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# Frequency of Withdrawal of Life-Sustaining Therapy for Perceived Poor Neurologic Prognosis

**OBJECTIVES:** To measure the frequency of withdrawal of life-sustaining therapy for perceived poor neurologic prognosis among decedents in hospitals of different sizes and teaching statuses.

**DESIGN:** We performed a multicenter, retrospective cohort study.

**SETTING:** Four large teaching hospitals, four affiliated small teaching hospitals, and nine affiliated nonteaching hospitals in the United States.

**PATIENTS:** We included a sample of all adult inpatient decedents between August 2017 and August 2019.

**MEASUREMENTS AND MAIN RESULTS:** We reviewed inpatient notes and categorized the immediately preceding circumstances as withdrawal of life-sustaining therapy for perceived poor neurologic prognosis, withdrawal of life-sustaining therapy for nonneurologic reasons, limitations or withholding of life support or resuscitation, cardiac death despite full treatment, or brain death. Of 2,100 patients, median age was 71 years (interquartile range, 60–81 yr), median hospital length of stay was 5 days (interquartile range, 2–11 d), and 1,326 (63%) were treated at four large teaching hospitals. Withdrawal of life-sustaining therapy for perceived poor neurologic prognosis occurred in 516 patients (25%) and was the sole contributing factor to death in 331 (15%). Withdrawal of life-sustaining therapy for perceived poor neurologic prognosis was common in all hospitals: 30% of deaths at large teaching hospitals, 19% of deaths in small teaching hospitals, and 15% of deaths at nonteaching hospitals. Withdrawal of life-sustaining therapy for perceived poor neurologic prognosis happened frequently across all hospital units. Withdrawal of life-sustaining therapy for perceived poor neurologic prognosis contributed to one in 12 deaths in patients without a primary neurologic diagnosis. After accounting for patient and hospital characteristics, significant between-hospital variability in the odds of withdrawal of life-sustaining therapy for perceived poor neurologic prognosis persisted.

**CONCLUSIONS:** A quarter of inpatient deaths in this cohort occurred after withdrawal of life-sustaining therapy for perceived poor neurologic prognosis. The rate of withdrawal of life-sustaining therapy for perceived poor neurologic prognosis occurred commonly in all type of hospital settings. We observed significant unexplained variation in the odds of withdrawal of life-sustaining therapy for perceived poor neurologic prognosis across participating hospitals.

**KEY WORDS:** critically ill; end-of-life care; epidemiology; neurologic disorders; prognosis; withdrawing treatment

Approximately 760,000 inpatient deaths occur in the United States annually. Few inpatients die after cardiopulmonary arrest despite full treatment. Instead, most deaths occur after withdrawal of life-sustaining therapies (WLSTs) (1, 2), although patterns in WLST vary by country and region and have changed over time (3–6).

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Providers may recommend WLST for perceived poor neurologic prognosis (WLST-N) (7) and/or non-neurologic reasons such as acute or chronic organ failure believed to be incompatible with recovery (8). Prognostication of neurologic complications often depends on various factors such as age, severity, and etiology of the condition as well as comorbidities. The process through which providers formulate a neurologic prognosis is complex and imprecise. Because gold standard prognostic tests do not exist for most neurologic illnesses, providers instead rely on specialized training, clinical experience, imperfect tests, and heuristics to predict patient outcome. Prior research has demonstrated significant interprovider variability, nonevidence-based practice, and poorly calibrated decisions in this context (9–12).

Studies describing the frequency of WLST have not differentiated WLST-N from WLST for nonneurologic reasons (1, 2, 4, 13). Understanding the prevalence and location of WLST-N is critical, since WLST-N may be the result of neurologic prognostication. We conducted a multicenter cohort study to determine the frequency of WLST-N. We hypothesized WLST-N would be common regardless of hospital or ICU characteristics.

