



Statistical and Machine Learning Approaches to Prediction

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Disclosures

Grants:

US National Institutes of Health (NIH): R01NS088475, R01CA213441,
R01AG056770, R01MH116156, R01NS122888 U01NS086090,
P30AR066262, UH3NS106899, U19AR076737, U24NS122732

US Veterans Affairs (VA): I01RX002245, I01RX002787, I01BX005871, I50BX005878

US Department of Defense (DoD): SC150198, SC150177

US Defense Advanced Research Projects (DARPA): N660012024046

US Department of Energy (DoE): LLNL

Craig H. Neilsen Foundation

Wings for Life Foundation

Data Science Consulting:

Santa Clara Valley Medical Center

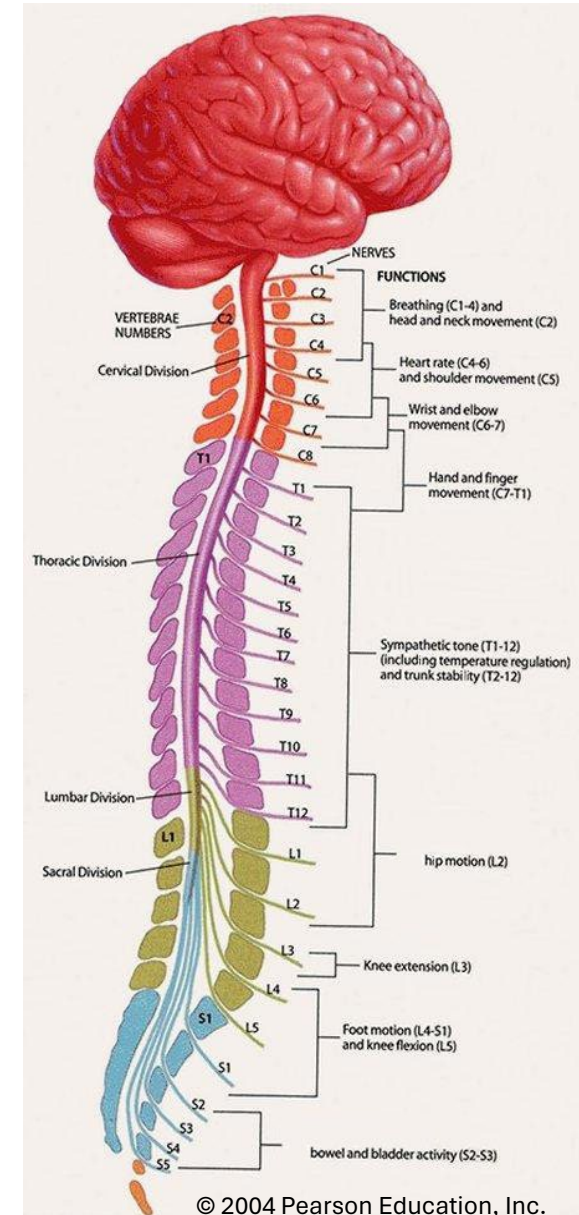
Neuronasal Inc.

SpineX Inc.

Industry Collaboration (in-kind):

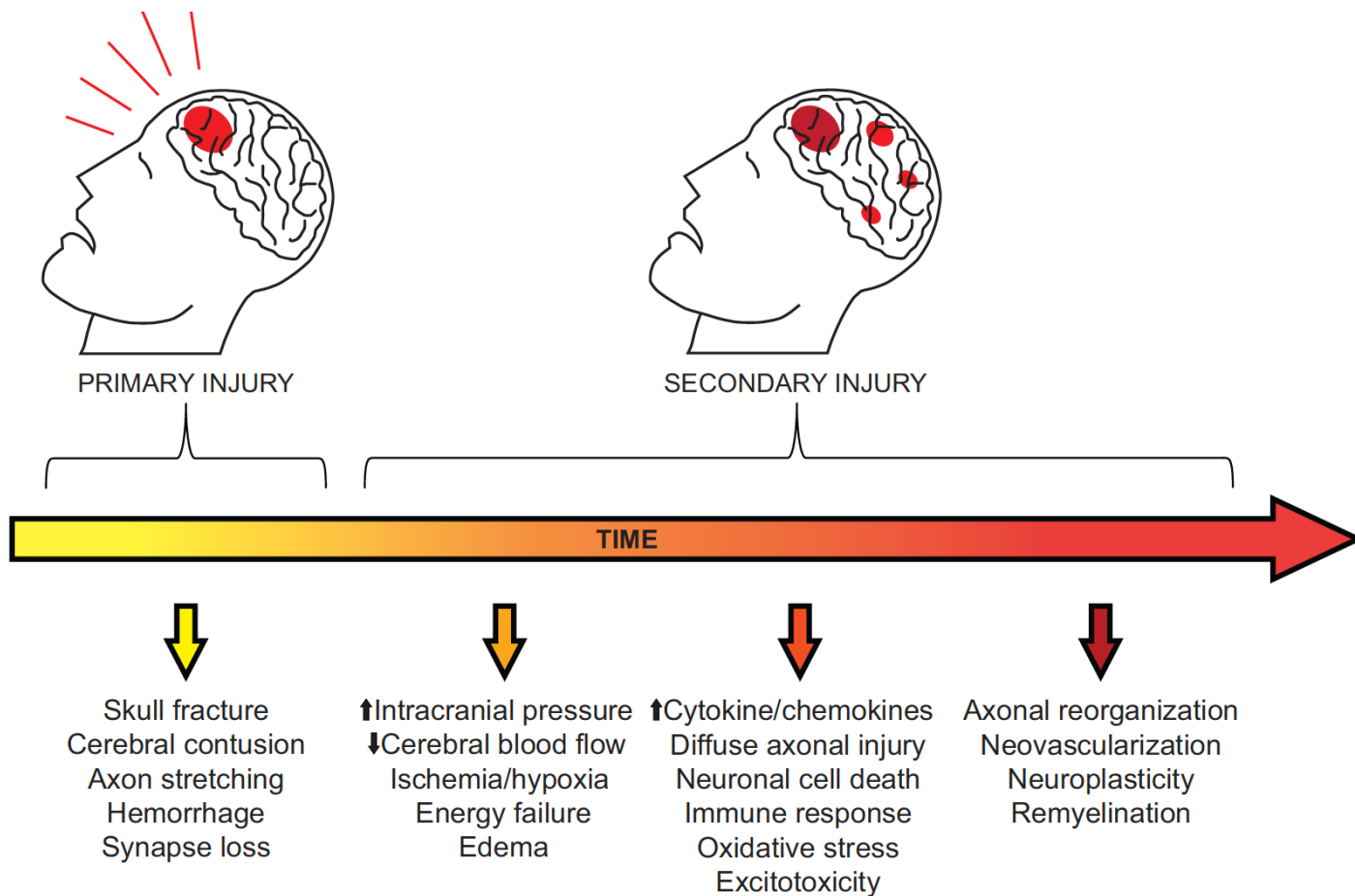
DataRobot: AI for Good program

TBI is Complex!

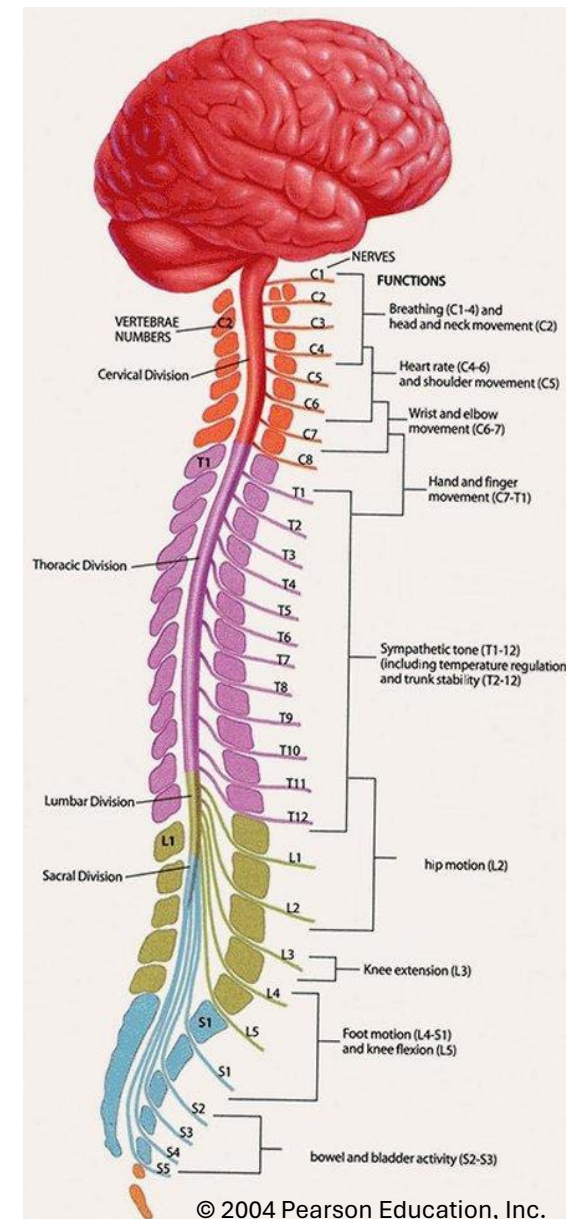


TBI is Complex!

Traumatic Brain Injury (TBI)

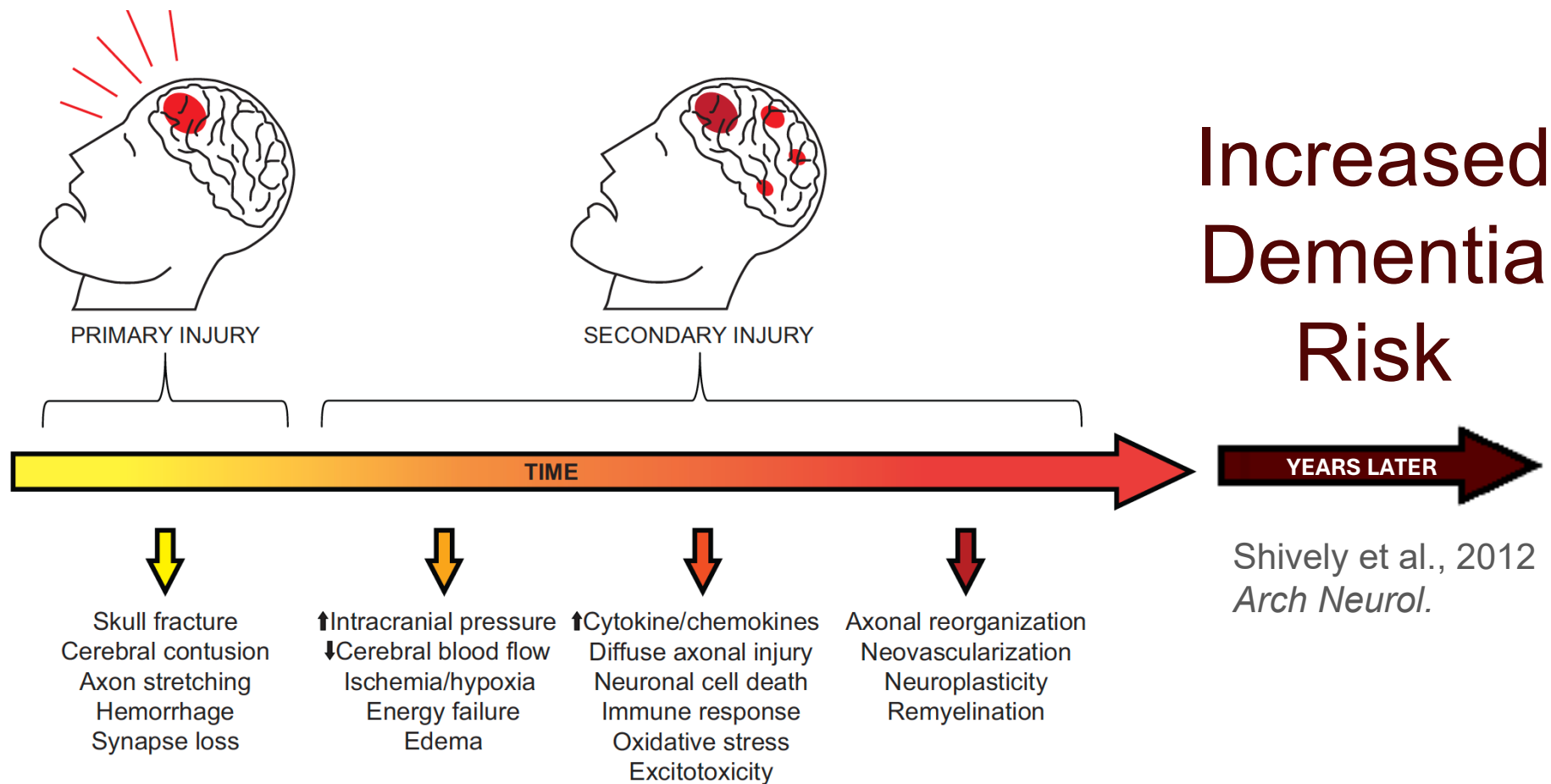


Irvine et al., 2018, *Pain Medicine*

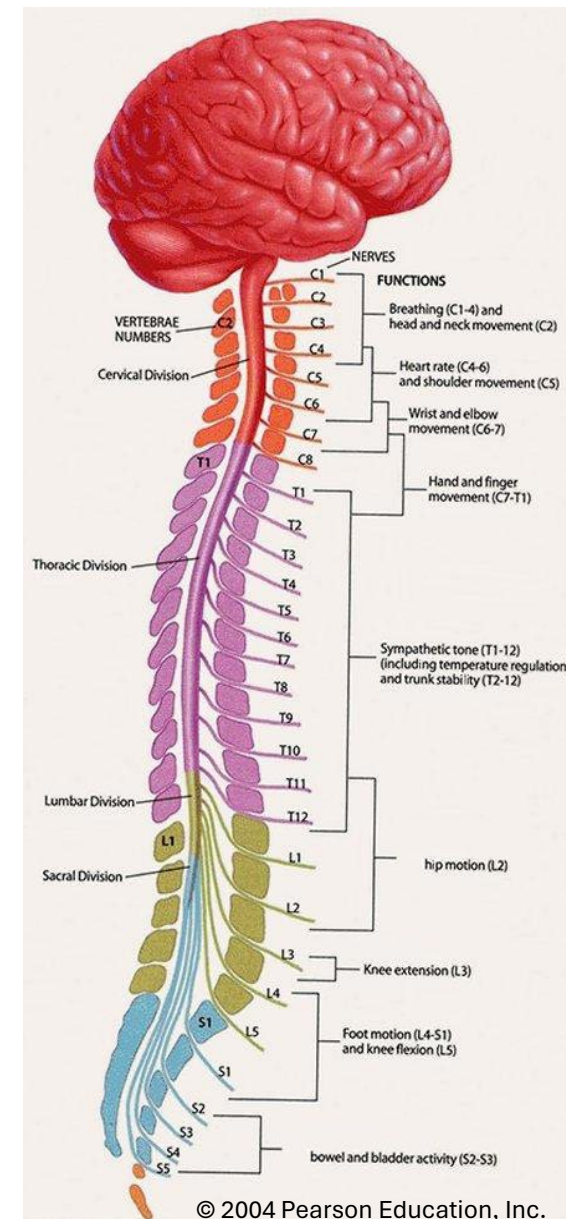


TBI is Complex!

