Chapter 13
Health Disparities in Critical Illness

Daniel Monroy Chaves and John Daryl Thornton

Key Points

- Health disparities are well described in most facets of critical illness.
- Racial and ethnic disparities are the most commonly described disparities in critical illness.
- However, race and ethnicity are often used as substitutes for other factors such as geographic location of residence or geographic location for receipt of health care that have an equal or greater effect on patient outcomes.
- Studies exploring the effects of specific health disparities (such as race and ethnicity) on outcomes of the critically ill need to account for as many additional factors as possible that may be involved in order to give a more detailed and accurate picture of the true factors affecting patient outcomes.
- Novel approaches to the design and evaluation of targeted interventions are needed to eliminate health disparities in critical illness.

D.M. Chaves, M.D.
Division of Pulmonary, Critical Care, and Sleep Medicine, The MetroHealth Campus of Case Western Reserve University, Cleveland, OH, USA

J.D. Thornton, M.D., M.P.H. (✉)
Division of Pulmonary, Critical Care, and Sleep Medicine and Center for Reducing Health Disparities, The MetroHealth Campus of Case Western Reserve University,
Cleveland, OH 44109, USA
e-mail: daryl.thornton@case.edu

L.B. Gerald, C.E. Berry (eds.), *Health Disparities in Respiratory Medicine*,
Respiratory Medicine, DOI 10.1007/978-3-319-23675-9_13

Background

The foundation for our current understanding of the practice of critical care medicine and the need for dedicated areas to care for the critically ill can be traced to Kommunehospitalet, the municipal hospital of Copenhagen, Denmark in 1953 [1]. The polio epidemic had ravaged the country and hospitals had exceeded their ability to care for those with respiratory failure [2]. Dr. Bjorn Ibsen, an anesthesiologist, not only described successful practices in the care of such patients, but he also conceived of a “special department, where they were under constant observation by a team, consulting epidemiologist, the ear, nose, and throat surgeon, and the anaesthetist, all working with help from an excellent and capable laboratory” [3]. Today, outcomes continue to be most favorable among critically ill patients that are cared for in an intensive care unit (ICU) and by a multidisciplinary care team with significant experience in dealing with such patients [4–6]. However, such care is resource exhaustive and relatively scarce. With an aging American population, the need for critical care services over the next few decades will likely dramatically increase, while the numbers of trained intensivists and pulmonologists will decrease below current levels [7, 8]. Many ICUs are already facing rapid increases in occupancy, having recently reached an alarming average occupancy of 68 %, leaving little room for the projected increases or for more acute needs in the setting of a pandemic [9, 10]. ICUs already buckling under the significant strain from the current increased demands for their services may not be able to sufficiently care for additional patients, which may lead to an increase in morbidity and mortality [11, 12]. Limited availability of critical care services will likely have the greatest impact among those who are most vulnerable and may lead to an increase in health disparities [13].

Research in health disparities related to critical illness has largely reflected health disparities research involving other aspects of medicine [14, 15] with early research being mostly descriptive (Table 13.1) [16, 17]. These descriptive studies established the prevalence of disparities in critical care and identified potential benchmarks for improvement. The next phase in health disparities research involved identifying the underlying mechanisms responsible for the described disparities. This has afforded us a deeper understanding of the root causes of health disparities, thereby assisting in the development of the third phase of research—evaluation of targeted interventions to eliminate health disparities. Unfortunately, this phase of health disparities research has been slow to evolve and is clearly where most of the work is needed [18]. This chapter provides a broad overview of health disparities in critical care and identifies mechanisms for the development and testing of novel disparities-related interventions. Gaps in our current understanding and areas of future need are emphasized (Table 13.2).

Table 13.1 State of health disparities research in critical care

Critical care settings	Descriptive studies	Mechanistic studies	Interventional studies
Emergency Department	*	_	_
Cardiac Critical Care	**	*	_
Medical Critical Care	***	**	_
Neurologic Critical Care	***	**	_
Surgical Critical Care	***	*	_

Table 13.2 Challenges and recommendations to further exploration of health disparities in critical illness

Challenge	Recommendation
1. Lack of clear guidelines regarding integral components of health disparities publications	Development of evidence-based guidelines and author checklists for health disparities publications
2. Racial and ethnic categories are static and mutually exclusive	Allow study participants to self-identify as many racial and ethnic categories as desired
3. Factors confounding racial, ethnic, age, and gender disparities are often missing	Aim to address all known factors affecting the relationship between disparities and health outcomes
4. Too few mechanistic and interventional studies	1. Creation of funding mechanisms devoted to exploring novel means to alleviate health disparities
	2. Increase in exposure of young investigators to health disparities research

Some Words About Race…

Racial disparities are perhaps the most studied aspect of health disparities, and differences in outcomes by race are well reported [15]. Osborn and Feit delineated the confusion associated with using race as a variable in research [19]. The common assumption in many studies is that the results reflect biological or genetic differences attributed to race. However, these studies often fail to account for the individual and societal complexities and lack of well-defined boundaries between the socially defined constructs of race and ethnicity [20]. Researchers have used race as a substitute for socioeconomic status, culture, and class, as well as genetic and ancestry-based biological constructs. With such wide variability in the definition, it is not surprising that study findings have been so disparate. To confound measures further, the assessment of race is also variable, ranging from direct observation to surrogate report, or by the optimal (unbiased and most detailed) method, self-report. Even well-regarded sources of data including the U.S. Census, state birth and death certificates, and hospital and payer records have substantial variability in the collection and ascertainment of race, despite the presence of federal guidelines [21]. Researchers reporting results of racial disparities are encouraged to be transparent and thorough in their assessment of race and include confounding factors that are commonly associated with race and adverse outcomes in their studies (see section "Factors Confounding Racial, Ethnic, Age, and Gender Disparities" below). In turn, readers of health disparities studies are encouraged to interpret the study results in the context of the information provided regarding the characterization of race. In this chapter, we have provided study results along with linking contextual information to promote a clearer understanding of the association between race and adverse outcomes among the critically ill.

Types of Health Disparities Affecting the Critically Ill

Race and Ethnicity

African Americans are more likely to be admitted into the ICU presumably due to a higher prevalence of conditions requiring critical care, a higher severity of illness, and an increased number of comorbid conditions that complicate management [22–24]. For example, African American men may be at greater risk for the development of sepsis from Grampositive bacteria and to have at least one acute organ dysfunction upon presentation compared to whites [25]. Using the New Jersey inpatient database, Dombrovskiy et al. found that African American adults with sepsis were younger, had more comorbid conditions, and were more likely to be admitted into the ICU compared to whites [26]. In a cohort study using data from the Acute Respiratory Distress Syndrome Network, African American patients with ARDS had the greatest severity of critical illness and were more likely to have complicating comorbidities such as HIV, end-stage renal disease, or cirrhosis [23]. After adjusting for demographic and clinical factors, African Americans and Hispanics with ARDS had a higher mortality rate compared to non-Hispanic whites with ARDS. However, after adjusting for severity of illness, African American race was no longer associated with mortality while the relationship between Hispanic ethnicity and mortality persisted.

A similar trend of increased ICU admission is seen in the pediatric population. However, the reasons for it may not be as clear as in adults. In a study of 4676 pediatric ICU admissions in Shelby County, Tennessee, African American children were more likely to be admitted to the pediatric ICU compared to non-Hispanic white children of similar severity of critical illness (OR: 2.1, 95 % CI: 1.7–2.7) [27]. Interestingly, full-term African American children had higher risks of admission compared to full-term white children (OR: 1.8, 95 % CI: 1.3–2.5) but there was no difference in risk for admission between preterm African American and preterm white children (OR: 1.4; 95 % CI: 0.9–2.2). In the region where the study was conducted, African Americans have a significantly higher prevalence of preterm births

(0.1 compared to 0.06 for non-Hispanic whites). Once admitted into the ICU, there was no difference in mortality between full-term African American and white children (4 % vs. 6 %, $p=0.2$) or preterm African American and white children (6.8 % vs. 8.9 %, $p=0.5$). The authors posit that African American children, particularly those with special needs, are less likely to receive primary care and therefore are more likely to be admitted to the ICU with exacerbations of unmanaged or undermanaged diseases [28–30]. A better understanding of factors affecting ICU admission and outcomes in the pediatric population is needed.

Once admitted into an ICU, African American patients receive disparate care compared to whites, despite no ultimate difference in mortality. In a study of over 15,000 patients admitted to one of 42 ICUs in 40 hospitals, Williams et al. found that African Americans received less technological monitoring, less laboratory testing, and less life-supporting treatments within the first 24 h following admission compared to whites. Adjusted ICU lengths of stay were also shorter [31]. Rapoport et al. found that critically ill African Americans of similar severity of illness to whites received fewer pulmonary artery catheters [32].

There are also ethnic barriers to optimal critical care. Limited English proficiency is a facet of ethnic disparities that has received a considerable amount of recent attention due to the alarming frequency of associated adverse outcomes including delayed care, permanent disability, or even death [33–36]. Some of the most influential factors associated with these poor outcomes include miscommunication, lack of cultural understanding, and poor social support. During the ICU family conference, patients' surrogates with limited English proficiency may receive less information regarding their loved one's current illness and proposed treatment and less emotional support from caregivers despite the presence of professional interpreters [37, 38]. It appears that the presence of interpreters attenuates but does not eliminate these adverse outcomes to patients with limited English proficiency [39, 40]. However, some data suggest that outcomes among patients with limited English proficiency may be equal to or better than those of English proficient patients. In a large cohort study of patients admitted to the ICU of two Boston hospitals between 1997 and 2007, patients whose primary language was not English had 31 % lower odds of 30-day mortality compared to patients whose primary language was English [41].

Age

Currently, patients older than 65 years of age comprise 56 % of all ICU days and patients older than 85 years of age comprise 14 % [7, 42]. With the population continuing to age, this percentage is expected to increase [43]. Using prospective data from Australian and New Zealand ICUs, Bagshaw et al. predicted that by 2015 the rate of patients 80 years of age and older will increase by 72 % to approximately 1 in 4 ICU admissions [44].

