GISMO 2022

XVIII CONGRESSO NAZIONALE

FRAGILITÀ MUSCOLO-SCHELETRICA
STILI DI VITA E APPROPRIATEZZA TERAPEUTICA

LE SFIDE PER IL FUTURO

Baveno
7 - 8 ottobre 2022

GISMO

Gruppo Italiano Studio
Malattie Metabolismo Osseo

- Osteoporosi
- Malattie Muscolo-Scheletriche
- Malattie Metaboliche
- Dolore
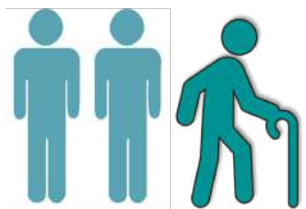- Nutrizione
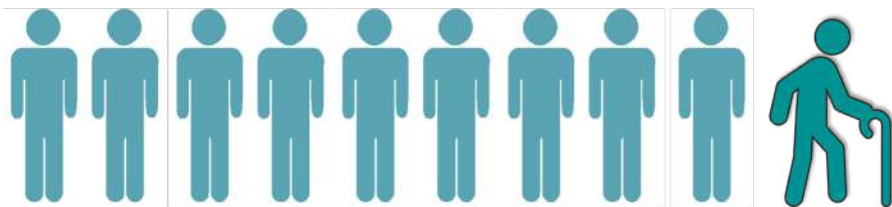
Professoressa Patrizia D'Amelio

Università di Losanna

*Osteoporosi nell'anziano:
to treat or not to treat?*

Aging world

In 2050, 1 person out of 3 will be older than 65 years

1 out of 10 will be older than 80

He W, et al. An aging world: 2015-International Population Reports. US Census Bureau, Washington, DC. 2016

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Fractures incidence increases with aging

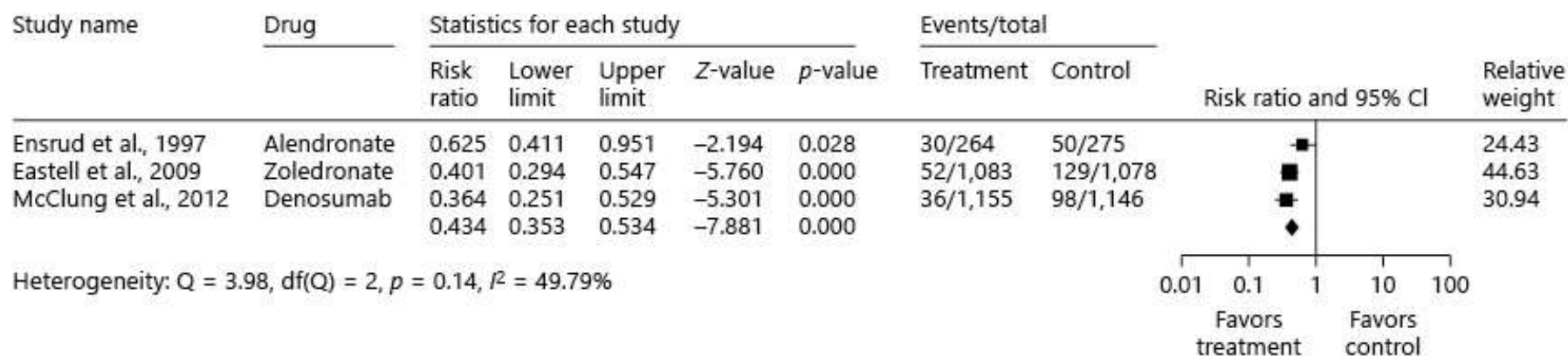*Bergh C. PLOS ONE 15(12): e0244291. 2020*

