COMORBIDITIES IN PATIENTS LIVING WITH HIV (PLWHIV) COMPARED TO MATCHED NON HIV CONTROLS: AN EPIDEMIOLOGICAL ANALYSIS USING A CLAIMS DATABASE IN FRANCE

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Background and objective

- Improvements in diagnosis and care, including the development of antiretroviral therapies (ART), has increased the life expectancy of people living with HIV (PLWHIV).

- For over the past ten years several studies have assessed the epidemiology of comorbidities in PLWHIV; however a gap remains to see the prevalence of these comorbidities when compared to a control group (non-HIV infected).

- The assessment of comorbidities becomes more important in a context of ageing PLWHIV populations. Exposure to certain ART is associated with many of these age-related comorbidities.

- We aimed to assess the current prevalence of comorbidities and their costs on PLWHIV and compare to a matched control group of people non infected with HIV.

Methods

This study is based on the analysis of the French claims EGB ("Echantillon Général des Bénéficiaires") database, which contains records of healthcare items reimbursed by Public Insurance schemes.

In this database, a retrospective cohort of PLWHIV diagnosed in 2011 and followed between 2011 and 2014 was extracted. HIV diagnosis was considered taking into account:

- ICD-10 codes related to HIV infection (B20, B21, B22, B23, B24, F02.4, Z21)
  - ✓ During hospital stay in 2011 or
  - ✓ For specific severe costly chronic disease in 2011
- The delivery for a drug specific to HIV in 2011
- A biology test specific to HIV: 0805 or 0806 (genotypic resistance testing)

Only patients with full follow-up in the database and patients who died within the period were included.

Each PLWHIV was matched to 2 non-HIV controls via a direct matching approach taking into account for 2011:

- Age
- Gender
- Place of residence (regional areas)
- Socioeconomic status, assessed by the advantage of the Universal Health Coverage (CMUc)

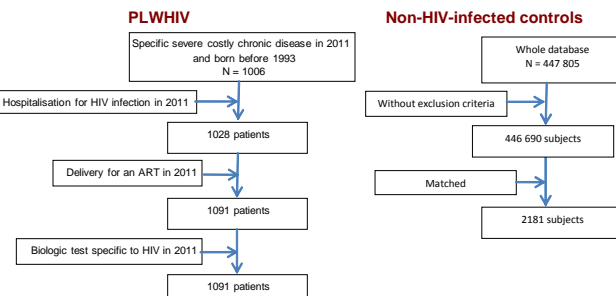Comorbidities were defined by the report of:

- A specific ICD-10 diagnosis during a hospitalization or for severe costly chronic disease
- The delivery of a specific drug in the time period (2011 to 2014)

Additionally, the most frequent 50 comorbidities in PLWHIV were identified and compared to matched controls.

The total direct costs (including reimbursed and non-reimbursed costs within ambulatory costs, transportation, pharmaceutical costs and hospitalization costs) were determined for 2014 or for the last 12 months of follow-up in patients who died during the considered study period.

A multivariate model (log-link function, gamma distribution, backward selection based on AIC) was used to assess the association of healthcare costs (without cost of ART) with comorbidities in PLWHIV.

Figure 1: Flowchart of the selection

PLWHIV
- Specific severe costly chronic disease in 2011 and born before 1993 N = 1006
- Hospitalisation for HIV infection in 2011
- 1028 patients
- Delivery for an ART in 2011
- 1091 patients
- Biologic test specific to HIV in 2011
- 1091 patients

Non-HIV-infected controls
- Whole database N = 447 805
- Without exclusion criteria
- 446 690 subjects
- Matched
- 2181 subjects

Patients characteristics

- In the PLWHIV group, the mean age in 2011 was 46.7 years, 68.8% were male and 15.6% had a low socioeconomic status.

- In the control group, before matching, the mean age in 2011 was 49.7 years, 48.7% were male and 6.3% had a low socioeconomic status.

For characteristics of the matched sample see Table 1.