Traumatic Brain Injury (TBI)



Shively et al., 2012
Arch Neurol.



Validated Prediction Models


BMJ**RESEARCH**

Predicting outcome after traumatic brain injury: practical prognostic models based on large cohort of international patients

MRC CRASH Trial Collaborators

BMJ: first published as 10.1136/bmj.39461.643438.25 on 12 February 2008.

CRASH Model

BMJ

Predicting
prognosis
in patients

MRC CRASH

BMJ: first published as 10.1136/bmj.b1000

CRASH Model

RESEARCH

OPEN ACCESS Freely available online

PLOS MEDICINE

Predicting Outcome after Traumatic Brain Injury: Development and International Validation of Prognostic Scores Based on Admission Characteristics

Ewout W. Steyerberg^{1*}, Nino Mushkudiani¹, Pablo Perel², Isabella Butcher³, Juan Lu⁴, Gillian S. McHugh³, Gordon D. Murray³, Anthony Marmarou⁴, Ian Roberts², J. Dik F. Habbema¹, Andrew I. R. Maas⁵

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PLOS Medicine | www.plosmedicine.org

1251

August 2008 | Volume 5 | Issue 8 | e165

IMPACT Model



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RESEARCH

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The BMJ logo is displayed in a large, blue, serif font.The word "RESEARCH" is written in a bold, dark blue, sans-serif font.

Predicting outcome after traumatic brain injury: practical prognostic models based on large cohort of international patients

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- Stratified model by economic development level (high income countries vs. low to middle income countries)

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- Glasgow Coma Score (GCS) ≤ 12

Web-based Prediction Calculators

The screenshot shows the IMPACT website interface. At the top is the IMPACT logo and a search bar. Below is a navigation menu with links to Home, TBI, IMPACT, Publications, References, Links, and Contact. A breadcrumb trail indicates the user is on the IMPACT Prognostic calculator page. The main content area is titled 'Prognostic calculator' and includes a text-based description of the calculator's purpose. To the right is a 'List of subpages' with links to Background, Mission & Aims, Collaboration, Investigators, Advisory Board, IMPACT database, Prognostic calculator, IMPACT recommendations, Common Data Elements (Draft), Data Sharing, and Acknowledgements. Below this is a section for 'Prognostic models in TBI' with sub-sections for Clinical Practice, Research, and Quality assessment of health-care delivery. The bottom section is titled 'Prediction models for 6 month outcome after TBI' and contains a form with various input fields for admission characteristics and a 'Calculate' button.

IMPACT
International Mission for Prognosis and Analysis of Clinical Trials in TBI

Home | TBI | IMPACT | Publications | References | Links | Contact

You are here: TBI-IMPACT.org » IMPACT » Prognostic calculator

Prognostic calculator

Based on extensive prognostic analysis the IMPACT investigators have developed prognostic models for predicting 6 month outcome in adult patients with moderate to severe head injury (Glasgow Coma Scale ≤ 12) on admission. By entering the characteristics into the calculator, the models will provide an estimate of the expected outcome at 6 months. We present three models of increasing complexity (Core, Core + CT, Core + CT + Lab). These models were developed and validated in collaboration with the CRASH trial collaborators on large numbers of individual patient data (the IMPACT database). The models discriminate well, and are particularly suited for purposes of classification and characterization of large cohorts of patients. Extreme caution is required when applying the estimated prognosis to individual patients.

Prediction models for 6 month outcome after TBI

Admission Characteristics	Value
Core	
Age (14-99 years)	
Motor Score	
Pupils	
Core+CT	
Hypoxia	
Hypotension	
CT Classification	
tSAH on CT	
Epidural mass on CT	
Core+CT+Lab	
Glucose (3-20 mmol/L)	mmol/L
Hb (6-17 g/dL)	g/dL

<http://www.tbi-impact.org/?p=impact/calc>

The screenshot shows the CRASH website interface. At the top is the CRASH logo. Below is a section titled 'Head injury prognosis' with a text-based description of the calculator's purpose. The main content area is titled 'Prediction' and contains a form with various input fields for patient characteristics and a 'Reset' button. Below the form is a red banner with the results of the calculation: 'Risk of 14 day mortality (95% CI)' and 'Risk of unfavourable outcome at 6 months'. At the bottom is a 'Reference' section with a citation and the text 'Online calculator by: Sealed Envelope Ltd'.

Head injury prognosis

CRASH

These prognostic models may be used as an aid to estimate mortality at 14 days and death and severe disability at six months in patients with traumatic brain injury (TBI). The predictions are based on the average outcome in adult patients with Glasgow coma score (GCS) of 14 or less, within 8 hours of injury, and can only support - not replace - clinical judgment. Although individual names of countries can be selected in the models, the estimates are based on two alternative sets of models (high income countries or low & middle income countries).

Country

Age, years

Glasgow coma score

Pupils react to light

Major extra-cranial injury?

CT scan available? ☐

Prediction

Risk of 14 day mortality (95% CI) -

Risk of unfavourable outcome at 6 months -

Reference:
The MRC CRASH Trial Collaborators. Predicting outcome after traumatic brain injury: practical prognostic models based on large cohort of international patients. BMJ 2008 doi:10.1136/bmj.39461.643438.25 2007;

Online calculator by: Sealed Envelope Ltd

<http://www.crash2.lshtm.ac.uk/Risk%20calculator/index.html>



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Hypotension
CT Classification
tSAH on CT
Epidural mass on CT

Core+CT+Lab

Glucose (3-20 mmol/L) mmol/L
Hb (6-17 g/dL) g/dL

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- [IMPACT recommendations](#)
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- [Acknowledgements](#)

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Prognostic models in TBI

1. Clinical Practice

- [informing relatives](#)
- [support treatment decisions](#)
- [allocating resources](#)

2. Research

- [Classification:](#)
 - [adjust for baseline characteristics](#)
 - [ordinal analyses:](#)
 - [sliding dichotomy](#)
 - [proportional odds model](#)
- [Clinical trials](#)

3. Quality assessment of health-care delivery



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3. Quality assessment of health-care delivery

This model predicts outcome in the following patients:

Adults with head injury, Glasgow Coma Scale 12 or less.

Prognostic Results:

Predicted probability of 6 month mortality: **Core model: 15%**

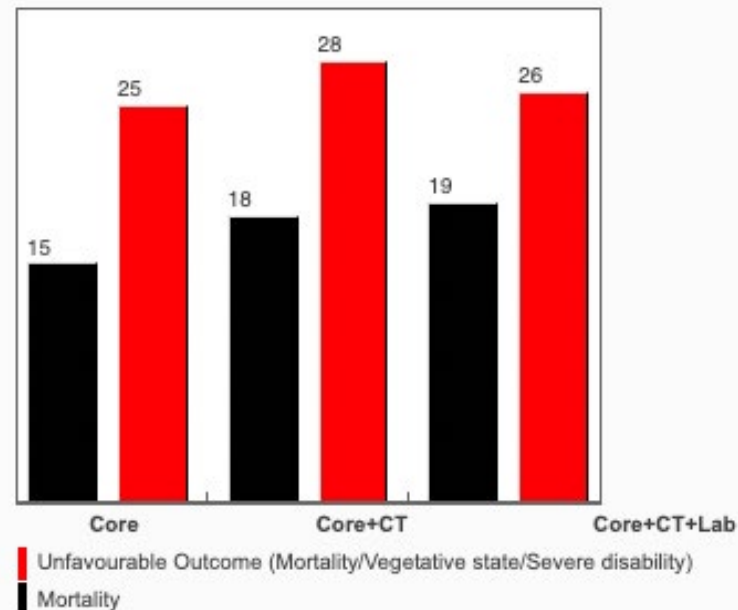
Predicted probability of 6 month unfavourable outcome: **Core model: 25%**

Predicted probability of 6 month mortality: **Core+CT model: 18%**

Predicted probability of 6 month unfavourable outcome: **Core+CT model: 28%**

Predicted probability of 6 month mortality: **Core+CT+Lab model: 19%**

Predicted probability of 6 month unfavourable outcome: **Core+CT+Lab model: 26%**





Performance of the IMPACT and CRASH prognostic models for traumatic brain injury in a contemporary multicenter cohort: a TRACK-TBI study

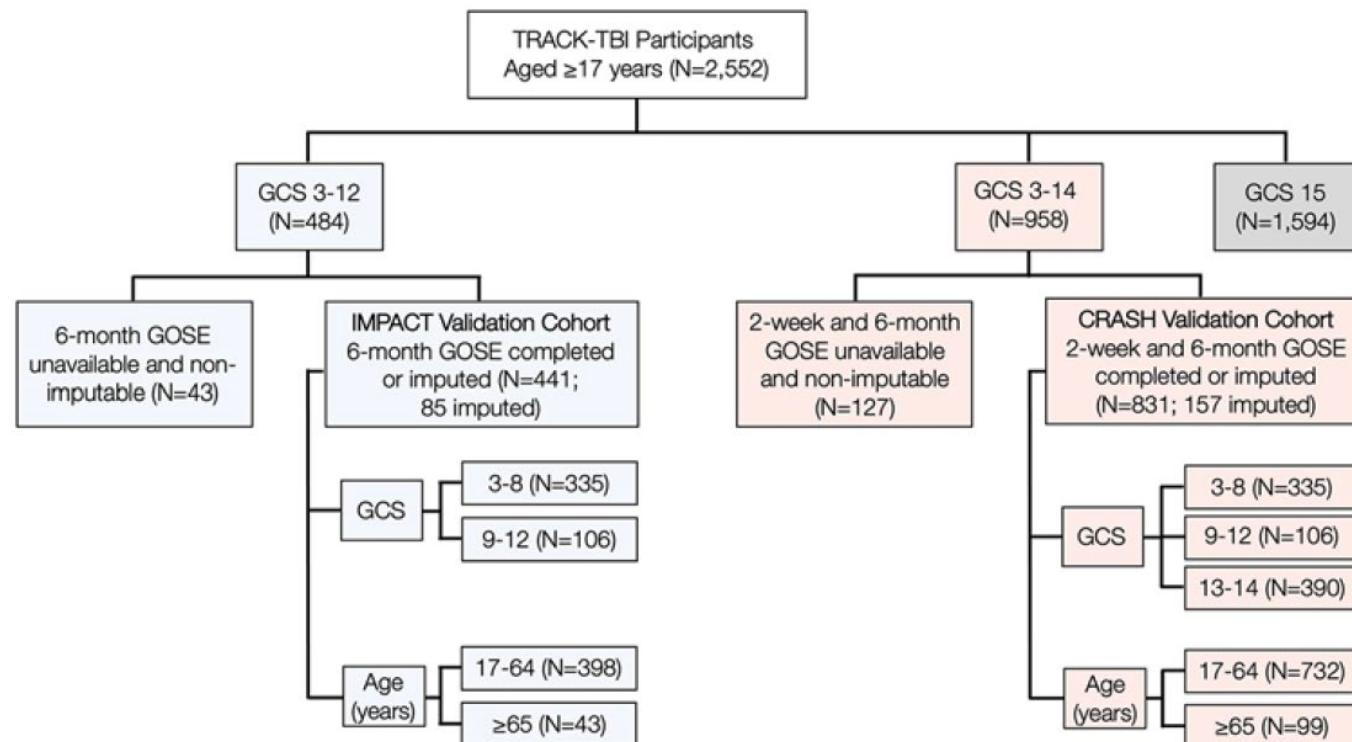
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Performance of the IMPA models for traumatic brain multicenter cohort: a TRA

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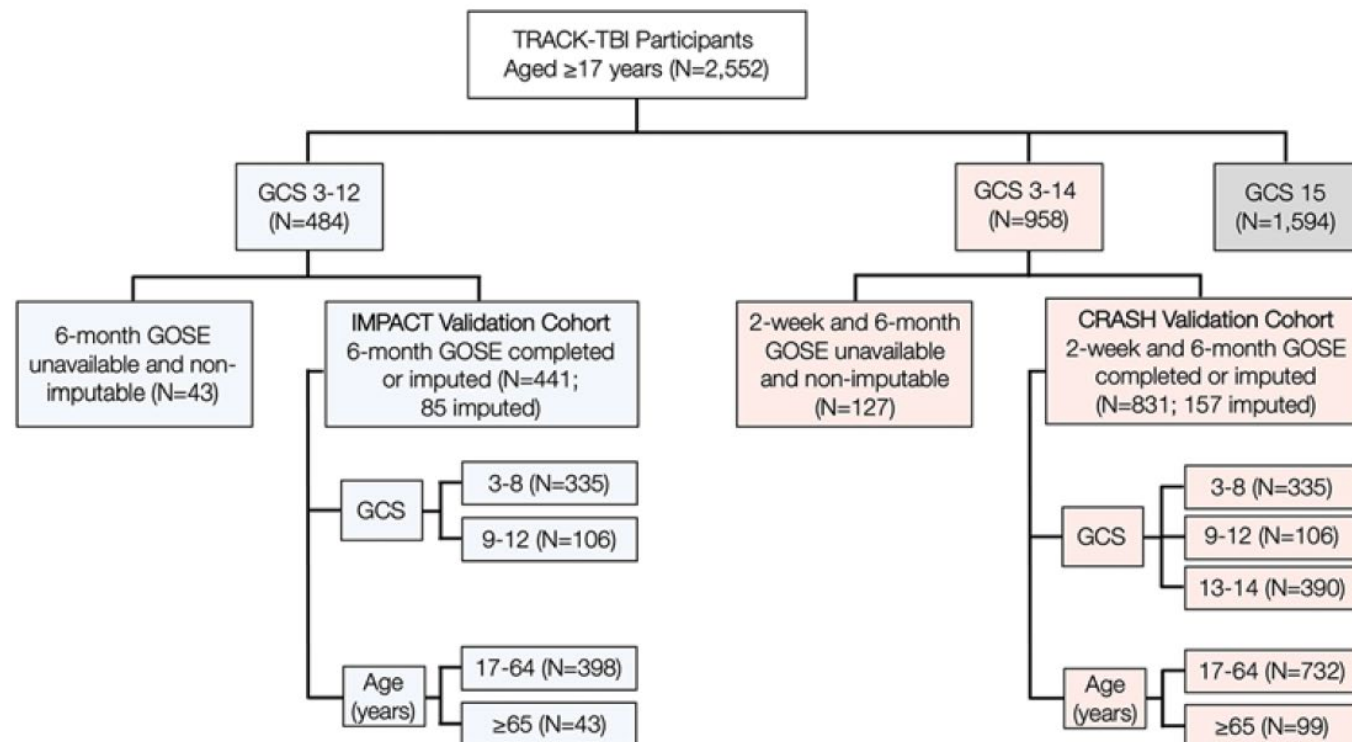




