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# Is There a Starling Curve for Intensive Care?

Hannah Wunsch, MD

Large differences exist in the provision of ICU beds worldwide, with a complicated mix of risks and benefits to the population of having either too few or too many beds. Having too few beds can result in delayed admission of patients to the ICU or no admission at all, with either scenario potentially increasing mortality. Potential societal benefits of having few beds include lower costs for health care and less futile intensive care at the end of life. With added ICU beds for a population, mortality benefit should accrue, but there is still the question of whether the addition of beds always means that more lives will be saved or whether there is a point at which no additional mortality benefit is gained. With an abundance of ICU beds may come the possibility of increasing harm in the forms of unnecessary costs, poor quality of deaths (ie, excessively intensive), and iatrogenic complications. The possibility of harm may be likened to the concept of falling off a Starling curve, which is traditionally used to describe worsening heart function when overfilling occurs. This commentary examines the possible implications of having too few or too many ICU beds and proposes the concept of a family of Starling curves as a way to conceptualize the balance of societal benefits and harms associated with different availability of ICU beds CHEST 2012; 141(6):1393-1399 for a population.

arge differences exist in the provision of ICU L beds worldwide. Even among the developed countries of Western Europe and North America, availability of beds varies dramatically, with up to eightfold differences among countries.<sup>1</sup> This large variation brings up the question of whether there is an optimal provision of ICU beds for a given population. Moreover, what are the consequences to society, in terms of both risks and benefits, of having either very few or many beds?

There are at least three potential models of the balance between risks and benefits associated with additional provision of ICU beds for a population. The first option is the more-is-better model, where

ing beyond mortality to encompass areas such as costs and patient and family experiences (Fig 2). Any delivery of intensive care involves a complex mix of trade-offs between the benefits and harms that will differ based on population, culture, and finances. This commentary examines the range of possible benefits and harms associated with differing provision of ICU beds for a population, with particular exploration of whether curve C (Fig 1) is plausible.

incremental increases in the provision of beds always

lead to additional societal benefits that outweigh

risks (Fig 1, curve A). The second is the flat model

where there is a level of provision that is needed

to minimize harm and the ratio of benefit to harm

remains stable with any additional delivery of inten-

sive care (Fig 1, curve B). The third model proposed—

the harm model-raises the possibility of increasing

harms associated with bed provision over a certain

number per capita, with little benefit accrued with

the added beds (Fig 1, curve C). This idea is similar

to the concept of falling off a Starling curve, which is

traditionally used to describe compromised heart

function in an overfilled heart.<sup>2</sup> It is important to recognize that this conceptual model is not unidi-

mensional (on the y-axis); instead, it includes a broad

mix of potential societal benefits and harms extend-

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Affiliations: From the Department of Anesthesiology, College of Physicians and Surgeons, Columbia University, and Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY.

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Correspondence to: Hannah Wunsch, MD, Department of Anesthesiology, Columbia University, 622 W 168th St, PH5-527D, New York, NY 10032; e-mail: hw2125@columbia.edu

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# POTENTIAL HARMS OF LOW PROVISION OF ICU BEDS

There are potentially large societal harms associated with too little delivery of intensive care for a population. The majority of low-income countries have very few ICU beds. But often the overall healthcare infrastructure, not just the delivery of intensive care, is unavailable. This fact makes it difficult to examine the true impact of a lack of ICU beds. However, other countries, such as the United Kingdom, provide universal health coverage, and yet have approximately one-sixth the ICU beds (three per 100,000 population) compared with the United States (~20 per 100,000 population).<sup>1</sup> Studies of intensive care in Britain, described later, allow us to understand at least some of the impact of such low provision of ICU beds per capita.<sup>3.6</sup>

The most obvious potential harm results from withholding intensive care from individuals because of a lack of ICU beds. Data used to examine the consequences of denied admission are surprisingly difficult to tease apart because of the complex nature of triage decisions in general,<sup>7</sup> variation in the ability to care for patients with higher severity of illness outside an ICU,<sup>8</sup> and different patient and family preferences regarding care.<sup>9</sup> Moreover, the difficulties of capturing the at-risk population, triage decisions, and outcomes for patients who have not received intensive care are logistical challenges, sometimes referred to as the denominator problem.<sup>10</sup>

