Outcome after Severe Stroke: What is Acceptable and Who Decides?

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Paint It Black

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Don’t Worry, Be Happy

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Figure 1: Distributions of the scores on the mRS and death after 12 months for patients treated with or without decompressive surgery.
Common question posed to potential investigators:

- What is the outcome that would justify a change in your clinical practice?
- What is the minimal difference in this outcome that will lead you to change your practice?
- Used in sample size planning and justifying value of intervention
- Named the “clinically meaningful difference”
Despite significant disability, most patients after decompressive craniectomy for large hemispheric stroke are satisfied with life and do not regret undergoing surgery (Rahme JNS 2012)

Larach DR et al. A life worth living: seven years after craniectomy, NCC 2009
- Cardiac anesthesiologist, left carotid dissection at age 49
- mRS 3 several years after stroke
Patient-Centered Outcomes Research (PCOR) helps people and their caregivers communicate and make informed healthcare decisions, allowing their voices to be heard in assessing the value of healthcare options. This research answers patient-centered questions, such as:

1. “Given my personal characteristics, conditions, and preferences, what should I expect will happen to me?”
2. “What are my options, and what are the potential benefits and harms of those options?”
3. “What can I do to improve the outcomes that are most important to me?”
4. “How can clinicians and the care delivery systems they work in help me make the best decisions about my health and health care?”
Regulatory Agencies

• “Hard” outcomes traditionally preferred
• FDA issued guidance on the use of patient reported outcomes (PROs) in evaluating drug and device efficacy
• Acceptable but must be justified a priori
  – Questionnaires
  – Symptom complex score
• After this released, # of PRO claims from industry dropped

Differing Viewpoints

- Clinical trial using “clinically meaningful difference” – physician centered
- Quality of Life – patient centered
- Regulatory agency – treatment centered
- Payor (government or insurance) – society centered

- How did we get here?
- Are these in conflict?
- Is this resolvable with compromise or which view supersedes?
“Respect of patient autonomy is arguably the ascendant ethical principle of ... medicine” – Manthous Chest 2007

WHO Report 2000 – autonomy as “universal” principle

What is autonomy?
- the right of individuals to self-determination
- rooted in society's respect for individuals' ability to make informed decisions about personal matters
Autonomy as Universal Principle

• Not so fast
• This is mainly a Western ethical construct
• Has really risen as a defining principle only in the last ~50 years

• Should patient be told diagnosis of cancer? (Blackhall JAMA 1995)
  – European Americans (87%), African-Americans (88%), Mexican-Americans (65%), Korean Americans (47%)
  – Similar trend for decision-making about life-support

• May not always be consistent with Islamist culture (Rathor JIMA 2011)
Ancient Chinese medical ethics rooted in Confucianism

- Respect for others (from physician)
- Respect for the physician

Hippocratic Oath “...I will comport myself and use my knowledge in a godly manner...”

Autonomy not explicitly described in either

- No clear rules for "respecting the autonomous choice" of patients

Sun Szu-miao (AD 581-682), a famous physician wrote monograph entitled “On the Absolute Sincerity of Great Physicians”
DESTINY-S: Attitudes of Physicians Toward Disability and Treatment in Malignant MCA Infarction

Hermann Neugebauer · Claire J. Creutzfeldt · J. Claude Hemphill III · Peter U. Heuschmann · Eric Jüttler

Multinational Survey

• 1860 physician respondents
• Asked about acceptability of various outcomes (on modified Rankin Scale)
• Decision-making on treatment for themselves in malignant MCA infarction
Different people look at things differently
• Gender, work experience, medical speciality, geographic location (proxy for culture)

Fig. 1 Acceptable and no longer acceptable outcome in Europe, North America, and Asia. NC no comment, mRS modified ranking scale. Rates were calculated based on the assumption that considering a certain mRS as acceptable means considering all lower mRS as also acceptable and vice versa for no longer acceptable outcome.
How Did We Get Here?

- People’s (and their family’s) viewpoint about life and death have evolved from cultural aspects that are thousands of years old.
- The ethics of what it means to be a physician are likewise very old and ingrained.
- We now are bringing in “new” concepts into the “old” paradigm:
  - High-tech procedures, individual rights, evidence-based medicine, payment for medical care by 3rd party (not patient or family)
  - Of course there will be conflict.
So What Are the Issues?

