

Delivering on the NASEM TBI Consensus Recommendation No. 1:

The NIH-NINDS CBI-M Framework for Characterization of Acute TBI

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National Institute of
Neurological Disorders
and Stroke

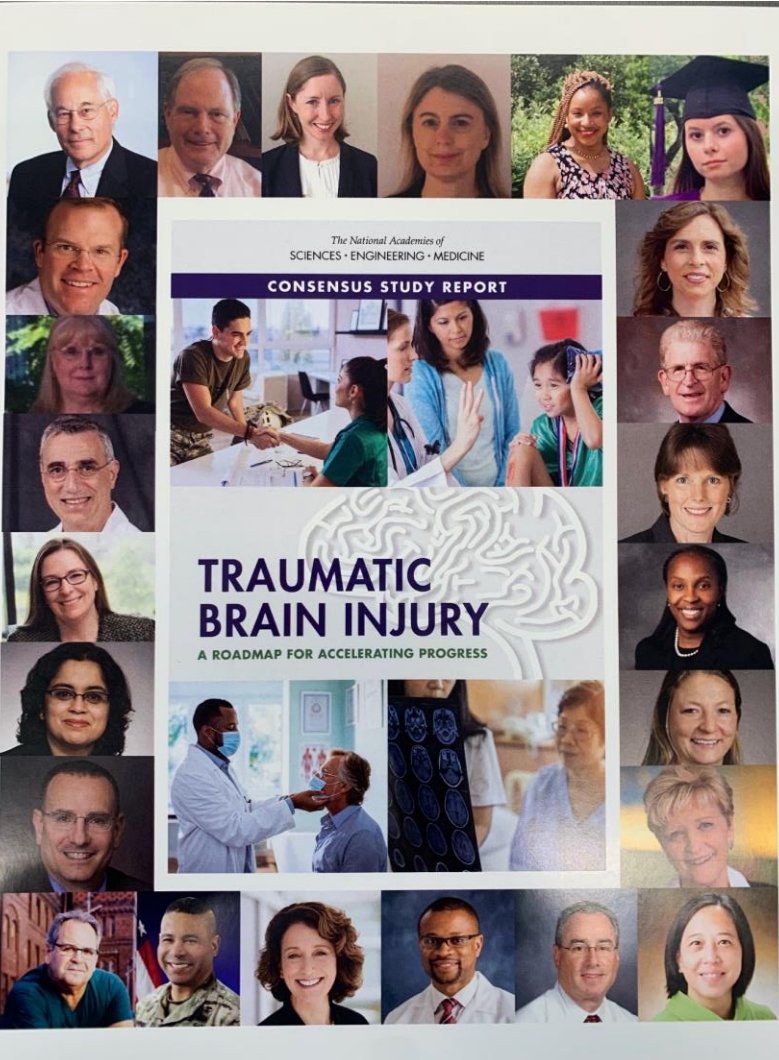


DISCLOSURES

- Dr. McCrea and the Center for Neurotrauma Research (CNTR) at Medical College of Wisconsin (MCW) receive funding from:
 - National Institutes of Health (NIH)
 - U.S. Department of Defense (DoD)
 - U.S. Department of Veterans Affairs (VA)
 - Centers for Disease Control and Prevention (CDC)
 - National Collegiate Athletic Association (NCAA)
 - National Football League (NFL)
 - Abbott Laboratories
 - MCW Clinical Translational Science Institute (CTSI)
 - Private foundations and philanthropic support
- Consultant to the Green Bay Packers, Milwaukee Brewers, Milwaukee Bucks, NFL Neurocognitive Testing Program (WoC)
- Travel support and speaker honorariums for professional activities.



NASEM: TBI a Roadmap for Accelerating Progress



1

Create and implement an **updated classification system** for TBI.

2

Integrate **acute** and **long-term** person- and family-centered **management** of TBI.

3

Reduce unwarranted **variability** and **gaps** in administrative and clinical **care guidance** to assure high quality care for TBI.

4

Enhance **awareness** and **identification** of TBI by healthcare providers and the public.

5

Establish and reinforce local and regional **integrated care delivery systems** for TBI.

6

Integrate the TBI system of **care** with TBI **research** into a **learning system**.

7

Improve the quality and **expand** the range of **TBI studies** and **study designs**.

8

Create and **promulgate** a **national framework** and **plan** for improvement of TBI care.

Commissioned by US Dept. of Defense (2022)



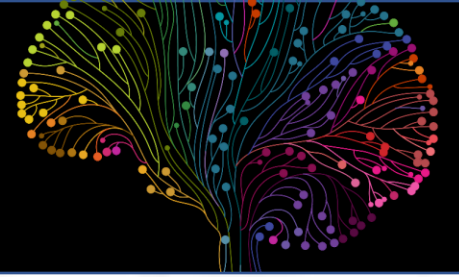
AIMS: This is the next step to leverage the findings over the past decade to move beyond mild, moderate, and severe TBI

- Produce a more precise framework for TBI Characterization, which will be validated and disseminated
- Identify current gaps and research topics that may inform refinement and updating of the new framework for TBI Characterization

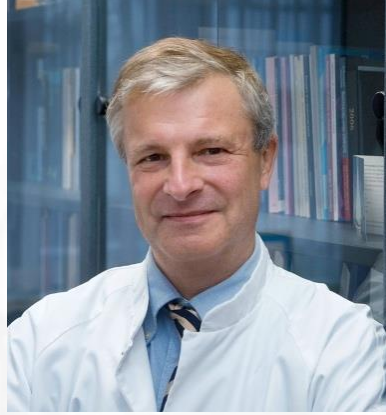
***Development & Implementation of a Global Solution for
Multi-Dimensional TBI Characterization***

MOVING US BEYOND “MILD, MODERATE, SEVERE”