## MATERIALS AND METHODS

We performed a multicenter retrospective cohort study of patients who died in one of 17 U.S. hospitals from August 2017 to August 2019. Each centers' Institutional Review Board approved this study or waived the need for approval (see **Supplemental Material**, <http://links.lww.com/CCX/A711> for each centers' board name and study approval/waiver number).

Participating hospitals included four large teaching hospitals, four small teaching hospitals, and nine nonteaching hospitals. The four large teaching hospitals were University of Pittsburgh Medical Center, Yale New Haven Hospital, Hospital of the University of Pennsylvania, and University of North Carolina Medical Center. Small teaching and nonteaching hospitals were all chosen based on affiliations with large teaching hospitals. Classification of hospitals was based on hospital size, ICU size, teaching status, and volume of organ donation.

We included all patients 18 years old and older, regardless of reason for admission. We excluded patients who died in the emergency department. Federal

regulatory compliance requires acute care hospitals to maintain a record of every in-hospital death. We obtained a list of patient deaths from each participating hospital.

From the list of all patient deaths, we selected a random sample of cases to include. For each participating site, we first obtained a list of all inpatient deaths, which we then deidentified. We then generated a random integer in Stata Version 15 (StataCorp, College Station, TX), sorted the list by this integer, and selected the first 300–600 cases, depending on the site. We initially estimated a sample size of 600 subjects, powered to detect a 15% difference in the incidence of WLST-N between any two equally sized subgroups and assuming 15% of outcomes could not be determined due to inadequate documentation in the electronic health record. Preliminary single-center data indicated this sample estimation was overly conservative, so for subsequent teaching sites, we reduced the required sample size to 300 per site. Because of a priori uncertainty in differences in the thoroughness of clinical documentation between teaching and nonteaching hospitals, which might have limited our ability to determine proximate cause of death reliably, we retained the initial sample size estimate of 600 for inclusion at nonteaching sites.

Two independent reviewers at each participating site completed a structured chart review using Research Electronic Data Capture (Clinical and Translational Sciences Institute at the University of Pittsburgh; the National Institutes of Health grant UL1-TR-001857). We reviewed all available clinical documentation but focused on physician and nursing notes from the day of and day prior to death. We recorded patients' age, sex, and hospital length of stay. We further recorded the unit in which a final prognostic decision leading to limitations in care was made (if any) and the unit in which death occurred. We reviewed daily clinical notes and death summaries to record the main organ system or disease process responsible for patients' death, which we coded as cancer, neurologic, cardiovascular, pulmonary, renal, hepatic, trauma, infection, multisystem organ failure, gastrointestinal, or other. We allowed for multiple selections of the primary pathology that was responsible for patients' death. We determined circumstances and decision-making preceding death by reading through all relevant clinical documentation in patients' chart, with particular focus

on physician and nursing documentation such as death summaries and family meeting synopses. We recorded the circumstances and decision-making preceding death, classified as WLST-N, WLST for nonneurologic reasons, limitations or withholding of life support or resuscitation, death despite full treatment (rearrest/intractable shock), or brain death (**Table 1**). Multiple selections were allowed for contributing circumstances of death in the case of WLST-N, WLST for nonneurologic reasons, and withholding/limitations. For example, a patient who developed a large hemispheric stroke and pneumonia leading to acute respiratory failure and then the decision from surrogate decision-makers was to WLST, the data abstractor would choose both WLST and WLST-N. If the patient died after full treatment or brain death, then the categories were mutually exclusive, and only one option could be picked. WLST-N was selected as a proximate cause of death if documentation specifically mentioned decision-making influenced by poor neurologic prognosis or there was any discussion of neurologic diseases (i.e., dementia, stroke, anoxic brain injury, subarachnoid hemorrhage) during end-of-life meetings. For patients treated after cardiac arrest, we classified death in the same manner. If documentation discussed only prognostication based on severe hypoxic-ischemic brain injury, we classified the case as WLST-N only. If the notes discussed only multisystem organ failure, we categorized these cases as nonneurologic WLST only. If

documentation discussed both perceived poor neurologic prognosis due to hypoxic-ischemic brain injury and multisystem organ failure, then we classified the case as both WLST-N and nonneurologic WLST.

