

Risk Assessment for Invasive Fungal Infections in the ICU

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Factors Involved in the Development of Opportunistic Mycosis

Factors

Fungal pathogens

Mucosal & cutaneous
disruption

Candida spp.

Aspergillus spp.

Neutrophil dysfunction

Candida spp.

Trichosporon spp.

Aspergillus and other molds

Defects in cell-med. immunity

Cryptococcus spp.

Endemic mycosis

Metabolic disorders

Zygomycetes

Candida spp.

Exposures

Endemic mycosis

Aspergillus and other molds

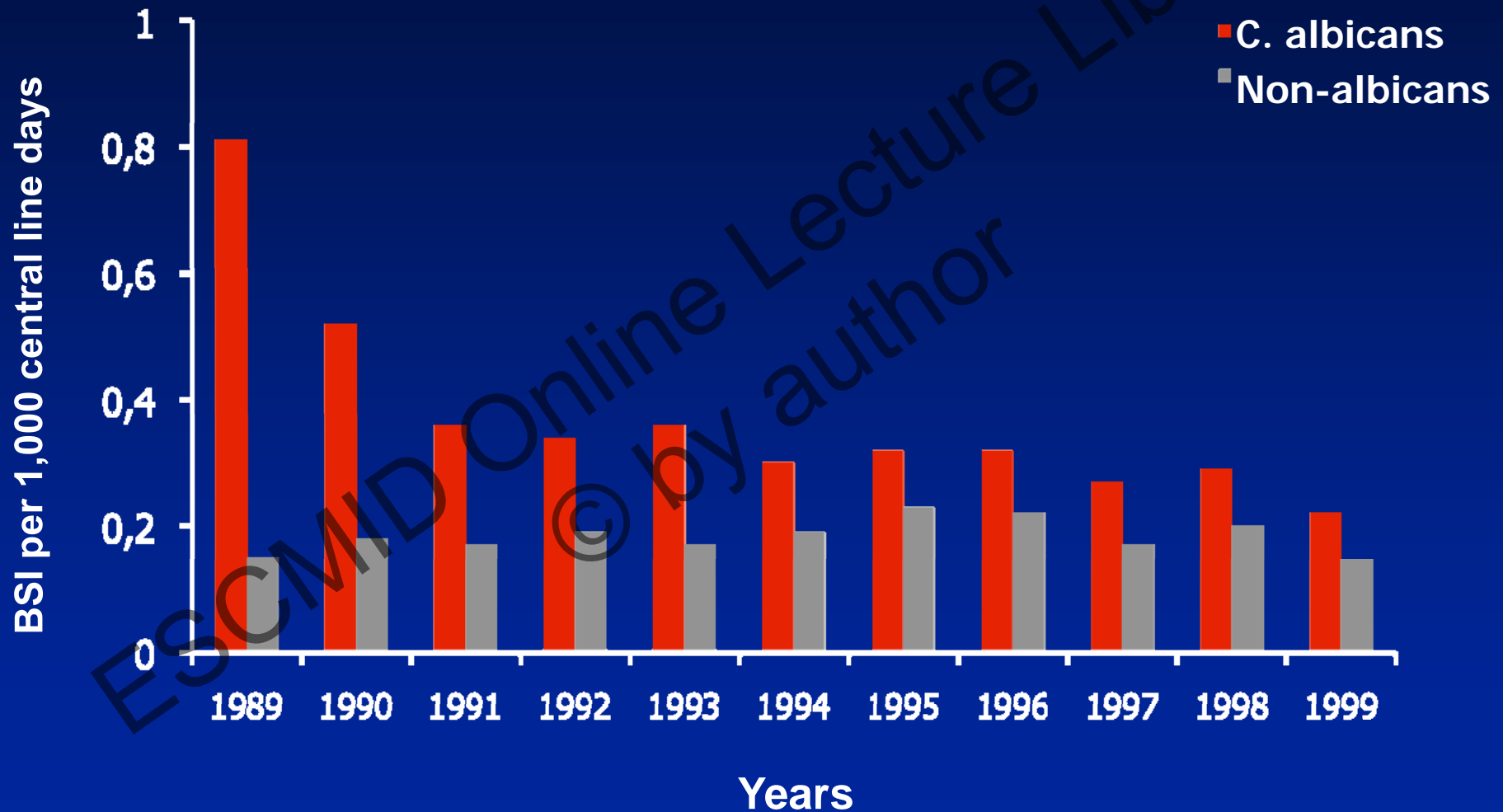
Extremes of age (<1 and >70 yr)

Candida spp.

Candida as a Nosocomial Pathogen

Rank	Pathogen	BSI per 10,000 admissions	Total (n=20,978)	% BSI		% Crude Mortality		
				ICU (n=10,515)	Non-ICU (n=10,515)	Total	ICU	Non-ICU
1.	CoNS	15.8	31.3	35.9	26.6	20.7	25.7	13.8
2.	S aureus	10.3	20.2	16.3	23.7	25.4	34.4	18.9
3.	Enterococcus spp	4.8	9.4	9.8	9.0	33.9	43.0	24.0
4.	Candida spp	4.6	9.0	10.1	7.9	39.2	47.1	29.0
5.	E coli	2.8	5.6	3.7	7.6	22.4	33.9	16.9
6.	Klebsiella spp	2.4	4.8	4.0	5.5	27.6	37.4	20.3
7.	P aeruginosa	2.1	4.3	4.7	3.8	38.7	47.9	27.6
8.	Enterobacter spp	1.9	3.9	4.7	3.1	26.7	32.5	18.0
9.	Serratia spp	0.9	1.7	2.1	1.3	27.4	33.9	17.1
10.	A baumannii	0.6	1.3	1.6	0.9	34.0	43.4	16.3

Incidence of Nosocomial Candidemia in ICU (NNIS)



