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Hilary H. Wang, MD
Panayiotis N. Varelas, MD, PhD
Galen V. Henderson, MD
Eelco F.M. Wijdicks, MD, PhD
David M. Greer, MD, MA

Correspondence to Dr. Greer: david.greer@yale.edu

ABSTRACT

Objective: To demonstrate that progress has been made in unifying brain death determination guidelines in the last decade by directly comparing the policies of the *US News and World Report*'s top 50 ranked neurologic institutions from 2006 and 2015.

Methods: We solicited official hospital guidelines in 2015 from these top 50 institutions, generated summary statistics of their criteria as benchmarked against the American Academy of Neurology Practice Parameters (AANPP) and the comparison 2006 cohort in 5 key categories, and statistically compared the 2 cohorts' compliance with the AANPP.

Results: From 2008 to 2015, hospital policies exhibited significant improvement ($p = 0.005$) in compliance with official guidelines, particularly with respect to criteria related to apnea testing ($p = 0.009$) and appropriate ancillary testing ($p = 0.0006$). However, variability remains in other portions of the policies, both those with specific recommendation from the AANPP (e.g., specifics for ancillary tests) and those without firm guidance (e.g., the level of involvement of neurologists, neurosurgeons, or physicians with education/training specific to brain death in the determination process).

Conclusions: While the 2010 AANPP update seems to be concordant with progress in achieving greater uniformity in guidelines at the top 50 neurologic institutions, more needs to be done. Whether further interventions come as grassroots initiatives that leverage technological advances in promoting adoption of new guidelines or as top-down regulatory rulings to mandate speedier approval processes, this study shows that solely relying on voluntary updates to professional society guidelines is not enough. ***Neurology*® 2017;88:562–568**

GLOSSARY

AAN = American Academy of Neurology; **AANPP** = American Academy of Neurology Practice Parameters.

The determination of death by neurologic criteria, or brain death as it is commonly called, has become codified through an extensive process over many decades.[1–3] The medical community has widely embraced and accepted brain death as a medical and legal diagnosis, and society has placed trust in the medical community to ensure good process and high reliability in this diagnosis.

The American Academy of Neurology (AAN) has taken the lead in providing guidelines and practice parameters for brain death determination, starting with the 1995 AAN Practice Parameters (AANPP).[4] However, members of our group who worked at different US institutions became concerned that variability in hospital policies might exist, which could lead to inaccurate brain death determination. We assessed this variability in 2008 in a study of the *US News and World Report* top 50 ranked institutions for neurology and neurosurgery[5] and indeed found significant variability not only between hospitals but also with accordance to the current AANPP

From the Department of Neurology (H.H.W., D.M.G.), Yale University School of Medicine, New Haven, CT; Department of Neurology (P.N.V.), Henry Ford Hospital, Detroit, MI; Department of Neurology (G.V.H.), Harvard Medical School, Cambridge, MA; and Department of Neurology (E.F.M.W.), Mayo Clinic, Rochester, MN.

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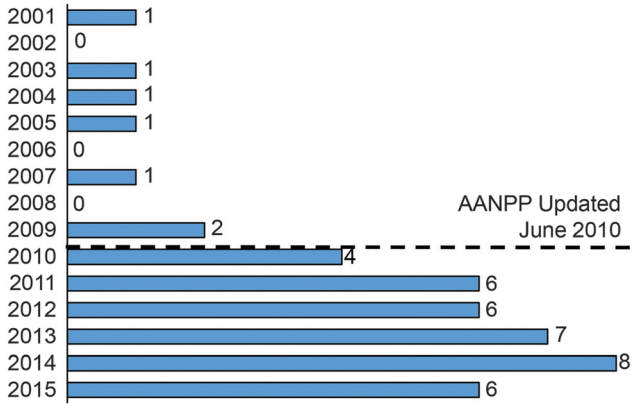
Figure 1 Year of most recent policy update/revision



The majority of institutions (74%) have updated their policies at a date after the June 2010 update to the American Academy of Neurology Practice Parameters (AANPP), while 16% did not and 10% made no mention of revision date, suggesting that most institutions had an opportunity to review the official guidelines before adopting their current policies, but 26% did not.

at that time. This led to an update of the AANPP in 2010,[6] which served not only to validate the central tenets of the 1995 practice parameters but also to be highly proscriptive in the details of brain death determination, including the provision of a detailed checklist and description of how determination is accurately performed. The mission of the guidelines was to provide a template that would allow hospitals to incorporate these new guidelines and the checklist into their hospital policies, thereby helping to ensure a sound and 100% accurate process.

