Neuroprognostication and Recurrent Hemorrhage Risk

Section: Intraparenchymal Hemorrhage: New Look at an Old Problem
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DISCLOSURES

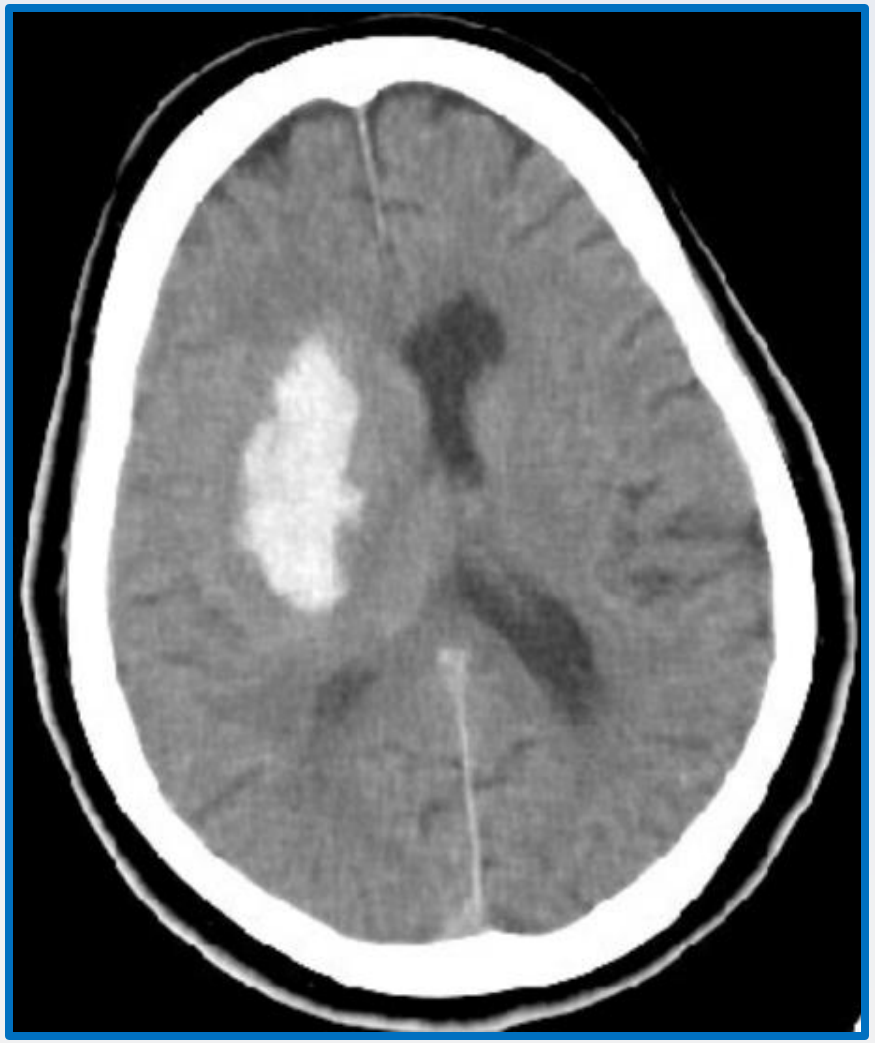
- None

OUTLINE

- Background
- Intracerebral hemorrhage (ICH) etiology
- Recurrent risk of ICH
- Prognostication in ICH
- ICH severity scores
- AHA guidelines
- Summary and future directions

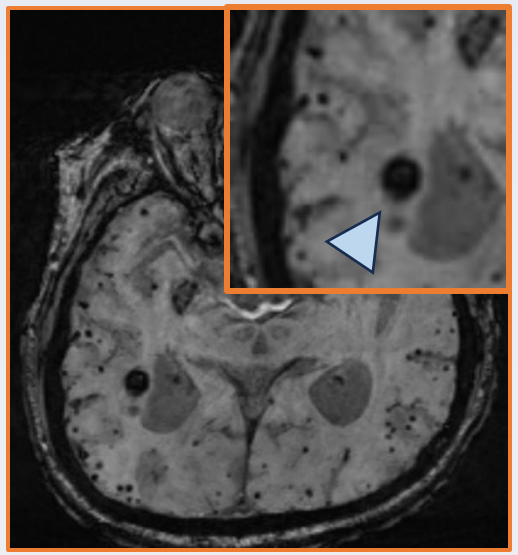
BACKGROUND

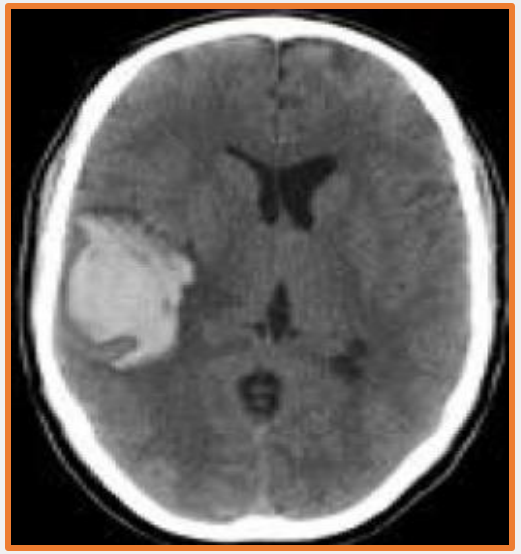
- ICH accounts for 10 to 20% of all strokes annually
- ICH accounts for higher morbidity and mortality than ischemic stroke
- Only 50% of patients survive for 1 year after ICH
- Most common cause of spontaneous ICH is cerebral small vessel disease (cSVD)

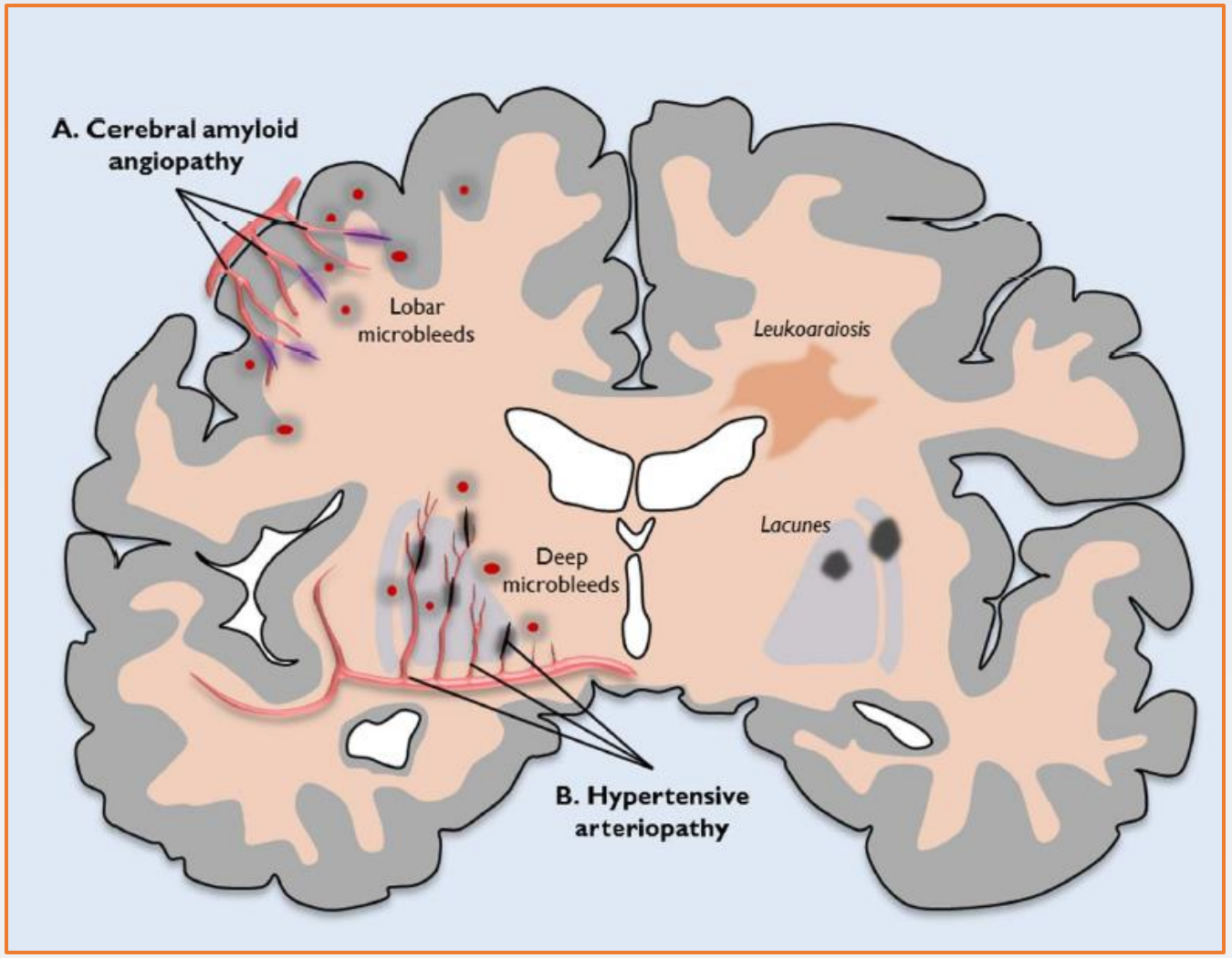


Puy L *et al. Nat Rev Dis Primers* (2023)

