

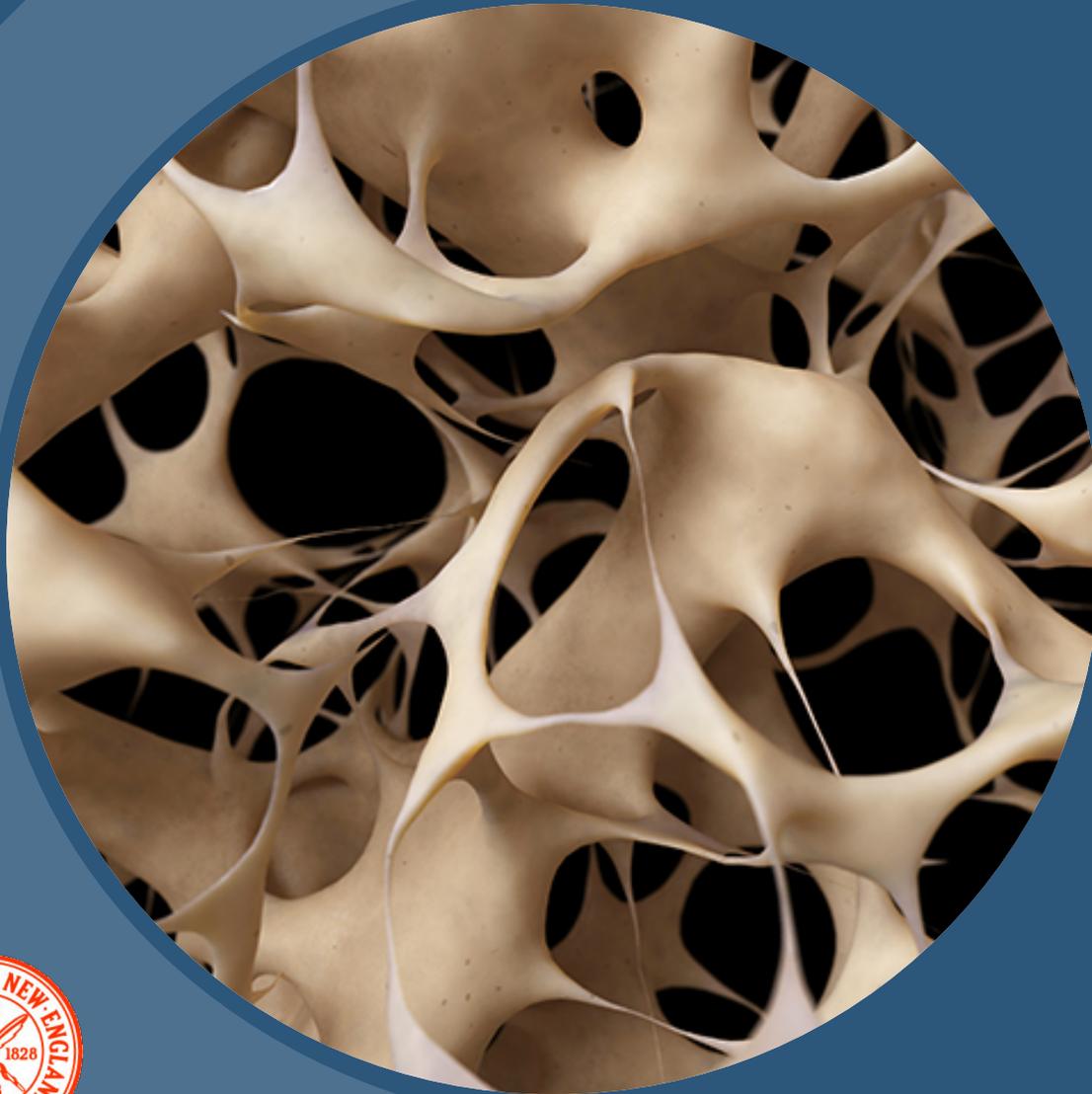


# Journal Watch

## Fracture Prevention with Zoledronate in Older Women with Osteopenia

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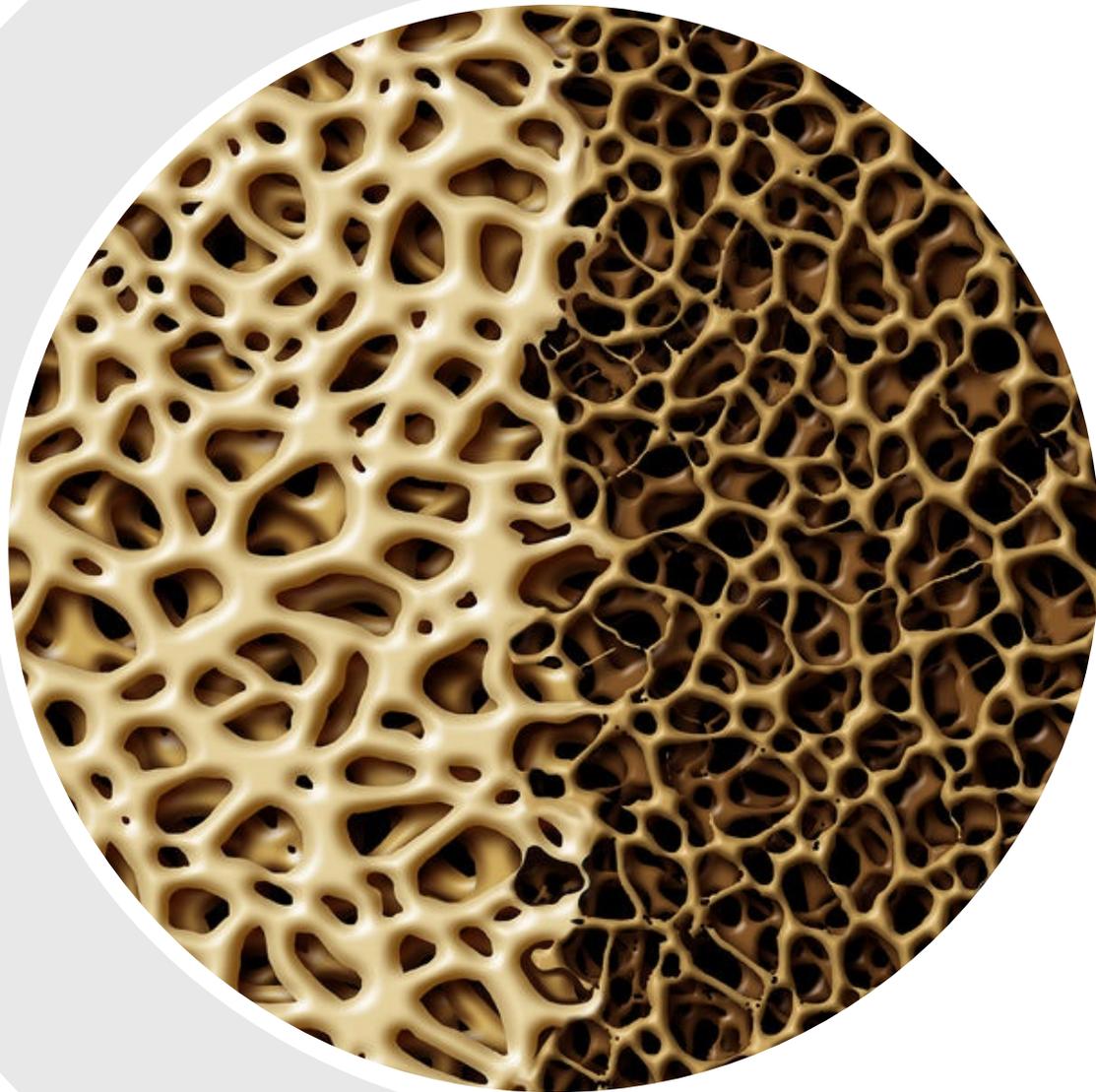
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# *BACKGROUND*



# INTRODUCTION



- **Bisphosphonate:** Principal class of medications used in management of postmenopausal osteoporosis
- It has been shown to prevent fracture
  - Most **clearly in patients with osteoporosis** (bone density T-score  $< -2.5$ )
  - Efficacy **in patients osteopenia alone is uncertain** (lack of evidence)
- **Fracture tend to occur** in larger group of women whose bone mineral density in **osteopenic range** (T-score of  $-1.0$  to  $-2.5$ )
- Therapy shown to be effective in women with osteopenia are needed

Need trial to assess **effect of bisphosphonate** on fracture in **post menopausal women** with BMD is characterized as **osteopenia**



# PREVIOUS CLINICAL TRIAL (OSTEOPOROSIS)



Bisphosphonate	Average relative risk (95% confidence interval)		
	Vertebral fracture	Nonvertebral fractures	Hip fracture
