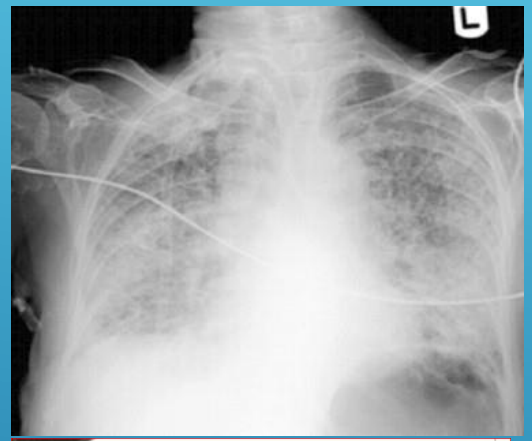
Spécificités des atteintes pulmonaires chez les patients immunodéprimés

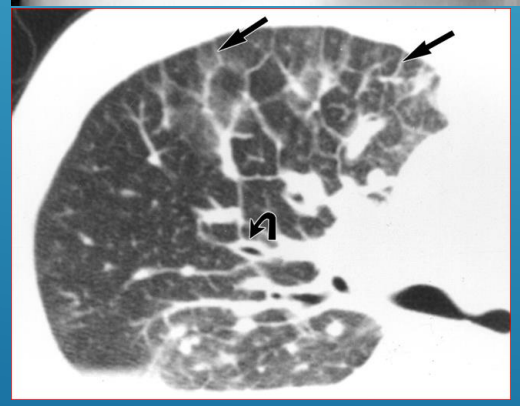
Élie Azoulay,
Université Paris, Hôpital St-Louis,
Groupe de Recherche Respiratoire en Réanimation Onco- Hématologique (Grrr-OH)

1 Patient de 57a,
Myélome autogreffe
HypoGamma

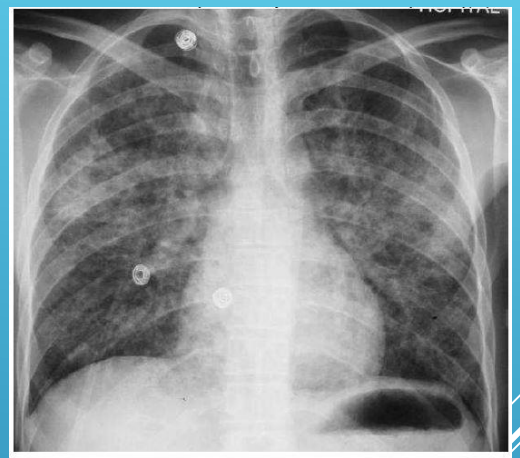
Méro
TMP-SMX
Amoxyciline
Ambisome
Amikacine

2 Patiente de 47a
LAM5b inaugurale
Caryo nl, NPM1 et IDH2 mutés
Infiltration pulm. leucémique





3 Patient de 34a,
LALT inaugurale
37,000 GB



A propos de trois patients d'hématologie (Sept. 2020)

Un tiers des patients de réanimation sont immunodéprimés

30%

70 %

35-70 %

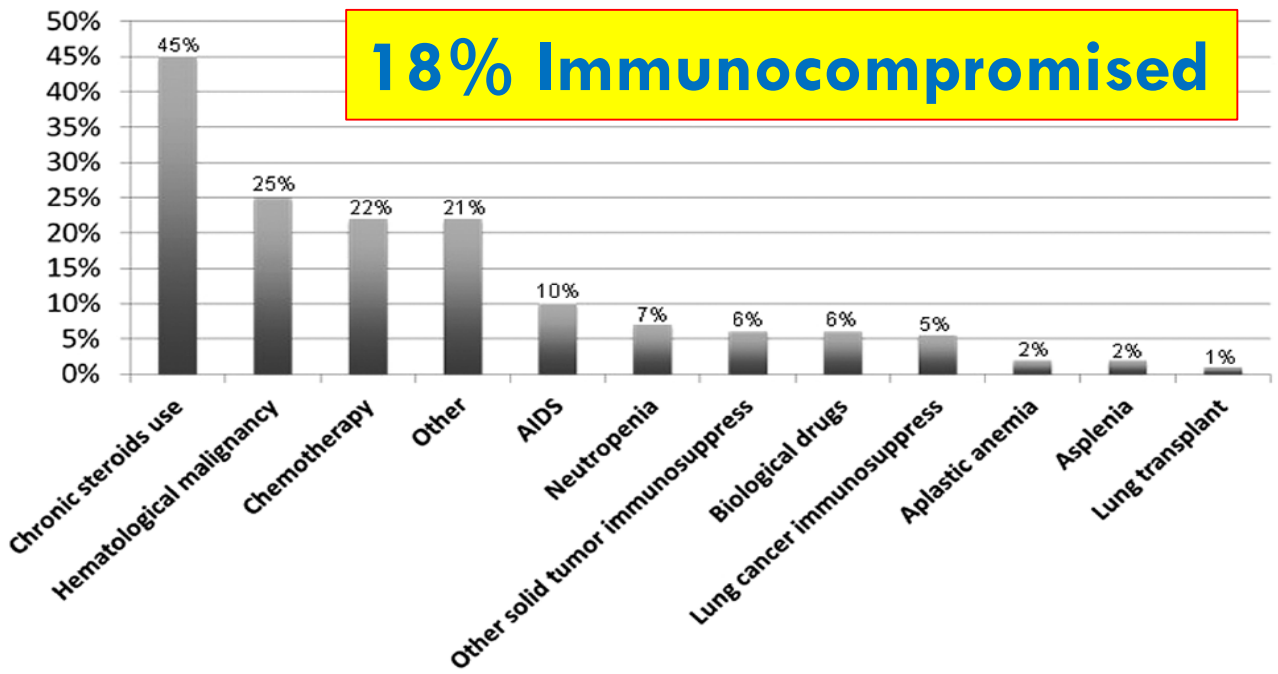
Clinical Infectious Diseases

MAJOR ARTICLE

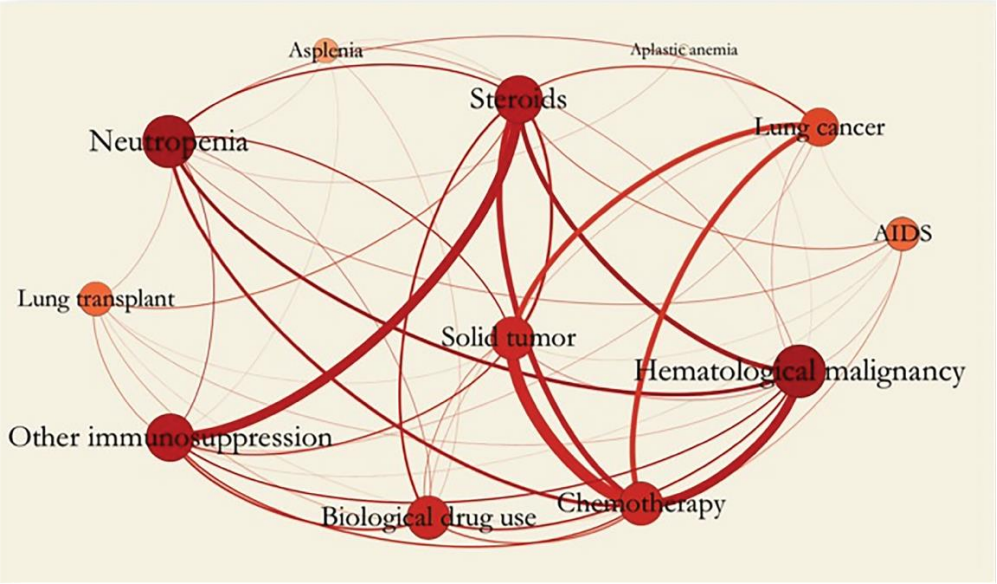
International study of patients with CAP from 222 hospitals in 54 countries.

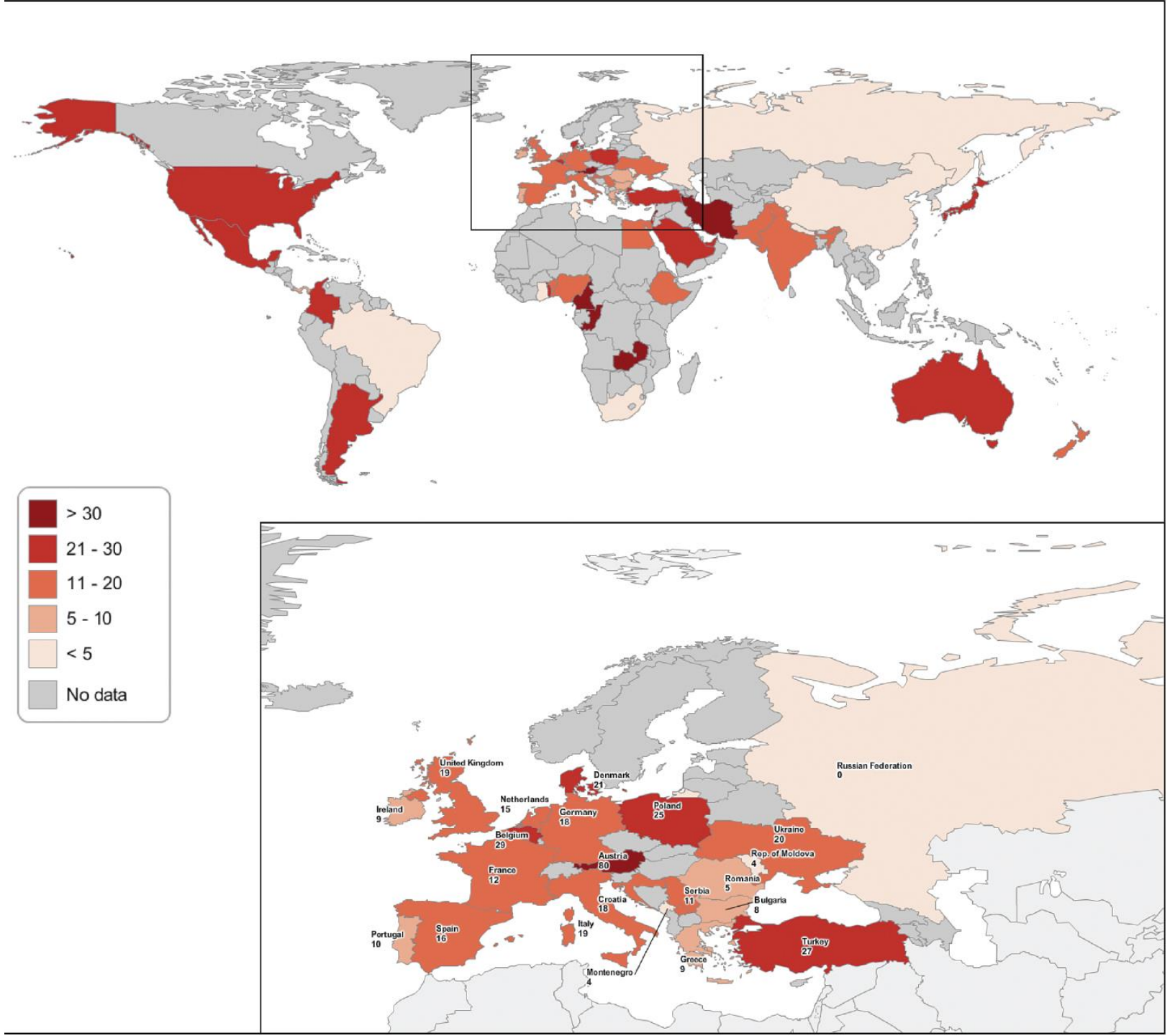
Prevalence and Etiology of Community-acquired Pneumonia in Immunocompromised Patients

Marta Francesca Di Pasquale,[1] Giovanni Sotgiu,[2] Andrea Gramegna,[1] Dejan Radovanovic,[3] Silvia Terraneo,[4] Luis F. Reyes,[5] Jan Rupp,[6] Juan González del Castillo,[7,8] Francesco Blasi,[1] Stefano Aliberti,[1] and Marcos I. Restrepo[9]; on behalf of GLIMP Investigators



CID 2019:68 (1 May) • Di Pasquale et al





GLIMP database

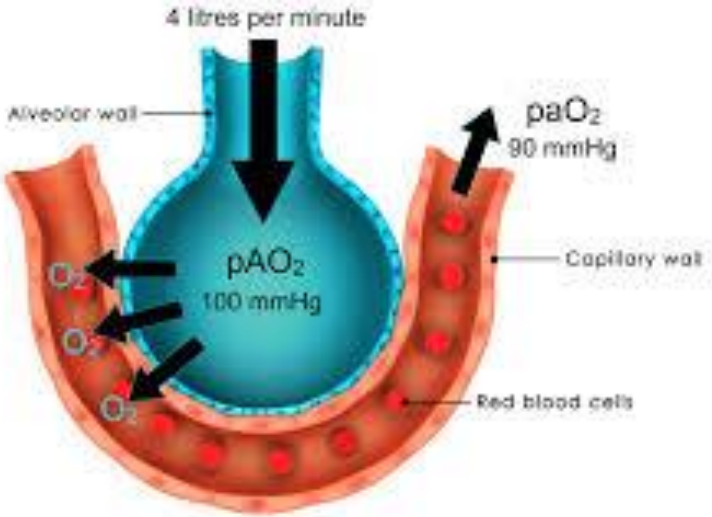
CID 2019:68 (1 May) • Di Pasquale et al

Acute Respiratory failure

1

2

3



Spécificités des atteintes pulmonaires chez les patients immunodéprimés

1. Incidence et sévérité et critères d'admission en réanimation
2. Stratégie diagnostique
3. Examens diagnostiques

Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America

hivma hiv medicine association

OXFORD

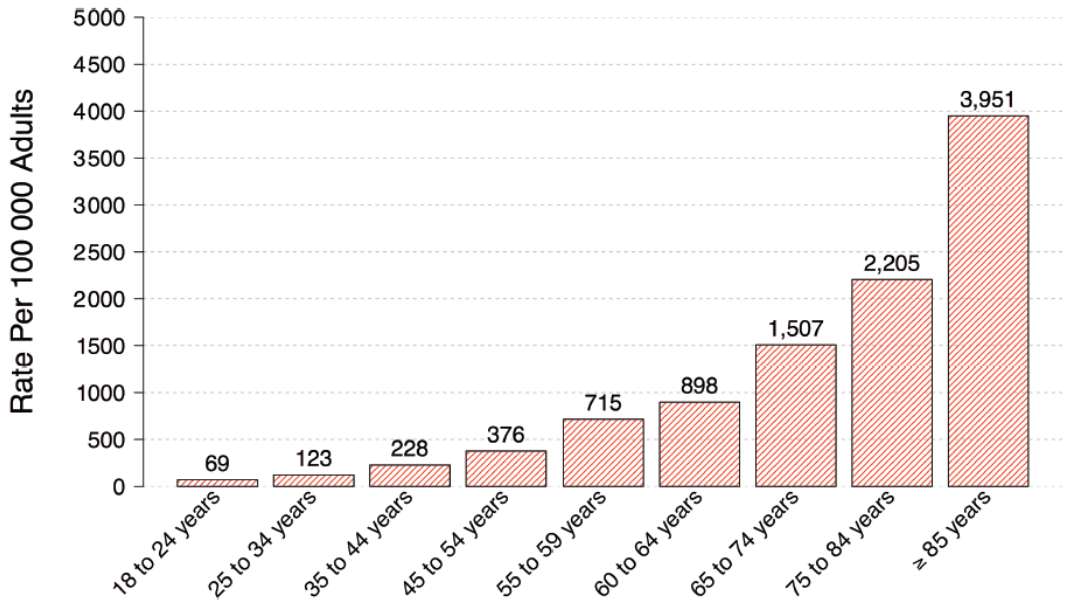
Population-based cohort study of adult from Louisville, Kentucky (June 2014-31 May 2016).