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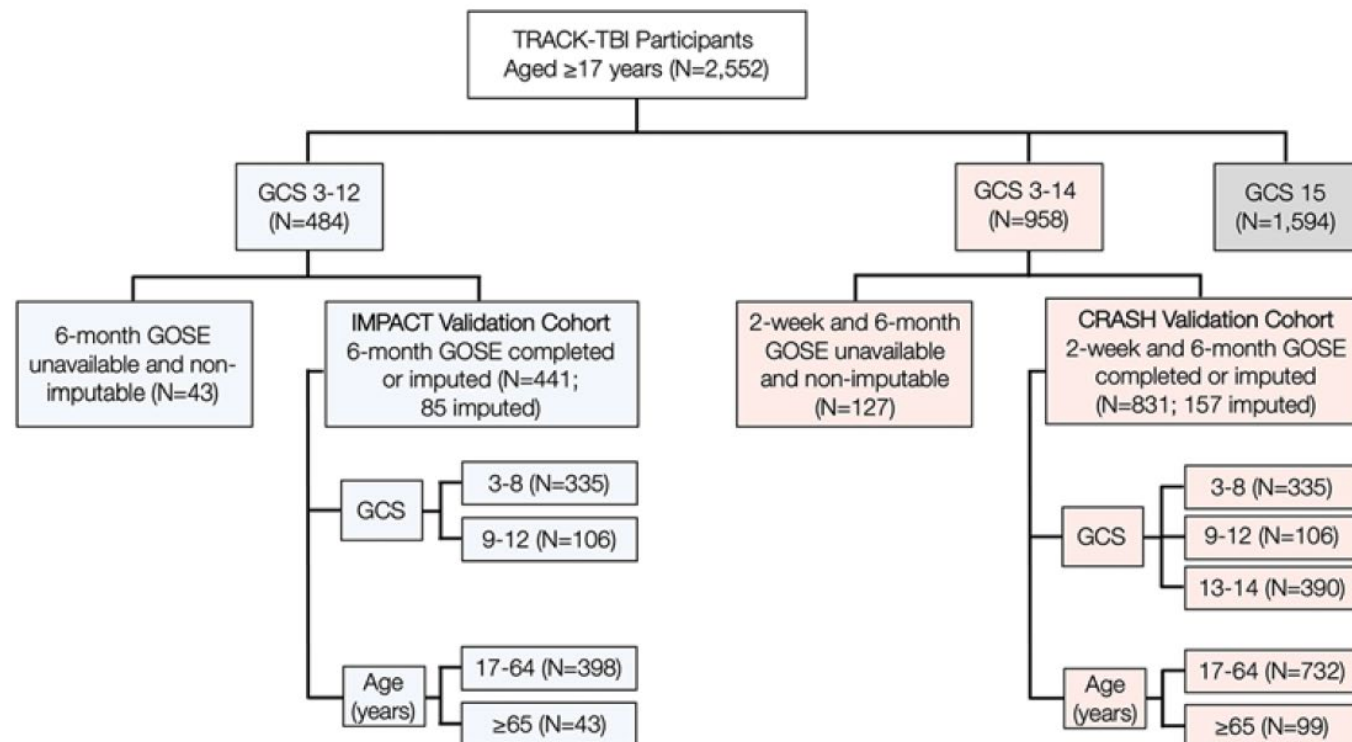
-The IMPACT and CRASH models adequately discriminated mortality and unfavorable outcome.



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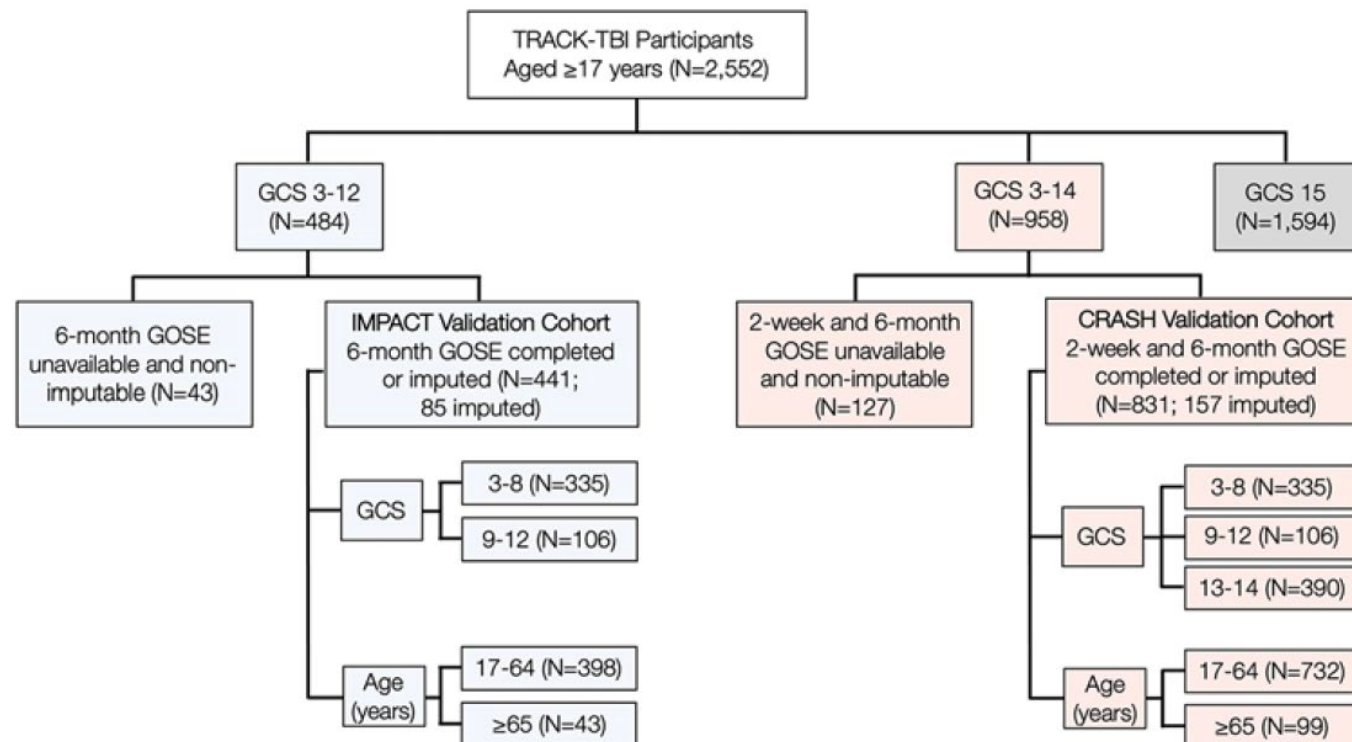
-IMPACT-Lab and CRASH-CT models overpredicted mortality in the overall cohort and for patients with severe or moderate TBI.



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and Geoffrey T. Manley, MD, PhD,^{1,2} on beha

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-The IMPACT and CRASH models adequately discriminated mortality and unfavorable outcome.

-IMPACT-Lab and CRASH-CT models overpredicted mortality in the overall cohort and for patients with severe or moderate TBI.

"This suggests the presence of **predictors in contemporary TBI care not accounted for by these models**, which were developed using data from over 2 decades ago."

**How do you navigate the full set of
potential predictors of TBI?**

How do you navigate the full set of potential predictors of TBI?

NEWS FEATURE

Predictable response:

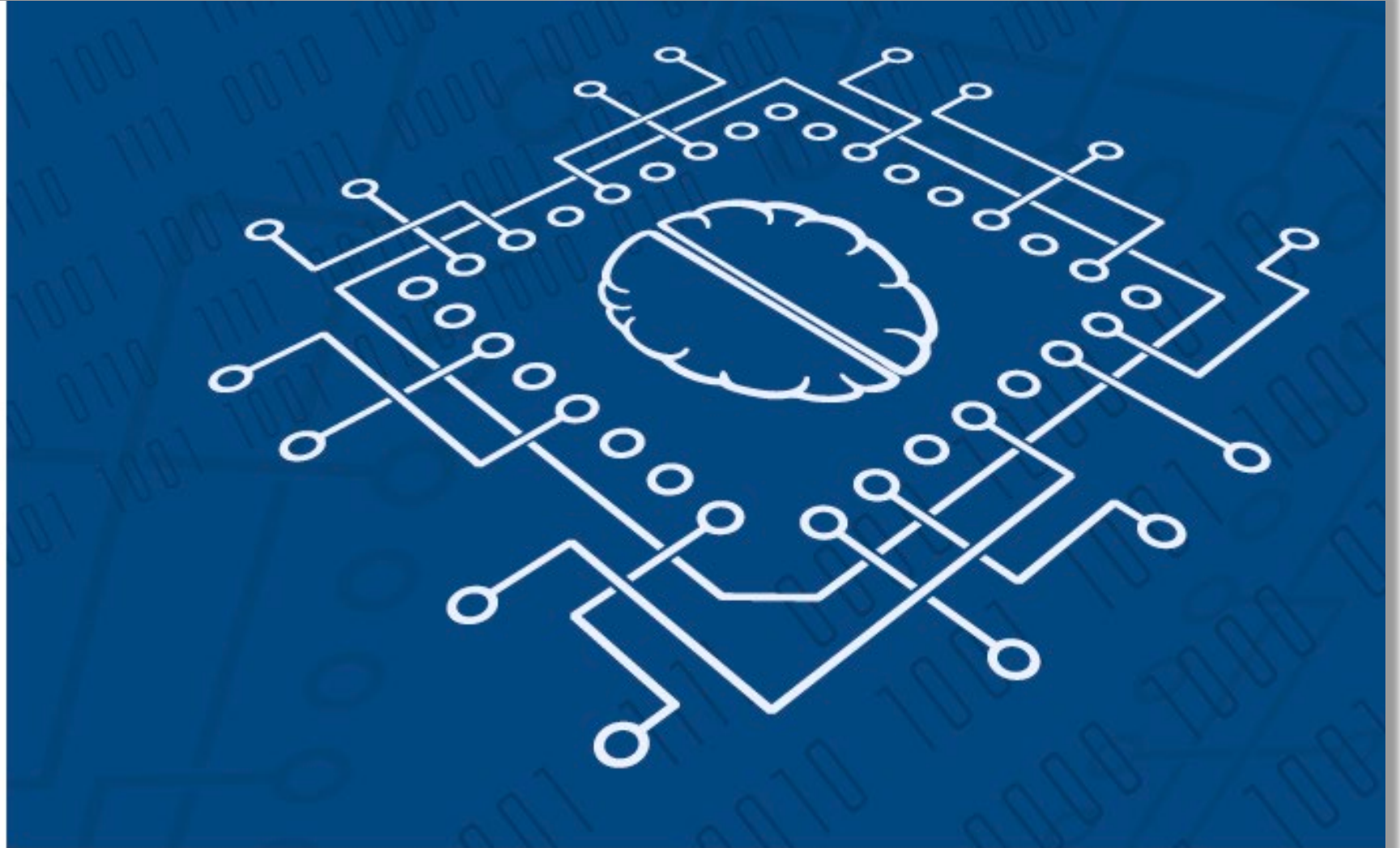
Finding optimal drugs and doses using artificial intelligence

By Shraddha Chakradhar

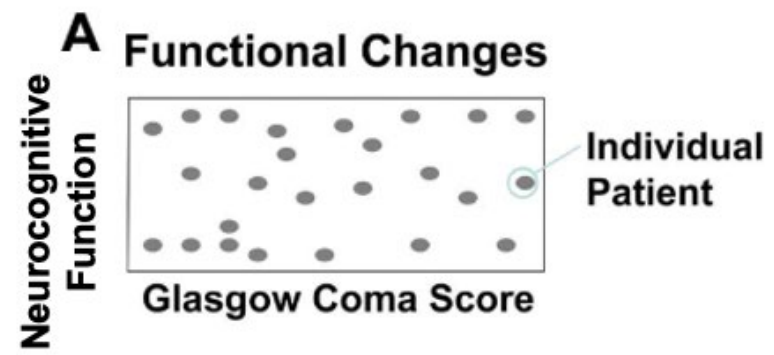
NATURE MEDICINE VOLUME 23 | NUMBER 11 | NOVEMBER 2017

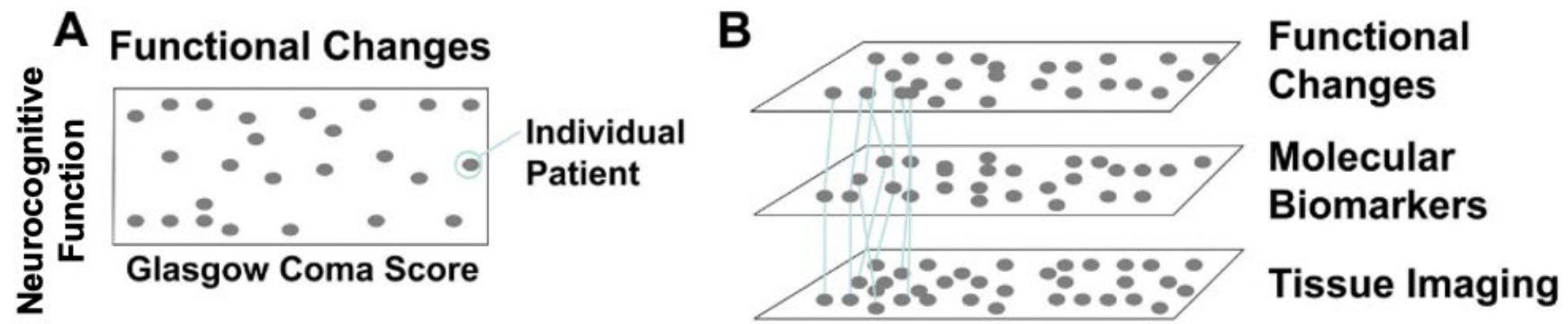
How do you navigate the full set of potential predictors of TBI?

