

Recent Advances in Neurocritical Care

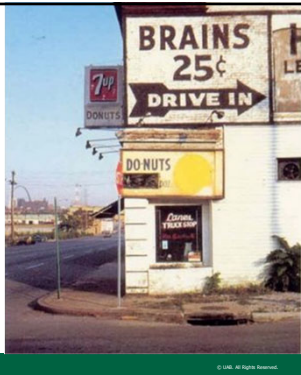
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Disclosures

- Financial disclosures
 - Site-PI for NIH-sponsored ICH grants
- Advisory Board for Legacy of Hope



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Brain Death

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Universal Determination of Death Act

1981: President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. Guidelines for Determination of Death.

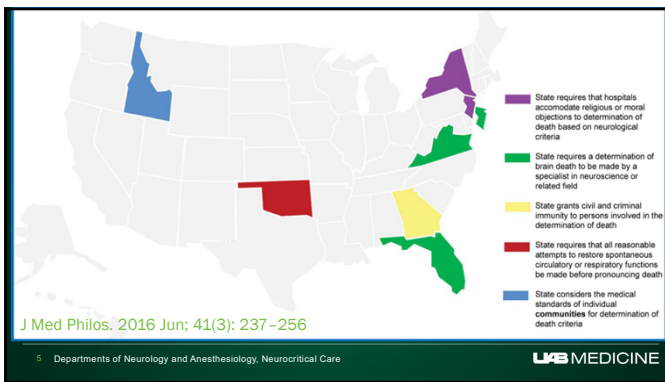
An individual who has sustained either (1) irreversible cessation circulatory and respiratory functions, or (2) irreversible cessation of all functions of the entire brain, including the brainstem, is dead.

A determination of death must be made in accordance with accepted medical standards

JAMA 1981; 246: 2184-2186.

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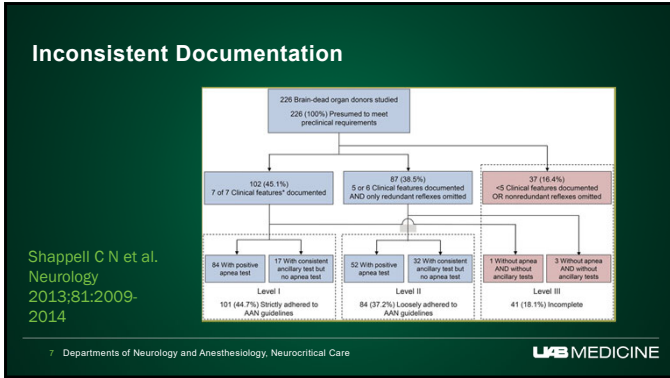
Institutional Variability

- Many centers specify which providers perform brain death evaluations: CC, Neuro, Neurosurgery, anesthesiologists, EM, trauma surgeons, etc.
 - APPs can do it in some places (Alaska, Georgia)
- Multiple clinical exams (71%), sometimes with different physicians
 - Interval varies from 1-24 hours
- Temperature requirements range from 32.2 to 36.5
- Hemodynamic instability is prohibited in most centers (71%), but definition varies

Greer DM, Varelas PN, Haque S, Wijdicks EFM. Variability of brain death determination guidelines in leading US neurologic institutions; Neurology 2008; 70 (4): 284-9.


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Aden Hailu

- Stomach Pain 4/1/15
 - Underwent appendectomy
- Persistent coma
- May 28th: apnea test



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In re guardianship of Hailu: The Nevada Supreme Court casts doubt on the standard for brain death diagnosis

Greg Yanke¹, Mohamed Y. Rady² and Joseph L. Verheijde³

Abstract
In the recent court case of In re Guardianship of Hailu, the Nevada Supreme Court cast doubt on the acceptability of the American Academy of Neurology's guidelines as a medical standard for determining brain death. The Uniform Determination of Death Act, which has been adopted in every state, requires that brain death diagnoses be made in accordance with accepted medical standards. The Court expressed concern that the guidelines fail to ensure that there is an irreversible cessation of all functions of a person's entire brain, which is a component of the Act's definition of death. Although the Nevada Supreme Court remanded the case to the District Court to hear more expert evidence concerning whether the guidelines constitute "accepted medical standards," the patient who was the subject of the case met the criteria for cardiopulmonary death several weeks prior to the hearing and the legal case became moot. As a result, the issue of whether the American Academy of Neurology guidelines, or some other criteria for determining brain death, are accepted medical standards for determining whether all brain function has ceased remains unresolved.