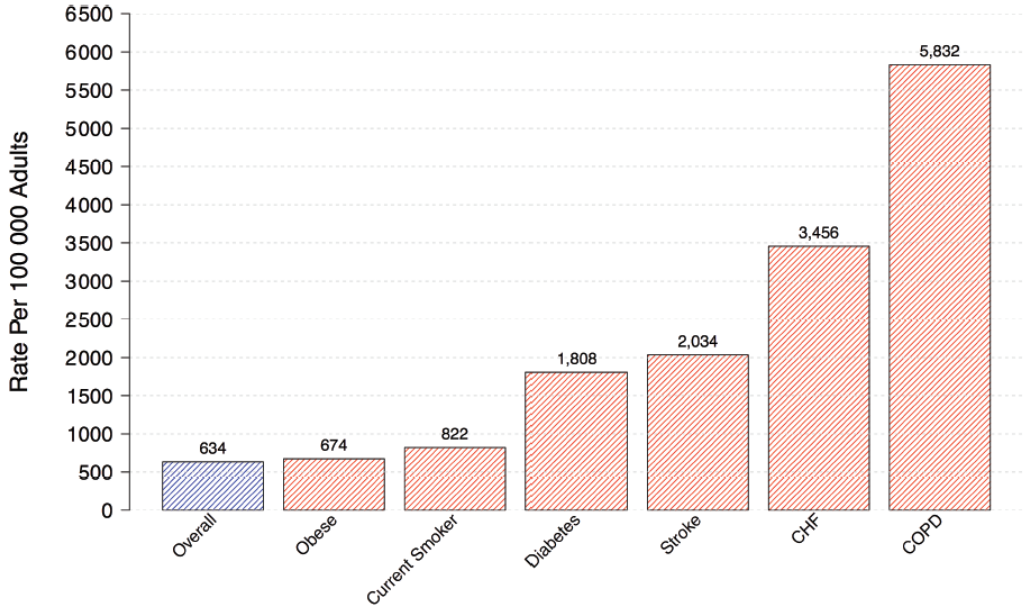
Adults Hospitalized With Pneumonia in the United States: Incidence, Epidemiology, and Mortality

Julio A. Ramirez,[1] Timothy L. Wiemken,[1] Paula Peyrani,[1] Forest W. Arnold,[1] Robert Kelley,[1] William A. Mattingly,[1] Raul Nakamatsu,[1] Senen Pena,[1] Brian E. Guinn,[1] Stephen P. Furmanek,[1] Annuradha K. Persaud,[1] Anupama Raghuram,[1] Francisco Fernandez,[1] Leslie Beavin,[1] Rahel Bosson,[1] Rafael Fernandez-Botran,[2] Rodrigo Cavallazzi,[3] Jose Bordon,[4] Claudia Valdivieso,[5] Joann Schulte,[6] and Ruth M. Carrico[1]; for the University of Louisville Pneumonia Study Group

- **7449 patients with CAP = annual age-adjusted incidence was 649/100 000 adults**
- **1,591825 annual adult CAP hospitalizations in the US**
- **Mortality during hospitalization was 6.5%,**

Age and comorbid conditions

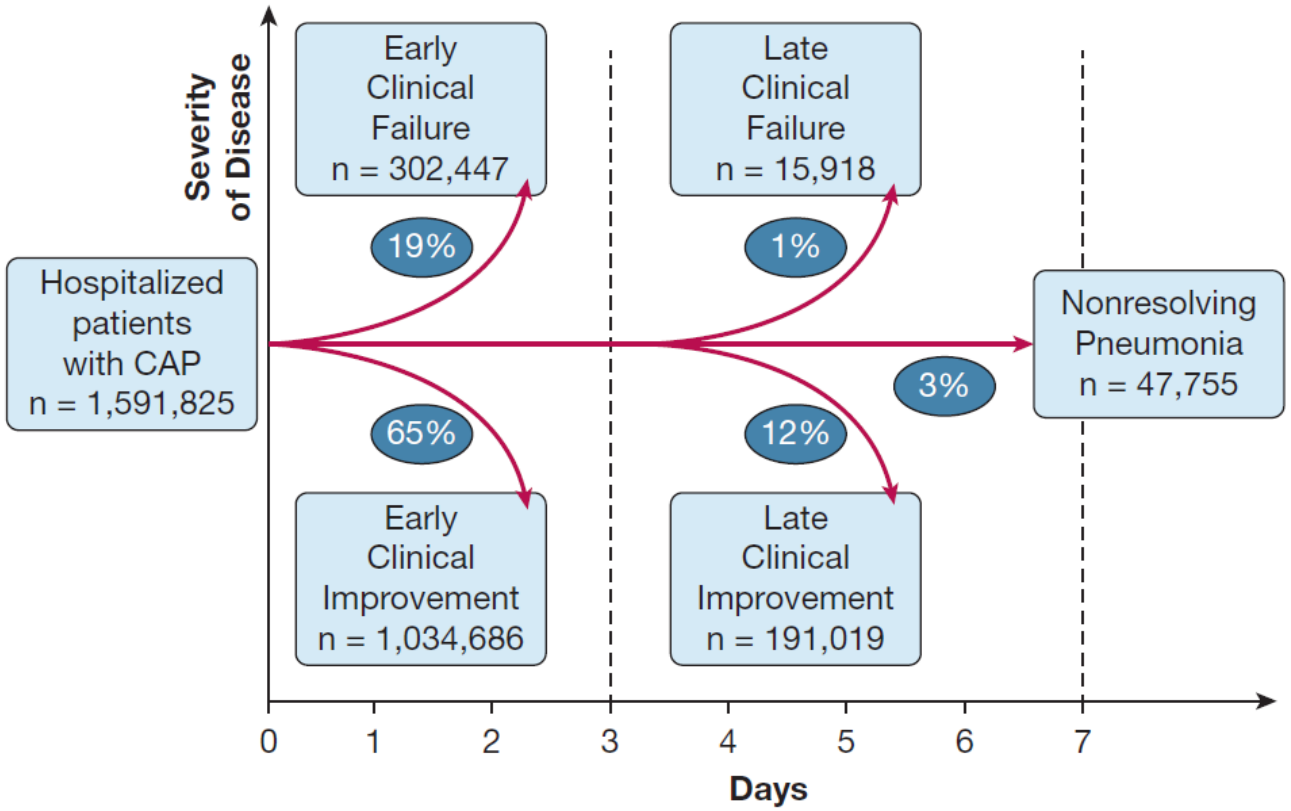




Incidence and Mortality of Adults Hospitalized With Community-Acquired Pneumonia According to Clinical Course

CHEST 2020; 157(1):34-41

Paula Peyrani, MD; Forest W. Arnold, DO; Jose Bordon, MD; Stephen Furmanek, MPH; Carlos M. Luna, MD; Rodrigo Cavallazzi, MD; and Julio Ramirez, MD



ARF Incidence according the type of ID

50
40
30
20
10
5
1

Allogeneic BMT/HSCT, AML

Prolonged Neutropenia

Lymphoproliferative disease

SOT (lung)

SOT (kidney), ALL, lymphoma

Lung cancer,
Syst diseases,
SOT heart
Solid tumors

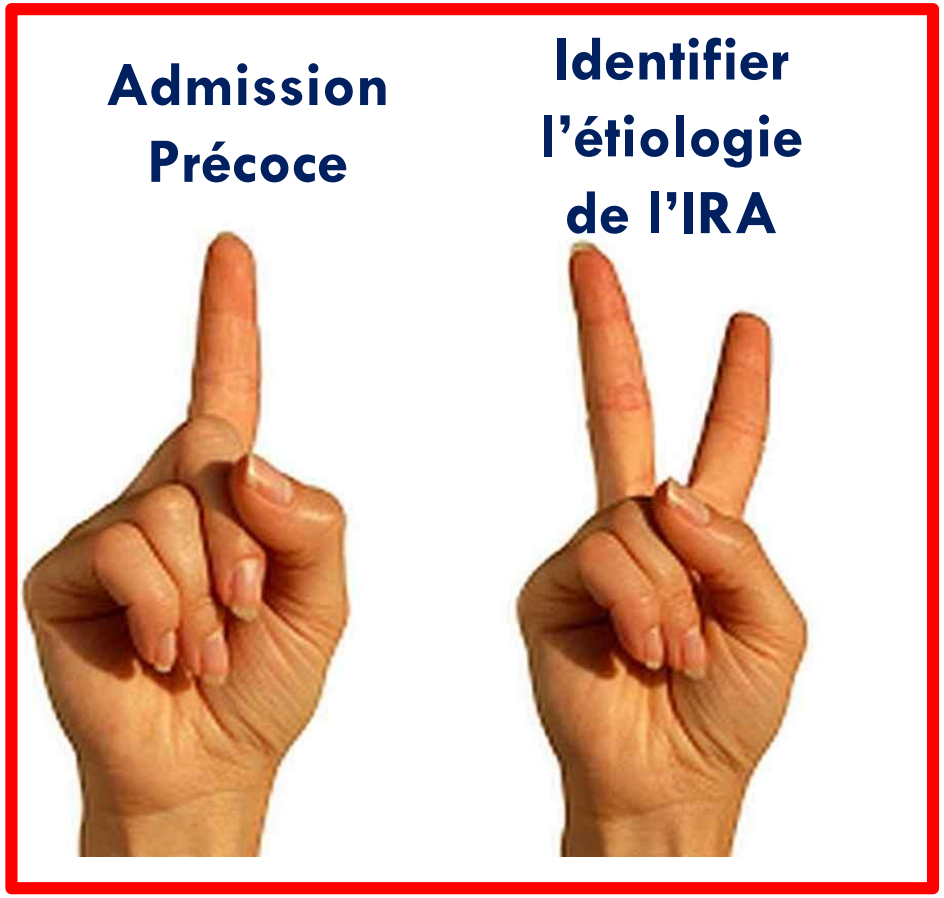
500,000 patients per year in Europe

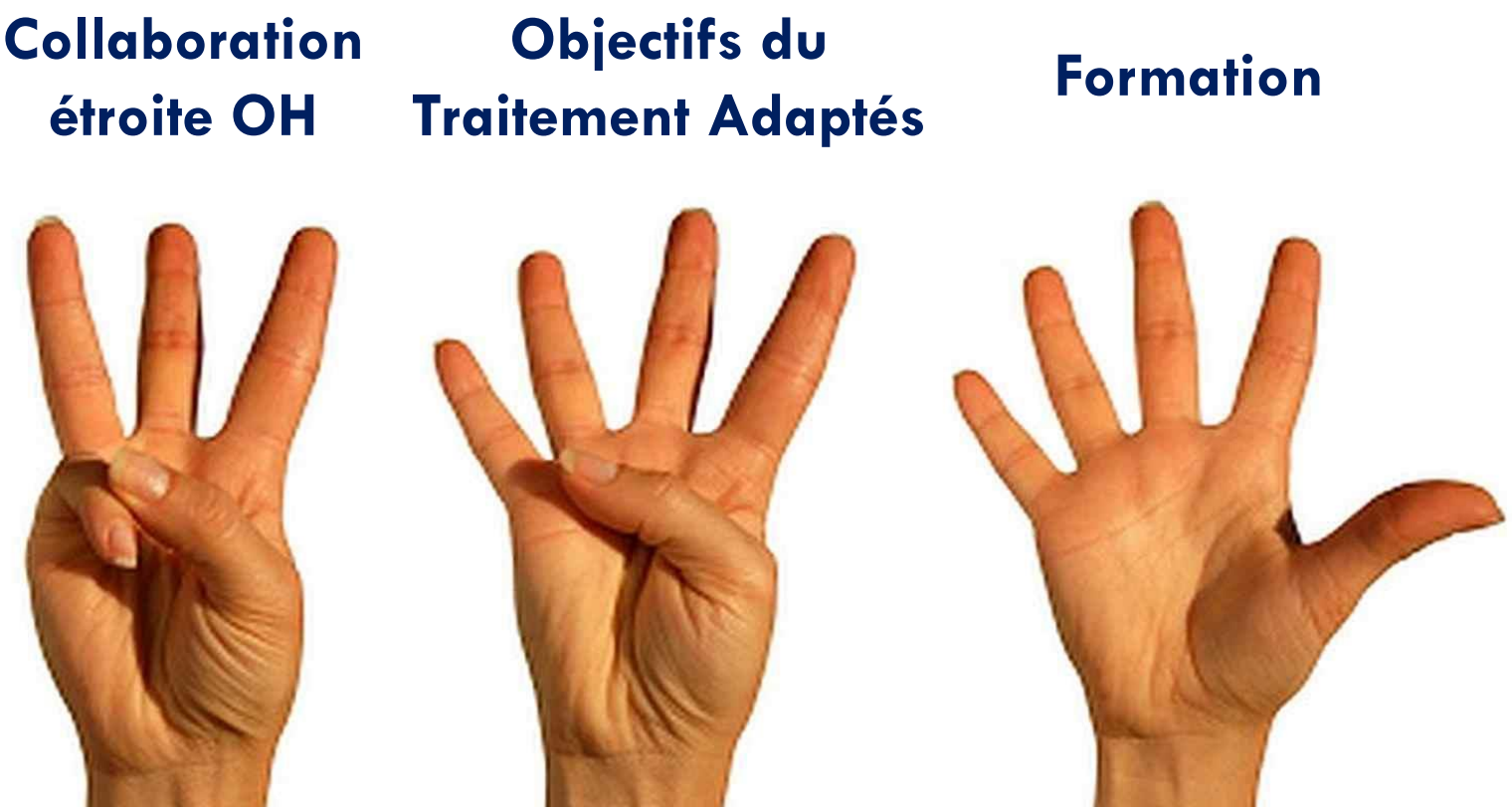
	Cumulative incidence of respiratory events		Need for ICU admission		Hospital mortality
Haematological malignancies					
Acute myeloid leukaemia	22%-84%		66%		45%
Acute lymphoblastic leukaemia	7%-18.5%		12%-15%		38.5%
Lymphoproliferative diseases	8%		8%		40-50%
Myelodysplastic syndrome	29.4%	AML	20%	+++	17%
Autologous HSCT	3%-28%		42%		3%-55%
Allogeneic HSCT	24%-30%		50%		51%
Prolonged neutropenia	8%-29.5%		11%-16%		5%-12%
					50%
Solid tumours					
Lung cancer	26%-50%	Lung Cancer	All	+++	11.2%-60%
Other solid tumours	0.7%-10.3%		All		6.1%-55%
Patients on immunotherapy	1.3%-3.6%		1.3% ¥		/
Solid organ transplantation					
Lung transplantation	14%	Lung Tx	All	+++	65%
Heart transplantation	12.5%		All		76.5%
Kidney transplantation	3.3%-4.8%		All		16.4%-22.5%

Table 1. Clinical and Severity Characteristics of the 2 Study Groups (Immunocompetent vs Immunocompromised)

Variable	Patients, No. (%)[a] Immunocompetent (n = 3050)	Immunocompromised (n = 652)	*P* Value
Age, median (IQR)	69 (54–81)	65 (52–74)	<.001
Underweight	125 (6.5)	41 (10.5)	.004
Malnutrition	243 (8.0)	80 (12.3)	<.001
Bedridden	355 (11.6)	60 (9.2)	.04
Chronic aspiration	224 (7.3)	33 (5.1)	.02
Bronchiectasis	136 (4.5)	42 (6.4)	.03
Severe COPD	72 (2.4)	28 (4.3)	.006
Interstitial lung disease	60 (2.0)	35 (5.4)	<.001
Lung transplantation	0 (0.0)	7 (1.1)	<.001
Tracheostomy	37 (1.2)	16 (2.5)	.02
Hypertension	1401 (45.9)	254 (39.0)	.001
Liver disease	103 (3.4)	37 (5.7)	.005
Cirrhosis	50 (1.6)	20 (3.1)	.02
Dementia	372 (12.2)	36 (5.5)	<.001
Enteral tube feeding	36 (1.2)	16 (2.5)	.01
Chronic renal failure	315 (10.3)	85 (13.0)	.04
Hemodialysis	34 (1.1)	18 (2.8)	.001
ICS use	462 (15.2)	128 (19.6)	.005
PPI use	777 (25.5)	251 (38.5)	<.001
Indwelling catheter	52 (1.7)	27 (4.1)	<.001
Prior mycobacteria diseases	70 (2.3)	26 (4.0)	.01
Prior ESBL	39 (1.3)	16 (2.5)	.02
Prior *Pseudomonas*	68 (2.2)	33 (5.1)	<.001
Severe CAP	840 (27.5)	190 (29.1)	.41

Pour améliorer la survie





ORIGINAL ARTICLE: CLINICAL

Leukemia & Lymphoma, August 2013; 54(8): 1724–1729

Delayed intensive care unit admission is associated with increased mortality in patients with cancer with acute respiratory failure

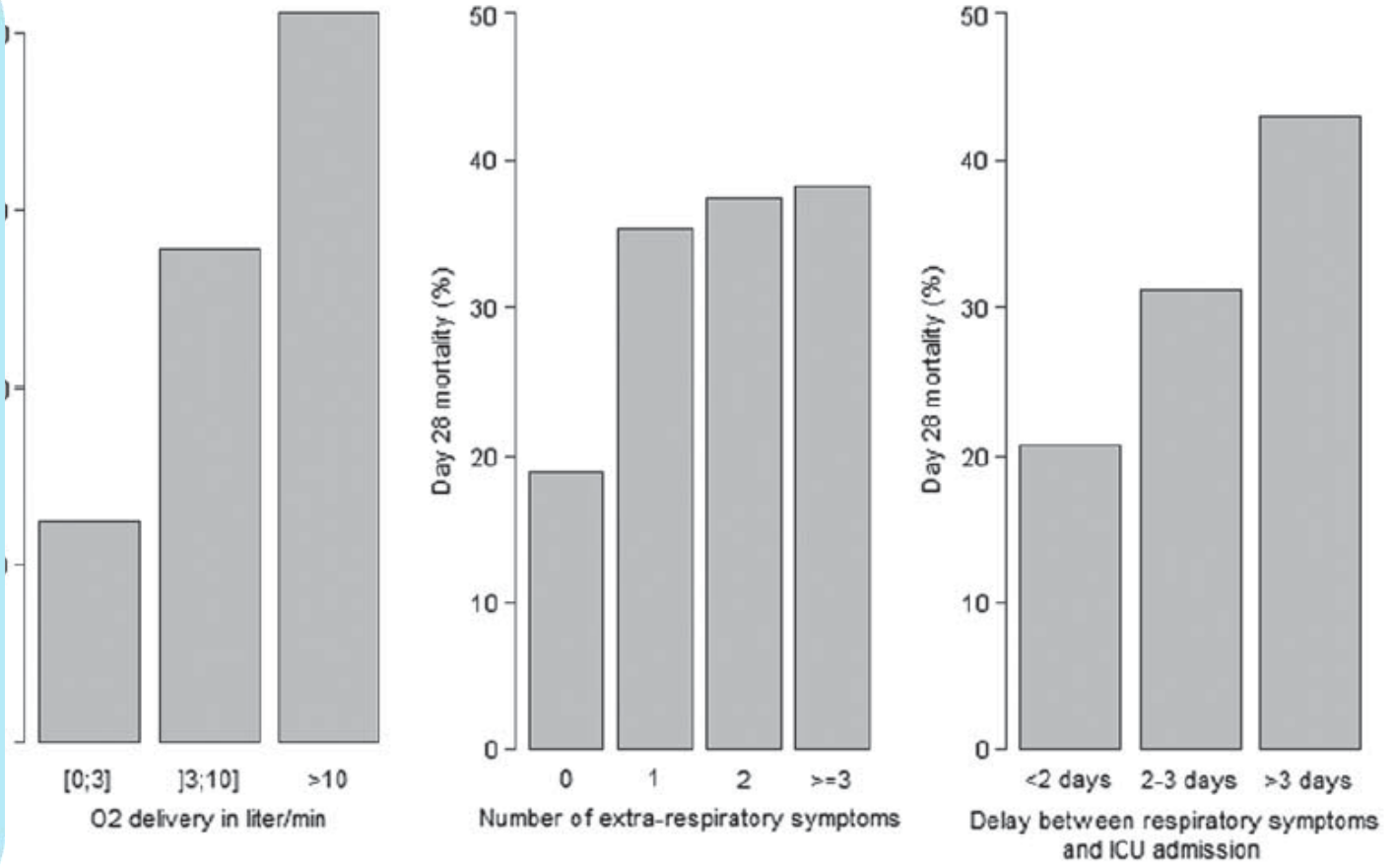
id Schnell[3], Louis Fouché[1], Antoine Rabbat[4], Achille Kouatchet[5],

ARF

2l O2 = 4x ICU

6l O2 = 40% MV

6l 02 = 25-30% mortality

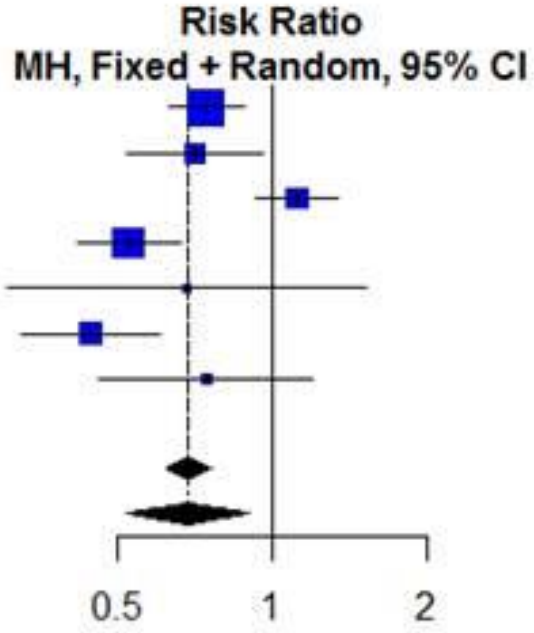


rvival according to O_2 delivery, extra-respiratory symptoms and delay between respiratory symptoms onset and ICU admission.

