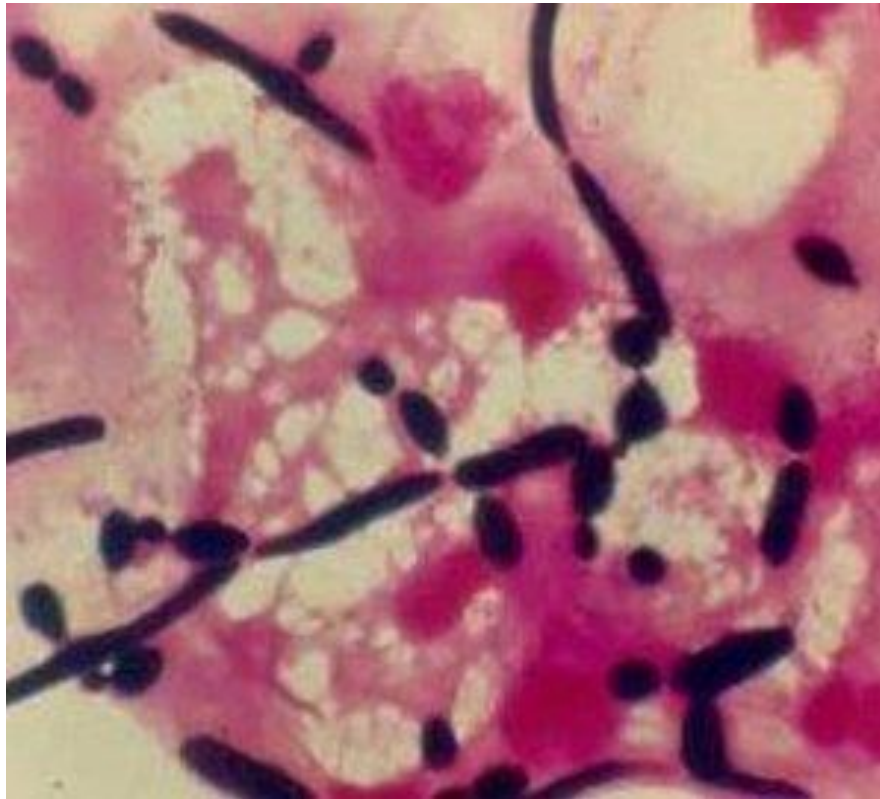


Antifungal Susceptibility of Invasive *Candida* Isolates from Canadian Hospitals: Results of the CANWARD 2013 Study

J. FULLER¹, S. SHOKOPLES¹, L. TURNBULL¹, R. RENNIE¹, H. ADAM^{2,3},
M. BAXTER², D. J. HOBAN^{2,3} and G. G. ZHANEL²

¹ Provincial Laboratory, Alberta Health Services, University of Alberta, Edmonton, AB; ² Medical Microbiology and Infectious Diseases, University of Manitoba, Winnipeg, MB; ³ Diagnostic Services of Manitoba, Winnipeg, MB

Candidemia



Canadian Surveillance of Candidemia

- Several published Canadian surveillance studies
 - 2006 is the most recent study period reported
 - Most are single-centre, retrospective
- Species distribution comparable to other studies and unchanging
 - *C. albicans* > *C. glabrata* > *C. parapsilosis*
- Activity of antifungal agents in vitro were excellent
 - No significant resistance issues identified with azoles and AmB
 - Echinocandins experience was limited (new class)

CANWARD

- A national population-based surveillance study of pathogens and antimicrobial susceptibility in medical centres across Canada
 - Coordinated out of HSC, University of Manitoba
- Invasive *Candida* surveillance
 - Characterize the species and MIC distribution of *Candida spp.* causing candidemia
 - 2007, 2010
 - **2011 to 2013**
 - Central test site, University of Alberta Hospital, Edmonton

