





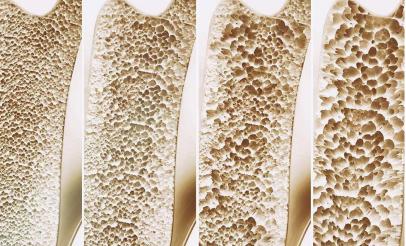
# An Update In The Prevention, Screening, Diagnosis, & Treatment Of **Osteoporosis**

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## Definition

- Osteoporosis is a systemic skeletal disease, defined by low bone mass and structural damage to bone tissue which Leads to increased bone fragility and high fracture risk.
- Osteoporosis is often referred to as a 'silent disease' because it progresses without symptoms until a fracture occurs. The World Health Organization defines classify osteoporosis as a BMD T-score of -2.5 or lower, indicating substantial fracture risk



Bartl, R., Frisch, B., Bartl, R., & Frisch, B. (2004). Definition of osteoporosis. Osteoporosis: Diagnosis, Prevention, Therapy. A Practical Guide for all Physicians—from Pediatrics to Geriatrics, 24-32.
 Larijani B, Mohageri Tehrani MR, Hamidi Z, Soltani A, Pajouhi M. Osteoporosis, prevention, diagnosis and treatment. J Reprod Infertil. 2005

## Causes Of Osteoporosis

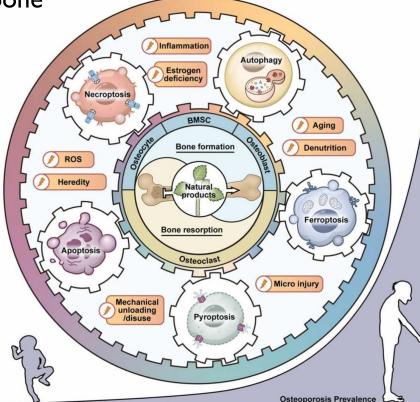
The imbalance of bone cell activity due to numerous factors can break the dynamic cycle of bone formation and bone resorption, thus affecting bone homeostasis and aggravating the condition of osteoporosis.

Heredity/Genetics

(~60-80%)

- Gender
- Nutrition
  - Energy intake
  - Protein intake
  - Calcium intake
  - Vitamin D

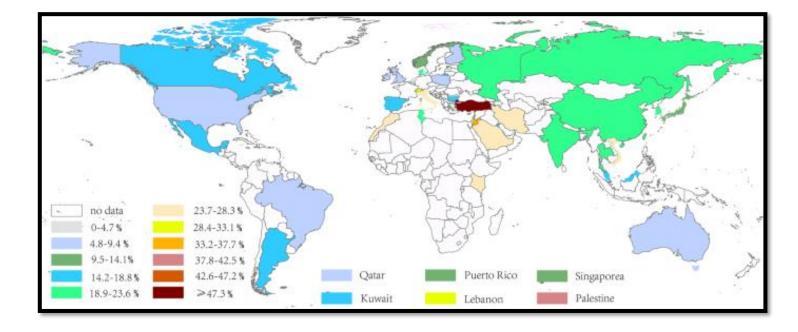
- Mechanical factors
  - Physical activity
  - Body weight
- Habitual Factors
  - Smoking
  - Alcohol
- Endocrine factors Sex steroids Calcitriol GH—IGF-1 axis



I. Li Z, Li D.... Cell death regulation: A new way for natural products to treat osteoporosis. Pharmacological Research. 2022 Dec

2. Keramat, A., Patwardhan, B., Larijani, B. et al. The assessment of osteoporosis risk factors in Iranian women compared with Indian women. BMC Musculoskelet Disord 9, 28 (2008).

## Global Distribution Of Osteoporosis June 2022



## The global prevalence of : Osteoporosis: **19.7%** Osteopenia: **40.4**%

The prevalence was higher in developing countries (22.1%) than in developed countries (14.5%)

## Prevalence And Burden Of Osteoporosis In MENA

A diverse prevalence rate of OP in the MENA region is obvious (ranged from 10.3-30%) and it is higher than that reported in Europe (20%)

Mortality rates post-hip fracture may be higher in this region than those reported from western populations. While such rates vary between 25-30% in western populations, they are 2-3 fold higher in populations from the Middle East and Africa region.

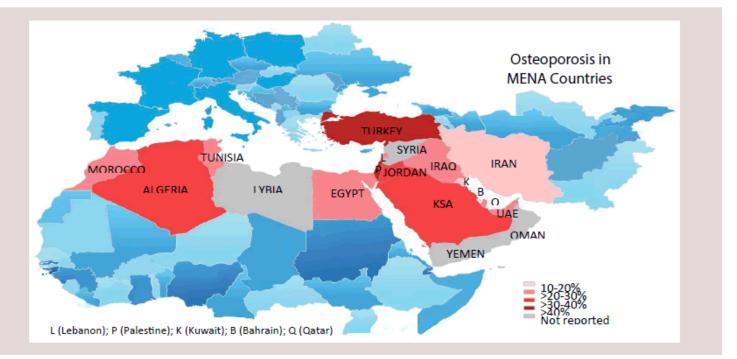


Figure 1. Prevalence of osteoporosis in adult female population in the Middle East and North Africa (MENA) region

# Prevalence Of Osteoporosis And Osteosarcopenia In Iran

Results of a large population-based study in Bushehr showed that:

- The age-standardized prevalence of osteoporosis is 41.5% in population aged ≥ 60 years (24.6% in men and 62.7% in women)
- The age-standardized prevalence of osteosarcopenia is 33.8 (95% CI 31.0–36.5) in men and 33.9 (30.9–36.8) in women

	Calcified Tissue International https://doi.org/10.1007/s00223-019-00646-6	
	ORIGINAL RESEARCH	
Archives of Osteoporo		Check for updates
nttps://doi.org/10.100	Prevalence of Osteosarcopenia and Its Association with Cardiovascular	
ORIGINAL ARTIC	Risk Factors in Iranian Older People: Bushehr Elderly Health (BEH)	
	Program	
Prevalence	of osteoporosis among the elderly population of Iran	

# Iranian Multi-center Osteoporosis Study (IMOS), 2021–2022

Khalagi et al. BMC Geriatrics (2022) 22:818 https://doi.org/10.1186/s12877-022-03532-3 BMC Geriatrics

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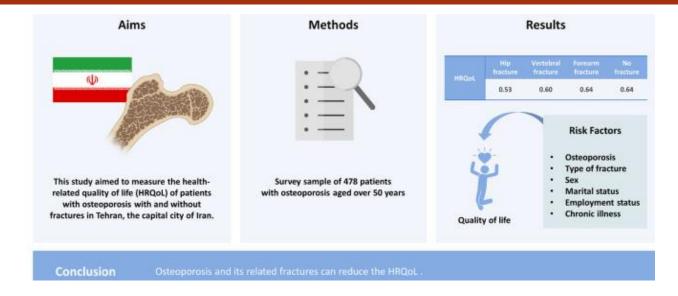
STUDY PROTOCOL

## Iranian Multi-center Osteoporosis Study (IMOS), 2021–2022: the study protocol

Kazem Khalagi<sup>1,2</sup>, Noushin Fahimfar<sup>1,3</sup>, Fatemeh Hajivalizadeh<sup>4</sup>, Mahnaz Sanjari<sup>1</sup>, Mohammad Javad Mansourzadeh<sup>1,5</sup>, Safoora Gharibzadeh<sup>6</sup>, Gita Shafiee<sup>7</sup>, Koorosh Kamali<sup>8</sup>, Farshid Alaeddini<sup>9</sup>, Farshad Farzadfar<sup>10</sup>, Samaneh Mohseni<sup>11</sup>, Nazli Namazi<sup>12</sup>, Farideh Razi<sup>13</sup>, Kobra Gorgani<sup>1</sup>, Katayoun Kateb Saber<sup>4</sup>, Nekoo Panahi<sup>14</sup>, Ramin Heshmat<sup>7</sup>, Alireza Raeisi<sup>15</sup>, Bagher Larijani<sup>16</sup> and Afshin Ostovar<sup>1\*</sup>

- IMOS will provide valuable information on the prevalence and determinants of osteoporosis and sarcopenia at the national level, and the results can be used in evaluating health system interventions and policymaking in the field of musculoskeletal diseases.
- IMOS is positioned to fill gaps in knowledge regarding osteoporosis and sarcopenia in Iran, building on previous rounds that primarily focused on urban populations. This research is crucial for understanding the national burden of these conditions and developing targeted health strategies.

# Quality Of Life And Osteoporosis



- Patients with fractures reported significantly lower HRQoL scores compared to those without fractures. This decline was attributed to increased pain, reduced mobility, and psychological effects such as anxiety and depression.
- The study highlighted that fracture patients experienced limitations in daily activities, contributing to a diminished quality of life.
- The fear of falling and subsequent fractures further exacerbated the decline in HRQoL among those with fractures.

# Novel Approaches To Reduce Osteoporosis Burden

- This study emphasizes the importance of novel preventive measures and treatment options for osteoporosis and sarcopenia. It highlights how addressing these conditions can also reduce the risk of other comorbidities in older adults, thereby improving overall health outcomes.
- The role of nutrition, particularly the intake of leucine and protein supplements, is as beneficial for muscle mass and physical function when combined with resistance exercises.
- osteoporosis is often associated with other health issues, such as cardiovascular disease (CVD).
- Resistance and balance training are effective interventions for improving quality of life and reducing fracture risk in patients with osteoporotic vertebral fractures.

Tabatabaei-Malazy, O., Tootee, A., Heshmat, R., Ostovar, A., Pan, A., Quyyumi, A. A., ... & Larijani, B. (2022). Reducing the Burden of Age-related Disease in relation to Osteoporosis, Sarcopenia and Osteosarcopenia. Frontiers in Medicine

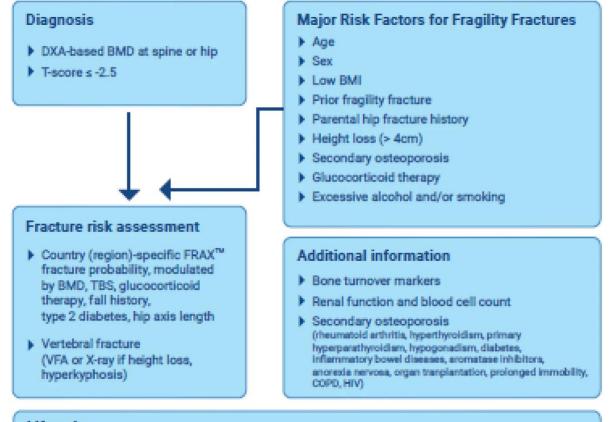
# **Projected Trends**

- The burden of osteoporosis and fragility fractures is projected to increase at a dramatic pace in the next decade taking in consideration the effect of the aging of the population alone.
- Of concern, there are individual and environmental factors that can further augment this trend. As an example, obesity and diabetes, which have increased in prevalence worldwide, have been largely associated with higher risk of fracture independently from bone mineral density (BMD).
- Sedentary lifestyle in younger individuals has also been associated with increased risk of osteoporosis later in life.
- Moreover, environmental air pollution, a well-known issue for present and future generations, has been linked with a substantial increase in the risk of osteoporosis and fractures.

