



COREVIH
ILE-DE-FRANCE NORD

Tabac et VIH : Risques et prévention



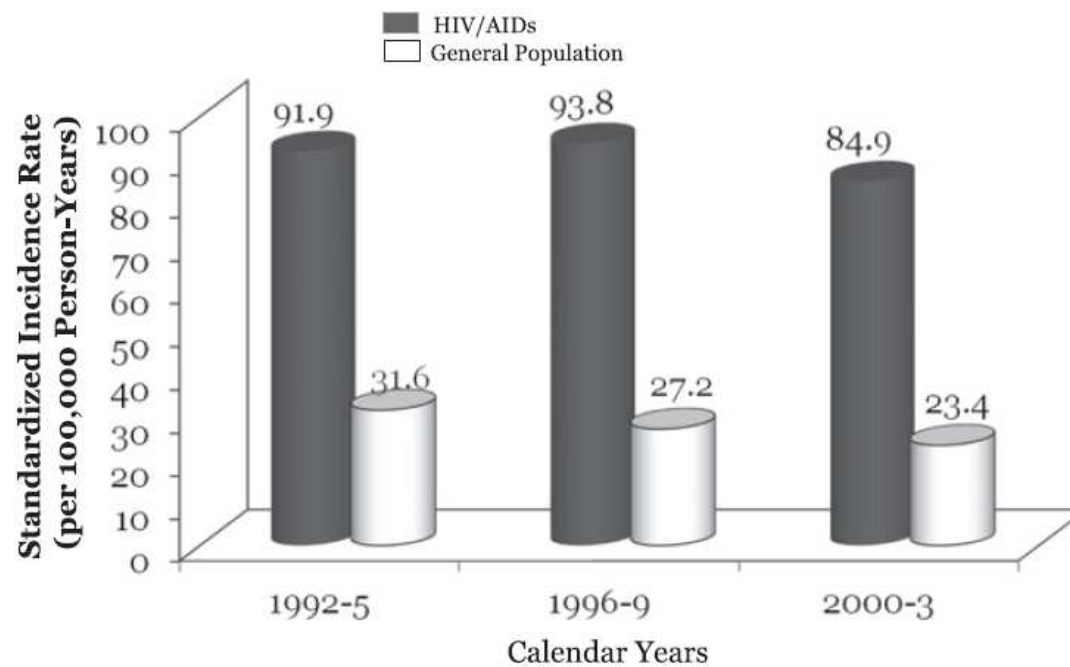
Quels risques pulmonaires et respiratoires spécifiques ?