The purpose of this study was to re-evaluate the top 50 ranked programs (as of 2015) to see whether policies were being updated to be in accordance with the current AANPP and whether variability still exists.

METHODS **Standard protocol approvals, registrations, and patient consents.** Informed consent and institutional review board approval were not required because the study involved no human participants and the guidelines were in the public domain and not considered private property.

The 2008 policy data were obtained directly from our previous similar study, which provides further details on methodology.[5] For the 2015 data, we referenced the 2015 *US News and World Report* top neurology and neurosurgery hospitals rankings.[7] Data acquisition took place July 2015 to January 2016 through solicitation of hospital policies via direct personal e-mail or assistance from local organ procurement organizations. Institutions were all provided assurance of anonymity of their policies and that the purpose of the study was to provide summary statistics across all institutions.

As in the original 2008[1] and expanded 2015[8] studies, we used 5 categories of data: determination performance (i.e., who was qualified to determine brain death), prerequisites for testing, details of the clinical examination, details of apnea testing, and details of ancillary testing. Using this framework, we created summary statistics for variability and commonality among institutions.

Data from both 2008 and 2015 were then assessed for a binary measure of compliance (either yes, precisely matched, or no, did not match) with the official AANPP at the time (either the 1995 AANPP for the 2008 cohort of policies or the 2010 update for the 2015 policies). Criteria for which the AANPP did not provide specific guidance were excluded from this analysis (e.g., waiting period between 2 examinations). A total of 55 policy criteria were assessed for 2015 hospitals and 57 for the 2008 cohort. The cohorts were then split into paired hospitals (those in the top 50 at both time points with both policies obtained, n = 29) and unpaired (n = 9 unique 2008 policies and n = 20 unique 2015 policies). Compliance data were compared by use of paired-sample, 2-tailed *t* tests for the paired group and 2-sample, 2-tailed *t* tests assuming unequal variance for the unpaired group. No change in rates of compliance was used as the null hypothesis in both instances. *p* Values for these 2 groups were then combined by use of the Fisher method.

RESULTS A total of 49 hospitals provided policies for the 2015 arm; of these, all (100%) had official guidelines for brain death determination at their institution. The 2008 study obtained 38 policies from 41 respondents, with 29 institutions contributing policies in both time periods. Of the 49 policies in the 2015 study, 76% had been instituted or revised at a time after the June 2010 update to the AANPP, while 16% did so before 2010 and 10% made no mention of their date of revision (figure 1). Multiple examinations were required in 71% of 2008 guidelines but only 61% of those in 2015.

Summary statistics. With regard to who was qualified to perform brain death determination, 23 (47%) of the 2015 policies required some type of education (e.g., training) or competency specific to brain death, while 21 (43%) did not and 5 (10%) made no mention. Further breakdown of specialties of providers found neurology or neurosurgery attendings stipulated most frequently, with 49% of policies explicitly encouraging their participation, followed by primary attendings (41%), an unspecific licensed physician (22%), intensivists (24%), and finally emergency medicine physicians (6%), with a further 10% making no mention. (Note that these percentages do not sum to 100% because multiple policies mentioned more than one type of provider.) Of note, no policy in 2015 explicitly stated that an advance-practice provider (e.g., nurse practitioner or physician assistant) could determine brain death.

Most hospitals required 2 brain death examinations (61%), with a minority requiring only one (27%), requiting either 1 or 2 (8%), or making no mention of how many (4%). Within the subset of 34 hospitals requiring 2 examinations, 28 (82%) specified that 2 separate physicians (rather than the same one) perform those examinations. A waiting

period between the first and second examinations was specified in 53% of those policies (18 of 34), with the majority (14 of 18) stipulating a period of 6 hours. Twenty-two percent of institutions also explicitly stipulated a waiting period for patients experiencing cardiac arrest. Sixty-four percent of these (7 of 11) specified 24 hours.

