Risk of progression to osteoporosis in HIV-infected subjects and role of protease inhibitors

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Barcelona, 15th September 2017

BACKGROUND

- Patterns of morbidity and mortality among HIV–infected individuals are changing
- Comorbidity because of non-AIDS diseases become more important in care
- Low bone mineral density (BMD), osteoporosis and fractures are more common in those living with HIV
  - Low rate of bone fracture attended in our daily clinical practice -> low sensitivity to consider the bone health?
- Osteoporosis in HIV and the epidemiology of fractures differ from the general population
  - VIH-infected people present high risk of osteoporosis due to factors related to the host and to the virus, the chronic inflammation and the antiretroviral treatment

OBJECTIVES

- To estimate the magnitude of the osteopenia and osteoporosis in HIV infected patients

- To assess
  - the evolution of BMD as a function of age
  - the effect of the antiretroviral therapy on BMD

METHODS

- Design
  - Retrospective
  - Longitudinal
  - Observational
  - DXA scans
  - HIV-infected patients with >=2 DXA
  - attended in our unit between January 1999 and December 2016

- Population
  - 3,726 DXA scans
  - 875 subjects

Bone Mineral Density (BMD)

- Dual-energy x-ray absorptiometry (DXA) test measures BMD (g/cm^2) at different parts of the body
  - Lunar Prodigy, GE Healthcare, Belgium

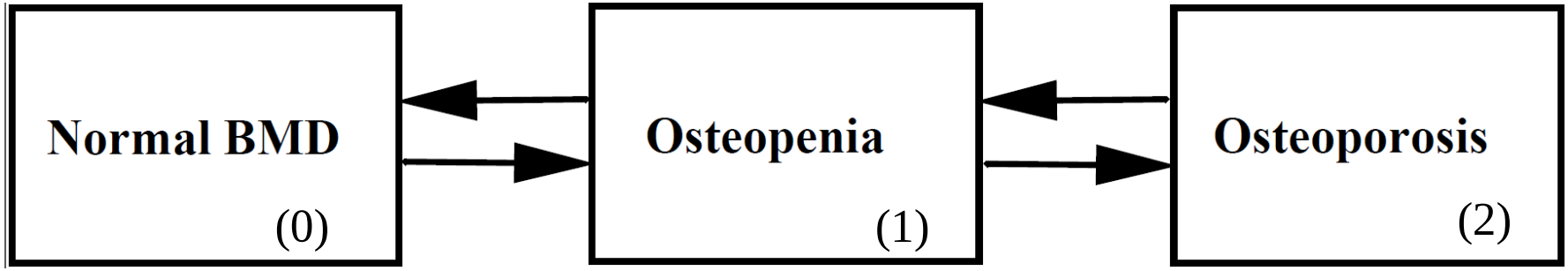
- BMD (g/cm^2) is compared it to established norms
  - T-score: comparison to 30-years-old healthy adult (same sex)

T-score	Diagnosis*
-1<= T	Normal
-2.5<=T<-1	Osteopenia
T<-2.5	Osteoporosis

- T score for the lumbar (L1-L4) spine and hip (femoral neck, trochanter and total femur)
- Minimum T-score ⟹ outcome variable

*NIH Osteoporosis and Related Bone Diseases National Resource Center

3-progressive bidirectional multistate model



- Multi-state process $\{X(a)\ a \in A\}$ with finite state space $S=\{0,1,2\}=\{Normal, Osteopenia, Osteoporosis\}$
  - a: patient's age at each DXS scan
  - $X(a) = s \in S$: patient's state at a
- Markov property assumed:
  - The future time course does only depend on the present state and not on the previous process history

Factors related to a change in the BMD evolution

- Age is used as time scale
- The effect of time is NOT the same at all "ages"
  - Time-inhomogeneous model
  - PCI for Age (<= 45, > 45)
- Models for women and men are fitted separately
- The use of antiretroviral drugs during the year prior to a DXA scan was included as a covariate in the model
- The effects of the covariates were studied by transition-specific hazard regression models
  - the hazard ratio is the effect size measure of interest

