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Changes in Incidence and Antifungal Drug Resistance in Candidemia: Results From Population-Based Laboratory Surveillance in Atlanta and Baltimore, 2008–2011

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Abstract

Background—Candidemia is common and associated with high morbidity and mortality; changes in population-based incidence rates have not been reported.

Methods—We conducted active, population-based surveillance in metropolitan Atlanta, Georgia, and Baltimore City/County, Maryland (combined population 5.2 million), during 2008–2011. We calculated candidemia incidence and antifungal drug resistance compared with prior surveillance (Atlanta, 1992–1993; Baltimore, 1998–2000).

Results—We identified 2675 cases of candidemia with 2329 isolates during 3 years of surveillance. Mean annual crude incidence per 100 000 person-years was 13.3 in Atlanta and 26.2 in Baltimore. Rates were highest among adults aged ≥65 years (Atlanta, 59.1; Baltimore, 72.4) and infants (aged <1 year; Atlanta, 34.3; Baltimore, 46.2). In both locations compared with prior surveillance, adjusted incidence significantly declined for infants of both black and white race (Atlanta: black risk ratio [RR], 0.26 [95% confidence interval {CI}, .17–.38]; white RR: 0.19 [95% CI, .12–.29]; Baltimore: black RR, 0.38 [95% CI, .22–.64]; white RR: 0.51 [95% CI: .29–.90]). Prevalence of fluconazole resistance (7%) was unchanged compared with prior surveillance; 32 (1%) isolates were echinocandin-resistant, and 9 (8 *Candida glabrata*) were multidrug resistant to both fluconazole and an echinocandin.

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Conclusions—We describe marked shifts in candidemia epidemiology over the past 2 decades. Adults aged ≥65 years replaced infants as the highest incidence group; adjusted incidence has declined significantly in infants. Use of antifungal prophylaxis, improvements in infection control, or changes in catheter insertion practices may be contributing to these declines. Further surveillance for antifungal resistance and efforts to determine effective prevention strategies are needed.

Bloodstream infections (BSIs) caused by *Candida* species, also known as candidemia, are an important public health problem in the United States. *Candida* species are among the most common causes of BSIs and are associated with high morbidity and mortality, as well as increases in hospital cost and length of stay [1–5].

Although most reports that describe the epidemiology of candidemia are from individual institutions or among specific patient groups, few reports in the United States have described the epidemiology of candidemia at a population level. Population-based data are important for describing infections in whole populations and across the entire spectrum of healthcare settings, and can be used to determine group-specific incidence rates to monitor and compare rates of infection over time. Previous population-based surveillance performed by the Centers for Disease Control and Prevention (CDC) and partners in Atlanta, Georgia (1992–1993), and Baltimore, Maryland (1998–2000), described incidence rates of 8.7 per 100 000 population in Atlanta and 24 per 100 000 population in Baltimore [6, 7]. During both surveillance periods, drug resistance to fluconazole was low: 3% of isolates were resistant in 1992, and 3.7% were resistant in 1998 [6–8].

Over the past decade, *Candida* species with reduced fluconazole susceptibility, such as *Candida glabrata*, have become more prevalent in some patient populations [8–12]. The newest class of antifungal medications, the echinocandins, are considered first-line empiric therapy for candidemia, and there are reports of echinocandin-resistant invasive infection [13, 14].

To evaluate changes in the epidemiology and antifungal drug resistance of candidemia, we conducted population-based prospective surveillance in metropolitan Atlanta, Georgia, and Baltimore City and County, Maryland, 2 areas where prior surveillance had been conducted.

MATERIALS AND METHODS

Surveillance Population

Surveillance for candidemia was conducted among residents of Atlanta, Georgia (Fulton, DeKalb, Cobb, Gwinnett, Clayton, Douglas, Newton, and Rockdale counties; 25 hospitals, population: 3.8 million) and Baltimore City and County, Maryland (14 hospitals, population: 1.4 million). Each catchment area is the same as prior surveillance (Atlanta, 1992–1993 [6]; Baltimore, 1998–2000 [7]).

