



What's New from the CDC?

Benjamin Park, MD

Mycotic Diseases Branch

U.S. Centers for Disease Control and
Prevention, Atlanta, Georgia

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CDC Mycotic Diseases Branch Epidemiology Team Staff

- Tom Chiller MD MPH – Team Leader
- Ben Park MD – Medical Epidemiologist
- Julie Harris, PhD - Epidemiologist
- Loretta Chang, MD, MPH – EIS Officer
- Debra Wagner MSPH – OTIP Coordinator
- Angela Ahlquist, MPH – Surveillance Epi

- Shawn Lockhart, PhD – Antifungals Unit
- Arun Balajee, PhD – Molecular Epi Unit
- Beatriz Gomez, PhD – Diagnostics Development Unit

Outbreaks and Investigations

Outbreak of Histoplasmosis- Iowa 2008

Initial Investigation

- 2 employees of “Office A” diagnosed with histoplasmosis within 2 days by a local MD
- Local health department finds
 - 7 of 9 had histo
- Investigation into Office A building begun
 - Shares courtyard with Office B
 - Recent landscaping

Initial Investigation Results

- Office A employees
 - 78% (7/9) had laboratory evidence
- Office B employees
 - 0% (0/15) had laboratory evidence
- 19 environmental samples tested by mouse peritoneal inoculation
 - All negative
- Was the office building the source?

Further Investigation

- Contacted other Office A employees who did not work at that office
- 23 Office A employees
 - 11 attended Office A awards ceremony at Governor's mansion
 - All were symptomatic and had laboratory evidence of histoplasmosis

Governor's Mansion

- Des Moines, Iowa
- Host tour groups, ceremonies and official dignitaries



51 Cases High Severity of Illness

Characteristic (N=51)	No.	%
Median estimated time to resolution of symptoms (95% CI)*	56 days	(53-58 days)
Ongoing symptoms at time of interview	21	58
Hospitalizations	0	0

*Kaplan-Meier Survival Analysis

Cohort Study

- Risk factors for infection
- Multivariable model
 - Outside during ceremony
 - RR_{adj} 3.3 (95% CI 1.6-6.8)
 - 4:00pm and 5:30pm
 - RR_{adj} 2.4 (95% CI 1.2-4.9)

Main Entrance on November 29



Environmental Sampling



Type of Sample	Results
Air Filter	Negative
Air Filter	Negative
Filter	Negative
Filter cassette	Negative
Bat Guano	Negative
Bat Guano	Negative
HVAC filter	Negative
HVAC filter	Negative
Soil	Negative

Probable Source

- Construction activity causing aerosolization of dust near main entrance
 1. Activity in attic disturbed bat guano
 2. Boards dropped down chute
 3. Digging grounding pits
- Ceremony attendees entered or spent time outside mansion via main entrance

Other Investigations

- Donor derived IFIs
 - Coccidioidomycosis (CA), zygomycosis (NC)
- Cluster of *C. neoformans* among immunocompetent persons in NC
- High cocci rates in a metro Phoenix community (AZ)
- Cocci among prison guards, CA
- Nosocomial *Aspergillus* in Neonatal ICU (England)

Subtyping Fungi for Outbreaks

- Subtyping is an essential component of public health
 - *Fusarium* keratitis contact lens solution outbreak
- Many subtyping methods exist, but best method for outbreaks not clear
- Led by Dr. Arun Balajee
 - Currently working on *Aspergillus*, *Candida*, *Zygomycetes*, *Coccidioides*
- Co-organizing meeting (fall 2009)
 - Methods for subtyping *Candida*, *Aspergillus* in outbreak settings
 - All are invited, look for announcements later in year

