



SDRA du patient immunodéprimé

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GrrrOH, Nine I

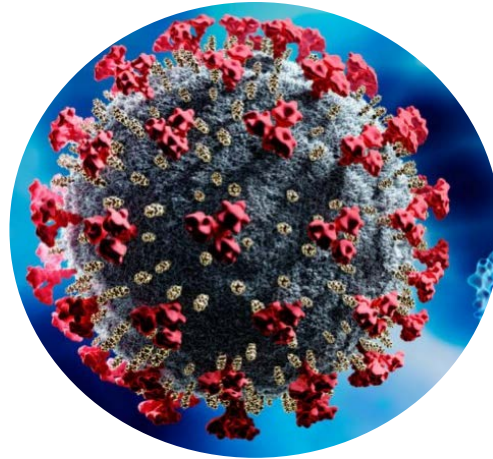
Liens d'intérêt

- Trésorière du GrrrOH
 - Gilead
 - Pfizer
 - Fisher-Paykel
 - Alexion
 - Sanofi
 - Jazzpharma

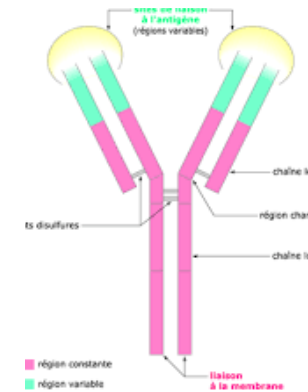
De qui parle-t-on ?



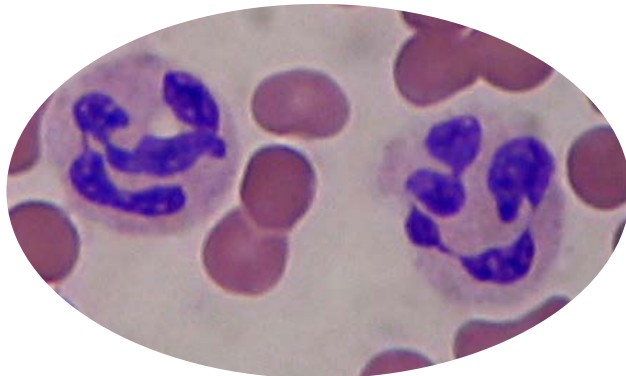
Déficit en macrophage



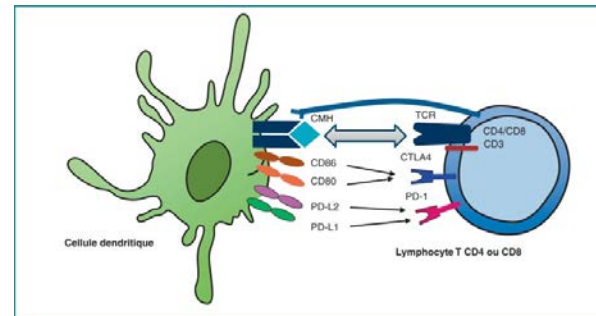
Déficit en population B



Déficit d'immunoglobulines



Neutropénie



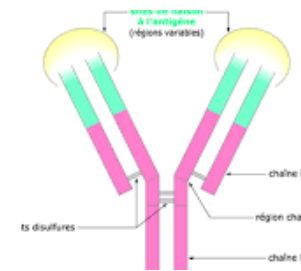
Déficit en population T



De quoi parle-t-on ?

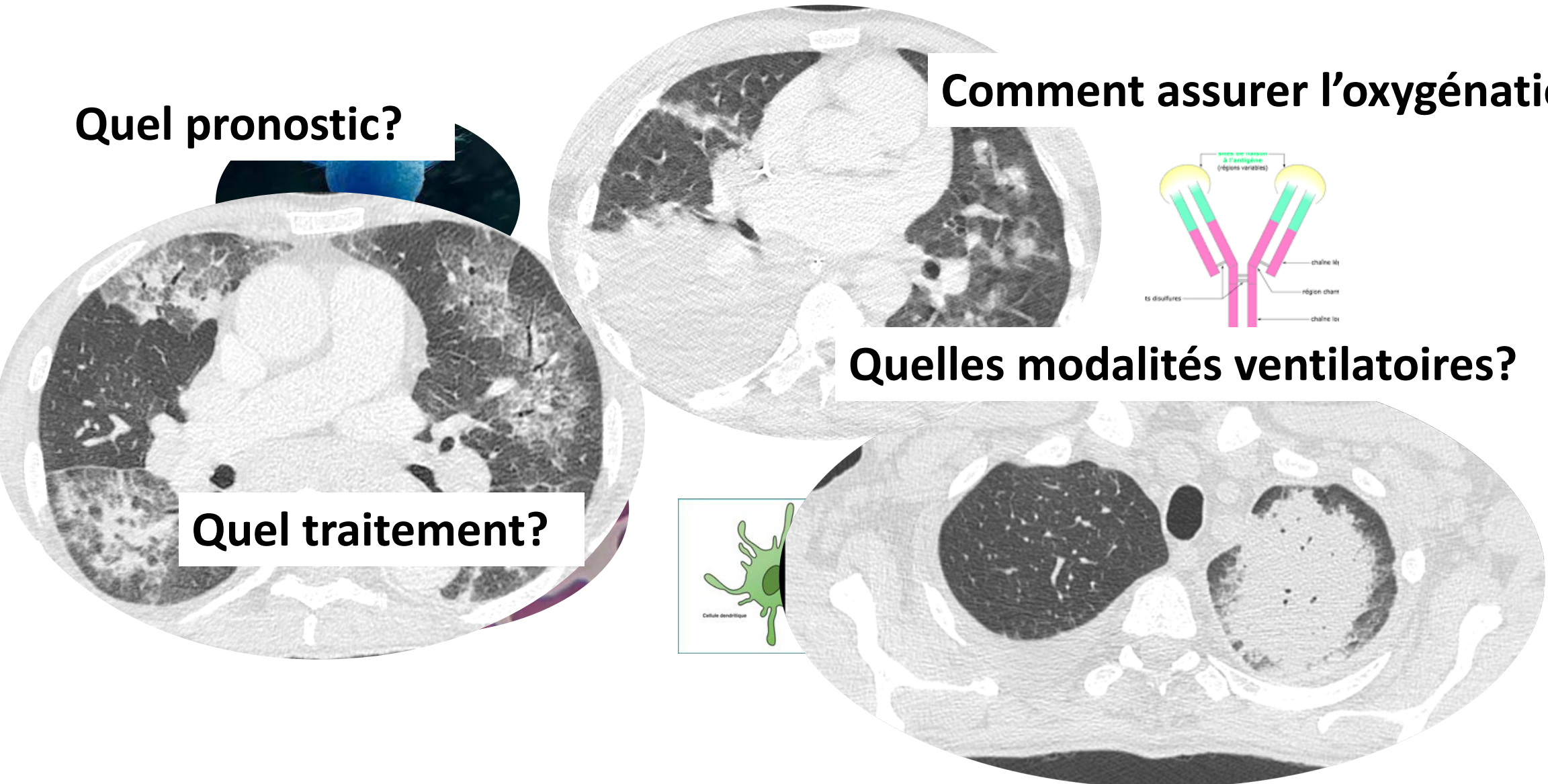
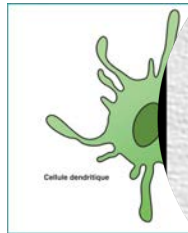
Quel pronostic?

Comment assurer l'oxygénation?








Quelles modalités ventilatoires?

Quel traitement?