# Advances In Diagnosis And Assessment

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# IOF Executive Summary Of The European Guidance For The Diagnosis And Management Of Osteoporosis In Postmenopausal Women

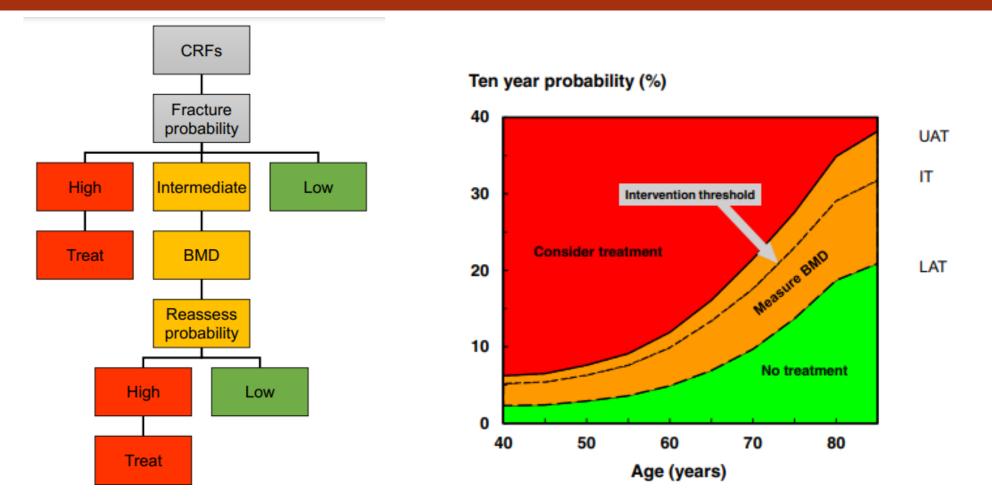


Kanis, J.A., Cooper, C., Rizzoli, R. et al. Executive summary of the European guidance for the diagnosis and management of osteoporosis in postmenopausal women. Calcif Tissue Int 104, 235–238 (2019).

#### Lifestyle

- Nutrition: calcium 800-1000 mg/day, protein ≥ 1g/kg BW/ day
- Vitamin D: 800 IU/day
- Daily weight-bearing physical activity
- Fall prevention measures

## Guidance For The Diagnosis And Management Of Osteoporosis



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Kanis, J., Cooper, C., Rizzoli, R. et al. European guidance for the diagnosis and management of osteoporosis in postmenopausal women. Osteoporos Int 30, 3-44 (2019). https://doi.org/10.1007/s00198-018-4704-5

# Diagnostic Tools

- I. Bone Mineral Density (BMD) Testing
  - Dual-Energy X-ray Absorptiometry (DXA): This is the most widely used method for diagnosing osteoporosis. It measures bone density at critical sites like the hip and spine, providing T-scores that indicate bone health relative to a young adult population. A T-score of -2.5 or lower indicates osteoporosis.
  - Quantitative Computed Tomography (QCT): This technique provides a three-dimensional assessment of bone density, particularly useful for evaluating the spine. However, it is less commonly used due to higher radiation exposure compared to DXA.
  - Peripheral Quantitative Computed Tomography (pQCT): This method measures bone density in peripheral sites like the forearm or tibia, but its clinical utility is limited compared to central measurements like DXA
- 2. Additional Imaging Techniques
  - Vertebral Fracture Assessment (VFA): Often performed alongside DXA, this technique uses low-dose X-rays to identify vertebral fractures, which can indicate osteoporosis2.
  - Magnetic Resonance Imaging (MRI): MRI can be used to evaluate vertebral fractures and assess underlying conditions like cancer that may affect bone health I.

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Lewiecki EM. Osteoporosis: Clinical Evaluation. [Updated 2021 Jun 7]. In: Feingold KR, Anawalt B, Blackman MR, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK279049/