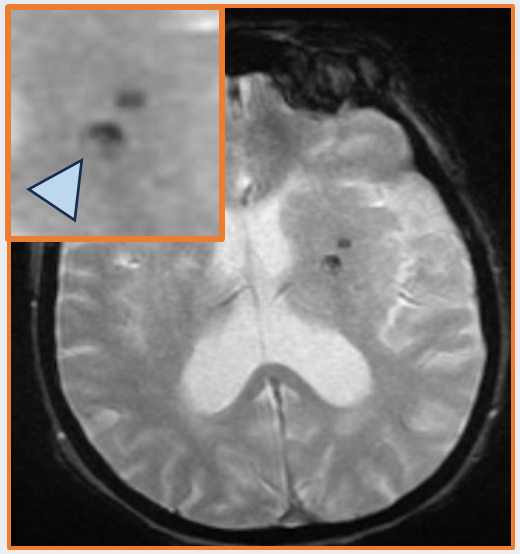
CAA

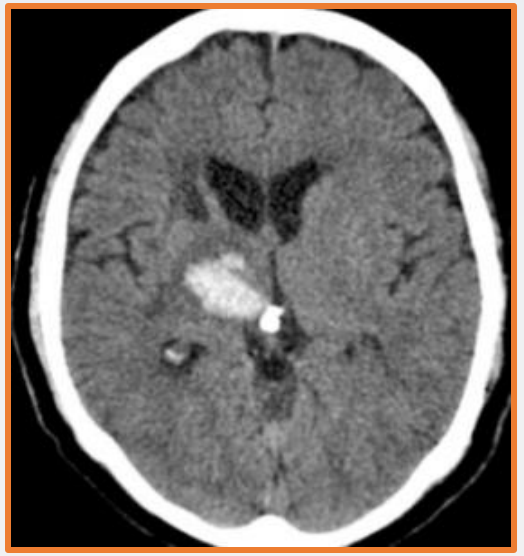






HA





Charidimou *et al*. *Front Neurol* (2012)

CSVD DISTRIBUTION

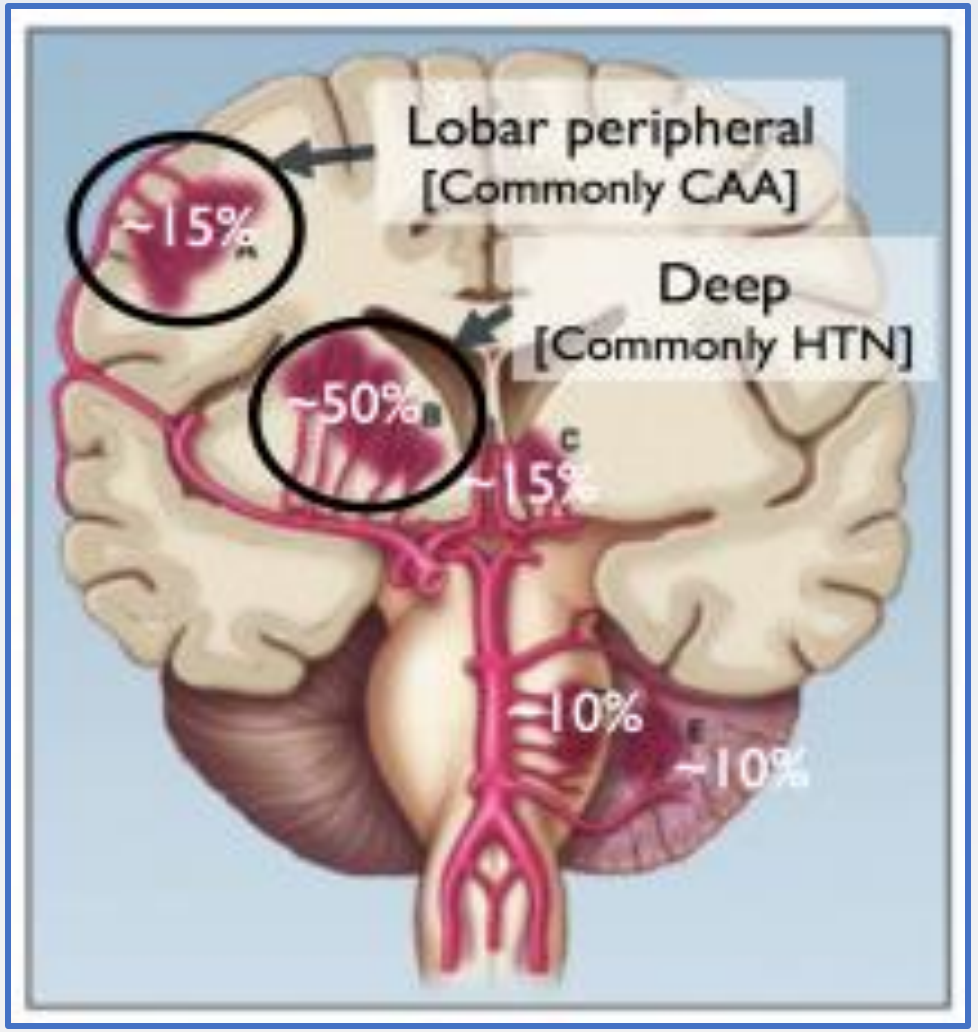
Small Vessel Disease Distribution

Hypertensive arteriopathy (85%)

- Basal ganglia (50%)
- Thalamus (15%)
- Brainstem (10%)
- Cerebellar (10%) (can also be CAA)

Cerebral amyloid angiopathy (15%)

- Lobar regions of the brain
- Cerebellum



DIAGNOSIS OF CSVD

- Diagnosis of cSVD relies on CT and MRI
- Deep hemorrhage → hypertensive arteriopathy
- Lobar hemorrhage → cerebral amyloid angiopathy
- Deep ICH – may not always need brain MRI if clear from CT
- Lobar ICH
  - Always obtain brain MRI
  - Utilize Boston criteria version 2.0 to diagnose CAA

CAA DIAGNOSIS

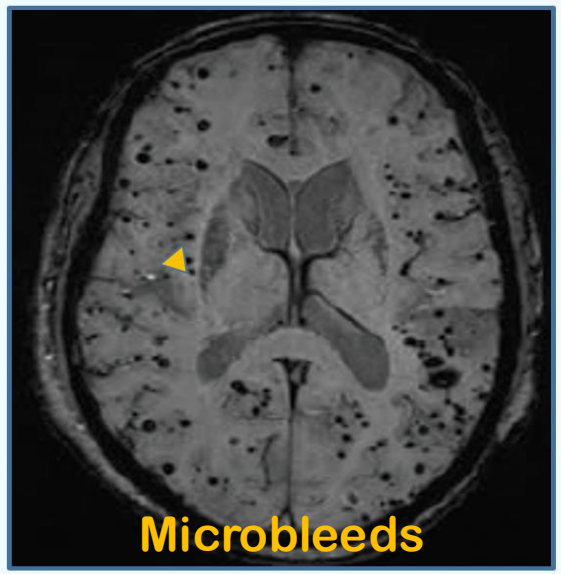
Non-hemorrhagic MRI markers

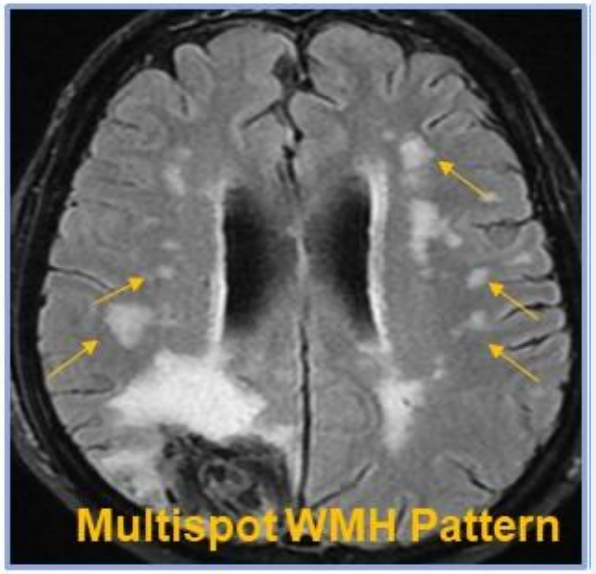
- White matter multi-spot pattern
- Centrum semiovale enlarged perivascular spaces (EVPS)

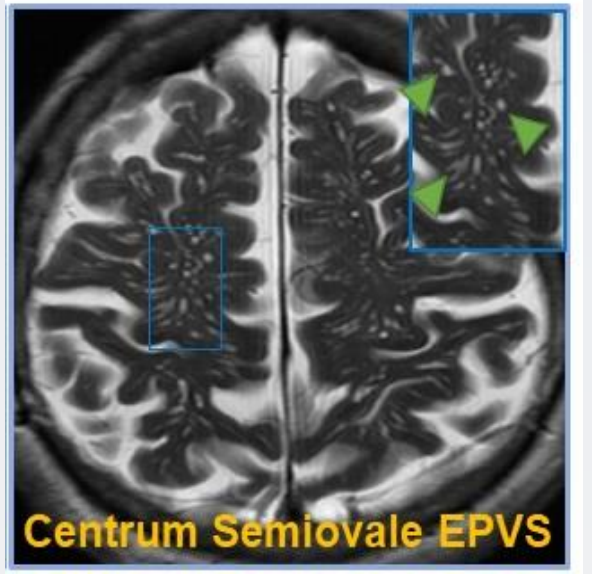
Hemorrhagic MRI markers

- Cerebral microbleeds
- Cortical superficial siderosis

MRI MARKERS OF CAA







BOSTON CRITERIA FOR CAA

- Age cutoff of 50 years old
- Categorizing likelihood of CAA into

  Requires pathology

  - Definite CAA – full post-mortem analysis
  - Probable with supporting pathology (obtained through biopsy or hematoma evacuation)