WORKSHOP STEERING COMMITTEE



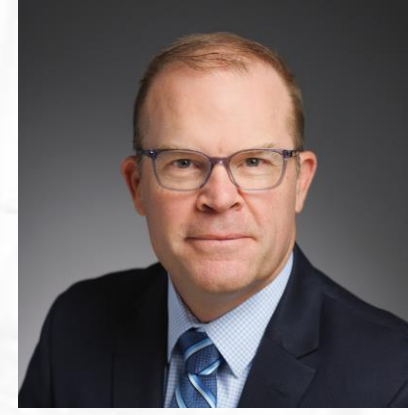
Kristen Dams O'Connor



Andrew Maas



Geoffrey Manley



Michael McCrea



Nsini Umoh

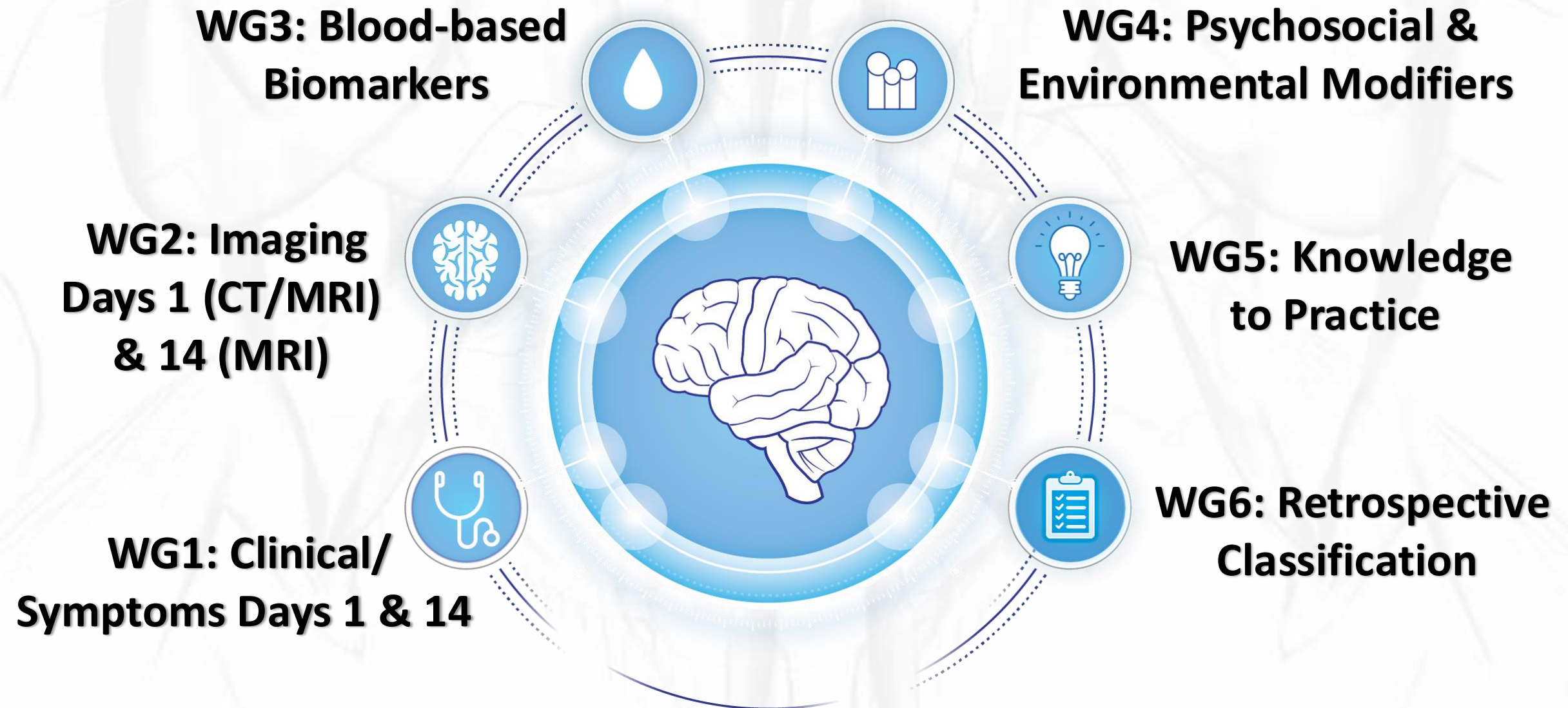
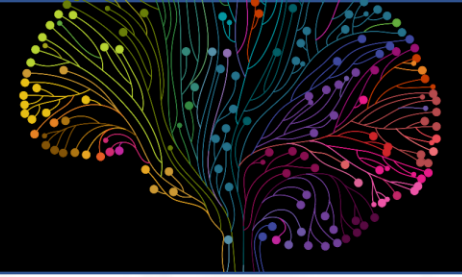


Hibah Awwad

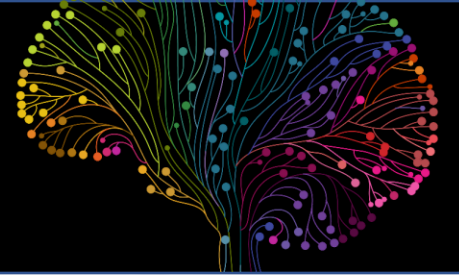


Adele Doperalski

WORKING GROUPS



WORKING GROUPS



WORKING GROUP CHAIRS

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Henrik Zetterberg
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CBI-M: Multi-Dimensional Framework for Characterization of Acute TBI



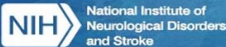
A new characterisation of acute traumatic brain injury: the NIH-NINDS TBI Classification and Nomenclature Initiative

Geoffrey T Manley*, Kristen Dams-O'Connor*, Michael L Alosco, Hibah O Awwad, Jeffery J Bazarian, Peter Bragge, John D Corrigan, Adele Doperski, Adam R Ferguson, Christine L Mac Donald, David K Menon, Molly M McNett, Joukje van der Naalt, Lindsay D Nelson, Dana Piscià, Noah D Silverberg, Nsini Umoh, Lindsay Wilson, Esther L Yuh, Henrik Zetterberg, Andrew I R Maas†, Michael A McCreath‡, on behalf of the members of the NIH-NINDS TBI Classification and Nomenclature Initiative‡

Lancet Neurol 2025; 24: 512-23
See [Comment](#) page 475
*Joint first author
†Joint last author
‡Members are listed in the appendix (pp 7-9)
Neurological Surgery, University of California, San Francisco, CA, USA
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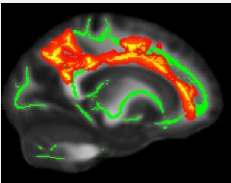
The clinical severity of traumatic brain injury (TBI) is commonly classified according to the Glasgow Coma Scale (GCS) sum score as mild (13-15), moderate (9-12), or severe (3-8). A new approach is needed for characterising TBI more accurately. In 2022, the US National Institutes of Health-National Institute of Neurological Disorders and Stroke launched an international initiative to address this need, with a focus on the acute phase of injury. Six working groups of TBI experts, implementation scientists, people with lived experience, and federal partners were established, involving 94 participants from 14 countries. The proposed new framework for the characterisation of acute TBI incorporates four pillars: a clinical pillar (full GCS and pupillary reactivity); a biomarker pillar (blood-based measures); an imaging pillar (pathoanatomical measures); and a modifier pillar (features influencing clinical presentation and outcome; CBI-M). The CBI-M framework provides a multidimensional characterisation of TBI to inform individualised clinical management and to improve scientific rigor. Research priorities include validation of the CBI-M framework, evaluation of its applicability beyond the acute phase of TBI, and strategies for clinical implementation.