Nevertheless, a number of studies from the United Kingdom demonstrate that some patients are not admitted to the ICU because of bed shortages.<sup>11</sup> In a study by Metcalfe et al,<sup>5</sup> 817 patients referred for admission to intensive care were tracked for 90 days. Of these, 168 were refused admission to an ICU at that time, and of these, 94 (56%) did not receive intensive care specifically because of the lack of available beds. Overall, the patients who were refused admission were noted to have a higher 90-day mortality (46%) than patients who received intensive care (37%). Sinuff et al<sup>11</sup> systematically reviewed 10 studies and found an overall odds of death of 3.04 (95% CI, 1.49-6.17) for patients refused admission compared with those admitted to an ICU. However, many of these studies had the recurring problem of mixing together patients refused admission specifically because of a lack of beds (inappropriate refusal) with patients who were refused admission for other reasons (appropriate refusal), such as perceived futility of intensive care. These patients will naturally have high death rates and confound data interpretation.

The impact of having too few beds may not always be complete refusal of admission to an ICU but, rather, delayed admission. A study comparing medical admissions to the ICU in the United States and United Kingdom demonstrated that the mean time to arriving in the ICU after admission to the hospital was substantially longer in the United Kingdom.<sup>12</sup> Many more patients were also admitted from the wards rather than directly from an ED. Because data suggest that early intervention may improve outcomes, particularly for patients with severe sepsis and septic shock,<sup>13,14</sup> these delays may be detrimental for patients. For example, in a study of patients with community-acquired pneumonia in the ED, patients who had delayed transfer to the ICU (defined as transfer to the wards and then to the ICU on day 2 or 3 of the hospital stay vs directly from the ED) had substantially increased hospital mortality (OR, 2.07; 95% CI, 1.12-3.85).  $^{15}$  A similar study by Chalfin et al  $^{16}$ of patients who stayed in the ED for >6 h vs those transferred to the ICU in < 6 h found that delayed admission increased the risk of hospital death and longer hospital stay.

Data from the United Kingdom also suggest that having few ICU beds may create pressure at the discharge end (ie, forcing a premature discharge in order to allow admission of another patient). The frequency of this practice in UK ICUs was quantified in a 1990s study that specifically examined time of and reason for discharges. The study demonstrated that 6% of UK patients in the ICU were being discharged at night, with 43% of these discharges specifically labeled as an early discharge due to shortage of ICU beds.<sup>6</sup> These patients experiencing premature nighttime discharge had substantially increased hospital mortality rates compared with patients discharged during the day.

# POTENTIAL BENEFITS OF LOW PROVISION OF ICU BEDS

Minimizing the use of intensive care does have some potential societal benefits, although at very low levels of provision, these benefits are very unlikely to outweigh the substantial concerns regarding increased mortality. One benefit may be that it improves the experience of dying patients by minimizing exposure to the discomforts of intensive care at the end of life. Although one in five Americans who die receive intensive care, only one in 20 experience intensive care in the United Kingdom.<sup>3</sup> The percentage of deaths that involve intensive care among children and young adults is similar in both countries, but the percentages diverge for elderly patients, with very few age > 85 years receiving intensive care before death in the United Kingdom. It is, of course, impossible to say whether some of these patients in the United Kingdom might have received benefit from intensive care. However, in either country, few people would choose to die in an ICU if given the choice.9,17



FIGURE 1. Schematic diagram of potential societal benefits and harms associated with increasing ICU bed provision for a population. Curve A represents the possibility of additional benefits accrued with additional ICU beds. Curve B, a plateau, represents a point beyond which no additional benefits are gained but with no additional harm either. Curve C shows the possibility of additional harms accruing beyond a certain provision of beds.

