

Fungal normalflora in immunocompromized hosts

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Two studies

- 1) Children with cancer
Children with cystic fibrosis (CF)
Healthy children
- 2) Adult patients with HIV

General background

- Antimicrobial therapy, including antifungals, change the normal flora
- Severely immunocompromised patients receive antimicrobials more often than other patient groups
- How do antimicrobials affect the normal fungal flora?
- Are these patients more prone to infections with drug resistant organisms?

Background:

Children with cancer (n=45)

- Long periods with neutropenia → infections → massive antibiotic treatment
- Typical antibiotics used in these patients:
 - Ampicillin + gentamycin
 - 3rd gen. cephalosporins, vancomycin, meropenem
 - Metronidazol, fluconazole, amphotericin-B
- Antifungal prophylaxis not common

Background:

Children with CF (n=33)

- Local "immunosuppression" of the lungs → severe lung infections → extensive antibiotic treatment
- Typical antibiotics used in these patients:
 - Oral ampicillin, cefalexin, trim-sulfa
 - Inhaled tobramycin and colistin
 - Intravenous tobramycin, ceftazidim, meropenem, (ciprofloxacin)
- Fungal treatment rare

Background:

Healthy children (n=47)

- Most Norwegian children receive very little antibiotic treatment
- Typical antibiotics used in general practice:
 - Penicillin, ampicillin
 - Erythromycin
 - Trimethoprim

Background:

Patients with HIV (n=107)

- Antimicrobial prophylaxis common:
 - PCP (49: tms 39, dps 5, ptm 5)
 - MAC (3)
- Antimicrobials therapeutically:
 - Antibacterials (9)
 - Fluconazole (5)
- Previous half year:
 - Antibacterials (25 therapeutically, 5 prophylactic)
 - Fluconazole (5)

Patients

- 1999-2000 + 2003-2004: Children with cancer (n=45)
 - From Ullevål and Rikshospitalet University Hospitals
 - 3-10 samples per patient
- 2004-2007: Children with CF (n=33*)
 - From Ullevål University Hospital out patient clinic
 - 4 samples during one year
- 2000-2001 + 2006-2007: Healthy children (n= 47*)
 - From day care centers and schools
 - 3 samples during one year
- 1998-1999: Patients with HIV (n=107)
 - From Ullevål University Hospital out patient clinic
 - 1-3 samples per patient

