



# ICPE 2022

August 24-28, 2022  
COPENHAGEN, DENMARK

[icpe2022.org](http://icpe2022.org)  
**#ICPE22 | @IntPharmacoEpi**



# Treatment patterns and outcomes in patients with osteoporosis in France

-  
*a study of the French national healthcare insurance database*

P. Bosco-Lévy<sup>1</sup>, J. O'Kelly<sup>2</sup>, K. Briot<sup>3</sup>, N. Mehsen-Cetre<sup>4</sup>, A. Fabre<sup>5</sup>, R. Lassalle<sup>1</sup>, A. Abouelfath<sup>1</sup>, A. Grelleau<sup>1</sup>, P. Blin<sup>1</sup>, C. Droz-Perroteau<sup>1</sup>

<sup>1</sup> Univ. Bordeaux, INSERM CIC-P1401, Bordeaux PharmacoEpi, 33000 Bordeaux, France

<sup>2</sup> Amgen Ltd, UK

<sup>3</sup> Université de paris, INSERM U1153, hôpital Cochin, rhumatologie, 75014, Paris

<sup>4</sup> CHU Bordeaux-Tripode, Service de Rhumatologie, 33076 Bordeaux

<sup>5</sup> Action Inc., Barcelona, Spain

## Disclosure

- This study was carried out
  - by BPE research platform
  - under the supervision of an independent scientific committee
- This study was funded by



# Context

- Data on **osteoporosis medications efficacy** in post menopausal women mainly from RCTs (*Roux C, Adamis S, Eular Course 2009, Tu KN, et al. 2018*)

	Vertebral fractures	Non-vertebral fractures	Hip fracture
Alendronate	+	+	+
Risedronate	+	+	+
Zoledronate	+	+	+
Raloxifen	+	-	-
Teriparatide	+	+	-
Denosumab	+	+	+

- 20 to 70 % ↓ of fracture risk depending on the localization (*Briot K et al. Joint Bone Spine 2018*)
- Limited data on their **effectiveness in clinical practice**

# Objective

- To estimate the **effectiveness** of each osteoporosis treatment by assessing the **longitudinal change in fracture incidence**
  - in postmenopausal women, between
    - the baseline period following initiation of treatment
    - and 3 subsequent risk assessment periods

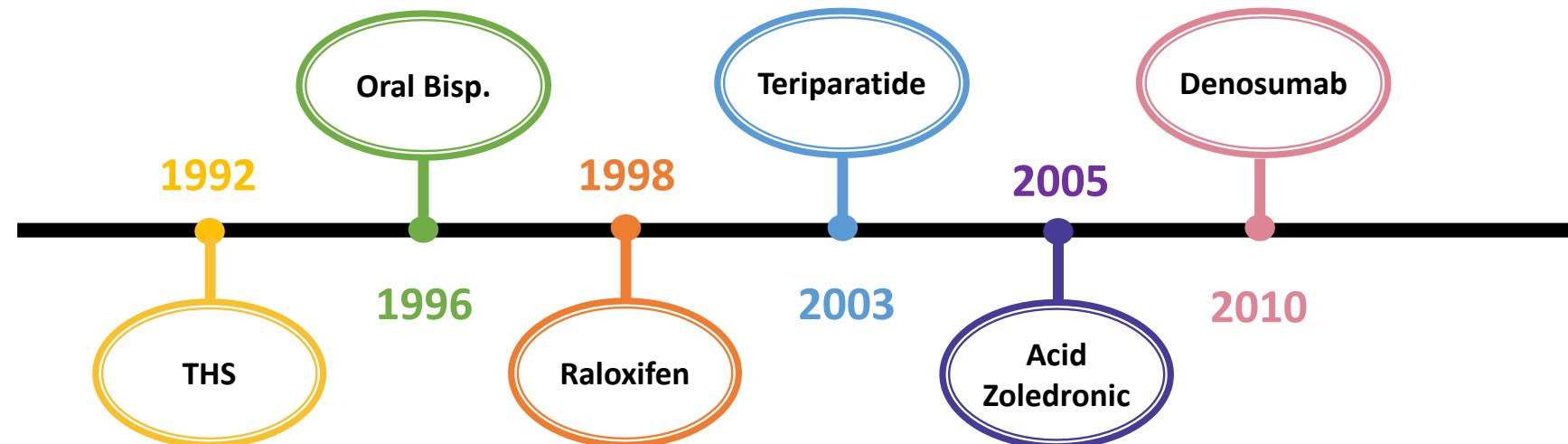
# Method (1)

- **Study design and data source**
  - Cohorts study using the French nationwide healthcare database (SNDS)
- **Study population**
  - All post-menopausal women ( $\geq 55$  years)
    - initiating an osteoporosis medication between 2014 and 2016
    - with 3 years of lookback period and  $\geq 2$  years of follow-up
    - with  $\geq 6$  months of treatment
    - without diagnosis of cancer nor Paget's disease in the previous year

