

DU de Réanimation des Pathologies Infectieuses – Paris, Vendredi 18 septembre 2020

Insuffisance respiratoire aiguë au cours de l'infection par le VIH



François Barbier, MD PhD

Médecine Intensive & Réanimation

Hôpital de la Source - CHR Orléans

francois.barbier@chr-orleans.fr



Liens d'intérêt potentiels

MSD

Pfizer

BioMérieux



Global summary of the AIDS epidemic | 2019

Number of people living with HIV

	Total	38.0 million	[31.6 million–44.5 million]
Adults	36.2 million	[30.2 million–42.5 million]	
Women (15+ years)	19.2 million	[16.4 million–22.2 million]	
Children (<15 years)	1.8 million	[1.3 million–2.2 million]	

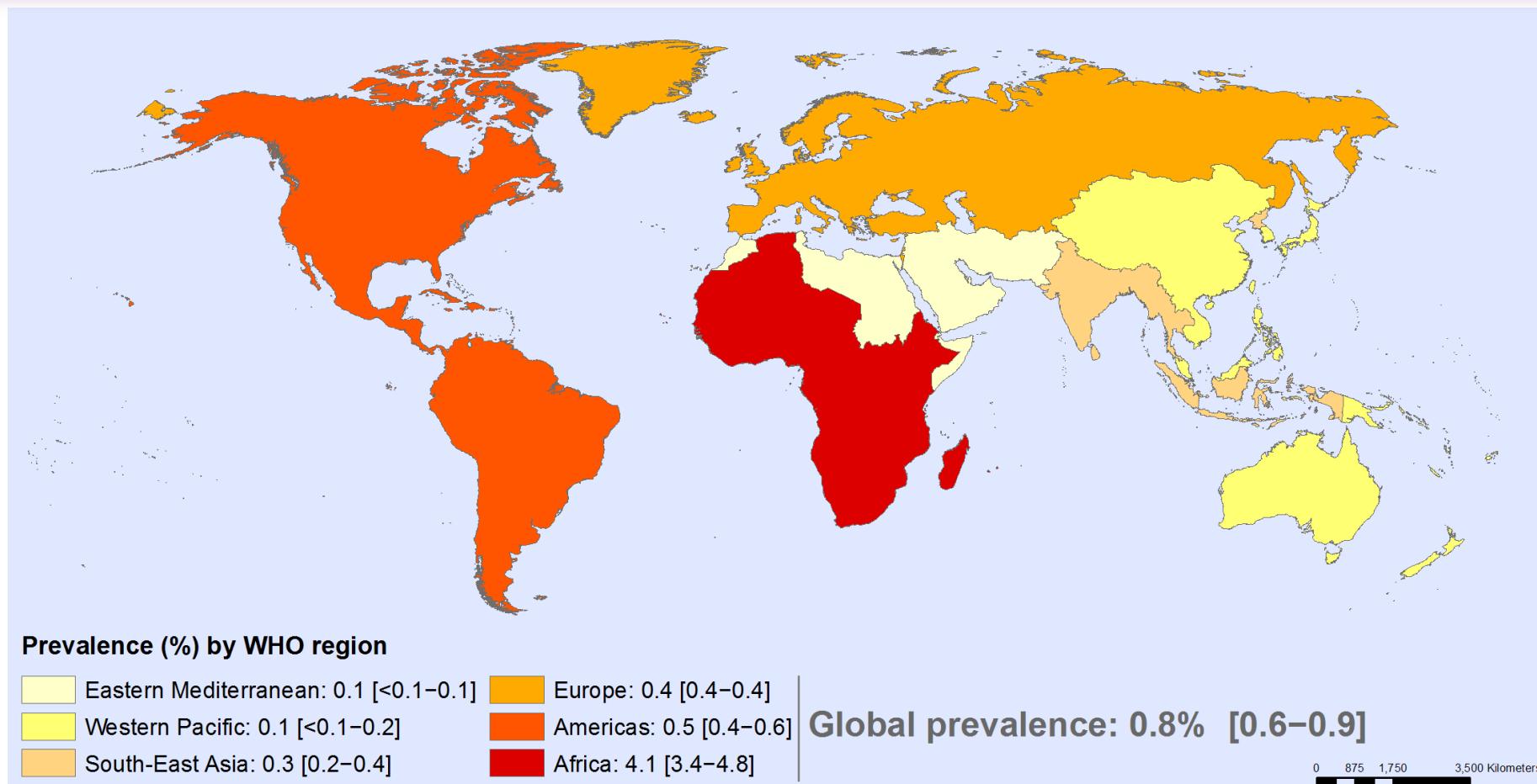
People newly infected with HIV in 2019

	Total	1.7 million	[1.2 million–2.2 million]
Adults	1.5 million	[1.1 million–2.0 million]	
Children (<15 years)	150 000	[94 000–240 000]	

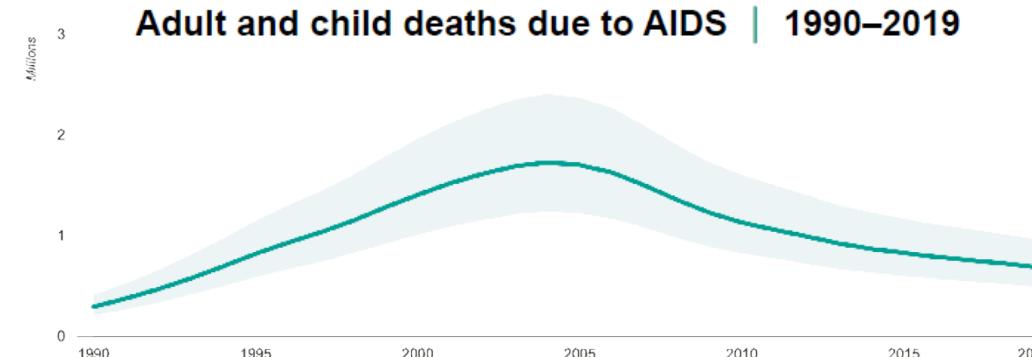
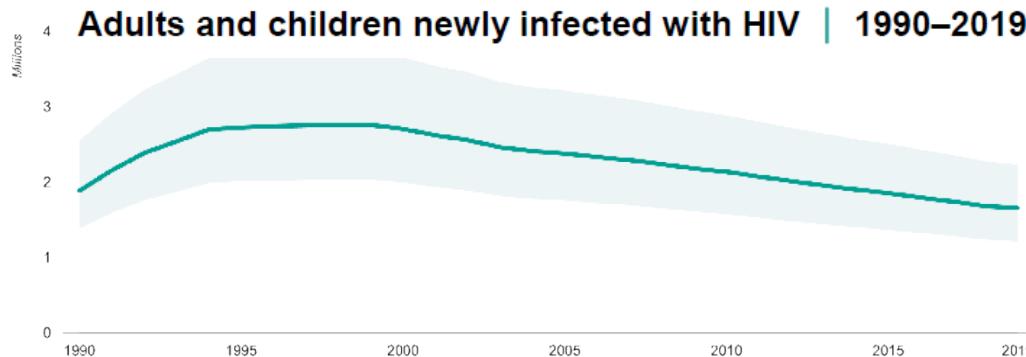
AIDS-related deaths in 2019

	Total	690 000	[500 000–970 000]
Adults	600 000	[430 000–840 000]	
Children (<15 years)	95 000	[61 000–150 000]	

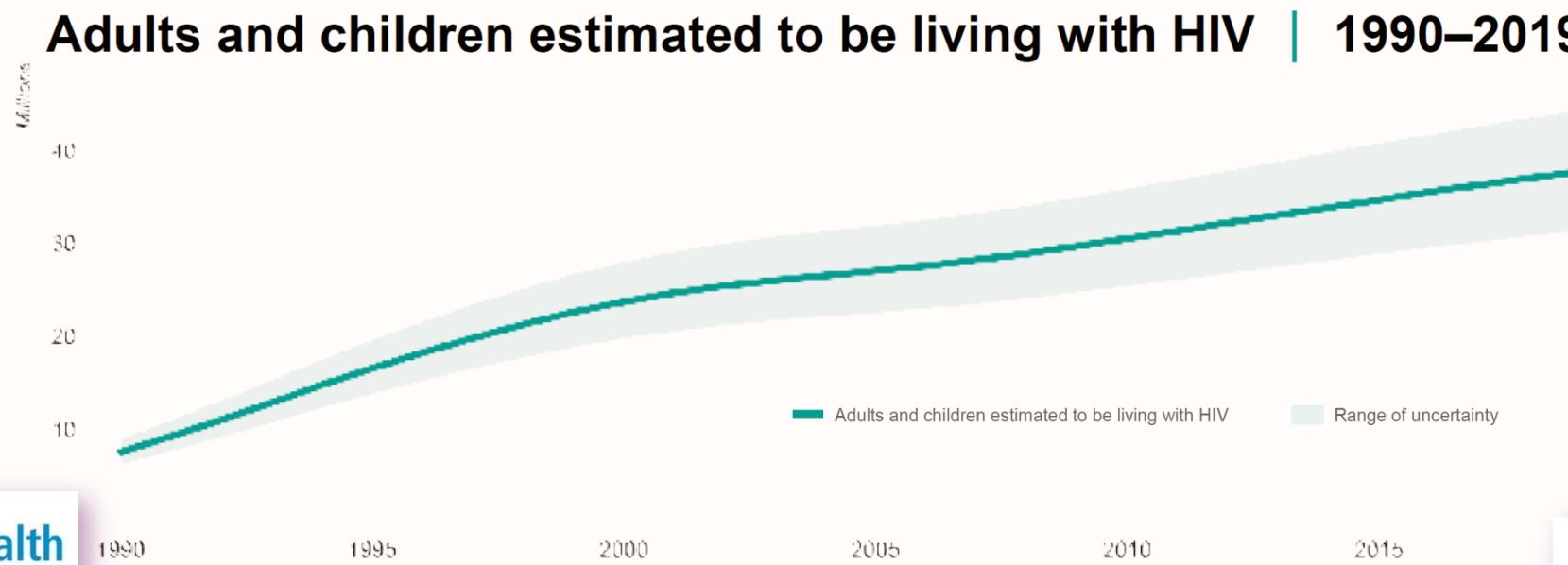
Global summary of the AIDS epidemic | 2019



Global summary of the AIDS epidemic | 2019



Adults and children estimated to be living with HIV | 1990–2019

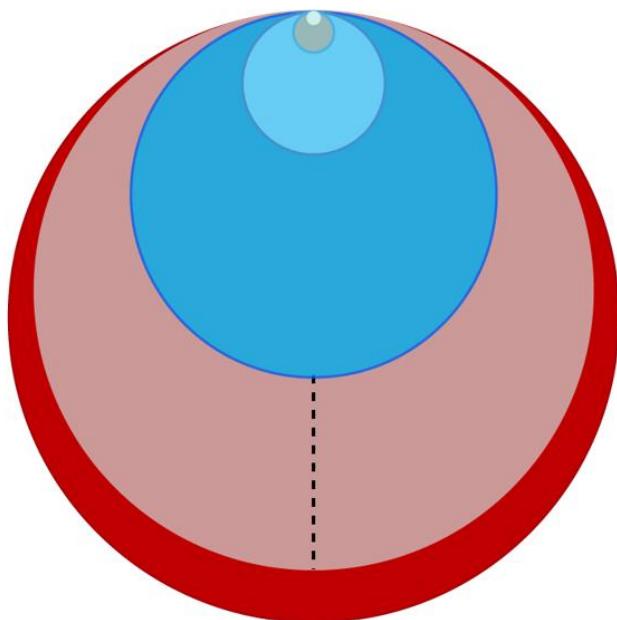


World Health Organization

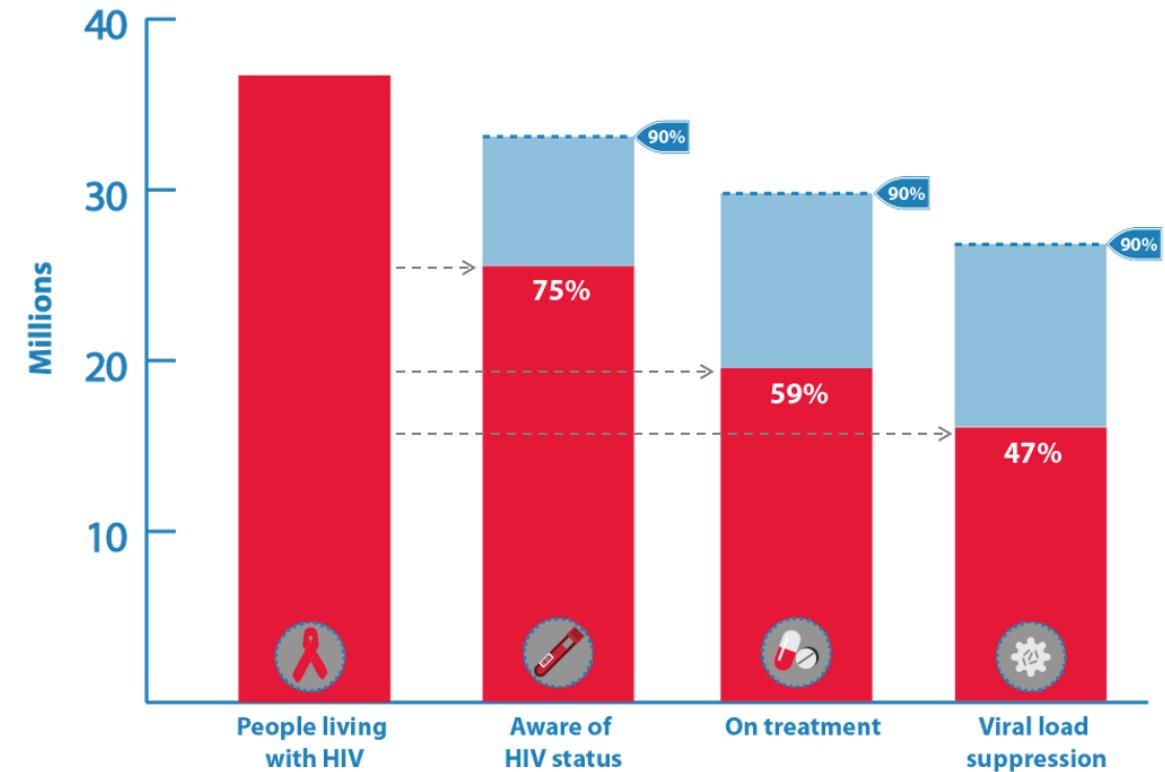


UNAIDS

Number of people receiving antiretroviral treatment



HIV testing and care continuum (2017)





Patients VIH+, France 2018

N = 200000 (IC 95%, 170000-240000)
soit ~0,3% de la pop° générale

Patients sous ARV : 81% (IC 95%, 69-94%)

Infections méconnues ~30000

www.santepubliquefrance.fr

www.unaids.org

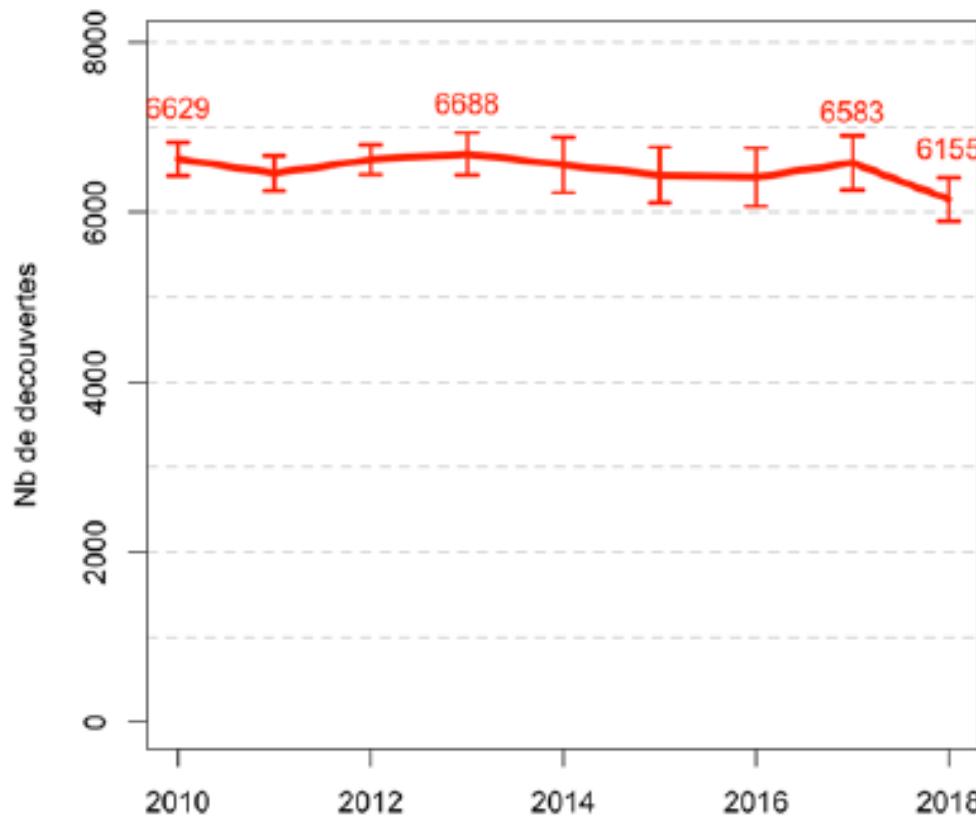


DÉCOUVERTES DE SÉROPOSITIVITÉ VIH ET DIAGNOSTICS DE SIDA - FRANCE, 2018

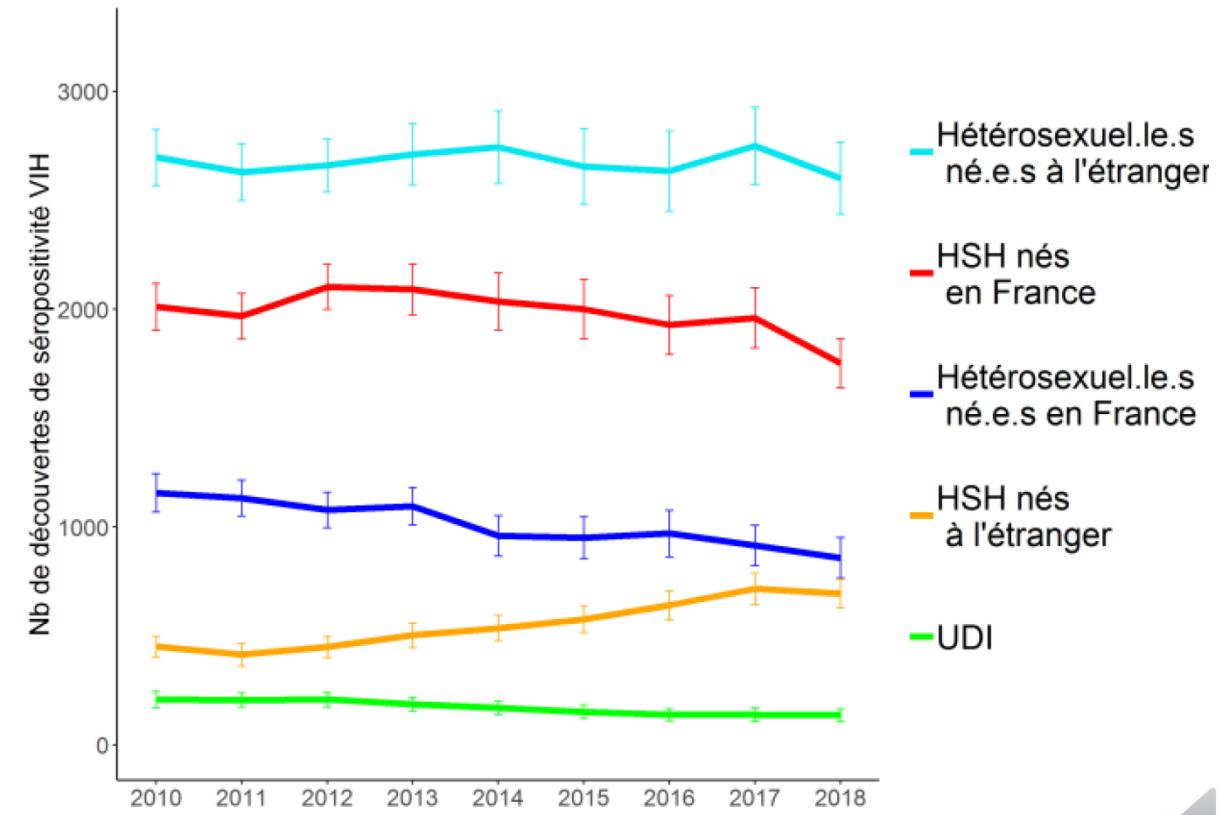
Bulletin de santé publique. 9 octobre 2019



Diagnostics de séropositivité, total

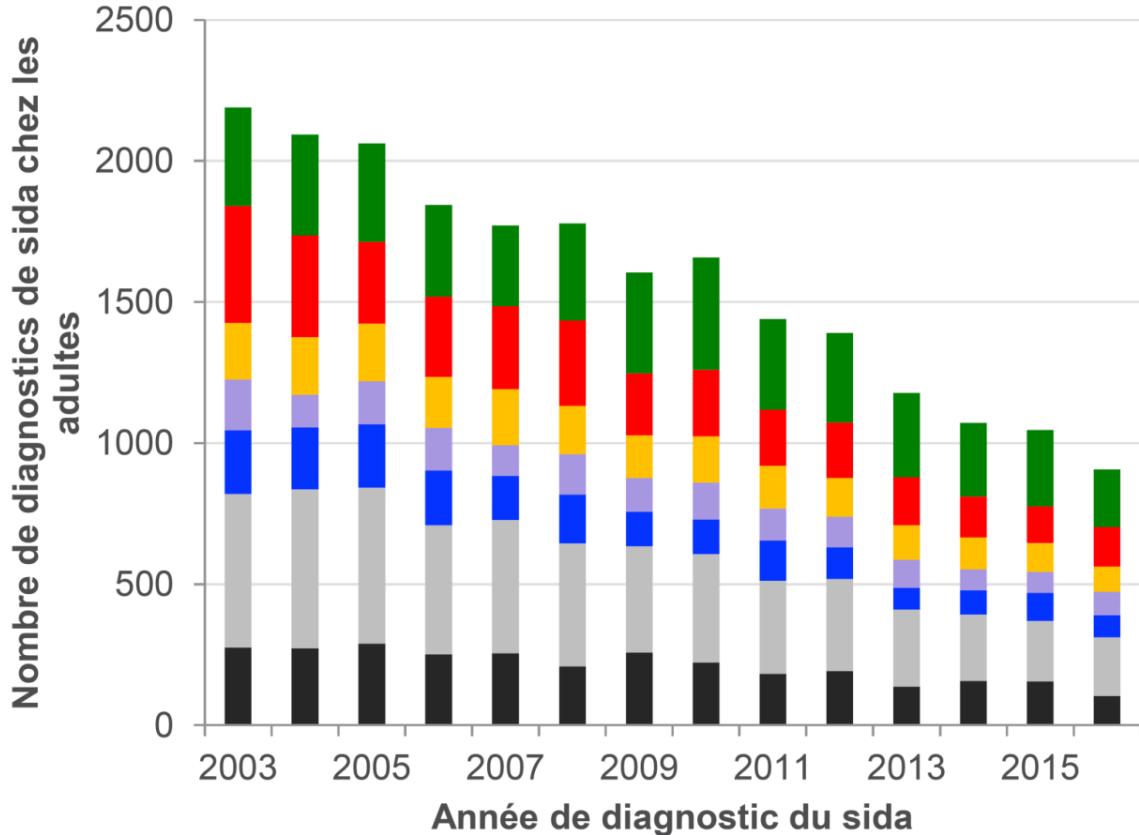


Diagnostics de séropositivité, sous-groupes



DÉCOUVERTES DE SÉROPOSITIVITÉ VIH ET DIAGNOSTICS DE SIDA - FRANCE, 2018

Bulletin de santé publique. 9 octobre 2019



**Diagnostics de SIDA en 2018 (~1200) :
Infections opportunistes inaugurales**

- Pneumocystose : 22%**
- Tuberculose : 7%
- Toxoplasmose SNC : 7%
- Sarcome de Kaposi : 7%
- Candidose oesophagienne : 8%
- Autres IO & lymphomes : 31%
- Pathologies multiples : 18%**



Garyphallia Poulakou
Matteo Bassetti
Jean-François Timsit

Critically ill migrants with infection: diagnostic considerations for intensive care physicians in Europe

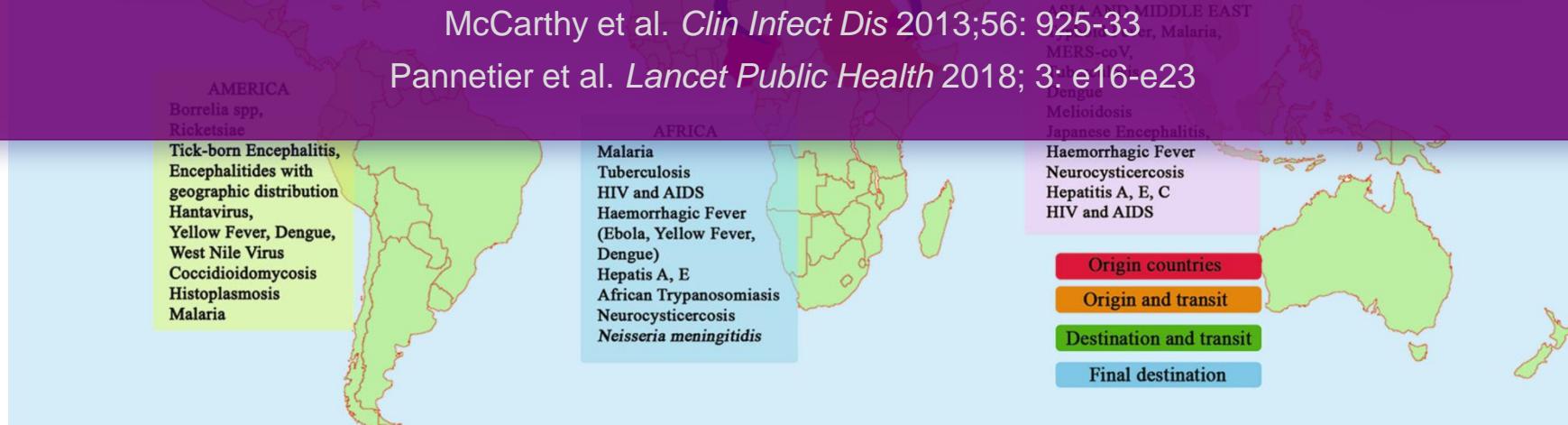


IO inaugurales importées (tuberculose++, histoplasmose)