## **Diagnostic Tools**

## 3. Bone Turnover Markers (BTM)

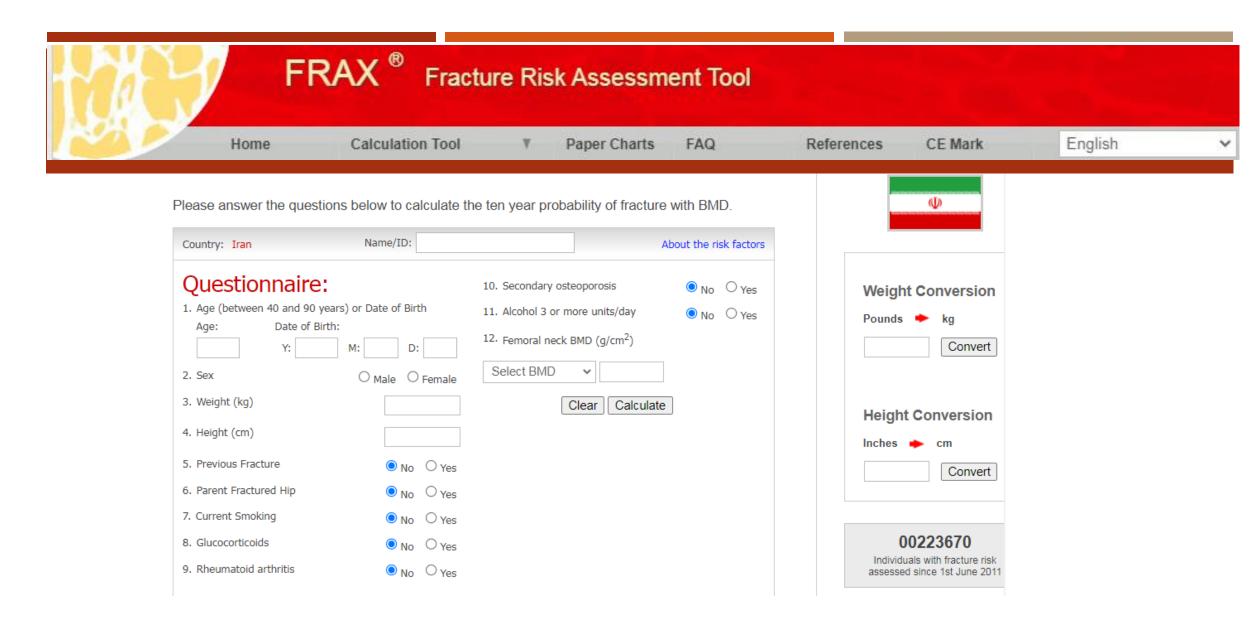
These markers can be measured in blood or urine samples and provide insights into bone metabolism. While they are useful in research settings, their diagnostic value for osteoporosis is limited; they cannot confirm or rule out the condition but may help monitor treatment efficacy

## 4. Fracture Risk Assessment Tools

FRAX®: Developed by the World Health Organization, this tool estimates the 10-year probability of major osteoporotic fractures based on clinical risk factors and BMD measurements. It helps in identifying individuals who may benefit from treatment236.

DXA remains the gold standard for measuring bone mineral density, while tools like FRAX® assist in evaluating fracture risk based on individual patient profiles. Additional methods such as BTMs and QUS provide supplementary information but are not substitutes for comprehensive BMD assessments.

Lewiecki EM. Osteoporosis: Clinical Evaluation. [Updated 2021 Jun 7]. In: Feingold KR, Anawalt B, Blackman MR, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK279049/



 In 2008, Sheffield university in the UK invented FRAX® as a fracture risk assessment tool for estimating the individualized 10-year probability of osteoporotic fractures. 16

# Explanations & Notes On Risk Factors

Age	The model accepts ages between 40 and 90 years. If ages below or above are entered, the programme will compute probabilities at 40 and 90 year, respectively.
Sex	Male or female. Enter as appropriate.
Weight	This should be entered in kg.
Height	This should be entered in cm.
Previous fracture	A previous fracture denotes more accurately a previous fracture in adult life occurring spontaneously, or a fracture arising from trauma which, in a healthy individual, would not have resulted in a fracture. Enter yes or no (see also notes on risk factors).
Parent fractured hip	This enquires for a history of hip fracture in the patient's mother or father. Enter yes or no.
Current smoking	Enter yes or no depending on whether the patient currently smokes tobacco (see also notes on risk factors).
Glucocorticoids	Enter yes if the patient is currently exposed to oral glucocorticoids or has been exposed to oral glucocorticoids for more than 3 months at a dose of prednisolone of 5mg daily or more (or equivalent doses of other glucocorticoids) (see also notes on risk factors).
Rheumatoid arthritis	Enter yes where the patient has a confirmed diagnosis of rheumatoid arthritis. Otherwise enter no (see also notes on risk factors).
Secondary osteoporosis	Enter yes if the patient has a disorder strongly associated with osteoporosis. These include type I (insulin dependent) diabetes, osteogenesis imperfecta in adults, untreated long-standing hyperthyroidism, hypogonadism or premature menopause (<45 years), chronic malnutrition, or malabsorption and chronic liver disease
Alcohol 3 or more units/day	Enter yes if the patient takes 3 or more units of alcohol daily. A unit of alcohol varies slightly in different countries from 8-10g of alcohol. This is equivalent to a standard glass of beer (285ml), a single measure of spirits (30ml), a medium-sized glass of wine (120ml), or 1 measure of an aperitif (60ml) (see also notes on risk factors).
Bone mineral density (BMD)	(BMD) Please select the make of DXA scanning equipment used and then enter the actual femoral neck BMD (in g/cm2). Alternatively, enter the T-score based on the NHANES III female reference data. In patients without a BMD test, the field should be left blank (see also notes on risk factors) (provided by Oregon Osteoporosis Center).



The following adjustments are currently available on FRAXplus<sup>®</sup>:

- Recency of osteoporotic fracture
- High exposure to oral glucocorticoids
- Type 2 diabetes mellitus
- Information on Trabecular Bone Score (TBS)
- Falls history
- Hip axis length (HAL)
- Concurrent data on Lumbar Spine BMD



# Previous Fracture And Subsequent Fracture Risk: A Meta-analysis To Update FRAX

- This study aimed to quantify the fracture risk linked to previous fractures globally
- The analysis included data from 665,971 men and 1,438,535 women across 64 cohorts in 32 countries, totaling 19.5 million person-years of follow-up.
- Findings indicated that individuals with a history of fractures had a significantly higher risk for future fractures
- The risk ratios were consistent across genders. Although low BMD contributed to some fracture risks (14% for clinical fractures, 17% for osteoporotic fractures, and 33% for hip fractures), the majority of the increased risk was independent of BMD.
- Additionally, the risk associated with prior fractures decreased when adjusted for age and time since the baseline examination.