# Method (2)

## – Exposure

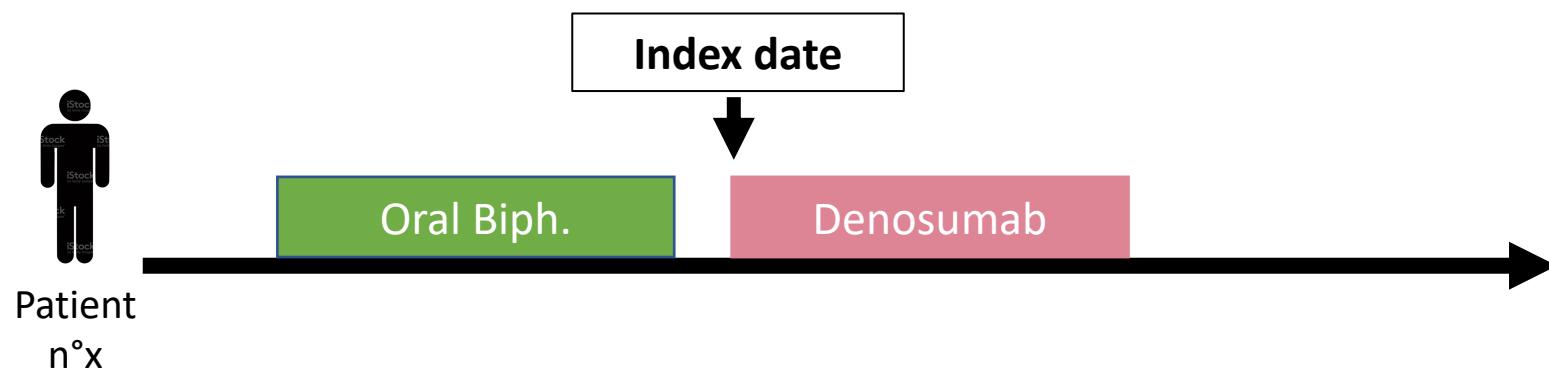
- Osteoporosis treatment
  - Patients assignment according to a **hierarchical approach** based on their relative order of entry into the French marketplace
    - late entry receiving = higher priority



# Method (2)

## – Exposure

- Osteoporosis treatment
  - Patients assignment according to a **hierarchical approach** based on their relative order of entry into the French marketplace
    - late entry receiving = higher priority

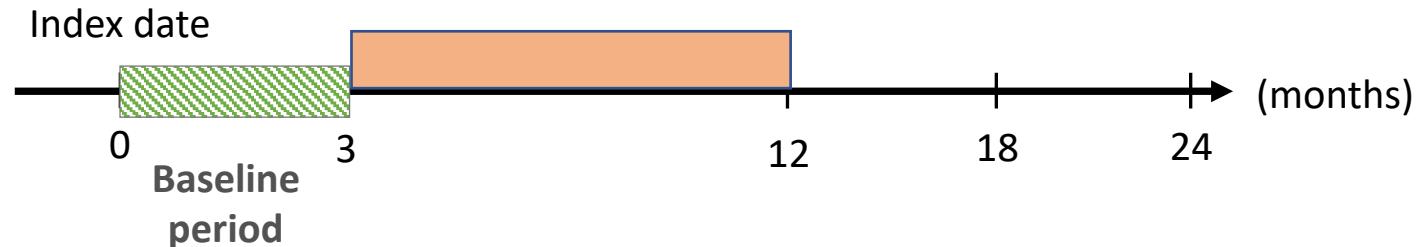


# Method (3)

- **Outcome**
  - **Fragility-related fractures**
    - using codes related to inpatient diagnosis (CIM-10) and medical procedures
    - categorization into **5 groups**: hip, wrist/forearm, vertebral, non-vertebral and non-hip/non-vertebral fractures
    - 2 consecutives fractures at the same body site must be **separated by  $\geq$  90 days** to be considered as **independent**

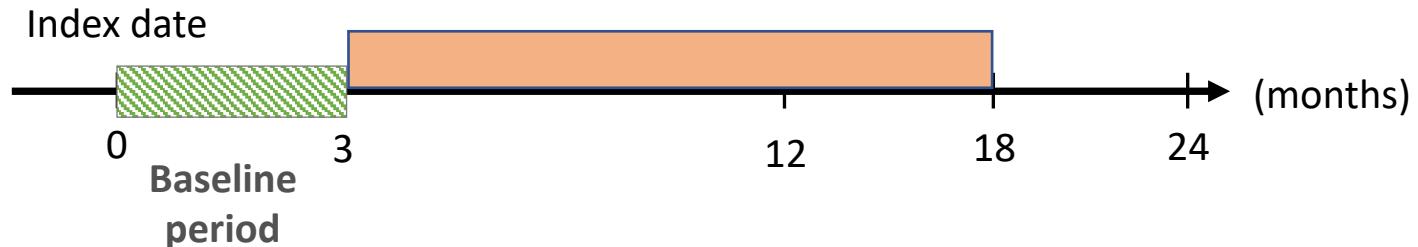
# Method (3)