- Doctors don’t want to provide futile care
- Avoid suffering of patients & family
- Limited doctor resources (money, time, equipment, space) – self-protection?
- Doctors aren’t always good at determining whether care is futile – self-fulfilling prophecy
- Maybe the patient/family don’t really understand the outcome
  - Clinical outcome
  - Impact on family and finances
- Substantial long-term costs to system/society
Galadriel tells Sam

“Remember that the Mirror shows many things, and not all have yet come to pass. Some never come to be, unless those that behold the visions turn aside from their path to prevent them. The Mirror is dangerous as a guide of deeds.”

J.R.R. Tolkien, *The Lord of the Rings*
Definition

• The self-fulfilling prophecy is, in the beginning, a false definition of the situation evoking a new behaviour which makes the original false conception come 'true'.

• This specious validity of the self-fulfilling prophecy perpetuates a reign of error.

• For the prophet will cite the actual course of events as proof that he was right from the very beginning.

Merton, Social theory and social structure, 1968
The toilet paper panic

The 1973 oil crisis resulted in the so-called "toilet paper panic." The rumor of an expected shortage in toilet paper—resulting from a decline in the importation of oil—led to people stockpiling supplies of toilet paper. This caused a shortage.

Slide courtesy of Tom Bleck, MD
If there is no proven treatment, does it matter what you do?

- **General hypothesis**
  - Patients treated in hospitals that have a “nihilistic” approach towards ICH do worse regardless of other factors

- **Formal hypothesis**
  - The rate at which a hospital uses early DNR orders in ICH patients (within 24 hrs of admission) is associated with outcome, even when adjusting for hospital case mix.
What about nihilism?

• Why DNR?
  – A step away from withdrawal of support
  – In strictest sense, DNR orders only influence care if patient has cardio-pulmonary arrest
  – DNR orders are often actually on continuum of efforts to limit care
  – DNR orders within 24 hours reflect that one of earliest decisions in care was ‘to limit care’

• OSHPD Database - 8233 ICH patients at 234 hospitals
  – Outcome – death during initial ICH hospitalization
  – Overall cohort
    » 37% in-hospital mortality
    » 25% of patients made DNR within first 24 hours ($P<0.001$)
    » Hospital DNR rate ranged from 0-70%
### ICH Outcome Predictors (n=8233)

<table>
<thead>
<tr>
<th>Patient Characteristic</th>
<th>Odds Ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Age</td>
<td>1.24 (1.18-1.31)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Patient was intubated or mechanically ventilated</td>
<td>14.37 (12.54-16.46)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hospital DNR Rate</td>
<td>3.28 (2.07-5.19)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hospital Craniotomy Rate</td>
<td>0.61 (0.27-1.37)</td>
<td>0.23</td>
</tr>
<tr>
<td>Hospital ICH Volume</td>
<td>0.99 (0.96-1.01)</td>
<td>0.35</td>
</tr>
<tr>
<td>Teaching Hospital</td>
<td>0.91 (0.74-1.13)</td>
<td>0.40</td>
</tr>
<tr>
<td>Rural Hospital</td>
<td>0.81 (0.60-1.08)</td>
<td>0.16</td>
</tr>
</tbody>
</table>

Analysis is adjusted for individual patient gender, race, and insurance status and hospital trauma center designation.

Being treated in a hospital that used DNR orders 10% more often than another hospital with a similar case mix increased a patient’s odds of dying during hospitalization by 13%. 

Hemphill *Stroke*, 2004
### Patient Characteristics by Adjusted DNR Use Quartile

<table>
<thead>
<tr>
<th></th>
<th>Lowest Quartile (n=2219)</th>
<th>Highest Quartile (n=1885)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (mean ± SD)</strong></td>
<td>68 ± 16</td>
<td>71 ± 15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td>1078 (49)</td>
<td>985 (52)</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Intubation or mechanical ventilation</strong></td>
<td>772 (35)</td>
<td>489 (26)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Comorbidities (median, IQR)</strong></td>
<td>3 (1,3)</td>
<td>3 (1,3)</td>
<td>0.49</td>
</tr>
<tr>
<td><strong>DNR within 24 hours</strong></td>
<td>230 (10)</td>
<td>803 (43)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Procedures performed</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Craniotomy</td>
<td>205 (9)</td>
<td>80 (4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ventriculostomy</td>
<td>139 (6)</td>
<td>40 (2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cerebral Angiogram</td>
<td>164 (7)</td>
<td>87 (5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MRI</td>
<td>136 (6)</td>
<td>133 (7)</td>
<td>0.23</td>
</tr>
<tr>
<td><strong>Length of stay (median, IQR)</strong></td>
<td>7 (4,15)</td>
<td>6 (3,11)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Hospital charges ($1000) (median, IQR)</strong></td>
<td>29 (14,70)</td>
<td>22 (12,48)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Length of stay and hospital charges include only patients who survived to hospital discharge.