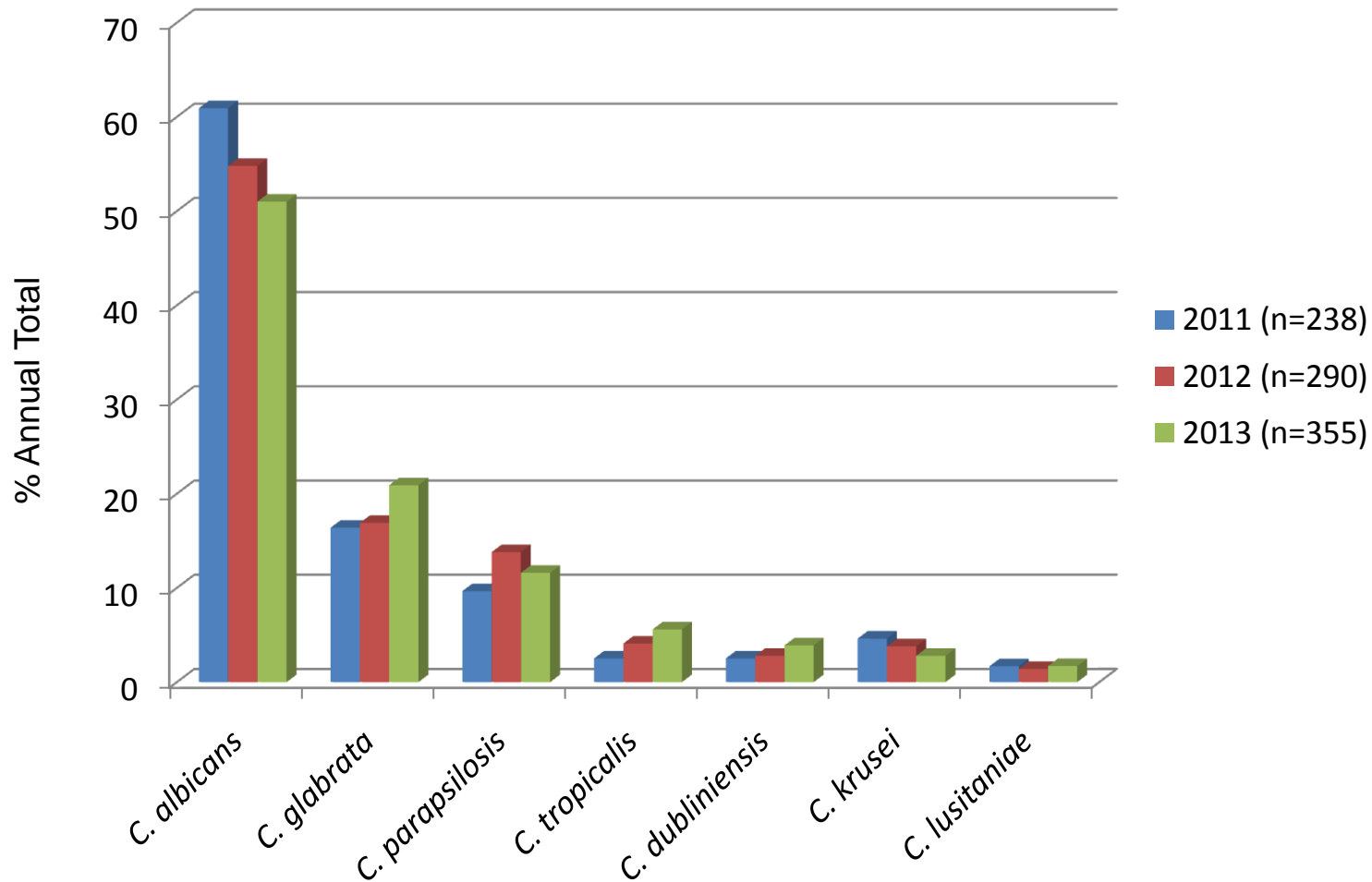
Methods – CANWARD 2011 to 2015

- Participating sites:
 - Tertiary care medical centres from 8 provinces
 - 12 clinical laboratories
- Isolate collection and inclusion:
 - *Candida* isolated from automated blood cultures
 - Patients attending hospital clinics, emergency rooms, medical/surgical wards, and intensive care units
- Antifungal susceptibility testing:
 - CLSI M27-S4, Broth microdilution guidelines

