Limitation of Life-Sustaining Care in the Critically Ill: A Systematic Review of the Literature

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When life-sustaining treatments (LST) are no longer effective or consistent with patient preferences, limitations may be set so that LSTs are withdrawn or withheld from the patient. Many studies have examined the frequency of limitations of LST in intensive care unit (ICU) settings in the past 30 years. This systematic review describes variation and patient characteristics associated with limitations of LST in critically ill patients in all types of ICUs in the United States. A comprehensive search of the literature was performed by a medical librarian between December 2014 and April 2017. A total of 1,882 unique titles and abstracts were reviewed, 113 were selected for article review, and 36 studies were fully reviewed. Patient factors associated with an increased likelihood of limiting LST included white race, older age, female sex, poor preadmission functional status, multiple comorbidities, and worse illness severity score. Based on several large, multicenter studies, there was a trend toward a higher frequency of limitation of LST over time. However, there is large variability between ICUs in the proportion of patients with limitations and on the proportion of deaths preceded by a limitation. Increases in the frequency of limitations of LST over time suggests changing attitudes about aggressive end-of-life-care. Limitations are more common for patients with worse premorbid health and greater ICU illness severity. While some differences in the frequency of limitations of LST may be explained by personal factors such as race, there is unexplained wide variability between units. Journal of Hospital Medicine 2019;14:303-310. Published online first February 20, 2019. © 2019 Society of Hospital Medicine

Access to life-sustaining treatment (LST) became a mainstay in hospitals across the United States in the 1970s. This has raised complex ethical questions surrounding the use of these therapies, particularly in the face of a poor prognosis or significant morbidity. The Society for Critical Care Medicine formed a consensus panel in 1989 to construct ethical guidelines regarding the initiation, continuation, and withdrawal of intensive care. These guidelines emphasized that withdrawing and withholding are not only permissible but may be necessary to preserve the balance between quantity and quality of life. Nevertheless, an increasing number of Americans are dying after aggressive LST in the hospital, and greater than one in five deaths occur after admission to the ICU. Understanding the factors associated with decisions to withhold or withdraw LST are important to policy makers, ethicists, and healthcare leaders because they affect resources used at the end of life and the need for palliative care and hospice in the ICU setting.

Several studies have characterized the patient characteristics, incidence, and variability associated with limitation of LST in various populations of critically ill patients in the US. We are unaware of another systematic review of the literature that has examined data from these studies in order to understand the process and outcomes of LST limitations. We defined limitations of LST as decisions to withdraw or withhold cardiopulmonary resuscitation through Do Not Resuscitate (DNR) orders, mechanical ventilation, renal replacement therapy, intravenous blood pressure support, or artificial nutrition (enteric or intravenous).

METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement was used for reporting. A comprehensive literature search was performed by a medical librarian (TWE) in Ovid MEDLINE, PubMed, Embase, the full Cochrane Library, CINAHL, PsycINFO, the Philosopher’s Index, Scopus, Web of Science, and Google Scholar. PubMed was limited to non-MEDLINE records in order to complement the Ovid results. The Georgetown Bioethics Research Library at the Kennedy Institute (https://bioethics.georgetown.edu/) was also searched for any unpublished literature. Initial searches were
conducted in December 2014, and an update was performed in April 2017. All databases were searched from inception, and bibliographies of relevant studies were reviewed for additional references (Appendix 1).

Database-specific subject headings and keyword variants for each of the five main concepts—intensive care, end-of-life, decision making, limitation of treatment, and death—were identified and combined. Results were limited to the adult population and to the English language.