Case Definitions

We defined an incident case of candidemia as the first blood culture positive for a *Candida* species collected from a resident of the surveillance area. An episode of candidemia was

defined by the 30-day period following the day of collection of the incident blood culture. Blood cultures with *Candida* collected >30 days after the incident blood culture were defined as new incident cases.

Candidemia episodes were categorized as hospital-onset (HO), healthcare-associated community-onset (HACO), or community-onset (CO). Hospital-onset candidemia was defined as candidemia occurring in patients whose incident blood cultures were collected on or after the third day of hospital admission, where admission date is the first day. Candidemia episodes obtained before the third day of hospital admission were categorized as either HACO or CO: candidemia episodes in patients with recent healthcare exposure were categorized as HACO if the patient (1) was a resident of a nursing home at the time of culture collection; (2) had a central venous catheter in place 2 days before, the day before, or on the day of culture collection; (3) had documentation of at least 1 of the following in the 90 days prior to candidemia: hospitalization, surgery, or hemodialysis; (4) was transferred from another acute care hospital; or (5) was a neonate (aged ≤30 days) at the time of candidemia, Patients without any of these criteria were classified as CO.

Data Collection

Surveillance data were collected for 3 years at each location (1 March 2008–28 February 2011 in Atlanta; 1 June 2008–31 May 2011 in Baltimore). Basic demographic and clinical information was collected on all cases, and additional clinical information (referred to as “enhanced surveillance”) on antifungal treatment and severity of illness was collected for the first 2 years of surveillance in each location (1 March 2008–28 February 2010 in Atlanta; 1 June 2008–31 May 2010 in Baltimore). Surveillance personnel used standardized case report forms to abstract data from medical records. Laboratory records from all participating laboratories were audited monthly, ensuring complete capture of all cases.

Isolate Collection, Identification, and Antifungal Susceptibility Testing

All available isolates were sent to the CDC for species confirmation and antifungal drug susceptibility testing. Isolates were identified using a Luminex assay or DNA sequencing of the D1-D2 subunit of the 28S recombinant DNA [15]. CDC-confirmed species are reported; if no isolate was received at the CDC, local laboratory species identifications are reported.

Antifungal susceptibility testing was performed by broth microdilution with fluconazole, itraconazole, voriconazole, posaconazole, flucytosine, anidulafungin, caspofungin, and micafungin as described by Clinical and Laboratory Standards Institute (CLSI) M27-A3 guidelines [16] using frozen RPMI microbroth trays (TREK Diagnostics, Cleveland, Ohio). We used the recently approved, species-specific CLSI 24-hour resistance breakpoints for fluconazole, voriconazole, and echinocandins [16]. Isolates of *Candida krusei* were considered intrinsically resistant to fluconazole. Amphotericin B susceptibility was performed using Etest as per the manufacturer’s instructions (bioMérieux, Durham, North Carolina); minimum inhibitory concentration values were read at 24 hours. Where comparisons were made to previous surveillance data [6, 7] the new breakpoints were applied to the old data [16], and thus resistance reported here differs from resistance previously reported. The testing protocols do not differ.

Statistical Methods and Denominators

All incidence rates were calculated using 2009 population estimates for Baltimore [17] and Atlanta [18] and are presented per 100 000 person-years. We used original case and isolate data to calculate incidence rates in Atlanta (1992–1993) [6] and Baltimore (1998–2000) [7]. Owing to inconsistency between Atlanta denominators obtained from the 1990 US census and prior published data, our reported 1992–1993 Atlanta rates are slightly higher than previously reported [6].

We report crude rates to describe the burden in the current population, as well as adjusted rates to describe changes over time. For adjusted rates, the data were first aggregated by several factors: time period, age group, race, sex, and species. Negative binomial regression models were then fit to the data to examine the relationship between those factors and the candidemia incidence rates, and to evaluate the change in average annual incidence rates between the 2 time periods. To assess the goodness of fit of a proposed model, we compared observed and expected rates under the assumed model. We found evidence of effect modification by age and race, and thus report group-specific relative risks to summarize changes in incidence over time. Patients with missing race data (<4% of all patients) were removed from multivariate modeling analyses.

Categorical variables were analyzed using χ^2 tests or Fisher exact tests. We used the Kaplan-Meier method to describe survival 30 days after incident candidemia. In all analyses, the level of significance was set at $\alpha = .05$.All analyses were done using SAS software (version 9.3; SAS Institute, Cary, North Carolina).

