

GISMO

Gruppo Italiano Studio
Malattie Metabolismo Osseo

- Osteoporosi
- Malattie Muscolo-Scheletriche
- Malattie Metaboliche
- Dolore
- Nutrizione

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XVIII CONGRESSO NAZIONALE

FRAGILITÀ MUSCOLO-SCHELETRICA
STILI DI VITA E APPROPRIATEZZA TERAPEUTICA
LE SFIDE PER IL FUTURO

Baveno

7 - 8 OTTOBRE 2022

LA GESTIONE DELL'OSTEOPOROSI SEVERA: IL PROGETTO SOS

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53100- Siena, Italy



Severe Osteoporosis

Table I. Classification of osteoporosis according to the WHO^[6] a

Diagnostic categories	Definition
Normal	A value for BMD within 1 SD of the young adult reference mean
Low bone mass (osteopenia)	A value for BMD >1 SD below the young adult mean but <2.5 SD below this value
Osteoporosis	A value for BMD >2.5 SD or more below the young adult mean
Severe osteoporosis	A value for BMD >2.5 SD below the young adult mean in the presence of one or more fragility fractures

a The value for BMD mentioned in each definition equals the T score.

BMD = bone mineral density.

Gaudio A et al, 2005

SEVERE= “critical or grave”.

This term is appropriate for a certain magnitude of severity in bone strength which is comprised of bone mineral density (BMD) and/or bone quality.

RISK FACTORS:

1. A prior low trauma fracture after the age of 50 years
2. Very low BMD (or T-scores) in older patients
3. A very high FRAX™ score

Table 2 - Proposed definition for osteoporosis and severe osteoporosis.

Osteoporosis	BMD T score ≤-2.5 SD or BMD T score ≥-2.5 SD in the presence of a prevalent fragility fracture
Severe osteoporosis	BMD T score ≤-2.5 with a prevalent fragility fracture or ≥2 prevalent fragility fractures independently of BMD values

This definition was endorsed by 83.3% of participants.
BMD: bone mineral density.

Nuti R et al, 2009

Miller PD et al, 2015

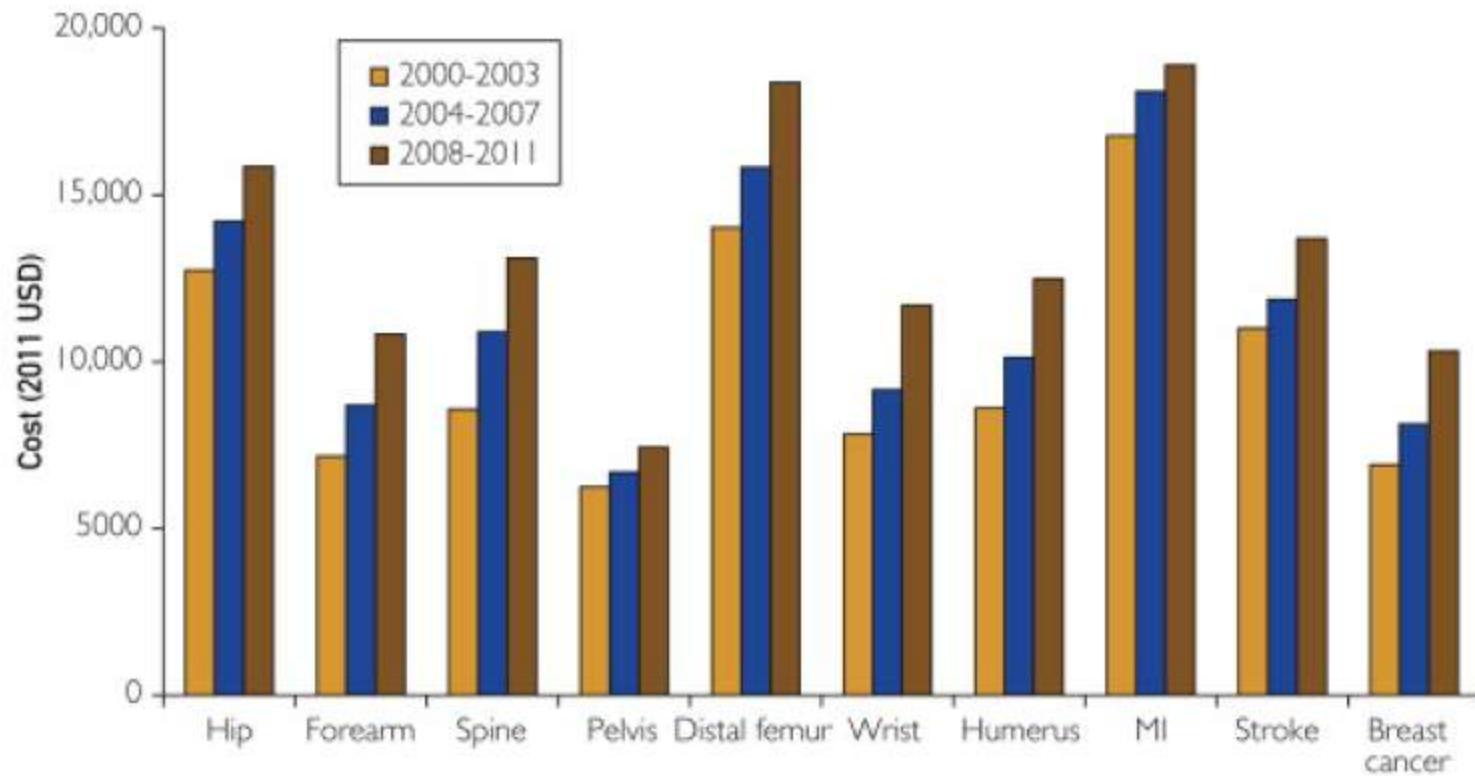
Conditions that might be associated with severe osteoporosis

1. Severe postmenopausal osteoporosis or severe male osteoporosis
2. Glucocorticoid-induced osteoporosis
3. Osteoporosis associated with systemic diseases that may also be associated with low bone formation and turnover:
 - diabetes mellitus;
 - chronic kidney disease,
 - multiple myeloma

(low bone formation associated with elevation in the serum of inhibitors of osteoblast poor bone quality.)
4. Osteoporosis associated with systemic diseases that are also associated with high bone turnover:
 - severe primary hyperparathyroidism;
 - immobilization (e.g. quadriplegia)
 - Osteoporosis associated with systemic diseases associated with frailty and a high risk for fractures from falls: Parkinson's disease, multiple sclerosis, polio, amyotrophic lateral sclerosis (ALS), and diseases associated with marked sarcopenia (deficiency of muscle mass and strength), particularly malabsorption syndromes, age-related sarcopenia, and myopathies of diffuse etiologies

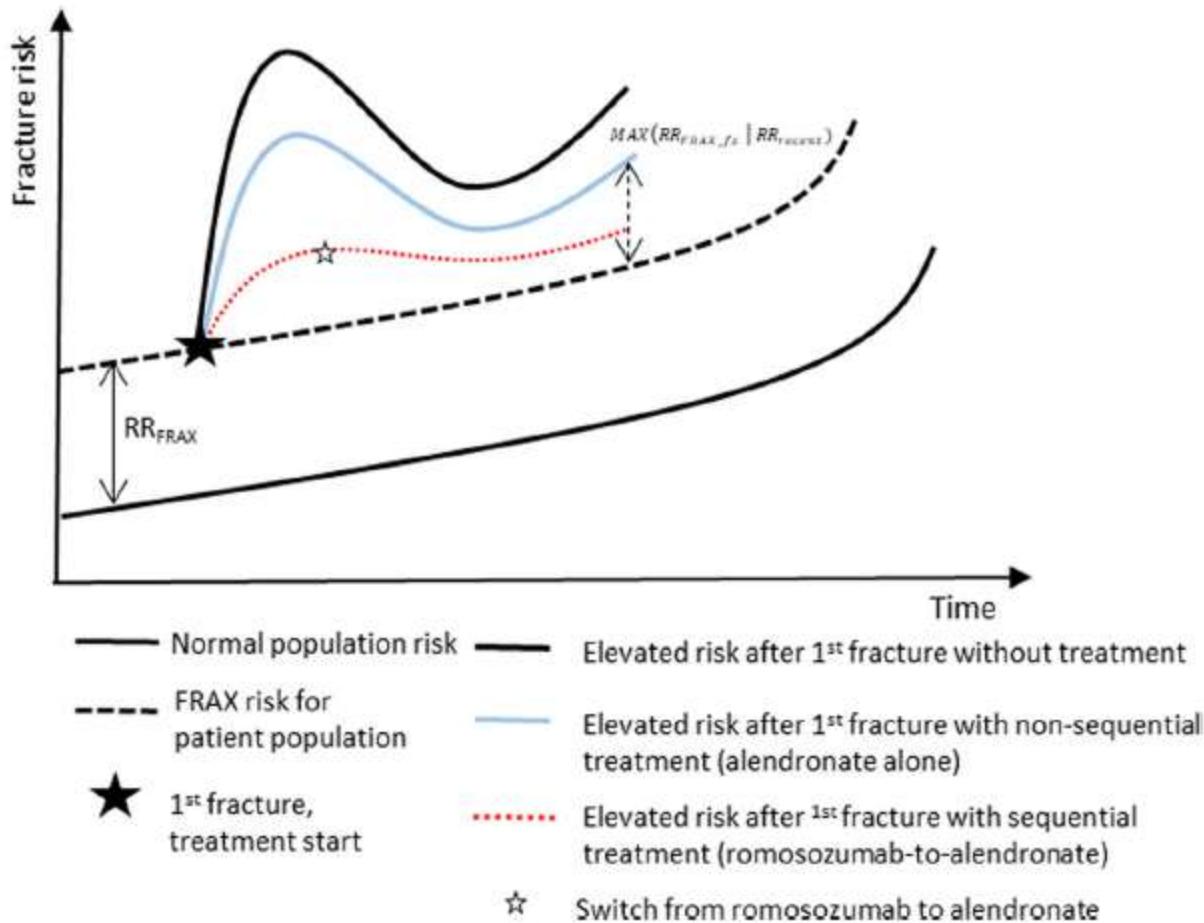
Miller PD et al, 2015

The annual costs of osteoporotic fractures as compared to the annual costs of 3 other major disease states



Singer A et al, 2015

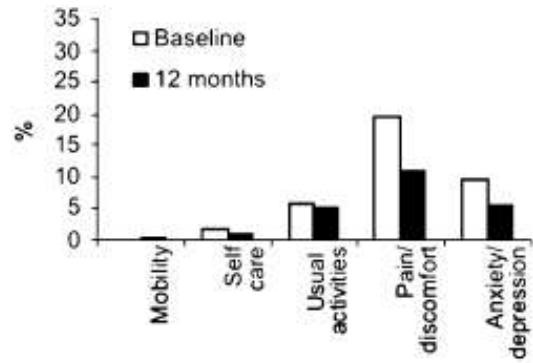
Trajectory of fracture risk after first fracture with sequential and non-sequential treatment and without treatment



