



Di.T.M.O

**Diagnostica e Terapia delle
Micosi Opportunistiche**

Genova, 22-23 giugno 2017

I DATABASE MULTICENTRICI ITALIANI

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PUBMED SEARCH FOR “candidemia and Italy”:

129 RESULTS

MULTICENTER ITALIAN STUDIES ABOUT CANDIDEMIA

1. Assessment of risk factors for candidemia in non-neutropenic patients hospitalized in Internal Medicine wards: A multicenter study. Falcone M, et al. Eur J Intern Med. 2017
2. Epidemiology and outcome of candidemia in internal medicine wards: A regional study in Italy. Tedeschi S, et al. Eur J Intern Med. 2016.
3. Nosocomial candidemia in patients admitted to medicine wards compared to other wards: a multicentre study. Luzzati R, et al. Infection. 2016.
4. Candidemia in Patients with Body Temperature Below 37° C and Admitted to Internal Medicine Wards: Assessment of Risk Factors. Tascini C, et al. Am J Med. 2016.
5. CAND-LO 2014-15 study: changing epidemiology of candidemia in Lombardy (Italy). Prigitano A, et al. Infection 2016.
6. Variable incidence of candidemia in patients admitted to ICUs or medical wards of large tertiary-care Italian hospitals. Tascini C, et al. Clin Microbiol Infect. 2015.
7. Candidemia in intensive care unit: a nationwide prospective observational survey (GISIA-3 study) and review of the European literature from 2000 through 2013. Montagna MT, et al. Eur Rev Med Pharmacol Sci. 2014.
8. A 1-year prospective survey of candidemia in Italy and changing epidemiology over one decade. Tortorano AM, et al. Infection. 2013.
9. Epidemiology of invasive fungal infections in the intensive care unit: results of a multicenter Italian survey (AURORA Project). Montagna MT, et al. Infection 2013.
10. Mortality in patients with early- or late-onset candidaemia. De Rosa FG, et al.. J Antimicrob Chemother. 2013.
11. Candida infective endocarditis: report of 15 cases from a prospective multicenter study. Falcone M, et al. Medicine (Baltimore). 2009.
12. Fungal infections in recipients of hematopoietic stem cell transplants: results of the SEIFEM B-2004 study--Sorveglianza Epidemiologica Infezioni Fungine Nelle Emopatie Maligne. Pagano L, et al. Clin Infect Dis. 2007.
13. Incidence, risk factors, and predictors of outcome of candidemia. Survey in 2 Italian university hospitals. Bassetti M, et al. Diagn Microbiol Infect Dis. 2007.
14. The epidemiology of fungal infections in patients with hematologic malignancies: the SEIFEM-2004 study. Pagano L, et al. Haematologica. 2006.
15. European Confederation of Medical Mycology (ECMM) prospective survey of candidaemia: report from one Italian region. Tortorano AM, et al. J Hosp Infect. 2002
16. Prevalence and outcome of invasive fungal infections in 1,963 thoracic organ transplant recipients: a multicenter retrospective study. Italian Study Group of Fungal Infections in Thoracic Organ Transplant Recipients. Grossi P, et al. Transplantation. 2000.
17. Candidemia in cancer patients: a prospective, multicenter surveillance study by the Invasive Fungal Infection Group (IFIG) of the European Organization for Research and Treatment of Cancer (EORTC). Viscoli C, et al. Clin Infect Dis. 1999.

CLINICAL RESEARCH ABOUT CANDIDEMIA IN ITALY

Significant interest towards diagnostics tools

Mainly single-center clinical studies

Largest multicenter studies in the ICU and in immunosuppressed hosts

Long-term epidemiological data are lacking

Increasing interest towards candidemia in Internal Medicine Wards in recent years

Overall epidemiological trends?

Clinical management in different clinical settings?

Risk factors for mortality?

**HOSPITAL-WIDE CANDIDEMIA:
FROM EPIDEMIOLOGY TO THE CANDIDEMIA
BUNDLE**

Primary objective

To compare in-hospital mortality before and after the implementation of a “candidemia bundle”, among patients with candidemia admitted to ICU and non-ICU wards.