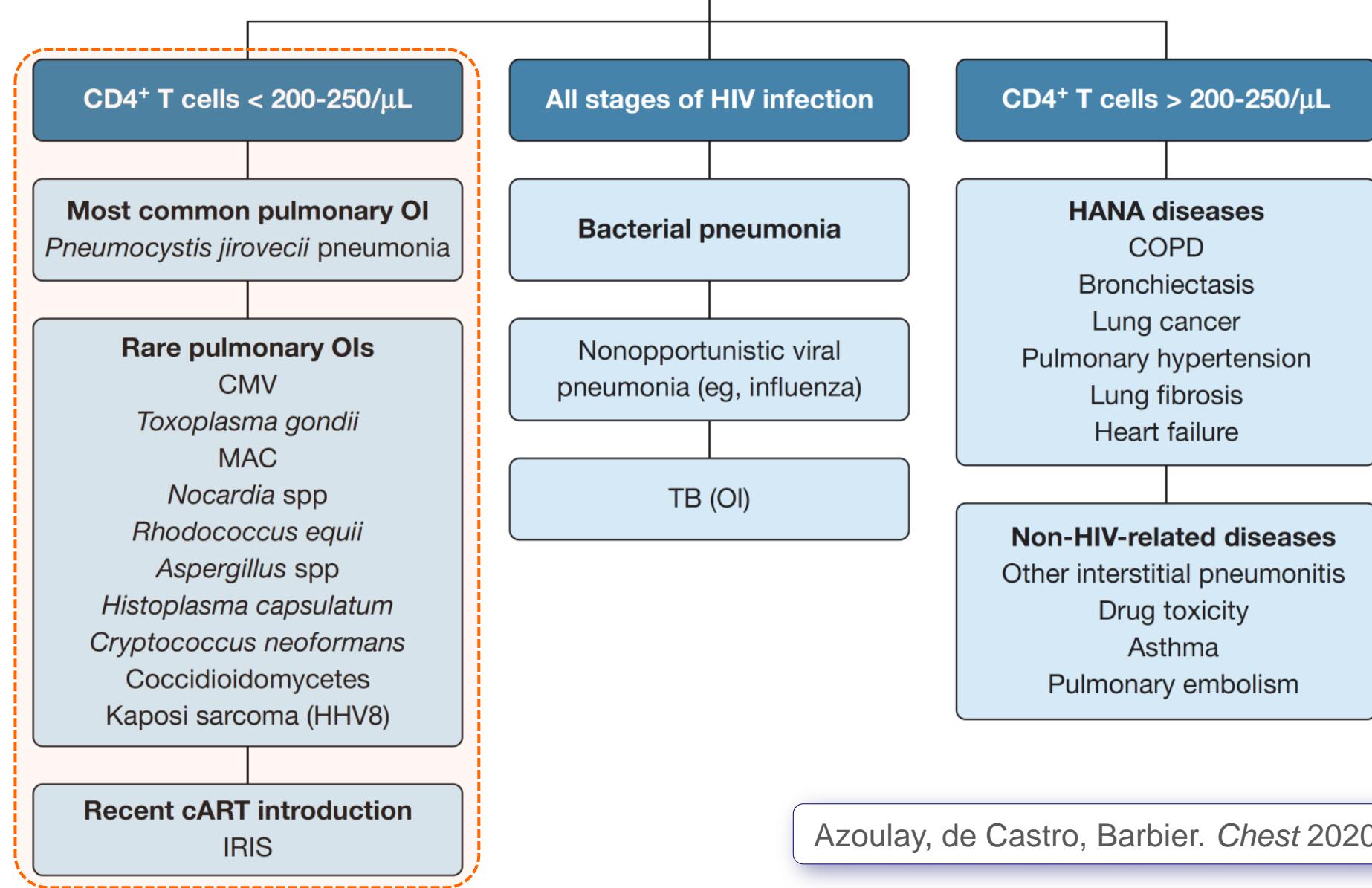
Infection par le VIH antérieure ou postérieure à la migration

McCarthy et al. *Clin Infect Dis* 2013;56: 925–33

Pannetier et al. *Lancet Public Health* 2018; 3:e16–e23



Acute respiratory failure in HIV-infected patients

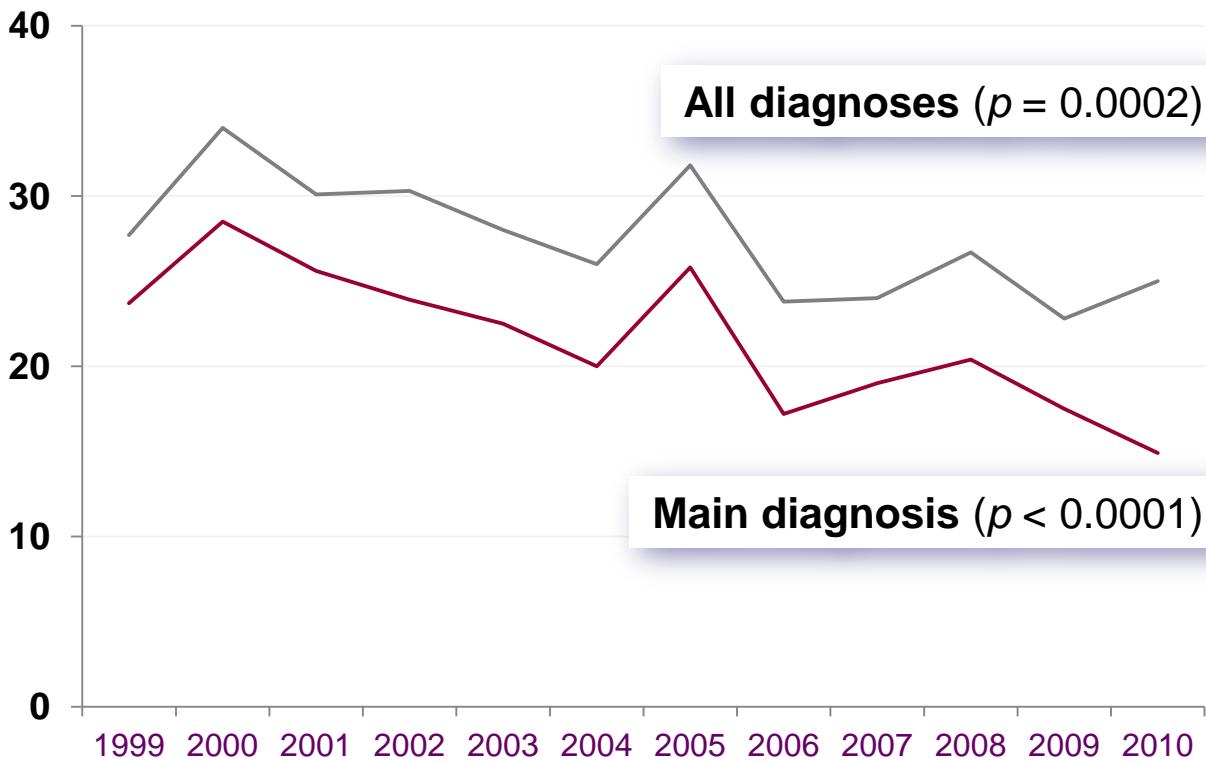


Azoulay, de Castro, Barbier. *Chest* 2020; 157: 293-309



François Barbier
Antoine Roux
Emmanuel Canet
Patricia Martel-Samb
Philippe Aegerter
Michel Wolff
Bertrand Guidet
Élie Azoulay

Temporal trends in critical events complicating HIV infection: 1999–2010 multicentre cohort study in France



34 ICUs (CUB-Rea Network), 1999–2010

6,673 HIV-infected patients

Prevalence of AIDS-defining opportunistic infections

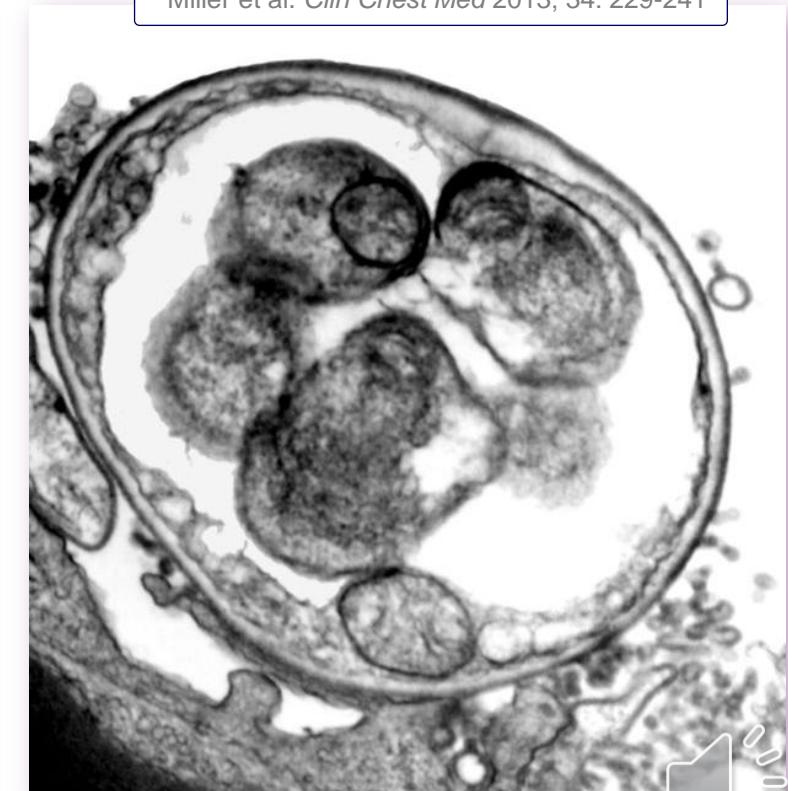
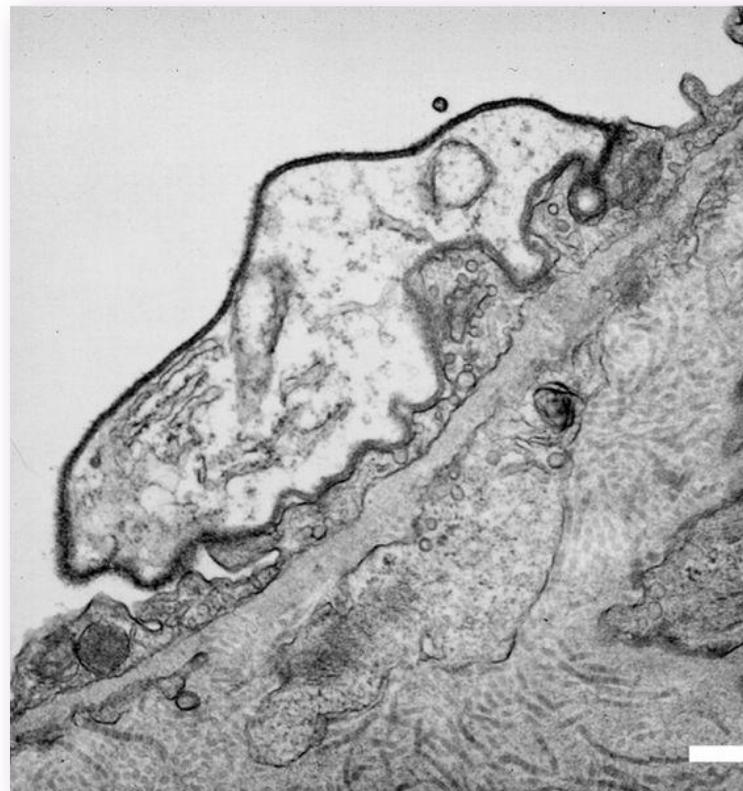
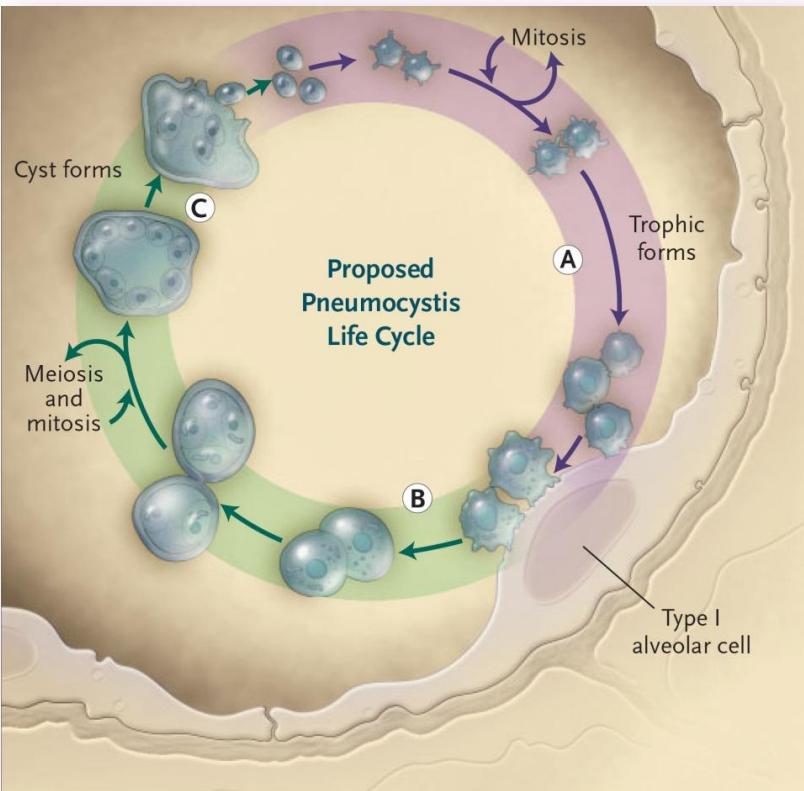
1. *Pneumocystis jirovecii* pneumonia : 608 (9.5%)
2. Cerebral toxoplasmosis : 400 (6.3%)
3. Tuberculosis (all forms) : 361 (5.7%)
4. CMV : 215 (3.4%)
5. Candidiasis : 103 (1.6%)
6. Cryptococcosis : 89 (1.4%)
7. MAC : 86 (1.3%)
8. Kaposi sarcoma : 63 (1.0%)
9. Histoplasmosis : 18 (0.3%)
10. PML (JC virus) : 14 (0.2%)



Pneumocystis jirovecii

- ***Pneumocystis* sp.** : champignon ubiquitaire, spécificité espèce/hôte (*P. jirovecii* / Homme)
- Exposition (= immunisation) quasi-constante dans les 2-4 premières années
- **Colonisation pulmonaire fréquente (VIH+++), transmission inter-humaine aéroportée**
- **PCP** : réinfection par une ou plusieurs souches de *P. jirovecii*

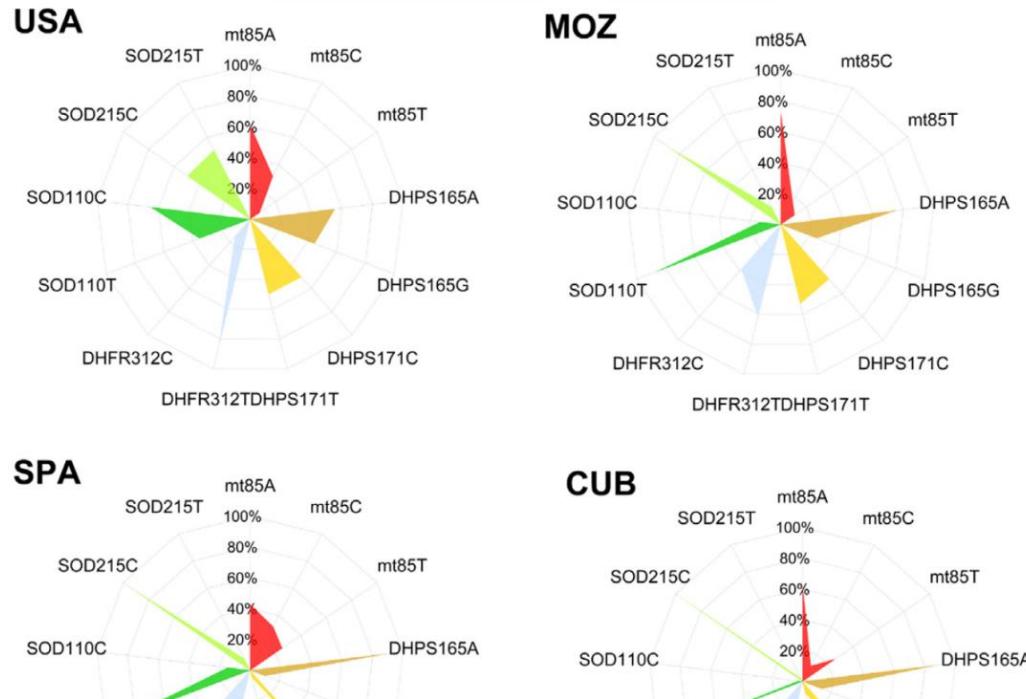
Kovacs et al. JAMA 2009; 301: 2578-2585
Miller et al. Clin Chest Med 2013; 34: 229-241



Multicentre study highlighting clinical relevance of new high-throughput methodologies in molecular epidemiology of *Pneumocystis jirovecii* pneumonia

F. Esteves¹, B. de Sousa², E. J. Calderón³, L. Huang⁴, R. Badura⁵, F. Maltez⁶, Q. Bassat^{7,8}, Y. de Armas⁹, F. Antunes¹⁰ and O. Matos¹¹

Clin Microbiol Infect 2016; 22: 566.e9–566.e19



« The haplotype DHFR312T/SOD110C/SOD215T was associated with severe AIDS-related PCP and high *P. jirovecii* burdens. Patients from the USA and Mozambique showed higher rates of DHPS mutants. »

Outbreak of *Pneumocystis jirovecii* Infection Among Heart Transplant Recipients: Molecular Investigation and Management of an Interhuman Transmission

William Vindrios,¹ Nicolas Argy,^{2,3,4} Solène Le Gal,^{5,6} François-Xavier Lescure,^{1,7} Laurent Massias,^{7,8} Minh Patrick Le,^{7,8} Michel Wolff,⁹ Yazdan Yazdanpanah,^{1,7} Gilles Nevez,^{5,6} Sandrine Houze,^{2,3,4} Richard Dorent,¹⁰ and Jean-Christophe Lucet^{7,11}

Clinical Infectious Diseases® 2017;65(7):1120–6

Table 2. *Pneumocystis jirovecii* Genotypes Obtained From Mitochondrial Large Subunit Ribosomal RNA, Superoxide Dismutase, and Cytochrome b and Sequences in 7 *P. jirovecii* Pneumonia Cases, 2 Colonized Patients, and 11 Unrelated Immunocompromised Control Patients

Patient	Sample	Date	Type of Immunosuppression	mtLSUrRNA	CYB ^a	SOD
Ctl1	IS	8 Jan 2015	Immunosuppressive treatment	1 + 2	CYB1	SOD1
Ctl2	BAL	22 Jan 2015	LTR	4	CYB2	SOD1
Ctl3	BAL	26 Jan 2015	HIV	3	CYB1	SOD1
Ctl4	BAL	5 Feb 2015	Immunosuppressive treatment	1	CYB1	SOD1
Ctl5	BAL	24 Feb 2015	Immunosuppressive treatment	1 + 2	CYB1 + CYB7	SOD1
Ctl6	IS	9 Mar 2015	HIV	1	CYB1	SOD2
Ctl7	BAL	21 Mar 2015	LTR	4	CYB2	SOD1
Ctl8	BAL	31 Mar 2015	Immunosuppressive treatment + neoplasia	1 + 4	mix	mix
Ctl9	BAL	13 Apr 2015	Neoplasia	2 + 3	CYB1 + CYB2	mix
Ctl10	IS	5 May 2015	Immunosuppressive treatment + neoplasia	3	CYB6	SOD1
Ctl11	BAL	7 May 2015	Immunosuppressive treatment	mix	mix	mix
Case 1	BAL	17 Mar 2015	HIV + RTR + HTR	4	CYB2	SOD1
Case 2	IS	12 May 2015	HTR	4	CYB2	SOD1
Case 3	BAL	15 July 2015	HTR	4	CYB2	SOD1
Case 4	BAL	28 July 2015	HTR	4	CYB2	SOD1
Case 5	BAL	06 Aug 2015	HTR	4	CYB2	SOD1
Case 6	BAL	24 Aug 2015	HTR	4	CYB2	SOD1
Case 7	BAL	2 Sept 2015	HTR	4	CYB2	SOD1
Col 8	NS	31 Aug 2015	HTR	4	CYB2	SOD1
Col 9	NS	2 Sept 2015	HTR	4	CYB2	SOD1
Col 10	NS	31 Aug 2015	HTR	NA ^b	NA ^b	NA ^b

« Genotyping and transmission chain confirmed inter-human transmission in all colonized/infected cases. Outpatient clinic layout and high encounters probably caused the outbreak. »





PCP/SIDA : incidence globale en diminution constante (ARV)
IO inaugurelle la plus fréquente (notamment en réanimation)



Environ 250 PCP inaugurales d'un SIDA en France en 2018



**Admission en réanimation nécessaire pour
~30% des patients VIH+ avec PCP**

Radhi et al. *BMC Infect Dis*. 2008; 8; 118

Roux et al. *Emerg Infect Dis* 2014; 20: 1490-7

Buchacz et al. *J Infect Dis* 2016; 214: 862-72



**Estimation pour l'année 2018 :
~80 admissions en réanimation pour PCP inaugurelle/SIDA**



Pneumonie à *P. jirovecii* (pneumocystose) associée au SIDA

Présentation « stéréotypée » au cours de l'infection par le VIH

Toux sèche, dyspnée crescendo, fièvre 39-40°C

Délai entre 1^{ers} symptômes et admission en MIR = 2-3 semaines

T CD4+ < 200/mm³ (le plus souvent < 50/mm³)

Elévation non-spécifique des LDH

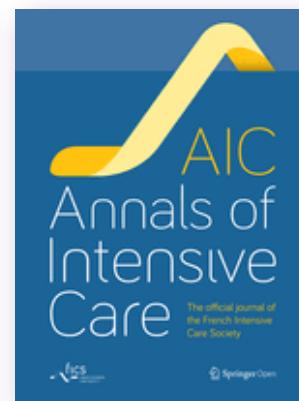
Hypoxémie profonde, relativement bien tolérée (installation subaiguë)

Tableau pulmonaire « pur »

**Une défaillance extra-respiratoire associée doit faire évoquer
un autre diagnostic ou une coinfection bactérienne**



Outcome and prognostic factors of *Pneumocystis jirovecii* pneumonia in immunocompromised adults: a prospective observational study

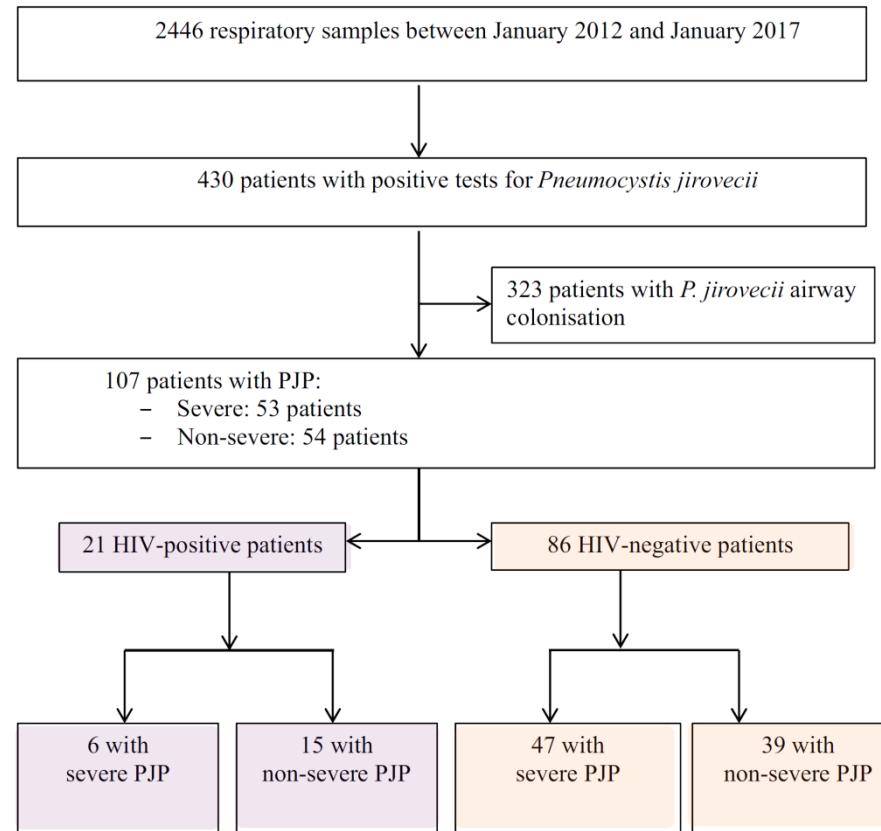


Gaborit et al. Ann. Intensive Care (2019) 9:131

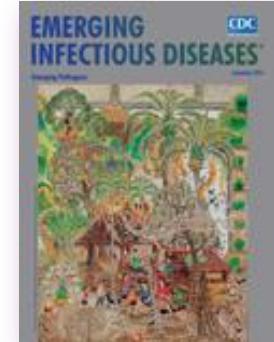
Cause of immunodeficiency, n (%)^a

Haematological malignancy	37 (34.6)
Solid organ transplant	27 (25.2)
HIV infection	21 (19.6)
HIV viral load, copies/mL, mean \pm SD	317,240 \pm 474,037
Systemic disease	13 (12.2)
Solid malignancy	12 (11.2)
Primary immunodeficiency	8 (7.5)
Ongoing immunosuppressive therapy, n (%)	83 (77.6)
Ongoing glucocorticoid therapy, n (%)	51 (47.7)
Prednisolone-equivalent dosage, mg/day, mean \pm SD	17 \pm 30
PJP prophylaxis, n (%) ^b	21 (19.6)

CHU Nantes, 2012-2017



***Pneumocystis jirovecii* Pneumonia in Patients with or without AIDS, France**



Antoine Roux, Emmanuel Canet, Sandrine Valade, Florence Gangneux-Robert, Samia Hamane, Ariane Lafabrie, Danièle Maubon, Anne Debourgogne, Solène Le Gal, Frédéric Dalle, Marion Leterrier, Dominique Toubas, Christelle Pomares, Anne Pauline Bellanger, Julie Bonhomme, Antoine Berry, Isabelle Durand-Joly, Denis Magne, Denis Pons, Christophe Hennequin, Eric Maury, Patricia Roux,¹ and Élie Azoulay

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 20, No. 9, September 2014

Table 2. Clinical management of 544 AIDS and non-AIDS patients after diagnosis with PCP, France, January 1, 2007–December 31, 2010*

Characteristic	AIDS patients, n = 223	Non-AIDS patients, n = 321	p value
Days from admission to treatment initiation, median (IQR)	1 (0–2)	2 (0–6)	<0.0001
Intensive care admission	65 (35)	134 (50)	0.0015
Immediate oxygen needed	87 (49)	160 (69)	<0.0001
Oxygen flow rate, L/min, mean (95% CI)	2 (1.3–2.8)	3.8 (2.8–4.8)	0.015
Mechanical ventilation			
Noninvasive needed	17 (8)	50 (16)	0.0053
Noninvasive failed	16 (8)	46 (15)	0.013
Invasive needed	25 (11.0)	98 (30.5)	<0.0001
Hospital deaths	8 (4)	75 (27)	<0.0001

*Values are no. (%) patients except as indicated. PCP, *Pneumocystis jirovecii* pneumonia; IQR, interquartile range.