Long-Term Studies

TRANSNET

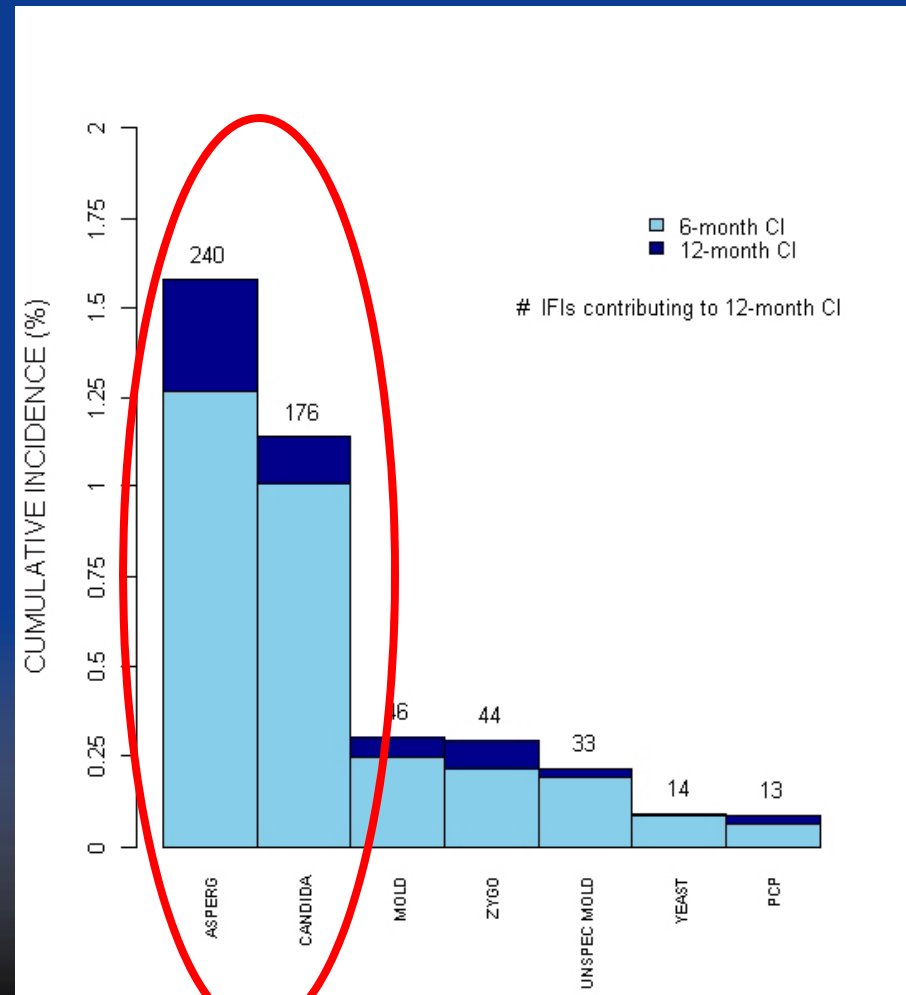
- 23 U.S. Transplant centers
- Prospective surveillance for proven/ probable IFIs
 - Hematopoietic stem cell transplants
 - Solid organ transplants
- 2001-2006
- Unique: enrolled and performed follow-up
 - 16,808 OTRs
 - 15% of all U.S. solid organ transplants
 - 16,220 HSCTs
 - 20% of all U.S. stem cell transplants

IFIs in TRANSNET

- 1,208 proven/ probable IFIs in OTRs
 - 639 invasive *Candida*
 - 227 *Aspergillus*
 - 97 *Cryptococcus*
- 983 in HSCTs
 - 425 *Aspergillus*
 - 276 *Candida*
 - 77 zygomycosis