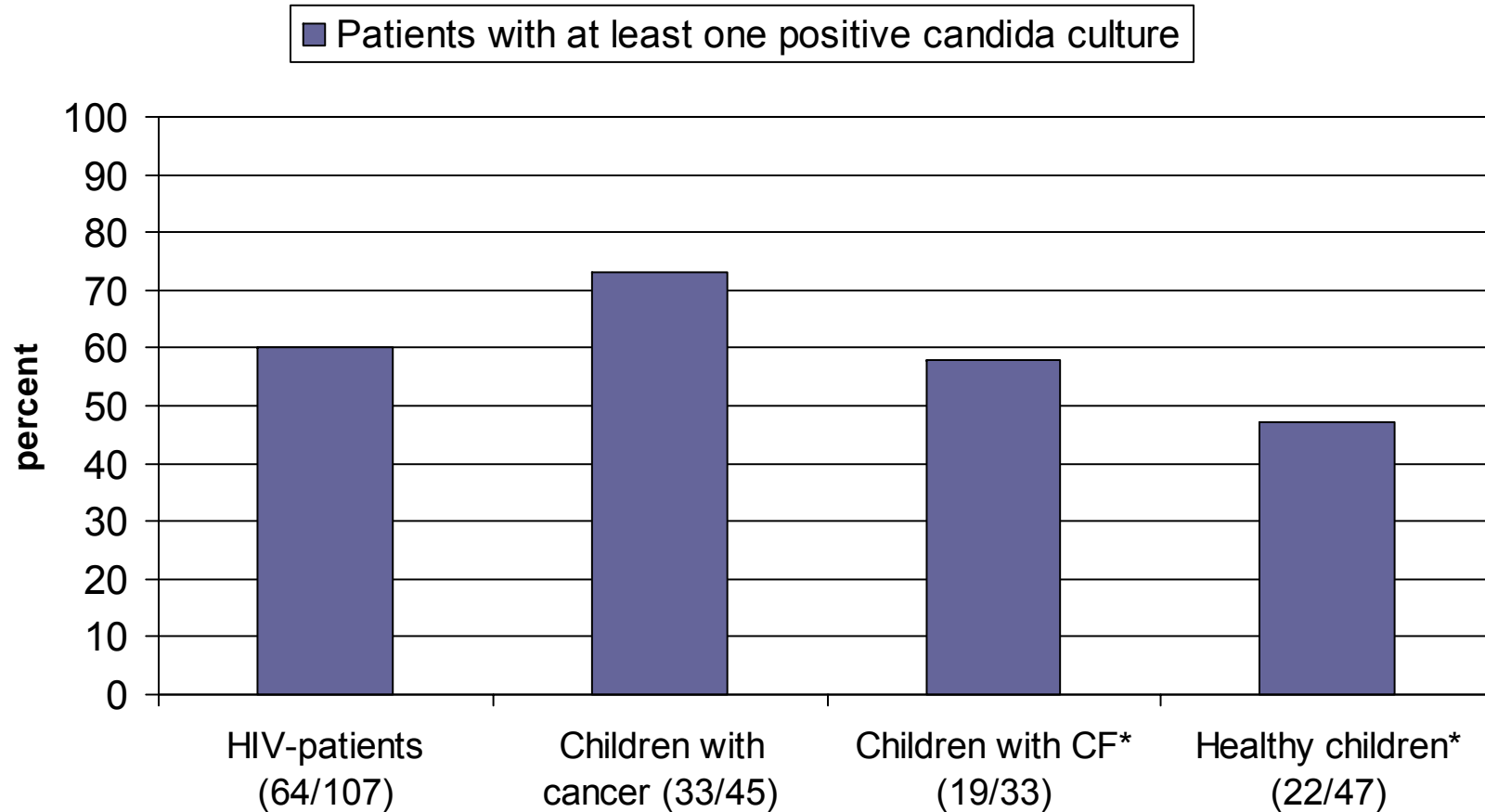
* Goal: 40 and 100 children respectively

Sampling and laboratory methods

- Throat swabs and fecal samples
- Plated out on sabouraud agar plates and incubated at 28°C for 5 days.
- Candida isolates were identified to species level
- Tested for susceptibility to different antifungal drugs.