PCP : aspects scannographiques

Lignes septales

Respect des régions sous-pleurales

Lésions kystiques

Verre dépoli diffus
ou focal/crazy paving

Pas de pleurésie, pas d'excavation, pas d'adénopathie



Research

Open Access

Critical care management and outcome of severe *Pneumocystis pneumonia* in patients with and without HIV infection

Xavier Monnet^{1,2}, Emmanuelle Vidal-Petiot^{1,2}, David Osman^{1,2}, Olfa Hamzaoui^{1,2},
Antoine Durrbach³, Cécile Goujard^{4,5}, Corinne Miceli^{5,6}, Patrice Bourée^{2,7} and Christian Richard^{1,2}

Critical Care 2008, 12:R28

Microbiological diagnosis

	HIV-negative cases n = 27	HIV-positive cases n = 46
Method of diagnosis, number (percentage of cases)		
BAL	23 (85)	42 (92)
Positive at staining	14	36
Positive at immunofluorescence	1 (4)	2 (4)
Induced sputum	1 (4)	2 (4)
Positive at staining	0	2
Positive at immunofluorescence	0	2
Tracheal aspiration	0	2 (4)
Positive at staining	0	2
Positive at immunofluorescence	0	2
Expectoration induced	0	2
Positive at staining	0	2
Positive at immunofluorescence	0	2
Density of <i>Pneumocystis jiroveci</i> on the BAL fluid ^a , percentage of all BAL	35%	81%
'Many'	65%	19%
'Few'		
Neutrophil count on the BAL, cells per microliter, median (range)	65,475 (6,000–733,500)	24,750 (320–480,000)

PCP au cours du SIDA

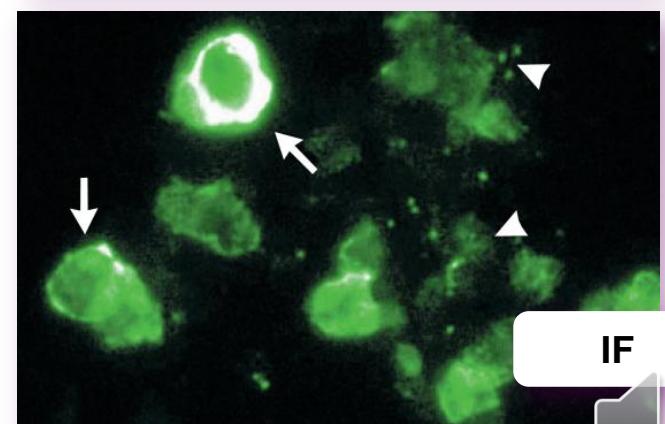
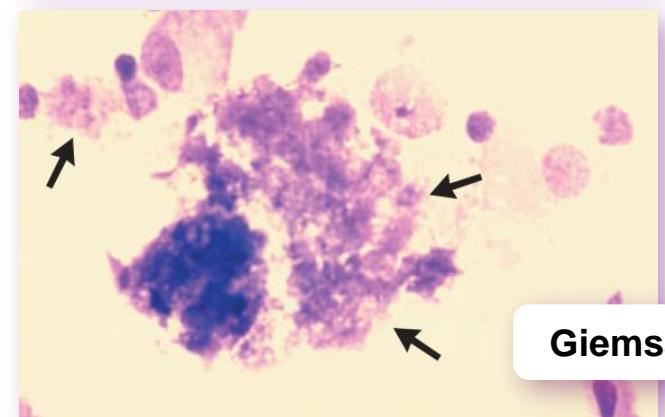
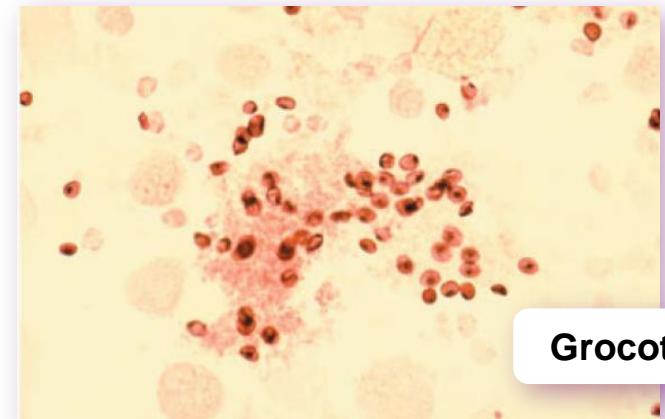
Examen direct (Giemsa, Grocott) et/ou
immunofluorescence

LBA : sensibilité > 95%¹

Expectoration induite : sensibilité 55-90%

Benito et al. Eur Respir J 2012; 39: 730-745

Azoulay et al. Chest 2020; 157:293-309



Intérêt de la PCR *Pneumocystis* pour le diagnostic de PCP au cours du SIDA?

- Colonisation respiratoire à *P. jirovecii* chez les patients VIH+ : 14 à 69%
- PCP/SIDA : colorations & IF très sensibles (inoculum >> autres formes d'ID)
- PCR qualitative sur LBA : Se >98% mais Sp médiocre (colonisation)
- PCR qualitative sur ENP ou bain de bouche : Se et Sp aléatoires
- Intérêt de la PCR quantitative pour différencier colonisation & PCP?
- Approche mixte : qPCR s/ LBA et dosage plasmatique du (1,3)β-D-glucane?
- **Seul intérêt démontré au cours du SIDA : VPN qPCR >95% sur LBA**

Louis et al. *J Clin Microbiol* 2015; 53 : 3870-3875

Fauchier et al. *J Clin Microbiol* 2016; 54 : 1487-1495

Guegan & Robert-Gangneux. *Curr Opin Infect Dis* 2019; 32 : 314-321



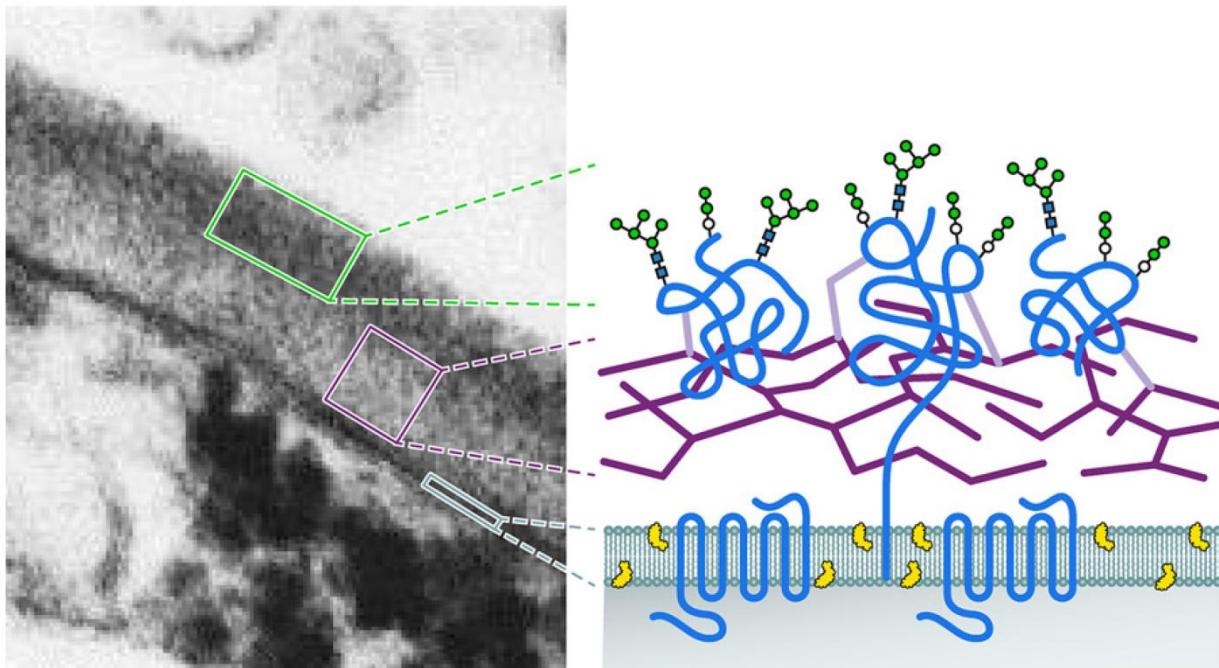
A Molecular Window into the Biology and Epidemiology of *Pneumocystis* spp.

Liang Ma,^a Ousmane H. Cissé,^a Joseph A. Kovacs^a

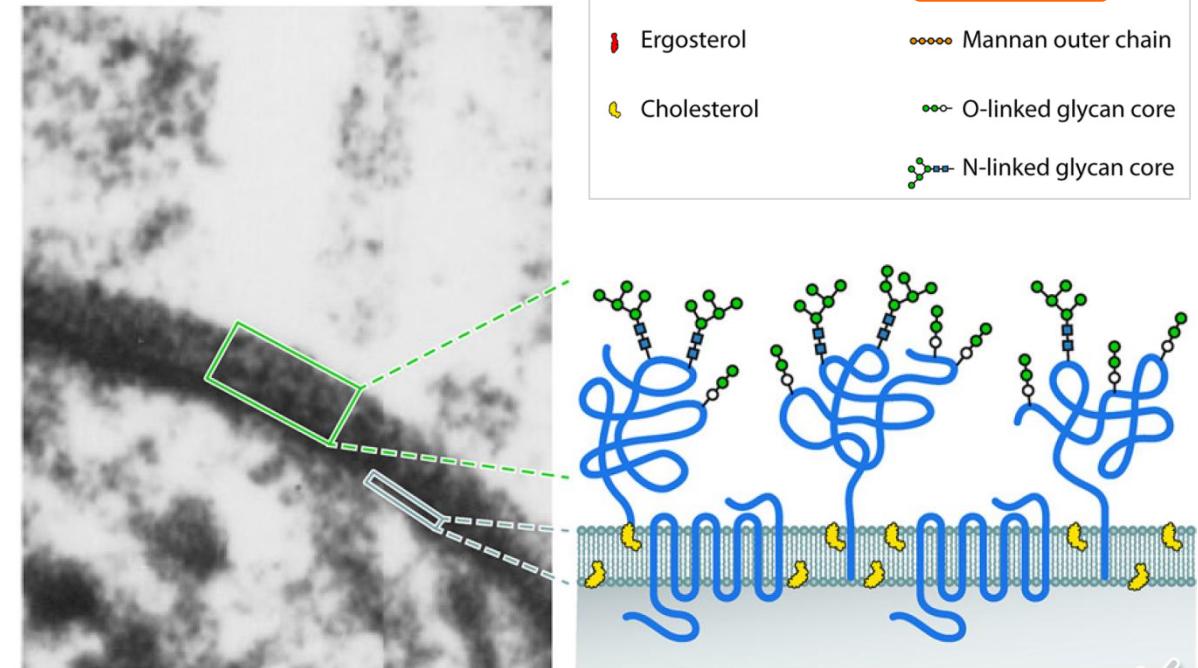
July 2018 Volume 31 Issue 3 e00009-18



B *Pneumocystis* cyst cell wall



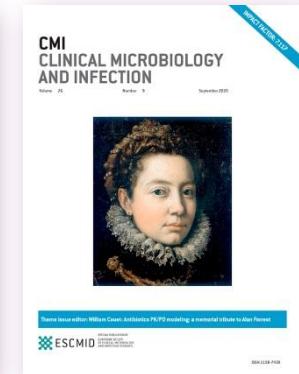
C *Pneumocystis* troph cell wall



Diagnostic accuracy of serum (1-3)- β -D-glucan for *Pneumocystis jirovecii* pneumonia: a systematic review and meta-analysis

Olivier Del Corpo,¹ Guillaume Butler-Laporte,² Donald C. Sheppard,^{2,3,4} Matthew P. Cheng,^{2,3} Emily G. McDonald,^{3,5,6} and Todd C. Lee,^{2,3,5,6}

Clinical Microbiology and Infection, September 2020, 26: 1137-1143

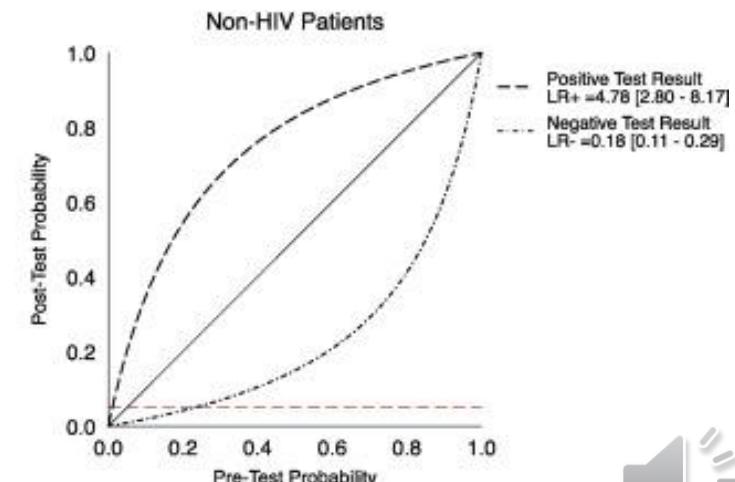
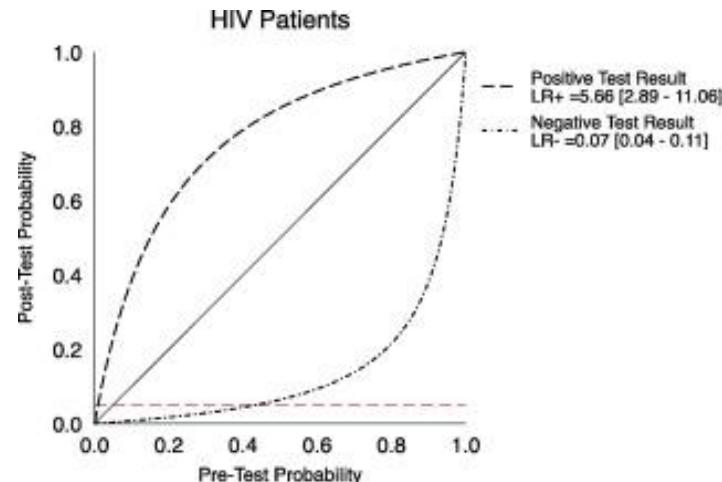


Cut-off value: 80 pg/ml

Pooled sensitivity: HIV 94% (95% CI, 91–96%) / non-HIV 86% (95% CI, 78–91%)

Pooled specificity: HIV 83% (95% CI, 69–92%) / non-HIV 83% (95% CI, 72–90%)

Negative BDG: associated with a low post-test probability of PJP ($\leq 5\%$) only for low-to-intermediate pre-test probability ($\leq 20\%$ in non-HIV and $\leq 50\%$ in HIV)



Traitements curatifs de la PCP au cours du SIDA

Guidelines HIVMA/IDSA 2018



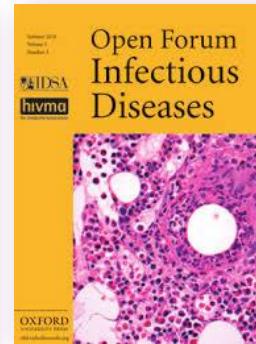
Première ligne dans les PCP sévères : Triméthoprime - Sulfaméthoxazole

- Y compris pour les PCP développées sous prophylaxie primaire par TMP-SMX
Mutation DHPS ? ⇒ Pas d'impact démontré à doses curatives
- **Posologie** : TMP 15-20 mg/kg/24h + SMX 75-100 mg/kg/24h
soit ~4 ampoules (TMP 80 mg / SMX 400 mg) x 3/24h IVL (poids 50-90 kg, fonction rénale normale)
- **Durée du traitement d'attaque** : 21 jours [relais *per os* possible : 2 cp (160 mg / 800 mg) x 3/24h]
Prophylaxie secondaire jusqu'à T CD4+ > 200/mm³ sous ARV
- **"Adding folinic acid to prevent myelosuppression during acute treatment is not recommended because efficacy is questionable and some evidence exists for a higher failure rate (AII)."**
- **Effets indésirables** : toxidermie 30-50%, fièvre 30-40%, leucopénie 30-40%, thrombopénie 15%, anémie hémolytique (déficit G6PD/pyruvate kinase), hépatite 20%, hyperkaliémie 10-20%



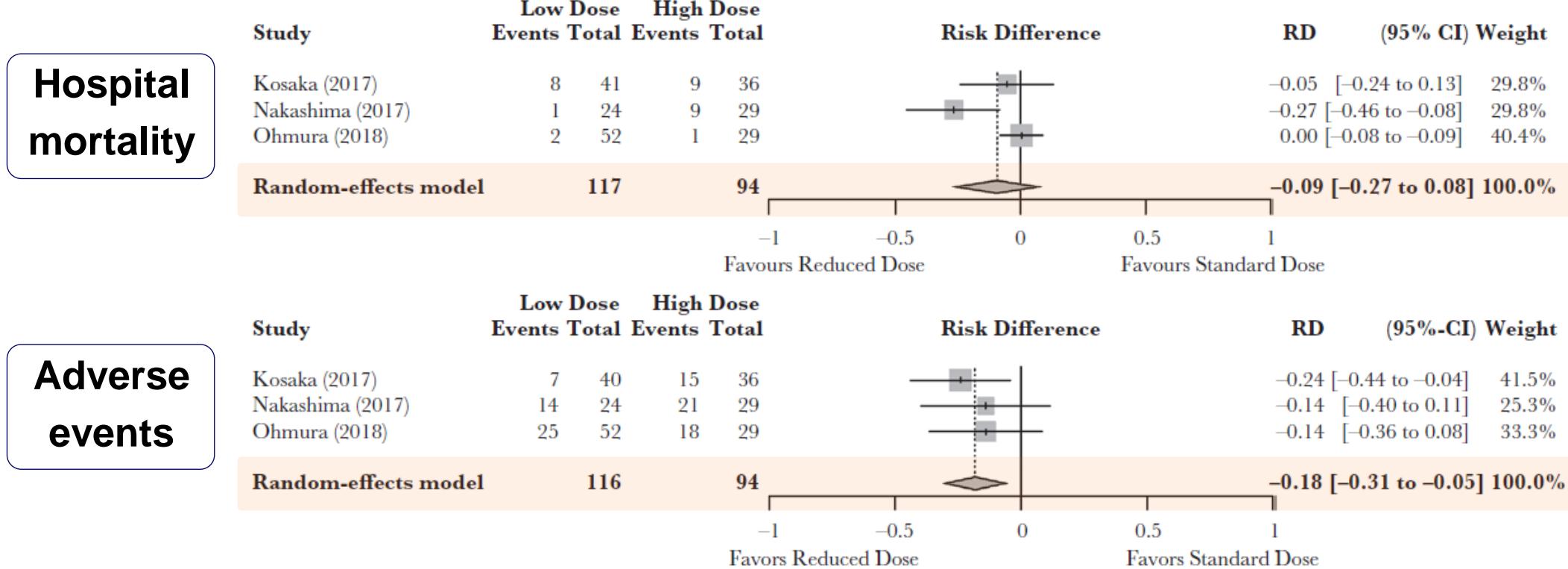
Low-Dose TMP-SMX in the Treatment of *Pneumocystis jirovecii* Pneumonia: A Systematic Review and Meta-analysis

Guillaume Butler-Laporte,^{1,◎} Elizabeth Smyth,² Alexandre Amar-Zifkin,³ Matthew P. Cheng,^{4,◎} Emily G. McDonald,^{1,2,5,6,7} and Todd C. Lee^{1,2,5,6,7,◎}



Open Forum Infect Dis 2020 (on-line first)

Standard dose (TMP 15-20 mg/kg/24h) versus lower doses (TMP ≤ 15 mg/kg/24h)



Traitemen^t curatif de la PCP au cours du SIDA

Guidelines HIVMA/IDSA 2018



Alternatives si intolérance ou allergie au SXT ?

- **Pentamidine : 4 mg/kg/24h en 1 injection (IVL > 1 heure)**
Versus SXT : efficacité comparable, toxicité plus fréquente
Principaux EI : tubulopathie, hypoglycémie, pancréatite aiguë, cytopénies, allongement du QT
- **Primaquine (+ clindamycine) : non disponible en France**
- **Echinocandines : non positionnées (cas décrits de PCP « émergeant » sous candines)**



FIGURE 1 | Mechanisms of action of traditional antifungal agents on cellular targets

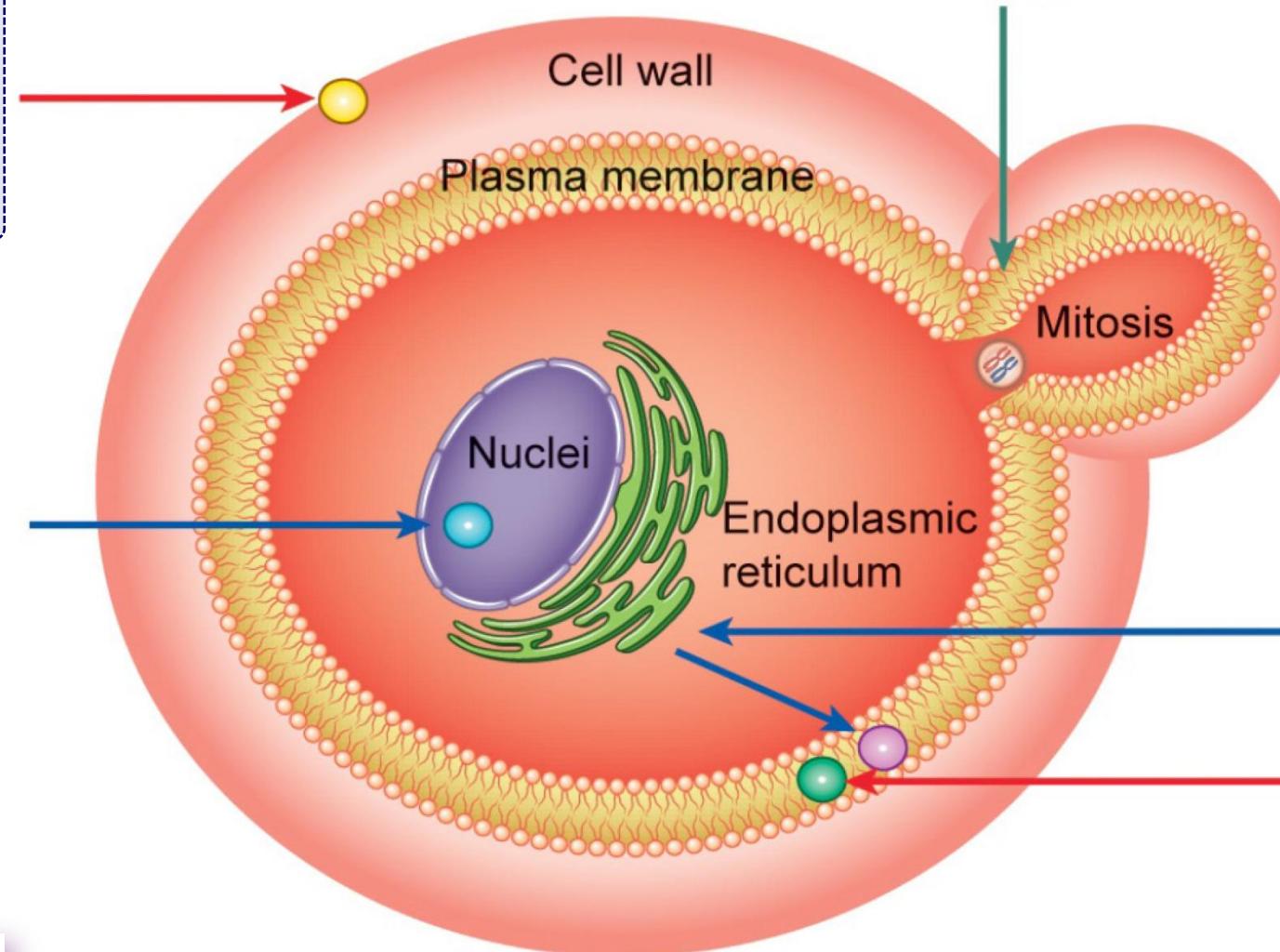
Echinocandins -
Inhibition of glucan
biosynthesis
pathway

Flucytosine -
Inhibition of
nucleic acid
synthesis

Griseofulvine - Inhibition of
microtubule synthesis

Azoles, Allylamines,
Thiocarbamates -
Inhibition of ergosterol
biosynthesis pathway

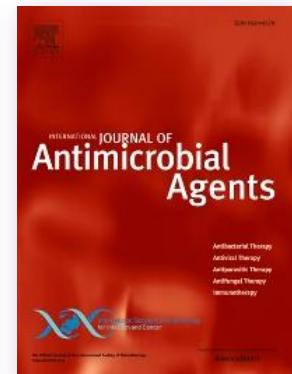
Polyenes - Binding to
ergosterol and disruption
of membrane integrity



Anidulafungin as an alternative treatment for *Pneumocystis jirovecii* pneumonia in patients who cannot tolerate trimethoprim/sulfamethoxazole

Po-Yi Chen^a, Chong-Jen Yu^a, Jung-Yien Chien^{a,*}, Po-Ren Hsueh^{a,b,*}

International Journal of Antimicrobial Agents 55 (2020) 105820



Factors associated with 60-day mortality in the univariate and multivariate analyses

Variable	Univariate analysis			Multivariate analysis		
	HR	95% CI	P-value	HR	95% CI	P-value
Alternative therapy with anidulafungin	1.171	0.641–2.136	0.608	1.202	0.645–2.240	0.563
Age ≥60 years	3.603	2.092–6.205	<0.001	1.840	1.039–3.259	0.036
SpO ₂ /FiO ₂ ratio in first 24 h	0.992	0.989–0.995	<0.001	0.994	0.990–0.998	0.005
Mechanical ventilation in first 24 h	4.172	2.448–7.109	<0.001	2.990	0.667–13.408	0.153
Vasopressor use in first 24 h	4.510	2.547–7.984	<0.001	1.877	0.971–3.628	0.061
ICU admission in first 24 h	3.543	2.058–6.100	<0.001	0.634	0.140–2.876	0.555
HIV infection	0.051	0.007–0.368	0.003	0.102	0.013–0.771	0.027
Solid organ tumour	2.627	1.490–4.632	0.001	1.317	0.720–2.410	0.372
Serum albumin (g/dL)	0.463	0.287–0.748	0.002	1.044	0.650–1.679	0.858
Blood urea nitrogen (mg/dL)	1.005	0.997–1.014	0.220	—	—	—

HR, hazard ratio; CI, confidence interval; SpO₂, oxygen saturation by pulse oximetry; FiO₂, fraction of oxygen in the inspired gas; ICU, intensive care unit; HIV, human immunodeficiency virus.



Scientific rationale for inhaled caspofungin to treat *Pneumocystis pneumonia*: A therapeutic innovation likely relevant to investigate in a near future . . .