Two authors independently reviewed article titles and abstracts (KM, AMT). The full text of potentially eligible studies was then reviewed for inclusion. All disputes were discussed and resolved by consensus. The criteria for inclusion were reporting of patient-level data, critical care patients only (or reported separately from other unit types), US setting, and reporting of data on limitations of LST. The exclusion criteria were studies published only as research abstracts, surveys of physicians or families, organ donors, studies of brain death, surveys, patients less than 18 years old, and long-term intensive care settings (ie, long-term acute care hospitals, long-term respiratory units). Also excluded were studies in which an intervention was performed; as a result, all included studies were observational. Research abstracts were excluded because they lacked sufficient detail from which to abstract study quality or results. Studies of organ donation, brain death, and pediatrics were excluded due to differences in the decision-making context that would make it difficult to draw conclusions about adult ICU care. Studies which included an intervention were excluded to avoid affecting the rate of limitation of LST as a result of the intervention, since our goal was to quantify the number of limitations of LST in usual medical practice.

For each article, we abstracted the number of patients who experienced a limitation of LST out of the total population and factors associated with the limitation. If a multivariable analysis was performed, we reported only variables that remained significant in this analysis. We also reported the number of patients who died, and of those, the number of decedents who underwent a limitation of LST before death. In some cases, this proportion was not reported in the manuscript but could be calculated based on the data presented. This number was calculated based on the number of deaths that were preceded by a limitation in life-sustaining care divided by the total number of deaths. Patients with brain death were not counted as having had a “limitation” if support was withdrawn after the declaration of brain death. We were unable to conduct a meta-analysis of the findings because of the wide variation in study populations and criteria used to define limitations of care.

To assess risk of bias in individual studies, the two raters independently made a yes/no determination regarding several quality metrics established at the outset of the review: clarity of the eligibility criteria for participant inclusion, whether a power or sample size calculation was done, adequacy of the description of the sampling approach and recruitment, and generalizability. Disagreements were resolved by consensus.

RESULTS
Study Selection
A total of 2,460 references were identified, and after removal of 578 duplicates, 1,882 unique titles and abstracts were reviewed. One hundred thirteen titles met the inclusion criteria. After review of complete texts, 83 were excluded based on the above criteria (Appendix). This led to a final number of 36 studies included for analysis.

Fifteen articles were prospective, observational studies. The rest were retrospective analyses of patient-level data. Seven were large, multicenter studies with greater than 20 centers involved (including Project IMPACT); six such studies included medical and surgical patients. The remaining large, multicenter study examined a surgical trauma cohort.

Fifteen of the studies addressed DNR as a limitation and 25 addressed other limitations such as withdrawing or withholding LST (several addressed both DNR and another limitation). Nine studies enrolled only patients who had died and the remaining 27 enrolled all ICU admissions.
Examination of the three studies that looked at >20 regional-ly diverse ICUs revealed a trend over time toward increased limitation prior to death (Figure). Jayes looked at the number of DNR orders preceding death from 1979 to 1980 then com-pared that to a cohort from 1988 to 1990; Prendergast included withholding/withdrawing of LST prior to death from 1994 to 1995; and Quill used the IMPACT database to examine limita-tions prior to death from 2001 to 2009.2,5

Effect of Unit Specialty
Twelve studies were mixed (surgical/medical or medical/neuro) ICUs, 11 were medical/cardiac units, five were neurologic units, and six were surgical/trauma units only. Two studies did not report unit specialty. Four studies that compared surgical and medical ICUs found that surgical patients were more likely to die with full intervention.4,7 In all of these studies, medical patients were more likely to have limitations of LST preceding death. Quill, et al. further detailed that emergency surgery was more likely to be associated with limitation than elective surgery.5

Patient Factors
In 15 studies, older age was associated with an increased like-lihood of limitations on LST.3,5-18 In one study, advanced age was associated with early versus late withdrawal.19 Poor performance status and multiple medical comorbidities were also associated with limitations of LST. The largest population-based study by Quill et al. found that being fully dependent on others upon admission to the ICU was associated with an increased likelihood of limiting LST.2 In Sise et al. found, in an analysis performed over 10 years in one trauma center, that increased age, comorbidities, and a fall as the reason for trauma admission were associated with limitation of LST.3 Salottolo et al. found that if the reason for trauma admission was a fall, there was an increased odds ratio of DNR status.18 Many studies found that having medical comorbidities prior to admission was associ-ated with increased likelihood of limiting LST in both medical and surgical patients.3,7,9,13,15,18