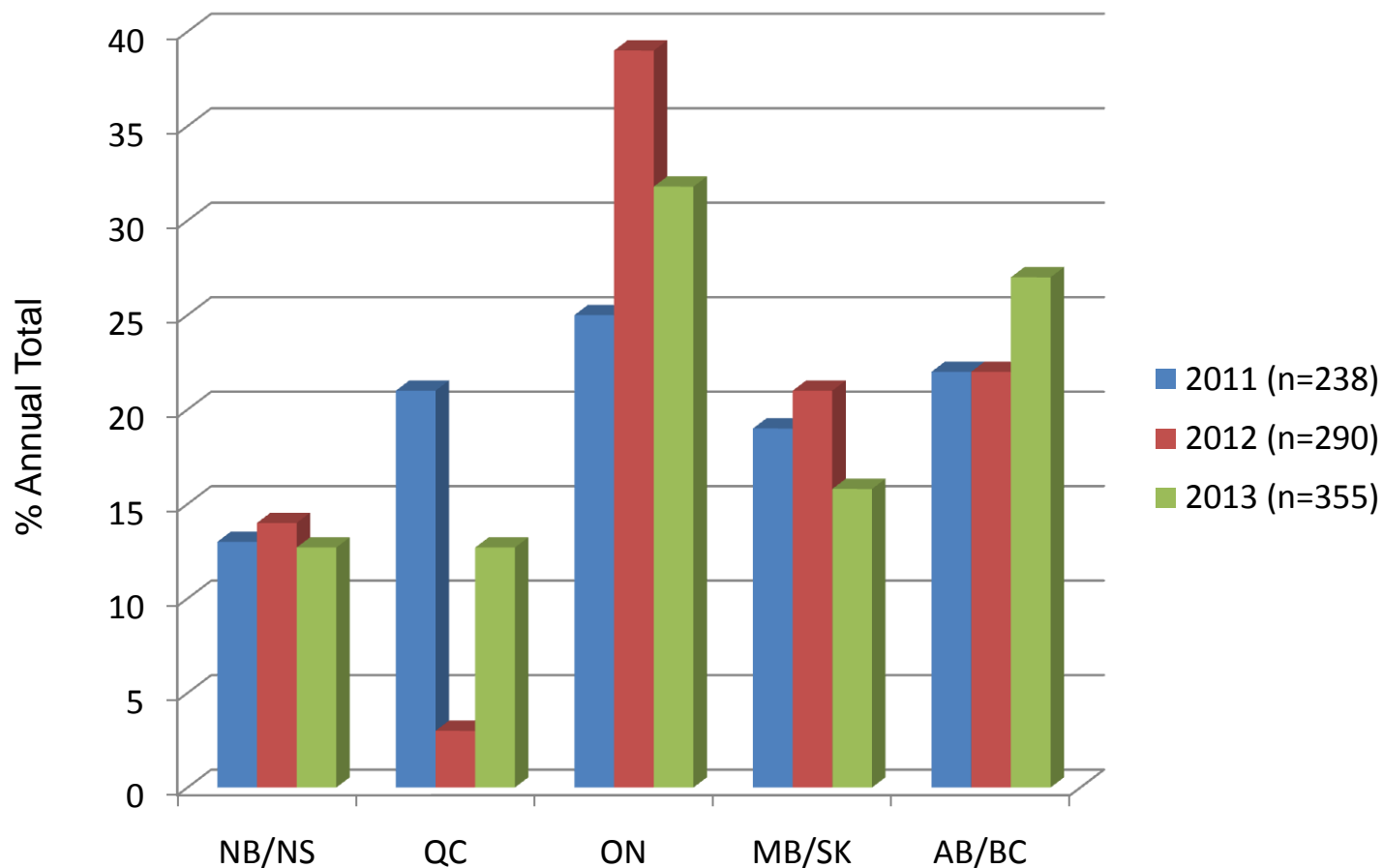
CANWARD Participating Investigators / Centres

- Dr. D. Roscoe – Vancouver Hospital, Vancouver
- Dr. R. Rennie/J. Fuller – University of Alberta Hospital, Edmonton
- Dr. J. Blondeau – Royal University Hospital, Saskatoon
- Drs. D.J. Hoban/G.G. Zhanel – Health Sciences Centre, Winnipeg
- Dr. M. John– London Health Sciences Centre, London
- Dr. S. Poutanen – University Health Network / Mount Sinai Hospital, Toronto
- Dr. L. Matukas – St. Michael's Hospital, Toronto
- Dr. F. Chan – Children's Hospital of Eastern Ontario, Ottawa
- Dr. M. Desjardins – The Ottawa Hospital, Ottawa
- Dr. M. Laverdière – Hôpital Maisonneuve-Rosemont, Montreal
- Dr. M. Goyette – CHRTR Pavillon Ste. Marie, Trois-Rivières
- Dr. M. Kuhn – South East Regional Health Authority, Moncton
- Dr. R. Davidson – Queen Elizabeth II HSC, Halifax

