MACHINE LEARNING IN PREDICTING AND MONITORING MENTAL HEALTH AND HUMAN PERFORMANCE

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Disclosure

No financial or professional conflict of interest.

I am Director of Computational Medicine and Artificial Intelligence and Assistant Professor in Behavioral and Cognitive Sciences at Columbia University, Department of Emergency Medicine.

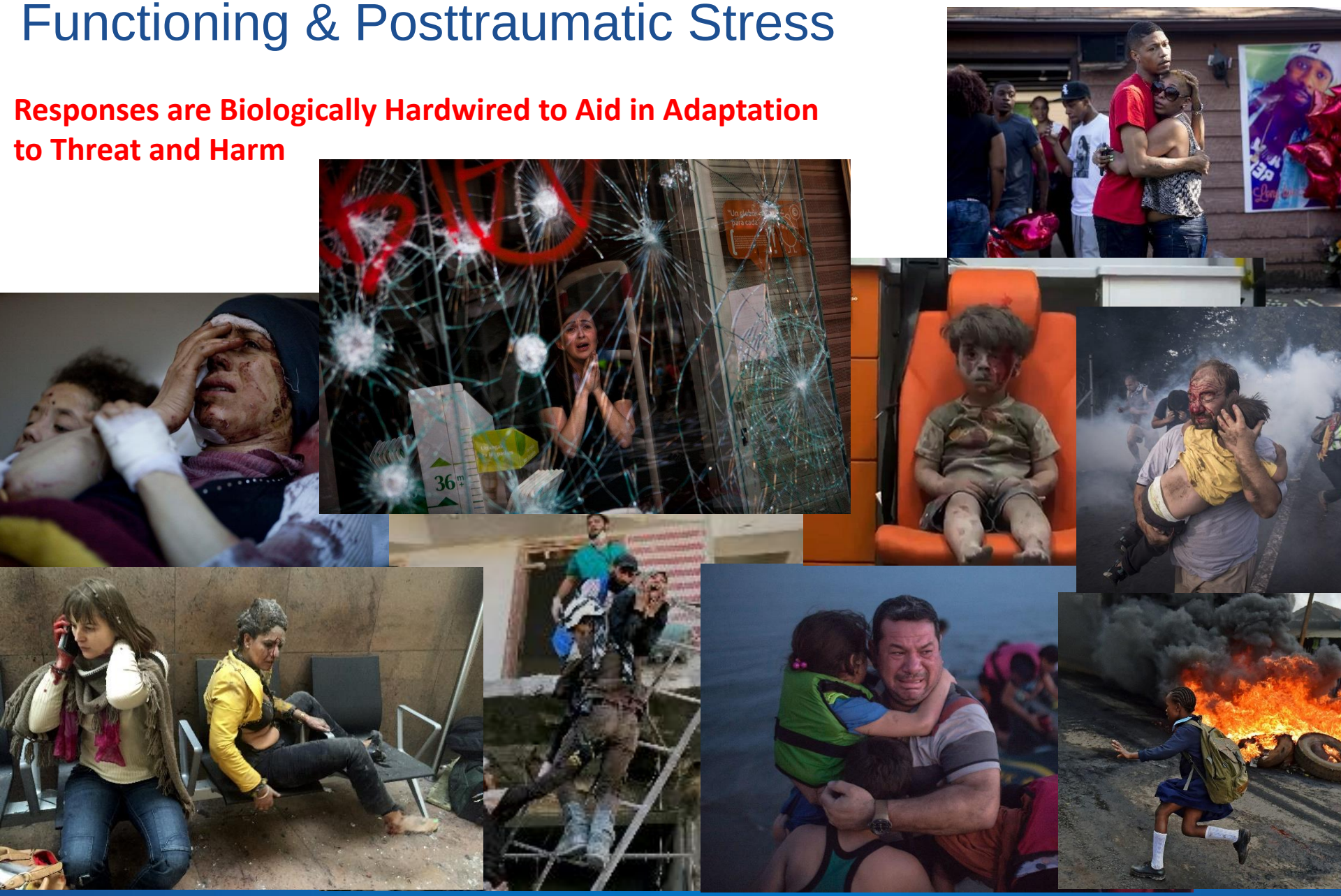
I only receive salary from Columbia University.

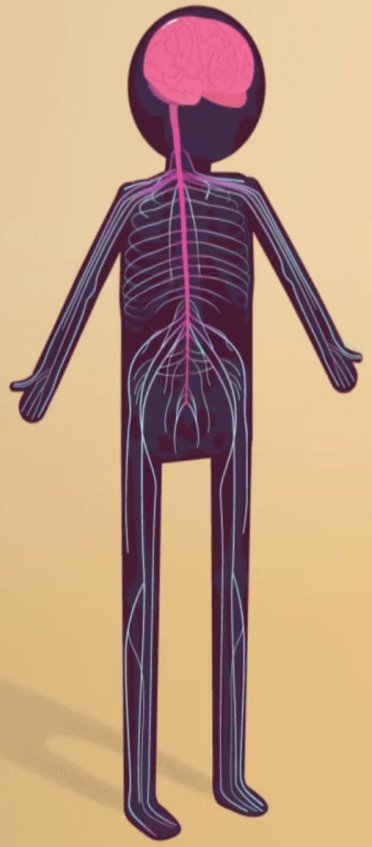
About 70% of the population experience a potentially traumatic event at some point in their lives.

Shalev, Liberzon, & Marmar (2017) NEJM

Functioning & Posttraumatic Stress

Responses are Biologically Hardwired to Aid in Adaptation to Threat and Harm





CENTRAL NERVOUS SYSTEM
CNS

PERIPHERAL NERVOUS SYSTEM
PNS

SENSORY DIVISION

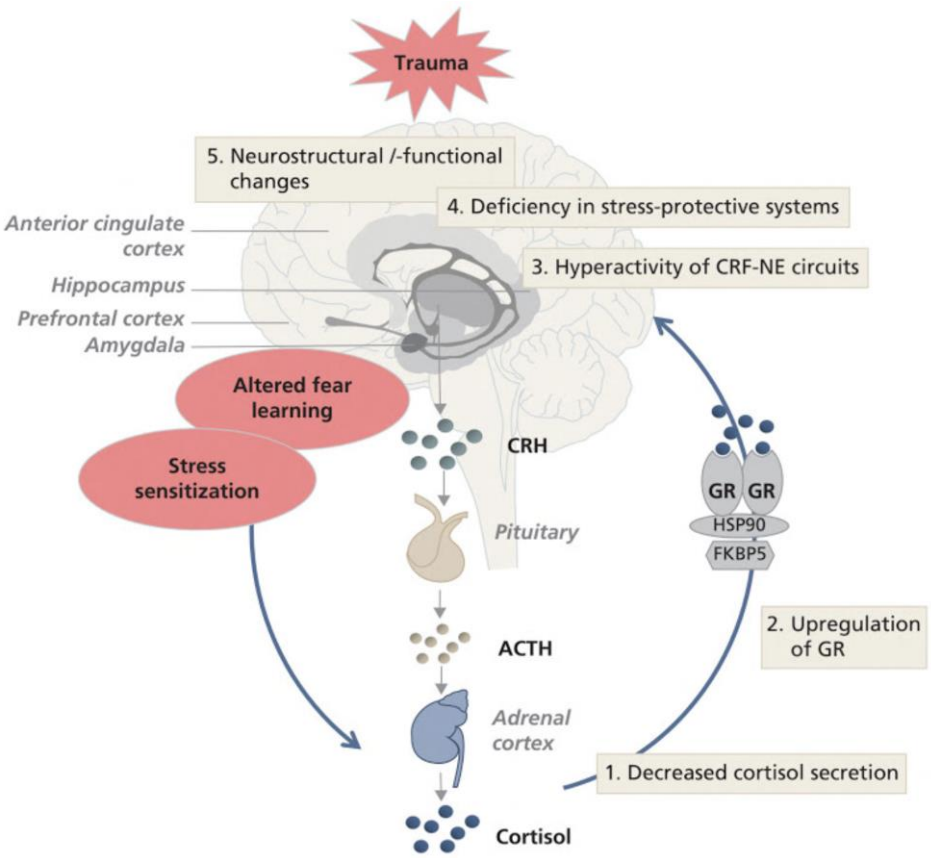
MOTOR DIVISION

SOMATIC NERVOUS SYSTEM

AUTONOMIC NERVOUS SYSTEM

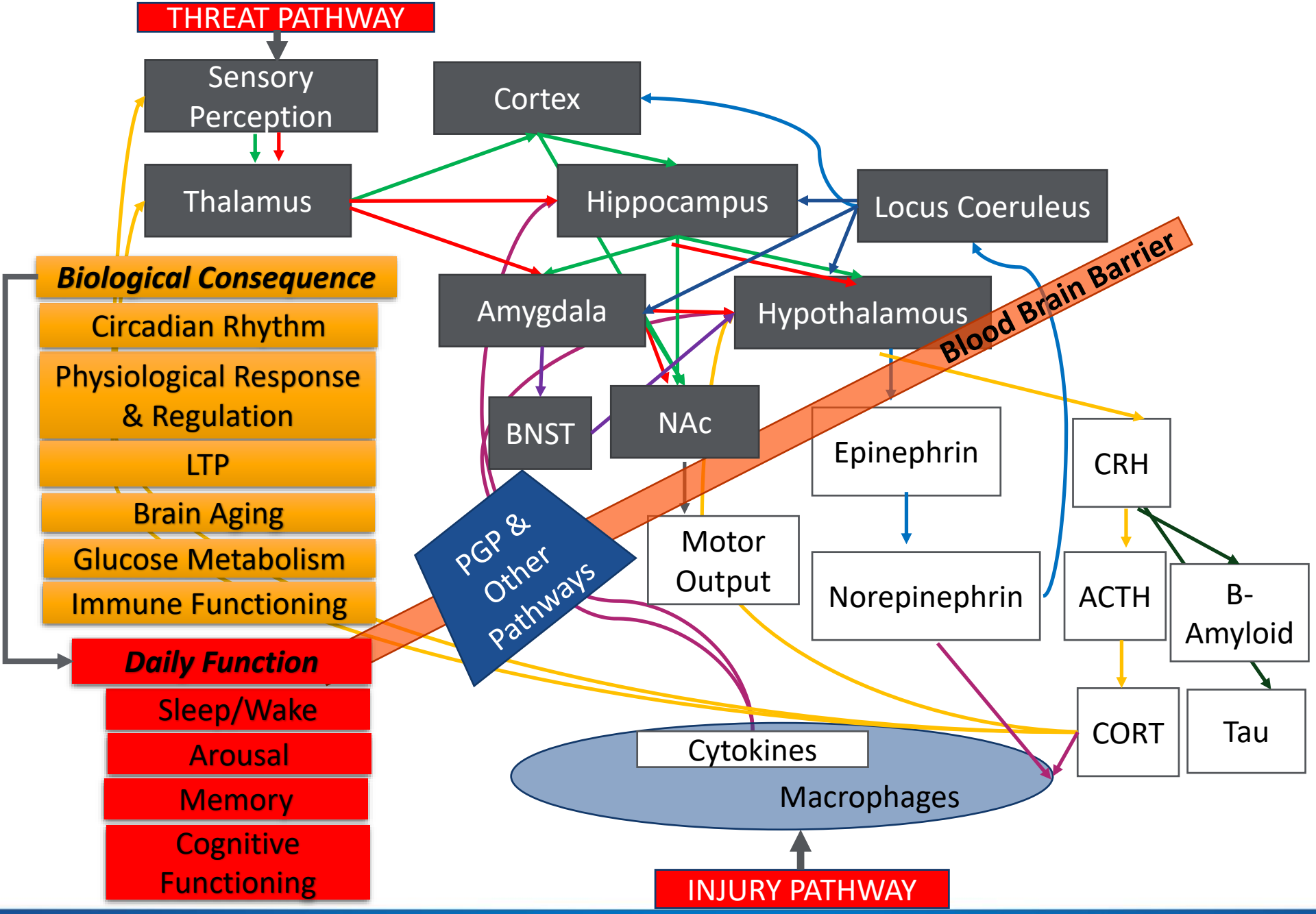
SYMPATHETIC DIVISION

PARASYMPATHETIC DIVISION



- Genetics and epigenetics
- Proteomics
- Transcriptomics
- Metabolomics
- Neuroendocrine functions
- Immunology
- Psychophysiological arousal
- Social environment and biography

Heim, C., **Schultebraucks, K.,** Marmar, C. R., & Nemeroff, C. B. (2018). Neurobiological Pathways Involved in Fear, Stress, and PTSD. *Post-Traumatic Stress Disorder*, 331.