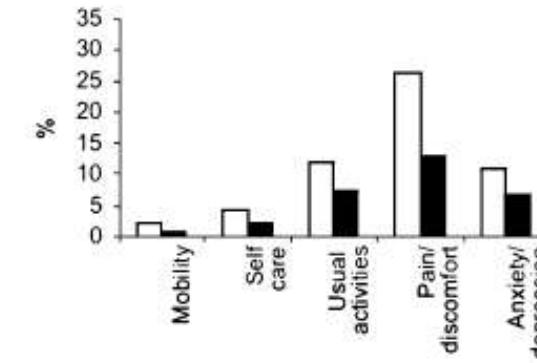
Fracture incidence and changes in quality of life in women with an inadequate clinical outcome from osteoporosis therapy: the Observational Study of Severe Osteoporosis (OSSO)

Percentage of patients reporting extreme problems in the domains of EQ-5D HSV according to prior and incident fracture status

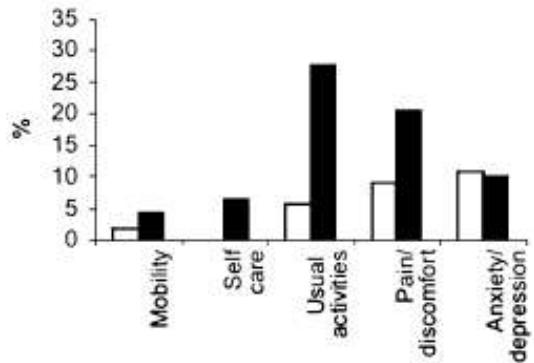
a No prior fracture/no incident fracture



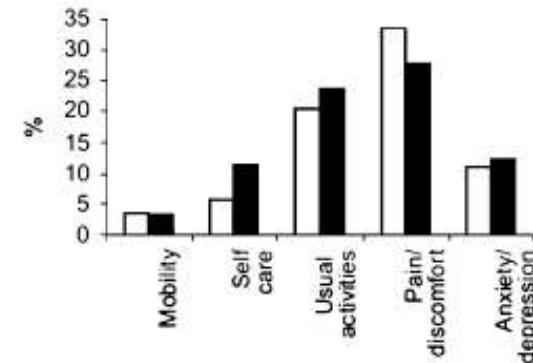
b Prior fracture/no incident fracture



c No prior fracture/incident fracture



d Prior fracture/incident fracture



Cooper C et al, 2008

Fracture risk decreases with osteoporosis medications

Molecules	Duration	Vertebral fracture risk reduction (%)	References
SERM	3 years	50% (if no prevalent VF)	Ettinger, JAMA 1999 [43]
Oral bisphosphonates	3 years	±50%	Chapurlat et al., Nat Clin Pract Endoc Metab 2006 [17]
IV bisphosphonates	3 years	75% (HORIZON) 62% (BONE, DIVA)	Black et al., NEJM 2007 [18] Chestnut et al., JBMR 2004 [19] Delmas et al., Arth Rhum 2006 [20]
Strontium ranelate	3 years	39% (TROPOS) 41% (SOTI)	Reginster et al., Arth Rheum 2008 [23] Meunier et al., NEJM 2004 [22]
Teriparatide	18 months	65%	Neer et al., NEJM 2001 [21]

Table II. Drugs approved by the US FDA for treatment of osteoporosis

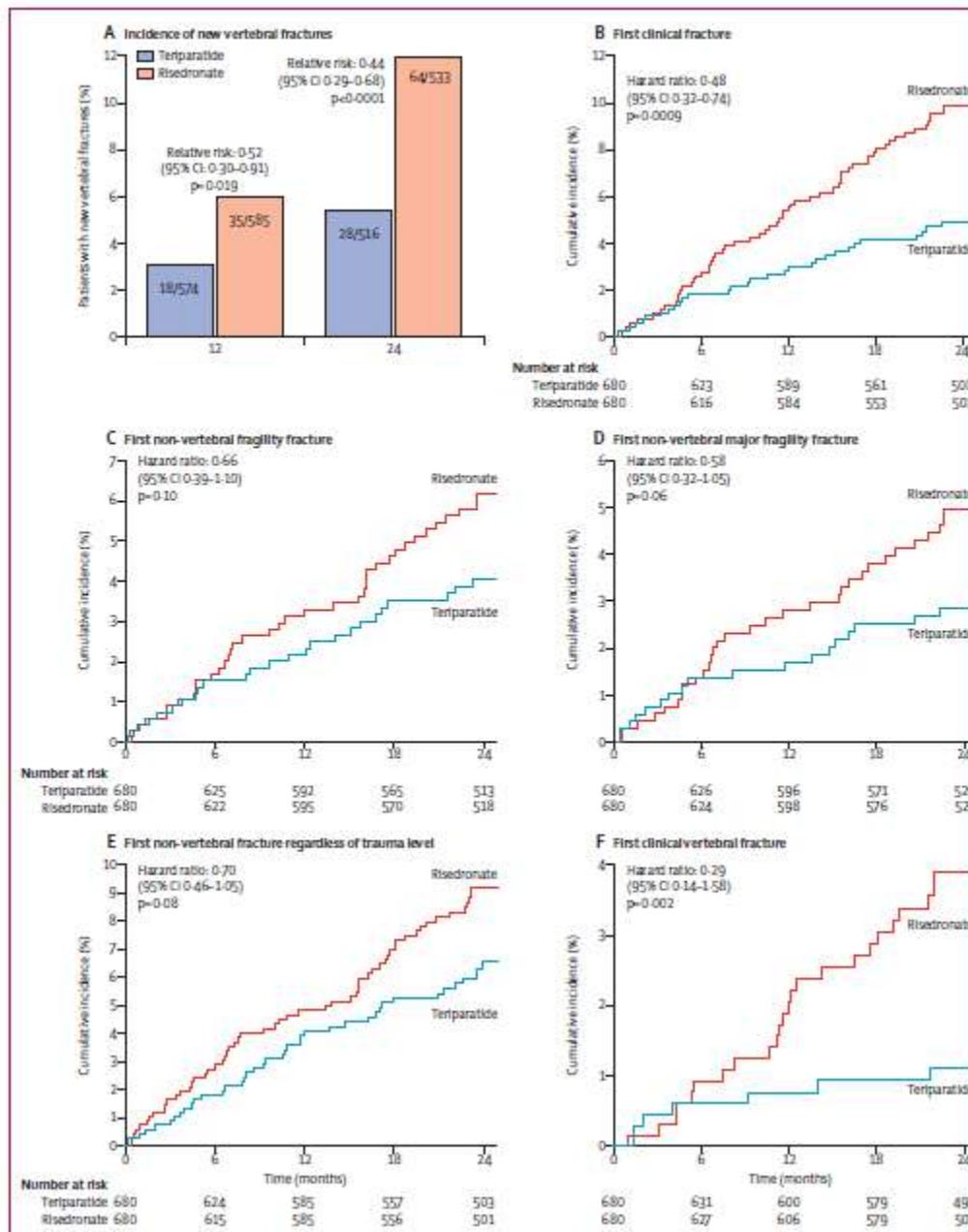
Drug	Available forms	Efficacy for preventing vertebral fractures	Efficacy for preventing femoral fractures
Alendronic acid	10mg tablets for daily administration and 70mg tablets for once-weekly administration	Yes	Yes
Risedronic acid	5mg tablets for daily administration and 35mg tablets for once-weekly administration	Yes	Yes
Calcitonin	Subcutaneously or intramuscularly administered injectable calcitonin (100 IU/day). Nasal calcitonin (200 IU/day)	Yes	NA
Raloxifene	60mg tablets for daily administration	Yes	NA
Teriparatide	Disposable pen device for subcutaneous injection (20 µg/day)	Yes	NA

NA = data not available.

Gaudio A et al, 2005



Effects of teriparatide and risedronate on new fractures in post-menopausal women with severe osteoporosis (VERO): a multicentre, double-blind, double-dummy, randomised controlled trial



DEFINING TREATMENT FAILURE IN SEVERE OSTEOPOROSIS

“an inadequate response to treatment for postmenopausal osteoporosis is the occurrence, in a patient with severe osteoporosis, adequate calcium and vitamin D intakes, and good treatment adherence, of any of the following: **incident major fracture within the first treatment year, more than one minor insufficiency fracture, or a bone mineral density decrease by at least the smallest significant amount (0.03 g/cm²) after 5 years or earlier in the event of a minor fracture**”.

Confavreux CB et al, 2010

OBSERVATIONAL STUDY ON SEVERE OSTEOPOROSIS (OSO):

“inadequate treatment response was defined as either **treatment discontinuation because of poor adherence or adverse events or a bone insufficiency fracture despite good adherence to osteoporosis therapy for at least 1 year**

Jacob F et al, 2006



New perspectives on the definition and the management of severe osteoporosis: The patient with two or more fragility fractures

Table 1 - Criteria used in this study for the evaluation of quality of evidence and strength of recommendations.

Quality evidence	
1	Randomized clinical trials
2	Other published studies
3	Expert opinion
Strength of recommendation	
A	Good
B	Moderate
C	Poor

Table 4 - Statements on clinical evaluation of patient with severe osteoporosis.

Statement	Quality of evidence	Strength of recommendation
1. Traditional radiography still plays an important role in defining the severity of vertebral fractures	1	A
2. New methodologies (SDI, DXA/VFA) have significant advantages when compared to other clinical signs such as a reduction in stature	1	A
3. During follow-up of patients with multiple fractures on medical therapy it is advisable to monitor biochemical parameters (markers)	2	C
4. During follow-up of patients with multiple fractures on medical therapy it is advisable to monitor BMD	2	B
5. During follow-up of patients with multiple fractures on medical therapy it is advisable to perform radiological monitoring	1	A/B
6. Radiological evaluation is necessary if clinical symptoms suggest a new fracture	1	A
7. Improvement of the QoL and disabilities have an important role in therapeutic strategies	1	A

SDI: spine deformity index; DXA: dual-energy X-ray absorptiometry; VFA: vertebral fracture assessment; BMD: bone mineral density; QoL: quality of life.