APPLICATION IN CLINICAL CARE *and* RESEARCH



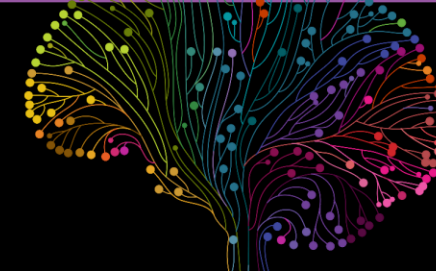
NINDS Traumatic Brain Injury (TBI) Classification and Nomenclature Workshop January 22-23, 2024 | NIH Campus | Bethesda, MD

NEW SYSTEM FOR CHARACTERIZATION TBI



C	CLINICAL
B	BIOMARKERS
I	IMAGING
M	MODIFIERS

C: CLINICAL PILLAR



Clinical Assessment on Days 1–14 for the Characterization of Traumatic Brain Injury: Recommendations from the 2024 NINDS Traumatic Brain Injury Classification and Nomenclature Initiative Clinical/Symptoms Working Group

David K. Menon,^{1,*} Noah D. Silverberg,^{2–4} Adam R. Ferguson,^{5,6} Thomas J. Bayuk,⁷ Shubhayu Bhattacharyay,⁸ David L. Brody,⁹ Scott A. Cota,^{10,†} Ari Ercole,¹¹ Anthony Figaji,¹² Guoyi Gao,¹³ Christopher C. Giza,^{14,15} Fiona Lecky,¹⁶ Rebekah Mannix,¹⁷ Ana Mikolic,¹⁸ Kasey E. Moritz,¹⁹ Claudia S. Robertson,²⁰ Abel Torres-Espin,^{21,22} Spyridoula Tsetou,²³ John K. Yue,²⁴ Hibah O. Awad,²⁵ Kristen Dams-O'Connor,^{26,27} Adele Doperalski,²⁸ Andrew I.R. Maas,^{29,30} Michael A. McCrea,³¹ Nnsini Umoh,³² and Geoffrey T. Manley³³

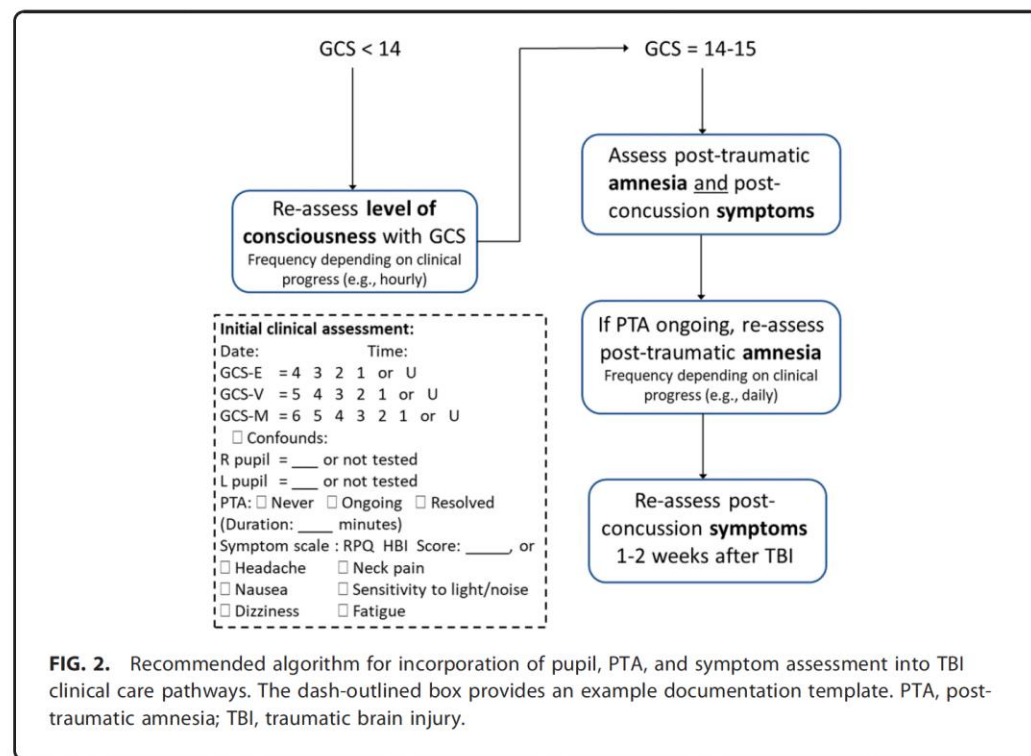


FIG. 2. Recommended algorithm for incorporation of pupil, PTA, and symptom assessment into TBI clinical care pathways. The dash-outlined box provides an example documentation template. PTA, post-traumatic amnesia; TBI, traumatic brain injury.

Basic clinical components

GCS score	GCS components
15	Eye:
14	☐ Spontaneous (4)
13	☐ To sound (3)
12	☐ To pressure (2)
11	☐ None (1)
10	☐ Untestable (u)
9	Verbal:
8	☐ Orientated (5)
7	☐ Confused (4)
6	☐ Words (3)
5	☐ Sounds (2)
4	☐ None (1)
3	☐ Untestable (u)
	Motor:
	☐ Obeys commands (6)
	☐ Localising (5)
	☐ Normal flexion (4)
	☐ Abnormal flexion (3)
	☐ Extension (2)
	☐ None (1)
	☐ Untestable (u)

Pupillary reactivity score

- ☐ Both pupils are reactive
- ☐ One pupil is reactive
- ☐ Both pupils are non-reactive