THREAT PATHWAY
Sensory Perception
Cortex
Thalamus
Hippocampus
Locus Coeruleus
Biological Consequence
Circadian Rhythm
Physiological Response & Regulation
LTP
Brain Aging
Glucose Metabolism
Immune Functioning
Amygdala
Hypothalamous
Blood Brain Barrier
BNST
NAc
Epinephrin
CRH
PGP & Other Pathways
Motor Output
Norepinephrin
ACTH
B-Amyloid
Daily Function
Sleep/Wake
Arousal
Memory
Cognitive Functioning
CORT
Tau
Cytokines
Macrophages
INJURY PATHWAY


EMERGENCY


OLD IRONSIDES
STRADLEY

NYU/Bellevue Stress and Resilience Study

- Every year In the US there are ~**30 million** discharges from the emergency room after a **potentially traumatic event**.

- 10-20% develop symptoms of posttraumatic stress after the discharge from emergency room.

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STUDIES IN CROP VARIATION.

II. THE MANURIAL RESPONSE OF DIFFERENT POTATO VARIETIES.

By R. A. FISHER, M.A. and W. A. MACKENZIE, B.Sc.

Rothamsted Experimental Station, Harpenden.

(With Two Charts.)

1. Introductory.

It is not infrequently assumed that varieties of cultivated plants differ not only in their suitability to different climatic and soil conditions, but in their response to different manures. Since the experimental error of field experiments is often underestimated, this supposition affords a means of explaining discrepancies between the results of manurial ex-

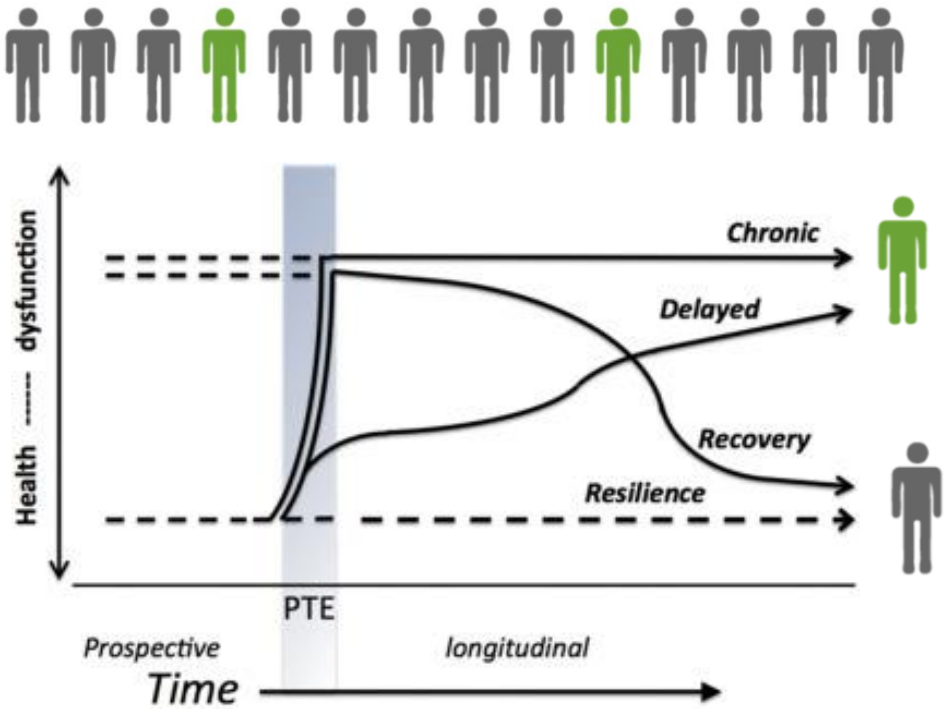
H_0: $\mu_1 = \mu_2 = \mu_3$

H_a: Mean values are different

P(Observation | H_0) with α =.05

Interestingly most of those risk factors we discussed earlier are routinely collected in the ED using electronic medical records

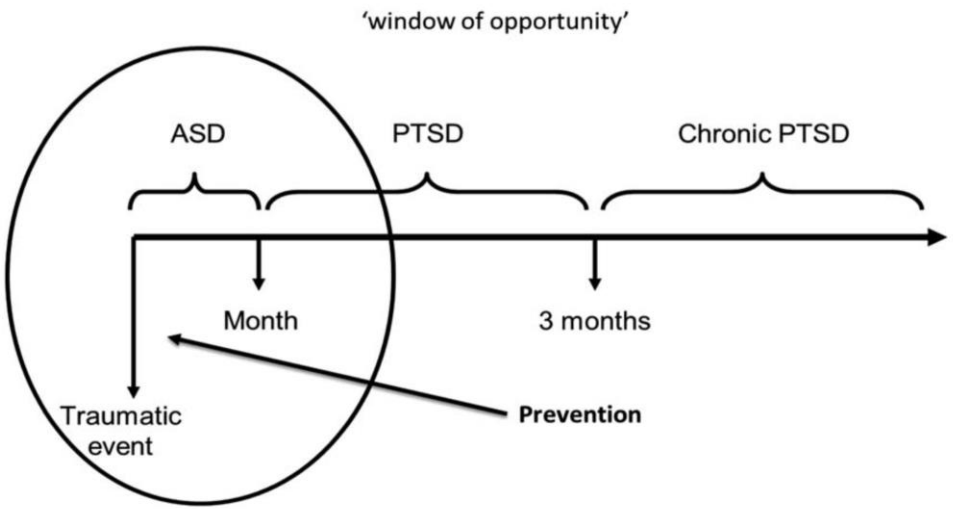
Currently there are no accurate methods to predict psychiatric risk in the immediate aftermath after a traumatic event.



Galatzer-Levy, I. R., Huang, S. H., & Bonanno, G. A. (2018). Trajectories of resilience and dysfunction following potential trauma: A review and statistical evaluation. *Clinical psychology review*.

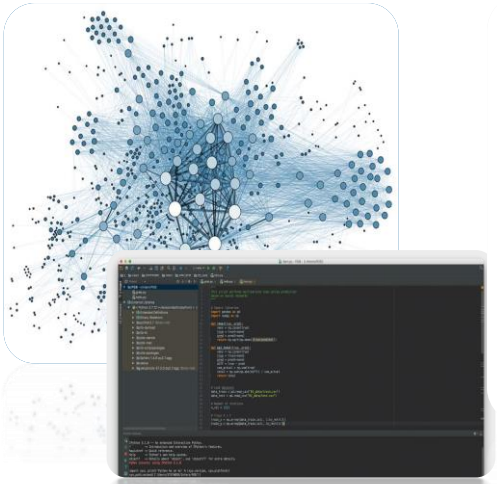
Development and implementation of a validated prediction model for PTSD risk could:

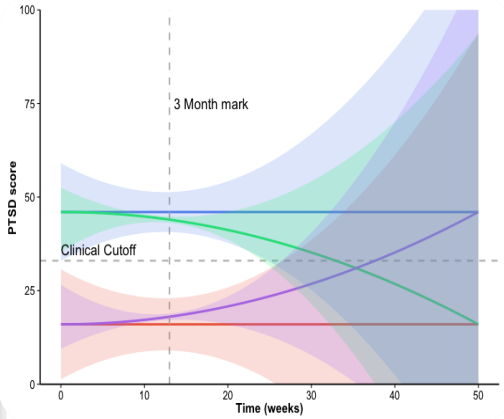
- Improve the likelihood of success of early interventions for posttraumatic stress
- Avoid potential overtreatment and unfavorable effects from blanket interventions.



Carmi, L., Fostick, L., Burshtein, S., Cwikel-Hamzany, S., & Zohar, J. (2016). PTSD treatment in light of DSM-5 and the "golden hours" concept. *CNS spectrums*, *21*(4), 279-282.

Previous studies have shown that early interventions are more likely to succeed if targeted at those who are at higher risk of PTSD.

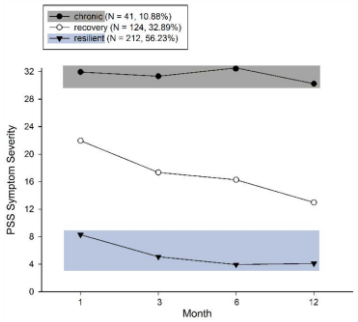




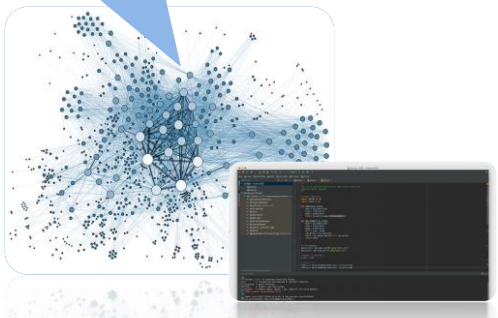
- Potential early interventions may require identification of patients at risk and application directly within the ED:
  - Clinically useful to be able to predict PTSD risk as early as possible
  - Using available ED data
- Develop a prediction model that is:
  - Accurate, but also scalable and cost-effective
  - Low additional burden to routine ED procedures.

1. Data collection of potential predictor variables in two Level 1 trauma centers:
1) Grady Memorial Hospital, Atlanta
2) Bellevue Hospital, NYC

2.

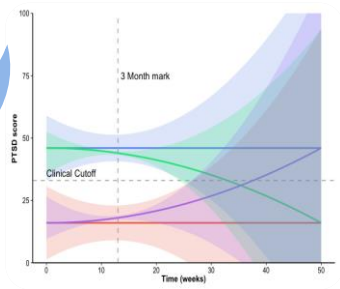


Model development sample: 12 months follow-up

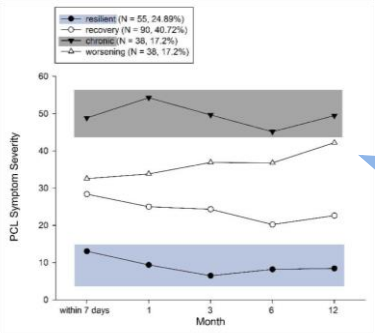


3. Deep Super Learner

Risk score for longitudinal symptom development



4.

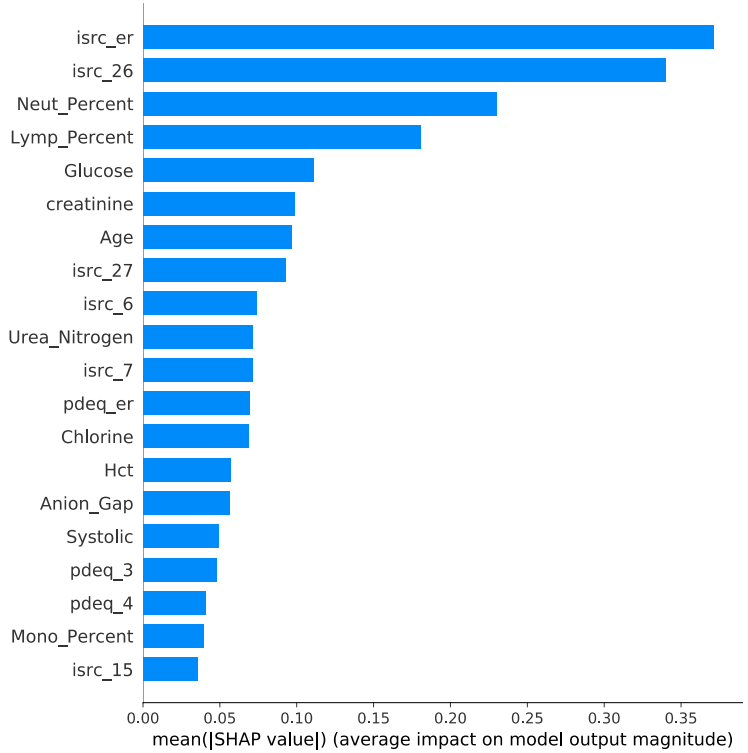


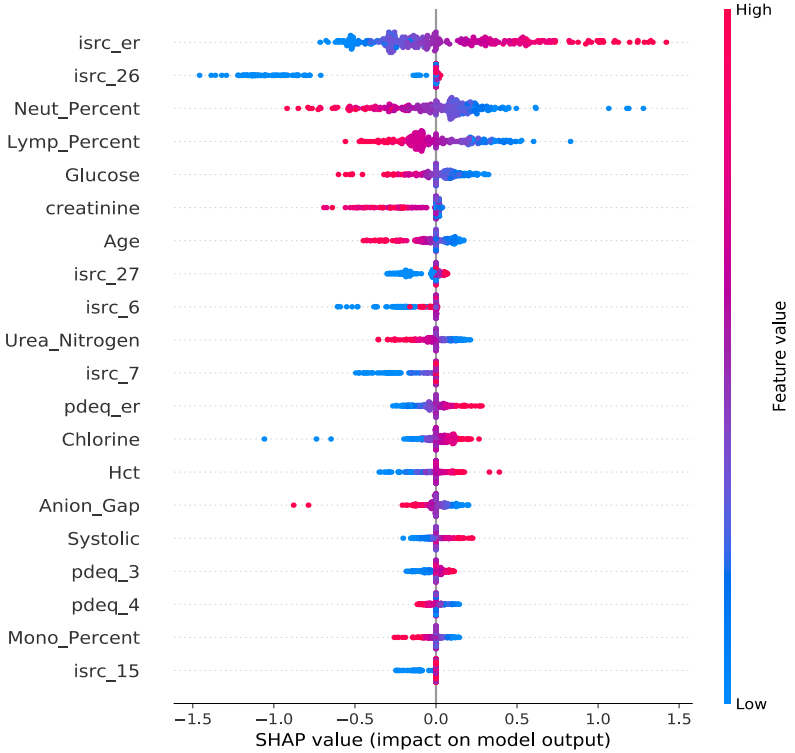
Independent external validation sample: 12 months follow-up