Trick WE, et al. Clin Infect Dis 2002;35:627

Candidaemia: the European Experience



International Journal of Antimicrobial Agents 27 (2006) 359–366

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Review

Candidaemia in Europe: epidemiology and resistance

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Hannelore Bernhardt^d, Lena Klingspor^e, Renee Grillo^f

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- September 1997- December 1999
- 6 European national societies
- 2089 reports from 106 participating centers

Tortorano et al., Int J Antimicrob Agents 2006; 27: 359-366

Candidaemia in Europe

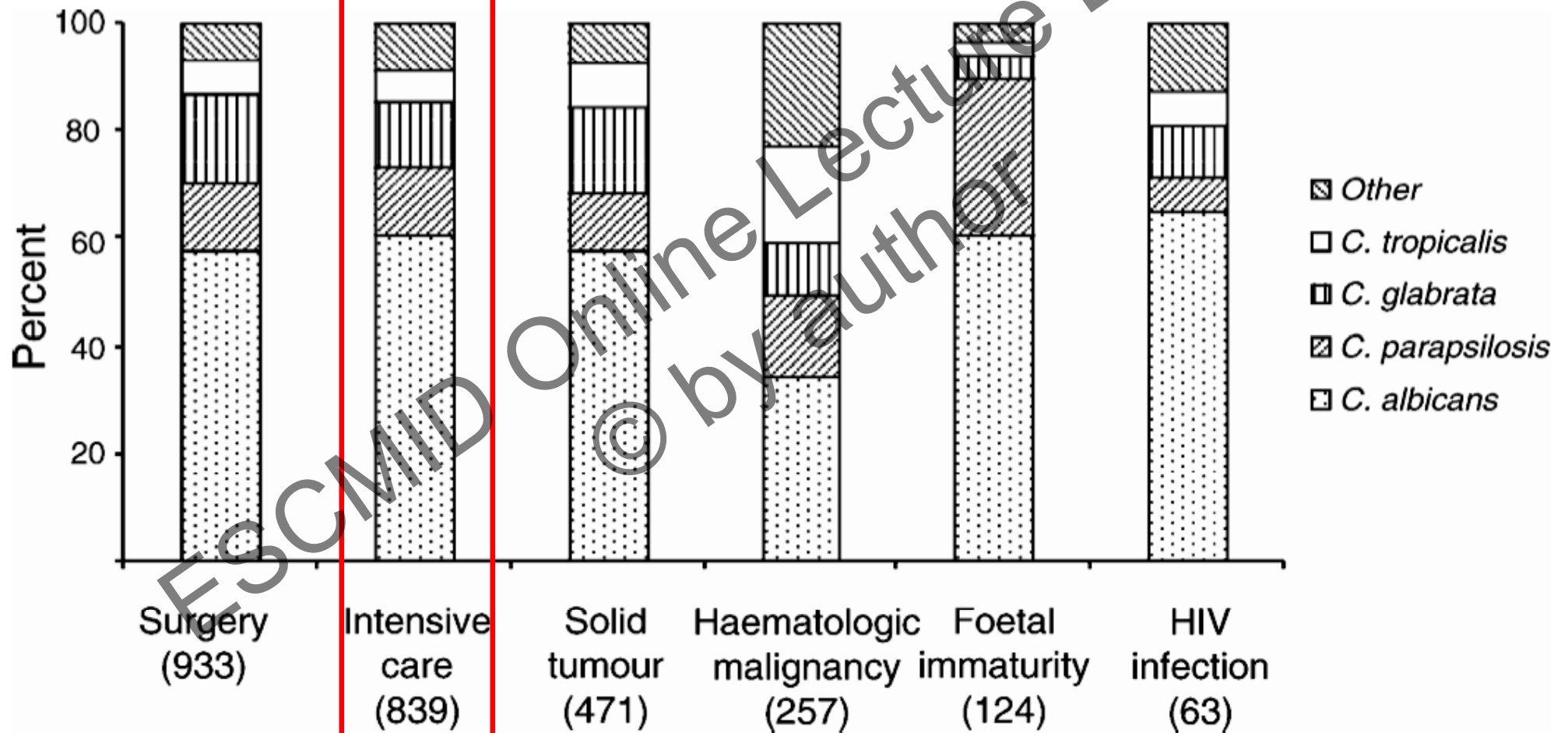
Underlying Pathology/Medical Care in Patients with Candidemia