Human Subjects

The CDC conducted ethical review of this surveillance project and deemed it a nonresearch activity; therefore, it was not subject to review by a CDC institutional review board. This activity was also evaluated individually at each location, and was either deemed a public health assessment or human subjects research and was approved by local review boards.

RESULTS

Demographic and Clinical Characteristics

We identified 2675 cases of candidemia in Atlanta and Baltimore during the 3-year surveillance period (Table 1). The median age of patients was 58 years (interquartile range [IQR], 45–71 years), and 51% were male; 217 patients (8%) had >1 episode of candidemia. The most common underlying conditions documented within the 3 months prior to candidemia were surgery (36%), diabetes (34%), and malignancy (21%). Most patients (n = 2265 [85%]) had a central venous catheter (CVC) in place within 2 days prior to incident candidemia, and of those, 1612 (71%) had all CVCs removed within 7 days of incident candidemia.

Most patients (n = 1775 [66%]) had infection occur during hospitalization (HO), or upon admission with documented exposures to healthcare (HACO; n = 787 [29%]); only 113 patients (4%) lacked recent documented healthcare exposure (CO, Table 1). Among the 787

HACO patients, 642 (82%) had documentation of a CVC within 2 days prior to or on the day of initial culture. CO patients were older than other patients (median age, 68 years vs 58 years in non-CO; $P < .001$), and more likely to have diabetes (39% vs 33% in non-CO; $P < .001$); *C. glabrata* was most frequently isolated in this group (n = 45 [40% of all species found in CO patients]), followed by Candida albicans (n = 36 [32%]) and *Candida parapsilosis* (n = 15 [13%]).

Enhanced Surveillance Results

During the 2 years of enhanced surveillance, we identified 1863 patients with candidemia. A total of 1143 patients (61%) were in an intensive care unit (ICU) within the 14 days before or after candidemia (Table 1). Among adult (aged ≥18 years) patients (n = 1749), 1333 (76%) met criteria for sepsis [19].

Antifungal medication data were available for 1807 patients (97% of 1863 patients) during the 2-year enhanced surveillance period, of whom 1616 (89%) received an antifungal following candidemia (Table 1); fluconazole (n = 1245 [77%]) or an echinocandin (n = 988 [61%]) was most commonly administered, and median treatment duration was 12 days (IQR, 6–17 days). For initial therapy, patients first received fluconazole (n = 938 patients [52%]) or micafungin (n = 371 [20%]). Most patients (n = 857 [53%]) received >1 antifungal. Among those who did not receive antifungal treatment (n = 191 [10%]), most (n = 109 [57%]) died or were discharged before the culture result was available to the clinician. A total of 278 patients (15%) had received an antifungal medication in the 14 days prior to candidemia; fluconazole was the most common choice (n = 177 [64%]), followed by an echinocandin (n = 41 [15%]).

Changes in Incidence Rates and Mortality

The average annual crude incidence rate per 100 000 person-years during 2008–2011 was 13.3 in Atlanta and 26.2 in Baltimore (Table 1). Rates were highest among persons aged ≥65 years (59.1 in Atlanta, 72.4 in Baltimore), persons <1 year of age (34.3 in Atlanta, 46.2 in Baltimore), and persons of black race (20.5 in Atlanta, 33.8 in Baltimore; Figure 1).

Although compared to prior surveillance periods overall crude incidence was 46% higher in Atlanta and 8% higher in Baltimore (Table 1), changes in rates varied by age group and race. Age- and race-specific strata illustrate variability in these differences between the 2 reporting sites (Figure 1). In both locations, rates significantly declined for all persons <20 years of age (Figure 2). Among persons aged ≥20 years, changes varied by location: In Atlanta, changes in incidence among persons aged ≥20 years were significant for all black persons aged ≥20 years and in all white persons aged ≥45, whereas in Baltimore, rates in persons aged ≥20 years changed little compared to prior surveillance, except for a slight increase in risk among white persons aged 45–64 years (Figure 2).