Results

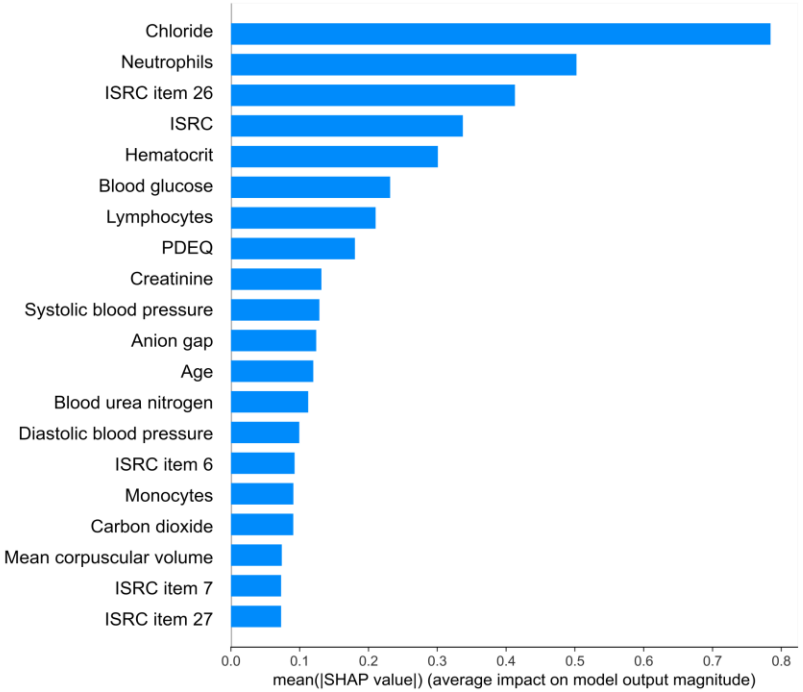
	Precision	Recall	F1-score	ROC-AUC	Positive events/Total events
Model development	.86	.84	.84	.84	27/164
Internal validation	.83	.64	.69	.7	14/89
External validation	**.86**	**.85**	**.85**	**.83**	**38/93**

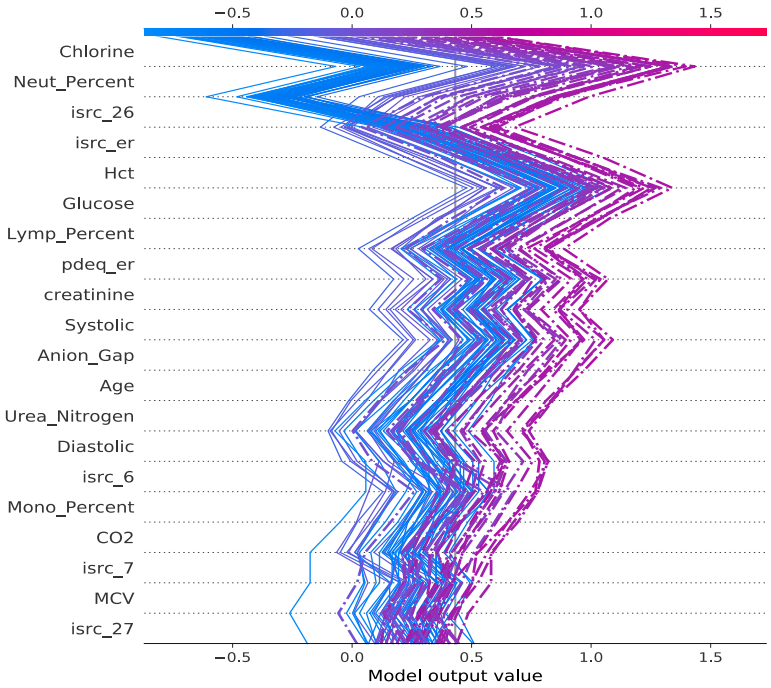
Variable importance using SHAP (SHapley Additive exPlanations) – Model development sample





Variable importance using SHAP (SHapley Additive exPlanations) – External validation set





Most important features

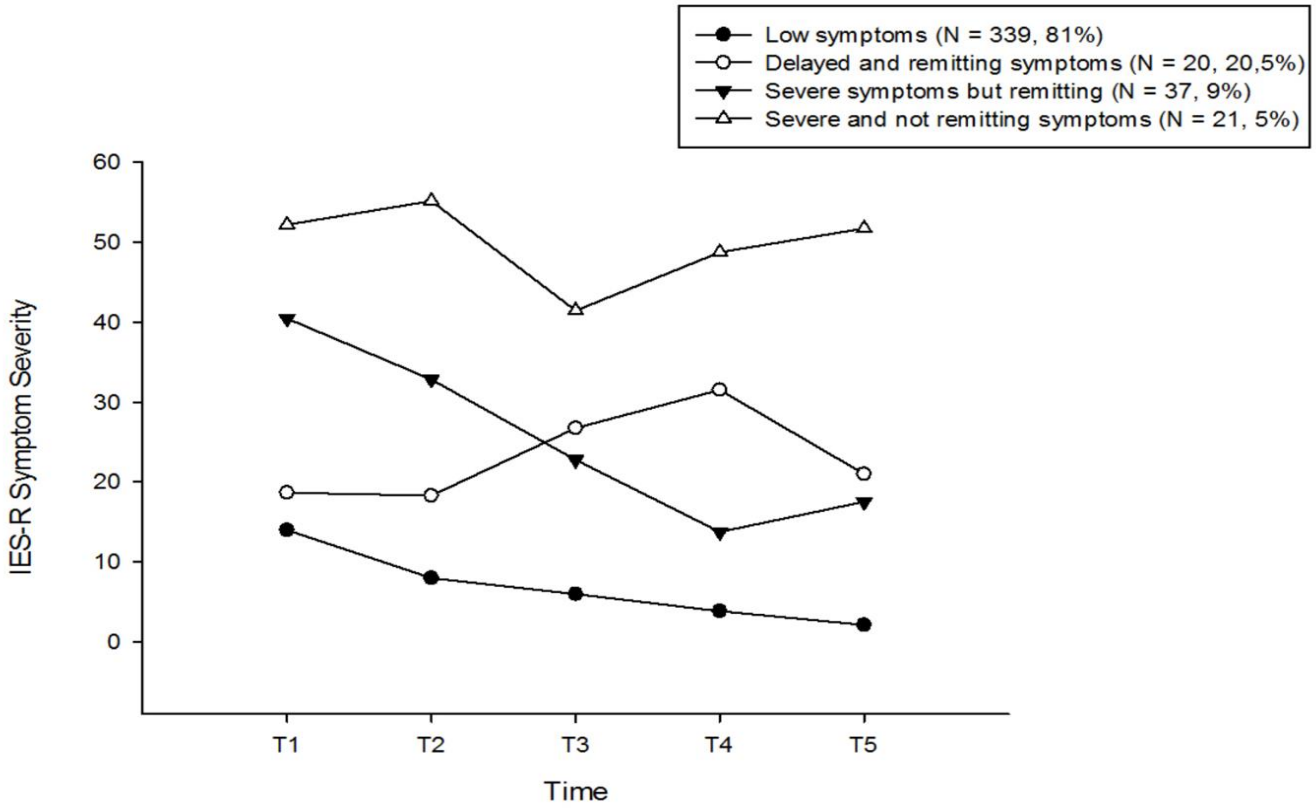
- Peripheral immune markers: neutrophils, lymphocyte, monocytes
- Acute stress disorder symptoms and peritraumatic dissociation
- Physiological marker of stress response
- Metabolic markers: blood glucose, carbon dioxide, chloride, anion gap

➢ Carbon dioxide has been shown to be associated with acute panicogenic and anxiogenic effects and panic attacks

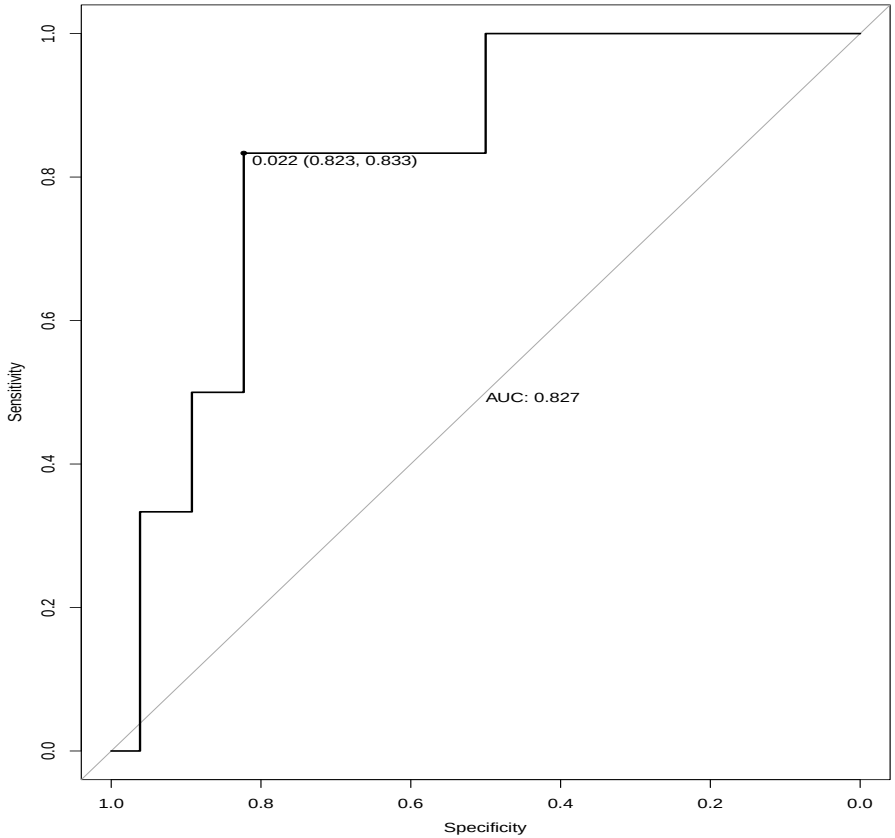
➢ Chloride and anion gap are critical measures of the body's pH (acid-base) status, and as with CO2, are associated with acidosis, which is associated with panic attack and fear in numerous studies. Whether or not chloride levels are mediated by potential blood and/or NaCl infusion warrants further investigation.