- **Outcome**
  - **Fragility-related fractures**
    - Fracture incidence assigned to different time periods
      - **Baseline period**
      - 3 subsequent risk assessment periods
        - **]3; 12] months**



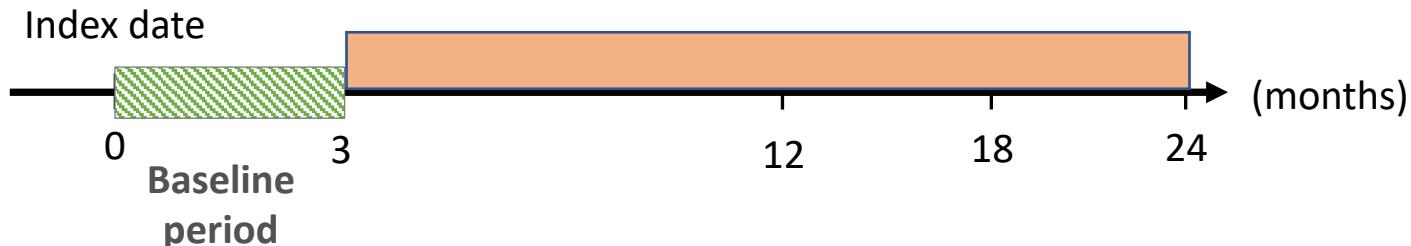
# Method (3)

- **Outcome**
  - **Fragility-related fractures**
    - Fracture incidence assigned to different time periods
      - **Baseline period**
      - 3 subsequent risk assessment periods
        - ]3; 12] months
        - **]3; 18]** months



# Method (3)

- **Outcome**
  - **Fragility-related fractures**
    - Fracture incidence assigned to different time periods
      - **Baseline period**
      - 3 subsequent risk assessment periods
        - $]3; 12]$  months
        - $]3; 18]$  months
        - **$]3; 24]$  months**



# Method (4)

- **Statistical analysis**
  - Incidence rate per 1000 Person-Year (% PY)
  - Incidence Rate Ratio (IRR) using a self-controlled analysis
    - comparing the **3 subsequent risk assessment periods** to the **baseline period**
  - Stratified analyses on potential confounders
    - Age, sex
    - Prior fracture
    - Prior use of corticosteroids or of osteoporosis medication
    - Dementia or other neurological dysfunctions
  - **Sensitivity analysis**
    - In patients with < 6 months of treatment
      - in OP users only +++

# Flow Chart

Post-menopausal women ( $\geq 55$  years) initiating an osteoporosis medication between 2014 and 2016  
**N = 694 402**

- >1 osteoporosis medication at index date, n = 746
- Pre-index period  $\leq 3$  years or Follow-up  $\leq 2$  years, n = 24 807
- History of cancer, n = 65 495
- History of Paget's disease, n = 317
- <6 months of osteoporosis medication after index date , n = 402 541  
(HRT=74%, **Oral BP=19%**, raloxifene=4%, denosumab, teriparatide and zoledronic acid =1%)

**Eligible women**  
**N = 200 496**

Denosumab n = 67 046 (33.4%)	Oral BP n = 52 914 (26.4%)	Zoledronic acid n = 41 700 (20.8%)	HRT n = 19 666 (9.8%)	Raloxifene n = 11 660 (5.8%)	Teriparatide n = 7 510 (3.7%)
------------------------------------	----------------------------------	--	-----------------------------	------------------------------------	-------------------------------------

# Baseline characteristics

	<b>Denosumab n = 67 046</b>	<b>Oral BP n = 52 914</b>	<b>Zoledronic acid n = 41 700</b>	<b>HRT n = 19 666</b>	<b>Raloxifene n = 11 660</b>	<b>Teriparatide n = 7 510</b>	<b>Total n = 200 496</b>
Age, Mean ( $\pm$ SD)	74.3 (9.2)	71.4 (9.4)	74.1 (9.8)	63.1 (8.4)	63.7 (6.7)	76.1 (9.2)	71.9 (10.0)
Comorbidities, n (%)							
Cardiovascular disease	15063 (22.5)	9899 (18.7)	11017 (26.4)	1805 (9.2)	704 (6.0)	2558 (34.1)	41046 (20.5)
Neurological disease	6958 (10.4)	4992 (9.4)	6056 (14.5)	1352 (6.9)	581 (5.0)	1215 (16.2)	21154 (10.6)
Diabetes	4465 (6.7)	4081 (7.7)	3777 (9.1)	1205 (6.1)	394 (3.4)	751 (10.0)	14673 (7.3)
In the previous 3 years, n (%)							
Factures							
1	7191 (10.7)	5284 (10.0)	6168 (14.8)	329 (1.7)	600 (5.1)	1434 (19.1)	21006 (10.5)
$\geq$ 2	2217 (3.3)	1238 (2.3)	1911 (4.6)	52 (0.3)	77 (0.7)	503 (6.7)	5998 (3.0)
Bone mineral density	46660 (69.6)	33632 (63.6)	26494 (63.5)	3059 (15.6)	8576 (73.6)	4623 (61.6)	123044 (61.4)
In the previous year							
Osteoporosis treatment	23737 (35.4)	5408 (10.2)	7878 (18.9)	257 (1.3)	1180 (10.1)	1578 (21.0)	40038 (20.0)
Corticosteroids	27917 (41.6)	20295 (38.4)	18163 (43.6)	6244 (31.8)	3473 (29.8)	3530 (47.0)	79622 (39.7)
Vit. D and Calcium	62518 (93.2)	49088 (92.8)	37952 (91.0)	9344 (47.5)	10352 (88.8)	6936 (92.4)	176190 (87.9)