We provided chart reviewers with a codebook outlining the process and standard definitions for categorization of limitations of care. Initially, one author (A.S.) trained each abstractor by jointly reviewing 20 deidentified patients at their site to ensure adequate calibration. At each site, two abstractors independently gathered the circumstances of death. There were two local abstractors at each site, who were chosen by the primary site investigator. In cases of disagreement, these abstractors would review the case together and discuss until consensus was reached. If consensus could not be reached, a senior physician (B.S.A., E.J.G., D.Y.H., W.L., J.E.) at the site reviewed the case and adjudicated the final decision. The senior physician was not previously involved in direct care of reviewed cases.

We used descriptive statistics to summarize patient demographics and hospital characteristics. For each site, we calculated percent agreement on initial independent chart review to quantify the proportion of cases in which final coding was the result of discussion between the two reviewers. We summarized the frequency with which each circumstance of death occurred in isolation or in combination and then compared these across sites, unit types and primary diagnoses, and other demographic features, with particular

**TABLE 1.**  
**Categories of Circumstances Before End of Life**

Categories	Definitions
Full resuscitation (rearrest/intractable shock)	Cardiopulmonary arrest despite maximal medical therapy. No care is actively withdrawn before death pronouncement.
Limitations or withholding of life support or resuscitation	Patient has preexisting or new wishes limiting implementation of NEW supportive care (i.e., no cardiopulmonary resuscitation, do not intubate), and patient dies because they did not receive the care based on their limitations. Includes not receiving life-saving surgeries or other interventions (dialysis).
Withdrawal of life support for perceived poor neurologic prognosis	Cessation or removal of ongoing medical therapy for reasons including poor neurologic prognosis (e.g., discussion of “brain injury,” “long-term function,” low chance of awakening from coma, etc.), with the intent not to substitute equivalent alternative therapy. Fully anticipated that the patient will die following the cessation of therapy.
Withdrawal of life support for non-neurologic reasons	Cessation or removal of ongoing medical therapy for systemic (nonbrain) problems (e.g., long-term need for dialysis, multisystem organ failure not predicted to recover, acute or chronic respiratory failure, or heart failure, etc.), with the intent not to substitute equivalent alternative therapy. Fully anticipated that the patient will die following the cessation of therapy.
Brain death	Death by neurologic criteria. No care is actively withdrawn before death pronouncement.

focus on the distribution of WLST-N. To test the association of WLST-N with hospital length of stay, we used a generalized linear model with a gamma distribution and log link to fit the skewed continuous outcome. We estimated the incidence of WLST-N nationally by using the total number of inpatient deaths stratified by hospital type (14) and multiplying by the point estimate from this study. We estimated CIs for our national estimate by taking simultaneous draws from the multivariate binomial distributions (stratified by hospital type) and multiplied the number of deaths nationally in each hospital type. To investigate variability of WLST-N between hospitals, we used unadjusted and adjusted mixed-effects logistic regression and calculated median odds ratios (MORs) and associated 95% CIs (15). For the adjusted model, we adjusted for age, sex, primary diagnosis, and hospital type. We used Stata Version 15 (StataCorp) for analysis.

## RESULTS

We included 2,100 decedents (Table 2). Median age was 71 years (interquartile range [IQR], 60–81 yr),

and 989 (47%) were female. Median length of stay was 5 days (IQR, 2–11 d), and 1,326 patients (63%) were treated in one of four large teaching hospitals. The most common primary diagnoses leading to death were infectious (528; 25%), neurologic (482; 23%), pulmonary (411; 20%), and multisystem organ failure (377; 18%) (Table 2). Overall, there was strong agreement between abstractors on the circumstances of death (86% overall; range 84–91% across sites) with stronger agreement for WLST-N (90%). A total of 17 hospitals were included in the study (Table 3). Four hospitals were large teaching hospitals, with more than 500 hospital and 100 ICU beds.