N=2089, more than one may be present in each episode

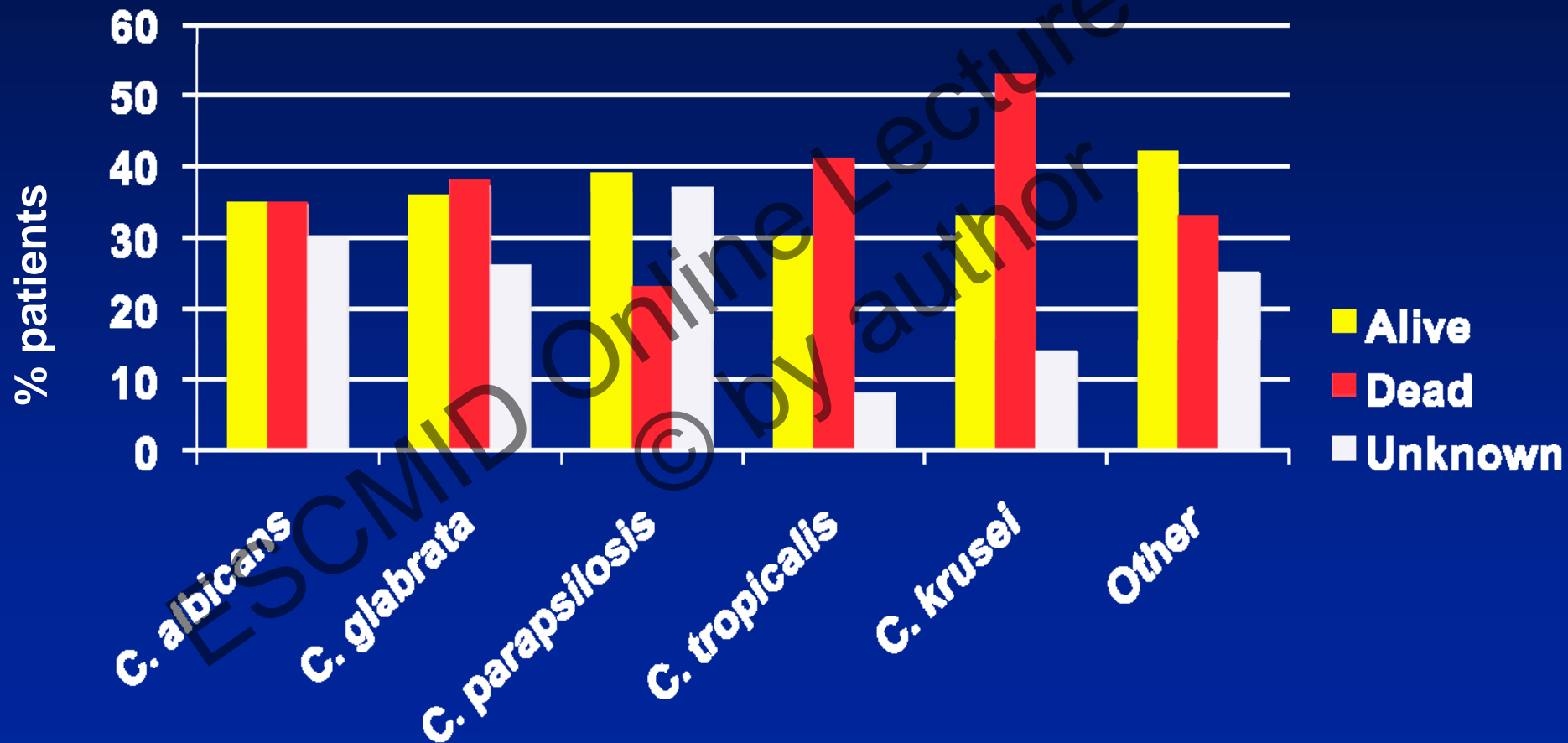
Underlying pathology/medical care	No.	%
Surgery	1007	48.2
Intensive care	839	40.2
Solid tumour	471	22.5
Steroids	364	17.4
Haematological malignancy	257	12.3
Premature birth	125	6.0
HIV infection	63	3.0
Burns	29	1.4

Candidaemia in Europe

Distribution of *Candida* species



Outcome of Invasive Candidiasis at 12th Week of Diagnosis PATH Registry



Invasive Candidiasis in the ICU

Risk Factors

- **Adult ICU**

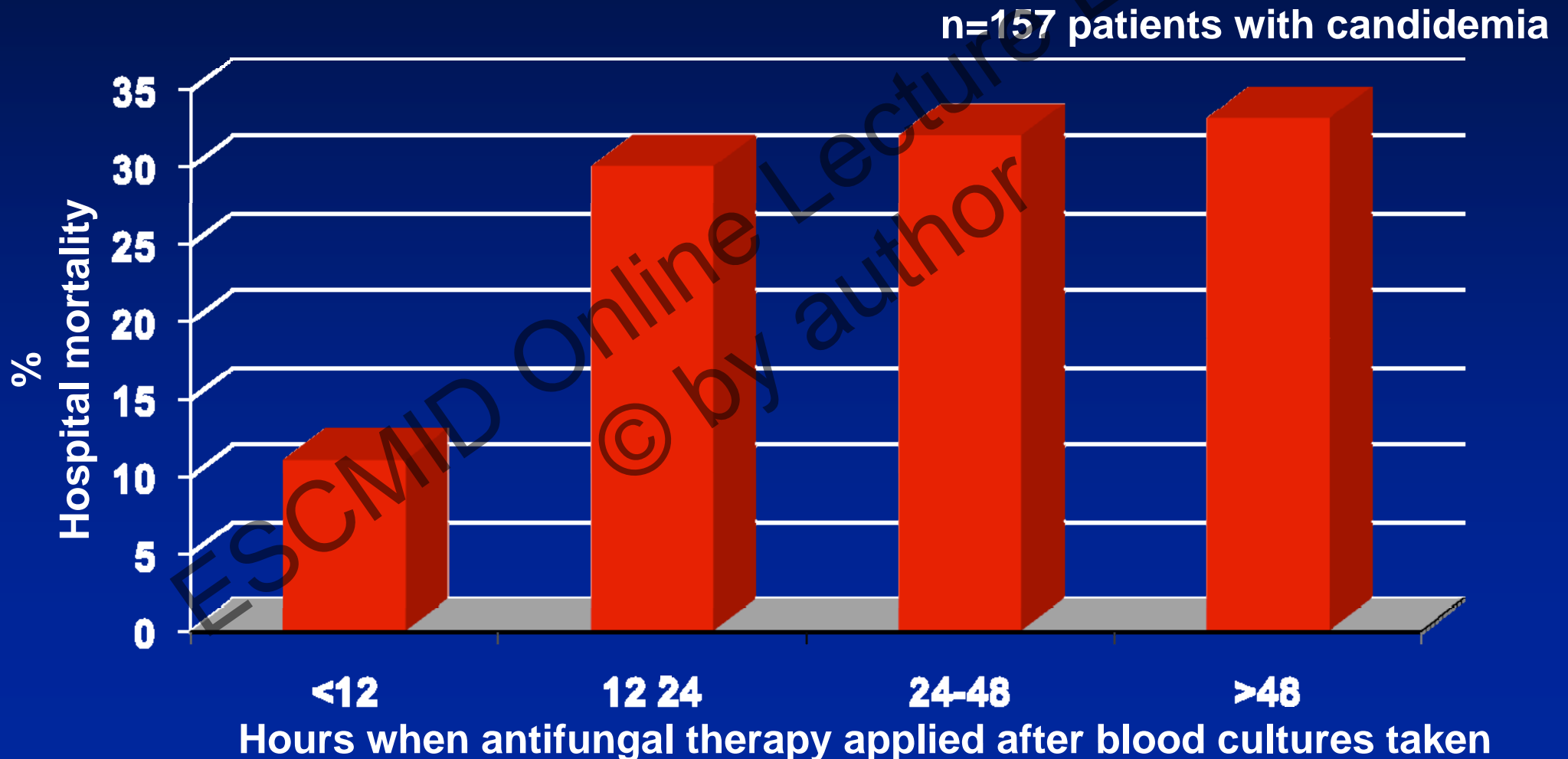
- Prolonged LOS
- Diabetes
- Renal failure
- CVC
- Parenteral nutrition
- Immunosupp. drugs
- Severe acut pancreatitis
- *Candida* colonization at multiple sites
- Transplantation
- Surgery

