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Molecular and Epidemiological Investigation of Fluconazole-resistant *Candida parapsilosis*—Georgia, United States, 2021

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Background. Reports of fluconazole-resistant *Candida parapsilosis* bloodstream infections are increasing. We describe a cluster of fluconazole-resistant *C parapsilosis* bloodstream infections identified in 2021 on routine surveillance by the Georgia Emerging Infections Program in conjunction with the Centers for Disease Control and Prevention.

Methods. Whole-genome sequencing was used to analyze *C parapsilosis* bloodstream infections isolates. Epidemiological data were obtained from medical records. A social network analysis was conducted using Georgia Hospital Discharge Data.

Results. Twenty fluconazole-resistant isolates were identified in 2021, representing the largest proportion (34%) of fluconazole-resistant *C parapsilosis* bloodstream infections identified in Georgia since surveillance began in 2008. All resistant isolates were closely genetically related and contained the Y132F mutation in the *ERG11* gene. Patients with fluconazole-resistant isolates were more likely to have resided at long-term acute care hospitals compared with patients with susceptible isolates ($P = .01$). There was a trend toward increased mechanical ventilation and prior azole use in patients with fluconazole-resistant isolates. Social network analysis revealed that patients with fluconazole-resistant isolates interfaced with a distinct set of healthcare facilities centered around 2 long-term acute care hospitals compared with patients with susceptible isolates.

Conclusions. Whole-genome sequencing results showing that fluconazole-resistant *C parapsilosis* isolates from Georgia surveillance demonstrated low genetic diversity compared with susceptible isolates and their association with a facility network centered around 2 long-term acute care hospitals suggests clonal spread of fluconazole-resistant *C parapsilosis*. Further studies are needed to better understand the sudden emergence and transmission of fluconazole-resistant *C parapsilosis*.

Keywords. azole-resistant; *Candida parapsilosis*; *ERG11* mutations; fungal outbreak; whole genome sequencing.

Candida parapsilosis is a frequent cause of *Candida* bloodstream infections (BSIs), also referred to as candidemia, in the United States and globally [1–3]. Compared with other *Candida* species, *C parapsilosis* is more readily transmitted within the healthcare environment because of its ability to form biofilms, adhere to healthcare workers' hands and medical equipment, and remain viable on surfaces up to 28 days [4–8]. Nosocomial outbreaks resulting from *C parapsilosis* have been well described and may be increasing in frequency, likely because of changes in infection prevention practices and healthcare delivery in the wake of the COVID-19 pandemic [9–16].

Antimicrobial resistance is a growing concern especially in non-albicans *Candida* species. Because there are limited classes of antifungal medications available to treat candidemia, treatment options for highly resistant cases are sparse. Studies examining the frequency of fluconazole resistance in *C parapsilosis* isolates have reported rates between 5% and 20% and as high as 90% in outbreak settings [11, 17–20].

The predominant mechanism for fluconazole resistance in *C parapsilosis* is a Y132F mutation in the *ERG11* gene, which an estimated 30% to 60% of fluconazole-resistant *C parapsilosis* isolates carry [21]. This mutation was first reported in 2015 in isolates from Atlanta, Georgia [22]. Since then, outbreaks associated with fluconazole-resistant *C parapsilosis* (FR-CP) harboring the Y132F mutation have been increasingly reported worldwide [2, 12, 23–25]. Previous investigations of *C parapsilosis* outbreaks employed multilocus sequence typing or microsatellite analysis to assess genetic relatedness [14]. Because *C parapsilosis* is among

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the most genetically homogeneous *Candida* species [3], highly resolutive techniques such as whole-genome sequencing (WGS) may better differentiate outbreak from nonoutbreak cases.

The Emerging Infections Program's (EIP) nationwide candidemia surveillance system identified an increase in FR-CP blood isolates collected in Georgia, United States, in 2021. We used WGS to assess the genetic relatedness between isolates and investigated epidemiological characteristics and patient movement between healthcare facilities to understand potential links to transmission.

METHODS

Data Collection and Definitions

EIP conducts active laboratory- and population-based surveillance for candidemia at 10 sites across the United States through a collaboration between the US Centers for Disease Control and Prevention, state health departments, and academic partners (https://www.cdc.gov/ncezid/dpei/eip/eip-about.html). This analysis included all incident *C parapsilosis* BSIs identified by Georgia EIP between January and December 2021 occurring in residents of the 8-county Atlanta catchment area, representing 39% of Georgia's population. Incident infections were defined as those without a prior *C parapsilosis* BSI in the preceding 30 days.