Christos Chouaid

CHI Créteil, Paris XII



Epidemic of Lung Cancer in Patients With HIV Infection



Study	Study Duration	Location	SIR	95% CI
Crulich et al ²⁹	1980-1993	Australia	3.8	1.39-8.29
Cooksley et al ³⁰	1975-1994	Texas	0.7	0.4-1.1
Gallagher et al ³¹	1981-1994	New York	3.3	2.86-3.75
Parker et al ¹³	1990-1995	Texas	6.5	4.5-8.9
Frisch et al ⁸	1978-1996	11 US areas	4.5	4.2-4.8
	1978-1996	...	2.8	2.4-3.1
Crulich et al ²⁹	1985-1999	Australia	1.44	0.84-2.30
Herida et al ³²	1996-1999 (men)	France	2.12	1.67-2.65
	1992-1995 (men)	...	1.13	0.71-1.72
	1996-1999 (women)	...	6.59	3.40-11.52
	1992-1995 (women)	...	1.08	0.01-5.98
Hessol et al ³³	1990-2000	San Francisco, CA	2.6	2.1-3.2
Engels et al ³	1980-1989	11 US regions	2.5	1.9-3.3
	1990-1995	...	3.3	2.9-3.8
	1996-2002	...	2.6	2.1-3.1
Bower et al ¹⁵	1986-1996	England	0.8	0.2-1.4
	1997-2002	...	6.7	3.5-9.9
Engels et al ³⁴	1991-2002	Multiple US areas	2.6	2.1-3.1
Clifford et al ³⁵	1985-2003	Switzerland	3.2	1.7-5.4
Patel et al ⁹	1992-1995	13 US areas	SRR = 3.5	2.5-4.9
	1996-1999	...	SRR = 3.8	2.8-5.0
	2000-2003	...	SRR = 3.6	2.8-4.6
Dal Maso et al ³⁶	1986-1996	Italy	2.1	1.2-3.3
	1997-2004	...	4.1	2.9-5.5
Bedimo et al ³⁷	1997-2004	United States	IRR = 2.0	1.8-2.2
Long et al ⁴	1996-2005	Baltimore, MD	5.5	3.7-8.0
Guiguet et al ²⁸	1998-2006 (CD4 count > 500)	France	RR = 1.0	...
	1998-2006 (CD4 count 350-499)	...	RR = 2.2	1.3-3.6
Powles et al ⁶	1983-1995	Europe	0	0.00-1.52
	1996-2001	...	3.1	1.34-6.11
	2002-2007	...	2.37	1.14-4.36
Silverberg et al ³⁸	1996-2007	California	RR = 1.9	1.4-2.5
Shiels et al ³⁹	1996-2007	Multiple US areas	3	2.8-3.2
Engsig et al ²⁵	1995-2009	Denmark	IRR = 2.38	1.61-3.53
Crulich et al ^{29, a}	1978-2003	Meta-analysis	2.72	1.91-3.87
Shiels et al ^{9, a}	1981-2005	Meta-analysis	2.6	2.1-3.1
Chaturvedi et al ^{40, b}	1980-2002 (-6 to +6 mo AIDS onset)	11 US regions	3.8	3.6-4.1
	1980-2002 (-6 to +3 mo AIDS onset)	...	10.5	9.7-11.4
Kirk et al ^{41, b}	1988-2003	Baltimore, MD	HR = 3.6 (risk of death)	1.6-7.9
Engels et al ^{18, b}	1989-2003	Baltimore, MD	SIR = 2.5	1.6-3.5
Shiels et al ^{42, b}	1988-2007	Baltimore, MD	HR = 2.3 (risk of lung cancer)	1.1-5.1
		...	HR = 3.8 (risk of death)	0.92-15

Table 1—The Clinical Characteristics of Individuals With HIV Infection and Lung Cancer