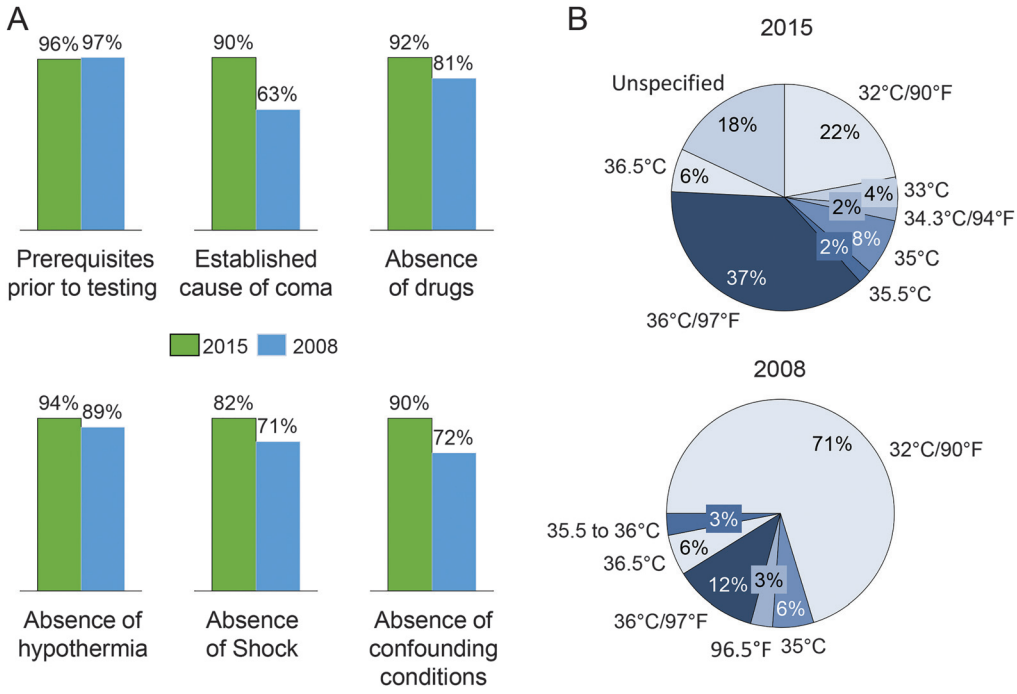
The vast majority of policies (96%) established prerequisites before a clinical examination was initiated to rule out confounders. These included the absence of hypothermia (94%); absence of drug effect (92%); absence of confounding conditions such as endocrine, acid-base, and electrolyte disorders (90%); assurance that providers can identify the cause of coma (90%); and establishment of the absence of shock (82%) (figure 2).

Specifically within the prerequisite criteria looking for the absence of drug effects, the 2015 policies largely ruled out potential confounding from both sedatives and paralytics (61%, plus 10% mentioning both and another drug) vs a minority of policies looking for only one or the other (6% sedatives, 2% paralytics, 2% paralytics + other). Thirty-seven percent of policies also specified acceptable drug level thresholds, and 31% stipulated the use of neuromuscular testing (i.e., "train of 4") to confirm the absence of ongoing neuromuscular blockade.

The minimum temperature thresholds to qualify for absence of hypothermia varied greatly, from 32°C/90°F (22%), 33°C (4%), 34.3°C/94°F (2%), 35°C (8%), 35.5°C (2%), and 36°C/97°F (37%), to 36.5°C (6%). Ten percent of policies did not specify a minimum core temperature but acknowledged the need for absence of hypothermia. Eighty-two percent of institutions required absence of shock as a prerequisite, but the definitions in the policies of a lowest acceptable blood pressure ranged from systolic blood pressures of 90 mm Hg (22%) or 100 mm Hg (22%) to mean arterial pressures of 60 mm Hg (10%) and 65 mm Hg (2%). Forty-four percent of these institutions requiring absence of shock did not define any lower threshold for blood pressure. Finally, most policies (92%) required patients to have no confounding medical conditions. Of these policies, 80% further stipulated the absence of acid-base, endocrine, and electrolyte derangements.