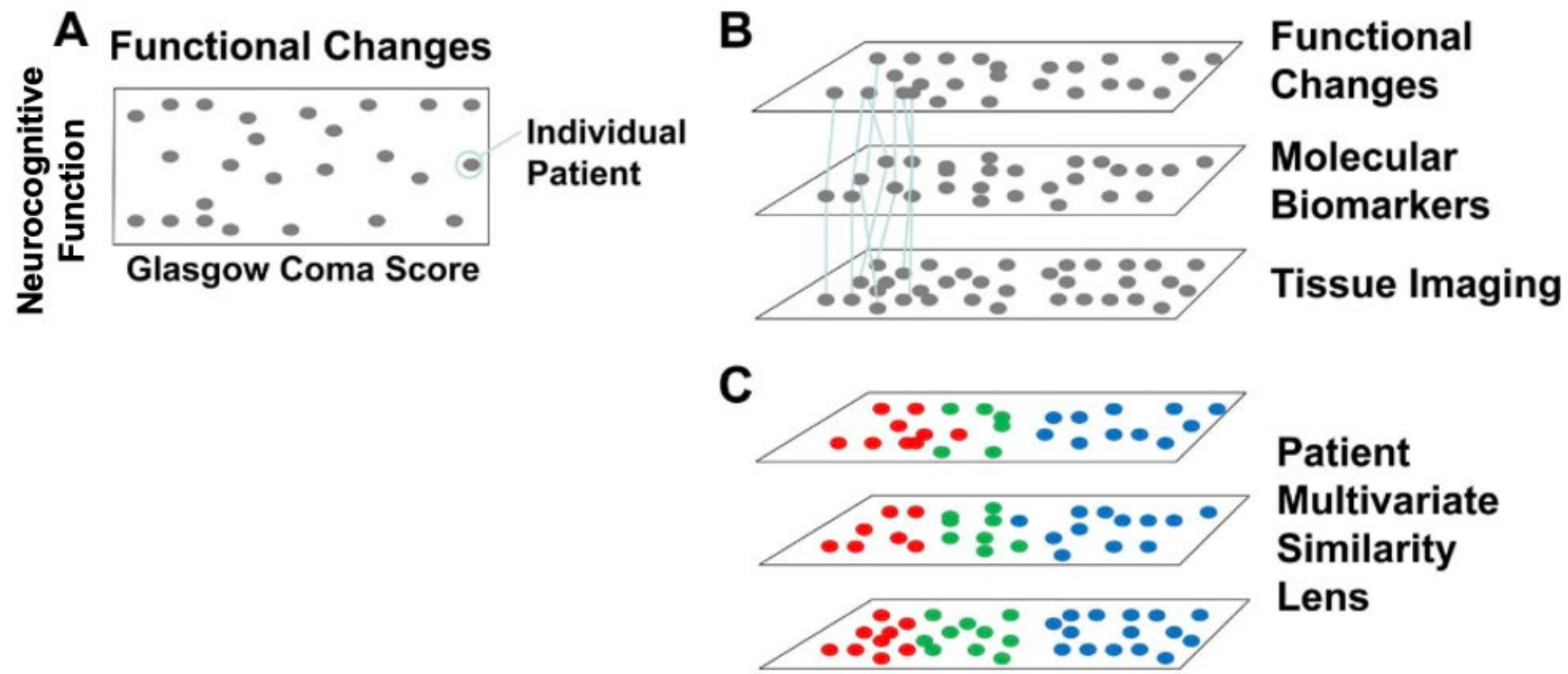
Predict
Finding optimal
By Shraddha Cha
NATURE MEDICINE

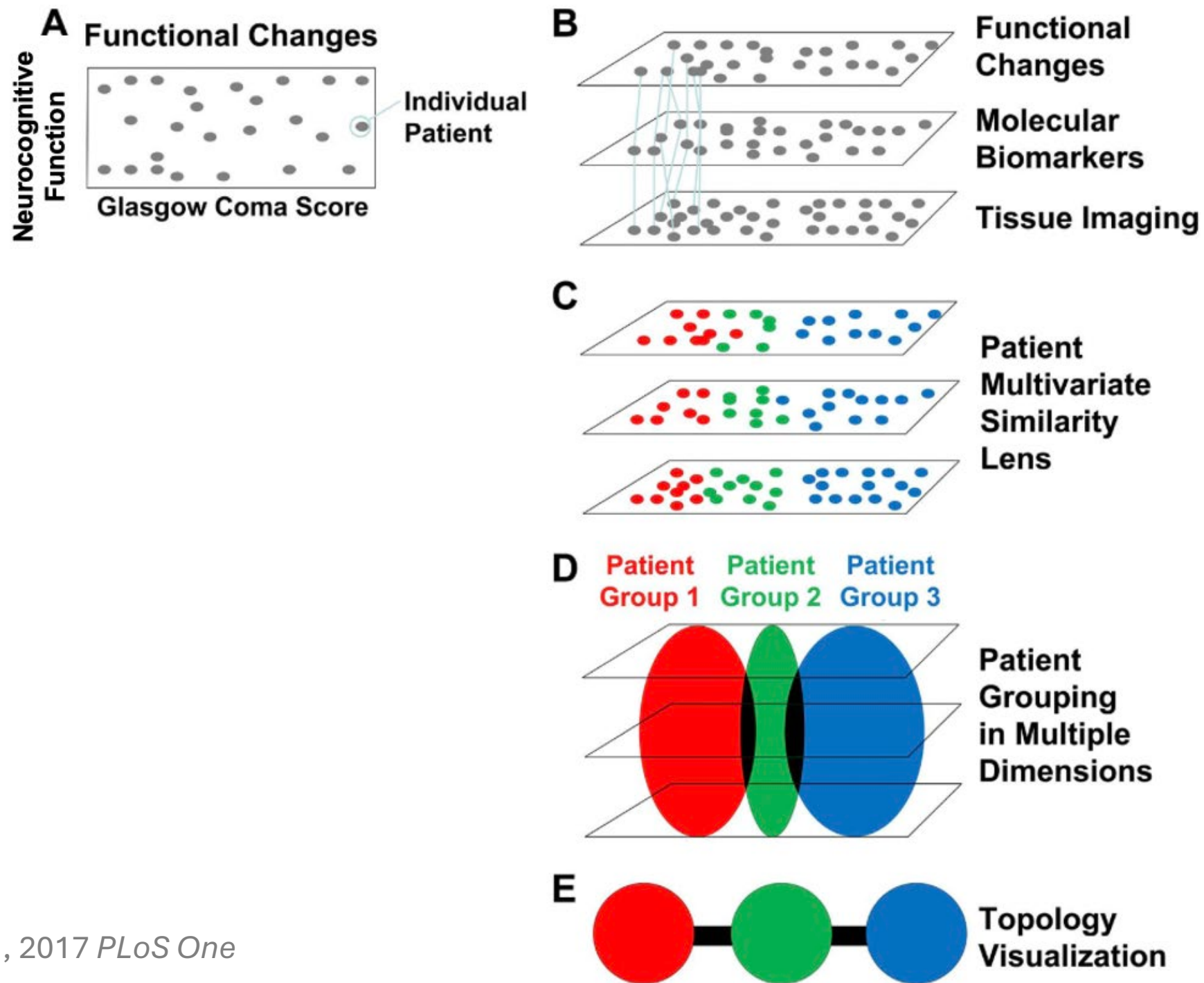


Mind-like machines: Machine learning is enabling the prediction of drug responses.









Clinical Trial

> [PLoS One](#). 2017 Mar 3;12(3):e0169490. doi: 10.1371/journal.pone.0169490.

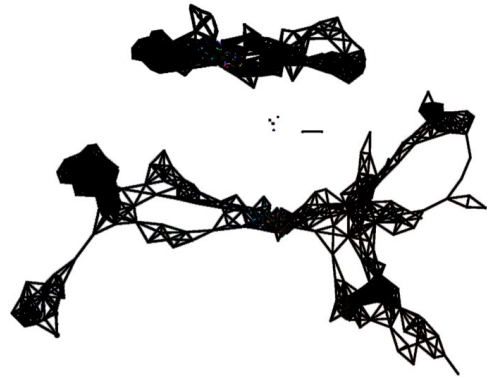
eCollection 2017.

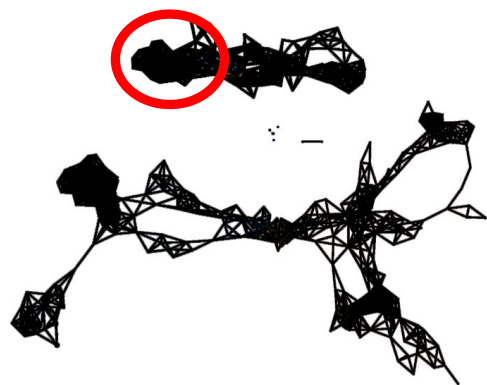
Uncovering precision phenotype–biomarker associations in traumatic brain injury using topological data analysis

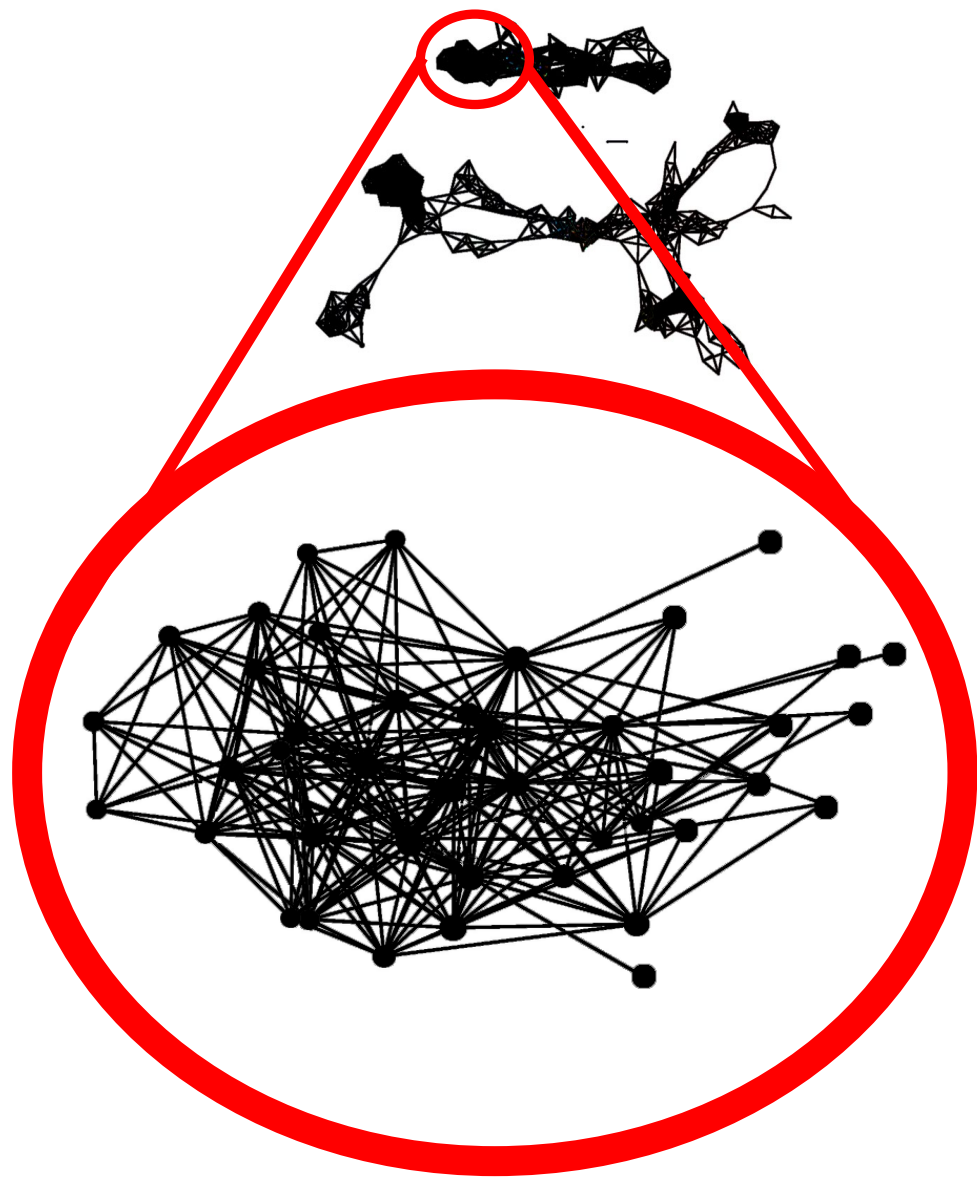
Jessica L Nielson ^{1 2}, Shelly R Cooper ^{1 2 3}, John K Yue ^{1 2}, Marco D Sorani ²,
Tomoo Inoue ^{1 2}, Esther L Yuh ³, Pratik Mukherjee ³, Tanya C Petrossian ⁴, Jesse Paquette ⁴,
Pek Y Lum ⁴, Gunnar E Carlsson ⁴, Mary J Vassar ^{1 2}, Hester F Lingsma ⁵, Wayne A Gordon ⁶,
Alex B Valadka ⁷, David O Okonkwo ⁸, Geoffrey T Manley ^{1 2}, Adam R Ferguson ^{1 2 9},
TRACK-TBI Investigators