Another societal benefit of low delivery of intensive care may be decreased costs of care for the health system as a whole. Although the costs associated with care should not be equated with quality, the two often must be balanced. There is some correlation between the provision of ICU beds per capita and health-care spending per capita across countries in North America and Western Europe.<sup>1</sup> Many studies of intensive care equate decreasing ICU length of stay with cost savings, but these savings are likely only realized if decreasing ICU length of stay leads to decreases in the number of ICU beds and fewer patients cared for in those beds or, alternatively, by having few beds to begin with.<sup>18</sup> This is due to the majority of costs in the ICU being fixed costs of care (salaries, costs of equipment, etc), which often are estimated to account for up to 80% to 85% of the total costs.<sup>19,20</sup> Therefore, minimizing the operating costs by having few beds generally will lower overall costs of care.



FIGURE 2. Schematic diagram of the individual potential societal benefits and harms associated with different provision of ICU beds for a population.

### POTENTIAL BENEFITS AND HARMS OF HIGH PROVISION OF ICU BEDS

In medicine, the assumption often is that more is better, leading to aggressive adoption of new technology,<sup>21</sup> interventions,<sup>22</sup> and increasing costs of care.<sup>23,24</sup> In the United States, the number of ICU beds per capita has steadily increased over the past 15 to 20 years, with a 26.1% increase from 1985 to 2000 and an additional 6.5% increase from 2000 to 2005.<sup>25,26</sup> There has been little examination in parallel of the potential societal benefits and harms of this high (and ever higher) provision of ICU beds for a population.

The epidemiologic studies on whether higherintensity care in the United States is associated with improved mortality are conflicting. Romley et al<sup>27</sup> recently examined data from California and found an association between increased hospital spending and decreased risk-adjusted inpatient mortality across six common medical conditions. Similarly, Barnato et al<sup>28</sup> found an association between higher end-of-life treatment intensity and lower short-term mortality among patients in Pennsylvania, suggesting that aggressive, intense care provides mortality benefit. But the study also concluded that there were decreasing marginal returns above average intensity and that those returns were further attenuated with longer follow-up. Other work failed to demonstrate additional mortality benefit or patient satisfaction associated with care in higher-spending regions in the United States.<sup>29</sup> With regard to mortality, therefore, it remains unclear whether there is a continued increasing benefit or a flattening of the curve with no mortality benefit beyond a certain point.

Higher availability of ICU beds for specific patients, such as those undergoing high-risk surgical procedures, may provide substantial mortality benefit. In the United Kingdom, Pearse et al<sup>30</sup> found that highrisk patients representing 12.5% of total surgical procedures accounted for 80% of surgical deaths and noted that only 15% of these patients were admitted to an ICU. A direct comparison of outcomes among high-risk surgical patients in a single hospital in the United States vs a single hospital in the United Kingdom found a fourfold increased risk of death in the UK cohort, even after risk adjustment.<sup>31</sup> The hospitals compared in the two countries served very different patient populations, raising the possibility of unknown confounders. However, the higher use of intensive care in the United States may at least partially explain the differences in mortality.

But there may also be a point after which potential harm begins to mount. Like a house officer enthusiastically ordering fluid for an underfilled heart, the benefits for the patient may be large at first, but a point of overload may occur beyond which additional fluid can cause harm. However, it is important to recognize that the harms of aggressive use of intensive care fall across many domains and currently can only be considered in the abstract.

There is certainly the possibility of unnecessary use of intensive care. Data from US studies of intensive care demonstrate low overall severity of illness and report mechanical ventilation rates of only 10% to 30%, with many patients admitted to US ICUs purely for monitoring.<sup>12,32</sup> In a model developed to identify patients in the United States who may not need ICU admission, 38.5% of all ICU admissions were for monitoring purposes, and only 11.5% of these patients went on to require any form of active treatment (defined using the Therapeutic Intervention Scoring System),<sup>32</sup> suggesting that >30% of ICU patients in the United States never require any ICU-level interventions. Another study of > 240,000 US patients in the ICU found that <30% of the patients were mechanically ventilated and that <25% received vasopressors.<sup>33</sup> Data are lacking on whether admission of patients to the ICU for monitoring improves outcomes in any way. A number of observational studies of patients undergoing carotid endarterectomy concluded that default admission of patients to the ICU for monitoring purposes did not improve outcomes but increased costs of care and length of hospital stay.<sup>34,35</sup> The concerns of iatrogenic complications,<sup>36</sup> risk of ICU-acquired infections,<sup>37</sup> immobilization,<sup>38</sup> and communication gaps associated with additional ICU admission and discharge<sup>39,40</sup> may all be underappreciated risks of intensive care, particularly for patients at low risk of death (Fig 2).