➢ Recent work from our group has identified nausea as a predictor variable for later PTSD development, which wasn't included in these analyses, however nausea is also associated with altered chloride, anion gap, and CO2 status

Trauma Tips Study

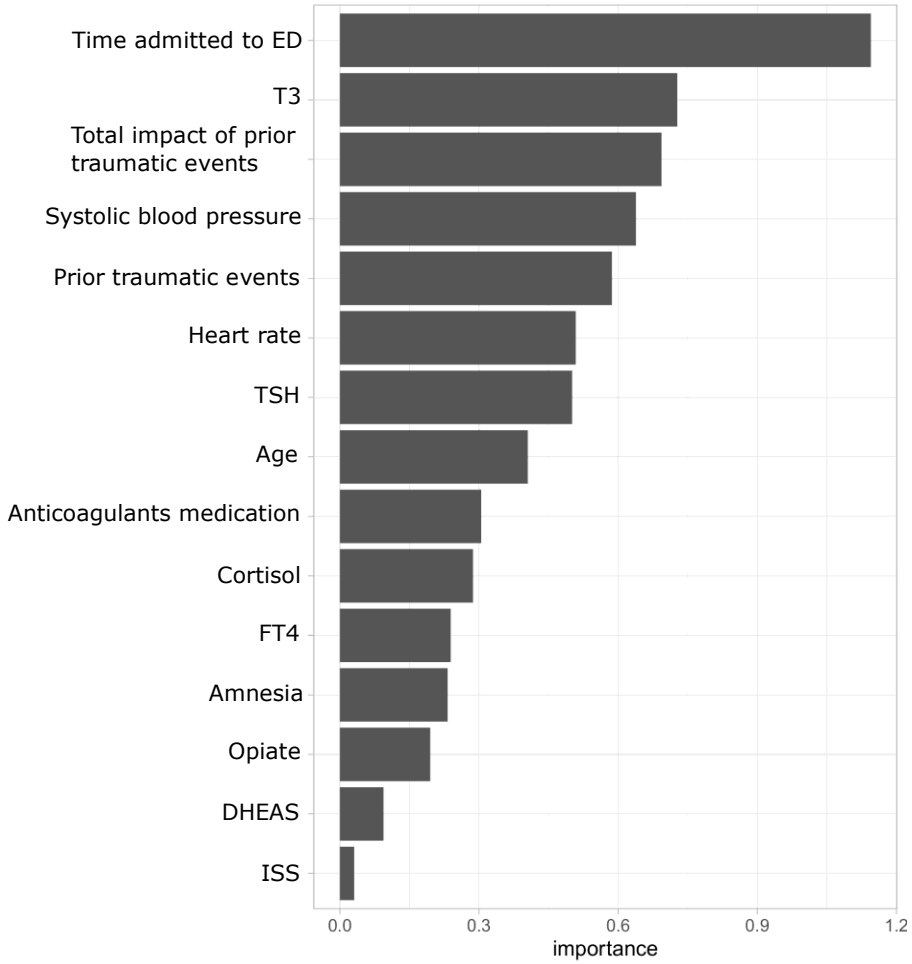


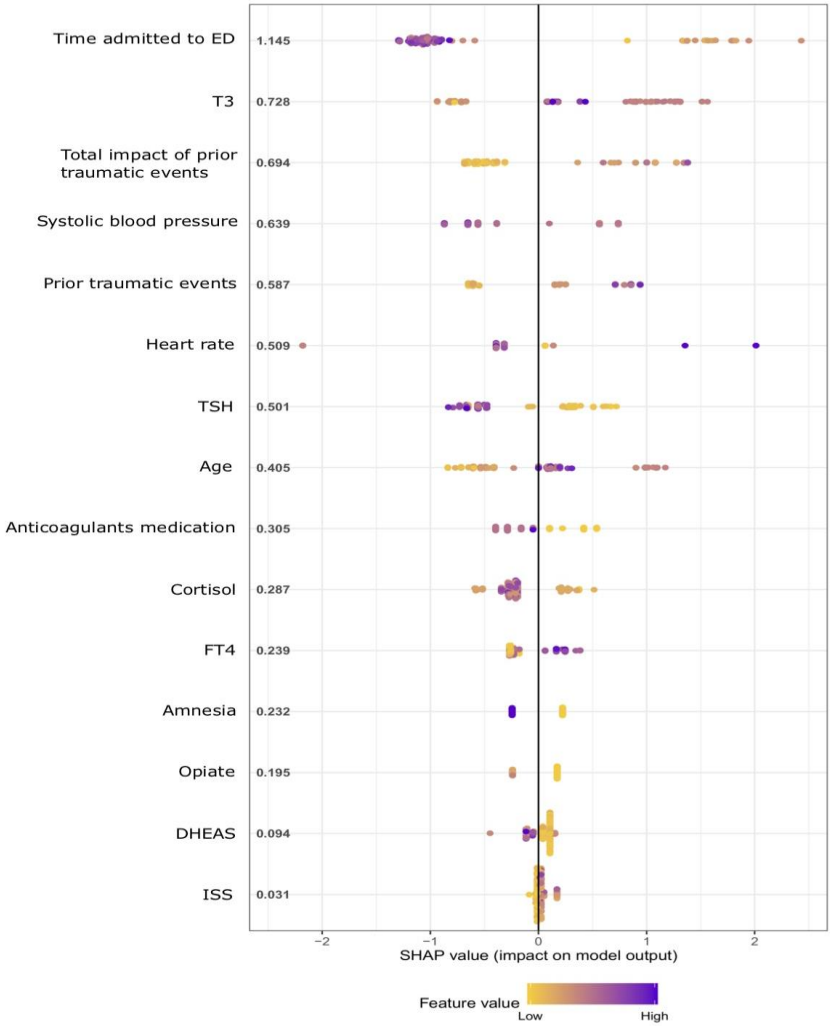
Schultebraucks, K., Sijbrandij, M., Galatzer-Levy, I., Mouthaan, J., Olff, M., van Zuiden, M. Forecasting Posttraumatic Stress Disorder Symptom Course in Emergency Medical Settings using Biomedical Data: a machine learning multicenter cohort study.

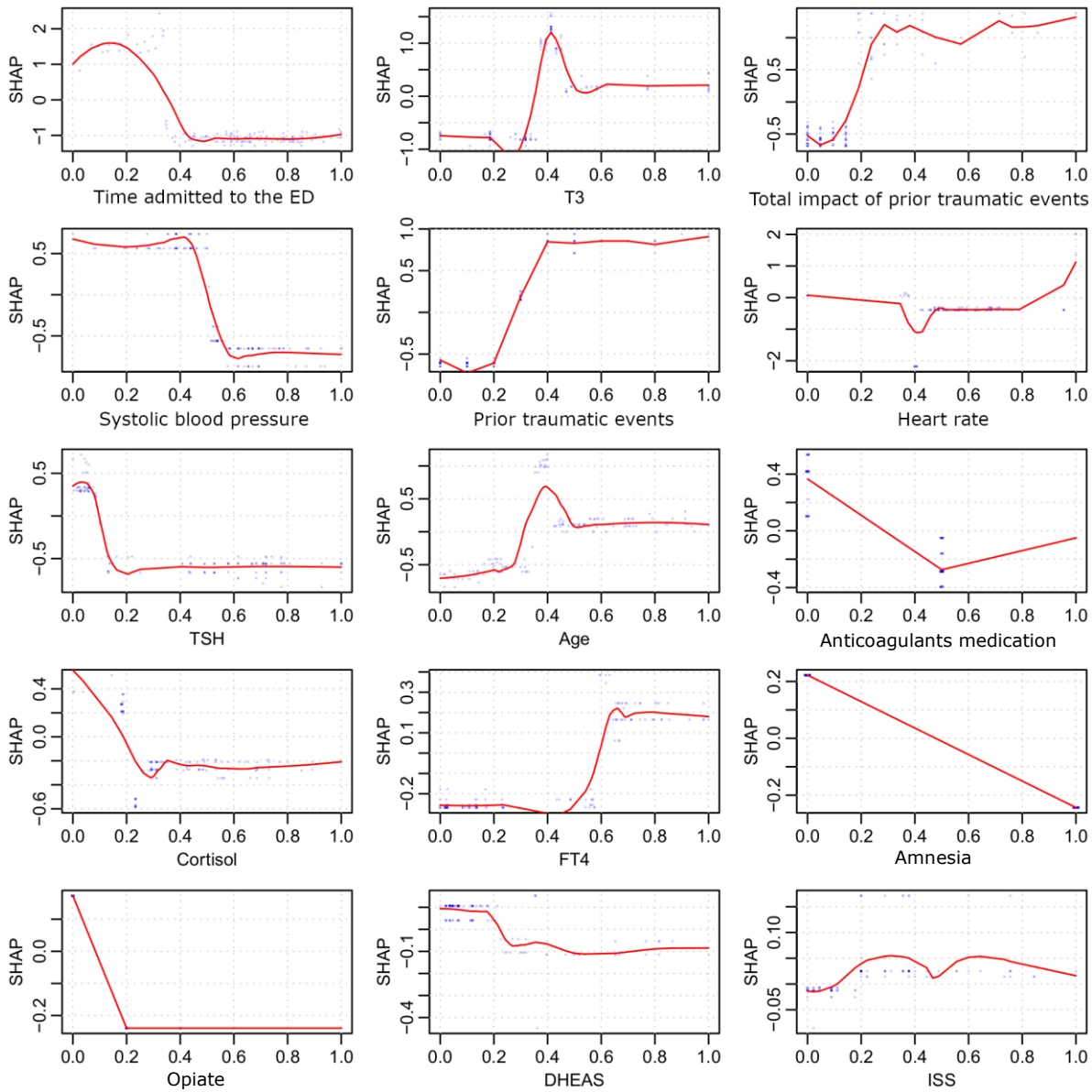


prediction of longitudinal PTSD symptom trajectories: multiclass **AUC = 0.89**

Prediction of clinician-rated PTSD (CAPS) at 12 months: **AUC = 0.83**


Time admitted to ED
T3
Total impact of prior traumatic events
Systolic blood pressure
Prior traumatic events
Heart rate
TSH
Age
Anticoagulants medication
Cortisol
FT4
Amnesia
Opiate
DHEAS
ISS
0.0
0.3
0.6
0.9
1.2
importance


Time admitted to ED 1.145
T3 0.728
Total impact of prior traumatic events 0.694
Systolic blood pressure 0.639
Prior traumatic events 0.587
Heart rate 0.509
TSH 0.501
Age 0.405
Anticoagulants medication 0.305
Cortisol 0.287
FT4 0.239
Amnesia 0.232
Opiate 0.195
DHEAS 0.094
ISS 0.031
−2
−1
0
1
2
SHAP value (impact on model output)
Feature value
Low
High


SHAP
Time admitted to the ED
T3
Total impact of prior traumatic events
Systolic blood pressure
Prior traumatic events
Heart rate
TSH
Age
Anticoagulants medication
Cortisol
FT4
Amnesia
Opiate
DHEAS
ISS

Summary

- Data collected in emergency rooms contain highly predictive information for PTSD.
- The algorithm can be implemented in medical emergency systems.
- The algorithm can be continuously updated and improved, using data from every patient who is discharged from the emergency room.
- Targeted prevention strategies can be implemented earlier, using the algorithm to inform clinical decision-making.

The clinical phenotype of PTSD is heterogeneous

How many different possibilities exist to fulfill the diagnosis of PTSD according to DSM-5?

$$\Sigma\binom{n}{k} \text{ mit } \binom{n}{k} = n!/\,k!(n-k)!$$

$$\Pi_{n=i}\left[\Sigma\binom{n}{k}\right]$$ **31 x 3 x 57 x 120** = ?

aps ASSOCIATION FOR PSYCHOLOGICAL SCIENCE

636,120 Ways to Have Posttraumatic Stress Disorder

Perspectives on Psychological Science
8(6) 651–662

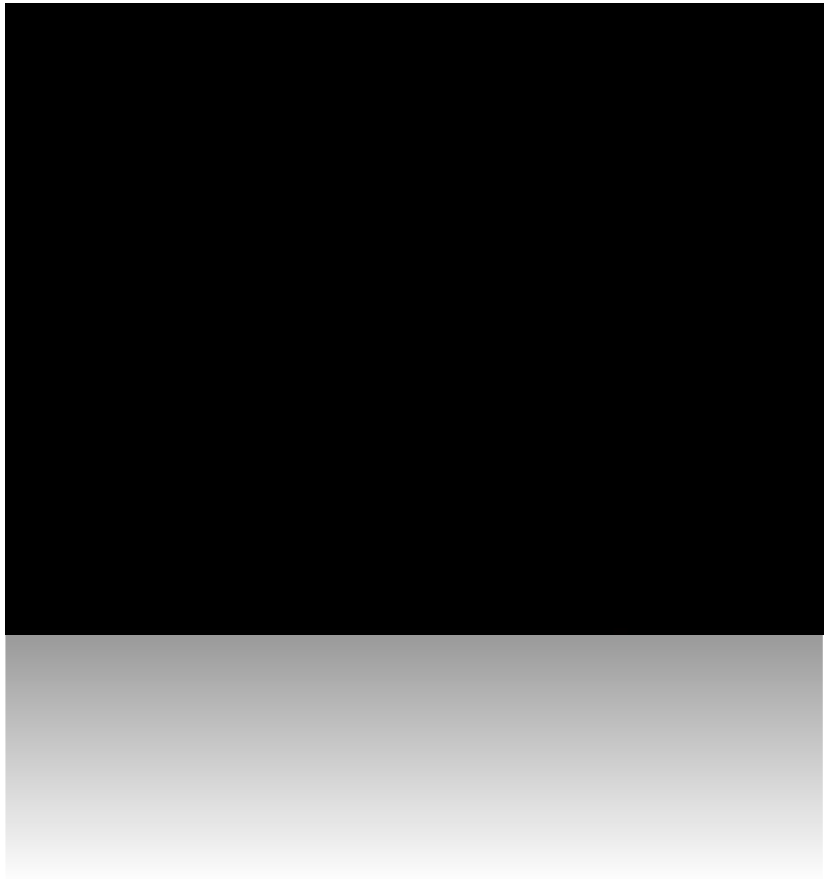
DOI: 10.1177/1745691613504115
pps.sagepub.com
SAGE

Isaac R. Galatzer-Levy[1] and Richard A. Bryant[2]
[1]New York University School of Medicine; and [2]University of New South Wales, Kensington, New South Wales, Australia

How can we get other measures of clinical functioning?