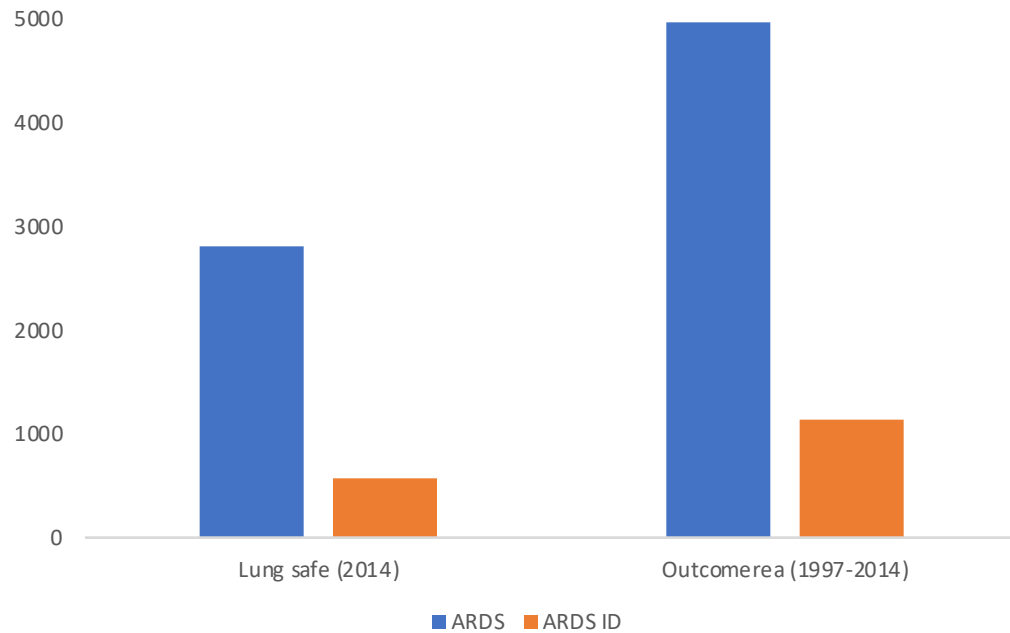


Les étiologies multiples

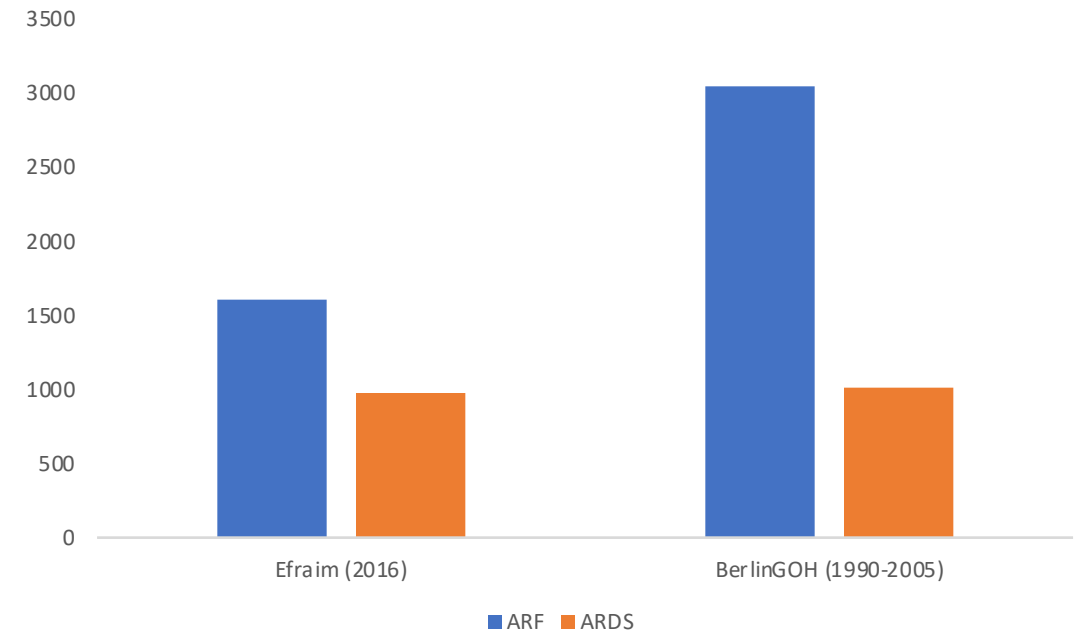
Immunological deficiency	Neutrophils 	Monocytes/dendritic cells/macrophages 	B lymphocytes 	T lymphocytes 	Humoral (antibody) immunity 
Diseases	Acute leukaemia; myelodysplastic syndrome; aplastic anaemia; chemotherapy and drug-related neutropenia	Hairy cell leukaemia; aplastic anaemia; allogeneic bone marrow transplant; malignant histiocytosis; acute myeloid leukaemia; chronic myeloid leukaemia; solid tumours; haemophagocytic lymphohistocytosis	Multiple myeloma; B-cell lymphoma; chronic lymphocytic leukaemia	T-cell leukaemia; T-cell lymphoma; Hodgkin disease	Multiple myeloma; chronic lymphoid leukaemia
Treatments	Chemotherapy-induced neutropenia	Steroids; basiliximab; antithymocyte globulin; tacrolimus; mycophenolate mofetil; belatacept	Chemotherapy; steroids; asplenia; rituximab	Steroids; fludarabine; cyclophosphamide; methotrexate; azathioprine; alemtuzumab; mycophenolate mofetil; cyclosporine; mTOR inhibitors (sirolimus); tacrolimus; 2-chlorodeoxyadenosine; daratumumab	Ibrutinib; rituximab; daratumumab; cyclophosphamide
Most frequently encountered infections	<ul style="list-style-type: none"> Gram-negative bacteria Gram-positive bacteria <i>Candida</i> <i>Aspergillus</i> <i>Nocardia</i> 	<ul style="list-style-type: none"> Non-tuberculous mycobacteria <i>Salmonella</i>, <i>Listeria</i>, <i>Legionella</i>, <i>Histoplasma</i>, <i>Brucella</i> Herpes simplex virus, varicella zoster virus, parainfluenza virus, respiratory syncytial virus <i>Candida parapsilosis</i> <i>Staphylococcus aureus</i>, <i>Enterococcus faecalis</i>, <i>Pseudomonas aeruginosa</i> 	<ul style="list-style-type: none"> Encapsulated bacteria (<i>Streptococcus pneumoniae</i>, <i>Streptococcus pyogenes</i>, <i>Haemophilus influenzae</i>) <i>Giardia lamblia</i>, <i>Campylobacter</i>, <i>Salmonella</i> <i>Mycoplasma</i> Enterovirus Recurrent infections 	<ul style="list-style-type: none"> Herpes simplex virus, cytomegalovirus, Epstein-Barr virus <i>Pneumocystis</i>, <i>Aspergillus</i>, <i>Cryptococcus</i> Mycobacterial infection Skin candidiasis Diarrhoea (rotaviruses, adenoviruses, <i>Cryptosporidium</i>, microsporidia, etc) John Cunningham virus 	<ul style="list-style-type: none"> Encapsulated bacteria (<i>S pneumoniae</i>, <i>S pyogenes</i>, <i>H influenzae</i>) <i>Mycoplasma</i>, <i>Ureaplasma urealyticum</i> Other infections related to associated T-cell defects

Proportion de SDRA chez les patients immunodéprimés

20% des SDRA en réa sont des patients immunodéprimés



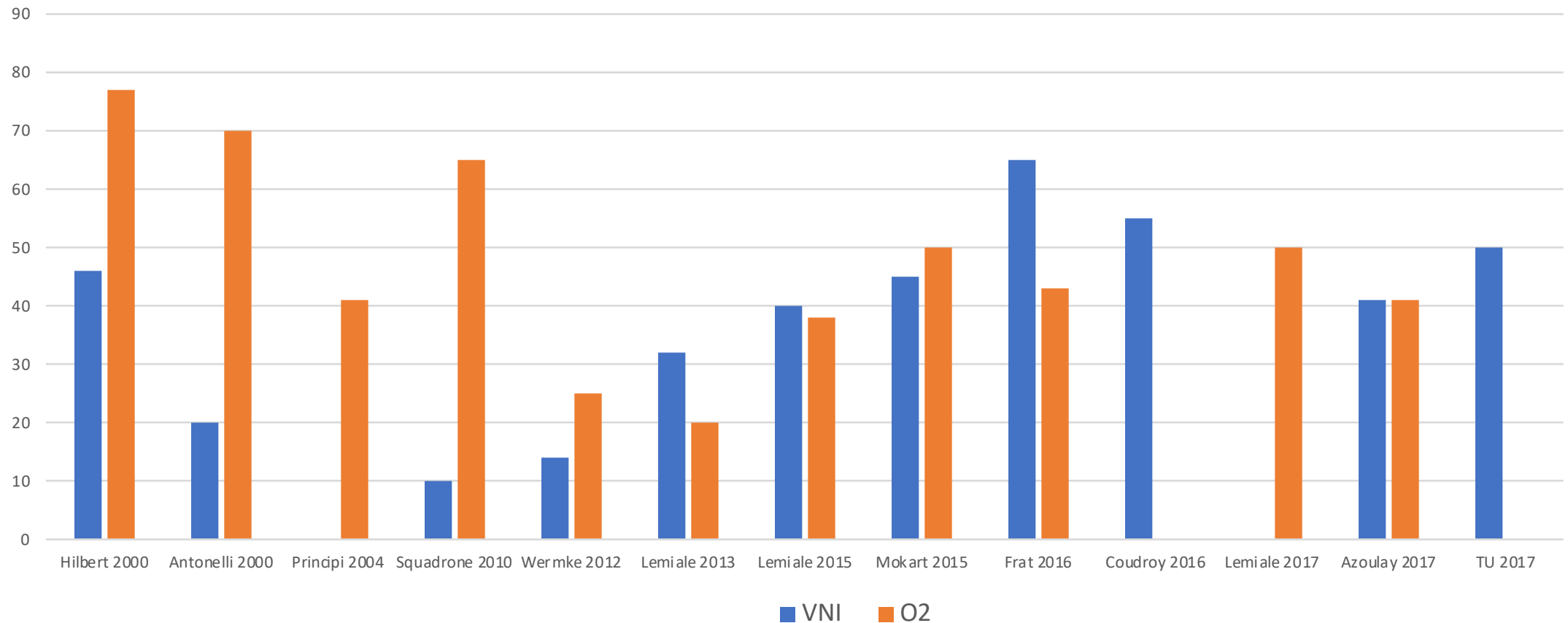
30 to 50 % des patients immunodéprimés en réa pour IRA sont en SDRA



Quel système d'oxygénation ?



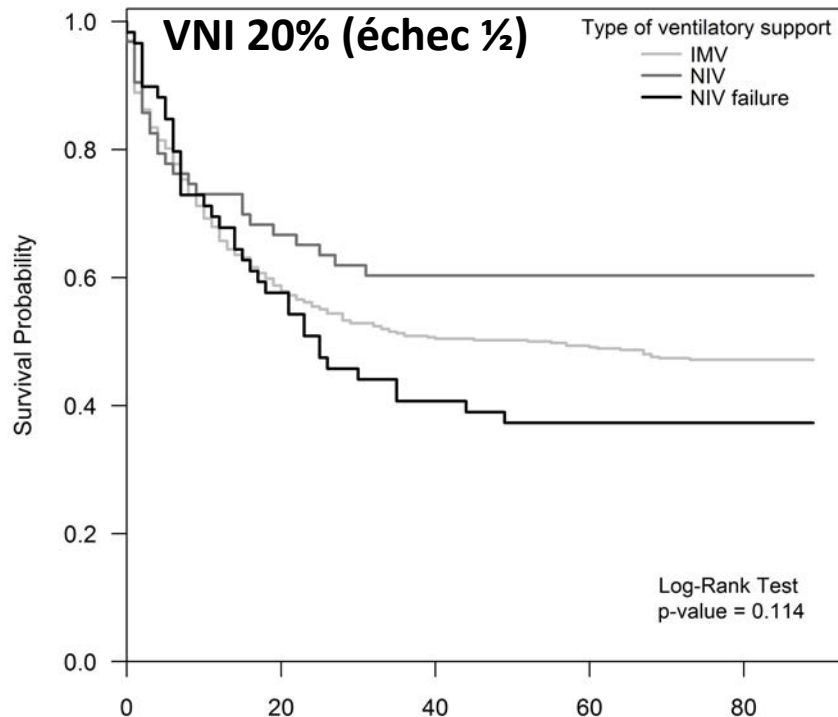
Taux d'intubation selon le type d'oxygénation



Quel système d'oxygénation ?



**584 patients
cohorte LUNG-SAFE**



# at risk	0	20	40	60	80
IMV	458	269	232	226	216
NIV	63	42	38	38	38
NIV failure	59	34	24	22	22

Cortegiani et al. *Critical Care* (2018) 22:157

Risques liés à l'échec de VNI

**1004 patients en ARDS
VNI 38% (échec 71%)**

**1614 patients ID
VNI 49% (échec 38%)**

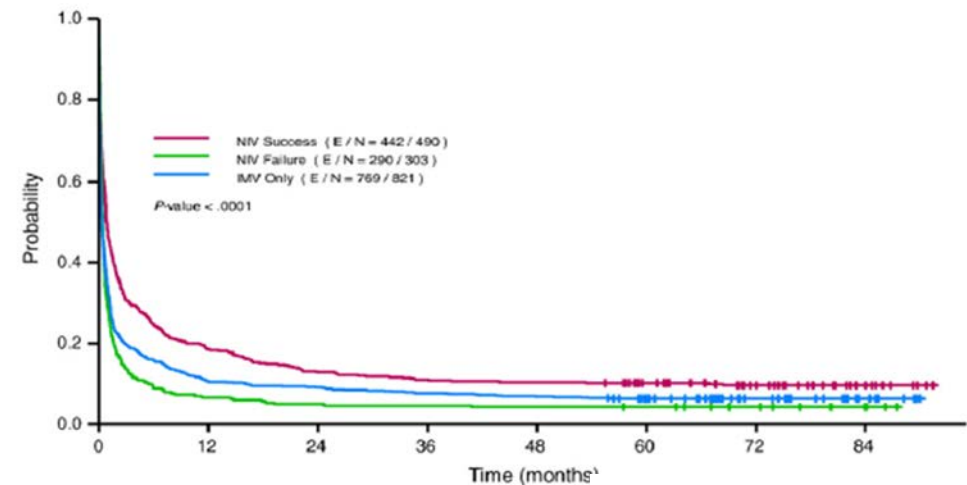
Factors associated with hospital mortality

	OR (95% CI)	P
Solid tumor (vs hematologic malignancy)	0.45 (0.19-1.09)	.08
Mild ARDS	1	
Moderate ARDS	0.92 (0.53-1.60)	.77
Severe ARDS	1.99 (1.09-4.28)	.02
SOFac	1.11 (1.04-1.19)	.001
NIV failure	2.63 (1.63-4.28)	<.001
Extrapulmonary infection	1.78 (0.94-3.37)	.08

SOFac indicates SOFA score without respiratory parameter.