<b>Alendronate</b>			
FIT-1 <sup>12</sup>	0.53 (0.41–0.68)	0.8 (0.63–1.01)	0.49 (0.23–0.99)
FIT-2 <sup>14</sup>	0.56 (0.39–0.8)	0.88 (0.74–1.04)	0.79 (0.43–1.44)
FLEX <sup>6</sup>	0.86 (0.6–1.22)	1.00 (0.76–1.32)	1.02 (0.51–2.10)
<b>Risedronate</b>			
VERT-NA <sup>13</sup>	0.59 (0.43–0.82)	0.6 (0.39–0.94)	Not available
VERT-MN <sup>17</sup>	0.51 (0.36–0.73)	0.67 (0.44–1.04)	Not available
HIP <sup>18</sup>	Not available	0.8 (0.7–1.0)	0.7 (0.6–0.9)
<b>Ibandronate</b>			
BONE <sup>15</sup>	0.5 (0.26–0.66)	Not available	Not available
Intermittent dosing			
<b>Zoledronate</b>			
HORIZON-PFT <sup>16</sup>	0.3 (0.24–0.38)	0.75 (0.64–0.87)	0.59 (0.42–0.83)
HORIZON-RFT <sup>19</sup>	0.54 (0.32–0.92)	0.73 (0.55–0.98)	0.7 (0.41–1.19)

**Abbreviations:** BONE, oral iBandronate Osteoporosis vertebral fracture trial in North America and Europe; FIT, Fracture Intervention Trial; FLEX, Fracture intervention trial Long-term EXtension; HIP, Hip Intervention Program; HORIZON-PFT; HORIZON-RFT; VERT-MN, Vertebral Efficacy with Risedronate Therapy-MultiNational; VERT-NA, Vertebral Efficacy with Risedronate Therapy-North America.