Thirty-day case fatality decreased significantly since 1998–2000 in Baltimore (28% in 2008–2011 vs 50% in 1998–2000, $P < 0.001$), but was similar between the 2 time periods for Atlanta (29% in 2008–2011 vs 35% in 1992–1993 $P = .09$).

Candida Species and Antifungal Susceptibility

Among 2675 total cases, the CDC received 2329 isolates from 2227 patients (83% of total cases); 99 patients (4%) had >1 isolate of different species available for testing, and 448 patients (17%) had no isolate. Incident isolates were available for 2136 (80%) patients. When species identifications from submitting laboratories were compared to CDC results, 107 isolates (5%) were discrepant (results not shown).

Species distributions and antifungal resistance testing results of the isolates received at the CDC are shown in Table 2. Among all isolates received at the CDC, *C. albicans* was the most common species (n = 877 [38%]), followed by *C. glabrata* (n = 670 [29%]), *C. parapsilosis* (n = 389 [17%]), and *Candida tropicalis* (n = 241 [10%]; Table 2).

Compared with prior surveillance, changes in species-specific incidence rates varied by location and age group (Table 3). In Atlanta, in persons aged ≥20 years, the risk for almost all *Candida* species increased compared with prior surveillance (Table 3); the increase was greatest in non–*C. albicans* species, particularly for *C. glabrata* and *C. parapsilosis* (increase in risk varied by age group; Table 3). In Baltimore, changes were less robust and limited to increases in *C. parapsilosis* in 2 of the 5 age groups (Table 3). In both locations, *C. albicans* decreased among all persons aged <20 years.

Overall, 165 isolates (7%) were resistant to fluconazole (Table 2). Thirty-one isolates (1%) were resistant to an echinocandin antifungal; the majority (n = 20 [65%]) were *C. glabrata*. Eight of the 9 isolates resistant to both an echinocandin and fluconazole were *C. glabrata*.

DISCUSSION

This report describes the largest prospective, population-based surveillance for candidemia in the United States and is the first to compare changes in the incidence of candidemia over time in large metropolitan areas. Importantly, we report substantial shifts in the epidemiology of candidemia among specific age groups. Infants, who previously had the highest incidence rates of all high risk groups, are now second to adult patients aged ≥65 years, and non–*C. albicans* species now comprise two-thirds of all *Candida* species isolated in blood.

Neonates and infants have historically been populations with some of the highest rates of candidemia [3, 6, 7, 20–23]. Although infants aged <1 year still have high rates, we observed a significant decline in incidence in this group compared to prior surveillance. This decline is consistent with other reports [21, 24]. We also observed a decline in incidence among infants aged <1 year in both locations during the 3 years of surveillance (results not shown). Prophylaxis with fluconazole in high-risk patients, such as neonates, has been shown to decrease risk of disease [21, 25–29]. However, it is unknown if the declines in neonatal candidemia have occurred only because of the increased use of azoles as prophylaxis in neonatal ICUs. Declines were also seen in other pediatric populations, and the possible contributions of improved infection control practices, such as hand hygiene and catheter care, deserve further study.

Persons aged ≥65 are now the highest-risk group for candidemia in both areas under surveillance. The shift in burden from neonates to adults is a major finding of this report. The reasons for the changing incidence are likely multifactorial; some contribution may be due to changes in the prevalence of risk factors in the adult population. Increases in common risk factors such as diabetes [30], ICU admissions [31, 32], or numbers of patients receiving immunosuppressive therapies [33] may have resulted in increases in the overall pool of patients at high risk for candidemia. Additionally, we report that CO patients were older and more likely to have diabetes than other patients. Thus, persons without recent healthcare exposures but with other chronic health conditions that are risk factors for candidemia may also be contributing to the increase in incidence in this age group.

Recent reports have documented significant and dramatic declines in some central line–associated BSIs (CLABSIs), such as those associated with *Staphylococcus aureus*, following adherence to established central line insertion practices; however, similar dramatic declines have been less evident for CLABSIs due to *Candida* species [20, 24, 34–36]. *Candida* species are commensals of the human gastrointestinal tract and can cause BSIs that are not the direct result of poor central line insertion practices, and instead may be more dependent on catheter maintenance after insertion [20, 22, 34] or may be unrelated to the central line. Therefore, interventions to reduce CLABSIs that focus solely on line insertion practices may be less effective in preventing candidemia. Further research is needed to define the proportion of candidemias that are central line related, and to identify catheter care strategies effective in preventing candidemia.