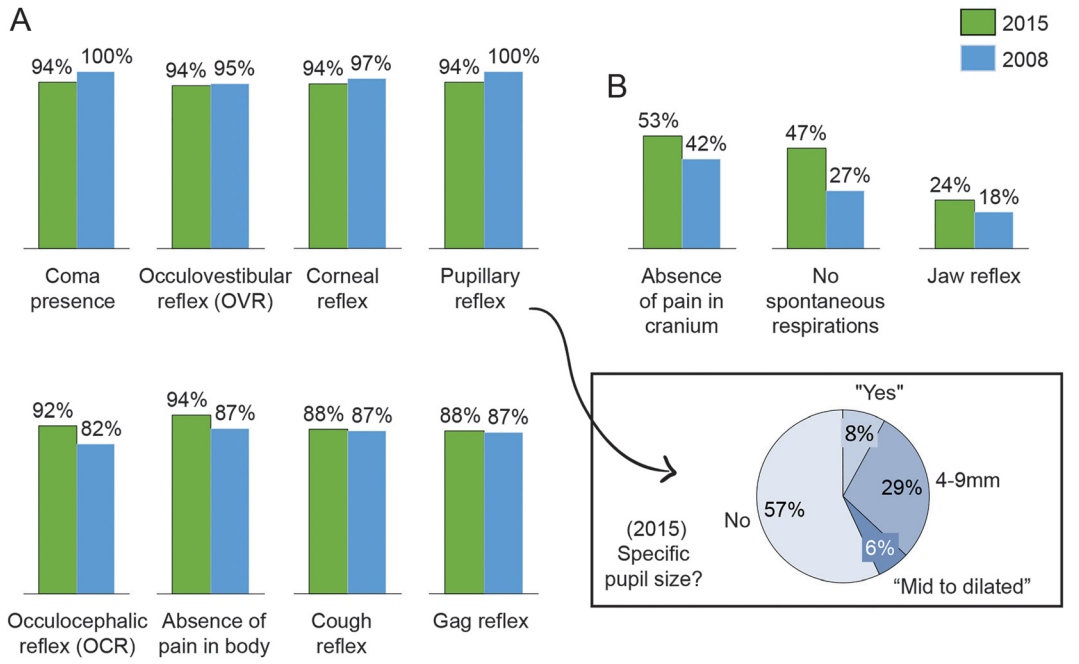
Within the clinical examination, the vast majority of policies looked for the presence of coma (94%), absence of pain response with peripheral stimulation (94%), and absence of oculovestibular (94%), oculocephalic (92%), corneal (94%), pupillary (94%), cough (88%), and gag (88%) reflexes. Approximately half of policies (43%) looked for specific pupil sizes in the 4 to 9 mm (29%) or mid to dilated (6%) range. Notably, consistently poor compliance was seen in absence of reaction to pain above the foramen magnum (53%), lack of spontaneous respirations (47%), and testing of the jaw jerk reflex (24%) (figure 3).

Figure 2 Prerequisites to testing



(A) The vast majority of 2015 policies (96%) required the perquisites listed by the American Academy of Neurology Practice Parameters, but the policies contained high variability in details (e.g., [B] the definition of hypothermia).

Figure 3 Clinical examination compliance with AANPP, 2015 vs 2008



(A) Consistent compliance to the majority of the clinical examination is shown, with additional specificity for pupil size in 45% of policies. (B) Areas of notably poor adherence in 2008 and 2015. AANPP = American Academy of Neurology Practice Parameters.

