

# Incidence and risk factors associated with osteoporosis-related fractures among people living with HIV in British Columbia, Canada.

José Barletta<sup>1</sup>, Monica Ye<sup>2</sup>, Michelle Lu<sup>2</sup>, Mia Kibel<sup>2</sup>, Robert Hogg<sup>2</sup>, Viviane D. Lima<sup>2</sup>, Silvia Guillemi<sup>2</sup>.

<sup>1</sup>Hospital Juan A. Fernández, Buenos Aires, Argentina. <sup>2</sup>British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada.

## Background.

- Life expectancy of people living with HIV (PLWHIV) receiving antiretroviral therapy (ART) has significantly increased. Prevalence of age-related comorbidities, including bone disease, remain high in this population.
- HIV-related factors and antiretroviral drugs were found to play a role in the pathogenesis of bone disease in PLWHIV.
- We investigated incidence and risk factors of osteoporosis-related fractures (ORF) among PLWHIV in British Columbia, Canada.

## Materials and Methods.

- These analyses were based on the Comparative Outcomes and Service Utilization Trends (COAST) cohort study. COAST is a population-based retrospective cohort study examining health outcomes and service use of PLWHIV and a 10% random sample of HIV negative individuals in BC.
- We examined incidence of ORF among PLWHIV from 1996 to 2013.
- ORF were defined as fractures of the wrist, vertebrae, humerus and hip; and identified using International Classification of Diseases (ICD) 9/10 codes in physician and hospital-based administrative data.
- Age and sex adjusted incidence rates were calculated using the 2011 Canada population as reference.
- The effect of the variables on the risk of ORF was assessed by logistic generalized estimating equation (GEE) model. For the GEE model, only ORFs occurring after ART initiation were considered; sex, age at ART initiation, previous injuries, injection drug use (IDU), ART initiation era and length of time (LOT) on antiretroviral-drug classes were covariates.

**Table 1. Characteristics of study population.**

Variable	HIV-Positive (n = 6846)		HIV-Negative (n = 514,619)		p value
	n/Median	%(Q1, Q3)	n/Median	%(Q1, Q3)	
<i>Covariates</i>					
<b>Sex</b>					
Female	1320	19	255874	50	<.0001
Male	5526	81	258745	50	
<b>Age at baseline (years)</b>	37.91	(31.54, 45.3)	35.50	(23.33, 49.75)	<.0001
<b>Intravenous Drug Use</b>					
No	3765	55	505351	98	<.0001
Yes	3081	45	9268	2	
<i>Covariates related to the first ORF</i>					
	<b>N=416</b>			<b>N=28028</b>	
<b>Age at first ORF (years)</b>	46.59	(37.95, 53.47)	61.87	(42.69, 78.83)	<.0001
<50	262	63	9441	34	<.0001
≥50	154	37	18587	66	
<b>Injuries before ORF</b>					
No	310	74.5	24613	88	<.0001
Yes	106	25.5	3415	12	
<b>Mental health disorder before ORF</b>					
No	96	23	19623	70	<.0001
Yes	320	77	8405	30	
<b>Substance use disorder before ORF</b>					
No	138	33	25370	90.5	<.0001
Yes	278	67	2658	9.5	
<b>Ever on corticosteroids before ORF</b>					
No	318	76.5	22958	82	0.01
Yes	98	23.5	5070	18	

## Results.

- A total of 6,846 PLWHIV and 514,619 HIV negative individuals were included in the incidence analysis.
- ORF occurred in 416 PLWHIV and 28,028 HIV negative individuals (6.08% versus 5.45% p=0.02). PLWHIV were younger at first ORF (median age 47 years Q1-Q3 38-53 versus 62 years Q1-Q3 43-79 p<0.0001).
- Age/sex adjusted ORF incidence rate was higher among PLWHIV (14.85 versus 6.43 per 1000 person-years, adjusted incidence rate ratio 2.31 95% confidence interval 1.97-2.65).
- Higher prevalence of comorbidities previously shown to be associated with increased risk of ORF was observed among PLWHIV. Demographics and characteristics of the study population are shown in Table 1.
- In a multivariate analysis, female sex, older age at ART initiation, IDU, previous injuries and ART initiation before 2008 were associated with increased likelihood of ORF.
- Neither NNRTI or PI exposure were associated with having an ORF in our population. Cumulative exposure to NRTI's was negatively associated with having an ORF. (Table 2)

**Table 2. Multivariate Factors associated with ORF among PLWHIV after 2001.**

Variable	Odds Ratio	95% Confidence Interval
<b>Sex</b>		
Female	1.49	1.02-2.18
Male [ref]	1	
<b>Intravenous Drug Use</b>		
No [ref]	1.00	
Yes	1.89	1.26-2.84
<b>Any injuries except falls before ORF*</b>		
No [ref]	1.00	
Yes	3.83	2.60-5.64
<b>Age at ART initiation (10 Years)</b>	1.63	1.37-1.94
<b>ART initiation era</b>		
2001-2003 [ref]	1.00	
2004-2007	0.57	0.38-0.86
≥2008	0.14	0.09-0.22
<b>Length of time on NRTI until ORF (1 year)*</b>	0.75	0.69-0.82
<b>Length of time on PI until ORF (1 year)*</b>	1.07	0.98-1.17

**Note.** ORF: Osteoporosis-related Fracture. ART: Antiretroviral Therapy. NRTI: Nucleoside/Nucleotide Reverse Transcriptase Inhibitors. PI: Protease Inhibitors. \*Are time-varying variables. Injuries include motor vehicle collision, land transportation injuries, self harm and assault. Mental health disorders include schizophrenia, mood disorders, dementia. Only ORF occurring after ART initiation are considered for the multivariate analysis.

## Conclusions.

- Higher rates of ORF at an earlier age were found among PLWHIV versus HIV negative individuals.
- In our study, ORF were associated with traditional risk factors in both populations.
- PLWHIV starting ART in later eras and those with longer ART exposure were less likely to have an ORF.
- Neither Antiretroviral classes were associated with risk for ORF

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