Expanded clinical components

Injury signs

- Post-traumatic amnesia
- Loss of consciousness
- Altered mental state

Standardised clinical assessment

- Symptoms
- Cognitive function*
- Vestibular-ocular function*
- Balance*

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GCS as Anchor of CBI-M

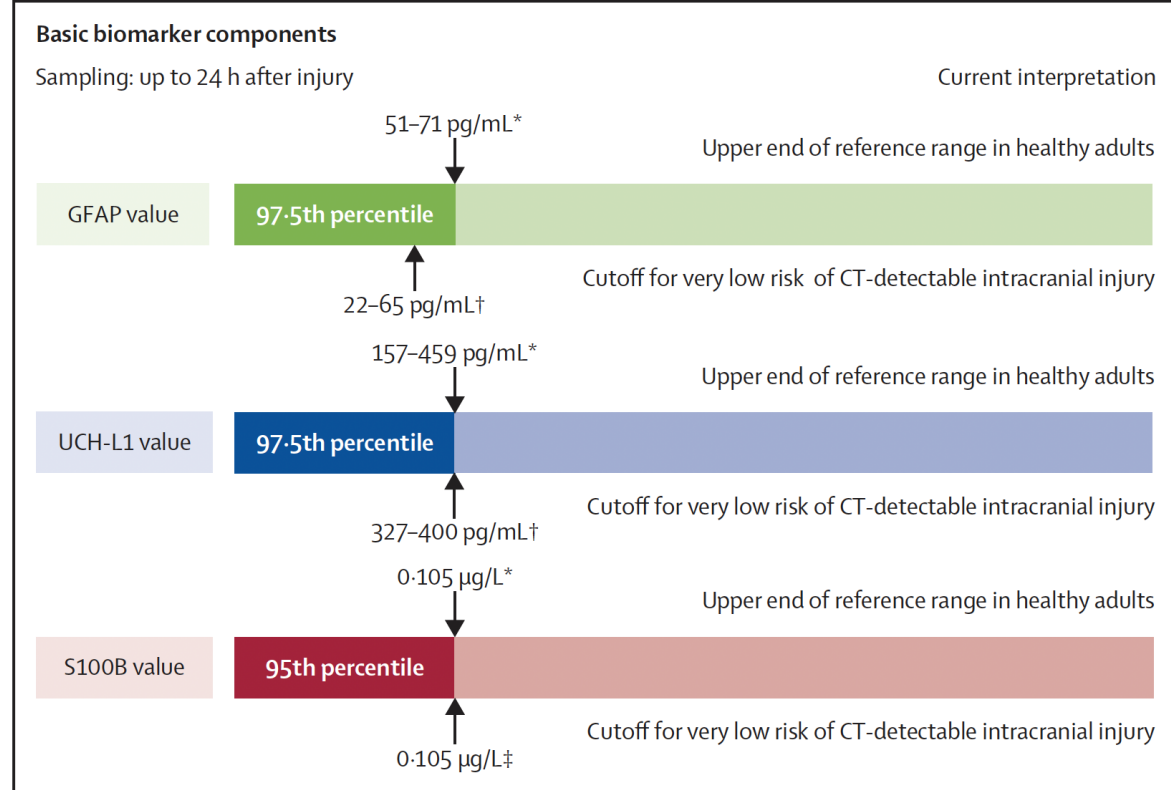
B: BIOMARKER PILLAR

Blood-Based Biomarkers for Improved Characterization of Traumatic Brain Injury: Recommendations from the 2024 National Institute for Neurological Disorders and Stroke Traumatic Brain Injury Classification and Nomenclature Initiative Blood-Based Biomarkers Working Group

Jeffrey J. Bazarian,^{1,*} Henrik Zetterberg,² András Buki,³ Bradley A. Dengler,⁴ Ramon Diaz-Arrastia,⁵ Frederick K. Korley,⁶ Rachel Lazarus,⁷ Timothy B. Meier,⁸ Stefania Mondello,⁹ Kasey Moritz,¹⁰ David O. Okonkwo,¹¹ Linda Papa,¹² James B. Phillips,¹⁰ Jussi P. Posti,¹³ Ava M. Puccio,¹¹ Stephanie Sloley,¹⁴ Ewout Steyerberg,¹⁵ Kevin K. Wang,^{16,17} Hibah O. Awwad,¹⁸ Kristen Dams-O'Connor,^{19,20} Adele Doperalski,²⁰ Andrew I.R. Maas,^{21,22} Michael A. McCrea,⁸ Nsini Umoh,²⁰ and Geoffrey T. Manley²³

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Biomarkers

- Neurology
- Neurotrauma
- Stroke
- Multiple Sclerosis
- Seizures
- Melanoma (S100B)

**Leveraging Advances in
POC Testing**

I: IMAGING PILLAR

Neuroimaging Characterization of Acute Traumatic Brain Injury with Focus on Frontline Clinicians: Recommendations from the 2024 National Institute of Neurological Disorders and Stroke Traumatic Brain Injury Classification and Nomenclature Initiative Imaging Working Group

Christine L. Mac Donald,^{1,†,*} Esther L. Yuh,^{2,†} Thijs Vande Vyvere,³ Brian L. Edlow,^{4,5} Lucia M. Li,⁶ Andrew R. Mayer,⁷ Pratik Mukherjee,² Virginia F.J. Newcombe,⁸ Elisabeth A. Wilde,^{9,10} Inga K. Koerte,¹¹ Deborah Yurgelun-Todd,¹² Yu-Chien Wu,¹³ Ann-Christine Duhaime,¹⁴ Hibah O. Awwad,¹⁵ Kristen Dams-O'Connor,^{16,17} Adele Doperalski,¹⁵ Andrew I.R. Maas,^{18,19} Michael A. McCrea,²⁰ Nsini Umoh,¹⁵ and Geoffrey T. Manley²¹

Basic imaging components

☐ Clinically not indicated

☐ No abnormalities detected

Acute TBI pathology:

- ☐ Epidural haematoma
- ☐ Subdural haematoma
- ☐ Traumatic subarachnoid haemorrhage
- ☐ Contusion
- ☐ Intracerebral haematoma
- ☐ Traumatic axonal and microvascular injury
- ☐ Intraventricular haemorrhage

☐ Skull fracture

Acute imaging studies:

- ☐ CT
- ☐ MRI

Lesion volume (eg, epidural, subdural, or intracerebral haematoma):

- ☐ ≥25 mL
- ☐ <25 mL

Mass effect:

- ☐ Cisternal compression
- ☐ Ventricular compression
- ☐ Midline shift
- ☐ Herniation

Other:

- ☐ Evidence of recent craniotomy
- ☐ Penetrating traumatic injury
- ☐ Ventriculomegaly
- ☐ Vascular

☐ Chronic or incidental lesions

Expanded imaging components

Lesion:

- ☐ Location
- ☐ Volume (quantitative)

Skull fracture:

- ☐ Vault and linear
- ☐ Vault and depressed
- ☐ Basilar

Traumatic subarachnoid haemorrhage:

- ☐ Cortical
- ☐ Basal or posterior fossa

Mass effect:

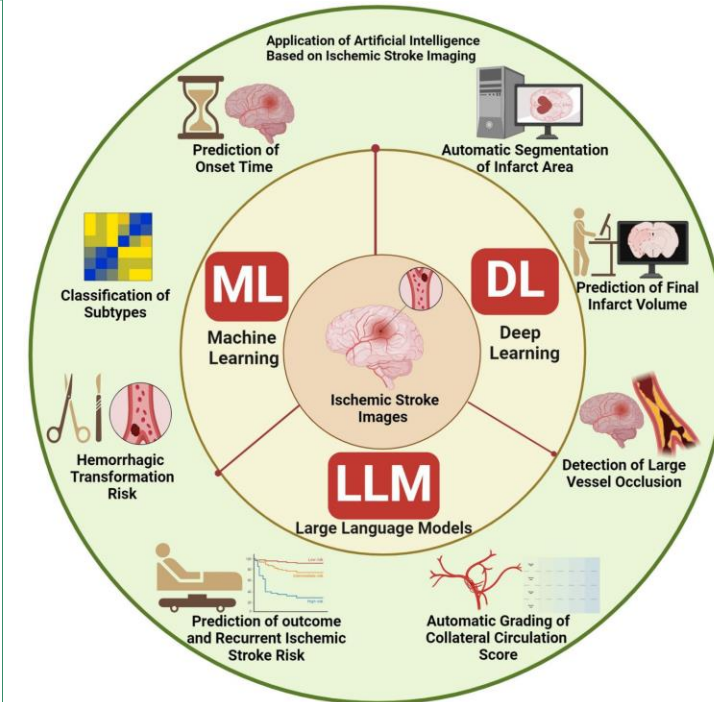
- ☐ Contributing factors other than intracranial haematoma
- ☐ Oedema
- ☐ Swelling

Vascular:

- ☐ Ischaemia
- ☐ Stroke
- ☐ Arterial dissection
- ☐ Traumatic pseudoaneurysm
- ☐ Venous sinus injury

Chronic or incidental lesions:

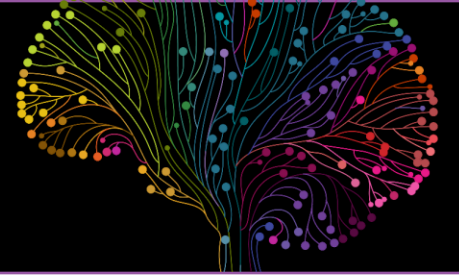
- ☐ Brain atrophy
- ☐ Focal encephalomalacia
- ☐ Enlarged perivascular spaces
- ☐ Chronic subdural haematoma or subdural effusion
- ☐ Non-traumatic haematoma
- ☐ Tumour
- ☐ Other incidental findings



Liu Y et al. (2024). Front. Neurol

Leveraging Modern AI Tools & Informatics Platforms in Clinical Workflow

M: MODIFIER PILLAR



Toward More Holistic Early Traumatic Brain Injury Evaluation and Care: Recommendations from the 2024 National Institute of Neurological Disorders and Stroke Traumatic Brain Injury Classification and Nomenclature Initiative Psychosocial and Environmental Modifiers Working Group

Lindsay D. Nelson,^{1,*} Lindsay Wilson,² Jennifer S. Albrecht,³ David B. Arciniegas,⁴ Ernest J. Barthélemy,⁵ Sarah N. Fontaine,⁶ Raquel C. Gardner,⁷ Shannon B. Juengst,⁸ Monique R. Pappadis,⁹ Jennie Ponsford,¹⁰ Danny G. Thomas,¹¹ Keith Owen Yeates,¹² Kristin Dams-O'Connor,¹³ Geoffrey T. Manley,¹⁴ Andrew I.R. Maas,¹⁵ Michael A. McCrea,¹⁶ Hibah O. Awwad,¹⁷ Adele Doperalski,¹⁷ and Nsini Umoh¹⁷

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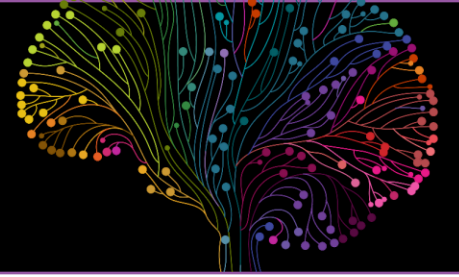
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Basic modifier components

Injury factors	• Mechanism of injury • Comorbid extracranial injury • Secondary insults • Early post-traumatic seizure • Stressful circumstances
Patient factors	• Age • Sex • Medical history and medication • Mental health condition • Developmental history • TBI history • Language or communication barrier
Community and society factors	• Social disadvantage or deprivation • No or partial health-care insurance