New perspectives on the definition and the management of severe osteoporosis: The patient with two or more fragility fractures

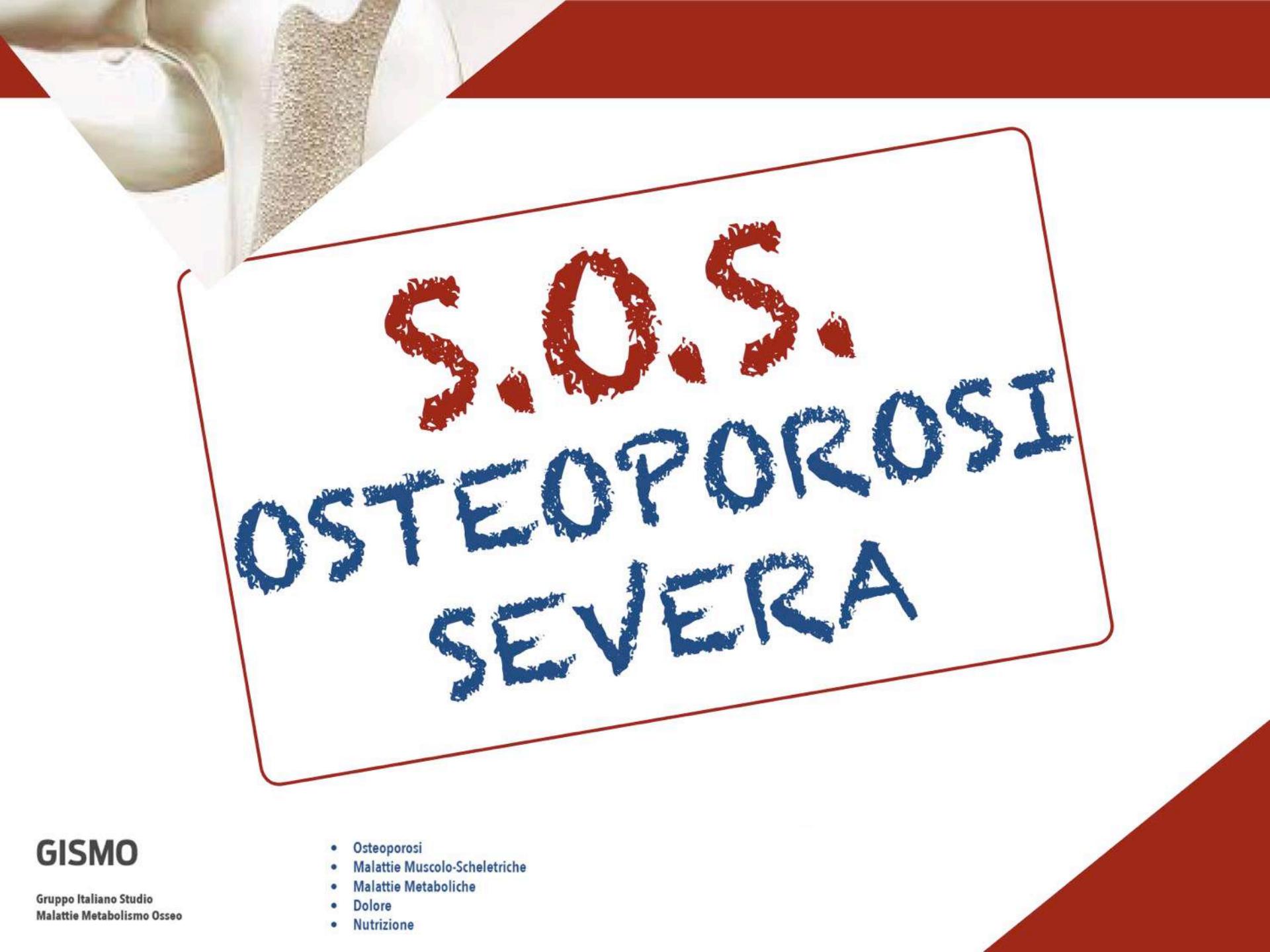
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Quality evidence	
1	Randomized clinical trials
2	Other published studies
3	Expert opinion
Strength of recommendation	
A	Good
B	Moderate
C	Poor

Table 5 - Management of severe osteoporosis in an orthopedic setting.

Statement	Quality of evidence	Strength of recommendation
1. The definition of osteoporosis can be extended to patients with poor bone quality found during surgical procedure independently of the BMD: - Thinning of the cortical bone - Enlargement of the medullary canal in long bones - Reduced capacity for surgical repair that may be perceived during surgical procedure as low resistance of bone tissue throughout the application of screw/nails and their instability after application; crack of femoral cortical bone during or immediately after prosthesis application; after surgical procedure as failure of surgical osteosynthesis or prosthesis instability	3	A
2. It is useful to evaluate the entity of osteoporosis in patients with low or moderate energy trauma causing fractures in the presence of known risk factors for osteoporosis	3	A
3. Clinical picture that can identify patients with the most severe form of osteoporosis: - Early fragility fractures - Advanced age - Presence of co-morbidities that are known to increase the risk of fracture - Location and characteristics of the fracture	2	B
4. What should be modified in the management of the most severe forms of osteoporosis in an orthopedic setting? - Establishment of a differential diagnostic protocol to define the entity of disease - Consequently, pharmacological treatment together with orthopedic-physical therapy	2	A
5. Necessity of defining a diagnostic algorithm for management of patients presenting to the emergency room with femoral fractures	3	A
6. Vertebroplasty and kyphoplasty - Both surgical indications may be considered - Both techniques have documented positive effects (reduction of pain and fracture stabilization) - Negative aspects have been documented (early increase in the risk of fracture of adjacent vertebra if pharmacological treatment is not associated)	2	A

BMD: bone mineral density.



S.O.S. OSTEOPOROSI SEVERA

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Osteoporosi severa e nota 79

 merletti4@unisi.it (non condiviso) [Cambia account](#) 

*Campo obbligatorio

Numero centro di riferimento (es: centro n. 1) *

La tua risposta

Numero scheda (indicare numero progressivo - es: scheda n. 1, scheda n.2) *

La tua risposta

Data compilazione scheda (es: 20/04/2022) *

La tua risposta

Nome e cognome medico (es: Mario Rossi) *

La tua risposta

Indicare iniziali del nome e cognome del paziente (es: A.T.) *

La tua risposta

Sesso *

Uomo

Donna

Fascia Età *

50-60

61-70

71-80

Peso *

Tra 40-50 kg

Tra 51-60 kg

Tra 61 e 70 kg

Tra 71 e 80 kg

Oltre 80 kg

Altezza *

- Inferiore a 140 cm
- Da 140 a 145 cm
- Da 146 a 150 cm
- Da 151 a 155 cm
- Da 156 a 160 cm
- Da 161 a 165 cm
- Da 166 a 170 cm
- Da 171 a 175 cm
- Da 176 a 180 cm
- Oltre 180 cm

Attività lavorativa *

- Agricoltore
- Artigiano
- Impiegato
- Libero Professionista
- Pensionato
- Altra occupazione

Dolore *

- Sì
- No

Paziente con nuova frattura da fragilità (trauma non efficiente)? *

- Sì
- No

[Avanti](#)

[Cancella modulo](#)

Non inviare mai le password tramite Moduli Google.

Osteoporosi severa e nota 79

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*Campo obbligatorio

Caratteristiche del paziente *

- Paziente con 3 o più fratture da fragilità
- Paziente con 1 o più fratture da fragilità + T-SCORE colonna o femore ≤ -4
- Paziente con 1 o più fratture da fragilità + trattamento > 12 mesi con prednisone o equivalenti $\geq 5\text{mg}/\text{die}$
- Paziente con nuova frattura vertebrale o femorale da fragilità nonostante trattamento in nota 79 da almeno 1 anno
- Nessuna delle precedenti

[Indietro](#)

[Avanti](#)

[Cancella modulo](#)

Fattori di rischio osteoporosi

Fumatore *

- Si
- No
- Ex fumatore

Alcol > 3U/die (pari a: 375ml di vino - 990ml di birra - 120ml di super-alcolico) *

- Si
- No

Altri fattori di rischio osteoporosi (è possibile indicare più di una risposta) *

- Familiarità per frattura di femore
- Uso di corticosteroidi
- Altre terapie osteopenizzanti
- Artride reumatoide
- Osteoporosi secondaria
- Nessuna delle precedenti

BMD (è possibile indicare più di una risposta) *

	da -1 a 2,4	da -2,5 a -4	> a -4	Non disponibile
--	-------------	--------------	--------	-----------------

- | | | | | |
|----------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| T-score L1-L4 | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| T-score collo femore | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Tscore femore totale | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

Analisi di laboratorio *

- Si
- No

Fratture pregresse da fragilità (trauma non efficiente): è possibile indicare più di una risposta *

- Polso
- Coste
- Vertebre
- Omero
- Femore
- Bacino
- Piede/caviglia
- Nessuna delle precedenti

Trattamento farmacologico *

- Si attualmente in corso
- Si trattamento pregresso
- Nessun trattamento

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[Avanti](#)

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Trattamento farmacologico *

- Si attualmente in corso
- Si trattamento pregresso
- Nessun trattamento

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Osteoporosi severa e nota 79

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*Campo obbligatorio

Trattamento farmacologico attualmente in corso

Terapia attualmente in corso *

- Alendronato
- Risedronato
- Ibandronato
- Teriparatide
- Denosumab
- Zoledronato
- Altro

Vitamina D *

- Si
- No

Se si quale Vitamina D

- Colecalciferolo
- Calcifediolo
- Calcitriolo

Calcio *

- Si
- No

[Indietro](#)

[Invia](#)

[Cancella modulo](#)

Trattamento farmacologico *

- Si attualmente in corso
- Si trattamento pregresso
- Nessun trattamento

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Trattamento farmacologico pregresso

Terapia pregressa sospesa? *

- Si
- No

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[Avanti](#)

[Cancella modulo](#)

Trattamento sospeso

Motivi della sospensione della terapia *

- Disturbi gastrointestinali
- Allergia
- Reazione di fase acuta
- Scarsa aderenza
- Altro

[Indietro](#)

[Invia](#)

[Cancella modulo](#)

Trattamento farmacologico *

- Si attualmente in corso
- Si trattamento pregresso
- Nessun trattamento

[Indietro](#)

[Avanti](#)

[Cancella modulo](#)

Sezione senza titolo

Terapia pregressa conclusa? *

- Si
- No

Terapia pregressa *

- Alendronato
- Risedronato
- Ibandronato
- Teriparatide
- Denosumab
- Zoledronato
- Altro