Over the past 20 years, the emergence of non–*C. albicans* species has been well documented [20, 37–42]. Our surveillance confirms these reports; non–*C. albicans* species now comprise two-thirds of all candidemias in Atlanta and in Baltimore City/County. We report little change among the overall proportion of isolates that were resistant to fluconazole; however, we also report an increase among some groups in the incidence of candidemia due to species with reduced fluconazole susceptibility, such as *C. glabrata*. As *C. glabrata* comprised more than half of the isolates resistant to 1 of the 2 drug classes (azoles and echinocandins), and 8 of the 9 isolates resistant to both classes, it is important to monitor this particular species for drug resistance. Additionally, echinocandin antifungals are a new class of drugs introduced in the past decade. Although the low overall level of resistance to echinocandins reported here is reassuring, especially among species like *C. parapsilosis*, it will also be important to monitor for the emergence of echinocandin resistance as this drug class is now first-line empiric therapy for candidemia.

This surveillance was subject to several limitations. Large medical centers in each metropolitan area contributed the most cases to the surveillance population, and the overall epidemiology in each area was influenced by the epidemiology in these centers. Thus, these data may not be nationally representative. However, they do represent one of the largest populations evaluated for changes in incidence of candidemia in the United States. The differences described in the epidemiology between the 2 locations surveyed emphasize the geographic and demographic variability of candidemia; surveillance in additional geographic areas will be important to further describe the epidemiology of this infection. We were unable to identify patients who received care outside the catchment area or from

healthcare facilities that sent blood cultures to labs outside of the catchment area, and were unable to collect isolates from one major federal institution. For these reasons, we may have underestimated the burden of disease in these areas.

This report demonstrates that the overall incidence of candidemia and the burden in adult populations has not declined in the past 20 years, and emphasizes the significant morbidity and mortality that candidemia contributes to the healthcare system. The changing face of healthcare is likely leading to growing populations of persons at risk for the development of candidemia. Our ability to prevent significant morbidity and mortality from candidemia remains a challenge. Although antifungal prophylaxis has been shown to be effective in selected patient populations, there is still debate on the application of risk prediction tools [43] and other preventive strategies. There is a continued need for surveillance of candidemia to develop and evaluate prevention strategies and to monitor for changes in incidence and resistance.

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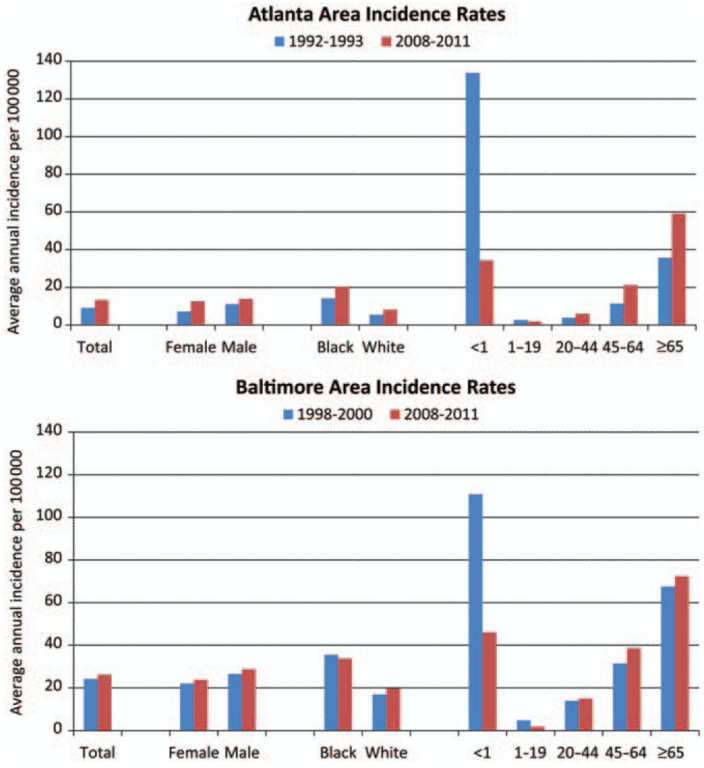

Figure 1.