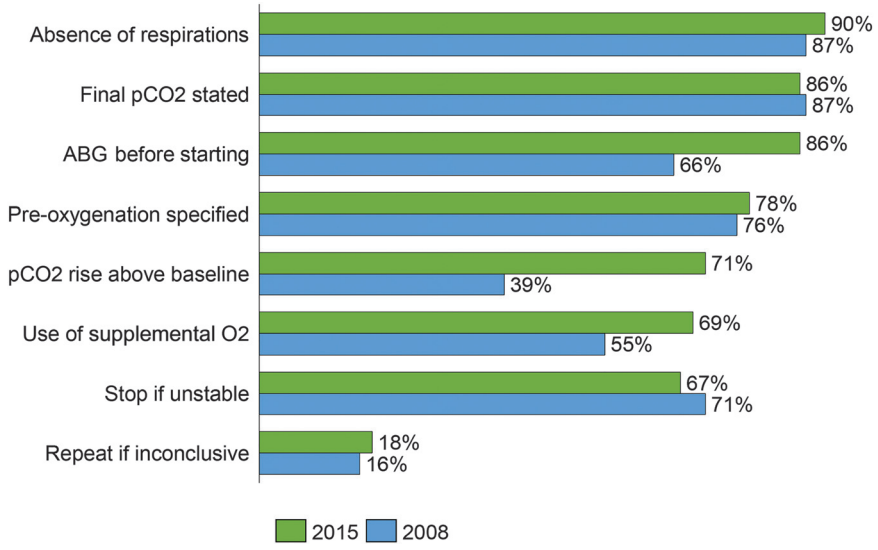
Apnea testing, in addition to the clinical examination, was required in all but one policy (98%), but the specifics of the testing technique varied widely across institutions. Sixty-one percent of 2015 policies specified a lowest acceptable body temperature (range 32°C–36.5°C), 86% specified the need for an arterial blood gas measurement before starting, and 78% specified preoxygenation. Most policies (69%) recommended maintenance of oxygenation via a cannula placed inside the endotracheal tube; a small minority permitted continued use of a mechanical ventilator on flow-by oxygenation with no delivery of breaths (6%). Supplemental oxygen rate during apnea testing was specified in 69% of policies, with specific flow rates ranging from 1 (3%), 4 (3%), 6 (56%), and 8 (6%) to 10 (9%) L/min and 100% fraction of inspired oxygen (6%). It is not clear why one policy did not stipulate apnea testing, and hospitals were not contacted for clarification or explanations of specific aspects of their policies.

A positive apnea test was specified by a final arterial P_{CO_2} of 60 mm Hg in 86% of 2015 guidelines (one policy stipulated 55 mm Hg). A secondary acceptable measurement of a rise in P_{CO_2} above baseline was specified in 71% of 2015 guidelines, with 100% of those policies referencing a minimum increase of 20 mm Hg above the patient's baseline. Sixty-seven percent of policies instructed examiners to stop apnea testing if the patient became unstable. Relatively few policies (18%) provided guidance on repeating apnea testing for inconclusive results or instability on the first attempt (figure 4).

Ancillary testing was optional in a majority of the 2015 institutions (78%), recommended in 12%, and unspecified in 10%. Eighty-four percent indicated specific situations in which ancillary testing would be recommended, most commonly related to an inability to complete the clinical (73%) or apnea (78%) testing, in addition to toxic drug levels (49%), chronic CO_2 retention (31%), and normal neuroimaging (6%). A majority of policies specified the use of the 4 AANPP-recommended ancillary tests: EEG (86%), transcranial Doppler (71%), angiography (80%), and radionuclide scintigraphy (88%). Unproven ancillary tests were stipulated in a minority of policies, specifically CT angiography (12%) and somatosensory evoked potentials (10%). In addition, relatively few policies gave specific instructions on how to administer these tests or to interpret results (49% for EEG, 37% for transcranial Doppler, 37% for angiography, and 43% for radionuclide scintigraphy) (figure 5).

Compliance statistics. Overall, the 2015 hospitals showed significant improvement in compliance with the AANPP compared with the 2008 cohort (p = 0.005, combined p value Fisher method). Looking at the subgroup comparisons, in the paired group of 29 hospitals with policies obtained in both 2008 and 2015, overall compliance with the AANPP did not