Hemphill *Stroke*, 2004
What does all this mean?

- Patients with the same DNR status were treated differently in different hospitals.
- Some additional aspect of care, which is reflected in the way hospitals use DNR orders, is in part responsible for the increased mortality risk in patients treated in high adjusted DNR hospitals.
- Adjusted hospital DNR use is probably a surrogate for overall aggressiveness of care.
- Confirmatory study from rural Texas cohort (Zahuranec, *Neurology* 2007)
Prospective ICH Outcomes Study

- Prospective observational study of outcome in ICH
- Patients with intent to treat without DNR orders for at least initial 5 days
- GCS $\leq 12$, no pre-existing DNR order
- N=109, 5 centers

- Specific Aim 1 – assess whether 30 day mortality is less than predicted by ICH Score
- Specific Aim 2 – if so, does this result in unacceptably high rate of disability at 90 days
3 Month mRS in ICH Patients

- Predicted
- Observed

Morgenstern Neurology 2015
Prognosticating in Individual Patients

• **Finley-Caulfield Neurology 2010**
  - 144 neurocritical care patients requiring $\geq$ 72 hours of mechanical ventilation
  - Neurointensivists predicted 6 month functional outcome
  - Dichotomized mRS (0-3 or 4-6)

• **Correctly predicted outcome in 80% (CI 72-86%)**
  - Poor outcome 94% (85-98%)
  - Good outcome 63% (50-74%)
### Table 2

Accuracy of neurointensivists’ (NI) predictions of functional outcome and quality of life at 6 months

<table>
<thead>
<tr>
<th>Modified Rankin scale</th>
<th>6 months</th>
<th>Predictive value</th>
<th>95% Confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-3, n</td>
<td>4-6, n</td>
<td></td>
</tr>
<tr>
<td>NI predicted, n = 142a</td>
<td>41</td>
<td>24</td>
<td>0.63</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>72</td>
<td>0.94</td>
</tr>
<tr>
<td></td>
<td>0-3</td>
<td>41</td>
<td>0.73</td>
</tr>
<tr>
<td></td>
<td>4-6</td>
<td>5</td>
<td>0.87</td>
</tr>
<tr>
<td>Quality of life</td>
<td>Good or excellent</td>
<td>Fair or poor</td>
<td></td>
</tr>
<tr>
<td>NI predicted, n = 60c</td>
<td>19</td>
<td>14</td>
<td>0.58</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>18</td>
<td>0.67</td>
</tr>
</tbody>
</table>

Histogram comparing predicted and actual 6-month mRS outcome for individual patients.
Daily Predictions of Longterm Outcome

- 66 SAH patients
- Daily prediction of 6 month mRS
- Among patients predicted to have a good outcome (mRS 0-2), 81% (71-92) actually did
- Among patients predicted to have a poor outcome (mRS 3-6), 88% (77-99%) actually did
- Prognostic accuracy did not improve over hospital course
- Factors worsening prognostic accuracy: increasing age, infection, mechanical ventilation, hydrocephalus, seizures

Navi Stroke 2012
Daily Prognostication

- 560 MICU patients
  - 23% in-hospital mortality
- Presume “trial of {aggressive} therapy”
- Patients will “declare themselves”
- Daily confidential question of primary nurse, resident, fellow, and attending
  - “Do you think this patient is going to die in the hospital or survive to hospital discharge?”
- Hypothesis – accuracy of prediction done daily would become more better over time

Power and limitations of daily prognostications of death in the medical intensive care unit

William Meadow, MD; Anne Pohlman, MD, PhD; Laura Frain, MD; Yaya Ren, JD; John Paul Kress, MD; Winnie Teuteberg, MD; Jesse Hall, MD

Objective: We tested the accuracy of predictions of impending death for medical intensive care unit patients, offered daily by their professional medical caretakers.

Design: For 560 medical intensive care unit patients, on each medical intensive care unit day, we asked their attending physicians, fellows, residents, and registered nurses one question: “Do you think this patient will die in the hospital or survive to be discharged?”