Milbrandt et al. posited that aging "predisposes to critical illness due to lifelong accumulation of molecular and cellular damage leading to decreased physiologic reserves and leaving the individual less able to respond to stressors" [43]. Therefore, it is not surprising that increasing age is positively associated with increasing mortality. In Bagshaw's study, patients 80 years of age and older had an adjusted odds of ICU and hospital mortality significantly higher than patients between the ages of 18 and 40 (OR: 2.7, 95 % CI: 2.4–3, and OR: 5.4, 95 % CI: 4.9–5.9, respectively). Factors associated with the higher odds of death among patients 80 and older included admission from a chronic care facility, nonsurgical admission, need for mechanical ventilation, comorbid conditions, a longer ICU stay, and a higher severity of illness. However, despite the increased odds of mortality compared to younger patients, approximately 80 % of patients 80 years of age and older survived to hospital discharge. In a cohort study spanning 7 years of ICU patients admitted to a single academic center in Massachusetts, patients over the age of 65 represented more than 45 % of the total ICU population. Mortality (28-day and 1-year) increased with age despite adjustment for gender, comorbidities, severity of critical illness, and presence of do not resuscitate orders [45].

Severe sepsis, a frequent cause of ICU stay and mortality, has enjoyed an increased survival rate over the last decade. Some have attributed the increase to a change in the age distribution or case fatality rate among those affected. Using a cohort of fee-for-service Medicare beneficiaries aged 65 and older, Iwashyna et al. found that the number of incident 3-year survivors of severe sepsis rose 119 % between 1999 and 2008. They attributed this increase in survivorship to an increased rate of organ dysfunction per patient hospitalized with infection rather than a change in the age distribution or better survival among patients. In fact, the 3-year case-fatality rates only decreased from 73 to 71 % over the period of analysis [46].

With the majority of older individuals surviving a hospitalization for severe sepsis, a new problem has emerged—that of chronic disability. Prospective data of 470 patients with severe sepsis admitted to 24 ICUs in Finland revealed a 2-year mortality of 45 % and a lower quality of life compared to age- and sex-adjusted reference values without sepsis [47]. The 2-year mortality was 35 % among those patients older than 55 years of age compared to younger patients (9.8 %, $p < 0.001$). As age increased, quality of life decreased, while the mean estimated cost per quality-adjusted life year (QALY) increased ranging from 325€ for those less than 24 years of age to 12,452€ for those over 81 years of age. The findings of significantly impaired quality of life following hospitalization and increased long-term mortality rates were confirmed in a 2010 systematic review of 30 studies [48]. The severity and duration of impairment was well delineated in another study by Iwashyna et al. They prospectively examined participants from the Health and Retirement Study whose data were linked with the Medicare database [49]. The prevalence of moderate to severe cognitive impairment was 11 % greater among the patients who had been hospitalized for severe sepsis compared to those who had been hospitalized for other conditions. Impairments in cognitive and physical functioning persisted for at least 8 years following hospitalization, suggesting that many patients may be unable to ever return to independent functioning.

Despite the fact that the majority of critically ill older patients survive hospitalization, age-related barriers to ICU admission appear to exist. In a prospective cohort study conducted in 15 French hospitals, 2646 patients of age 80 years and older were triaged in the emergency room. The authors used standardized admission criteria to determine patient eligibility for admission. Of the 1426 patients who met definite admission criteria, only 31 % were referred for ICU admission, and only 52 % of those referred were admitted [50]. Increasing age was an independent factor associated with no referral for ICU admission (OR: 1.04, 95 % CI: 1.02–1.07 for every 1 year increase). Another study demonstrated that once admitted into the ICU, elderly patients are less likely than younger patients to receive intensive treatments such as mechanical ventilation and renal replacement therapy, perhaps due to the subjective perception among healthcare providers of a potential lack of benefit from treatment [42]. In both of these studies, it is unclear what role patient preferences may have played in decisions regarding admission and intensity of care.

Patient and provider decisions regarding care of the critically ill older patient may be based on incomplete or faulty information. In 1995, there were 215,000 deaths attributable to severe sepsis representing 9.3 % of all deaths in the United States and equivalent to the number of deaths attributed to acute myocardial infarction (AMI). The burden of severe sepsis is significant among the older population. The incidence of severe sepsis is 26/1000 among those 85 years and older compared to 5/1000 for adults between that ages of 60 and 64. Moreover, mortality from severe sepsis is 38 % among those ≥85 years of age and <30 % for those between 60 and 64. Despite the increased burden, observational studies of severe sepsis and clinical trials of sepsis therapies often exclude the elderly due to perceptions of increased risk of death or lack of response to treatment. It is important to note that the majority of elderly patients admitted to the ICU with severe sepsis are discharged alive. In addition, as pointed out by Angus et al., with the elderly comprising a substantial proportion of the critically ill population, excluding them from such studies threatens external validity and prevents a comprehensive public policy approach from being created [43, 51].

It is also important to consider the effect of multiple demographic factors on patient outcomes. For example, age and race may be interacting to uniquely affect health outcomes. In a study using data from the National Hospital Discharge Survey, Martin et al. found that African American men presented with the highest rates of sepsis (331 cases/100,000), the youngest age at onset (47 years), and the highest mortality (23 %) [52]. The reasons were not explored, but the authors presented several possible mechanisms including genetic, social, and clinical differences, and called for further investigation to be performed.

Gender

Although women comprise a larger proportion of the US population, the evidence suggests that men have a higher incidence of critical illnesses such as sepsis (mean annual relative risk: 1.3, 95 % CI: 1.2–1.3) [52]. Despite the increased incidence, men do not appear to have a higher case-fatality rate compared to women [25]. In surgical ICUs in the US, for example, men were found to have a higher incidence of sepsis and septic shock compared to women but no difference in hospital or postdischarge mortality [53]. Men are also at risk of prolonged ICU stays compared to women of a similar severity of illness [54]. This may represent differences in end-of-life care, personal preferences regarding care, or other unmeasured factors.

In Europe, some data suggest women have a higher severity of illness and receive a lower overall intensity of care compared to men, but there are no apparent differences in mortality by gender. For example, among 25,998 adults admitted to one of 31 ICUs in Austria, women had higher severity of illness scores (SAPS II 28 vs. 26, $p<0.001$) and in-hospital mortality rates (18 % vs. 17 %, $p=0.04$) compared to men [55]. However, after adjustment for severity of illness, the mortality rate did not differ between men and women. Men received more intensive care compared to women including mechanical ventilation, vasoactive medication, placement of central venous and pulmonary artery catheters, and renal replacement therapy compared to women. These results suggest that the SAPS II score did not fully capture patient severity of illness or other factors besides severity of illness are associated with disparate receipt of intensive therapies between men and women.

Gender differences in receipt of therapies are found in other parts of the world as well. In the U.S., evidence suggests that critically ill men are more likely to receive thrombolytic therapy, emergent surgery, mechanical ventilation, and even coronary artery bypass graft surgery more frequently than critically ill women [56]. Similar results were found in Canada [57]. In a retrospective examination of almost 25,000 critically ill patients admitted to Ontario hospitals over a 2-year period, women were less likely to be admitted into an ICU compared to men (40 % compared to 60 %, $p<0.001$). In fact, older women (≥50 years of age) had 32 % lower odds of being admitted compared to older men. Older women were also less likely to receive mechanical ventilation and pulmonary artery catheterization, and they had shorter ICU stays but longer overall stays in the hospital. Most concerning was the fact that ICU and in-hospital mortality rates were greater for older women compared to older men.

While race, ethnicity, age, and gender all play substantial roles in the development of disparate outcomes, other factors linked to these demographic indices may be equally if not more important. Studies that have explored the root causes of disparities have often found that much of the effect attributed solely to race, ethnicity, gender, or age is significantly attenuated upon consideration of potential confounders. Unfortunately, few studies have incorporated detailed adjustments of these confounding factors into their analyses. A deeper understanding of the effects of these confounding factors is warranted.

Factors Confounding Racial, Ethnic, Age, and Gender Disparities

Genetic Predisposition

Emerging evidence suggests that genetic predisposition may play a role in many disorders affecting the critically ill. However, the extent to which genetic predisposition plays a role in the development of health disparities has not been well described. Perhaps the best evidence linking genetics and premature mortality among the critically ill was from a case–control study of 976 adult Danish nonfamilial decedent adoptees and their biological and adoptive parents [58, 59]. Sørensen et al. found an increased mortality among the biological parents of decedent children but not among their adoptive parents. The associated causes of death included all of the major sources of critical illness: infectious causes (HR: 1.9, 95 % CI: 1.1–3.5), vascular causes (HR: 2.0, 95 % CI: 1.2–3.1), and even natural causes (HR: 1.2, 95 % CI: 1.0–1.4). However, there was no adjustment for demographic or socioeconomic factors. Other studies have identified only a few heritable mutations predisposing to critical illness that are limited mainly to a handful of families. For example, Picard et al. described 3 unrelated children with inherited interleukin-1 receptor-associated kinase (IRAK-4) deficiency rendering them susceptible to recurrent pyogenic bacterial infections [60]. Recent genetic epidemiologic studies have focused on the more prevalent genetic variations [61]. Differing allelic frequencies have been found by both race and gender in patients with ARDS and sepsis. The myosin light chain kinase gene (*MYLK*) encodes a multifunctional protein involved in the inflammatory response [62]. Different single-nucleotide polymorphisms of *MYLK* were found to be associated with sepsis and sepsis-associated ARDS among African Americans and whites. The functional *T-46C* polymorphism in the Duffy antigen/receptor for chemokines (*DARC*) gene is found almost exclusively in persons of African descent and associated with worse clinical outcomes among African Americans with ARDS, perhaps due to an increase in circulating IL-8 [63].

Part of the difficulty in identifying genetic influences on health disparities is due to the wide variability in genetic variants between people of different ancestries. When diverse populations are studied, the associations with a clinical phenotype may be mistaken for being associated with the presence of multiple specific genetic variants determining a predisposing genotype, rather than with an association with prevalence/incidence due to patient ancestry [61]. This spurious association confounding can be overcome by stratifying the case and control groups with different fractions of ancestry from each ancestral subpopulation [64]. Unfortunately, this level of detail is often missing from genetic epidemiology studies in critical illness.

Geographic Residence and Location of Care

Vulnerable critically ill patients are at high risk of experiencing poor health outcomes because of poor access to acute and chronic care, lower socioeconomic status, lower levels of education, higher rates of unemployment, and a higher burden of chronic disease compared to the majority of patients [65]. The imbalances in the geographical distribution of resources, available technological advancements, and distribution of wealth have intentional and unintentional repercussions that have left increasing numbers of the general population unprotected. In the United States, for example, minority populations frequently live clustered together in neighborhoods separated from white populations. Due to the need for emergent care, critically ill patients are often cared for in hospitals nearest to their homes. As a result, critically ill minority patients are more likely to receive care in different hospitals compared to critically ill white patients. The resources available to persons living in minority-predominant neighborhoods are often fewer compared to majority-predominant neighborhoods. This is true in health care as well. Indeed, a recent analysis of Medicare data revealed that only 25 % of hospitals in the United States care for almost 90 % of elderly African American patients [66]. These hospitals tended to be larger and more often were teaching hospitals situated in the southern United States. They also tended to have worse measures of quality of care including treatment of AMI, heart failure, and pneumonia compared to hospitals caring for lower proportions of African American patients.