A. Neuschwander et al / *Journal of Critical Care* 38 (2017) 295-299

Overall Survival by Treatment from ICU Admission



N.K. Rathi et al / *Journal of Critical Care* 39 (2017) 56-61

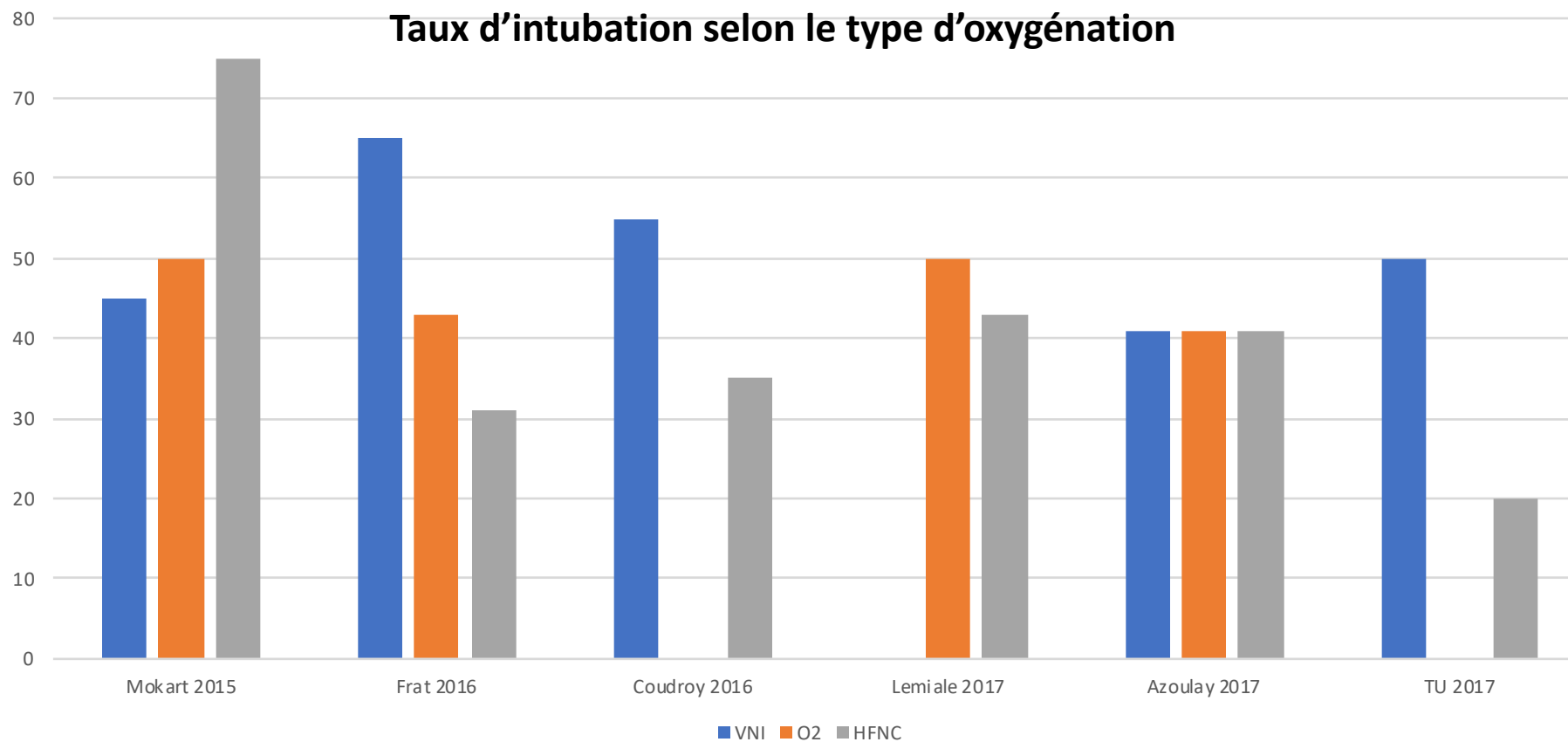
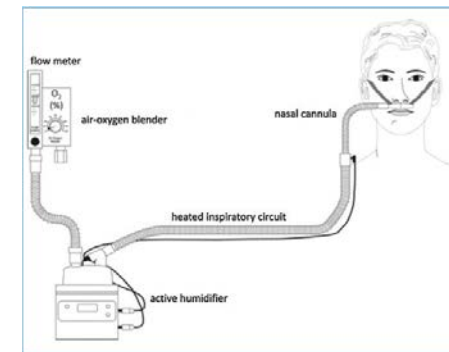
Fig. 1. Overall survival of treatment groups.

Quel système d'oxygénation ?

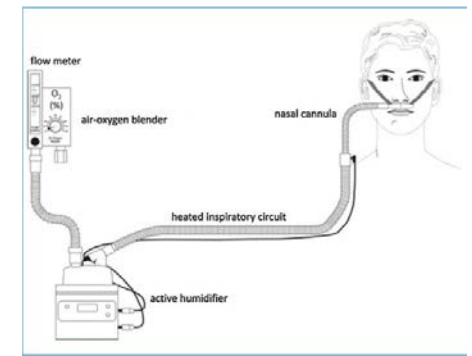


- Peu confortable
- Risque d'échec plus fréquent que chez le patient non immunodéprimé : 10% vs 6% Cortegiani et al. *Critical Care* (2018) 22:157
- Echec associé à la mortalité

Quel système d'oxygénation ?



Quel système d'oxygénation ?

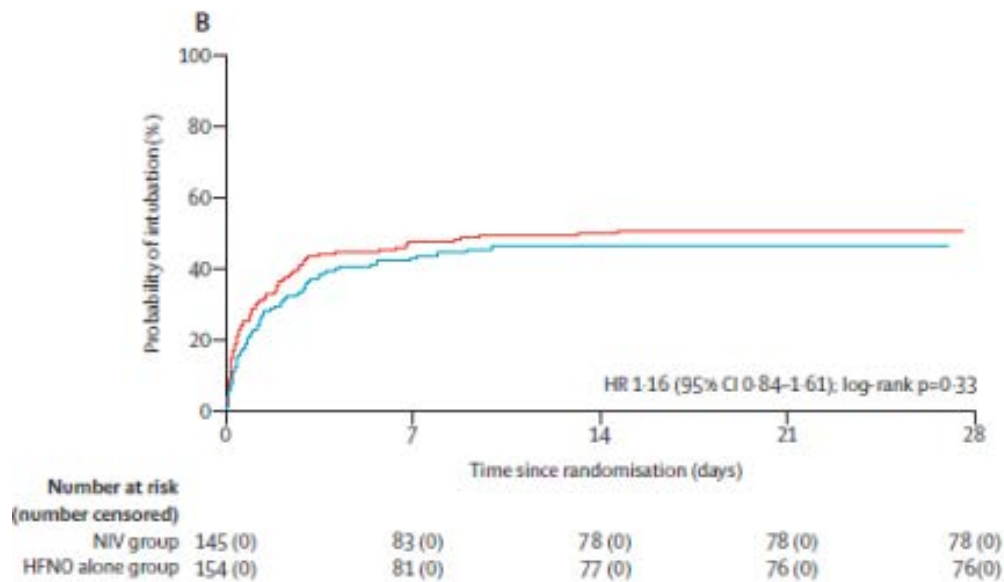
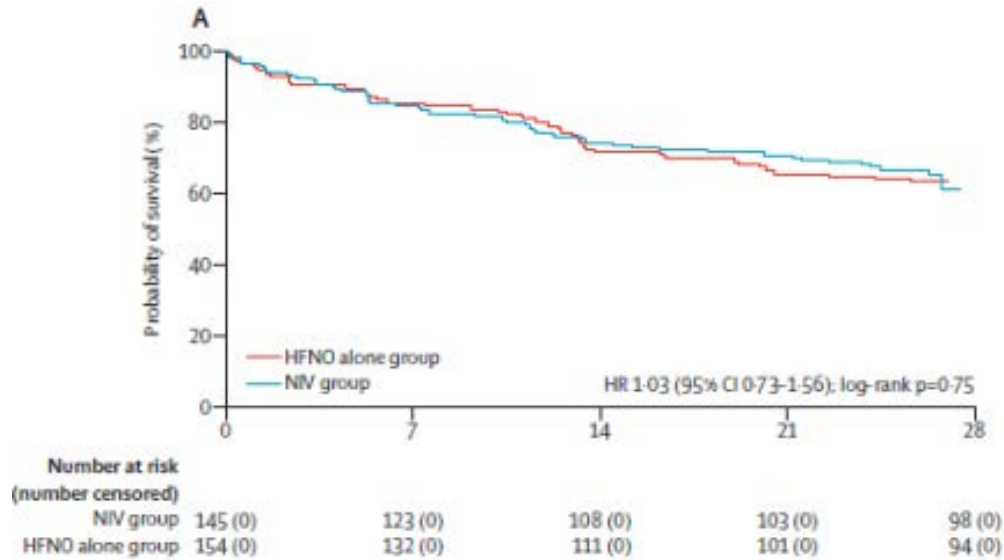
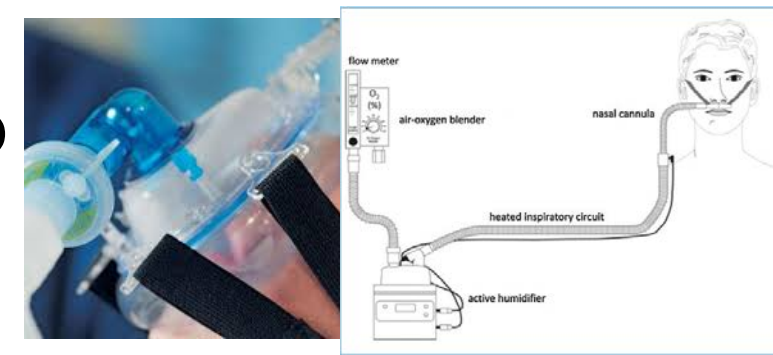


778 patients en détresse respiratoire aigue >6l/min
80% de pathologie hématologique
Randomisation Oxygène vs HFNC

