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Decreasing Case-Fatality But Not Death Following Admission to ICUs in Australia, 2005-2018

To the Editor:

Death is the most common outcome measure used in observational and interventional studies in critical care medicine.[1] Death, as an outcome measure, has the merits of being an objective, binary, and clinically relevant variable and may be expressed as a case-fatality (deaths per 100 cases, percentage) or as a mortality rate (deaths per 100,000 population). Although related by the numerator of each as number of deaths, the denominators differ with associated interpretive implications. Although conditions with high case-fatality (ie, rabies, >99%) have major implications for affected patients, they will be associated with low mortality rates when occurrence is rare. On the other hand, conditions with low overall case-fatality (ie, coronavirus disease 2019 [COVID-19], <5%) may be associated with devastating mortality rates in a pandemic setting.

Numerous studies conducted in ICUs have reported that the survival outcome associated with critical illness has improved over the past several decades.[2-7] Because few new therapeutic interventions or strategies have been demonstrated to reduce mortality rates effectively, these observations have been attributed partially to general improvements in quality of care.[8] When outcomes from critical illness and evaluating trends are reported over time, it is important to consider the differences between case-fatality and mortality rates in drawing conclusions. We therefore sought to examine the case-fatality and mortality rates associated with admission to ICUs in Australia between 2005 and 2018 to evaluate whether the outcome of critical illness may be changing.

Patients and Methods

A population-based cohort of all admissions to Australians among residents ≥20 years old registered in the Australian and New Zealand Intensive Care Society Adult Patient Database between 2005 and 2018 was assembled. The Australian and New Zealand Intensive Care Society Adult Patient Database is a well-established database that is estimated to include >90% of admissions to Australian ICUs and has been described in detail previously.[9] This study was approved with waiver of individual informed consent by The Alfred Hospital Human Research Ethics Committee (No. 693/19).

Basic demographics (age and sex), hospital admission and discharge dates, discharge vital status, and Australia and New Zealand risk of death (ANZROD) score were obtained for each admission.[10] Only a patient's first admission was included. Deaths at 30-days after the admission date were identified. Patients who were discharged from hospital alive prior to 30 days were classified as survivors. Case-fatality was calculated by the number of deaths at 30 days per 100 admissions and was reported as a percent. The number of admissions and 30-day deaths were used to calculate incidence and mortality rates per 100,000 population, respectively. These were further adjusted by directly standardizing annual rates by sex and age (in 5-year strata from ages 20 to 85 years and then ≥85 years) referenced to the Australian 2016 national population. Analysis was descriptive.

Results

During the 14-year study period, there were 1,545,395 first admissions to ICUs among Australian adult residents. Among these, 130,084 patients died within 30 days, which corresponds to a case-fatality of 8.42% and an adjusted mortality rate of 57.21 per 100,000 population. The median age of this cohort was 65.5 years (interquartile range, 51.7 to 75.7), 890,081 (57.61%; n = 1,544,972) were men; the median ANZROD score was 1.82% (ie, 1.82% risk for death; interquartile range, 0.57% to 7.35%).

The case-fatality associated with ICU admission decreased by more than one-third between 2005 (10.96%) and 2018 (6.88%) (Fig 1). The decreasing annual case-fatality was mirrored by an increase in the adjusted incidence of admissions (Fig 1). Although there was moderate year-to-year variability with a peak in 2005 (59.84 per 100,000) and nadir in 2013 (54.46 per 100,000), no evident consistent linear trend in the adjusted annual mortality rates occurred during the study years as shown in Figure 1.