International Journal of Infectious Diseases 95 (2020) 464–467

Ehrmann S. et al

References	Models	Intervention	Observed effects and major findings
Huang et al. (2018)	2 patients with auto-immune diseases (retrospective trial)	Daily IV caspofungin in combination with co-trimoxazole	Resulted in 100% overall survival

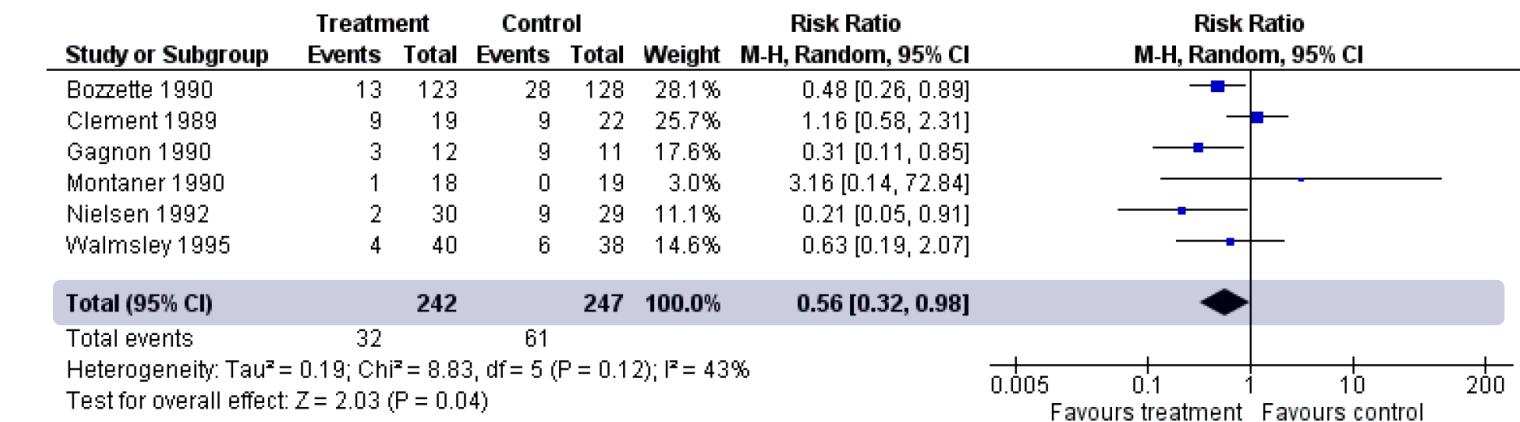
Caspofungine
PM élevé, forte liaison protidique
Faible diffusion pulmonaire par voie IV (<5% cc° plasmatiques)
Intérêt de la voie inhalée??

NCT03978559 (actual study start date: August 14, 2019)	61 HIV-negative patients (prospective trial)	Daily IV caspofungin in combination with co-trimoxazole for 21 days	Ongoing
--	--	---	---------

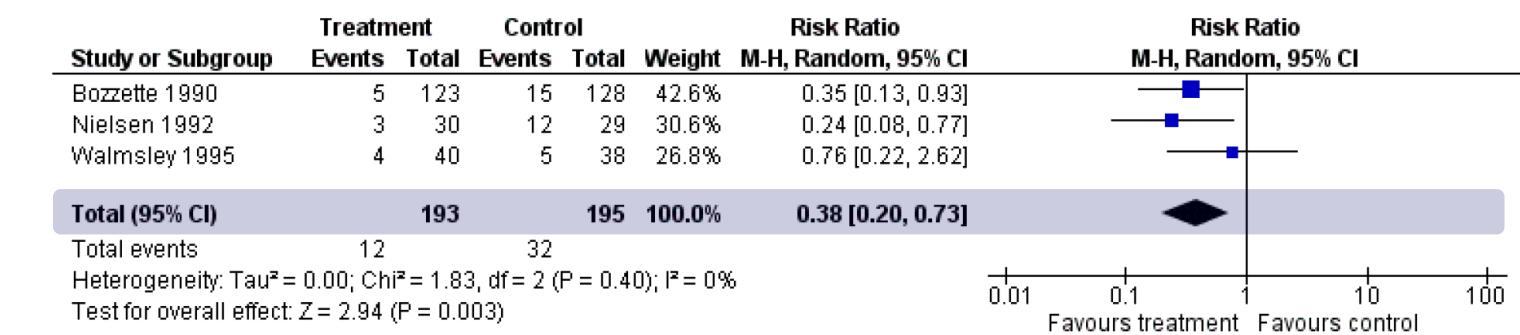


Adjunctive corticosteroids for *Pneumocystis jiroveci* pneumonia in patients with HIV infection (Review)

**Figure 3. Forest plot of comparison: I Adjunctive corticosteroids versus no such treatment, outcome: I.1
Death at 1 month; adults.**



**Figure 6. Forest plot of comparison: I Adjunctive corticosteroids versus no such treatment, outcome: I.4
Need for mechanical ventilation at 1 month; adults.**



Adjunctive corticosteroids for *Pneumocystis jiroveci* pneumonia in patients with HIV infection (Review)

Figure 3. Forest plot of comparison: I Adjunctive corticosteroids versus no such treatment, outcome: I.1
Death at 1 month; adults.

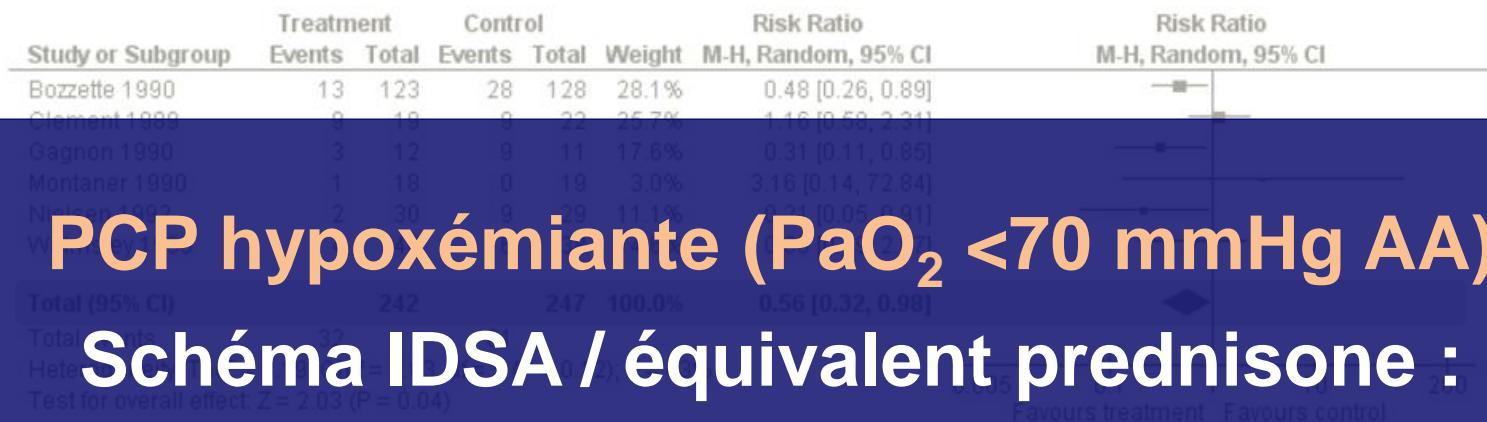
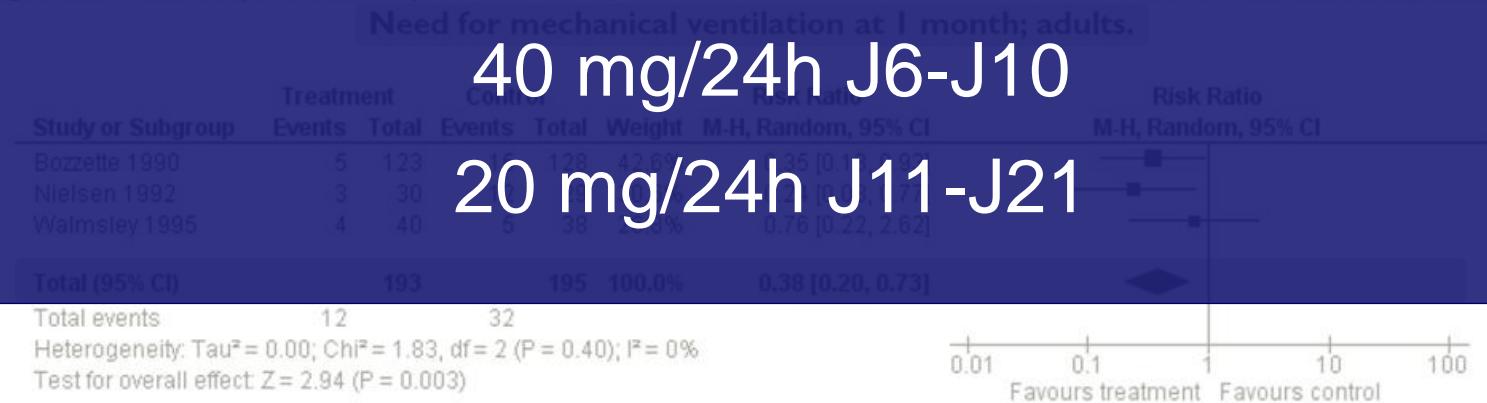


Figure 6. Forest plot of comparison: I Adjunctive corticosteroids versus no such treatment, outcome: I.4



AIDS-related PCP : points-clé

1. Continuer à y penser (formes inaugurales / test rapide VIH)
2. Diagnostic : Giemsa et IF sur LBA (ou expectoration induite)
3. PCR *Pneumocystis* : pas de place pour le diagnostic positif de PCP au cours du SIDA (intérêt = VPN>95-98% sur LBA)
4. Co-infections 15-30% (pyogènes > CMV et autres IO)
5. Formes graves : débuter le traitement (SXT/corticoïdes) sans attendre la confirmation diagnostique si forte suspicion clinique
6. Bilan bactériologique usuel et antibiothérapie empirique type PAC sévère

Cytomegalovirus infection in HIV-infected patients in the era of combination antiretroviral therapy

Perello et al. BMC Infectious Diseases

(2019) 19:1030

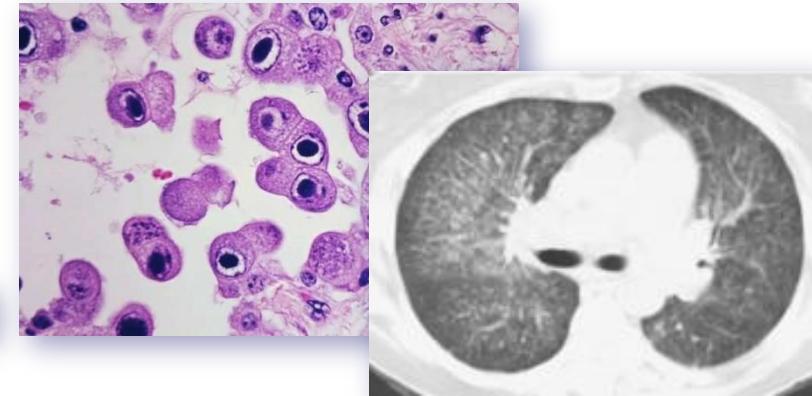


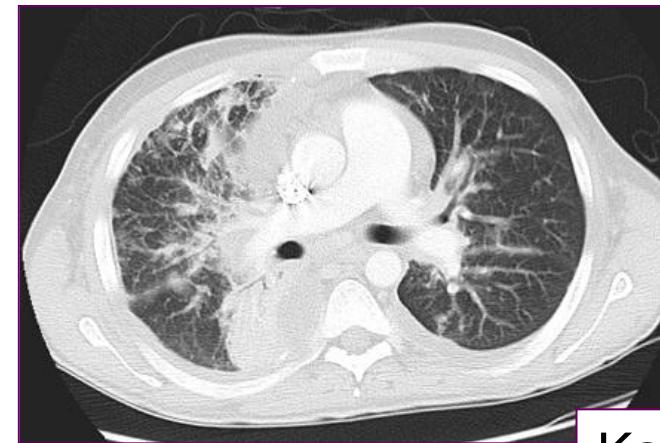
Table 1 Characteristics of the patients according system involvement of the whole cohort $n = 56$

Variable	Overall $n = 56$	Respiratory involvement $n = 17$	Systemic involvement $n = 24$	Digestive involvement $n = 8$	Neurological $N = 4$
Pneumonie sévère à CMV au cours du SIDA					
Age in years, Median (IQR)	39 (31–47)	39 (31–47)	38 (31–50)	35 (28–42)	36 (34–51)
Sex, male n, (%)	44 (79)	13 (78)	21 (87)	7 (88)	1 (25)
Fever n, (%)	33 (59)	12 (71)	18 (75)	1 (13)	2 (50)
ICU admission n, (%)	19 (34)	8 (47)	7 (30)	1 (13)	2 (50)
Mechanical Ventilation, yes n, (%)	12 (21)	6 (35%)	3 (13)	1 (13)	1 (25)
Mortality n, (%)	10 (18%)	3 (18%)	4 (17)	1 (13)	1 (25)
Une PCR CMV fortement positive sur le LBA ne suffit pas au diagnostic					
Critères diagnostiques (HIVMA/www.idsociety.org) : (i) infiltrats pulmonaires (ii) effet cytopathogène sur le LBA (iii) absence de diagnostic alternatif (?)					
HIV viral load cop/ml $\times 10^5$ Median, (IQR)*	514 (272–888)	356 (180–860)	514 (289–653)	727 (494–941)	319 (123–649)
Traitemennt (3-4 semaines) : Ganciclovir (5 mg/kg/12h, IV), foscarvir en 2ème ligne					
CMV*** blood VL Median (IQR)*copies/ml $\times 10^3$	3.7 (1.09–24.9)	3.9 (1.2–43.6)	1.2 (0.7–15)	1.2 (0.56–31.1)	0.4 (0.1–122)



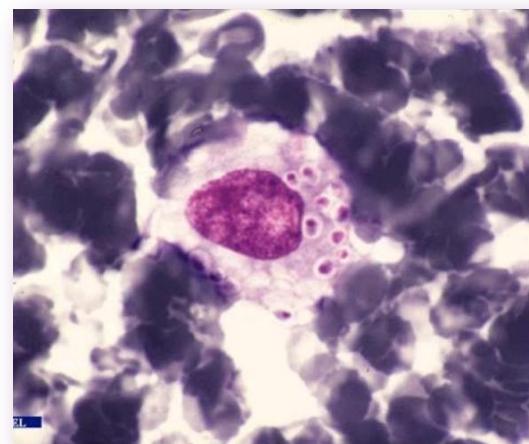
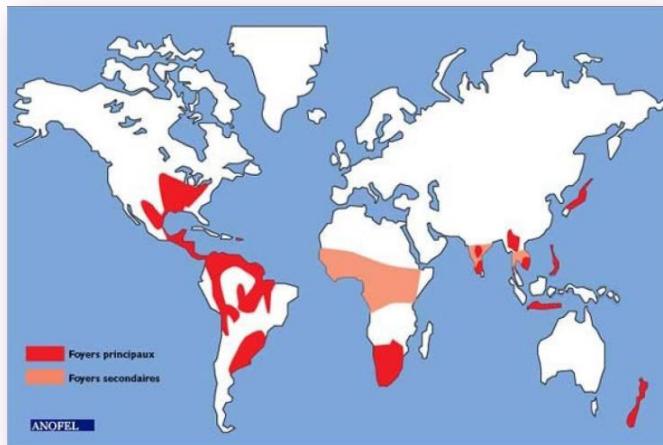
Infections à HHV8 au cours du SIDA

- **Angiosarcome de Kaposi** (lésions pulmonaires et/ou pleurales, hémoptysie) – CD4 <<200/mm³
- **Maladie de Castelman** (œdème pulmonaire lésionnel sur SALH)
- **Lymphomes des séreuses** – PEL (localisations pleurales / péricardiques)



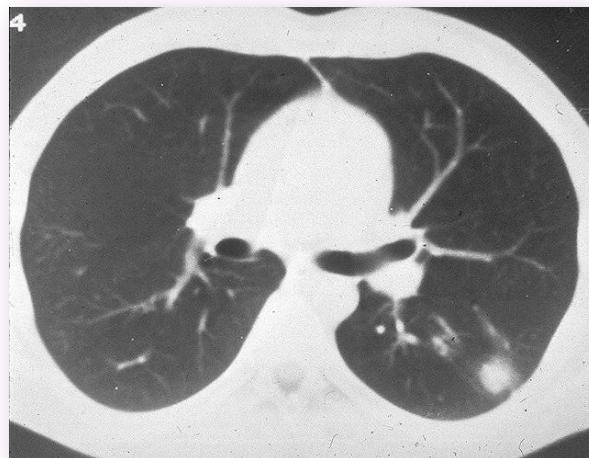
Histoplasmose au cours du SIDA

- Mycose opportuniste d'importation / Levure : *Histoplasma capsulatum*
- Transmission : inhalation de spores (déjections de chauve-souris)
- Formes disséminées au cours du SIDA ($CD4 < 150/\text{mm}^3$) « tuberculosis-like » (AEG fébrile, HSMG, polyADP, poumon, tube digestif, peau, SNC, SAM)
- Diagnostic : ex. direct, culture (LBA, sang, moelle, biopsies), galactomannane, antigène soluble
- Guidelines IDSA : Amphotéricine B liposomale 3 mg/kg/24h pendant ≥ 2 semaines puis Itraconazole 200 mg x 2/24h pendant ≥ 12 mois

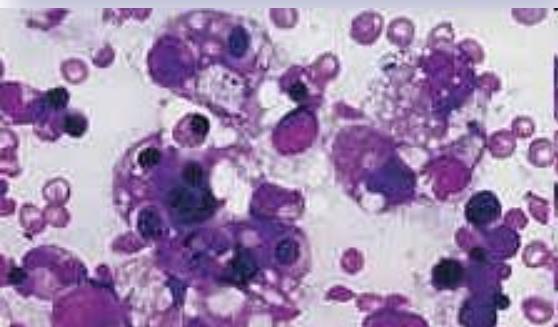
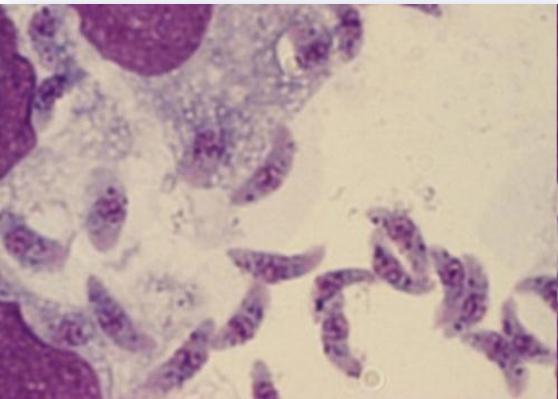


Histoplasmose au cours du SIDA

- Mycose opportuniste d'importation / Levure : *Histoplasma capsulatum*
- Transmission : inhalation de spores (déjections de chauve-souris)
- Formes disséminées au cours du SIDA ($CD4 < 150/\text{mm}^3$) « tuberculosis-like » (AEG fébrile, HSMG, polyADP, poumon, tube digestif, peau, SNC, SAM)
- Diagnostic : ex. direct, culture (LBA, sang, moelle, biopsies), galactomannane, antigène soluble
- Guidelines IDSA : Amphotéricine B liposomale 3 mg/kg/24h pendant ≥ 2 semaines puis Itraconazole 200 mg x 2/24h pendant ≥ 12 mois



Toxoplasmose disséminée au cours du SIDA



- Choc septique +/- cardiogénique (myocardite), SAM, SDRA, SDMV¹
- Mortalité > 50%¹
- Diagnostic : PCR *Toxoplasma gondii* (sang, LBA, LCR)
- 1^{ère} intention (SNG) : pyriméthamine + sulfadiazine
- Alternative (IV) : cotrimoxazole + clindamycine

¹ Schmidt et al. *Clin Infect Dis* 2013; 57: 1535-1541



TABLE 2

Common radiographical appearances of pulmonary infections in HIV patients

Chest radiograph or CT abnormality

Acute or subacute onset

Chronic onset

Autres IO pulmonaires associées au SIDA (<<5% des IRA)

Focal consolidation

Any organism, but especially pyogenic bacteria

Mycobacteriosis

Nocardiosis

Mycobacterium avium-intracellulare complex

Diffuse interstitial infiltrate

Legionellosis

Fungi (aspergillosis, endemic fungal infections, cryptococcosis)

Mycobacteriosis

Autres mycobactéries atypiques

Pneumocystis jirovecii
Haemophilus influenzae
 (influenza, CMV)

Fungal pneumonia, especially cryptococcal

Toxoplasmosis

CMV

Nocardiosis

Fungi

Cryptococcus neoformans

Nodules

Tuberculosis

Aspergillus sp

Fungi (cryptococcosis, aspergillosis)

Bacteria

Rhodococcus equi

Tuberculosis

Mycobacteriosis

Endemic fungal infections

Nocardia asteroides

Tuberculosis

Mycobacteriosis

Nocardiosis

Fungi

Mucormyces

Staphylococcus aureus (IDU)

Mycobacteriosis

Coccidioidomycose...

Fungi

Nocardiosis

Fungi

Pleural effusion

Anaerobes

Rhodococcus equi

Pseudomonas aeruginosa

Legionellosis

Le plus souvent à un stade très avancé d'ID (T CD4+ << 50/mm³)

Pyogenic bacteria

Fungi

Tuberculosis

Pneumocystis jirovecii

Pneumothorax



Updates annuels disponibles sur www.idsociety.org

Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents



Recommendations from the Centers for Disease Control,
the National Institutes of Health, and the HIV Medicine Association
of the Infectious Diseases Society of America



Immune reconstitution inflammatory syndrome in patients starting antiretroviral therapy for HIV infection: a systematic review and meta-analysis

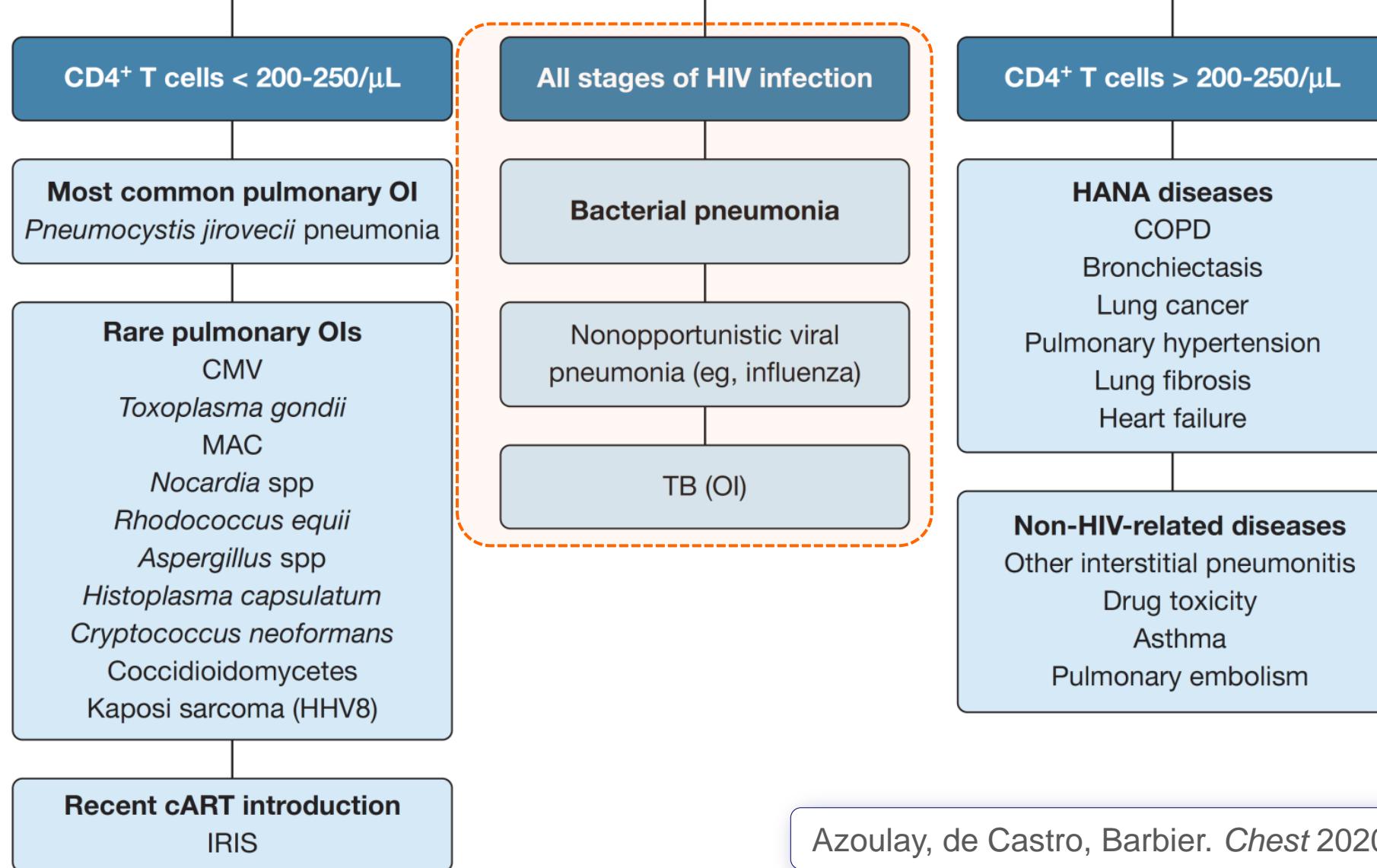
Lancet Infect Dis 2010;
10: 251-61

Monika Müller, Simon Wandel, Robert Colebunders, Suzanna Attia, Hansjakob Furrer, Matthias Egger, for leDEA Southern and Central Africa



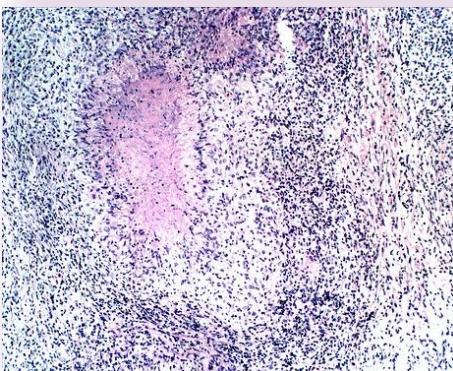
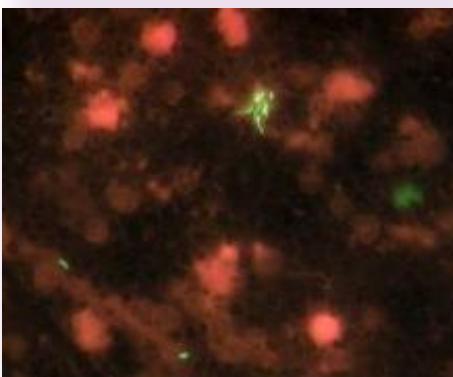
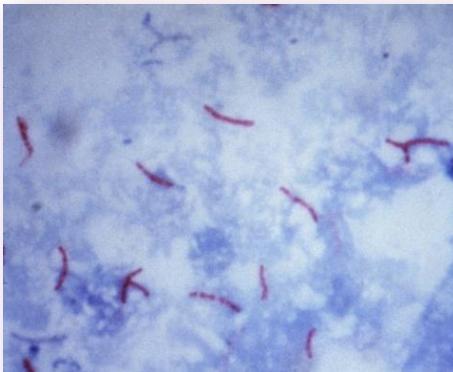
Figure 3: Incidence of immune reconstitution inflammatory syndrome (IRIS) according to CD4 cell count at the start of antiretroviral therapy
Data are provided for 22 studies. Circle size is proportional to weighting in the random-effect model.