Many patients and families express a wish to die at home or to die with comfort measures.<sup>9</sup> Yet, many die in ICUs in ways that do not match their stated preferences, with  $\sim 20\%$  of Americans receiving intensive care before death.<sup>41</sup> Although some of this aggressive care is justifiable or may represent a change in preferences, many families of patients who die in the ICU would not choose this end-of-life experience.9 These data suggest that there may be room to improve the delivery of end-of-life care by matching preferences with care. Such alignment does not require any rationing of care but does require moreaggressive measures by health-care workers to address end-of-life preferences early to ensure the most appropriate care.42,43 With high availability of ICU beds, it often may be easier for clinicians to avoid the question and continue to treat. We know, for example, that it is not just variation in patient preferences that explain large regional variations in end-of-life spending across the United States.9 However, recent data suggest that use of advance directives specifying limitations in end-of-life care do reduce the likelihood of in-hospital death and increase use of hospice care in regions with high overall end-of-life spending.  $^{\rm 44}$ 

Finally, interwoven with all of these other aspects of the delivery of critical care is the question of costs. In an idealized system with no cost constraints, spending on intensive care would be a separate concern. However, every health-care system faces budgetary restrictions that are associated with the delivery of care.45 In our current system with escalating healthcare costs, large numbers of ICU beds represent an expensive fixed cost for hospitals and a large part of societal costs of health care, particularly in the United States.<sup>20</sup> Recent efforts to quantify the costs of intensive care in the United States as a percentage of hospital costs estimated that intensive care represented between 17.4% and 39.0% of all hospital costs<sup>46</sup> and that critical care now accounts for 0.66% of the US gross domestic product.<sup>26</sup> The system may also develop a spiraling cost cycle. As the percentage of ICU beds relative to hospital beds increases, there may be substantial delays in finding a ward bed for an ICU patient. With delayed discharge comes further cost for the higher level care that is not needed.<sup>4</sup>

## What Happens When the Provision of ICU Beds Changes?

According to the Starling curve analogy, changing the availability of ICU beds should change the relative harms and benefits for a population, depending on the starting point on the curve. Does this happen? England provides us with a test case of this possibility at the low end of the curve. Based on data generated during the 1990s, it became apparent that there was a significant lack of ICU beds across the country.<sup>5,6</sup> Beginning in 2000, the Department of Health worked to modernize critical care, with increased expenditure and a 35% increase in the number of staffed beds in general ICUs over 5 years—a substantially greater rate of growth than for the underlying population.<sup>4</sup> Of note, the majority of these new beds were level 2 beds with two-to-one nursing rather than level 3 beds with one-to-one nursing and the ability to provide a full range of organ support. The predicted mortality for patients admitted to the ICUs decreased by only 0.7% over this time period, suggesting that there was a previously unmet need for intensive care as the severity of illness remained relatively steady. But the changes in actual mortality were striking, with a steady decrease in the relative risk of both ICU and hospital mortality starting in 2003 to 2004 and continuing through 2006. Moreover, there was a significant drop in the percentage of patients who were identified as being discharged

from the ICU too early. Other intensive care initiatives were implemented over a similar time period, including a ventilator bundle in many hospitals, an increase in the number of rapid response teams in hospitals to identify deteriorating patients, and the establishment of critical care networks. Therefore, changes in outcomes may not be attributable solely to changes in the availability of beds.<sup>4</sup>

What about the opposite end of the curve? Few studies have examined the impact of closing ICU beds and decreasing the availability of beds for a population. One older study examined ICU admission decisions during variable periods of ICU bed availability in a single center. The authors found that severity of illness of patients admitted to the ICU increased with decreasing availability of beds, and although patients were discharged sooner from the ICU under crowded conditions, there was no discernible difference in outcomes.<sup>47</sup> However, the study authors were unable to comment on the patients who were denied ICU admission. Another study of a closure of beds in a single hospital because of a nursing shortage found a reduction in the proportion of patients admitted primarily for monitoring, with no demonstrated changes in mortality for either patients admitted to the ICU or for those cared for elsewhere in the hospital.48 These few studies suggest that there may be room at the top of the curve to decrease ICU beds and decrease costs without substantial harm in some settings.