gismo.net
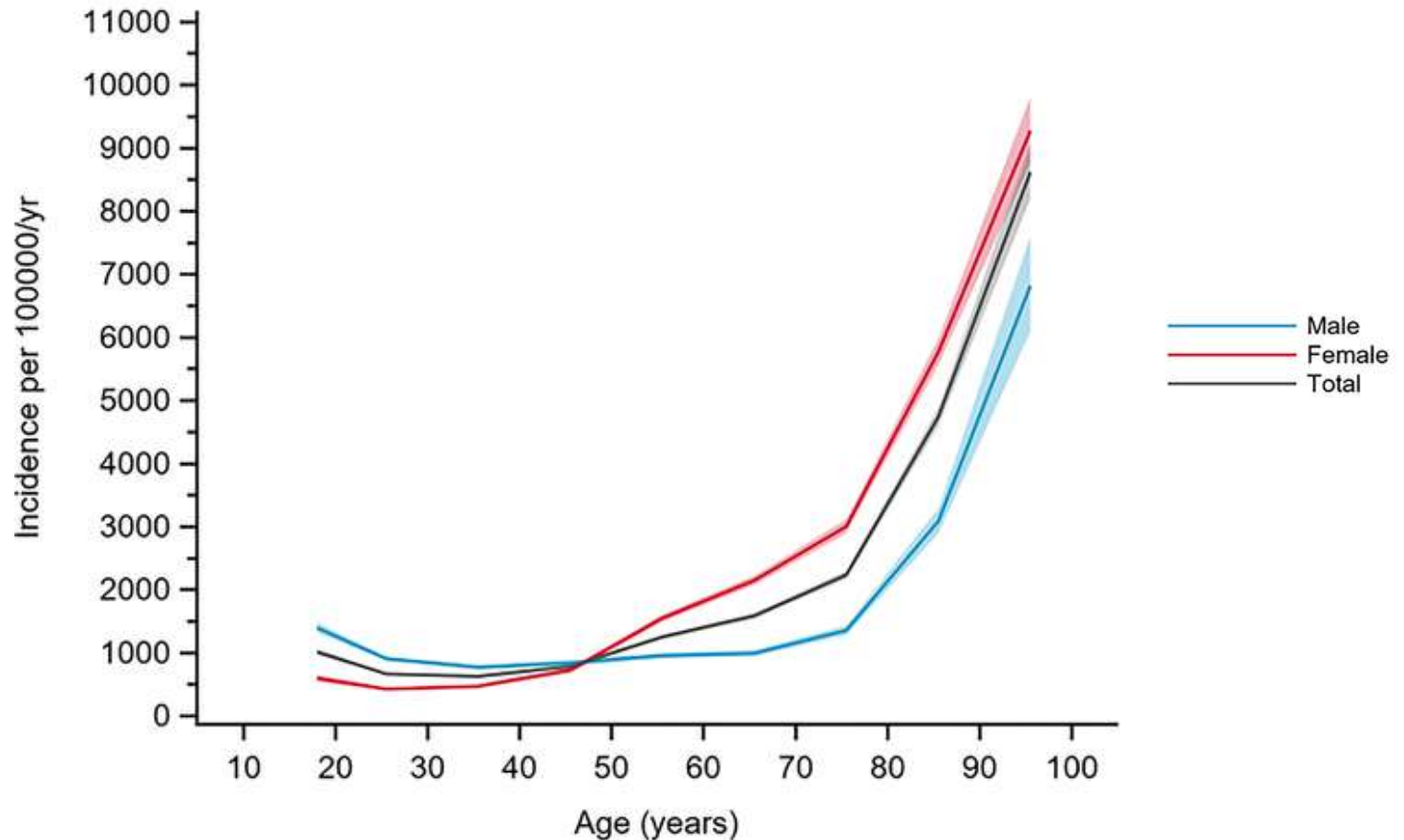
Why shouldn't we treat an old patient?
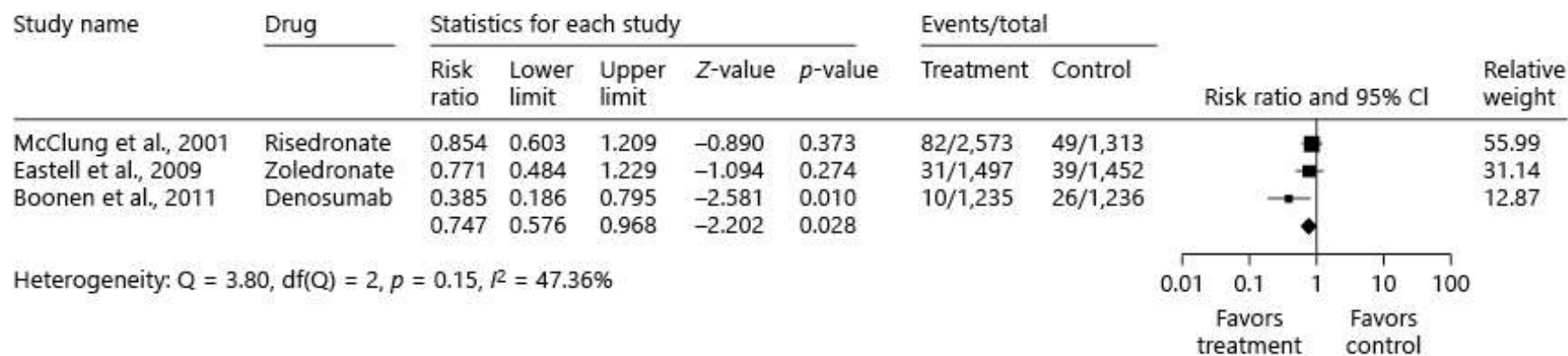# Or
When a prescription is not appropriate?

- Lack of efficacy?

- Increase in adverse events?