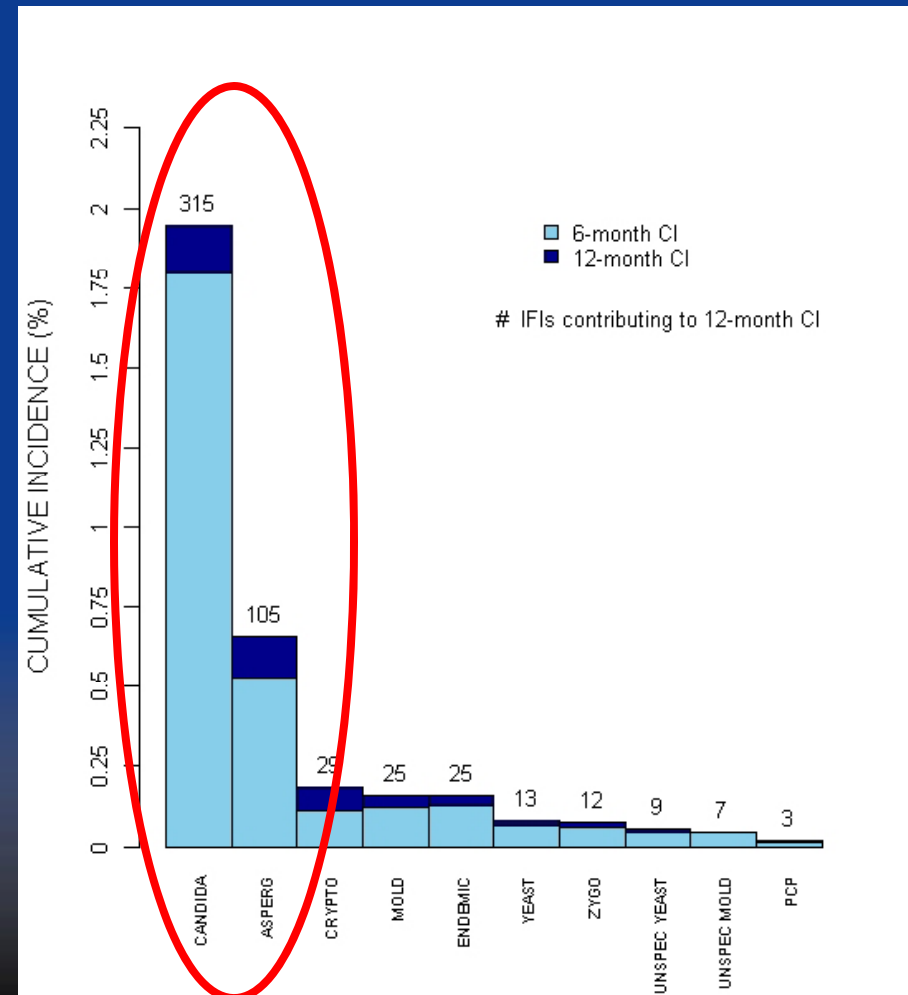
Incidence in HSCT

- 12-month cumulative incidence post-transplant
 - For any IFI: 3.4%
 - *Aspergillus*: 1.6%
 - *Candida*: 1.1%



Incidence in OTR

- 12-month cumulative incidence post-transplant
 - For any IFI: 3.1%
 - *Candida*: 1.9%
 - *Aspergillus*: 0.7%