Hospital level factors may influence health disparities more than patient-level factors. For example, in a study of patients admitted to 28 hospitals for community-acquired pneumonia, African American patients were less likely to receive timely or guideline-adherent antibiotics [67]. Within each hospital, African American and white patients received a similar quality of care. However, among hospitals serving a greater proportion of African American patients, African American and white patients with community-acquired pneumonia were less likely to receive timely antibiotics (OR = 0.8, 95 % CI: 0.8–0.9) and were more likely to receive mechanical ventilation (OR = 1.6, 95 % CI: 1.0–2.4). In a retrospective population-based cohort study including six U.S. states (Florida, Massachusetts, New Jersey, New York, Virginia, and Texas), African Americans had the highest age- and sex-standardized population-based incidence of severe sepsis and hospital-acquired infections and the highest ICU case fatality rates compared to Hispanic and non-Hispanic whites [22]. However, adjustment for clinical characteristics and the treating hospital fully explained the higher case fatality rate.

It appears that when it comes to health care in general in the US, separate may not be equal. For example, risk-adjusted mortality after AMI is higher among African American and white patients admitted to hospitals caring for the highest proportion of African American patients compared to those caring for the lowest [68]. Hospitals with large proportions of African American patients also have worse cardiac arrest outcomes compared to hospitals with predominantly white patients

[69, 70]. This might explain the disparities in survival following cardiac arrest noted between African Americans and whites. Among patients discharged to home following evaluation in emergency rooms in Arizona, Massachusetts, and Utah, African American and Asian patients had lengths of stay ranging from 2 to 14 % shorter than white patients in teaching hospitals, and 1.6 to 16 % longer than white patients in nonteaching hospitals, potentially leading to incomplete clinical evaluations [71]. Finally, in critical care at the end of life, Barnato et al. found differences in ICU use between African Americans, Hispanics, and whites that were attributed to admission into different hospitals with varying ICU utilization patterns at the end of life rather than effects of patient race or ethnicity on ICU use within the hospitals [72]. These studies provide a compelling case to adjust for type and locations of hospitals in all studies of health disparities affecting the critically ill.

The Department of Housing and Urban Development conducted a study that provided insight into successful interventions that may overcome the harmful effects of poverty and segregation on health outcomes [73]. Between 1994 and 1998, 4498 women and children living in public housing in high-priority urban census tracts were randomized to one of three groups. The first group was assigned to receive housing vouchers which could be redeemed only if the participant family moved to a census tract where <10 % of the residents were impoverished and if the participant received counseling regarding moving. Participants in the second group were assigned to receive unrestricted, traditional vouchers with no additional counseling on moving, and participants in the third group served as a control group that received neither vouchers nor counseling. Ten to 15 years later, participants were contacted to determine their body mass index and glycated hemoglobin levels as proxies for the development of high-risk morbid conditions. Participants who had received the vouchers to move to low poverty census tracts combined with counseling on moving were less likely to be obese and had lower glycated hemoglobin levels than participants in the control group. There were no differences in body mass index or glycated hemoglobin among participants in the unrestricted voucher group and participants in the control group. Whether this or similar interventions will have an effect on critical illness outcomes remain to be seen.

Chronic Illness and Access to Care

Comorbid conditions have a significant effect on critical care outcomes [74], and differential prevalence of comorbid conditions as well as differential receipt of treatment of such conditions may explain a significant portion of observed racial and ethnic differences in critical care outcomes. African Americans are more likely to be hospitalized for ambulatory care-sensitive conditions—conditions for which appropriate ambulatory care could prevent hospitalizations—compared to whites [75, 76]. Among patients admitted to ICUs in 35 California hospitals, Erikson et al. found no racial or ethnic differences in in-hospital mortality or ICU length of stay after adjusting for severity of illness, socioeconomic status, and insurance status [77]. They did find that African American patients were more likely to be admitted with a higher severity of illness and more metabolic derangements suggesting poor access to care and poor control of comorbid conditions prior to admission. The lack of a difference in mortality when compared to white patients could be due to the fact that providing initial care for exacerbations of chronic diseases altered the trajectory of the critical illness. For example, African Americans between the ages of 45 and 64 are 2.5 times more likely to die of heart failure compared to whites of similar age [78]. An African American patient may be admitted to the ICU with an acute exacerbation of previously untreated heart failure with reduced ejection fraction due to poor access to ambulatory care and consequently an inability to initiate routine first-line therapy such as diuretics or ACE inhibitors. With prompt initiation of these agents upon ICU admission, his ICU mortality may improve even though his acute severity of illness on presentation was high, as these agents have previously been demonstrated to be effective in reducing mortality among patients with his degree of CHF. A white patient presenting with a similar CHF exacerbation and an equal acute severity of illness may have an equal or worse mortality as he may have had better access to evidence-based treatments for heart failure while in the ambulatory setting and therefore may already be taking several medications that are indicated for the treatment of CHF. The current measures of ICU severity of illness such as APACHE and SAPS do not account for severity of chronic illness nor do they account for degree of optimization of comorbid conditions. The African American patient may appear sicker according to such severity of illness measures, but require less aggressive treatment from the care team and have a lower ICU mortality. Another explanation for the lack of mortality difference between African American and white patients in this study may be that the participating hospitals were located in the west coast, which care for a higher proportion of white patients and may therefore deliver superior care compared to hospitals in other regions of the country which serve predominantly African American patients.

Uninsurance and Under Insurance

Almost 100 million people worldwide are forced into poverty each year because of catastrophic household medical expenses [79]. As evident in other areas of healthcare, lack of adequate health insurance adversely affects critical care outcomes. For example, low-income and uninsured individuals residing in large metropolitan areas are much less likely to visit with a physician compared to those with higher income or health insurance [80]. Uninsured patients experiencing new serious or morbid symptoms are less likely to receive medical care even though they think they need it [81]. In a systematic review of 29 studies examining the association between insurance status and critical care delivery and outcomes, uninsured patients were less likely to receive critical care services than those who were insured [82]. Following admission, uninsured patients also received fewer procedures compared to insured patients. Most importantly, lack of insurance was associated with an increased risk of death. In a more recent study not included in the systematic review, Lyon and colleagues performed a retrospective review of patients admitted to Pennsylvania hospitals in 2005 and 2006 [13]. They performed comprehensive patient clinical and demographic adjustments while also considering hospital-level effects and found an increased 30-day mortality among uninsured patients compared to privately insured patients (5.7 % vs. 4.6 %, $p<0.001$). Uninsured patients were also less likely to receive a central venous catheter (7.3 % vs. 9.8 %, $p<0.001$), acute hemodialysis (0.7 % vs. 1.1 %, $p<0.001$), or tracheostomy (8.6 % vs. 22 %, $p<0.001$). As pointed out by the authors, adjusting for hospital-level effects in the analysis allowed comparisons between uninsured and private patients cared for at the same hospitals. Therefore, the lower receipt of critical care procedures and higher mortality rate seen among the uninsured compared to private patients in this study were most likely due to factors occurring within each care setting.

With expansion of insured care under the Affordable Care Act, one might expect greater utilization of critical care services and even a decrease in observed mortality among the critically ill. However, in a comprehensive analysis of Massachusetts data before and after healthcare reform compared to four states that did not enact reform (New York, Washington, Nebraska, and North Carolina), no difference was noted in ICU utilization, discharge destination, or hospital mortality [83]. However, the number of critically ill patients with insurance increased, as was expected. The authors cited several hypotheses for their lack of observed mortality difference, including the unique patient demographics of Massachusetts where only 9 % of patients were uninsured compared to a national average of 17 %. The population of Massachusetts also has a higher baseline socioeconomic status and less racial and ethnic diversity compared to the rest of the nation. Another possibility is that the association between lack of health insurance and mortality observed in prior studies may have been due to other unmeasured factors for which lack of insurance served as a proxy (i.e., poverty). These unmeasured factors may not have changed immediately following insurance expansion. In a study comparing 5 years before Medicaid to have expansion to 5 years after expansion in New York, Maine, and Arizona were found to have a relative reduction in all-cause mortality of 6.1 % or 20 deaths per 100,000 adults compared to neighboring states that did not undergo Medicaid expansion [84]. Mortality reductions were greatest among older adults, nonwhites, and residents of poorer counties.

In 2008, Oregon used a lottery system to select from those individuals waiting for Medicaid expansion. About 2 years after the lottery, 6387 adults who had been selected to apply for Medicaid coverage were compared with 5842 adults who had not been selected [85]. Medicaid coverage was associated with a decreased likelihood of a positive screen for depression (−9 %, 95 % CI: −17 to −1.6 %, $p=0.02$), increased use of many preventive services, and nearly complete elimination of potentially catastrophic out-of-pocket medical expenditures. Among those covered by Medicaid, more cases of diabetes were diagnosed (3.8 % increase, 95 % CI: 1.9–5.7 %) and a higher proportion of patients were using diabetes medications (5.4 % increase, 95 % CI: 1.4–9.5 %). There was no difference in the use of medications for hypertension or hyperlipidemia, nor was there a difference in average glycated hemoglobin levels. While physical health failed to improve in the first 2 years following expanded Medicaid coverage, there was greater healthcare utilization and reduced financial strain.

Work Trajectory and Unemployment

Work may offer many people a sense of accomplishment and well-being, but for some individuals, work can have deleterious effects on health [86]. Over the last half-century, women have had increased representation in the labor force. Despite this increased representation, African American and white women have had significantly different work trajectories. Black women are more likely to work in jobs with lower earnings, little room for advancement, and high risk of termination [87]. Using data from the National Longitudinal Survey of Mature Women, Shippee et al. found that Black working women who had felt that their work had progressed in the past 10 years had a 24 % lower mortality risk compared to those who felt that their work was static or had regressed. This result persisted despite adjusting for personal demographics, type of occupation, health characteristics, family life, and personal and household wealth. We were unable to find any studies exploring the effects of work trajectory on critical care outcomes.

Income Inequality

Income has a significant effect on health outcomes. Low income is associated with low birth weight, poor educational outcomes, unemployment, work disability, lack of medical insurance, increased medical expenditures, smoking, and sedentary activity [88]. It should come as no surprise, therefore, that income inequality is also associated with differences in all-cause age-adjusted mortality [89]. Across Europe, countries with a lower proportion of their population in relative poverty have higher average life expectancies [90].