WLST-N occurred in 516 patients (25%) and was the sole contributing factor in 331 patients (15%) (Table 4). WLST-N was common in all hospitals but occurred most often (30% of all deaths; 394 patients) at large teaching hospitals, compared with 19% of deaths (39 patients) in small teaching hospitals and 15% of deaths (84 patients) at nonteaching hospitals. Demographics of patients who had WLST-N preceding death were similar to the entire cohort, except that a neurologic diagnosis as the

**TABLE 2.**  
**Demographics of Patients**

Characteristics	All Hospitals (N = 2,100)	Large Teaching (N = 1,326)	Small Teaching (N = 196)	Nonteaching (N = 578)
Age, median (interquartile range)	71 (60–81)	66 (56–76)	67 (57–87)	77 (68–87)
Female sex, n (%)	964 (46)	602 (46)	99 (51)	263 (47)
Length of stay, median (interquartile range)	5 (2–11)	6 (2–13)	3 (1–8)	3 (2–8)
Primary pathology leading to death <sup>a</sup> , n (%)				
Infectious	528 (25)	285 (21)	57 (29)	186 (32)
Neurologic	482 (23)	385 (29)	25 (13)	72 (13)
Pulmonary	411 (20)	190 (14)	37 (19)	184 (32)
Multiple organ failure	377 (18)	198 (15)	34 (17)	145 (25)
Cardiac	304 (15)	189 (14)	30 (15)	85 (15)
Cancer	276 (13)	145 (11)	31 (16)	100 (17)
Gastrointestinal	130 (6)	78 (6)	9 (5)	43 (7)
Trauma	110 (5)	94 (7)	5 (3)	11 (2)
Liver	84 (4)	65 (5)	7 (4)	12 (2)
Renal	53 (3)	32 (2)	10 (5)	11 (2)
Other	182 (9)	145 (11)	24 (12)	13 (2)

<sup>a</sup>Totals sum to > 100% of the cohort because multiple primary pathologies could be selected for a single case.



**TABLE 3.**  
**Hospital Characteristics**

Characteristics	n (%)
Hospital size, beds	
< 100	2 (12)
100–250	7 (41)
250–500	2 (12)
> 500	6 (35)
ICU size, beds	
< 10	4 (24)
10–20	4 (24)
20–50	5 (29)
> 100	5 (29)
Teaching status	
Nonteaching	9 (53)
Small teaching	4 (24)
Large teaching	4 (24)
ICU specialty type <sup>a</sup>	
General/mixed ICU	12 (33)
Medical	6 (16)
Surgical	6 (16)
Neurologic	5 (14)
Cardiac	3 (8)
Other	5 (14)

<sup>a</sup>n sums to more than the number of hospitals since hospitals may have multiple ICUs, percentages are expressed for the total number of ICUs.

primary cause of death occurred more commonly (384 patients; 74%) (Table 5). Rate of WLST-N did not vary by age or sex. WLST-N was associated with shorter length of stay (median 4 [IQR, 1.5–10] vs 5 [IQR, 2–11];  $p < 0.001$ ).

WLST-N happened frequently across all ICUs and floors, with 146 patients (73%) in neonatal ICUs, 318 (22%) in other ICUs, and 50 (13%) outside of critical care settings. For patients with or without a neurologic disease leading to death, WLST-N occurred commonly in 382 patients (79%) and 134 patients (8%), respectively. We observed significant variability in the odds of WLST-N between sites (MOR, 1.59; 95% CI, 1.32–2.18;  $p < 0.001$  for likelihood ratio test vs a fixed-effects model). This persisted after adjusting for measured patient and hospital characteristics (adjusted MOR, 1.59; 95% CI, 1.26–2.18;  $p < 0.001$ ).