  Requires clinical data and MRI

  - Probable
  - Possible

BOSTON CRITERIA FOR CAA

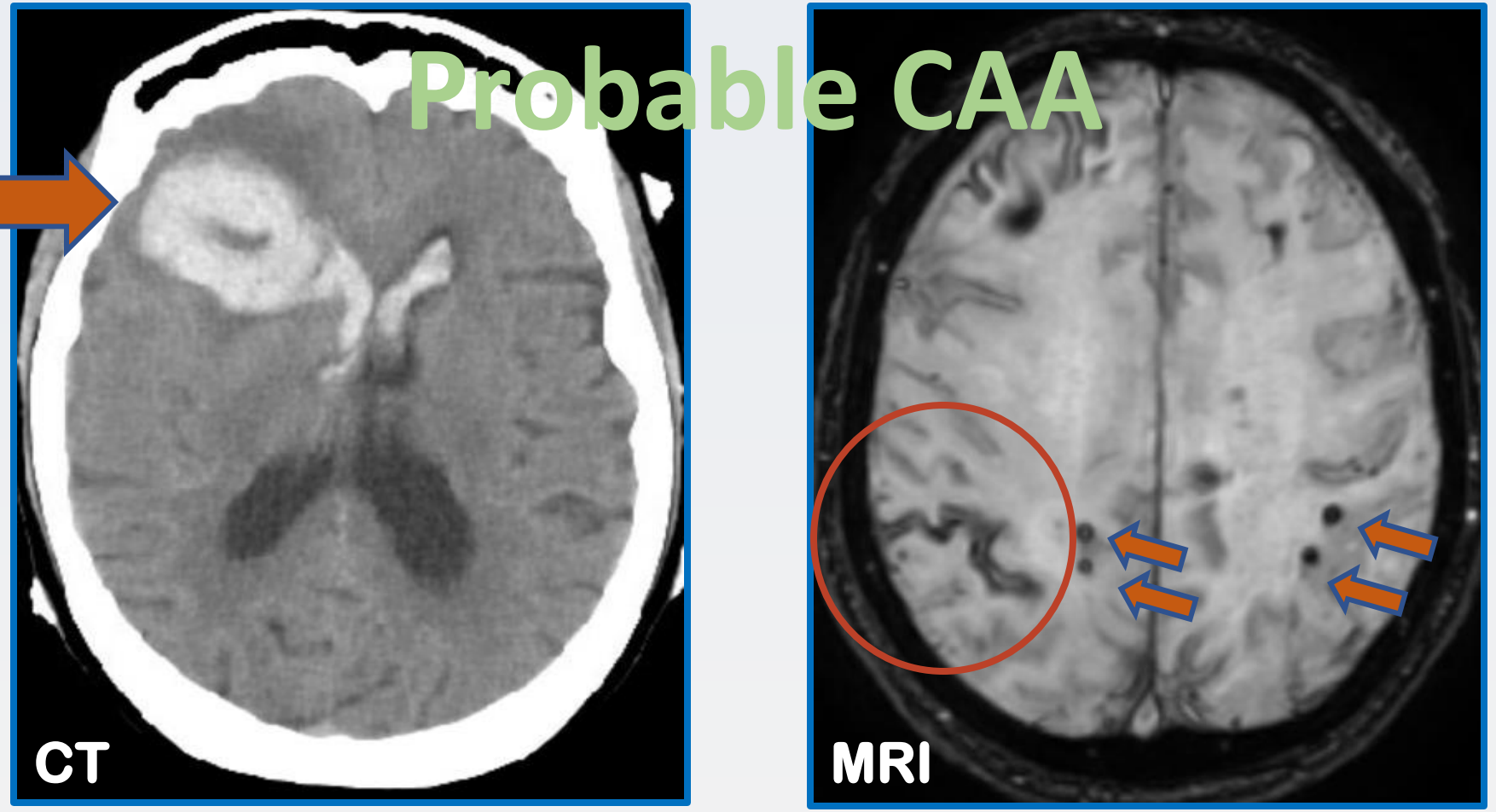
- Possible CAA – all patients with a lobar ICH on CT meet criteria
- Probable CAA – lobar ICH + one of any of the following
  - Prior lobar ICH
  - Microbleed
  - Cortical superficial siderosis
  - Centrum semi-ovale EPVS
  - Multispot pattern

  } MRI Markers

- Presence of any deep ICH/microbleeds excludes CAA

Charidimou *et al*. *Lancet Neurol* (2022)

CAA DIAGNOSIS



RECURRENT HEMORRHAGE RISKS

- CAA-ICH carries high risk of recurrent ICH (7%–10%/year)
- HA-ICH carries lower risk of recurrent ICH (1%–3%/year)
- In addition to cSVD subtype, follow-up ICH risk modulated by
  - Clinical factors (age, post-ICH ambulatory hypertension, Black race)
  - Genetic factors
  - Anti-thrombotic therapy
  - Imaging markers
- Prior ICH increases risk for recurrent hemorrhage (HR 4.8)

Charidimou *et al*. *Brain* (2017)

RECURRENT HEMORRHAGE RISKS

- Hemorrhagic markers on MRI increase future ICH risk
  - Lobar microbleeds (risk increases with burden)
    - 1 microbleed → HR 1.88 (95% CI 0.5–7.6)
    - 2–4 microbleeds → HR 2.93 (95% CI 1.3–4.0)
    - > 4 microbleeds → HR 4.12 (95% CI 1.6–9.3)
  - Cortical superficial siderosis (HR 4.69)
- Carriers of apolipoprotein E genotypes at increased risk
  - Ɛ2 (HR 3.3)
  - Ɛ4 (HR 2.5)

Biffi *et al*. Neurology (2010)

RECURRENT HEMORRHAGE RISK

- Antithrombotic therapy (aspirin, dAPT, anticoagulation) increase the risk of recurrent ICH, especially in lobar ICH
- Resumption timing and choice of antithrombotic should balance risks associated with ICH size and cSVD subtype against indication for therapy (mechanical valves, AF, etc.)
- *Example*: Patient with small deep hypertensive basal ganglia hemorrhage on aspirin for coronary disease → reasonable to consider restarting therapy

ICH IN PATIENTS WITH AFIB

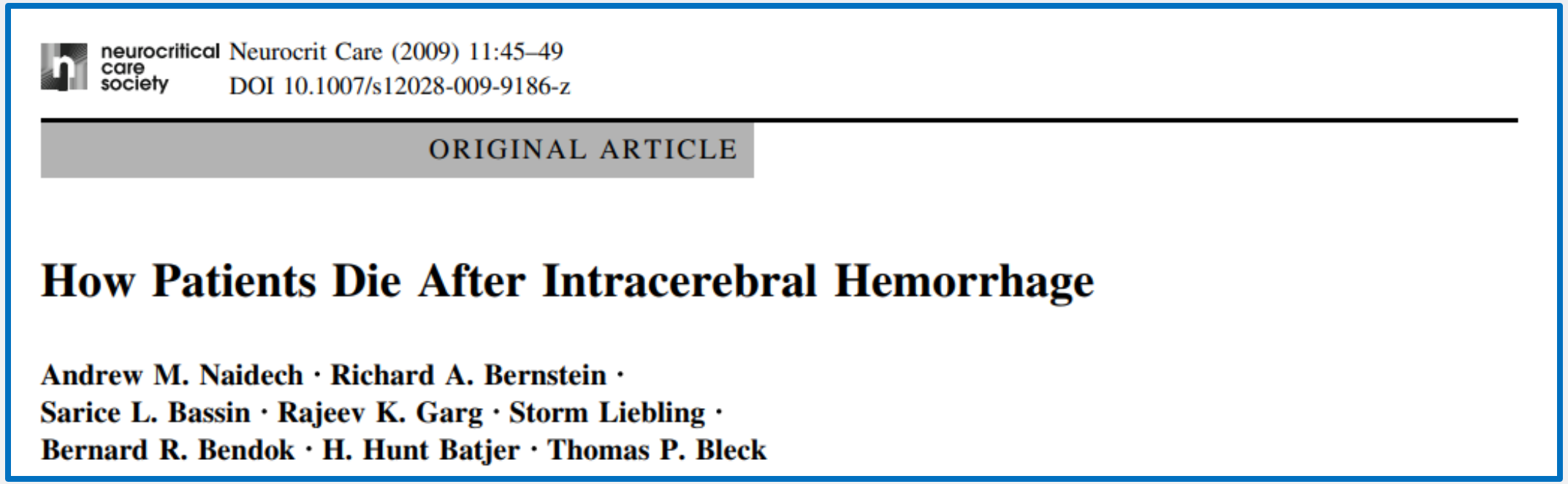
- Anticoagulation for AF after ICH → high risk of recurrent ICH
- PRESTIGE-AF trial → resumption of NOACs in AF increases hemorrhagic risk but reduces stroke risk
- Ongoing trials evaluating resumption of anticoagulation (ASPIRE)
- Left atrial appendage closure (LAAC) may be option in patients with AF and ICH
- Ongoing trials evaluating LAAC in this population (A3ICH, STROKECLOSE, CLEARANCE)

Veltkamp *et al. Lancet* (2025)

PROGNOSTICATION IN ICH

MORTALITY IN ICH

- Non-traumatic ICH carries a high 30-day mortality (~30-50%)
- What is the predominant cause of mortality in these patients?



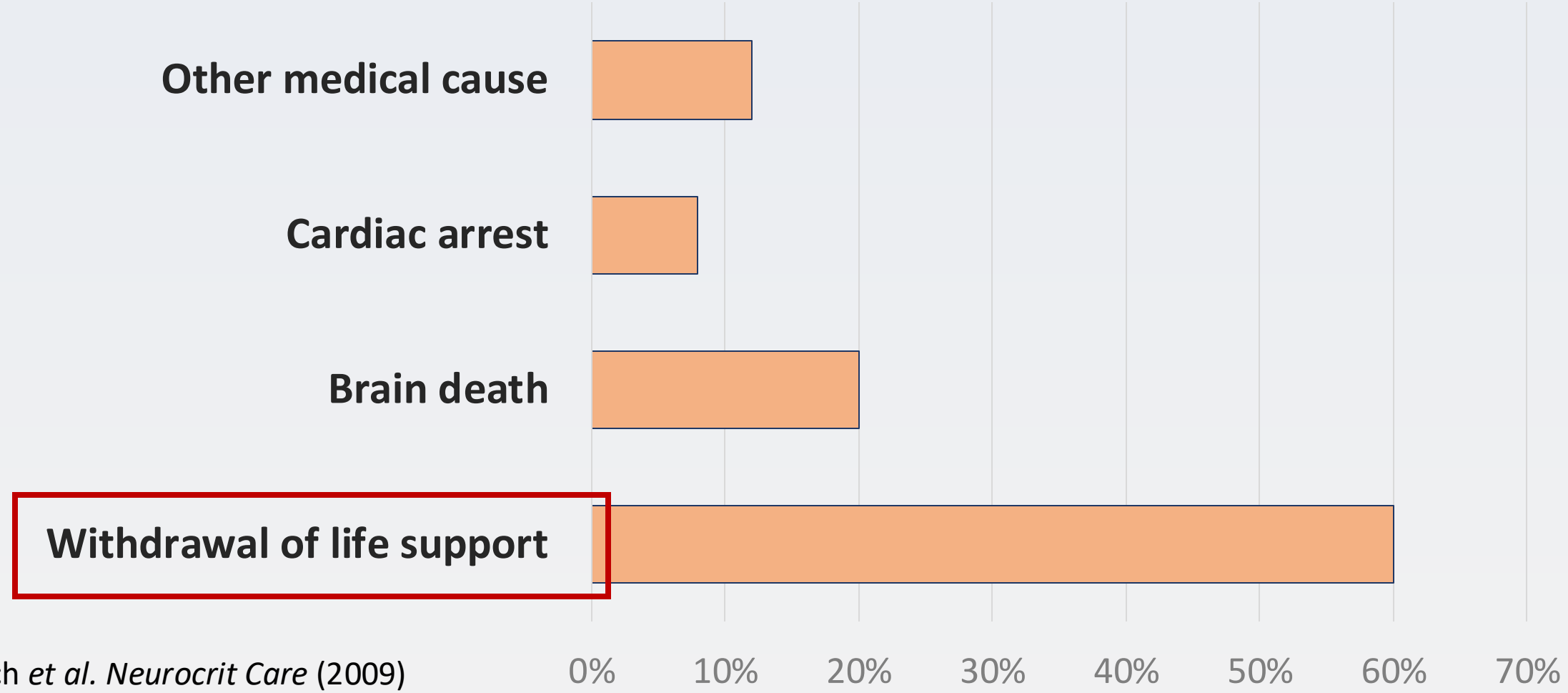
neurocritical care society Neurocrit Care (2009) 11:45–49
DOI 10.1007/s12028-009-9186-z