Figure 4 Apnea testing compliance with AANPP, 2015 vs 2008

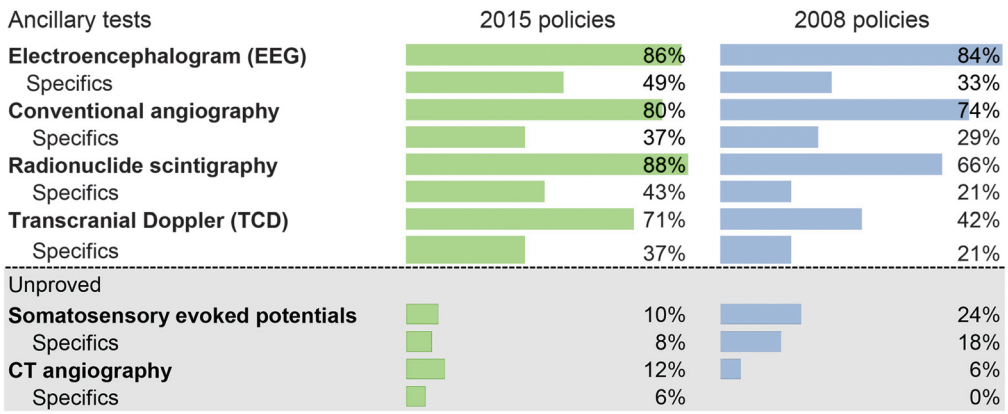


Apnea testing criteria showed a notably higher proportion of policies requiring arterial blood gas (ABG) measurement before beginning apnea testing (86% vs 66%) and a Pco_2 rise of 20 mm Hg above baseline for the test to qualify as positive (71% vs 39%). Overall compliance to the American Academy of Neurology Practice Parameters (AANPP) guidelines was greater in 2015 than in 2008 ($p < 0.04$).

show statistical improvement ($p = 0.054$, 2008 average compliance = 59.3% vs 2015 = 68.0%). However, in the unpaired hospitals, compliance showed a statistical improvement ($p = 0.011$, 2008 average compliance = 52.9% vs 2015 = 72.0%).

Breaking this overall measure of compliance into its subgroups of key categories of the brain death examination shows that most of this improvement is driven by increased uniformity in apnea testing and ancillary testing. In the paired group, 51% of 2008 hospitals complied with apnea guidelines vs 63% in 2015 ($p = 0.072$), and in the unpaired group, 42% complied in 2008 vs 71% in 2015 ($p = 0.016$). Combined, the 2015 hospitals significantly improved their compliance from 2008 ($p = 0.0091$). Similarly, for ancillary testing, both the paired and unpaired groups significantly improved their compliance from 2008 to 2015 (paired: 53%–64%, $p = 0.020$; unpaired: 47%–71%, $p = 0.003$, in combination $p = 0.0006$). In contrast, compliance for prerequisites to testing (64% to 68% from 2008 to 2015, combined paired and unpaired $p = 0.500$) and clinical

Figure 5 Policies in 2015, similar to 2008, continue to name ancillary tests much more frequently than describing their specific details (e.g., 86% look for EEG as an ancillary test, only 49% stipulate specifics)



Radionuclide scintigraphy appears in a notably greater proportion of 2015 policies (88%) than 2008 policies (66%) and with greater details (43% scintigraphy specifics in 2015 vs 21% in 2008). Unproved tests (shaded gray) continue to be endorsed by a minority of policies.

examination criteria (71% to 81%, combined $p = 0.0673$) did not differ significantly.

DISCUSSION The findings of the original 2008 study[1] on variability in brain death determination in the United States drew attention to a lack of uniformity among policies at highly ranked neurology and neurosurgery institutions. Its publication spurred the update of the AANPP in 2010,[6] designed to be simple and straightforward, conclusive, yet sufficiently detailed for practical use. Disappointingly, 16% of policies sampled in 2015 were last revised before the June 2010 publication of the AANPP update, and an additional 10% did not specify a date of creation/revision. Thus, by default, >25% of institutions might not have benefited from the AANPP update.

In assessing progress made in improving policy uniformity, we looked to 4 areas of concern highlighted by the 2008 study: low rates of neurologist/neurosurgeon involvement, strikingly high variability in numeric thresholds (temperatures, blood pressures), details of apnea testing, and ancillary testing specifics. The portions of policies detailing apnea testing ($p = 0.0091$) and ancillary testing ($p = 0.0006$) showed a statistically greater compliance to 2010 AANPP. This encouraging result is suggestive of an effect of the revised brain death guidelines on hospital policies, but this cannot be fully established. However, variability continued to be high in terms of policies specifying neurology or neurosurgery involvement, and it is conventional wisdom that a specialist in the acute neurosciences would be preferred, but comparative studies are not available and are difficult to perform. Data from simulation scenarios suggest differences between critical care and neurology trainees.[9]

These results suggest primarily a good response to the 2010 AANPP revision, which appears to have had a positive effect on the content of individual institutional policies. We suggest 2 possible theories for why some policies have not been updated: a false sense of security and lack of regulatory oversight driving change.