Demographic and clinical data for patients were collected from medical records using a standardized case report form. All-cause, 90-day mortality was obtained from the Georgia Vital Statistics database. Infections were described as hospital onset, healthcare-associated community onset, or community onset as determined by the patient's residence and healthcare interaction around the time of isolate collection. Hospital onset was defined as incident candidemia that occurred more than 72 hours after an admission to an acute care hospital (ACH). Healthcare-associated community onset was defined as incident candidemia that was not identified at an acute care hospital, but the patient had an admission to a healthcare facility in the 90 days before infection or was on chronic dialysis. Community onset was defined as incident candidemia that occurred less than 72 hours into an admission to an ACH or long-term acute care hospital (LTACH) or occurred in the community without a prior admission to a healthcare facility in the past 90 days.

Isolate Collection and Testing

As part of ongoing EIP candidemia surveillance, isolates were submitted to Centers for Disease Control and Prevention for species identification, antifungal susceptibility testing, and WGS. Fluconazole resistance was defined in concordance with Clinical and Laboratory Standards Institute breakpoints with resistant defined as an minimum inhibitory concentration (MIC) $\geq$ 8 mg/L and susceptible-dose dependent (SDD) as an MIC = 4 mg/L [26].

WGS was completed on 45 of 61 (74%) Georgia *C parapsilosis* isolates from 2021, prioritizing all resistant isolates. Two resistant isolates were excluded because of poor sequencing data quality. Fourteen other isolates were not sequenced because of poor viability or workflow limitations. Additional supplementary WGS was completed on all viable FR-CP isolates from the Georgia catchment area in 2019 and 2020 (n = 14) and from other EIP sites in 2020 and 2021 (n = 12). Additional details on methods are described in the Supplementary material.

Read data were submitted to the Sequence Read Archive database from the National Center for Biotechnology Information, BioProject accession PRJNA106854.

Single-nucleotide Polymorphism Calling and Phylogenetic Reconstruction

For the single-nucleotide polymorphism (SNP) calling and phylogenetic reconstruction, MycoSNP-nf v1.4 (https://github.com/CDCgov/mycosnp-nf), a NextFlow workflow was used (Supplementary material; Bagal UR et al 2022). The genome sequence of *C parapsilosis* CDC317, a fluconazole-resistant isolate with the Y132F mutation in the *ERG11* gene, was used as a reference for read mapping and SNP calling.

Phylogeny was estimated using FastTree v2.1.10 and the pairwise distances were calculated with MEGA X. For tree visualization, we used the web-based JavaScript application, Microreact v252. In-house R scripts were used to compute the SNP medians and compare groups of samples by azole susceptibility phenotype; data visualizations were created with ggplot2 and ggpubr R packages.

SnpEff was used to identify mutations. From the variant call format file obtained with MycoSNP-nf workflow, the SNPs were annotated using the database available in SnpEff for *C parapsilosis* GCA 000182765. Several filters were applied to the annotated variant call format to identify the mutations present in *ERG11*.

Epidemiological Analysis

Bivariate analysis was performed comparing epidemiological variables among fluconazole-resistant and fluconazole-susceptible (including SDD) isolates. Categorical variables were analyzed using chi-squared (or Fisher test as appropriate), whereas continuous variables were analyzed using Wilcoxon rank-sum test because of data nonnormality. All data were analyzed using SAS 9.4, and a 2-sided P value of $<.05$ was considered significant.

Facility Network Analysis

Patient information was linked to the Georgia Discharge Data System (Office of Health Indicators for Planning, Atlanta, GA) to identify all nonfederal acute care facilities (ACH, LTACH, and in-patient rehabilitation facilities) where a patient with a *Candida* BSI had stayed in overnight in the 1 year before the index culture and 3 months after the discharge date associated with the index culture. Using an adjacency matrix, we calculated the betweenness and degree (in-degree and out-degree)

for patients with susceptible and resistant isolates. Degree describes the number of admissions into (in-degree) and out of (out-degree) a facility. Betweenness describes the connectedness of facilities. R igraph library was used to create the social network.

RESULTS

Proportion of Fluconazole-resistant *C parapsilosis* Over Time

In 2021, 61 *C parapsilosis* BSIs were identified in the Georgia surveillance area. The proportion of FR-CP isolates doubled from 17% in 2020 to 34% in 2021 resulting in the highest number (n = 20) and proportion of FR-CP reported in all years of surveillance since EIP candidemia surveillance began in 2008 (Figure 1).