Early ICU Admission for Hematology patients

Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight (fixed)	Weight (random)	Risk Ratio MH, Fixed + Random, 95% CI
Azoulay , 2013	144	451	241	560	37.8%	17.4%	0.74 [0.63, 0.88]
Bird, 2012	41	107	50	92	9.5%	15.1%	0.71 [0.52, 0.96]
Doukhan, 2017	193	246	38	54	11.0%	17.1%	1.11 [0.93, 1.34]
Lee, 2015	64	221	168	304	24.9%	16.4%	0.52 [0.42, 0.66]
lengline, 2012	10	42	7	20	1.7%	7.1%	0.68 [0.30, 1.52]
Song , 2012	32	100	72	99	12.7%	15.0%	0.44 [0.32, 0.60]
Thiery, 2005	48	105	8	13	2.5%	11.8%	0.74 [0.46, 1.20]
Total (fixed effect, 95% CI)		**1272**		**1142**	**100.0%**	**--**	**0.69 [0.62, 0.76]**
Total (random effects, 95% CI)					**--**	**100.0%**	**0.69 [0.52, 0.90]**

Heterogeneity: $Tau^2 = 0.10$; $Chi^2 = 40.64$, df = 6 ($P < 0.01$); $I^2 = 85\%$
Test for overall effect (fixed effect): Z = -7.56 ($P < 0.01$)
Test for overall effect (random effects): Z = -2.72 ($P < 0.01$)



Hourmant & Darmon, Submitted. Journal of Critical Care 2020

Spécificités des atteintes pulmonaires chez les patients immunodéprimés

1. Incidence et sévérité et critères d'admission en réanimation
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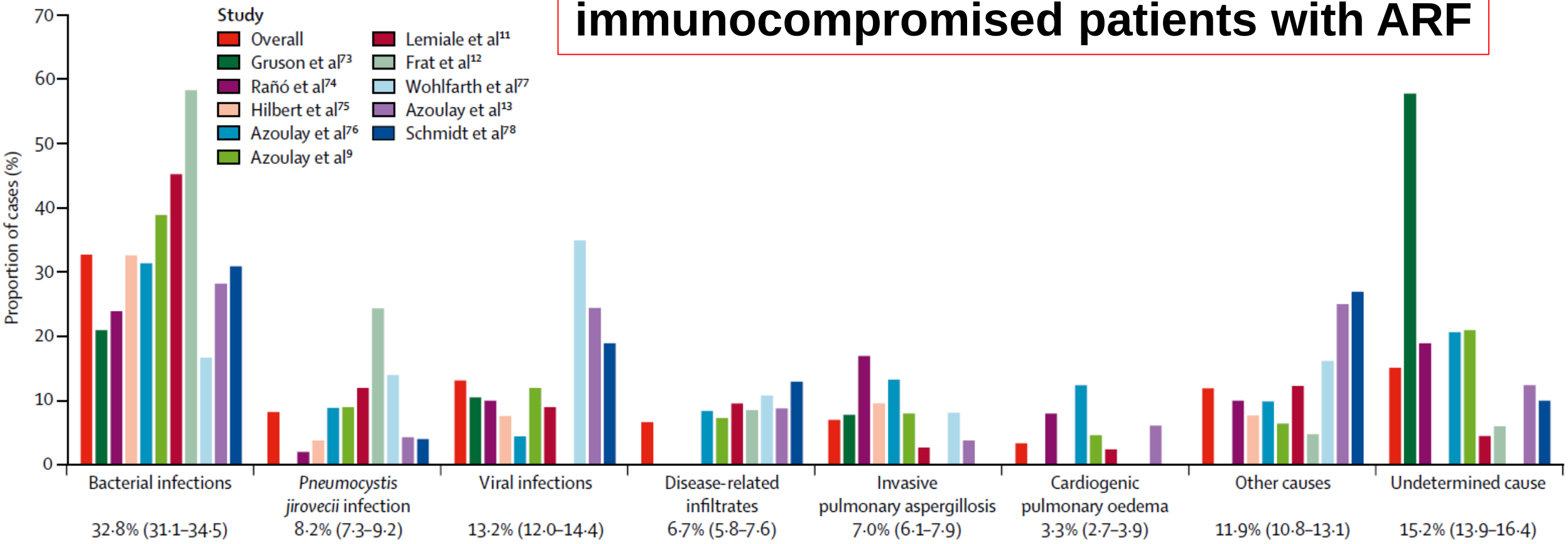
Acute respiratory failure in immunocompromised adults

Elie Azoulay, Djamel Mokart, Achille Kouatchet, Alexandre Demoule, Virginie Lemiale

Azoulay et al. Lancet Respiratory Medicine 2018

Causes of pulmonary infiltrates in immunocompromised patients with ARF



Azoulay et al. Lancet Respiratory Medicine 2018

Intensive Care Med
DOI 10.1007/s00134-006-0129-2

REVIEW

Élie Azoulay
Benoît Schlemmer

Diagnostic strategy in cancer patients with acute respiratory failure

The DIRECT approach: a guide to select initial antimicrobial treatments and appropriate investigations

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Delay since malignancy onset or BMT
Patterns of **I**mmune deficiency
Radiographic appearance
Clinical **E**xperience and knowledge of the literature
Clinical picture
Findings by the high resolution computed **T**omodensitometry (HRCT)

The GPS = clinical stratification for the pre-test probability (*to identify the most probable ARF etiologies)*

1

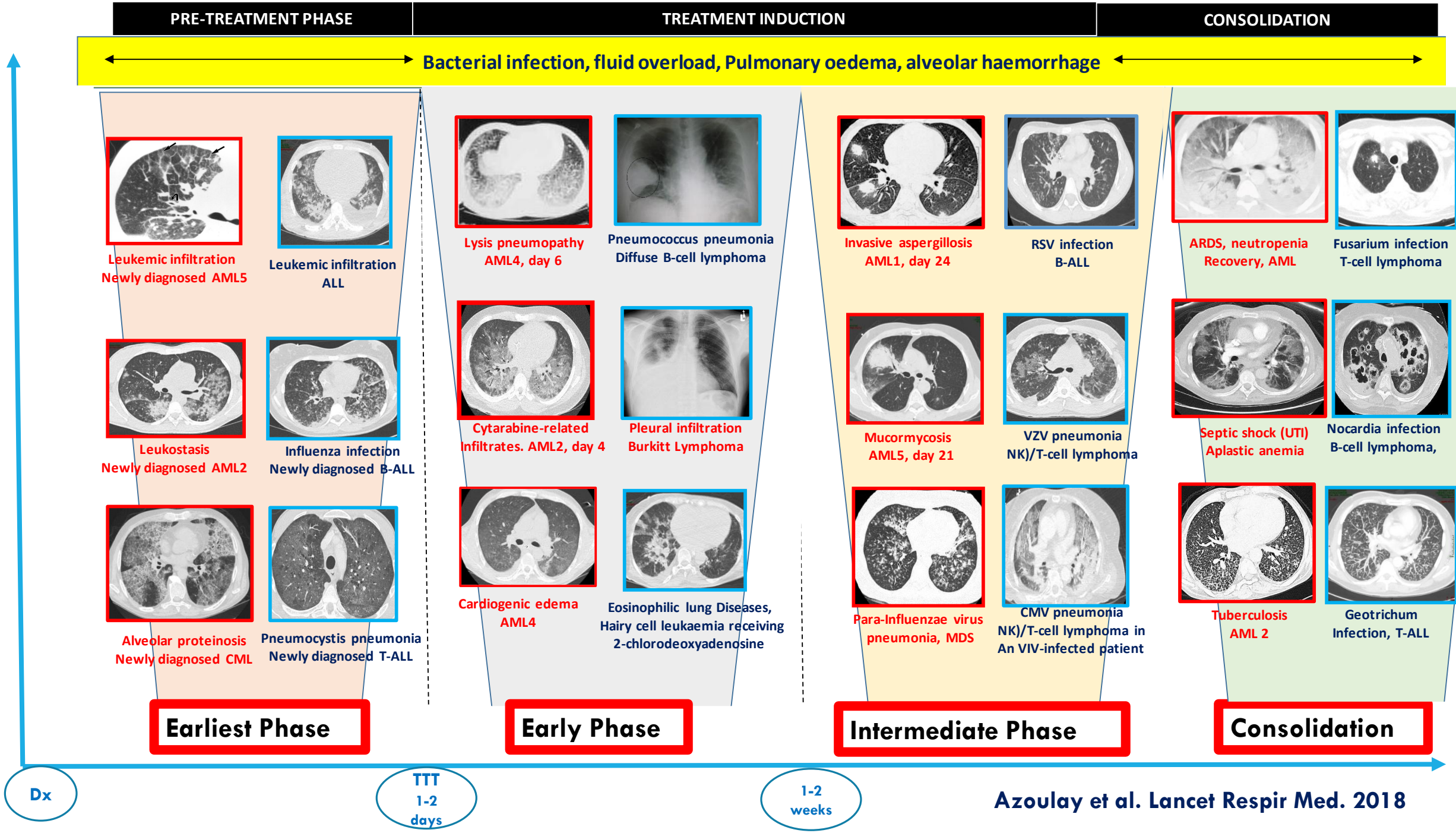
Use the GPS to provide early and adequate TTT, select the appropriate diagnostic strategy and sometimes avoid risky procedures

2

Perform the appropriate diagnostic strategy to document and confirm the initial approach. Give priority to NIT

3

Use innovative tests, oMICs technology and integrative biology to distinguish colonization from infection


PRE-TREATMENT PHASE
TREATMENT INDUCTION
CONSOLIDATION
Bacterial infection, fluid overload, Pulmonary oedema, alveolar haemorrhage
Leukemic infiltration
Newly diagnosed AML5
Leukemic infiltration
ALL
Leukostasis
Newly diagnosed AML2
Influenza infection
Newly diagnosed B-ALL
Alveolar proteinosis
Newly diagnosed CML
Pneumocystis pneumonia
Newly diagnosed T-ALL
Lysis pneumopathy
AML4, day 6
Pneumococcus pneumonia
Diffuse B-cell lymphoma
Cytarabine-related
Infiltrates. AML2, day 4
Pleural infiltration
Burkitt Lymphoma
Cardiogenic edema
AML4
Eosinophilic lung Diseases,
Hairy cell leukaemia receiving
2-chlorodeoxyadenosine
Invasive aspergillosis
AML1, day 24
RSV infection
B-ALL
Mucormycosis
AML5, day 21
VZV pneumonia
NK)/T-cell lymphoma
Para-Influenzae virus
pneumonia, MDS
CMV pneumonia
NK)/T-cell lymphoma in
An VIV-infected patient
ARDS, neutropenia
Recovery, AML
Fusarium infection
T-cell lymphoma
Septic shock (UTI)
Aplastic anemia
Nocardia infection
B-cell lymphoma,
Tuberculosis
AML 2
Geotrichum
Infection, T-ALL
Earliest Phase
Early Phase
Intermediate Phase
Consolidation
Dx
TTT
1-2
days
1-2
weeks
Azoulay et al. Lancet Respir Med. 2018

Infectious risk and immunologic dysfunctions

DISEASES:
Acute leukaemia;
Myelodysplastic syndrome;
Aplastic anaemia;
Chemotherapy and drug-related neutropenia;

- Gram negative bacteria
- Gram positive bacteria
- Candida
- Aspergillus
- Herpes Virus
- Nocardia
- Salmonella

NEUTROPHILS

DISEASES:
Hairy cell leukemia; Aplastic anemia; Allogeneic BMT; Malignant histiocytosis; AML; CML; Solid tumours; HLH

TREATMENTS:
Steroids; Basiliximab; ATG; Alemtuzumab; Tacrolimus; Cyclosporine; MMF; Betalacept; mTOR inhibitors (sirolimus)

- Mycobacteria
- Salmonella, Listeria, Legionella, Histoplasma, Brucella
- HSV, VZV, PIV, RSV,
- Candida
- S. pneumoniae, S. aureus, E. faecalis, P aeruginosa
- Pneumocystis jirovecii

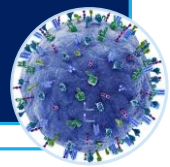
MACROPHAGES

DISEASES:
Multiple myeloma;
B-cell lymphoma;
Chronic lymphocytic leukaemia;

TREATMENTS:
Chemotherapy;
Steroids;
Asplenia;
Rituximab

- Encapsulated bacteria (S. pneumoniae, S. pyogenes, H influenzae, and S aureus)
- Giardia lamblia
- Mycoplasma
- Enterovirus
- Recurrent infections

B LYMPHOCYTES

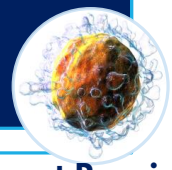


DISEASES:
T-cell leukaemia;
Hodgkin disease;

TREATMENTS:
Steroids; Fludarabin; Cyclophosphamide; Methotrexate; Azathioprine; Mycophenolate mofetil; Ciclosporin; Tacrolimus.

- Pneumocystis jiroveci, Aspergillus, CMV,
- Mycobacterial infection,
- Candida
- Diarrhoea (rotaviruses, adenoviruses….).

T LYMPHOCYTES

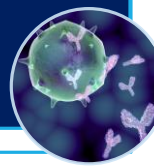


DISEASES:
Multiple myeloma
Chronic lymphoid leukemia

TREATMENTS:
Ibrutinib; Rituximab

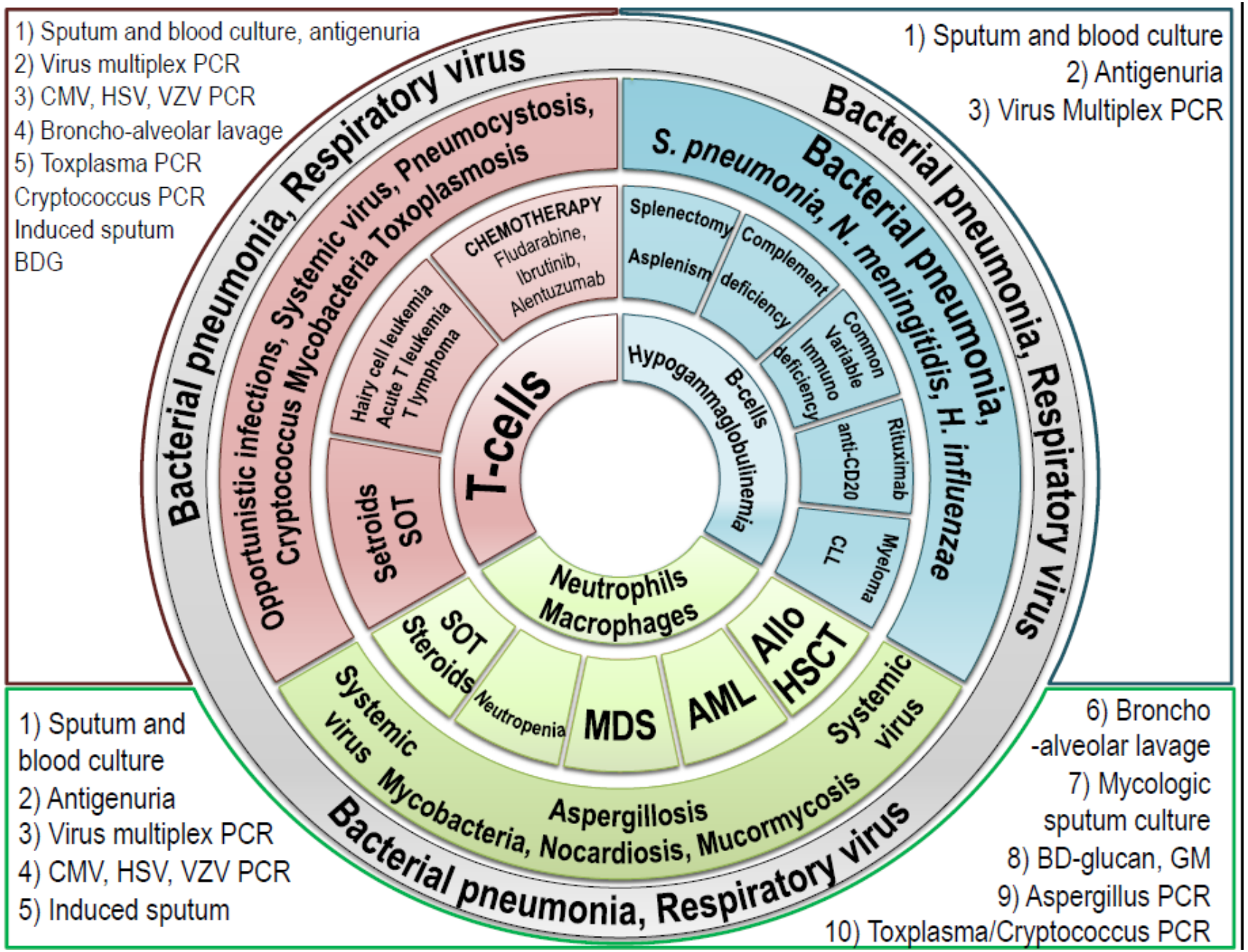
- Encapsulated bacteria (S. pneumoniae, S. pyogenes, H influenzae, and S aureus)
- Mycoplasma,
- Mycobacteria