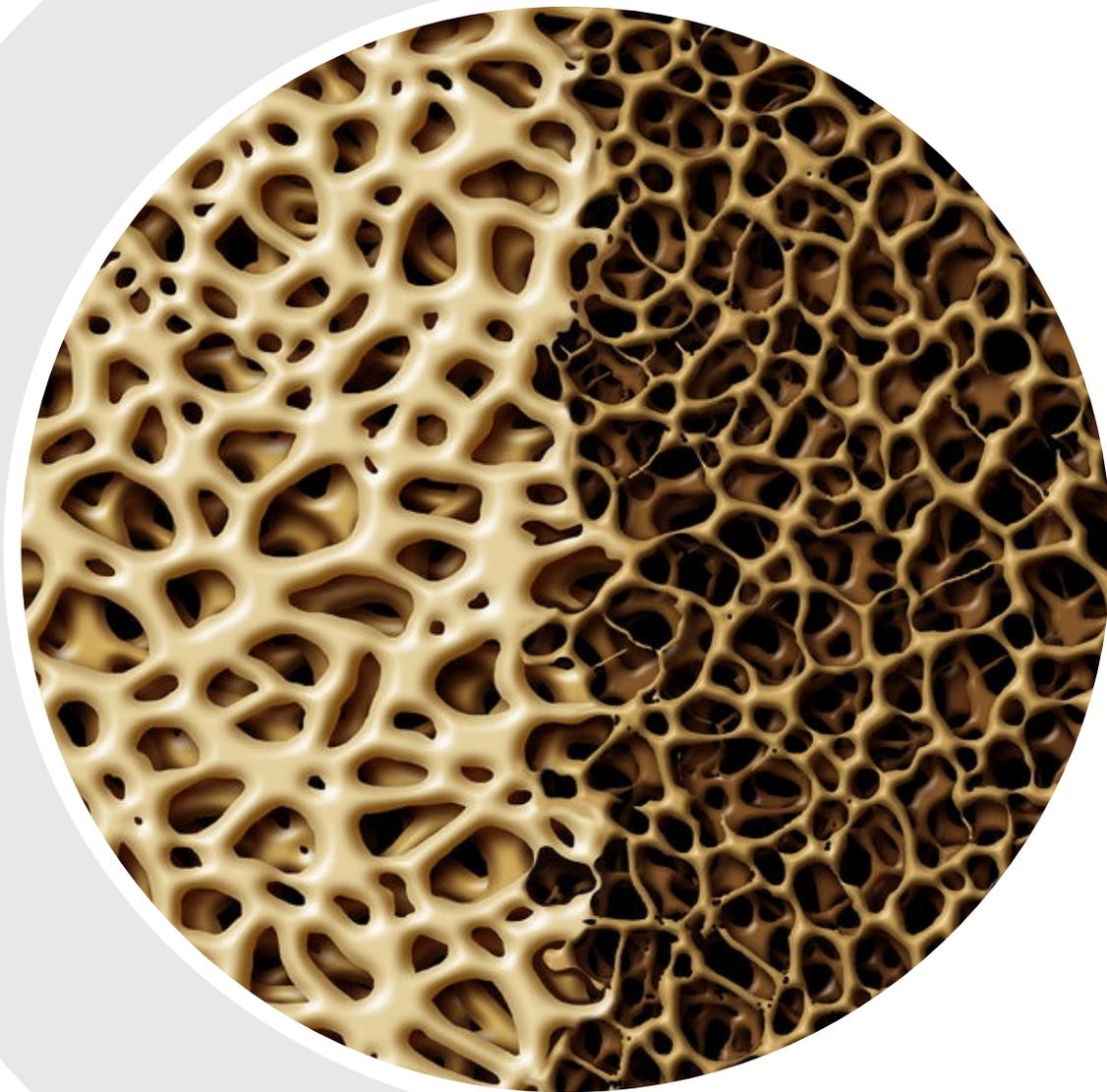
# PREVIOUS CLINICAL TRIAL (OSTEOPENIA)



- **Alendronate** 
  - No significant lower risk of clinical fractures with alendronate than placebo among women with osteopenia
- **Risedronate** 
  - Suggested fracture prevention among patients who had osteopenia
- **Clodronate** 
  - Found to reduce incidence of total fracture among community-dwelling women older than 75 years of age

**Benefit** of treatment of bisphosphoate in **patient with osteopenia**  
**remain unclear** (controversial study)





# *METHODS*

Zoledronate 5 mg  
q 18 months x 4

Normal saline  
q 18 months x 4



Study time  
**6 years**



Zoledronate Group

Placebo Group

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4,552 Participants were assessed for eligibility

2,552 Did not meet inclusion criteria

2,000 Patients underwent randomization

**Zoledronate**  
1,000 Patients

**Normal saline**  
1,000 Patients

41 Died  
28 Withdrew  
    18 Withdrew for medical reasons  
    10 Withdrew for personal reasons  
6 Loss follow up

27 Died  
34 Withdrew  
    17 Withdrew for medical reasons  
    17 Withdrew for personal reasons  
3 Loss follow up

925 Patients  
Complete follow up at 6 years

936 Patients  
Complete follow up at 6 years

**Place**

- Auckland region of New Zealand

**Time**

- Enrolled from September 2009 through October 2011
- Last trial: January 2018



# PARTICIPANTS



## Inclusion criteria

- Ambulatory postmenopausal women
- $\geq 65$  years old
- T score of -1.0 to -2.5 (either total hip or femoral neck)