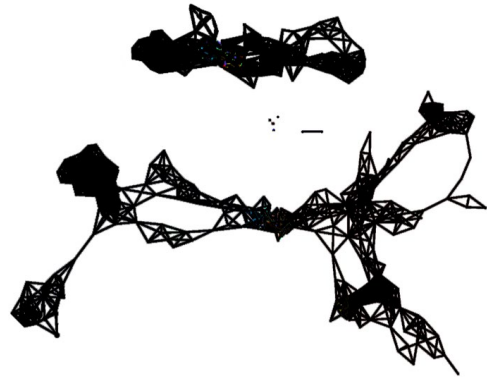
Affiliations [+ expand](#)

PMID: 28257413 PMCID: [PMC5336356](#) DOI: [10.1371/journal.pone.0169490](#)

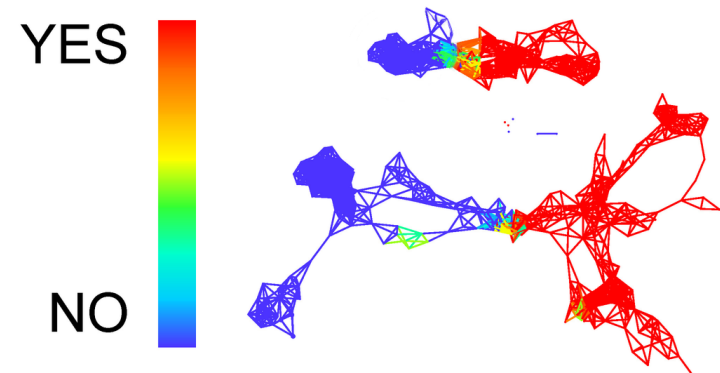




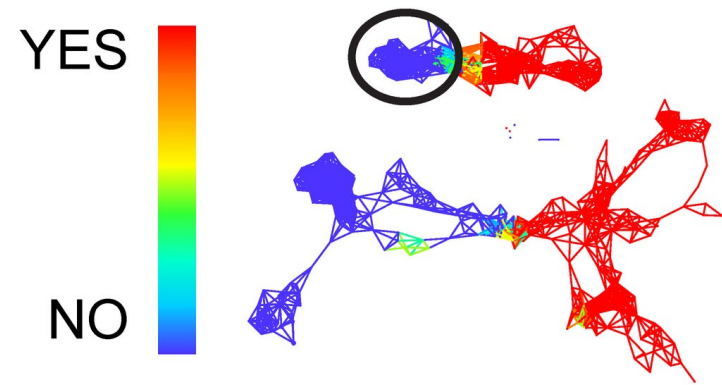


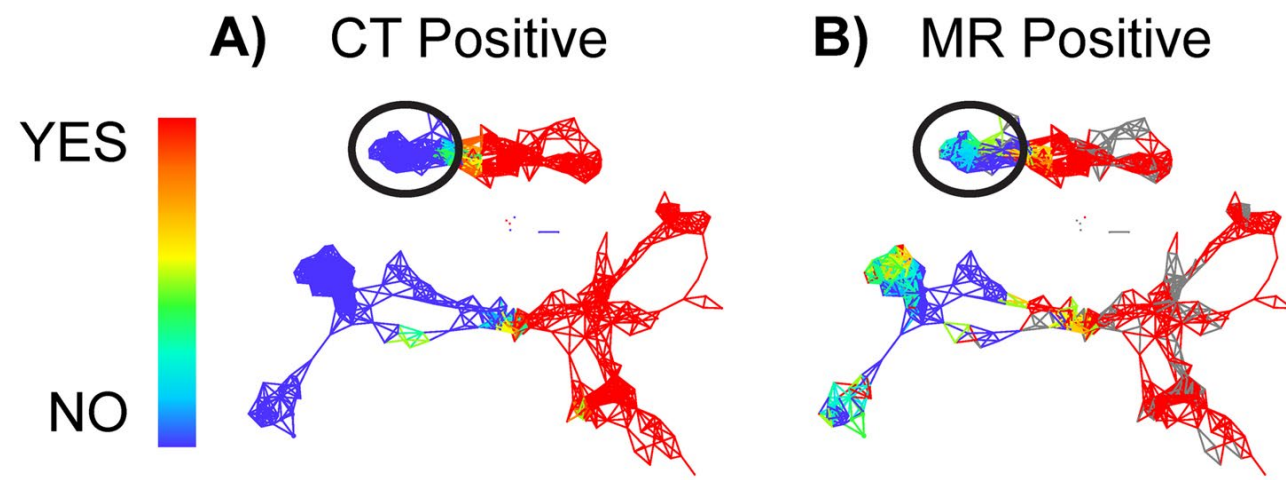


A) CT Positive

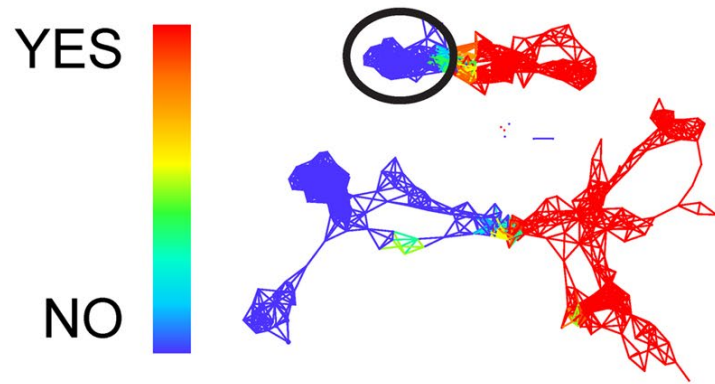


A) CT Positive

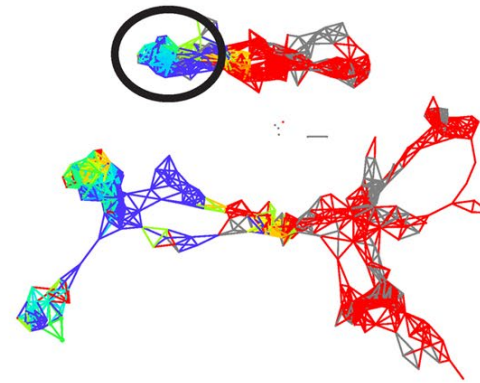




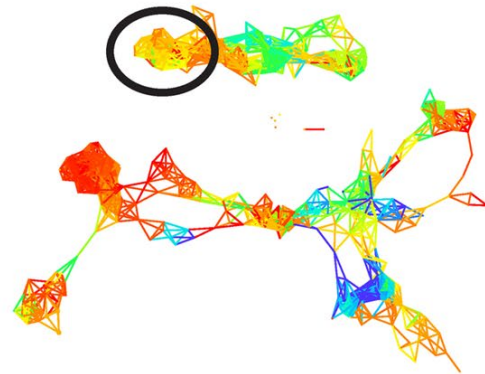
A) CT Positive



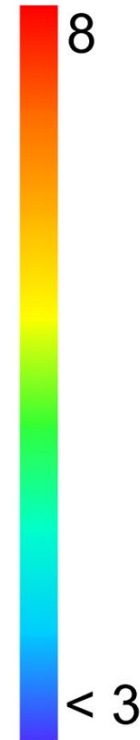
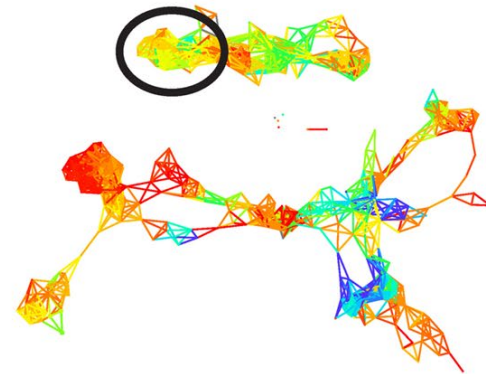
B) MR Positive

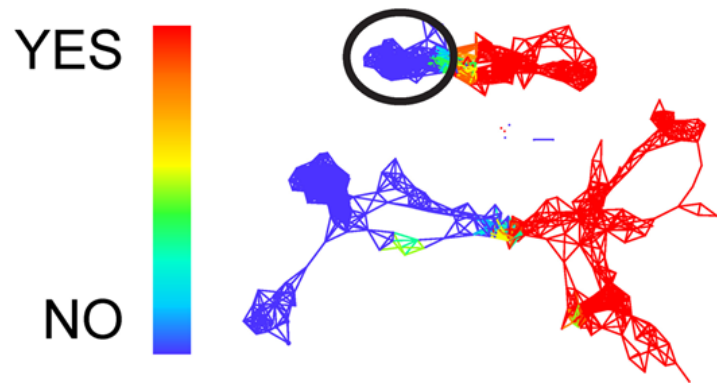
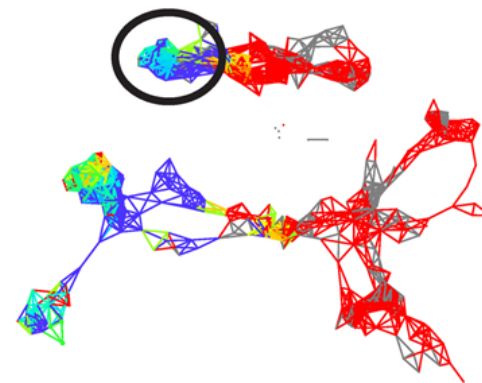
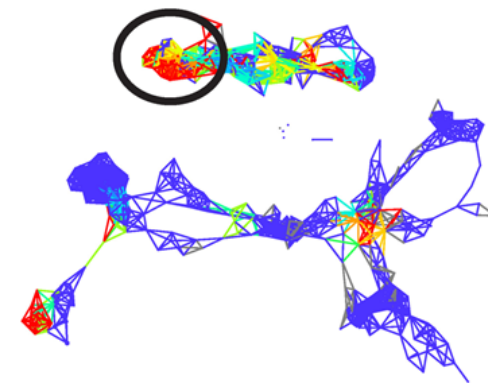
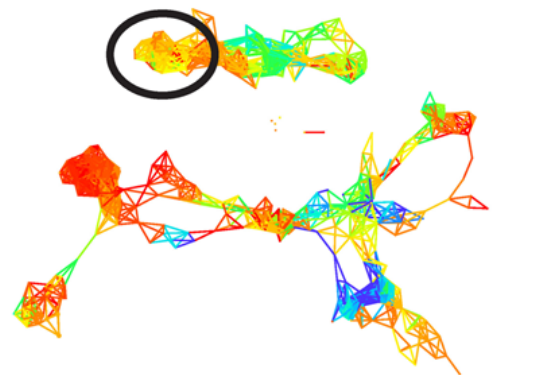
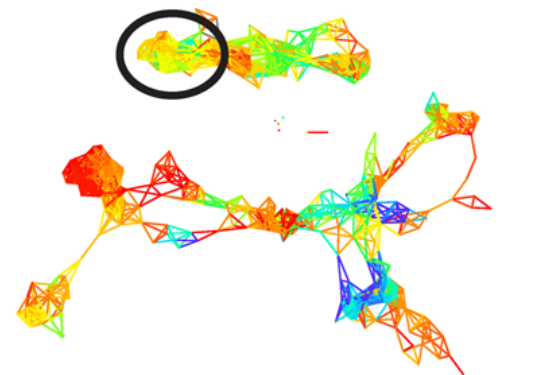
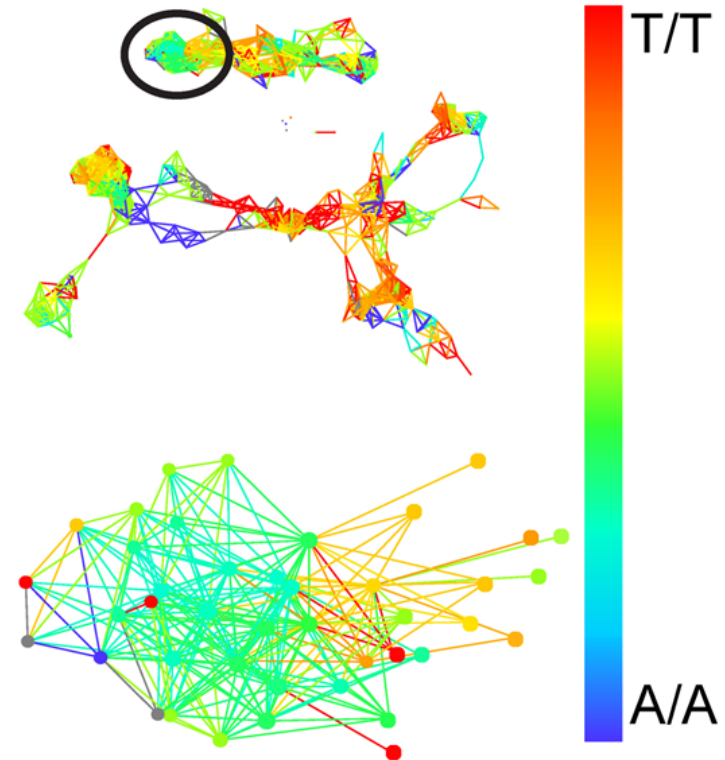