- Unfavorable cost/benefit ratio?

- Therapeutic futility?

Meta-analysis of the effect of antiresorptive agents on vertebral fracture risk reduction in patients aged ≥75 years.

Study name	Drug	Statistics for each study					Events/total		Risk ratio and 95% CI	Relative weight
		Risk ratio	Lower limit	Upper limit	Z-value	p-value	Treatment	Control		
Ensrud et al., 1997	Alendronate	0.625	0.411	0.951	−2.194	0.028	30/264	50/275		24.43
Eastell et al., 2009	Zoledronate	0.401	0.294	0.547	−5.760	0.000	52/1,083	129/1,078		44.63
McClung et al., 2012	Denosumab	0.364	0.251	0.529	−5.301	0.000	36/1,155	98/1,146		30.94
		0.434	0.353	0.534	−7.881	0.000				

Heterogeneity: Q = 3.98, df(Q) = 2, p = 0.14, I^2 = 49.79%

0.01 0.1 1 10 100

Favors treatment — Favors control

Wang Q.-Y. et al. Gerontology 2021;67:639–649

gismo.net
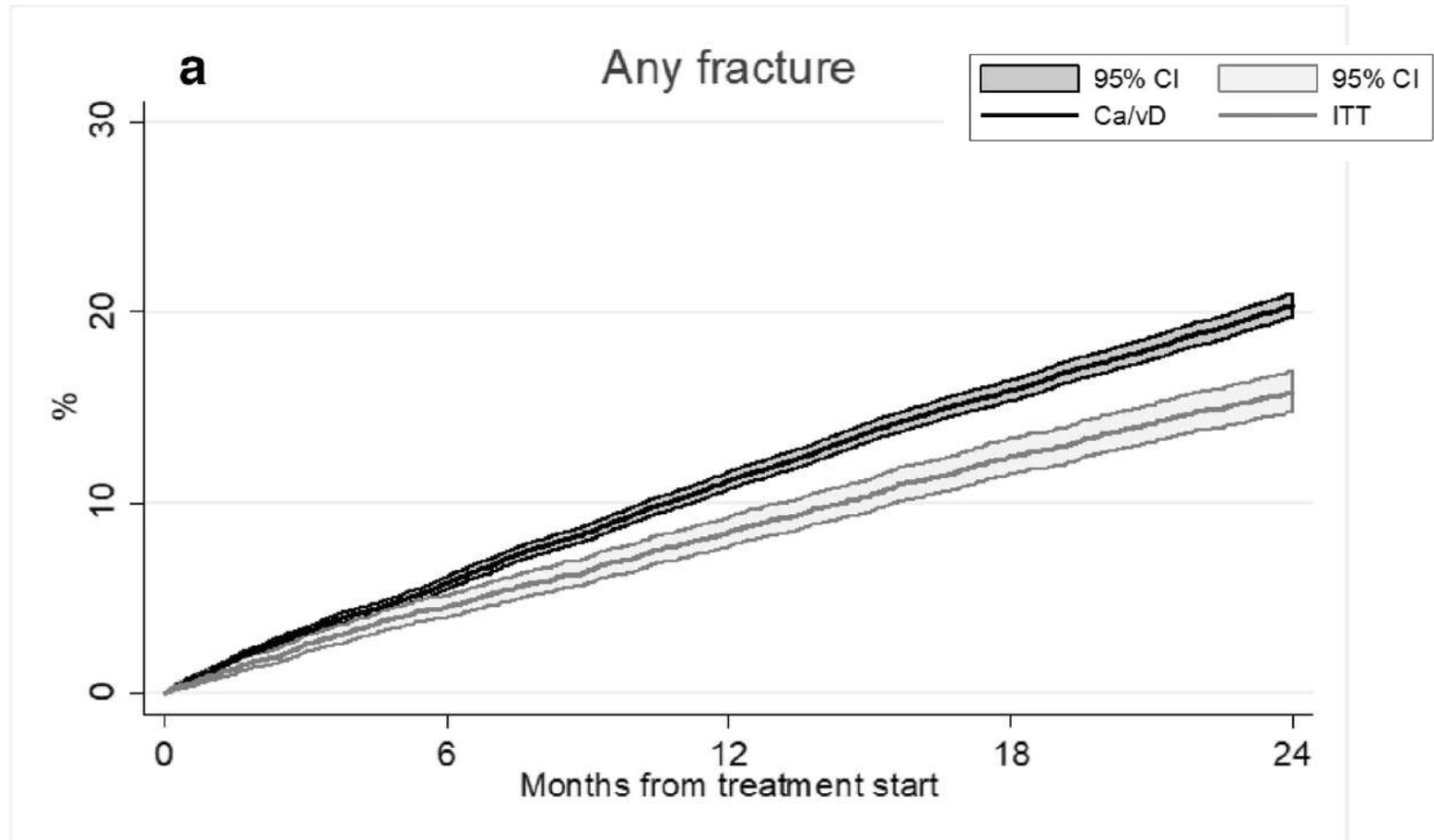
Meta-analysis of the effect of antiresorptive agents on reducing the risk of femur fracture in patients aged ≥75 years