## DISCUSSION

A quarter of all inpatient deaths in our cohort occurred after WLST-N. Although the frequency varied, WLST-N was common across all individual centers, hospital types, ICU specialties, and primary diagnoses. Given that there are 760,000 inpatient deaths in the United States annually (113,483 in large teaching hospitals, 258,536 small teaching hospitals, and 398,881 nonteaching hospitals) (14), if our results are generalizable to the entire United States, our findings suggest that WLST-N precedes approximately 143,000 deaths annually (95% CI, 125,157–161,577). Given challenges with accurate neurologic prognostication, especially in the acute care setting, we hypothesize there is considerable risk for avoidable deaths resulting from therapeutic nihilism or incorrect prediction of poor outcome. We also observe considerable between-hospital variability in the odds of WLST-N, although our study did not capture factors such as physicians' demographics or patients' socioeconomic status, which may explain some or all of this (16).

Factors that inform WLST-N are complex. WLST-N occurs when a clinician formulates a neurologic prognosis and then communicates that to patients' families and loved ones, who ultimately make decisions about end-of-life care. Neurologic prognostication is challenging and complex. Understanding the neurologic examination and localization is paramount for accurate neurologic prognostication. Objective data such as neurophysiologic testing (e.g., electroencephalography and somatosensory evoked potentials), neuroimaging (e.g., computerized tomography, MRI), blood biomarkers (e.g., neuron-specific enolase, neurofilament light change) have utility in many acute illnesses, although appropriate timing and combination of testing vary on a disease-specific and case-by-case basis. By contrast, prognostication in chronic neurodegenerative conditions such as dementia often relies on understanding the baseline clinical status and disease trajectory for the individual patient. Decisions about prognostic data acquisition, interpretation, and synthesis into a treatment recommendation require considerable expertise. Even in expert hands, when evidence-based algorithms are strictly adhered to, prognosis is often uncertain (17). One reason for the lower incidence of WLST-N in small teaching and nonteaching hospitals may be a lack of available neurologic expertise or that

**TABLE 4.**  
**Preceding Events Prior to Death**

Characteristics	Patients (N = 2,100), n (%)	Large Teaching (n = 1,326), n (%)	Small Teaching (n = 196), n (%)	Non-teaching (n = 578), n (%)
WLST for perceived poor neurologic prognosis	516 (25)	394 (30)	39 (19)	84 (15)
Sole cause	331 (15)	274 (21)	14 (7)	43 (7)
WLST for non-neurologic reasons	1,168 (56)	695 (52)	133 (68)	340 (59)
Sole cause	886 (42)	526 (40)	105 (54)	255 (44)
Limitations	387 (18)	206 (16)	31 (16)	150 (26)
Sole cause	250 (12)	121 (10)	27 (14)	102 (18)
Full treatment	244 (12)	145 (11)	16 (8)	83 (14)
Brain death	61 (3)	58 (4)	1 (1)	2 (1)
Unable to determine	18 (1)	12 (1)	2 (1)	4 (1)

WLST = withdrawal of life-sustaining therapy.

**TABLE 5.**  
**Demographics of Patients Where  
 Withdrawal of Life-Sustaining Therapy for  
 Perceived Poor Neurologic Prognosis  
 Preceded Death**

Characteristics	Patients (N = 516)
Age, median (interquartile range)	70 (59–80)
Female sex, n (%)	235 (46)
Length of stay, median (interquartile range)	4 (2–10)
Primary pathology leading to death <sup>a</sup> , n (%)	
Infectious	75 (15)
Neurologic	382 (74)
Pulmonary	52 (10)
Multiple organ failure	62 (12)
Cardiac	47 (9)
Cancer	27 (5)
Gastrointestinal	14 (3)
Trauma	47 (9)
Liver	3 (1)
Renal	7 (1)
Other	23 (4)

<sup>a</sup>Totals sum to > 100% of the cohort because multiple primary pathologies could be selected for a single case.

patients with more severe neurologic injury are transferred to affiliated, larger teaching hospitals.