Kanis JA, Johansson H, McCloskey EV, et al. Previous fracture and subsequent fracture risk: a meta-analysis to update FRAX. Osteoporos Int. 2023;34(12):2027-2045. doi:10.1007/s00198-023-06870-z

	Outcome fracture	Number of cohorts	<i>I</i> <sup>2</sup> (%)	HR	95% CI
Women					0
	Any	56	94	1.84	1.72-1.97
	Hip	51	81	1.71	1.57-1.86
	MOF	50	94	1.77	1.63-1.93
	MOF without hip fracture	45	91	1.80	1.65-1.95
	Osteoporotic	51	94	1.82	1.70-1.96
Men					
	Any	34	97	1.92	1.56-2.34
	Hip	29	91	1.99	1.53-2.59
	MOF	31	96	1.90	1.51-2.39
	MOF without hip fracture	30	94	1.79	1.43-2.25
	Osteoporotic	31	97	1.92	1.55-2.38
Men and women					
	Any	62	98	1.85	1.69-2.02
	Hip	56	92	1.77	1.59-1.98
	MOF	55	97	1.80	1.61-2.01
	MOF without hip fracture	51	96	1.80	1.62-2.01
	Osteoporotic	56	98	1.84	1.68-2.03
HR		HR			
2. Caller	fracture P=0.0031	3.0 MOF		P=0.00	95
5		2.5	•••		
4		2.0			
3		1.5			
2		1.0			19
-					

Age (years)

Age (years)

# The Importance Of Recent Prevalent Fracture Site For Imminent Risk Of Fracture

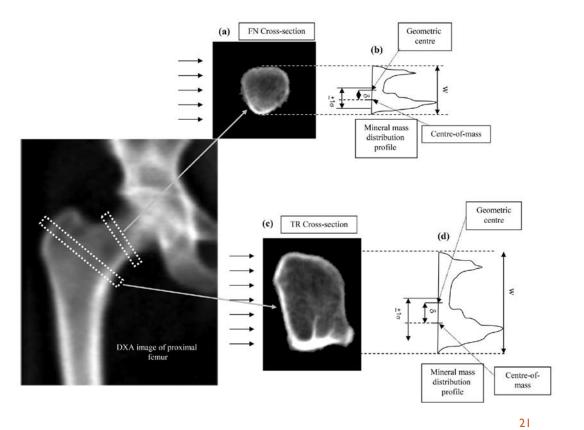
- The object of this study was to assess how the site of a recent fracture influences the risk of future fractures in individuals aged 50 and older.
- Individuals with recent fractures (both MOF and non-MOF) had a significantly higher risk of subsequent fractures:
  - Recent MOF: HR = 2.11 (95% CI: 2.08-2.14)
  - Recent Non-MOF: HR = 2.24 (95% CI: 2.21-2.27)
  - Old Fractures: HR = 1.77 (95% Cl: 1.76-1.78)
- The research highlights that All recent fractures, MOFs, and non-MOFs, as well as older fractures, increase the risk of subsequent fracture, suggesting that all recent fractures should be included in fracture liaison services and that case-finding strategies for those with older fractures may be warranted to prevent subsequent fractures.

Axelsson KF, Litsne H, Lorentzon M. The Importance of Recent Prevalent Fracture Site for Imminent Risk of Fracture - A Retrospective, Nationwide Cohort Study of Older Swedish Men and Women. J Bone Miner Res. 2023;38(6):851-859.

S021 base of skull, n = 485		
S920 calcaneus, <i>n</i> = 627		
S121 second cervical vertebra, n = 481		
S122 other specified cervical vertebra, n = 468		
S220 thoracic vertebra, n = 1644		
S822 shaft of tibia, n = 1010		
S520 upper end of ulna, n = 1638		
S420 clavicle, n = 2914		
S820 patella, n = 1803		
S325 pubis, n = 3045		
S821 upper end of tibia, n = 2730		_
S223 rib, n = 6727	+	
S023 orbital floor, $n = 521$		
S424 lower end of humerus, n = 1238		
S029 skull and facial bones unspecified, $n = 480$		
S224 multiple ribs, $n = 1755$		
S328 other and unspecified parts of lumbar, $n = 1682$		
S324 acetabulum, n = 694		
S422 upper end of humerus, $n = 11984$		
S422 shaft of humerus, $n = 1227$		
M485 collapsed vertebra not elsewhere classified, $n = 6815$		
S622 first metacarpal bone, $n = 522$		
S625 thumb, <i>n</i> = 1232		
S623 other metacarpal bone, $n = 2993$		
S724 lower end of femur, <i>n</i> = 1058		
S823 lower end of tibla, n = 986		
S323 lower end of tibla, $n = 360$ S320 lumbar vertebra, $n = 2663$		
S723 shaft of femur, n = 1110		
S721 pertrochanteric fracture, $n = 8464$		
Size periodianteric fractore, $n = 6404$ S626 other finger, $n = 4911$		
S825 medial malleolus, n = 768		
Se25 medial maneolog, $n = 768$ S925 other toe, $n = 1445$		
S620 scaphoid bone of hand, $n = 1204$		
S620 scaphold bone of hand, $n = 1204$ S421 scapula, $n = 946$		
S526 lower end of both ulna and radius, n = 2051		
Size lower end of both una and radius, $n = 2051$ Size other parts of lower leg, $n = 4340$		
Size other parts of lower leg, $n = 4340$ Size subtrochanteric fracture, $n = 1861$		
S722 Subtrochamenc macture, n = 1661 S924 great toe, n = 963		
S024 malar and maxillary bones, $n = 565$		
S024 malar and maximary bones, n = 565 S022 nasal bones, n = 1899		
S525 lower end of radius, $n = 22313$		
S525 lower end of radius, $n = 22313$ S521 upper end of radius, $n = 2204$		
S923 metatarsal bone, n = 3689		
S824 fibula alone, $n = 1274$		20
S621 other carpal bones, n = 753		20
S720 neck of femur, <i>n</i> = 12412		
S826 lateral malleolus, $n = 6535$		
S523 shaft of radius, n = 457 Dective,		
	0.0 0.5 1.0 1.5 2.0 2.5 3.0 3.5	
	Hazard ratio	