Keywords
Aden Hailu, bioethics, brain death, Uniform Determination of Death Act

However, on appeal, the Nevada Supreme Court, in a November 16, 2015, decision, held that it is not clear that the AAN guidelines are "accepted medical standards" under Nevada's Uniform Determination of Death Act (UDDA).³

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J. Med. Toxicol. (2017) 13:271–279
DOI 10.1007/s13181-017-0466-6

POSITION STATEMENT

ACMT Position Statement: Determining Brain Death in Adults After Drug Overdose

Mark J. Nevins¹ · Andrew Strohbach² · David M. Green¹ · Lewis S. Nelson¹ · Shaw W. Scaife³ · Jeffrey Brown⁴ · Laura M. Terrence-Holmes⁵ · On behalf of the American College of Medical Toxicology

- **"5 half-lives" recommendation may be insufficient in cases of drug overdose**
- $0.5^5 = 0.03125 \rightarrow < 3\%$ of the drug remains
- In the case of a very large overdose, 3% may be clinically relevant
- Half-life may be prolonged:
 - Delayed gastric emptying
 - Extended-release preparations
 - Hypomotility/hypoperfusion of the gut
 - Hypothermia
- For example: baclofen $-t_{1/2}$ is 2.4 hours
 - In overdose patients coma may last up to 7d

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Metabolic Derangements That May Confound DNC Evaluation

Laboratory Result	Value
Ammonia	> 75 umol/L
Blood Urea Nitrogen	>75 mg/dL
Calcium (or ionized calcium)	< 7 mg/dL or > 11 mg/dL
Glucose	< 70 mg/dL or > 300 mg/dL
Magnesium	< 1.5 mg/dL or > 4 mg/dL
Potassium	< 3 mmol/L or > 6 mmol/L
Sodium	<130 mmol/L or > 160 mmol/L
pH	< 7.3 or > 7.5
Total T4	< 3 mg/dl or > 30 mg/dL
Free T4	≤ 0.4 ng/dL or > 5 ng/dL

https://cdn-links.lww.com/permalink/wnl/di/wnl_2023_10_03_wessels_1_sd04.pdf

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Apnea Testing

- **"Clinicians must perform at least 1 apnea test."**
 - Several described methods:
 - Apneic oxygenation
 - PEEP valve
 - CPAP
 - Abort if sats < 85%
- **Criteria for Demonstrating Apnea**
 - $CO_2 \geq 60$ and ≥ 20 from baseline
 - pH < 7.30
 - Chronic CO_2 retention:
 - Ancillary test if baseline CO_2 is unknown

Gent, M., Scaravilli, V., Colomito, S.M., Confalonieri, A., Len, R., Meggioni, E., Aelli, L., Vargiolu, A., & Clerico, G. (2015). Apnea test during brain death assessment in mechanically ventilated and EDMO patients. *Intensive Care Medicine*, 42, 72-81.

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Ancillary Testing

- **Recommends against routine use**
- **Necessary if:**
 - Some portions of the exam cannot be completed
 - Patient retains CO₂ at baseline and baseline is unknown
 - Metabolic derangements cannot be adequately corrected
 - Cardiopulmonary instability precluding apnea test
- **Cannot be used in the setting of hypothermia or high levels of sedating drugs**



Image Credit: Pedro Fregoso Costa
https://www.researchgate.net/publication/328542740_A_Technologist's_Guide_to_Brain_Imaging

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Ancillary Testing: Recommendations

Recommended

- 4-vessel catheter angiography
- Radionuclide perfusion scintigraphy
- Radionuclide angiography
- TCD (adults only)

Not Recommended

- EEG
- SSEPs/AEPs
- CTA
- MRA

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Primary Posterior Fossa Injury

Recommendation 40 Rationale

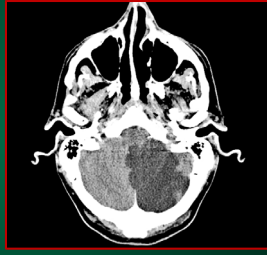
Patients with primary posterior fossa injury may be clinically comatose with brainstem areflexia and apnea; however, they may retain some cortical function.e31

Recommendation Statement 40

To avoid determining BD/DNC in patients with primary posterior fossa injury and retained supratentorial function, clinicians should ensure that the posterior fossa process has also led to catastrophic supratentorial injury as demonstrated on a conventional neuroimaging study before initiating the BD/DNC evaluation (Level B).