- more reliable
- more efficient
- more patient-relevant
- more comprehensive
- much easier available

Behavior is indicative of clinical functioning



Individual with Major Depressive Disorder

- Lowered gaze
- Lack of eye contact
- Facial expressivity
- Slow movement
- Verbal valence
- Speech content

Behavior allows interviewer to assess clinical state

$$\underbrace{Y}_{\text{Clinical Phenotype}} = \underbrace{\beta_0 + \beta_1 X1 + \beta_2 X2 .. + \beta_n Xn}_{\text{Genes, Circuits, Proteins}}$$

What is a phenotype?

the set of observable characteristics of an individual resulting from the interaction of its genotype with the environment

A clinical description

Phenotype is what you see - the visible or observable expression of the results of genes, combined with the environmental influence on an organism's appearance or behavior. For example:

It is the expression of gene information which is observable with the senses (like the sound of a bird's chirping or the color of a cat's hair)

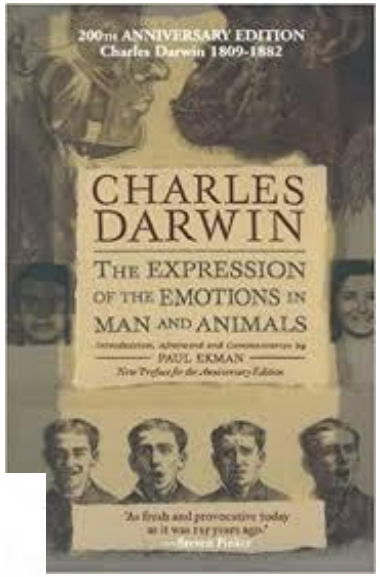
Behavioral & Physiological Phenotypes

Biologically conserved

Ecologically valid

Transdiagnostic

Quantifiable

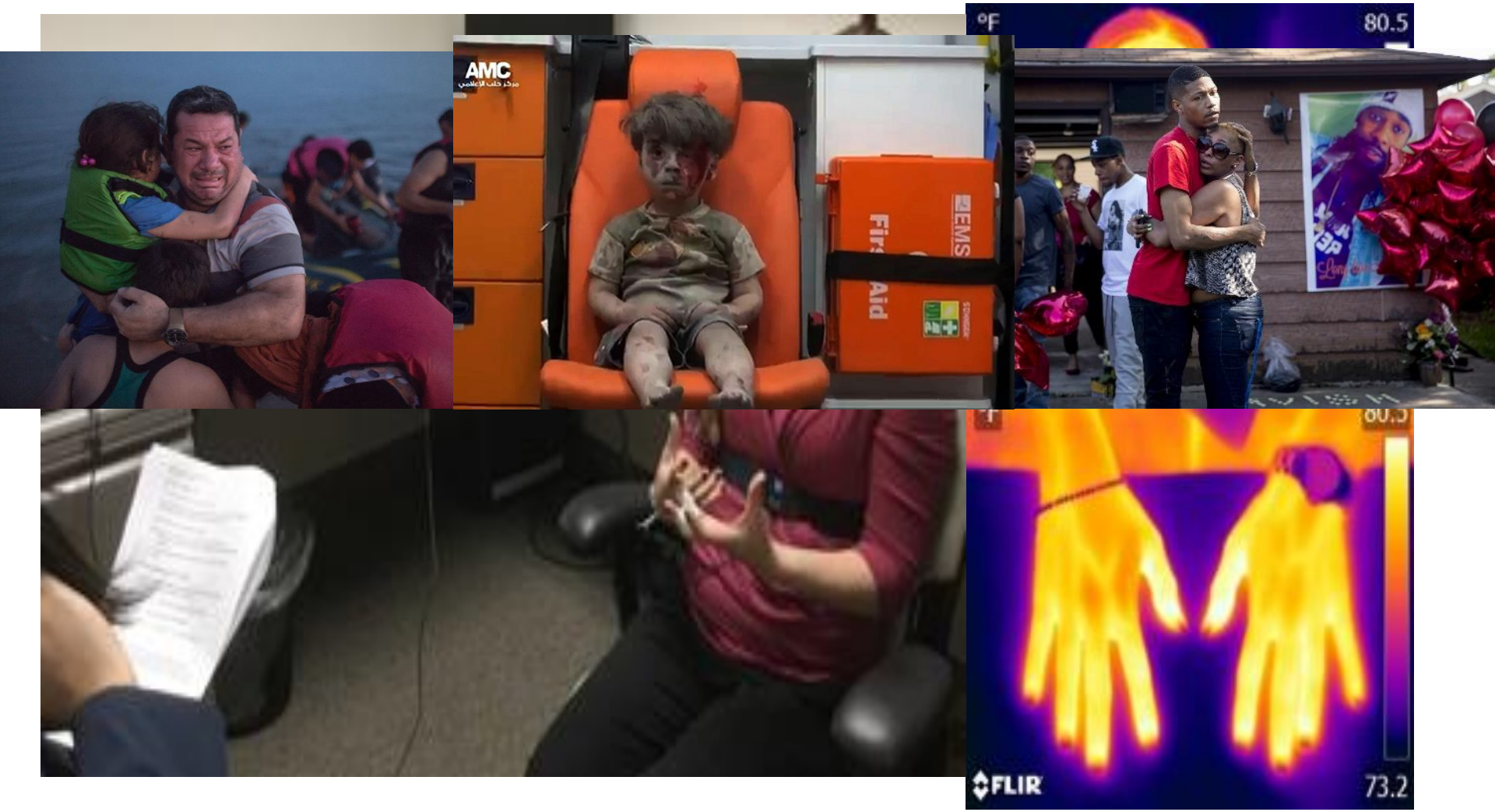


Digital Phenotyping

Insel, T. R. "Bending the Curve for Mental Health: Technology for a Public Health Approach." (2019): S168-S170.

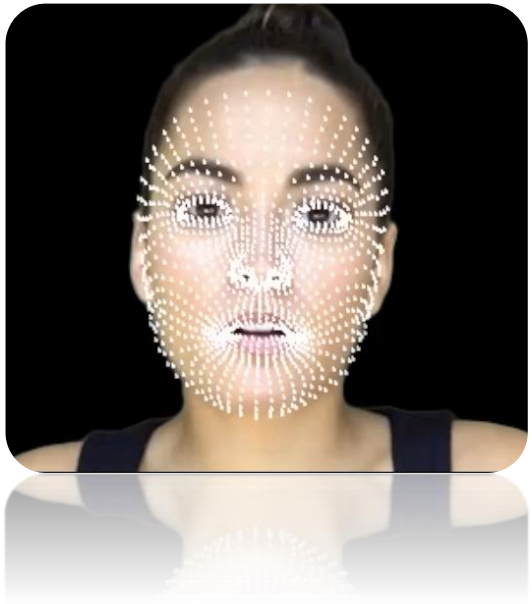
Insel, T. R. (2019). Deep Medicine: How Artificial Intelligence Can Make Healthcare Human Again. *Nature*, *567*(7747), 171-173.

Digital Phenotyping



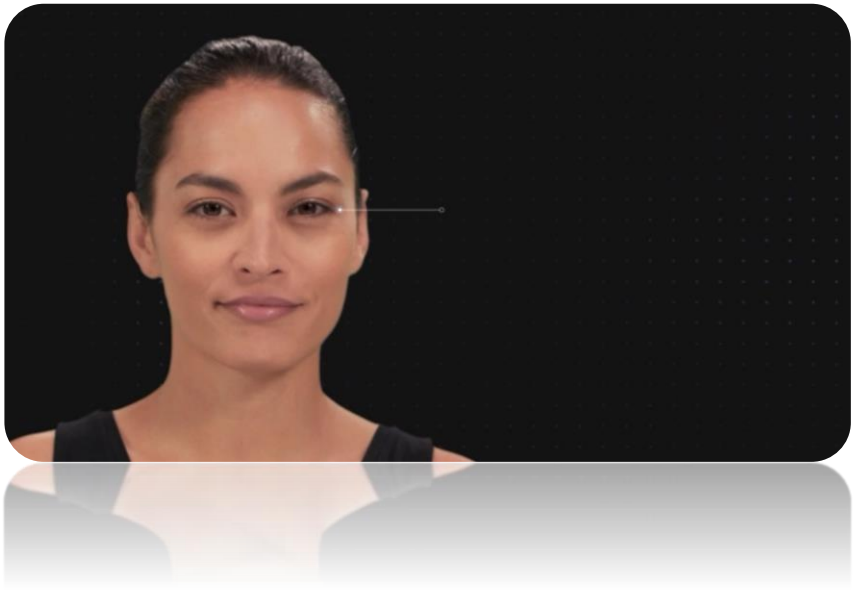
Physiologically Enhanced Qualitative Interview

Facial features

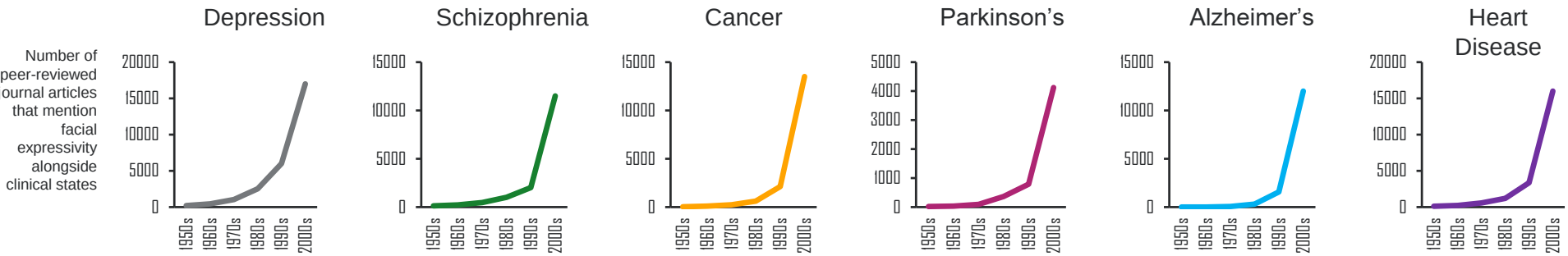


Emotional expressivity

- Happiness
- Sadness
- Anger
- Fear
- Contempt
- Disgust
- Surprise
- Composite

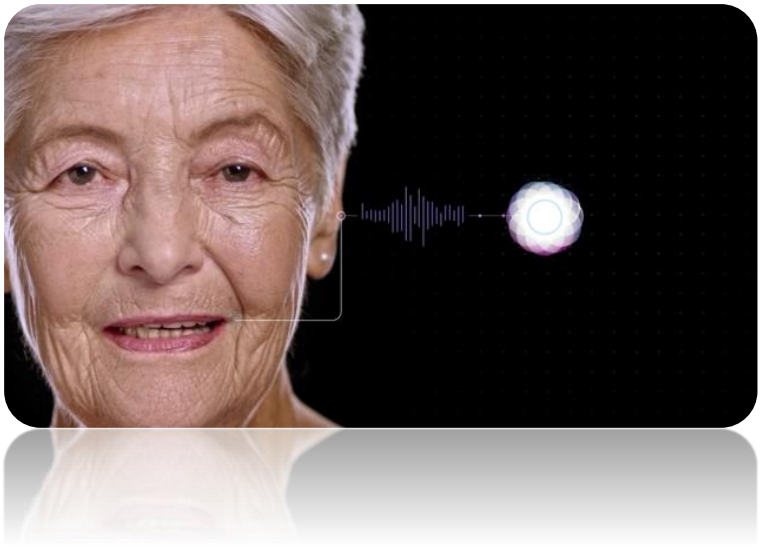


Facial expressivity has been shown to be relevant in distinguishing clinical populations



AiCure CDx

Voice features



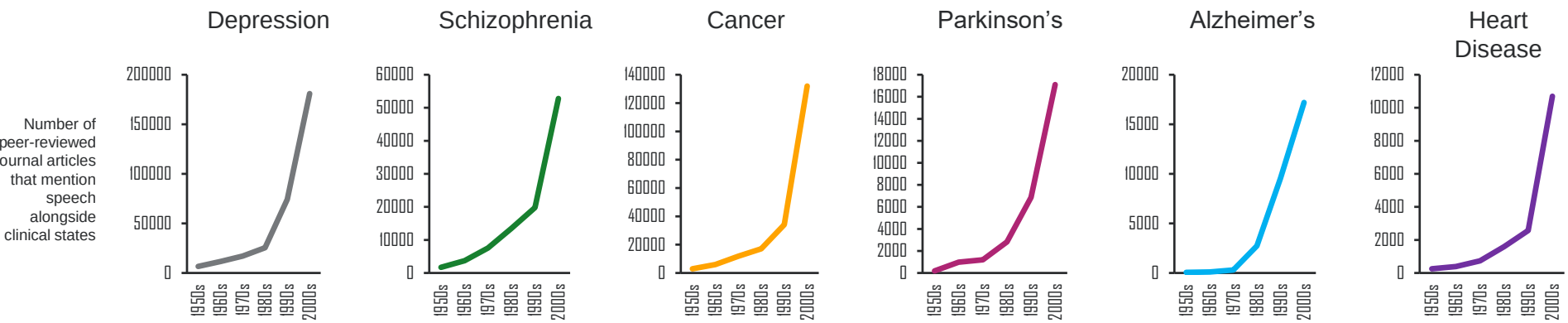
Verbal features

- Expressivity
- Pitch
- Harmonic noise ratio
- Guttural noise excitation
- Normalized amplitude quotient
- Formant variability