- **Neonatal and Pediatric ICU**

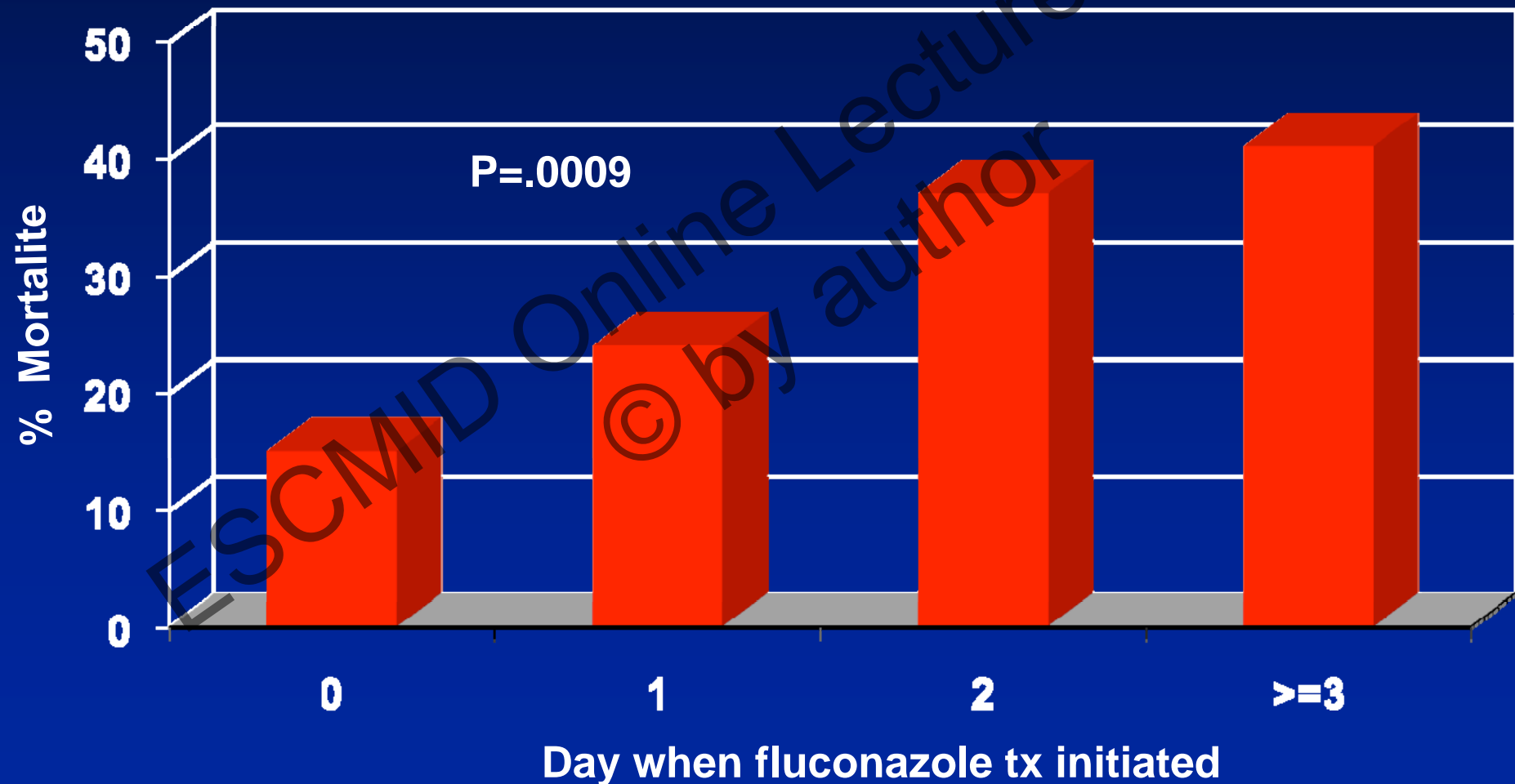
(In addition to adult risk factors)