Bein et al. prospectively administered a questionnaire that assessed patient socioeconomic status (level of education, occupation, income, marital, and health insurance status) to the surrogates of 1006 patients in a 24-bed surgical ICU of a tertiary hospital in Germany [91]. They found patients of lower socioeconomic status had a higher adjusted odds for ICU length of stay and a lower adjusted odds for visits from friends and family compared to patients with higher socioeconomic status. This result has not been replicated in the United States. In the previously mentioned study involving multiple hospitals in California, Erickson et al. found that socioeconomic status (and higher admission severity of illness) attenuated the increased ICU length of stay identified in African Americans [77]. This demonstrates the importance of including multiple patient level factors in disparities studies.

In spite of the previously mentioned associations between low income and increased mortality, a retrospective study of 38,917 patients admitted to either of two academic medical centers in Boston between 1997 and 2007 found that the percentage of census tract residents below the federal poverty line was not associated with all cause 30-day, 90-day, or 1-year mortality [92]. It was also found to not be associated with 90- and 365-day mortality postcritical care initiation. The study did not include severity of illness information based on physiologic parameters but did include comorbid conditions.

In summary, several factors may confound the relationship between race, ethnicity, age and gender, and health outcomes, including genetic predisposition, geographic location, chronic illness, access to care, and socioeconomic status. Such factors should be adequately addressed in any study of health disparities before valid conclusions can be made.

Critical Care Settings and Conditions Where Health Disparities Have Been Described

Emergency Department

The emergency department remains the primary source of ICU admissions. Despite this, there is a paucity of data regarding emergency department care of the critically ill [93]. To our knowledge, there are no national databases tracking critically ill patients in the emergency department. This leads to an inability to accurately assess the proportion of emergency department patients that are critically ill, the quality of the care that is delivered to them, and how our care delivery in this setting has changed over time.

Even with the lack of national emergency department data on critical illness, important work in health disparities has been performed in the emergency department. A seminal study in health disparities was conducted in an emergency department in Los Angeles in 1993, involving chart review for 139 Hispanic and non-Hispanic white adult patients who presented to the emergency department of a level I trauma center with isolated long-bone fractures [94]. Hispanics remained more likely than non-Hispanic whites to not receive pain medication for their acute fractures after adjustment for several patient and physician characteristics (odds ratio: 7.5, $p < 0.01$). A follow-up study in the same setting found that despite Hispanics receiving less analgesia they did not differ from non-Hispanic whites in their delineation of pain and their physicians rated their pain similar to non-Hispanic whites [95]. This suggests that other factors were responsible for lack of an equitable receipt of analgesia among Hispanic patients.

Factors affecting triage of critically ill patients in the emergency department may also influence disparities, and prehospital therapy may influence outcomes in critical illness by affecting appropriate triage. In one study of patients with sepsis, patients that arrived by ambulance had a higher likelihood of receiving immediate care (including a shorter time to first antibiotics and a shorter time to initiation of early goal directed therapy) compared to "walkins" [96]. For patients who are unable to afford the cost of an ambulance and instead present to their local emergency department by their own means, this can significantly affect their survival. How this further modifies existing racial, ethnic, gender, and age-related disparities is unclear.

Delayed transfer of patients from the ED to the ICU also has a significant impact in outcomes. A study conducted using the Project IMPACT database demonstrated increased ICU and inhospital mortality rates and prolonged hospital lengths of stay following ICU discharge for patients with at least a 6 h delay in ICU transfer from the ED [97]. Unfortunately, few patient level demographics were available to look for associations with health disparities. However, similar findings were demonstrated in a Brazilian study [98]. Such delays are not uncommon and are related to availability of critical care beds in the same institution, the need for interhospital transfer due to need for higher level resources, and physician and nursing staffing in the emergency department and ICU.

Intensive Care Unit

The intensive care unit is the setting for the majority of studies evaluating health disparities among the critically ill. Common conditions encountered in the ICU have received significant attention.

Acute Respiratory Distress Syndrome

In 2012, the definition of ARDS was updated. The new Berlin definition is less ambiguous and has better predictive validity for mortality compared to the previous standard, implemented in 1994 by the American-European Consensus Conference (AECC) [99]. However, the vast majority of ARDS research in general and ARDS health disparities research in particular has relied on the AECC definition. At present, it is unclear what effect the new definition will have on identifying health disparities in ARDS.

Epidemiologic data regarding the incidence and outcomes of ARDS has been hampered by inconsistent definitions, diagnostic misclassification, single-center studies, and limited durations of observation. One of the few studies to overcome these limitations evaluated data from 18 hospitals in King County, Washington as well as 3 hospitals in adjacent counties [100]. The crude incidence of ARDS was 78.9 per 100,000 person-years, and the age-adjusted incidence was 86.2 per 100,000 person-years. In hospital mortality was 38.5 %. The incidence of ARDS varied by age ranging from 16 cases per 100,000 person-years among those between the ages of 15 and 20 years to 306 cases per 100,000 person-years among those between the ages of 75 and 85 years. In-hospital mortality was also found to vary with age, ranging from 24 % among those 15–19 years old to 60 % among those 85 years and older. However, the residents of King County were more affluent, younger, and had a different racial distribution compared to the United States population, and as a result, ARDS incidence and mortality data for minorities and individuals of lower socioeconomic status could not be determined in this study. Using data of patients who participated in the National Heart, Lung, and Blood Institute multicenter, randomized trials of the ARDS Network, Ely and colleagues found similar disparities in mortality among older patients with ARDS. Patients at least 70 years of age had longer times on the mechanical ventilator (median of 19 vs. 10 days, $p < 0.001$), longer ICU stays (21 vs. 16 days, $p < 0.01$), and a higher risk of in-hospital death (hazard ratio: 2.5, $p < 0.001$) [101]. Even after passing spontaneous breathing trials, older patients needed an additional day to obtain unassisted breathing compared to younger patients ($p = 0.002$), and 3 additional days before leaving the ICU ($p = 0.005$). However, older patients had fewer preexisting comorbid conditions compared to the younger group.

A study using the Multiple Cause Mortality Files from 1979 through 1996 for records containing ICD-9 codes consistent with ARDS found a higher risk of ARDS among women compared to men and African Americans compared to whites [102]. African American men had the highest ARDS-associated mortality compared to white men and men of other minority groups (12.8 per 100,000 individuals per year, compared to 9.1 and 8.6, respectively). African American women similarly had higher ARDS-associated mortality compared to white women and women of other minority groups (7.4 per 100,000 individuals per year, compared to 5.4 and 4.7, respectively). Of particular interest is the fact that a high proportion of African American decedents with ARDS (27 %) were younger than 35 years of age. In contrast, the vast majority of white decedents with ARDS (91 %) were older than 75 years of age. It is unclear whether the higher ARDS-associated mortality rate in African Americans is due to a higher incidence of acute lung injury (ALI) among African Americans or a higher case fatality rate among those with ALI. For example, the excess mortality may have been due to a higher prevalence of comorbid conditions, and the authors were unable to adjust for such confounders in their analysis. Recent work from the ARDS Network found higher 60-day mortality rates among Hispanics (33 %) and blacks (33 %) compared to whites (29 %) [23]. However, after adjustment for gender, receipt of low-tidal volume ventilation, presence of comorbid conditions, cause and severity of ARDS, and severity of acute illness, the association between black race and mortality was no longer significant, but it persisted among Hispanics. The authors found that 30 % of the association between black race and mortality was accounted for in severity of illness. Hispanic ethnicity was not only associated with increased mortality, but also with fewer ventilator-free days. The associations between race/ethnicity and mortality and race/ethnicity and ventilator-free days were not affected by accounting for patient clustering within hospitals. This supports that there were no hospital-specific differences in quality of care as has been suggested in prior studies. An essential consideration that should be made when accounting for ARDS outcomes is that long-term survival in ARDS may not be related to the presence of ARDS, but to the age of the patient, the risk factor for ARDS development, and comorbidity [103].

Given the higher burden of ARDS and severity of illness among minorities and older persons, some have questioned whether such patients are adequately represented in clinical trials. One study compared the rates of enrollment in the ARDS Network studies at the University of California, San Francisco (UCSF) Moffitt-Long University Hospital, which is a large academic medical center, and San Francisco General Hospital, which is the regional safety net hospital [104]. Because both hospitals were part of the same study site, similar screening practices were utilized. A total of 7434 patients were screened and 902 (12 %) were enrolled. The most common reason for not being enrolled was not being medically eligible (45 % at Moffitt-Long compared to 37 % at San Francisco General). Among eligible patients, 89 % of patients at Moffitt-Long were enrolled compared to 29 % as San Francisco General ($p<0.001$). The biggest factor that influenced enrollment among eligible patients at San Francisco General was the lack of available surrogates (40 % of eligible patients compared to only 1 % at Moffitt-Long, $p<0.001$). Patient and family refusal was also higher at San Francisco General (6 % vs. 1 % at UCSF, $p<0.02$). This was particularly common among minority families.

In a larger study that examined enrollment across the ARDS Network studies, Cooke et al. found no differences in the likelihood of enrollment across all racial and ethnic groups [105]. Among excluded patients, minority patients were more likely to be excluded due to patient inability to consent or lack of a surrogate. African American patients were more likely to be excluded compared to white patients as a result of patient or family refusal. Patients over 75 years of age were less likely to be enrolled than younger patients, but older women were more likely to be enrolled than older men. Medical comorbidity had the largest effect on enrollment among older patients. Enrolled patients had lower PAO_2/FIO_2 ratios and were more often cared for in medical compared to surgical ICUs than nonenrolled patients.

Delirium

The reported incidence of delirium among critically ill patients ranges 16–89 % depending on the criteria used for assessment and the populations studied. An important risk factor for the development of delirium in the intensive care unit is receipt of mechanical ventilation [106, 107]. Patients who experience delirium upon admission are more likely to have prolonged hospitalizations. Mortality is higher among patients with delirium compared to patients without delirium (34 % vs. 15 %, HR: 3.2, $p=0.008$) [108]. The risk for delirium increases with increasing age with a prevalence of 14 % among those over age 85 [109]. Among older patients, dementia is a significant risk factor for the development of delirium [110]. Unfortunately, delirium is often missed by both intensivists and ICU nurses due to its overlap with dementia, its fluctuating nature, and infrequent use of validated screening instruments [111]. Little information is available regarding the effects of patient and hospital factors and delirium-related outcomes.