Acute respiratory failure in HIV-infected patients

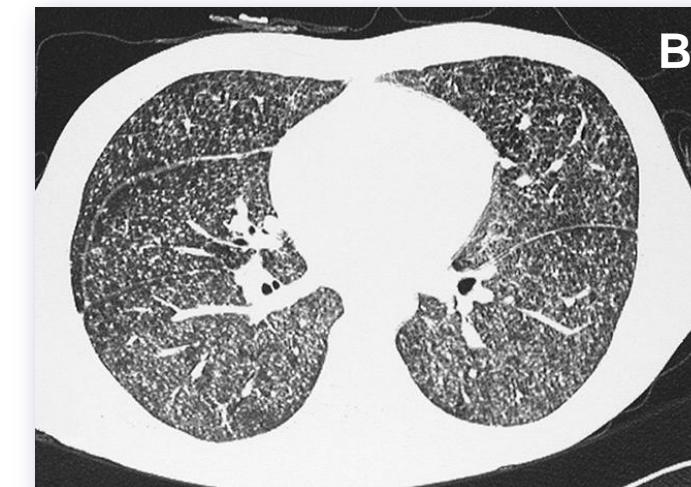
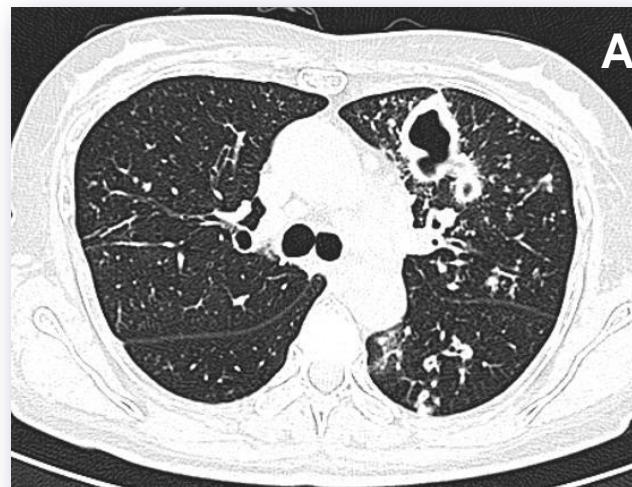


Azoulay, de Castro, Barbier. *Chest* 2020; 157: 293-309

Tuberculose au cours de l'infection par le VIH



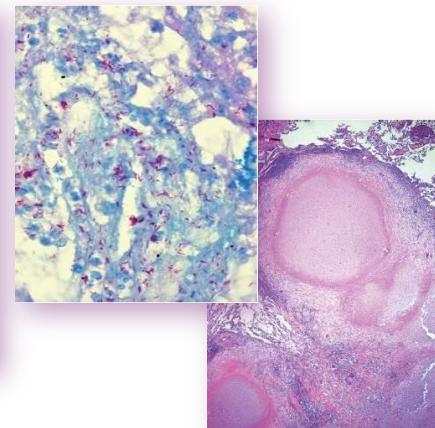
- Risque majeur de TBC à tous les stades de l'infection par le VIH
- **5 à 10% des IRA chez les patients VIH+**
- Pathologie inaugurale fréquente, notamment chez les migrants originaires de zones à prévalence élevée (Afrique, Asie du Sud-Est)
- **Tuberculose classique si T CD4+ > 300-350/mm³ (A)**
Atteintes pulmonaires focales (nodules, condensations, excavation – apex)
- **Formes disséminées (hématogènes) fréquentes si T CD4+ << 200/mm³ (B)**
Pneumonie diffuse, miliaire, localisations extra-pulmonaires



Tuberculosis in the intensive care unit: a descriptive analysis in a low-burden country

J-P. Lanoix,* S. Gaudry,† R. Flicoteaux,‡ R. Ruimy,§ M. Wolff†

INT J TUBERC LUNG DIS 18(5):581-587



Tuberculose grave (ICU) chez les patients VIH+

Atteinte pulmonaire quasi-constante (95%)

Formes disséminées plus fréquentes (vs VIH-)

Table 4 Clinical and radiological involvement of TB in the ICU

	HIV-positive (n = 40) n (%)	HIV-negative (n = 57) n (%)	Total n (%)
Organs involved			
Pleuro-pulmonary TB	38 (95)	51 (89.5)	89 (91.8)
Neurological TB*	9 (22.5)	12 (21)	21 (21.6)
Haematological TB*	6 (15)	2 (3.5)	8 (8.2)
Disseminated TB*	9 (22.5)	7 (12.3)	16 (16.5)
Clinical and radiological forms			
Pleurisy	9 (22.5)	13 (22.8)	22 (22.6)
Cavity	6 (15)	15 (26.3)	21 (21.6)
Lobar pneumonia	2 (5)	13 (22.8)	15 (15.5)
Meningitis	7 (17.5)	12 (21)	19 (19.5)
Tuberculoma	1 (2.5)	1 (1.7)	2 (2.06)
Radiological miliary	3 (7.5)	10 (17.5)	13 (13.4)
Haemoptysis	2 (5)	8 (14)	10 (10.3)



Tuberculosis in the intensive care unit: a descriptive analysis in a low-burden country

J-P. Lanoix,* S. Gaudry,† R. Flicoteaux,‡ R. Ruimy,§ M. Wolff†

INT J TUBERC LUNG DIS 18(5):581–587

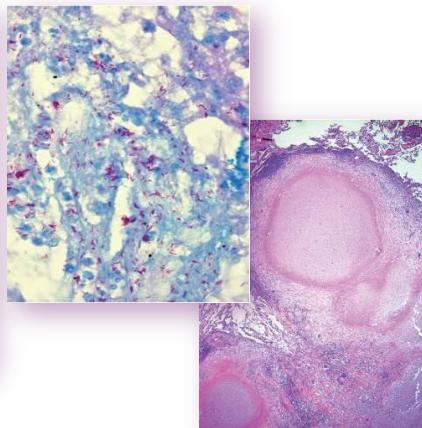


Table 5 ICU features of TB patients

	HIV-positive (n = 40, 41.2%) n (%)	HIV-negative (n = 57, 58.8%) n (%)	Total (n = 97) n (%)
Mechanical ventilation	18 (45)	27 (47.4)	45 (46.4)
ARDS	5 (12.5)	8 (14)	13 (29.5)
Ventilation duration, days, median (range)	5.5 (1–97)	9 (1–129)	8 (1–129)
Vasopressor medication	13 (32.5)	23 (40.4)	36 (37.1)
Dialysis	4 (10)	5 (8.8)	9 (9.3)
SAPS II, median (range)	46 (23–121)	33 (6–105)	38 (6–121)
SOFA score, median (range)	4 (0–17)	3 (0–14)	4 (0–17)
Associated non-tuberculous infection			
One infection	13 (32.5)	16 (28.1)	29 (29.9)
Two infections	4 (10)	1 (1.7)	5 (5.2)
Death in ICU	9 (22.5)	12 (21)	21 (21.6)
In-hospital death	13 (32.5)	19 (33.3)	32 (33.3)



Tuberculose pulmonaire chez le patient VIH+

Modalités diagnostiques

- **LBA, aspiration trachéale, tubage gastrique, expectorations** : Auramine-Ziehl / culture MGIT / PCR *M. tuberculosis*
- **Histologie (plèvre, ganglion)** : Ziehl, MGIT, granulome, PCR *M. tuberculosis*
- Hémoculture isolator
- Dosage de l'adénosine désaminase (ADA) si épanchement pleural ?
- **Interferon-gamma release assays (IGRA)** : pas de place pour le diagnostic positif (négativité : jusqu'à 30% des patients VIH+ avec tuberculose confirmée)

Boehme et al. *N Engl J Med* 2010; 363: 1005-1015

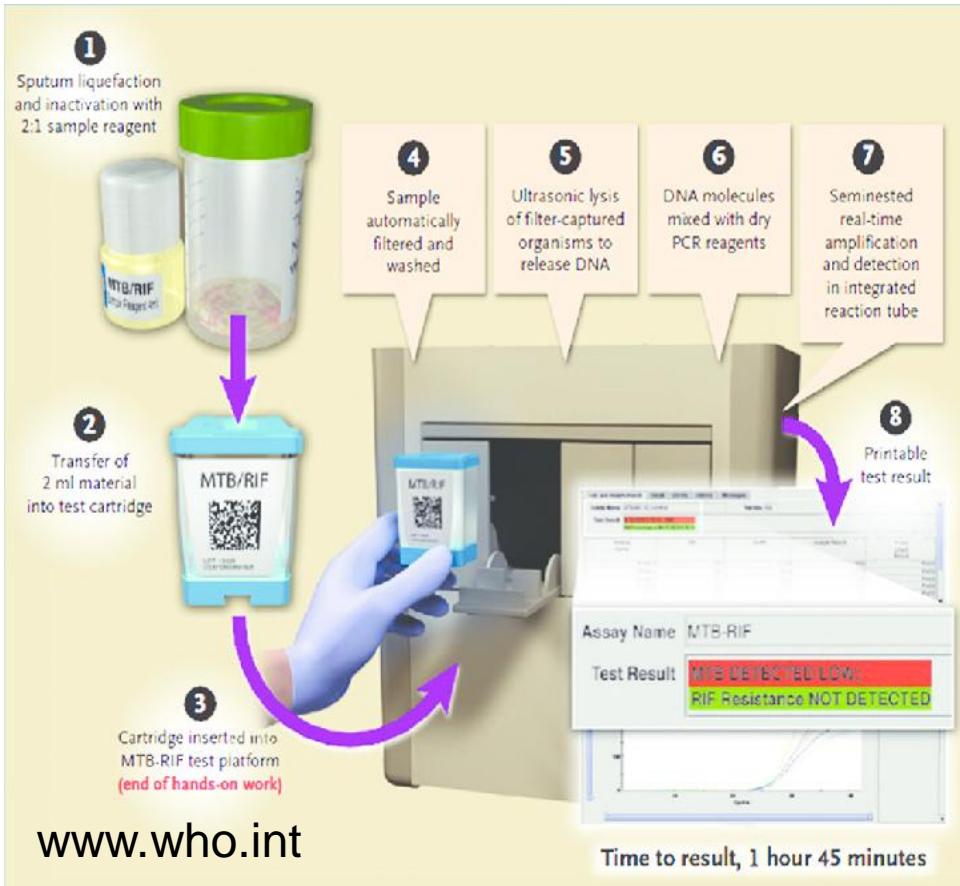
Dorman et al. *Lancet Infect Dis* 2018; 18: 76-84

www.hivma.org



Tuberculose pulmonaire chez le patient VIH+

Modalités diagnostiques



PCR *M. tuberculosis*

(NAAT : *nucleic acid amplification test*)

Sur prélèvements respiratoires : positive dans 50% à 80% des TB pulmonaires avec culture positive / Ziehl négatif

Guidelines WHO : systématique sur ≥ 1 plvt respiratoire chez tout patient VIH+ suspect de TB pulmonaire

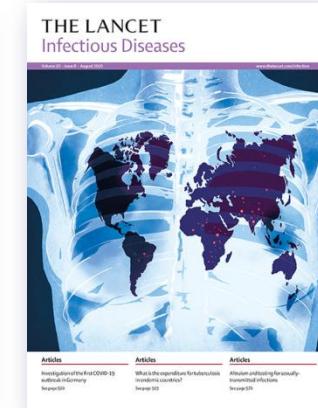
Si BAAR+ : distinction *M. tuberculosis* vs autres mycobactéries (ex. *M. avium-intracellulare*)

Détection précoce des résistances (rifampicine +/- INH)

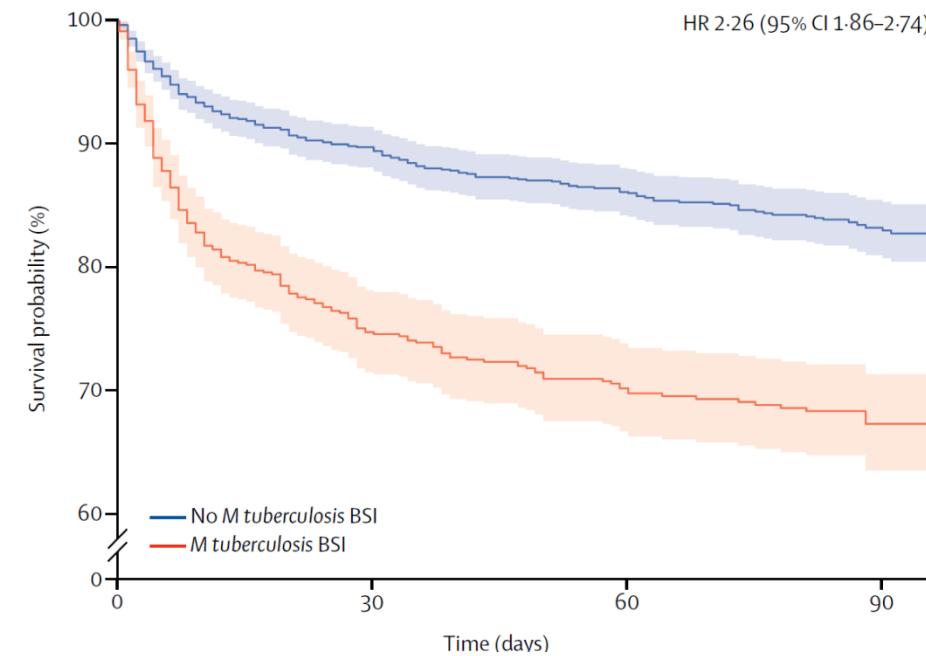
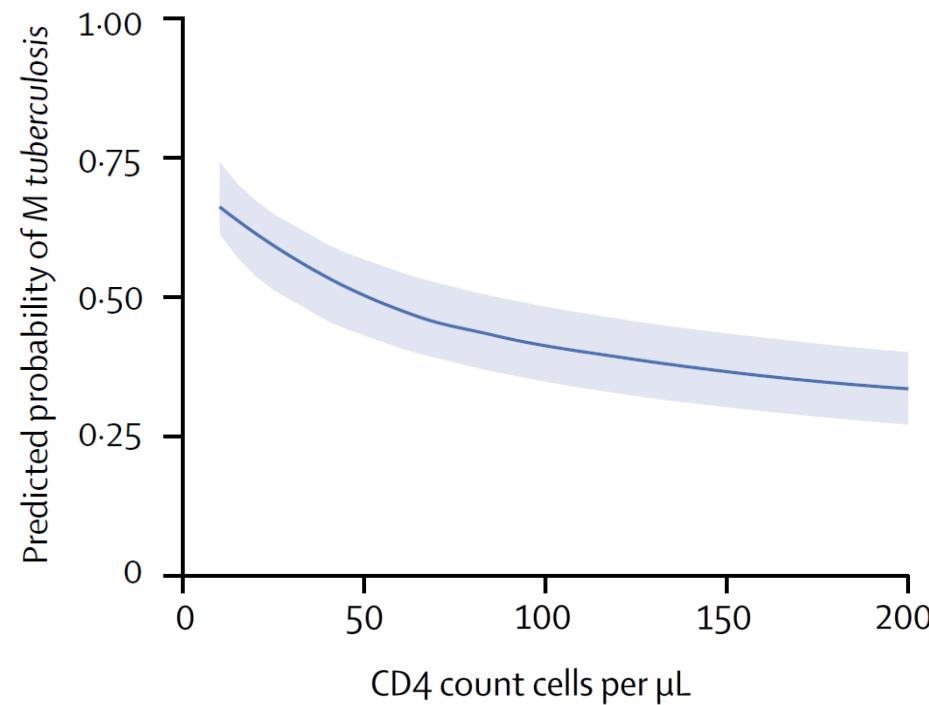


Mycobacterium tuberculosis bloodstream infection prevalence, diagnosis, and mortality risk in seriously ill adults with HIV: a systematic review and meta-analysis of individual patient data

Lancet Infect Dis 2020;
20: 742–52



5751 patients (med. CD4 cells, 76/ μ L) - Pooled prevalence of BSI: 45% (95% CI 38-52)



Jean-Ralph Zahar
Elie Azoulay
Elise Klement
Arnaud De Lassence
Jean-Christophe Lucet
Bernard Regnier
Benoît Schlemmer
Jean-Pierre Bedos

Delayed treatment contributes to mortality in ICU patients with severe active pulmonary tuberculosis and acute respiratory failure

99 patients
HIV 38%
TB pulm. 59%

Table 5 Multivariate analysis: independent predictors of 30-day mortality

	Odds-ratio	95 % CI	p value
Number of organ failures	3.11	(1.45–6.65)	0.003
Number of lobes involved on chest radiograph	1.83	(1.12–2.98)	0.01
Serum albumin < 20 g/l	3.73	(1.09–15.31)	0.04
Time from symptoms to treatment > 1 month	3.73	(1.06–13)	0.02



Tuberculose pulmonaire chez le patient VIH+

Traitement

Guidelines HIVMA/IDSA

Quadrithérapie conventionnelle d'attaque dans la plupart des situations :

Isoniazide 5 mg/kg/24h (*per os/SNG/IV*)

Rifampicine 10 mg/kg/24h (*per os/SNG/IV*)

Ethambutol 20 mg/kg/24h (*per os/SNG/IV*)

Pyrazinamide 30 mg/kg/24h (*per os/SNG*)

Si ARV : interactions possibles à discuter avec les infectiologues, notamment avec rifampicine

Intérêt probable des **dosages plasmatiques** dans les formes sévères

Durée : 2 mois (attaque) puis 4 à 7 mois (bithérapie RIF/INH selon antibiogramme) voire 10 mois si atteinte SNC associée

Corticoïdes si miliaire (HAS - ex : méthylprednisolone 1 mg/kg24h) et si péricardite et/ou méningite



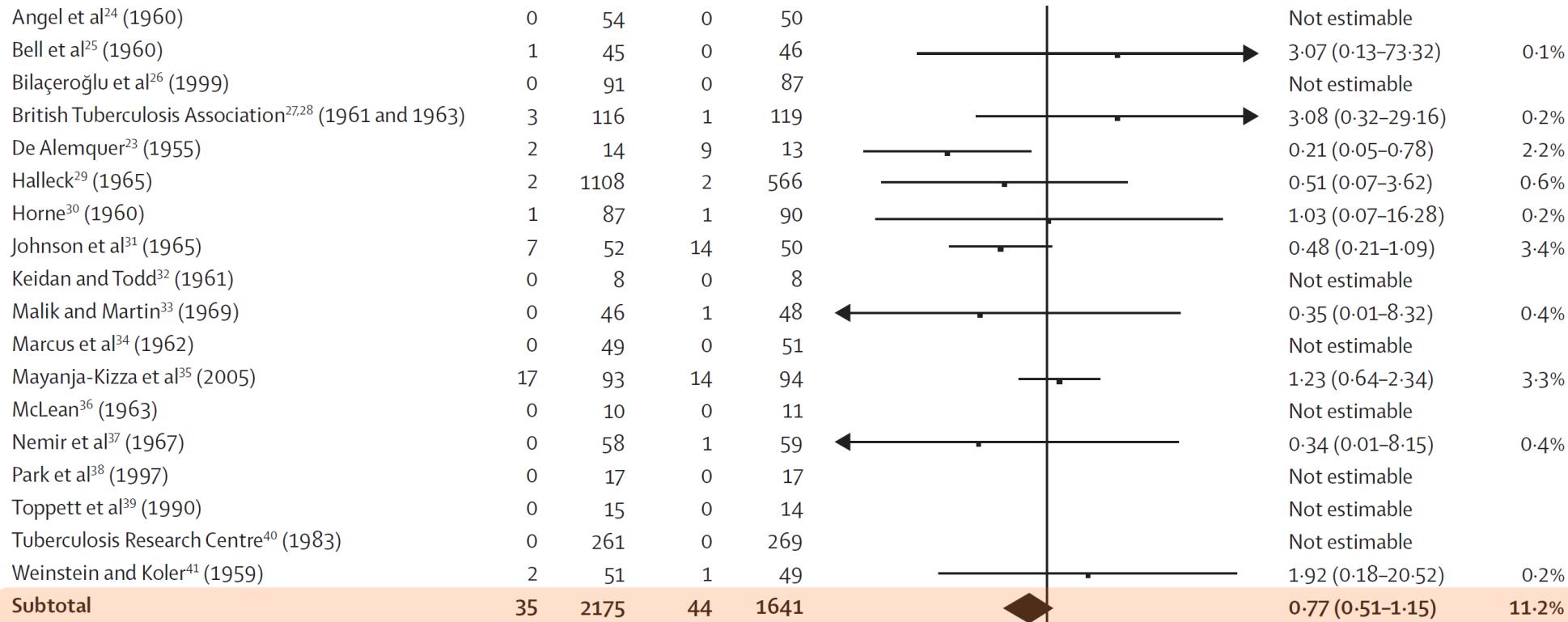
Corticosteroids for prevention of mortality in people with tuberculosis: a systematic review and meta-analysis

Julia A Critchley, Fiona Young, Lois Orton, Paul Garner

Lancet Infect Dis 2013;
13: 223-237



Pulmonary tuberculosis



Heterogeneity: $\chi^2=10.48$, $df=9$ ($p=0.31$); $I^2=14\%$. Test for overall effect: $Z=1.30$ ($p=0.20$)



Effects of Corticosteroids on Critically Ill Pulmonary Tuberculosis Patients With Acute Respiratory Failure: A Propensity Analysis of Mortality

Ji Young Yang,^{1,a} Minkyu Han,^{2,a} Younsuck Koh,³ Woo-Sung Kim,³ Jin-Woo Song,³ Yeon-Mok Oh,³ Sang-Do Lee,³ Sei Won Lee,³ Jae-Seung Lee,³ Chae-Man Lim,³ Chang-Min Choi,³ Jin-Won Huh,³ Sang-Bum Hong,³ Tae Sun Shim,³ and Kyung-Wook Jo³

Clinical Infectious Diseases® 2016;63(11):1449–55

1 December 2016
Volume 63
Number 11
IDSA
hivma
by infection prevention

Clinical
Infectious
Diseases



OXFORD
UNIVERSITY PRESS
cid.oxfordjournals.org

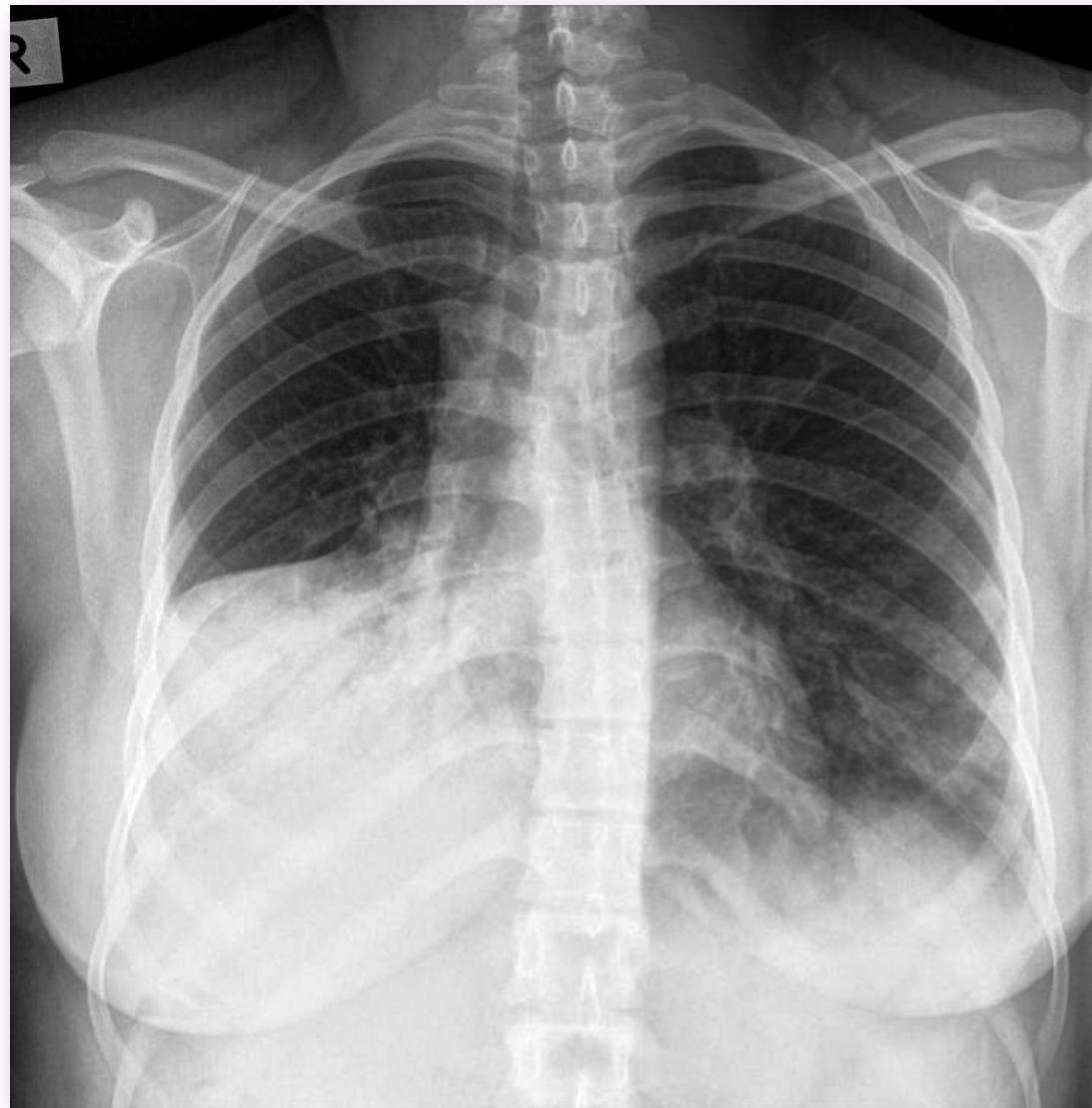
Cohorte rétrospective monocentrique (Corée du Sud)

124 patients avec IRA hypoxémique sur tuberculose pulmonaire (aucun patient VIH+)

Table 3. Analysis of Steroid Treatment Related to 90-Day Mortality in the Study Patients

Analysis	90-Day Mortality	P Value
Crude OR (95% CI)	0.94 (.46–1.92)	.875
Adjusted OR (95% CI) ^a	0.46 (.18–1.19)	.110
Adjusted OR by IPTW (95% CI)	0.47 (.22–0.98)	.049

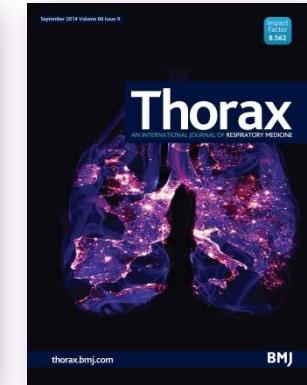




Risk factors for community-acquired pneumonia in adults in Europe: a literature review

Antoni Torres,¹ Willy E Peetermans,² Giovanni Viegi,^{3,4} Francesco Blasi⁵

Thorax 2013;68:1057–1065.