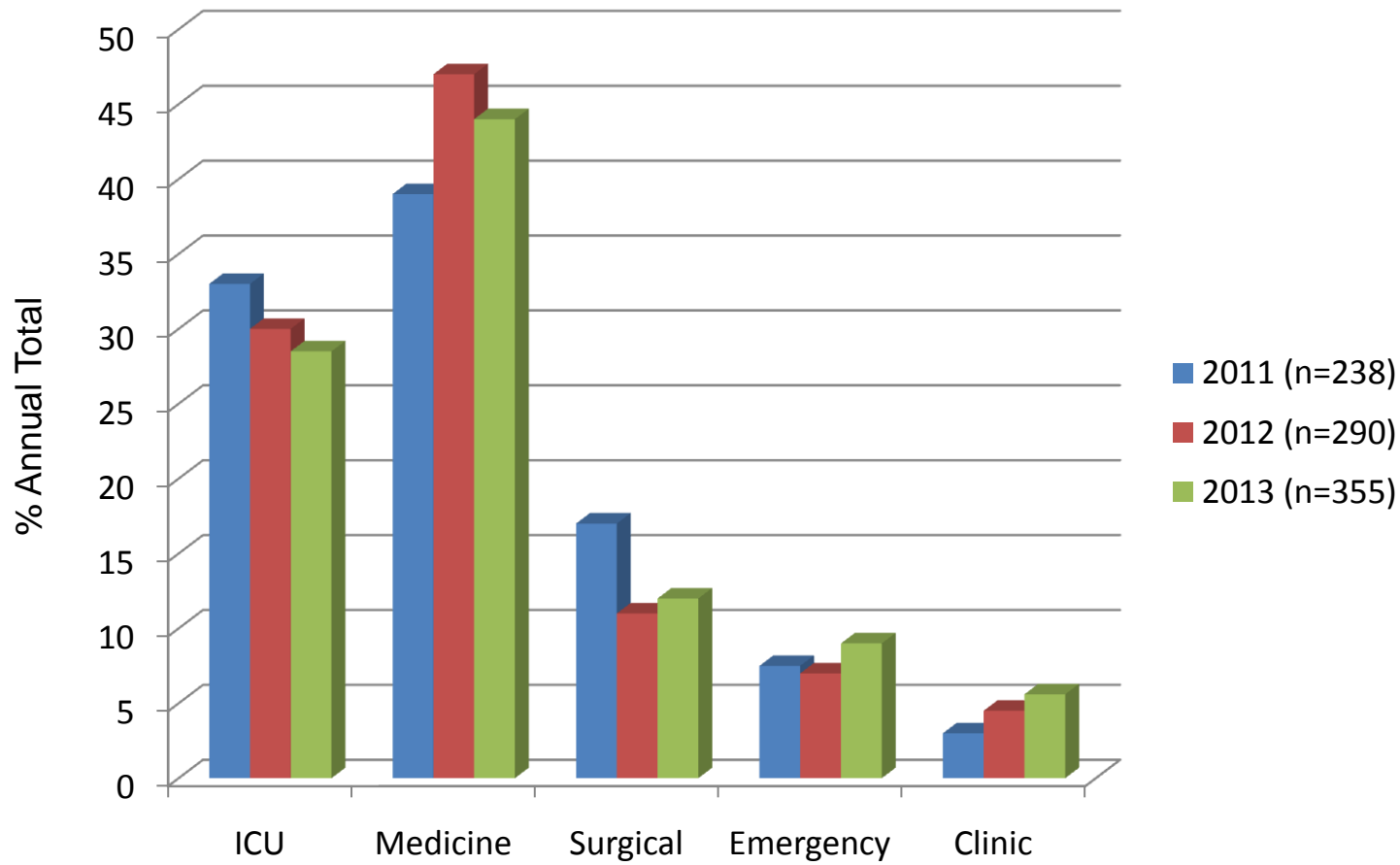
Temporal Distribution of the Most Common *Candida* Species Causing Candidemia