A comparison of crude average annual incidence rates per 100 000 persons in Atlanta (1992–1993 vs 2008–2011) and Baltimore (1998–2000 vs 2008–2011), overall, and by sex, race, and age group.

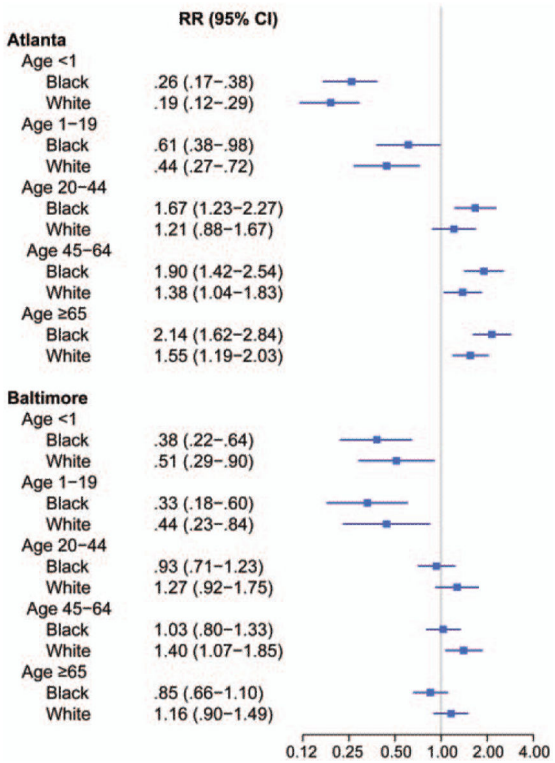

Figure 2.

A comparison of adjusted incidence rate ratios, by age group and race, comparing rates in the previous time period (1992–1993 in Atlanta, 1998–2000 in Baltimore) to rates in the current time period (2008–2011). 95% confidence interval. The line represents a relative risk of 1. Rates to the right of the line are an increase in risk compared to prior surveillance; rates to the left of the line are a decrease in risk compared to prior surveillance. Abbreviations: CI, confidence interval; RR, relative risk.

Table 1

Selected Demographic and Clinical Characteristics of Persons With Candidemia in Atlanta and Baltimore (Comparison of Prior Surveillance With Current Surveillance Data)

	No. (%) of Patients			
	Atlanta		Baltimore	
Characteristic	**1992–1993 (n = 428)**	**2008–2011 (n = 1554)**	**1998–2000 (n = 680)**	**2008–2011 (n = 1121)**
Crude incidence rate (per 100 000 person-years)	9.1	13.3	24.2	26.2
Sex[a]				
Female	173 (40)	748 (48)	328 (48)	540 (48)
Male	253 (59)	806 (52)	352 (52)	579 (52)
Race[a]				
White	175 (41)	525 (34)	260 (38)	447 (40)
Black	193 (45)	929 (60)	406 (60)	623 (56)
Median age, years (IQR)	46 (6–69)	58 (44–70)	57 (40–73)	58 (45–72)
Age (years)[a]				
<1	85 (20)	61 (4)	39 (6)	27 (2)
1–19	35 (8)	62 (4)	34 (5)	18 (2)
20–44	85 (20)	271 (17)	143 (21)	230 (21)
45–64	92 (21)	598 (38)	198 (29)	428 (38)
≥65	129 (30)	562 (36)	265 (39)	411 (37)
Underlying or prior conditions				
Surgery in the 3 months prior[b]	80 (19)	588 (38)	319 (47)	366 (33)
Abdominal surgery	54 (13)	367 (24)	178 (26)	222(20)
Nonabdominal surgery	26 (6)	312 (20)	NA	201 (18)
Diabetes	55 (13)	508 (33)	193 (28)	392 (35)
Malignancies	113 (26)	339 (22)	145 (51)	212 (19)
Renal conditions	NA	250 (16)	202 (30)	203 (18)
Liver diseases	9 (2)	126 (8)	108 (16)	199 (18)
HIV or AIDS	29 (7)	55 (4)	72 (11)	95 (8)