HUMORAL (antibody) IMMUNITY

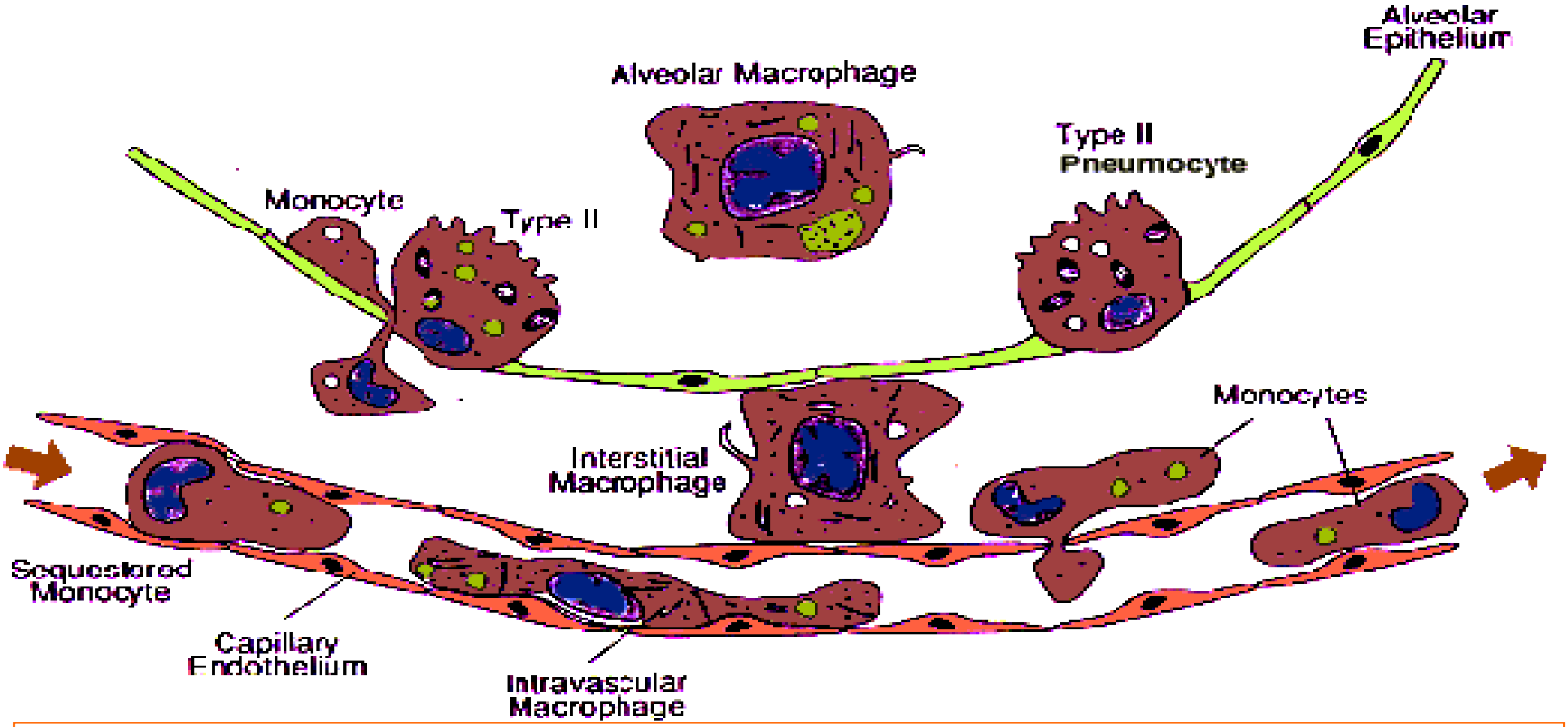


Azoulay et al. Lancet Respir Med. 2018

Pulmonary Infections according to immunosuppression



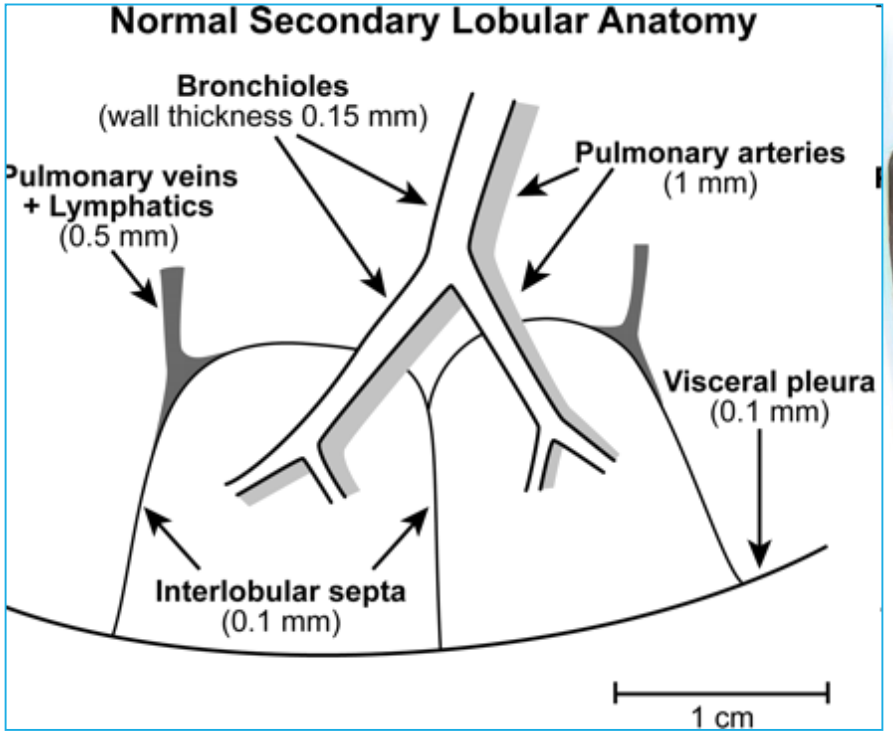
Azoulay et al. In Press 2020

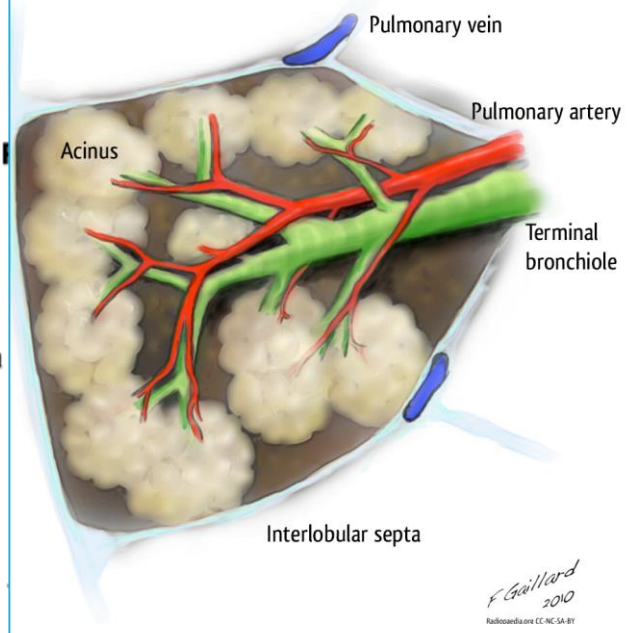


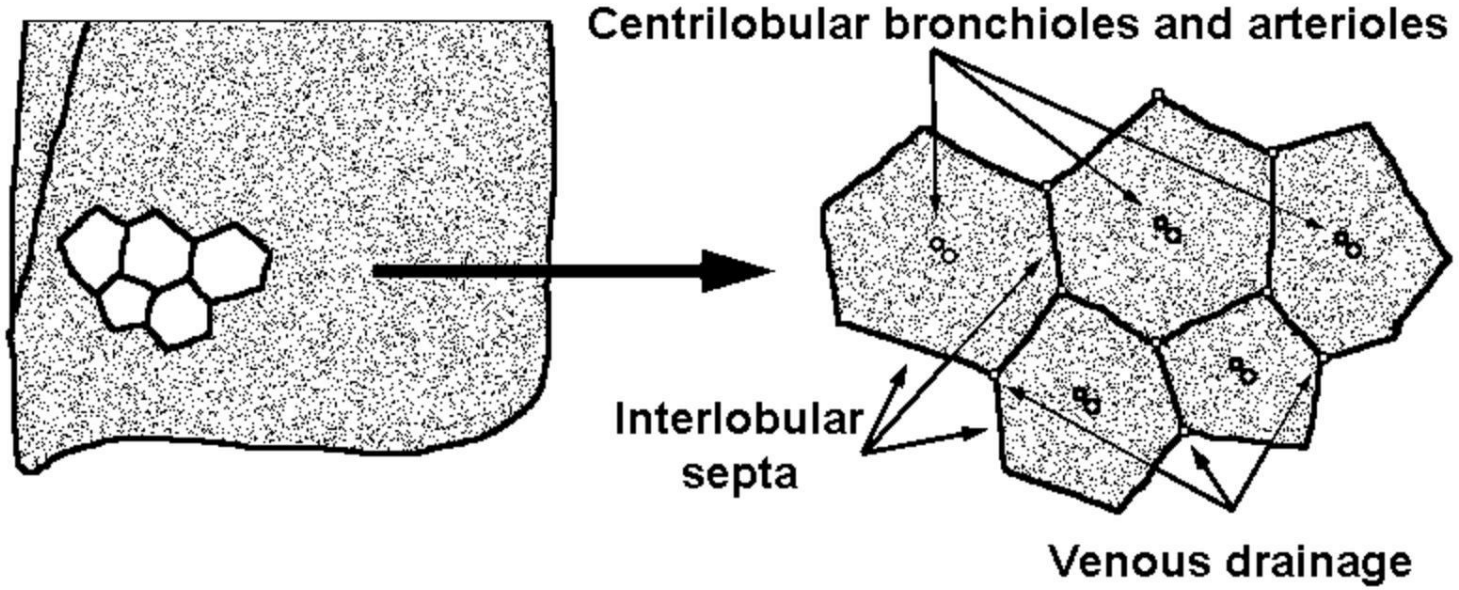
Portion of the lung between epithelial and endothelial membranes

http://www.bioscience.org/1997/v2/d/longwort/2.htm

Secondary pulmonary lobular anatomy







CHESTRADIOLOGY.NET

Heussel et al. JCO 1999

	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Ground Glass				
> 0%	74	71	55	85
> 25%	31	82	45	71
> 50%	13	88	35	68
In > 1 lobe	56	79	56	79
Consolidation	33	89	59	73
Ill defined Nodules	57	86	66	81
In > 1 lobe	44	88	64	77
Linear Opacities				
opacities	18	94	58	70
Cavitation	11	98	78	70
Effusion	25	88	50	71

NODULAR LESIONS
- **Bacterial pneumonia**
- **Aspergillosis**
- **Nocardiosis**
- **Mucormycosis**

- Sputum and blood culture
- Antigenuria
- Sputum with mycologic culture
- PCR Aspergillus and mucormycosis
- Galactomannan, BD-glucan
- Broncho-alveolar lavage

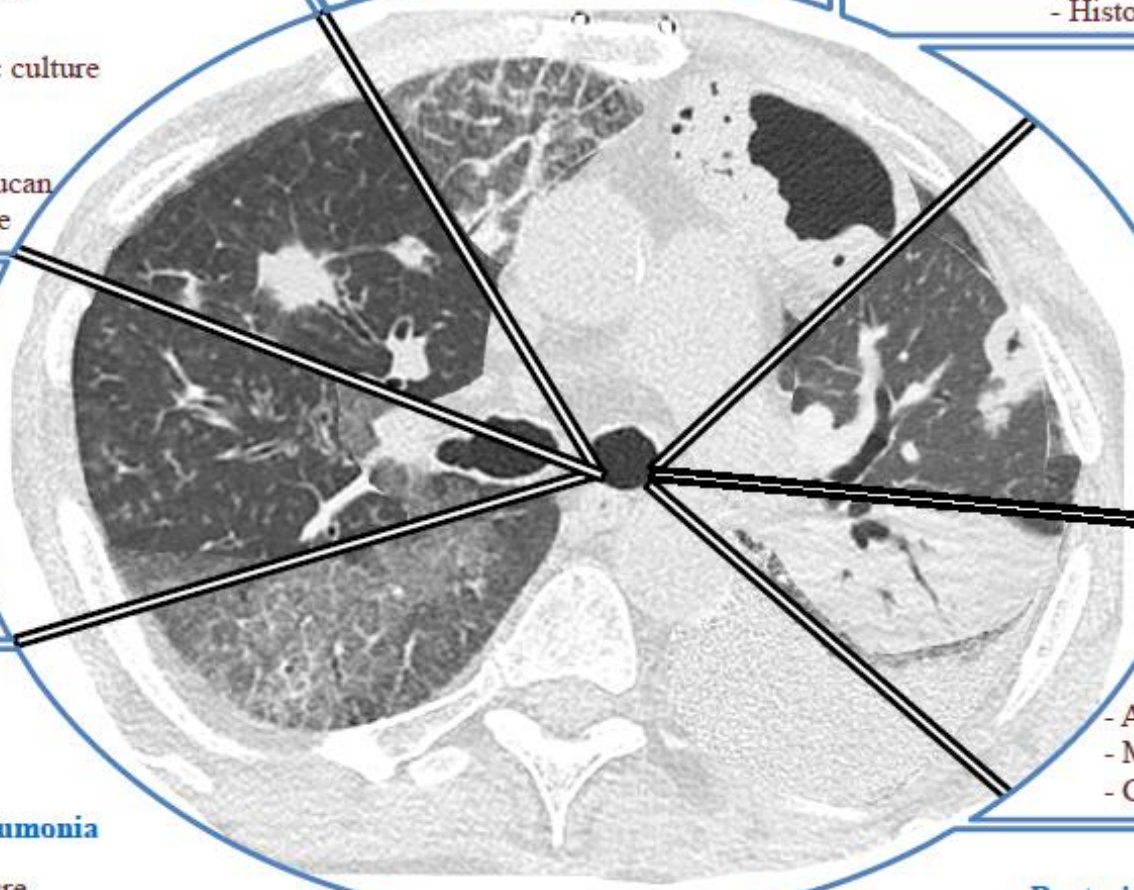
SEPTAL THICKENING
- **Atypical bacterial pneumonia**

- Sputum and blood culture
- Antigenuria
- Broncho-alveolar lavage

CAVITATION
- **Mycobacteria**
- **Histoplasma**
- **Bacterial pneumonia** (*S. aureus*)

- Sputum and blood culture
- Mycobacteria culture
- Histoplasma PCR

MICRONODULES
- **Bacterial pneumonia**
- **Viral pneumonia**
- **Mycobacteria**
- Sputum and blood culture
- Multiplex virus PCR
- Mycobacteria culture
- CMV, VZV, HSV PCR



EXCAVATED NODULES
- **Bacterial pneumonia**
- **Mucormycosis**
- **Nocardiosis**
- **Actinomyces**
- **Aspergillosis**
- Sputum & blood culture
  - Mucor PCR
  - Nocardia PCR
  - BD-glucan
  - Galactomannan
  - Aspergillus PCR

CONSOLIDATION
- **Bacterial pneumonia**
- **Aspergillosis**
- Sputum and blood culture
- Antigenuria
- Mycologic sputum culture
- GM, BD-glucan

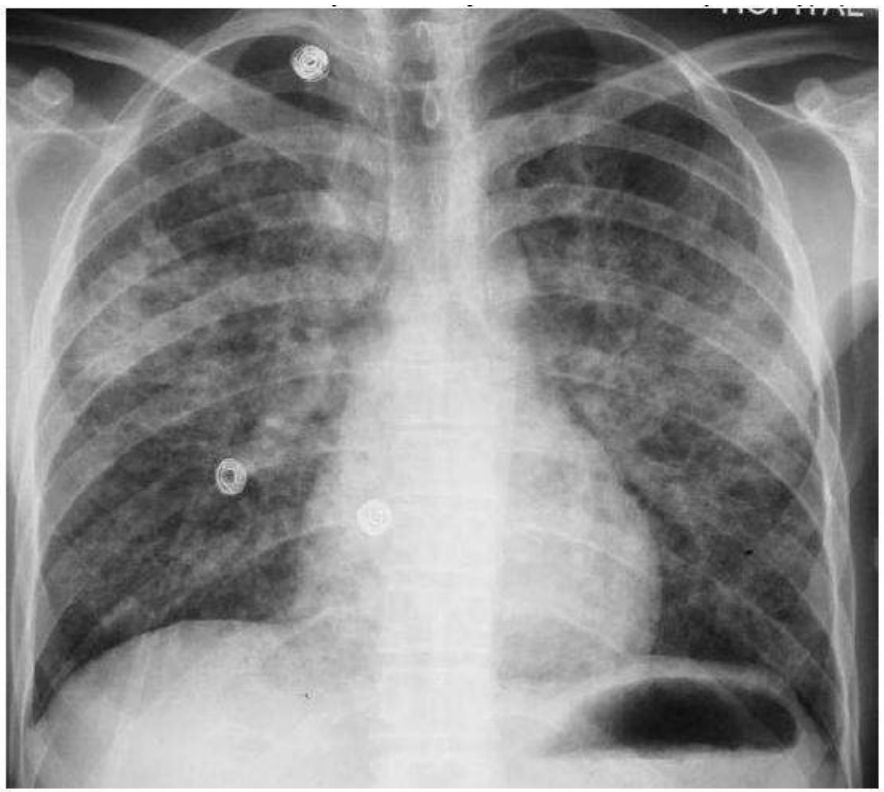
GROUND GLASS OPACITIES
- **Pneumocystosis**
- **Viral pneumonia**
- **Atypical bacterial pneumonia**

- Sputum and blood culture
- Legionella antigenuria
- Induced sputum for Pneumocystis search
- BD-glucan
- Multiplex virus PCR
- CMV, VZV, and HSV blood PCR
- Broncho-alveolar lavage, Pneumocystis IF and PCR

PLEURAL EFFUSION
- **Bacterial pneumonia**
- **Tuberculosis**

- Sputum and blood culture
- Antigenuria
- Mycobacteria blood culture
- Pleural effusion punction and culture

34yo man, T-cell leukemia. Acute respiratory failure



bjh research paper

Quantification of the effect of chemotherapy and steroids on risk of *Pneumocystis jiroveci* among hospitalized patients with adult T-cell leukaemia

© 2014 John Wiley & Sons Ltd
British Journal of Haematology, 2015, **168,** 501–506

bjh BRITISH JOURNAL OF HAEMATOLOGY

214 PCP cases

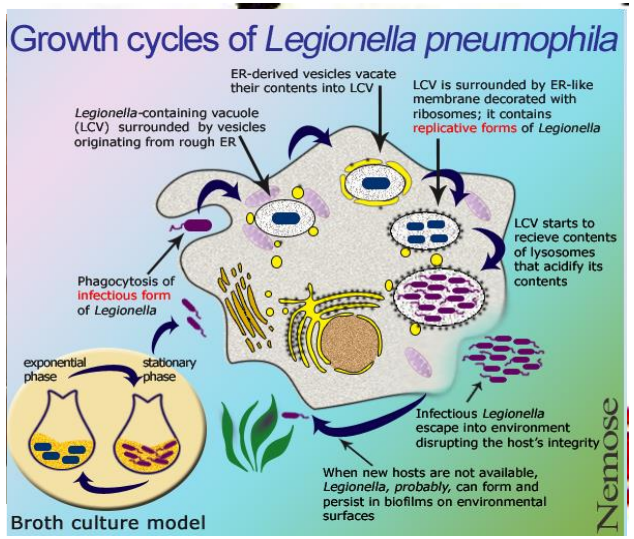
	PCP		Crude		
	n	%	OR	95% CI	*P*-value
Treatment group					
No agent	30	3·2		Reference	
Chemotherapy	10	9·7	3·21	1·52–6·77	0·002
Chemotherapy plus steroid	80	10·0	3·32	2·15–5·10	<0·001
Steroid	94	16·6	5·94	3·88–9·10	<0·001

A 49a yo man with fever, pancytopenia, spleen enlargement: diagnosis of HCL

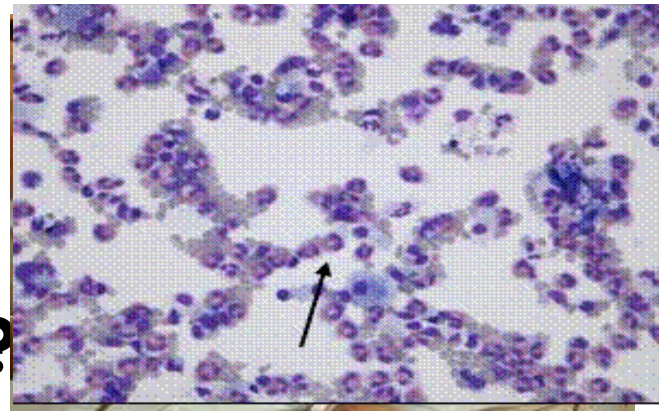
The DIRECT approach:
ments and appropriate in

Delay since malignancy
Patterns of Immune defi
Radiographic appearanc
Clinical Experience and
Clinical picture
Findings by the high res
(HRCT)

Are we at day 0?