- Prematurity
- Low APGAR Score
- Congenital malformations

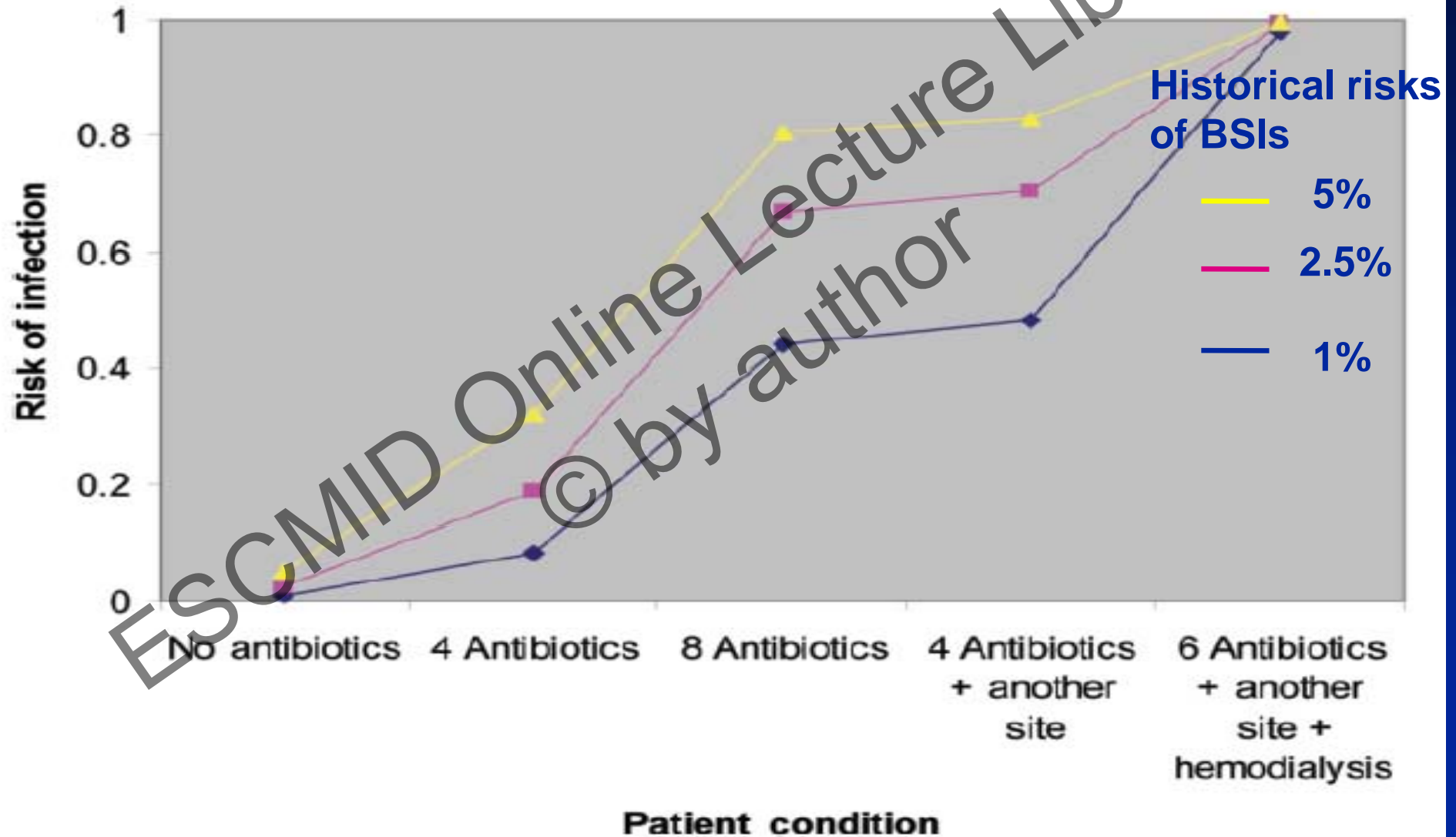
Delaying the Empirical Treatment of Candidemia



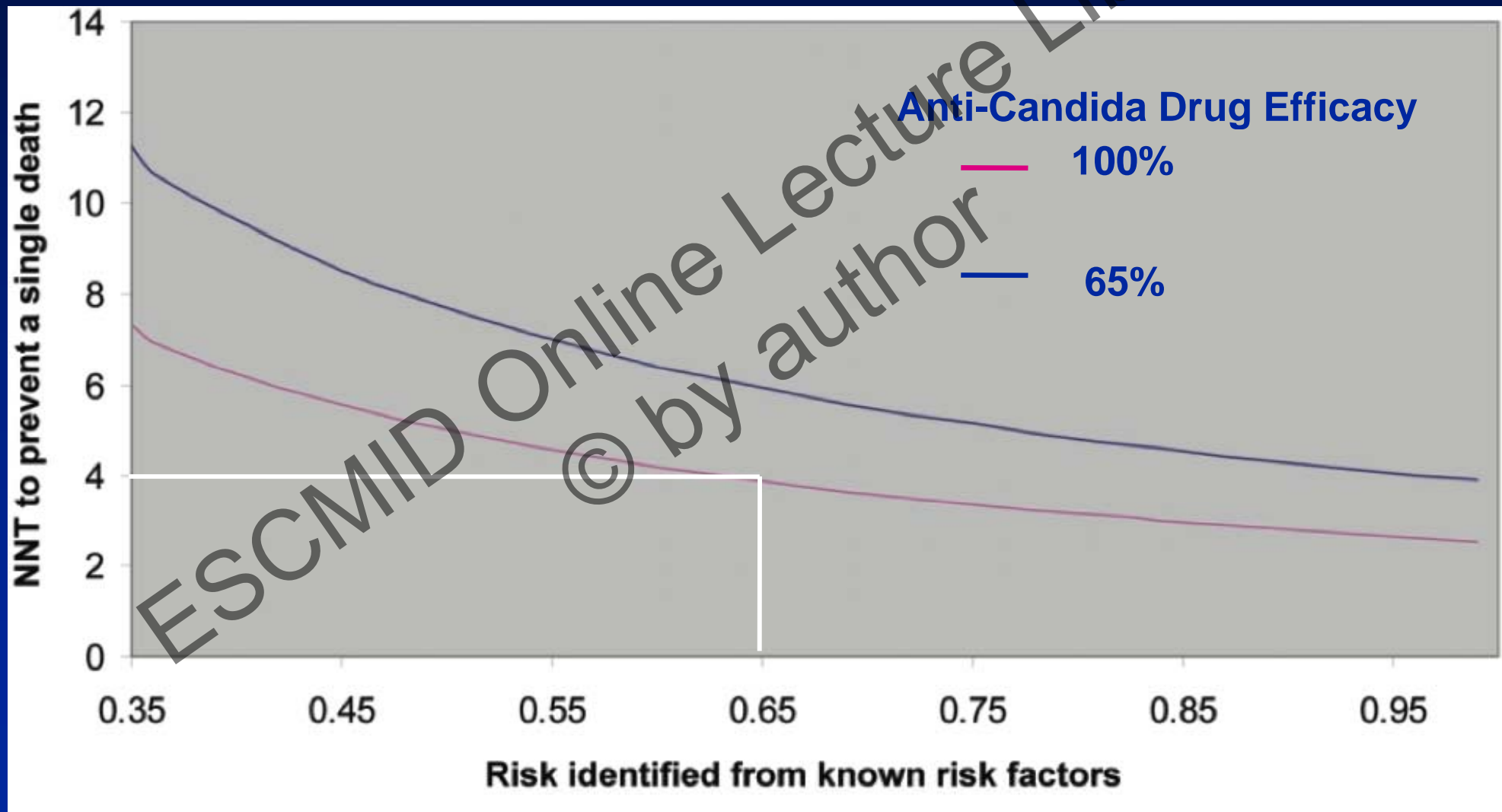
Mortality due to Candidemia and Time for Initiating Fluconazole Therapy