Results: We obtained >6,000 predictions on 2018 medical intensive care unit patient days. Seventy-five percent of MICU patients who stayed ≥4 days had discordant predictions; that is, at least one caretaker predicted survival, whereas others predicted death before discharge. Only 107 of 206 (52%) patients with a prediction of “death before discharge” actually died in hospital. This number rose to 66% (96 of 145) for patients with 1 day of corroborated (i.e., >1) prediction of “death,” and to 84% (79 of 94) with at least 1 unanimous day of predictions of death. However, although positive predictive value rose with increasingly stringent prediction criteria, sensitivity fell so that the area under the receiver-operator characteristic curve did not differ for single, corroborated, or unanimous predictions of death. Subsets of older (>65 yrs) and ventilated medical intensive care unit patients revealed parallel findings.

Conclusions: 1) Roughly half of all medical intensive care unit patients predicted to die in hospital survived to discharge nonetheless. 2) More highly corroborated predictions had better predictive value; although, approximately 15% of patients survived unexpectedly, even when predicted to die by all medical caretakers. (Crit Care Med 2011; 39:474–479)

Key Words: prognostication; medical intensive care unit; clinical predictions; medical intensive care unit survival
"The eventual outcomes for MICU patients became progressively less clear, not more clear, over time."

Figure 3. Predictive power of increasing number of predictions of “death before discharge.” Fifty-two percent of patients with any prediction of death before discharge actually died in hospital. Increasingly stringent caretaker predictions of “death” had higher positive predictive value (PPV), although 16% of patients with a unanimous prediction of death, survived to discharge nonetheless.
Facing Future Reality

- **Economic truism** – supply is finite and insufficient to meet all demand

- **EBM truism** – money spent when a patient dies is not cost effective (if the outcome is favorable clinical status)

- There is an inevitable intersection between prognostic decision-making, cost of care, and resource allocation
Saving Money

- ICU as ideal place to save money at end-of-life
  - Critical care is expensive
  - Life-sustaining treatment not cost-effective

- Luce *Am J Respir Crit Care Med* 2002
  - Closest effort to “CUA” for end-of-life ICU care
  - Fallacy of cost savings
    - Fixed v. variable costs
    - Cost shifting not cost saving
    - Only way to really save money – close ICUs and fire nurses/RTs

- Fundamental social change might save costs to “the system”
Focus on End-of-Life Care

- Consider goal of interaction

1. Managing expectations
   - Patients come to hospital (and esp ICU) with expectation of care, not expectation of death

2. Ask-Tell-Ask
   - Talking about death brings it on

3. Communicating risk
   - Natural frequency
     - (40 out of 100, better understood than 40% chance)

4. Unweighting prognosis
   - 1st meeting is about information, not decision
The Dark Side

• “Intent to Obfuscate”
  – *To alter code while preserving its behavior but conceal its structure and intent*
  – Data is supposed to be neutral

• “The family won’t really understand”

• “These patients always do badly”

• “Here is what we want to get out of this family meeting”

• This is not consistent with ancient medical ethics or autonomy

• Rarely discussed; very sensitive issue
Communicating Prognosis

• Do families (surrogates) believe our prognoses?
  – 88% of surrogates expressed doubt about physicians' ability to prognosticate for critically ill patients (Zier *CCM* 2008)
  – 64% of surrogates expressed doubt about the accuracy of physicians' futility predictions (Zier *Chest* 2009)

• Do families (surrogates) want physicians' recommendations on whether to limit life support?
  – 42% preferred not to receive a recommendation (White *Am J Respir Crit Care Med* 2009)
Figure 1. Surrogate decision makers’ interpretations of physicians’ prognostic statements.
Prognosis for What?

- Differing outcomes may be considered acceptable for different patients/surrogates/physicians
  - Alive
  - mRS $\leq 3$
  - Wheelchair bound and total care, but living with family
  - Only want to survive if they could still play tennis
  - Minimally conscious state but can still imagine playing tennis
- People don’t always know what would be acceptable
  - Ubel et al. Misimagining the unimaginable: the disability paradox and health care decision making. *Health Psychology* 2005
Quality of Communication in the ICU and Surrogate’s Understanding of Prognosis

Jared Chiarchiaro, MD\textsuperscript{1,2}; Praewpannarai Buddadhumaruk, MS, RN\textsuperscript{2}; Robert M. Arnold, MD\textsuperscript{3,4}; Douglas B. White, MD, MS\textsuperscript{2,5,6}

![Graph](image)

**Figure 3.** Surrogates who rate quality of communication the highest are also the most optimistic.
"It’s not just what the doctor tells me:” Factors that influence surrogate decision-makers’ perceptions of prognosis

Elizabeth A. Boyd, PhD; Bernard Lo, MD; Leah R. Evans, Med; Grace Malvar, BA; Latifat Apatira, BA; John M. Luce, MD; Douglas B. White, MD, MAS

Objective: Physicians and surrogate decision-makers for seriously ill patients often have different views of patients’ prognoses. We sought to understand what sources of knowledge surrogates rely on when estimating a patient’s prognosis.