The frequency with which WLST-N occurs outside of neuroscience ICUs is not surprising. Neurologic diseases are the leading cause of disability and the second leading cause of death worldwide (18), and cerebrovascular disease is a common cause of death in the United States (19). Smaller teaching and nonteaching hospitals in the United States do not typically have specialty ICUs. Although care for brain trauma and stroke are regionalized (20), care for most other acute neurologic conditions is not. Patients with anoxic encephalopathy, meningitis, and status epilepticus are commonly cared for in general ICUs. In addition, all critically ill patients are at high risk for developing acute neurologic emergencies while admitted to the hospital (21–23).

We found that WLST-N occurred in one in 12 patients without a primary neurologic diagnosis. There are several possible explanations for this. End-stage dementia predisposes patients to having oropharyngeal dysfunction resulting in pneumonia, a leading cause of all inpatients deaths (19). Cancer is another leading cause of death (19), and development of brain metastases is common and may inform WLST-N. Finally, elderly patients who become critically ill are more likely to undergo WLST-N if they have baseline neurocognitive deficits or other preexisting comorbidities (24).

Abundant data in numerous conditions including brain trauma (10, 25), hypoxic-ischemic brain injury (11, 12, 26), stroke (9, 27), subarachnoid hemorrhage (28), and status epilepticus (29) highlight that accurate neurologic prognostication in the acute setting is extremely challenging (30). It is striking that patients who died after WLST-N had significantly shorter hospital lengths of stay compared with other decedents. This offers indirect evidence that decisions about WLST-N and subsequent death may often be made before reliable prognostic data are available. Other factors such as severity of illness, which we did not explore, may also contribute. Clinical nihilism, knowledge deficits, fear of survival with severe brain injury, and other provider factors may all contribute to premature WLST-N (9, 10, 25, 31, 32). Availability of experts in neurology or neurocritical care in the United States is limited, with many community centers in particular facing acute shortages (33). Taken together, the frequency and complexity of WLST-N and possibly the paucity of available expertise suggest the potential for avoidable mortality attributable to inaccurate prognostication. However, further research and different methodology would be needed to understand the prevalence and factors that lead to inaccurate neurologic prognostication for all inpatient deaths.

There are several limitations to our study. The retrospective design of our study can lead to ascertainment biases. Even though we used two independent abstractors, the events preceding death can be difficult to definitively establish through chart review and are subject to error. Given the high percent agreement (86%) between the two abstractors, this seems less likely. The retrospective methodology creates another limitation—there is a difference between studying patients who have already died and studying patients who may eventually die (34). This would bias toward an underestimation of the frequency of WLST-N. Our methods may further underestimate the true frequency of WLST-N due to instances where prognostication did not lead to withdrawal during hospitalization (e.g., favorable prognosis, family chose not to withdraw, etc.) or when WLST-N resulted in death in another setting such as hospice. Another limitation of our study is the generalizability. We included nine community hospitals, all of which were part of the same regional health system, and only four academic medical centers. Thus,

the extent to which our findings generalize nationally and internationally is unknown. The focus of our investigation was to define the incidence and hospital-level variability of WLST-N. Numerous patient factors including race, ethnicity, values and preferences, prior advanced directives, premorbid function, comorbidities, socioeconomic status, and severity of illness are also likely to affect decisions about WLST-N and are important areas of ongoing investigation not addressed by this study. Hospital factors such as neurology or palliative care consults may also influence rates of WLST-N and are also something that we did not investigate. There are also certainly many cases in which WLST-N is appropriate, even in the face of residual prognostic uncertainty. Physicians and surrogates may make reasonable decisions to limit care based on available clinical information and thoughtful consideration of patients' and their families' values and preferences. Our study lacked the granularity to adjudicate the appropriateness of prognostication or influence of subjective factors like patient preferences. Finally, we could not address the basis for perceived poor neurologic prognosis because of the retrospective study and reliance on clinician documentation.

In conclusion, a quarter of inpatient deaths in this large multicenter cohort occurred after WLST-N, and in no setting was WLST-N rare. Improving provider accuracy of predicting neurologic outcome is important for care of critically ill patients and may avert both avoidable deaths and perpetuation of self-fulfilling prophecies.

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