SD= Standard Deviation; HRT= Hormonal Replacement Therapy

# Baseline characteristics

	<b>Denosumab n = 67 046</b>	<b>Oral BP n = 52 914</b>	<b>Zoledronic acid n = 41 700</b>	<b>HRT n = 19 666</b>	<b>Raloxifene n = 11 660</b>	<b>Teriparatide n = 7 510</b>	<b>Total n = 200 496</b>
Age, Mean ( $\pm$ SD)	74.3 (9.2)	71.4 (9.4)	74.1 (9.8)	63.1 (8.4)	63.7 (6.7)	76.1 (9.2)	71.9 (10.0)
Comorbidities, n (%)							
Cardiovascular disease	15063 (22.5)	9899 (18.7)	11017 (26.4)	1805 (9.2)	704 (6.0)	2558 (34.1)	41046 (20.5)
Neurological disease	6958 (10.4)	4992 (9.4)	6056 (14.5)	1352 (6.9)	581 (5.0)	1215 (16.2)	21154 (10.6)
Diabetes	4465 (6.7)	4081 (7.7)	3777 (9.1)	1205 (6.1)	394 (3.4)	751 (10.0)	14673 (7.3)
In the previous 3 years, n (%)							
Factures							
1	7191 (10.7)	5284 (10.0)	6168 (14.8)	329 (1.7)	600 (5.1)	1434 (19.1)	21006 (10.5)
$\geq$ 2	2217 (3.3)	1238 (2.3)	1911 (4.6)	52 (0.3)	77 (0.7)	503 (6.7)	5998 (3.0)
Bone mineral density	46660 (69.6)	33632 (63.6)	26494 (63.5)	3059 (15.6)	8576 (73.6)	4623 (61.6)	123044 (61.4)
In the previous year							
Osteoporosis treatment	23737 (35.4)	5408 (10.2)	7878 (18.9)	257 (1.3)	1180 (10.1)	1578 (21.0)	40038 (20.0)
Corticosteroids	27917 (41.6)	20295 (38.4)	18163 (43.6)	6244 (31.8)	3473 (29.8)	3530 (47.0)	79622 (39.7)
Vit. D and Calcium	62518 (93.2)	49088 (92.8)	37952 (91.0)	9344 (47.5)	10352 (88.8)	6936 (92.4)	176190 (87.9)

SD= Standard Deviation; HRT= Hormonal Replacement Therapy

# Baseline characteristics

	Denosumab n = 67 046	Oral BP n = 52 914	Zoledronic acid n = 41 700	HRT n = 19 666	Goserelin n = 11 650	Teriparatide n = 7 510	Total n = 200 496
Age, Mean ( $\pm$ SD)	74.3 (9.2)	71.4 (9.4)	74.1 (9.8)	63.1 (8.4)	63.7 (8.0)	76.1 (9.2)	71.9 (10.0)
Comorbidities, n (%)							
Cardiovascular disease	15063 (22.5)	9899 (18.7)	11017 (26.4)	1805 (9.2)	11046 (20.5)		
Neurological disease	6958 (10.4)	4992 (9.4)	6056 (14.5)	1352 (6.9)	12154 (10.6)		
Diabetes	4465 (6.7)	4081 (7.7)	3777 (9.1)	1205 (6.1)	14673 (7.3)		
In the previous 3 years, n (%)							
Factures							
1	7191 (10.7)	5284 (10.0)	6168 (14.8)	329 (1.7)	91	21006 (10.5)	
$\geq$ 2	2217 (3.3)	1238 (2.3)	1911 (4.6)	52 (0.3)	77 (0.7)	503 (6.7)	5998 (3.0)
Bone mineral density	46660 (69.6)	33632 (63.6)	26494 (63.5)	3059 (15.6)	8576 (73.6)	4623 (61.6)	123044 (61.4)
In the previous year							
Osteoporosis treatment	23737 (35.4)	5408 (10.2)	7878 (18.9)	257 (1.3)	1180 (10.1)	1578 (21.0)	40038 (20.0)
Corticosteroids	27917 (41.6)	20295 (38.4)	18163 (43.6)	6244 (31.8)	3473 (29.8)	3530 (47.0)	79622 (39.7)
Vit. D and Calcium	62518 (93.2)	49088 (92.8)	37952 (91.0)	9344 (47.5)	10352 (88.8)	6936 (92.4)	176190 (87.9)