Characteristic	No. (%) of Patients			
	Atlanta		Baltimore	
	1992–1993 (n = 428)	2008–2011 (n = 1554)	1998–2000 (n = 680)	2008–2011 (n = 1121)
Central venous catheter usage				
CVC at time of candidemia	NA	1342 (86)	520 (76)	923 (82)
CVC was removed within 7 days of candidemia	NA	907 (68)	435 (64)[c]	705 (76)
Onset of candidemia				
Candidemia ≤2 days after admission or no admission	110 (28)[d]	443 (29)	229 (34)	461 (41)
Acquisition of candidemia				
Hospital onset	NA	1114 (72)	NA	661 (59)
Health care-associated community-onset	NA	386 (25)	NA	401 (36)
Community-onset	NA	54 (3)	NA	59 (5)
Severity of illness				
Crude 30-day all-cause mortality[e]	35%	29%	50%	28%
Had >1 episode of candidemia	18 (4)	99 (6)	33 (3)	118 (11)
SIRS at time of candidemia (age ≥18 years only)[f]	NA	798 (81)	NA	535 (70)
In ICU within 14 days before or after candidemia[f]	NA	756 (49)	NA	494 (44)
In ICU at time of candidemia[f]	NA	508 (33)	218 (32)	333 (30)
Treatment[f]				
Treatment information available	NA	1052 (98)	NA	755 (95)
Received antifungals in the 14 days prior to candidemia	NA	195 (18)	NA	83 (10)
Received antifungals after candidemia	NA	956 (90)	NA	660 (83)
Species[g]				
C. albicans	223 (52)	629 (40)	289 (43)	369 (33)
Non-*C. albicans*	205 (48)	925 (60)	391 (58)	752 (67)
C. glabrata	51 (12)	403 (26)	188 (28)	325 (29)
C. tropicalis	43 (10)	129 (8)	14 (98)	131 (12)
C. parapsilosis	90 (21)	262 (17)	72 (11)	172 (15)

Data are number (%) of all cases unless otherwise indicated.

Abbreviations: CVC, central venous catheter; HIV, human immunodeficiency virus; ICU, intensive care unit; IQR, interquartile range; NA, not applicable as question was not asked in surveillance time period; SIRS, systemic inflammatory response syndrome.

[a] Some variables could not be collected for every case.

[b] Patients could have >1 type of surgery.

[c] Question in 1998–2000 was: "Was CVC removed or changed after diagnosis of candidemia?"

[d] A total of 386 patients had admission information available in 2008–2010.

[e] Crude 30-day all-cause mortality calculated using Kaplan-Meier method.

[f] Data collected in 2 years of enhanced surveillance.

[g] Species are reported per patient. In cases where no isolate was available to be sent to the Centers for Disease Control and Prevention, local lab identification is used.

Table 2

Candida Species Distribution and Antifungal Resistance to Fluconazole and Echinocandins of Total Isolates Received at the Centers for Disease Control and Prevention, 2008–2011, Compared With Prior Surveillance in Atlanta and Baltimore

	Atlanta Area				Baltimore Area			
		2008–2011				2008–2011		
Species	1992–1993 Fluconazole Resistant, No. (%)	Fluconazole Resistant, No. (%)	Echinocandin Resistant, No. (%)	Total Isolates, No. (%)	1998–2000 Fluconazole Resistant, No. (%)	Fluconazole Resistant, No. (%)	Echinocandin Resistant, No. (%)	Total Isolates, No. (%)
C. albicans	1 (1)	11 (2)	5 (1)	489 (41)	8 (3)	9 (2)	1 (0)	388 (34)
Non–*C. albicans*	15 (12)	83 (12)	10 (1)	709 (59)	32 (10)	62 (9)	15 (2)	743 (66)
C. glabrata	7 (20)	42 (13)	10 (3)	318 (27)	12 (8)	38 (11)	10 (3)	352 (31)
C. tropicalis	1 (3)	9 (9)	0 (0)	103 (9)	7 (9)	6 (4)	3 (2)	138 (12)
C. parapsilosis	1 (2)	12 (6)	0 (0)	212 (18)	0 (0)	4 (2)	1 (1)	177 (16)
C. krusei	0 (0)	19 (100)	0 (0)	19 (2)	0 (0)	13 (100)	0 (0)	13 (1)
C. dubliniensis	0 (0)	1 (20)	0 (0)	5 (<1)	0 (0)	1 (3)	1 (3)	31 (3)
C. lusitaniae	0 (0)	0 (0)	0 (0)	22 (2)	0 (0)	0 (0)	0 (0)	12 (1)
Other species	0 (0)	0 (0)	0 (0)	30 (3)	0 (0)	0 (0)	0 (0)	20 (2)
All species	16 (7)	94 (8)	15 (1)	1198 (100)	40 (7)	71 (6)	16 (1)	1131 (100)