Are we at day 15?



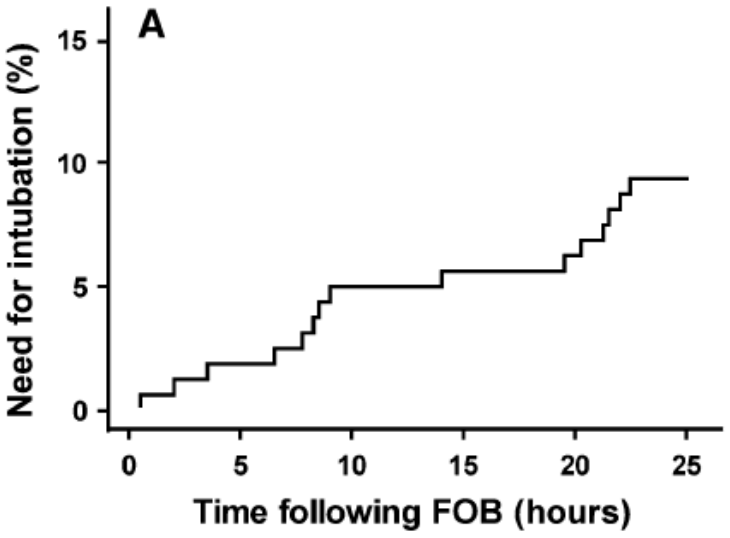
Spécificités des atteintes pulmonaires chez les patients immunodéprimés

1. Incidence et sévérité et critères d'admission en réanimation
2. Stratégie diagnostique
3. Examens diagnostiques

Christophe Cracco
Muriel Fartoukh
Hélène Prodanovic
Elie Azoulay
Cécile Chenivesse
Christine Lorut
Gaëtan Beduneau
Hoang Nam Bui
Camille Taille
Laurent Brochard
Alexandre Demoule
Bernard Maitre

Safety of performing fiberoptic bronchoscopy in critically ill hypoxemic patients with acute respiratory failure

Intensive Care Med (2013) 39:45–52
DOI 10.1007/s00134-012-2687-9



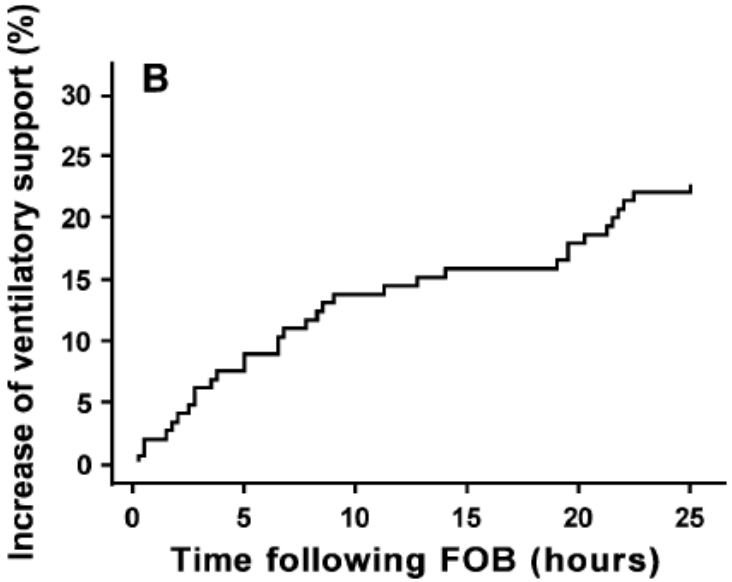


Table 4 Factors associated with initiation of invasive ventilation within 24 h after bronchoscopy in multivariable analysis

	Odds ratio	95 % confidence interval	*p* value
COPD	5.3	1.6–17.8	0.007
Immunosuppression	5.4	1.7–17.2	0.004

ORIGINAL

Benefit-to-risk balance of bronchoalveolar lavage in the critically ill. A prospective, multicenter cohort study

Toufik Kamel[1], Julie Helms[2], Ralf Janssen-Langenstein[3], Achille Kouatchet[4], Antoine Guillon[5], Jeremy Bourenne[6], Damien Contou[7], Christophe Guervilly[8,9], Rémi Coudroy[10,11], Marie Anne Hoppe[12], Jean Baptiste Lascarrou[13], Jean Pierre Quenot[14], Gwenhaël Colin[15], Paris Meng[16], Jérôme Roustan[17], Christophe Cracco[18], Mai-Anh Nay[1], Thierry Boulain[1*] and Clinical Research in Intensive Care Sepsis Group (CRICS-TRIGGERSEP)

483 patients dans 16 ICUs, la moitié immunodéprimés

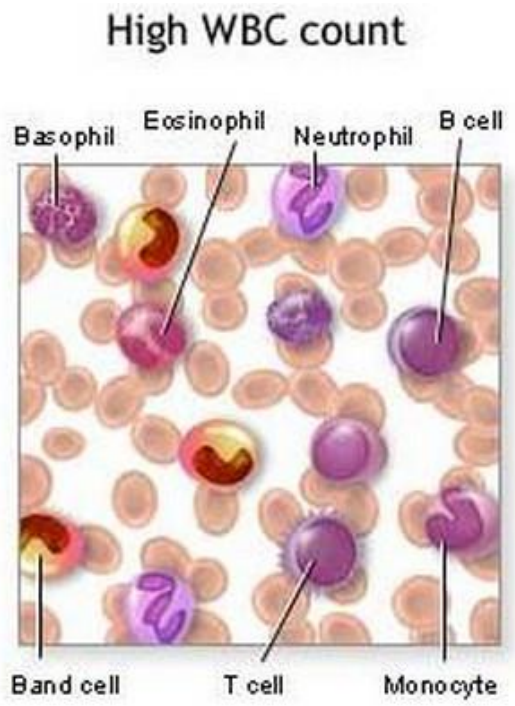
LBA chez patients non intubés dans 20% des cas

14% d'effets secondaires sévères

- **Surtout si la fibroscopie est faite par un médecin moins expérimenté (<10a d'experience, quelle que soit la spécialité)**

Diagnostic Criteria

Fever



Hyperleukocytosis

Biomarkers

Rapid Pathogen Detection

Diagnostic Strategy for Hematology and Oncology Patients with Acute Respiratory Failure

Randomized Controlled Trial

Am J Respir Crit Care Med Vol 182. pp 1038–1046, 2010

Élie Azoulay[1], Djamel Mokart[2], Jérôme Lambert[3], Virginie Lemiale[4], Antoine Rabbat[5], Achille Kouatchet[6], François Vincent[7], Didier Gruson[8], Fabrice Bruneel[9], Géraldine Epinette-Branche[1], Ariane Lafabrie[1], Rebecca Hamidfar-Roy[10], Christophe Cracco[11], Benoît Renard[12], Jean-Marie Tonnelier[13], François Blot[14], Sylvie Chevret[3], and Benoît Schlemmer[1]

Etiologies	MAXI N=113	MINI N=106
Bacteria	47 (41%)	39 (37%)
Viruses	7 (6%)	19 (18%)
Fongi	14 (12%)	9 (8.5%)
Pneumocystis	9 (8%)	10 (9.4%)
Malignant infiltration	10 (9%)	6 (6%)
Cardiac Pulm. Edem	7 (6%)	3 (3%)
More than one diagnosis	9 (8%)	9 (8.4%)

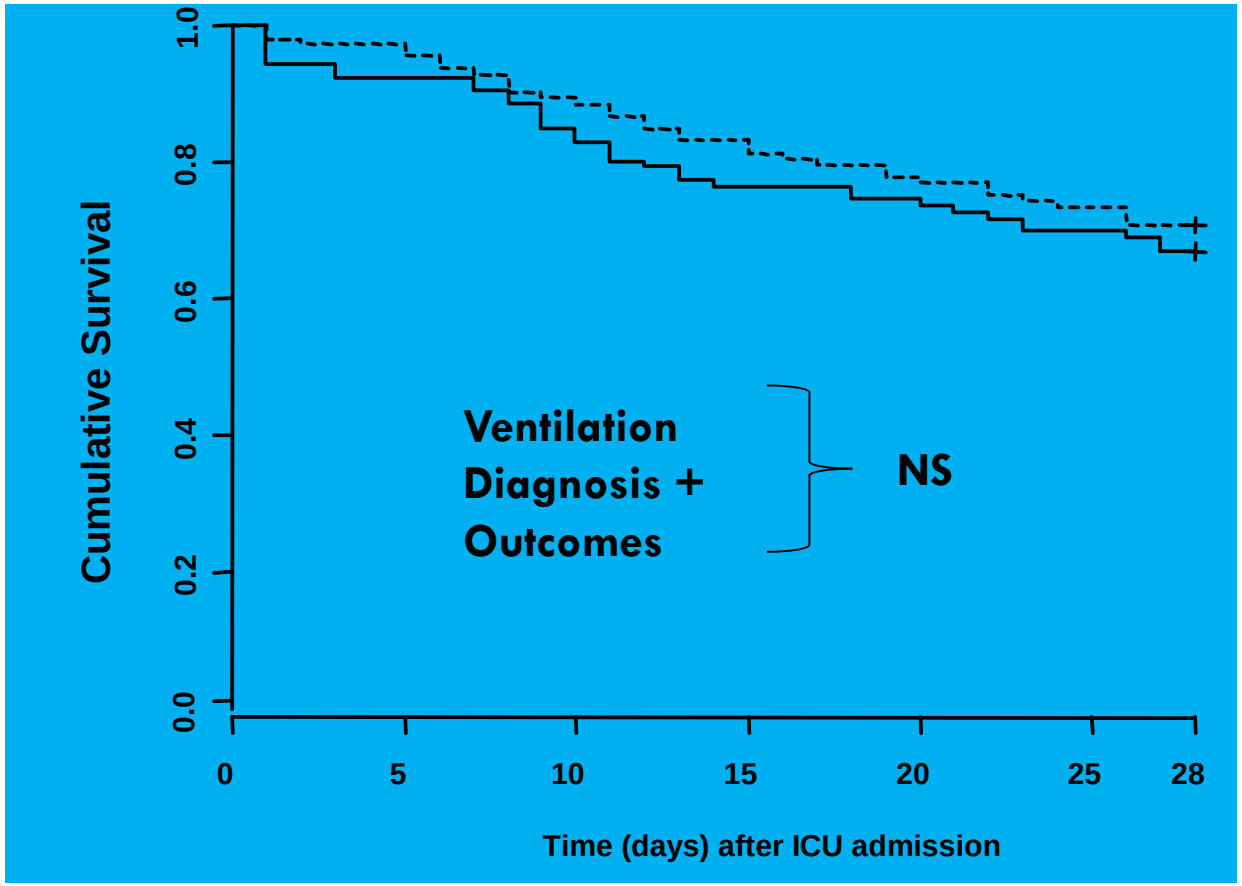
Diagnoses	Diagnosis made by NIT
CPO: 10	10 (100%)
Fungi: 23	22 (95.6%)
Aspergilus: 18	17 (94%)
Virus: 26	24 (92.3%)
Malignancy: 16	13 (81%)
Pneumocystis: 19	15 (79%)
Bacteria: 86	57 (66.3%)

Diagnostic Strategy for Hematology and Oncology Patients with Acute Respiratory Failure

Randomized Controlled Trial

Am J Respir Crit Care Med Vol 182. pp 1038–1046, 2010

Élie Azoulay[1], Djamel Mokart[2], Jérôme Lambert[3], Virginie Lemiale[4], Antoine Rabbat[5], Achille Kouatchet[6], François Vincent[7], Didier Gruson[8], Fabrice Bruneel[9], Géraldine Epinette-Branche[1], Ariane Lafabrie[1], Rebecca Hamidfar-Roy[10], Christophe Cracco[11], Benoît Renard[12], Jean-Marie Tonnelier[13], François Blot[14], Sylvie Chevret[3], and Benoît Schlemmer[1]