Design: Prospective, mixed-methods study using face-to-face, semistructured interviews with surrogate decision-makers.

Setting: Four intensive care units at the University of California, San Francisco Medical Center in 2006 to 2007.

Participants: Participants were 179 surrogate decision-makers for 142 incapacitated, critically ill patients at high risk for death.

Main Results: Less than 2% (3 of 179) of surrogates reported that their beliefs about the patients’ prognoses hinged exclusively on prognostic information provided to them by physicians. The majority cited other factors in addition to physicians’ predictions that also contributed to their beliefs about the patients’ prognoses, including perceptions of the patient’s individual strength of character and will to live; the patient’s unique history of illness and survival; the surrogate’s own observations of the patient’s physical appearance; the surrogate’s belief that their presence at the bedside may improve the prognosis; and the surrogate’s optimism, intuition, and faith. For some surrogates, these other sources of knowledge superseded the importance of the physician’s prognostication. However, most surrogates endeavored to balance their own knowledge of the patient with physicians’ biomedical knowledge.

Conclusions: Surrogates use diverse types of knowledge when estimating their loved ones’ prognoses, including individualized attributes of the patient, such as their strength of character and life history, of which physicians may be unaware. Attention to these considerations may help clinicians identify and overcome disagreements about prognosis. (Crit Care Med 2010; 38: 1270–1275)
Deciding to Withdraw Support

• Values based decision
  – People see a 2 in 100 chance differently
    » PTSD in families of critically ill
  – Data is neutral
    » “intent to obfuscate”
  – Society is not yet deciding for us (cost, rationing, etc)

• Principle of autonomy

• Next-of-kin & surrogates incorrectly predict a patient’s end-of-life cares wishes 1/3 of the time (Shalowitz Arch Intern Med 2006)
Deciding to Withdraw Support

- This is not easy
  - Neuro catastrophes usually hyper-acute
  - Understanding acute family grief
  - Managing staff expectations

- We have insufficient tools to help families understand what disability looks like

- Usually requires more than 1 meeting
  - Most people “get it”
  - Given time

- Palliative Care as a
  - Skill of neurointensivsts and distinct specialty
  - Measure of quality care
  - AHA Palliative Care in Stroke Guidelines
So What Are We To Do?

• Get over it
• Accept (and embrace) differences in
  - Acceptable outcomes
  - Prognostic decisions
  - Value of a treatment, even if structured outcomes (e.g. mRS) are understood
• The real issues are
  - Discordance between physicians and patients/families (generally when physicians don’t want to do something)
  - Who pays the bills (generally when families expect someone else to pay)
• Have we gone as far as we can go with modeling on “traditional” predictors?

• Major leap will come from fundamental new biological insights (and tools to assess these clinically)
  – EEG
  – Functional neuroimaging
  – TMS
Consciousness supporting networks
Athena Demertzi, Andrea Soddu and Steven Laureys

Functional neuroimaging shows that patients with disorders of consciousness exhibit disrupted system-level functional connectivity. Unresponsive/“vegetative state” patients

For instance, every night when falling asleep, we experience a decrease of the level of wakefulness up to the point we lose awareness of our environment. Awareness is more
My Opinions

1. In general we should listen to our patients/families regarding their view of an “acceptable outcome”

2. “Knowledge is power”
   - If you provide data, then provide confidence intervals
   - Acknowledge uncertainty
   - Improve ways of communicating what disability looks like

3. Understand and acknowledge colleagues’ opinions, and work much of this out ahead of time

4. Society needs honest discussion about cost of care limitations. But doctors should not be expected to solve this on a case-by-case basis.

5. Clinical trials should use more patient-centered outcomes and we should accept this as legitimate
Ethical Decision-Making in Severe Stroke

- Prognostication is important and appropriate in the care of severely ill stroke patients
- We are actually pretty good at prognosticating and have fairly good guidance from outcome models and studies
- Uncertainty is inherent
- Self-fulfilling prophecy is real
- Family/surrogate communication is challenging and often discordant. Don’t be impatient.
- Focus on patient and surrogate preferences, this drives the decision whether to withdraw support (in a society where autonomy is primary)
- Cost and cultural aspects are relevant
- We need to guide how society evolves these decisions