The last of fungUs?
Recent developments in fungal infections in the German hospital setting

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Introduction

- Invasive fungal diseases are rising, particularly among immunocompromised populations, often resulting in death or severe chronic illnesses.[1]
- However, fungal infections receive limited attention and resources compared to other global public health topics, leading to a lack of data on disease distribution and antifungal resistance patterns.
- In 2022, the World Health Organization (WHO) released the first fungal priority pathogens list, which systematically prioritizes fungal pathogens.[2]
- Additionally, antifungal resistances exacerbate the challenge of managing these infections effectively.[3]
- This study aims to provide an overview of fungal infections and antifungal resistances in the inpatient setting in Germany.

Methods

- This retrospective data analysis was based on German hospital data from the Institute for the Hospital Remuneration System (InEK) spanning from January 1st, 2019, December 31st, 2023.
- Fungal infections (main discharge diagnosis) and antifungal resistance (secondary discharge diagnosis) were identified by the following ICD-10-GM codes:
  - B37.- "Candidiasis"
  - B44.- "Aspergillosis"
  - B45.- "Cryptococcosis"
  - U83.- "Human pathogenic fungi with resistance to antimycotics"
- Since 2023, the ICD-10-GM catalogue allows a more precise specification of the antifungal resistance, considering the pathogen as well as antifungal group.
- Due to coding limitations preventing exact species identification, this assessment focused on the three fungal genus classifications from the WHO critical priority group (Cryptococcus, Candida, Aspergillus).
- Antifungal applications of patients with a diagnosed resistance to antimycotics (U83.-) were identified in 2023 by operation and procedure keys (OPS codes). All codes from chapter 6 "Application of drugs" were considered.
- Hospitalization rates with 95% confidence intervals (CI) were calculated.

Conclusions

- Between 2019 and 2023, patients hospitalized due to fungal infections from WHO's critical priority group were mostly male and ≥60 years old.
- Increase in hospitalization rates due to "Cryptococcus" and "Aspergillus" affirms the WHO concerns.
- The stable ratio of hospitalizations with fungal infections versus overall hospitalizations, does not necessarily indicate a realistic trend of hospitalizations rates, as the analyzed years were impacted by the COVID-19 pandemic.
- Further observation and research are necessary to estimate the burden and future risks of invasive fungal diseases.

References

1. Bongomin F, Gago S, Oladele RO, Denning DW. Global and multi-national prevalence of fungal diseases – estimate precision. J Fungi (Basel). 2017;3(4).
2. WHO fungal priority pathogens list to guide research, development and public health action. Geneva: World Health Organization; 2022.
3. Hendrickson JA, Hu C, Aitken SL, Beyda N. Antifungal Resistance: a Concerning Trend for the Present and Future. Curr Infect Dis Rep 21, 47 (2019).

Results

- Between 2019 and 2023, n=39,199 patients were hospitalized due to infections with fungal pathogens of critical priority. The majority of these patients (68.7%) were ≥60 years old (**Figure 1**). Looking at individual priority groups, B37.- "Candidiasis" was mostly diagnosed in patients ≥60 years old (70.9%), whereas B45.- "Cryptococcosis" was mostly diagnosed in patients younger than 60 years of age (69.0%) (**Figure 2**).
- Overall, the patient population consisted of more men (52.9%), which was most prominent for patients with B45.- "Cryptococcosis" (68.0% male) as main discharge diagnosis (**Figure 3**).
- Set in relation to the total number of hospitalizations in Germany, the proportion of hospitalizations with main discharge diagnoses for fungal infections did not increase from 2019 (0.049%) to 2023 (0.045%).