Whole-genome Sequencing

Phylogenetic analysis of *C parapsilosis* isolates revealed 7 distinct clades that were each separated by a minimum of 935 SNPs (clades V and VII) and a maximum of 2617 SNPs (clades I and VI; Figure 2*A*; Supplementary Table 1). Clade II included all the resistant isolates from 2021, 1 susceptible isolate, 1 SDD isolate, as well as the reference resistant isolate, CDC317 (Figure 2*B* and 2*C*). The observed median SNP difference between fluconazole-resistant isolates within a clade was significantly lower than that between the susceptible isolates within a clade (7 SNPs vs 93 SNPs; $P < .001$; Supplementary Figure 1). All fluconazole-resistant isolates from 2021 and 1 SDD isolate from the resistant cluster harbored the Y132F substitution in the *ERG11* gene (Supplementary Table 2). None of the susceptible isolates possessed this mutation. The R398I amino acid substitution was found in 11 susceptible isolates (Figure 2*A*). Of the 14 additional FR-CP Georgia isolates from previous years (2019-2020), 13 were genetically related to the resistant isolates from 2021. Conversely, none of the additional FR-CP isolates from other states was closely related to the Georgia FR-CP isolates, and none contained the Y132F mutation (Supplementary Figure 2).

Epidemiological Analysis

Of the 61 patients with CP BSIs in 2021, 54% were male and the median age was 66 years (interquartile range 54-72). Most patients (88%) were hospitalized at the time of specimen collection (Table 1). Most patients (77%) had a central line in place in the 2 days before specimen collection, and 87% had received systemic antibiotics in the 30 days before candidemia episode (Table 1). Patients with a susceptible isolate were more likely to have received piperacillin-tazobactam compared to patients with FR-CP (59% vs 27%; $P = .04$), to have been hospitalized at the time of infection identification ($P = .03$), and to have been diagnosed with a malignancy ($P = .02$) (Table 1). Patients with FR-CP were more likely to have been admitted to an LTACH in the past 90 days (35% vs 7%; $P = .01$). Among patients with FR-CP compared to patient with a susceptible isolate, there was a trend toward (1) increased receipt of any azole antifungal agent in the 30 days before infection ($P = .06$), (2) increased colonization with multidrug-resistant organisms (MDROs; $P = .06$), (3) more mechanical ventilation in the 30 days before BSI ($P = .08$), and (4) a higher median number of days on the ventilator ($P = .12$) (Table 1). The 90-day all-cause mortality was 45% for the entire cohort and similar between patients with FR-CP and susceptible isolates (Table 1).

Network Facilities Analysis

The networks of healthcare facilities associated with patients with susceptible and FR-CP isolates were distinct (Figure 3), and the network of patient movement for those with FR-CP BSIs specifically centered around 2 LTACHs. Furthermore, the 5 most frequently encountered facilities (by degree) for patients with FR-CP and susceptible isolates were nonoverlapping (Figure 3).

DISCUSSION

Through nationwide candidemia surveillance, we identified an increase of FR-CP BSIs in Georgia with isolates that were highly genetically related, suggesting transmission of a single resistant strain. Genetically related FR-CP isolates from previous years suggest that this FR-CP strain was circulating before 2021. Patients identified in 2021 with fluconazole-resistant isolates had increased exposure to LTACHs. Social network analysis further confirmed that the FR-CP BSIs were associated with a facility network based around 2 LTACHs, and this network was unique from the network for patients with susceptible isolates. This increase in FR-CP BSIs in Atlanta in 2021 mirrors reports from around the world [2, 12, 14, 24–30] and shows the importance of monitoring for the emergence of antimicrobial-resistant infections. Many clinical microbiology laboratories lack the ability to perform highly reliable antifungal susceptibility testing on *Candida* spp. and if clinicians and microbiologists are not aware of high rates of resistance in their area, patients with resistant infections may be improperly treated.