RESULTS

	875 patients
Gender, men, n (%)	659 (75.3%)
Age, years	41.7 (36.1; 47.8)
DXA scans per patient, number	3 (2; 18)
Patients and DXA scans, n (%)	
Two DXA scans	294 (33.6%)
Three DXA scans	188 (21.5%)
Four DXA scans	118 (13.5%)
Five or more DXA scans	275 (31.4%)
Time from the first to the last DXA scan, years	5 (2.2; 9.6)
Time between consecutive DXA scans, years	1.1 (0.6 – 2.2)
Antiretroviral therapy during the year before DXA, number of DXA scans (%) *	
PI + TDF	567 (16.1%)
Only PI	1290 (36.7%)
Only TDF	734 (20.9%)
Neither PI, nor TDF	925 (26.3%)
Among subjects receiving a PI, number of DXA scans (%)	
Darunavir	519 (27.9%)
Lopinavir	616 (33.2%)
Atazanavir	253 (13.6%)
Other PIs	469 (25.3%)

TABLE. Epidemiological and clinical data at first DXA scan among 875 patients.
Values are expressed as median (IQR) or number (%).

Prevalence and transitions

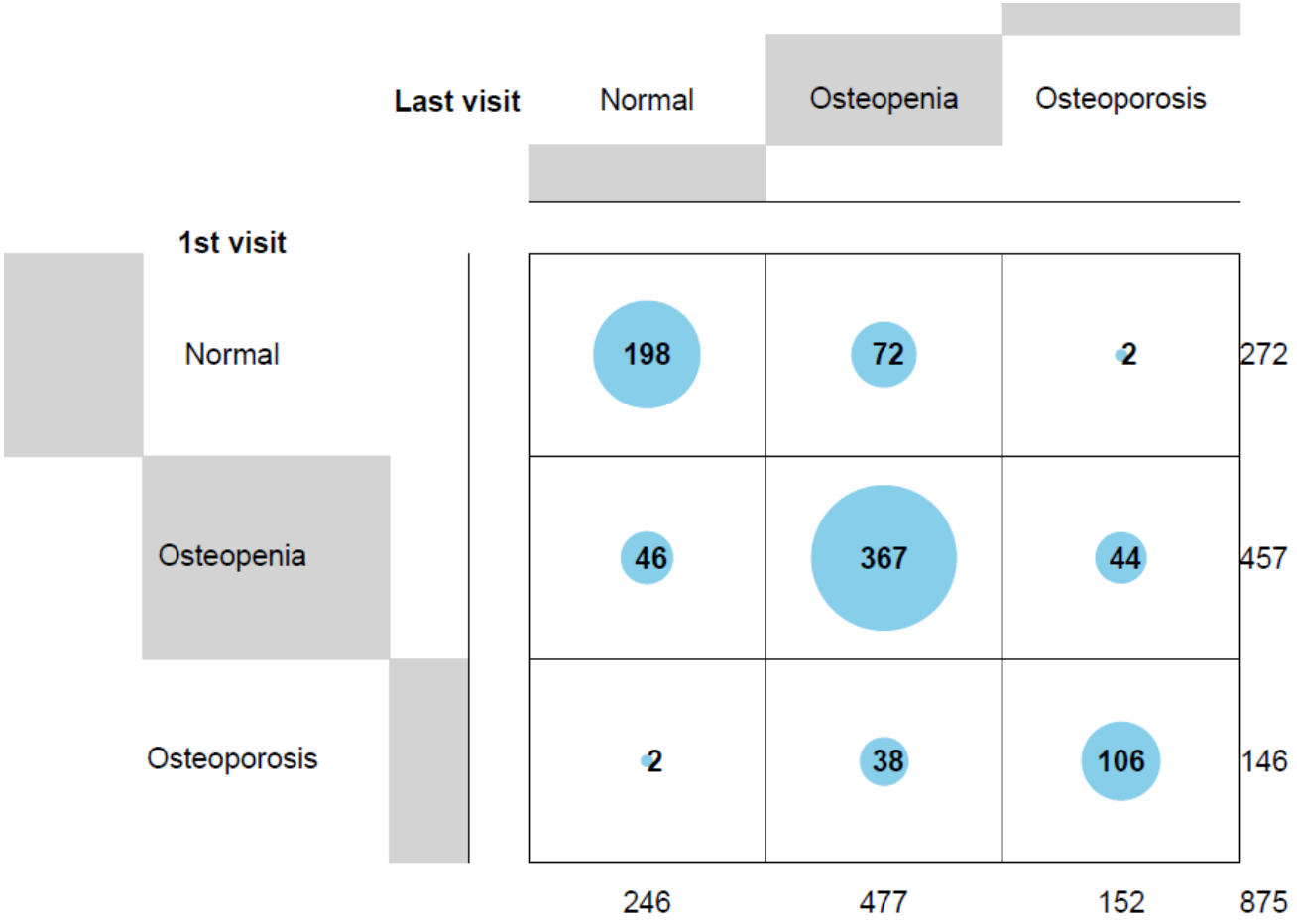


FIGURE: Transitions from first to last DXA among all HIV-infected patients.