D) GOS-E 3M

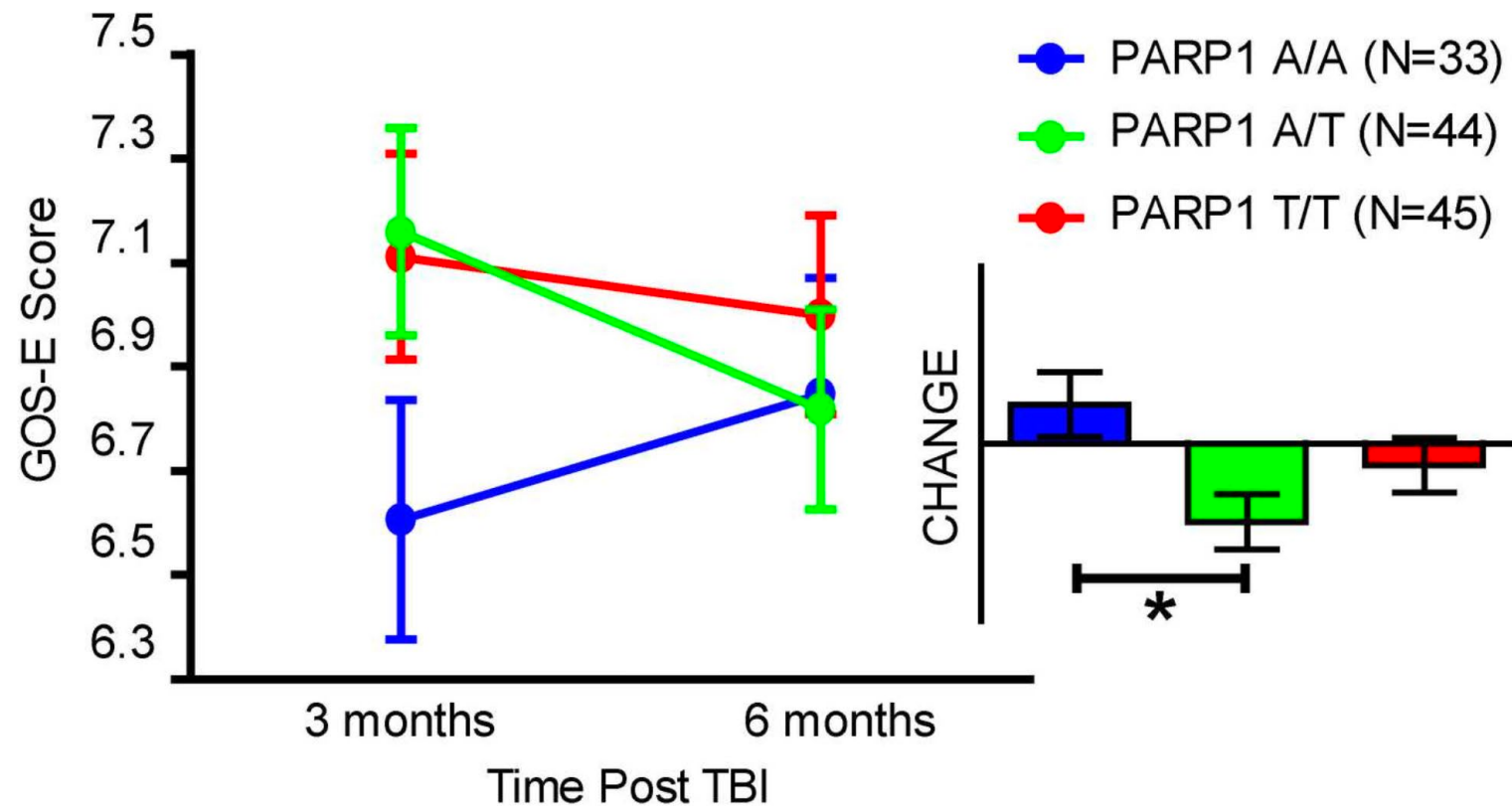


E) GOS-E 6M



A) CT Positive**B) MR Positive****C) PTSD Positive****D) GOS-E 3M****E) GOS-E 6M****F) PARP1**

A) GOS-E Recovery: CT- Patients

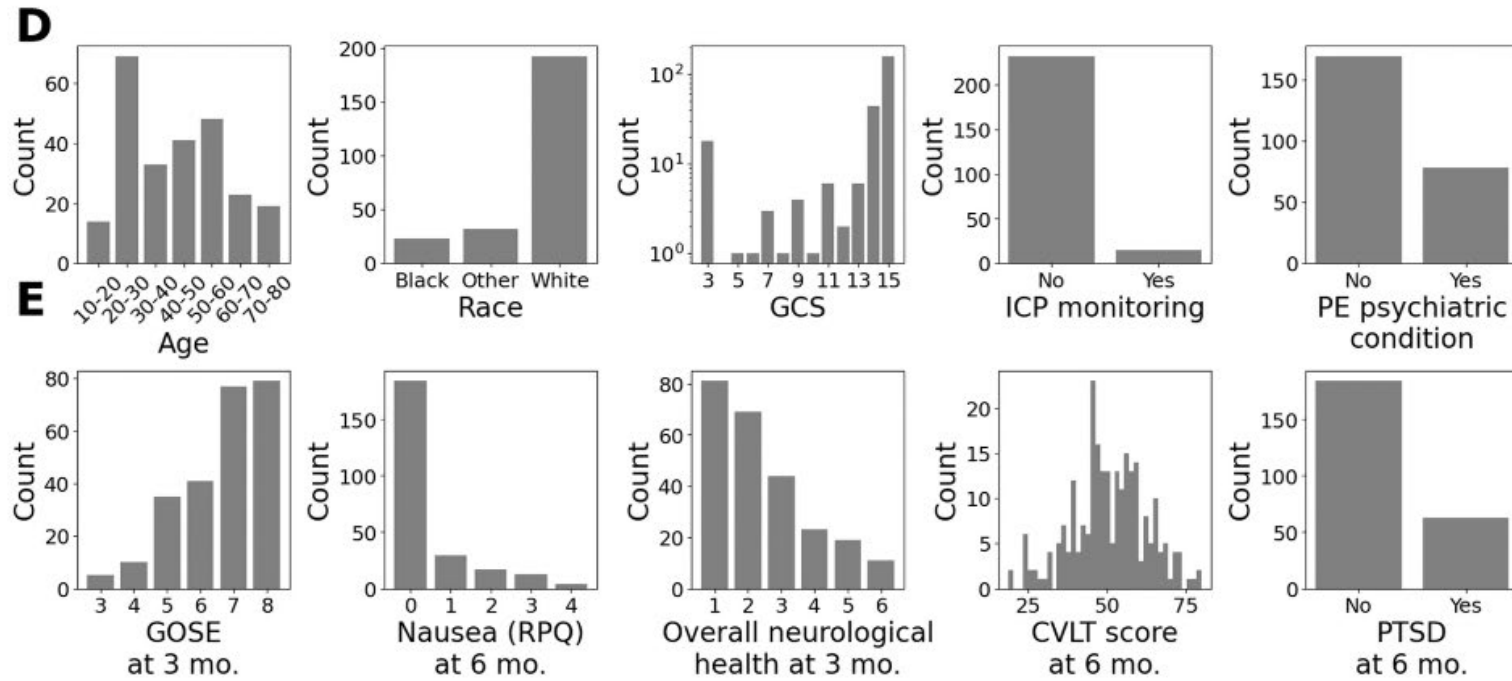
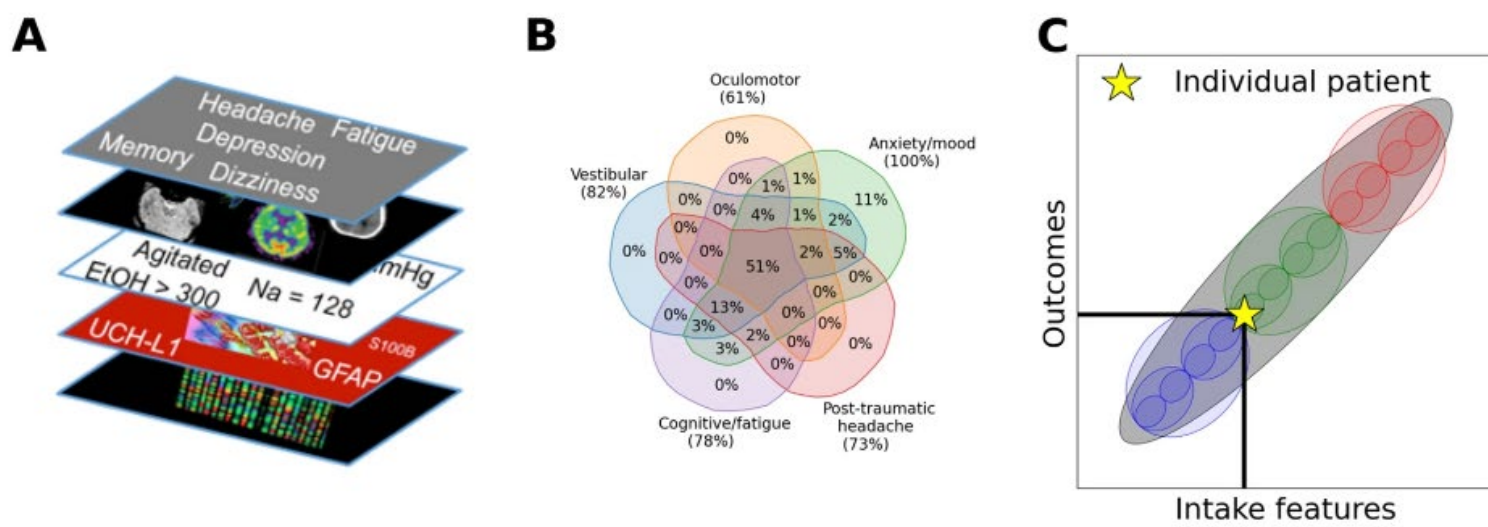




OPEN

Data-driven distillation and precision prognosis in traumatic brain injury with interpretable machine learning

Andrew Tritt¹, John K. Yue^{2,3}, Adam R. Ferguson^{2,3,4}, Abel Torres Espin^{2,3},
Lindsay D. Nelson⁵, Esther L. Yuh^{2,3}, Amy J. Markowitz^{2,3}, Geoffrey T. Manley^{2,3,6,7},
Kristofer E. Bouchard^{7,8,9,10}✉ & the TRACK-TBI Investigators*