ORIGINAL ARTICLE

How Patients Die After Intracerebral Hemorrhage

Andrew M. Naidech · Richard A. Bernstein ·
Sarice L. Bassin · Rajeev K. Garg · Storm Liebling ·
Bernard R. Bendok · H. Hunt Batjer · Thomas P. Bleck

CAUSES OF DEATH AFTER ICH



Naidech *et al. Neurocrit Care* (2009)

MORTALITY AFTER ICH

- Withdrawal of life-sustaining therapy (WLST) is the most common cause of death in ICH (~60 to 78%)!
- In ICH, life-sustaining treatment is often ventilatory support
- WLST occurs when there is a belief that the prognosis from the ICH is poor, ongoing care will be futile

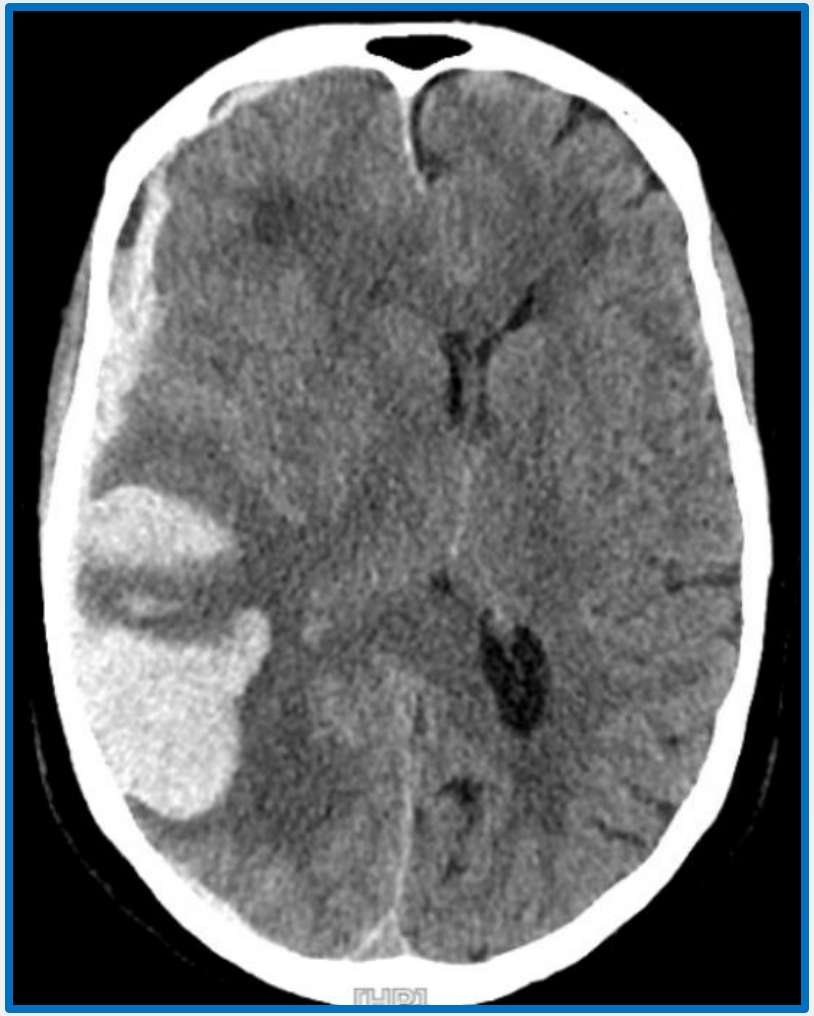
Question 1: How is prognosis determined?

Question 2a: Who determines prognosis? → **Treatment team**

Question 2b: If treatment team determines prognosis, are they good at it?

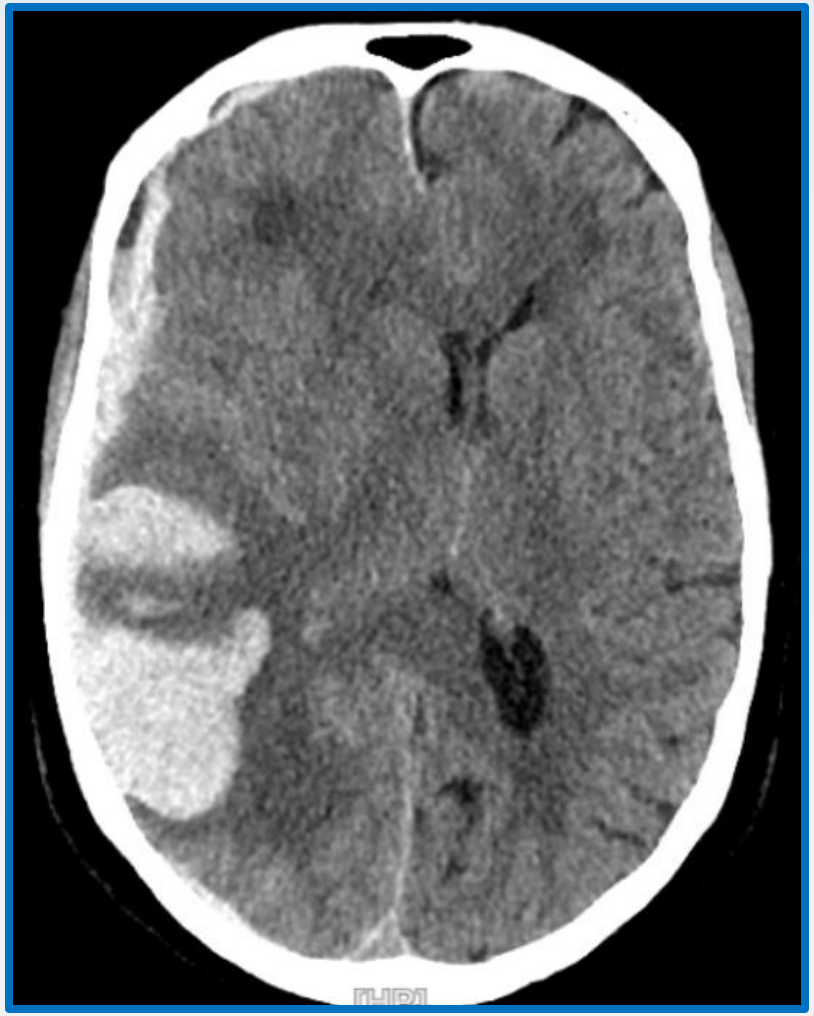
HOW DO WE PROGNOSTICATE?

- Clinical variables
  - Age
  - Comorbidities
  - Baseline functional/cognitive status
- ICH presentation
  - GCS score
  - Hematoma size
  - Hematoma location
  - Midline shift/herniation
- Neurological examination



HOW DO WE PROGNOSTICATE?

- Use the totality of information to determine best and worst case scenarios for long-term recovery
- Attempt to assign relative probabilities to possible outcomes (e.g., very low chance the patient will return back to his functional baseline)
- Prognostication geared toward the purpose of making clinical decision with the patient's proxies/families