Secondary objectives:

- To compare the two periods before and after the implementation of the “candidemia bundle”, in terms of 30-day mortality and of candidemia-related length of stay (from first positive blood culture to discharge/death);
- To describe *Candida* species epidemiology as causative agent of candidemia and epidemiological trends.
- To assess risk factors for mortality among patients with candidemia.
- To assess risk factors for initial inappropriate therapy (if associated to poorer outcome)

MULTICENTRE, QUASI EXPERIMENTAL PRE-POST STUDY

Phase 1: Multicenter, retrospective cohort study on all candidemia episodes in adult patients occurred at participating centers from 1st January 2009 to 31st December 2012.

Phase 2: Multicenter, prospective study on all candidemia episodes in adult patients occurred at participating centers from 1st January 2016 to 30th June 2017 (data collection ongoing).

Participating centers: Bologna (Sant'Orsola), Genova (San Martino), Roma (Gemelli), Torino (Molinette), Udine (S. Maria della Misericordia), Pavia (Biostatistics Unit IRCCS S.Matteo)

**HOSPITAL-WIDE CANDIDEMIA:
FROM EPIDEMIOLOGY TO THE CANDIDEMIA
BUNDLE**

**RESULTS OF THE RETROSPECTIVE PRE-BUNDLE
PHASE**

Primary objective

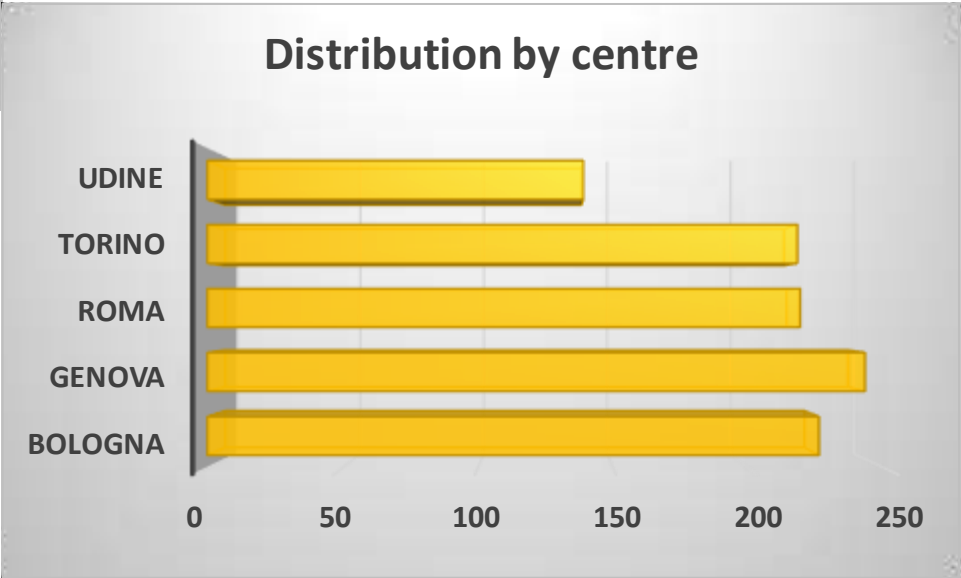
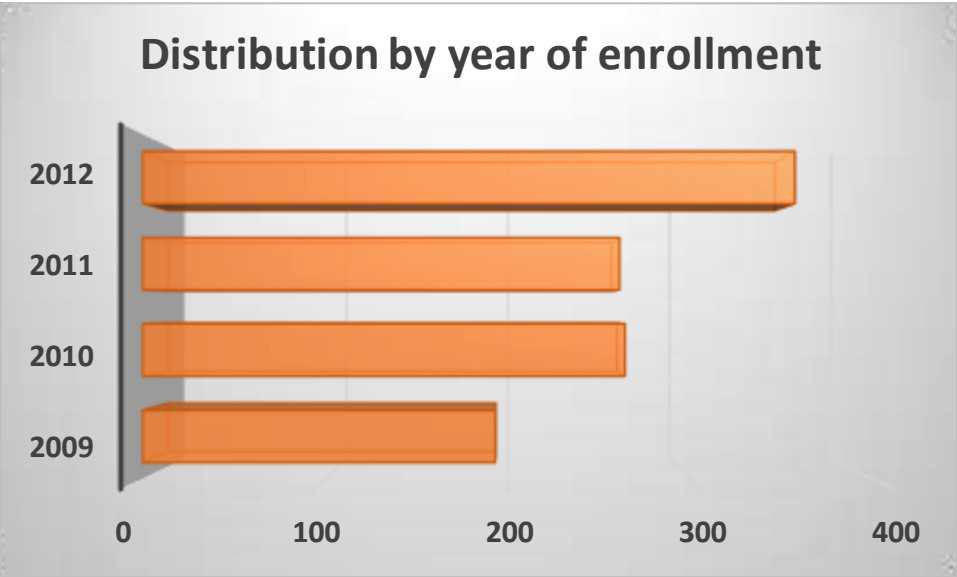
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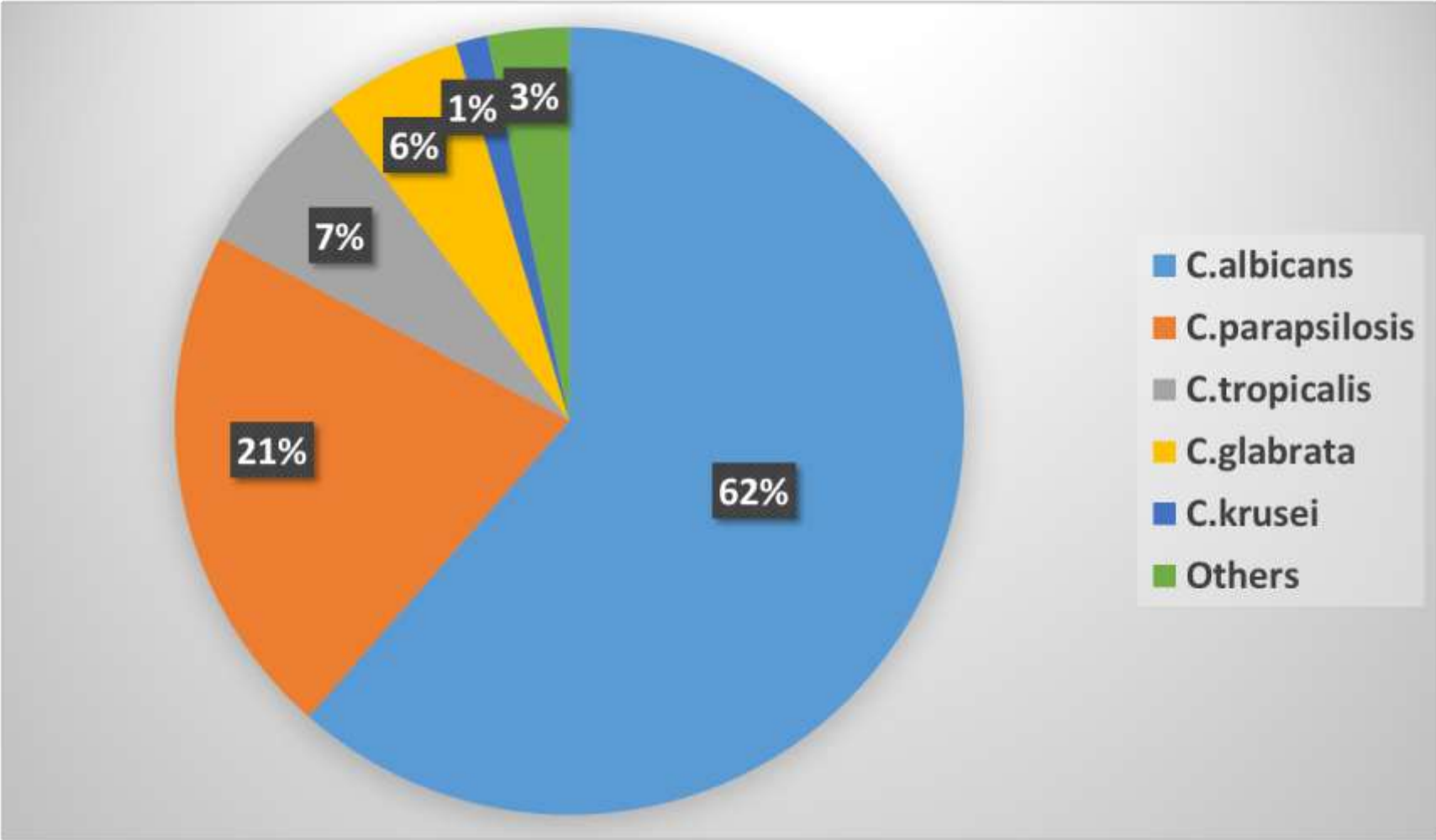
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STUDY POPULATION