Low Genetic Diversity Among Fluconazole-resistant Isolates

There are limited publications describing WGS of *C parapsilosis*; therefore, an SNP difference threshold for defining the clonal relationship between isolates has not been determined. Still, our results clearly show that FR-CP isolates were more related than susceptible isolates. All FR-CP isolates except 1 shared a recent common ancestor, suggesting the presence of a single population of FR-CP that likely expanded via transmission. Our study, which spanned multiple facilities, further suggests that FR-CP may be easily transmissible and can spread across

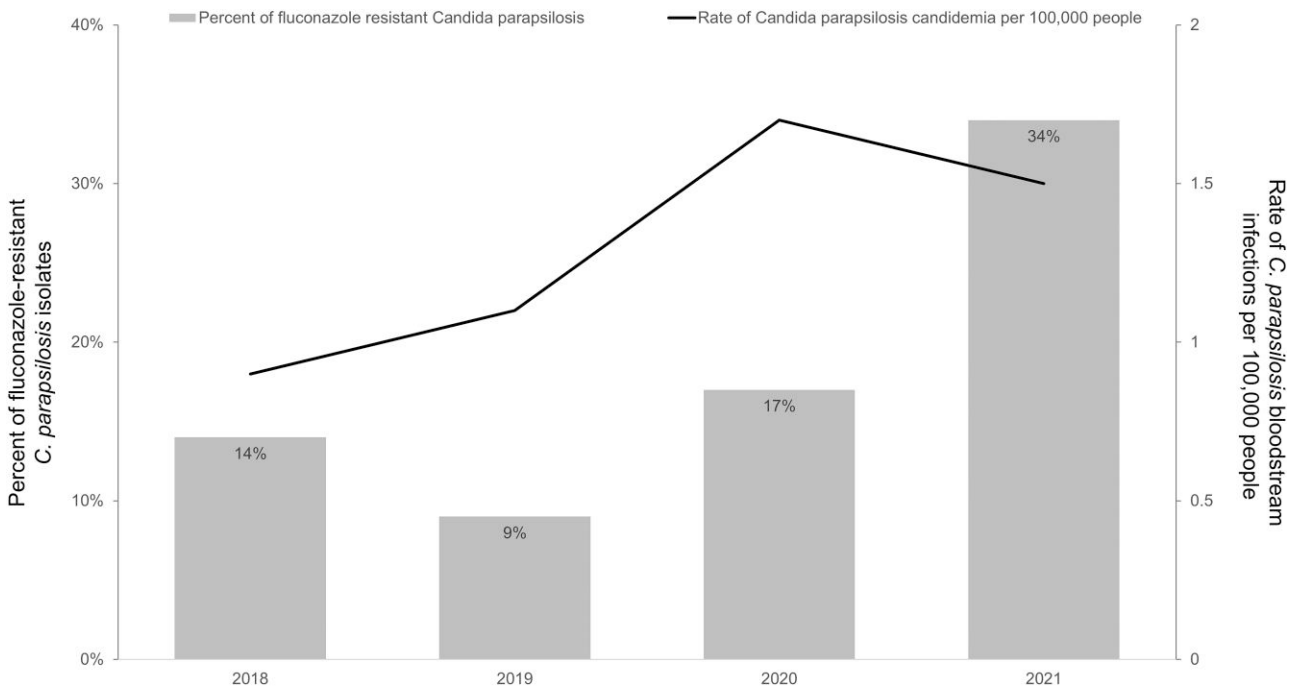

Figure 1. Rate of incident *Candida parapsilosis* bloodstream infections by year with percent of fluconazole-resistant isolates.