Figure 1. Age of patients with fungal infections, total (2019-2023)
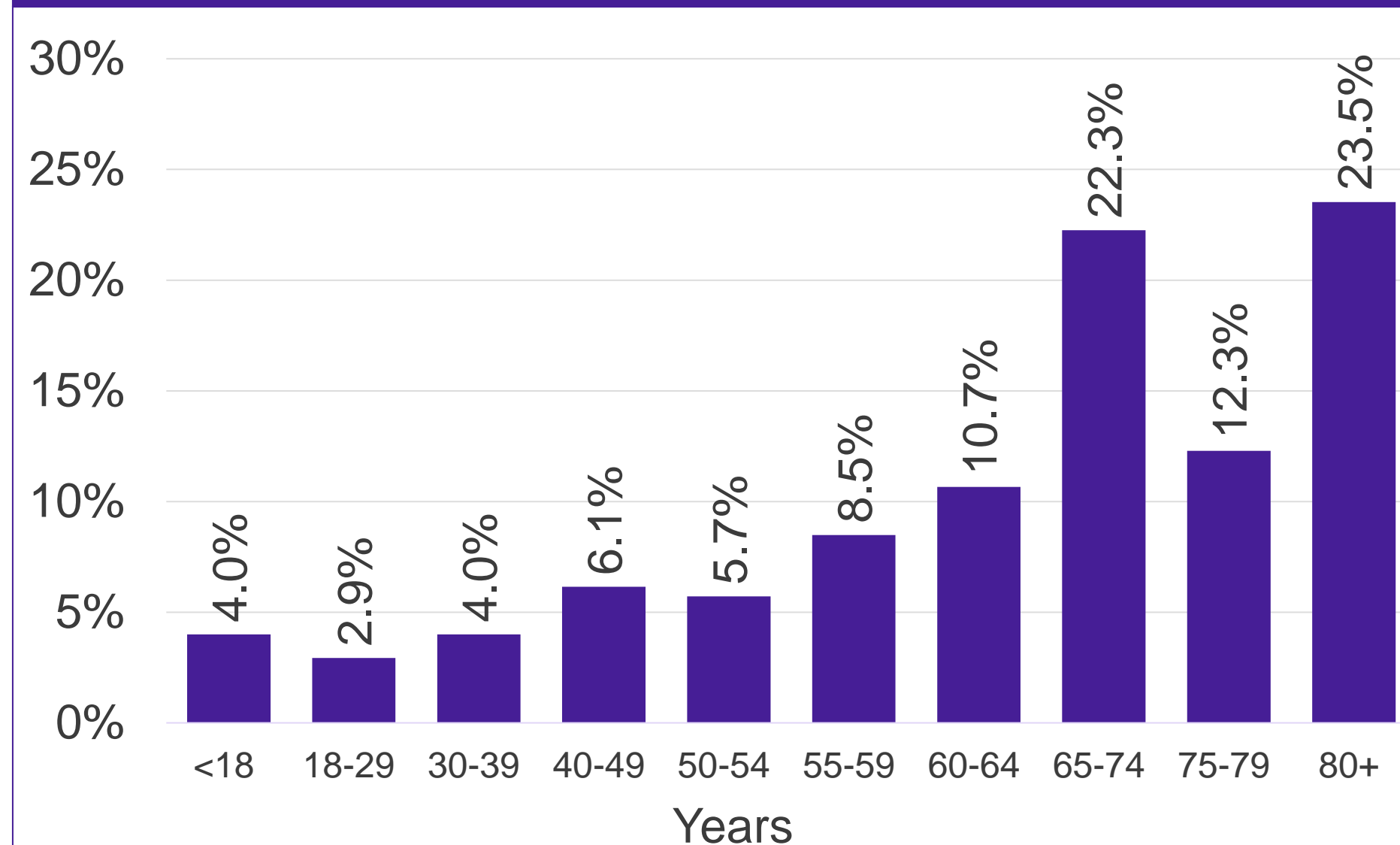