Stroke

Most disparities-related research in the field of neurocritical care has focused on patients with stroke. In 1999, the Centers for Disease Control and Prevention listed decline in deaths from coronary heart disease and stroke as one of the ten greatest public health achievements in the US [112]. However, while the mortality from stroke continues to decline, the mortality among different subgroups with stroke is widening suggesting worsening of health disparities. In 2010, non-Hispanic whites between the ages of 45 and 64 years had a mortality rate from stroke of 16.8 per 100,000 population compared to 18.5 per 100,000 in Hispanics and 46.2 per 100,000 among African Americans of the same age [113]. Hispanics may have a higher stroke incidence, but they have a similar stroke mortality compared to non-Hispanic whites. This may be due to the varied effects of stroke among Hispanic subgroups. For example, Mexicans may have a lower mortality from stroke compared to Puerto Ricans and Cubans [114]. Researchers suggest that observational studies with oversampling of Hispanic participants are needed to better understand these findings.

The mortality rate ratio for stroke has not improved significantly for African Americans compared to whites, and African Americans continue to have a 2–3 times greater prevalence. This widening of the mortality rate is generally attributed to whites having more timely access to intensive stroke-related critical care services compared to African Americans [115]. Another reason is the impact of conditions conferring an increased risk for stroke such as smoking and elevated blood pressure. Using data from the REGARDS study, Howard et al. found that a 10 mmHg increase in systolic blood pressure was associated with an 8 % (95%CI: 10–16 %) increase in stroke risk in whites, but a 24 % (95 % CI: 14–35 %) increase among African Americans [116]. In a Cox proportional hazard model adjusting for gender and use of hypertensive medications, African Americans between the ages of 45 and 64 with systolic blood pressures less than 120 mmHg had a similar risk of death compared to whites of the same age (HR: 0.9, 95 % CI: 0.5–1.6). However, with systolic blood pressure between 140 and 159 mmHg, African Americans had an increased risk of death compared with whites (HR: 2.4, 95 % CI: 1.2–4.7). In the Greater Cincinnati/Northern Kentucky Stroke Study (GCNKSS), African Americans were found to have twice as many small-vessel strokes and strokes of undetermined cause compared to whites [117]. African Americans also had 40 % more large-vessel strokes. The unequal distribution of different types of strokes by race suggests additional factors may be playing a role that have yet to be identified.

Socioeconomic status is also strongly associated with stroke outcomes. In the previously mentioned GCNKSS study, 39 % of the excess risk for stroke among African Americans compared to whites was due to poverty [118]. In the Netherlands, lower education levels were associated with higher disability rates within the 3 years following a stroke and a greater likelihood of requiring institutionalized care [119]. When education and income were combined into a proxy measure for socioeconomic status, low socioeconomic status was associated with increased stroke mortality in men ($p<0.001$) and accounted for 14–46 % of excess stroke risk in

African Americans ($p < 0.05$) [120]. Among women, the same relationship between socioeconomic status and mortality was not found.

Despite accounting for over 60 % of patients presenting with stroke, women have a 30 % lower odds of receiving rt-PA treatment compared to men [121]. This gender disparity exists in spite of ample data demonstrating the cost effectiveness of thrombolysis in acute stroke in both men and women [122, 123]. Part of the explanation may be gleaned from a study conducted in 12 hospitals in the Netherlands where women were more likely to present with stroke at an older age and after the allotted 4-h time window for administration [124]. Unfortunately, in the US, the rates of thrombolysis for acute stroke are extremely low for all patients and have been slow to improve (1.4 % in 2001 to 4.5 % in 2009) despite rt-PA being available for use since 1996 [125]. With such abysmal rates of utilization overall, differences by race or gender are difficult to detect.

Regional disparities have been well defined in regards to stroke outcomes. For over four decades, we have noted a significant difference in stroke outcomes of patients residing in the 11 state region extending from Louisiana to Virginia [126]. In fact, the average mortality is 20–25 % higher in this "Stroke Belt" compared to the rest of the nation [115]. The NIH-sponsored Reasons for Geographic and Racial Differences in Stroke (REGARDS) project is a population-based longitudinal cohort study examining the risk factors for stroke among 30,239 African American and white persons over age 45. Participants were recruited from 2003 through 2007 and followed through 2011. African Americans and inhabitants of the "Stroke Belt" were oversampled. A recent finding from that study demonstrated that only 20 % of African American and white stroke participants were evaluated in a Joint Commission-certified primary stroke center. While race and gender were not associated with clinical evaluation at a Joint Commission accredited primary stroke center, both rural residence (OR: 0.39; 95 % CI: 0.22–0.67) and a history of previous stroke (OR: 0.46; 95 % CI: 0.27–0.78) were [127]. A study by the Neurocritical Care Society found the greatest need for neurocritical care units was located in the South, where access is the poorest [128]. This region of the US may also have a higher incidence of cognitive decline suggesting the risk for additional adverse neurologic events may also be prevalent [129]. However, preliminary work has not demonstrated a relationship between residing in a health professional shortage area and use of less cardiovascular disease preventative medications [130].

Trauma

Disparities have been documented for critically ill patients following traumatic injury. Using the National Trauma Data Bank, which is the largest database of trauma inpatients in the United States comprising almost 700 trauma centers and hospitals, Haider et al. found that race and insurance status were associated with mortality [131]. African Americans and Hispanics with insurance had higher mortality rates compared to whites with insurance (OR: 1.2, 95 % CI: 1.1–1.2 and OR: 1.5, 95 % CI: 1.4–1.6). However, uninsured African Americans and Hispanics had even higher rates compared to whites with insurance (OR: 1.8, 95 % CI: 1.6–1.9 and OR: 2.3, 95 % CI: 2.1–2.5). In a subsequent reevaluation of the National Trauma Data Bank including adjustment for centers caring for a high proportion of minority patients (≥50 %), Haider et al. found that the association between race and mortality was significantly attenuated after accounting for the overall high mortality rates observed in hospitals carrying for predominantly minority trauma patients [132, 133]. As stated previously, consideration of factors confounding the relationship between race, ethnicity, and adverse outcomes must be included in disparities research to derive an accurate understanding of the underlying mechanisms at work.

Following trauma-related ICU stays, African American and Hispanic patients are less likely to be transferred to a rehabilitation service compared with non-Hispanic whites (OR 0.85; 95 % CI 0.8–0.9, $p<0.0001$) [134]. This may be explained by lack of health insurance [135].

In a review of adult trauma patients with a hospital length of stay >72 h in the National Trauma Data Bank, women experienced a 21 % lower adjusted odds of death compared to men [136]. Women were also less likely to experience many of the complications following trauma that men experienced including ARDS, pulmonary embolism, and acute kidney injury. Women did have an increased risk of respiratory tract infections compared to men.

Elderly trauma patients have a greater risk of complications and an increased risk of death compared to younger trauma patients. The mortality risk for trauma increases significantly after age 57 (OR: 5.6, $p=0.04$) compared to the youngest patients [137]. Given this increased risk, elderly patients derive a significant mortality benefit from admission to a trauma center (OR: 0.83, $p=0.04$). In fact, the number needed to transfer to prevent one death decreases as the patient's age increases. Despite this compelling evidence, many elderly patients continue to be improperly triaged to less than ideal settings rather than high-level trauma centers.

Pulmonary Embolism

Pulmonary embolism (PE) represents a significant cause of morbidity and mortality, contributing to at least 100,000 deaths in the United States each year. As the most common preventable cause of mortality during hospitalization, pulmonary embolism is known to be a risk factor for short- and long-term complications with an attributed mortality of 2–6 % in stable patients and up to 30 % in those presenting with hemodynamic instability or shock. In a very large sample (1.3 million) of surgical and nonsurgical patients from the Nationwide Inpatient Sample, the proportion of white patients diagnosed with pulmonary embolism decreased from 83 % in 1998 to 76 % in 2004 while the proportion of African American patients diagnosed with pulmonary embolism increased from 12 % in 1998 to 16 % in 2004. The overall case fatality rate from pulmonary embolism decreased from 12.3 % in 1998 to 8.2 % in 2005 [138]. However, the nationwide the case fatality rate stratified by race was not reported. Heit et al. found racial differences in presentation and risk factors for pulmonary emboli among 2397 patients enrolled from seven centers of the CDC

Thrombosis and Hemostasis Centers Research and Prevention Network between 2003 and 2009 [139]. African American were less likely to present with deep venous thromboses and pulmonary emboli compared to whites (20 % vs. 27 %, p = 0.006). African Americans were also less likely to present with isolated deep venous thromboses without pulmonary emboli compared to whites (52 % vs. 58 %, p = 0.02). However, African Americans were more likely than whites to present with pulmonary emboli without deep venous thromboses (28 % vs. 14 %; $p < 0.0001$). African Americans also had a lower prevalence of identifiable risk factors such as family history, diagnosed thrombophilia, oral contraceptive use, recent trauma, recent surgery, and infection. However, African Americans were more likely to be obese and to have hypertension, diabetes mellitus, HIV, sickle cell anemia, and end-stage renal disease. The authors posit that African Americans may have undiscovered heritable factors that may be conferring an increased risk for pulmonary emboli. Among patients admitted to Pennsylvania hospitals, African American patients had a higher 30-day mortality from pulmonary embolism compared to white patients after adjusting for risks for thromboembolic disease, pulmonary embolism prognosis, hospital bed size, insurance status, and treatment (OR: 1.3, 95 % CI: 1.1–1.6) [140]. It is unclear if the mortality differences were attributable to differences in treatment, pattern of thrombosis, or other unidentified factors.

Challenges to Exploring the Topic of Health Disparities in Critical Illness

Over a decade ago, Judith Kaplan and Trude Bennett challenged us to rethink how we use race and ethnicity in biomedical publications [20]. Yet, many of the concerns that they expressed remain unresolved today (Table 13.2). Race and ethnicity continue to be used as fixed, mutually exclusive categories, ignoring the fact that an increasing number of individuals identify with more than one racial/ethnic group and that racial and ethnic self-identification may change with time. Race and ethnicity also continue to be used as poor substitutes for the true factors that need to be identified including income, insurance status, location where healthcare was delivered, neighborhood of residence, and work trajectory. This not only leads to false declarations, but it prevents the field from moving forward as it implies that such factors and their associated outcomes are not modifiable.

It is time for the field of health disparities in critical illness to quickly leap forward from descriptive to intervention-oriented research. Moreover, future research needs to emphasize the specific mechanisms serving as the basis for health disparities development by including more detailed analyses incorporating patient, provider, and hospital-level factors. Journals can facilitate this change by creating consensus guidelines for the publication of health disparities research. A clearer understanding of the underlying factors at work may facilitate the design of novel interventions that can be rigorously evaluated to determine their effect on reducing health disparities. With the rapid changes to critical care looming on the horizon due to a surging demand for services, we cannot afford to continue to be spectators in this crisis.