Risk of progression

The risk of progression of bone loss or bone gain as a function of age (<= vs. >45 years)

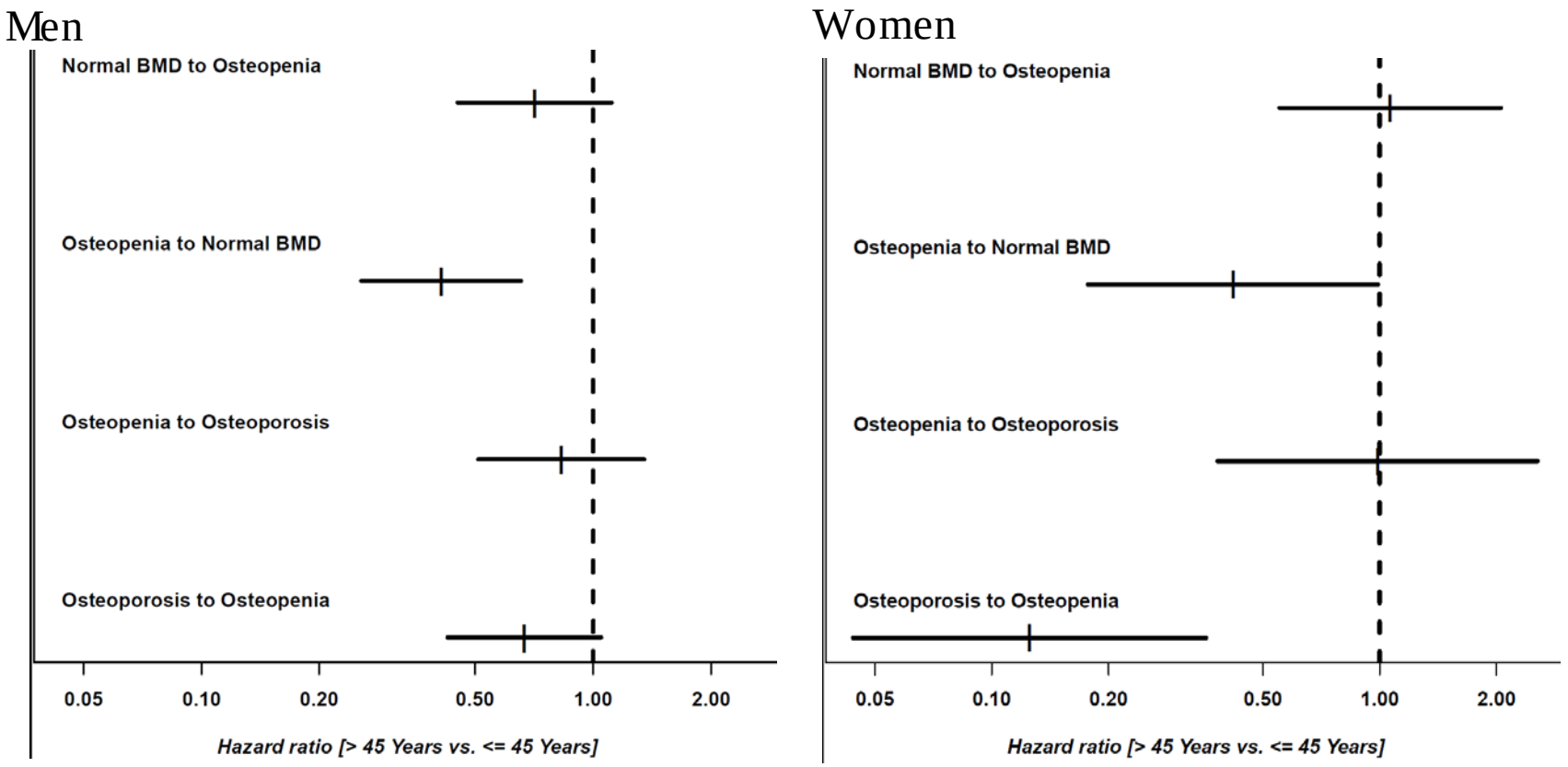
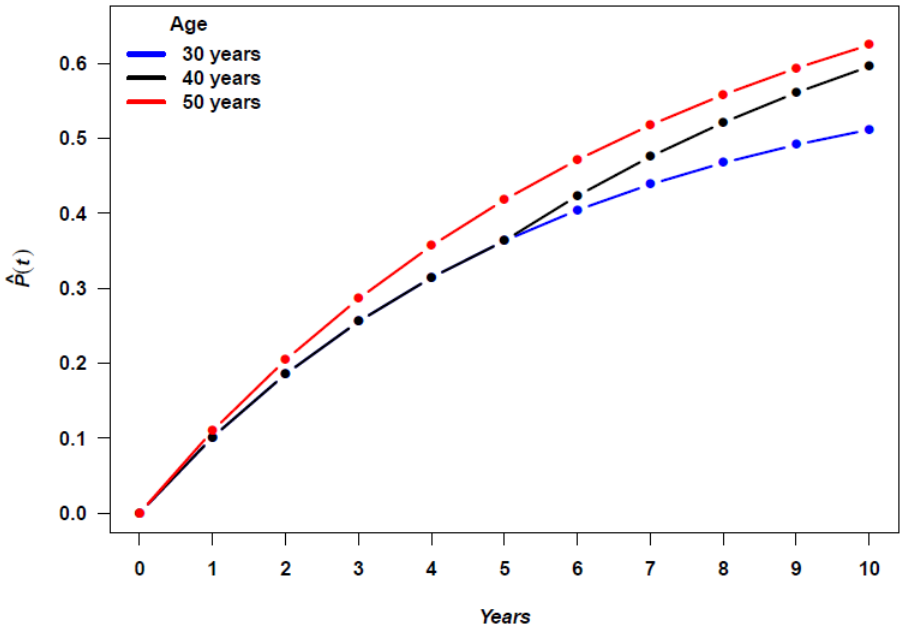