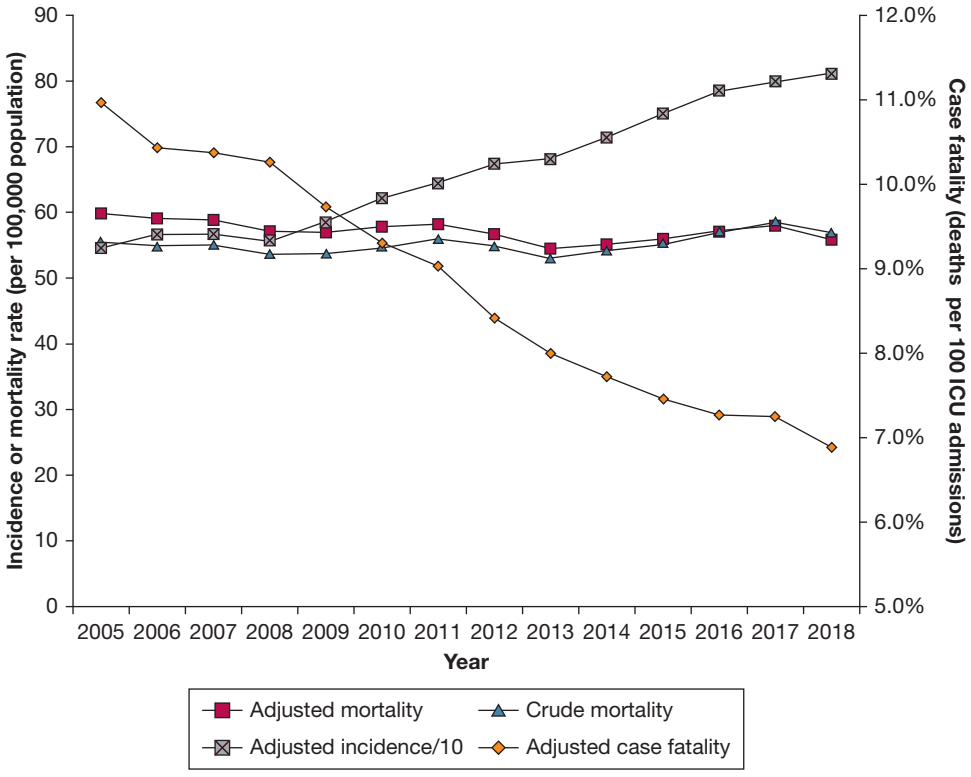

Figure 1 – *Annual case-fatality and mortality rate associated with admission to Australian ICUs, 2005-2018.*