### Primary end point

- Time to first occurrence fragility fracture

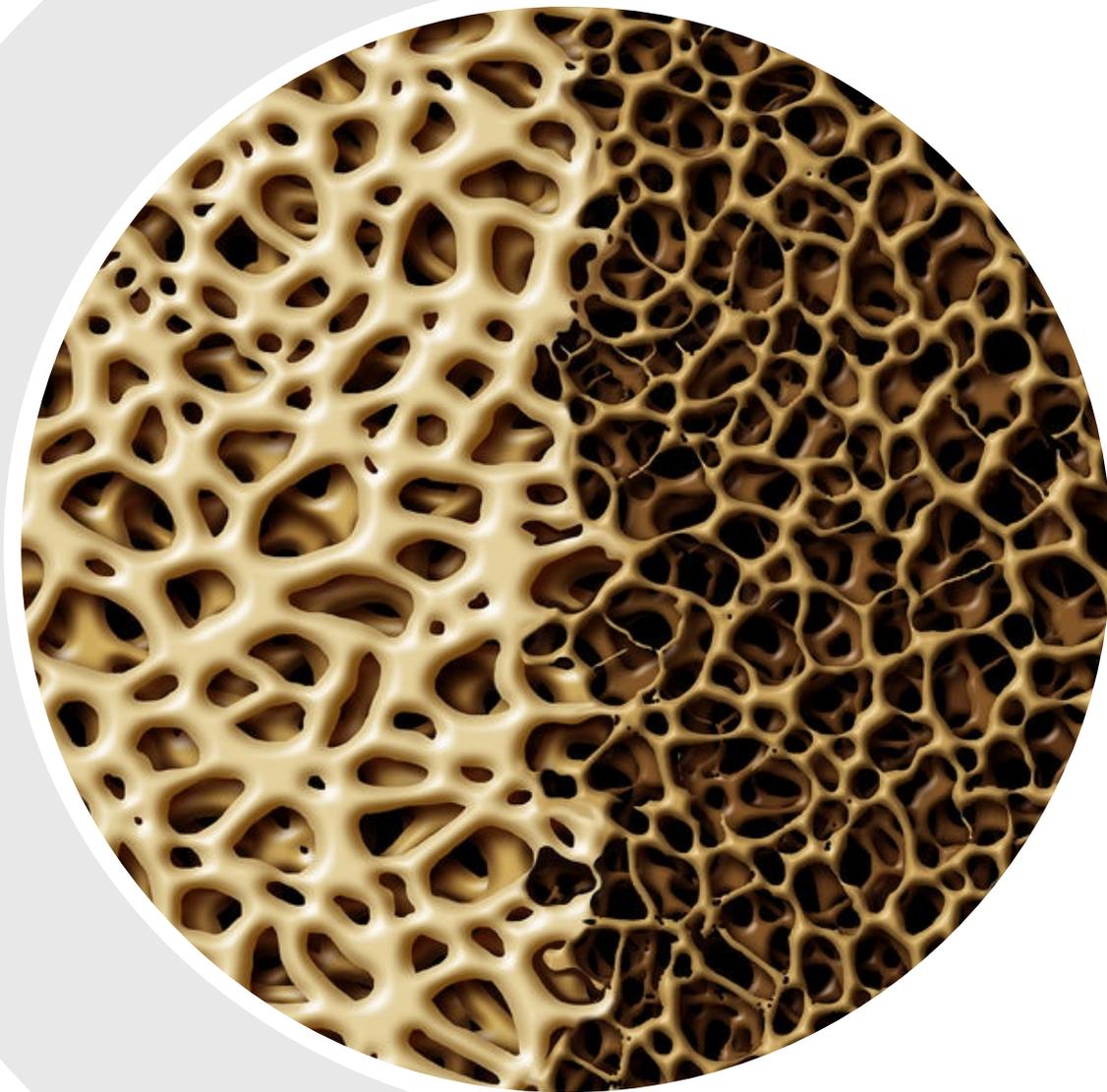
### Secondary end points

- Occurrence of symptomatic (clinical) fracture
- Occurrence of vertebral fracture
- Change in height
- Mortality

## Exclusion criteria

- eGFR  $< 30$  ml/min/1.73 m<sup>2</sup> of BSA
- Major systemic disease
- Cancer in previous 2 years
- Metabolic disease
- Regular use of bone-active drugs in previous year (including bisphosphonates, estrogen, antiestrogen, and prednisolone  $\geq 2.5$  mg/day or equivalent)