FIGURE: Estimated hazard ratios for all the transitions associated to age <=45 vs. >45 years.

Probability of progression

Estimated transition probabilities from normal bone mineral density to osteopenia/osteoporosis throughout 10 years for HIV-infected patients of ages 30, 40, and 50 years.



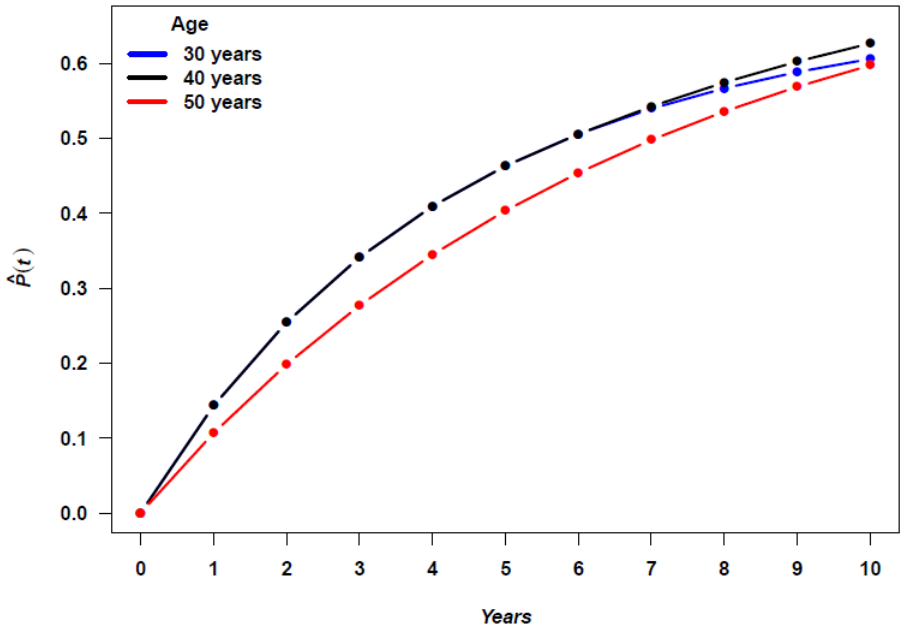
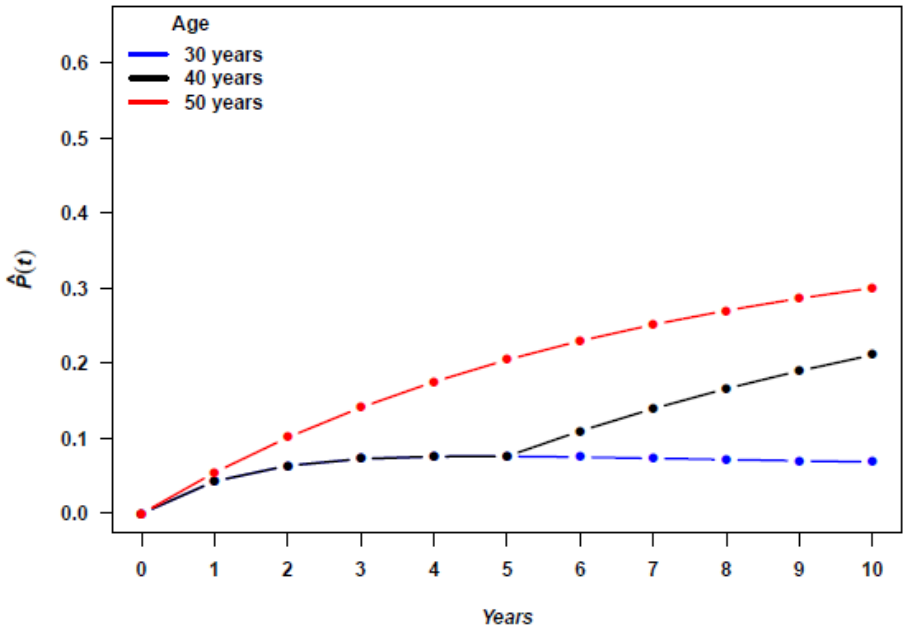