How does a system change? In the case of a national health service, the decisions can be made at a national level, and changes are implemented across the country.<sup>4</sup> Changes in a country such as the United States are not as easy. The first step may be to align monetary incentives among patients, physicians, hospitals, and society so that high-quality but low-cost care is more often the default. A few states have now implemented laws requiring that palliative care information and counseling be offered to patients with terminal illnesses (eg, New York Public Health Law section 2997-c, AB 2747). Whether such requirements have an impact on care patterns at the population level is unknown.

The current US system often rewards physicians financially for doing more tests or procedures or providing ICU-level care.<sup>49</sup> A recent editorial reviewed the impact of different reimbursement schemes, suggesting that one alternative approach is the use of extensive panels of quality indicators in conjunction with another reimbursement system to ensure best care.<sup>50</sup> However, there is little agreement about which quality indicators should be measured to assess a hospital's performance; the best approach for alignment of incentives in either the United States or Europe remains unclear.

Currently, there is great heterogeneity in the provision of ICU beds across the United States.<sup>51</sup> It is important to recognize that the ICU bed needs of an individual hospital or health-care system vary, making it difficult to assess whether any individual hospital or local system is overprovisioned. One option that combines local needs with a more population-based approach to care may be regionalization of care so that ICU beds and specific technology, such as extracorporeal membrane oxygenation or high-frequency ventilation, are concentrated within regions.<sup>52,53</sup> Such a system makes sense from the perspective of queuing theory, which shows that the likelihood of a delay in admission occurring goes down as the total number of beds in the system increases.<sup>54</sup> Therefore, treating ICUs not as silos but as part of a larger system of beds may decrease the lack of available beds. The creation of critical care networks and the more frequent transfer of patients between hospitals is one way in which the United Kingdom may optimize its use of fewer beds.55,56

#### IS THERE A RIGHT NUMBER OF BEDS?

Like assessment of optimal heart function, there are many factors that can affect the shape of an ICU Starling curve and the best number of beds per capita for any given region or country. Moreover, like the recognition that there is a family of Starling curves, there are many factors that might shift the optimal spot on the curve or the entire curve itself, such as the health of the underlying population.<sup>57</sup> For example, data comparing the United States and United Kingdom demonstrate that middleaged Americans have approximately twice the burden of chronic illness compared with a similar population in the United Kingdom.<sup>58</sup> Given the association between chronic illnesses and critical illness, the overall ICU needs of a sicker population will likely be higher. Different availability of services on general wards and stepdown beds will also affect this calculation. The increasing use of noninvasive mechanical ventilation, which often can be delivered to patients outside an ICU, may create a substantial downward shift in the demand for traditional ICU beds that can accommodate patients receiving mechanical ventilation.59

Any optimal availability of ICU beds must also include some slack in the system to ensure that a population is adequately served. As mentioned earlier, queuing theory provides information regarding the required ICU needs at a local level because it accounts for the problem of fixed capacity with random demand. Although operating at 90% to 100% occupancy may appear to be most efficient in terms of use of ICU beds, this level of occupancy is likely to result in delayed

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or denied admission and decreased efficiency for the health-care system as a whole.<sup>54,60</sup> Moreover, systems that are operating on the edge of overload are ill equipped to deal with any surge in demand, such as that seen in an epidemic. This situation occurred in Toronto, Canada, during the severe acute respiratory syndrome outbreak, with too few additional beds available when some ICU beds needed to be closed to contain the disease.<sup>61</sup>

We do not yet have the sophistication to quantify the many risks and benefits of intensive care and to decide the relative weights in the trade-offs among additional survival, complications, costs, and care experience. At the low end, the United Kingdom assessed its care across these many domains and concluded that it needed more beds. Up until now, there has been little assessment of what is gained or lost with the relentless addition of ICU beds in the United States.