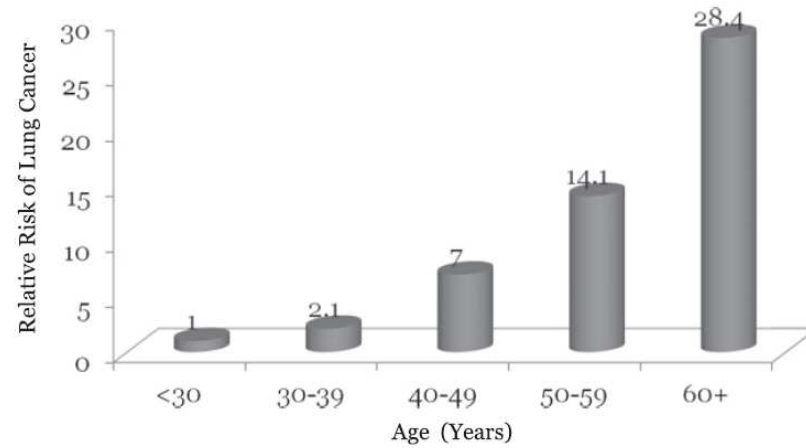
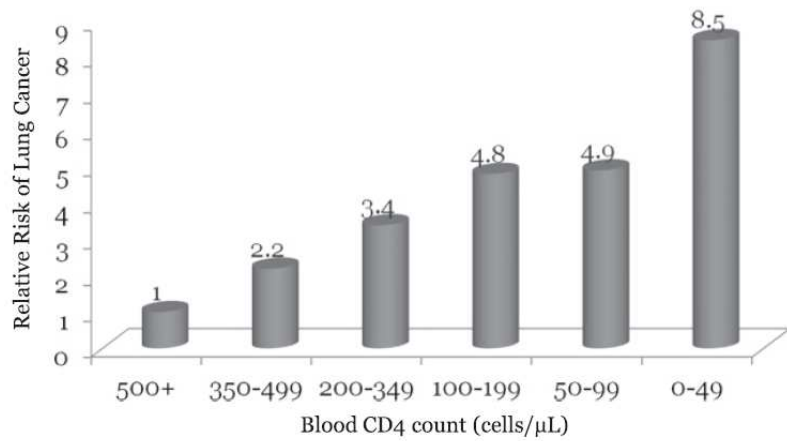
Study	Study Period	Sample Size	No. With Lung Cancer	Average Age, y	Male Sex, %	Smoker, %	IVDU, %	cART, %	CD4 Count, cells/ μ L	Histology (% of Total)	Stage (% of Total)	Survival, mo
Karp et al ¹⁰	1983-1991	205	7	38	86	100	100	0	N/A	Adeno (100)	IV (100)	1
Sridhar et al ¹¹	1986-1991	1,336	19	47	100	N/A	21	0	121	Adeno (42)	IV (58)	3
Alshafie et al ²	1990-1994	127	11	50	82	90	82	N/A	329	Adeno (45)	IV (45)	3
Vyzula and Remick ¹²	1988-1995	N/A	16	45	94	N/A	63	0	184	Adeno (50)	N/A	5.4
Parker et al ¹³	1990-1995	26,181	36	49	97	N/A	N/A	0	N/A	Adeno (33)	IIIB/IV (89)	N/A
Tirelli et al ¹⁴	1986-1998	138	36	38	89	N/A	69	8	150	Adeno (42)	IV (55)	5
Bower et al ¹⁵	1986-2001	8,400	11	45	91	N/A	N/A	55	160	Adeno (45)	IV (54)	2
Spano et al ¹⁶	1993-2002	N/A	22	45	86	N/A	23	N/A	364	Squamous(50)	III/IV (75)	7
Powles et al ¹⁷	1996-2002	36	9	45	N/A	N/A	N/A	N/A	160	Adeno(66)	IV (66)	4
Engels et al ¹⁸	1989-2003	5,238	33	46	67	69	57.5	57.1	> 200	Adeno(48)	N/A	N/A
Hakimian et al ¹⁹	1996-2003	N/A	34	44	68	N/A	86	60	> 200	NSCLC (88)	IV (53)	8.2
Brock et al ²⁰	1986-2004	5,065	92	46	67	89	58	62	305	Adeno (48)	IV (69)	6.3
Lavol� et al ²¹	1996-2007	5,170	49	46	86	N/A	35	73	350	Adeno (67)	III/IV (84)	8.1
Bertolaccini et al ²²	2003-2007	N/A	26	39	85	N/A	58	85	143	NSCLC (81)	IV (33)	23
Pakkala et al ²³	1995-2008	N/A	80	52	80	N/A	25	55	304	Adeno (38)	IV (49)	6.1
D'Jaen et al ²⁴	1996-2008	36,569	75	50	83	76	30	80	340	Adeno (46)	IIIB/IV (77)	9
Engsig et al ²⁵	1995-2009	5,053	29	57	93	71	10	69	299	Squamous (28)	N/A	2
Ruiz ²⁶	2002-2009	2,060	16	49	69	N/A	N/A	100	211	Adeno (67)	IIIB/IV (85)	N/A
Clifford et al ²⁷	1985-2010	405	68	50	79	73	37	74	N/A	Adeno (32)	N/A	N/A

Adeno = adenocarcinoma; cART = combination antiretroviral therapy; IVDU = IV drug use; N/A = not available; NSCLC = non-small cell lung cancer.



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Theory	Mechanisms	Key References
Direct oncogenic effect of HIV	Virus-inducing microsatellite alterations and widespread genomic instability. <i>Tat</i> , an essential gene for HIV-1 replication, increases expression of protooncogenes and proliferation of the human adenocarcinoma cell line by downregulating tumor suppressor gene p53. Downregulation of HIV <i>Tat</i> -interacting protein (TIP30) has been found to promote metastasis of lung cancer.	Wistuba et al ⁴³ el-Solh et al ⁴⁴ Baker et al, ⁴⁵ Tong et al ⁴⁶
HIV-induced immunosuppression	Conflicting evidence, wherein immunosuppression may lead to a reduction in tumor surveillance, thus enabling tumor growth.	Bower et al, ¹⁵ Engels ⁴⁷
Chronic inflammation	Chronic inflammation has been recognized as a risk factor for lung cancer. Individuals with HIV infection and chronic pneumonia and asthma are at higher risk of lung cancer. The rate of pneumonia is nearly six times higher in patients with HIV infection and CD4 counts > 500 cells/ μ L than in control subjects without HIV.	Engels ⁴⁸ Shebl et al, ⁴⁹ Kirk et al ⁴¹ Sogaard et al ⁵⁰
Cigarette smoking	Smoking is an independent risk factor for lung cancer in individuals with HIV infection. Smoking is two to three times more prevalent among individuals with HIV infection than in the general population.	Guiguet et al ²⁸ Engels et al, ¹⁸ Giordano and Kramer ⁵¹
IV drug use	IV drug users with HIV infection have an increased risk of lung cancer compared with nonusers with HIV.	Serraino et al ⁵²