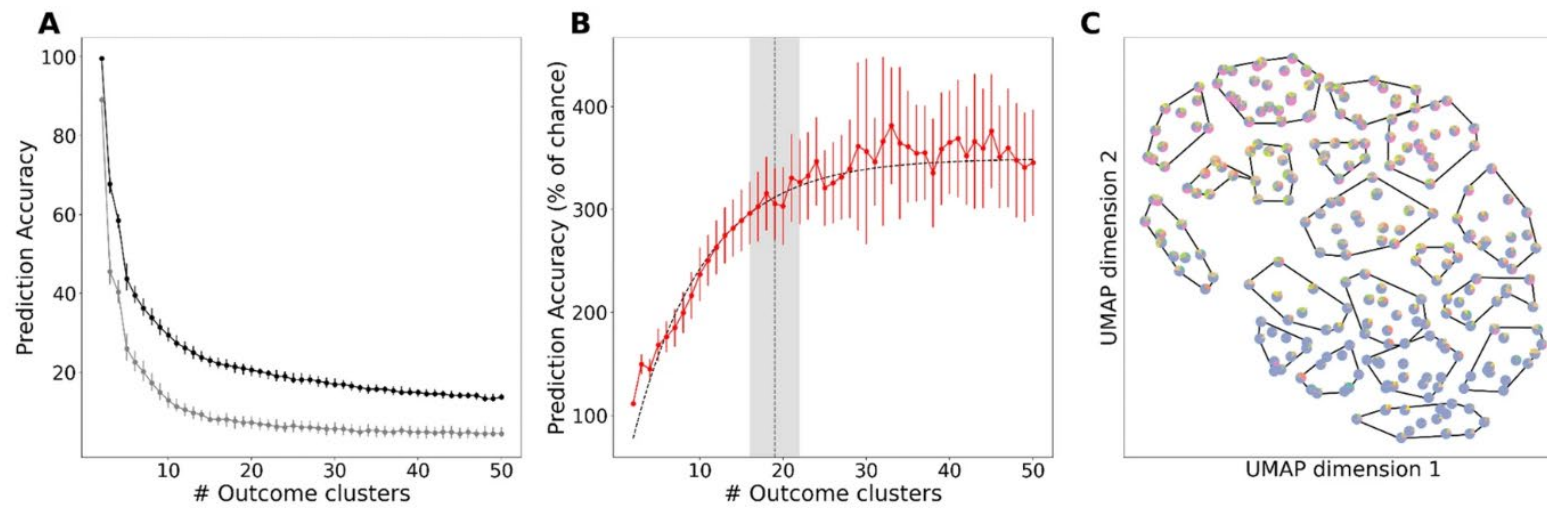
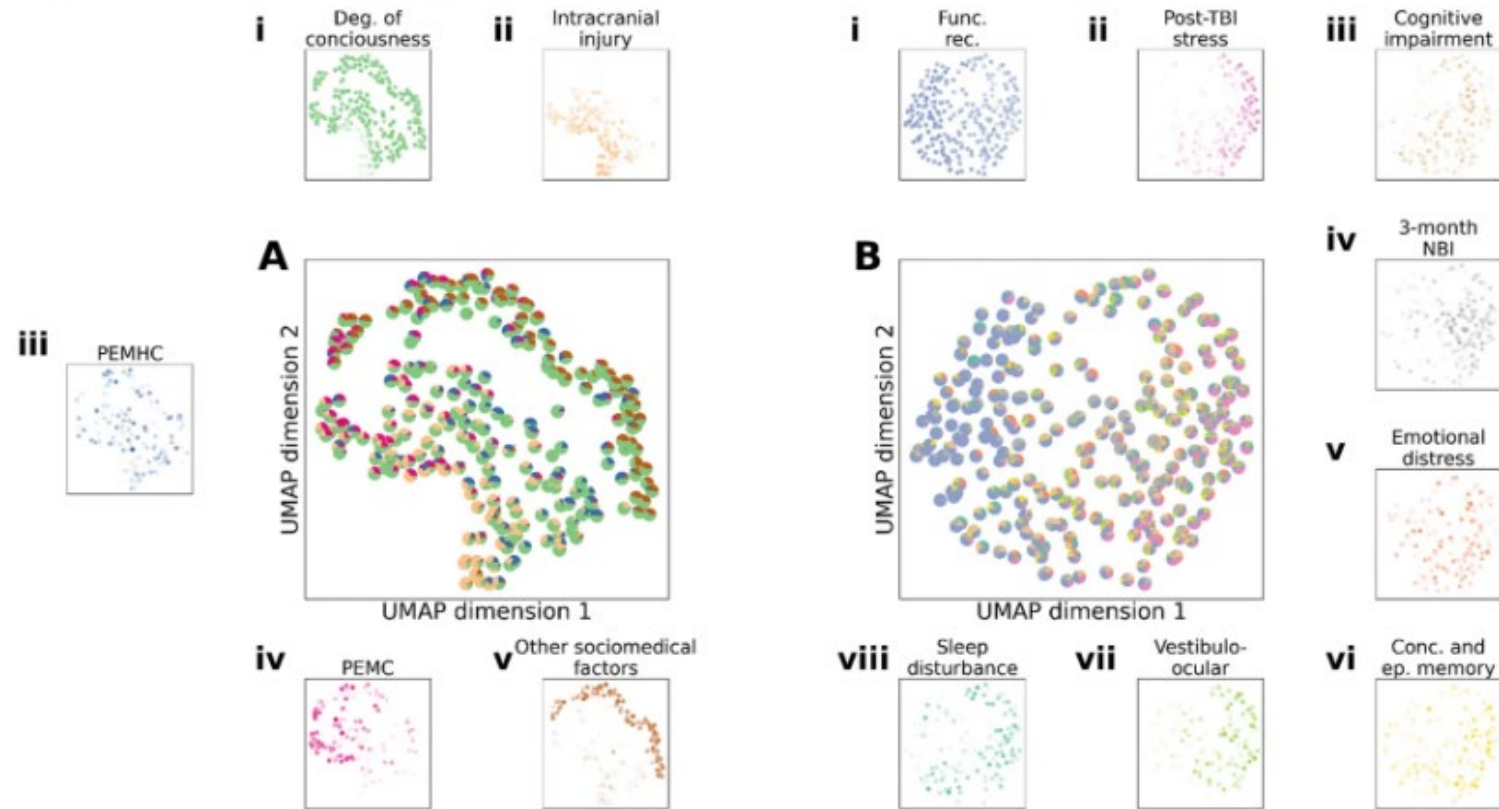
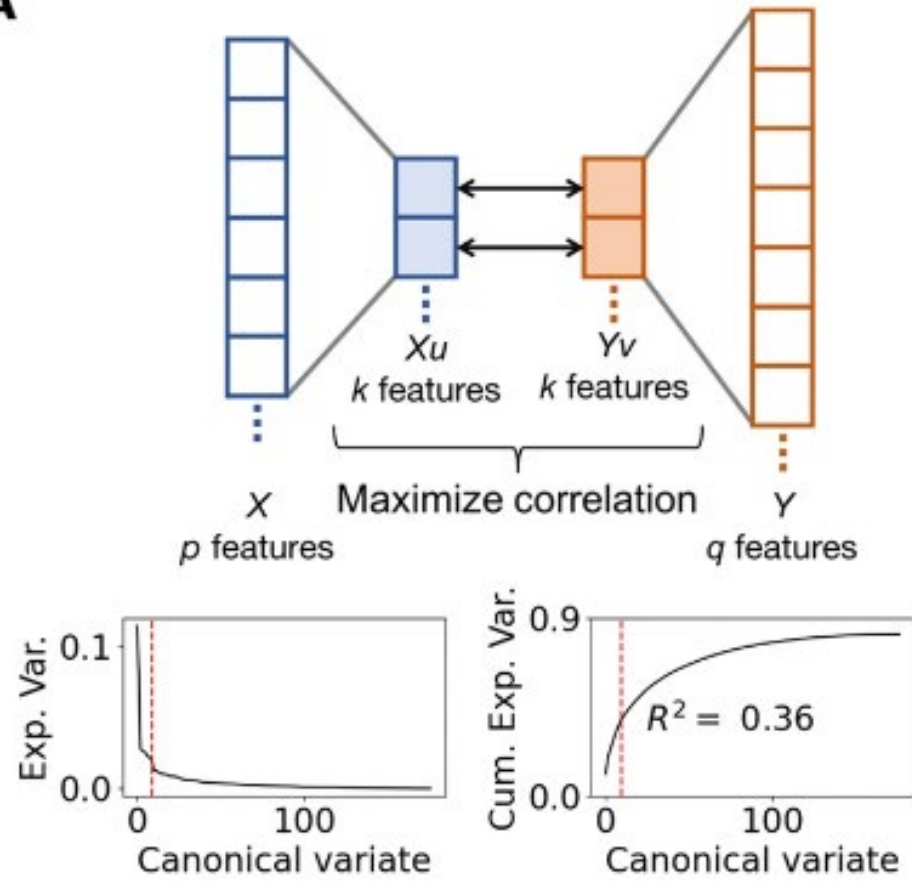
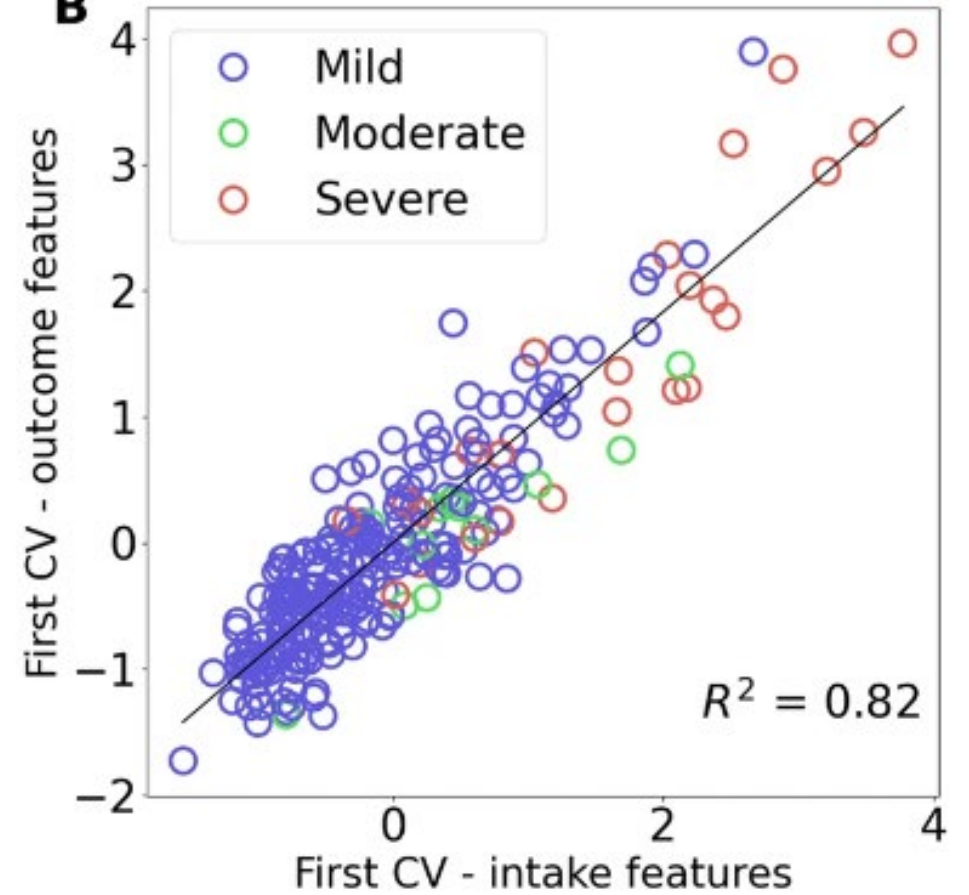


Figure 3

From: [Data-driven distillation and precision prognosis in traumatic brain injury with interpretable machine learning](#)



A**B**

Mixture Model Framework for Traumatic Brain Injury Prognosis Using Heterogeneous Clinical and Outcome Data

Alan D. Kaplan , *Member, IEEE*, Qi Cheng, *Senior Member, IEEE*,
K. Aditya Mohan , *Senior Member, IEEE*, Lindsay D. Nelson, Sonia Jain , Harvey Levin,
Abel Torres-Espin , Austin Chou , J. Russell Huie, Adam R. Ferguson, Michael McCrea,
Joseph Giacino , Shivshankar Sundaram, Amy J. Markowitz, and Geoffrey T. Manley

Mixture Model Framework for Traumatic Brain Injury Prognosis Using Heterogeneous

www.nature.com/scientificreports

scientific reports



OPEN

Refining outcome prediction after traumatic brain injury with machine learning algorithms

D. Bark¹, M. Boman^{2,3}, B. Depreitere⁴, D. W. Wright⁵, A. Lewén¹, P. Enblad¹, A. Hånell^{1,7} & E. Rostami^{1,6,7}✉

**OK, but what about real world
implementation of prediction models?**

Effectiveness of Computerized Decision Support Systems Linked to Electronic Health Records: A Systematic Review and Meta-Analysis

Lorenzo Moja, MD, MSc, PhD, Koren H. Kwag, BSc, MSc, Theodore Lytras, MD, MPH, Lorenzo Bertizzolo, MD, Linn Brandt, MD, Valentina Pecoraro, BSc, Giulio Rigon, MD, MSc, Alberto Vaona, MD, MSc, Francesca Ruggiero, BA, MA, Massimo Mangia, Alfonso Iorio, MD, PhD, Ilkka Kunnamo, MD, PhD, and Stefanos Bonovas, MD, MSc, PhD

e12 | Systematic Review | Peer Reviewed | Moja et al.

American Journal of Public Health | December 2014, Vol 104, No. 12

Twenty-eight RCTs were included (N = 37,395 patients)

“A statistically significant effect [of Decision Support Systems] were evident in the prevention of morbidity, any disease.”

RESEARCH

Electronic Health Record Technology Designed for the Clinical Encounter

MS NeuroShare

Riley Bove, MD, MMSc, Christa A. Bruce, MPH, Chelsea K. Lunders, MA, Jennifer R. Pearce, MPA, Jacqueline Liu, BS, Erica Schleimer, BS, Stephen L. Hauser, MD, Walter F. Stewart, PhD, and J.B. Jones, PhD

Correspondence

Dr. Bove
Riley.Bove@ucsf.edu

Neurology: Clinical Practice August 2021 vol. 11 no. 4 318-326 doi:10.1212/CPJ.0000000000000986

“In neurologic care, insights generated from research must be brought from academic centers to clinics and transformed into actionable information to enable patient-centered care.”

A

MS SHARE

Patient
Sex
Age
Marital Status
Insurance
Age of Onset
MS Type
MS Status
Last Visit with Me
Welcome

21
RRMS
Active Progressive

MS Management

Clinician Entered
MS Activity

Age of Onset: 21
MS Type: Relapsing-Remitting
MS Status: Active Progressive

Clinician Entered
Karla's Reported Relapses

Patient Reported Date	Clinician Confirmed
Mid May 2016	Yes ☒ No ☐
Late Aug 2016	Yes ☒ No ☐
Late Feb 2016	Yes ☐ No ☒

Electronic Health Record
Imaging

Image Type	Ordered	Link to Image
Image Type 01	10/18/16	See Image
Image Type 02	10/18/16	See Image
Image Type 03	10/18/16	See Image
Image Type 04	10/18/16	See Image

Electronic Health Record
Disease Modifying Therapy

	Name	Route	Ordered	Patient Reported Start
Current	COPAXONE	Injectable	11/16/16	Mid Nov 2016
Last	TECFIDERA	Oral	05/16/17	Late May 2017

Electronic Health Record
Labs

Lab Test	Result Value	Normal Range	Result Date
	Hematocrit (%)	44	4.5 - 11.0
White Blood Cells (K/uL)	6.7	14 - 46	06/02/18
Lymphocyte (c/uL)	860	850 - 2000	06/02/18
Platelet Count (K/uL)	268	140 - 415	06/02/18
Aspartate Amino (IU/L)	62	0 - 40	06/02/18
Alanine Transferase (IU/L)	58	0 - 40	06/02/18
Thyroid-sti. Hormone (uIU/mL)	6.2	0.35 - 5.5	06/02/18
Vitamin D (ng/mL)			
Anti - JCV (IU/ML)			
Anti - VZV (IU/ML)			
OCB			
IgG Index			

Electronic Health Record
Vitamin D

Ordered	Patient Reported
02/02/15	03/10/15

Electronic Health Record
Important Vaccinations

Name	Ordered
Influenza (Flu)	02/02/08
Varicella	10/15/95
Zoster	02/02/08
Hepatitis B	10/15/00

Patient Reported
Karla's Concerns

RELAPSES ☒
NEED A REFILL ☒
MEDICATION CONCERNS ☐
OUT OF RANGE SYMPTOMS
Tingling / Numbness ☐
Bowel ☐
Arm Use ☒
OTHER
My insurance changed ☐
Is there new research? ☐

Decision Support
MD Tips

A

MS SHARE Patient Sex Age Marital Status Insurance Age of Onset 21 MS Type RRMS MS Status Active Progressive Last Visit with Me Welcome

MS Management

Clinician Entered

MS Activity

Age of Onset: 21

MS Type: Relapsing-Remitting

MS Status: Active Progressive Update

Clinician Entered

Karla's Reported Relapses

Patient Reported Date	Clinician Confirmed
Mid May 2016	Yes ☒ No ☐
Late Aug 2016	Yes ☒ No ☐
Late Feb 2016	Yes ☐ No ☒

Graph It

Electronic Health Record

Imaging

Image Type	Ordered	Link to Image
Image Type 01	10/18/16	See Image
Image Type 02	10/18/16	See Image
Image Type 03	10/18/16	See Image
Image Type 04	10/18/16	See Image

Electronic Health Record

Disease Modifying Therapy

	Name	Route	Ordered	Patient Reported Start
Current	COPAXONE	Injectable	11/16/16	Mid Nov 2016
Last	TECFIDERA	Oral	05/16/17	Late May 2017

Electronic Health Record

Labs

Patient Reported

Karla's Concerns

RELAPSES ☒

NEED A REFILL ☒

MEDICATION CONCERNS ☐

OUT OF RANGE SYMPTOMS ☐

Tingling / Numbness ☐

B

neuroSHARE Patient Sex Age Marital Status Insurance Age of Onset 21 MS Type RRMS MS Status Active Progressive Last Visit with Me

MS Related

Remove Virtual Caseload

2015 2016 2017

Today

Imaging

Study	Ordered	See Data
Brain W Contrast	08/05/15	
Cervical Spine W/O Contrast	08/05/15	
Thoracic Spine W/O Contrast	08/05/15	

EDSS Score

2.0 2.5 2.5 3.0 3.5

Vitamin D2 ... Vitamin D3 ...

Rebif ... Tysabri ... Tecfidera ...