Calculated Risk of Invasive Candidiasis



The Number Needed to Treat to Prevent a Single Death



Clinical Prediction Rule for Invasive Candidiasis in ICU

- **Multicenter, retrospective study in USA and Brazil**
- **2890 patients, stayed ≥ 4 d in hospital**
 - Overall incidence of invasive Candida infections 3%

Clinical Prediction Rule for Invasive Candidiasis in ICU

- The best performing rule:
 - Any systemic antibiotic (days 1-3) **OR**
 - Presence of a CVC (days 1-3) **AND** at least **TWO** of the following
 - Total parental nutrition (days 1-3)
 - Major surgery (-7-0)
 - Pancreatitis (-7-0)
 - Use of steroids (-7-3)
 - Use of other immunosuppressives (-7-0)

Usefulness of the Rule

- Among patients meeting the rule
 - The rate of invasive candidiasis 9.9%
 - RR 4.36
 - Sensitivity 34%
 - Specificity 90%
 - PPV 1%
 - NPV 97%

Improvement of the Rule

- The previous one could be applicable <10% of all patients in ICU
- Retro review of 597 records in 6 sites
 - Mean APACHE II score 14.4
 - Mean ICU stay 12.5 days
 - Mean ventilation time 10.7 days
- Mechanical ventilation **plus**
- Presence of a CVC **plus**
- Broad spectrum antibiotics on days 1-3 **plus**
- An additional risk factor
- Applicable 18% of patients

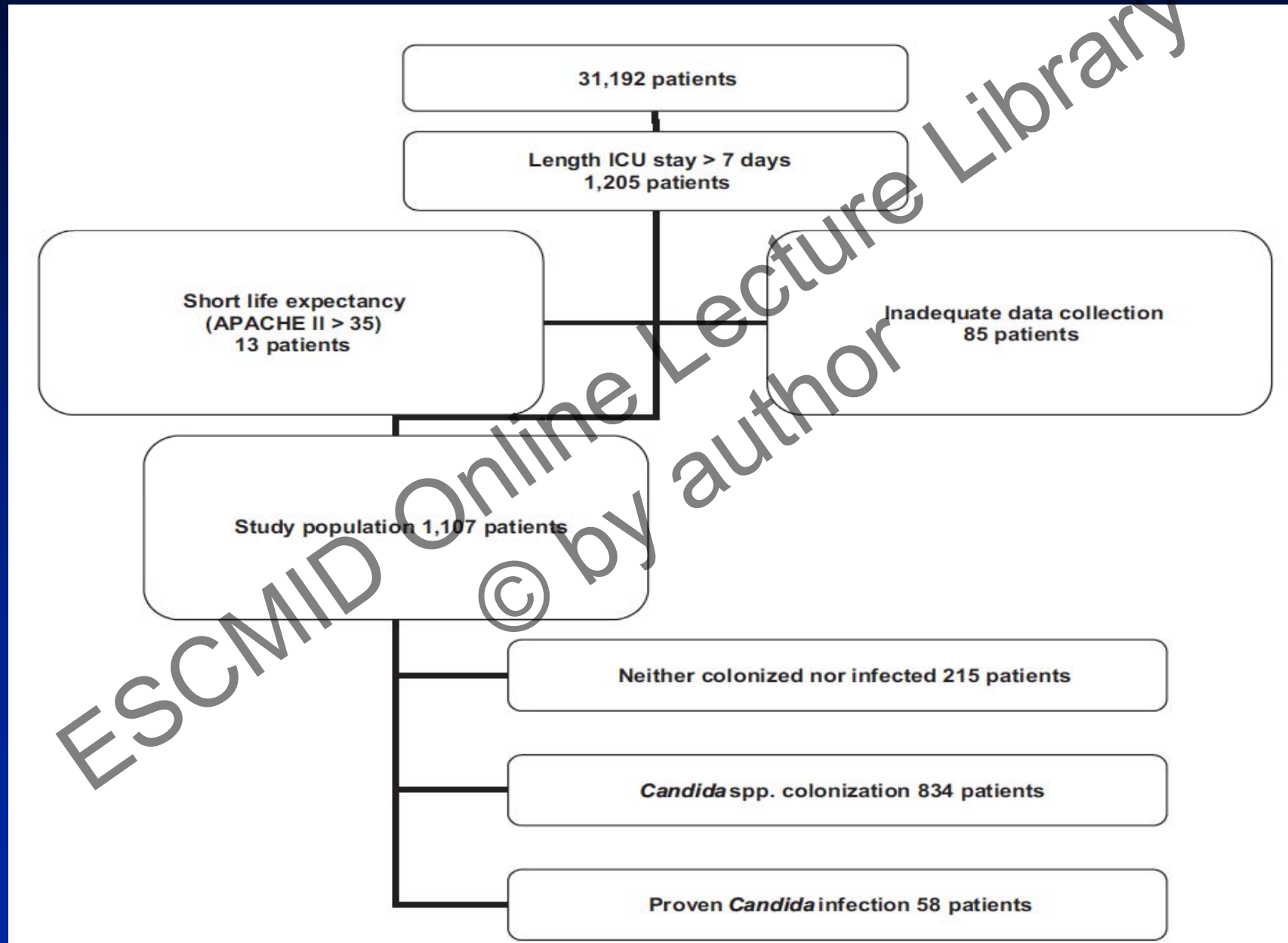
“*Candida* Score” in Critically Ill Patients