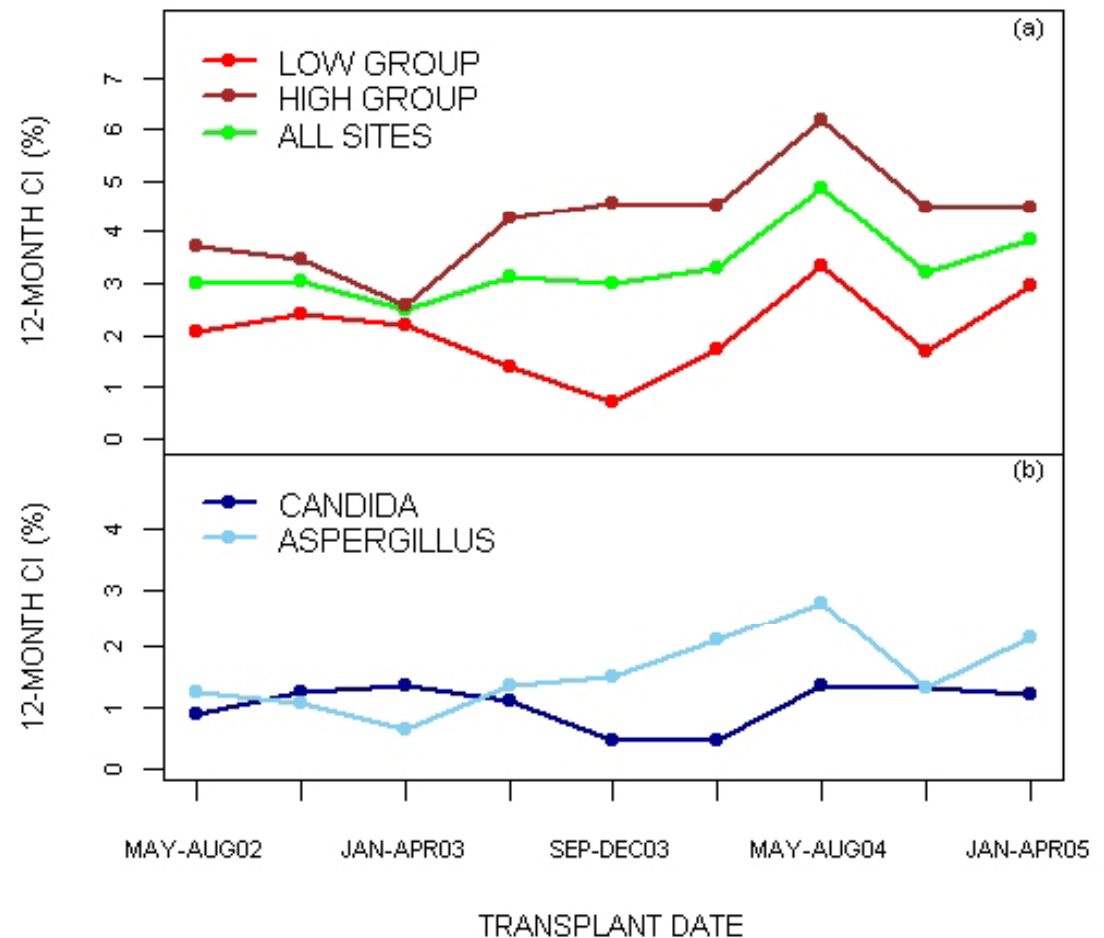


Is Incidence Lower than Reported?

- Other reports- higher incidence
- Actually large site-to-site variability
 - Range in SCTs= 0.9% - 13.2%
- Diverse institutions, not all high risk transplants
- Likely variability in case finding or diagnostic methods

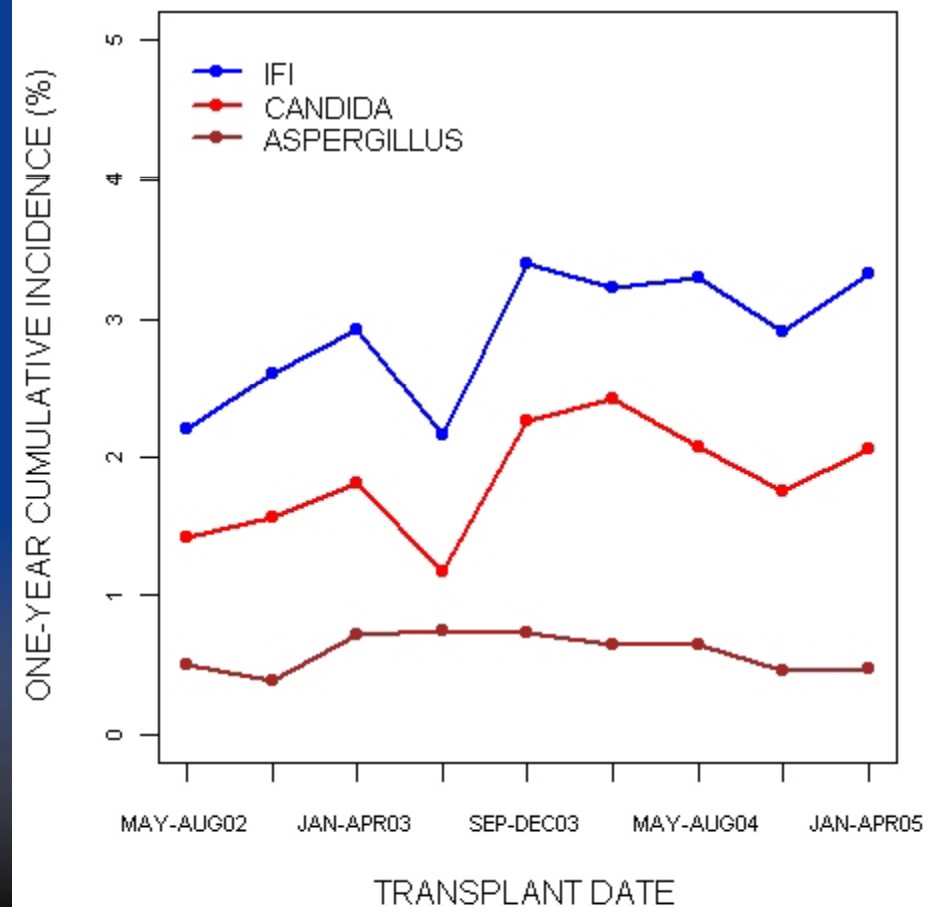
Trend in 12-month CI: SCT

- Split to “low risk” and “high risk” site groups according to % allo HSCTs
 - No clear increase or decrease by site
- By organism
 - No increase in *Candida*
 - Increase in *Aspergillus*?