Geographic Distribution of Surveillance Isolates

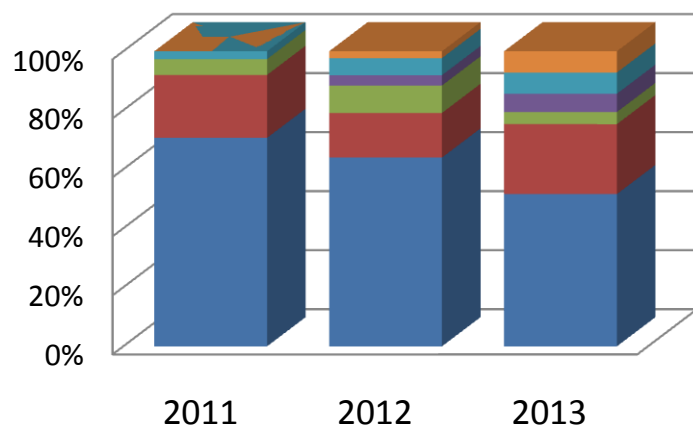


Distribution of *Candida* Species Causing Candidemia Based on Patient Location

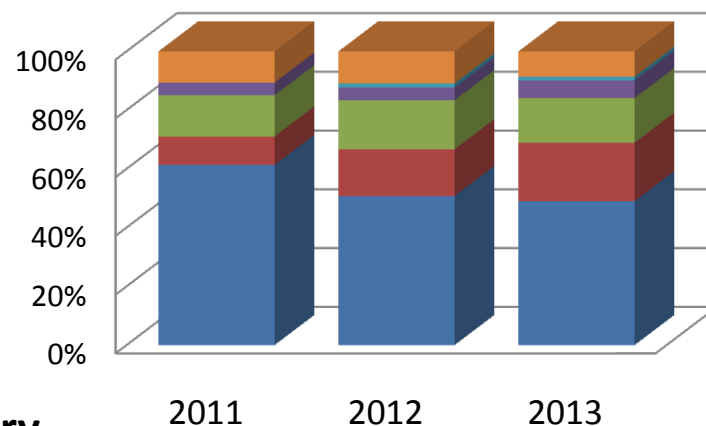


Rank Distribution of the Most Common Species by Ward per Year

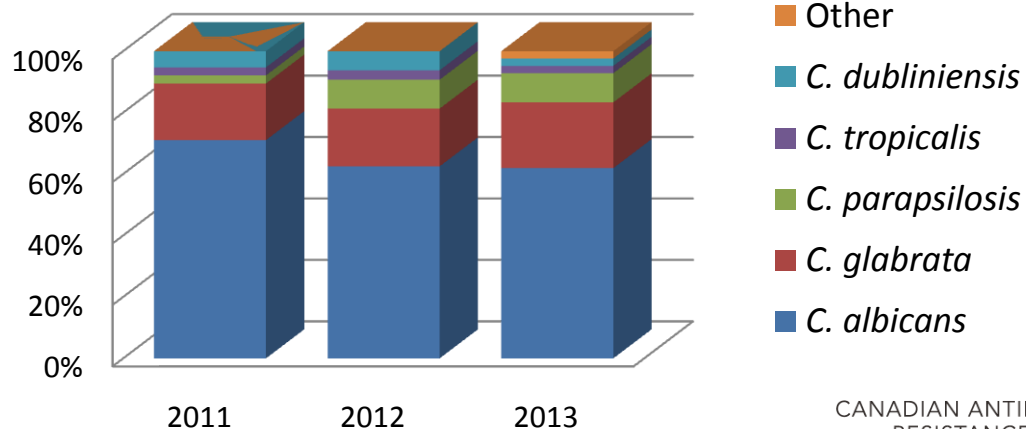
ICU



Medicine



Surgery



C. albicans MIC Distribution Summary

Species	Agent	Year	No. Tested	Mode	MIC90	Geom Mean	CBP	% Non-susceptible (#)
<i>C. albicans</i>	MICA	2011	145	0.015	0.015	0.015	≤0.25	0
		2012	159	0.007	0.007	0.007	≤0.25	0.63 (1)
		2013	181	0.007	0.007	0.008	≤0.25	0
	CASP	2011	145	0.015	0.06	0.021	≤0.25	1.38 (2)
		2012	159	0.03	0.125	0.038	≤0.25	0
		2013	181	0.007	0.125	0.03	≤0.25	0.55 (1)

Echinocandin MIC Distribution Against *C. albicans*

Year (no. tested)	Agent	Number of Isolates at MIC												
		0.007	0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32
2011	MICA		144	0	0	0	1							
(145)	CASP		112	13	9	8	1	2						
2012	MICA	152	5	1	0	0	0	1						
(159)	CASP	19	32	40	29	28	11							
2013	MICA	163	13	4	0	0	1							
(181)	CASP	51	28	26	34	31	10	1						

C. glabrata MIC Distribution Summary

Species	Agent	Year	No. Tested	Mode	MIC90	Geom Mean	CBP	% Non-susceptible (#)
<i>C. glabrata</i>	MICA	2011	39	0.015	0.015	0.016	≤0.06	2.56 (1)
		2012	49	0.007	0.015	0.010	≤0.06	0
		2013	74	0.007	0.015	0.011	≤0.06	6.76 (5)
	CASP	2011	39	0.25	0.5	0.166	≤0.12	
		2012	49	0.25	0.5	0.261	≤0.12	
		2013	74	0.25	0.5	0.254	≤0.12	

Echinocandin MIC Distribution Against *C. glabrata*

Year (no. tested)	Agent	Number of Isolates at MIC												
		0.007	0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32
2011	MICA		37	1	0	1								
(39)	CASP		2	2	1	12	17	4	1					
2012	MICA	38	8	3	0	0								
(49)	CASP	1	1	2	0	1	29	14	1	0				
2013	MICA	55	12	2	0	2	0	2	0	0	1			
(74)	CASP	1	0	1	1	12	42	12	4	0	1			

Interlaboratory Variability of Caspofungin MICs for *Candida* Species

- Unacceptably high interlaboratory variation in caspofungin MIC values for *Candida* species increasingly being reported
 - Modal MIC values differ by up to 5 doubling dilutions
 - Effect most severe with *C. glabrata*
- Source of variation has yet to be identified
 - Limited number of laboratories contributing to MIC data pool used for CBP analysis likely prevented earlier discovery
- Evidence sufficient to allow micafungin as surrogate marker to predict susceptibility

Pfaller et al. JCM. 2014;52:108-114.

Espinel-Ingroff et al. AAC. 2013;57:5836-5842.

C. albicans MIC Distribution Summary

Species	Agent	Year	No. Tested	Mode	MIC90	Geom Mean	CBP	% Non-susceptible (#)
<i>C. albicans</i>	FLUC	2011	145	0.125	0.25	0.149	≤2	1.38 (2)
		2012	159	0.125	0.25	0.175	≤2	1.26 (2)
		2013	181	0.125	0.25	0.147	≤2	0
	VORI	2011	145	0.015	0.015	0.018	≤0.12	1.38 (2)
		2012	159	0.015	0.015	0.016	≤0.12	0.63 (1)
		2013	181	0.015	0.015	0.016	≤0.12	0

Azole MIC Distribution Against *C. albicans*

Year (no. tested)	Agent	Number of Isolates at MIC												
		0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	>64
2011	FLUC			15	109	12	3	1	3	0	0	0	0	2
(145)	VORI	138	0	4	1	0	0	0	0	0	0	2		
2012	FLUC			5	86	63	3	0	0	0	1	0	0	1
(159)	VORI	153	3	0	2	0	0	0	0	0	0	1		
2013	FLUC			17	110	49	4	0	1					
(181)	VORI	170	9	2	0	0								