Vitamina D *

- Si
- No

Se si quale Vitamina D

- Colecalciferolo
- Calcifediolo
- Calcitriolo

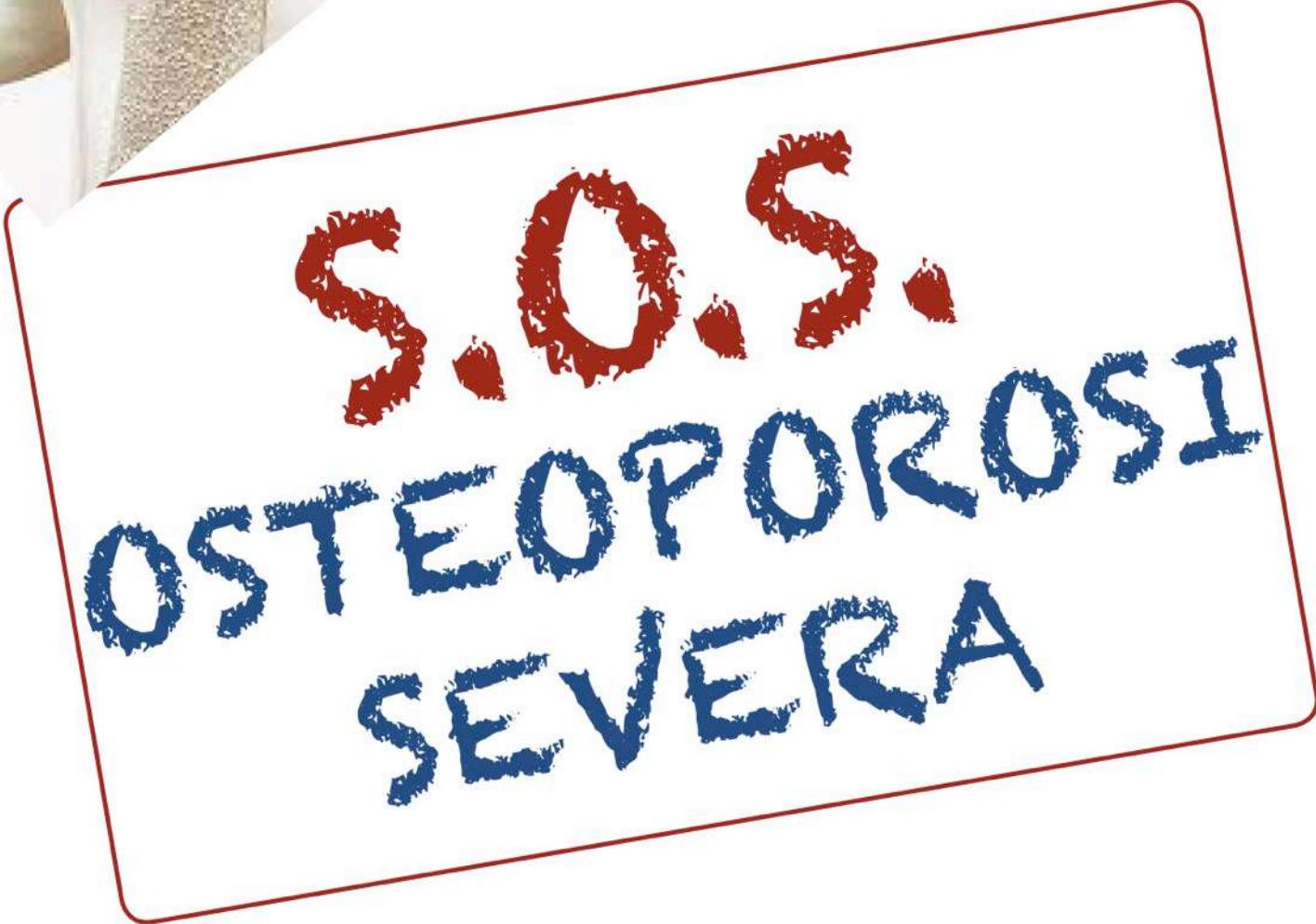
Calcio *

- Si
- No

[Indietro](#)

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OSTEOPOROSI
SEVERA

GISMO

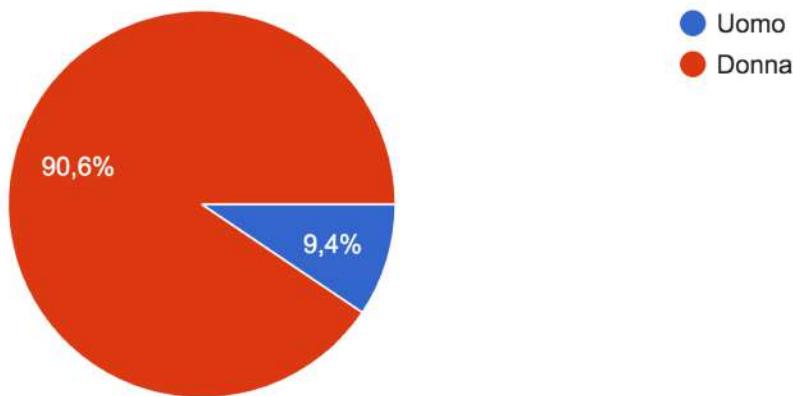
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RISULTATI