- **73 medical-surgical ICU in Spain**
- **1699 patients, ≥ 7 d stay in ICU**
 - **Multifocal colonization (+1)**
 - **Parenteral nutrition (+1)**
 - **Surgery (+1)**
 - **Severe sepsis (+2)**

“*Candida* Score” in Critically Ill Patients

- **A score ≥ 3 accurately selects for early antifungal therapy**
 - **61 % sensitivity**
 - **86 % specificity**
 - **Risk ratio >7.75 (95% CI 4.74 to 12.66)**

Validation of “*Candida* Score”



Rates of Invasive Candidiasis per Candida Score

Cutoff value	Incidence rate (%) (95% CI)	Relative risk (95% CI)
<3	2.3 (1.1-3.5)	1
3	8.5 (4.2-12.7)	3.7 (1.8-7.7)
4	16.8 (9.7-23.9)	7.3 (3.7-14.5)
5	23.6 (12.4-34.9)	10.3 (5.0-21.0)

Candida Score vs Colonization Index Discriminatory Power

	Candida Score ≥ 3	Colon. Index ≥ 0.5
Area under ROC curve	0.774	0.663
Sensitivity	77.6	72.4
Specificity	66.2	47.4
PPV	13.8	8.7
NPV	97.7	96.1
Relative risk for IC	5.98	2.24

of Patients Needed to Predict an Invasive Candidiasis

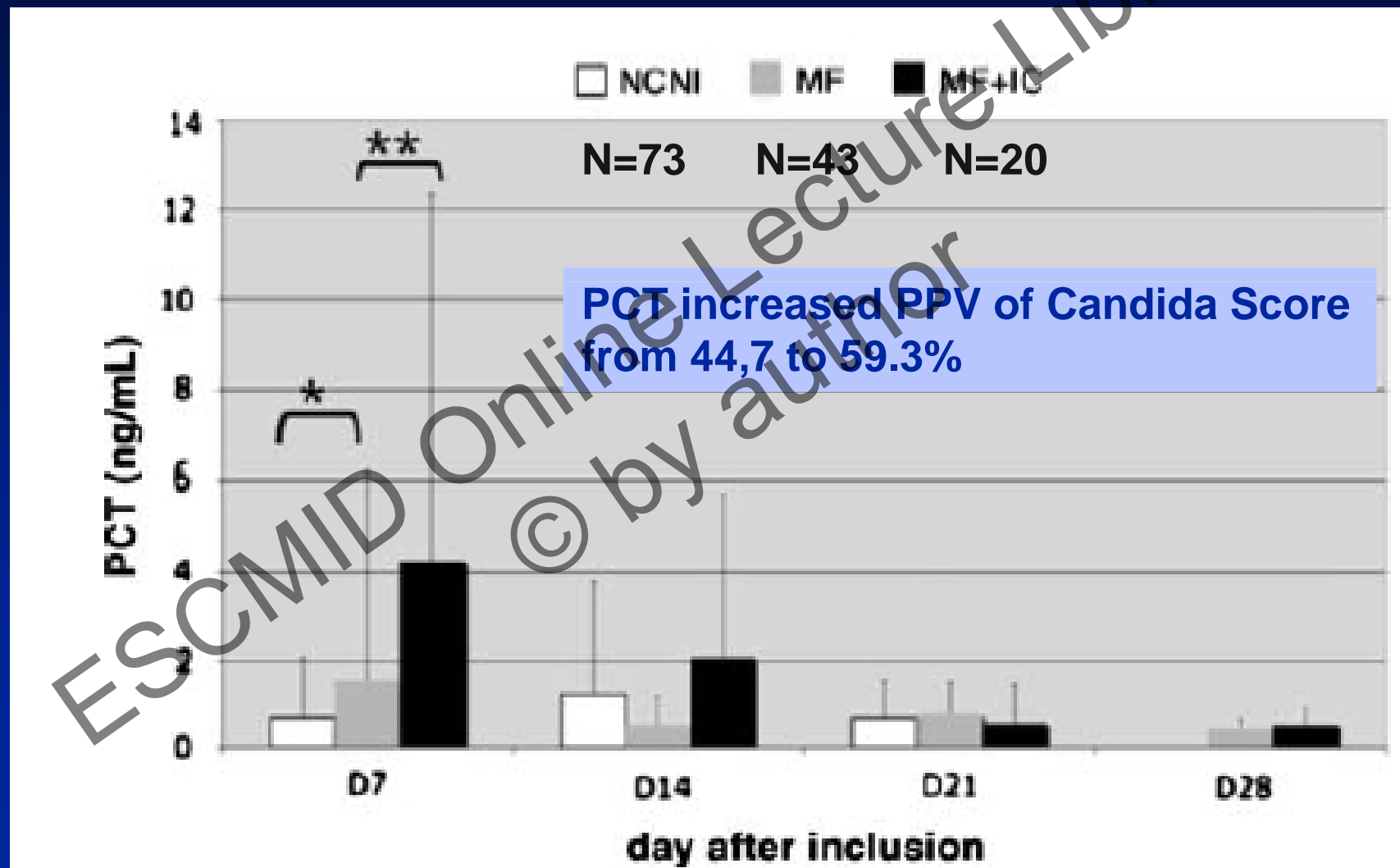
	Colonized (n)	Invasive candidiasis (%)	Patients to be included*
Candida score <3	565	13 (2.3)	
Candida score ≥ 3	327	45 (13.8)	8.7
Col. index <0.5	411	16 (3.9)	
Col. index ≥ 0.5	481	42 (8.7)	20.8