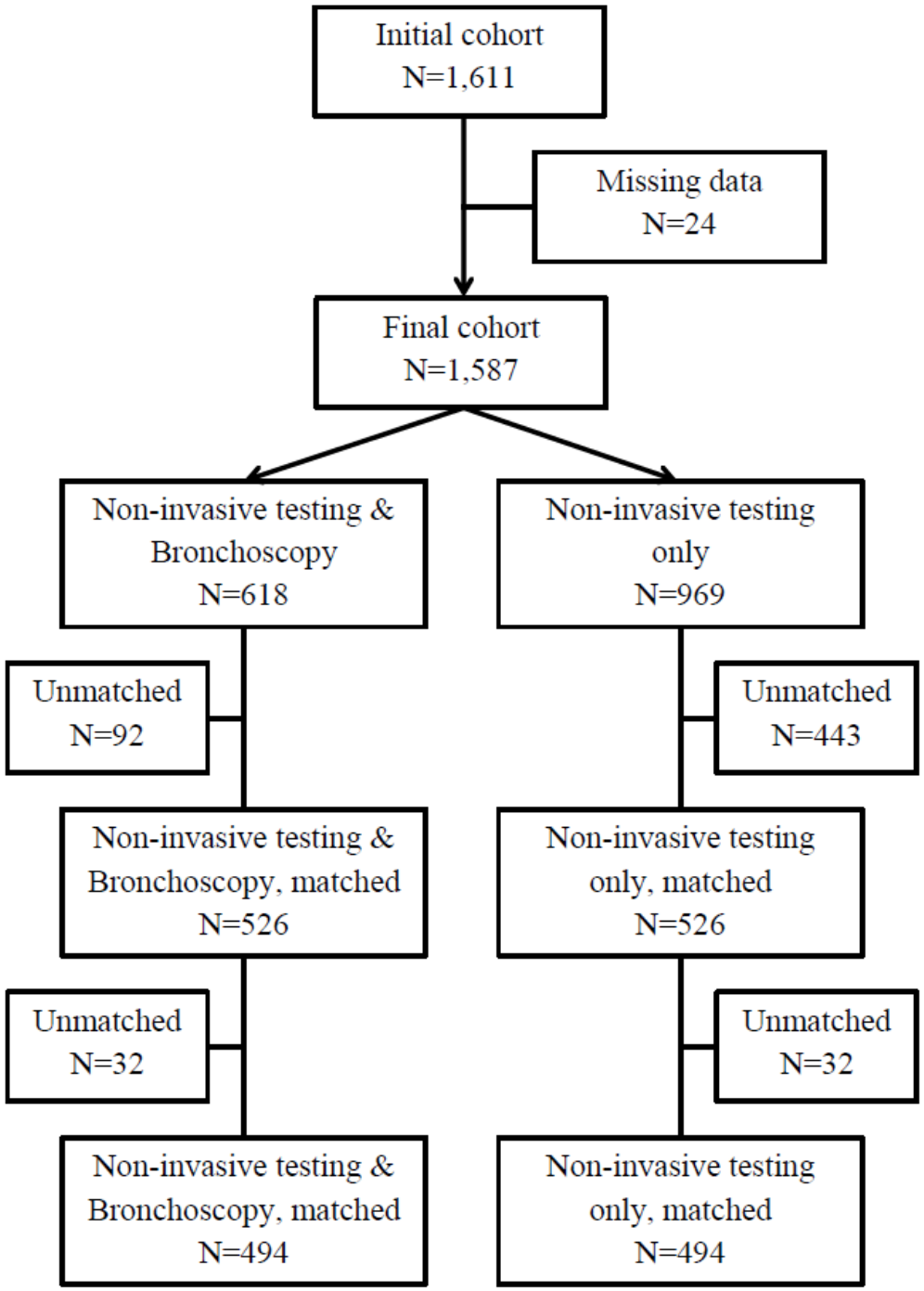


EUR ORY journal
L OF ERS

Diagnosis and C atory Failure in Immu Bronchoscopy

Substudy of Efraim

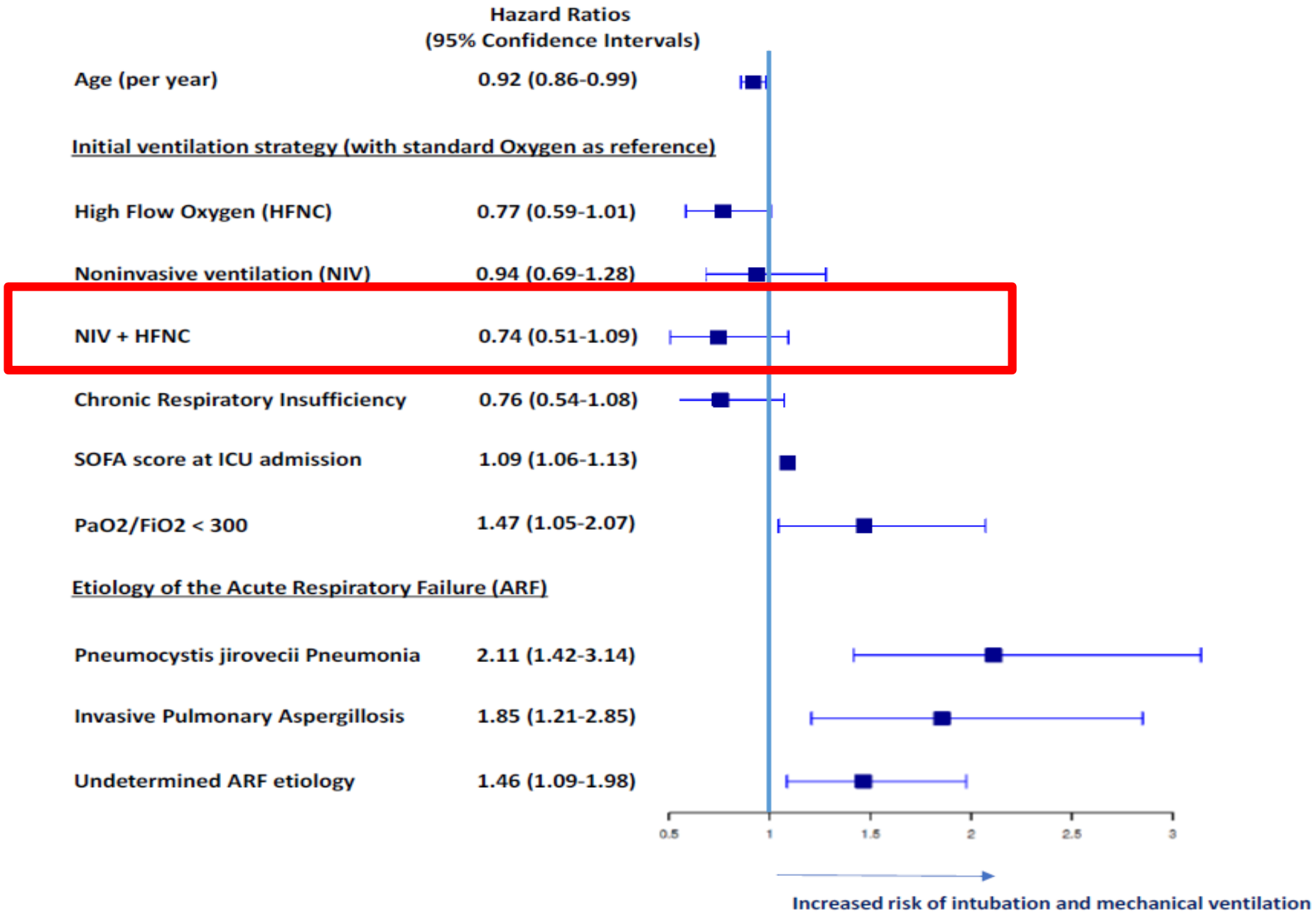
Philippe R. Bauer, Sylvie Ch Pickkers, Ramin B. Bukan, Jordi Rello, Andry van de L acio Martin-Loeches, Brian Marsh, Lorenzo Socias Cresp Karin Amrein, Martin Balik, Massimo Antonelli, Martine Bergmans, Angélique M.E. Spoelstra-de Man, Anne Kuit a Metaxa, Virginie Lemiale, Gaston Burghi, Alexandre D oia, Pål Klepstad, Ann M. Møller, Djamel Mokart, Elie A udy group



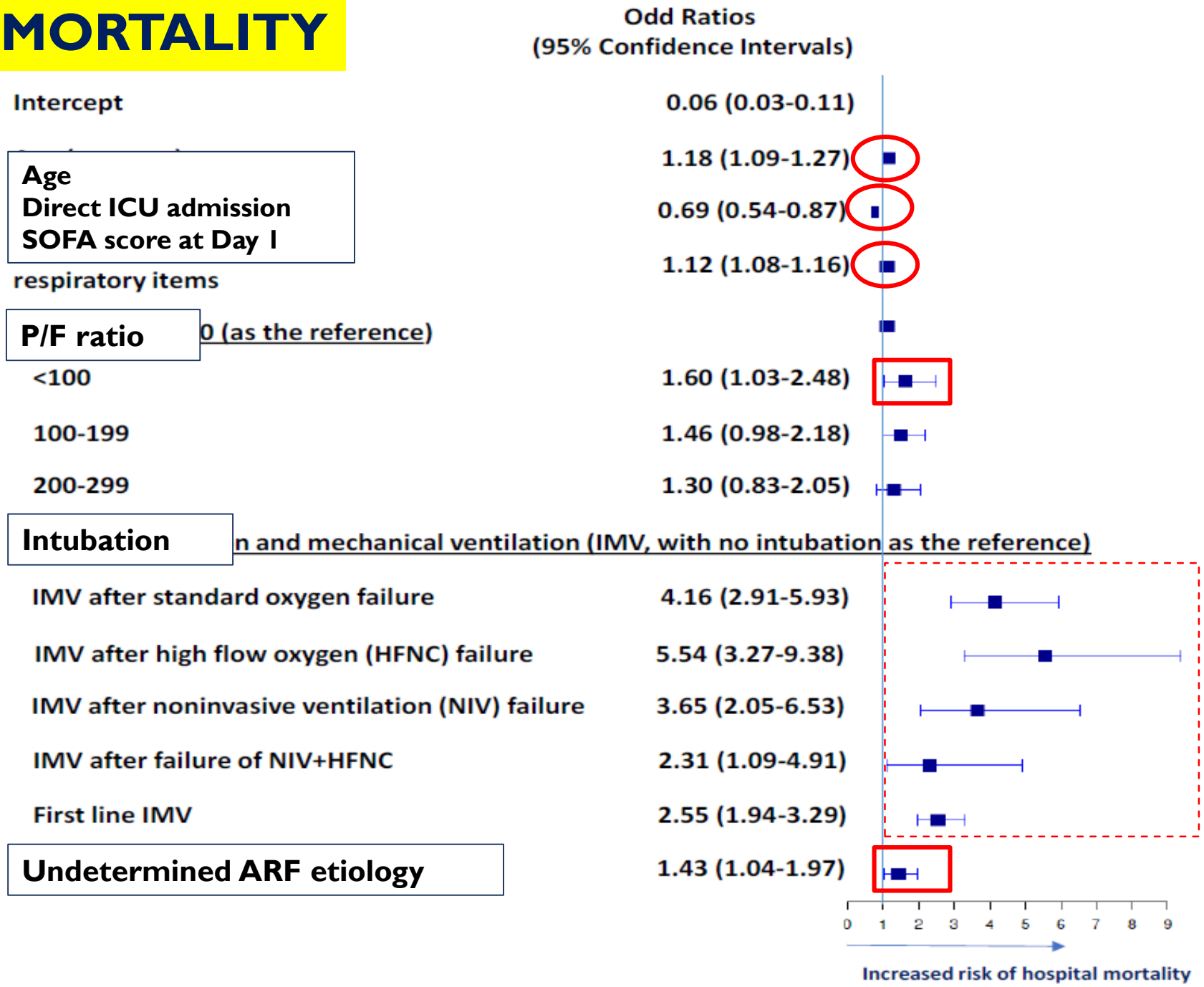
The Price of Undertermined ARF etiology

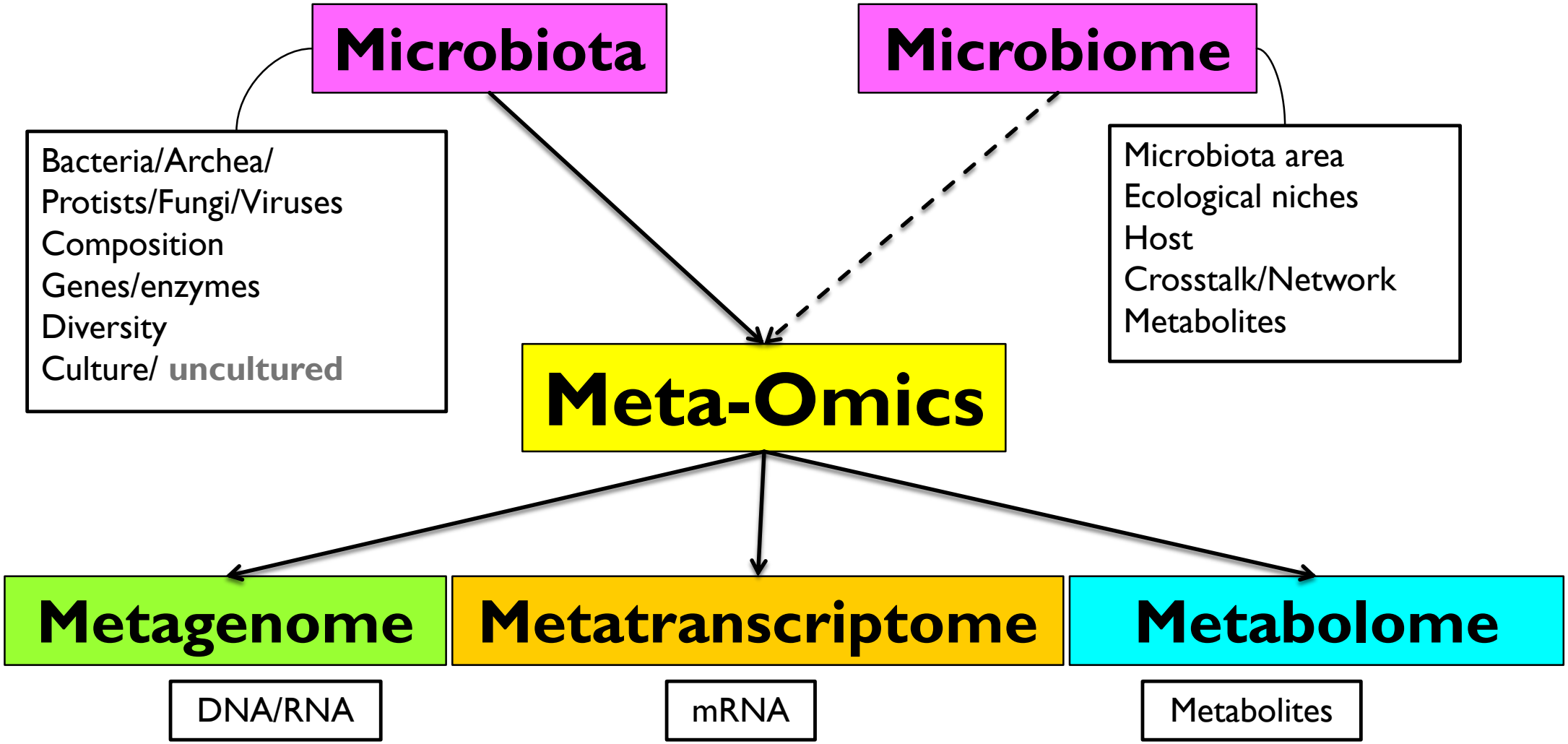
Authors	Reference	Population	Prevalence	Impact on outcomes
Masur	Medicine 1991	AIDS	/	(autopsy study)
Ewig	ERJ 1998	Hematology	**31%**	Not evaluated
Gruson	ERJ 1999	BMT	**58%**	**Increased mortality**
Rano	Thorax 2001	All IC patients	**19%**	Not evaluated
Rano	Chest 2002	All IC patients	**22%**	**Increasd mortality if time to diagnosis > 5d**
Danès	JCM 2002	All IC patients	**16%**	Not evaluated
Azoulay	Medicine 2004	Cancer	**21%**	**Increased mortality**
Contejean	AIC 2016	Hematology	**12.9%**	**Increased mortality**
Azoulay	ICM 2017	All IC patients	**13.2%**	**Increased mortality**

INTUBATION

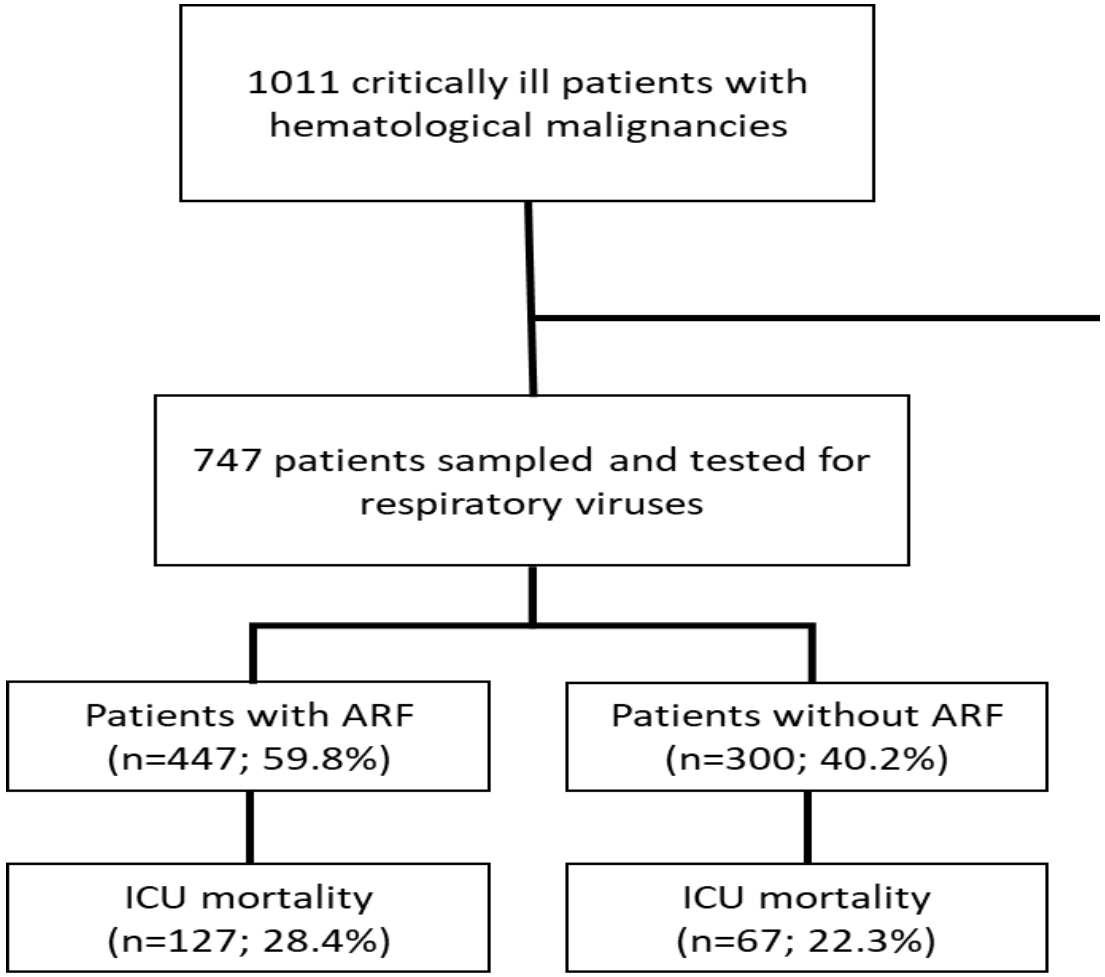

Hazard Ratios
(95% Confidence Intervals)
Age (per year) 0.92 (0.86-0.99)
Initial ventilation strategy (with standard Oxygen as reference)
High Flow Oxygen (HFNC) 0.77 (0.59-1.01)
Noninvasive ventilation (NIV) 0.94 (0.69-1.28)
NIV + HFNC 0.74 (0.51-1.09)
Chronic Respiratory Insufficiency 0.76 (0.54-1.08)
SOFA score at ICU admission 1.09 (1.06-1.13)
PaO2/FiO2 < 300 1.47 (1.05-2.07)
Etiology of the Acute Respiratory Failure (ARF)
Pneumocystis jirovecii Pneumonia 2.11 (1.42-3.14)
Invasive Pulmonary Aspergillosis 1.85 (1.21-2.85)
Undetermined ARF etiology 1.46 (1.09-1.98)
0.5
1
1.5
2
2.5
3
Increased risk of intubation and mechanical ventilation

MORTALITY


Odd Ratios
(95% Confidence Intervals)
Intercept
0.06 (0.03-0.11)
Age
1.18 (1.09-1.27)
Direct ICU admission
0.69 (0.54-0.87)
SOFA score at Day 1
1.12 (1.08-1.16)
respiratory items
P/F ratio
0 (as the reference)
<100
1.60 (1.03-2.48)
100-199
1.46 (0.98-2.18)
200-299
1.30 (0.83-2.05)
Intubation
n and mechanical ventilation (IMV, with no intubation as the reference)
IMV after standard oxygen failure
4.16 (2.91-5.93)
IMV after high flow oxygen (HFNC) failure
5.54 (3.27-9.38)
IMV after noninvasive ventilation (NIV) failure
3.65 (2.05-6.53)
IMV after failure of NIV+HFNC
2.31 (1.09-4.91)
First line IMV
2.55 (1.94-3.29)
Undetermined ARF etiology
1.43 (1.04-1.97)
0 1 2 3 4 5 6 7 8 9
Increased risk of hospital mortality


Microbiota
Microbiome
Bacteria/Archea/
Protists/Fungi/Viruses
Composition
Genes/enzymes
Diversity
Culture/ uncultured
Microbiota area
Ecological niches
Host
Crosstalk/Network
Metabolites
Meta-Omics
Metagenome
Metatranscriptome
Metabolome
DNA/RNA
mRNA
Metabolites