# Differences In Femoral Neck And Trochanteric Structure In Elderly Women Prior To Hip Fracture: Role In Hip Fracture Prediction

- The object of this study was to analyze the structural characteristics of the femoral neck and trochanteric area in older women to improve predictions of hip fracture risk.
- Structural Differences: Significant differences were identified in the geometric and mechanical properties of the femoral neck and trochanteric regions between the two groups.
- Women who later fractured exhibited reduced cortical thickness and altered trabecular microarchitecture.
- Predictive Value: The study found that specific structural characteristics in these areas could serve as predictive markers for hip fracture risk, emphasizing the importance of targeted assessments in clinical settings.



Prince, Richard et al. "Differences in Femoral Neck and Trochanteric Structure in Elderly Women Prior to Hip Fracture: Role in Hip Fracture Prediction." Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research vol. 38,6 (2023): 869-875.

# Risk Of Falls And Fractures In Individuals With Cataract, Age-related Macular Degeneration, Or Glaucoma

This study showed that individuals with cataract, AMD, or glaucoma have a significantly higher risk of both falls and fractures compared to those without these conditions. It emphasizes the need for enhanced awareness and preventive measures for falls among this population.

				- Age related matural deg				C Glaucoma conort			
	No. of events				No. of events	5			No. of events		
Source	Individuals with cataract	Control individuals	HR (95% CI)	Source	Individuals with AMD	Control individuals	HR (95% CI)	Source	Individuals with glaucom	Control a individuals	HR (95% CI)
Primary outcome				Primary outcome				Primary outcome			
Incident falls	121855	283274	1.36 (1.35-1.38)	Incident falls	121855	283274	1.25 (1.23-1.27)	Incident falls	22553	57531	1.38 (1.36-1.41)
Incident fractures	58954	67715	1.28 (1.27-1.30)	Incident fractures	58 954	67715	1.18 (1.15-1.21)	Incident fractures	11032	32898	1.31 (1.27-1.35)
Secondary outcome (incident fractures by body s	site)			Secondary outcome (incident fractures by body s	ite)			Secondary outcome (incident fractures by body site	2)		
Hip	11933	52332	1.28 (1.27-1.30)	Нір	11933	52332	1.06 (1.04-1.09)	Hip	2012	9383	1.00 (0.94-1.07)
Spine	7478	15257	1.39 (1.34-1.44)	Spine	7478	15257	1.26 (1.18-1.35)	Spine	1217	3142	1.25 (1.14-1.37)
Forearm/wrist	7571	20084	1.34 (1.30-1.39)	Forearm/wrist	7571	20084	1.27 (1.19-1.36)	Forearm/wrist	1459	3976	1.44 (1.33-1.56)
Skull/facial bones	1604	5843	1.11 (1.03-1.19)	Skull/facial bones	1604	5843	1.19 (1.03-1.37)	Skull/facial bones	293	1131	0.97 (0.82-1.15)
Pelvis	3121	11401	1.10 (1.05-1.16)	Pelvis	3121	11401	1.13 (1.03-1.24)	Pelvis	550	2071	1.06 (0.93-1.21)
Ribs/sternum	2994	8938	1.18 (1.12-1.25)	Ribs/sternum	2994	8938	1.10 (0.99-1.23)	Ribs/sternum	575	1859	1.26 (1.11-1.44)
Lower limb	9628	22988	1.46 (1.41-1.51)	Lower limb	9628	22988	1.25 (1.17-1.34)	Lower limb	2026	4982	1.49 (1.38-1.61)