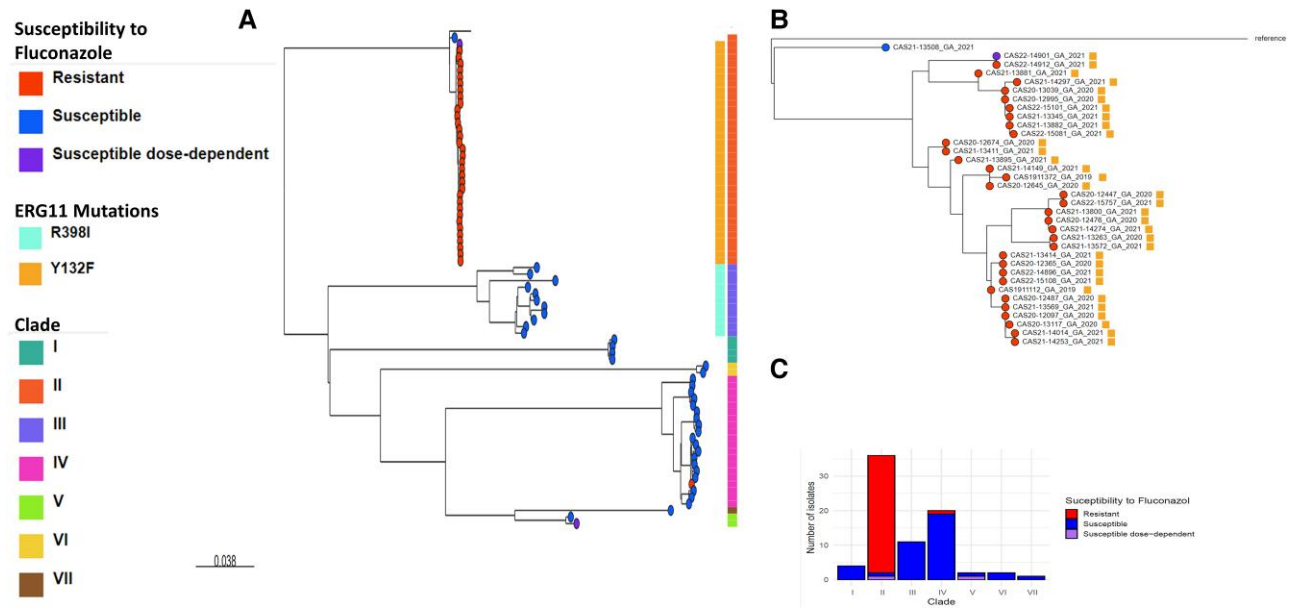

Figure 2. *A*, Phylogenetic tree using the neighbor-joining method. Isolates clustered into 7 clades. Taxa colors represent susceptibility profile and boxes represent mutations in the *ERG11* gene. *B*, Zoom view of clade II. *C*, Frequency distribution of *C parapsilosis* isolates by clade. Bars are divided by colors that represent the number of susceptible dose-dependent, susceptible, or fluconazole-resistant isolates.

facilities in a network. Similarly, Daneshnia et al described a *C parapsilosis* outbreak in a Brazilian intensive care unit (ICU) and found that 85% of resistant isolates clustered together, whereas susceptible isolates were distributed among varying lineages [31]. Of note, Daneshnia et al used multilocus sequence typing, a genotyping technique based on a small number of loci across the genome [31]. These techniques are not as sensitive as WGS, which considers all polymorphic positions in

Table 1. Characteristics of Patients With *Candida parapsilosis* Infections in Atlanta, GA, 2021, by Fluconazole Susceptibility

	Total (n = 61) n (%)[a]	Fluconazole Resistant (n = 20) n (%)[a]	Fluconazole Susceptible (n = 41) n (%)[a]	*P* Value
Age, median (IQR)	66 (54–72)	67 (62–74)	64 (43–72)	.06
Sex	…	…	…	.32
Female	28 (46)	11 (55)	17 (41)	…
Race[b]	…	…	…	.84
Black	34 (60)	12 (63)	22 (58)	…
White	17 (30)	6 (32)	11 (29)	…
Other	6 (10)	1 (5)	5 (13)	…
Ethnicity	…	…	…	.68
Hispanic	3 (5)	0 (0)	3 (7)	…
Location	…	…	…	.38
Community onset	5 (8)	2 (10)	3 (7)	…
Healthcare-associated community onset	19 (31)	9 (45)	10 (24)	…
Long-term acute facility onset	7 (11)	4 (20)	3 (7)	…
Hospital onset	37 (60)	9 (45)	28 (68)	…
Colonized with multidrug-resistant organism[b]	10 (17)	6 (31)	4 (10)	.06
Additional associated infection/colonization[b]	14 (30)	5 (29)	9 (30)	.97
Hospitalized at time of culture	54 (88)	15 (75)	39 (95)	.03
Hospitalized in 90 d before infection	30 (49)	12 (60)	18 (44)	.24
Overnight in LTACH 90 d before infection	10 (16)	7 (35)	3 (7)	.01
Overnight in LTCF 90 d before infection	10 (16)	4 (20)	6 (15)	.72
Surgery in 90 d before infection	20 (33)	7 (35)	13 (31)	.8
Prior candidemia episode	4 (7)	1 (5)	3 (7)	1
In ICU before culture	26 (43)	8 (40)	18 (44)	.77
Diabetes	19 (47)	12 (60)	17 (41)	.17
History of gastrointestinal disorders	7 (11)	1 (5)	6 (15)	.41
History of immunocompromising conditions	2 (3)	0 (0)	2 (5)	1
History of malignancy	9 (14)	0 (0)	9 (22)	.02
History of pancreatitis[b]	2 (3)	0 (0)	2 (5)	1
Concurrent neutropenia[b]	10 (17)	4 (21)	6 (15)	.71
Central venous catheter in place 2 d prior	47 (77)	14 (70)	33 (80)	.52
Mechanically ventilated in 30 d prior	30 (49)	13 (65)	17 (41)	.08
Days of ventilation, median (IQR)[b]	16.5 (5–36)	39 (14–58)	14 (5–19)	.12
Chronic dialysis[b]	5 (8)	2 (11)	3 (7)	.64
Systemic antibiotic therapy 30 d before infection[b]	52 (87)	18 (94)	34 (83)	.6
Cefepime	11 (21)	3 (16)	8 (23)	.44
Piperacillin-tazobactam	25 (48)	5 (27)	20 (59)	.04
Daptomycin	6 (11)	2 (11)	4 (12)	.46
Vancomycin	39 (75)	14 (78)	25 (73)	.37
Carbapenem	24 (46)	7 (39)	17 (50)	.56
Systemic steroids	22 (36)	7 (35)	15 (36)	.9
Total parental nutrition	36 (60)	12 (63)	24 (58)	1
Systemic antifungals in 30 d before infection[b]	18 (30)	8 (42)	7 (24)	.33
Fluconazole	8 (13)	5 (25)	3 (7)	.1
Any azole therapy[c]	10 (16)	6 (30)	4 (10)	.06
Amphotericin	1 (2)	1 (2)	0 (0)	…
Echinocandin (micafungin)	13 (21)	3 (15)	10 (24)	.52
Given CHG bath in the 5 d before infection[b]	27 (45)	7 (37)	20 (49)	.77
Number of CHG baths, median (IQR)	4 (3–5)	3 (3–5)	4 (3–5)	.47
90-d mortality[b]	26 (45)	8 (42)	18 (46)	.77