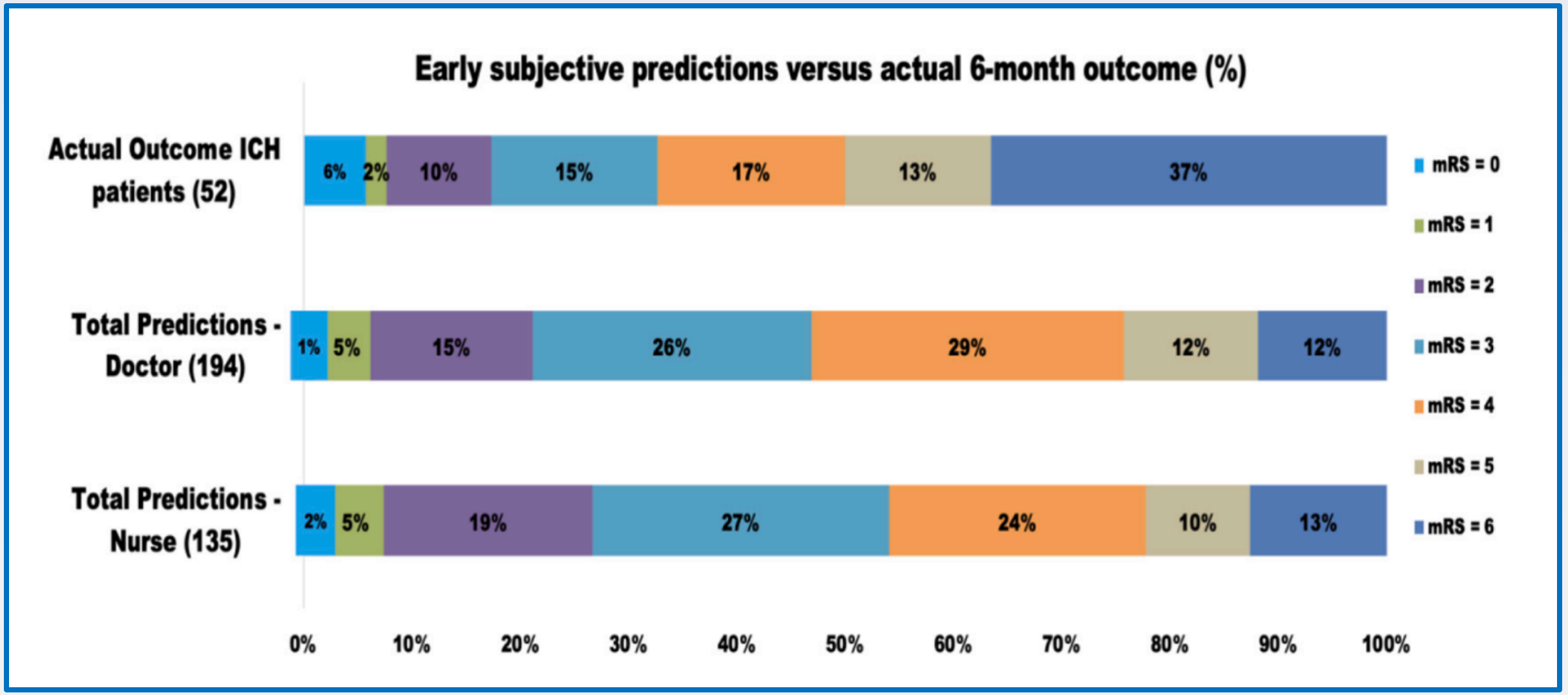


ARE WE GOOD AT PROGNOSTICATION?

Predictions of Outcome by Physicians and Nurses after ICU Admission			
	Physicians' Predictions C Statistic (95% CI)	**Nurses' Predictions C Statistic (95% CI)**	***p* value**
Hospital mortality	0.67 (0.61–0.73)	0.68 (0.62–0.74)	0.81
6-month mortality	0.76 (0.72–0.81)	0.69 (0.64–0.74)	0.02
Unable to return home at 6 months	0.70 (0.65–0.75)	0.67 (0.61–0.72)	0.24
Unable to ambulate up 10 stairs at 6 months	0.72 (0.63–0.82)	0.70 (0.60–0.79)	0.93
Abnormal cognition at 6 months	0.61 (0.54–0.68)	0.55 (0.48–0.62)	0.13

Detsky *et al. JAMA* (2017)

For good (mRS 0–3) versus poor (mRS 4–6), outcome, accuracy of predictions was 68% and exact agreement 29%



Lernon *et al*. *eNeurologicalSci* (2023)

BARRIERS TO ACCURATE PROGNOSTICATION

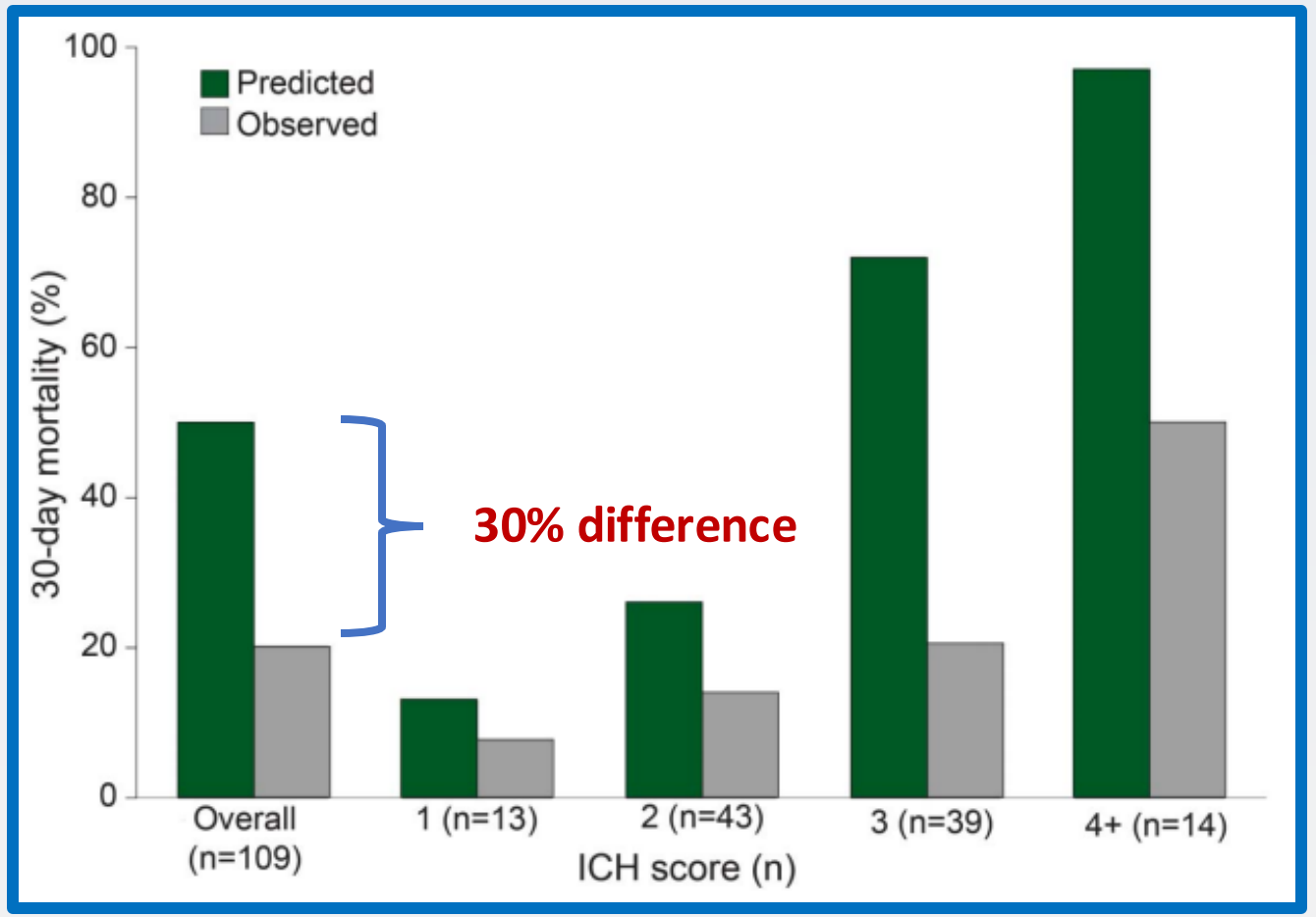
- Patient families make decisions based on how clinicians relay prognosis and frame long-term clinical outcomes
- Accurate neuro prognostication is the holy grail of neurocritical care
- Significant complexities and barriers that limit fully accurate prognostication
  - Prognosis is relayed too early, before patients have had a chance to “declare themselves”
  - DNR orders influence treatment decisions
  - Physicians have inherent biases that influence prognostication

BARRIERS TO ACCURATE PROGNOSTICATION: DNR ORDERS

- DNR order specifically apply to cardiac arrest scenarios
- Often lead to withholding care in other aspects of care
  - Lower likelihood of admission to a stroke unit
  - Less use of guideline-concordant care for VTE prophylaxis
  - Fewer surgical procedures
  - Earlier institution of end-of-life care
  - Increased mortality
- **Decisions to limit these other aspects of care should be part of shared decision-making discussions**

Hemphill. *Crit Care* (2007)

MORTALITY WITHOUT EARLY DNR ORDERS (< 5 DAYS)



Morgenstern *et al. Neurology* (2015)

BAR
PRO S

Cognitive bias	Description	Example
Confirmation bias	To look for or to interpret evidence to support prior hypothesis rather than look for disconfirming evidence.	Looking for evidence to support the presumed prognosis rather than contradictory elements.
Availability bias	Judgments of likelihood or percentages based on ease of recall (greater 'availability' in memory) rather than on actual probabilities.	Overestimate the likelihood of a prognosis based on a recent experience with a similar case.
Anchoring effect	To rely heavily on one piece of information when making decisions (usually the first piece of information acquired: the 'anchor').	Focusing on salient features in the patient's presentation too early in the prognosis process and failing to adjust this initial impression in the light of new information.
Framing effect	To draw different conclusions from the same information, depending on how that information is presented.	Allowing the way evidence is framed or whom the information came from to influence prognosis making.
Loss aversion	To view losses as looming larger than corresponding gains.	Continue with a given prognosis, even though it may not fit the new evidence (avoiding the loss of 'being right').
Attribute substitution	Answering a complex, difficult question by substituting it by a related but simpler one.	Translate a legitimate high confidence in diagnosis elements into overconfidence on prognosis issue.
Sunk-cost effect	To allow previously spent time, money, or effort to influence present or future decisions.	Overestimation of a good prognosis if a lot of resources (typically surgery or organ supply) have been successful (in terms of short outcome).
Dunning–Krúger effect	Tendency for unskilled individuals to overestimate their own ability ('illusory superiority') and the tendency for experts to underestimate their own ability.	Being overconfident in a prognosis in case of a lack of knowledge in this specific field (in comparison to an expert).
Bandwagon effect	To do (or believe) things because many other people do (or believe) the same.	Rely too much on apparent consensus and/or common practices.
Commission bias	To favour action rather than inaction.	Jumping to a withdrawal of care procedure (with/without organ donation) rather than giving more time to get more information.
Blind obedience	To show undue deference to authority or technology.	Relying too much on a unique expert opinion or test results.

Rohaut and Claassen. *BJA* (2018)

HOW TO INCREASE ACCURACY?