As the 2010 AANPP highlighted, although the legitimacy of death determination by neurologic criteria has faced some opposition since its inception, there has never been a single reported case of recovery of neurologic function after the clinical diagnosis of brain death was made with full adherence to the 1995 AANPP.[6] Given this tremendous nationwide success of declaring death by neurologic criteria, hospitals may be lulled into a false sense of security in the validity and sufficiency of their existing policies. However, this logical fallacy masks the fact that the primary reason why the criteria have been afforded accurate diagnosis is the regular, precautionary updates that aim to identify what might lead to misdiagnosis before it can occur. Indeed, we know from the 1981 President's Commission that, by earlier criteria, physicians would have misdiagnosed toxic drug ingestions and other conditions as brain death. The crucial detail in the success of brain death determination thus far lies in its tremendous evolution since the original 1968 Harvard criteria and reaffirms the importance of participation in this iterative process at the local level.

Second, change is a costly, time-consuming process for any institution, particularly voluntarily change that may not directly influence a hospital financially. Without enforced accountability for having up-to-date brain death policies, institutions may understandably react slowly and partially to any updates in practice parameters. Aside from these broad theories, explanations for lack of uniformity may be specific to an institutional level. For example, the culture of a particular hospital may wish to leave the details of determination to the discretion of the physician.

This study made a key assumption that the adoption of an official hospital policy for brain death determination is indicative of actual practice. That is, it is assumed that the physicians practicing in those hospitals made regular use of and adhered to those policies. This is certainly not a guarantee at institutions employing many physicians at various stages of training (who may also have spent time practicing the different policies of a previous employer). It has been shown that documentation of brain death determination also varies widely across hospitals.[10] Therefore, actual practice could be either more or less variable than the policies suggest (e.g., if only a few physicians within an institution diagnose the majority of brain deaths and they mutually decide to follow the AANPP criteria without changing the hospital policy to match or vice versa). Another limitation is the sample bias of only looking at highly ranked neurologic institutions, which are not representative of many smaller, community hospitals in the nation. In addition, within the statistical analysis of this highly ranked group, the sets of hospitals in 2008 and 2015 were only partially overlapping, with more of the significance in improvements deriving from the unpaired, nonoverlapping institutions.

For physicians to preserve the legitimacy of the diagnosis of brain death and to maintain the public's trust in the medical community, brain death needs to be accurately diagnosed 100% of the time. Patients and their loved ones deserve the peace of mind of knowing that to be true no matter where the diagnosis takes place. However, because even the top 50 neurologic institutions in one of the most medically advanced nations are not in agreement after 2

decades of efforts toward uniformity, room for improvement remains.

Our recent study attempted to further quantify the magnitude of variability in brain determination of all hospitals with intensive care capabilities in the United States.[8] Among the 508 nationwide hospitals it queried, a similar lack of consensus existed.[8] Variability in brain death policies is a now a known national problem, one that does not seem be adequately addressed solely with an update to professional society guidelines. This raises deeper questions of the current capacity of medicine to react in a timely and unified way to changes in our understanding of best practices for patient care. Thus far, one encouraging move to modernize and accelerate the pace of policy updates is the Neurocritical Care Society's online tool kit for brain death, which includes an online course, video demonstrations of clinical examination techniques, and sample policies and checklists for institutions to easily adopt and implement.[11] In addition, there are currently ongoing efforts to create templates within existing electronic medical records to improve the ease and accuracy of documentation and to help ensure good practice.

However, beyond the promotion of user-friendly, digital resources, The Joint Commission or the Department of Public Health, in its ongoing assessments of hospitals nationwide, may consider adding the standardization of brain death determination to its roster of requirements for accreditation. Regulatory oversight, rather than voluntary participation, may be the missing driver to accelerate AANPP adoption.

AUTHOR CONTRIBUTIONS

Hilary Wang: acquisition of data, analysis and interpretation of the data, drafting and revising the manuscript for intellectual content. Panayiotis Varelas, Galen Henderson, and Eelco Wijdicks: revision of the manuscript for intellectual content. David Greer, acquisition of data, design and conceptualization of the study, analysis and interpretation of the data, and drafting and revising the manuscript for intellectual content.

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DISCLOSURE

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