Five studies found a statistically significant difference be-tween women and men in the likelihood of limitation of LST,3,5,9,14,16 and another study reported that women who were trauma patients had an increased odds ratio of changing to DNR code status.18 Only one study found that males were as-soociated with an increased likelihood of limiting aggressive treatment.20

White race was associated with increased limitation of LST in nine studies.4,5,10,11,14,16,21,22 One study in neurocritical care pa-tients found that both white and Hispanic races were correlat-ed with a higher likelihood of limitations.23 Muni et al. found that nonwhite patients had a statistically significantly lower likelihood of having comfort measures and DNR orders written prior to death, but discussion of prognosis was more likely to be documented in nonwhite patients.21

In summary, white race, female gender, and older age were the most frequent factors associated with a higher likelihood of limiting LST.

Factors Related to Critical Illness
There were several illness severity indicators that were associ-ated with limitations. The Acute Physiology and Chronic Health Evaluation (APACHE) scores were the most common for medical patients and Glasgow Coma Scale (GCS) was the most common for patients with neurologic injury. Eight studies reported that a higher APACHE score was associated with an increased likelihood of limitations.3,7,10,15,17,20,22,24 Similar associations were found based on the Sepsis Related Organ Failure Assessment score in one study and a scoring system developed by the author in a second study.25,26

Seven studies, consisting of three neurologic, two medica-l-surgical, and two trauma cohorts, reported that a lower GCS score increased the likelihood that the patient would have limited LST.3,5,10,11,13,14,18,22 Additionally, Geocadin and col-leagues discussed the difficulty with neurological prognostica-tion in clinical practice; they reported that the cortical evoked potential (CEP) was correlated with the time to withdraw LST if the CEP was malignant, and the time to withdraw LST was less in malignant than in benign CEP.27

Mortality and End Effects of Limiting LST
Chen and colleagues used propensity scores to control for mortality differences between patients who had full inter-ventions versus those with limitations and found that higher mortality correlated with the decision to withhold or withdraw LST.10 Weimer and colleagues used modeling to predict the probable outcome of patients who experienced an intracranial hemorrhage who had limitation of LST. Based on this model, nearly all the patients in their study would have died or had severe disability at 12 months despite having maximal therapy; they concluded that withdrawal of LST may not have been a self-fulfilling prophecy as others have proposed.28 Mulder and colleagues reported that in a small cohort of out-of-hospital cardiac arrest survivors admitted to the hospital, over one-third had good neurological outcomes after coding after 72 hours.29 The study highlighted the importance of timing in neurological prognostication.

Variation in Limitation Rates among Centers
In the 36 studies, we found an overall range of DNR orders from 5.4%1 to 82.0%.30 For other limitations, the rates ranged from 6.3%13 to 80.4%.31 Hart reported a low rate of limitations (4.8%) at the time of ICU admission.32 Four large, multicenter studies drew attention to the large variability between critical care centers and the limitation of end-of-life care.3,5,14 Jayes first described this phenomenon when examining the frequency of DNR orders from 1979 to 1980 and 1988 to 1990.3 This study found a range from 1.5% to 22%. Later, in another large, multicenter study, Prendergast et al. looked at 131 ICUs at 110 dif-ferent institutions in 38 states that participated in postgraduate training and found variability in CPR attempts prior to death between 4% and 79%.3 In 2008, Nathens et al. reported signif-icant variation in DNR rates across trauma centers; they found a higher incidence of DNR orders when there was an open ICU structure.14
### TABLE. Main Results of the 36 Final Manuscripts

