

2008

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## Recommended Citation

Zilberberg, Marya D.; Shorr, Andrew F.; and Kollef, Marin H., "Secular trends in candidemia-related hospitalization in the United States, 2000-2005." *Infection Control and Hospital Epidemiology*,. 978-980. (2008).

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Reviewed work(s):

Source: *Infection Control and Hospital Epidemiology*, Vol. 29, No. 10 (October 2008), pp. 978–980

Published by: [The University of Chicago Press](#) on behalf of [The Society for Healthcare Epidemiology of America](#)

Stable URL: <http://www.jstor.org/stable/10.1086/591033>

Accessed: 19/04/2012 17:10

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## CONCISE COMMUNICATION

## Secular Trends in Candidemia-Related Hospitalization in the United States, 2000–2005

Marya D. Zilberberg, MD; Andrew F. Shorr, MD, MPH; Marin H. Kollef, MD

In the United States, from January 1, 2000, through December 31, 2005, the incidence of candidemia-related hospitalization per 100,000 population rose by 52%, from 3.65 to 5.56 cases; and the incidence per 1,000 hospitalizations rose by 49%, from 0.28 to 0.42 cases. The proportion of all candidemia-related hospitalizations in which candidemia was the principal diagnosis remained stable at approximately 14%.

*Infect Control Hosp Epidemiol* 2008; 29:978–980

Hospitals in the United States are experiencing unprecedented growth in the incidence of infection due to antibiotic-resistant organisms, such as methicillin-resistant *Staphylococcus aureus* and *Clostridium difficile*. The common thread that ties many of these infections is the host's prior exposure to antibiotics. Another group of pathogens for which infection is associated with exposure to antibiotics is *Candida* species, common causes of nosocomial bloodstream infections that have high morbidity, mortality, and costs.<sup>1–3</sup> Although studies examining fungal bloodstream infection epidemiology in the 1980s noted a near quintupling of *Candida* bloodstream infection rates during that decade in the US hospitals,<sup>1</sup> up-to-date population data that make it possible to understand the full burden of candidemia in the United States are lacking. To fill this gap, we sought to quantify current population trends in the incidence of adult hospitalization with candidemia in the US hospitals.

### METHODS

We identified candidemia-related hospitalizations for 2000–2005 from the Nationwide Inpatient Sample data, available on the Healthcare Costs and Utilization Project Net Web site, administered by the Agency for Healthcare Research and Quality.<sup>4</sup> Candidemia was identified by the presence of the *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* diagnosis code 112.5 (disseminated candidiasis), and the numbers of discharges per year were age-stratified. To benchmark candidemia incidence against the general growth in hospitalizations over time, we obtained age-stratified numbers of total hospitalizations from Healthcare Costs and Utilization Project Net for each year and derived the candidemia-related hospitalization incidence as a function of total annual number of hospitalizations in the

United States. We also obtained census and intercensal data on the numbers and demographic characteristics of the US population between 2000 and 2005 from the US Census Bureau, and we calculated age-specific population hospitalization incidence rates. Finally, we examined time trends for candidemia as the principal diagnosis. The Nationwide Inpatient Sample definition of a principal diagnosis is “that condition established after study to be chiefly responsible for occasioning the admission of the patient to the hospital for care. The principal diagnosis is always the reason for admission.”<sup>4</sup>

### RESULTS

The number of adult discharges from US hospitals with a diagnosis of candidemia rose from 10,299 in 2000 to 16,500 in 2005, equating to a population incidence of 3.65 cases per 100,000 in 2000 to 5.56 cases per 100,000 in 2005 (Table). We noted approximately an order of magnitude difference in the candidemia-related hospitalization incidence between the youngest group (1.42 cases per 100,000 population among those aged 18–44 years) and the oldest group (17.29 cases per 100,000 population among those aged at least 85 years) in the year 2000, a relationship that persisted throughout the study period (Table). Each group experienced a similar rise in the incidence of candidemia-related hospitalizations from January 1, 2000, through December 31, 2005: an increase of 41% among people aged 18–44 years, 50% among those aged 45–64 years, 49% among those aged 65–84 years, and 45% among those aged at least 85 years.

An examination of the trends in the incidence of candidemia-related hospitalizations compared with the total annual number of hospitalizations in the United States yielded similar results, although, for the oldest group, the rise in hospitalization incidence was greater than the rise in the population incidence (51% increase vs 45% increase) (Table). In the analysis of candidemia as the principal diagnosis, the percentage of total candidemia-related hospitalizations in which candidemia was the principal diagnosis remained stable at approximately 14% during the study period (Figure). Although minor fluctuations in the proportion of total candidemia-related hospitalizations in which candidemia was the principal diagnosis were noted for the 3 younger groups, the fluctuations seen among the group aged at least 85 years were more pronounced, ranging from 28.9% in 2001 to 15.4% in 2004 (Figure).