OTR: Trend in 12-month CI

- By organism
 - No increase in *Aspergillus*
 - Increase in *Candida*



Conclusions- TRANSNET

- IFIs in transplant recipients remain a substantial problem
 - *Candida* in OTR
 - *Aspergillus* in HSCT
- Epidemiology may be shifting
 - No decrease in incidence, even in age of prophylaxis
 - *Candida* may be increasing in OTR
 - *Aspergillus* may be increasing in HSCT

Candidemia in United States

- *Candida*- 3rd or 4th most common nosocomial BSI
- Incidence approximately 10 cases/ 100,000 population
 - Determined by CDC population-based surveillance

Population-Based Surveillance

- All cases in a certain defined area (usually geographic) are counted
 - Only residents of the area
- Population is defined (denominator)
 - Census
- Incidence can be calculated
 - Numerator= number of cases among residents
 - Denominator= population
- Resource-intensive, but accurate representation of truth

Candida Surveillance Overview

- CDC population-based surveillance
 - 1992-93: Atlanta and Houston
 - 1998-2000: Baltimore and Connecticut
 - 2008-2010: Atlanta and Baltimore
- Atlanta surveillance start date: March 01, 2008
 - 25 hospitals in 8 counties, population = 3.6 million
- Baltimore surveillance start date: May 01, 2008
 - 15 hospitals in Baltimore city/ county, population = 1.4 million
- To date, 821 cases detected total

Baltimore

Preliminary *Candida* Sp.

Species	2008-2010*	1998-2000
Total cases	273	680
<i>Candida albicans</i>	98 (36)	289 (43)
<i>Candida glabrata</i>	66 (24)	188 (28)
<i>Candida parapsilosis</i>	60 (22)	72 (11)
<i>Candida tropicalis</i>	38 (14)	98 (14)
<i>Candida krusei</i>	11 (4)	--
Other	19 (7)	33 (5)

Atlanta

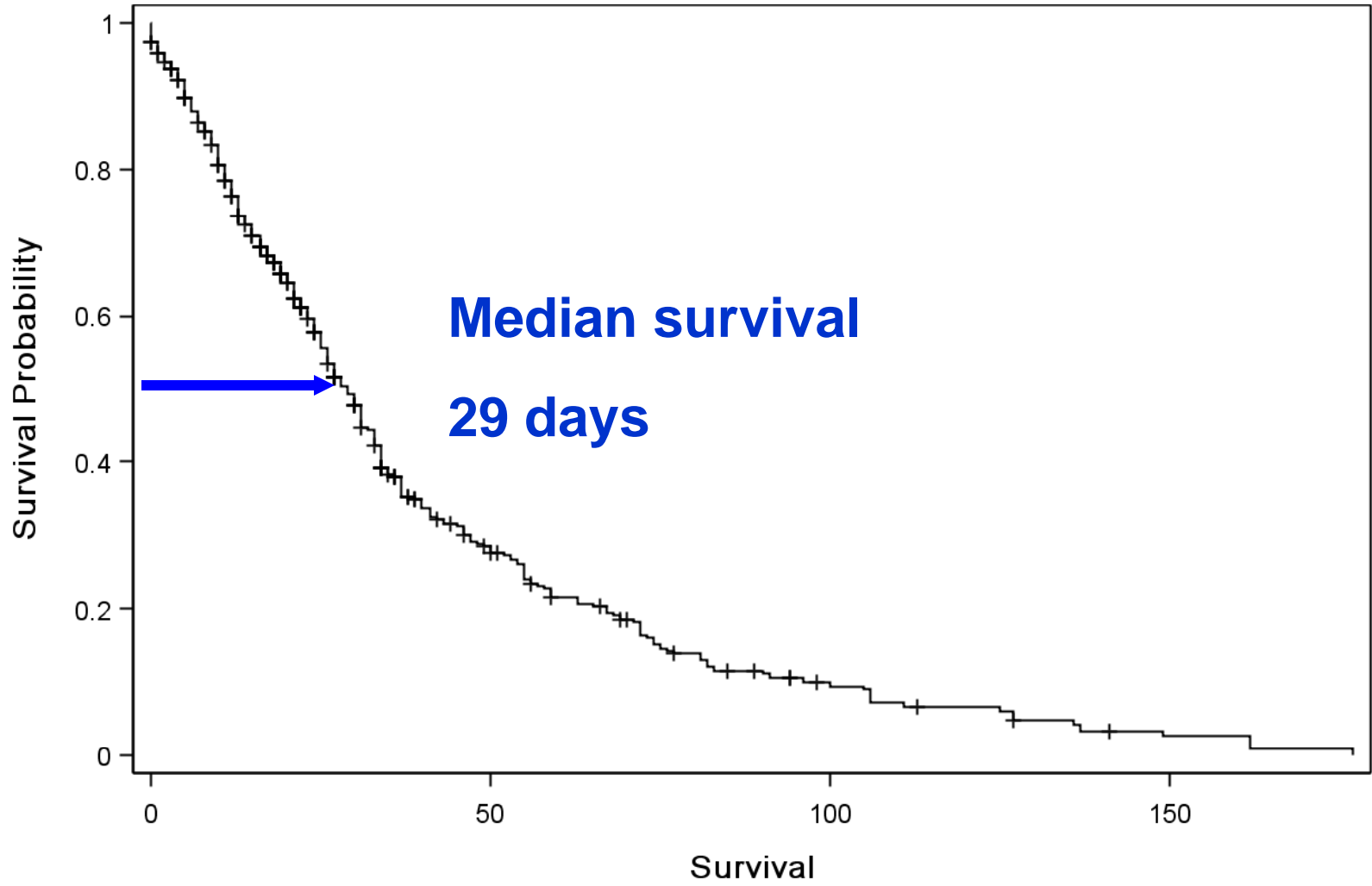
Preliminary *Candida* Sp.