Speech features

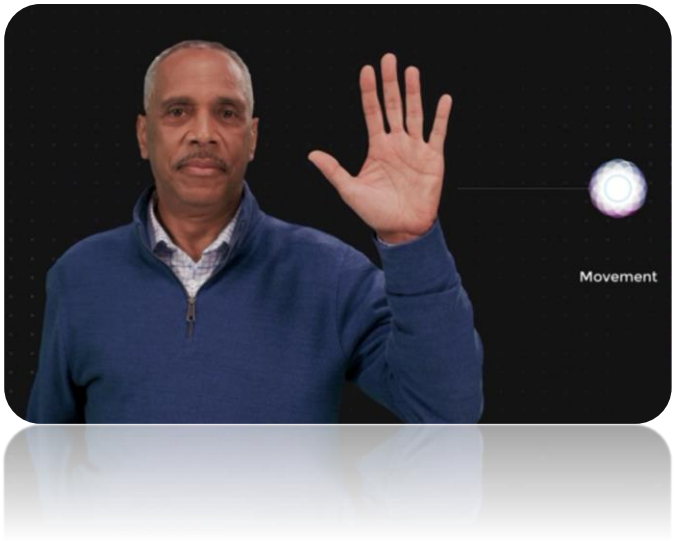
- Content valence
- Speech intent
- Speech rate
- Speech repetition

Verbal and speech features have been shown to be relevant in distinguishing clinical populations



AiCure CDx

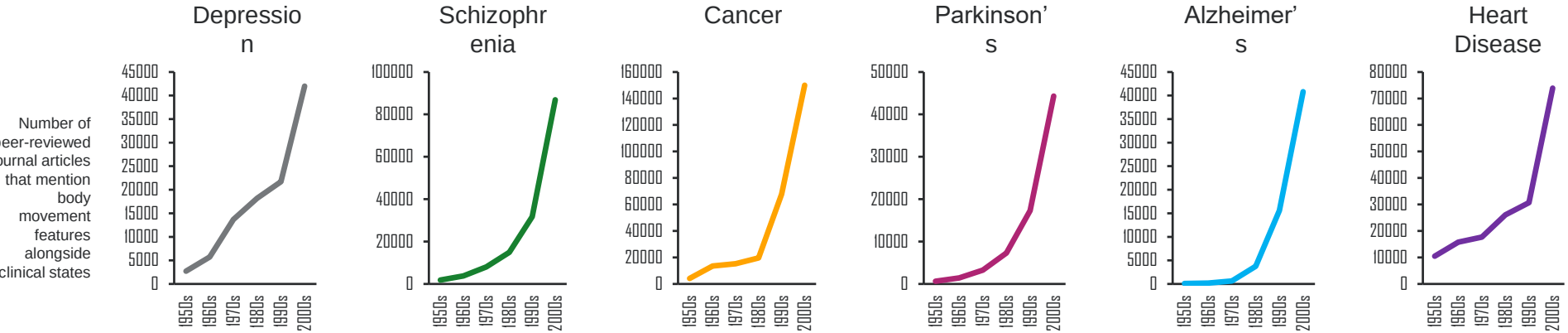
Movement features



Measuring movement

- General body movement
- Tremor analysis using
  - Body movement
  - Movement of facial musculature
  - Variations in speech