<table>
<thead>
<tr>
<th>Article Year</th>
<th>Period of Data Collection</th>
<th>Study Population (Number, Description, Study)</th>
<th>Limitation Addressed in the Study</th>
<th>Type of Intensive Care Unit</th>
<th>Study Design</th>
<th>Number (%) with Limitation of LST</th>
<th>Of Those Who Died, What Number (%) Had Limitations</th>
<th>Patient Characteristics Associated with Limitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albaeni 2014</td>
<td>2004-2010</td>
<td>189 survivors of out-of-hospital cardiac arrest pts; 1 unit</td>
<td>Withdrawal of LST</td>
<td>Cardiac/medical</td>
<td>Retrospective</td>
<td>99/189 (52%)</td>
<td>In hospital death 94/147 (63.9%)</td>
<td>No associations were found</td>
</tr>
<tr>
<td>Brown 2016</td>
<td>2003-2008</td>
<td>829 pts who died in ICUs from ILD, COPD, or metastatic; 15 hospitals, 2 neuro ICUs, and 5 non-neuro ICUs</td>
<td>DNR, withdrawal of LST</td>
<td>Medical</td>
<td>Secondary analysis of randomized trial</td>
<td>DNR 681/829 (82.1%); Withdraw LST 621/829 (74.9%)</td>
<td>DNR 681/829 (82.1%); Withdraw LST 621/829 (74.9%)</td>
<td>Not reported</td>
</tr>
<tr>
<td>Chen 2008</td>
<td>2002-2005</td>
<td>2,211 consecutive ICU admissions; 1 unit</td>
<td>Withholding LST, excluded withdraw of treatment</td>
<td>Medical</td>
<td>Retrospective</td>
<td>201/2,211 (9.1%)</td>
<td>Not reported</td>
<td>Age, GCS, APACHE II, race</td>
</tr>
<tr>
<td>Creutzfeldt 2015</td>
<td>2001-2008</td>
<td>200 admission to 2 neuro ICUs who met palliative care triggers, 1,909 admissions to 5 other ICUs in the same hospitals who met triggers (Project IMPACT)</td>
<td>DNR, withholding LST</td>
<td>Neuro vs other</td>
<td>Retrospective</td>
<td>Neuro ICU DNR 16/175 (9.1%); WD/WH 36/175 (20.6%); Non-neuro ICU DNR 212/1,711 (12.4%); WD/WH 195/1,711 (11.4%)</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Diringer 2001</td>
<td>1994-2000</td>
<td>2,109 pts treated with mechanical ventilation; 1 unit</td>
<td>Withdrawal of mechanical ventilation</td>
<td>Neurology/Neurosurgery</td>
<td>Retrospective analysis of prospectively collected clinical database</td>
<td>284/2,109 (13.5%)</td>
<td>279/720 (38.8%)</td>
<td>Surgical pts, age, GCS, race</td>
</tr>
<tr>
<td>Geocadin 2006</td>
<td>Dates not given</td>
<td>58 comatose pts after cardiac arrest consulted on by the neurology service; 1 unit</td>
<td>Withholding and withdrawal of LST</td>
<td>Cardiac, medical</td>
<td>Prospective observational cohort</td>
<td>40/58 (70.0%)</td>
<td>40/48 (83.3%)</td>
<td>Not reported</td>
</tr>
<tr>
<td>Hamel 2002</td>
<td>1989-1994</td>
<td>596 Non-traumatic coma pts (SUPPORT); 5 medical centers</td>
<td>Withholding CPR and ventilation</td>
<td>Unknown</td>
<td>Secondary analysis of prospective study</td>
<td>121/549 (22.0%)</td>
<td>Not reported</td>
<td>Higher risk assessment score</td>
</tr>
<tr>
<td>Hart 2015</td>
<td>2001-2008</td>
<td>277,693 ICU admissions (Project IMPACT); 141 ICUs in 105 hospitals</td>
<td>Treatment limitation at the time of ICU admission</td>
<td>Mixed</td>
<td>Retrospective</td>
<td>13,405/277,693 (4.8%)</td>
<td>Not reported</td>
<td>Age, gender, race, pre-admission functional status</td>
</tr>
<tr>
<td>Huynh 2013</td>
<td>2005-2006</td>
<td>322 ICU pts who died; 1 hospital</td>
<td>Withdrawal of mechanical ventilation</td>
<td>Not specified</td>
<td>Retrospective</td>
<td>159/322 (49.4%)</td>
<td>159/322 (49.4%)</td>
<td>Age, nonsurgical pts</td>
</tr>
<tr>
<td>Kerlin 2015</td>
<td>2001-2008</td>
<td>270,742 ICU admissions (Project IMPACT); 143 ICUs</td>
<td>Limitation of LST</td>
<td>Mixed</td>
<td>Retrospective</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Kish Wallace4</td>
<td>1994-1996</td>
<td>270 admissions to ICU; 1 hospital</td>
<td>DNR</td>
<td>Medical ICU in cancer hospital</td>
<td>Matched pairs case control</td>
<td>41/270 (15.2%)</td>
<td>Unable to determine</td>
<td>Matched groups</td>
</tr>
<tr>
<td>Kowalski 2013</td>
<td>1991-2009</td>
<td>1,134 aneurysmal SAH pts; 2 units</td>
<td>Withdrawal of LST</td>
<td>Neurology/neurosurgery</td>
<td>Prospective observational</td>
<td>72/1,134 (6.3%)</td>
<td>In hospital deaths 72/207 (34.7%)</td>
<td>GCS, age, comorbidities</td>
</tr>
<tr>
<td>Lissauer 2011</td>
<td>2008-2010</td>
<td>151 surgical ICU pts who died; 1 unit</td>
<td>Withdrawal and withholding of LST</td>
<td>Surgical</td>
<td>Retrospective analysis of prospectively collected data</td>
<td>111/151 (73.5%)</td>
<td>111/151 (73.5%)</td>
<td>Sex, APACHE IV score</td>
</tr>
</tbody>
</table>