Species	2008-2010*	1992-1993 ATL only ^a
<i>Total cases</i>	375	428
<i>Candida albicans</i>	143 (38)	230 (54)
<i>Candida glabrata</i>	120 (32)	49 (11)
<i>Candida parapsilosis</i>	64 (17)	79 (18)
<i>Candida tropicalis</i>	34 (9)	42 (10)
<i>Candida krusei</i>	4 (1)	5 (1)
<i>Other</i>	10 (3)	23 (5)

Antifungal Treatment (n=554)

Antifungal	N	%
Fluconazole	271	48.92
Micafungin	114	20.58
Caspofungin	100	18.05
Anidulafungin	24	4.33
Voriconazole	20	3.61
Amphotericin B deoxycholate	9	1.62
Amphotericin B lipid complex	8	1.44
Liposomal amphotericin B	3	0.54
Amphotericin B colloidal dispersion	2	0.36
Itraconazole	1	0.18
Flucytosine	1	0.18
Posaconazole	1	0.18

Product-Limit Survival Function Estimate



No. of Subjects	Event	Censored	Median Survival (95% CL)
418	75% (312)	25% (106)	29.00 (26.00 32.00)

Preliminary FLU Susceptibility- All species

Year	Site	Drug	MIC50	MIC90
1992-3	Atlanta/ SF	FLU	0.5	16
1998-00	Baltimore/ CT	FLU	0.5	8
2008	Atlanta	FLU	2	32
	Baltimore	FLU	2	32

C. glabrata

- Dramatic rise in *C. glabrata* isolates susceptible-dose-dependent or resistant to Fluconazole
- S - DD 52% (prev. 26%)
- R 16% (prev. 13%)