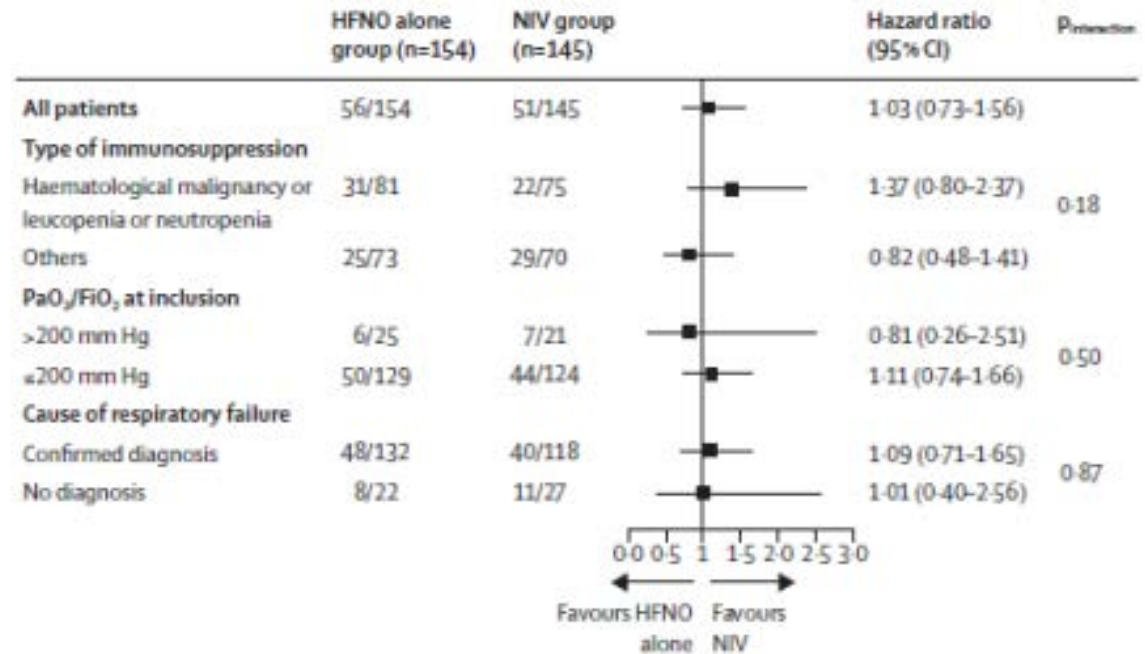
End Points	No. (%)		Mean Difference, % (95% CI) ^b	Relative Difference (95% CI)	P Value
	High-Flow Oxygen Therapy (n = 388)	Standard Oxygen Therapy (n = 388)			
Primary					
All-cause day-28 mortality	138 (35.6)	140 (36.1)	-0.5 (-7.3 to 6.3)	HR, 0.98 (0.77 to 1.24)	.94
Secondary					
Invasive mechanical ventilation ^c	150 (38.7)	170 (43.8)	-5.1 (-12.3 to 2.0)	HR, 0.85 (0.68 to 1.06) ^d	.17
ICU-acquired infection	39 (10.0)	41 (10.6)	-0.6 (-4.6 to 4.1)	HR, 1.01 (0.96 to 1.06) ^d	.91
ICU mortality	123 (31.7)	122 (31.4)	0.3 (-6.3 to 6.8)	RR, 1.01 (0.82 to 1.24)	.64
Hospital mortality	160 (41.2)	162 (41.7)	-0.5 (-7.5 to 6.4)	RR, 0.99 (0.84 to 1.17)	.77
Length of stay, median (IQR), d					
ICU	8 (4-14)	6 (4-13)	0.6 (-1.0 to 2.2)	NA ^e	.07
Hospital	24 (14-40)	27 (15-42)	-2 (-7.3 to 3.3)	NA ^e	.60

Pas de différence de mortalité chez les patients finalement intubés

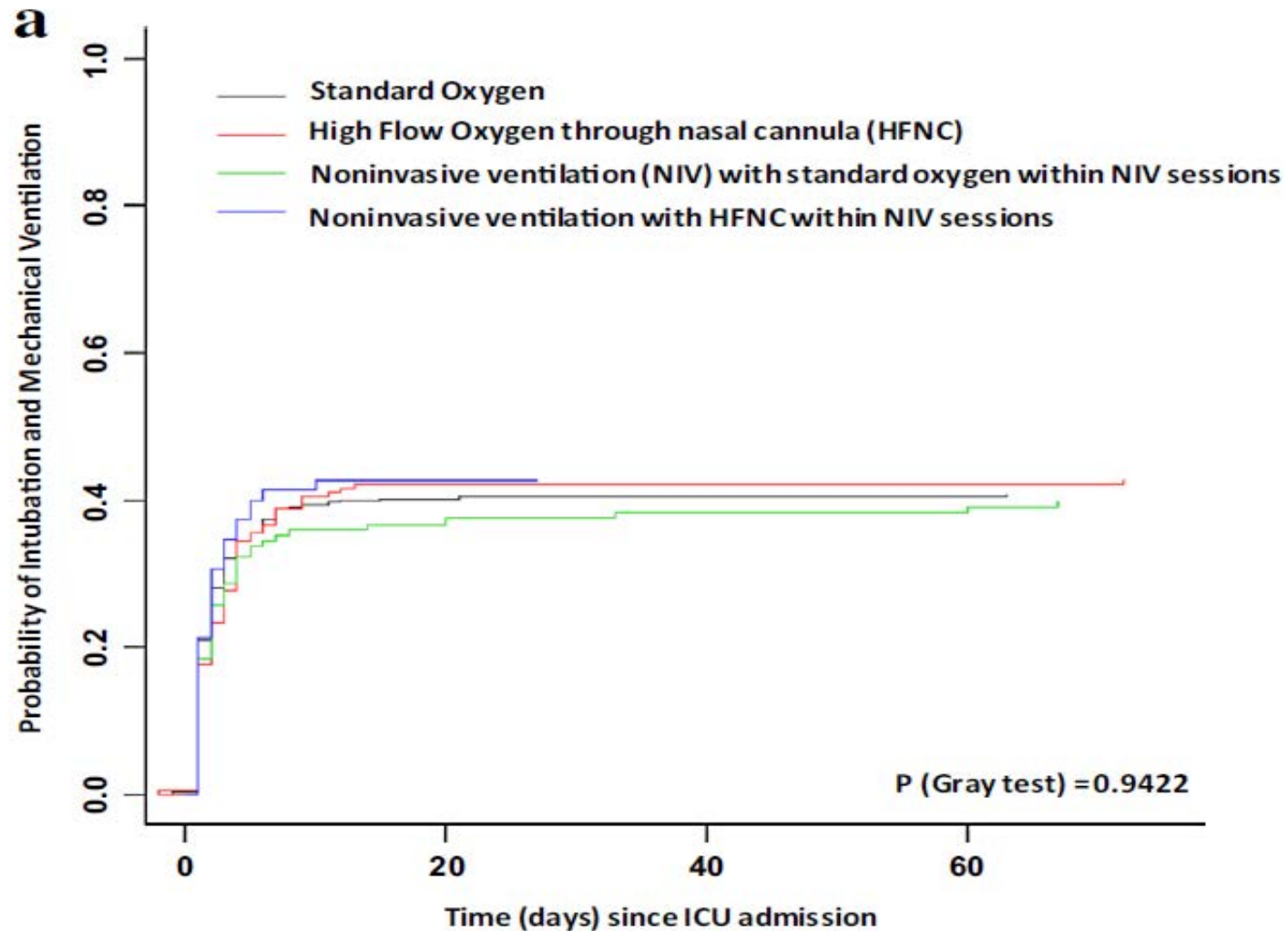
Quel système d'oxygénation ?



299 patients immunodéprimés
Randomisés VNI +OHD vs OHD seule

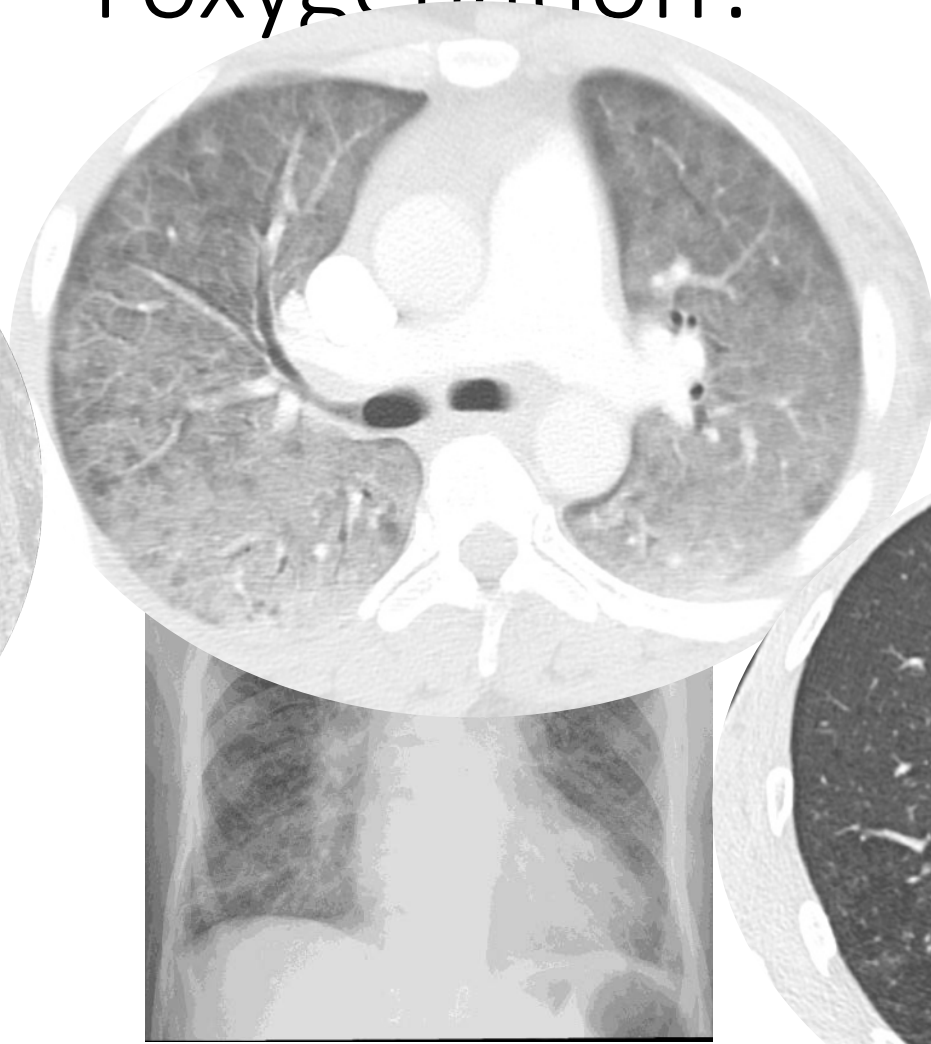
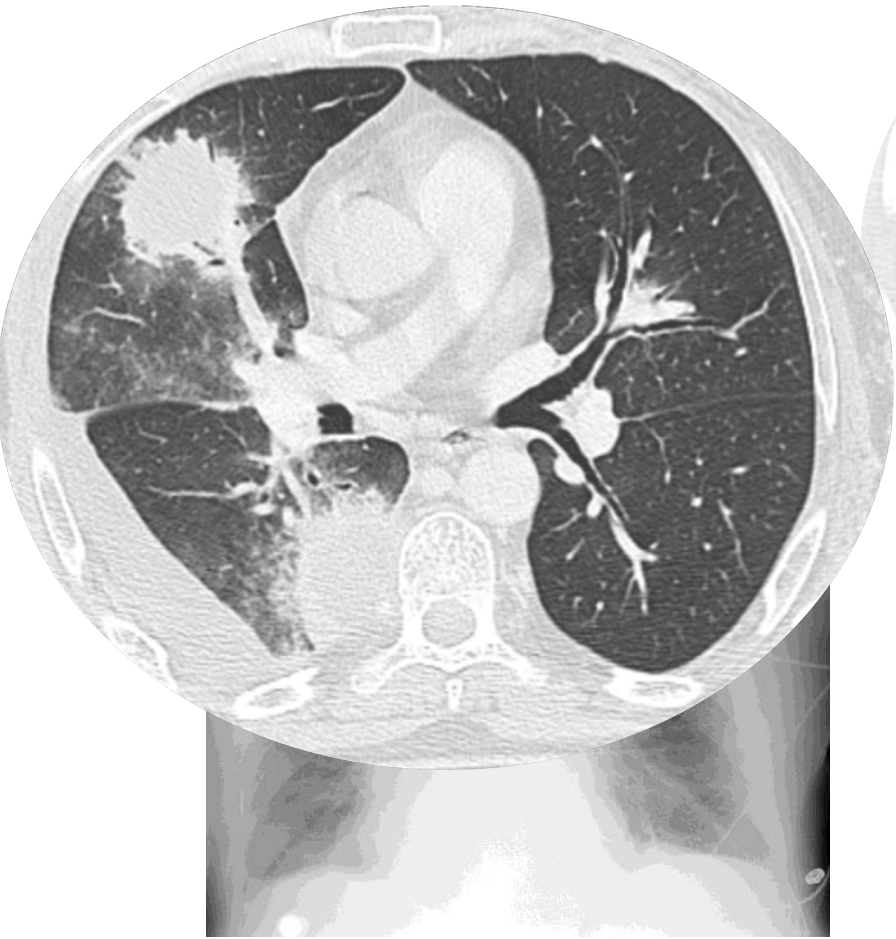