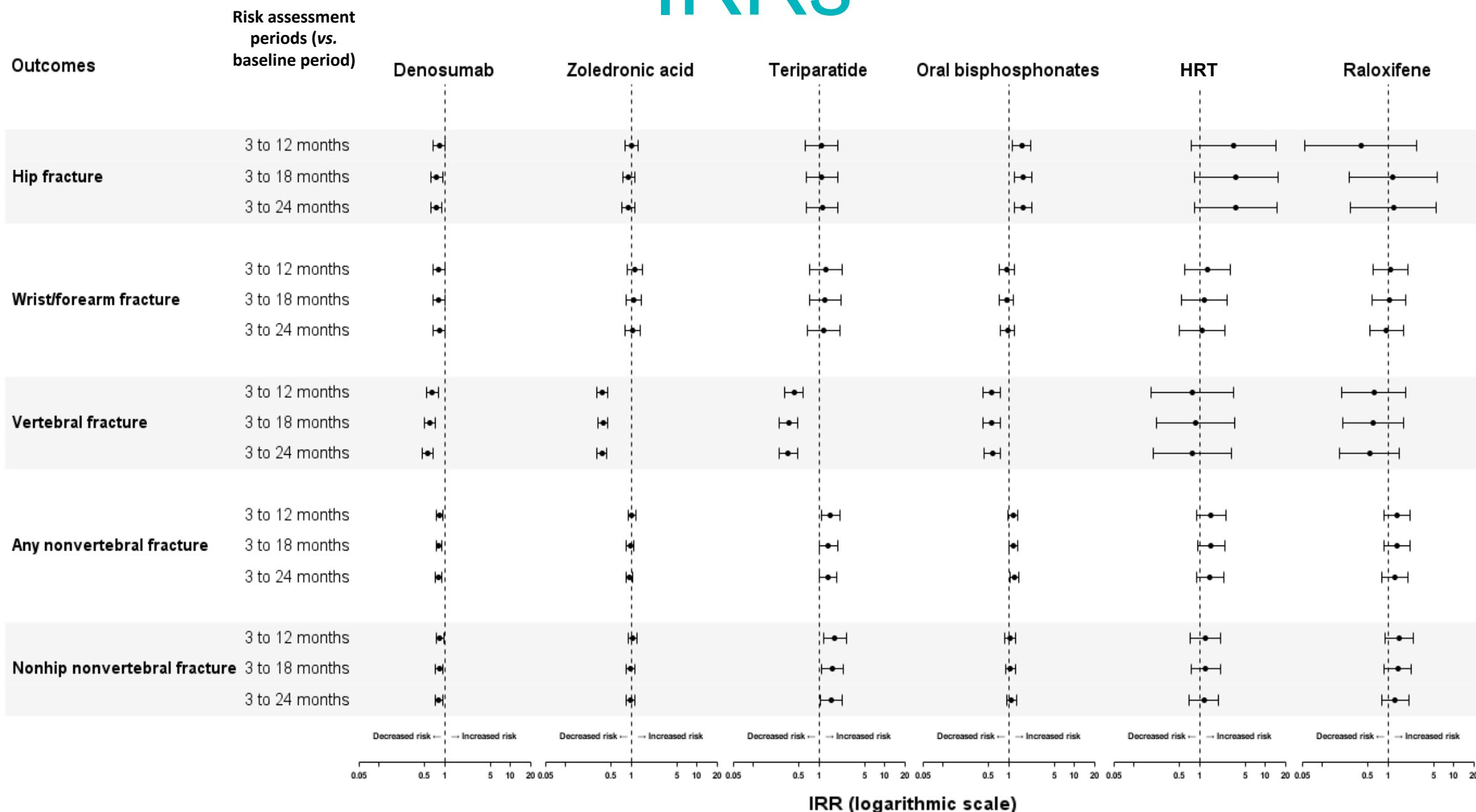
SD= Standard Deviation; HRT= Hormonal Replacement Therapy