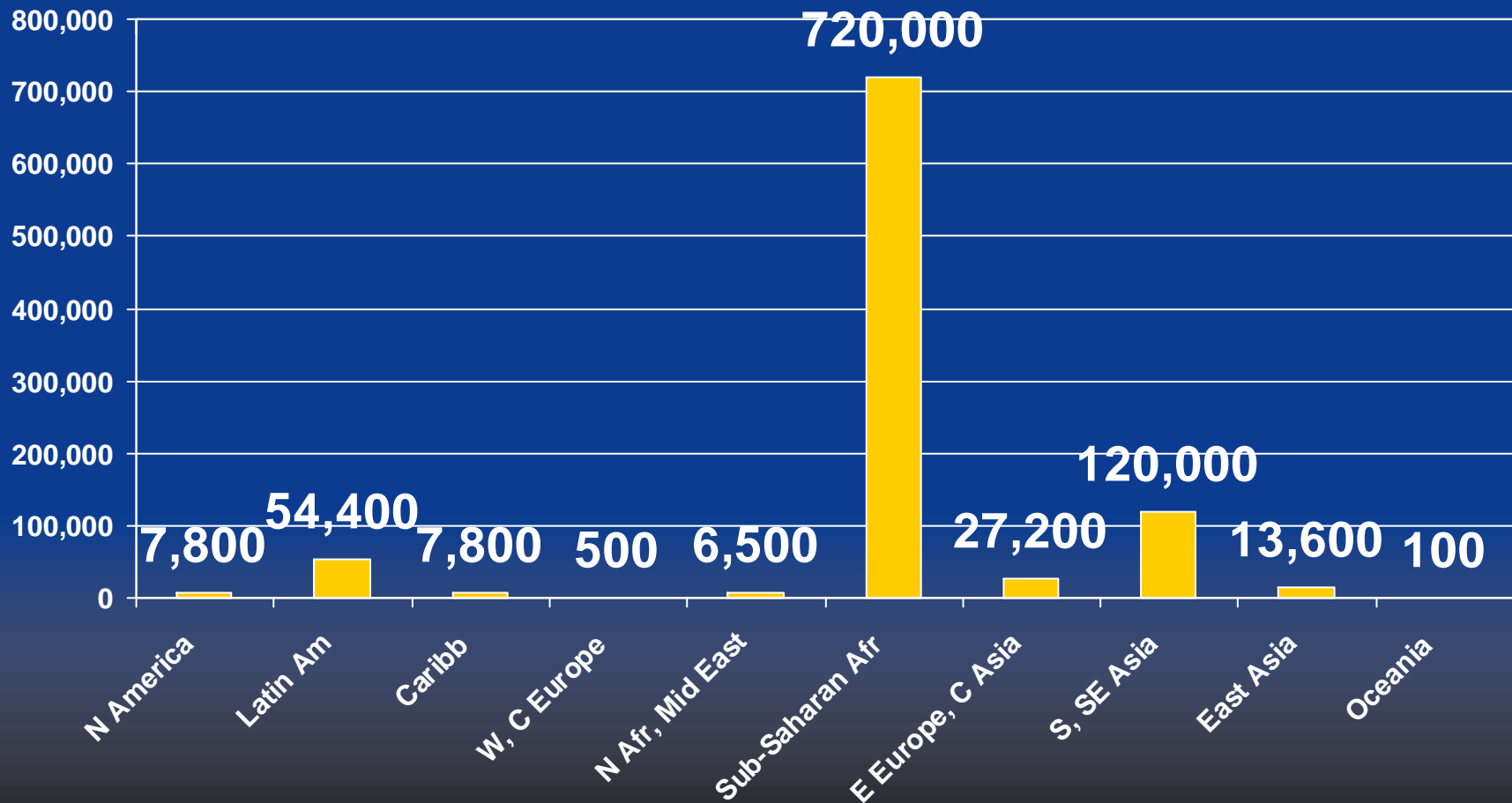
- Additional 7 isolates resistant (Atlanta) to all azoles, and one or more echinocandins

Cryptococcus in HIV Globally

- One of the most important HIV-related OIs
- Probably very common
- How to place in context of other diseases?
- Calculate the global burden of disease*
 - Frequently performed by public health agencies
 - Important to plan and prioritize needed resources for disease prevention and control