References

1. Berthelsen PG, Cronqvist M. The first intensive care unit in the world: Copenhagen 1953. Acta Anaesthesiol Scand. 2003;47(10):1190–5.
2. Reisner-Sénélar L. The birth of intensive care medicine: Björn Ibsen's records. Intensive Care Med. 2011;37(7):1084–6. doi:10.1007/s00134-011-2235-z.
3. Ibsen B. The anaesthetist's viewpoint on the treatment of respiratory complications in poliomyelitis during the epidemic in Copenhagen, 1952. Proc R Soc Med. 1954;47(1):72–4.
4. Kahn JM, Goss CH, Heagerty PJ, Kramer AA, O'Brien CR, Rubenfeld GD. Hospital volume and the outcomes of mechanical ventilation. N Engl J Med. 2006;355(1):41–50. doi:10.1056/NEJMsa053993.
5. Treggiari MM, Martin DP, Yanez ND, Caldwell E, Hudson LD, Rubenfeld GD. Effect of intensive care unit organizational model and structure on outcomes in patients with acute lung injury. Am J Respir Crit Care Med. 2007;176(7):685–90. doi:10.1164/rccm.200701-165OC.
6. Cooke CR, Watkins TR, Kahn JM, et al. The effect of an intensive care unit staffing model on tidal volume in patients with acute lung injury. Crit Care. 2008;12(6):134. doi:10.1186/cc7105.
7. Angus DC, Kelley MA, Schmitz RJ, White A, Popovich J, Committee on Manpower for Pulmonary and Critical Care Societies (COMPACCS). Caring for the critically ill patient. Current and projected workforce requirements for care of the critically ill and patients with pulmonary disease: can we meet the requirements of an aging population? JAMA. 2000;284(21):2762–70.
8. Angus DC, Shorr AF, White A, et al. Critical care delivery in the United States: distribution of services and compliance with Leapfrog recommendations. Crit Care Med. 2006;34(4):1016–24. doi:10.1097/01.CCM.0000206105.05626.15.
9. 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. doi:10.1097/CCM.0b013e3181b090d0.
10. 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):1371–2. doi:10.1001/jama.2010.394.
11. Gabler NB, Ratcliffe SJ, Wagner J, et al. Mortality among patients admitted to strained intensive care units. Am J Respir Crit Care Med. 2013. doi:10.1164/rccm.201304-0622OC.
12. Wagner J, Gabler NB, Ratcliffe SJ, Brown SES, Strom BL, Halpern SD. Outcomes among patients discharged from busy intensive care units. Ann Intern Med. 2013;159(7):447–55. doi:10.7326/0003-4819-159-7-201310010-00004.
13. Lyon SM, Cooke CR, Iwashyna TJ, Ratcliffe SJ, Kahn JM. The effect of insurance status on mortality and procedural use in critically ill patients. Am J Respir Crit Care Med. 2011;184(7):809–15. doi:10.1164/rccm.201101-0089OC.
14. Epstein AM, Ayanian JZ. Racial disparities in medical care. N Engl J Med. 2001;344(19):1471–3.
15. Smedley BD, Stith AY, Nelson ARAR, Institute of Medicine (U.S.). Committee on Understanding and Eliminating Racial and Ethnic Disparities in Health Care. Unequal treatment: confronting racial and ethnic disparities in health care. Washington, DC: National Academy Press; 2003.
16. Foreman MG, Willsie SK. Health care disparities in critical illness. Clin Chest Med. 2006;27(3):473–86; vii. doi:10.1016/j.ccm.2006.04.007.
17. Soto GJ, Gong MN. Healthcare disparities in critical illness. Crit Care Med. 2013;41(12):2784–93. doi:10.1097/CCM.0b013e3182a84a43.
18. Cooke CR, Kahn JM. Deconstructing racial and ethnic disparities in critical care. Crit Care Med. 2010;38(3):978–80. doi:10.1097/CCM.0b013e3181cc15d3.
19. Osborne NG, Feit MD. The use of race in medical research. JAMA. 1992;267(2):275–9.
20. Kaplan JB, Bennett T. Use of race and ethnicity in biomedical publication. JAMA. 2003;289(20):2709–16. doi:10.1001/jama.289.20.2709.

21. Laws MB, Heckscher RA. Racial and ethnic identification practices in public health data systems in New England. Public Health Rep. 2002;117(1):50–61.
22. Barnato AE, Alexander SL, Linde-Zwirble WT, Angus DC. Racial variation in the incidence, care, and outcomes of severe sepsis: analysis of population, patient, and hospital characteristics. Am J Respir Crit Care Med. 2008;177(3):279–84. doi:10.1164/rccm.200703-480OC.
23. Erickson SE, Shlipak MG, Wheeler AP, et al. Racial and ethnic disparities in mortality from acute lung injury. Crit Care Med. 2009;37(1):1–6. doi:10.1097/CCM.0b013e31819292ea.
24. Mayr FB, Yende S, Linde-Zwirble WT, et al. Infection rate and acute organ dysfunction risk as explanations for racial differences in severe sepsis. JAMA. 2010;303(24):2495–503. doi:10.1001/jama.2010.851.
25. Esper AM, Moss M, Lewis CA, Nisbet R, Mannino DM, Martin GS. The role of infection and comorbidity: factors that influence disparities in sepsis. Crit Care Med. 2006;34(10):2576–82. doi:10.1097/01.CCM.0000239114.50519.0E.
26. Dombrovskiy VY, Martin AA, Sunderram J, Paz HL. Occurrence and outcomes of sepsis: influence of race. Crit Care Med. 2007;35(3):763–8. doi:10.1097/01.CCM.0000256726.80998.BF.
27. Turner D, Simpson P, Li S-H, Scanlon M, Quasney MW. Racial disparities in pediatric intensive care unit admissions. South Med J. 2011;104(9):640–6. doi:10.1097/SMJ.0b013e3182296e52.
28. Newacheck PW, Stein REK, Bauman L, Hung Y-Y, Research Consortium on Children With Chronic Conditions. Disparities in the prevalence of disability between black and white children. Arch Pediatr Adolesc Med. 2003;157(3):244–8.
29. Newacheck PW, Hung Y-Y, Wright KK. Racial and ethnic disparities in access to care for children with special health care needs. Ambul Pediatr. 2002;2(4):247–54.
30. Newacheck PW, Inkelas M, Kim SE. Health services use and health care expenditures for children with disabilities. Pediatrics. 2004;114(1):79–85. doi:10.1542/peds.114.1.79.
31. Williams JF, Zimmerman JE, Wagner DP, Hawkins M, Knaus WA. African-American and white patients admitted to the intensive care unit: is there a difference in therapy and outcome? Crit Care Med. 1995;23(4):626–36.
32. Rapoport J, Teres D, Steingrub J, Higgins T, McGee W, Lemeshow S. Patient characteristics and ICU organizational factors that influence frequency of pulmonary artery catheterization. JAMA. 2000;283(19):2559–67.
33. Derose KP, Baker DW. Limited English proficiency and Latinos' use of physician services. Med Care Res Rev. 2000;57(1):76–91.
34. Flores G. Language barriers to health care in the United States. N Engl J Med. 2006;355(3):229–31. doi:10.1056/NEJMp058316.
35. DuBard CA, Gizlice Z. Language spoken and differences in health status, access to care, and receipt of preventive services among US Hispanics. Am J Public Health. 2008;98(11):2021–8. doi:10.2105/AJPH.2007.119008.
36. Peterson PN, Shetterly SM, Clarke CL, et al. Health literacy and outcomes among patients with heart failure. JAMA. 2011;305(16):1695–701. doi:10.1001/jama.2011.512.
37. Pham K, Thornton JD, Engelberg RA, Jackson JC, Curtis JR. Alterations during medical interpretation of ICU family conferences that interfere with or enhance communication. Chest. 2008;134(1):109–16. doi:10.1378/chest.07-2852.
38. Thornton JD, Pham K, Engelberg RA, Jackson JC, Curtis JR. Families with limited English proficiency receive less information and support in interpreted intensive care unit family conferences. Crit Care Med. 2009;37(1):89–95. doi:10.1097/CCM.0b013e3181926430.
39. Baker DW, Hayes R, Fortier JP. Interpreter use and satisfaction with interpersonal aspects of care for Spanish-speaking patients. Med Care. 1998;36(10):1461–70.
40. Laws MB, Heckscher R, Mayo SJ, Li W, Wilson IB. A new method for evaluating the quality of medical interpretation. Med Care. 2004;42(1):71–80. doi:10.1097/01.mlr.0000102366.85182.47.
41. Mendu ML, Zager S, Moromizato T, McKane CK, Gibbons FK, Christopher KB. The association between primary language spoken and all-cause mortality in critically ill patients. J Crit Care. 2013;28(6):928–34. doi:10.1016/j.jcrc.2013.07.057.