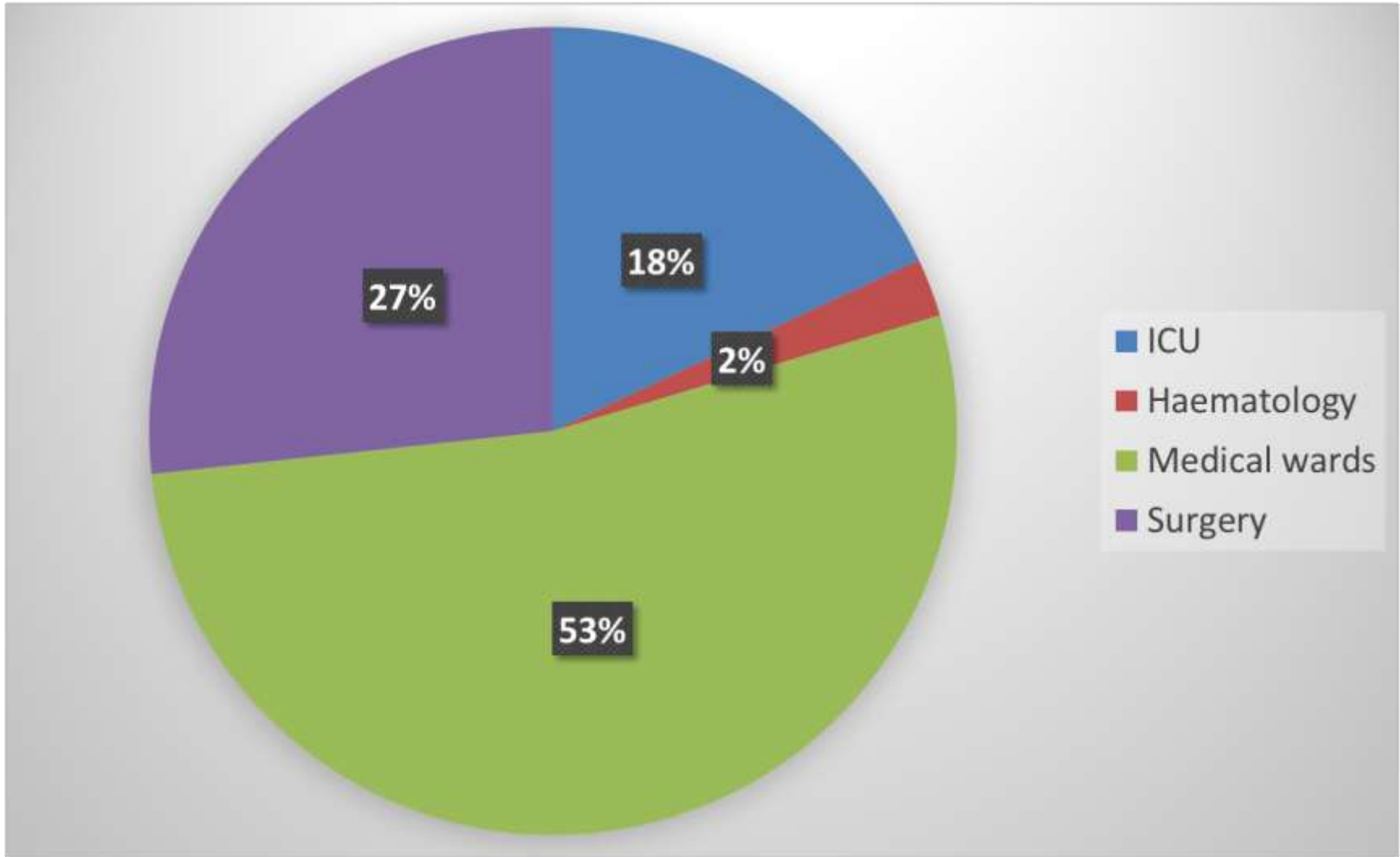
1075 patients in 4 years



SPECIES DISTRIBUTION



DISTRIBUTION IN HOSPITAL WARDS



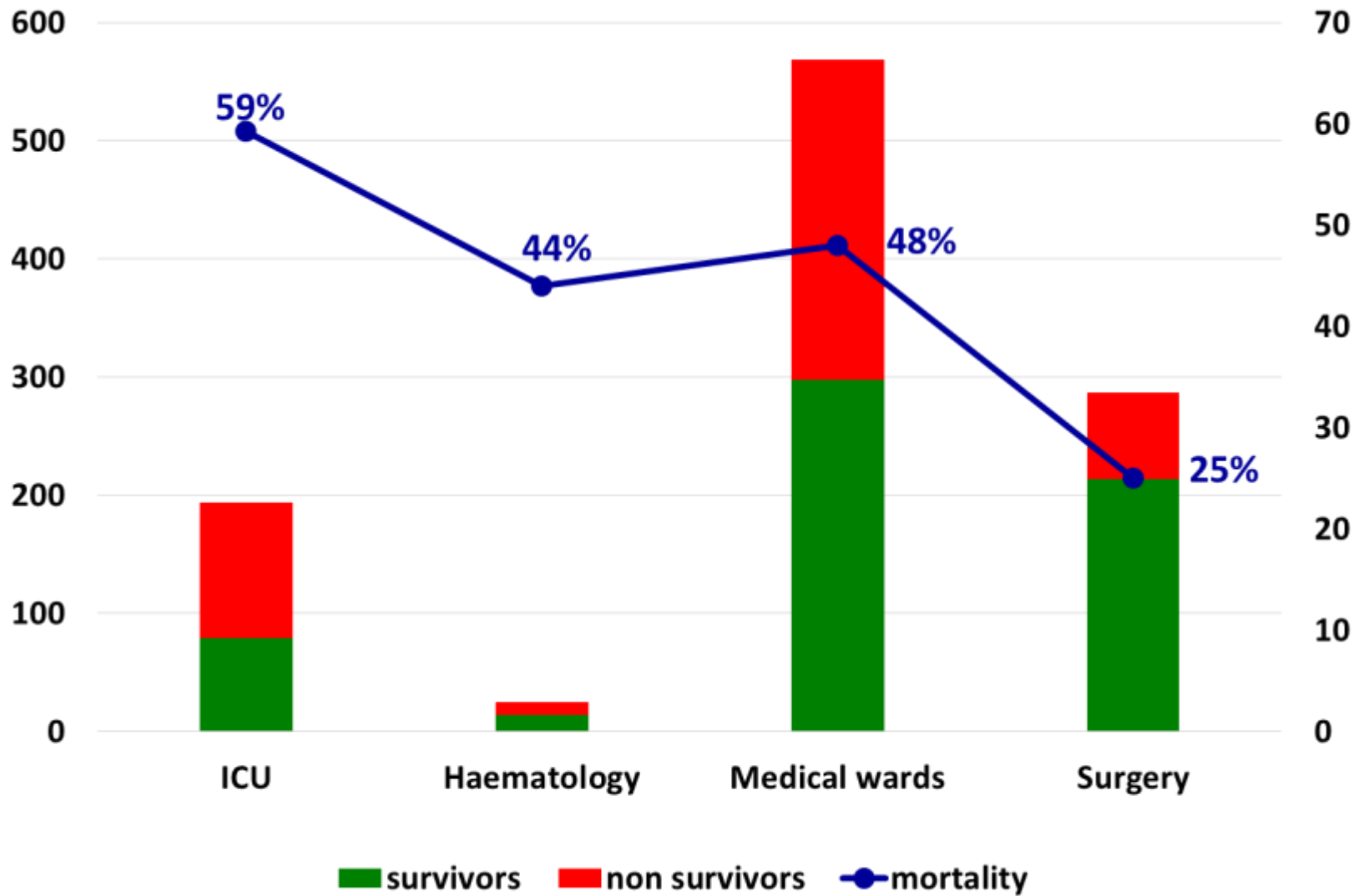
CHARACTERISTICS OF STUDY POPULATION

Variable	N° (%)
Age (years) – median (IQR)	70 (59 – 79)
Male sex	630 (59)
LOS at index blood culture (days) – median (IQR)	19 (8-34)
Severe sepsis/septic shock	229 (21)
Presence of CVC	817 (76)