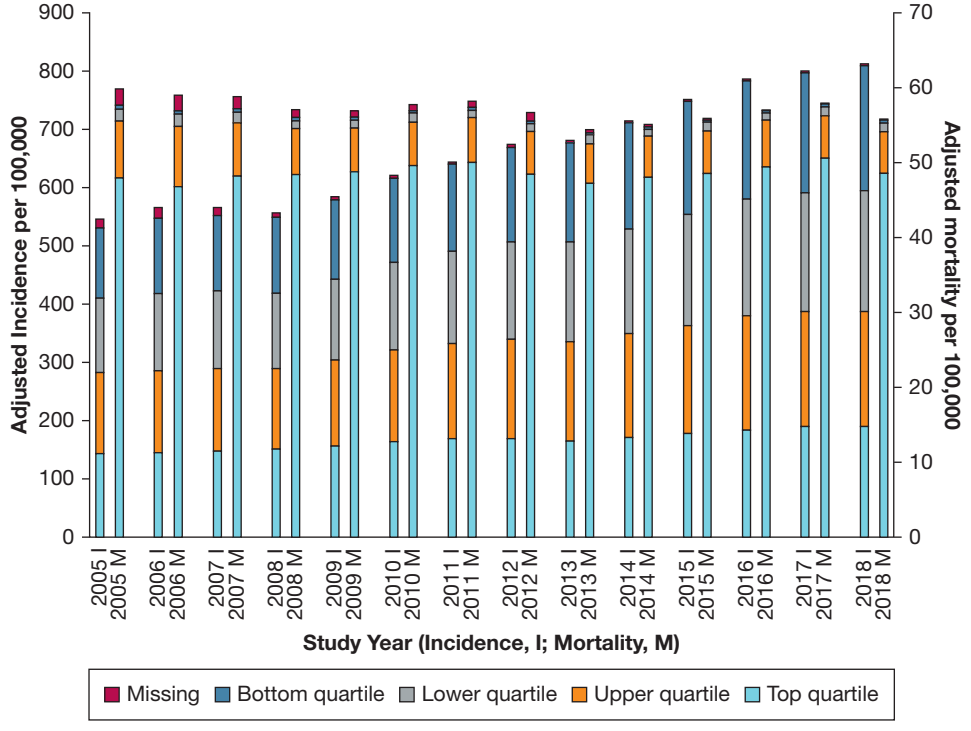

Figure 2 – *Age- and sex-adjusted admission incidence and mortality rate by quartiles of Australia and New Zealand Risk of Death scores, 2005-2018.*

TABLE 1] Influence of Testing or Admission Frequency on Case Fatality and Mortality Rate[a]

Variable	Example A[b]	Example B[c]	Example C[d]
Admissions or cases (baseline)	1,000 high risk	1,000 high risk plus 1,000 low risk	1,000 high risk plus 10,000 low risk
Case fatality	100/1,000 = 10%	100/1,000 plus 10/1,000; 110/2,000 = 5.5%	100/1,000 plus 100/10,000; 200/11,000 = 1.8%
Mortality rate	100/100,000	110/100,000	200/100,000
Admissions or cases (preventive intervention to reduce disease by 50%)	50% × 1,000 high risk = 500	50% × (1,000 high risk plus 1,000 low risk) = 1,000	50% × (1,000 high risk plus 10,000 low risk) = 5,500
Case fatality	50/500 = 10%	50/500 plus 5/500; 55/1,000 = 5.5%	50/500 plus 50/5,000; 100/5,500 = 1.8%
Mortality rate	50/100,000	55/100,000	100/100,000

[a]Hypothetical example with population of 100,000 residents; true risk for death 1% of low-risk and 10% for high-risk cases; at baseline and after implementation of a preventive intervention that reduced cases by 50%.
[b]Only high-risk cases admitted or tested.
[c]High-risk and some low-risk cases admitted or tested.
[d]High-risk and many low-risk cases admitted or tested.

Increasing adjusted incidence of admission during the study period occurred proportionally across quartiles of ANZROD scores (Fig 2). The adjusted annual mortality rates for the first (lowest), second, third, and fourth (highest) quartiles of ANZROD scores were 0.34, 1.24, 6.08, and 48.68 per 100,000, respectively, and these were similar throughout the study (Fig 2).

Discussion

In this study, we demonstrate that the case-fatality has decreased progressively but that the mortality rate associated with admissions to ICUs in Australia between 2005 and 2018 has not. This is an important observation, because readers of medical literature may not recognize or appreciate the important differences between case-fatality and mortality rate. However, this is becoming increasingly topical related to the current COVID-19 pandemic. Issues surrounding large variations in case-fatality between countries and in relation to population differences and testing rates have been presented in the medical literature and the lay press. It may be expected that, as compared to a region with a restrictive testing policy for high-risk patients, a region that has higher testing rates for COVID-19, especially inclusive of asymptomatic or younger healthy individuals who are low risk for death, will have a lower case-fatality but comparable mortality rate. An illustrative hypothetical example is shown in Table 1.

There is no preferred measure of death outcome; use of case-fatality or mortality rates remain dependent on the study objective. On one hand, case-fatality is generally a preferred measure for expressing the severity of an illness, is clinically relevant for patient care, and may be used as an outcome in clinical trials. On the other hand, mortality rate is superior for evaluating the burden of an illness and, unlike case-fatality, is responsive to preventative measures (Table 1).

In summary, this letter highlights the importance of differentiating case-fatality and mortality rate. These data suggest that, although there have been significant successes in critical care management in Australia with improved case-fatality, the death burden has not changed appreciably. Our data support the precise use of the terms case-fatality and death and argue for careful interpretation of studies that aim to define the burden of a disease or examine changes in outcome over time.

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