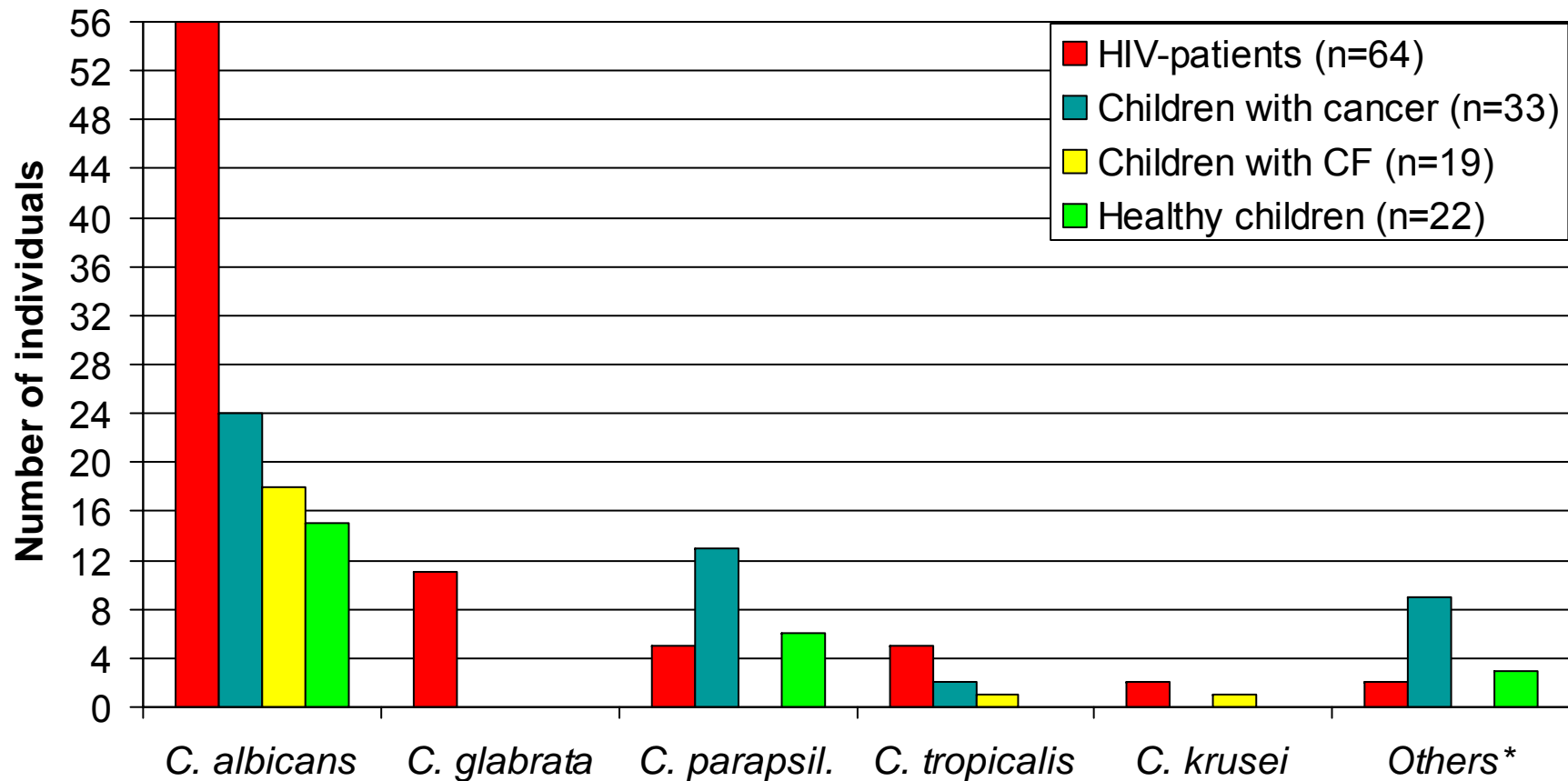
Results

Positive candida cultures



* Preliminary results;
sampling still ongoing

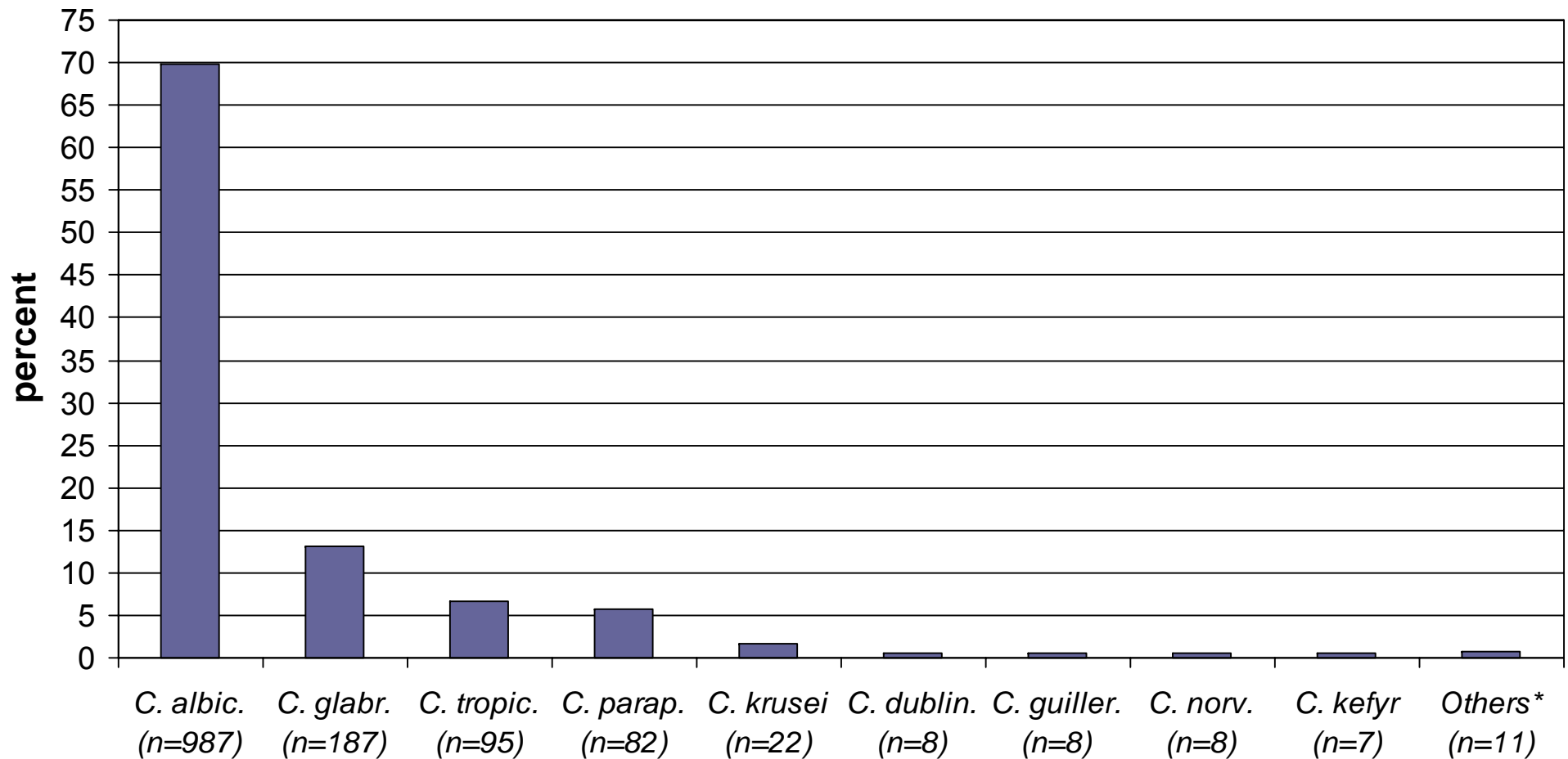
Positive candida cultures



* *C. dubliniensis*, *C. famata*, *C. guilliermondii*, *C. lambica*, *C. lusitaniae*, *C. magnolia*, *C. rugosa*, *C. sphaerica*