- Avoid self-fulfilling prophecy of poor outcome due to clinical nihilism (e.g., treatment is not beneficial)
- Initial aggressive guideline-concordant care is recommended for all ICH patients (unless specific limitations to care were previously documented)
- Optimal and sufficient duration of a trial of aggressive treatment remains uncertain
- Approach of aggressive care without early DNR orders may lead to better-than-expected outcomes

PROGNOSTIC MODELS FOR OUTCOME: ICH SCORE

- Categories included are independent predictors of 30-day mortality
- Higher ICH score → higher mortality rate
- GCS score determined on initial presentation (or after resuscitation)
- ICH volume is determined by $\frac{ABC}{2}$

ICH Score	Points
GCS score *	
3–4	2
5–12	1
13–15	0
ICH volume **	
≥ 30 cm^3	1
< 30 cm^3	0
IVH ***	
Yes	1
No	0
Infratentorial origin of ICH	
Yes	1
No	0
Age	
≥ 80	1
< 80	0
ICH Total Score	0-6

Hemphill *et al*. *Stroke* (2001)

Predictors of 30-day mortality after intracerebral hemorrhage

Patient Characteristics	Odds Ratio (95% CI)	*p* value
Supratentorial only (*n* = 122)		
GCS	0.69 (0.58–0.82)	<0.001
Age (≥80 y)	9.55 (2.40–38.07)	0.001
ICH volume	1.40 (1.06–1.84)	0.017
Infratentorial only (*n* = 30)		
GCS	0.64 (0.46–0.88)	0.007
IVH	10.52 (0.84–131.19)	0.067
All ICH patients (*n* = 152)		
GCS	0.69 (0.59–0.80)	<0.001
Age (≥80 y)	9.84 (2.58–37.47)	0.001
Infratentorial	4.24 (1.15–15.65)	0.030
IVH	2.97 (0.99–8.92)	0.052
ICH Volume	1.31 (1.00–1.71)	0.047

Hemphill *et al*. *Stroke* (2001)

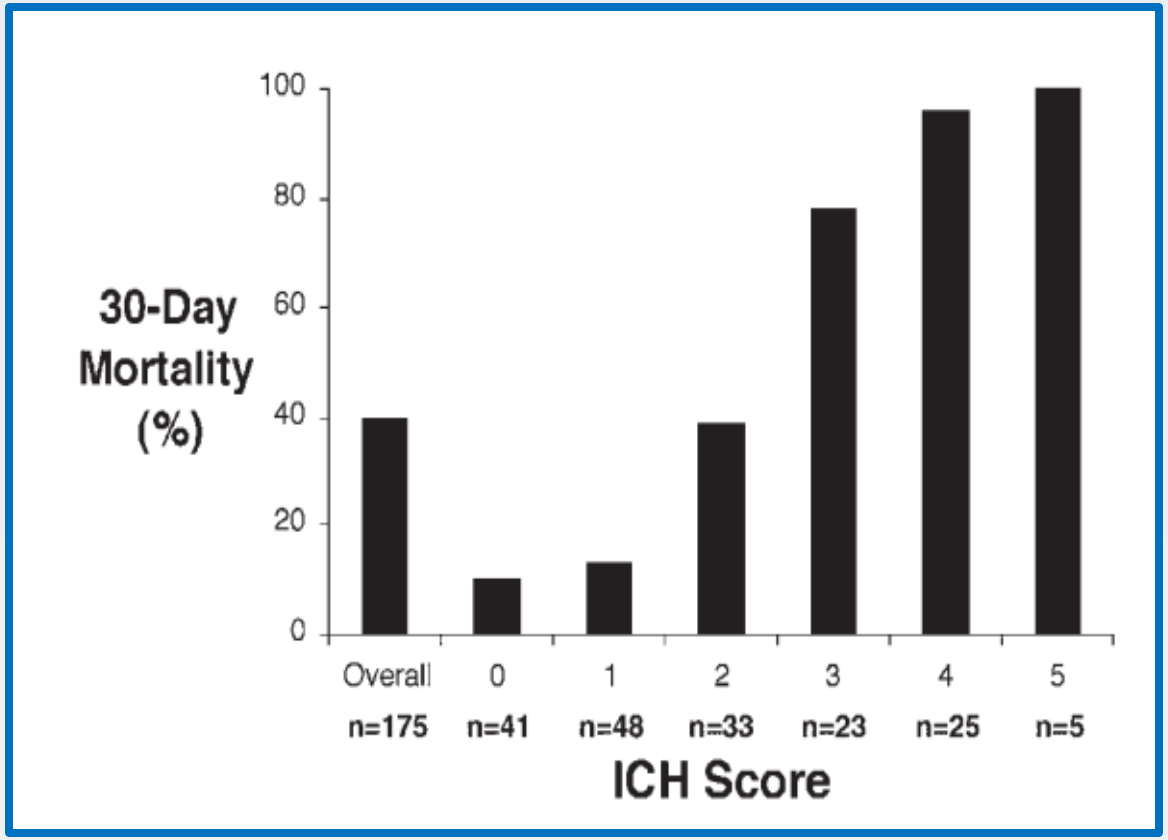
PROGNOSTIC MODELS FOR OUTCOME: ICH SCORE

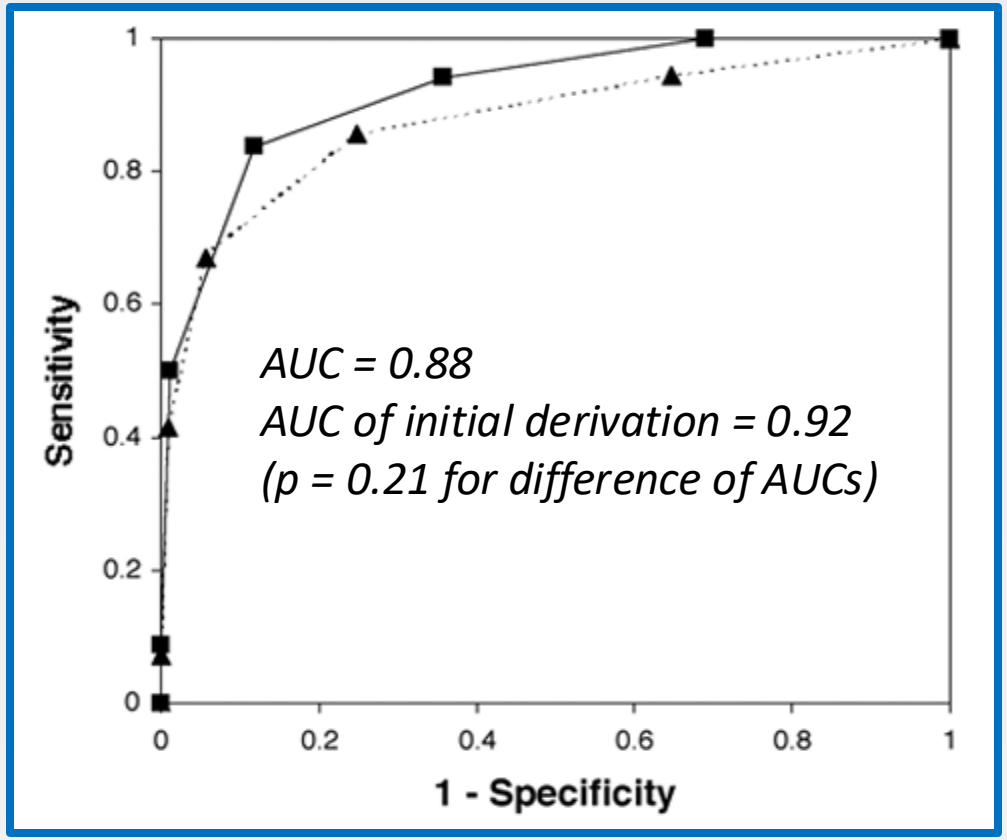
ICH Score	30-Day Mortality
0	0%
1	13%
2	26%
3	72%
4	97%
5	100%
6	100%

Hemphill *et al*. *Stroke* (2001)

PROGNOSTIC MODELS FOR OUTCOME: ICH SCORE

Externally validated in other cohorts



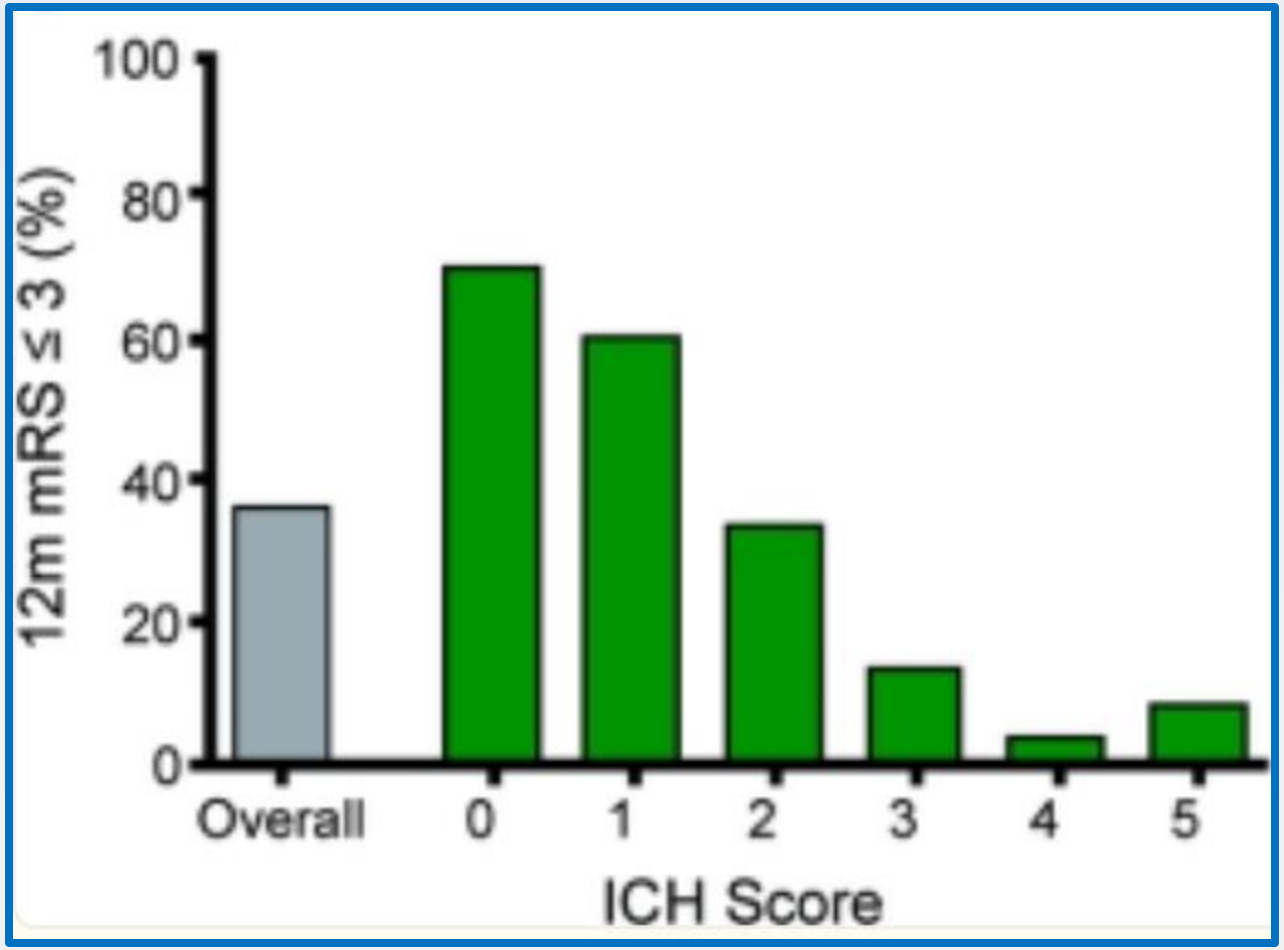


All patients with ICH score of 5 died

Clarke *et al*. *Neurocritical Care* (2004)