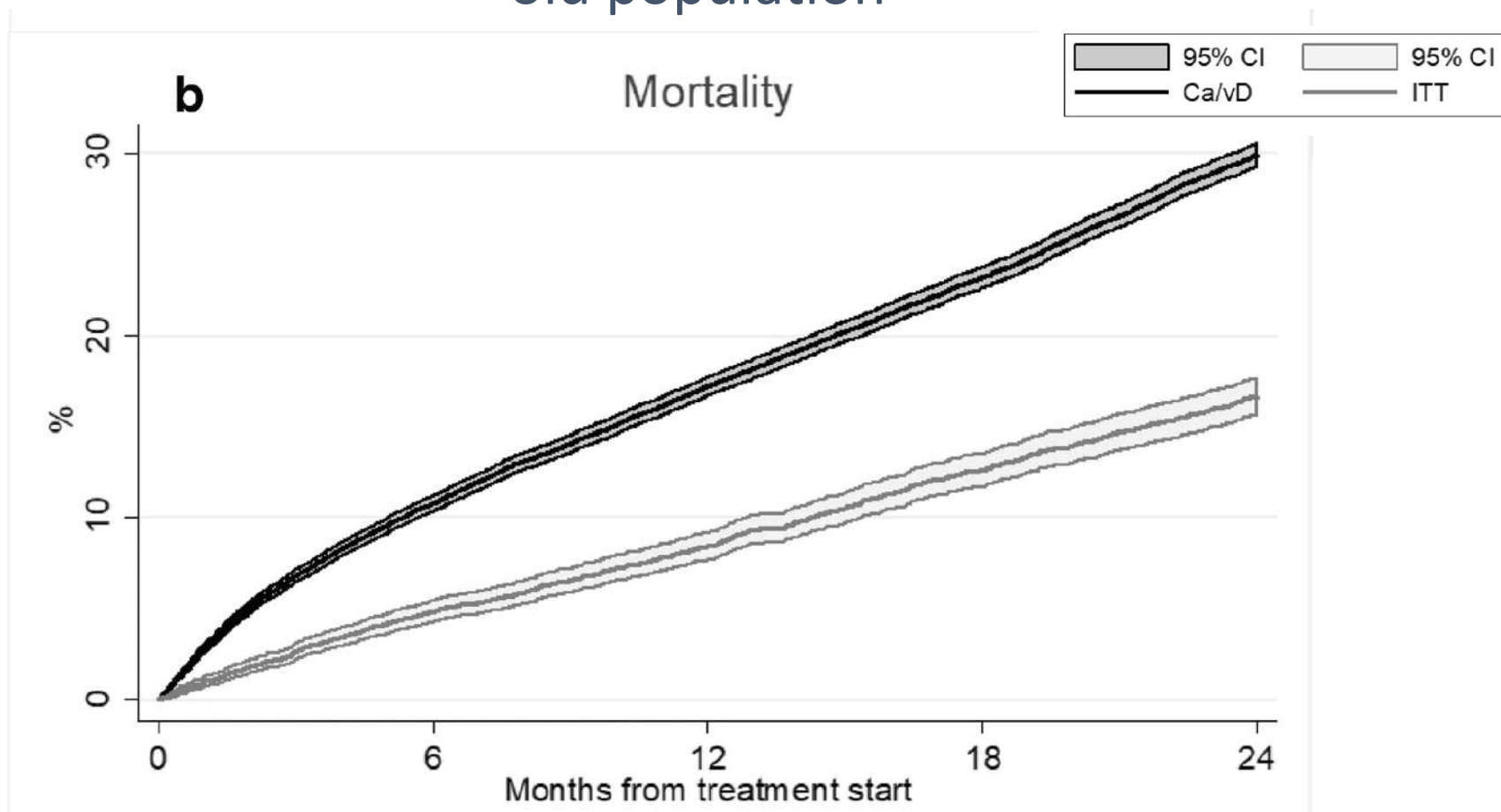| Study name	Drug	Risk ratio	Lower limit	Upper limit	Z-value	p-value	Treatment	Control	Risk ratio and 95% CI	Relative weight
		Statistics for each study					Events/total			
McClung et al., 2001	Risedronate	0.854	0.603	1.209	−0.890	0.373	82/2,573	49/1,313		55.99
Eastell et al., 2009	Zoledronate	0.771	0.484	1.229	−1.094	0.274	31/1,497	39/1,452		31.14
Boonen et al., 2011	Denosumab	0.385	0.186	0.795	−2.581	0.010	10/1,235	26/1,236		12.87
		0.747	0.576	0.968	−2.202	0.028				