Table 1: Socio-demographic description of PLWHIV and matched controls

After matching	2011		2014	
	PLWHIV	Matched controls	PLWHIV	Matched controls
	1,091	2,181	1,052	2,151
Sex male	751 (68.8%)	1,502 (68.9%)	718 (68.3%)	1,476 (68.6%)
Age in 2011: mean (SD)	46.7 (11.5)	46.6 (11.5)	49.4 (11.5)	49.4 (11.4)
Age in 2011				
[18-30] years	70 (6.4%)	140 (6.4%)	39 (3.7%)	78 (3.6%)
[30-39] years	226 (20.7%)	452 (20.7%)	169 (16.1%)	342 (15.9%)
[40-49] years	403 (36.9%)	806 (37.0%)	344 (32.7%)	702 (32.6%)
[50-59] years	250 (22.9%)	500 (22.9%)	326 (31.0%)	667 (31.0%)
[60-69] years	101 (9.3%)	201 (9.2%)	121 (11.5%)	261 (12.1%)
>= 70 years	41 (3.8%)	82 (3.8%)	53 (5.0%)	101 (4.7%)
Low socioeconomic status	170 (15.6%)	334 (15.3%)	141 (13.4%)	239 (11.1%)
Time since onset of full coverage for HIV (years): mean (SD)	10.2 (6.2)	NA	13.0 (6.4)	NA

By the end of 2014 the proportions of subjects still alive were:
- 96% (CI95%=[94%; 97%]) in the PLWHIV group
- 98% (CI95%=[97%; 99%]) in the control group

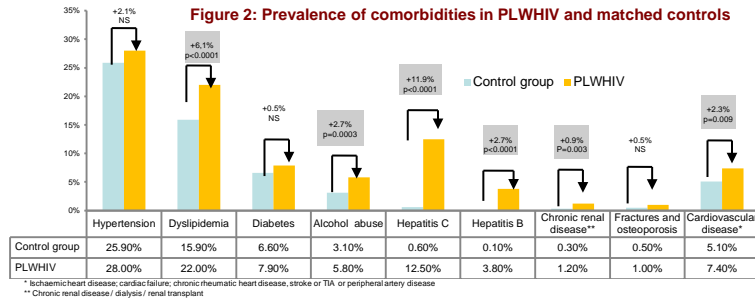The differences are statistically significant (p<0.001).

Comorbidities

The prevalence of the age-related comorbidities commonly associated with HIV (Figure 2) is significantly higher in PLWHIV patients than for matched controls:

- Dyslipidaemia (p<0.0001)
- Alcohol abuse (p=0.0003)
- Hepatitis B and hepatitis C (p<0.0001)
- Chronic renal disease (p=0.003)
- Cardiovascular disease (p=0.009)

Within cardiovascular disease, all considered conditions were more frequent in PLWHIV than in controls with peripheral artery disease reaching statistical significance:
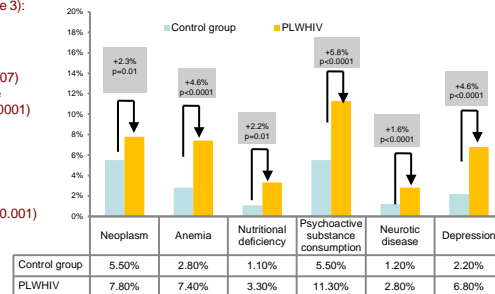
- Peripheral artery disease (2.5% vs 1.4%, p=0.02)
- Chronic rheumatic heart disease (0.3% vs 0.1%, p=0.3)
- Cardiac failure (1.6% vs 1.2%, p=0.3)
- Stroke or TIA (1,1% vs 0,7%, p=0.2)
- Ischemic heart disease (4.5% vs 3.4%, p=0.14)

Figure 2: Prevalence of comorbidities in PLWHIV and matched controls

	Hypertension	Dyslipidemia	Diabetes	Alcohol abuse	Hepatitis C	Hepatitis B	Chronic renal disease**	Fractures and osteoporosis	Cardiovascular disease*
Control group	25.90%	15.90%	6.60%	3.10%	0.60%	0.10%	0.30%	0.50%	5.10%
PLWHIV	28.00%	22.00%	7.90%	5.80%	12.50%	3.80%	1.20%	1.00%	7.40%

* Ischaemic heart disease; cardiac failure; chronic rheumatic heart disease, stroke or TIA or peripheral artery disease
** Chronic renal disease/ dialysis / renal transplant