PROGNOSTIC MODELS FOR OUTCOME: ICH SCORE

- Also validated for long-term functional outcomes
- Higher the ICH score the lower the percentage of mRS ≤ 3
- Notable exceptions: 1 patient with ICH score of 1 achieved an mRS of 2 at 1 year



Hemphill *et al*. *Neurology* (2009)

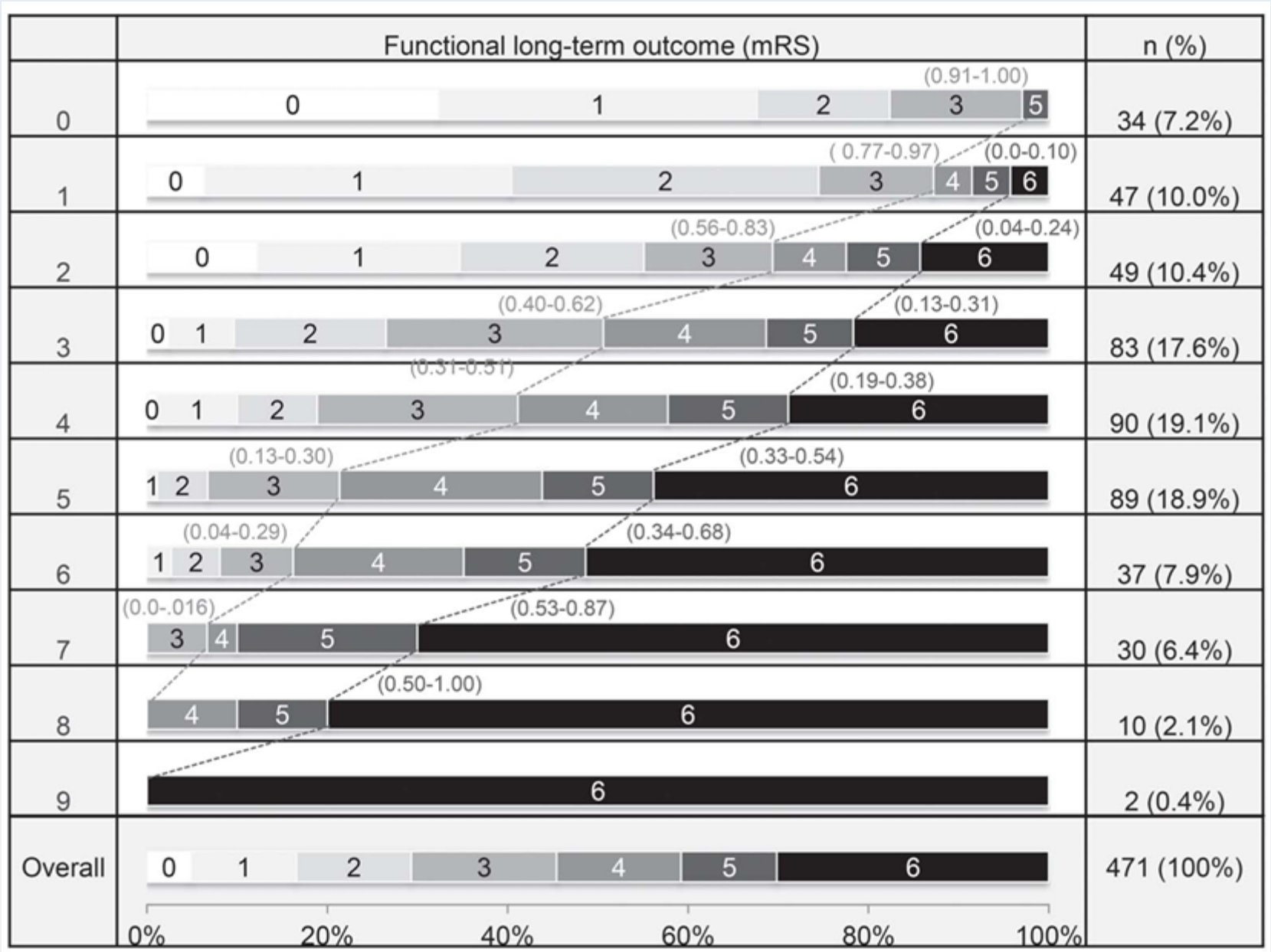
MAX-PROGNOSTIC MODELS FOR OUTCOME: MAX-ICH SCORE

- Max-ICH score predicts mortality and unfavorable long-term functional outcome at 1-year
- Max-ICH score ranges from 0 to 10, incorporates more characteristics than ICH score
- Shown to be more superior than ICH score at determining mortality
- Each 1-point increase score associated with an OR of 1.24 for an unfavorable outcome

Sembill *et al*. *Neurology* (2017)

Max-ICH Score	
NIHSS	
0–6	**0**
7–13	**1**
14–20	**2**
≥ 21	**3**
Age, years	
≤ 69	**0**
70–74	**1**
75–79	**2**
≥ 80	**3**
Lobar hematoma volume ≥ 30 mL	**1**
Non-lobar hematoma volume ≥ 10 mL	**1**
Intraventricular hemorrhage	**1**
Oral anticoagulation	**1**

Sembill *et al*. *Neurology* (2017)



Sembill JA *et al*. *Neurology* (2017)

ICH SEVERITY SCORE RECOMMENDATIONS

- Most baseline severity scores incorporate
  - Age
  - ICH location
  - Clinical deficits (e.g., GCS scores)
- Administering ICH score is level 1 guideline (AHA guideline)
- ICH severity scores should not be used as sole basis for making clinical decisions
- Optimal timing of administration of scores is unclear (~ 24 hours)
- Prognostication should be individualized to the patient

AHA RECOMMENDATIONS

In patients with spontaneous ICH, administering a baseline measure of overall hemorrhage severity is recommended as part of the initial evaluation to provide an overall measure of clinical severity. **(Class 1)**

In patients with spontaneous ICH, a baseline severity score should not be used as the sole basis for forecasting individual prognosis or limiting life-sustaining treatment. **(Class 3)**

PROGNOSTICATION RECOMMENDATIONS

- Exonerate reversible confounders (e.g., sedation, hydrocephalus, delirium, etc.)
- Avoid early decision making (< 48 hours)
- Limit interpretation of DNR orders to only cardiac arrest → should not influence decisions surrounding surgery, WLST
- Incorporate shared-decision making with surrogates

AHA RECOMMENDATIONS

In patients with spontaneous ICH who do not have preexisting documented requests for life-sustaining therapy limitations, aggressive care, including postponement of new DNAR orders or withdrawal of medical support until at least the second full day of hospitalization, is reasonable to decrease mortality and improve functional outcome **(Class 2a)**

In patients with spontaneous ICH who are unable to fully participate in medical decision-making, use of a shared decision-making model between surrogates and physicians is reasonable to optimize the alignment of care with patient wishes and surrogate satisfaction **(Class 2a)**

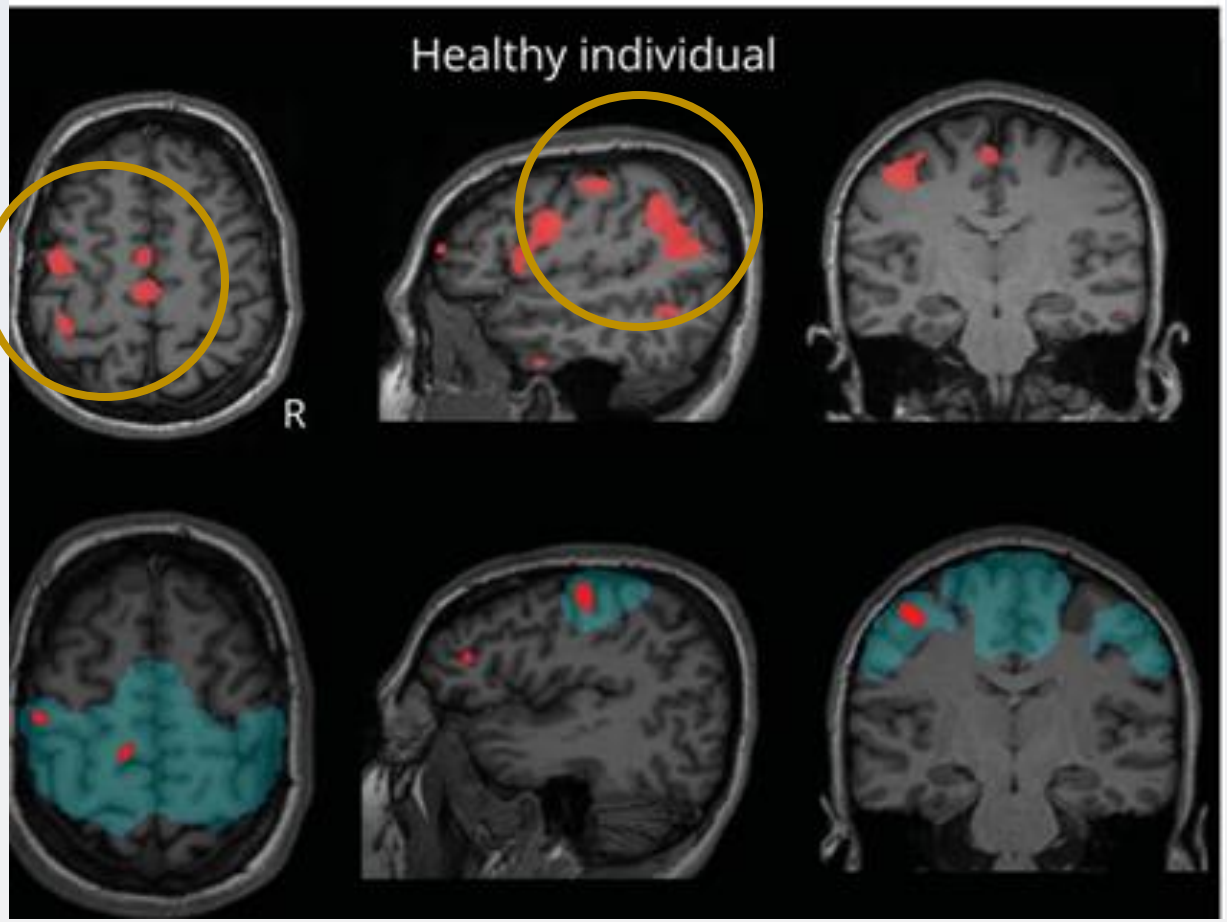
In patients with spontaneous ICH who have DNAR status, limiting other medical and surgical interventions, unless explicitly specified by the patient or surrogate, is associated with increased patient mortality. **(Class 3)**