Heterogeneity: $Q = 3.80$, $df(Q) = 2$, $p = 0.15$, $I^2 = 47.36\%$

Favors treatment — Favors control

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Real-world effectiveness of osteoporosis treatment in the old population

O. Ström, R. et al Osteoporosis International 2020

gismo.net

Real-world effectiveness of osteoporosis treatment in the old population

O. Ström, R. et al Osteoporosis International 2020
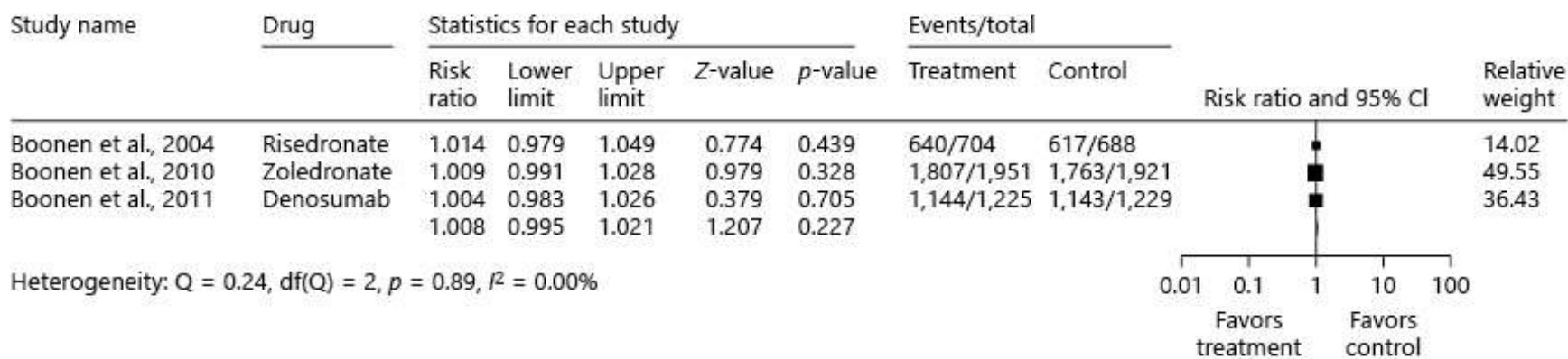
Why shouldn't we treat an old patient?
Or
When a prescription is not appropriate?

- Lack of evidence of effectiveness? NO!

- Increase in adverse events?

- Unfavorable cost/benefit ratio?

- Therapeutic futility?

# Meta-analysis of the safety of anti-resorptive agents in terms of any adverse event in patients aged ≥75 years.

Study name	Drug	Statistics for each study					Events/total		Risk ratio and 95% CI	Relative weight
		Risk ratio	Lower limit	Upper limit	Z-value	p-value	Treatment	Control		
Boonen et al., 2004	Risedronate	1.014	0.979	1.049	0.774	0.439	640/704	617/688		14.02
Boonen et al., 2010	Zoledronate	1.009	0.991	1.028	0.979	0.328	1,807/1,951	1,763/1,921		49.55
Boonen et al., 2011	Denosumab	1.004	0.983	1.026	0.379	0.705	1,144/1,225	1,143/1,229		36.43
		1.008	0.995	1.021	1.207	0.227				