### DISCUSSION

We have documented an approximately 50% increase in the incidence of hospitalization with candidemia in US hospitals

TABLE. Annual Population Incidence and Hospitalization Incidence of Candidemia-Related Hospitalization, by Age Group, United States, 2000–2005

Incidence measure, patient age group	2000	2001	2002	2003	2004	2005
No. of cases per 100,000 population						
18–44 years	1.42	1.53	1.80	2.20	2.26	2.01
45–64 years	4.53	5.06	5.97	6.16	6.66	6.81
65–84 years	12.52	14.16	15.51	16.84	16.49	18.64
≥85 years	17.29	17.32	19.46	21.48	21.86	25.01
No. of cases per 1,000 hospitalizations						
18–44 years	0.16	0.17	0.20	0.25	0.25	0.23
45–64 years	0.38	0.43	0.49	0.51	0.55	0.57
65–84 years	0.38	0.41	0.46	0.50	0.50	0.57
≥85 years	0.29	0.28	0.33	0.37	0.39	0.43

from January 1, 2000, through December 31, 2005. Consistently, the highest incidence was seen in the oldest group of patients and the lowest incidence in the youngest. Although the proportion of candidemia-related hospitalizations in which candidemia was the primary diagnosis remained stable overall, substantial fluctuations were noted for the oldest group of patients.

*Candida* species are recognized as important causes of bloodstream infections, particularly among critically ill and immunocompromised patients.<sup>1</sup> A recent systematic review documented that the attributable mortality for candidemia ranged from 5% to 71%,<sup>2</sup> and survivors of this disease incur substantial increases in the duration and the costs of hospitalization.<sup>3</sup> Furthermore, although in 1990 nearly 80% of isolates representing candidemia were *Candida albicans*, more

recently this percentage has decreased to less than 50%, raising the probability of resistance to azoles.<sup>5,6</sup> Because of these clinical and economic implications of bloodstream infection due to *Candida*, it is critical to understand its epidemiologic trends, and our data provide the needed generalizable information on the current state of the population incidence of hospitalization with infection due to this evolving pathogen.

Several prior investigations reported trends in candidemia-related hospitalizations over time both in the United States and abroad. For example, Martin et al.,<sup>7</sup> utilizing the ICD-9-CM codes 117.9 (disseminated fungal infection), 112.5 (disseminated candidiasis), and 112.81 (candidal endocarditis), documented a substantial rise in fungal sepsis incidence in the United States between 1979 and 2001. Because this study did not report specifically on candidemia, we are unable to

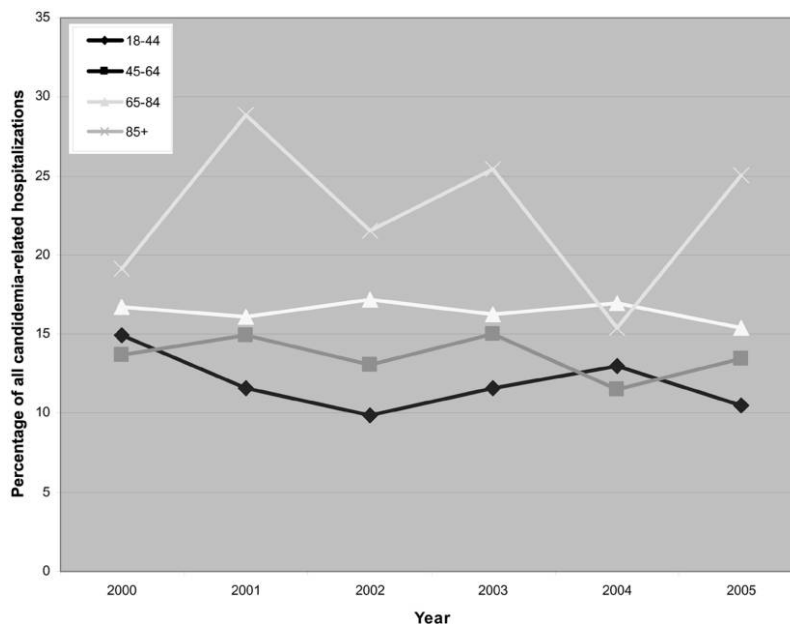


FIGURE. The proportion of all candidemia-related hospitalizations in which candidemia is the principal diagnosis, by age group (in years), 2000–2005.

make direct comparisons with our results with regard to the magnitude of change. Other studies from abroad have noted increases in the incidence of hospitalization with candidemia that were similar in magnitude to the increase in our study.<sup>8</sup>

Our analysis has multiple limitations. It relied on ICD-9-CM coding to identify candidemia-related hospitalizations, which may have predisposed our case ascertainment to misclassification. Although the accuracy of the coding for candidemia is unknown, giving credence to our numbers is the report by Zaoutis et al.,<sup>9</sup> who, in an approach similar to ours, noted candidemia incidence to be 30 cases per 100,000 adults hospitalized in the United States in 2000; in our analysis we found 28.3 cases per 100,000 hospitalizations in the same year. Additional support is provided by the relative stability over time of the proportion of all candidemia-related hospitalizations in which candidemia was the principal diagnosis. Nevertheless, the administrative nature of the data set is likely to have resulted in an underestimate of the full burden of candidemia.

The incidence of candidemia has risen by 50% in the time period between 2000 and 2005, and age-adjusted estimates confirm a rise among all adult age groups. Given the magnitude of attributable morbidity, mortality, and costs of this disease, the implications of this increase are likely not trivial. Our findings, in combination with reports of the increasing incidence of recovery of azole-resistant isolates from patients with candidemia, should compel a closer examination of this emerging disease and its impact on patient and systemwide outcomes.

#### ACKNOWLEDGMENTS

*Potential conflicts of interest.* All authors report no conflicts of interest relevant to this study.

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Received May 13, 2008; accepted June 9, 2008; electronically published August 20, 2008.

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