# Baseline characteristics

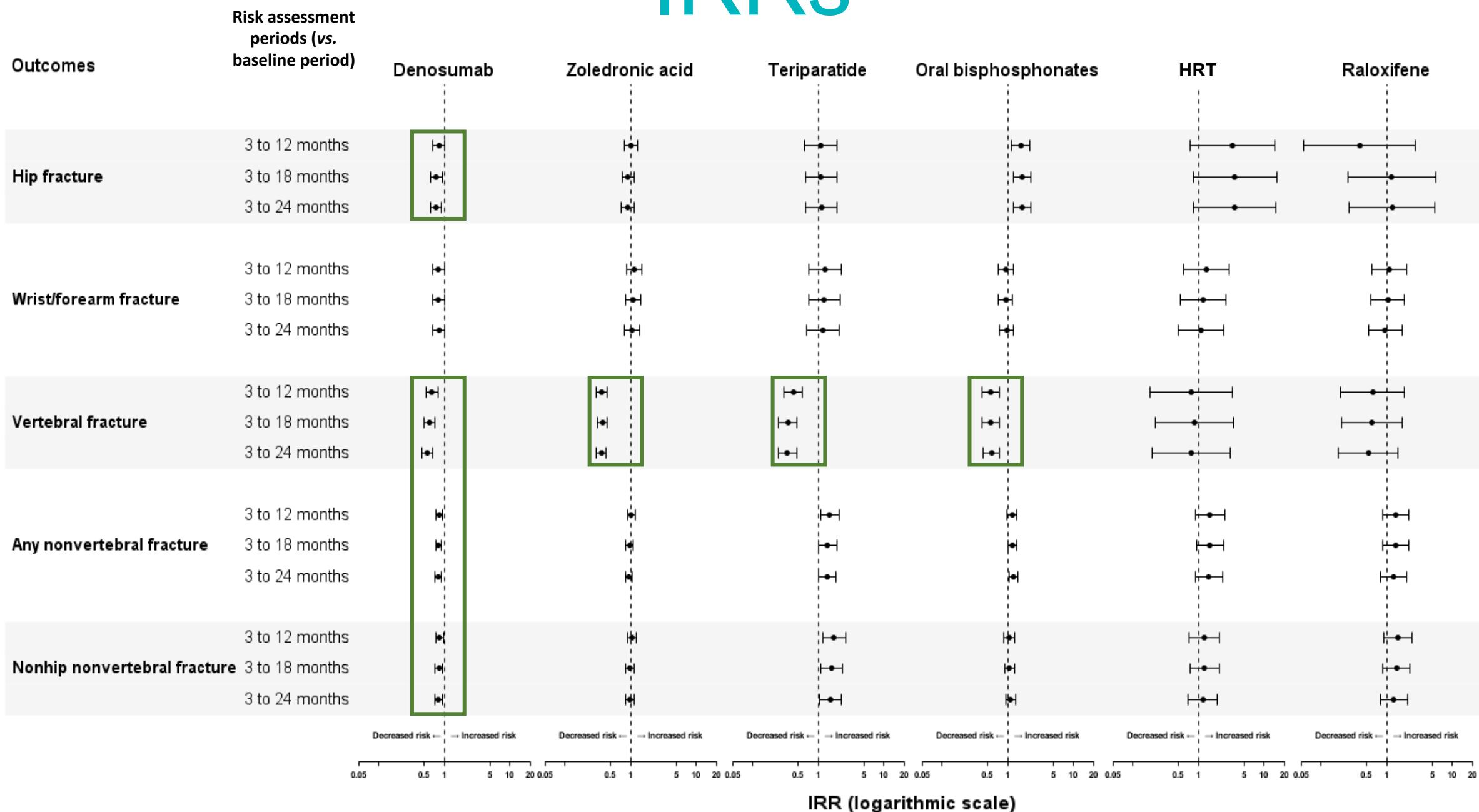
	<b>Denosumab n = 67 046</b>	<b>Oral BP n = 52 914</b>	<b>Zoledronic acid n = 41 700</b>	<b>HRT n = 19 666</b>	<b>Raloxifene n = 11 660</b>	<b>Teriparatide n = 7 510</b>	<b>Total n = 200 496</b>
Age, Mean ( $\pm$ SD)	74.3 (9.2)	71.4 (9.4)	74.1 (9.8)	63.1 (8.4)	63.7 (6.7)	76.1 (9.2)	71.9 (10.0)
Comorbidities, n (%)							
Cardiovascular disease	15063 (22.5)	9899 (18.7)	11017 (26.4)	1805 (9.2)	704 (6.0)	2558 (34.1)	41046 (20.5)
Neurological disease	6958 (10.4)	4992 (9.4)	6056 (14.5)	1352 (6.9)	581 (5.0)	1215 (16.2)	21154 (10.6)
Diabetes	4465 (6.7)	4081 (7.7)	3777 (9.1)	1205 (6.1)	394 (3.4)	751 (10.0)	14673 (7.3)
In the previous 3 years, n (%)							
Factures							
1	7191 (10.7)	5284 (10.0)	6168 (14.8)	329 (1.7)	600 (5.1)	1434 (19.1)	21006 (10.5)
$\geq$ 2	2217 (3.3)	1238 (2.3)	1911 (4.6)	52 (0.3)	77 (0.7)	503 (6.7)	5998 (3.0)
Bone mineral density	46660 (69.6)	33632 (63.6)	26494 (63.5)	3059 (15.6)	8576 (73.6)	4623 (61.6)	123044 (61.4)
In the previous year							
Osteoporosis treatment	23737 (35.4)	5408 (10.2)	7878 (18.9)	257 (1.3)	1180 (10.1)	1578 (21.0)	40038 (20.0)
Corticosteroids	27917 (41.6)	20295 (38.4)	18163 (43.6)	6244 (31.8)	3473 (29.8)	3530 (47.0)	79622 (39.7)
Vit. D and Calcium	62518 (93.2)	49088 (92.8)	37952 (91.0)	9344 (47.5)	10352 (88.8)	6936 (92.4)	176190 (87.9)