THERAPEUTIC MANAGEMENT

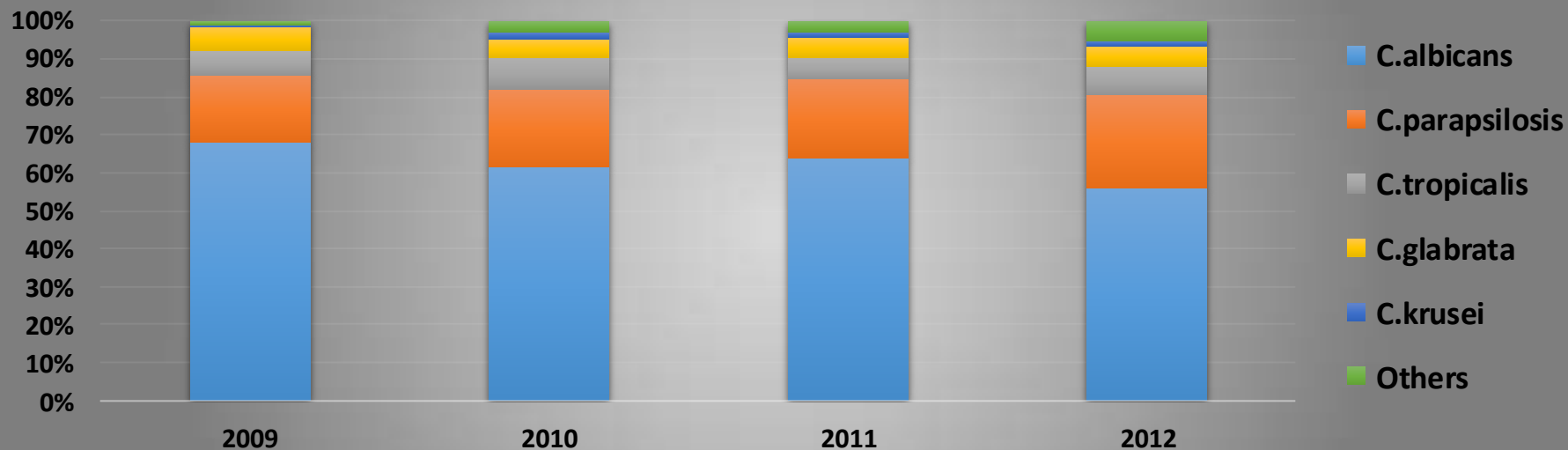
	N= 1075 (%)
Antifungal prophylaxis ongoing	96 (9)
Any antifungal treatment administered	848 (79)
Timing of antifungal treatment from blood cultures (n=848)	
Ongoing	184 (21)
< 24 h	124 (15)
24-48 h	103 (12)
48-72 h	176 (21)
>72	261 (31)