Every treatment is a balance between risks and benefits. When the risk of death from the associated acute illness is high, the decision to use an ICU bed generally becomes easy. Delivery of high-intensity treatment is clearly life saving in many circumstances. Moreover, no clinician ever wants to be in the position of being unable to provide the appropriate bed and resources for a patient in need. But overprovision of ICU beds, like an overfilled heart, may ultimately generate harm that is less easily quantified but important to recognize. We often speak of number needed to treat but rarely emphasize the number needed to harm. As the volume of patients in the ICU goes up and the severity of illness goes down, the calculation that health-care providers do daily in their heads to assess the need for ICU admission becomes even more complex and should at least include a possible coefficient for harm. Our understanding of health-care systems, and critical care in particular, is not yet sophisticated enough to place real numbers on these curves or even to be sure which Starling curve is right. We must continue, however, to question our needs and seek to understand the individual and societal impact of the provision of intensive care.

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#### References

 Wunsch H, Angus DC, Harrison DA, et al. Variation in critical care services across North America and Western Europe. *Crit Care Med.* 2008;36(10):2787-2793.

- Starling EH. The Linacre Lecture on the Law of the Heart. Given at Cambridge, 1915. London, England: Longmans, Green & Co; 1918.
- Wunsch H, Linde-Zwirble WT, Harrison DA, Barnato AE, Rowan KM, Angus DC. Use of intensive care services during terminal hospitalizations in England and the United States. *Am J Respir Crit Care Med.* 2009;180(9):875-880.
- Hutchings A, Durand MA, Grieve R, et al. Evaluation of modernisation of adult critical care services in England: time series and cost effectiveness analysis. *BMJ*. 2009;339:b4353.
- Metcalfe MA, Sloggett A, McPherson K. Mortality among appropriately referred patients refused admission to intensivecare units. *Lancet*. 1997;350(9070):7-11.
- Goldfrad C, Rowan K. Consequences of discharges from intensive care at night. *Lancet*. 2000;355(9210):1138-1142.
- Azoulay E, Pochard F, Chevret S, et al; PROTOCETIC Group. Compliance with triage to intensive care recommendations. *Crit Care Med.* 2001;29(11):2132-2136.
- Lieberman D, Nachshon L, Miloslavsky O, et al. Elderly patients undergoing mechanical ventilation in and out of intensive care units: a comparative, prospective study of 579 ventilations. *Crit Care*. 2010;14(2):R48.
- Barnato AE, Herndon MB, Anthony DL, et al. Are regional variations in end-of-life care intensity explained by patient preferences? A study of the US Medicare population. *Med Care*. 2007;45(5):386-393.
- Wunsch H. A triage score for admission: a holy grail of intensive care. Crit Care Med. 2012;40(1):321-323.
- Sinuff T, Kahnamoui K, Cook DJ, Luce JM, Levy MM; Values Ethics and Rationing in Critical Care Task Force. Rationing critical care beds: a systematic review. *Crit Care Med.* 2004;32(7):1588-1597.
- Wunsch H, Angus DC, Harrison DA, Linde-Zwirble WT, Rowan KM. Comparison of medical admissions to intensive care units in the United States and United Kingdom. *Am J Respir Crit Care Med.* 2011;183(12):1666-1673.
- Kumar A, Roberts D, Wood KE, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. *Crit Care Med.* 2006;34(6):1589-1596.
- Rivers E, Nguyen B, Havstad S, et al; Early Goal-Directed Therapy Collaborative Group. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med. 2001;345(19):1368-1377.
- Renaud B, Santin A, Coma E, et al. Association between timing of intensive care unit admission and outcomes for emergency department patients with community-acquired pneumonia. *Crit Care Med.* 2009;37(11):2867-2874.
- Chalfin DB, Trzeciak S, Likourezos A, Baumann BM, Dellinger RP; DELAY-ED study group. Impact of delayed transfer of critically ill patients from the emergency department to the intensive care unit. *Crit Care Med.* 2007;35(6): 1477-1483.
- National Audit Office. End of Life Care: Report by the Comptroller and Auditor General. HC 1043 Session. London, England: National Audit Office; 2008.
- Luce JM, Rubenfeld GD. Can health care costs be reduced by limiting intensive care at the end of life? *Am J Respir Crit Care Med.* 2002;165(6):750-754.
- Roberts RR, Frutos PW, Ciavarella GG, et al. Distribution of variable vs fixed costs of hospital care. JAMA. 1999;281(7): 644-649.
- Kahn JM. Understanding economic outcomes in critical care. Curr Opin Crit Care. 2006;12(5):399-404.
- Al-Khatib SM, Hellkamp A, Curtis J, et al. Non-evidencebased ICD implantations in the United States. JAMA. 2011; 305(1):43-49.