SD= Standard Deviation; HRT= Hormonal Replacement Therapy

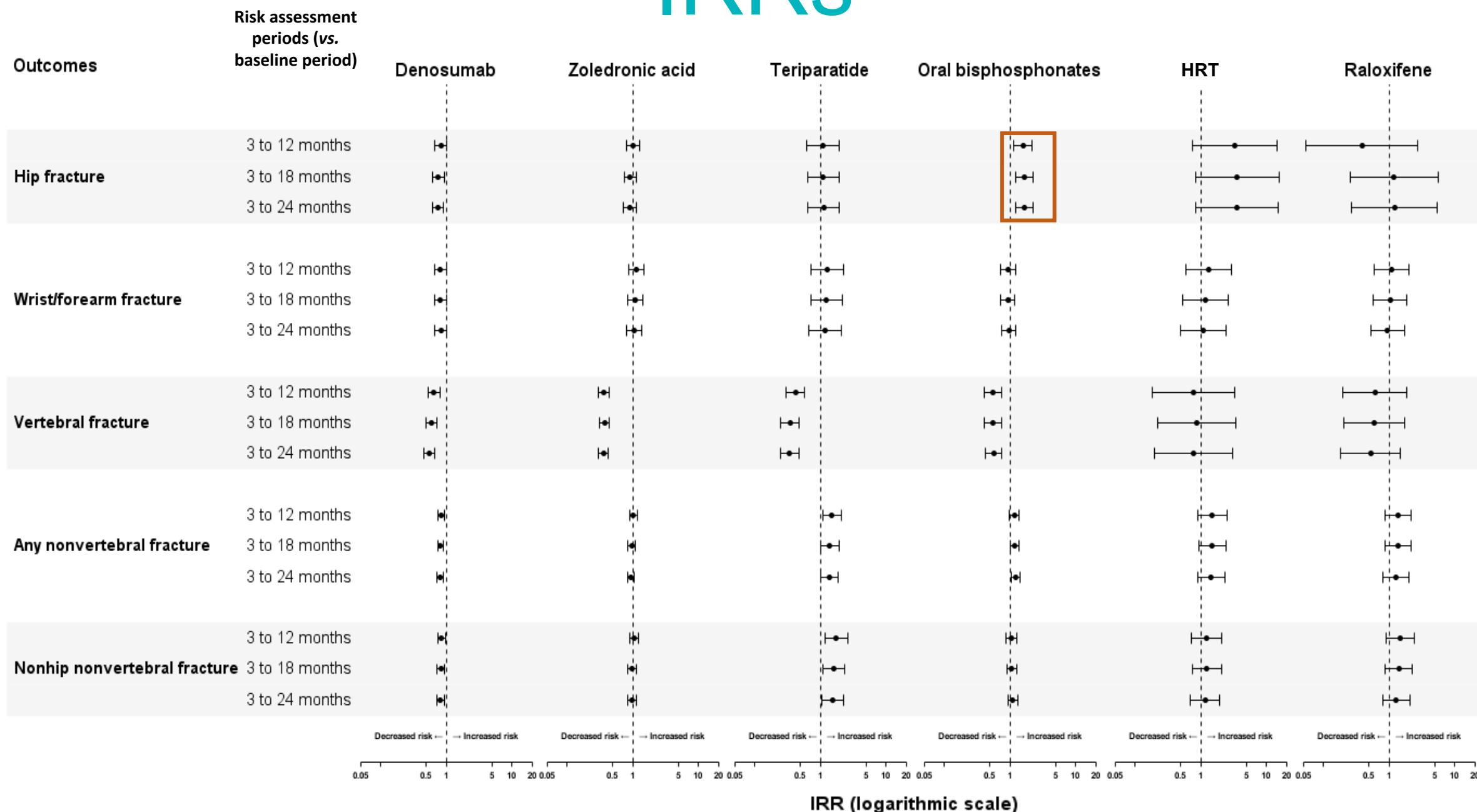
# IRRs



# IRRs



# IRRs

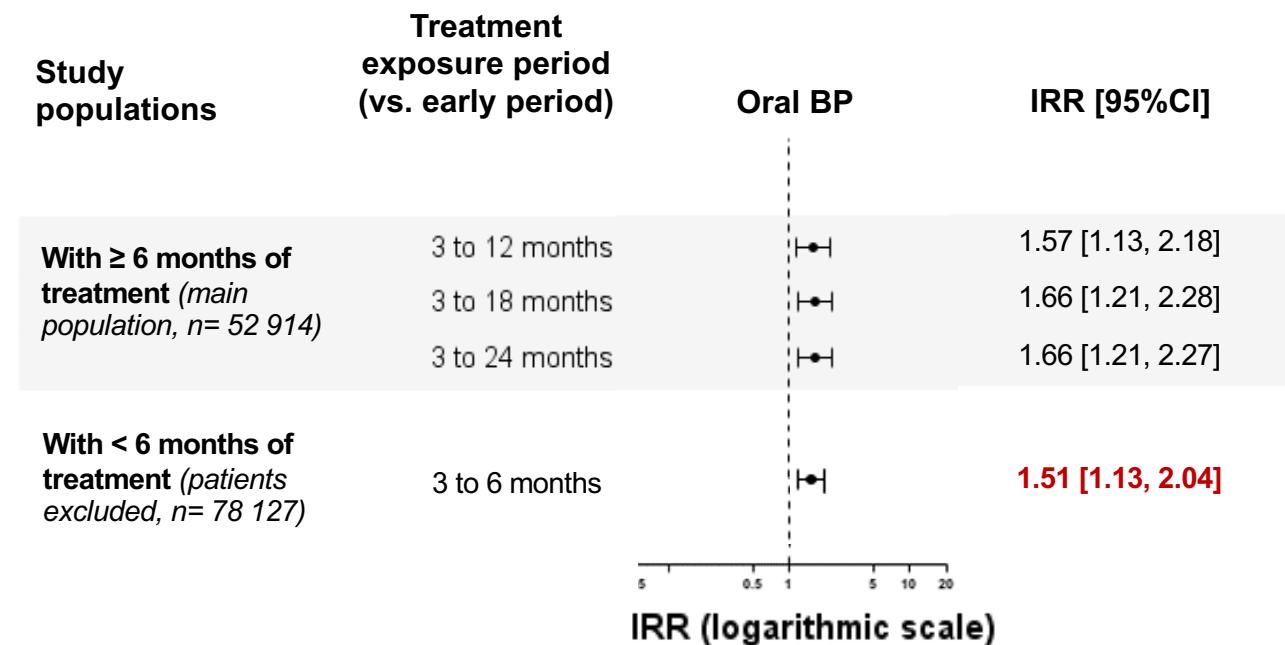


# Stratified analyses

- **Similar results found** whatever the stratification variables used
  - some IRRs become non-significant given the small size of the groups
  - minor variation observed among age groups
    - ↓ IRR in the youngest, who initiated
      - zoledronic acid for hip fracture (IRR=0.3 [0.1;0.7] in [55; 64] years)
      - teriparatide for hip fracture (IRR=0.3 [0.1;0.9] in [65; 74] years) and for wrist/forearm fracture (IRR=0.3 [0.1;0.9] in [55; 64] years)
    - ↑ IRR in the oldest, who initiated
      - oral BP for hip fracture (IRR=3.0 [1.1;8.4] in [75; 79] years and IRR=1.7 [1.1;2.5] in  $\geq 80$  years)

# Sensitivity analysis

- Among oral BP users with < 6 months of treatment
  - ↑ IRR also observed for hip fracture



# Discussion

- This study highlights
  - A **significant decrease** in
    - Vertebral fracture among patients treated with denosumab, zoledronic acid, teriparatide and oral BP
    - Hip and peripheral fractures among patients treated with denosumab
  - A **significant increase** in **hip fractures** among patients treated with oral BP
    - Confirmed by a previous observational study (IRR of 1.05 [1.00-1.09] in Bourrion et al. Int J Environ Res Public Health 2021)
    - Could be explained by an insufficient duration of treatment to be effective

# Thank you for your attention



[pauline.bosco-levy@u-bordeaux.fr](mailto:pauline.bosco-levy@u-bordeaux.fr)

Bordeaux PharmacoEpi - <http://www.bordeauxpharmacoeipi.eu>  
Plateforme de recherche en Pharmaco-épidémiologie  
CIC Bordeaux CIC1401  
INSERM - Université de BORDEAUX - CHU de Bordeaux - Adera  
Bâtiment Le Tondu - case 41 - 146 rue Léo Saignat - 33076 Bordeaux Cedex  
Acc. +33 (0)5 57 57 46 75 – Fax +33 (0)5 57 57 47 40

---  [www.bordeauxpharmacoeipi.eu](http://www.bordeauxpharmacoeipi.eu) ---

---  @BxPharmacoEpi ---

---  [/company/bordeauxpharmacoeipi/](https://www.linkedin.com/company/bordeauxpharmacoeipi/) ---