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Uniform Determination of Death Act

Uniform Law Commission

2021 | Determination of Death Committee

The committee will update the Uniform Determination of Death Act. Issues to be considered include the medical criteria for determining death, the distinction between irreversible versus permanent cessation of brain functions, the relevant regions of the brain, and several other issues identified by the study committee that recommended this project.

Chair	Members	Reporters	Advisors
Chair: Thomas Samuel, Wake Forest	Members: Rebecca Samuel, Wake Forest; Blake Bell	Reporters: Karoline Nita, Duke University School of Law	Advisors: [List of names and affiliations]

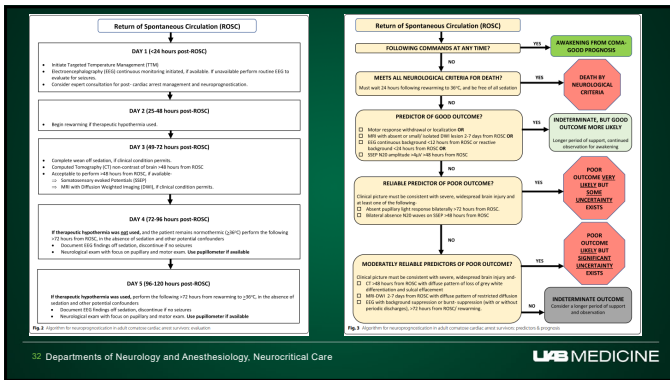
Prognosis

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Moderately Reliable

- **Exam Findings:**
 - Absent pupillary reflexes at 72 h
- **Neuroimaging:**
 - CT: Diffuse loss of GW
 - > 48 h from ROSC
 - MRI: Diffuse diffusion restriction
 - 2-7d from ROSC
- **Electrodiagnostics:**
 - EEG: suppressed background or burst suppression
 - > 72 h from ROSC or rewarming
 - SSEP: bilaterally absent N20
 - > 48h from ROSC



ICH

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ENRICH:

- Randomized, adaptive, comparative-effectiveness design
- Included patients with lobar and anterior basal ganglia hemorrhages
 - 18-80 years, 30-80cc, GCS 5-14
 - ABG arm terminated early
- Improved outcomes (Uw-MRS at 180 days) in the surgical arm
 - Mortality: 20.0% (S) vs 23.3% (MM)
 - Uw-MRS: 0.458 vs 0.374; difference = 0.084
 - Bayesian posterior probability of superiority of 0.9813



<https://www.medscape.com/viewarticle/991805>

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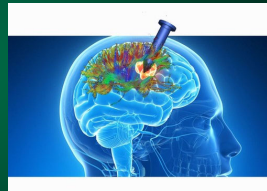
ENRICH:

Enrolled patients with lobar or ABG ICH who could be treated within 24h

- ICH volume 30-80 cc

BG arm was stopped due to futility
Demonstrated improved outcomes (UWmRS at 6 mo) in the surgical arm

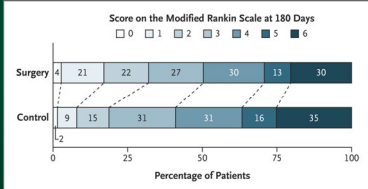
- Also shorter LOS
- Benefit restricted to lobar hemorrhages
- NNT 8 to prevent bad outcome



N Engl J Med 2024;390:1745-55.
DOI: 10.1056/NEJMoa2313040/



End Point	Surgery Group (N=150)	Control Group (N=150)	Estimated Difference (95% Credible Interval)	Posterior Probability of Superiority
Death by 30 days — no. (%)	14 (9.3)	27 (18.0)	-8.7 (-16.4 to -1.0)	0.987
Postoperative rebleeding associated with neurologic deterioration — no. (%)†	5 (3.3)	NA		NA
Change in hematoma volume — mL‡	-43.9;30.09	4.0;37.82	-47.91 (-53.59 to -42.36)	>0.999
One or more serious adverse events — no. (%)	95 (63.3)	118 (78.7)	-15.3 (-25.4 to -5.2)	0.998
Death in the hospital after randomization — no. (%)	7 (4.7)	19 (12.7)	-8.0 (-14.5 to -1.5)	0.994