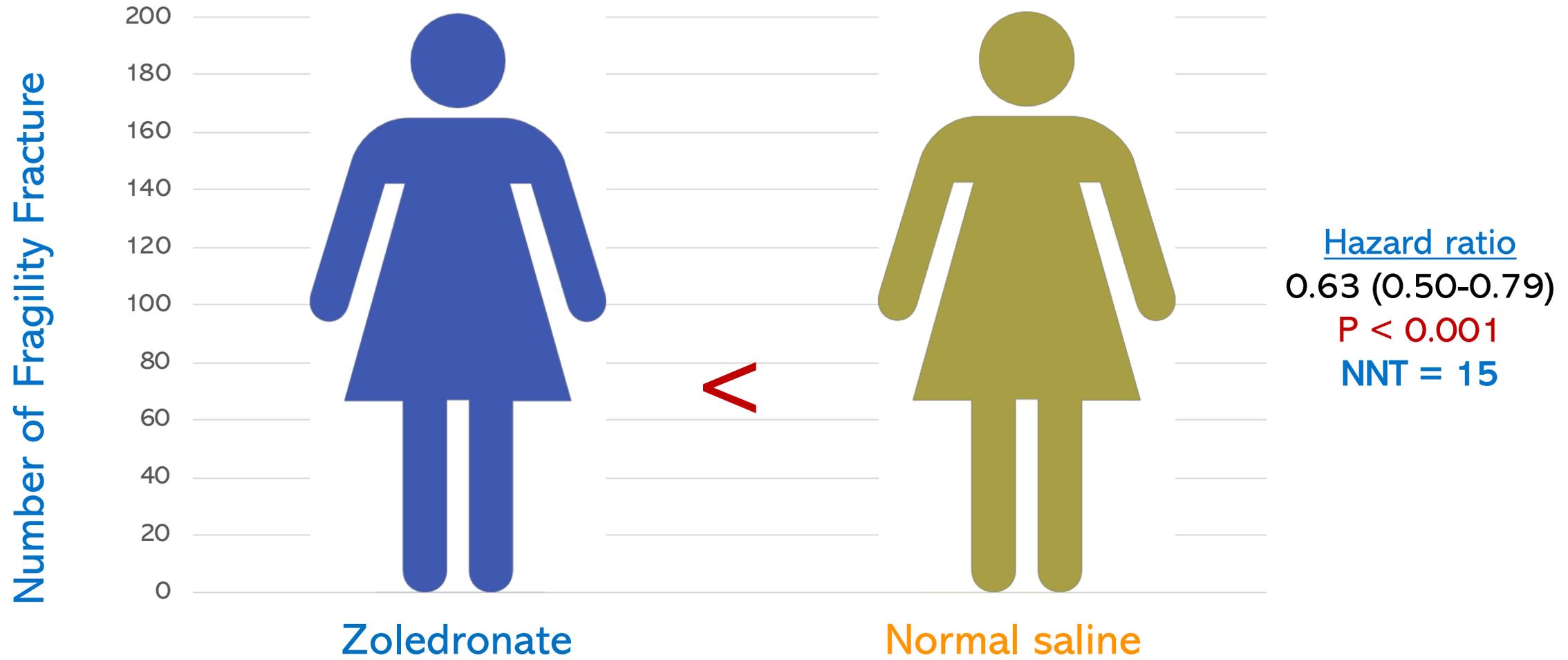




# RESULTS

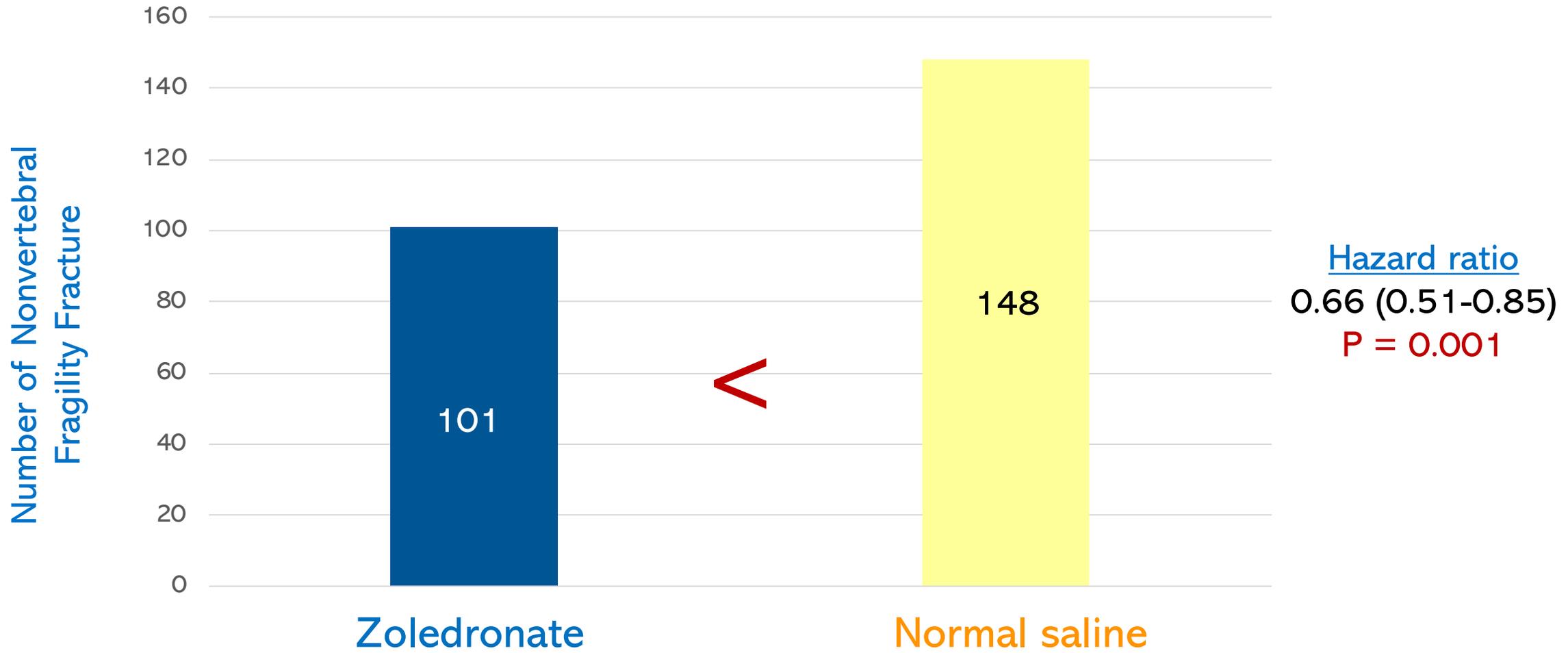
# Primary End Point

## Fragility Fracture after 6-Year Follow up



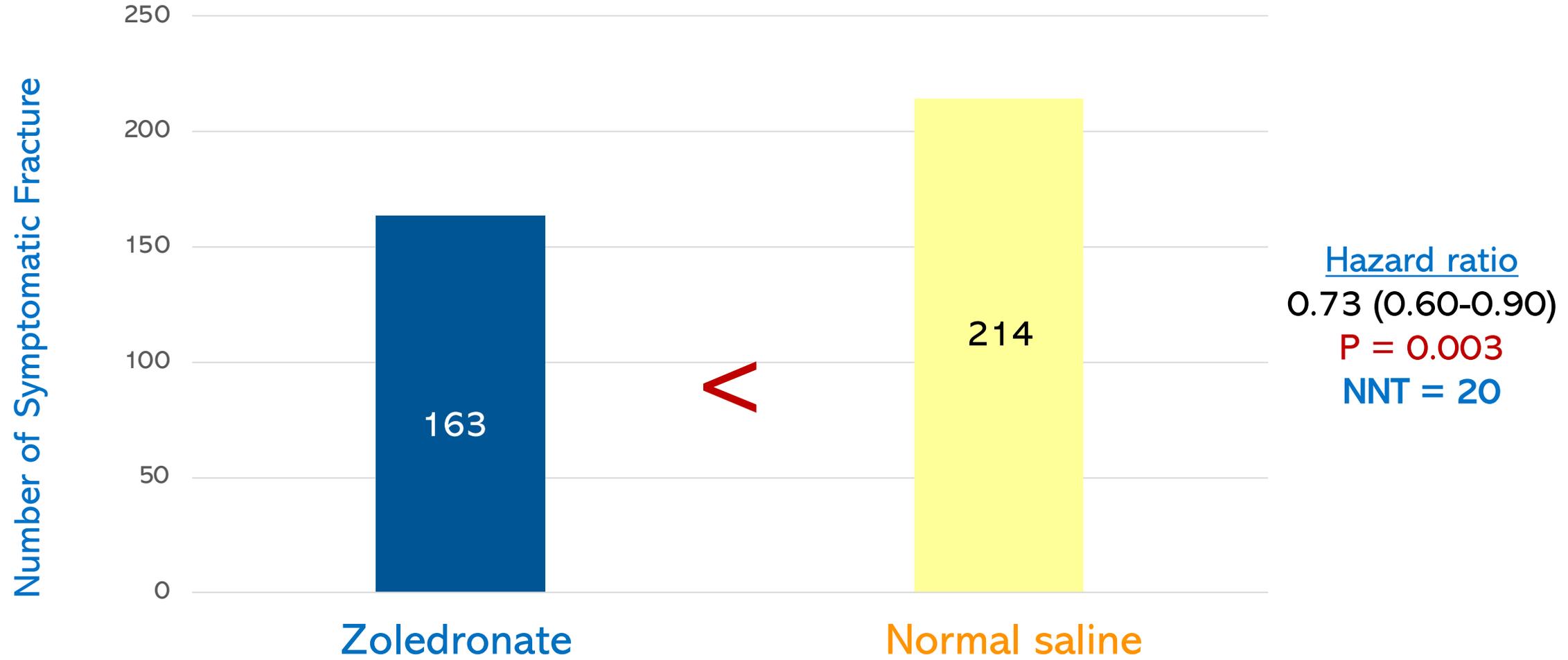
# Primary End Point

## Non vertebral fragility Fracture after 6-Year Follow up



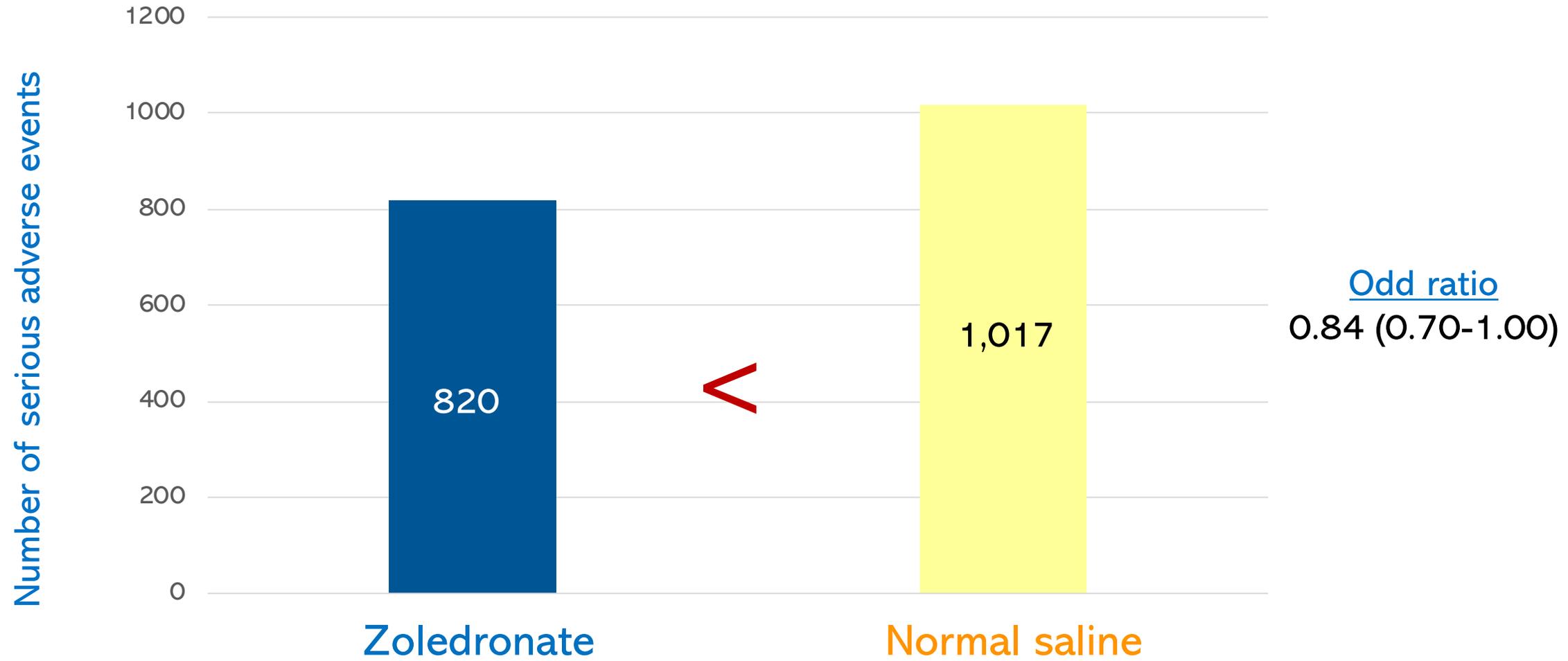