Risk of CAP after adjustment on confounders:

aOR = 2.48 for HIV infection without AIDS (95% CI, 1.34 to 4.58)

aOR = 5.90 for AIDS (2.55 to 13.64)

The incidence of CAP in patients with HIV in France was 12.0 (9.9 to 14.0) per 1000 patient-years.

HAART appears to reduce the risk of CAP, with a French study reporting a reduction from 10.6 (5.4 to 15.7) per 1000 patient-years in the pre-HAART era to 2.5 (1.4 to 3.6) in the post-HAART era.



PAC sévères au cours de l'infection par le VIH

- 35 à 50% des admissions pour IRA chez les patients VIH+ dans les séries récentes
- Fréquence plus élevée que dans les séries <1996 (introduction ARV)
- Pneumonies bactériennes « récurrentes » = *AIDS-defining illness* (classification CDC)
- **Facteurs de risque de PAC chez les patients VIH+ : CD4 <200/mm³ et virémie HIV détectable (effet protecteur des ARV)**, tabagisme, alcoolisme, âge, dénutrition, IVDU, diabète, comorbidités respiratoires (BPCO)
- Altérations fonctionnelles précoces induites par le VIH à toutes les étapes de la réaction immunitaire (lymphocytes T CD4+/B, PNN, macrophages alvéolaires)

Benito et al. *Eur Respir J* 2012; 39: 730–745

Segal et al. *Proc Am Thor Soc* 2012; 8: 282-287

Cilloniz et Torres. *Expert Rev Anti Infect Ther* 2018; 16: 579-588

Barbier et al. *Intensive Care Med* 2020; 46: 329-342



HIV-associated changes in the enteric microbial community: potential role in loss of homeostasis and development of systemic inflammation

Curr Opin Infect Dis 2017, 30:31–43

David B. Gootenberg^{a,b}, Jeffrey M. Paer^a, Jesus-Mario Luevano^{a,b},
and Douglas S. Kwon^{a,b,c}

"HIV-driven destruction of gastrointestinal CD4 T cells may disturb the microbiota–mucosal immune system balance, **disrupting the stable gut microbiome and leading to systemic inflammation** and chronic HIV pathogenesis manifested as NCD such as CVD."

Gut microbiota in HIV–pneumonia patients is related to peripheral CD4 counts, lung microbiota, and in vitro macrophage dysfunction

Shenoy et al. *Microbiome* (2019) 7:37

"Compared with patients with high CD4+ cell counts, those with low counts possessed more compositionally similar airway and gut microbiota, evidence of microbial translocation, and their associated gut microbiome products reduced macrophage activation and IL-10 expression and increased IL-1 β expression in vitro. These findings suggest that **the gut microbiome is related to CD4 status and plays a key role in modulating macrophage function, critical to microbial control in HIV-infected patients with pneumonia.**"



Épidémiologie des PAC chez les patients VIH+

	Hors réanimation [1, 2, 3]	Réanimation [4, 5, 6]
<i>Streptococcus pneumoniae</i>	~70%	25-39%
<i>Pseudomonas aeruginosa</i>	<5%	9-25%
<i>Haemophilus influenzae</i>	~10%	8-14%
<i>Staphylococcus aureus</i>	~10%	5-10%
Entérobactéries	~5%	6-8%
<i>Legionella pneumophila</i>	~5%	<5%

¹ Benito et al. *Eur Respir J.* 2012; 39: 730-745

³ Figueiredo-Mello et al. *Medicine (Baltimore)* 2017; 96: e5778

⁵ Almeida et al. *Int J STD AIDS* 2016; 27: 998-1004

² Head et al. *Pneumonia* 2017; 9: 12

⁴ Barbier et al. *Intensive Care Med.* 2009; 35: 1678-1686

⁶ Elabbadi et al. *Ann Intensive Care* 2020 ; 10:123



Challenges in severe community-acquired pneumonia: a point-of-view review

Intensive Care Med (2019) 45:159–171



Antoni Torres^{1,2,3*} James D. Chalmers⁴, Charles S. Dela Cruz⁵, Cristina Domínguez⁶, Marin Kollef⁷, Ignacio Martín-Loeches^{3,8}, Michael Niederman⁹ and Richard G. Wunderink¹⁰

“We recommend empirically covering PES pathogens in SCAP when ≥ 2 specific risk factors are present.”

Table 3 Risk factors for PES pathogens in patients with severe CAP (Modified from Webb et al. [27])

Therapy related risk factors	Patients related risk factors	Antibiotic selection pressure
Hospitalization for more than 2 days in the past 90 days ^a	Chronic lung diseases: bronchiectasis, severe COPD, tracheostomy ^b	Systemic antibiotic in the past 3–6 months ^a
Gastric acid suppression therapy	Poor functional status ^a (Barthel's index < 50, need for tube feeding, not ambulatory)	
Hemodialysis ^c	MRSA colonization ^c	
Immune suppressive therapy ^a	<i>Pseudomonas aeruginosa</i> colonization ^b	
Home wound care	Prior PES pathogen infection	
	Recurrent skin infections ^c	
	Residence in a long-term care facility	

PES : *P. aeruginosa*, ESBL, MRSA



Burden and risk factors for *Pseudomonas aeruginosa* community-acquired pneumonia: a multinational point prevalence study of hospitalized patients

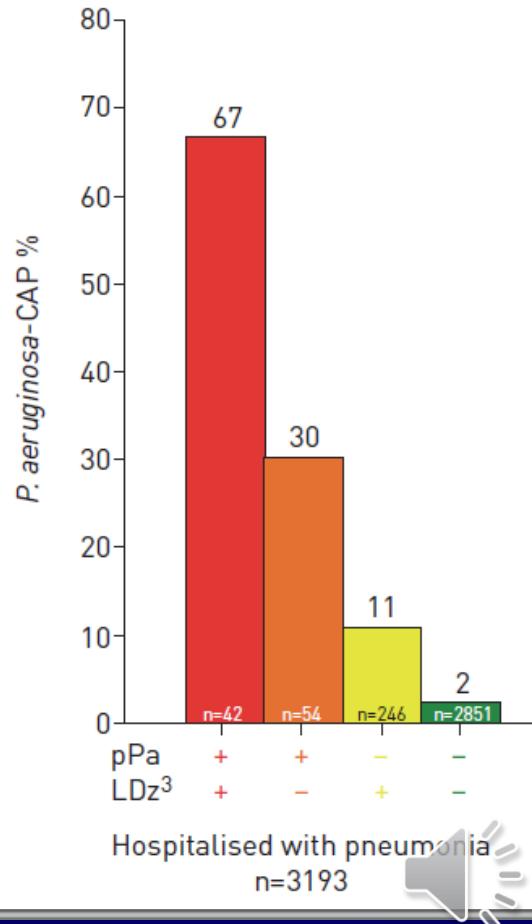
Restrepo et al. *Eur Respir J* 2018; 52 (2): pii 1701190



- 3193 patients avec PAC documentée (54 pays)
 - **PAC à *P. aeruginosa* (ensemble de la cohorte : 4,2%)**
 - ✓ Patients sans facteur de risque : 2%
 - ✓ Patients avec antécédent de colonisation/infection à *P. aeruginosa* et comorbidité respiratoire (BPCO sévère, DDB, trachéotomie) : **67%**

TABLE 3 Multivariate analysis of risk factors for *Pseudomonas aeruginosa*-community-acquired pneumonia (CAP), antibiotic-resistant *P. aeruginosa*-CAP, multidrug-resistant (MDR) *P. aeruginosa*-CAP and specific antibiotic resistance patterns

	Subjects	Prior <i>P. aeruginosa</i>	IRVS	Tracheostomy	Bronchiectasis	COPD	Very severe COPD
<i>P. aeruginosa</i>-CAP	133	16.10 [9.48–27.35]	2.33 [1.44–3.78]	6.50 [2.61–16.19]	2.88 [1.65–5.05]		2.76 [1.25–6.06]
Antibiotic-resistant <i>P. aeruginosa</i>-CAP	64	17.29 [9.95–33.42]	3.12 [1.63–5.97]	5.55 [1.73–17.80]			
Anti-pseudomonal cephalosporins	38	17.79 [7.32–43.22]				2.58 [1.07–6.19]	
Piperacillin/tazobactam	30	9.72 [3.88–24.36]	4.14 [1.75–9.81]		3.33 [1.21–9.19]		
Carbapenems	34	10.62 [4.26–26.45]	2.70 [1.14–6.34]	10.77 [3.09–37.52]			
Aminoglycosides	31	17.32 [7.21–41.61]	3.02 [1.24–7.31]				
Quinolones	50	17.35 [8.28–36.38]	2.84 [1.39–5.78]	4.35 [1.21–15.60]			
MDR <i>P. aeruginosa</i>-CAP	33	12.34 [5.05–30.14]	3.42 [1.47–7.97]			2.69 [1.10–6.55]	



Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Am J Respir Crit Care Med Vol 200, Iss 7, pp e45–e67, Oct 1, 2019



Table 4. Initial Treatment Strategies for Inpatients with Community-acquired Pneumonia by Level of Severity and Risk for Drug Resistance

	Standard Regimen	Prior Respiratory Isolation of MRSA	Prior Respiratory Isolation of <i>Pseudomonas aeruginosa</i>	Recent Hospitalization and Parenteral Antibiotics and Locally Validated Risk Factors for MRSA	Recent Hospitalization and Parenteral Antibiotics and Locally Validated Risk Factors for <i>P. aeruginosa</i>
Nonsevere inpatient pneumonia*	β-Lactam + macrolide [†] or respiratory fluoroquinolone [‡]	Add MRSA coverage [§] and obtain cultures/nasal PCR to allow deescalation or confirmation of need for continued therapy	Add coverage for <i>P. aeruginosa</i> and obtain cultures to allow deescalation or confirmation of need for continued therapy	Obtain cultures but withhold MRSA coverage unless culture results are positive. If rapid nasal PCR is available, withhold additional empiric therapy against MRSA if rapid testing is negative or add coverage if PCR is positive and obtain cultures	Obtain cultures but initiate coverage for <i>P. aeruginosa</i> only if culture results are positive
Severe inpatient pneumonia*	β-Lactam + macrolide [†] or β-lactam + fluoroquinolone [‡]	Add MRSA coverage [§] and obtain cultures/nasal PCR to allow deescalation or confirmation of need for continued therapy	Add coverage for <i>P. aeruginosa</i> and obtain cultures to allow deescalation or confirmation of need for continued therapy	Add MRSA coverage [§] and obtain nasal PCR and cultures to allow deescalation or confirmation of need for continued therapy	Add coverage for <i>P. aeruginosa</i> and obtain cultures to allow deescalation or confirmation of need for continued therapy



Excess mortality risk from sepsis in patients with HIV – A meta-analysis

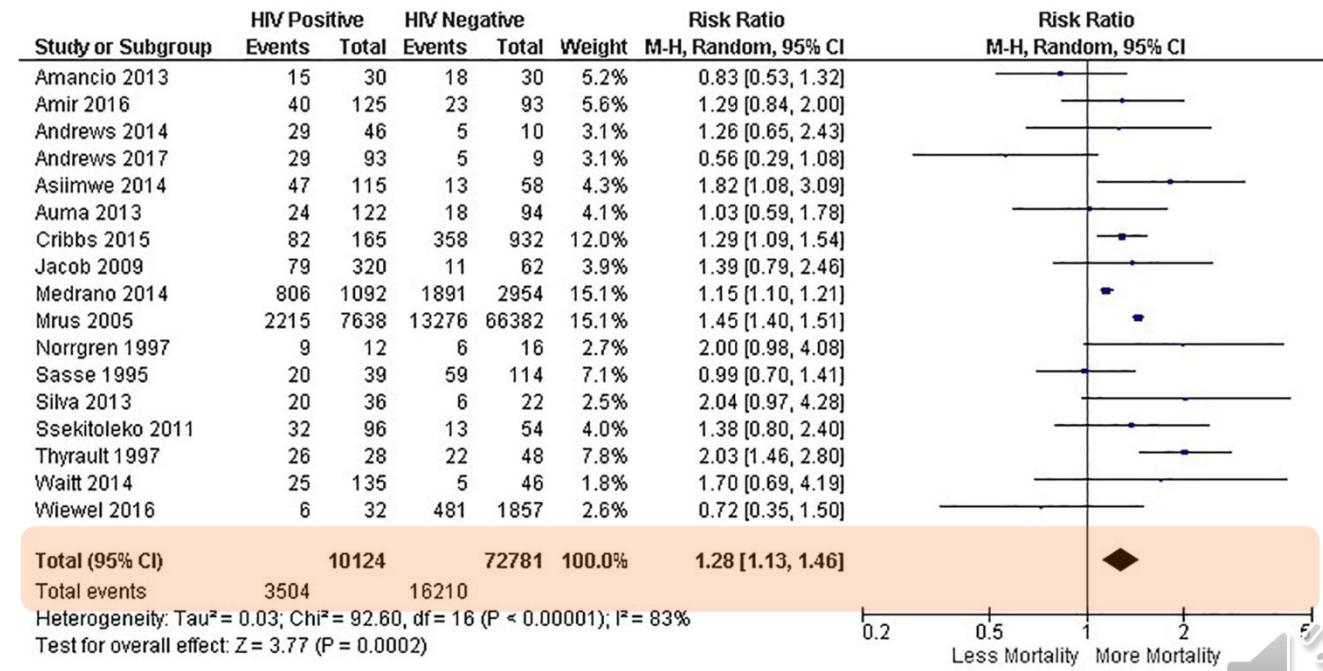
Fahim F. Pyarali, MD, MPH ^{a,1,*}, Roumen Iordanov, MD ^a,
Ana Palacio, MD, MPH ^{a,b}, Leonardo Tamariz, MD, MPH ^{a,b}

Journal of Critical Care 59 (2020) 101–107



"Sepsis mortality was 28% higher in HIV-positive patients (95% CI 1.13–1.46). Relative risk of mortality was higher in patients treated in low-income countries (RR 1.43, vs. 1.29 in high-income countries.)"

Author, year	Average age	% male	Average CD4 of HIV + (cells/mm3)	% patients on ARTs
Amancio 2013	49	66.5	72	57.0%
Amir 2016	35 (median)	50.5	78	66.4%
Andrews 2014	34.8	53.6	70	35.6%
Andrews 2017	35.8	53.4	65 (median)	49.5%
Asiimwe 2014	–	–	–	–
Auma 2013	32 (median)	49	75	36.0%
Cribbs 2015	52.6	62.3	41 (median)	22.0%
Jacob 2009	34.8	40.8	52	11.9%
Medrano 2014	–	–	–	–
Mrus 2005	49.1	55.2	–	–
Norrgren 1997	–	–	103	–
Sasse 1995	56.8	58.2	–	–
Silva 2013	42.1	58.7	25	42.9%
Ssekitoleko 2011	35.4	62.7	–	22.0%
Thyrault 1997	46.7	65.8	67	–
Waitt 2014	33 (median)	42	–	43.0%
Wiewel 2016	60.2	52.3	70	70.7%

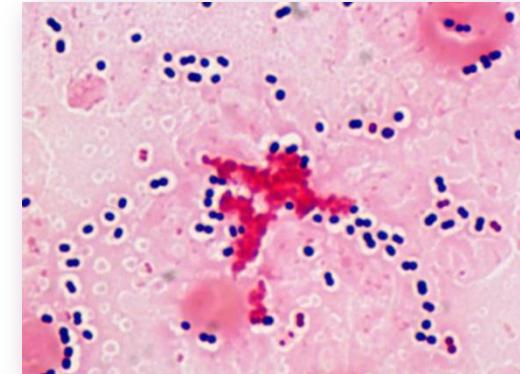


Community-Acquired Pneumococcal Pneumonia in Virologically Suppressed HIV-Infected Adult Patients

A Matched Case-Control Study

CHEST 2017; 152(2):295-303

Catia Cillóniz, PhD; Antoni Torres, MD; Christian Manzardo, MD; Albert Gabarrús, MSc; Juan Ambrosioni, MD; Adriana Salazar, MD; Felipe García, MD; Adrián Ceccato, MD; Josep Mensa, MD; Jorge Puig de la Bella Casa, MD; Asunción Moreno, MD; and Jose M. Miró, MD



Case-control study, Hospital Clinic, Barcelona, Spain (2001-2016)

HIV-negative controls matched by age, sex, comorbidities, and year of diagnosis

TABLE 3] Clinical Outcomes

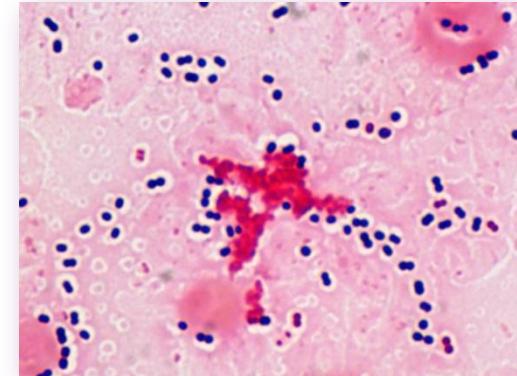
Variables	Case Patients (HIV Infection) (n = 50)	Control Patients (Non-HIV Infection) (n = 100)	P
ICU admission, No. (%)	9 (18)	27 (27)	.22
Mechanical ventilation, No. (%)	6 (12)	8 (8)	.43
Length of hospital stay, median (IQR), d	7.0 (5.0; 11.0)	7.0 (4.0; 11.0)	.76
30-d mortality, No. (%)	0 (0)	0 (0)	...



Community-Acquired Pneumococcal Pneumonia in Virologically Suppressed HIV-Infected Adult Patients A Matched Case-Control Study

CHEST 2017; 152(2):295-303

Catia Cillóniz, PhD; Antoni Torres, MD; Christian Manzardo, MD; Albert Gabarrús, MSc; Juan Ambrosioni, MD; Adriana Salazar, MD; Felipe García, MD; Adrián Ceccato, MD; Josep Mensa, MD; Jorge Puig de la Bella Casa, MD; Asunción Moreno, MD; and Jose M. Miró, MD



Case-control study, Hospital Clinic, Barcelona, Spain (2001-2016)

HIV-negative controls matched by age, sex, comorbidities, and year of diagnosis

CONCLUSIONS: Pneumococcal pneumonia episodes requiring hospitalization in virologically suppressed patients with HIV with > 350 CD4+ T-cell count/mm³ were neither more severe nor had worse prognosis compared with uninfected patients. These results support the fact that such patients do not need treatment, admission, or care sites different to the general population.

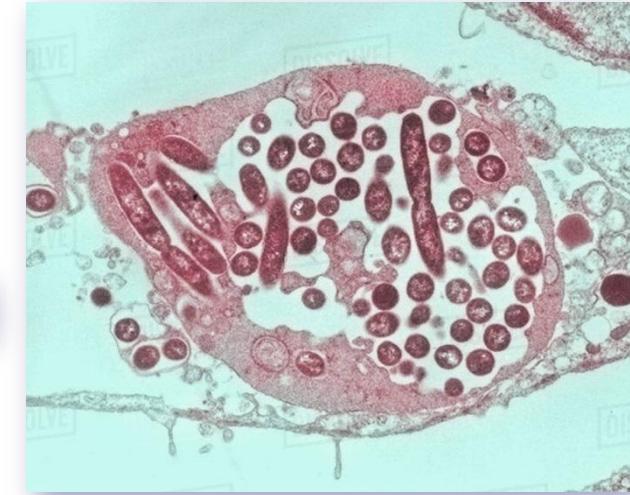


Community-Acquired *Legionella* Pneumonia in Human Immunodeficiency Virus-Infected Adult Patients: A Matched Case-Control Study

Clinical Infectious Diseases®

2018;67(6):958–61

Catia Cillóniz,^{1,2} Lucia Miguel-Escuder,³ María Luisa Pedro-Bonet,^{4,5,6}
Vicenç Falcó,³ Yessica Lopez,^{4,5,6} Carolina García-Vidal,⁷
Albert Gabarrús,¹ Asunción Moreno,⁷ Antoni Torres,¹ and José M. Miró⁷;
for the *Legionella*-HIV Researchers^a



We investigate whether the clinical presentations and outcomes of *Legionella* pneumonia in human immunodeficiency virus (HIV)-infected patients were comparable to those seen in non-HIV-infected patients (case-control design). HIV-infected individuals presented neither a more severe disease nor a worse clinical outcome than matched HIV-negative control patients.

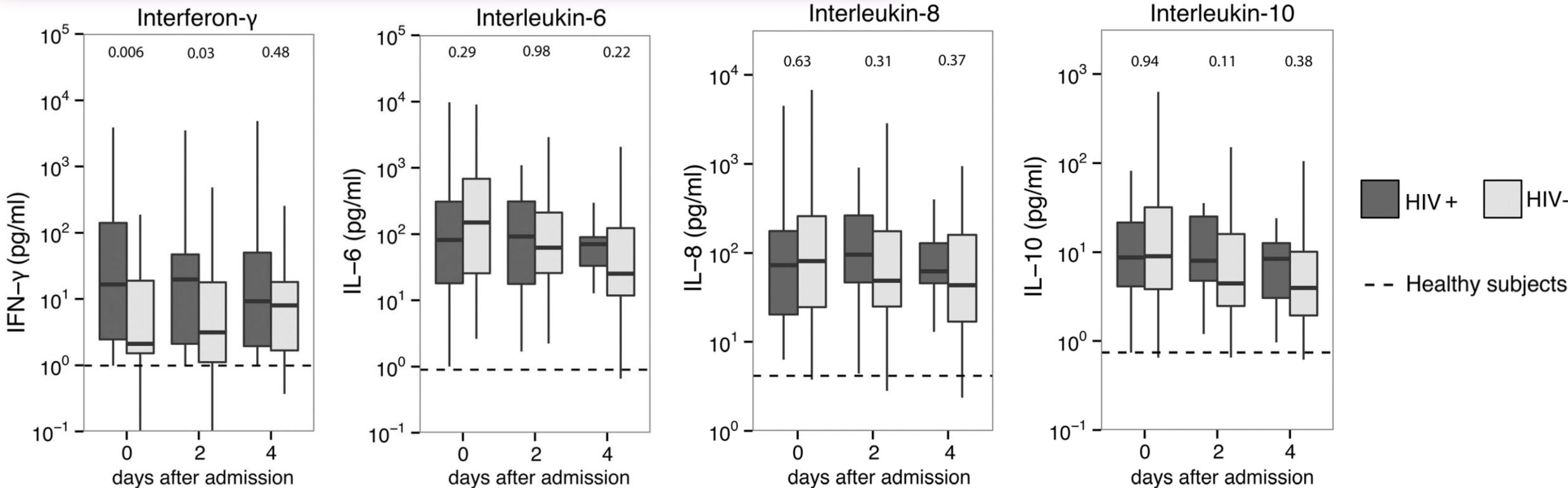


Impact of HIV infection on the presentation, outcome and host response in patients admitted to the intensive care unit with sepsis; a case control study

Wiewel et al. Critical Care (2016) 20:322



30 HIV-patients versus 90 seronegative controls
Sepsis / community-acquired pneumonia



Disease severity and mortality up to one year after admission did not differ according to HIV status.

HIV infection has little impact on host response during sepsis.



