We Are Seeing More Sepsis .... But Are We Seeing the Whole Picture?

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(See the Major Article by Gohil et al on pages 695–703.)

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In determining how to most effectively allocate limited resources, it is imperative to accurately define the burden of a given disease. As the number of data sources available for epidemiologic analyses continues to increase, clearly elucidating the relative strengths and weaknesses of these potentially valuable resources is imperative. Evaluating emerging trends in the incidence of specific conditions is vital in most efficiently directing efforts to preventive or therapeutic initiatives. These efforts must, however, be based on the careful examination of the source data as well as the potential impact of external forces.

In this context, it is useful to consider the recent work focused on sepsis. Sepsis is the most costly condition in the United States, and costs continue to increase at a rate much higher than for overall hospital stays [1, 2]. Several studies have reported a recent rise in the incidence of sepsis [3, 4]. This work contributed to the development of large-scale campaigns, most notably the Surviving Sepsis Campaign, to improve the diagnosis and treatment of sepsis [5]. Although overall mortality related to sepsis has been increasing due to the general increased incidence of sepsis, the case-fatality rate has been decreasing over a similar period of time. This has been thought to be, in part, an effect of such campaigns. More work is needed to clearly define trends in sepsis incidence and outcomes to evaluate the effectiveness of such interventions.

In this light, the work by Gohil and colleagues in this issue of Clinical Infectious Diseases represents an important advance in the field [6]. The authors sought to assess the potential impact of Centers for Medicare and Medicaid Services (CMS) guidance regarding International Classification of Diseases, 9th Revision (ICD-9) coding and Medical Severity Diagnosis Related Group (MS-DRG) systems on trends in sepsis. The authors included all adult patients hospitalized in the state of California over a period of 10 years. This comprehensive cohort captured the entire at-risk population, allowing for comprehensive determination of incidence and outcomes. Segmented regression analyses of time-series data were employed to examine the temporal changes in sepsis incidence and mortality. The authors further strengthened their findings by using logistic regression analysis to identify factors independently associated with the diagnosis of sepsis as well as with mortality.

Gohil and colleagues found that the incidence of sepsis increased at a rate higher than would have been predicted by baseline trends and that these increases were temporally associated with both the introduction of CMS sepsis coding guidance and the MS-DRG reimbursement change. Sepsis-related mortality, meanwhile, decreased in a similar fashion. Policy changes were independently associated with both the increase in incidence of sepsis and the decrease in mortality from sepsis. The increase in sepsis incidence was primarily driven by increases in diagnosis of severe sepsis. Additionally, the mean comorbidity score increased over time. Given the high attributable mortality associated with severe sepsis (20%–50%) [7], one would expect mortality rates to increase in parallel. However, the opposite trend was noted. This suggests, as the authors conclude, the “upcapture” not only of sepsis diagnoses but also improved documentation of comorbidities and severity of illness. Sepsis incidence increased despite lack of change in overall admission rates, indicating that these findings are specific to the sepsis diagnosis and not an increase in hospitalizations overall.

This article represents a significant advance in elucidating the numerous drivers of sepsis incidence. Most important, the authors reveal the considerable effect of external policy changes on the identified incidence of sepsis, helping to better place recently observed trends in sepsis incidence in context. While acknowledging the demonstrated impact of policy changes, it is also important to note that the incidence of sepsis does appear to be rising, albeit likely at a slower rate than the current trends indicate. This increase in incidence has also been noted in other countries, such as the United Kingdom [8], Croatia [9], and Australia and New Zealand [10]. Several other factors may be at play in the observed increase in sepsis,
including enhanced identification of sepsis (particularly on admission), improved identification and documentation through electronic health records, and increases in the aged population. In fact, diagnosis of severe sepsis increased most dramatically among elderly individuals in this study.

The decrease in sepsis-related mortality over time has also been reported in other studies [4]. As discussed by the authors, this could be due to improvement in recognition and management of sepsis, but also may, in part, be the result of uptake of less severely ill patients after the policy changes. In addition, it is important to note that the primary outcome in this study was in-hospital mortality. However, as care is being increasingly continued outside of acute care hospitals (eg, long-term acute care) [2, 3], failure to account for outcomes occurring after discharge to these facilities could lead to an underestimation of true mortality rates.

Several methods have been used to identify cases of sepsis/severe sepsis. These methods, developed by Angus et al [11], Martin et al [12], Wang et al [13], and Dombrovskyi et al [14], use ICD-9 codes for infection paired with at least 1 diagnosis of end-organ dysfunction. However, the methods vary widely in terms of the number of diagnoses used for infection and inclusion of sepsis-specific codes, and incidence rates of sepsis have been found to vary depending on the method used [4]. Notably, the Dombrovsky method was used in this study and is considered to be more specific in defining sepsis. Given that the current study is examining changes related to coding, it would be interesting to see if the impact of these policy changes would differ using the other methods, such as the ones that use more infection codes.

This study was conducted using data from only adults. Given increased attention to sepsis in pediatrics, it would be valuable to see if these trends and effects of policy changes are also evident among children. Although California is a populous state with a diverse racial and ethnic population, the responses to policy trends may not be fully generalizable nationwide given potential differences in CMS education and guidance from state to state.

Finally, Gohil and colleagues confirmed the finding that nonwhite patients are more likely to have a diagnosis of sepsis. This has been reported in several prior studies [12, 15–17] and has been linked to increased infection rate as well as higher risk of organ dysfunction [16]. Some explanations for these disparities include differences in chronic disease burden (ie, higher incidence of chronic kidney disease and diabetes in nonwhites); differences in the immune response to infection, as genetic polymorphisms in proteins involved in the host response to infection have been found in patients of African descent [18]; and social and environmental factors, such as receiving care at hospitals that provide poorer quality of care [19]. The reasons behind these disparities need to be further elucidated in order to target efforts to improve outcomes in this higher-risk population of patients.

In summary, Gohil and colleagues have provided a timely and important examination of the impact of changes in CMS coding and guidance as well as a change in the reimbursement system on the incidence and outcomes related to sepsis. These results highlight the fact that characterization of the epidemiology of sepsis from administrative databases may be susceptible to coding and policy initiatives. The varying past approaches employed to define sepsis in administrative databases offer additional challenges in this line of research. Rigorous efforts such as those of Gohil and colleagues are urgently needed to better characterize the evolving epidemiology of sepsis. Only through these efforts can we most effectively target treatment and prevention initiatives appropriately and inform future policies on performance measures.

Note
Potential conflict of interest. Both authors: No reported conflicts. Both authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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