Recent Increase in Fluconazole-Nonsusceptible Candida parapsilosis in a Global Surveillance with the Expansion of the Erg11 Y132F genotype and a Rapid Detection Method to Detect This Alteration

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Objective

- We evaluated the rates of fluconazole-nonsusceptible *C. parapsilosis* among isolates from 2018 to 2021.
- Additionally, we developed a PCR assay for the rapid detection of the Y132F Erg11 alteration in *C. parapsilosis*.

Methods

- 1,103 *C. parapsilosis* isolates from invasive candidiasis were submitted to the SENTRY Antifungal Surveillance Program.
- Isolates were susceptibility tested using the CLSI reference broth microdilution method.
- Fluconazole-nonsusceptible isolates (MIC, ≥4 mg/L) were submitted to a PCR assay to detect the Erg11 Y132F alteration.
- Positive (n=38) and negative (n=18) controls previously submitted to whole genome sequencing were tested to evaluate this method.

Conclusions

- Fluconazole-nonsusceptible C. parapsilosis rates increased from 10.2% in 2018 to 15.4% in 2021.
- These isolates were detected in 12 of 30 surveyed countries.
- The highest rates of Erg11 Y132F were observed in Europe (92.7%), followed by the US (60.9%).
- The Y132F Erg11 alteration was detected in 83.2% of the isolates (104/125) collected during 2018–2021 by the designed PCR method.
- Y132F Erg11-positive isolates were mostly resistant to voriconazole, but posaconazole and itraconazole MIC values were all wildtype.
- Continuous monitoring is needed for isolates carrying the globally disseminated Y132F Erg11 alteration and their rapid detection is critical.

Acknowledgments

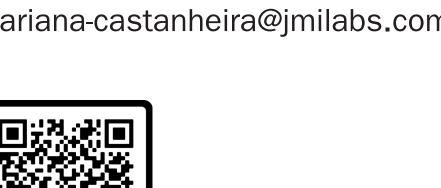
This study was performed at JMI Laboratories. No funding was received to perform this analysis.

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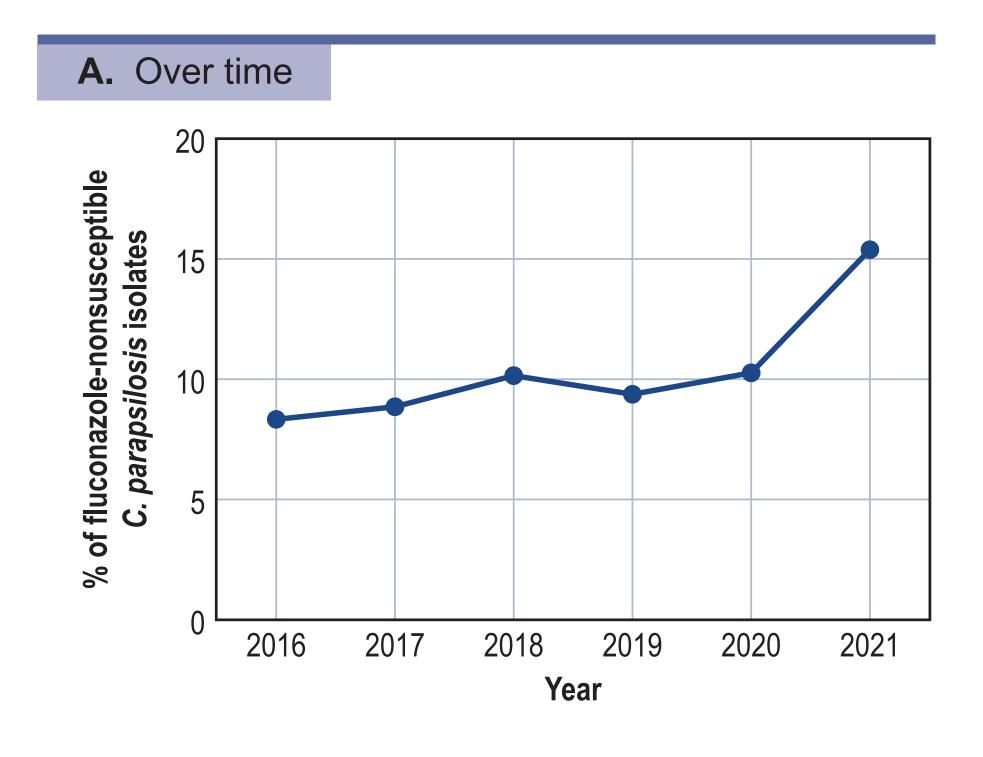