Scientific literature studying movement extends beyond movement disorders

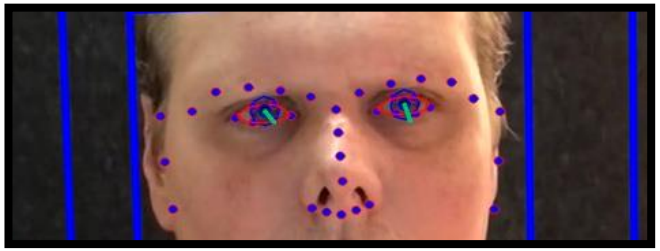


AiCure CDx

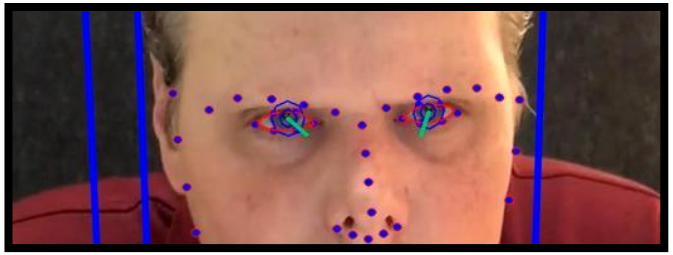
Behavioral indicators of health

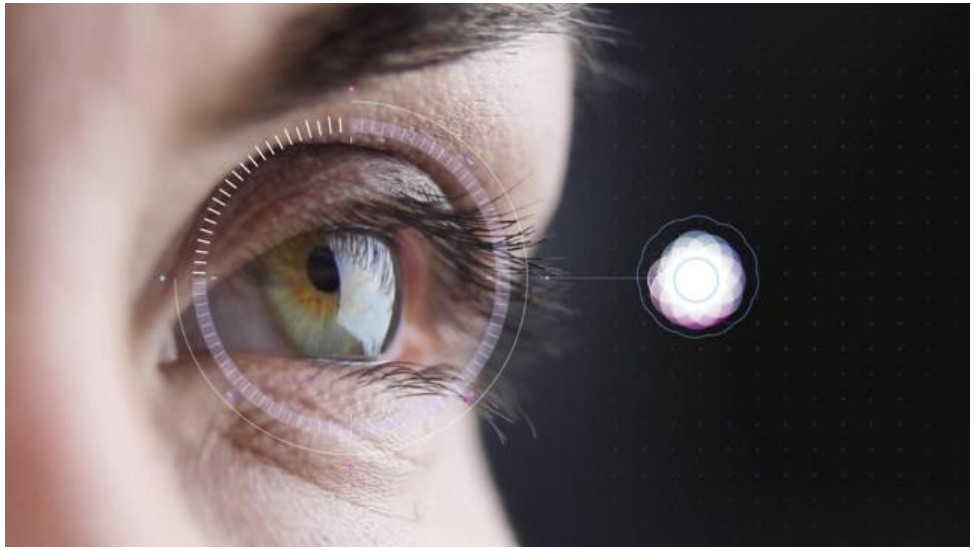
Eye-tracking

Gaze during countdown

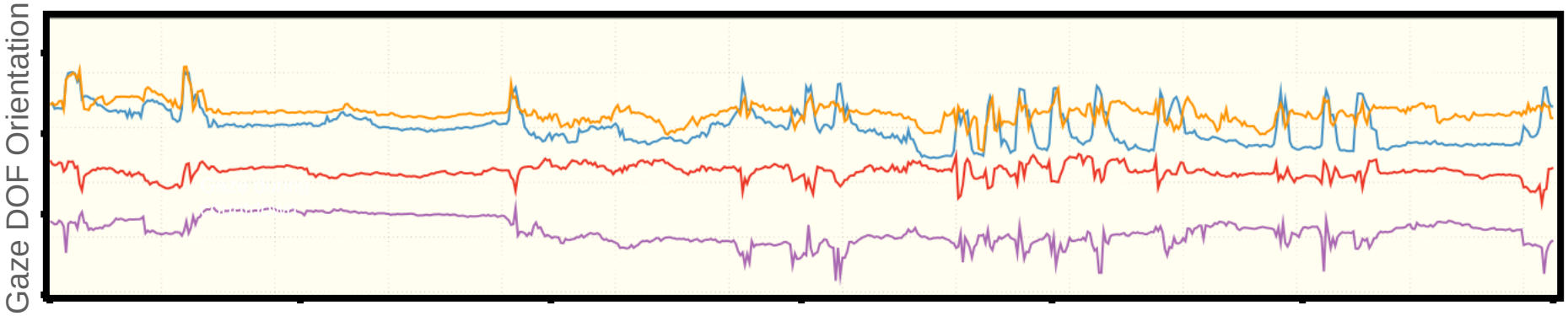


Gaze when image is revealed

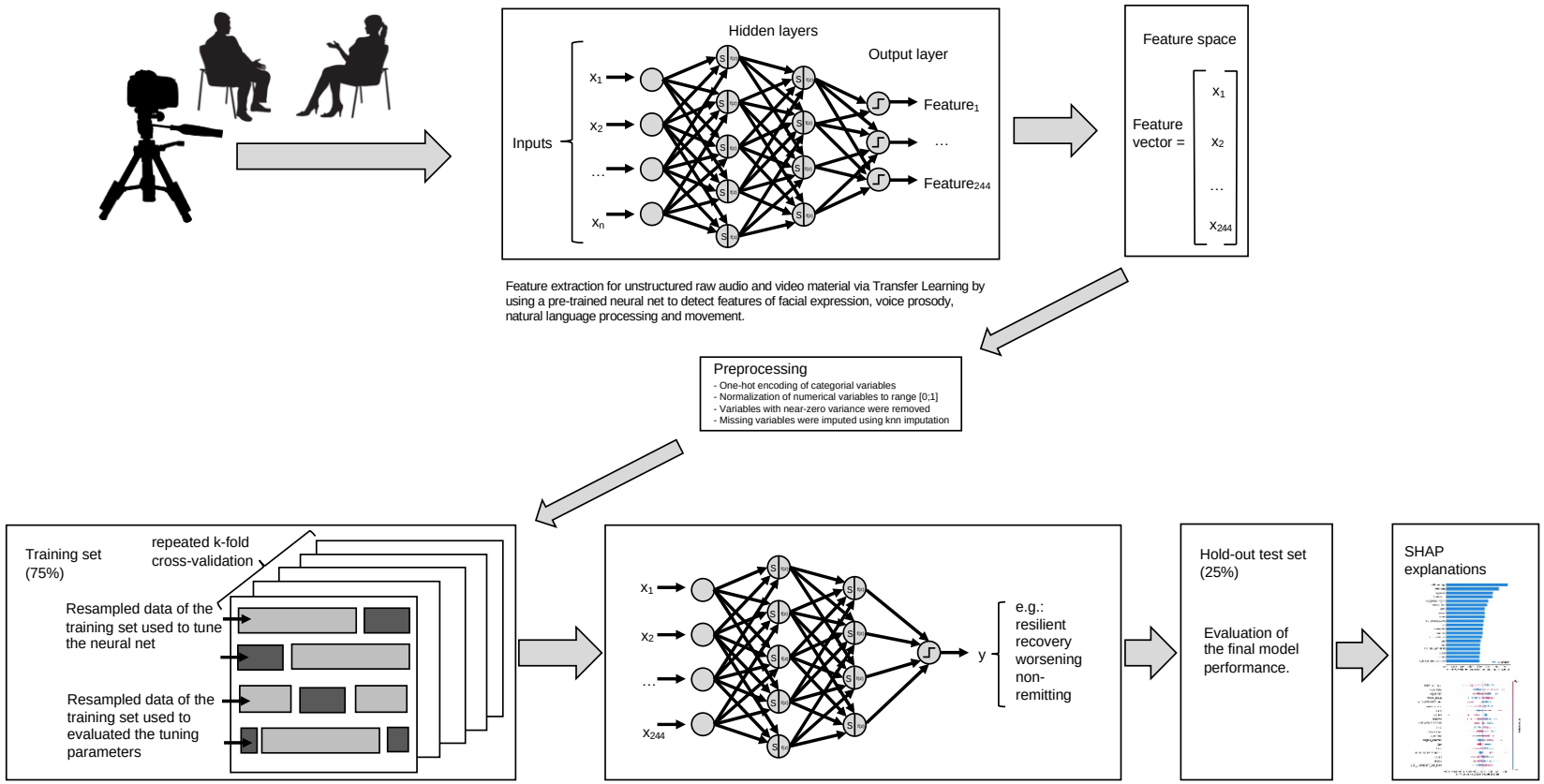




Gaze Tracking



Predictive model development



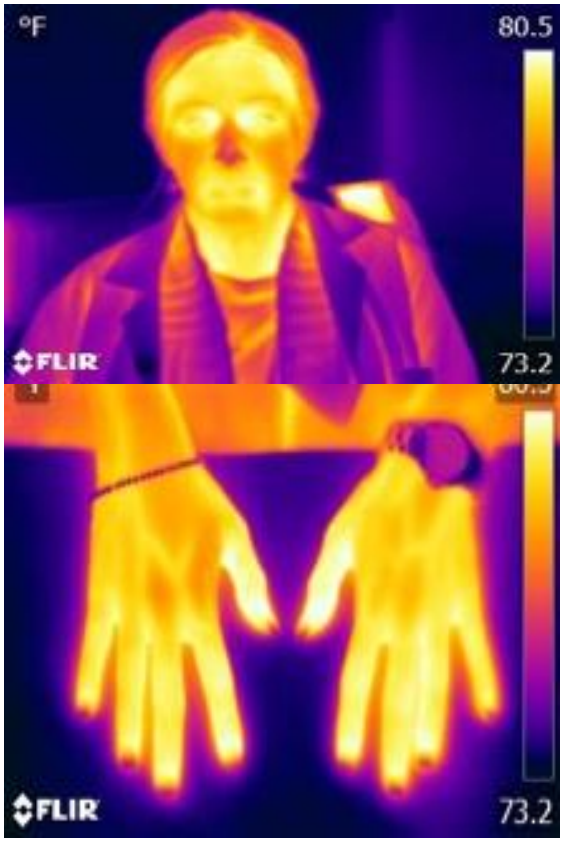
4 Min Each

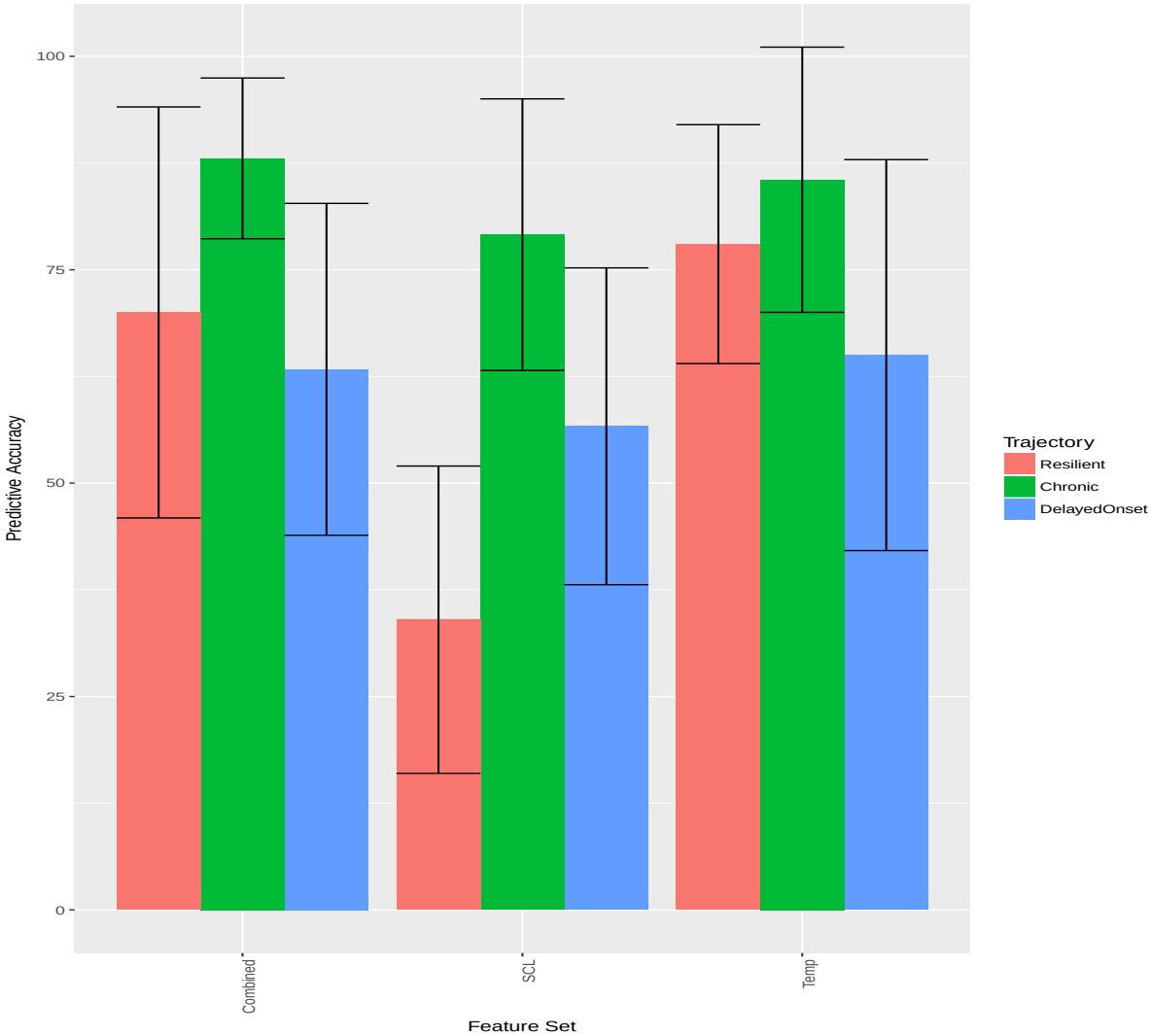
Tell me about what brought you to the hospital

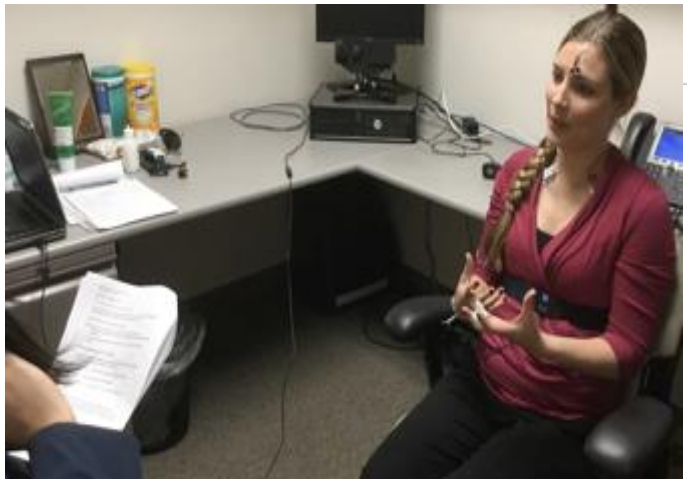
Tell me about your experience in the hospital

Tell me about the past month

NN Classification Results based on Interview







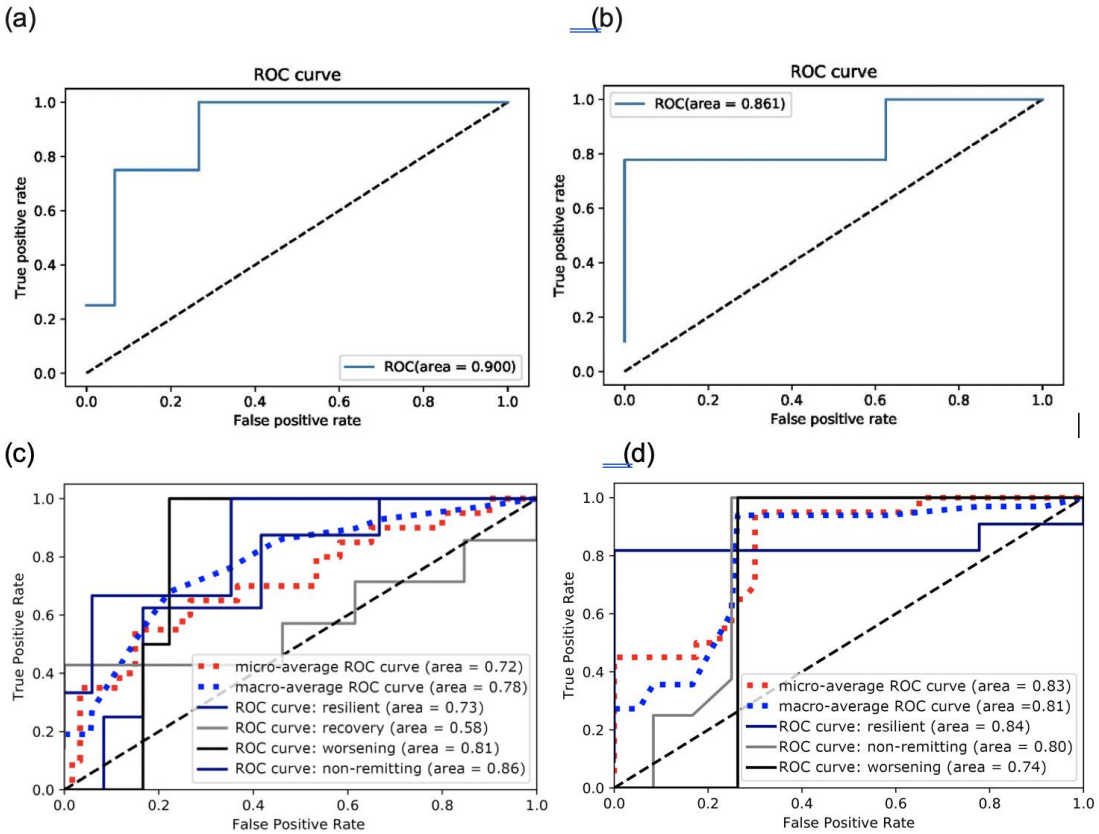
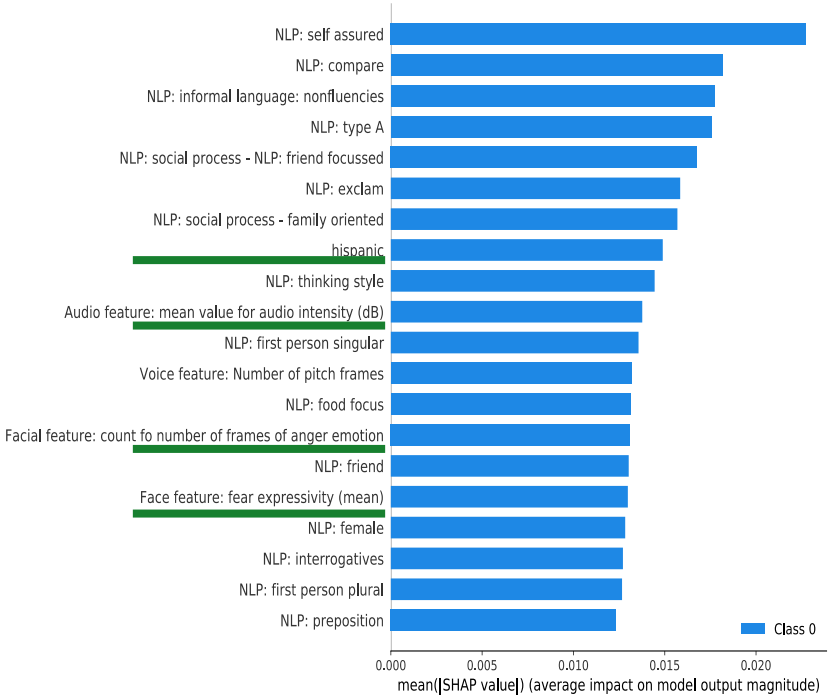
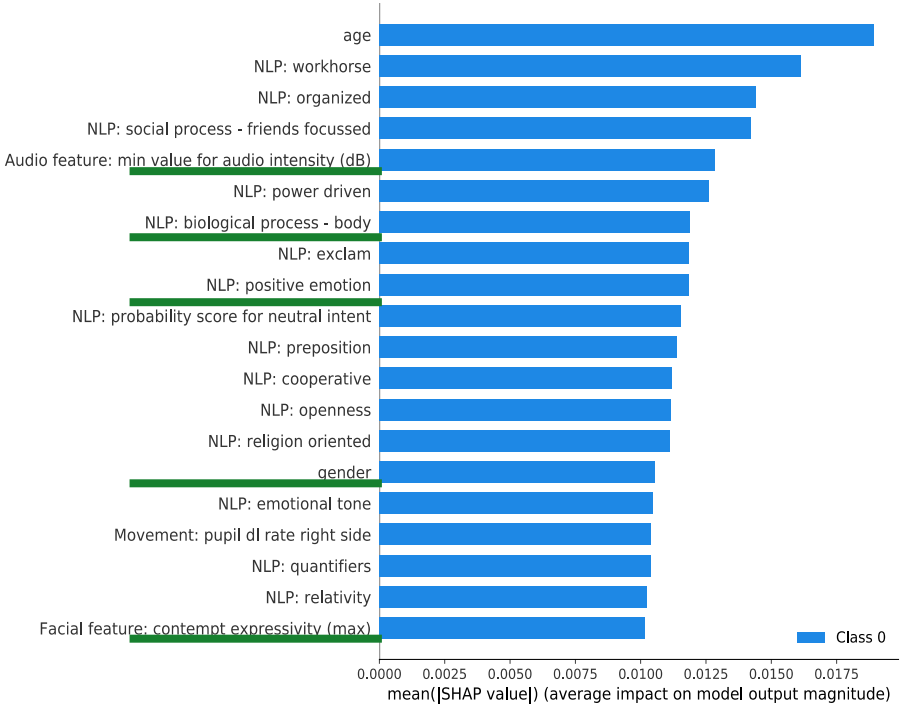


Figure 3. Receiver operating characteristic (ROC) curve of the internal test set for predicting (a) PCL-5 cut-off ≥ 33 (AUC = .90), (b) CES-D cut-off ≥ 23 (AUC = .86), (c) PTS symptom trajectories (non-remitting AUC = .86) and (d) depressive symptom trajectories (non-remitting AUC = .80).