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### TABLE. Main Results of the 36 Final Manuscripts (continued)

<table>
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<th>Patient Characteristics Associated with Limitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mayer 199923</td>
<td>1994-1997</td>
<td>105 neurocritical ICU pts who died; 1 unit</td>
<td>Withdrawal of ventilation</td>
<td>Neuro</td>
<td>Retrospective</td>
<td>50/105 (47.6%)</td>
<td>50/105 (47.6%)</td>
<td>Race</td>
</tr>
<tr>
<td>Mehter 201417</td>
<td>2000-2005</td>
<td>809 ICU pts with ARDS and documented code status; multicenter</td>
<td>DNR, withdrawal and withholding of LST</td>
<td>Medical</td>
<td>Retrospective</td>
<td>232/809 (28.7%); WW/HW 195/809 (24.1%)</td>
<td>90 day mortality DNR 225/284 (79.2%)</td>
<td>APACHE III score</td>
</tr>
<tr>
<td>Mulder 201310 and 201416</td>
<td>2007-2011</td>
<td>154 comatose survivors out of hospital cardiac arrest survivors admitted to the ICU; 1 center</td>
<td>Withdrawal of LST</td>
<td>Medical</td>
<td>Prospective observational</td>
<td>63/154 (40.9%)</td>
<td>63/78 (80.8%)</td>
<td>Not reported</td>
</tr>
<tr>
<td>Muni 201121</td>
<td>2003-2008</td>
<td>3,138 ICU pts who died; 15 ICUs</td>
<td>DNR, comfort care, RRT, MV, pressors, enteral feedings</td>
<td>Medical</td>
<td>Retrospective</td>
<td>2,274/1,321 (72.90%)</td>
<td>2,274/1,321 (72.90%)</td>
<td>Race</td>
</tr>
<tr>
<td>Naib 201514</td>
<td>2012</td>
<td>1,368 pts; 1 CICU</td>
<td>Withdrawal and withholding of LST</td>
<td>Cardiac</td>
<td>Retrospective</td>
<td>Not reported</td>
<td>ICU deaths: 85/117 (72.6%)</td>
<td>Not reported</td>
</tr>
<tr>
<td>Nathens 200814</td>
<td>2001-2002</td>
<td>6,765 trauma pts; 68 centers</td>
<td>DNR</td>
<td>Trauma, mixed</td>
<td>Prospective observational</td>
<td>464/6,765 (6.9%)</td>
<td>408/603 (67.7%)</td>
<td>Age, race, sex, global injury severity score, admission GCS</td>
</tr>
<tr>
<td>Plaisier 200211</td>
<td>1994-1998</td>
<td>102 trauma pts who died; 1 unit</td>
<td>Withdrawal and withholding of LST</td>
<td>Trauma</td>
<td>Retrospective</td>
<td>82/102 (80.4%)</td>
<td>82/102 (80.4%)</td>
<td>Not reported</td>
</tr>
<tr>
<td>Prendergast 199710</td>
<td>1987-1993</td>
<td>1,719 ICU admissions; 2 hospitals</td>
<td>Withdrawal and withholding of LST</td>
<td>Medical/surgical</td>
<td>Retrospective</td>
<td>114/224 (6.6%); 177/1711 (10%)</td>
<td>1987-1988 114/1,711 (6.6%); 1992-1993 179/200 (89.5%)</td>
<td>Not reported</td>
</tr>