ICH Score and Functional Outcome

- 12 month outcomes
- 34% improved between hospital discharge and 1 year.
- 13% improved by at least 2 grades

1 patient (cerebellar ICH who underwent surgery)

Hemphill, Farrant, O'Neill. *Neurology*. 2009;73(14):1088-1094. 2009 by Lippincott Williams & Wilkins

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Figure 1 Comparison of mortality rates

ICH Score	ICH score predicted mortality (%)	Observed mortality of entire cohort (%)	Observed mortality in maximally treated patients (%)
0	10	10	10
1	15	15	15
2	25	30	25
3	70	55	35
4	95	75	45
5	100	90	50

Jochen A. Sembill et al. *Neurology* 2517:89-423-431

AMERICAN ACADEMY OF NEUROLOGY

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From: One-Year Outcome Trajectories and Factors Associated with Functional Recovery Among Survivors of Intracerebral and Intraventricular Hemorrhage With Initial Severe Disability

JAMA Neurol. 2022;79(5):856-868. doi:10.1001/jamaneurol.2022.1991

Date of download: 10/27/2023

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ARTICLES | VOLUME 402, ISSUE 10395, P27-40, JULY 01, 2023 [Download Full Issue](#) PDF [787 KB] Figures Save

The third Intensive Care Bundle with Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial (INTERACT3): an international, stepped wedge cluster randomised controlled trial

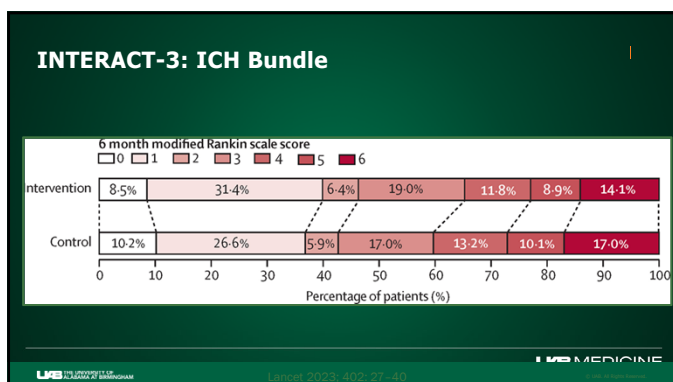
Prof Lu Ma, MD * • Xin Hu, MD * • Lili Song, PhD * • Xiaoying Chen, PhD * • Menglu Ouyang, PhD • Prof Laurent Billot, MRes • et al. [Show all authors](#) • [Show footnotes](#)

[Open Access](#) • Published: May 25, 2023 • DOI: [https://doi.org/10.1016/S0140-6736\(23\)00806-1](https://doi.org/10.1016/S0140-6736(23)00806-1)

Intervention arm:

- Blood Pressure: SBP 130-140 w/in 1h
- Glucose: 110-140 (-DM) or 140-180 (+DM)
- Temperature: T ≤ 37.5
- Anticoagulation: Reverse in 1h (warfarin only)

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INTERACT 3: Outcomes

Figure S5. Kaplan-Meier curve of mortality over 6 months

HR (95%CI): 0.79 (0.68, 0.93) P value: 0.02

Adverse Events			
	Bundle	Usual	
Total	16.0%	20.1%	0.0098
Stroke	1	11	
PNA	26	48	
AHRF	18	34	

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Code ICH: A Call to Action

Qi Li, MD, PhD, Aleksandra Yakhkind, MD, MS, Anne W. Alexandrov, PhD, AGACNP-BC, ANVP-BC, Andrei V. Alexandrov, MD, Craig S. Anderson, MBBS, PhD, Dar Dowlatshahi, MD, PhD, Jennifer A. Frontera, MD, ... [SHOW ALL](#), and Stephan A. Mayer, MD

AUTHOR INFO & AFFILIATIONS

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