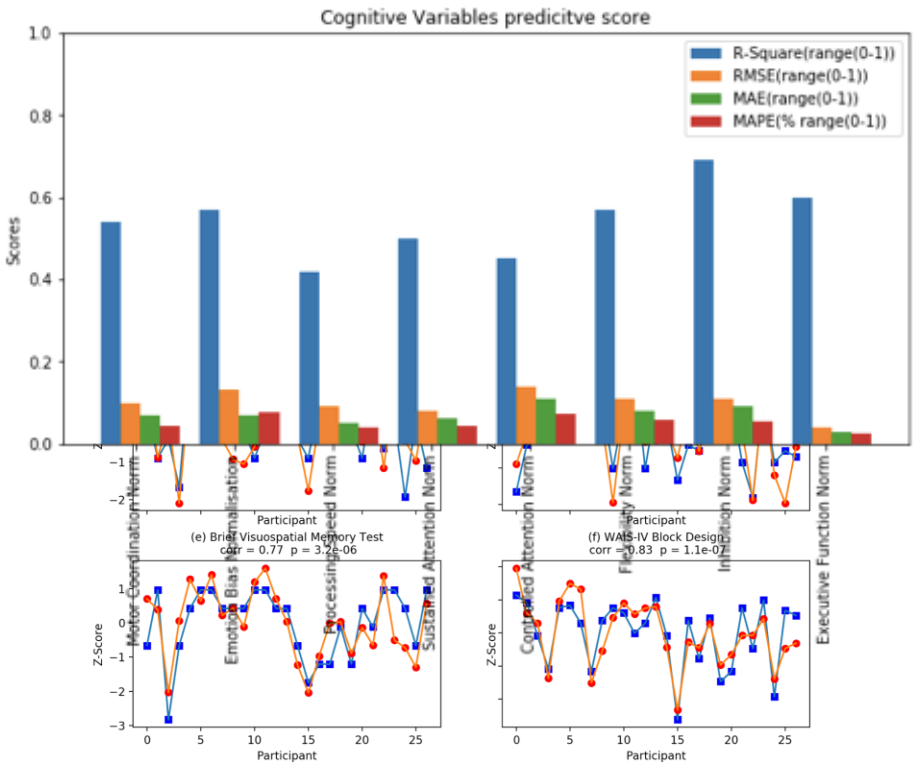


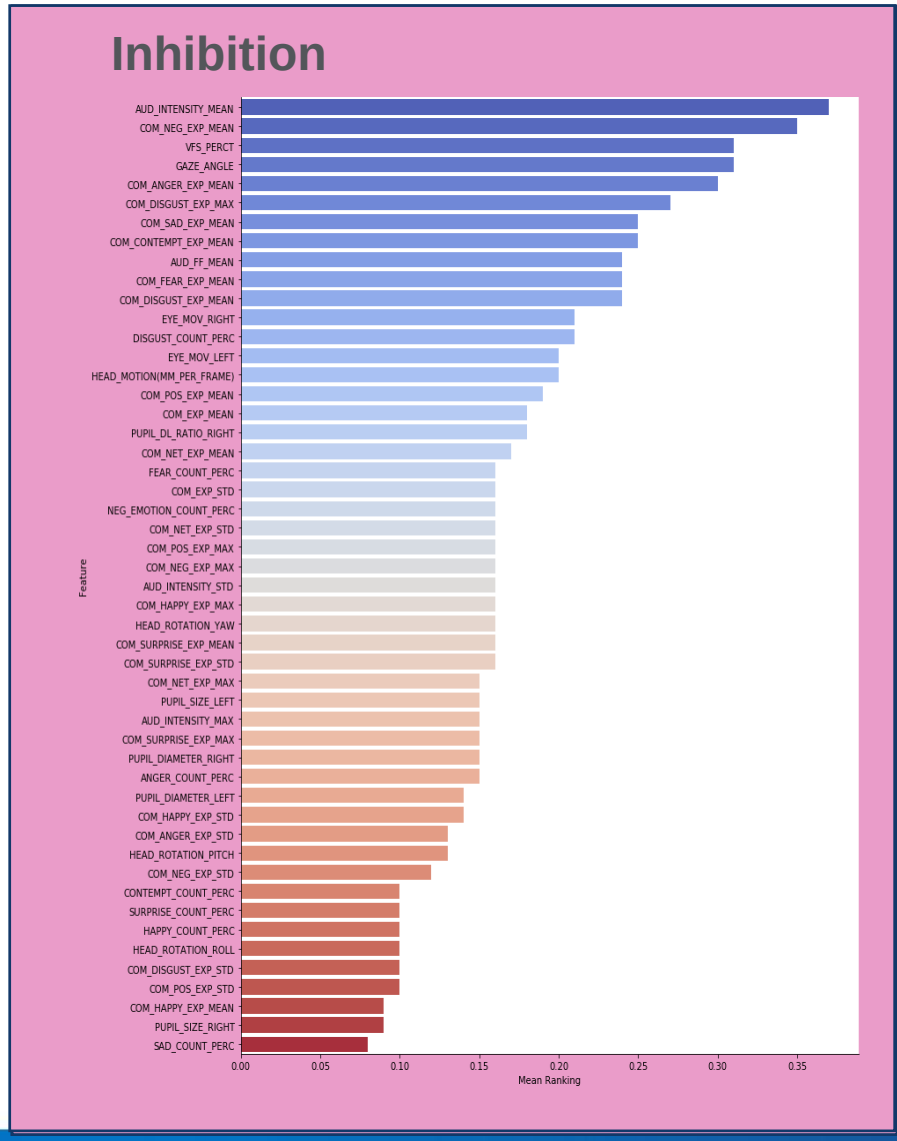
PTSD Classification



Depression Classification

Digital Signals of Cognitive Functioning





How can we scale-up the clinical utility of this technology?

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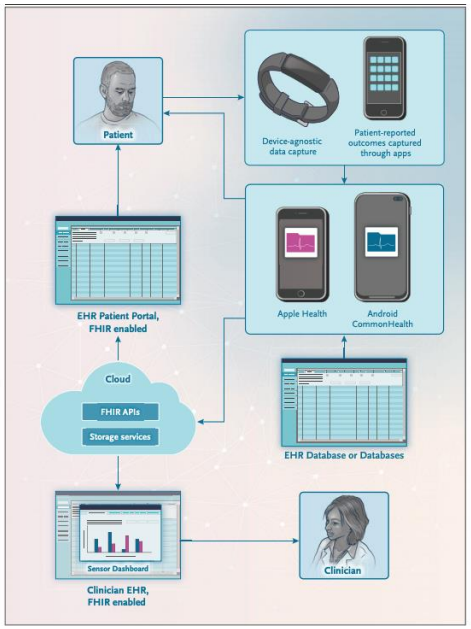
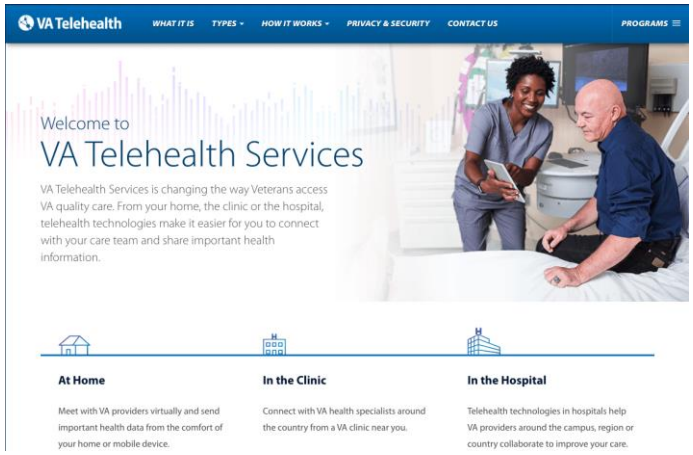
Creating a Learning Health System through Rapid-Cycle, Randomized Testing

Leora I. Horwitz, M.D., M.H.S., Masha Kuznetsova, M.P.H., and Simon A. Jones, Ph.D.





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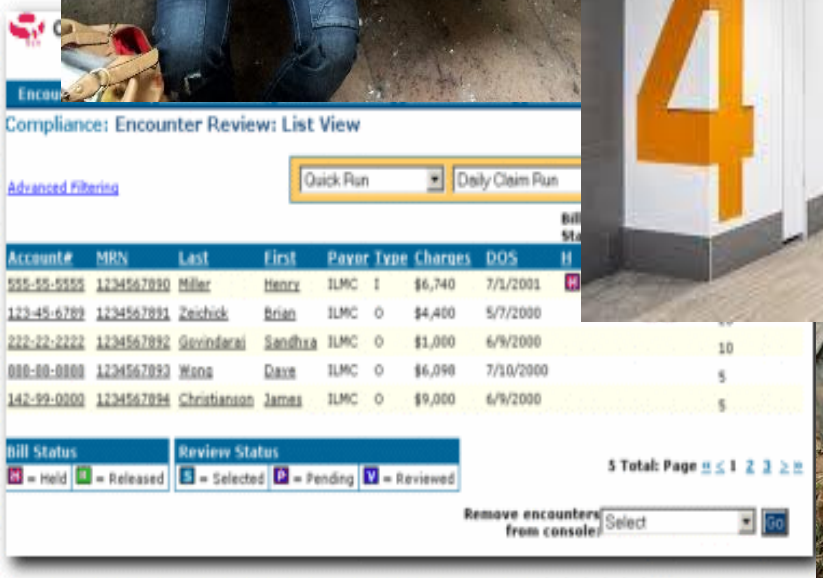
REVIEW ARTICLE

FRONTIERS IN MEDICINE

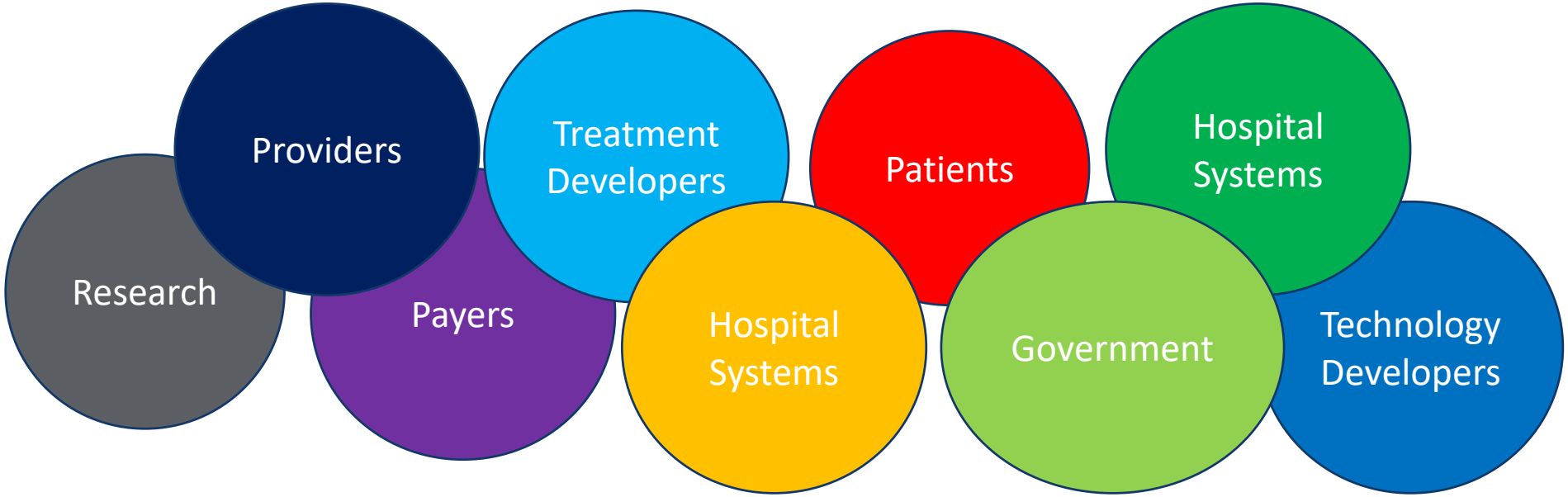
Mobile Devices and Health

Ida Sim, M.D., Ph.D.

At what point in time can we implement it?



Stakeholder engagement is crucial to sucess



Thank you very much for your attention!

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DFG Deutsche Forschungsgemeinschaft SCHU 3259/1-1

NIH National Institute of Mental Health