IN-HOSPITAL MORTALITY

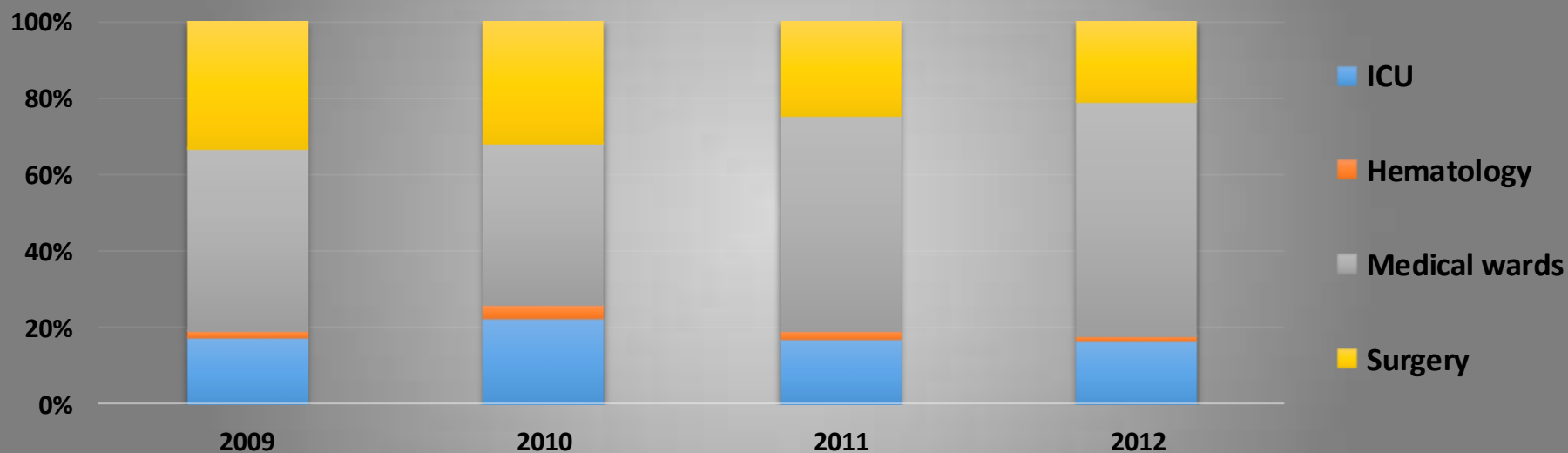


TEMPORAL TRENDS

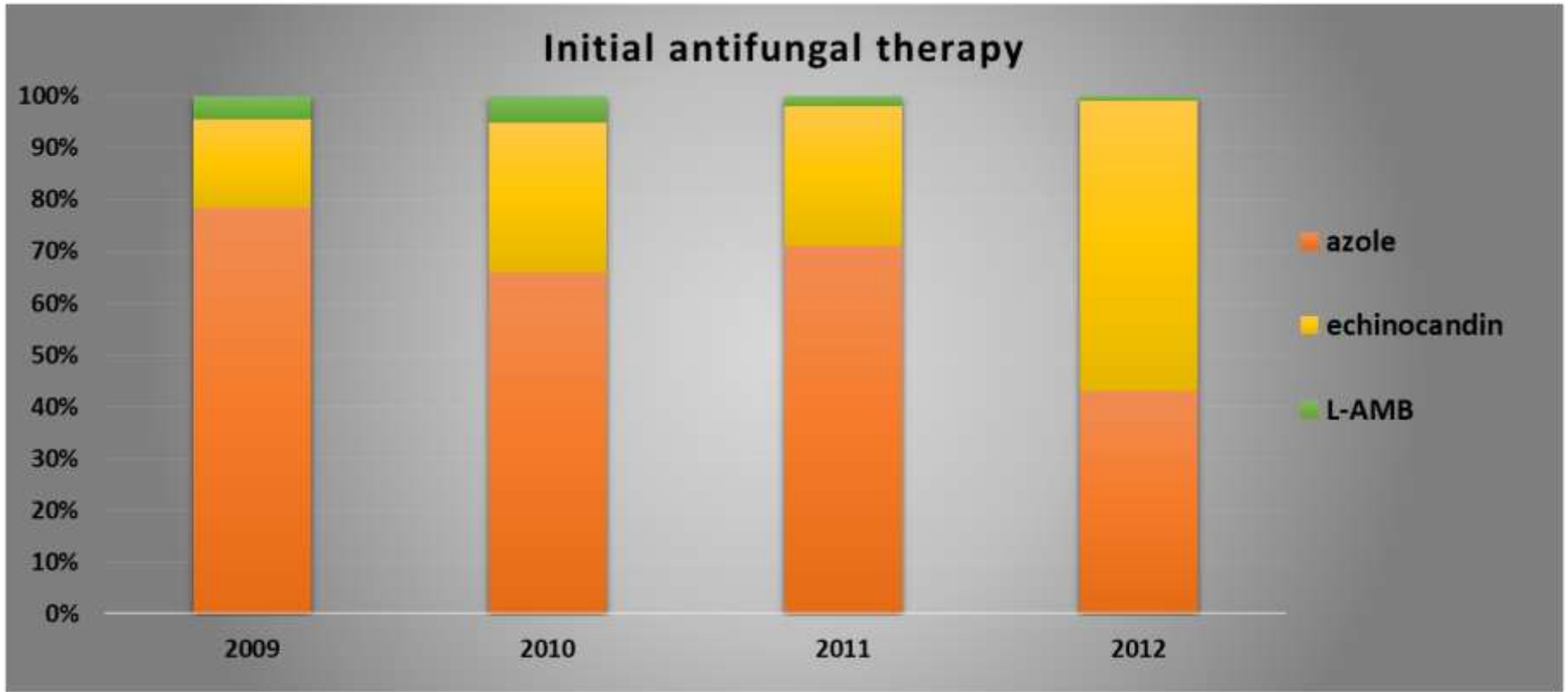
Species distribution



Distribution by hospital wards



TEMPORAL TRENDS



	IDSA Guidelines 2009	ESCMID Guidelines 2012
Primary therapy	FLC ECH in unstable pts or those with prior azole exposure	ECH
Alternative therapy	AMB-D, Lipid-AMB or VCZ	Lipid-AMB , VCZ, FLC

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RISK FACTORS FOR MORTALITY: UNIVARIATE ANALYSIS

	Survivors N=605 (%)	Non survivors N=470 (%)	p
Age	67 (56-77)	75 (64-82)	<0.001
Male sex	352 (58)	278 (59)	0,749
LOS at index blood culture	17 (7-33)	21 (9-36)	0.019
Severe sepsis/septic shock	66 (11)	163 (35)	<0.001
Presence of CVC	465 (56)	352 (43)	0.376