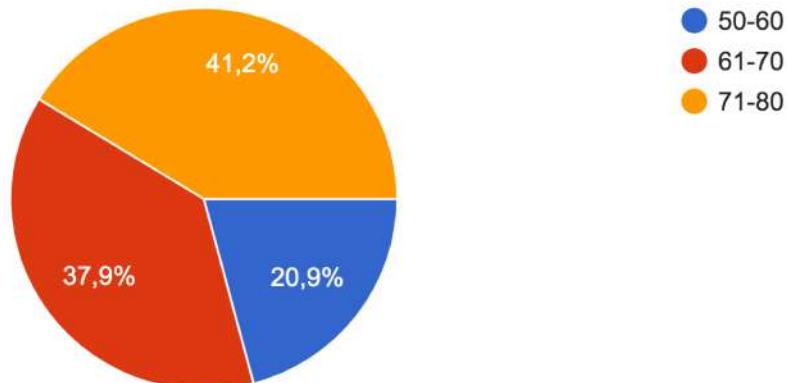
Sesso

657 risposte



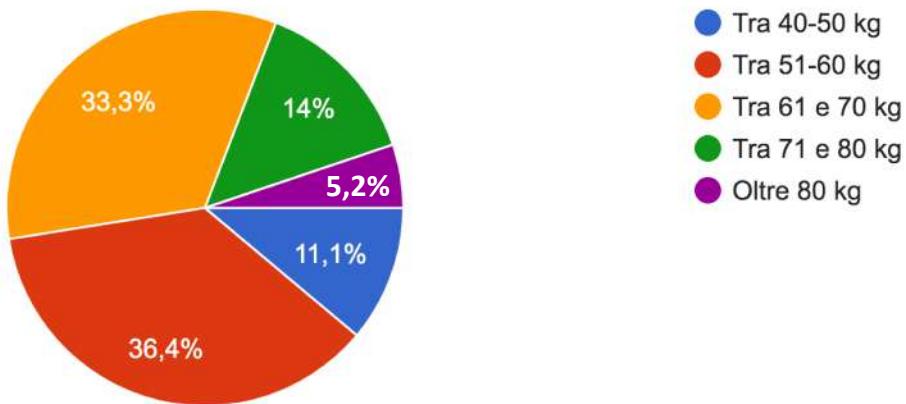
Fascia Età

657 risposte



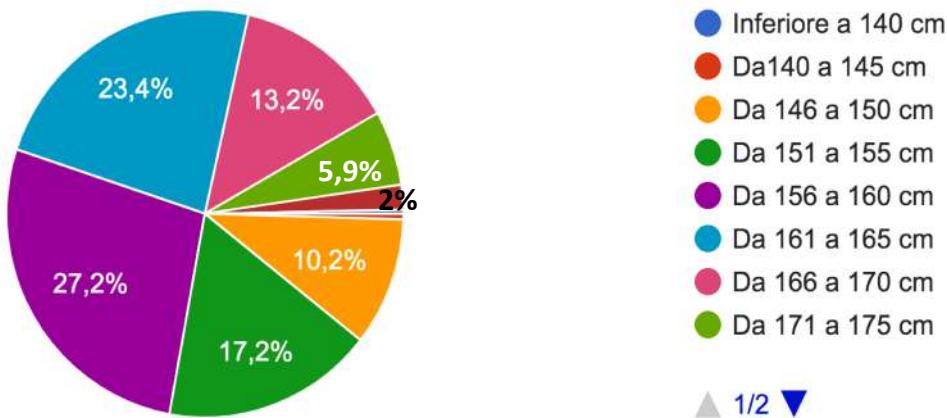
Peso

657 risposte



Altezza

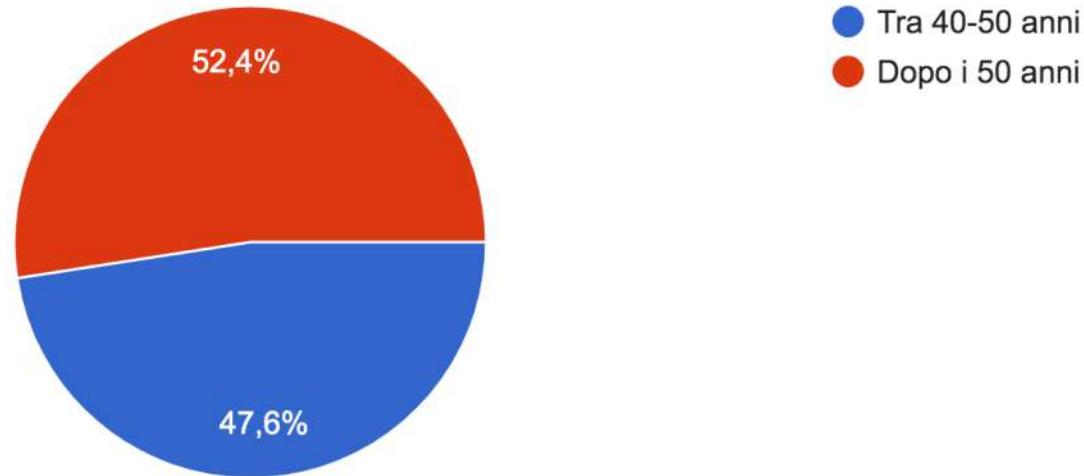
657 risposte



▲ 1/2 ▼

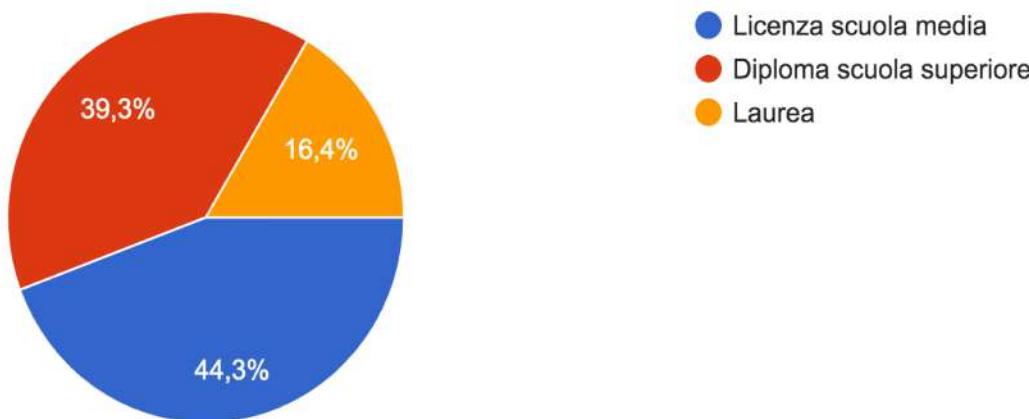
Menopausa

593 risposte



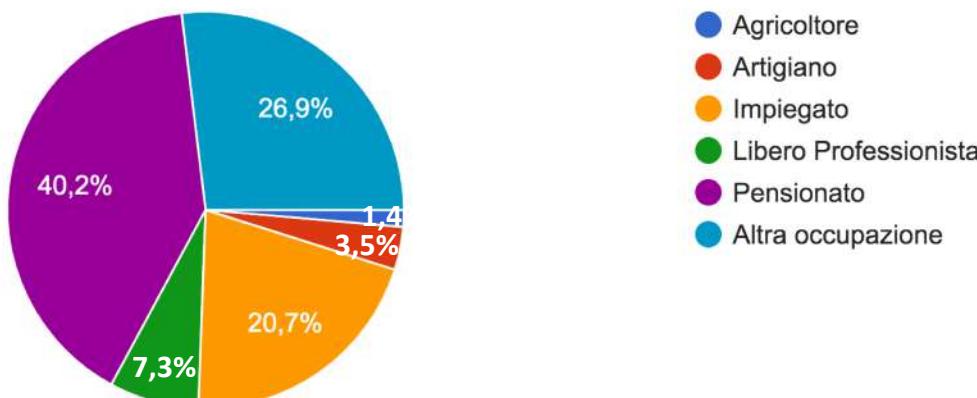
Titolo di Studio

657 risposte



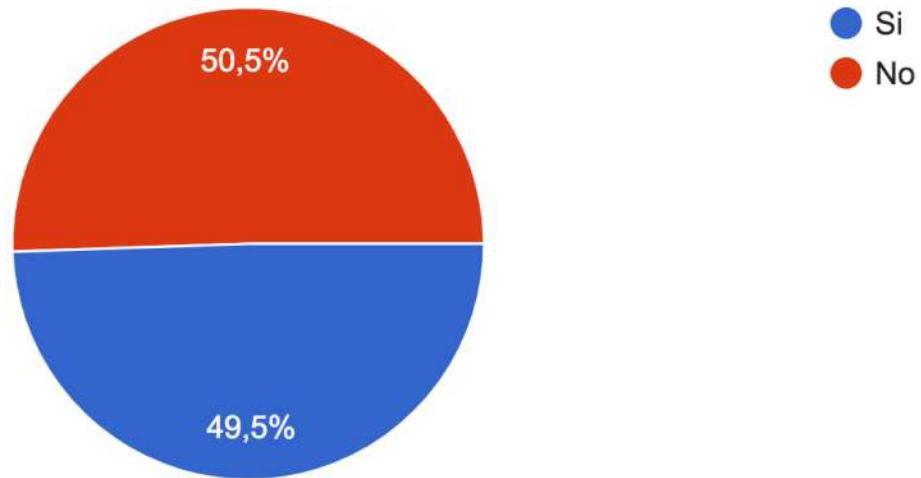
Attività lavorativa

657 risposte



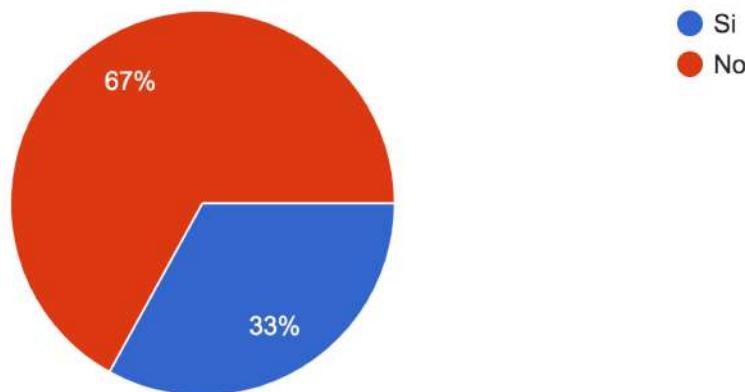
Dolore

657 risposte



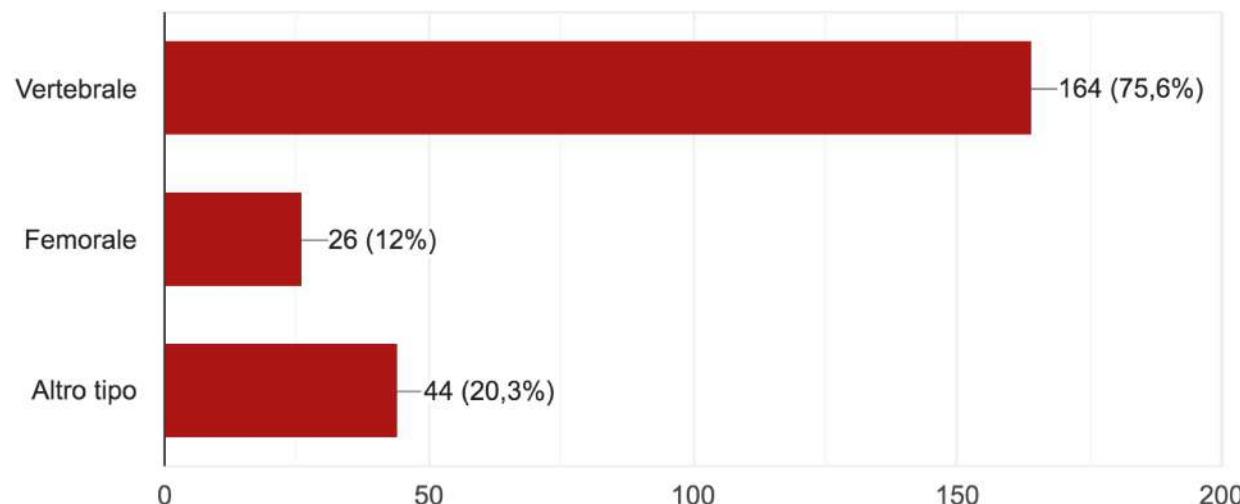
Paziente con nuova frattura da fragilità (trauma non efficiente)?

657 risposte



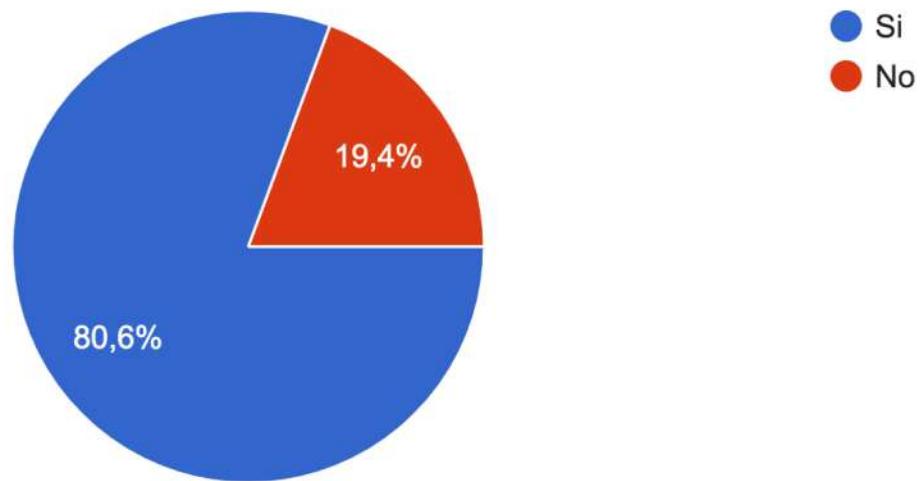
Se si quale tipo di frattura? (è possibile indicare più di una risposta)

217 risposte



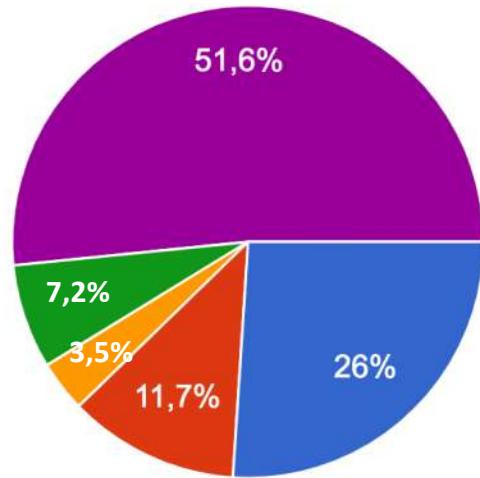
Ha effettuato RX da meno di sei mesi

217 risposte



Caratteristiche del paziente

657 risposte

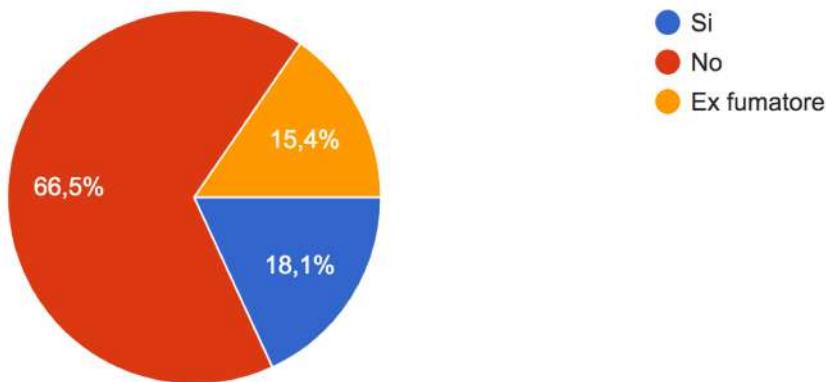


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- Paziente con nuova frattura vertebrale o femorale da fragilità nonostante trattamento in nota 79 da almeno 1 anno
- Nessuna delle precedenti