#### B Age-related macular degeneration cohort

A Cataract cohort

C Glaucoma cohort

# Updates on Osteoporosis Treatment Strategies



## **Overview Of Medicines For Prevention And Treatment**

## **Bisphosphonates**

## Antiresorptive Agents

Alendronate	Fosamax®, Fosamax Plus D™	Oral (tablet, solution)	Daily/Weekly	Women & Men			
Alendronate	Binosto®	Oral (effervescent tablet)	Weekly	Women & Men			
Ibandronate	Boniva®	Oral (tablet)	Monthly	Women			
Ibandronate	Boniva®	Intravenous (IV) injection	Every 3 months	Women			
Risedronate	Actonel®	Oral (tablet)	Daily/Weekly/Monthly	Women & Men			
Risedronate	Atelvia~	Oral (tablet)	Weekly	Women			
Zoledronic Acid	Reclast®	Intravenous (IV) infusion	One Time per Year/Once every two years	Women & Men			
RANK ligand (RANKL)	) inhibitor						
Denosumab	Prolia®	Injection	Every 6 Months	Women & Men			
Estrogen* (Hormone T	'herapy)						
Estrogen	Multiple Brands	Oral (tablet)	Daily	Women			
Estrogen	Multiple Brands	Transdermal (skin patch)	Twice Weekly/Weekly	Women			
Estrogen Agonists/Antagonists also called selective estrogen receptor modulators (SERMs)							
Raloxifene	Evista®	Oral (tablet)	Daily	Women			
Tissue Specific Estroge	en Complex (TSEC)						
Estrogen/Bazodoxifene	Duavee®	Oral (tablet)	Daily	Women			

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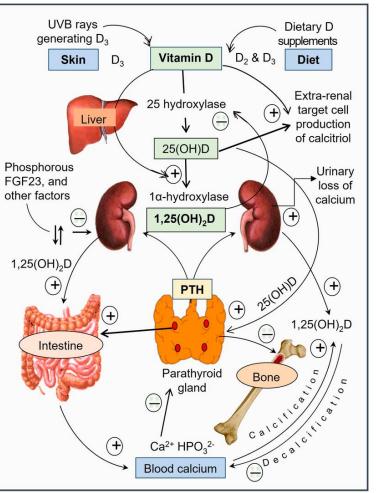
## **Anabolic Agents**

## **Sclerostin Inhibitor**

Romosozumab-aqqg	Evenity®	Injection	2 injections once monthly for 12 months	Women			
Parathyroid Hormone (PTH) Analog							
Teriparatide	Forteo®	Injection	Daily	Women & Men			
Teriparatide	Bonsity®	Injection	Daily	Women & Men			
Parathyroid Hormone-Related Protein (PTHrp) Analog							
Abaloparatide	Tymlos®	Injection	Daily	Women & Men			

## Antiresorptive Agents: Calcium And Vitamin D

- Calcium and vitamin D play distinct parts in bone physiology
- Different combinations of these two treatments and the relative effect of each is not clear
- Calcium supplementation alone does not provide any beneficial effects on bone mineral density
- Vitamin D supplementation is only beneficial in patients with low vitamin D concentrations



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Ebrahimi M, Khashayar P, Keshtkar A, Etemad K, Dini M, Mohammadi Z, Ebrahimi H, Chaman R, Larijani B. Prevalence of vitamin D deficiency among Iranian adolescents. Journal of Pediatric Endocrinology and Metabolism. 2014 Jul 1;27(7-8):595-602.

## Effectiveness Of Calcium Supplementation

Supplementation

- Calcium Supplements:
  - Recommended for individuals unable to meet dietary needs. However, excessive supplementation may lead to side effects such as constipation or kidney stones.
- Vitamin D Supplements:
  - Beneficial for those with low levels, particularly in populations with limited sun exposure. Recommended dosages typically range from 400 to 800 IU per day.
- Combined Supplements:
  - Many products combine calcium and vitamin D to support bone health effectively.

Lifestyle Factors

- Regular weight-bearing and resistance exercises are emphasized as vital for maintaining bone density.
- A balanced diet rich in calcium and vitamin D is crucial for optimal bone health.

## Effectiveness Of Vitamin D Supplementation

- some trials from the past 5 years have had new and unexpected adverse events. These adverse events include increased fractures, falls, and hospitalizations in older people (aged >65 years) include increased fractures after annual injections of 300 000 IU and after annual bolus oral doses of 500 000 IU; increased falls after 500 000 IU annually
- more attention should be paid to the safety of high doses of vitamin D supplementation, particularly in older people





Volume 11, Issue 5, May 2023, Pages 362-374

Personal View

Vitamin D: 100 years of discoveries, yet controversy continues

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## Vitamin D for the Prevention of Disease: An Endocrine Society Clinical Practice Guideline

## Recommendation 1

In children and adolescents aged 1 to 18 years, we suggest empiric vitamin D supplementation to prevent nutritional rickets and potentially lower the risk of respiratory tract infections.  $(2 \mid \oplus \oplus \bigcirc \bigcirc)$ 

## **Recommendation 3**

In the general adult population younger than age 50 years, we suggest against routine 25(OH)D testing. (2  $|\oplus \bigcirc \bigcirc \bigcirc$ )

## **Recommendation 5**

In the general population aged 50 to 74 years, we suggest against routine 25(OH)D testing.  $(2 | \oplus \bigcirc \bigcirc \bigcirc)$ 

## **Recommendation 2**

In the general adult population younger than age 50 years, we suggest against empiric vitamin D supplementation.  $(2 | \oplus \bigcirc \bigcirc \bigcirc)$ 

## **Recommendation 4**

In the general population aged 50 to 74 years, we suggest against routine vitamin D supplementation.  $(2 \mid \oplus \oplus \oplus \bigcirc)$ 

## **Recommendation 6**

In the general population aged 75 years and older, we suggest empiric vitamin D supplementation because of the potential to lower the risk of mortality.  $(2 \mid \oplus \oplus \oplus \bigcirc)$ 

### **Recommendation 7**

In the general population aged 75 years and older, we suggest against routine testing for 25(OH)D levels. (2 |  $\oplus \bigcirc \bigcirc \bigcirc$ )