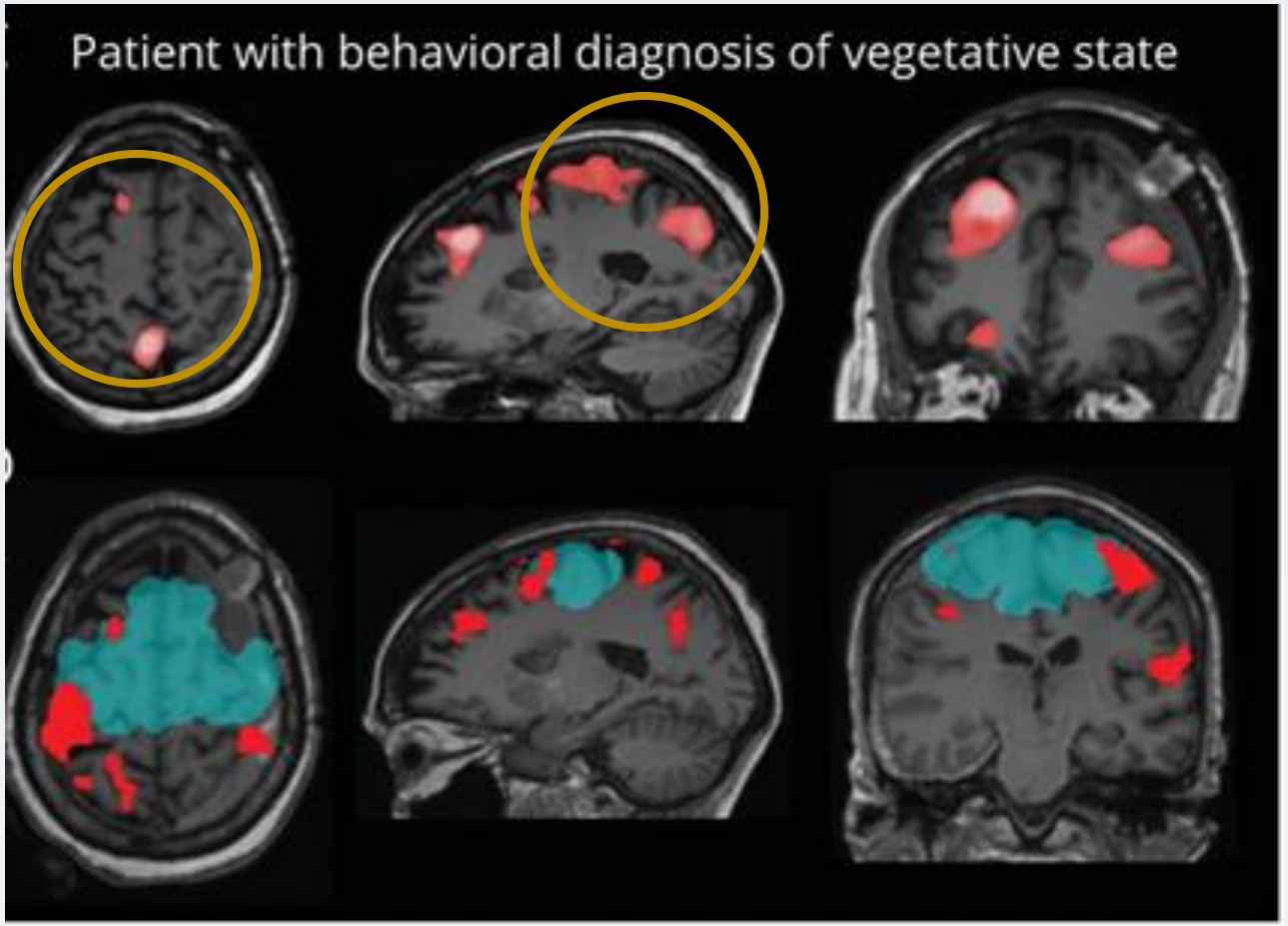
SUMMARY

- Spontaneous ICH caused by cSVD: CAA and HA
- CAA carries a high risk of recurrent ICH, compounded by oral anticoagulation, and hemorrhagic MRI markers
- Diagnosis of CAA in lobar ICH patients is critical, may impact secondary stroke prevention strategies
- Physicians should avoid 1) early DNR orders 2) liberal interpretation of DNR orders 3) therapeutic nihilism
- Clinical decision making should not solely rely on ICH scores; shared-decision making should be used

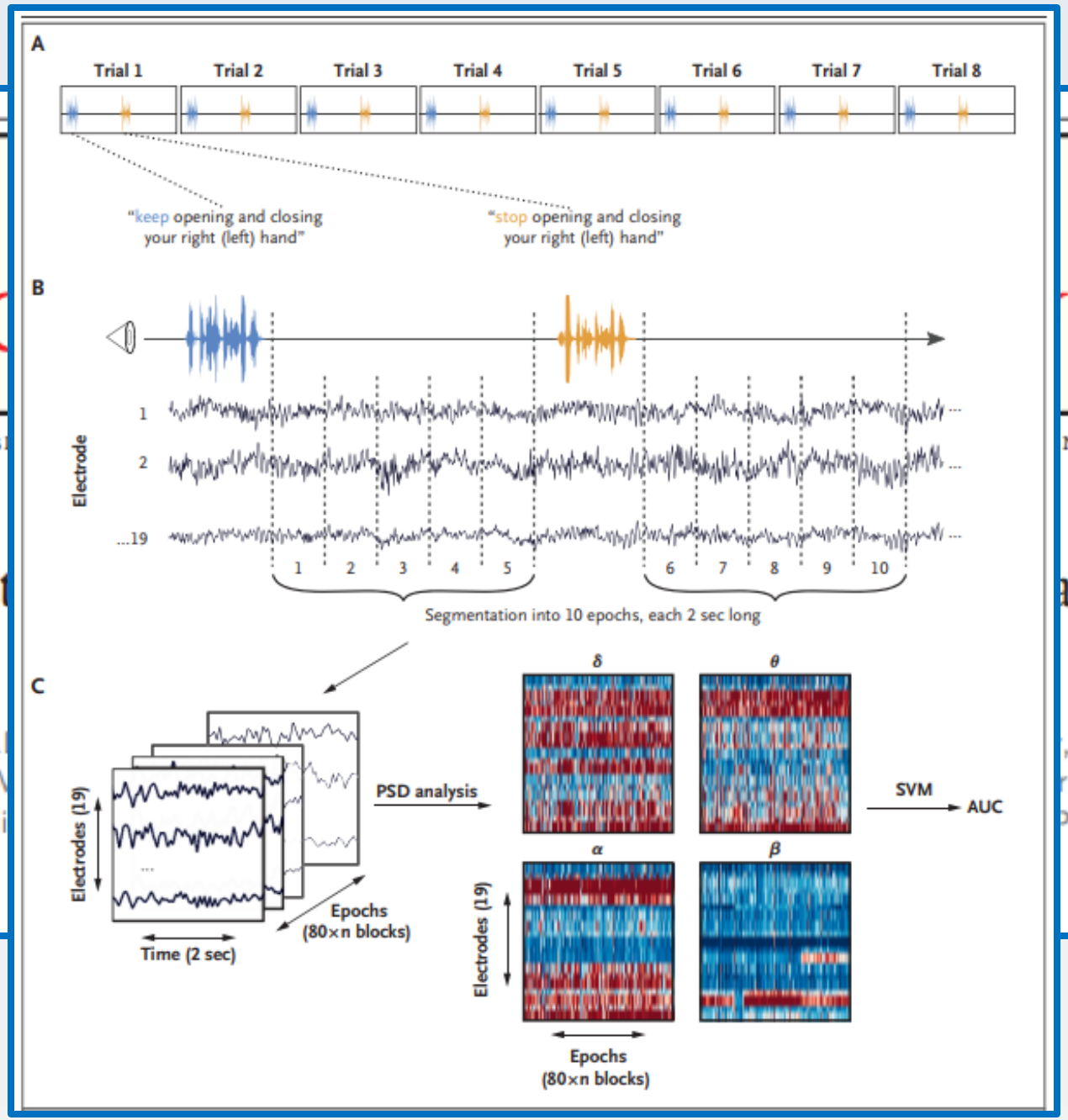
FUTURE DIRECTIONS

Imagine open and closing right hand





Bodien *et al. Neurol Clin Pract*. (2025)



Claassen *et al. NEJM* (2019)

THANK YOU