Vir-OH study: the pre-oMICs era
PCR testing in 747 hematology patientys

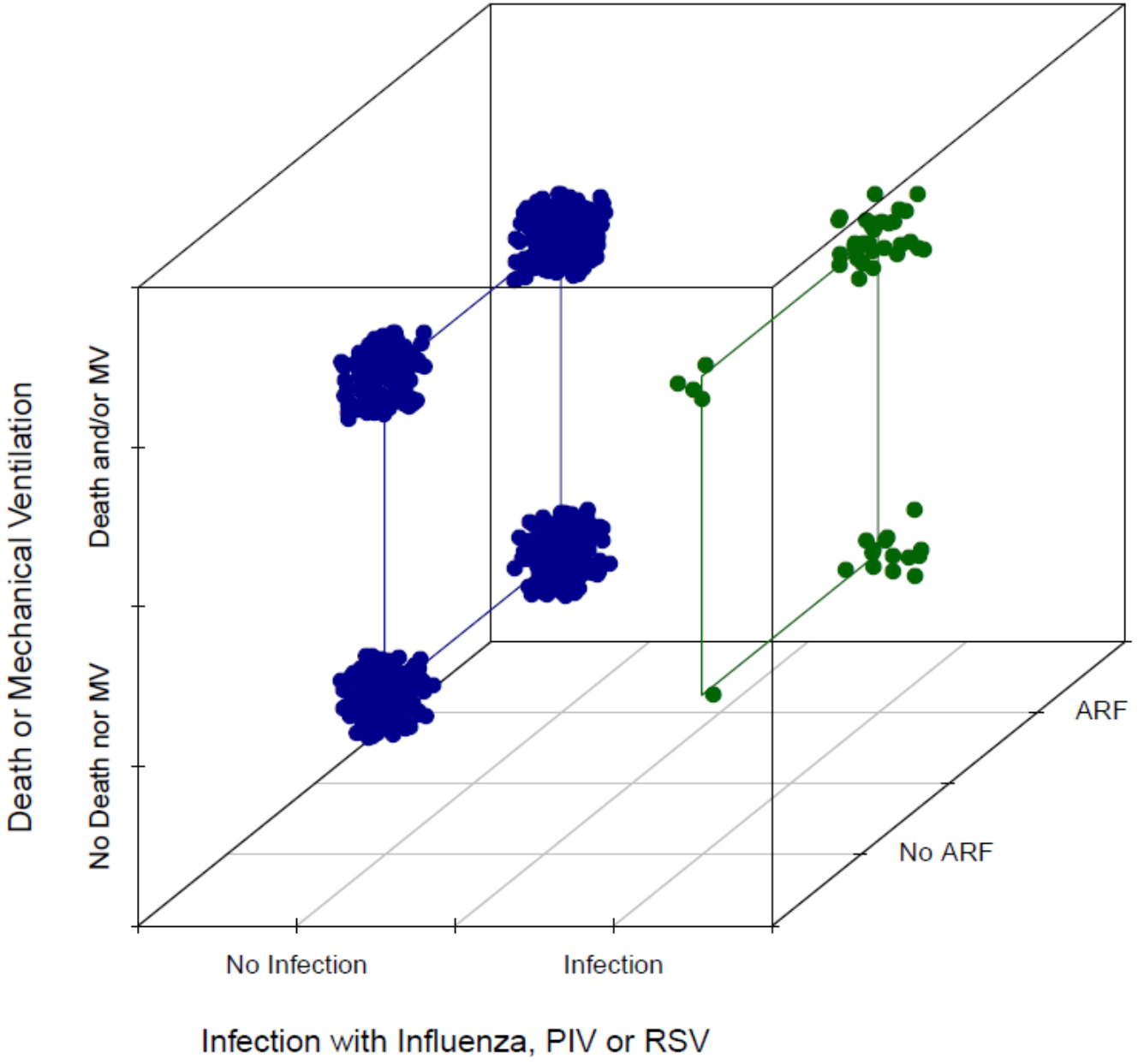


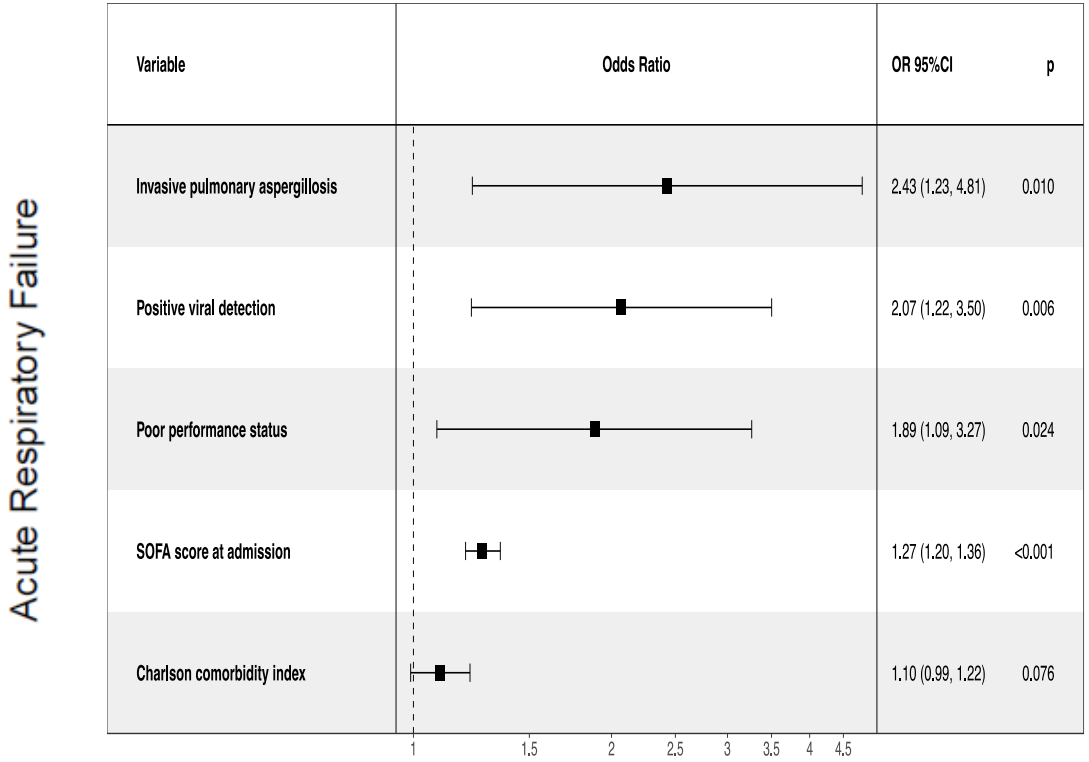
Overtakes 15% of diagnoses

Allow to risk-stratify patients for their risk of mortality

Le Goff J, Zucman N, et al. GRRR-OH AJRCCM 2018

Vir-OH study (Multiplex)





Le Goff J, et al. GRRR-OH AJRCCM 2018

Integrating host response and unbiased microbe detection for lower respiratory tract infection diagnosis in critically ill adults

Charles Langelier et al. PNAS 2018;115:52:E12353-E12362

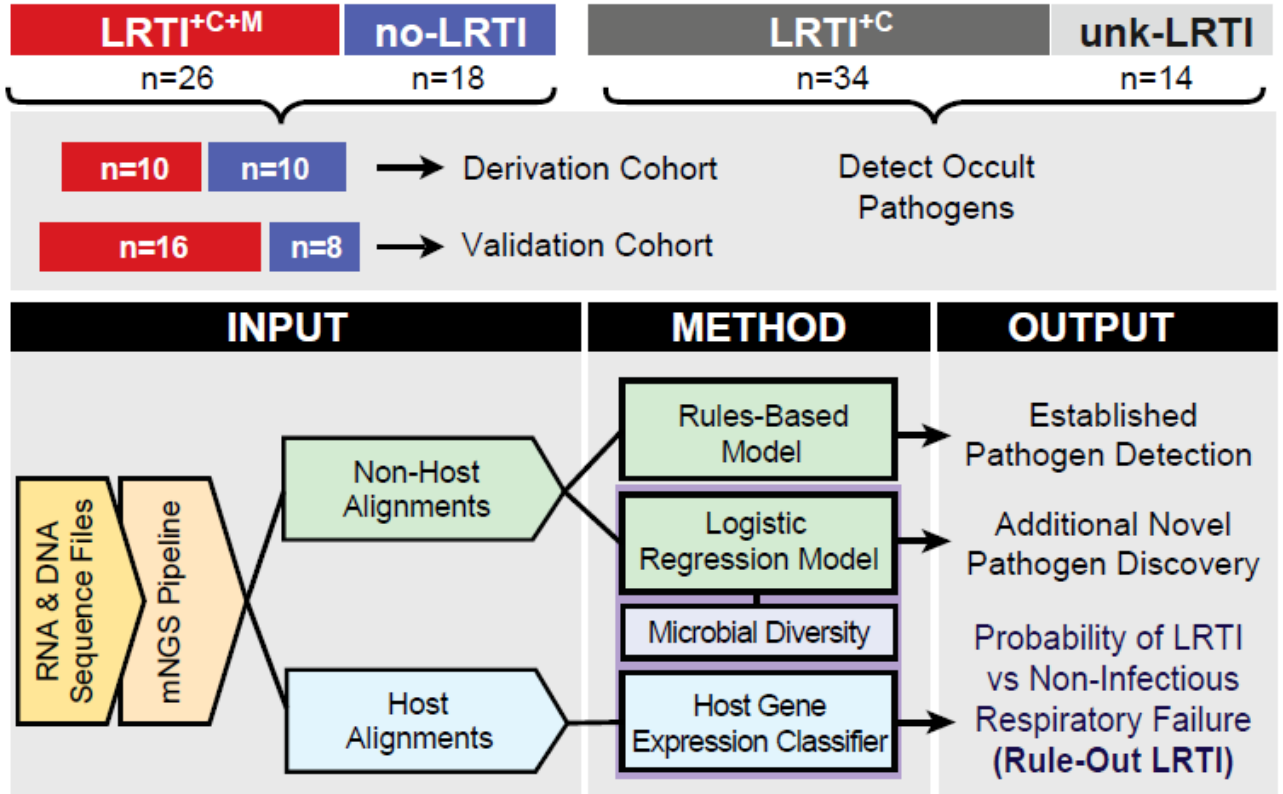
PNAS

Charles Langelier[a,b,1], Katrina L. Kalantar[c,1], Farzad Moazed[d], Michael R. Wilson[e,f], Emily D. Crawford[b,c], Thomas Deiss[d], Annika Belzer[d], Samaneh Bolourchi[d], Saharai Caldera[a,b], Monica Fung[a], Alejandra Jauregui[d], Katherine Malcolm[g], Amy Lyden[b], Lillian Khan[c], Kathryn Vessel[d], Jenai Quan[b,c], Matt Zinter[h], Charles Y. Chiu[a,i], Eric D. Chow[c], Jenny Wilson[j], Steve Miller[i], Michael A. Matthay[d,k,l], Katherine S. Pollard[b,m,n,o,p,q], Stephanie Christenson[d], Carolyn S. Calfee[d,h,2], and Joseph L. DeRisi[b,c,2,3]

A streamlined protocol offering

1/ an integrated genomic portrait of pathogen (metagenomic next-generation sequencing (mNGS),
2/ airway microbiome,
3/ host transcriptome

Negative pred. value of 100%

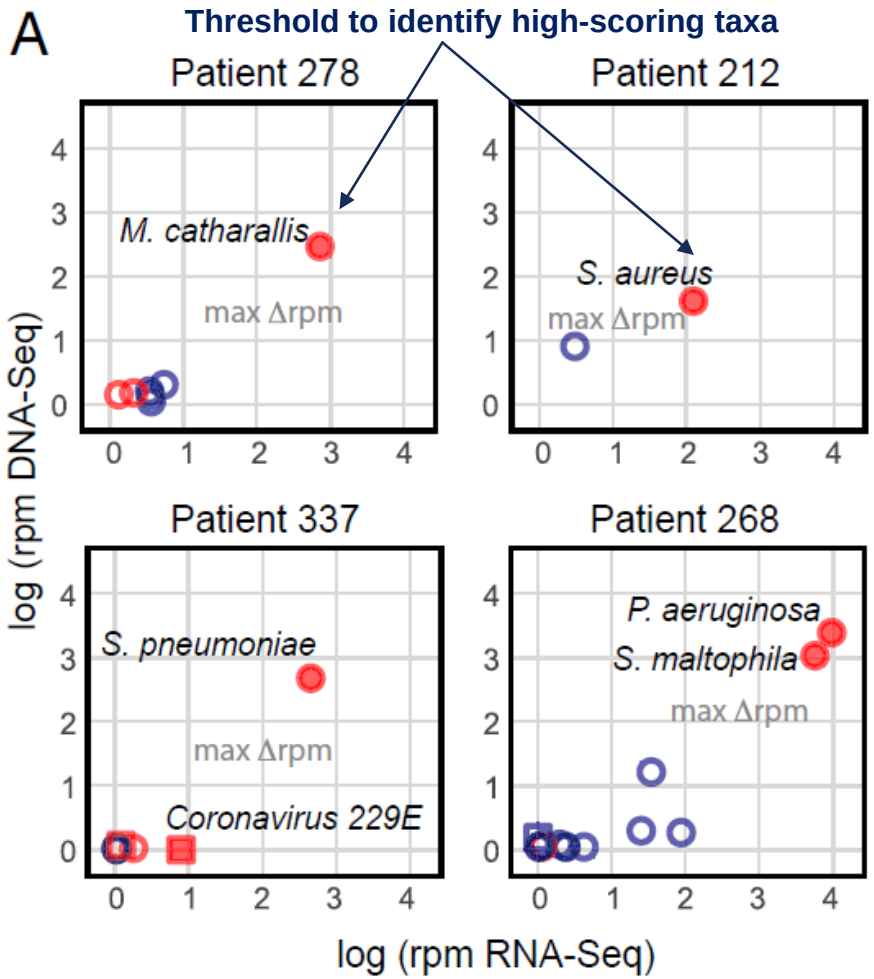


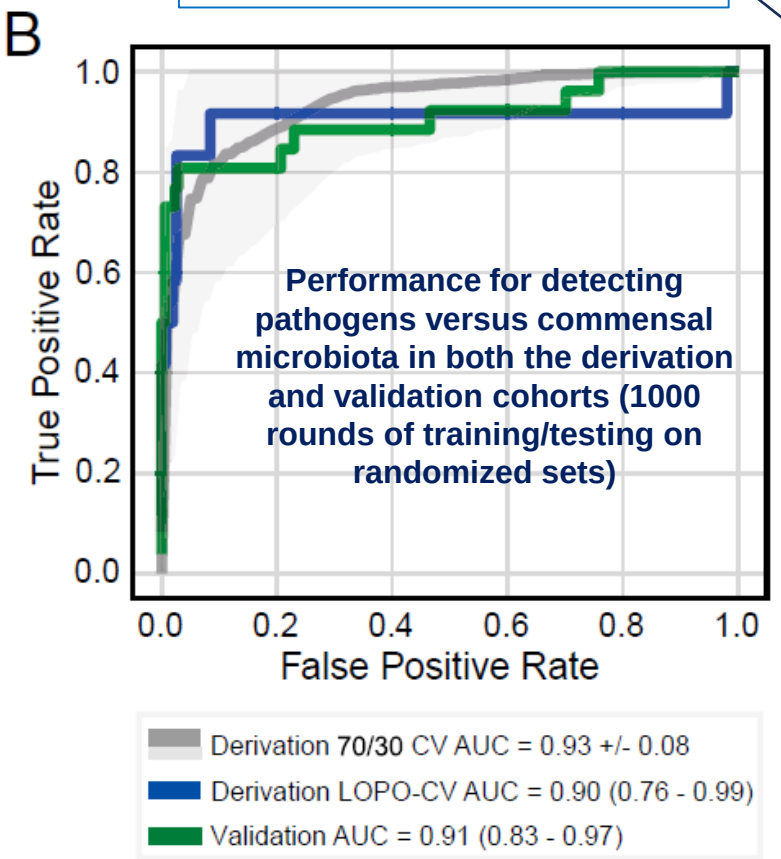
Algorithmic approach for distinguishing LRTI pathogens from respiratory commensals

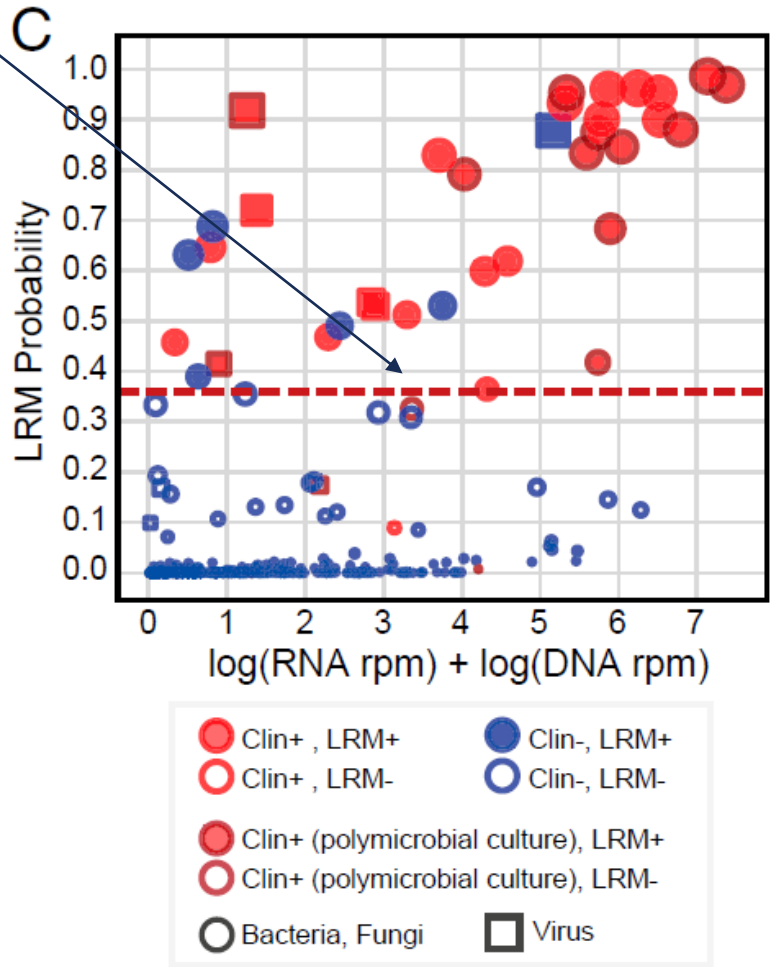
Microbial relative abundance RNAxDNA in Representative cases

optimized probability threshold for pathogen assignment

Microbes predicted to represent putative pathogens







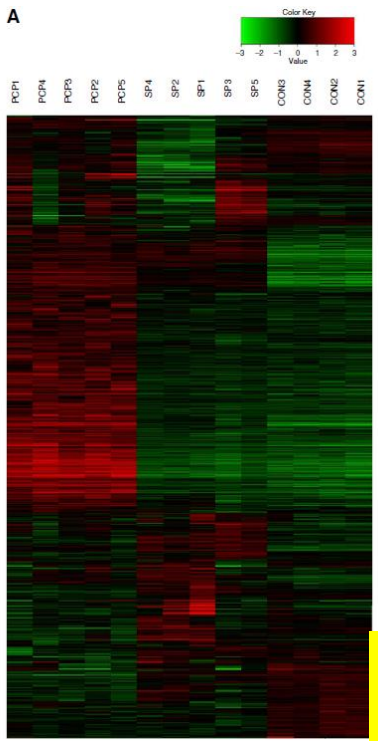
Langelier et al. PNAS 2018;115:52

ORIGINAL RESEARCH

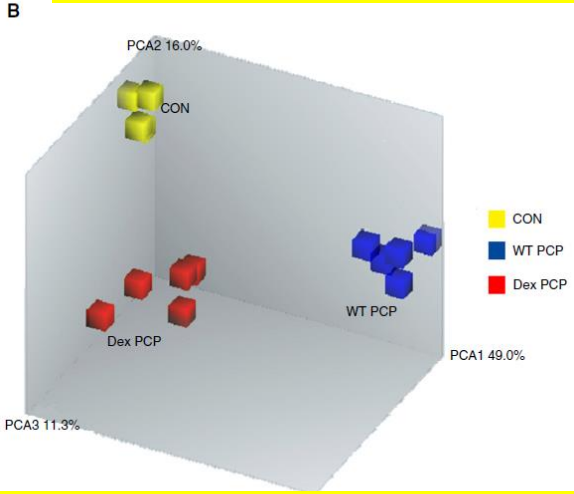
Transcriptomic Analysis Reveals Significant B Lymphocyte Suppression in Corticosteroid-Treated Hosts with *Pneumocystis* Pneumonia