Etiology of Pulmonary Infections in Human Immunodeficiency Virus-infected Inpatients Using Sputum Multiplex Real-time Polymerase Chain Reaction

Gary Maartens,^{1,1D} Rulan Griesel,¹ Felix Dube,^{2,a} Mark Nicol,^{2,b} and Marc Mendelson³

Clinical Infectious Diseases®

2020;70(6):1147–52

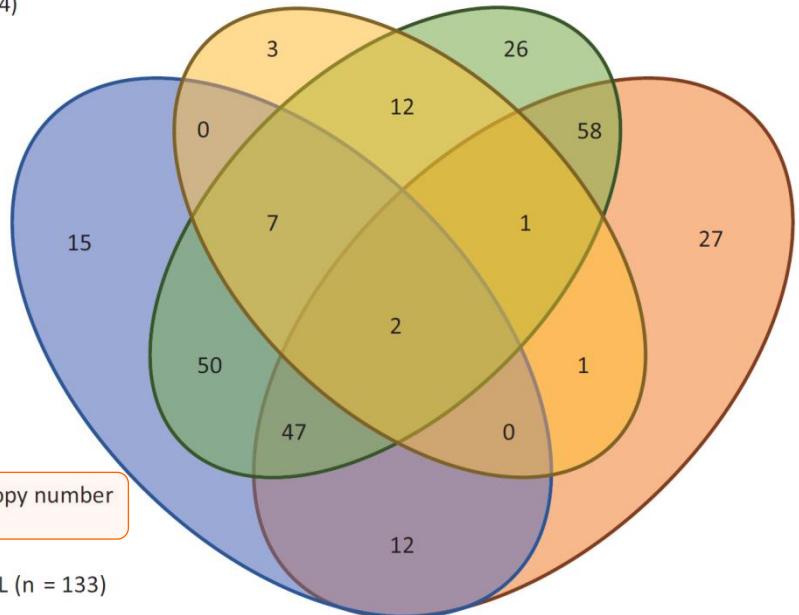


Clinical
Infectious
Diseases

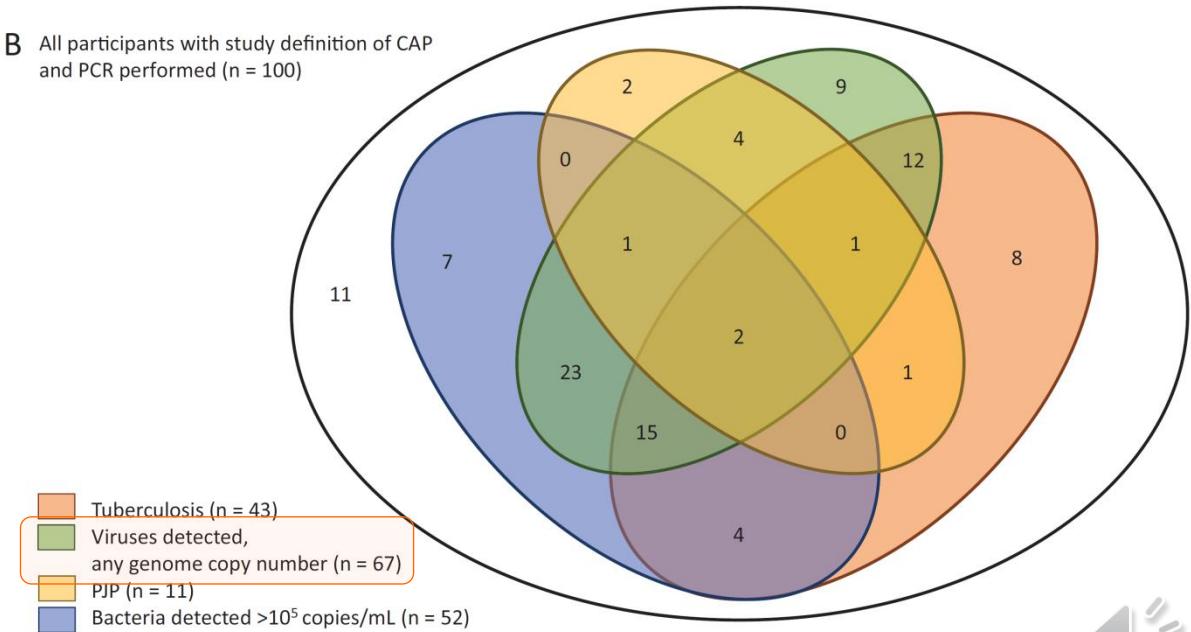


South Africa, 284 HIV-infected patients (median CD4 97 cells/ μ L, cART 38%)

A All participants with PCR done (n = 284)

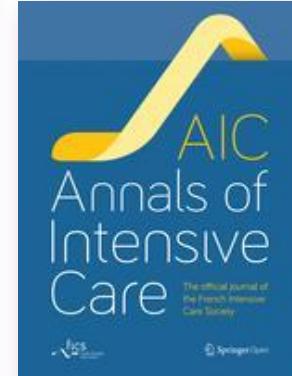


B All participants with study definition of CAP and PCR performed (n = 100)



Respiratory virus-associated infections in HIV-infected adults admitted to the intensive care unit for acute respiratory failure: a 6-year bicenter retrospective study (HIV-VIR study)

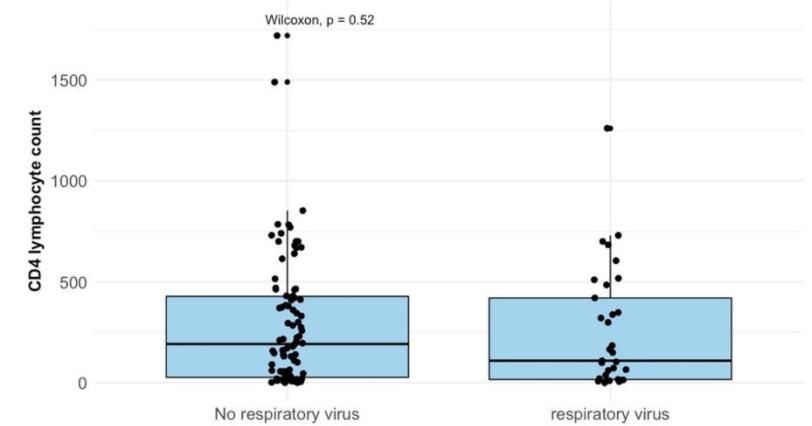
Alexandre Elabbadi¹, Jérémie Pichon¹, Benoit Visseaux^{2,3}, Aurélie Schnuriger⁴, Lila Bouadma^{3,5}, Quentin Philippot¹, Juliette Patrier⁵, Vincent Labb  ^{1,6}, St  phane Ruckly³, Muriel Fartoukh^{1,6}, Jean-Fran  ois Timsit^{3,5} and Guillaume Voiriot^{1,6*} 



Ann. Intensive Care (2020) 10:123

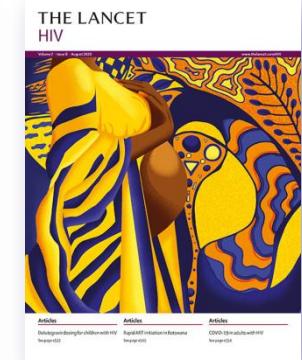
Table 2 Causative diagnosis of acute respiratory failure in 123 HIV-infected patients admitted to the ICU

Patients	All patients (n = 123)	CD4 ≤ 200 (n = 66)	CD4 > 200 (n = 57)
Pneumocystis jirovecii pneumonia	29 (23.6)	26 (39.4)	3 (5.3)
Other opportunistic lung infection ^a	9 (7.3)	7 (10.6)	2 (3.5)
Non-opportunistic acute lung infection	59 (48)	22 (33.3)	37 (64.9)
Bacteria	53	21	32
Virus	25	13	12
Rhinovirus	8	6	2
Adenovirus	2	1	1
Coronavirus	1	1	0
Influenza virus	6	2	4
Human metapneumovirus	1	0	1
Parainfluenza virus	3	2	1
Respiratory syncytial virus	4	1	3
Bacteria–virus coinfection	12	8	4
Virus–virus coinfection	2	2	0



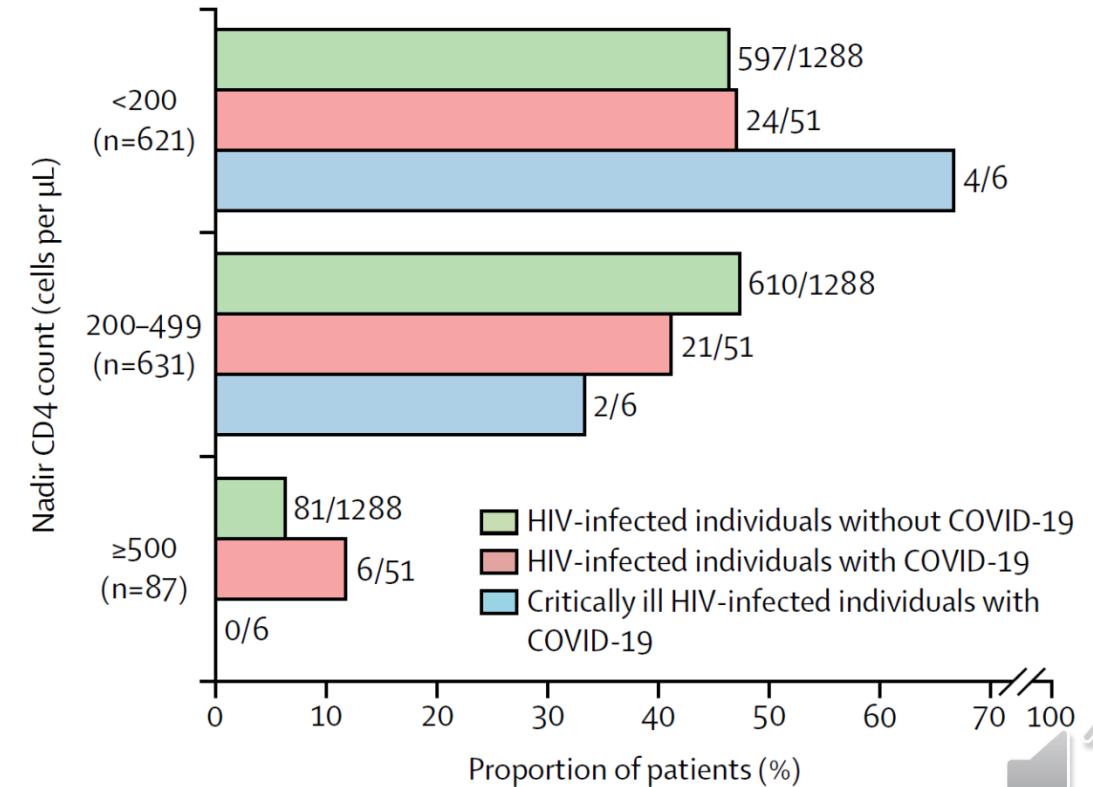
Description of COVID-19 in HIV-infected individuals: a single-centre, prospective cohort

Pilar Vizcarra, María J Pérez-Elías, Carmen Quereda, Ana Moreno, María J Vivancos, Fernando Dronda, José L Casado, on behalf of the COVID-19 ID Team*



Lancet HIV 2020; 7: e554-64

- Spain (Madrid), 51 HIV+ patients with COVID-19 (age 53.9 ± 9.5 y., cART 99%)
- Age and CD4 cells: similar to those in 1288 HIV-infected individuals without COVID-19
- **At least one comorbidity, mostly hypertension and diabetes : 63% vs 38% ($P = 0.0006$)**
- Clinical/radiological presentation: similar to the general population
- **Hospital admission 55%, ICU 12%, death 4%**



Incidence and Severity of COVID-19 in HIV-Positive Persons Receiving Antiretroviral Therapy

A Cohort Study

Julia del Amo, MD, PhD; Rosa Polo, MD, PhD; Santiago Moreno, MD, PhD; Asunción Díaz, MD, PhD; Esteban Martínez, MD, PhD; José Ramón Arribas, MD, PhD; Inma Jarrín, PhD; and Miguel A. Hernán, MD, DrPH; for The Spanish HIV/COVID-19 Collaboration*



Annals of Internal Medicine



2020. doi:10.7326/M20-3689

Whole population:

Hospital admission 63.9%
ICU 6.3%, death 8.5%

Patients receiving ART ($n = 77\,590$)

Patients with PCR-confirmed diagnosis ($n = 236$)

0.3%

Hospitalized patients ($n = 151$)

Nonhospitalized patients ($n = 85$)

ICU admissions ($n = 15$)

Died ($n = 3$)

Recovered ($n = 82$)

Died ($n = 5$)

Recovered ($n = 10$)

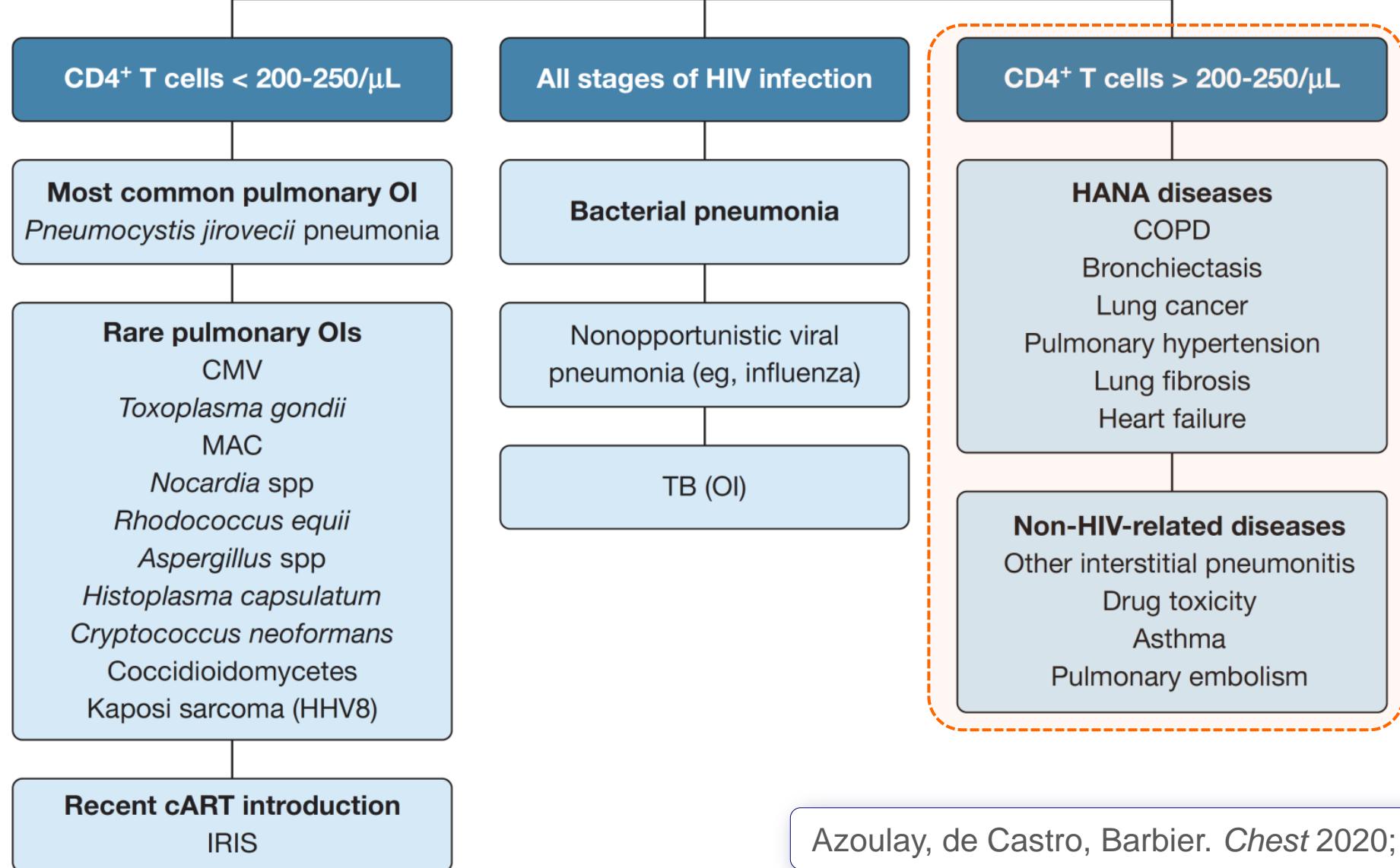
Non-ICU admissions ($n = 136$)

Died ($n = 12$)

Recovered ($n = 124$)

1 February - 15 April 2020

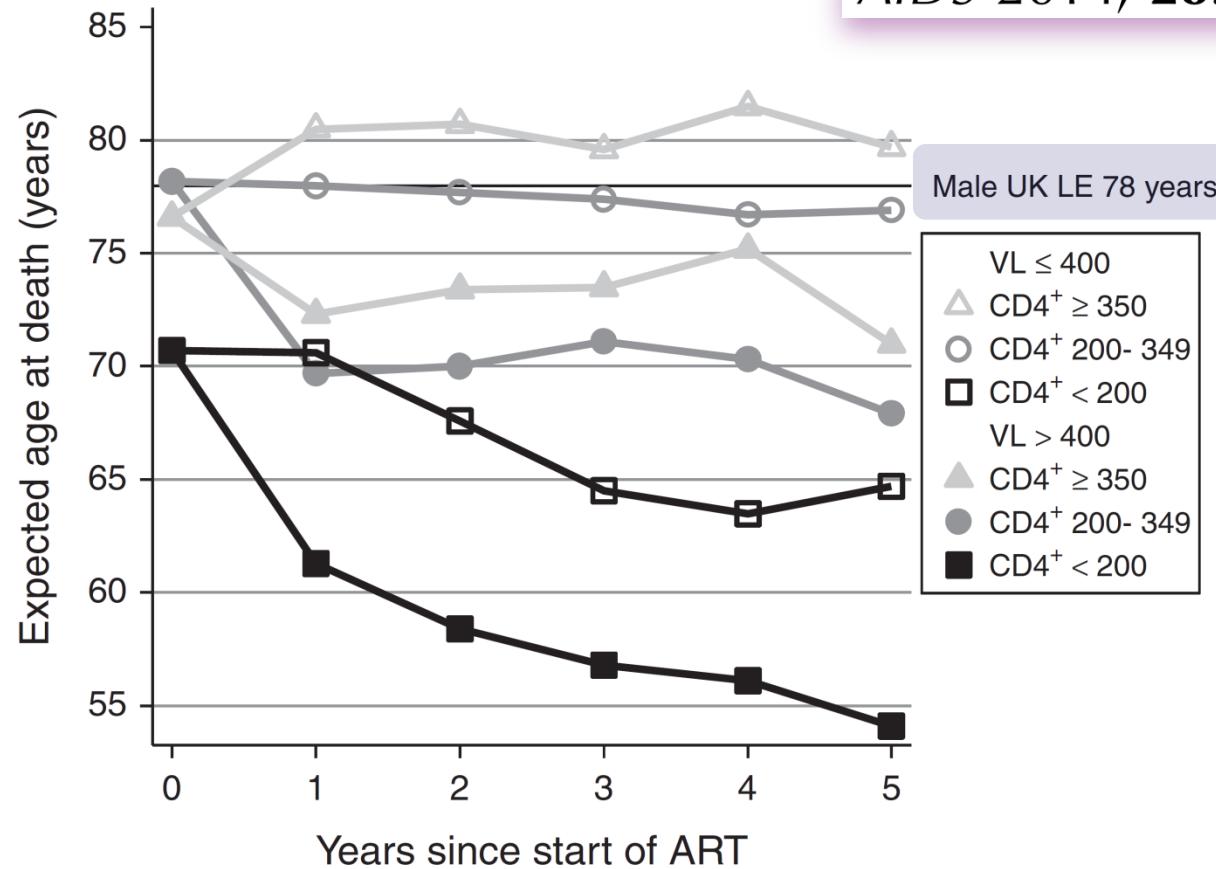
Acute respiratory failure in HIV-infected patients



Azoulay, de Castro, Barbier. *Chest* 2020; 157: 293-309

Impact on life expectancy of HIV-1 positive individuals of CD4⁺ cell count and viral load response to antiretroviral therapy

AIDS 2014, 28:1193–1202



Conclusion: Successfully treated HIV-positive individuals have a normal life expectancy. Patients who started ART with a low CD4 cell count significantly improve their life expectancy if they have a good CD4 cell count response and undetectable viral load.

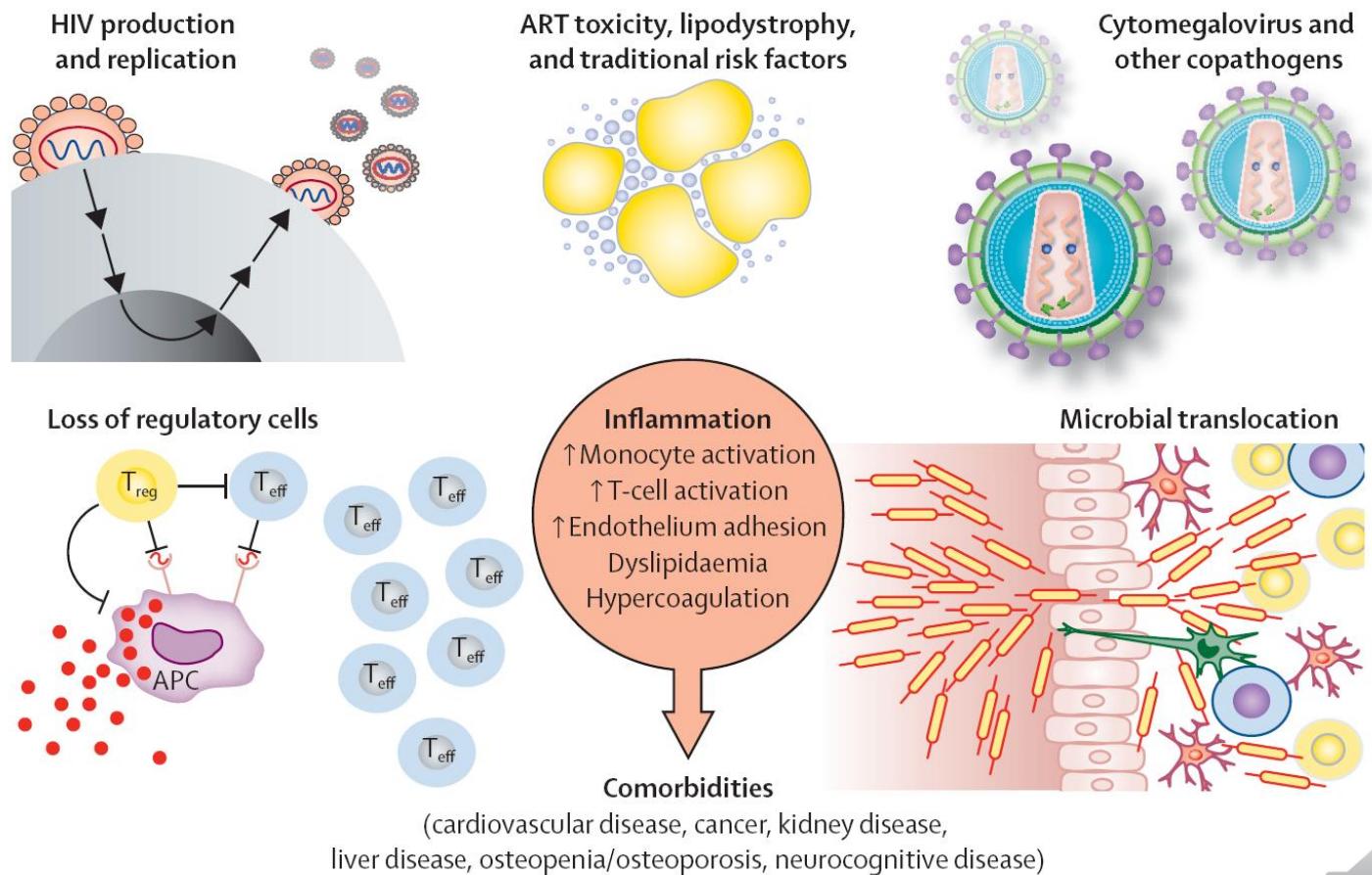
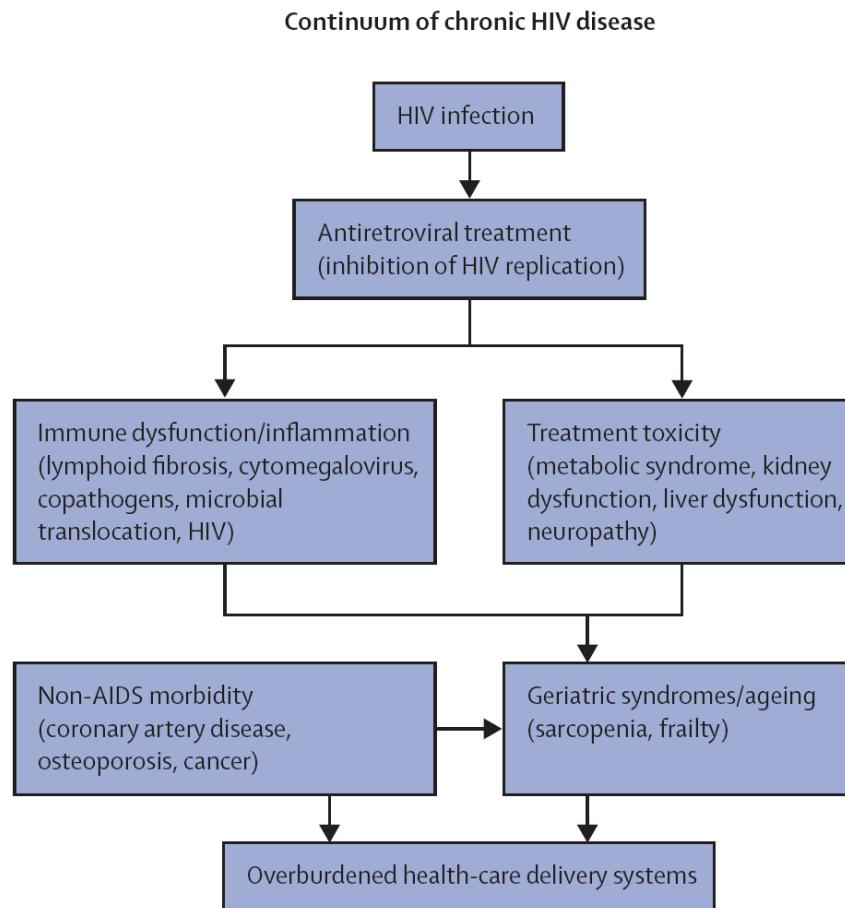


The end of AIDS: HIV infection as a chronic disease

Steven G Deeks, Sharon R Lewin, Diane V Havlir

Lancet 2013; 382: 1525–33

"HIV is a wily beast, but recent insights seem to offer tangible clues about how to begin to corral the AIDS pandemic to the dustbin of history."



Mechanisms Underlying HIV-Associated Noninfectious Lung Disease

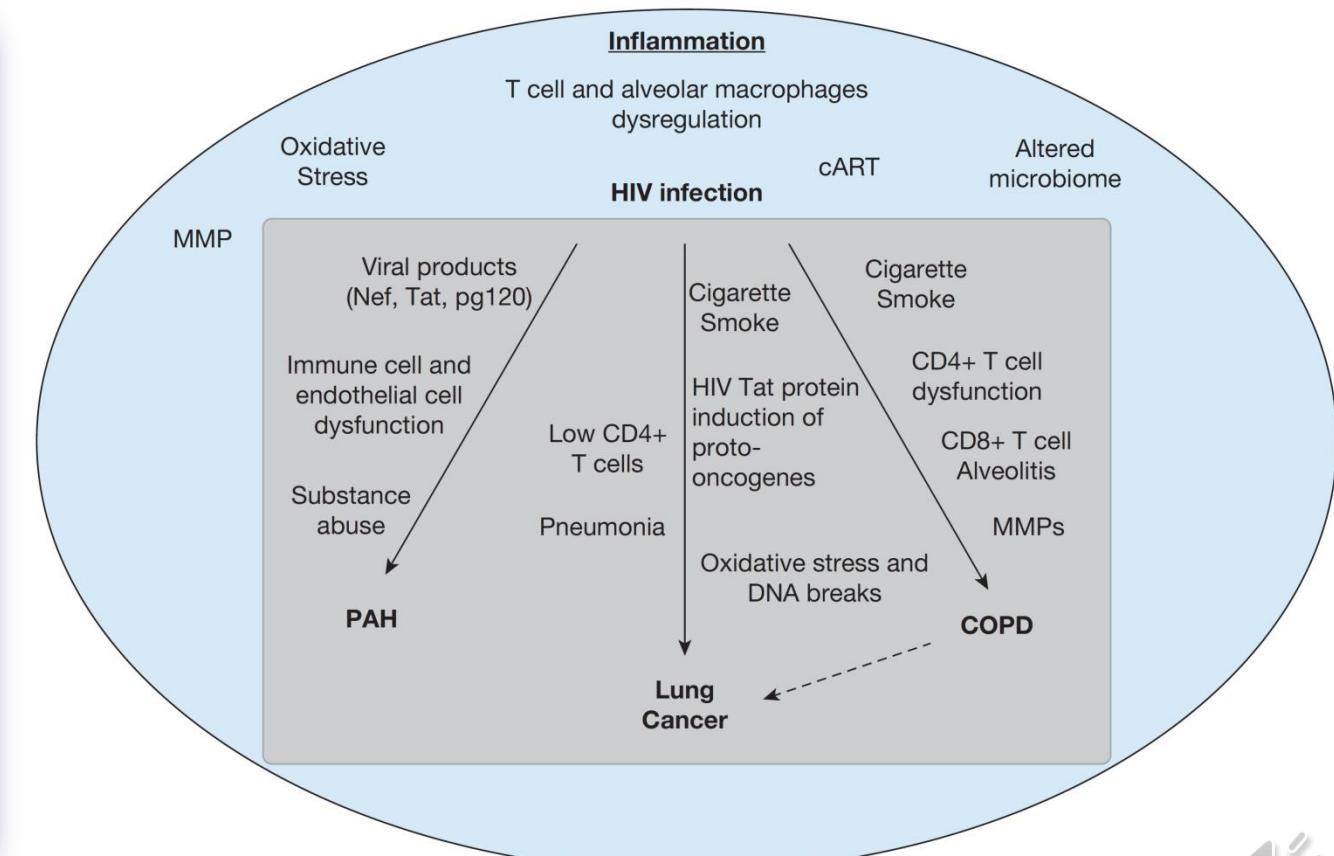
Rachel M. Presti, MD, PhD; Sonia C. Flores, PhD; Brent E. Palmer, PhD; Jeffrey J. Atkinson, MD; Catherine R. Lesko, PhD; Bryan Lau, PhD; Andrew P. Fontenot, MD; Jesse Roman, MD; John F. McDyer, MD; and Homer L. Twigg III, MD



CHEST 2017; 152(5):1053-1060

“Recent research suggests that oxidative stress, expression of matrix metalloproteinases and genetic instability may result in lung damage, which predisposes HIV-patients to lung cancer, COPD and pulmonary hypertension.”

