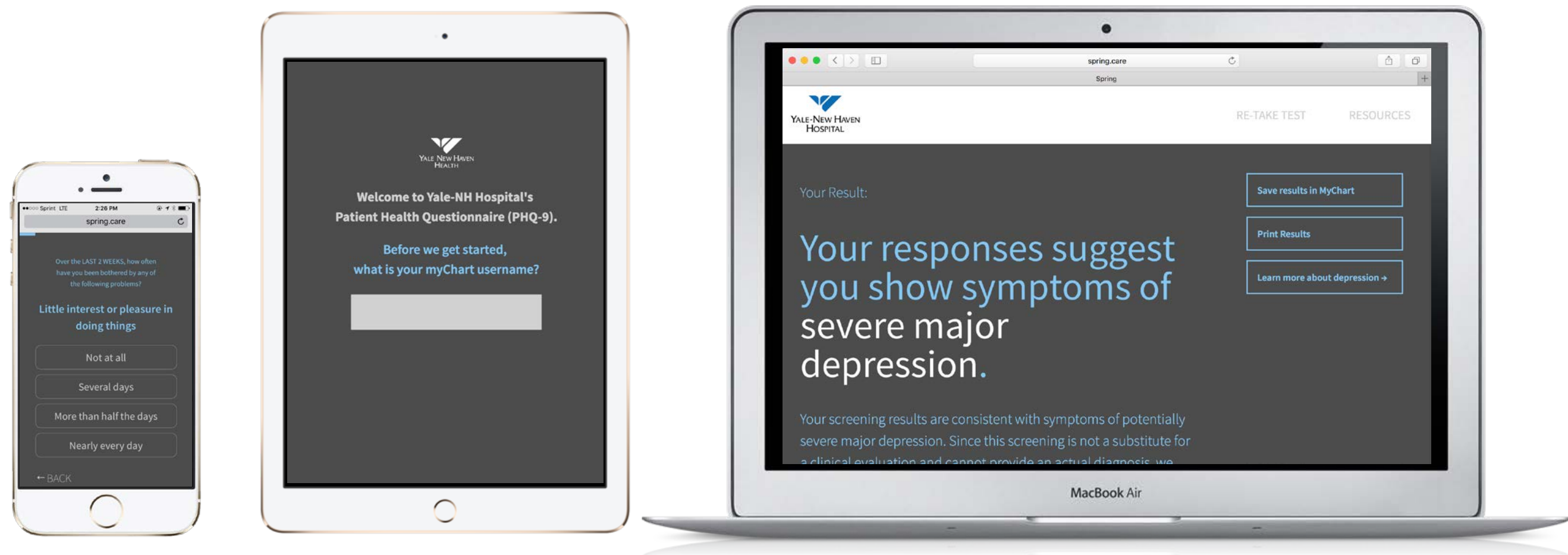
Outperformed more expensive genetic
and biological tests

Doubled clinical accuracy

Patients are 2-6x more likely to get better

ALGORITHM → QUESTIONNAIRE

10-minute test (e.g. in a waiting room)



www.spring.care

CLINICAL WORKFLOW

Primary Care



Amanda



PHQ-9
Depression Screening



Tablet in waiting room



**Automatically triggered Spring Assessment
if patient is depressed**



Efficient, actionable recommendations for PCP



Track progress via mobile phone

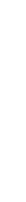


Efficient Screening



**Machine-learning
treatment selection**

spring



**Clinical
decision support**



Outcomes Tracking

BENEFITS FOR PROVIDERS

- **Efficient, smart clinical care**
- **Integrated behavioral health in primary care**
- **Reduced total cost of care per patient**
by prescribing medication most likely to work for patient
- **Healthier, happier patients & better outcomes**

PILOT AGREEMENTS



YALE-NEW HAVEN
HOSPITAL

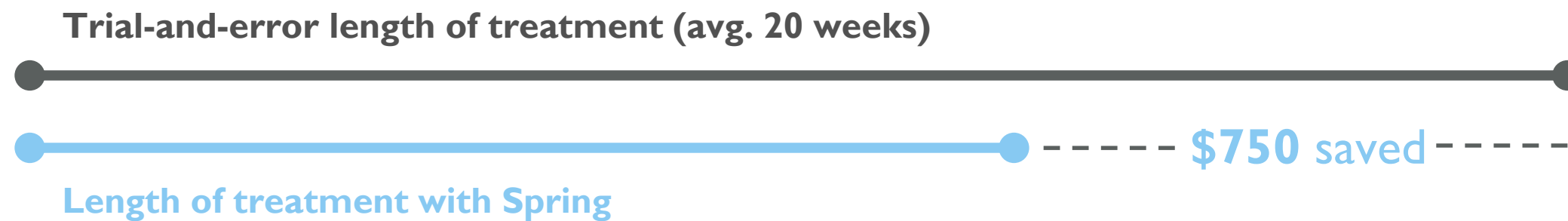


50,000+
patients



BUSINESS MODEL

Medical Cost Savings = \$750/patient
Charge up to 50% to value-based providers and insurers



Yale-New Haven
saves

\$24M

CareFirst BCBS
saves

\$158M

Medicare
saves

\$2.7B



vs

spring

method

uses genomics
(saliva sampling)

10min digital
questionnaire

efficiency

slower

immediate results

cost

more expensive
(\$2000-\$3000/test)

affordable

accuracy

no data

65%

3 Technical Founders from Yale

Founded in May 2016



April Koh
CEO

- Yale BA
- Raised \$5M as an undergraduate
- CS & Sociology



Adam Chekroud
Chief Scientist

- Yale PhD Psychology
- Oxford BA, MSc
- Neuroscience & Statistics



Abhishek Chandra
CTO

- Yale BS
- Google
- PatientBank
- CS & Economics

Scientific Advisory Board

Support from Leaders In Psychiatry



John Krystal, MD

Yale-New Haven Hospital
Chief of Psychiatry



Martin Paulus, MD

**Laureate Institute for Brain
Research**
Scientific Director and President



**Nikolaos Koutsouleris,
MD**

Ludwig-Maximilians-University of Munich
World expert in personalized psychiatry

WHAT'S NEXT?

Looking forward to the future features and products

**Comprehensive precision medicine platform
for behavioral and chronic health**

✓ **depression**

✓ **psychosis**

✓ anxiety

✓ OCD

✓ eating disorders

✓ chronic pain

✓ allergies

✓ birth control