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Figure 1. Fluconazole nonsusceptible C. parapsilosis (A) over time and (B) by country



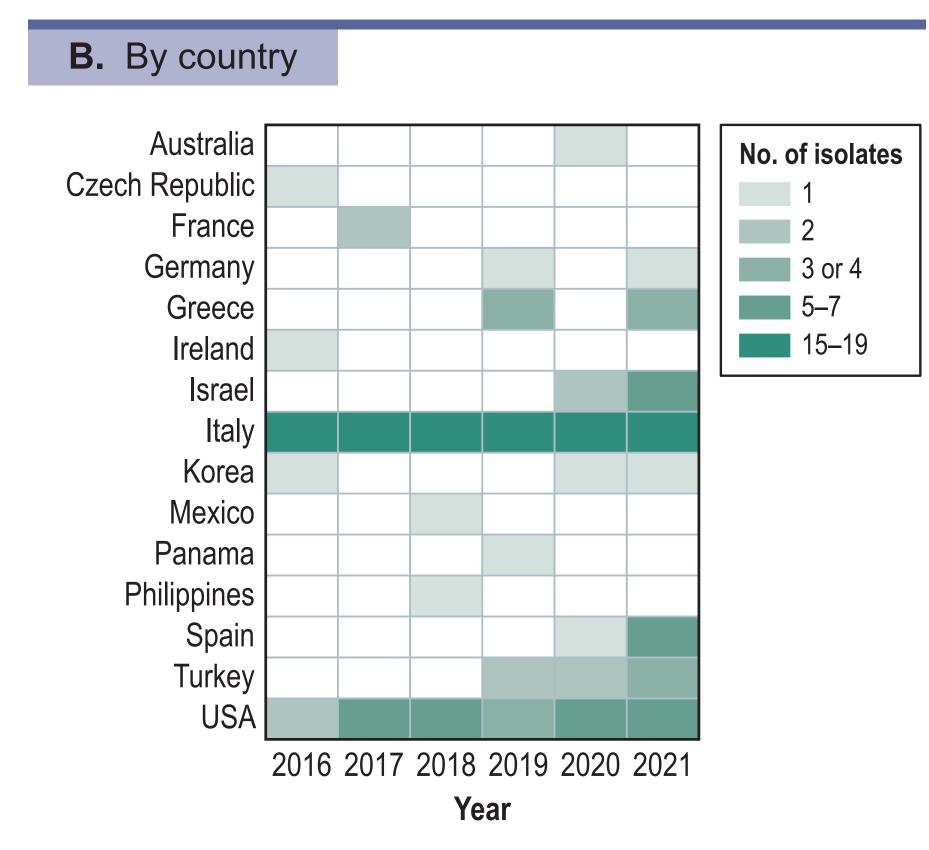
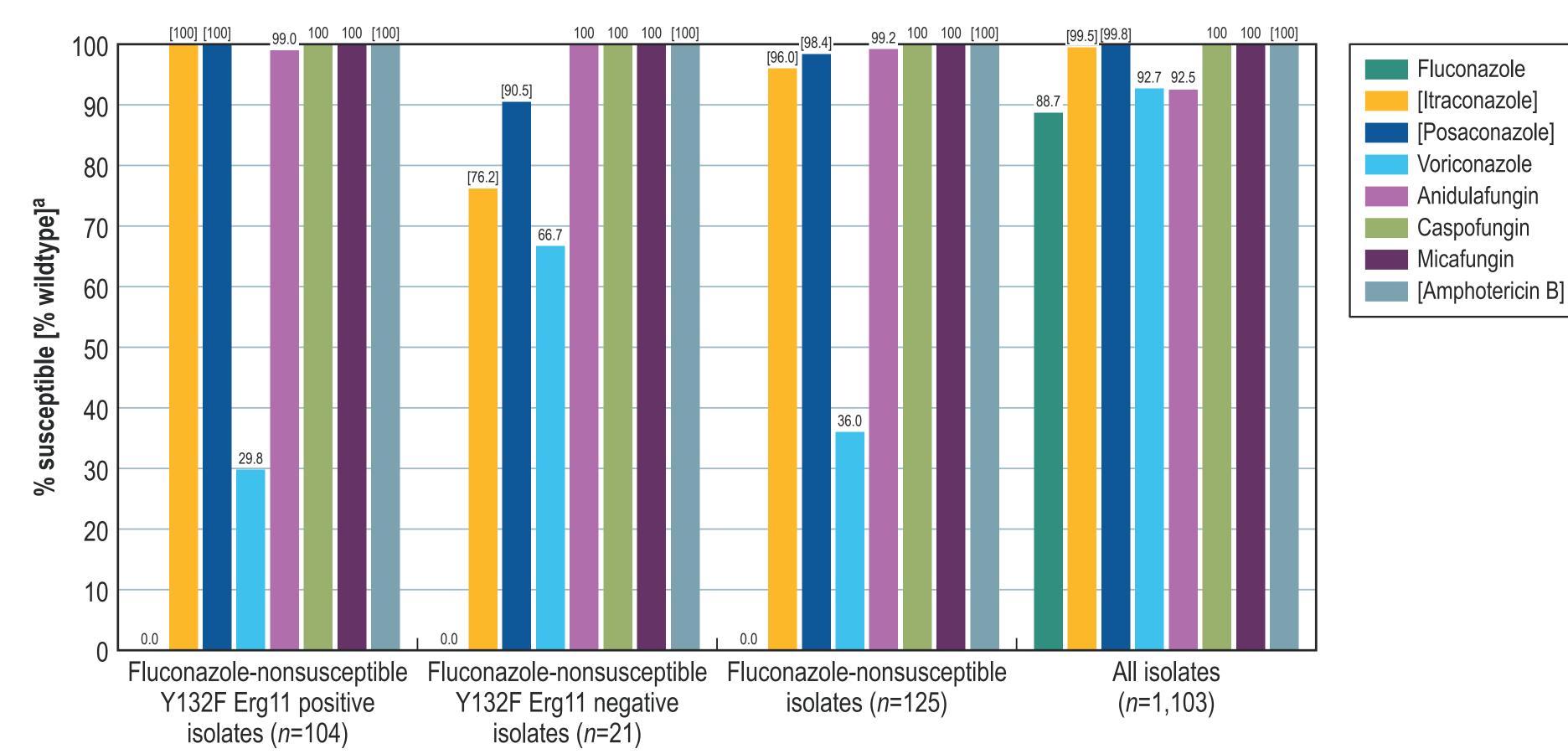