# Secondary End Point

## Symptomatic Fracture after 6-Year Follow up



# Secondary End Point

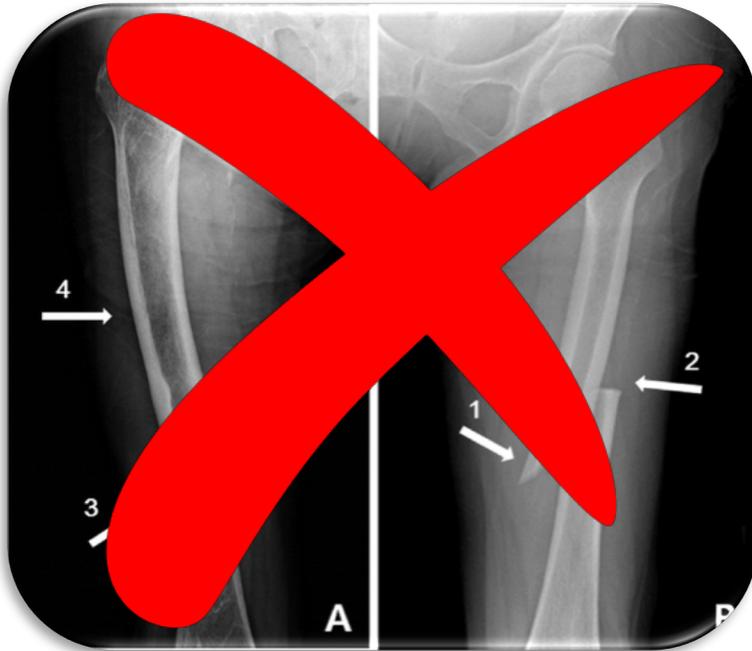
## Serious adverse events



# RESULTS



No atypical femoral fractures  
in either group

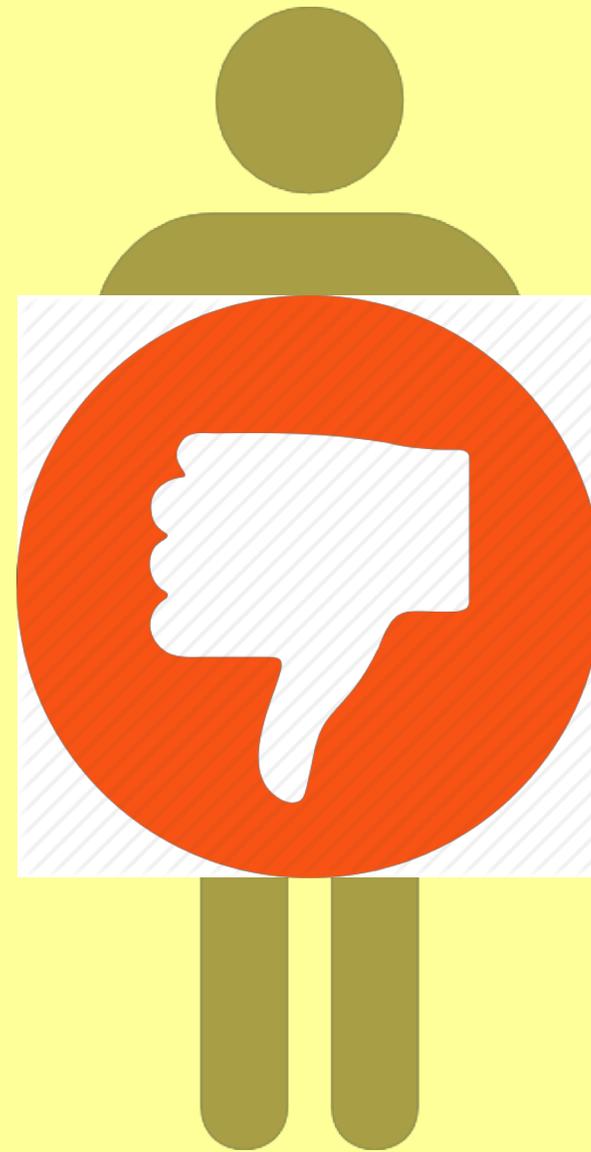


No osteonecrosis  
in either group





Zoledronate Group



Placebo Group

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# CONCLUSION

# CONCLUSION



- Risk of nonvertebral or vertebra fragility fractures was **significantly lower** in women with osteopenia who received **zoledronate** than in women who received placebo
- **NNT = 15 (To prevent 1<sup>st</sup> fragility fracture)**
- Funded by
  - Health Research Council of New Zealand