Quel est le meilleur système d'oxygénation?

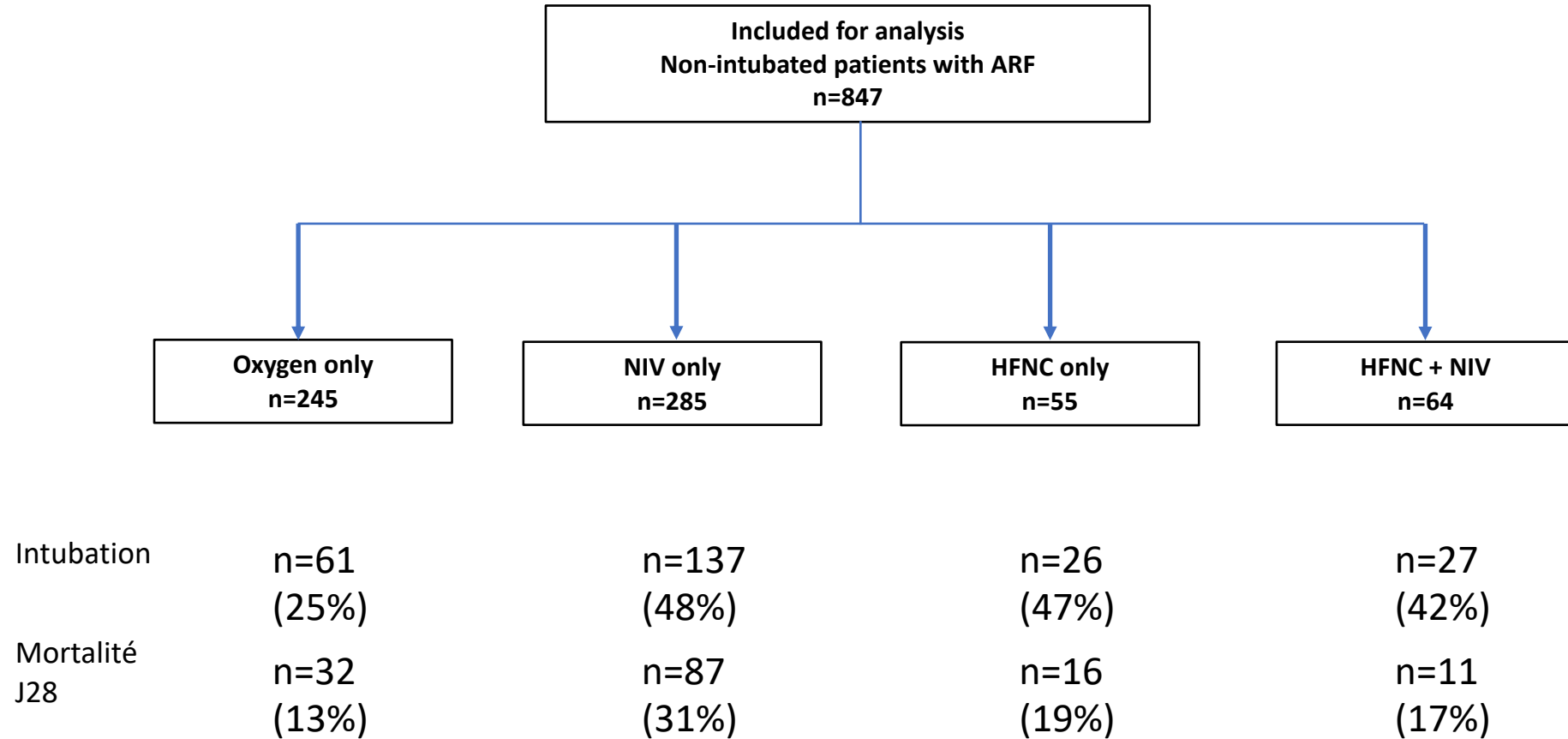


1611 patients ID
16 pays, 68 ICU
Taux d'intubation 62%

Tous les patients ont-ils la même réponse à l'oxygénation?



Réponse à la stratégie d'oxygénation

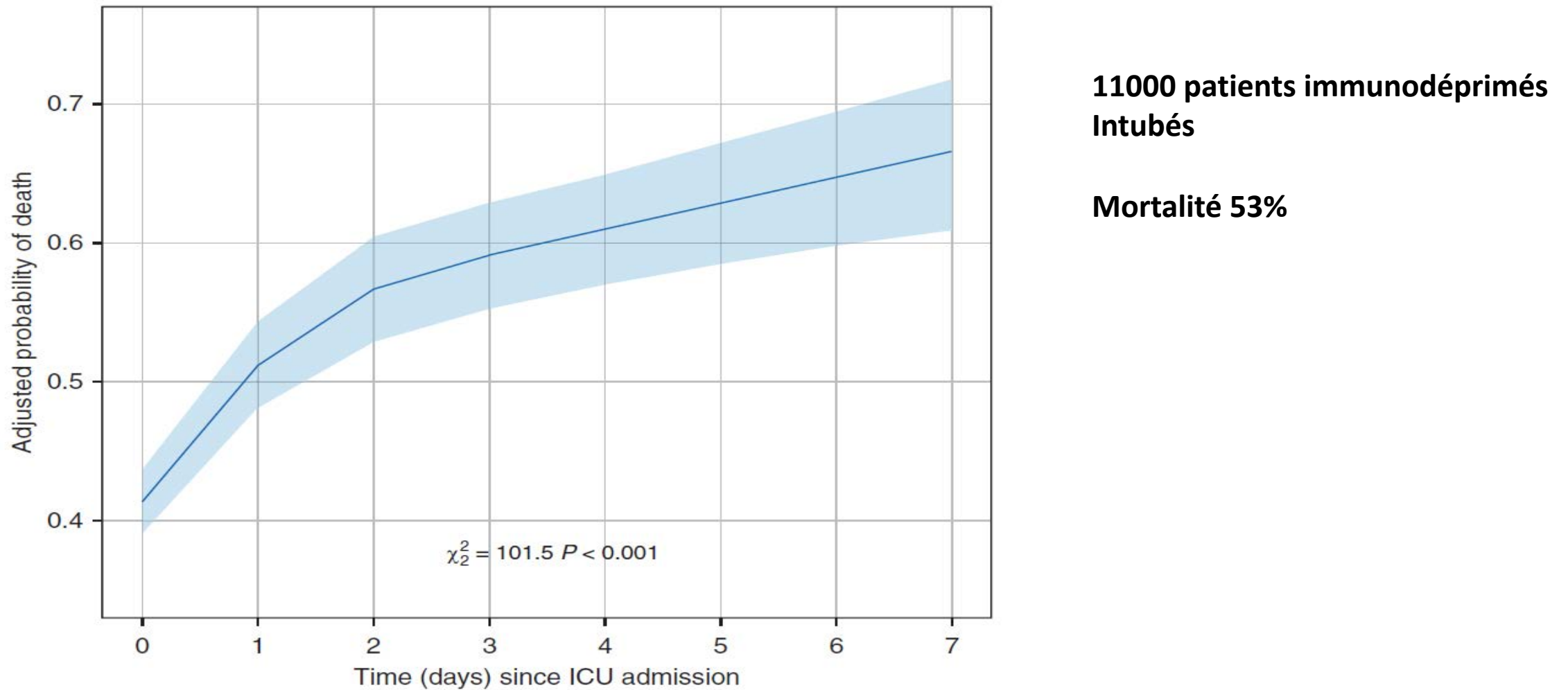


Tous les patients ont-ils la même réponse à l'oxygénation?

Variables	OR	p
Mode of oxygenation		
Oxygen only	1	
NIV only	2.85 (1.73-4.70)	<0.001
HFNC only	2.19 (0.99-4.85)	0.05
NIV and HFNC	1.70 (0.83-3.49)	0.14
Severity of ARF		
SOFA score without respiratory item at admission	1.19 (1.10-1.28)	<0.001
PaO ₂ / FiO ₂ <100 at ICU admission	1.96 (1.27-3.02)	0.0002
Diagnosis		
Other identified causes	1	
Bacterial or viral pneumonia	1.98 (1.07-3.65)	0.03
Opportunistic infection	4.75 (2.23-10.1)	<0.001
Lung involvement by the underlying disease or Drug-related pulmonary toxicity	2.13 (0.96-4.73)	0.06
No identified cause	1.48 (0.70-3.11)	0.30
Radiologic pattern at ICU admission		
Bilateral alveolar	1.67 (1.03-2.69)	0.04