Data are No. (%) of all isolates by Candida species resistant to either fluconazole or an echinocandin antifungal drug, and overall No. (%) of all isolates, by location and time period.

Table 3

Changes in *Candida* Species, by Age Group: Comparison of Rates in the Previous Time Period (1992–1993 in Atlanta, 1998–2000 in Baltimore) With Rates in the Current Time Period (2008–2011)

	Atlanta			Baltimore		
	Incidence Density[a]			Incidence Density[a]		
Species by Age Group	1992–1993	2008–2011	Relative Risk (95% CI)	1998–2000	2008–2011	Relative Risk (95% CI)
<1 year						
C. albicans	66.82	17.44	0.26 (.16–.42)*	70.70	19.86	0.28 (.14–.58)*
C. glabrata	0.00	3.61	…	12.29	7.22	0.59 (.15–2.35)
C. parapsilosis	39.11	7.22	0.18 (.09–.37)*	27.66	12.64	0.46 (.17–1.23)
Other *Candida* spp	6.52	3.01	0.46 (.12–1.72)	6.15	5.42	0.88 (.15–5.27)
1–19 years						
C. albicans	1.06	0.59	0.23 (.11–.47)*	2.19	0.51	0.23 (.08–.64)*
C. glabrata	0.25	0.61	2.49 (.62–9.96)	0.44	0.20	0.46 (.08–2.78)
C. parapsilosis	1.14	0.43	0.37 (.18–.80)*	0.29	0.41	1.39 (.26–7.62)
Other *Candida* spp	0.25	0.40	1.61 (.46–5.72)	2.04	0.61	0.30 (.11–.78)*
20–44 years						
C. albicans	1.85	2.56	1.38 (.96–1.99)	6.31	4.98	0.79 (.56–1.11)
C. glabrata	0.38	3.80	10.01 (4.77–21.01)*	4.24	3.25	0.77 (.50–1.16)
C. parapsilosis	0.47	1.13	2.37 (1.20–4.69)*	1.03	2.63	2.54 (1.27–5.10)*
Other *Candida* spp	0.85	1.10	1.29 (.75–2.22)	3.00	4.22	1.41 (.90–2.19)
45–64 years						
C. albicans	6.28	8.49	1.35 (.99–1.83)	12.89	11.80	0.92 (.69–1.21)
C. glabrata	1.38	15.06	10.89 (5.91–20.06)*	9.09	12.27	1.35 (.99–1.85)
C. parapsilosis	1.26	3.44	2.74 (1.42–5.26)*	5.19	5.11	1.35 (.83–2.19)
Other *Candida* spp	1.88	3.25	1.73 (1.00–2.98)*	6.28	9.57	1.52 (1.05–2.21)*
≥65 years						
C. albicans	14.81	22.58	1.52 (1.13–2.06)*	30.13	24.27	0.81 (.63–1.03)
C. glabrata	4.47	28.61	6.40 (3.83–10.70)*	20.52	23.18	1.13 (.85–1.50)

	Atlanta			Baltimore		
	Incidence Density[a]			Incidence Density[a]		
Species by Age Group	1992–1993	2008–2011	Relative Risk (95% CI)	1998–2000	2008–2011	Relative Risk (95% CI)
C. parapsilosis	3.63	8.81	2.42 (1.35–4.36)*	5.19	9.96	1.92 (1.15–3.20)*
Other *Candida* spp	6.43	10.02	1.56 (.99–2.46)	11.43	12.68	1.11 (.76–1.62)

Abbreviation: CI, confidence interval.

*Significant at $P < .05$.

[a]Per 100 000 person-years.