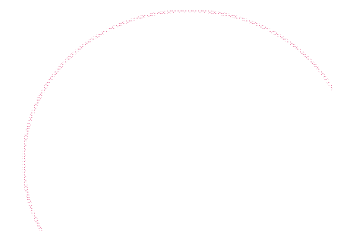
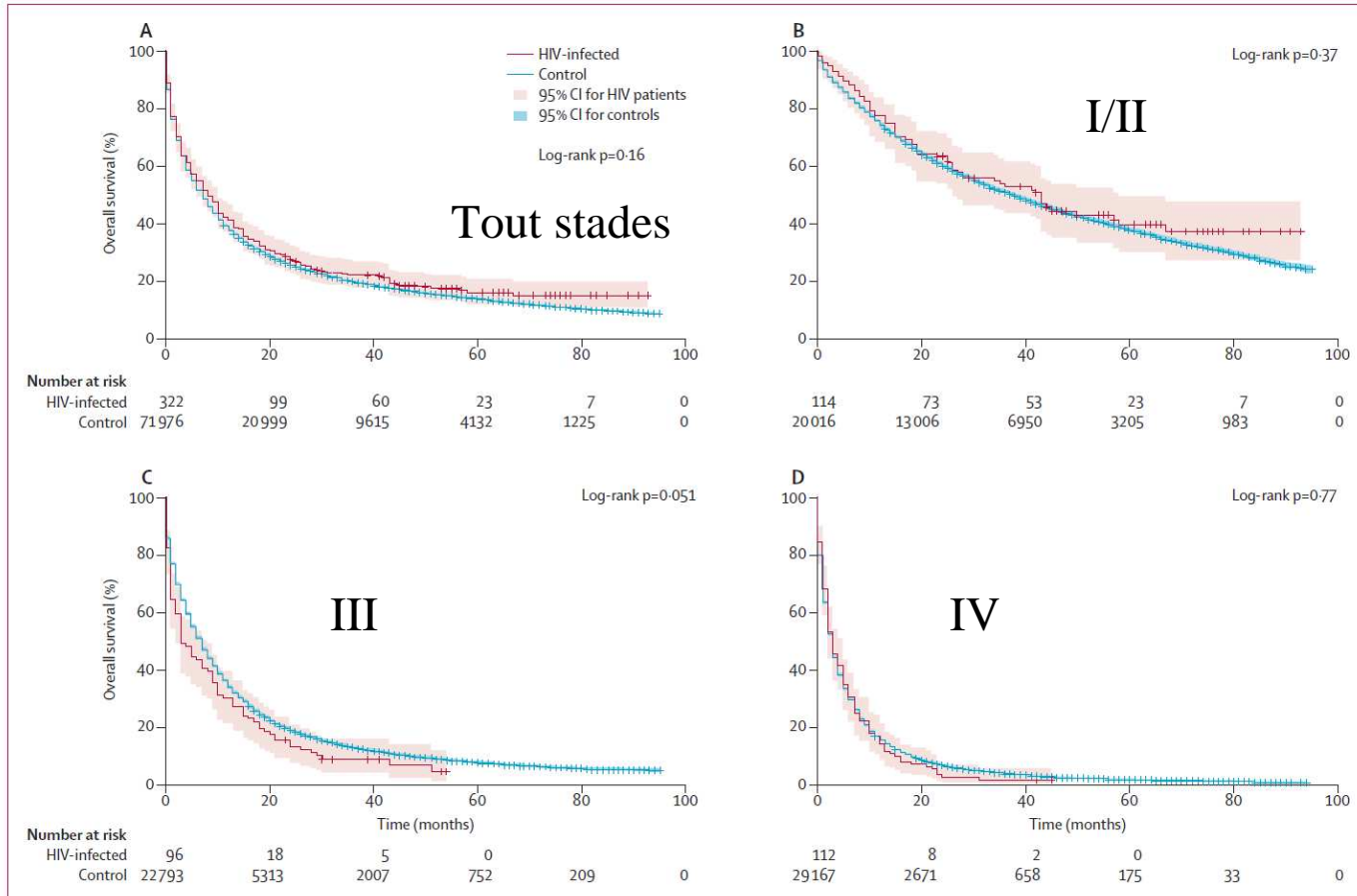