FDR d'intubation

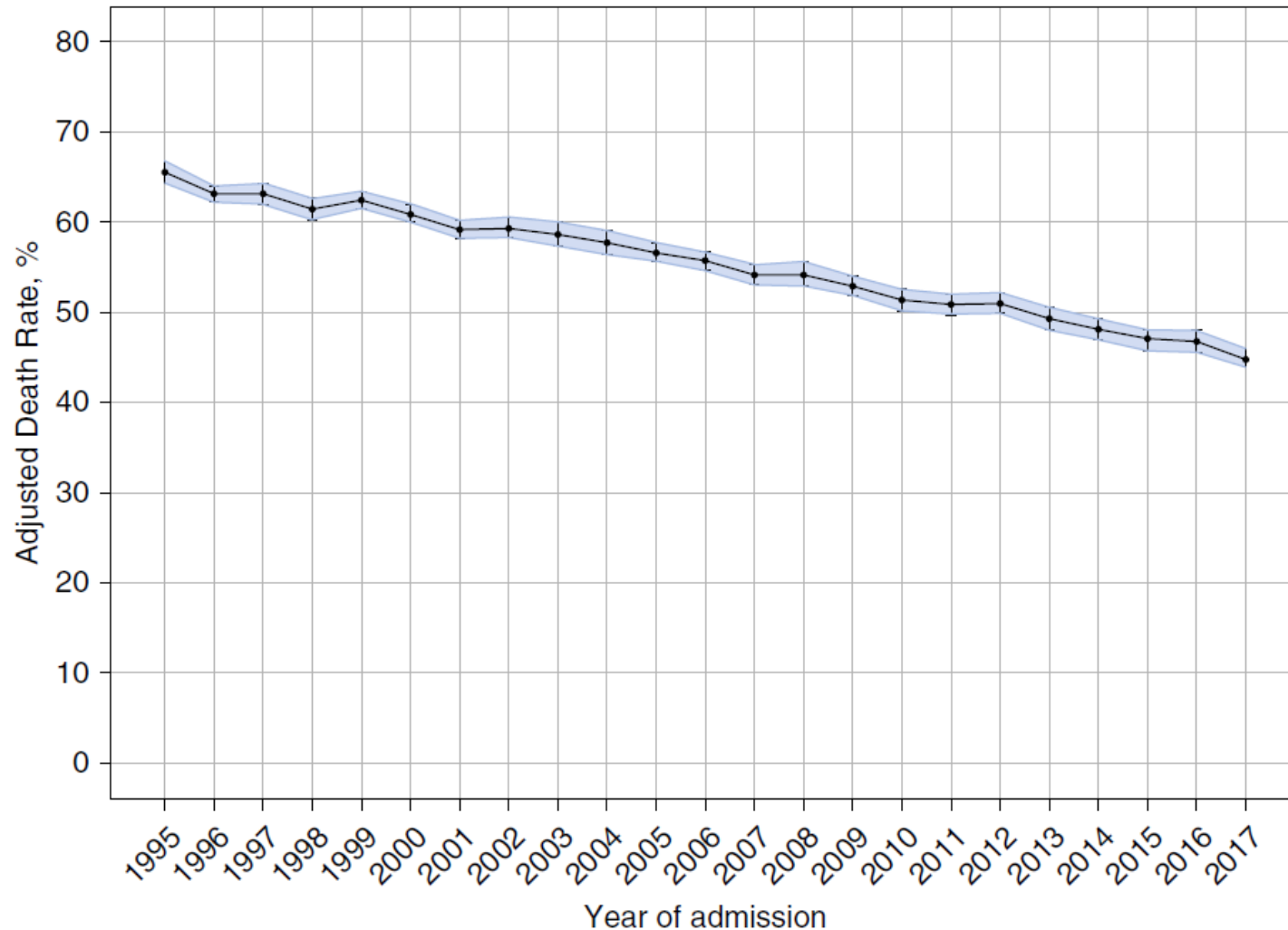
Poids de l'intubation retardée



Complications particulières liées à la VMI

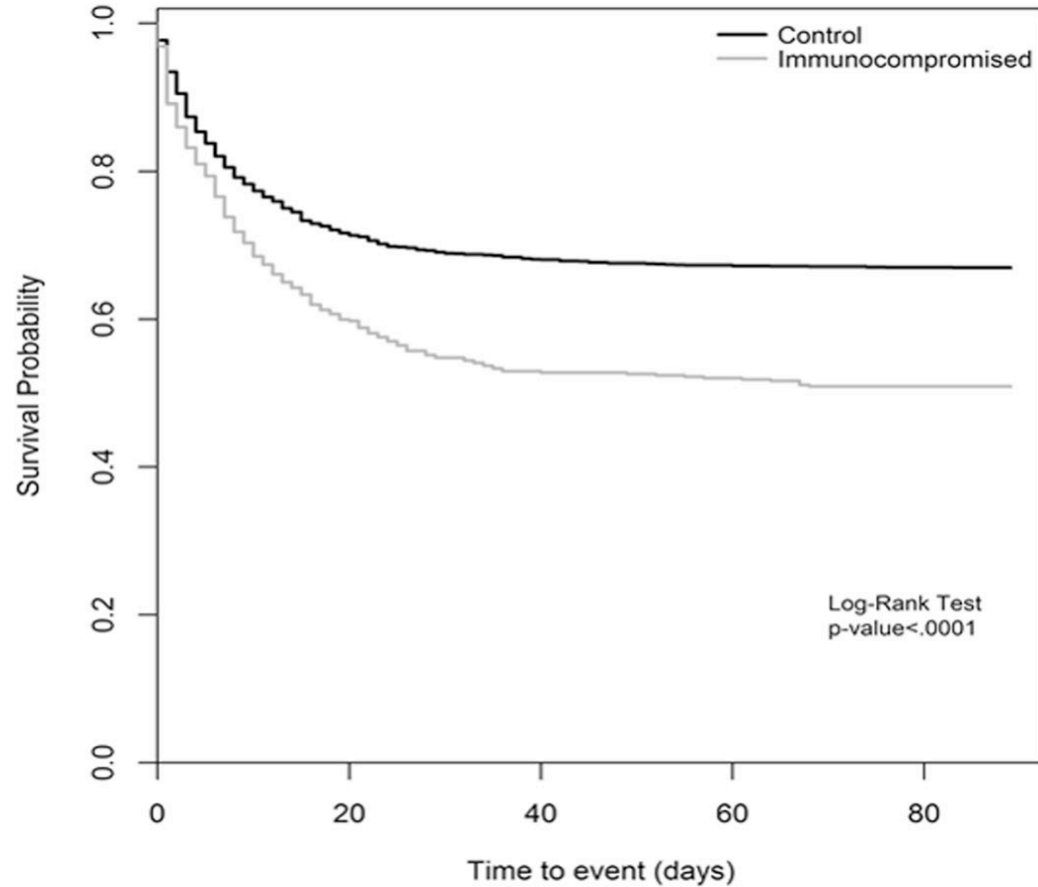
- L'intubation:
 - Hypoxémie sévère
 - Mucite
- Au cours la ventilation mécanique invasive
 - Fréquence des pathologies infectieuses
 - Fréquence des atteintes fongiques
 - Conséquences de l'atteinte neuro-musculaire et perte de poids sur la poursuite du traitement de la pathologie sous-jacente

Pronostic de la ventilation mécanique



**11000 patients
immunodéprimés
Déficit immunitaire :**
- Hématologie 30%
- Tumeur solide 23%
- Autre cause 46%

Pronostic des patients en SDRA



# at risk	0	20	40	60	80
Control	2111	1512	1437	1420	1414
Immunocompromised	542	325	287	282	276

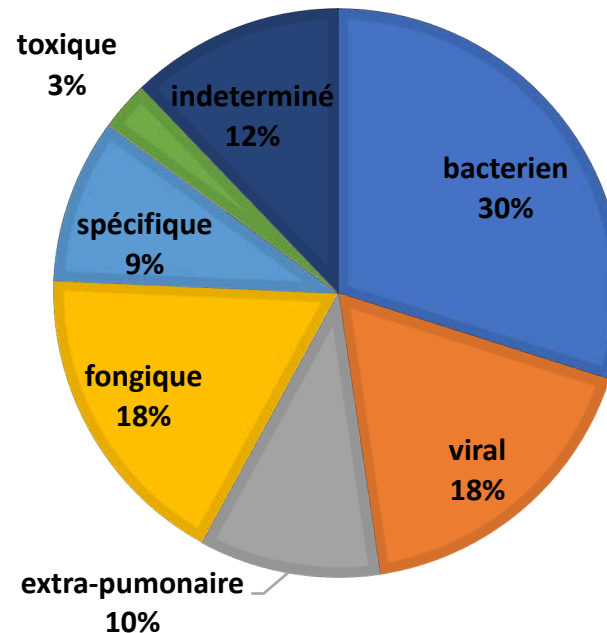
4500 patients dont 20% patients immunodéprimés

Chez les patients immunodéprimés :

- **Moins de comorbidité**
- **Le plus souvent pneumonie bactérienne**
- **VNI plus fréquente (20.9 vs 15.9,9%, p=0,004)**
- **Fréquence des échecs de VNI (10.4% vs 6,1%, p=0,002)**
- **Fréquence des décisions de fin de vie**

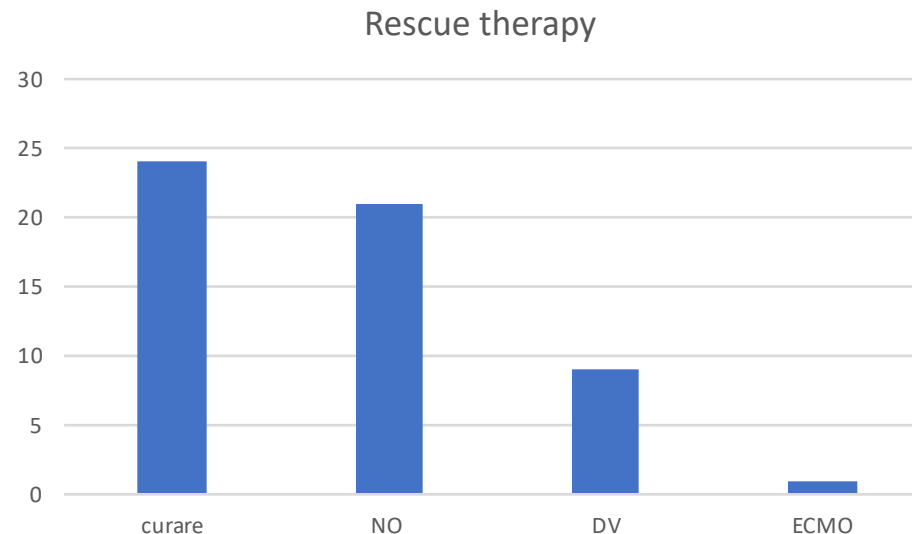
Ventilation mécanique du SDRA

- 1611 patients en IRA
- 789 patients ventilés dont 494 avec données mécaniques
- Survie 43.7%
- Étiologies