Today's Actions

- ☐ Need a refill
- ☒ Medication concerns
- ☐ New workforce Accommodation need

MS Related Care

- ☒ Review relapses
- ☒ Review MRI Images
- ☒ Review symptom status
- ☒ Review MS type/status
- ☒ Review DMTs
- ☐ Review monitoring labs
- ☐ Review Vitamin D
- ☐ Review other related meds
- ☐ Review symptoms referrals

Journal of the American Medical Informatics Association, 29(3), 2022, 424–434

<https://doi.org/10.1093/jamia/ocab270>

Advance Access Publication Date: 16 December 2021

Research and Applications



OXFORD

Research and Applications

Embedding electronic health records onto a knowledge network recognizes prodromal features of multiple sclerosis and predicts diagnosis

Charlotte A. Nelson^{1,2}, Riley Bove ³, Atul J. Butte^{2,4}, and Sergio E. Baranzini ^{1,2,3}

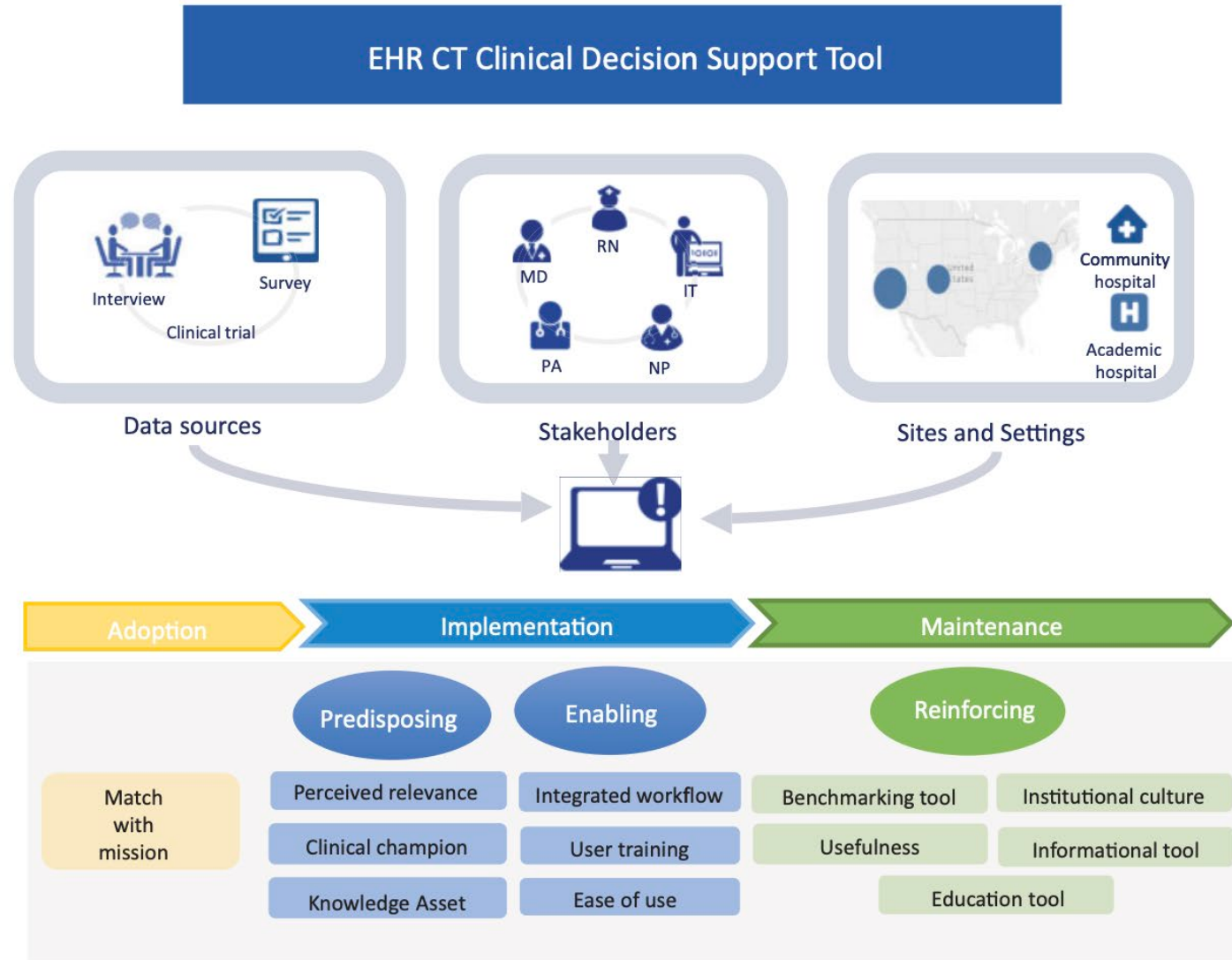
**OK, but what about real world
implementation *in TBI*?**

Applying the RE-AIM Framework for the Evaluation of a Clinical Decision Support Tool for Pediatric Head Trauma: A Mixed-Methods Study

Ruth M. Masterson Creber¹ Peter S. Dayan² Nathan Kuppermann³ Dustin W. Ballard^{4,5}
 Leah Tzimenatos³ Evaline Alessandrini⁶ Rakesh D. Mistry⁷ Jeffrey Hoffman⁸ David R. Vinson^{5,9}
 Suzanne Bakken^{10,11} for the Pediatric Emergency Care Applied Research Network (PECARN) and the
 Clinical Research on Emergency Services and Treatments (CREST) Network

Applying the RE-AIM Clinical Decision Support Tool Trauma: A Mixed-Methods Study

Ruth M. Masterson Creber¹ Peter S. Lehmann² Leah Tzimenatos³ Evaline Alessandri⁴ Suzanne Bakken^{10,11} for the Pediatric Clinical Research on Emergency Services (PACES) Study Group



Individual QI projects from single institutions

OPEN

Quality Improvement in Pediatric Head Trauma with PECARN Rules Implementation as Computerized Decision Support

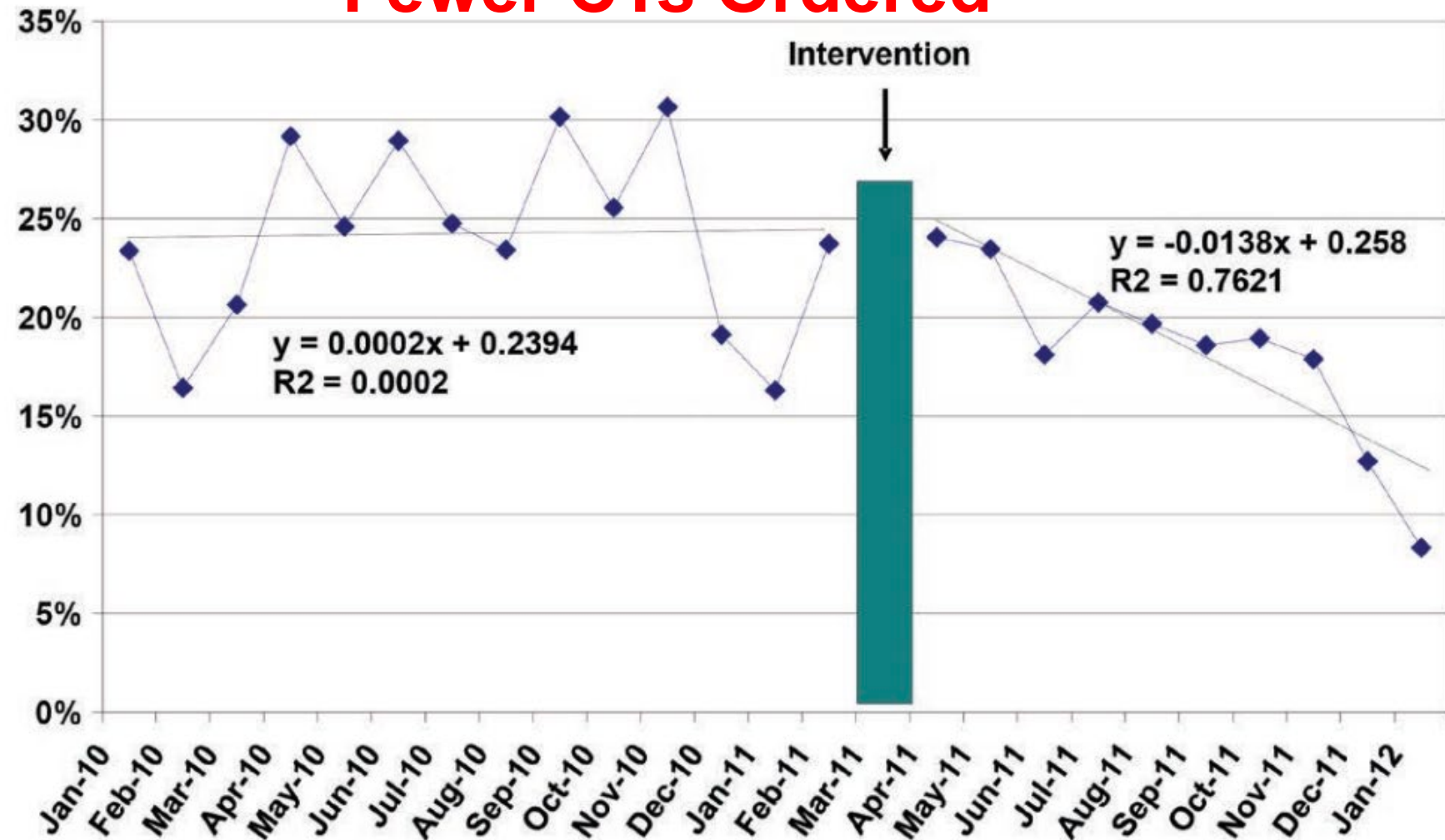
Shireen M. Atabaki, MD, MPH†; Brian R. Jacobs, MD*†; Kathleen M. Brown, MD*†; Samira Shahzeidi, BS*; Nia J. Heard-Garris, MD*†; Meghan B. Chamberlain*; Robert M. Grell, BS*†; and James M. Chamberlain, MD*†*

Individual

Quality
with
Comp

Shireen M.
Samira Sh
and James

Fewer CTs Ordered



Individual QI projects from single institutions

OPEN

Quality Improvement in Pediatric Head Trauma with PECARN Rules Implementation as Computerized Decision Support

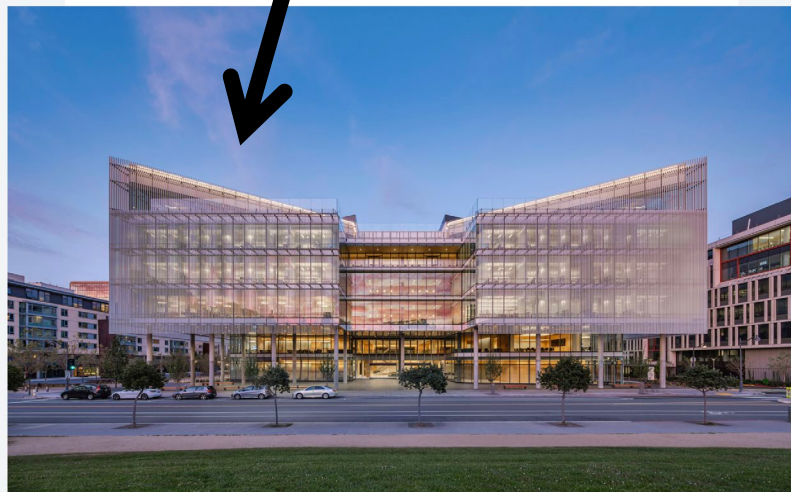
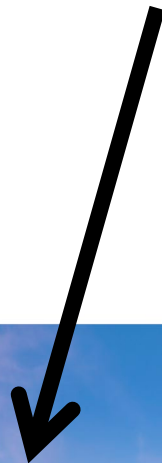
Shireen M. Atabaki, MD, MPH†; Brian R. Jacobs, MD*†; Kathleen M. Brown, MD*†; Samira Shahzeidi, BS*; Nia J. Heard-Garris, MD*†; Meghan B. Chamberlain*; Robert M. Grell, BS*†; and James M. Chamberlain, MD*†*

- Fewer CTs Ordered
- No significant change in the rate of return visits to the ED within 7 days.
- None of these returns was associated with a missed diagnosis

Key Takeaways

- Statistical models for predicting TBI outcomes are being developed using large datasets.
- Machine learning approaches can integrate various data sources to improve TBI prediction.
- The implementation of these technologies in electronic health records (EHRs) is key for clinical translation.
- The EHR may be used to educate physicians about TBI and guide their decision-making through clinical decision support pathways

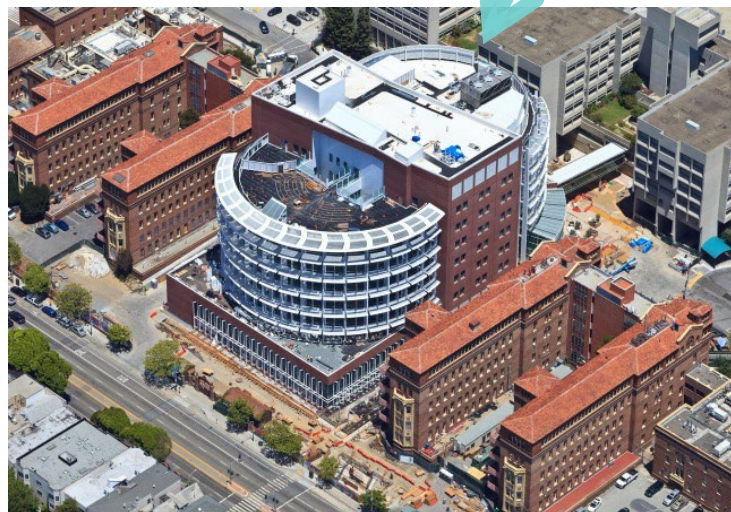
Weill Neurohub



The UCSF Weill Neurosciences Building. Photo by Tim Griffith

UCSF Weill Institute for
Neurosciences

Brain and Spinal
Injury Center



ZUCKERBERG
SAN FRANCISCO GENERAL
Hospital and Trauma Center



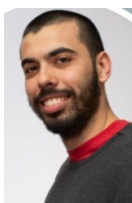
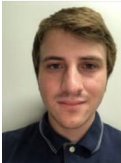
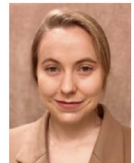
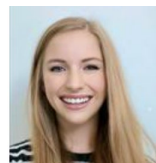
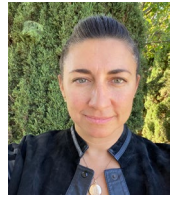


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Funding

US National Institutes of Health (NIH): R01NS088475, R01CA213441, R01AG056770, R01MH116156, R01NS122888; U01NS086090, P30AR066262, UH3NS106899, U19AR076737; U24NS122732
US Veterans Affairs: 1I01RX002245, 1I01RX002787, 1I01BX005871, 1I01BX005878
US Department of Defense: SC150198, SC150177
US DARPA
US Department of Energy
Craig H. Neilsen Foundation
Wings for Life Foundation
UC Noyce Initiative