FATTORI DI RISCHIO OSTEOPOROSI

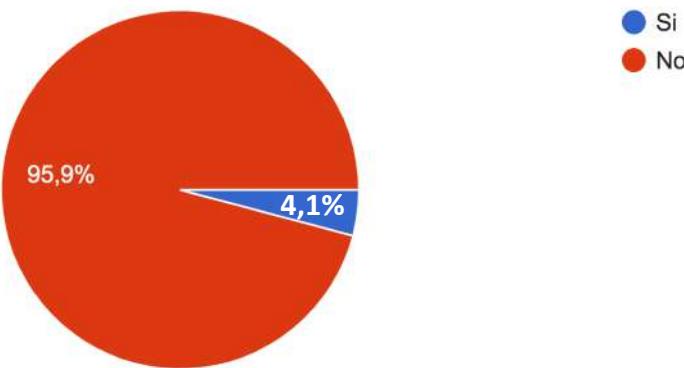
Fumatore

657 risposte



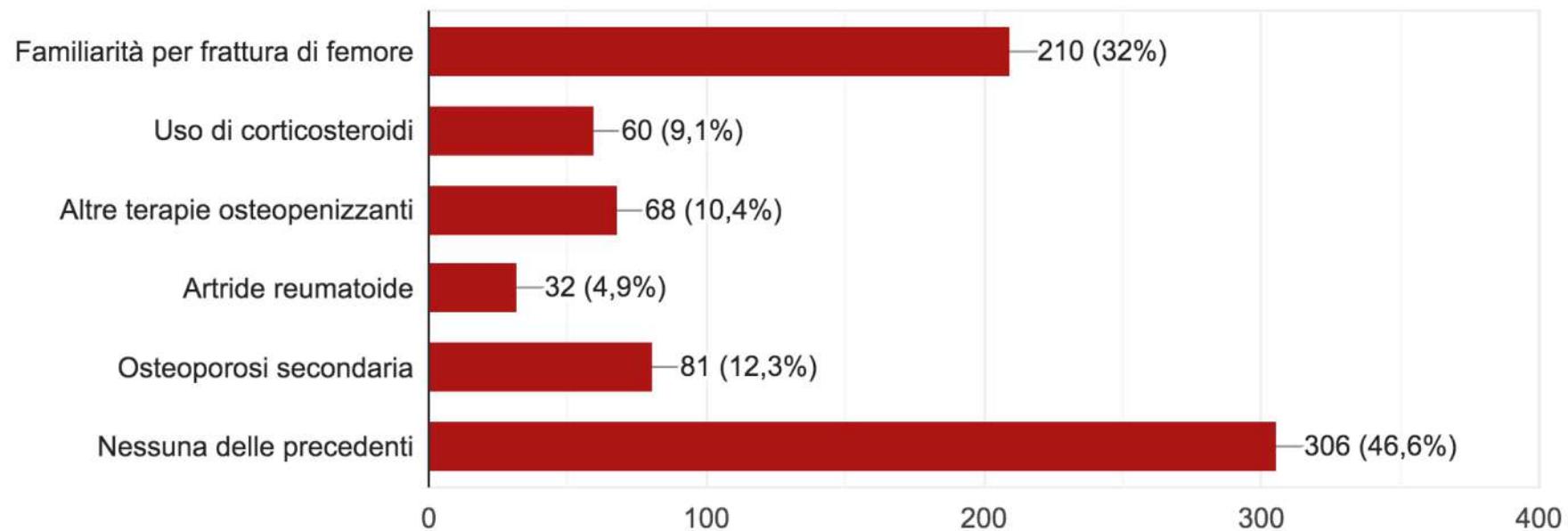
Alcol > 3U/die (pari a: 375ml di vino - 990ml di birra - 120ml di super-alcolico)

657 risposte

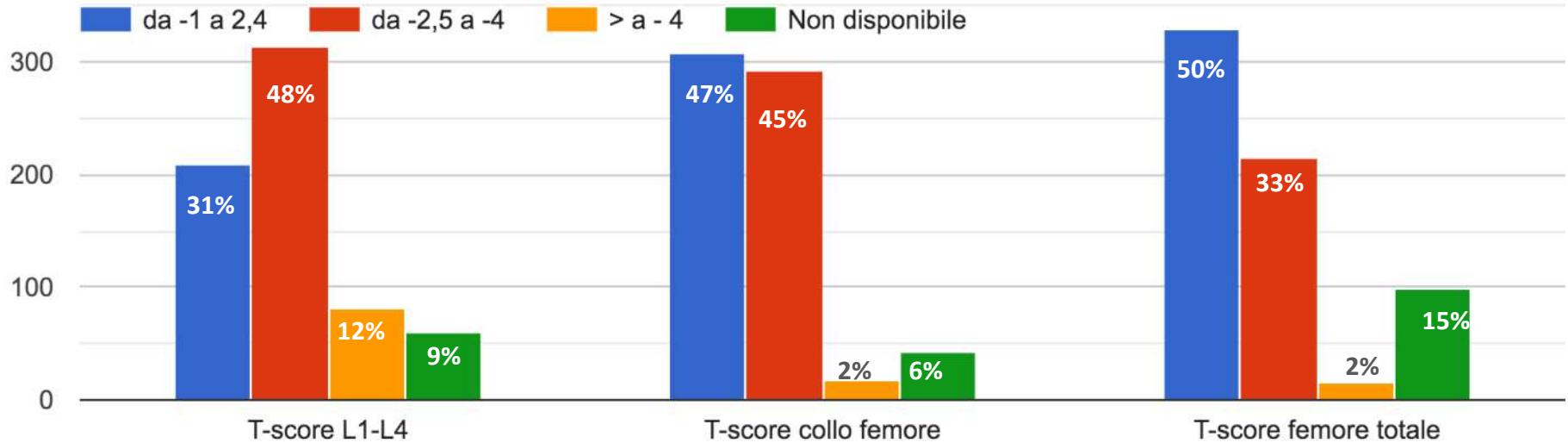


Altri fattori di rischio osteoporosi (è possibile indicare più di una risposta)

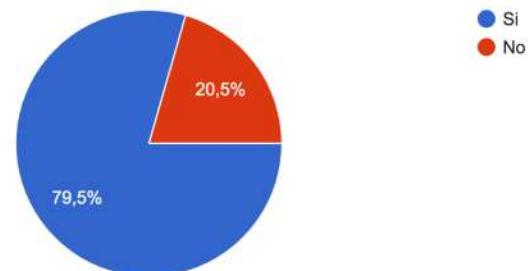
657 risposte



BMD (è possibile indicare più di una risposta)

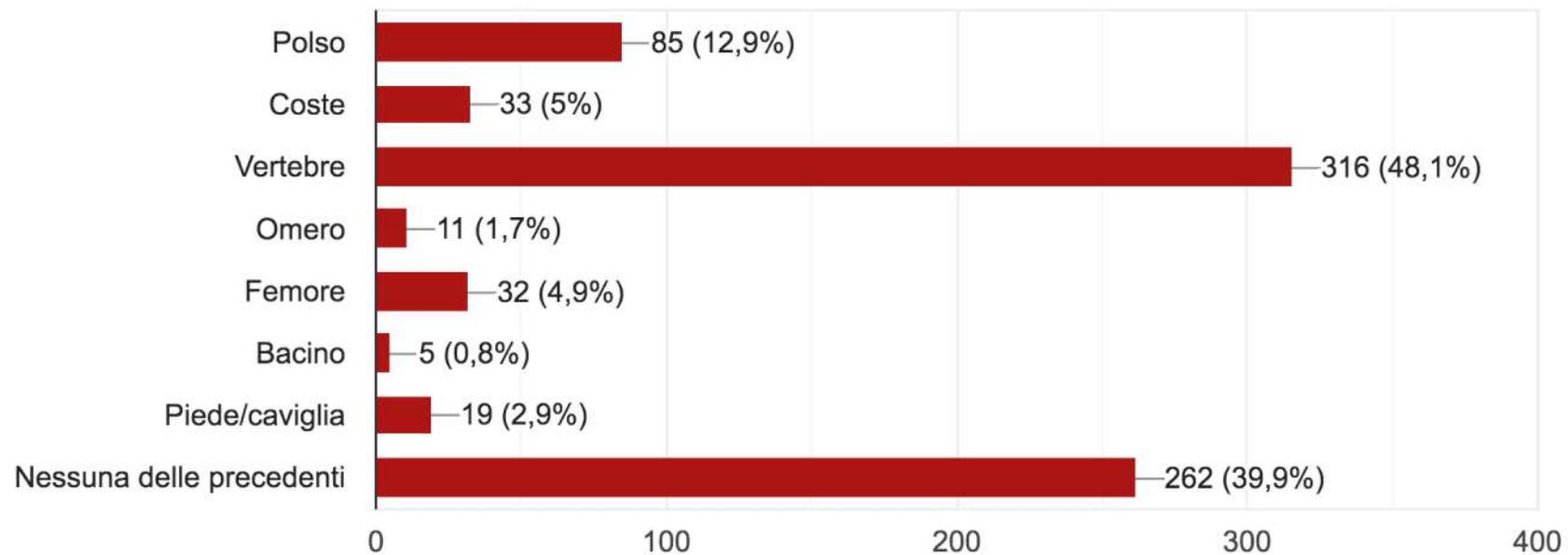


Analisi di laboratorio
657 risposte



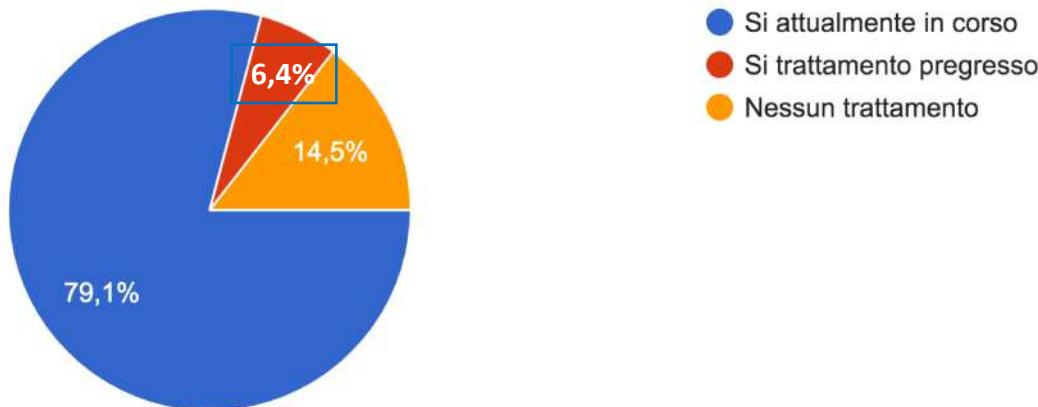
Fratture pregresse da fragilità (trauma non efficiente): è possibile indicare più di una risposta