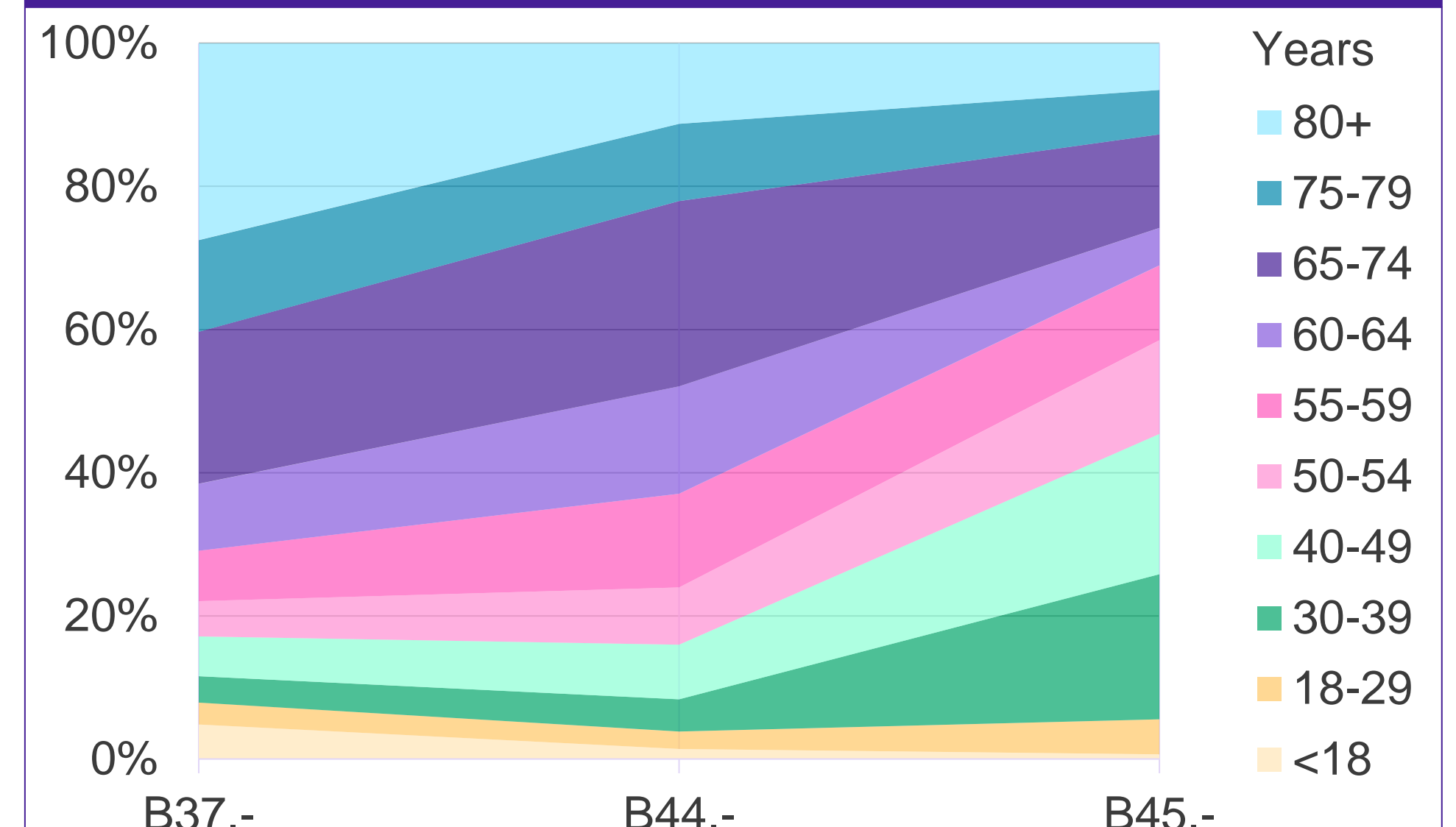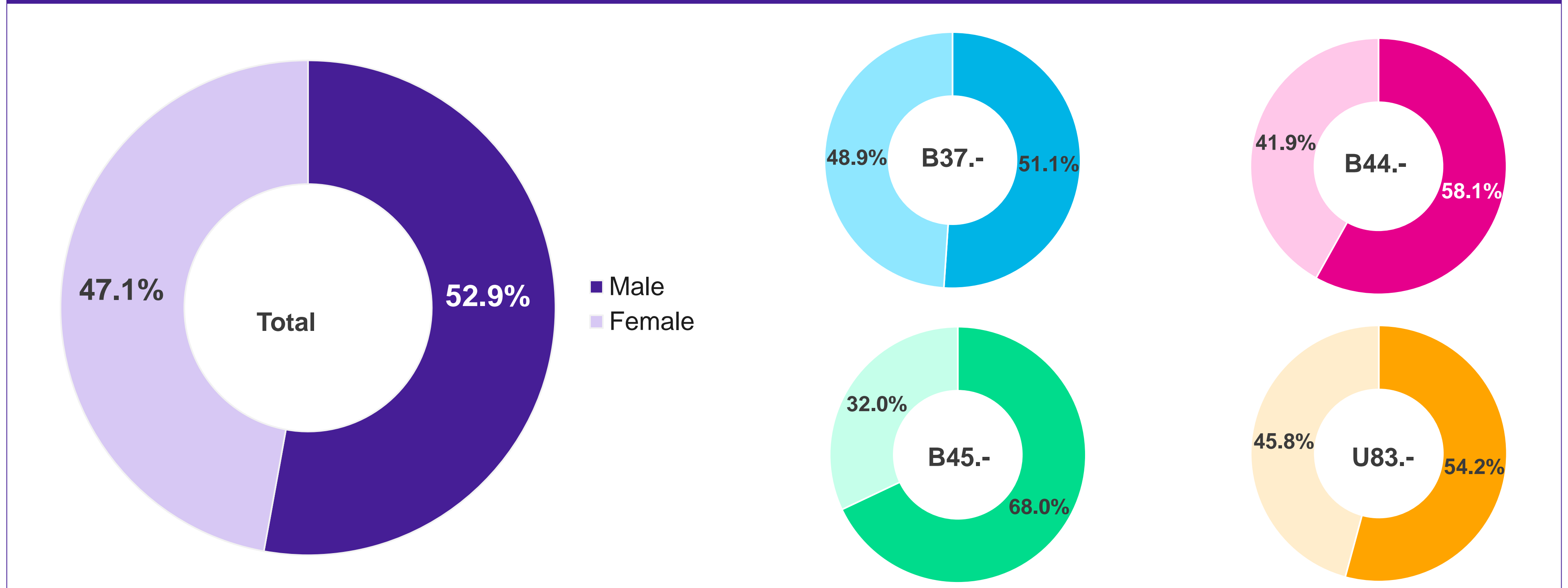Figure 2. Age of patients with fungal infections, by priority group (2019-2023)