42. Nguyen Y-L, Angus DC, Boumendil A, Guidet B. The challenge of admitting the very elderly to intensive care. Ann Intensive Care. 2011;1(1):29. doi:10.1186/2110-5820-1-29.
43. Milbrandt EB, Eldadah B, Nayfield S, Hadley E, Angus DC. Toward an integrated research agenda for critical illness in aging. Am J Respir Crit Care Med. 2010;182(8):995–1003. doi:10.1164/rccm.200904-0630CP.
44. Bagshaw SM, Webb SAR, Delaney A, et al. Very old patients admitted to intensive care in Australia and New Zealand: a multi-centre cohort analysis. Crit Care. 2009;13(2):R45. doi:10.1186/cc7768.
45. Fuchs L, Chronaki CE, Park S, et al. ICU admission characteristics and mortality rates among elderly and very elderly patients. Intensive Care Med. 2012;38(10):1654–61. doi:10.1007/s00134-012-2629-6.
46. Iwashyna TJ, Cooke CR, Wunsch H, Kahn JM. Population burden of long-term survivorship after severe sepsis in older Americans. J Am Geriatr Soc. 2012;60(6):1070–7. doi:10.1111/j.1532-5415.2012.03989.x.
47. Karlsson S, Ruokonen E, Varpula T, Ala-Kokko TI, Pettilä V, Finnsepsis Study Group. Long-term outcome and quality-adjusted life years after severe sepsis. Crit Care Med. 2009;37(4):1268–74. doi:10.1097/CCM.0b013e31819c13ac.
48. Winters BD, Eberlein M, Leung J, Needham DM, Pronovost PJ, Sevransky JE. Long-term mortality and quality of life in sepsis: a systematic review. Crit Care Med. 2010;38(5):1276–83. doi:10.1097/CCM.0b013e3181d8cc1d.
49. Iwashyna TJ, Ely EW, Smith DM, Langa KM. Long-term cognitive impairment and functional disability among survivors of severe sepsis. JAMA. 2010;304(16):1787–94. doi:10.1001/jama.2010.1553.
50. Garrouste-Orgeas M, Boumendil A, Pateron D, et al. Selection of intensive care unit admission criteria for patients aged 80 years and over and compliance of emergency and intensive care unit physicians with the selected criteria: an observational, multicenter, prospective study. Crit Care Med. 2009;37(11):2919–28.
51. Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. Crit Care Med. 2001;29(7):1303–10.
52. Martin GS, Mannino DM, Eaton S, Moss M. The epidemiology of sepsis in the United States from 1979 through 2000. N Engl J Med. 2003;348(16):1546–54. doi:10.1056/NEJMoa022139.
53. Wichmann MW, Inthorn D, Andress HJ, Schildberg FW. Incidence and mortality of severe sepsis in surgical intensive care patients: the influence of patient gender on disease process and outcome. Intensive Care Med. 2000;26(2):167–72.
54. Higgins TL, McGee WT, Steingrub JS, Rapoport J, Lemeshow S, Teres D. Early indicators of prolonged intensive care unit stay: impact of illness severity, physician staffing, and pre-intensive care unit length of stay. Crit Care Med. 2003;31(1):45–51. doi:10.1097/01.CCM.0000038743.29876.3C.
55. Valentin A, Jordan B, Lang T, Hiesmayr M, Metnitz PGH. Gender-related differences in intensive care: a multiple-center cohort study of therapeutic interventions and outcome in critically ill patients. Crit Care Med. 2003;31(7):1901–7. doi:10.1097/01.CCM.0000069347.78151.50.
56. Mahmood K, Eldeirawi K, Wahidi MM. Association of gender with outcomes in critically ill patients. Crit Care. 2012;16(3):R92. doi:10.1186/cc11355.
57. Fowler RA, Sabur N, Li P, et al. Sex-and age-based differences in the delivery and outcomes of critical care. CMAJ. 2007;177(12):1513–9. doi:10.1503/cmaj.071112.
58. Sørensen TI, Nielsen GG, Andersen PK, Teasdale TW. Genetic and environmental influences on premature death in adult adoptees. N Engl J Med. 1988;318(12):727–32. doi:10.1056/NEJM198803243181202.
59. Petersen L, Nielsen GG, Andersen PK, Sørensen TIA. Case-control study of genetic and environmental influences on premature death of adult adoptees. Genet Epidemiol. 2002;23(2):123–32. doi:10.1002/gepi.1122.
60. Picard C, Puel A, Bonnet M, et al. Pyogenic bacterial infections in humans with IRAK-4 deficiency. Science. 2003;299(5615):2076–9. doi:10.1126/science.1081902.

61. Wurfel MM. Genetic insights into sepsis: what have we learned and how will it help? Curr Pharm Des. 2008;14(19):1900–11.
62. Gao L, Grant A, Halder I, et al. Novel polymorphisms in the myosin light chain kinase gene confer risk for acute lung injury. Am J Respir Cell Mol Biol. 2006;34(4):487–95. doi:10.1165/rcmb.2005-0404OC.
63. Kangelaris KN. The association between a DarcGene polymorphism and clinical outcomes in African American patients with acute lung injury. Chest. 2012;141(5):1160. doi:10.1378/chest.11-1766.
64. Pritchard JK, Rosenberg NA. Use of unlinked genetic markers to detect population stratification in association studies. Am J Hum Genet. 1999;65(1):220–8. doi:10.1086/302449.
65. Landrine H, Corral I. Separate and unequal: residential segregation and black health disparities. Ethn Dis. 2009;19(2):179–84.
66. Jha AK, Orav EJ, Li Z, Epstein AM. Concentration and quality of hospitals that care for elderly black patients. Arch Intern Med. 2007;167(11):1177–82. doi:10.1001/archinte.167.11.1177.
67. Mayr FB, Yende S, D'Angelo G, et al. Do hospitals provide lower quality of care to black patients for pneumonia? Crit Care Med. 2010;38(3):759–65. doi:10.1097/CCM.0b013e3181c8fd58.
68. Skinner J, Chandra A, Staiger D, Lee J, McClellan M. Mortality after acute myocardial infarction in hospitals that disproportionately treat black patients. Circulation. 2005;112(17):2634–41. doi:10.1161/CIRCULATIONAHA.105.543231.
69. Merchant RM, Becker LB, Yang F, Groeneveld PW. Hospital racial composition: a neglected factor in cardiac arrest survival disparities. Am Heart J. 2011;161(4):705–11. doi:10.1016/j.ahj.2011.01.011.
70. Ehlenbach WJ, Barnato AE, Curtis JR, et al. Epidemiologic study of in-hospital cardiopulmonary resuscitation in the elderly. N Engl J Med. 2009;361(1):22–31. doi:10.1056/NEJMoa0810245.
71. Karaca Z, Wong HS. Racial disparity in duration of patient visits to the emergency department: teaching versus non-teaching hospitals. West J Emerg Med. 2013;14(5):529–41. doi:10.5811/westjem.2013.3.12671.
72. Barnato AE, Berhane Z, Weissfeld LA, et al. Racial variation in end-of-life intensive care use: a race or hospital effect? Health Serv Res. 2006;41(6):2219–37. doi:10.1111/j.1475-6773.2006.00598.x.
73. Ludwig J, Sanbonmatsu L, Gennetian L, et al. Neighborhoods, obesity, and diabetes—a randomized social experiment. N Engl J Med. 2011;365(16):1509–19. doi:10.1056/NEJMsa1103216.
74. Esper AM, Martin GS. The impact of comorbid [corrected] conditions on critical illness. Crit Care Med. 2011;39(12):2728–35. doi:10.1097/CCM.0b013e318236f27e.
75. Laditka JN, Laditka SB, Mastanduno MP. Hospital utilization for ambulatory care sensitive conditions: health outcome disparities associated with race and ethnicity. Soc Sci Med. 2003;57(8):1429–41. doi:10.1016/S0277-9536(02)00539-7.
76. O'Neil SS, Lake T, Merrill A, Wilson A, Mann DA, Bartnyska LM. Racial disparities in hospitalizations for ambulatory care-sensitive conditions. Am J Prev Med. 2010;38(4):381–8. doi:10.1016/j.amepre.2009.12.026.
77. Erickson SE, Vasilevskis EE, Kuzniewicz MW, et al. The effect of race and ethnicity on outcomes among patients in the intensive care unit: a comprehensive study involving socioeconomic status and resuscitation preferences. Crit Care Med. 2011;39(3):429–35. doi:10.1097/CCM.0b013e318206b3af.
78. Centers for Disease Control and Prevention (CDC). Mortality from congestive heart failure—United States, 1980-1990. MMWR Morb Mortal Wkly Rep. 1994;43(5):77–81.
79. Commission on Social Determinants of Health. Closing the gap in a generation. Geneva: World Health Organization; 2008. p. 1–256.
80. Andersen RM, Yu H, Wyn R, Davidson PL, Brown ER, Teleki S. Access to medical care for low-income persons: how do communities make a difference? Med Care Res Rev. 2002;59(4):384–411. doi:10.1177/107755802237808.

81. Baker DW, Shapiro MF, Schur CL. Health insurance and access to care for symptomatic conditions. Arch Intern Med. 2000;160(9):1269–74.
82. Fowler RA, Noyahr L-A, Thornton JD, et al. An official American Thoracic Society systematic review: the association between health insurance status and access, care delivery, and outcomes for patients who are critically ill. Am J Respir Crit Care Med. 2010;181(9):1003–11. doi:10.1164/rccm.200902-0281ST.
83. Lyon SM, Wunsch H, Asch DA, Carr BG, Kahn JM, Cooke CR. Use of intensive care services and associated hospital mortality after Massachusetts Healthcare Reform. Crit Care Med. 2014;42(4):763–70. doi:10.1097/CCM.0000000000000044.
84. Sommers BD, Baicker K, Epstein AM. Mortality and access to care among adults after state Medicaid expansions. N Engl J Med. 2012;367(11):1025–34. doi:10.1056/NEJMsa1202099.
85. Baicker K, Taubman SL, Allen HL, et al. The Oregon experiment—effects of Medicaid on clinical outcomes. N Engl J Med. 2013;368(18):1713–22. doi:10.1056/NEJMsa1212321.
86. Kivimäki M, Batty GD, Hamer M, et al. Using additional information on working hours to predict coronary heart disease: a cohort study. Ann Intern Med. 2011;154(7):457–63. doi:10.1059/0003-4819-154-7-201104050-00003.
87. Shippee TP, Rinaldo L, Ferraro KF. Mortality risk among Black and White working women: the role of perceived work trajectories. J Aging Health. 2012;24(1):141–67. doi:10.1177/0898264311422743.
88. Kaplan GA, Pamuk ER, Lynch JW, Cohen RD, Balfour JL. Inequality in income and mortality in the United States: analysis of mortality and potential pathways. BMJ. 1996;312(7037):999–1003. doi:10.1136/bmj.312.7037.999.
89. Lynch JW, Kaplan GA. Understanding how inequality in the distribution of income affects health. J Health Psychol. 1997;2(3):297–314. doi:10.1177/135910539700200303.
90. Wilkinson RG. Income distribution and life expectancy. BMJ. 1992;304(6820):165–8.
91. Bein T, Hackner K, Zou T, et al. Socioeconomic status, severity of disease and level of family members' care in adult surgical intensive care patients: the prospective ECSSTASI study. Intensive Care Med. 2012;38(4):612–9. doi:10.1007/s00134-012-2463-x.
92. Zager S, Mendu ML, Chang D, et al. Neighborhood poverty rate and mortality in patients receiving critical care in the academic medical center setting. Chest. 2011;139(6):1368–79. doi:10.1378/chest.10-2594.
93. Halpern NA. Critical care in the emergency department: it's critical to know what's going on! Crit Care Med. 2013;41(5):1367–8. doi:10.1097/CCM.0b013e318283d161.
94. Todd KH, Samaroo N, Hoffman JR. Ethnicity as a risk factor for inadequate emergency department analgesia. JAMA. 1993;269(12):1537–9.
95. Todd KH, Lee T, Hoffman JR. The effect of ethnicity on physician estimates of pain severity in patients with isolated extremity trauma. JAMA. 1994;271(12):925–8.
96. Studnek JR, Artho MR, Garner CL, Jones AE. The impact of emergency medical services on the ED care of severe sepsis. Am J Emerg Med. 2012;30(1):51–6. doi:10.1016/j.ajem.2010.09.015.
97. Chalfin DB, Trzeciak S, Dellinger RP. Impact of delayed transfer of critically ill patients from the emergency department to the intensive care unit. Crit Care Med. 2007;35(6):1477–83. doi:10.1097/01.CCM.0000266585.74905.5A.
98. Cardoso LTQ, Grion CMC, Matsuo T, et al. Impact of delayed admission to intensive care units on mortality of critically ill patients: a cohort study. Crit Care. 2011;15(1):R28. doi:10.1186/cc9975.
99. ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, et al. Acute respiratory distress syndrome: the Berlin Definition. JAMA. 2012;307:2526–33. doi:10.1001/jama.2012.5669.
100. Rubenfeld GD, Caldwell E, Peabody E, et al. Incidence and outcomes of acute lung injury. N Engl J Med. 2005;353(16):1685–93. doi:10.1056/NEJMoa050333.
101. Ely EW, Wheeler AP, Thompson BT, Ancukiewicz M, Steinberg KP, Bernard GR. Recovery rate and prognosis in older persons who develop acute lung injury and the acute respiratory distress syndrome. Ann Intern Med. 2002;136(1):25–36.
102. Moss M, Mannino DM. Race and gender differences in acute respiratory distress syndrome deaths in the United States: an analysis of multiple-cause mortality data (1979-1996). Crit Care Med. 2002;30(8):1679–85.