	HIV+ (n=322)	%	Control (n=71 976)	%	χ^2 p value
Stage I/II	114	35.40%	20 016	27.81%	0.002
Stage IIIA/IIIB	96	29.81%	22 793	31.67%	0.48
Stage IV	112	34.78%	29 167	40.50%	0.04
Median age (IQR)	75 (69–81)		75 (69–81)		0.99
Race					
White	231	71.74%	62 859	87.33%	<0.0001
African American	76	23.60%	6 056	8.41%	<0.0001
Other	15	4.66%	3 061	4.25%	0.72
Comorbidities					
0	16	4.97%	6 164	8.56%	0.02
1	28	8.70%	11 660	16.20%	0.0003
2 or more	278	86.34%	54 152	75.24%	<0.0001
Median income in bottom two quartiles (range in US dollars)	139	43.17 (7–32 492)	33 117	46.01 (7–32 492)	0.65

Table: Patient characteristics

Programme SEER – 1 Janv 2000 – 31 decembre 2005

Ramesh Rengan, *Lancet Oncol* 2012; 13: 1203-09





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Stade I/II vers III/IV

Etat général

Patient sous ARV

CD 4 ?



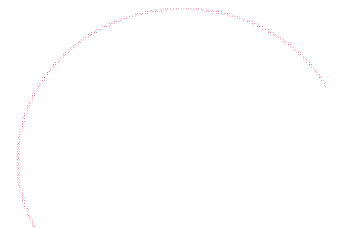


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Sevrage tabagique +++

Surveillance pulmonaire rigoureuse = diagnostic
précoce

**Early Lung Cancer Diagnosis in HIV Infected Population With an Important
Smoking History With Low Dose CT: a Pilot Study (EP48 HIV CHEST)**





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Identique à la population générale

Tenir compte des co morbidités

Chimiothérapie moins bien toléré, plus de complication

Essai de phase II évaluant l'efficacité et la tolérance de l'association carboplatine-pemetrexed stade III /IV





Year of publication	First author Reference	Study period	Type of study	Focus	Number of patients	Main findings
1993	Moscato G [12]	NR	"One day" Case-control	Bronchial hyper-responsiveness	25 (25 controls)	Prevalence of bronchial hyper-responsiveness identical in the two populations
1997	Wallace JM [11]	1988-1994	Cohort Case-control	Bronchial hyper-responsiveness	62 (62 controls)	Prevalence of bronchial hyper-responsiveness identical in the two populations
2001	Poirier CD [10]	1995-1996	prospective Case-control	Bronchial hyper-responsiveness	248 (236 controls)	Prevalence of bronchial hyper-responsiveness identical in the two populations Among smokers, bronchial hyper-responsiveness more frequent in HIV-infected men than in controls
2003	Diaz PT [13]	1993-1998	Cohort Case-control	Chronic bronchitis	327 (52 controls)	Chronic bronchitis more frequent in HIV-infected patients than in controls (26.9% versus 13.5%, $p < 0.05$)
1998	Shaw RJ [16]	NR	Prospective? descriptive	Airway obstruction	34	Lung infections (PCP, bacterial pneumonia) associated with lower FEV ₁ and peak flow rates
1988	O'Donnell CR [14]	1983-1986	Retrospective?	Airway obstruction	99 (AIDS)	Estimated prevalence of lower forced expiratory. flow rates: 33%
1999	Gelman M [15]	NR	Prospective Case-control	Air trapping/CT	48 (11 controls)	Degree of air trapping correlated with duration of HIV infection
2000	Hnizdo E [18]	1995-1996	Cohort Case-control	Impairment of lung function and tuberculosis	305 (1038 controls)	Functional respiratory decline due to tuberculosis not aggravated by HIV co infection
2000	Morris AM [17]	1988-1994	Cohort descriptive	Airway obstruction	141	Acceleration of decline in FEV ₁ , FVC and FEV ₁ /FVC, for several months after acute episode
1989	Kuhlman JE [21]	NR	Retrospective descriptive	Emphysema CT findings	55	CT signs of emphysema, bullous lesions and cysts in 42% of cases
1996	Guillemi SA [22]	NR	Prospective descriptive	Emphysema CT findings	32	CT signs of emphysema in 31% of cases
1999	Diaz PT [20]	NR	Prospective Case-control	Emphysema	96 (30 controls)	CT signs of emphysema in 50% of cases in patients with reduced D _{L, CO}
2000	Diaz PT [23]	1994-1997	Prospective Case-control	Emphysema	114 (44 controls)	Increased incidence of emphysema in the HIV-infected population (15% versus 2% in controls ($p = 0.025$)).
1993	Nieman RB [25]	1986-1991	Cohort descriptive	T _{L, CO}	84 (AIDS)	Decline in T _{L, CO} significantly associated with more rapid progression to AIDS
1993	Mitchell DM [27]	NR	Cohort descriptive	D _{L, CO}	474	D _{L, CO} decline in case of acute respiratory disease. Decline not specific for PCP diagnosis.
1995	Rosen MJ [29]	1988-1994	Prospective Case-control	D _{L, CO}	1127 (167 controls)	CD4 < 200/mm ³ , ethnic origin, smoking, IV drug use associated with D _{L, CO} decline