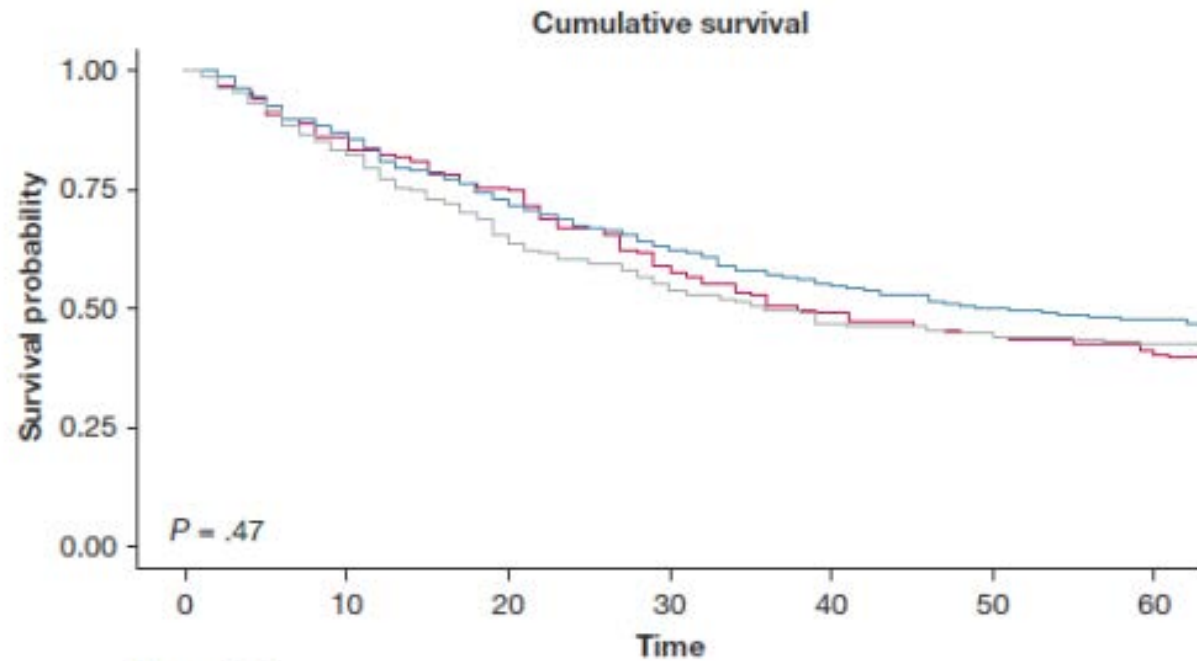


Ventilation mécanique du SDRA

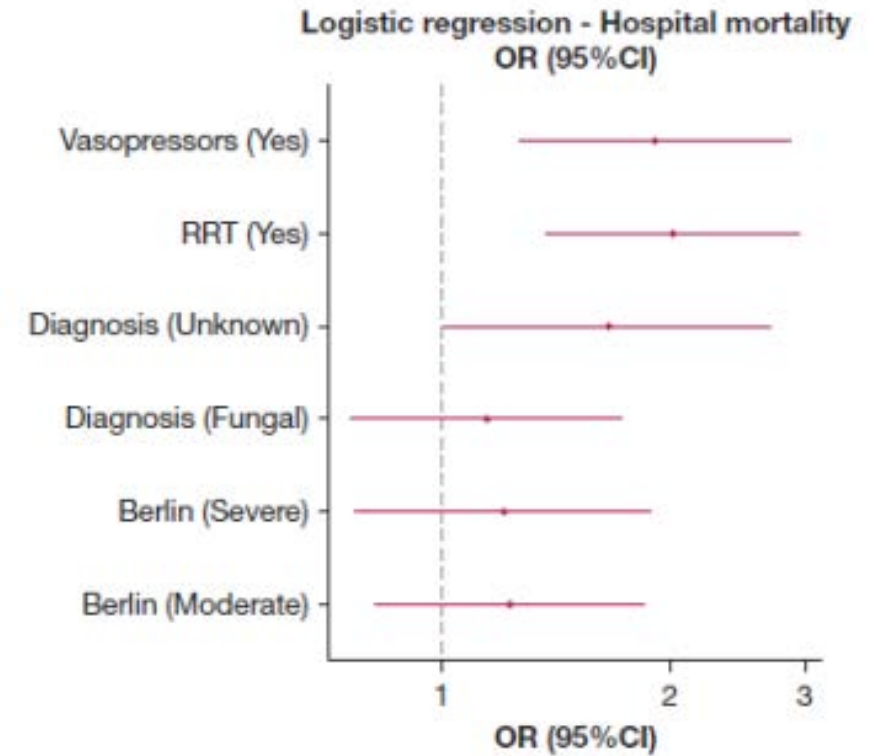
- SDRA modéré 21%, modéré 47%, sévère 32%
- Vt 6.8 (6.1-7.8) ml/Kg, Peep 10 (7-12)
- Pression plateau 23 (20-28), Driving pressure 14 (11-18)
- Compliance 30 (23-41)



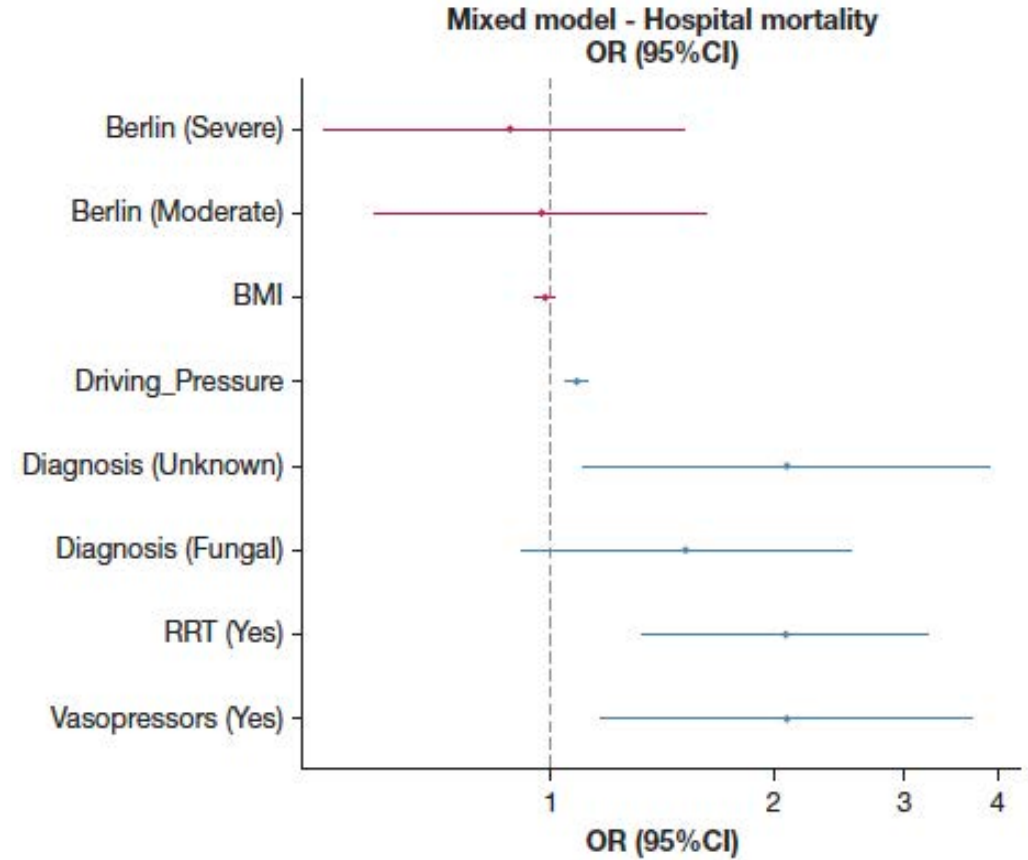
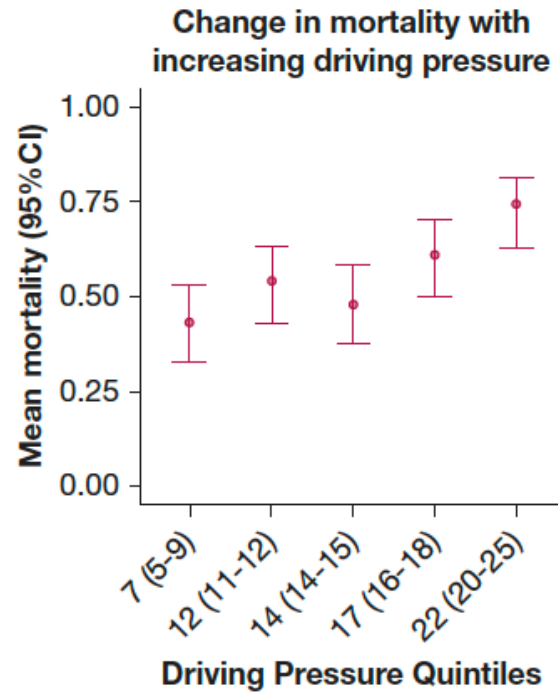
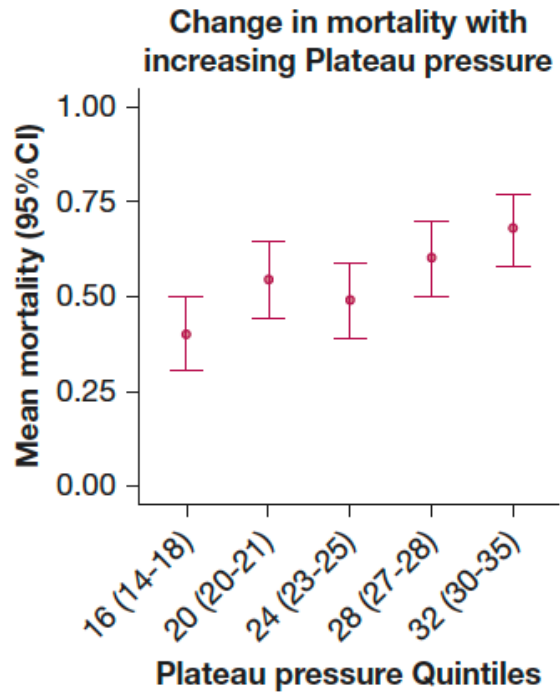
Pronostic du SDRA