<tr>
<td>Prendergast 199810</td>
<td>1994-1995</td>
<td>6,303 ICU pts who died; 131 ICUs</td>
<td>Withdrawal and withholding of LST</td>
<td>Medical/surgical</td>
<td>Prospective observational</td>
<td>5,006/6,303 (75.5%); LST 3,036/6,303 (48.2%)</td>
<td>1987-1998 114/1,224 (50.9%); 1992-1993 179/200 (89.5%)</td>
<td>Not reported</td>
</tr>
<tr>
<td>Quill 201415</td>
<td>2001-2009</td>
<td>269,002 full code ICU admissions; 153 units</td>
<td>Withdrawal and withholding of LST</td>
<td>Medical/surgical</td>
<td>Retrospective</td>
<td>31,408/269,002 (11.7%)</td>
<td>ICU deaths: 18,460/21,758 (84.8%); Hospital deaths: 23,469/33,910 (69.2%)</td>
<td>Surgery type, age, race, sex, GCS score, dependent pre-admission status</td>
</tr>
<tr>
<td>Reicher 200616</td>
<td>2002-2004</td>
<td>47 lung cancer pts admitted to ICU/1 unit</td>
<td>DNR/terminal extubation</td>
<td>Medical</td>
<td>Retrospective</td>
<td>DNR on ICU admission 12/47 (25.5%); any DNR order 35/47 (74.5%); terminally extubated 5/47 (10.6%)</td>
<td>Not reported</td>
<td>Sore SOFA score</td>
</tr>
<tr>
<td>Rubin 201415</td>
<td>2002-2009</td>
<td>1885 pts with neurologic injury with a GCS &lt; 9, and mechanical ventilation; 1 unit</td>
<td>Withdrawal of ventilation, DNR</td>
<td>Neuro</td>
<td>Prospective observational</td>
<td>529/1,885 (28%); withdrawal ventilation; 714/1,885 (37.9%)</td>
<td>DNR 533/788 (67.6%)</td>
<td>Nonsurgical pts low GCS, high APACHE II white race</td>
</tr>
<tr>
<td>Salottolo 201518</td>
<td>2008-2013</td>
<td>10,053 trauma pts; 1 ICU</td>
<td>DNR, withdrawal of LST noted for deaths only</td>
<td>Surgical trauma</td>
<td>Retrospective</td>
<td>1,523 (15.1%)</td>
<td>In hospital death or hospice discharge; DNR 536/455 (73.8%); withdraw LST 45/455 (9.9%)</td>
<td>Age, sex, GCS score, Charlson Comorbidity Index, frailty/issue admission status</td>
</tr>
<tr>
<td>Sise 201210</td>
<td>2000-2009</td>
<td>698 trauma pts who died; 1 unit</td>
<td>Withdrawal or withholding of LST</td>
<td>Trauma</td>
<td>Retrospective</td>
<td>375/698 (53.7%)</td>
<td>375/698 (53.7%)</td>
<td>Age, sex, ISS score, GCS score, fall, Charlson Comorbidity Index, trauma consult</td>
</tr>
<tr>
<td>Smedira 199010</td>
<td>1987-1988</td>
<td>1,719 ICU patient; 2 hospitals</td>
<td>Withdrawal or withholding of LST</td>
<td>Medical/surgical</td>
<td>Prospective observational</td>
<td>97/1,719 (5.6%)</td>
<td>ICU deaths: 71/109pts (62.1%)</td>
<td>Not reported</td>
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</table>