657 risposte



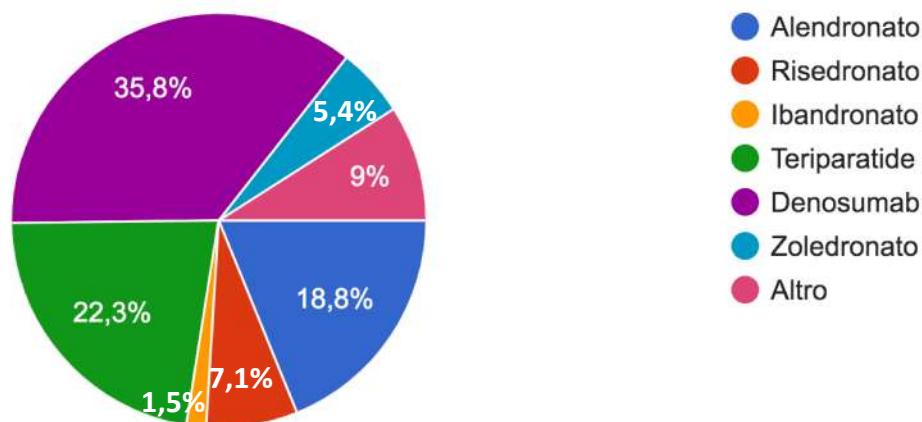
Trattamento farmacologico

657 risposte



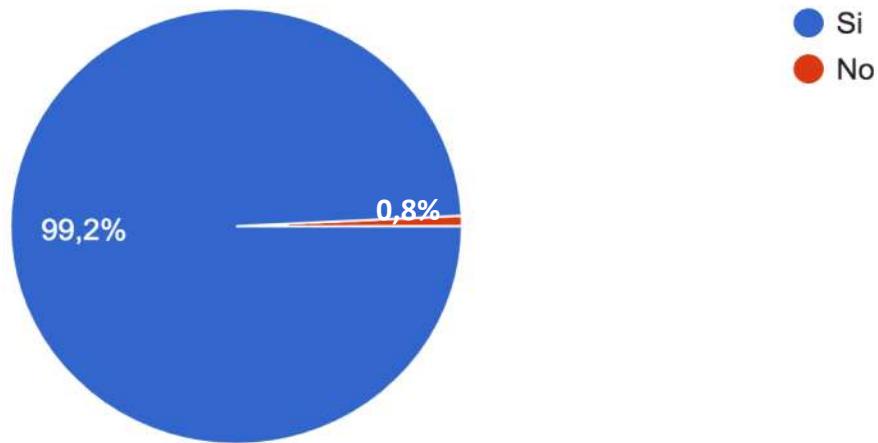
Terapia attualmente in corso

520 risposte



Vitamina D

520 risposte

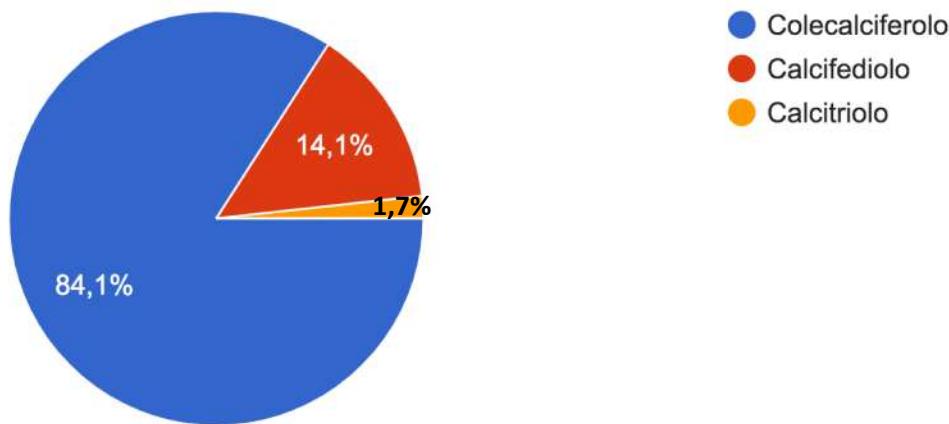


Si

No

Se si quale Vitamina D

516 risposte



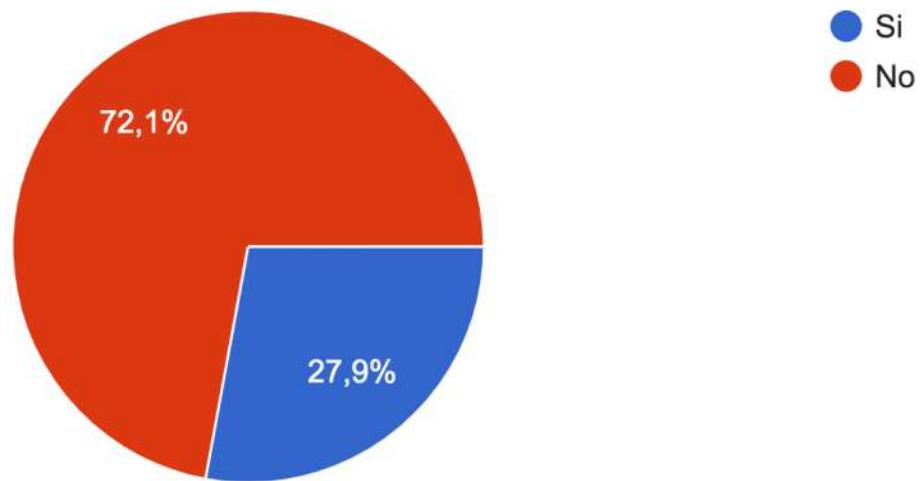
Colecalciferolo

Calcifediolo

Calcitriolo

Calcio

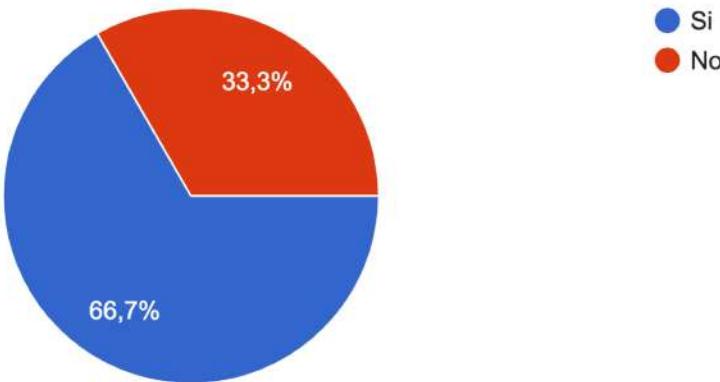
520 risposte



TRATTAMENTO FARMACOLOGICO PREGRESSO

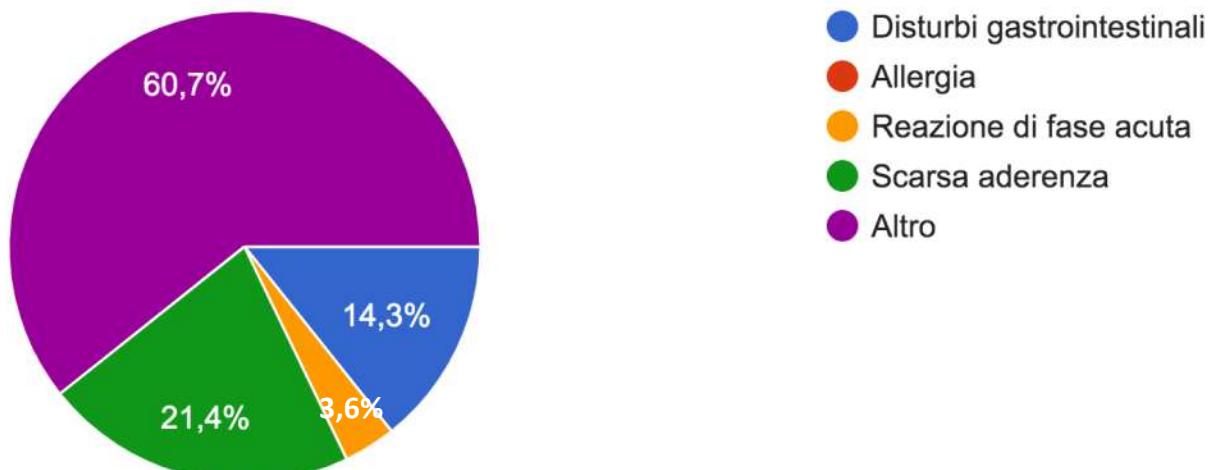
Terapia pregressa sospesa?

42 risposte



Motivi della sospensione della terapia

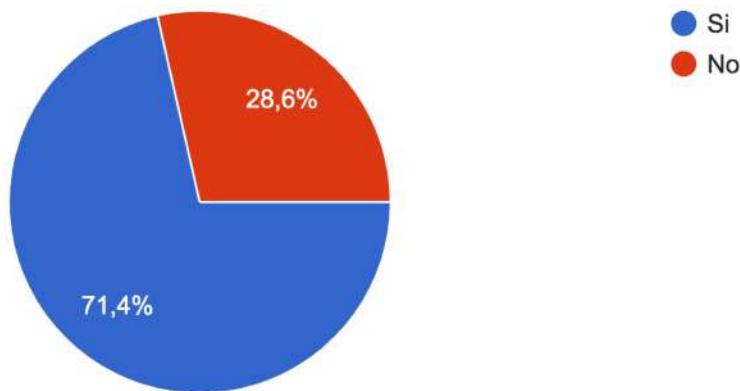
28 risposte



TRATTAMENTO FARMACOLOGICO PREGRESSO

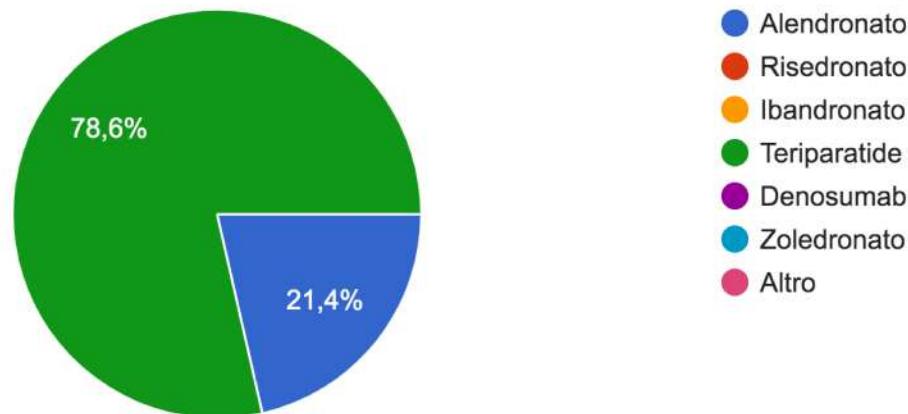
Terapia pregressa conclusa?