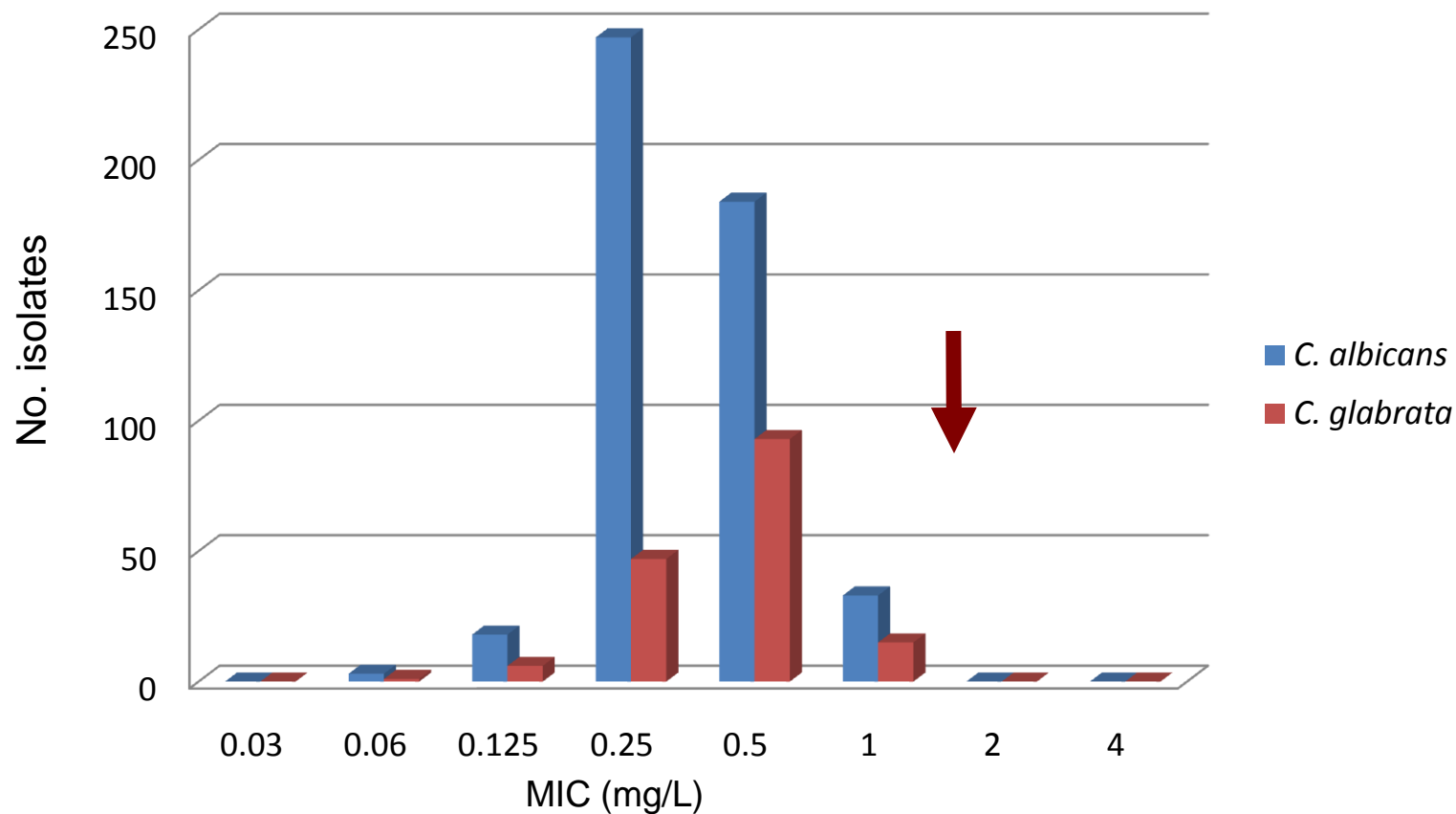
C. glabrata MIC Distribution Summary

Species	Agent	Year	No. Tested	Mode	MIC90	Geom Mean	CBP (ECV)	% Non-susceptible (#)
<i>C. glabrata</i>	FLUC	2011	39	4	4	1.79	≤32	0
		2012	49	2	8	2.65	≤32	0
		2013	74	2	4	2.78	≤32	4.05 (3)
	VORI	2011	39	0.06	0.25	0.079	(≤0.5)	2.56 (1)
		2012	49	0.125	0.25	0.125	(≤0.5)	2.04 (1)
		2013	74	0.06	0.25	0.100	(≤0.5)	8.11 (6)