Gastrointestinal disease: diverticular disease, inflammatory bowel disease, peptic ulcers, or short gut. Immunocompromising conditions: HIV, primary immunodeficiency, hematopoietic stem cell transplant, solid organ transplant.

Abbreviations: CHG, chlorhexidine gluconate; ICU, intensive care unit; IQR, interquartile range; LTACH, long-term acute care hospitals; LTCF, long-term care facility.

[a]Percent values may not sum to 100 because of rounding.

[b]Missing data: race (2), multidrug-resistant organism (1), neutropenia (2), pancreatitis (1), associated infection (13), chronic dialysis (1), systemic antibiotics 30 d (1), total parental nutrition (1), CHG (2), ventilator days (2), antifungals (1), mortality (3).

[c]Other azole antifungals included isavuconazole (1) and posaconazole (1).

A

Facility	Type	Degree	In-degree	Out-degree	Betweenness
A1	ACH	71	43	28	78.71
C1	ACH	33	13	20	47.06
H5	ACH	32	16	16	0.00
I2	ACH	32	15	17	0.00
B1	ACH	31	18	13	9.35

B

Facility	Type	Degree	In-degree	Out-degree	Betweenness
H1	ACH	27	16	11	0
E1	LTACH	19	12	7	11
A6	LTACH	19	9	10	16
F2	ACH	13	6	7	1
A5	ACH	12	3	9	12