Year of publication	First Author reference	Study period	Type of study	Focus	Number of patients	Main findings
2005	Crothers K [32]	1999-2000	Observational study prospective cohort	Respiratory symptoms	867	Smoking associated with increase in respiratory symptoms; cough and dyspnea found in 44% of smokers and 25% of non smokers
2006	Crothers K [31]	2001-2002	Observational study Prospective Case-control Cohort	COPD (self-assessment and coding data)	1014 (713 controls)	Self-assessment: prevalence of COPD significantly higher in HIV-infected patients (15% vs 12%, p = 0.04); HIV infection = independent risk factor for COPD
2009	George MP [33]	2003-2004	Observational study Prospective	Respiratory symptoms. airway obstruction	234	Prevalence of airway obstruction: 6.8%. Age, pack-years, history of bacterial pneumonia and HAART = independent risk factors for airway obstruction
2009	Morris A [43]	NR	Observational study Prospective	<i>Pneumocystis</i> colonization and airway obstruction	42	Colonization by <i>Pneumocystis jirovecii</i> (26% of cases) associated with increase in airway obstruction and sputum metalloprotease (MMP 12) levels
2010	Drummond MB [36]	1988-?	Observational study Prospective Cohort Case-control	Respiratory symptoms. Airway obstruction	288 (686 controls)	Prevalence of airway obstruction: 15.5%. No influence of HIV status
2010	Cui Q [35]	NR	Observational study Prospective	Respiratory symptoms. Airway obstruction	119	No acceleration of FEV ₁ decline relative to published data for general population
2010	Gingo RM [34]	2007-2009	Cross-sectional analysis	Airway obstruction	167	64% of patients had impaired diffusion. 21% of patients had irreversible airway obstruction. Irreversible airway obstruction was independently associated with HAART, pack-years smoked and intravenous drug use.
2011	Crothers K [37]	1999-2007	Observational study prospective Cohort Case-control	Coding data	3707 (9980 controls)	HIV-infected patients more likely to have diagnoses of COPD (20.3 per 1000 person-years versus 17.5 per 1000 person-years - p < 0.001).



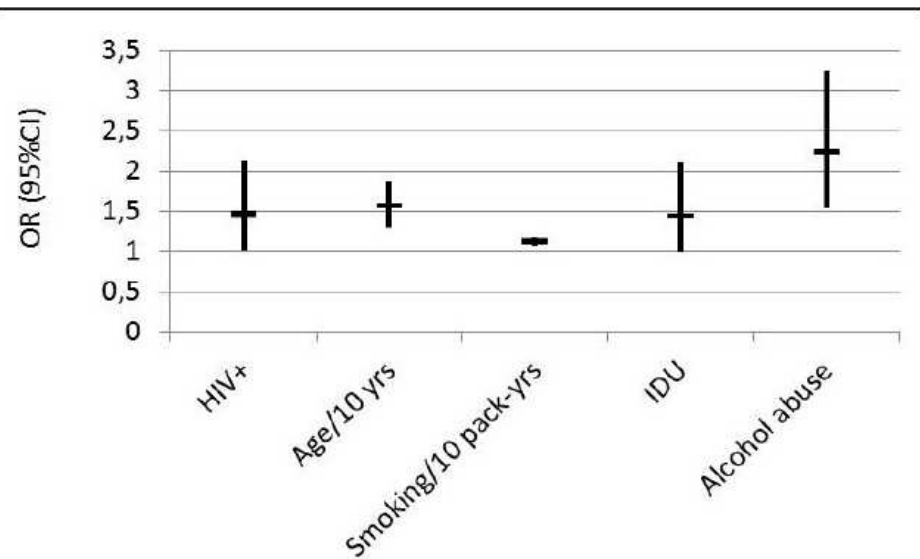


Figure 1 Predictors of COPD (OR with 95%CI) for some of the risk factors identified (using ICD-9 codes) in multivariate analysis as independently associated with a diagnosis of chronic airflow obstruction, among 1014 HIV-positive and 713 HIV-negative US veterans [31].