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Overall, there was wide variation in the proportion of deaths preceded by limitation of LST, ranging from 29.5% in one study of trauma patients to 92% in another study of trauma patients whose death occurred after 24 hours of care. In the largest study to date by Quill and colleagues utilizing the IMPACT database, they found large variability in the number of deaths preceded by full intervention based on differences in practice patterns of critical care centers.

Bias
All studies indicated clear eligibility criteria for inclusion and described their sampling approach in adequate detail. All but one stated their method of participant recruitment, and the one remaining study was a secondary analysis and referenced the earlier manuscript. No study provided a power or sample size calculation, and sample sizes varied widely. Generalizability was most affected by the fact that many studies were conducted in a single ICU.

**DISCUSSION**
This systematic review of LST in US ICUs found several patient and illness factors that were associated with limitation of LST. The association of preadmission functional status and comorbidities with limitation of LST suggest that prior health is a factor in decision making. Further, ICU severity of illness, as measured by several commonly used indices, was associated with limitations. Although variations in study design precluded meta-analysis, examination of the largest studies suggests that limitations are becoming more frequent over time. Also, early studies generally addressed DNR status, while later studies included withdrawal or withholding of LST, most commonly artificial ventilation. These findings reflect the current consensus in US medicine that it is ethically acceptable to limit LSTs in cases when they no longer benefit the patient or the patient would no longer want them.

Some studies found variability by unit type, suggesting that decision making may differ among surgical, medical, and neurologic illness. Mayer and Kossoff concluded, in study of a cohort of neurocritical care ICU patients, that medical patients often have issues of physiologic futility and imminent death, whereas neurologic patients more often confront issues of quality of life. They also note that there is a difference in how patients with differing illnesses die; medical patients will have issues of physiologic futility and imminent death, whereas neurologic patients more often confront issues of quality of life. Other authors have documented that African American patients are more likely to choose end-of-life care for themselves or their family members, which may be due to cultural or religious factors as well as to a history of unequal access to health care.