Figure 2. Antifungal susceptibility rates of *C. parapsilosis* isolates



^a The breakpoint criteria and epidemiological cut-off values used were published by CLSI in the third edition of the M2744S (2022) and the fourth edition of the M57 (2022).

Table 1. PCR-based Erg11-Y132F detection results for fluconazole-nonsusceptible *C. parapsilosis* isolates from 2018–2021

| Continent (no. tested) Country (no. tested) | No. (%) of NS isolates | No. (%) of NS isolates detected as | |
|---|------------------------|------------------------------------|----------------|
| | | Y132F positive | Y132F negative |
| All geographical regions (1,103) | 125 (11.3) | 104 (83.2) | 21 (16.8) |
| Asia Pacific (127) | 4 (3.1) | 0 (0) | 4 (100.0) |
| Australia (37) | 1 (2.7) | 0 (0) | 1 (100.0) |
| Korea (33) | 2 (6.1) | 0 (0) | 2 (100.0) |
| Philippines (16) | 1 (6.2) | O (O) | 1 (100.0) |
| Europe (466) | 96 (20.6) | 90 (93.8) | 11 (11.5) |
| Germany (51) | 2 (3.9) | O (O) | 2 (100.0) |
| Greece (15) | 7 (46.7) | 6 (85.7) | 1 (14.3) |
| Israel (13) | 7 (53.8) | 7 (100.0) | 0 (0) |
| Italy (209) | 66 (31.6) | 63 (95.5) | 3 (4.5) |
| Spain (47) | 6 (12.8) | 6 (100.0) ^b | 0 (0) |
| Turkey (31) | 8 (25.8) | 8 (100.0) | 0 (0) |
| Latin America (124) | 2 (1.6) | 0 (0) | 2 (100.0) |
| Mexico (42) | 1 (2.4) | 0 (0) | 1 (100.0) |
| Panama (20) | 1 (5.0) | O (O) | 1 (100.0) |
| North America (386) | 23 (6.0) | 14 (60.9) | 9 (39.1) |
| USA (383) | 23 (6.0) | 14 (60.9) | 9 (39.1) |

Abbreviations: NS, nonsusceptible.

a Countries without NS isolates are

a Countries without NS isolates are not shown.

b Five isolates from Spain carried a dual Erg11 genotype, each of which harbored 1 Y132F allele and 1 WT allele. These isolates should be treated as having a positive resistance genotype.