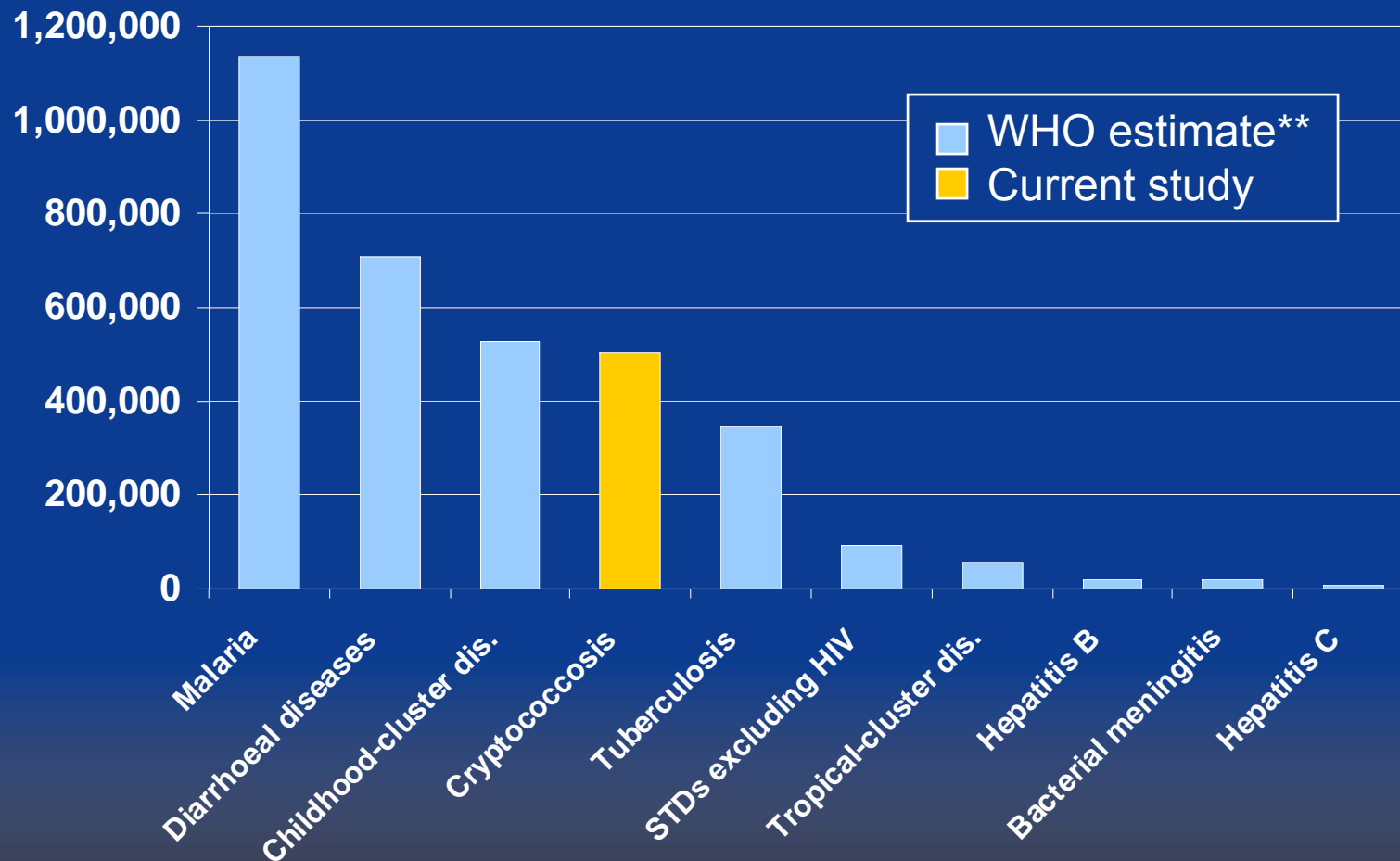
Benjamin J. Park, Kathleen A. Wannemuehler, Barbara J. Marston, Nelesh Govender, Peter G. Pappas, and Tom M. Chiller, Estimation of the current global burden of cryptococcal meningitis among persons living with HIV/AIDS. *AIDS* 2009 23:525-30.

Approximately 1M Cases/ Yr Globally



*Park BJ, Wannemuehler KA, Marston B, et al. AIDS 2009

Sub-Saharan Africa- Estimated Deaths/ Yr



*Park BJ, Wannemuehler KA, Marston B, et al. AIDS 2009

*Excluding HIV/ AIDS

**WHO. Revised Global Burden of Disease (GBD) 2002 Estimates. 2002 [Available from: <http://www.who.int/healthinfo/bodgbd2002revised/en/index.html>].

More Work Needed

- CDC is working with partners to explore best prevention methods
 - Primary prophylaxis- no studies in SSA
 - Pre-emptive treatment using serum CrAg as screening
- More efforts sorely needed
 - Tracking epidemiology of disease
 - Improved diagnostics
 - Optimize treatment strategies in many areas

Other Studies

- *Cryptococcus gattii* in Pacific NW
- Organ Transplant Infection Project (OTIP) – cohort study of lung and allo stem cell transplants
- Invasive mold infections in Japan
- Burden of coccidioidomycosis in Arizona
- More to come...

Future Directions and Challenges in Public Health Mycology

- Subtyping methods for use in outbreaks
- Emerging molds
 - How to perform surveillance and identify trends
- Prevention of endemic mycoses
 - PPE? Avoiding exposure?
- Environmental sources/ testing

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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