- 22. Carson SS, Cox CE, Holmes GM, Howard A, Carey TS. The changing epidemiology of mechanical ventilation: a population-based study. *J Intensive Care Med.* 2006;21(3): 173-182.
- Bodenheimer T. High and rising health care costs. Part 1: seeking an explanation. Ann Intern Med. 2005;142(10):847-854.
- Bodenheimer T. High and rising health care costs. Part 2: technologic innovation. Ann Intern Med. 2005;142(11): 932-937.
- Halpern NA, Pastores SM, Thaler HT, Greenstein RJ. Changes in critical care beds and occupancy in the United States 1985-2000: Differences attributable to hospital size. *Crit Care Med.* 2006;34(8):2105-2112.
- Halpern NA, Pastores SM. Critical care medicine in the United States 2000-2005: an analysis of bed numbers, occupancy rates, payer mix, and costs. *Crit Care Med.* 2010;38(1): 65-71.
- Romley JA, Jena AB, Goldman DP. Hospital spending and inpatient mortality: evidence from California: an observational study. *Ann Intern Med.* 2011;154(3):160-167.
- Barnato AE, Chang CC, Farrell MH, Lave JR, Roberts MS, Angus DC. Is survival better at hospitals with higher "end-oflife" treatment intensity? *Med Care*. 2010;48(2):125-132.
- Fisher ES, Wennberg DE, Stukel TA, Gottlieb DJ, Lucas FL, Pinder EL. The implications of regional variations in Medicare spending. Part 2: health outcomes and satisfaction with care. *Ann Intern Med.* 2003;138(4):288-298.
- Pearse RM, Harrison DA, James P, et al. Identification and characterisation of the high-risk surgical population in the United Kingdom. *Crit Care*. 2006;10(3):R81.
- Bennett-Guerrero E, Hyam JA, Shaefi S, et al. Comparison of P-POSSUM risk-adjusted mortality rates after surgery between patients in the USA and the UK. *Br J Surg.* 2003; 90(12):1593-1598.
- Zimmerman JE, Kramer AA. A model for identifying patients who may not need intensive care unit admission. J Crit Care. 2010;25(2):205-213.
- Lilly CM, Zuckerman IH, Badawi O, Riker RR. Benchmark data from more than 240,000 adults that reflect the current practice of critical care in the United States. *Chest*. 2011;140(5):1232-1242.
- Kraiss LW, Kilberg L, Critch S, Johansen KJ. Short-stay carotid endarterectomy is safe and cost-effective. Am J Surg. 1995; 169(5):512-515.
- Back MR, Harward TR, Huber TS, Carlton LM, Flynn TC, Seeger JM. Improving the cost-effectiveness of carotid endarterectomy. *J Vasc Surg.* 1997;26(3):456-462.
- 36. Garrouste-Orgeas M, Timsit JF, Vesin A, et al; OUTCOMEREA Study Group. Selected medical errors in the intensive care unit: results of the IATROREF study: parts I and II. Am J Respir Crit Care Med. 2010;181(2):134-142.
- Grundmann H, Bärwolff S, Tami A, et al. How many infections are caused by patient-to-patient transmission in intensive care units? *Crit Care Med.* 2005;33(5):946-951.
- Schweickert WD, Pohlman MC, Pohlman AS, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. *Lancet*. 2009;373(9678):1874-1882.
- Horwitz LI, Moin T, Krumholz HM, Wang L, Bradley EH. Consequences of inadequate sign-out for patient care. Arch Intern Med. 2008;168(16):1755-1760.
- Bell CM, Brener SS, Gunraj N, et al. Association of ICU or hospital admission with unintentional discontinuation of medications for chronic diseases. *JAMA*. 2011;306(8): 840-847.
- Angus DC, Barnato AE, Linde-Zwirble WT, et al; Robert Wood Johnson Foundation ICU End-Of-Life Peer Group.