Heterogeneity: Q = 0.24, df(Q) = 2, p = 0.89, I^2 = 0.00%

0.01   0.1   1   10   100

Favors treatment   Favors control

Wang Q.-Y. et al. Gerontology 2021;67:639–649

gismo.net

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Consequences of fractures

COMPLETE RECOVERY   PARTIAL RECOVERY   DEATH
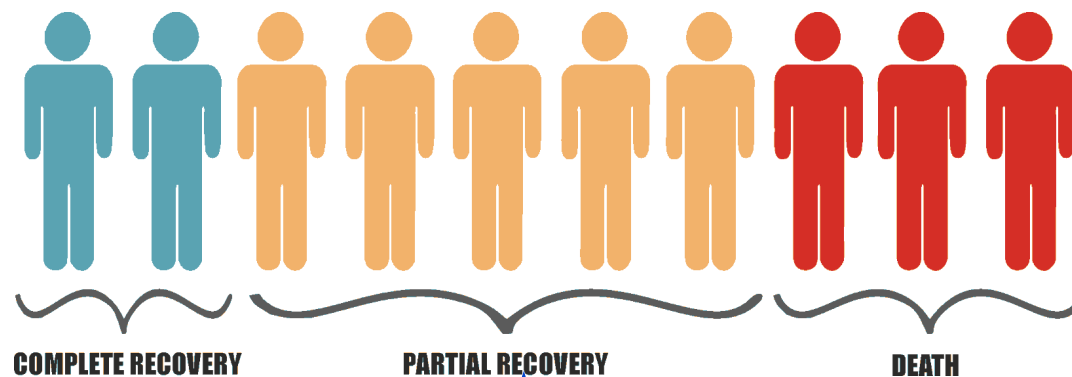
LOSS OF INDEPENDENCE

80%

After a fracture cannot climb the stairs

50%

Loose independence
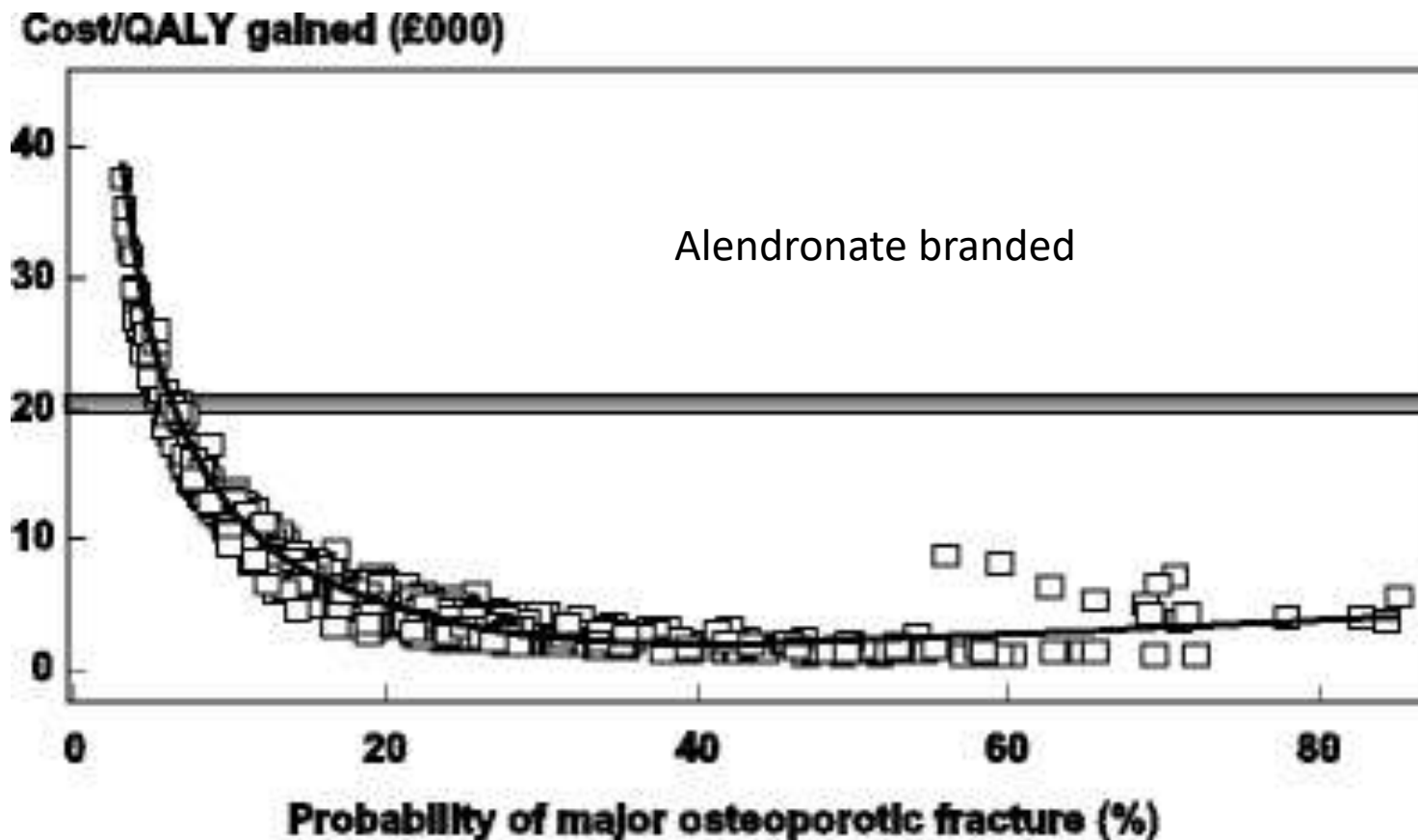
HIGH MORTALITY RATE

30%

Within a year of hip fracture

Costi socio-sanitari: un altro prezzo da pagare

- degenza
- cura e riabilitazione
- invalidità transitoria o permanente
- impegno socio-assistenziale per i pazienti non più autonomi
- mortalità precoce

EUROPA
31.7
MILIARDI

Costi diretti delle fratture da osteoporosi

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Cost/effectiveness of alendronate