It's About Injury, Who Comes to Injury, & Response to Injury

CBI-M: REAL WORLD DATA

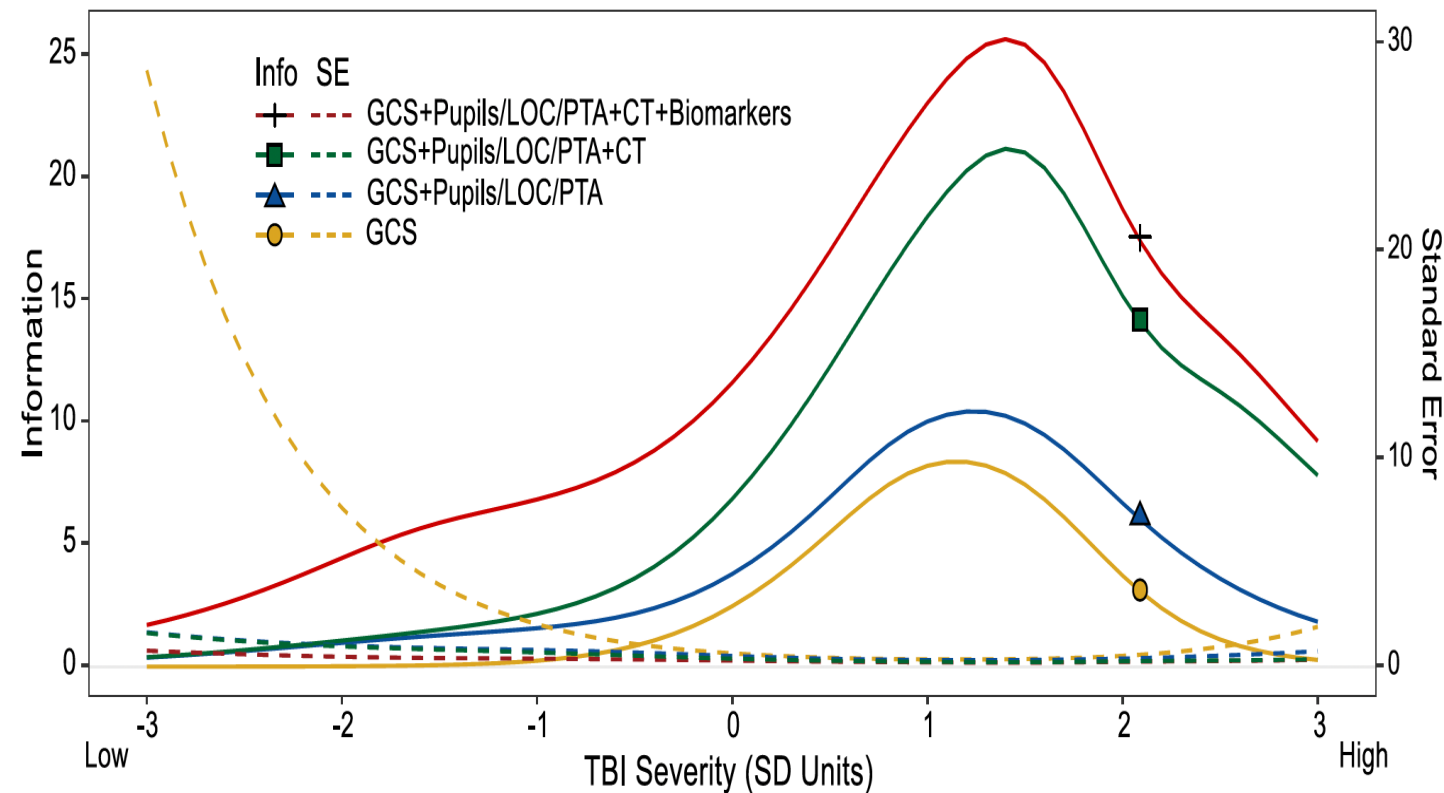


IMPROVED CHARACTERIZATION OF TBI SEVERITY

Beyond mild, moderate, and severe traumatic brain injury:
modelling severity from clinical, neuroimaging, and
blood-based indicators

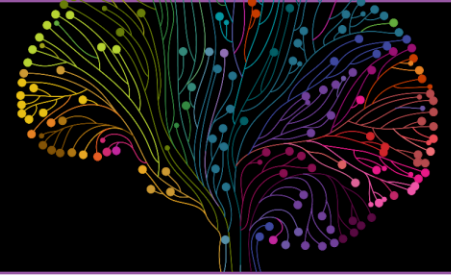
Lindsay D. Nelson,^{a,*} Brooke E. Magnus,^b John K. Yue,^c Steve Balsis,^d Christopher J. Patrick,^e Nancy Temkin,^f Esther L. Yuh,^g Ramon Diaz-Arrastia,^h
Ehri Ryu,^b Andrew I. R. Maas,ⁱ David K. Menon,^j Lindsay Wilson,^k and Geoffrey T. Manley,^c the TRACK-TBI Investigators^j, on behalf of the
CENTER-TBI Participants and Investigators^l

*Item response theory (IRT) to
develop a new method for
quantifying TBI severity using 24
clinical, head CT, and blood-based
biomarker variables familiar to
clinicians and researchers.*



ADDED VALUE OF MULTI-DIMENSIONAL CHARACTERIZATION OF TBI

CBI-M: REAL WORLD DATA



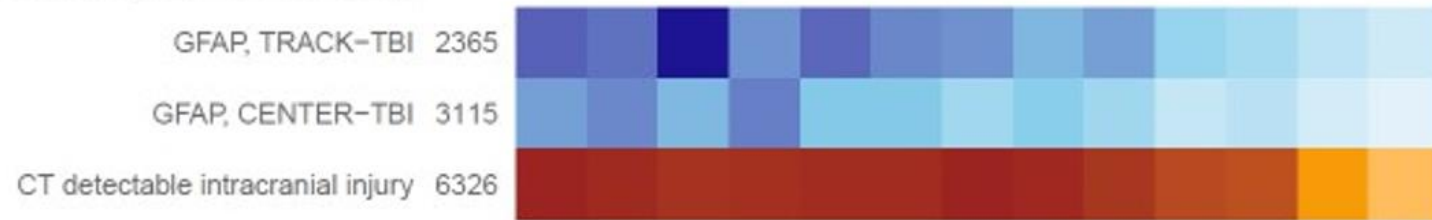
DIAGNOSTIC CHARACTERIZATION & PROGNOSTIC UTILITY:

Associations
Between CBI Pillar
Components in
CENTER-TBI and
TRACK-TBI

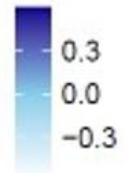
Clinical (GCS)
Biomarkers (GFAP)
Imaging (CT)