FIGURE: Normal BMD to osteopenia and osteoporosis (Left panel:Women).

Probability of progression

Estimated transition probabilities from osteopenia to osteoporosis throughout 10 years for HIV-infected patients of ages 30, 40, and 50 years.



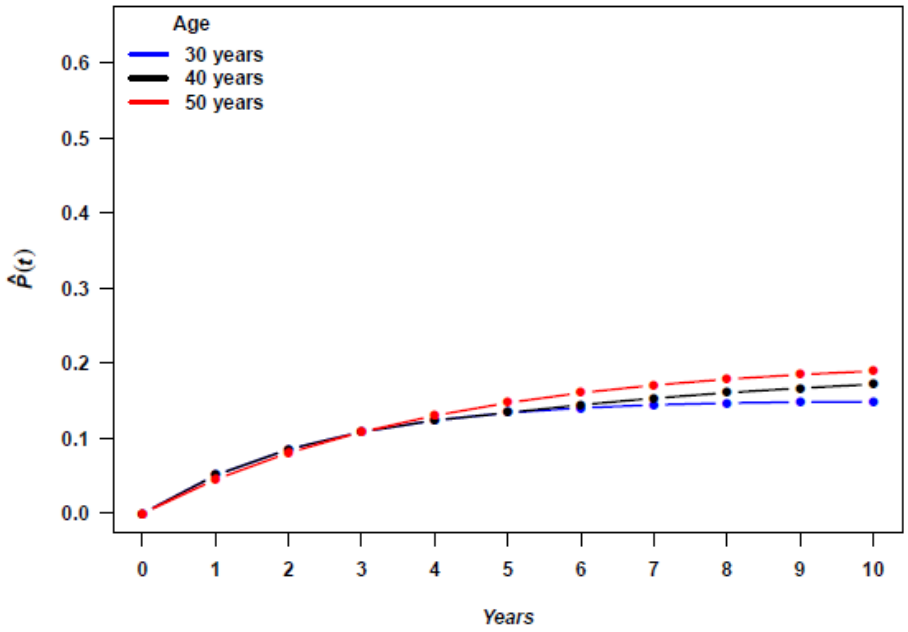
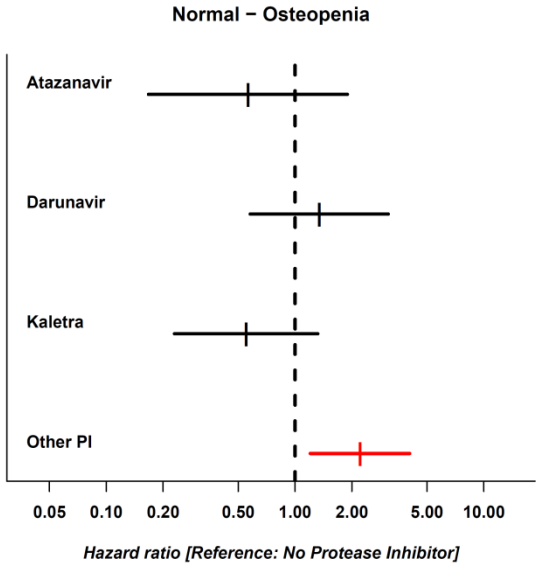
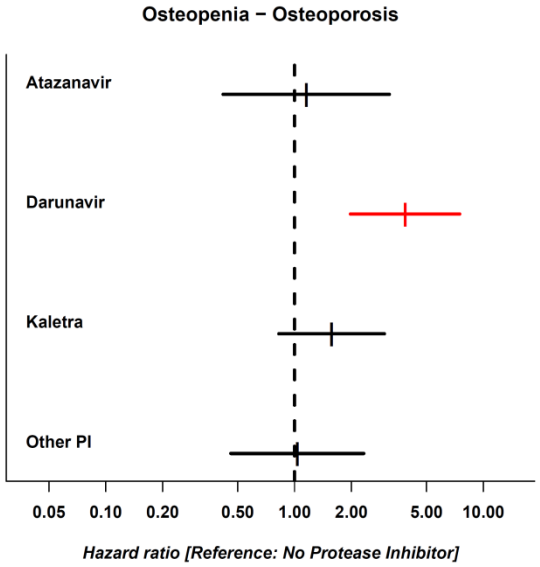