Among the 50 most frequent comorbidities in PLWHIV the following were also found to have a statistically significantly increased prevalence when compared to matched controls (Figure 3):

- Mental diseases:
  - ✓ Depression (p<0.0001)
  - ✓ Neurotic, stress-related and somatoform disorders (p=0.0007)
  - ✓ Disorders due to psychoactive substance consumption (p<0.0001)
- Nutritional deficiency (p<0.0001) and anaemia (p<0.0001)
- Neoplasm (p=0.01), and among neoplasms:
  - ✓ Digestive organ neoplasm (p=0.001)
  - ✓ Lymphoid or haematopoietic neoplasm (p<0.0001)
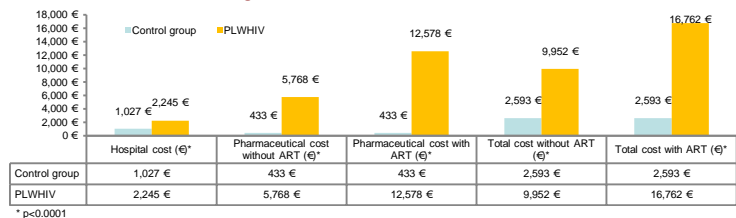 - ✓ Connective and soft tissue neoplasms (p=0.01)

Figure 3: Other comorbidities with increased prevalence in PLWHIV

	Neoplasm	Anemia	Nutritional deficiency	Psychoactive substance consumption	Neurotic disease	Depression
Control group	5.50%	2.80%	1.10%	5.50%	1.20%	2.20%
PLWHIV	7.80%	7.40%	3.30%	11.30%	2.80%	6.80%

Costs

Annual healthcare costs were significantly higher in PLWHIV than in matched controls, with 6 times higher total costs, 4 times higher total costs without ART, and 2 time higher hospital costs.

Figure 4: Costs in PLWHIV and controls

	Hospital cost (€)*	Pharmaceutical cost without ART (€)*	Pharmaceutical cost with ART (€)*	Total cost without ART (€)*	Total cost with ART (€)*
Control group	1,027 €	433 €	433 €	2,593 €	2,593 €
PLWHIV	2,245 €	5,768 €	12,578 €	9,952 €	16,762 €

* p<0.0001

A multivariate regression model was used to identify factors correlated with total costs excluding ART in PLWHIV (Table 2). The significant predictors of higher cost (incremental cost) were:

- Older age (+42€ per year)
- Metastatic carcinoma (+6,880€)
- Hepatitis C (+6,705€)
- Moderate or severe liver disease (+6,299€)
- Chronic cardiovascular disease (+3,003€)

Table 2 : Parameter estimates of the multivariate model

	Parameter estimate	p	Incremental cost	95% Confidence Interval	
				Inf	Sup
Age (in 2011)	0.014	0.003	42 €	12 €	72 €
Low socioeconomic status (ref=no)	-0.238	0.11			
Chronic cardiovascular disease (ref=no)	0.703	0.0006	3,003 €	1,143 €	6,043 €
Chronic renal disease (ref=no)	0.766	0.13			
Hepatitis C (ref=no)	1.187	<0.0001	6,705 €	3,944 €	10,927 €
Chronic Pulmonary Disease (ref=no)	0.349	0.19			
Rheumatic Disease (ref=no)	0.888	0.26			
Paraplegia and Hemiplegia (ref=no)	0.724	0.17			
Metastatic Carcinoma (ref=no)	1.205	0.016	6,880 €	1,030 €	26,599 €
Moderate/Severe Liver Disease (ref=no)	1.144	0.003	6,299 €	1,641 €	18,594 €

Conclusions

In PLWHIV, with mean age approaching 50, prevalence of relevant comorbidities such as cardiovascular and chronic renal disease are significantly higher than those of age-matched controls, together with some risk factors, neoplasms and mental conditions.

Healthcare costs of PLWHIV were significantly higher than those of matched-controls. The comorbidities that showed significant independent association with healthcare costs were chronic cardiovascular disease, hepatitis C coinfection and other moderate/severe liver diseases, and metastatic cancers.

As costly comorbidities may be associated with selected ART treatment, optimal ART regimen choice may help reduce the burden of comorbidity.

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