RISK FACTORS FOR MORTALITY: UNIVARIATE ANALYSIS

	Survivors N=605 (%)	Non survivors N=470 (%)	p
<i>Candida</i> species			
<i>C.albicans</i>	356 (59)	305 (65)	0.043
<i>C.glabrata</i>	35 (5.8)	26 (5.5)	0.845
<i>C.parapsilosis</i>	144 (24)	84 (18)	0.016
<i>C.tropicalis</i>	41 (6.8)	34 (7.2)	0.786
Hospital ward			
ICU	79 (13.1)	115 (24.5)	<0.001
Haematology	14 (2.3)	11 (2.3)	0.977
Medical	298 (49)	271 (58)	0.006
Surgical	214 (70)	73 (37)	<0.001

RISK FACTORS FOR MORTALITY: UNIVARIATE ANALYSIS

	Survivors N=605 (%)	Non survivors N=470 (%)	p
Antifungal prophylaxis	47 (7.8)	49 (10.4)	0.009
Any antifungal treatment	497 (82)	351 (75)	0.003
Antifungal treatment < 72 h from BC	345 (57)	242 (52.5)	0.07
Appropriate initial antifungal	435 (71)	258 (54)	<0.001
Initial antifungal drug			
Azole	324 (58)	205 (58)	0.871
Echinocandin	160 (29)	134 (38)	0.003
L-AMB	12 (2.1)	12 (3.4)	0.242

RISK FACTORS FOR MORTALITY: MULTIVARIATE COX REGRESSION ANALYSIS

	aHR (95% CI)	p
Age	1.02 (1.01 – 1.03)	<0.001
Severe sepsis/septic shock	1.82 (1.43 – 2.38)	< 0.001
Parenteral nutrition	1.29 (1.05 – 1.58)	0.01
Diabetes	1.41 (1.15 – 1.74)	0.001
Liver cirrhosis	1.76 (1.27 – 2.44)	0.001
Chronic corticosteroids	1.32 (1.05 – 1.65)	0.01
Hospital ward		
ICU	2.72 (1.36 – 5.44)	0.005
Medical ward	2.20 (1.13 – 4.30)	0.02
Surgery	0.21 (0.11 – 0.44)	<0.001
Appropriate initial antifungal therapy	0.64 (0.48 – 0.85)	0.002
Antifungal therapy < 72 h from BCs	0.77 (0.63 – 0.95)	0.01

RISK FACTORS FOR MORTALITY: MULTIVARIATE COX REGRESSION ANALYSIS

Subgroup of patients with CVC

	aHR (95% CI)	p
Age	1.02 (1.01 – 1.03)	<0.001
Severe sepsis/septic shock	2.38 (1.78 – 3.19)	< 0.001
Diabetes	1.52 (1.21 – 1.92)	<0.001
Liver cirrhosis	1.56 (1.08 – 2.26)	0.02
Hospital ward		
ICU	2.91 (1.04 – 6.05)	0.004
Medical ward	2.42 (1.20 – 4.90)	0.01
Surgery	0.18 (0.08 – 0.39)	<0.001
CVC removal	0.39 (0.30 – 0.49)	<0.001

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RISK FACTORS FOR INITIAL INAPPROPRIATE ANTIFUNGAL THERAPY

	Appropriate N=693 (%)	Inappropriate N=382 (%)	p
Age	67 (56-77)	75 (64-82)	<0.001
LOS at index blood culture	17 (7-33)	21 (9-36)	<0.001
Severe sepsis/septic shock	55 (8)	174 (45)	<0.001
● Presence of CVC	544 (79)	273 (72)	0.01
Antifungal prophylaxis ongoing	53 (7.3)	43 (11.3)	0.05
Comorbidities			
Solid tumour	239 (34)	122 (32)	0.397
Hematological malignancy	45 (6.5)	27 (7.1)	0.656
Diabetes	164 (24)	102 (27)	0.270
ESRD on dialysis	51 (7.4)	41 (10.7)	0.05
Liver cirrhosis	44 (6.3)	29 (7.6)	0.438
Hospital ward			
ICU	104 (15)	90 (23)	<0.001
Hematology	18 (2.6)	7 (1.8)	0.426
Medical ward	361 (52)	208 (54)	0.459
● Surgery	210 (30)	30 (20)	<0.001
Candida species			
C.albicans	425 (61)	236 (62)	0.884
● C.parapsilosis	160 (23)	68 (18)	0.04
C.tropicalis	46 (6.6)	29 (7.6)	0.557
C.glabrata	30 (4.3)	31 (8.1)	0.01

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