FIGURE: Osteopenia to osteoporosis (Left panel:Women).

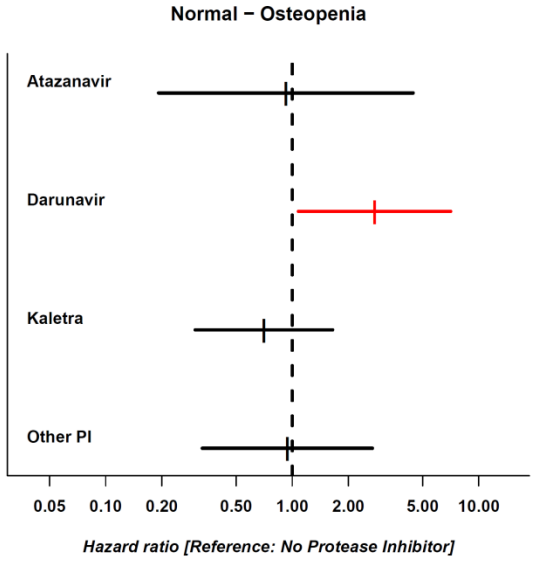
Risk of low BMD according to the PI

Men





Women



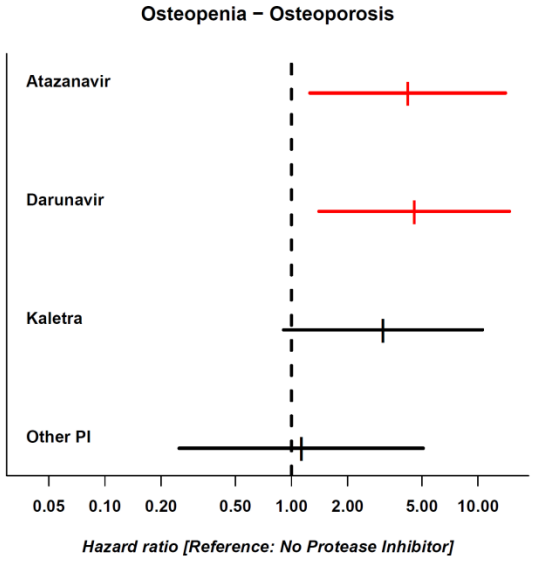


FIGURE: Estimated hazard ratios associated to PIs.

CONCLUSIONS

- In this large cohort of HIV-infected people, the progression to osteoporosis was high for those subjects aged 45 years over 5 years, mainly for women.
  - NEED OF MONITORING THE BMD

- Osteoporosis can be related to the use of protease inhibitors, in particular with darunavir.
  - CHANGES IN SOME ANTIRETROVIRAL DRUGS

THANK YOU FOR YOUR ATTENTION