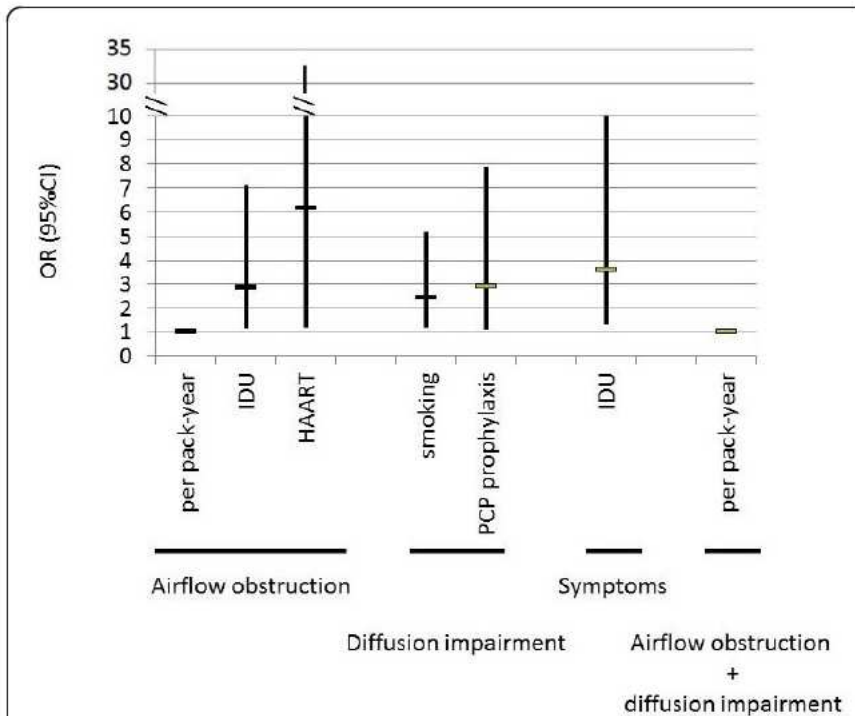


Figure 2 Predictors of COPD (OR with 95%CI) for risk factors independently associated with airflow obstruction, diffusion impairment, both, and symptoms in a cohort of 167 HIV-infected subjects [34]. Age/10 y: age in ten-year periods. Smoking/10 pack-years: smoking per ten pack-years.