103. Davidson TA, Rubenfeld GD, Caldwell ES, Hudson LD, Steinberg KP. The effect of acute respiratory distress syndrome on long-term survival. Am J Respir Crit Care Med. 1999;160(6):1838–42. doi:10.1164/ajrccm.160.6.9903058.
104. Glassberg AE, Luce JM, Matthay MA, National Heart Lung and Blood Institute Clinical Trials Network. Reasons for nonenrollment in a clinical trial of acute lung injury. Chest. 2008;134(4):719–23. doi:10.1378/chest.08-0633.
105. Cooke CR, Erickson SE, Watkins TR, Matthay MA, Hudson LD, Rubenfeld GD. Age-, sex-, and race-based differences among patients enrolled versus not enrolled in acute lung injury clinical trials. Crit Care Med. 2010;38(6):1450–7. doi:10.1097/CCM.0b013e3181de451b.
106. Ely EW, Inouye SK, Bernard GR, et al. Delirium in mechanically ventilated patients: validity and reliability of the confusion assessment method for the intensive care unit (CAM-ICU). JAMA. 2001;286(21):2703–10.
107. Thomason JWW, Shintani A, Peterson JF, Pun BT, Jackson JC, Ely EW. Intensive care unit delirium is an independent predictor of longer hospital stay: a prospective analysis of 261 non-ventilated patients. Crit Care. 2005;9(4):R375–81. doi:10.1186/cc3729.
108. Ely EW, Shintani A, Truman B, et al. Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. JAMA. 2004;291(14):1753–62. doi:10.1001/jama.291.14.1753.
109. Inouye SK. Delirium in older persons. N Engl J Med. 2006;354(11):1157–65. doi:10.1056/NEJMra052321.
110. Pisani MA, Murphy TE, van Ness PH, Araujo KLB, Inouye SK. Characteristics associated with delirium in older patients in a medical intensive care unit. Arch Intern Med. 2007;167(15):1629–34. doi:10.1001/archinte.167.15.1629.
111. Spronk PE, Riekerk B, Hofhuis J, Rommes JH. Occurrence of delirium is severely underestimated in the ICU during daily care. Intensive Care Med. 2009;35(7):1276–80. doi:10.1007/s00134-009-1466-8.
112. Centers for Disease Control and Prevention (CDC). Ten great public health achievements—United States, 1900-1999. MMWR Morb Mortal Wkly Rep. 1999;48(12):241–3.
113. Centers for Disease Control and Prevention (CDC). Underlying cause of death, 1999-2011 request. Available at: http://wonder.cdc.gov/controller/datarequest/.
114. Gillum RF. Epidemiology of stroke in Hispanic Americans. Stroke. 1995;26(9):1707–12.
115. Howard G. Ancel keys lecture: adventures (and misadventures) in understanding (and reducing) disparities in stroke mortality. Stroke. 2013;44(11):3254–9. doi:10.1161/STROKEAHA.113.002113.
116. Howard G, Lackland DT, Kleindorfer DO, et al. Racial differences in the impact of elevated systolic blood pressure on stroke risk. JAMA Intern Med. 2013;173(1):46–51. doi:10.1001/2013.jamainternmed.857.
117. Schneider AT, Kissela B, Woo D, et al. Ischemic stroke subtypes: a population-based study of incidence rates among blacks and whites. Stroke. 2004;35(7):1552–6. doi:10.1161/01.STR.0000129335.28301.f5.
118. Kleindorfer DO, Lindsell C, Broderick J, et al. Impact of socioeconomic status on stroke incidence: a population-based study. Ann Neurol. 2006;60(4):480–4. doi:10.1002/ana.20974.
119. van den Bos GAM, Smits JPJM, Westert GP, van Straten A. Socioeconomic variations in the course of stroke: unequal health outcomes, equal care? J Epidemiol Community Health. 2002;56(12):943–8.
120. Howard G, Russell GB, Anderson R, et al. Role of social class in excess black stroke mortality. Stroke. 1995;26(10):1759–63.
121. Reeves M, Bhatt A, Jajou P, Brown M, Lisabeth L. Sex differences in the use of intravenous rt-PA thrombolysis treatment for acute ischemic stroke: a meta-analysis. Stroke. 2009;40(5):1743–9. doi:10.1161/STROKEAHA.108.543181.
122. Boudreau DM, Guzauskas G, Villa KF, Fagan SC, Veenstra DL. A model of cost-effectiveness of tissue plasminogen activator in patient subgroups 3 to 4.5 hours after onset of acute ischemic stroke. Ann Emerg Med. 2013;61(1):46–55. doi:10.1016/j.annemergmed.2012.04.020.

123. Penaloza-Ramos MC, Sheppard JP, Jowett S, et al. Cost-effectiveness of optimizing acute stroke care services for thrombolysis. Stroke. 2014;45:1–22. doi:10.1161/STROKEAHA.113.003216.
124. de Ridder I, Dirks M, Niessen L, Dippel D, PRACTISE Investigators. Unequal access to treatment with intravenous alteplase for women with acute ischemic stroke. Stroke. 2013;44(9):2610–2. doi:10.1161/STROKEAHA.113.002263.
125. Kleindorfer D, de los Rios La Rosa F, Khatri P, Kissela B, Mackey J, Adeoye O. Temporal trends in acute stroke management. Stroke. 2013;44(6 Suppl 1):S129–31. doi:10.1161/STROKEAHA.113.001457.
126. Borhani NO. Changes and geographic distribution of mortality from cerebrovascular disease. Am J Public Health Nations Health. 1965;55:673–81.
127. Mullen MT, Judd S, Howard VJ, et al. Disparities in evaluation at certified primary stroke centers: reasons for geographic and racial differences in stroke. Stroke. 2013;44(7):1930–5. doi:10.1161/STROKEAHA.111.000162.
128. Ward MJ, Shutter LA, Branas CC, Adeoye O, Albright KC, Carr BG. Geographic access to US Neurocritical Care Units registered with the Neurocritical Care Society. Neurocrit Care. 2012;16(2):232–40. doi:10.1007/s12028-011-9644-2.
129. Wadley VG, Unverzagt FW, McGuire LC, et al. Incident cognitive impairment is elevated in the stroke belt: the REGARDS Study. Ann Neurol. 2011;70(2):229–36. doi:10.1002/ana.22432.
130. Brown TM, Parmar G, Durant RW, et al. Health Professional Shortage Areas, insurance status, and cardiovascular disease prevention in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study. J Health Care Poor Underserved. 2011;22(4):1179–89. doi:10.1353/hpu.2011.0127.
131. Haider AH, Chang DC, Efron DT, Haut ER, Crandall M, Cornwell EE. Race and insurance status as risk factors for trauma mortality. Arch Surg. 2008;143(10):945–9. doi:10.1001/archsurg.143.10.945.
132. Haider AH, Ong'uti S, Efron DT, et al. Association between hospitals caring for a disproportionately high percentage of minority trauma patients and increased mortality: a nationwide analysis of 434 hospitals. Arch Surg. 2012;147(1):63–70. doi:10.1001/archsurg.2011.254.
133. Haider AH, Hashmi ZG, Zafar SN, et al. Minority trauma patients tend to cluster at trauma centers with worse-than-expected mortality: can this phenomenon help explain racial disparities in trauma outcomes? Ann Surg. 2013;258(4):572–9; discussion 579–81. doi:10.1097/SLA.0b013e3182a50148.
134. Shafi S, la Plata de CM, Diaz-Arrastia R, et al. Ethnic disparities exist in trauma care. J Trauma. 2007;63(5):1138–42. doi:10.1097/TA.0b013e3181568cd4.
135. Heffernan DS, Vera RM, Monaghan SF, et al. Impact of socioethnic factors on outcomes following traumatic brain injury. J Trauma. 2011;70(3):527–34. doi:10.1097/TA.0b013e31820d0ed7.
136. Haider AH, Crompton JG, Oyetunji T, et al. Females have fewer complications and lower mortality following trauma than similarly injured males: a risk adjusted analysis of adults in the National Trauma Data Bank. Surgery. 2009;146(2):308–15. doi:10.1016/j.surg.2009.05.006.
137. Goodmanson NW, Rosengart MR, Barnato AE, Sperry JL, Peitzman AB, Marshall GT. Defining geriatric trauma: when does age make a difference? Surgery. 2012;152(4):668–74; discussion 674–5. doi:10.1016/j.surg.2012.08.017.
138. Park B, Messina L, Dargon P, Huang W, Ciocca R, Anderson FA. Recent trends in clinical outcomes and resource utilization for pulmonary embolism in the United States: findings from the nationwide inpatient sample. Chest. 2009;136(4):983–90. doi:10.1378/chest.08-2258.
139. Heit JA, Beckman MG, Bockenstedt PL, et al. Comparison of characteristics from White- and Black-Americans with venous thromboembolism: a cross-sectional study. Am J Hematol. 2010;85(7):467–71. doi:10.1002/ajh.21735.
140. Ibrahim SA, Stone RA, Obrosky DS, Sartorius J, Fine MJ, Aujesky D. Racial differences in 30-day mortality for pulmonary embolism. Am J Public Health. 2006;96(12):2161–4. doi:10.2105/AJPH.2005.078618.