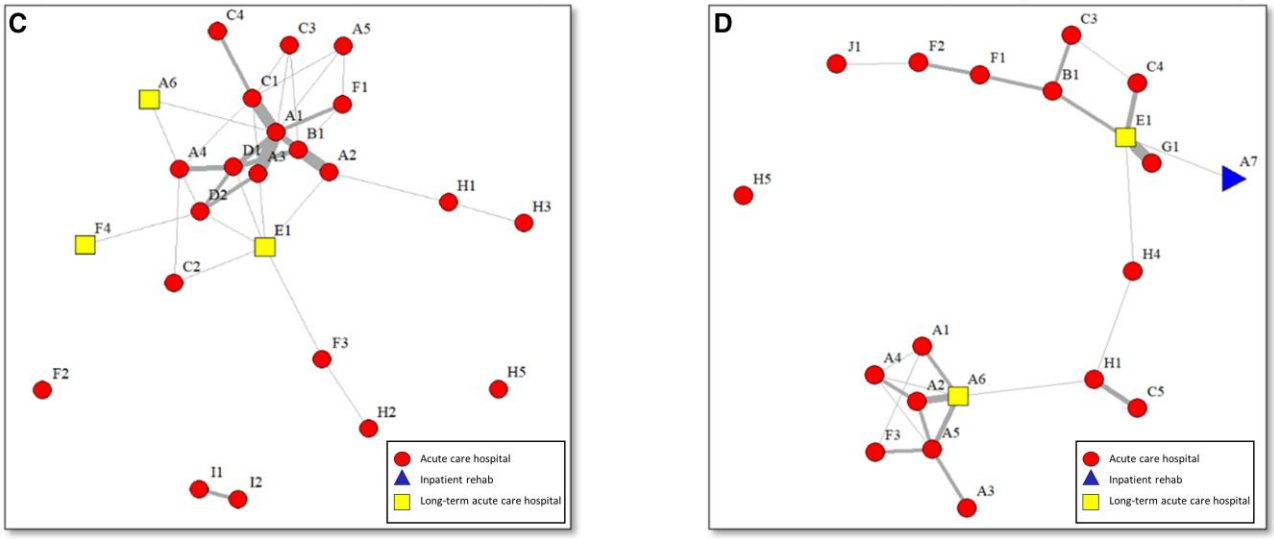

Figure 3. Social network analysis results. Tables *A* and *B* list the 5 most encountered facilities (by degree) for patients with susceptible (*A*) and resistant (*B*) isolates. Graphics show the facility network of patients with susceptible (*C*) and resistant (*D*) isolates. Node shape represents type of facility, whereas edge thickness is proportional to the number of patients moving between facilities as either direct or indirect transfers (1 y before receipt at facility or up to 3 mo after discharge from a facility). Movement to and from the same facility (such as readmissions) are not shown but are accounted for in degree calculation.

the genome. Additional FR-CP isolates from other states were genetically separate from those from Georgia (Supplementary Figure 2), reinforcing the hypothesis of local transmission.

Interestingly, we identified a single susceptible isolate of the same lineage but more distant from the resistant isolates (56 SNPs) and therefore unlikely to be related to transmission of this strain. The susceptible isolate may represent a remnant of the wild-type ancestral lineage.

Mutations Associated With Azole Resistance and the *EGR11* Gene

All isolates in the resistant cluster had the Y132F mutation, which is consistent with prior reports of outbreaks associated with isolates with the Y132F mutation [24, 25]. In contrast, Daneshnia et al found that only 36% of FR-CP isolates in a Brazilian outbreak contained a mutation in *ERG11* gene but all carried an L518F mutation in the *TAC1* gene and significantly overexpressed CDR1 [31]. The only nonsynonymous substitution that we found in *ERG11* beyond Y132F was R398I, a mutation frequently reported among susceptible isolates from the United States [22] and identified among only susceptible isolates in this study [22]. We did not identify a K143R mutation in the *EGR11* gene in any Georgia isolates, despite it previously being described in resistant isolates from the United States [32]. This may speak to the clonality of these isolates or a low prevalence of this mutation in this geographic area. We did identify the Y132F mutation in a fluconazole SDD isolate, which may be due to the inherent technical limitation of the microdilution test because there is only 1 drug dilution separating samples considered SDD and those considered resistant [33]. Molecular detection of the Y132F mutation in clinical microbiology laboratories could allow for more rapid identification of resistant strains with greater potential to spread and potentially earlier identification of outbreaks.

Potential Link Between Resistance and Fitness

Prior studies have postulated that the Y132F mutation may convey multiple clinically relevant genetic changes to aid in persistence of *C parapsilosis* in the healthcare environment, which allows it to cause outbreaks more readily than susceptible strains [7, 19, 34–36]. One outbreak investigation in a Brazilian ICU in 2017 found that 10 of 14 isolates were fluconazole nonsusceptible, and these isolates formed biofilms with low biomass activity [11]. The same authors reported an ongoing, multicenter FR-CP outbreak linked to a contaminated computed tomography machine with isolates all demonstrating the Y132F mutation [13]. Our investigation did not include

environmental sampling to assess for *C parapsilosis* on healthcare surfaces, nor did we assess infection prevention practices at the facilities to understand potential breakdowns in healthcare workers' hand hygiene or cleaning and disinfection practices that may have led to transmission. However, we did analyze adherence to chlorhexidine bathing, which did not differ between patients with susceptible and resistant isolates.