Alendronate branded

gismo.net

Cost/effectiveness of Denosumab

T score	Previous fracture			
	Age (years)			
Den/no treat	60	65	70	75
≤-2,5	2400	Cost saving	Cost saving	Cost saving
≤-3,0	Cost saving	Cost saving	Cost saving	Cost saving
≤3,5	Cost saving	Cost saving	Cost saving	Cost saving
≤-4,0	Cost saving	Cost saving	Cost saving	Cost saving
Den/alendronate				
≤-2,5	9890	4102	Cost saving	Cost saving
≤-3,0	3932	Cost saving	Cost saving	Cost saving
≤3,5	Cost saving	Cost saving	Cost saving	Cost saving
≤-4,0	Cost saving	Cost saving	Cost saving	Cost saving

*Darbà J et al. Clinico econ Outcomes Res. 2015*

gismo.net

Cost/effectiveness of teriparatide
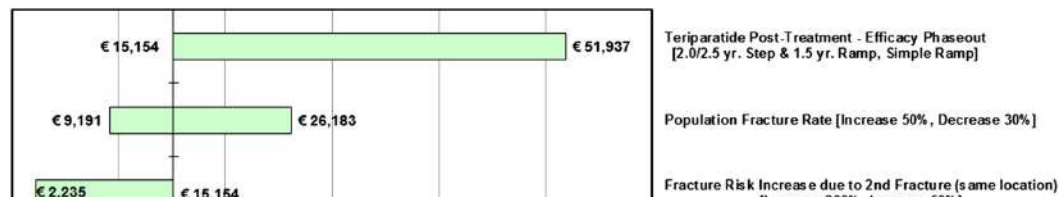
The results from this study demonstrate that there are high-risk osteoporosis patient cohorts where teriparatide use as a first-line agent is a cost-effective treatment option compared to bisphosphonates or to no treatment.

Murphy et al. BMC Musculoskeletal Disorders 2012

gismo.net
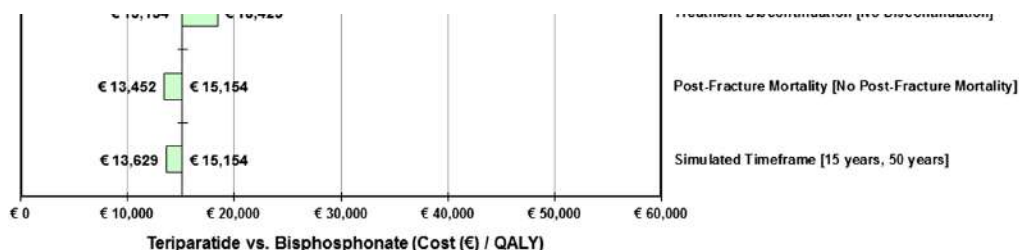
Cost-effectiveness of a secondary fracture prevention intervention