Clinical & Functional
Outcome

Blood-based biomarkers and imaging N



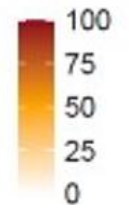
Median scaled
GFAP level
per score



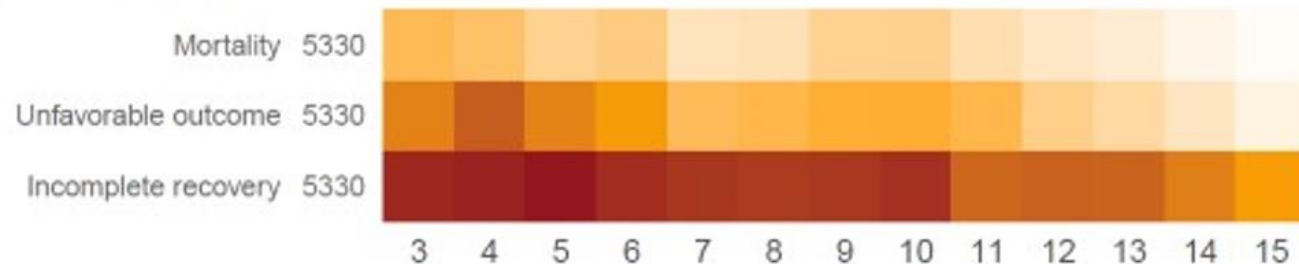
Clinical decision-making



Percentage
with endpoint
per score



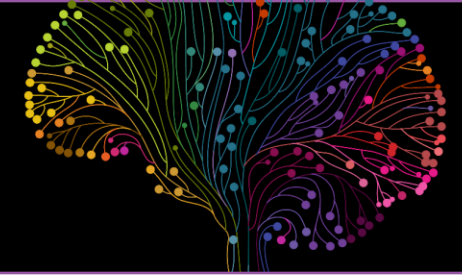
Clinical outcomes at 6 months



GCS Score

Foundational utility of GCS, Enhanced by Biomarkers & Imaging

CBI-M: REAL WORLD DATA



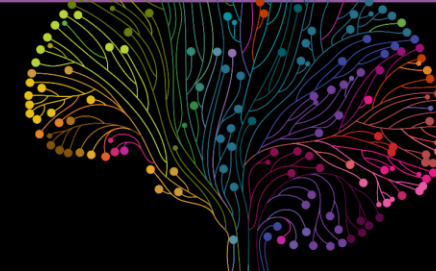
ADDED PROGNOSTIC VALUE

Discriminatory Performance (AUC) of CBI-M for TBI Endpoints

DIAGNOSTIC/CARE PATH	CENTER-TBI	TRACK-TBI
	FULL MODEL	FULL MODEL
CT Abnormalities	0.90	0.88
ICU Admission	0.94	0.92
ICP Monitoring	0.83	0.94
Major Intracranial Surgery	0.93	0.98
OUTCOME		
Mortality	0.92	0.95
Unfavorable Outcome (GOSE<5)	0.89	0.91

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CBI-M: REAL WORLD DATA



IMPROVED OUTCOME PREDICTION

General neurology

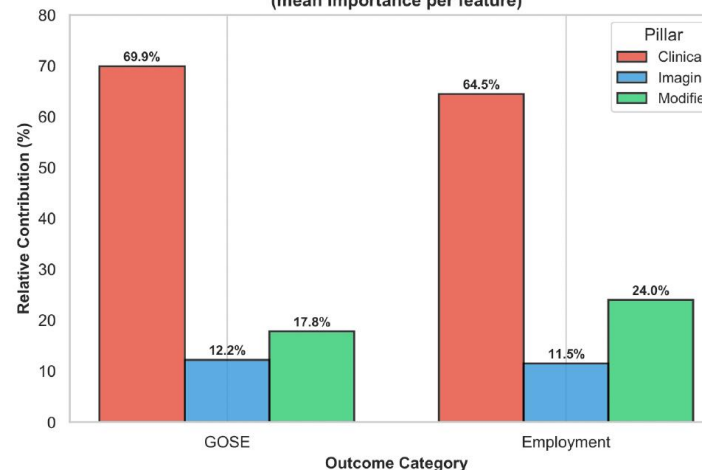
Original research

Long-term prediction of traumatic brain injury outcome using the CBI-M framework

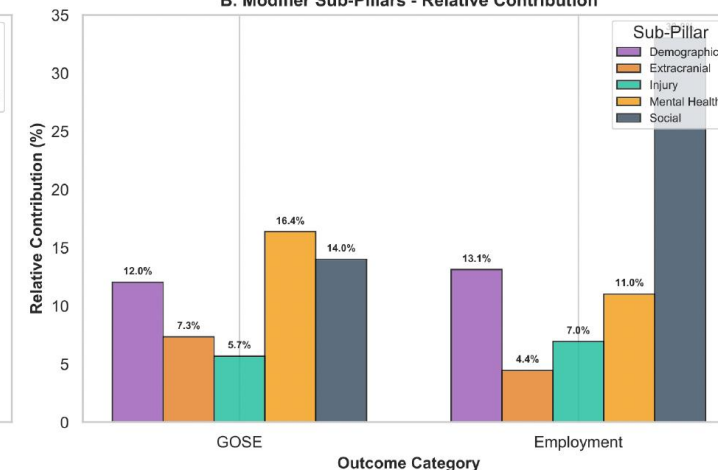
Gershon Spitz ,^{1,2,3} Marina Downing,^{1,3} Megan Carty,³ Jennie L Ponsford³

CBI-M framework predicts functional and vocational outcomes up to 10 yrs post-TBI.

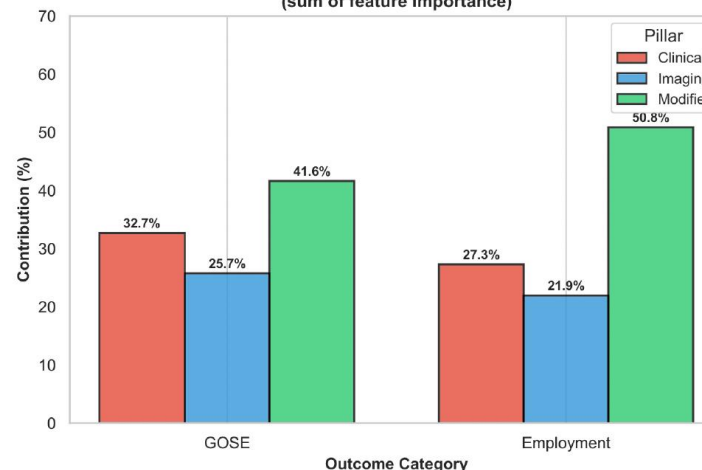
A. Major Pillars - Relative Contribution (mean importance per feature)