Figure 3. Sex of patients with fungal infections, total and by priority group (2019-2023)

- Most hospitalizations were due to Candida infections (75.8%; CI: 74.9-76.6%). However, the share of hospitalizations with "Candidiasis" decreased from 2019 (77.4%; CI: 75.7-79.2%) to 2023 (74.8%; CI: 72.9-76.7%).
- In contrast, hospitalizations due to B37.- "Cryptococcus" infections increased between 2019 (0.6%; CI: 0.5-0.8%) and 2023 (0.9%; CI: 0.7-1.1%).
- A significant trend was observed for hospitalizations due to infections with B44.-"Aspergillus" from 2019 (21.9%; CI: 21.0-22.9%) to 2023 (24.3%; CI: 23.2-25.4%) (**Figure 4**).
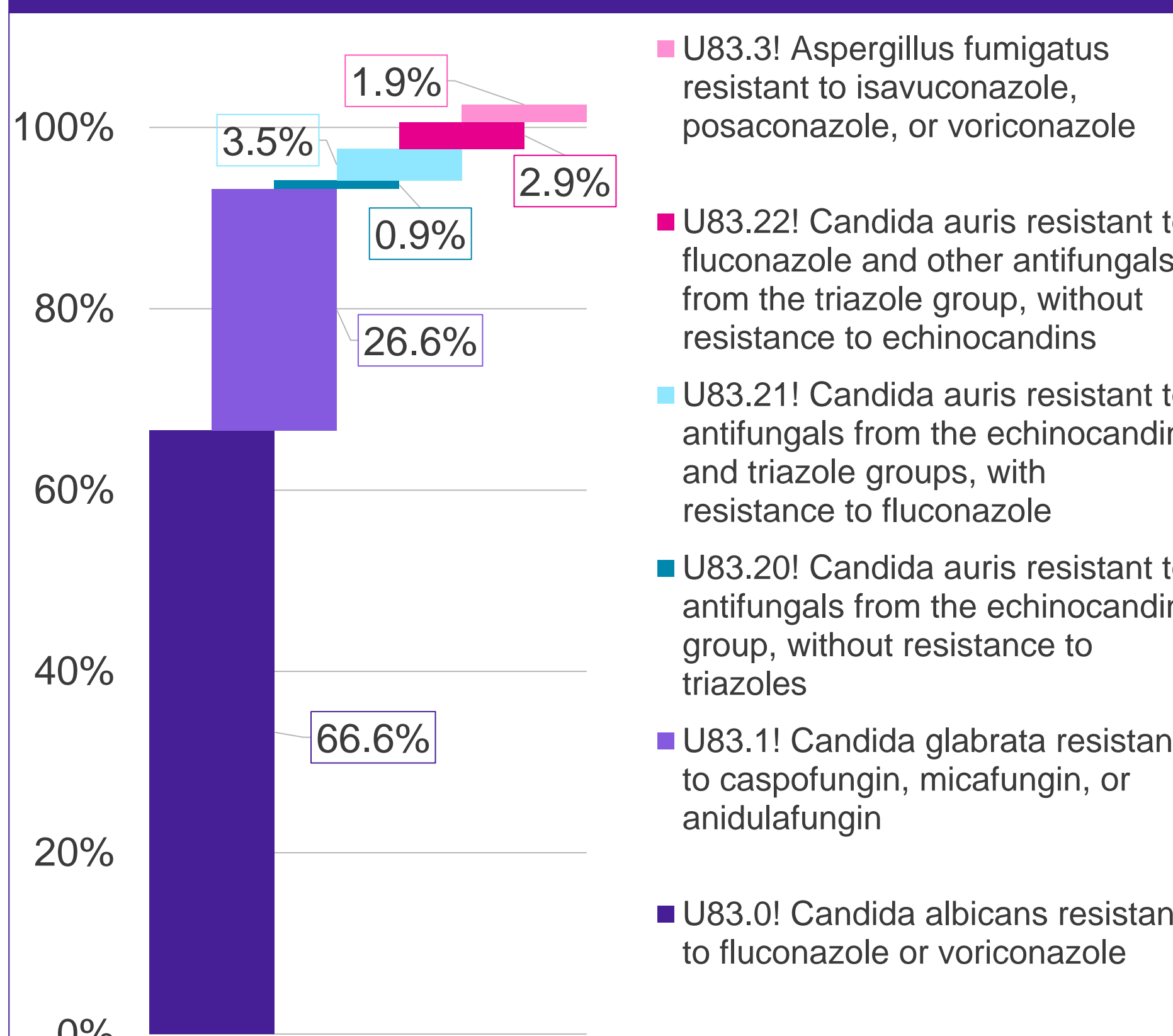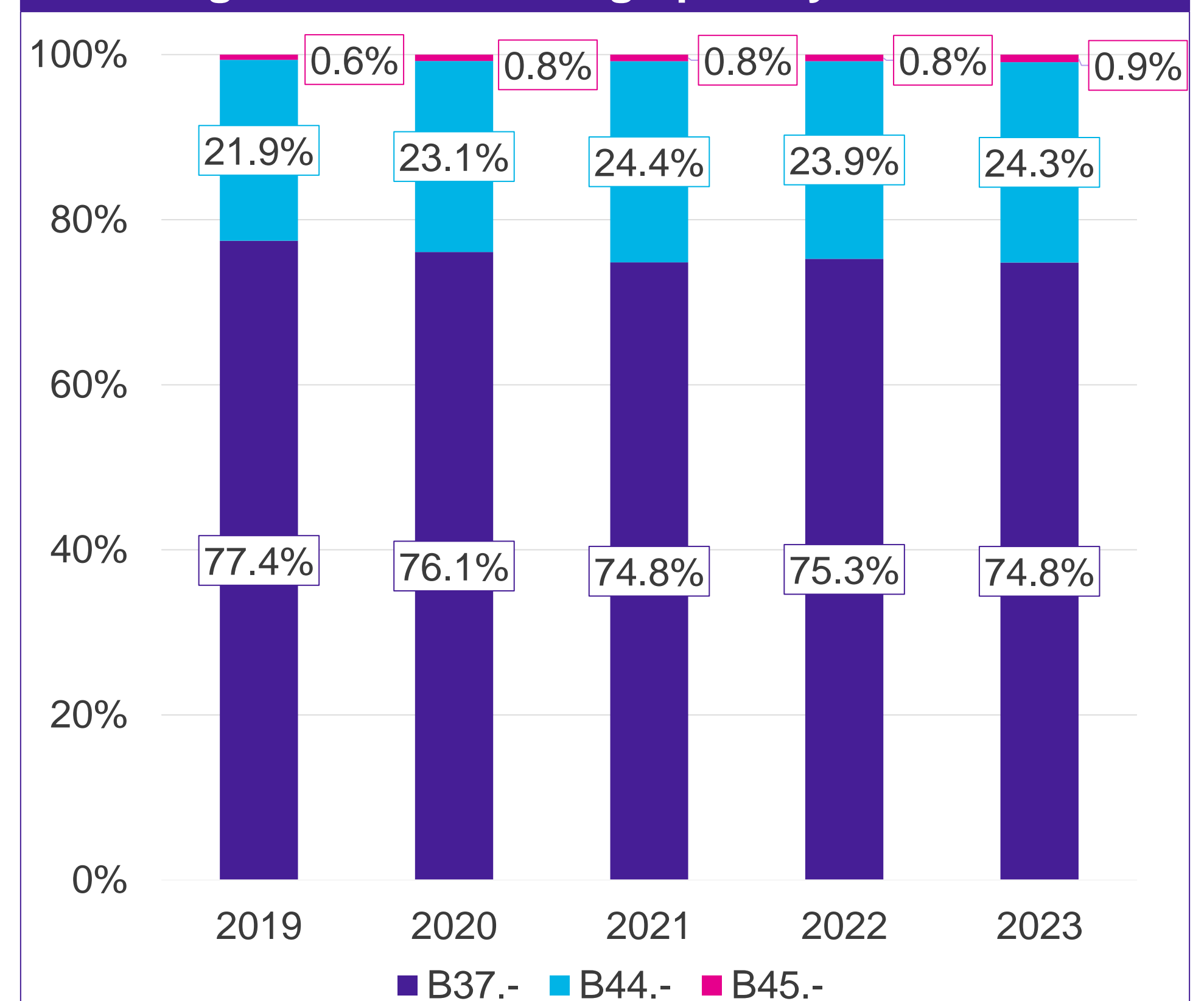

Figure 4. Distribution of main discharge diagnoses with fungal infections of high priority

Figure 5. Distribution of antifungal resistance ICD-10-GM codes in 2023

- U83.3! Aspergillus fumigatus resistant to isavuconazole, posaconazole, or voriconazole
- U83.22! Candida auris resistant to fluconazole and other antifungals from the triazole group, without resistance to echinocandins
- U83.21! Candida auris resistant to antifungals from the echinocandin and triazole groups, with resistance to fluconazole
- U83.20! Candida auris resistant to antifungals from the echinocandin group, without resistance to triazoles
- U83.1! Candida glabrata resistant to caspofungin, micafungin, or anidulafungin
- U83.0! Candida albicans resistant to fluconazole or voriconazole

- Between 2019 and 2023, n=7,183 hospitalized patients were diagnosed with an antifungal resistance (U83.-). Among these patients, the most frequently applied antifungal drug was caspofungin, followed by anidulafungin, and voriconazole.
- Among n=1,194 patients with a recorded antifungal resistance in 2023, n=1,224 cases were documented, indicating that some patients had more than one antifungal resistance (**Figure 5**).
- The most frequent documented resistance group was "Candida albicans resistant to fluconazole or voriconazole" (**Figure 5**).

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