Usual care
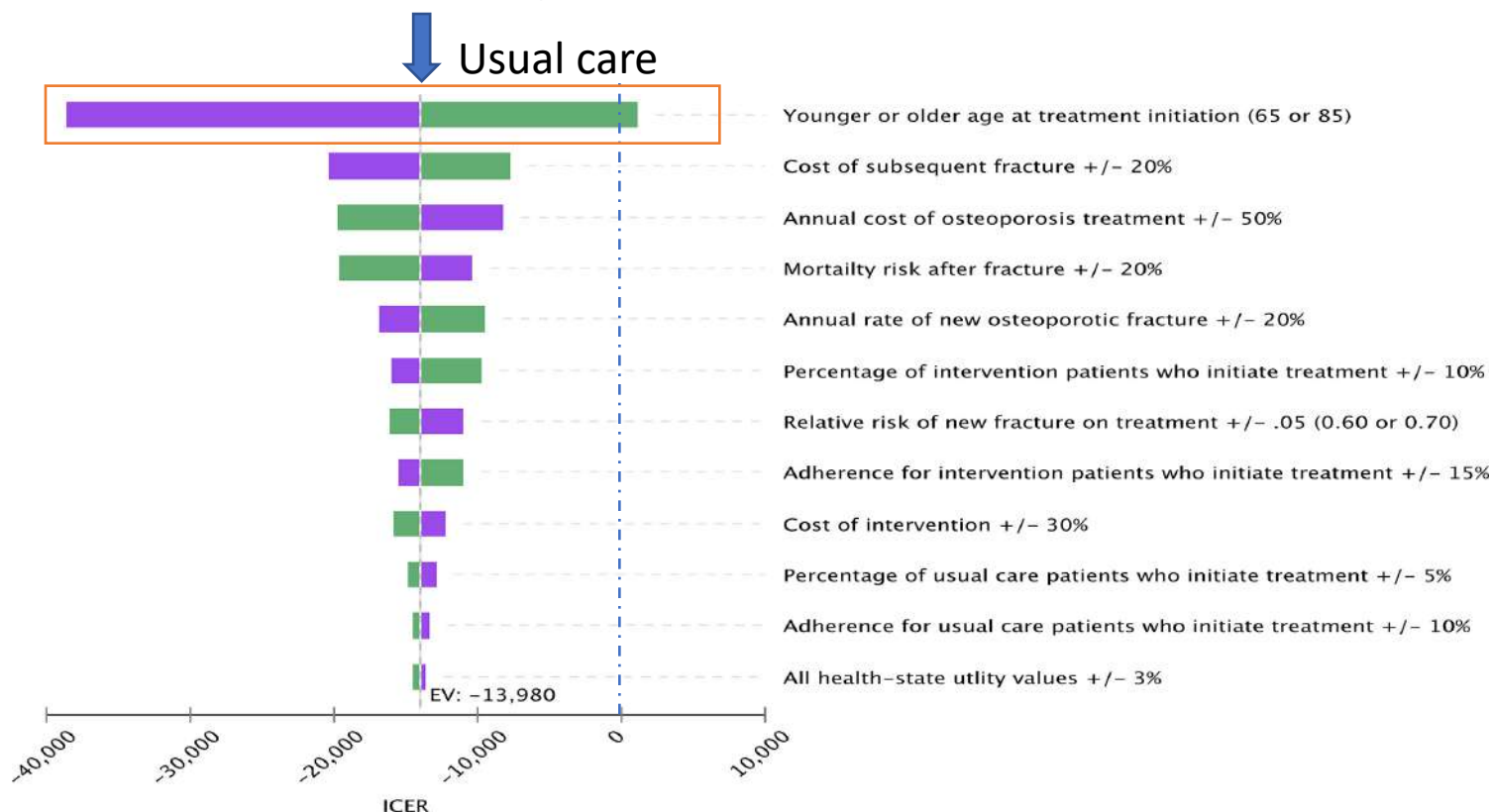
incremental cost-effectiveness value (ICER)

Nayak S, Singer A, Greenspan SL. J Am Geriatr Soc. 2021

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- Increase in adverse events?   **NO!**

- Unfavorable cost/benefit ratio?   **NO!**

- Therapeutic futility?

JAMA Internal Medicine | Original Investigation

Time to Benefit of Bisphosphonate Therapy for the Prevention of Fractures Among Postmenopausal Women With Osteoporosis
A Meta-analysis of Randomized Clinical Trials

William James Deardorff, MD; Irena Cenzer, PhD; Brian Nguyen, BA; Sei J. Lee, MD, MAS

10 RCTs comprising 23 384 postmenopausal women with osteoporosis.
The pooled meta-analysis found that 12.4 months (95%CI, 6.3-18.4 months)were
needed to avoid 1 non vertebral fracture per 100 postmenopausal women receiving
bisphosphonate therapy

Association of Disease Definition, Comorbidity Burden, and Prognosis With Hip Fracture Probability Among Late-Life Women

Kristine E. Ensrud, MD, MPH; Allyson M. Kats, MS; Cynthia M. Boyd, MD; Susan J. Diem, MD, MPH; John T. Schousboe, MD, PhD; Brent C. Taylor, PhD, MPH; Douglas C. Bauer, MD; Katie L. Stone, PhD; Lisa Langsetmo, PhD; for the Study of Osteoporotic Fractures (SOF) Research Group

Key Points

Question What is the association of disease definition, comorbidity burden, and prognosis with 5-year hip fracture probabilities among women 80 years and older?

Findings This prospective cohort study found that the 5-year hip fracture probability, taking into account the competing risk of death, was over 3-fold higher among women with osteoporosis compared with women without osteoporosis but at high fracture risk. The difference between groups in hip fracture probabilities was even more pronounced in women with a greater number of comorbidities or poorer prognosis.

Meaning Women 80 years and older with osteoporosis, including those with more comorbidities or poorer prognosis, have a high hip fracture probability despite accounting for competing mortality risk and may be the group most likely to be candidates for drug treatment to prevent hip fractures.

Why shouldn't we treat an old patient?
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- Lack of evidence of effectiveness? **NO!**

- Increase in adverse events? **NO!**

- Unfavorable cost/benefit ratio? **NO!**

- Therapeutic futility? **To be evaluated!**

Take home messages

✓ Antiresorptive and anabolic agents are effective treatments

for reducing fracture risk in old patients

La vecchiaia…

«la vecchiaia è una malattia sessualmente trasmissibile…
Con una progressione lenta ed un tasso di mortalità del
100%"

P. Cadrobbi

Senectus ipsa est morbus

P. Terenzio Afro

Grazie!!!!