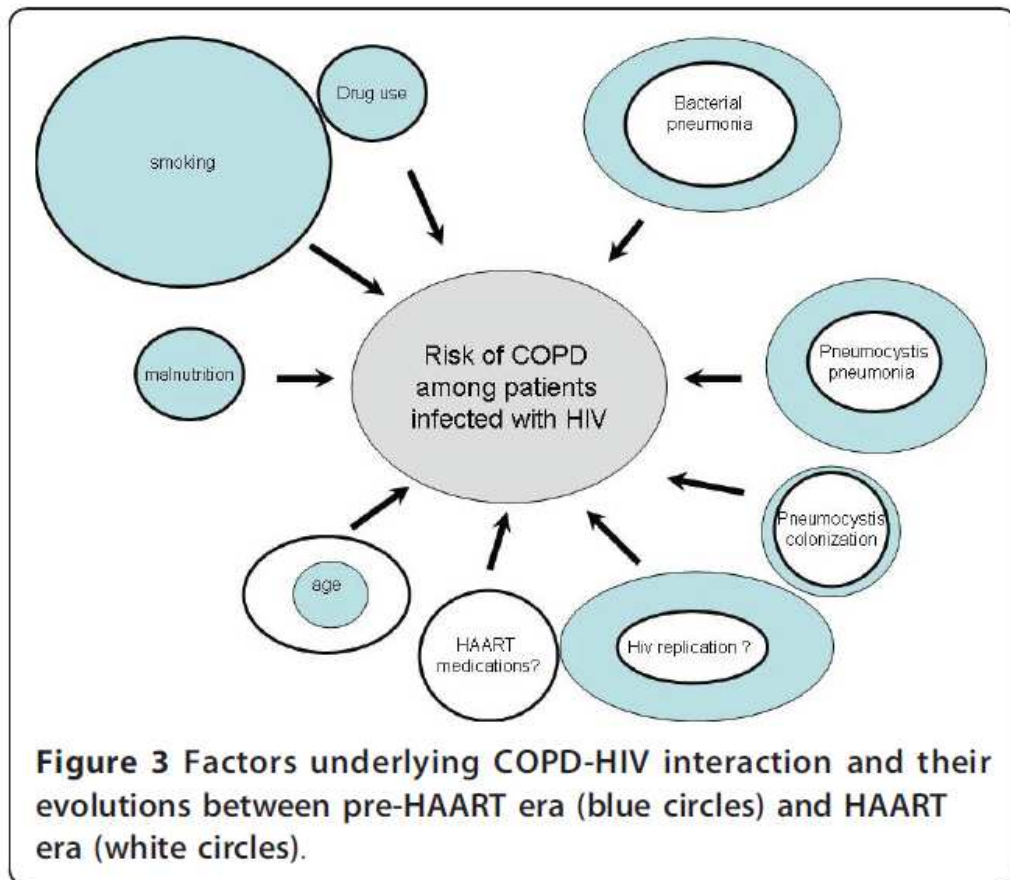
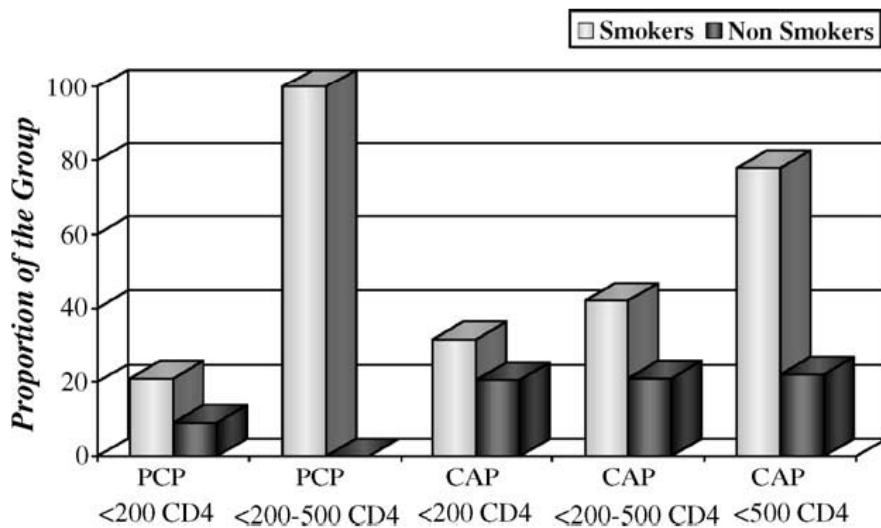


Figure 3 Factors underlying COPD-HIV interaction and their evolutions between pre-HAART era (blue circles) and HAART era (white circles).

Table 1 Study group characteristics.

Variables	Smokers (<i>n</i> = 328)	Non-smokers (<i>n</i> = 193)
Gender		
Men (<i>n</i> = 300)	197	103
Women (<i>n</i> = 221)	131	90
Race/ethnicity		
African Americans	74%	26%
Haitians	19%	81%
Hispanics	61%	39%
Caucasians	95%	5%
Asian	0	100%*
Substance use		
Alcohol users	52%	31%
Crack/cocaine	40%	10%
Marijuana	26%	6%
Heroin	2%	0%
Years living with HIV (<i>n</i> = years)	8 ± 6	5.7 ± 5.5
CDC classification		
HIV	17%	22%
AIDS	83%	78%



	Wald	Odds ratio	Significance <i>p</i> -value
Tuberculosis			
Smoking	0.728	1.309	0.394
CD4	3.960	2.377	0.047
PCP			
Smoking	14.159	3.500	0.000
CD4	11.899	6.458	0.001
Pneumonia			
Smoking	12.586	2.278	0.000
CD4	0.206	1.118	0.650



(2005) 9, 208–217



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Le tabac n'est jamais le facteur unique MAIS

- incidence plus élevée de cancers du poumon

- incidence plus élevée de BPCO et infections type PCP

Le sevrage reste une priorité