14 risposte



Terapia pregressa

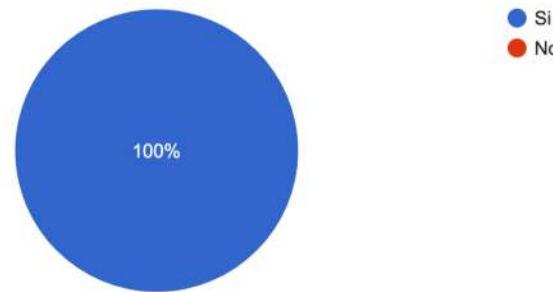
14 risposte



TRATTAMENTO FARMACOLOGICO PREGRESSO

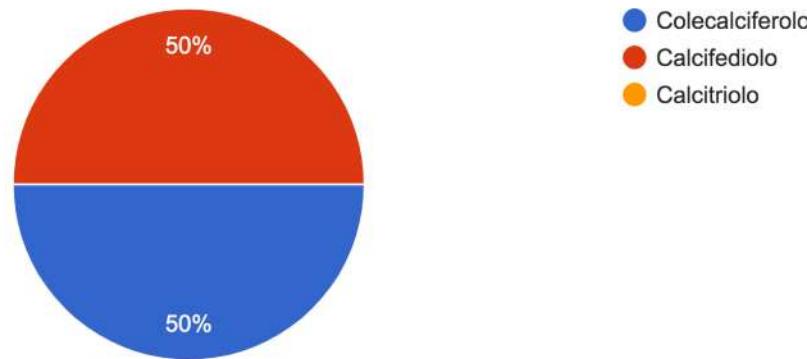
Vitamina D

14 risposte



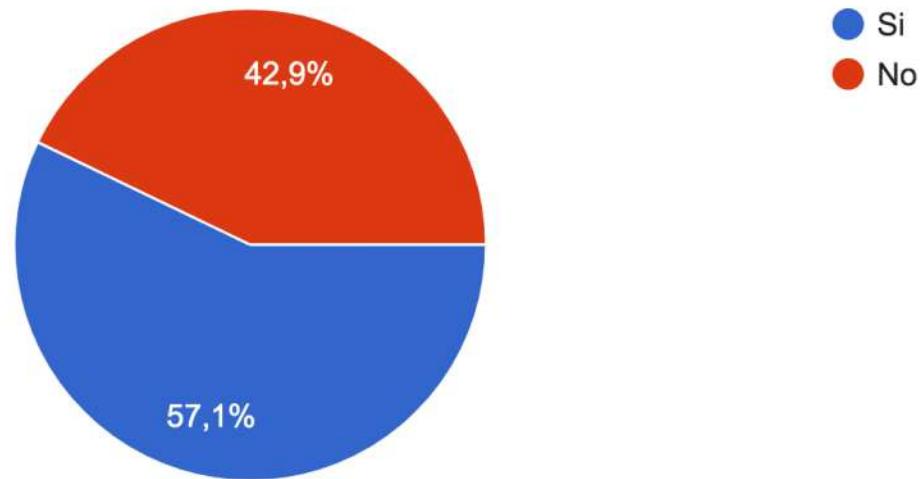
Se si quale Vitamina D

14 risposte



Calcio

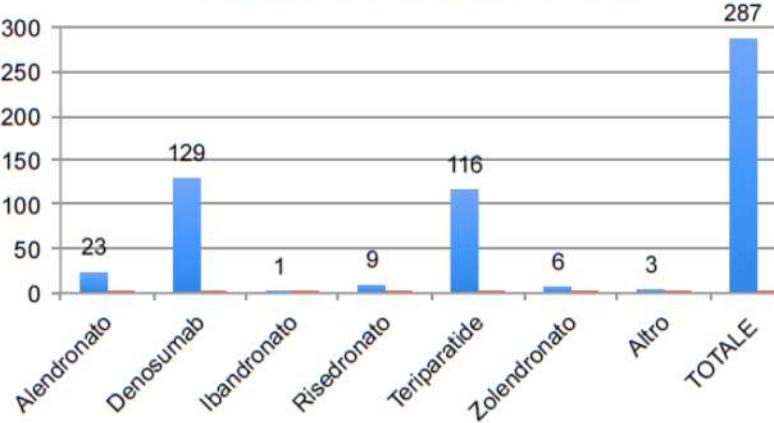
14 risposte



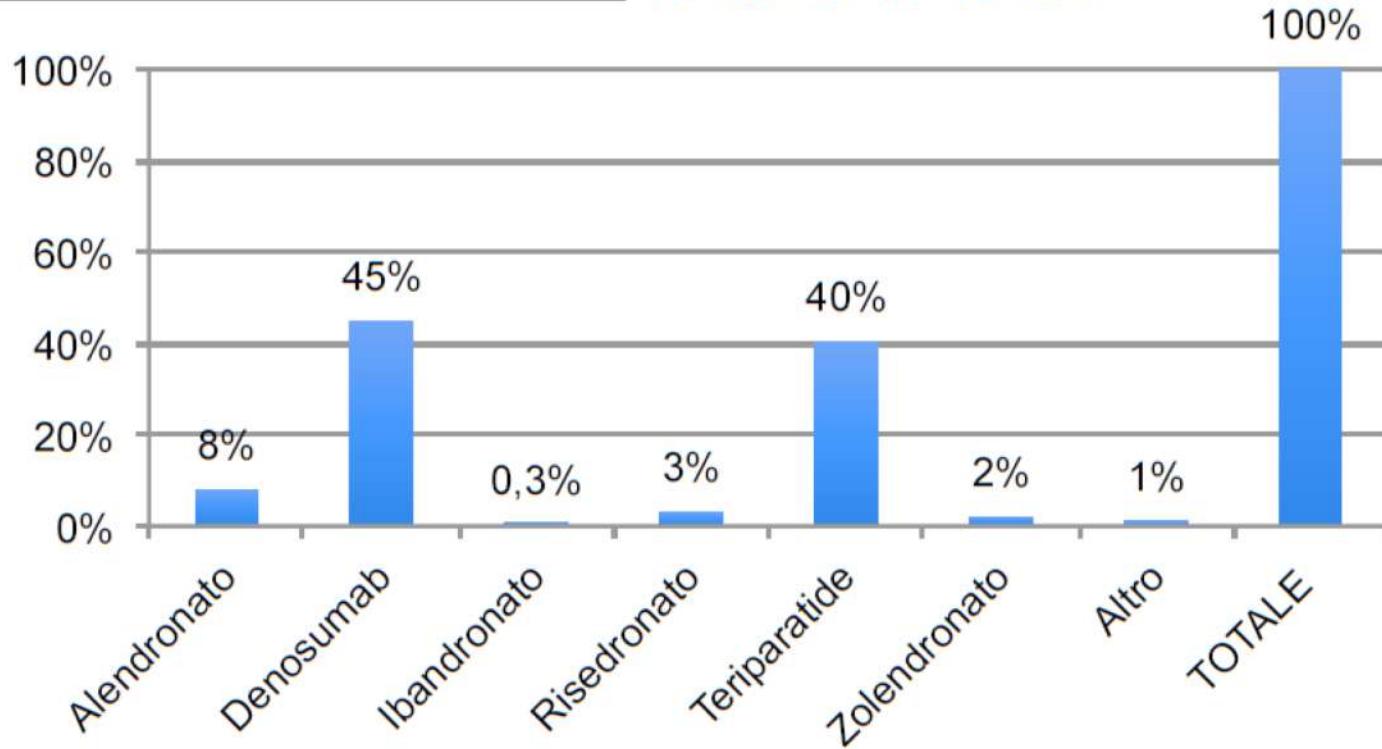
GISMO

Gruppo Italiano Studio
Malattie Metaboliche Ossee

■ PAZIENTI CON OSTEOPOROSI SEVERA



OSTEOPOROSI SEVERA



SUMMARY

- Nello **Studio SOS** il 33% dei pazienti presenta una nuova frattura da fragilità prevalentemente a livello vertebrale (75%) con diagnosi radiologica (80.6%) negli ultimi 6 mesi
- Il 26% dei pazienti presenta 3 o più frattura da fragilità mentre il 12% circa dei pazienti presenta 1 o più frattura da fragilità + TSCORE colonna o femore <-4
- Il fattore di rischio principale (32%) è risultata la familiarità per frattura di femore
- Nel 40-50% dei casi la BMD è risultata fra -2.5 e -4 di TSCORE
- Il 48% dei paziente riferiva una pregressa frattura vertebrale ed il 5% una pregressa frattura di femore
- Il 79% dei pazienti risulta in trattamento:
 - Denosumab 35%
 - Teriparatide 22%
 - Bisfosfonati 34%
- Il 99% dei pazienti assume supplementazione con Vitamina D prevalentemente colecalciferolo (84%). Solo il 28% dei pazienti assume supplementi di calcio
- Il 67% dei pazienti riferisce una pregressa terapia sospesa per scarsa aderenza nel 24% dei casi e disturbi gastrointestinali nel 14.3% dei casi
- Il 78% dei pazienti riferisce di essere già stato sottoposto a trattamento: teriparatide (78%) e alendronato (21%). Tutti avevano assunto supplementazione con vitamina D (colecalciferolo e calcifediolo) associato a calcio nel 57.1% dei casi
- Tra i pazienti con osteoporosi severa solo il 40% è in terapia anabolica con Teriparatide.

TAKE HOME MESSAGES

- **Severe osteoporosis** is currently defined by the threshold of bone density value **below the -2.5 SDS of T-score, determined by dual energy X-ray absorptiometry, and the presence of one or more fragility fractures.** This definition does not entirely reflect the spectrum of severity of the disease that provides a variable increase in fracture risk
- **Patients who sustain a vertebral fracture are at particularly high risk of another vertebral fracture within the following year**, which has been estimated to be about 3-to-5 fold higher than the risk of subjects without fractures. This can be translated to an absolute risk of 10.8% to develop a new clinical fracture within the next 2 year.
- It has been widely documented that **mortality increases significantly and proportionally with the number and the severity of vertebral fractures**
- **The main aim for the pharmacological treatment of severe osteoporosis is prevention of “fracture cascade”** triggered by the first vertebral fracture.
- **Quality of life is significantly reduced in patients with fragility fractures.** Multiple and severe vertebral fractures are typically associated with exponential deterioration of quality of life

TAKE HOME MESSAGES

- Nel progetto SOS il 50% dei pazienti risultava osteoporotico con pregresse fratture prevalentemente a livello vertebrale.
- L' evento fratturativo predispone i pazienti ad una nuova frattura sintomatica radiologica prevalentemente a livello vertebrale
- La maggior parte dei pazienti riceve adeguato trattamento antiriassorbitivo ma il 20% dei pazienti con osteoporosi severa non è trattato
- Una discreta porzione di pazienti con osteoporosi interrompe il trattamento per scarsa compliance
- La maggior parte dei pazienti con osteoporosi severa non riceve adeguata terapia anabolica
- E' pertanto necessaria una maggiore consapevolezza del problema a livello sanitario e sociale per una migliore gestione del paziente con osteoporosi severa ed una ottimizzazione della spesa sanitaria correlata.
- Sarebbe auspicabile, specialmente nei soggetti con osteoporosi severa, poter eseguire una terapia sequenziale a lungo termine nell' ottica di una "medicina personalizzata"