### TABLE. Main Results of the 36 Final Manuscripts (continued)

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<thead>
<tr>
<th>Article Year</th>
<th>Period of Data Collection</th>
<th>Study Population (Number, Description, Study)</th>
<th>Limitation Addressed in the Study</th>
<th>Type of Intensive Care Unit</th>
<th>Study Design</th>
<th>Number (%) with Limitation of LST</th>
<th>Of Those Who Died, What Number (%) Had Limitations</th>
<th>Patient Characteristics Associated with Limitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turnbull 2014*</td>
<td>2004-2007</td>
<td>490 acute lung injury patient; 13 ICUs</td>
<td>Withdrawal or withholding of LST</td>
<td>Medical/surgical</td>
<td>Prospective observational</td>
<td>192/490 (39.2%) ICU deaths 166/214 (77.60%)</td>
<td>Patient type, age</td>
<td></td>
</tr>
<tr>
<td>Van Scoy 2013**</td>
<td>2006-2008</td>
<td>100 pts who died after 72 hour stay in the ICU; 1 hospital</td>
<td>DNR</td>
<td>Medical/surgical</td>
<td>Retrospective</td>
<td>52/100 (52.0%) 52/100 (52.0%) APACHE II score</td>
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</tr>
<tr>
<td>Weimer 2016**</td>
<td>2008-2011</td>
<td>383 intracranial hemorrhage pts; 1 ICU</td>
<td>Withdrawal of LST</td>
<td>Neuro</td>
<td>Retrospective analysis of prospectively collected data</td>
<td>26/383 (6.8%) (26/67) 38.8% None</td>
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<tr>
<td>Weimer 2014**</td>
<td>2008-2012</td>
<td>536 trauma pts who died; 1 unit</td>
<td>Withdrawal of LST</td>
<td>Trauma</td>
<td>Retrospective analysis of prospectively collected data</td>
<td>158/536 (29.5%) 158/536 (29.5%) Older age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White 2006**</td>
<td>2003-2004</td>
<td>303 ICU pts; 1 hospital</td>
<td>DNR, limitation of LST</td>
<td>Medical</td>
<td>Prospective observational</td>
<td>DNR 13/49 (26.5%); Withdrawal LST 8/49 (16.3%); DNR 9/13 (69.2%); Withdrawal of LST 8/13 (61.5%)</td>
<td>Age, race, APACHE score, pre-admission health status</td>
<td></td>
</tr>
<tr>
<td>Youngner 1985**</td>
<td>1983-1983</td>
<td>506 MICU admissions; 1 unit</td>
<td>DNR</td>
<td>Medical</td>
<td>Prospective observational</td>
<td>71/506 (14%) Hospital deaths 62/123 (50.4%)</td>
<td></td>
<td>Age, race, APACHE score, pre-admission health status</td>
</tr>
<tr>
<td>Zimmerman 1986**</td>
<td>1979-1982</td>
<td>7265 ICU admissions; 13 units</td>
<td>DNR</td>
<td>Mixed</td>
<td>Prospective observational</td>
<td>393/7,265 (5.4%); ICU deaths 237/611 (39%)</td>
<td>Surgery type, age, APACHE score, pre-admission health status</td>
<td></td>
</tr>
</tbody>
</table>

*Pts who were brain dead were not counted as having life-sustaining treatments withdrawn or withheld.

Abbreviations: APACHE, acute physiology and chronic health evaluation; COPD: chronic obstructive pulmonary disease; DNR, do not resuscitate; GCS, Glasgow coma scale ICU, intensive care unit; IMPACT, informing the pathway of COPD treatment; LST, life-sustaining treatments; MV, mechanical ventilation; Pts, patients; RRT, rapid response team; SAH, subarachnoid hemorrhage; SUPPORT: study to understand prognoses and preferences for outcomes and risks of treatments; WD, withdraw; WH, withhold.
medical care.³⁴ Reasons for the finding that women are more likely to have limitations has not been as well described. Further research could explore whether this is due to differences in patient preferences by gender or to other factors.  

Even when examining patient-level factors, illness severity and type of ICU, the wide variability in end-of-life care in critical care units across the country is still large. A worldwide review and type of ICU, the wide variability in end-of-life care in critical research could explore whether this is due to differences in patient-level factors, illness severity, and type of ICU in which they receive their care. Further research could consider during goals of care discussions. Further research could also be useful including preferences, illness type, or changes over time.

The limitations of this review include the wide variety of LSTs assessed, including code status change, ventilator withdrawal, removal of pressors, and cessation of renal replacement therapy. Also, there was variation in sample size and the number of included units. There was also significant heterogeneity in the outcomes addressed and the variety of methods used in the included studies. We attempted to address this with an analysis of the quality of the studies, but given the wide variability, we were unable to account for all of the differences; unfortunately, this is a standard issue within studies that utilize systematic reviews, as well as similar concepts such as meta-analyses.

In conclusion, the increase in the frequency of limitations of LST in critically ill patients and a change in the nature of limitations from DNR order to withdrawal or withholding of LST suggests a trend toward growing acceptance of limiting treatments in critical illness. The wide variation in withdrawal of care in US ICUs does not seem fully explained by patient variables including preferences, illness type, or changes over time. Factors such as poor prefunctional status, a higher number of comorbid conditions prior to critical illness, and the severity of critical illness are likely important for surrogates and clinicians to consider during goals of care discussions. Further research is needed to explore why patients may receive very different types of care at the end of life depending the institution and ICU in which they receive their care.

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References