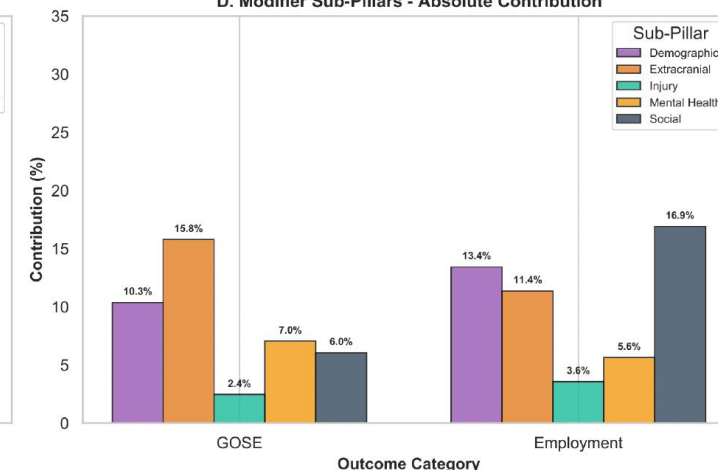
B. Modifier Sub-Pillars - Relative Contribution



C. Major Pillars - Absolute Contribution (sum of feature importance)



D. Modifier Sub-Pillars - Absolute Contribution



ADDED VALUE OF MULTI-DIMENSIONAL CHARACTERIZATION OF TBI

CBI-M: IMPLEMENTATION STRATEGIES & TACTICAL PLANNING

Starting with the End in Mind: Recommendations to Optimize Implementation of a Novel TBI Classification from the 2024 NINDS TBI Classification and Nomenclature Workshop's Knowledge to Practice Working Group

Peter Bragge,^{1,*} Molly McNett,² Mark Bayley,³ Maureen Dobbins,⁴ Risa Nakase-Richardson,⁵ Corinne Peek-Asa,⁶ Alexis F. Turgeon,^{7,8} Hibah Awwad,⁹ Kristen Dams-O'Connor,^{10,11} Adele Doperalski,¹² Andrew Maas,^{13,14} Mike McCrea,¹⁵ Nsini Umoh,¹² and Geoff Manley¹⁶

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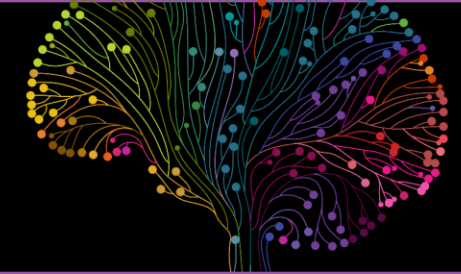
**LOOKING TO
ENGAGE
LEADERS IN TBI
CARE &
RESEARCH**

Legacy and
Prospective
Validation Studies

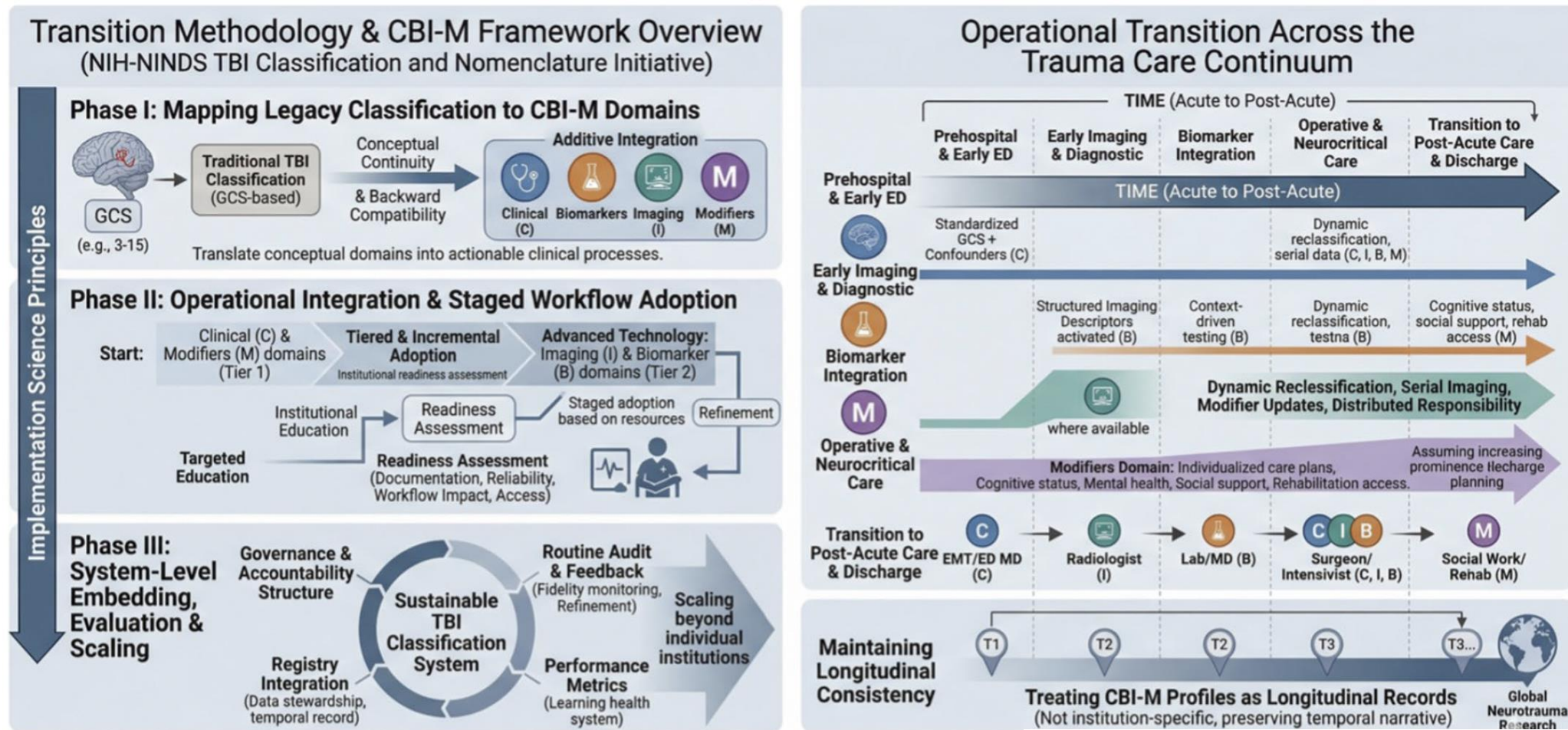
Strategies & Tactical
Planning for Clinical
Implementation

Ongoing Refinement,
Optimization

CBI-M: REAL WORLD IMPLEMENTATION



The Framework of Policy Transition in TBI: From GCS to CBI-M



CBI-M: A NEW ERA IN TBI



**Moving Beyond the
Limitations of
“Mild, Moderate, Severe”**

C

CLINICAL

B

BIOMARKERS

I

IMAGING

M

MODIFIERS