Yang Hu[1]*, Dong Wang[1]*, Kan Zhai[2], and Zhaohui Tong[1]

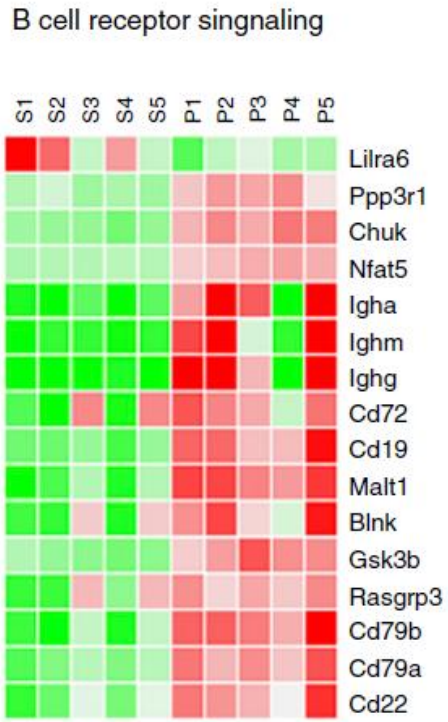
Transcriptome = complete set of RNA transcripts produced by the genome (microarray analysis). Comparison of transcriptomes allows the identification of genes that are differentially expressed in distinct cell populations, or in response to different treatments.



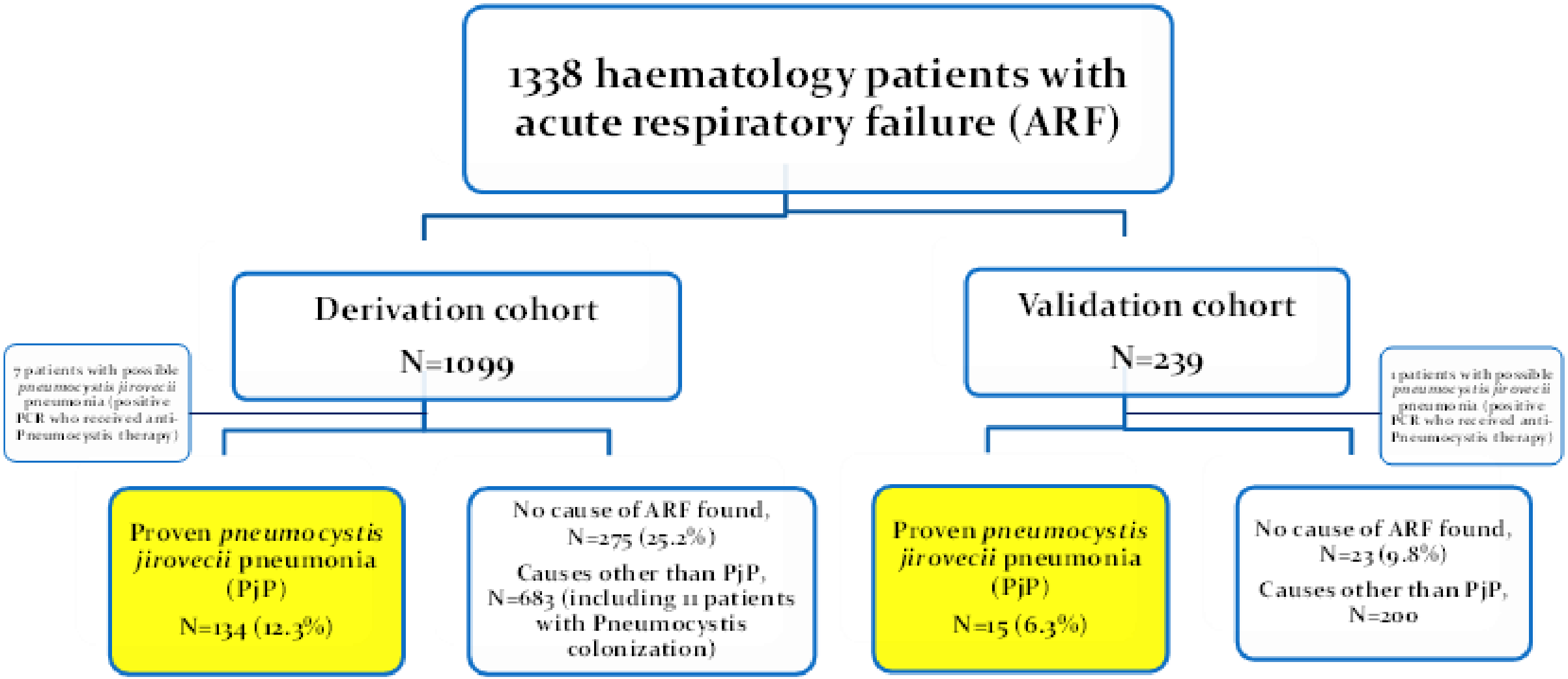
Principle component analysis (PCA) of the microarray data



Clustering of gene expression profiles based on the microarray result



Our study focused on the differences of immune reaction in immunocompetent and corticosteroid-treated hosts by transcriptomic analysis to reveal the mechanism by which corticosteroids prompt *Pneumocystis* pneumonia. Results show that hosts with corticosteroids have significant defects in B cell immunity, even more prominent than the defect of T cell immunity. The findings stress the importance of B cell immunity in the anti-*Pneumocystis* defense.



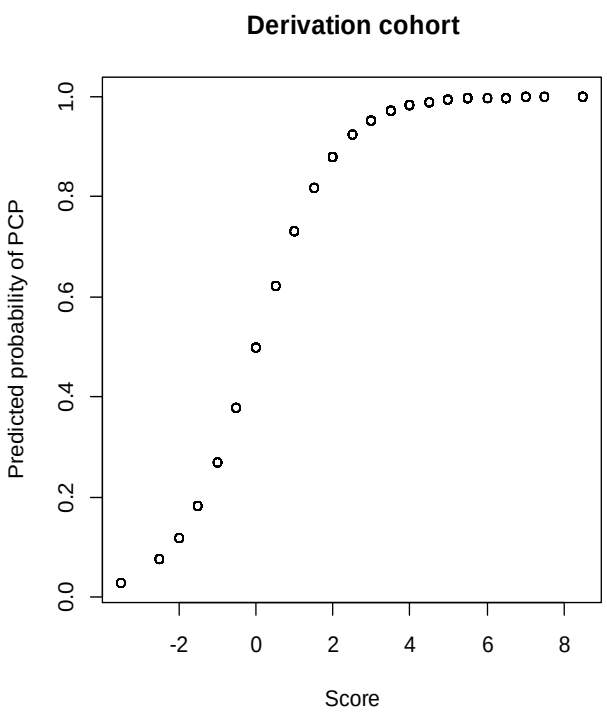
Azoulay et al. GRRR-OH. AJRCCM 2018

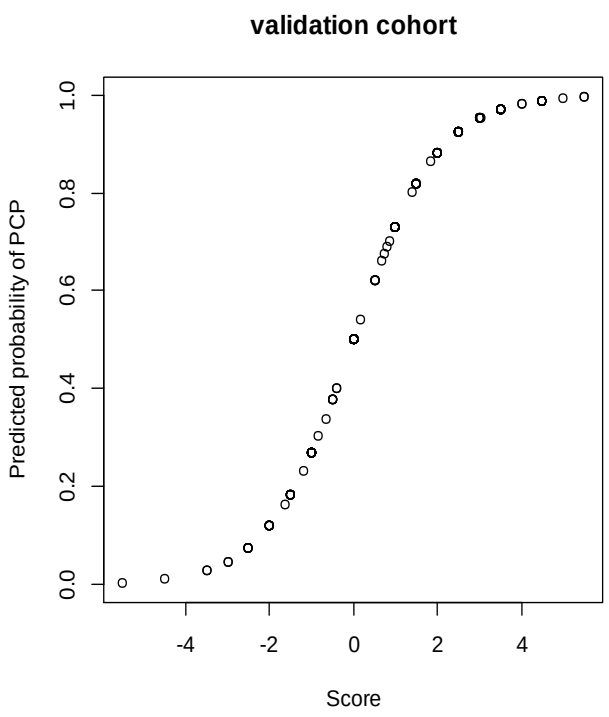
Clinical score for PjP

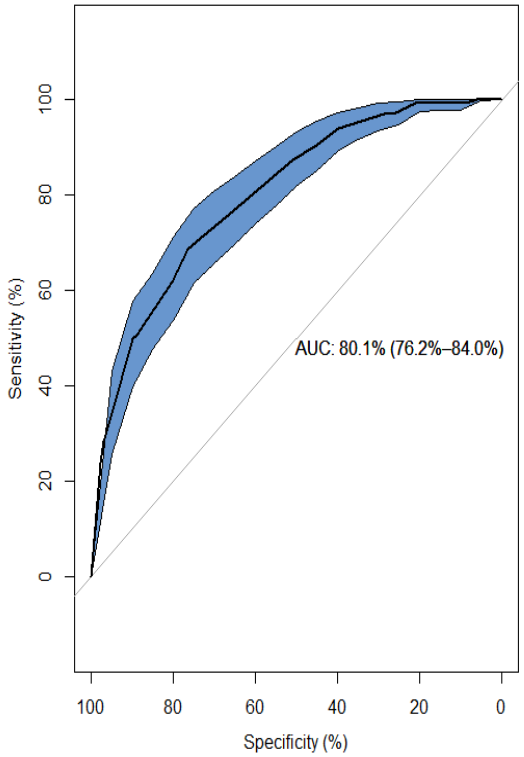
Variables	Category	N points
Age	<50	0
	50-70	-1.5
	>70	-2.5
Lymphoproliferation		+2
No prophylaxis		+1
Time from symptoms	3-5 days	+3
	>5 days	+3
Shock		-1.5
Interstitial pattern		+2.5
Pleural involvement		-2

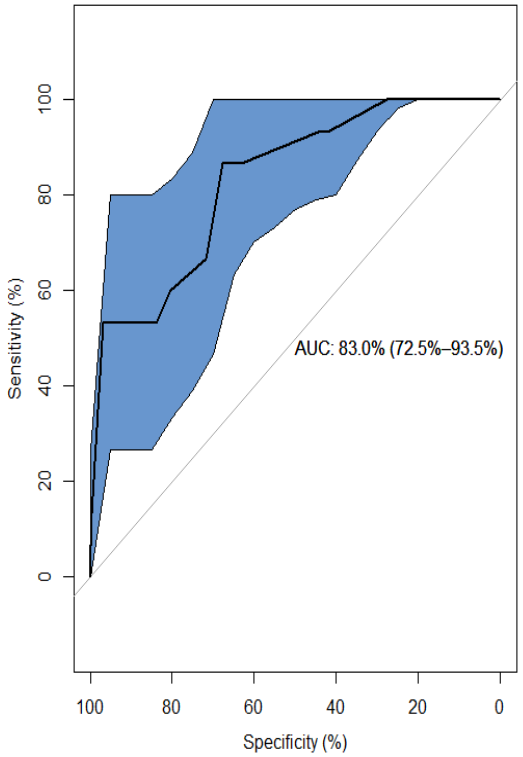
Azoulay et al. GRRR-OH. AJRCCM 2018

The Pneumocystis Score

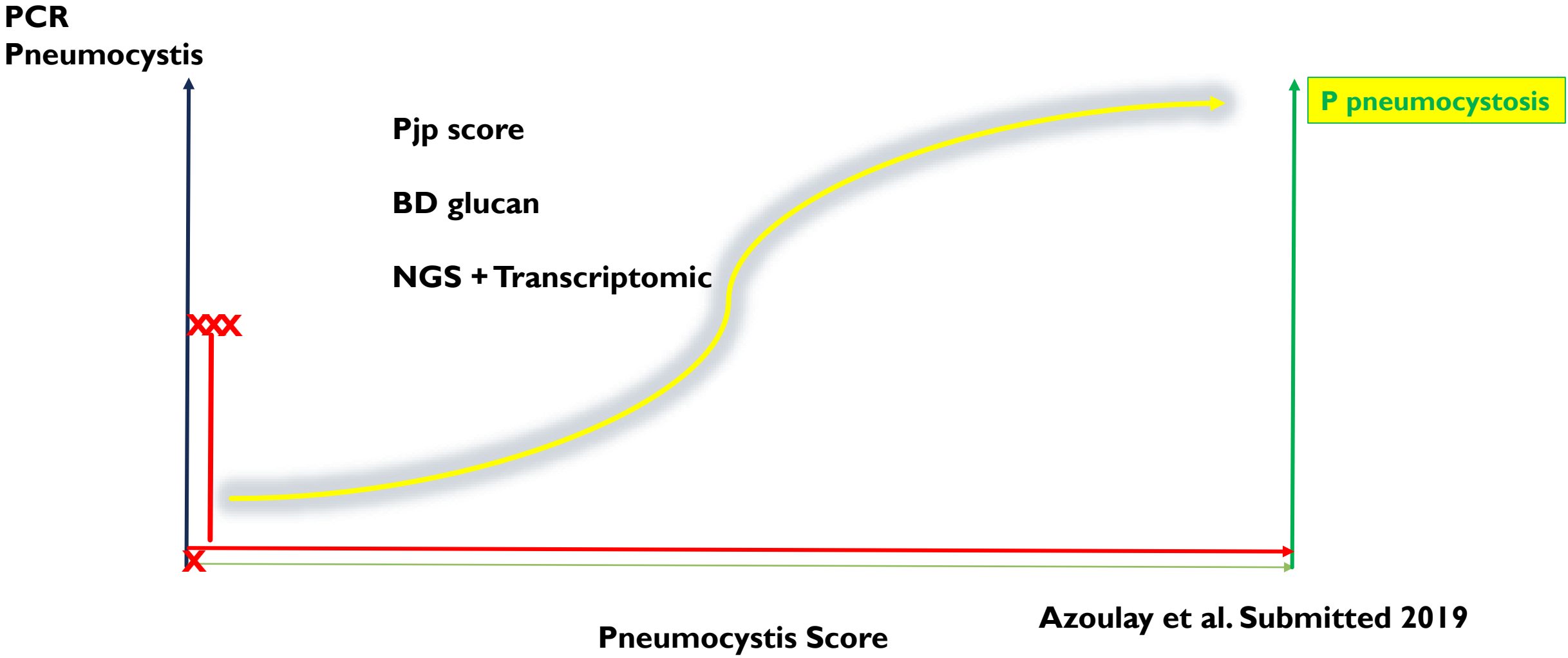








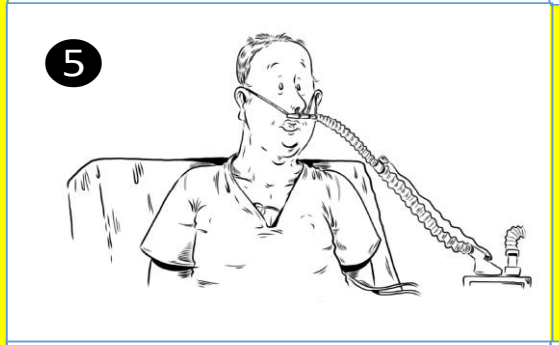
PjP Score + NGS + transcriptomic biomarkers



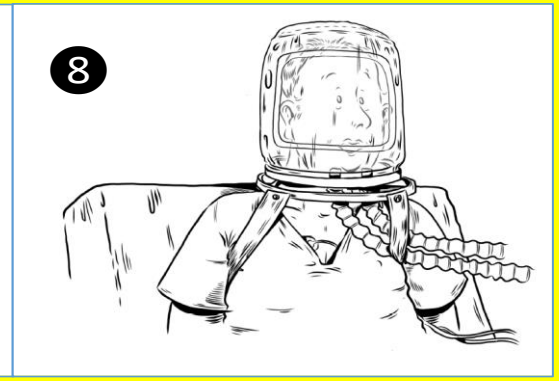
Azoulay et al. Submitted 2019

Standard Oxygen

High Flow Oxygen Therapy



Noninvasive Ventilation



Intubation and Mechanical Ventilation

Oxygénation et ventilation

	Flow (l/min)	FiO2	Device
Nasal Canula	1-6 L/min	25-40%	
Face Mask	5-10 L/min	40-60%	
Face tent	10-15 L/min	40%	
Venturi Mask	2-15 L/min	24-60%	
Non-Rebreather	10-15 L/min	80-95%	
HFNC	60 L/min	21-100%	

- Regardez le patient
- Stratégie Diagnostique
- Temporalité

Spécificités des atteintes pulmonaires chez les patients immunodéprimés

1. Incidence et sévérité et critères d'admission en réanimation
2. Stratégie diagnostique
3. Examens diagnostiques