Postmenopausal women (age  $\geq$  65 years old) with osteopenia **may have benefit from zoledronate** to prevent fragility fracture

**Cost**  
55,648 baht / 6 years  
9,275 baht / year

< Zoledronic Acid

Trade Name(s)

ZOLENNIC  
ZOMETA  
ACLASTA

ราคาและเงื่อนไข (Price and Prescription Condition)

TRADE NAME	DOSAGE FORM	STRENGTH /PACKAGE SIZE	ราคาขาย	บัญชียาหลักแห่งชาติ
ZOLENNIC	inj	4 mg, 5 mL	2,886.00	X
ZOMETA	inj	4 mg, 100 mL	13,655.00	X
ACLASTA	inj	5 mg, 100 mL	13,912.00	X





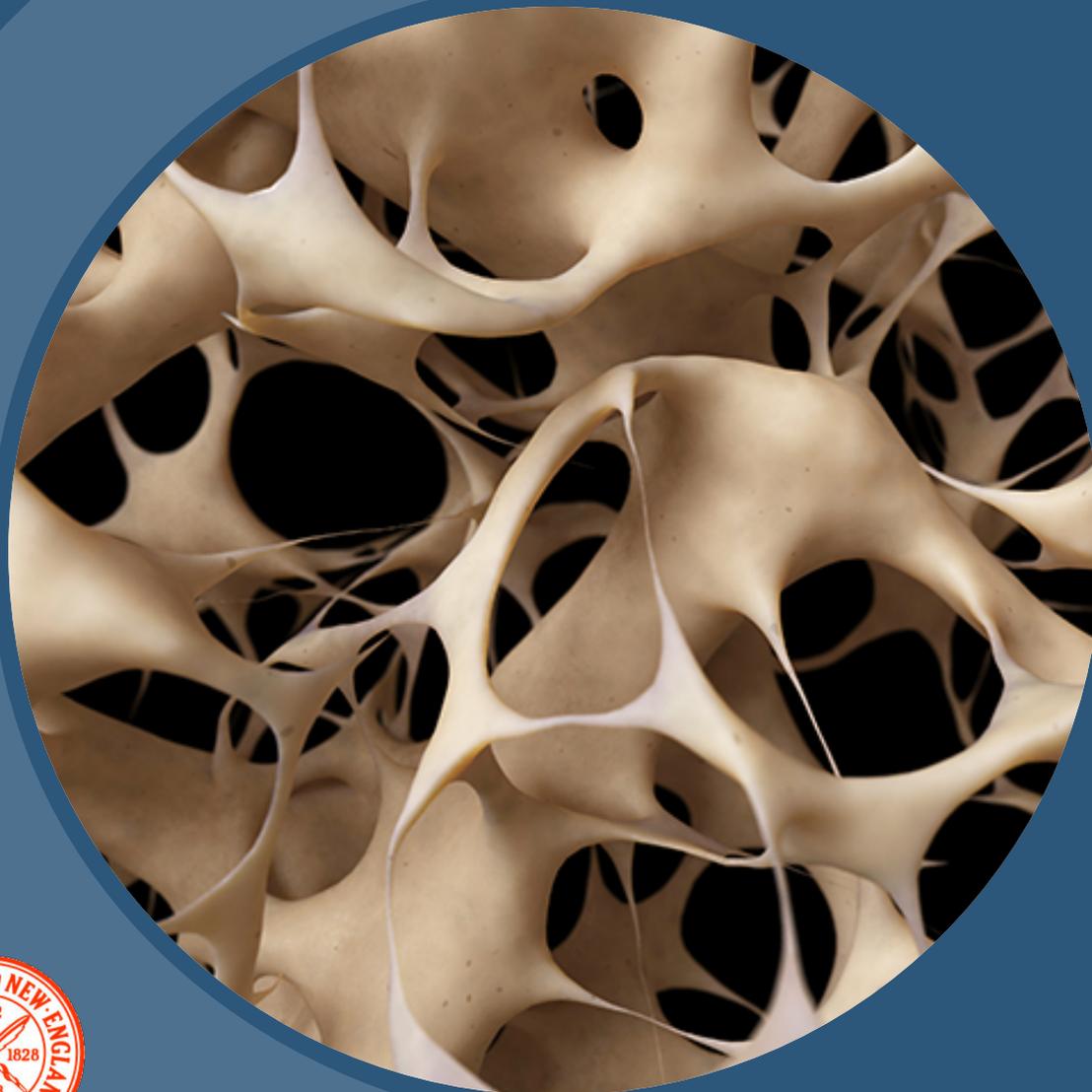
# *Journal Watch*

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**The End**  
**Thank you for your attention**

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