Epidemiological Investigation

Our epidemiological investigation revealed an association between LTACH admission and FR-CP; an association previously described for *Candida auris* but not for *C parapsilosis* [37]. Long-term acute care hospitals are specialized facilities in the United States that provide highly complex medical care, such as mechanical ventilation and weaning, complex wound care, or multiple intravenous medication infusions but do not require extensive diagnostic procedures. As such, patients housed at LTACHs are severely ill and often have multiple indwelling medical devices such as central venous or hemodialysis catheters and tracheostomy tubes. This uniquely sick and healthcare-experienced population, combined with lower staffing resources, has traditionally led to high levels of MDRO colonization and outbreaks in patients cared for in LTACHs. Patients with FR-CP were also more likely to have been exposed to any azole antifungal in the 30 days before infection, although this did not reach statistical significance. At least 1 previous study showed that more than 70% of patients with Y132F isolates had a history of azole use [24]. However, many other studies reported no association between azole therapy and the Y132F mutation [2, 12, 25]. This suggests transmission of FR-CP rather than patients developing FR-CP individually because of antifungal pressure. It is also possible that azole usage is more prevalent in the specific facilities that patients with FR-CP were admitted to, or that prior azole use impacted the fungal microbiome of these patients, leading to colonization with a resistant strain that eventually caused a bloodstream infection. There was no difference in frequency of prior episodes of candidemia between those with resistant and susceptible isolates, which might result in a difference in azole exposure. There was a similar trend toward increased colonization with an MDRO in patients with FR-CP, which may suggest a preexisting disruption of the microbiome allowing for colonization with resistant organisms, including *Candida*, or it may reflect transmission pathways similar to other MDROs, for example that they are amplified in LTACHs. Prior use of piperacillin-tazobactam was more frequent in patients with susceptible isolates; however, this may simply be a surrogate for interaction with specific healthcare facilities that use more piperacillin-tazobactam. This interaction requires further evaluation because it is possible that piperacillin-tazobactam has a unique effect on the bacterial microbiome, which in turn could affect the fungal microbiome. Our study found no difference in 90-day mortality in patients with FR-CP compared to patients with susceptible isolates. Thomaz et al analyzed ongoing spread of azole-resistant *C parapsilosis* in an adult ICU at a Brazilian cancer center and found that 30-day mortality of patients with azole-resistant *C parapsilosis* was 63.8% compared to 20% for susceptible isolates [11]. We also found that patients with malignancy were more likely to have susceptible isolates. This likely represents differences in facilities because specific facilities within the network serve as cancer hospitals and are more likely to interact with patients with malignancies.

Social Network Analysis

Prior work examining patient movement for carbapenem-resistant *Enterobacterales* suggested that movement of patients with carbapenem-resistant *Enterobacterales* mirrors general movement of patients [38]. Conversely, we found that the movement of patients with FR-CP was distinct from the movement of patients with susceptible isolates and was centered around 2 LTACHs, which reinforces our belief that the spread of FR-CP represents an outbreak with multiple transmission events. To our knowledge, ours is the only social network analysis of the movement of patients with *C parapsilosis* BSIs.

Limitations

This study has several limitations. First, although we showed a difference in prior receipt of antifungal agents, we did not have complete data regarding why these medications were provided. Therefore, we cannot verify whether this observed difference was due to a prior infection or was simply empiric treatment reflecting practice patterns of the facilities where patients were previously cared for. We did not include environmental sampling and did not have information on facility adherence to infection prevention and control practices such as hand hygiene, central line care, or respiratory care bundles. Therefore, we cannot link this spread to environmental or definitively prove transmission event(s). Similarly, we did not have information regarding general cleaning and disinfection practices for each hospital, nor rates of facility-specific COVID-19 admissions that may have affected the propagation of this clone. Last, our study was small which may limit our ability to identify associated exposures.

CONCLUSIONS

We present an investigation of a regional cluster of highly related fluconazole-resistant *C parapsilosis* BSIs, where all isolates possessed a Y132F mutation suggesting transmission among a network of facilities centered around LTACHs. These findings highlight the importance of continued candidemia surveillance and the potential utility of incorporating WGS into infection prevention investigations to rapidly identify outbreaks of resistant strains and implement infection control

practices to stop their spread. Further studies are required to investigate the possible link between the Y132F mutation and environmental persistence contributing to transmission.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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Disclaimer. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. Use of trade names is for identification only and does not imply endorsement.

Data availability. Genomic sequences underlying this study were deposited in the National Center for Biotechnology Information (NCBI) Sequence Read Archive (SRA) database, accession number PRJNA1068541.

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Patient consent statement. This activity was reviewed by the CDC and received nonresearch determination. It does not include factors necessitating patient consent.

Potential conflicts of interest. The authors: No reported conflicts of interest.

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