Factors that drive these processes include tobacco and other substance use, direct HIV infection and expression of specific HIV proteins, inflammation, and shifts in the microbiome toward pathogenic and opportunistic organisms.”



Prevalence of chronic obstructive pulmonary disease in the global population with HIV: a systematic review and meta-analysis

Jean Joel Bigna, Angeladine Malaha Kenne, Serra Lem Asangbeh, Aurelie T Sibetcheu

Lancet Glob Health 2018;
6: e193-202

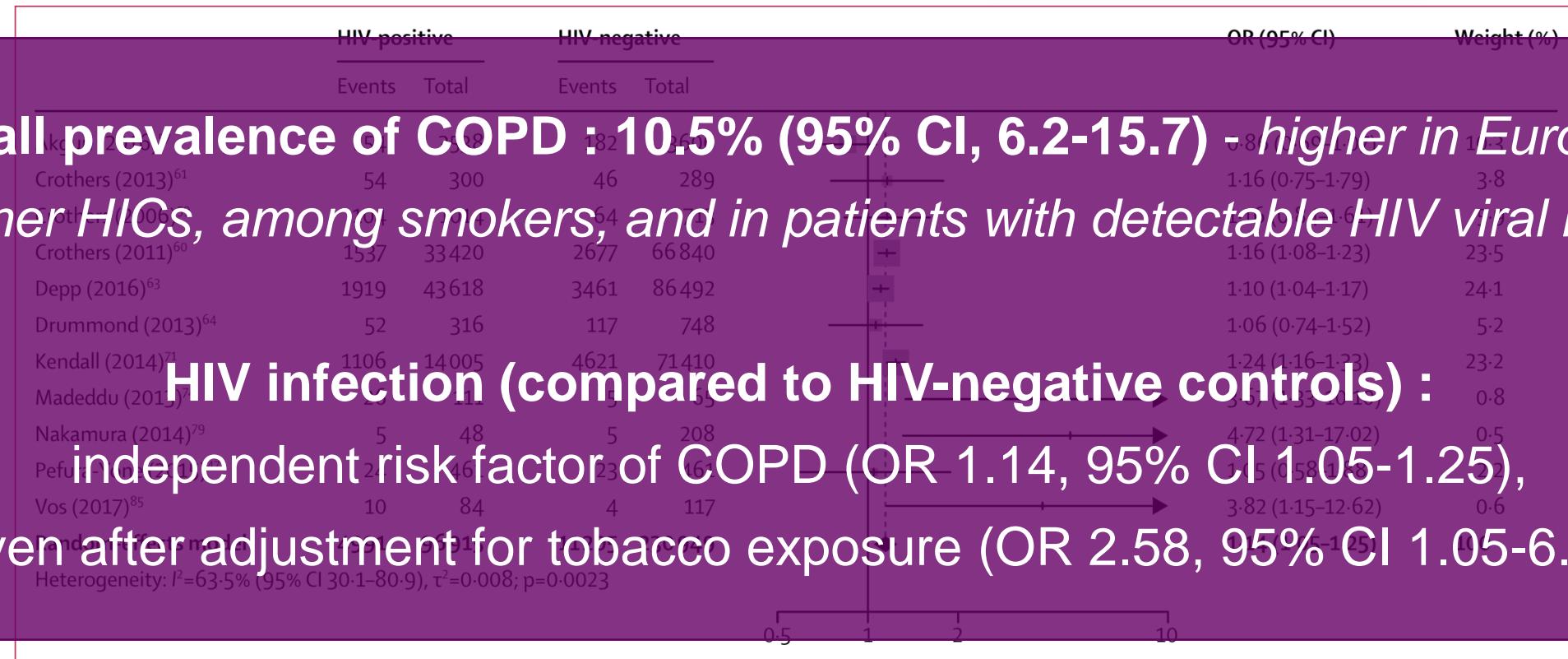


Figure 3: Forest plot of the association between exposure to HIV infection and COPD



HIV-Associated Cancers and Related Diseases

N Engl J Med 2018;378:1029-41.

Robert Yarchoan, M.D., and Thomas S. Uldrick, M.D.

Table 1. Principal HIV-Associated Tumors.*

Cancer	Estimated No. of Cases/Yr in the United States among Persons with AIDS†	SIR after Combination ART in the United States‡	Role of Immunosuppression from HIV Infection	Etiologic Virus	Other Causative Factors
AIDS-defining					
Non-Hodgkin's lymphoma	1194	11.5	++ to ++++ for different types	EBV§	
Kaposi's sarcoma	765	498.1	+++	KSHV	
Cervical cancer	106	3.2	+	HPV	Tobacco
Non-AIDS-defining					
Lung cancer	376	2.0	+	?	Smoking, pulmonary infections
Anal cancer	313	19.1	+	HPV	
Hodgkin's lymphoma	179	7.7	++	EBV	
Oral cavity and pharyngeal cancer	100	1.6¶	0 to + for different types	HPV	Tobacco, alcohol
Hepatocellular carcinoma	117	3.2	0 or +	HBV, HCV	Alcohol, other hepatic insults
Vulvar cancer	15	9.4	+	HPV	
Penile cancer	13	5.3	+	HPV	



Risk Factors for Hospitalization and Medical Intensive Care Unit (MICU) Admission Among HIV-Infected Veterans

Kathleen M. Akgün, MD,*† Kirsha Gordon, MS,*† Margaret Pisani, MD, MPH,‡ Terri Fried, MD,‡‡

Kathleen A. McGinnis, MS,§ Janet P. Tate, ScD, MPH,*† Adeel A. Butt, MD, MS,||¶

Cynthia L. Gibert, MD, MSc,# Laurence Huang, MD, ** Maria C. Rodriguez-Barradas, MD,††††

David Rimland, MD,§§ Amy C. Justice, MD, PhD,*† and Kristina Crothers, MD||||



Volume 62, Number 1, January 1, 2013

Cohorte prospective de 3410 patients VIH+ (âge médian 49 ans, ARV 71%)

1141 patients (33,5%) hospitalisés dans les 2 ans suivant l'inclusion dont 203 (6%) en réanimation

TABLE 3. Multivariable Model for Odds of MICU Admission Within 2 Years of Enrollment Among Those Hospitalized (n = 1141)*

Characteristic	Odds Ratio (95% CI)
VACS Index score/5-point change	1.11 (1.08 to 1.15)
Hypertension	1.38 (0.97 to 1.96)
CAD/CHF	2.88 (1.66 to 5.01)
History of any cancer	2.06 (1.15 to 3.68)



François Barbier
Antoine Roux
Emmanuel Canet
Patricia Martel-Samb
Philippe Aegerter
Michel Wolff
Bertrand Guidet
Élie Azoulay

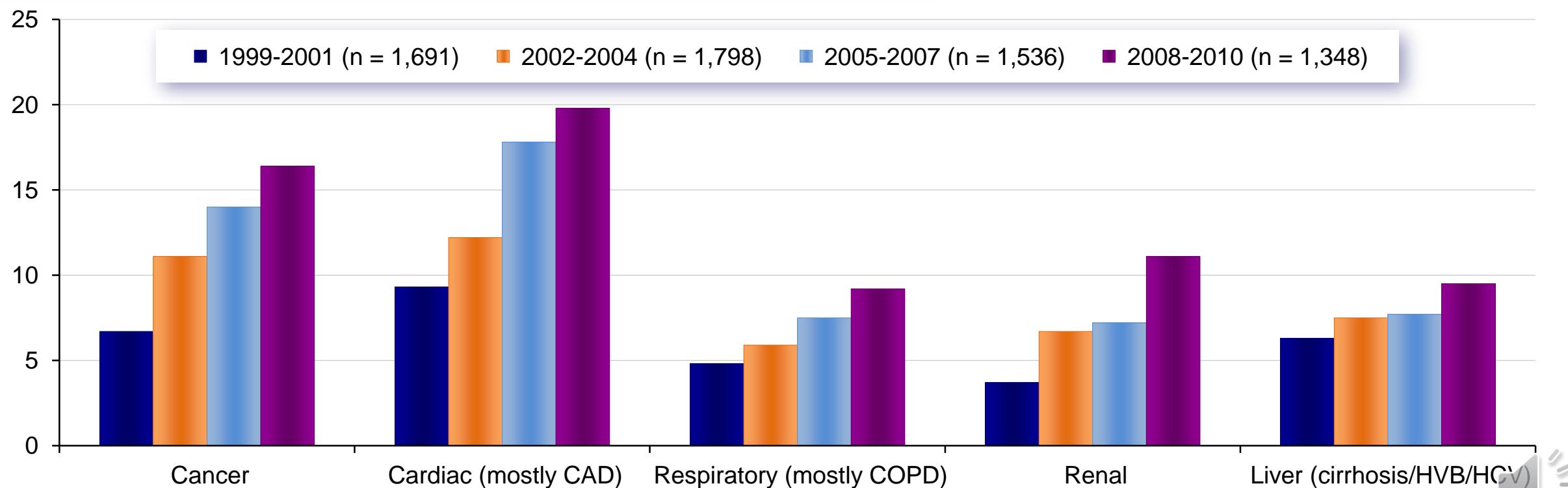
Temporal trends in critical events complicating HIV infection: 1999–2010 multicentre cohort study in France

34 ICUs (CUB-Rea Network)

6,673 HIV-infected patients

Prevalence of chronic diseases (%)

($p < 0.001$ for all trends)



Challenges in solid organ transplantation in people living with HIV

Intensive Care Med (2019) 45:398–400

Jose M. Miro^{1*}, Paolo A. Grossi² and Christine M. Durand³

« **Any organ can be transplanted to HIV-infected patients.** (...) Finally, mid- and long-term survival rates of kidney, liver and heart transplantation are lower than in matched HIV-negative recipients but are still acceptable. HCV co-infection negatively affects these results. »

Table 1 Long-term survival of kidney, liver and heart transplants in HIV-infected recipients compared with HIV-negative controls

Type of SOT/country (references)	Period	Number of patients	Years						<i>P</i> value
			1	2	3	4	5	10	
Kidney/USA [1]	2002–2011	HIV+ HCV– (<i>n</i> =362)	96%	–	92%	–	89%	64%	0.096
		HIV– HCV– (<i>n</i> =3620)	97%	–	94%	–	89%	78%	
Kidney/USA [1]	2002–2011	HIV+ HCV+ (<i>n</i> =104)	91%	–	77%	–	67%	29%	0.001
		HIV– HCV+ (<i>n</i> =1050)	94%	–	86%	–	79%	56%	
Liver/Spain [2]	2002–2006	HIV+/HCV+ (<i>n</i> =84)	88%	71%	62%	60%	54%	–	0.008
		HIV-/HCV+ (<i>n</i> =252)	90%	81%	76%	73%	71%	–	
Liver/Spain [3]	2002–2009	HIV+/HCV+ SVR (<i>n</i> =16)	93%	87%	79%	79%	79%	–	0.093
		HIV-/HCV+ SVR (<i>n</i> =64)	98%	98%	98%	92%	92%	–	
Liver/USA [4]	2002–2011	HIV+/HCV+ (<i>n</i> =117)	77%	–	59%	–	52%	44%	<0.001
		HIV-/HCV+ (<i>n</i> =15,581)	88%	–	76%	–	69%	60%	
Liver/USA [5]	2001–2007	HIV+/HBV+ (<i>n</i> =22)	85%	–	85%	–	85%	–	0.090
		HIV-/HBV+ (<i>n</i> =20)	100%	–	100%	–	100%	–	
Heart/USA [6]	1999–2004	HIV+ (<i>n</i> =20)	86%	–	79%	–	–	–	0.950
		HIV– (<i>n</i> =9174)	90%	–	90%	–	–	–	
Heart/USA [7]	2004–2016	HIV+ (<i>n</i> =35)	100%	–	88%	–	88%	–	0.149
		HIV– (<i>n</i> =21,400)	89%	–	83%	–	77%	–	



Influence of HIV status on the management of acute asthma exacerbations

Muhammad Adrish ¹, Gabriella Roa Gomez,² Enny Cancio Rodriguez,³
Nikhitha Mantri²

BMJ Open 2020 (on-line first)

Table 2 Outcomes by HIV status

Variables	HIV-negative n=358	HIV-positive n=104	P value
Non-invasive positive pressure ventilation use, N (%)	91 (25.4%)	57 (54.8%)	<0.001
Length of stay on non-invasive positive pressure ventilation, Mean (SD) days	2.670 (1.571)	2.723 (1.873)	0.861
Mechanical ventilation use, N (%)	3 (0.8%)	0 (0%)	0.808
Need for ICU admission, N (%)	30 (8.4%)	6 (5.8%)	0.533
Length of stay in hospital, Mean (SD) days	2.813 (1.712)	3.346 (2.693)	0.015



Insuffisance respiratoire aiguë au cours de l'infection par le VIH : quel pronostic?





0090-3493/89/1702-0113\$02.00/0
CRITICAL CARE MEDICINE
Copyright © 1989 by The Williams & Wilkins Co.

Vol. 17, No. 2
Printed in U.S.A.

clinical investigations

Crit Care Med 1989

Admission of AIDS patients to a medical intensive care unit: Causes and outcome

PAUL L. ROGERS, MD; H. CLIFFORD LANE, MD; DAVID K. HENDERSON, MD; JOSEPH PARRILLO, MD;;
HENRY MASUR, MD

Série monocentrique ($n = 216$), Pittsburgh, Pensylvanie, 1981-1987

Patients VIH+ sous ventilation mécanique pour insuffisance respiratoire aiguë
(étiologie principale : pneumocystose)

Mortalité en réanimation : 66% (!)

Mortalité à 3 mois : 85% (!!!)



Patients VIH+ admis pour IRA : quel pronostic à court terme ?

Mortalité hospitalière globale :
entre 20 et 30% dans les séries récentes



Amélioration nette du pronostic sur les deux dernières décennies

Bénéfice de la ventilation protectrice (ARDS)

Admission plus précoce

Prise en charge diagnostique et thérapeutique mieux codifiée ?

Amélioration globale des pratiques en réanimation +++

Akgun & Miller. *Semin Respir Crit Care Med* 2016; 37: 303-17

Azoulay, de Castro & Barbier. *Chest* 2019 (e-pub)



François Barbier
Antoine Roux
Emmanuel Canet
Patricia Martel-Samb
Philippe Aegerter
Michel Wolff
Bertrand Guidet
Élie Azoulay

Temporal trends in critical events complicating HIV infection: 1999–2010 multicentre cohort study in France

34 ICUs (CUB-Rea Network)
6,673 HIV-infected patients
Independent predictors of in-hospital mortality

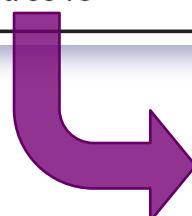
Table 3 Independent predictors of hospital mortality in critically ill HIV-infected patients: results of multivariate logistic regression analysis

Variable	OR (95 % CI)	p value
Chronic liver disease	3.4 (2.6–4.5)	<0.0001
Cancer/haematological malignancy	2.5 (2.0–3.1)	<0.0001
Medical versus surgical admission	5.0 (3.6–7.0)	<0.0001
Delayed (>24 h) versus direct admission	1.7 (1.5–2.0)	<0.0001
SAPS II >44 at ICU admission	2.4 (2.0–2.8)	<0.0001
Admission for cardiac arrest	5.1 (3.1–8.2)	<0.0001
Cytomegalovirus infection ^a	1.7 (1.2–2.5)	0.006
Aspergillosis ^a	3.2 (1.5–6.9)	0.003
Cryptococcosis ^a	4.0 (2.2–7.2)	<0.0001
Invasive candidiasis ^a	2.4 (1.4–4.1)	0.002
Mechanical ventilation during the ICU stay	3.5 (2.9–4.2)	<0.0001
Vasopressors use during the ICU stay	4.4 (3.7–5.2)	<0.0001
Renal replacement therapy during the ICU stay	2.1 (1.7–2.5)	<0.0001



Initiation d'un premier traitement ARV / avril 2018

IO	Délai préférable d'introduction des ARV par rapport à l'initiation du traitement de l'IO	Force de la recommandation
Tuberculose (sauf méningite)		
CD4 < 50/mm ³	≤ 2 semaines	AI
CD4 > 50/mm ³	2 à 4 semaines	AI
Méningite tuberculeuse	Amélioration clinique et biologique de la méningite ; ≥ 4 semaines	BIII
Cryptococcose neuroméningée *		
traitement comprenant de l'amphotéricine B	≥ 4 semaines	AII
traitement ne comportant pas d'amphotéricine B	Fin du traitement d'attaque	BIII
Autres IO	≤ 2 semaines	AI



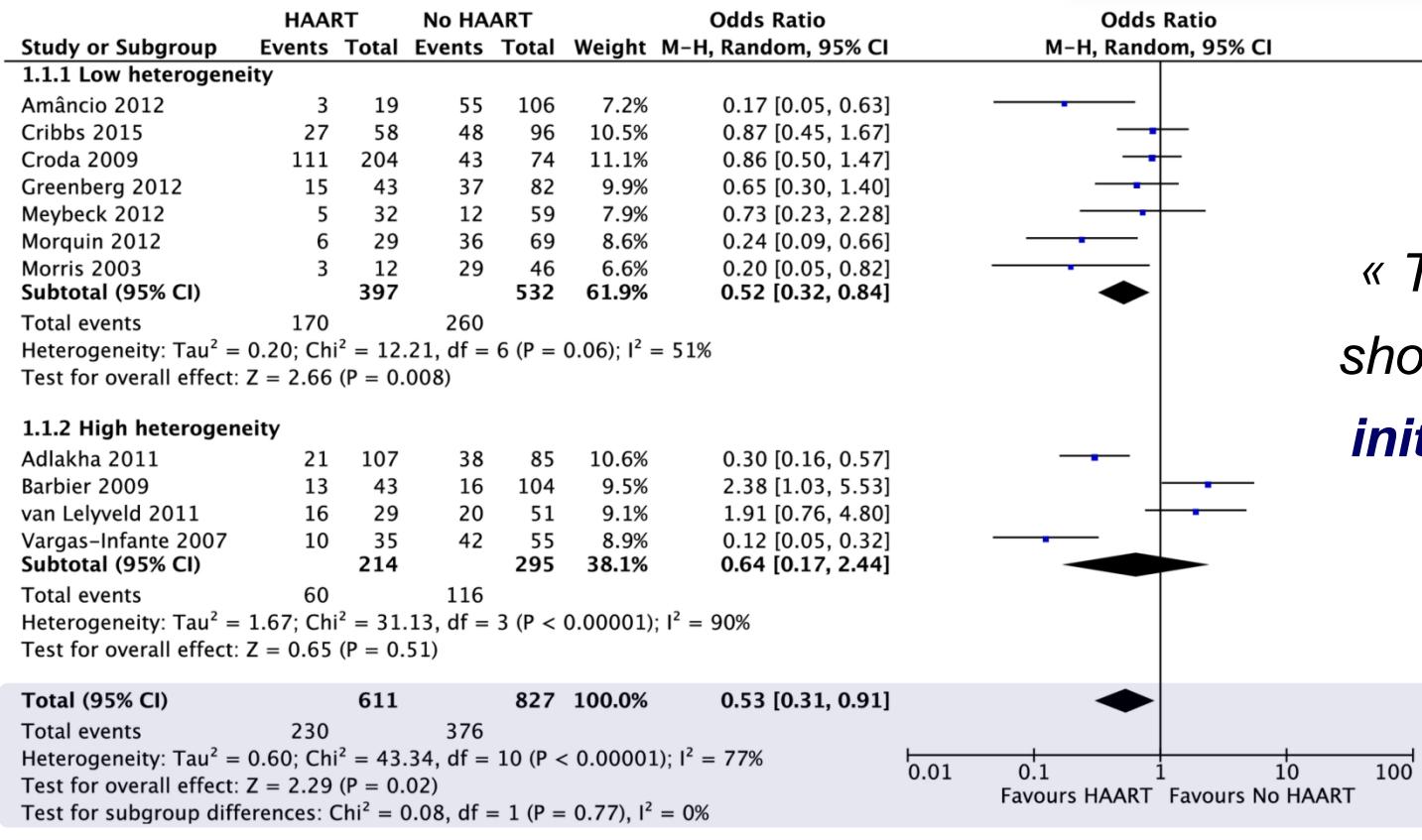
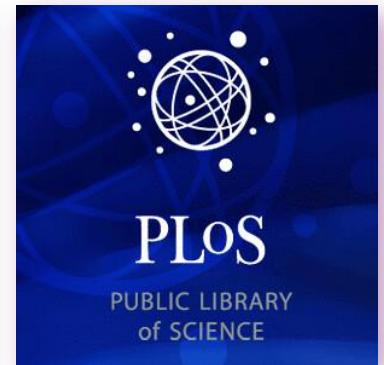
PCP, toxoplasmose, CMV,
HSV, IO sans traitement spécifique

**PRISE EN CHARGE
MÉDICALE DES PERSONNES
VIVANT AVEC LE VIH**
RECOMMANDATIONS DU GROUPE D'EXPERTS
Sous la direction du Pr Philippe Morlat
et sous l'égide du CNS et de l'ANRS



Highly active antiretroviral therapy for critically ill HIV patients: A systematic review and meta-analysis

PLoS ONE 12(10): e0186968.



« *The short-term mortality meta-analysis showed a significant beneficial effect of initiating or maintaining HAART during the ICU stay (OR 0.53, p = 0.02).* »

Fig 2. Forest plot of the effects of highly active antiretroviral therapy (HAART) on short-term mortality-random effects odds ratio.

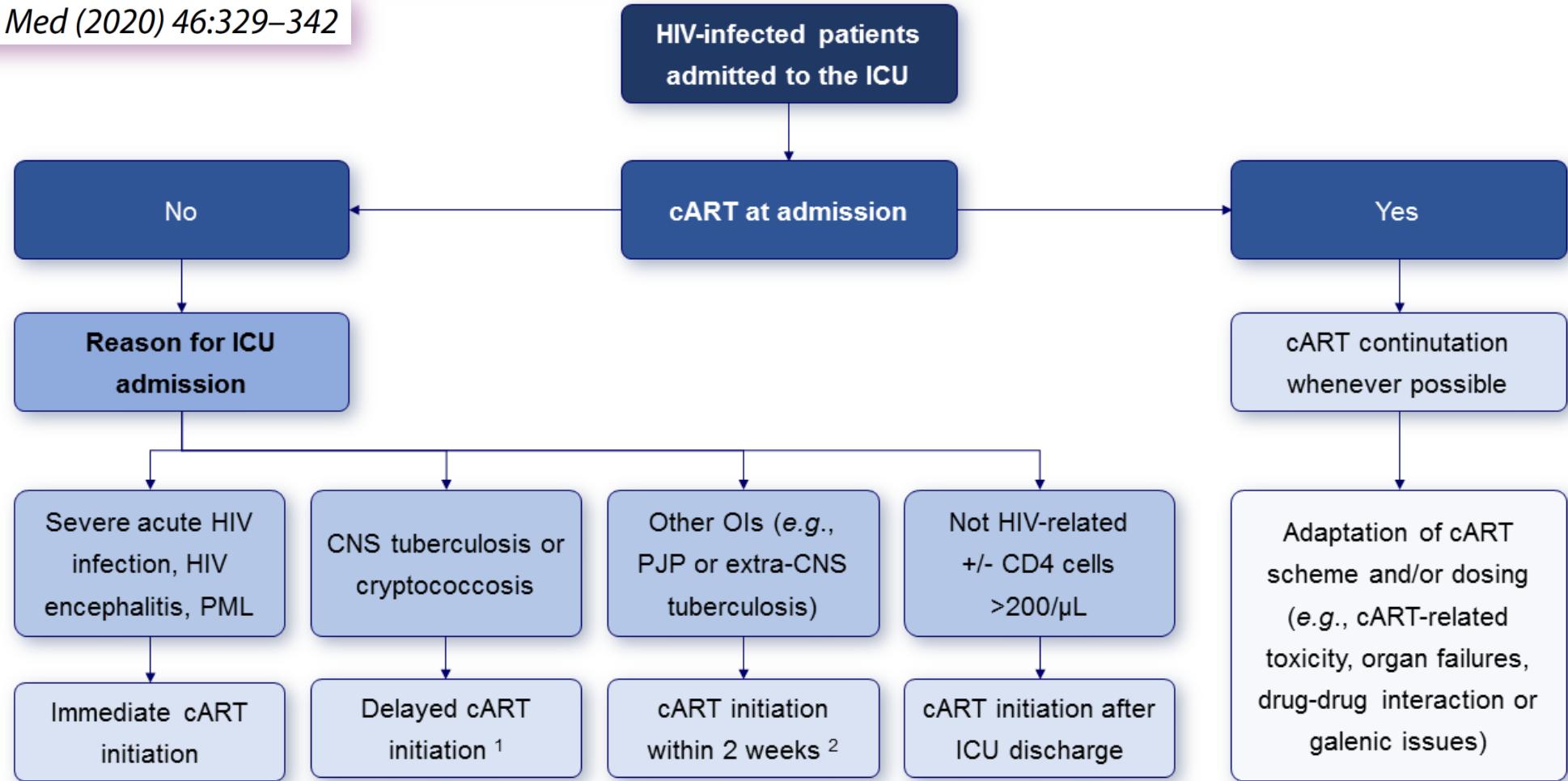


Management of HIV-infected patients in the intensive care unit

François Barbier^{1*} , Mervin Mer^{2,3}, Piotr Szychowiak¹, Robert F. Miller⁴, Éric Mariotte⁵, Lionel Galicier⁶, Lila Bouadma^{7,8}, Pierre Tattevin⁹ and Élie Azoulay^{5,10*}

Intensive Care Med (2020) 46:329–342

Initiation d'un traitement ARV : algorithme proposé en réanimation (absence de guidelines)



Critically Ill Patients With HIV

40 Years Later

Élie Azoulay, MD, PhD; Nathalie de Castro, MD, PhD; and François Barbier, MD, PhD



CHEST 2020; 157(2):293-309

IRA chez le patient VIH+ : situation relativement fréquente en réanimation

Principale cause : pneumonies bactériennes (30-50%)

Augmentation des admissions pour IRA non liées au SIDA (population vieillissante, comorbidités, ARV $\geq 70\%$) : BPCO, néoplasies, HTAP, IC

Chez les patients avec CD4 < 200/mm³ :

- 1- PCP : principale étiologie (inaugurale ou non compliance ARV/prophylaxie)
- 2- Plusieurs IO peuvent coexister+++ (LBA « complet », TDM thoracique)



Critically Ill Patients With HIV 40 Years Later

Élie Azoulay, MD, PhD; Nathalie de Castro, MD, PhD; and François Barbier, MD, PhD



CHEST 2020; 157(2):293-309

Amélioration du pronostic à court terme lié aux progrès généraux de la réanimation, et non à l'amélioration de la prise en charge spécifique

CD4, charge virale, SIDA, ARV avant réanimation : pas d'impact indépendant sur la mortalité hospitalière

Hors sepsis grave (?) : **pronostic à court terme comparable à celui d'un patient séronégatif à âge, comorbidités et défaillances d'organes identiques**

Pronostic à long terme mal connu (bénéfice d'une introduction précoce des ARV si IO évolutive – interactions avec infectiologues+++)