* No. of patients with CS ≥ 3 to predict one infection

Role of Beta-D-Glucan

- In 240 patients with colonization, serum levels was measured
- 18 developed invasive candidiasis
- For a cutoff value of 75 pg/mL
 - 77.8% sensitivity
 - 52.7% specificity
- Both CS and beta-glucan were independent predictors

Serum Procalcitonin Levels in 136 Patients in ICU



Significance of *Candida* Isolation from Airway Samples in ICU

2004-2006
17-bed MICU
1900-bed hospital

1587 admissions

301 died (19%)

232 autopsies (77%)

135 pts w pneumonia (%58)

97 pts w/o pneumonia (42%)

77 pts w resp. samples (+) for *Candida*

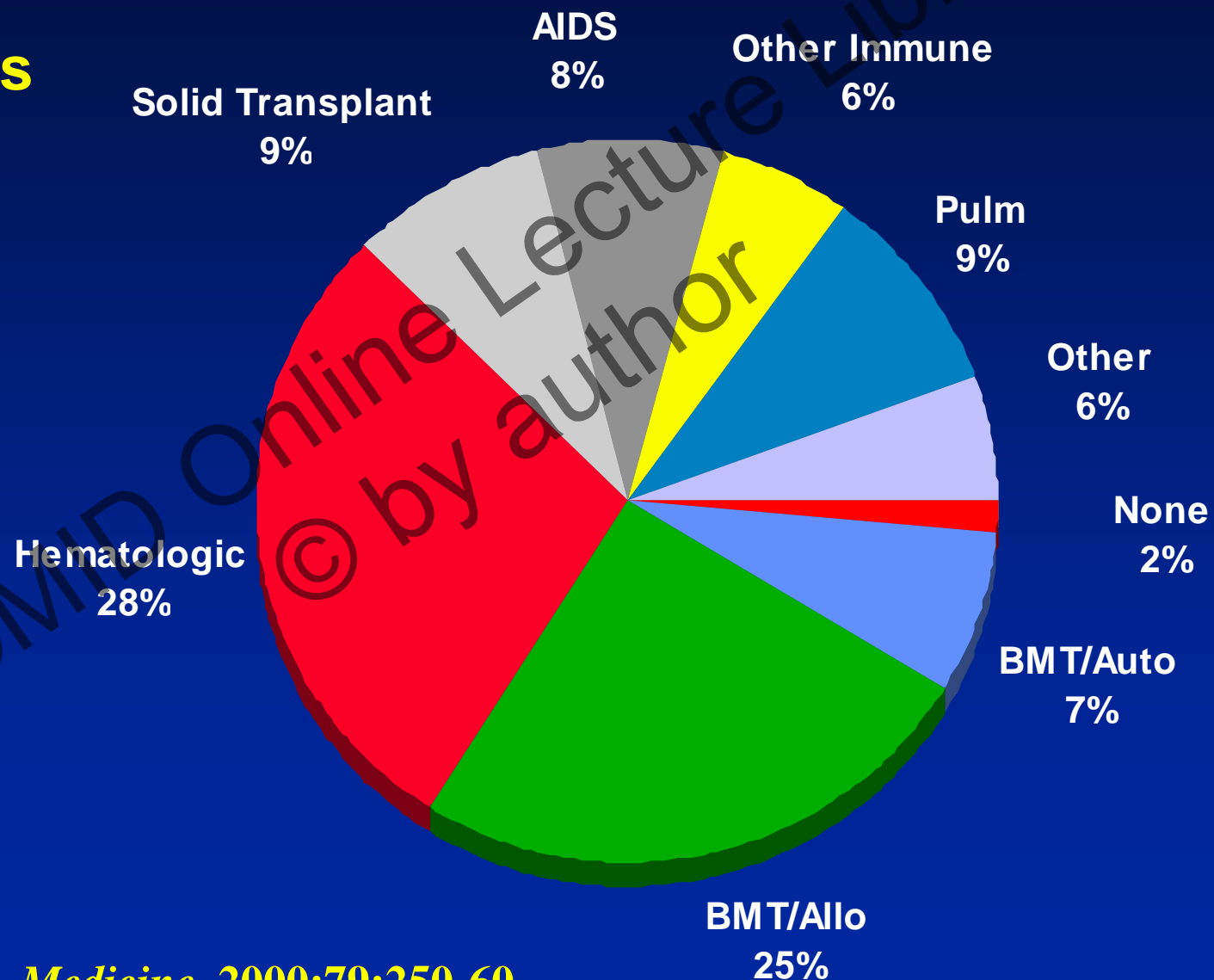
58 pts w resp. samples (-) for *Candida*

Candida pneumonia
N=0

Conditions	Patients
Chronic obstructive pulmonary disease	16
Cirrhosis	13
ARDS ^a	10
Hematological malignancy	9
Solid organ malignancy	7
Cardiogenic shock	5
Systemic disease	5
Miscellaneous ^b	5
Solid organ transplant recipients	5
Pancreatitis	2

Primary Diagnosis in Patients with Invasive Aspergillosis

595 patients



Risk Factors for Invasive Aspergillosis in ICU

- COPD plus prolonged steroid use
- High-dose steroid use >3 weeks
- Chronic renal failure with dialysis
- Liver cirrhosis/Acute hepatic failure
- Near-drowning
- Diabetes mellitus

Galactomannan in BAL

- 110 ICU patients admitted to ICU
 - Only 22% neutropenic
 - 26 proven IA (16 in non-neutropenics)
- GM detection in BAL fluid
 - 88% sensitivity
 - 87% specificity
- Serum GM sensitivity 42%
- In 11 cases BAL culture and serum GM (-), BAL GM (+)

Conclusions

- **Invasive candidiasis causes significant mortality in ICU patients**
 - Early treatment is essential
 - Early diagnosis is problematic
 - Various prediction rules are available
 - May be used in conjunction with other tests; i.e. PCT, serum β -glucan
- **No prediction rules for aspergillus and other mold infections**
 - High-level suspicion in risk groups