Candidemias in Norway 1991-2003

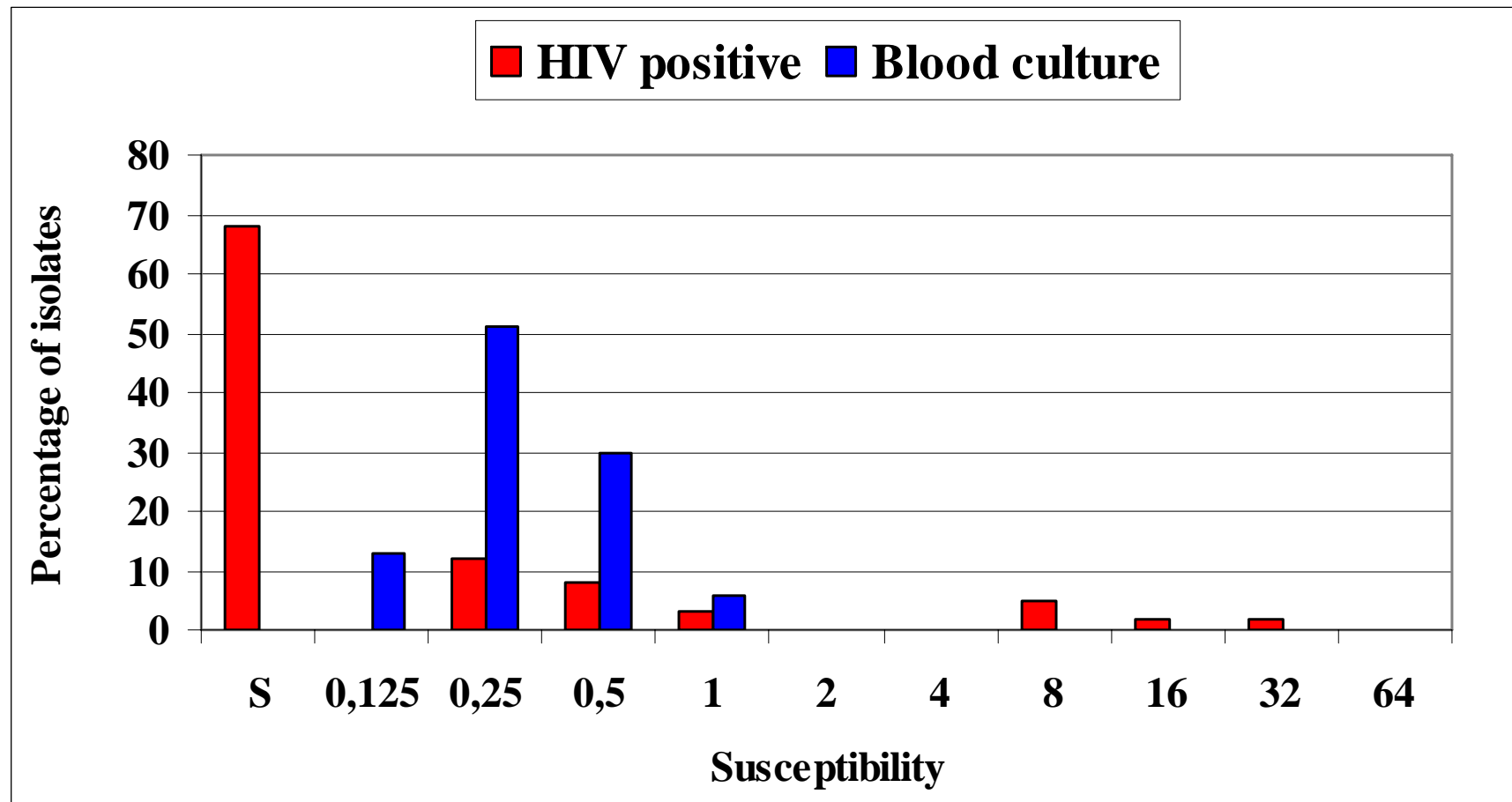
n=1415



Sandven P et al. In press (J Clin Microbiol. 2006 June issue)

* *C. blankii*, *C. inconspic.*, *C. lusitaniae*,
C. Sake, *Candida sp.*, *unspec. yeast*

Susceptibility of *C. albicans* isolates to fluconazole



Risk factors for fluconazole resistance in patients with HIV

- Independent risk factors for carrying *C. albicans* isolates with decreased susceptibility:
 - treatment with antimycotics
 - hospitalisation in the half year prior to the sampling
- Significant relationship between fluconazole use and the isolation of *Candida* species other than *C. albicans*
- Similar finding by others:
 - Sandven P et al. Antimicrob Agents Chemother. 1993;37:2443.
 - Sobel JD et al. J Infect Dis. 2001;183:286
 - ...and many other publications...

Conclusion

- *Candida* carriage seems to be very common, both in the adult and paediatric population.
- *C. albicans* is by far the most dominating species, and for the most part completely susceptible to fluconazole except for 5 strains found in 5 different HIV-patients.
- However, several other *Candida*-species and yeast species less susceptible to fluconazole were often present. These are frequently found fungemias in paediatric cancer patients*

*Krupova Y et al. Support Care Cancer. 2000 Sep;8:427

Mullen CA et al. Support Care Cancer. 2003 May;11:321

Conclusion

- How do antimicrobials affect the normal fungal flora?
 - **Reduced susceptibility in some species and strains**
- Are immunocompromized patients more prone to infections with drug resistant organisms?
 - **Yes** (in many cases, anyway)

Thank you!