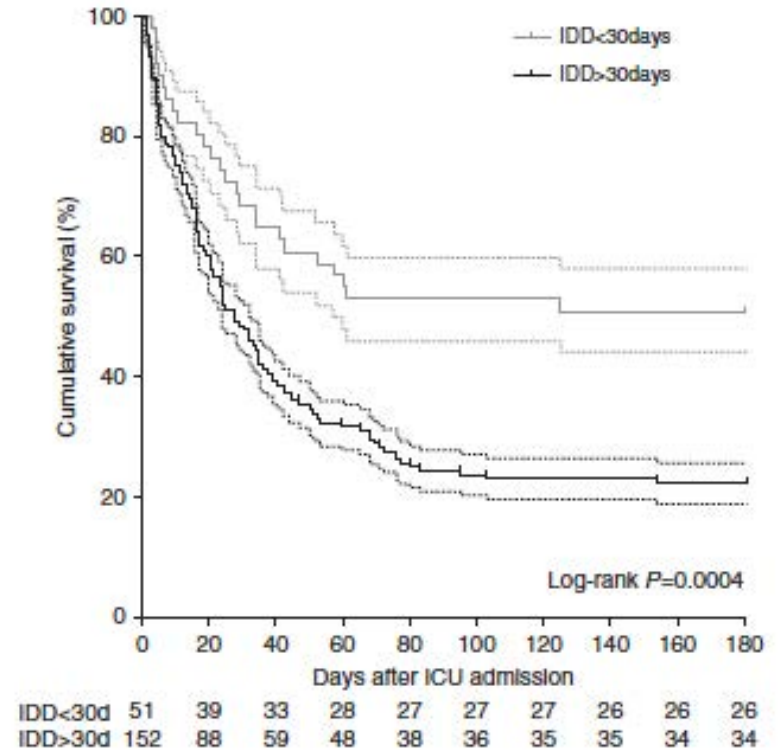
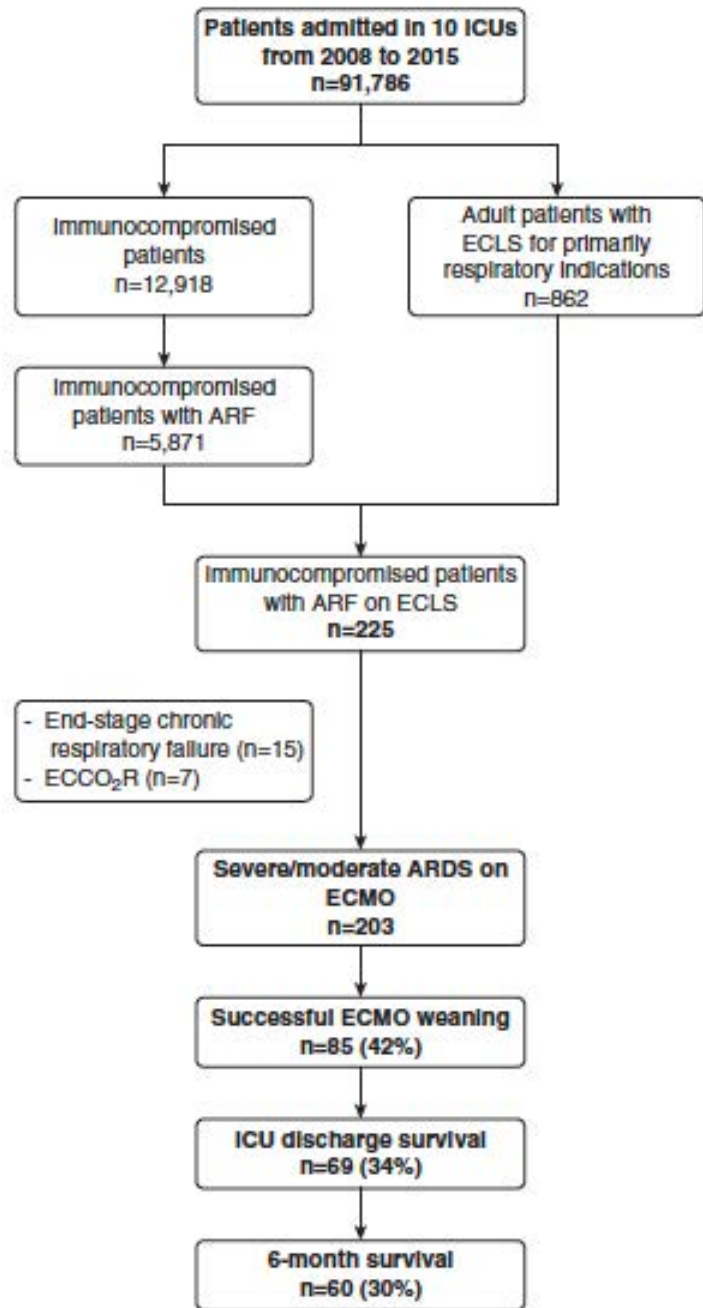
	No. at risk						
Berlin = Mild	127	109	96	75	62	57	52
Berlin = Moderate	300	261	220	189	166	150	143
Berlin = Severe	213	177	139	117	100	95	90



Pronostic du SDRA

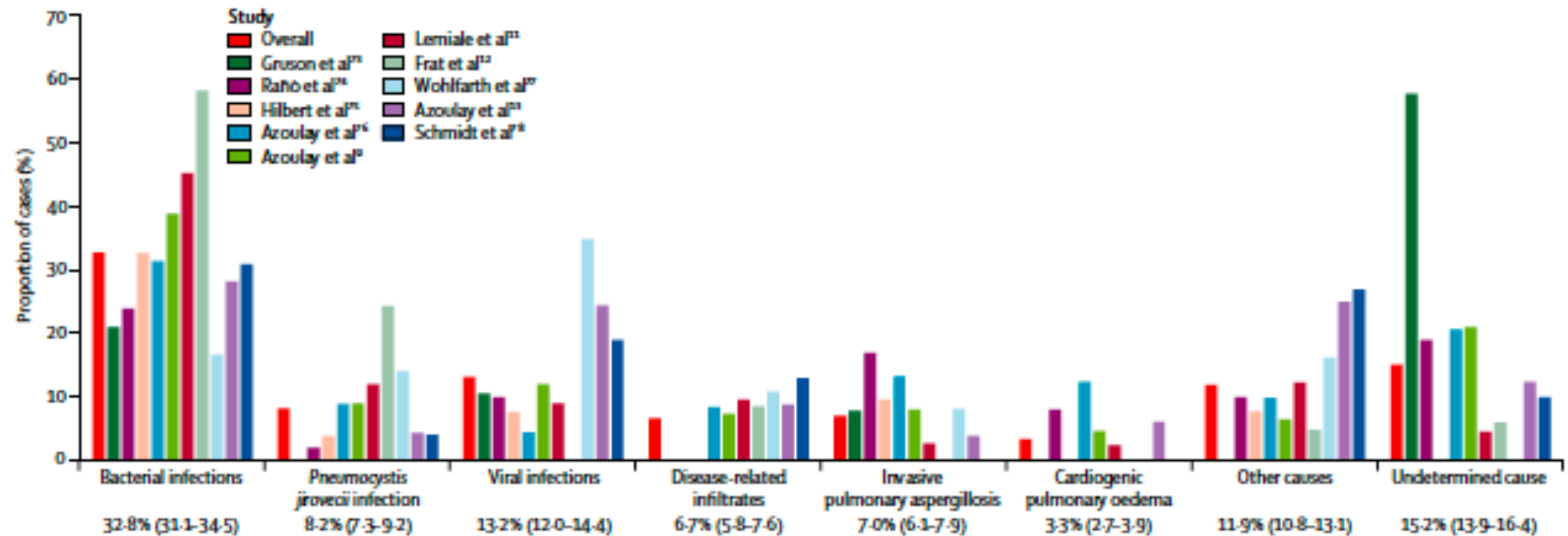


ECMO



Variable*	OR (95% CI)	P Value
Recently diagnosed immunodeficiency [†]	0.364 (0.148–0.899)	0.028
Platelet count	0.996 (0.992–0.999)	0.008
P _{CO2}	1.031 (1.005–1.058)	0.019
Age	1.032 (1.002–1.062)	0.035
Driving pressure	1.079 (1.001–1.164)	0.047

Intérêt du diagnostic étiologique



Absence de diagnostic et mortalité

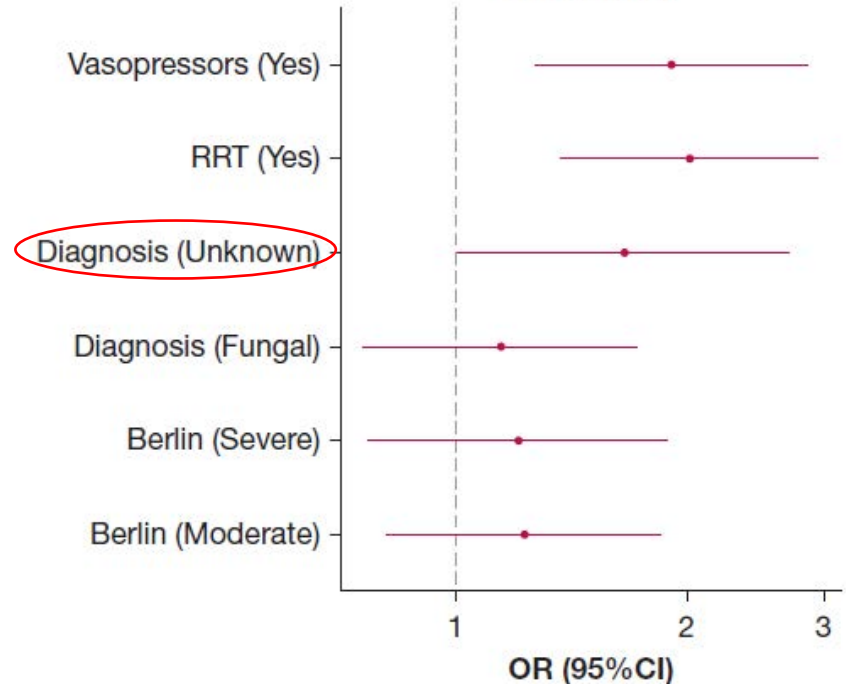
Invasive mechanical ventilation (1st 24hr)
 Undetermined diagnosis
 SOFA score > 7
 Invasive pulmonary aspergilosis



604 hematological patients with ARF
 12,9 % undetermined diagnosis

Contejean et al. *Ann. Intensive Care* (2016) 6:102

Logistic regression - Hospital mortality
 OR (95%CI)



789 ID with ARDS
 13 % undetermined diagnosis

Demoule et al, *Chest* (2020) :1947-1957

Neutropenia after chemotherapy associated with bacterial infection
Steroid treatment associated with pneumocystis infection
Multiple myeloma associated with pneumococemia

Bronchial endoscopy

Immunofluorescence for PCP
Cell count for toxicity

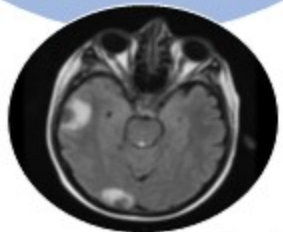
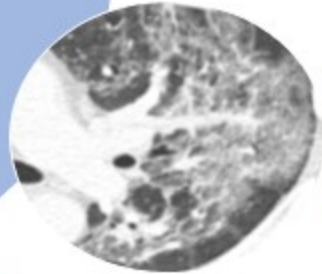
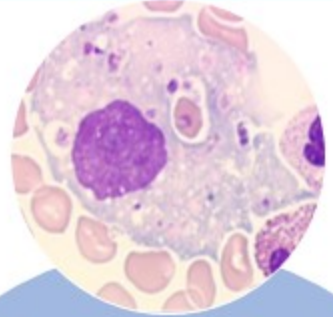
Non invasive exams

Blood culture for bacterial infection
PCR on nasal swab
Blood galactomannan for fungal infection

CT scan

Ground glass opacity related to pneumocystis
Nodular lesion related to fungal disease
Alveolar disease related to pneumococemia

Etiology of ARF



Length of symptoms

Few minutes for acute cardiogenic oedema
One week for pneumocystis infection
Few weeks for lung toxicity

Respiratory examination

Hemoptysis related aspergilosis infection
Crackles related to bacterial pneumonia
Wheezing related to aspergillus trachéobronchitis

Symptoms outside the lung

Cutaneous lesion related to fungal infection or toxicity
Brain impairment related to nocardia or specific infiltration
Kidney failure related to immune disease

Perspectives d'amélioration?

- Améliorer la prise en charge. Etude Expert-is : conseil de télémédecine des centres experts vers des centres non-experts
- Traitement probabiliste : étude efrain2 : traitement probabiliste par antifongique et/ou corticoïdes pour les patients sans diagnostic

Conclusion

- SDRA fréquent chez le patient immunodéprimé
- Aucun système d'oxygénation ne permet d'éviter totalement l'intubation
- Mortalité élevée en cas d'intubation
- Poids de l'absence de diagnostic étiologique
- Poids du retard d'intubation

Merci pour votre attention