Use of intensive care at the end of life in the United States: an epidemiologic study. *Crit Care Med.* 2004;32(3):638-643.

- 42. Wright AA, Zhang B, Ray A, et al. Associations between end-of-life discussions, patient mental health, medical care near death, and caregiver bereavement adjustment. *JAMA*. 2008;300(14):1665-1673.
- 43. Zhang B, Wright AA, Huskamp HA, et al. Health care costs in the last week of life: associations with end-of-life conversations. Arch Intern Med. 2009;169(5):480-488.
- 44. Nicholas LH, Langa KM, Iwashyna TJ, Weir DR. Regional variation in the association between advance directives and end-of-life Medicare expenditures. *JAMA*. 2011;306(13): 1447-1453.
- Emanuel EJ. Where are the health care cost savings? JAMA. 2012;307(1):39-40.
- 46. Coopersmith CM, Wunsch H, Fink MP, et al. A comparison of critical care research funding and the financial burden of critical illness in the United States. *Crit Care Med.* 2012; 40(4):1072-1079.
- Strauss MJ, LoGerfo JP, Yeltatzie JA, Temkin N, Hudson LD. Rationing of intensive care unit services. An everyday occurrence. *JAMA*. 1986;255(9):1143-1146.
- Singer DE, Carr PL, Mulley AG, Thibault GE. Rationing intensive care—physician responses to a resource shortage. *N Engl J Med.* 1983;309(19):1155-1160.
- Murray JP, Greenfield S, Kaplan SH, Yano EM. Ambulatory testing for capitation and fee-for-service patients in the same practice setting: relationship to outcomes. *Med Care*. 1992;30(3):252-261.
- Vincent JL, Takala J, Flaatten H. Impact of reimbursement schemes on quality of care: a European perspective. Am J Respir Crit Care Med. 2012;185(2):119-121.
- Carr BG, Addyson DK, Kahn JM. Variation in critical care beds per capita in the United States: implications for pandemic and disaster planning. *JAMA*. 2010;303(14): 1371-1372.
- Kahn JM, Linde-Zwirble WT, Wunsch H, et al. Potential value of regionalized intensive care for mechanically ventilated medical patients. Am J Respir Crit Care Med. 2008; 177(3):285-291.
- Noah MA, Peek GJ, Finney SJ, et al. Referral to an extracorporeal membrane oxygenation center and mortality among patients with severe 2009 influenza A(H1N1). *JAMA*. 2011; 306(15):1659-1668.
- Green LV. How many hospital beds? *Inquiry*. 2002-2003; 39(4):400-412.
- Mackenzie PA, Smith EA, Wallace PG. Transfer of adults between intensive care units in the United Kingdom: postal survey. *BMJ*. 1997;314(7092):1455-1456.
- Fried MJ, Bruce J, Colquhoun R, Smith G. Inter-hospital transfers of acutely ill adults in Scotland. *Anaesthesia*. 2010; 65(2):136-144.
- 57. Sarnoff SJ, Berglund E. Ventricular function. I. Starling's law of the heart studied by means of simultaneous right and left ventricular function curves in the dog. *Circulation*. 1954;9(5):706-718.
- Banks J, Marmot M, Oldfield Z, Smith JP. Disease and disadvantage in the United States and in England. JAMA. 2006;295(17):2037-2045.
- Nava S, Hill N. Non-invasive ventilation in acute respiratory failure. *Lancet*. 2009;374(9685):250-259.
- McManus ML, Long MC, Cooper A, Litvak E. Queuing theory accurately models the need for critical care resources. *Anesthesiology*. 2004;100(5):1271-1276.
- Booth CM, Stewart TE. Severe acute respiratory syndrome and critical care medicine: the Toronto experience. *Crit Care Med.* 2005;33(suppl 1):S53-S60.