Azole MIC Distribution Against *C. glabrata*

Year (no. tested)	Agent	Number of Isolates at MIC												
		0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64
2011	FLUC			1	4	0	4	2	10	15	1	0	2	
(39)	VORI	4	6	12	10	3	3	1						
2012	FLUC					1	2	4	18	18	5	1		
(49)	VORI	1	3	12	19	12	1	0	1					
2013	FLUC				2	2	5	8	24	20	3	2	5	3
(74)	VORI	5	9	26	18	5	5	3	3					

Amphotericin B MIC Distribution Against *C. albicans* and *C. glabrata*



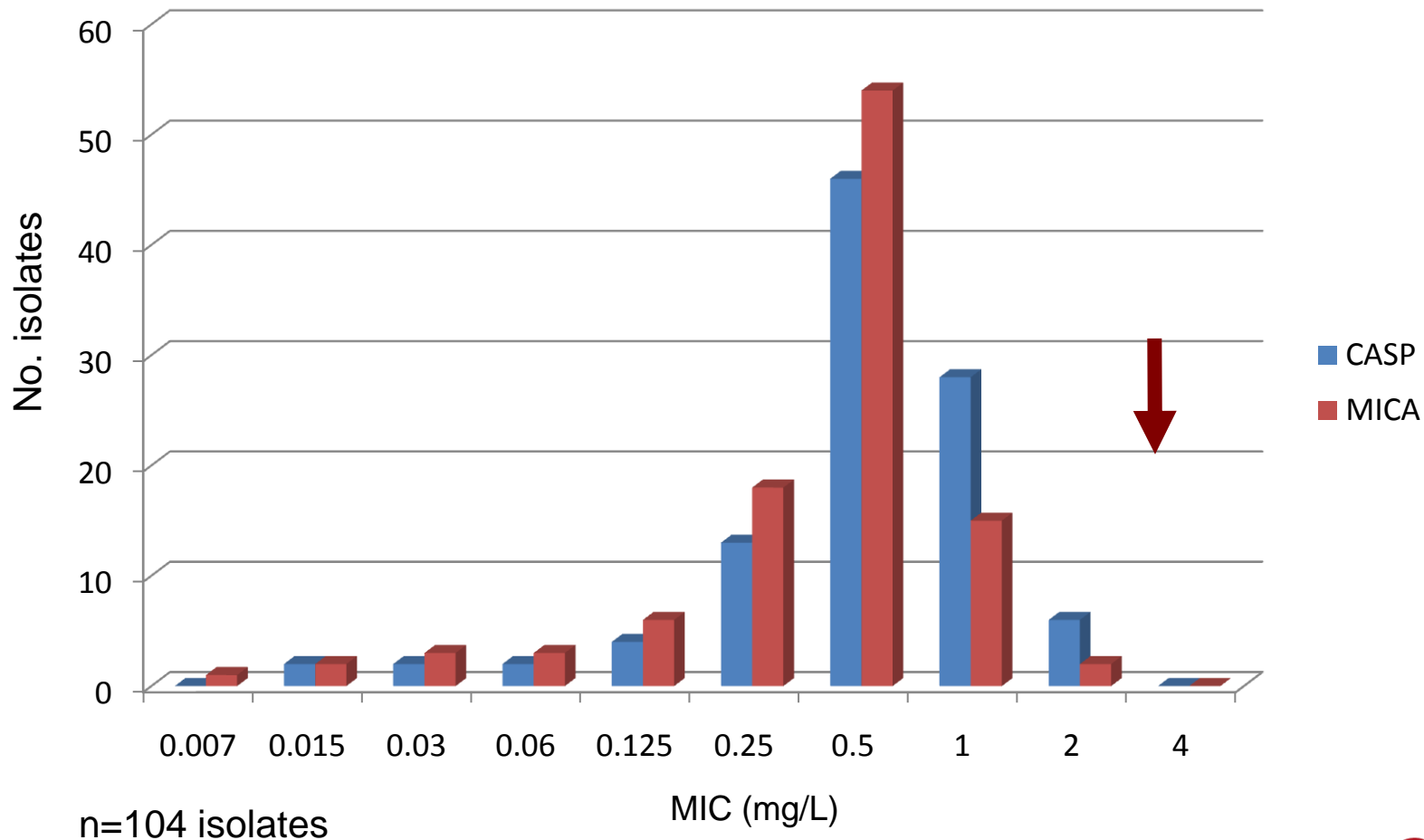
ECOFF ≤ 2 mg/L

Ca, n=485; Cg, n= 162

CANADIAN ANTIMICROBIAL
RESISTANCE ALLIANCE

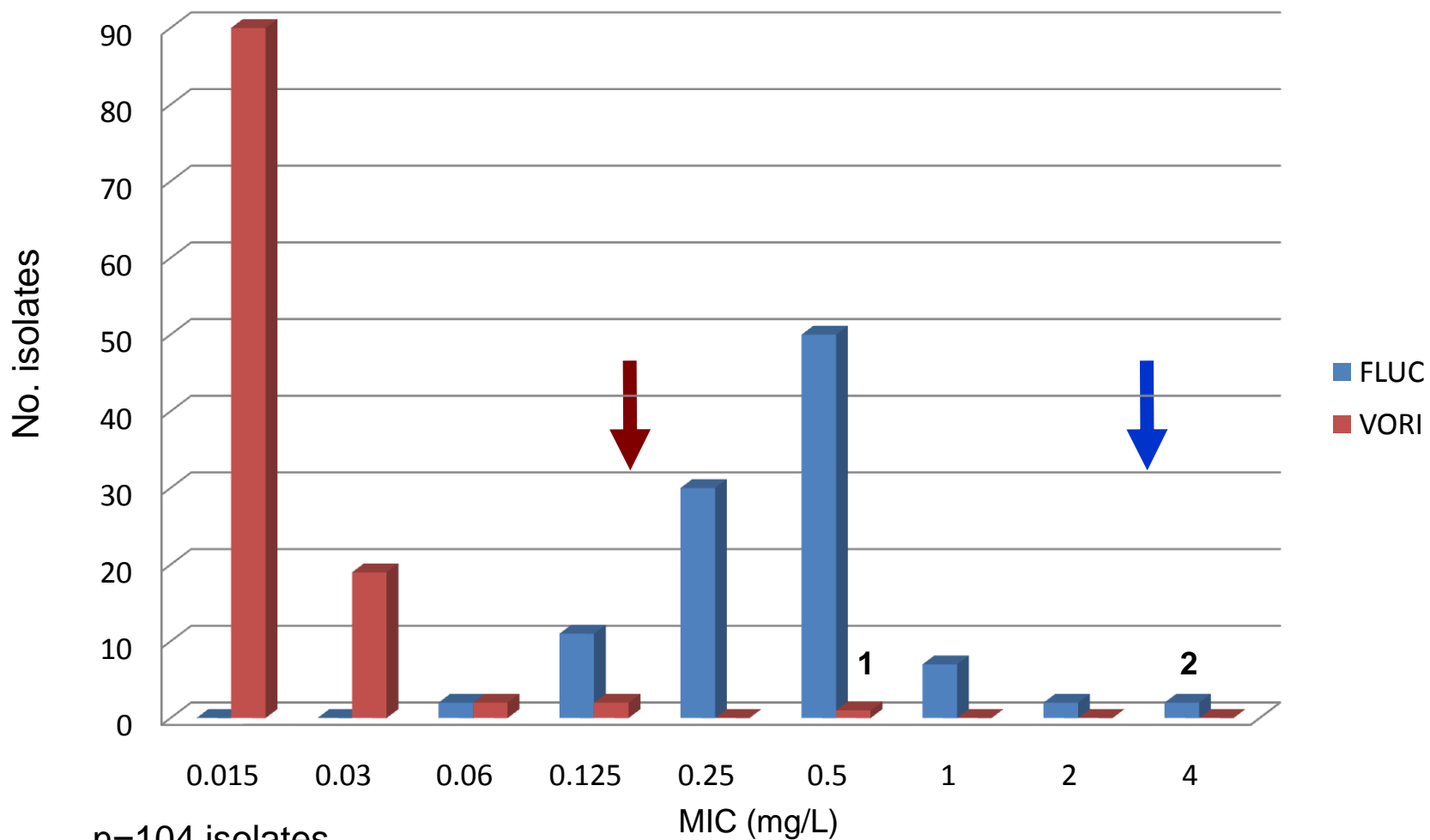


Echinocandin MIC Distribution Against *C. parapsilosis*



n=104 isolates

Azole MIC Distribution Against *C. parapsilosis*



n=104 isolates

Less Common *Candida* Species

- *C. tropicalis*, *C. dubliniensis*, *C. krusei*, *C. lusitaniae* identified in surveillance (<5% prevalence each)
- Numbers are too small to identify trends or changes
- Fully susceptible or within the wild-type population
- It remains important to follow these less common species
 - Selection pressures of antifungal practices may promote species expansion

CANWARD - Total *Candida* Resistance

2011-13	Overall Resistance (%)			
Species	Fluconazole	Voriconazole	Micafungin	Ampho B
<i>C. albicans</i>	0.83	0.62	0.20	0
<i>C. glabrata</i>	1.85	(4.94)	3.70	0
<i>C. parapsilosis</i>	1.92	0.96	0	0

- Antifungal activities of azoles and echinocandins are high against the most common causes of candidemia in Canada
- *C. glabrata* and resistance will be important for continued surveillance
- MIC distributions are normal with unchanging mode and geometric mean values (wild-type population)

Summary

- CANWARD 3-year surveillance has collected ~900 *Candida* isolates bloodstream infections
- Species prevalence indicates that the epidemiology has not significantly changed
- MIC results confirm that activity of available antifungals remains excellent
- Azole and echinocandin resistance in *C. glabrata* warrants continued surveillance
- CBP revisions have improved the quality of antifungal susceptibility testing, detection of resistance, and clinical relevance of laboratory results for the treating physician

CANWARD Candidemia is supported, in part, by grant support from Astellas