#### **Recommendation 9**

During pregnancy, we suggest against routine 25(OH) D testing. (2  $| \oplus \bigcirc \bigcirc \bigcirc$ )

### **Recommendation 11**

In adults aged 50 years and older who have indications for vitamin D supplementation or treatment, we suggest daily, lower-dose vitamin D instead of nondaily, higher-dose vitamin D. (2  $| \oplus \oplus \bigcirc \bigcirc$ )

#### **Recommendation 13**

In adults with dark complexion, we suggest against routine screening for 25(OH)D levels. (2  $| \oplus \bigcirc \bigcirc \bigcirc$ )

#### **Recommendation 8**

We suggest empiric vitamin D supplementation during pregnancy, given its potential to lower risk of preeclampsia, intra-uterine mortality, preterm birth, small-for-gestational-age (SGA) birth, and neonatal mortality. (2  $| \oplus \oplus \bigcirc \bigcirc$ )

#### **Recommendation 10**

For adults with high-risk prediabetes, in addition to lifestyle modification, we suggest empiric vitamin D supplementation to reduce the risk of progression to diabetes. (2  $| \oplus \oplus \oplus \bigcirc$ )

#### **Recommendation 12**

In healthy adults, we suggest against routine screening for 25(OH)D levels.  $(2 | \oplus \bigcirc \bigcirc \bigcirc)$ 

#### **Recommendation 14**

In adults with obesity, we suggest against routine screening for 25(OH)D levels.  $(2 | \oplus \bigcirc \bigcirc \bigcirc)$ 

# The Effects Of Dairy Product Supplementation On Bone Health Indices In Children Aged 3 To 18 Years: A Meta-analysis Of Randomized Controlled Trials

- Dairy supplementation significantly increased:
  - Whole-body bone mineral content (BMC) by +25.37 g, Areal BMD by +0.016 g/cm<sup>2</sup>, Height by +0.21 cm
  - Total hip BMC by +0.49 g and aBMD by +0.013 g/cm<sup>2</sup>, Femoral neck BMC by +0.06 g and aBMD by +0.030 g/cm<sup>2</sup>, Lumbar spine BMC by +0.85 g and aBMD by +0.019 g/cm<sup>2</sup>
- This study showed that dairy product supplementation during growth leads to small but significant increases in bone mineral mass parameters and height in children and adolescents. These findings are consistent across various subgroups based on sex, geographical region, baseline calcium intake, and other factors.

Churcher	BMD		0/
Study		WMD (95% CI)	% Weight
Whole-body Cadogan (1997) [9] Merrilees (2000) [10] Volek (2003) [12] Du (2004) [13] Lau (2004) [14] Cheng (2005) [15] Zhu (2006) [18] Cohen (2017) [23] Ikedo (2018) [25] Lu (2019) [27] Overall (I-squared = 44.0%, p = 0.06	6)	0.010 (0.000, 0.020) 0.010 (-0.095, 0.115) 0.014 (-0.564, 0.592) 0.034 (0.016, 0.052) 0.006 (-0.005, 0.017) 0.010 (-0.034, 0.054) 0.030 (0.018, 0.042) 0.012 (-0.020, 0.044) -0.003 (-0.047, 0.041) 0.000 (-0.033, 0.033) 0.016 (0.006, 0.025)	22.46 0.75 0.03 14.15 21.74 3.78 20.51 6.64 3.87 6.08 100.00
Total hip Lau (2004) [14] Cheng (2005) [15] Lu (2019) [27] Overall (I-squared = 0.0%, p = 0.714	4) <b>þ</b>	0.010 (-0.006, 0.026) 0.020 (-0.002, 0.042) -0.001 (-0.071, 0.069) 0.013 (0.000, 0.026)	64.28 32.49 3.23 100.00
Femoral neck Merrilees (2000) [10] Lau (2004) [14] Cheng (2005) [15] Overall (I-squared = 76.7%, p = 0.01	(4) <b>♦</b>	0.050 (0.031, 0.069) 0.010 (-0.008, 0.028) 0.030 (-0.006, 0.066) 0.030 (0.002, 0.058)	36.74 37.43 25.84 100.00
Lumbar spine Chan (1995) [8] Merrilees (2000) [10] Volek (2003) [12] Lau (2004) [14] Cheng (2005) [15] Cohen (2017) [23] Ikedo (2018) [25] Lu (2019) [27] Overall (I-squared = 45.1%, p = 0.07	78)	0.070 (0.025, 0.115) 0.020 (0.001, 0.039) 0.002 (-0.103, 0.107) 0.030 (0.019, 0.041) 0.010 (-0.030, 0.050) -0.006 (-0.052, 0.040) -0.001 (-0.072, 0.070) -0.003 (-0.028, 0.022) 0.019 (0.004, 0.033)	7.99 22.14 1.81 29.36 9.62 7.85 3.79 31 17.43 100.00
I -1	0	1 1	

Hidayat K, Zhang LL, Rizzoli R, Guo YX, Zhou Y, Shi YJ, Su HW, Liu B, Qin LQ. The Effects of Dairy Product Supplementation on Bone Health – Indices in Children Aged 3 to 18 Years: A Meta-Analysis of Randomized Controlled Trials. Adv Nutr. 2023 Sep;14(5):1187-1196.

## Milk Intake And Hip Fracture Incidence In Community-dwelling Old Icelandic Adults

- The study included 4,614 subjects with a mean age of 76 years, recruited between 2002 and 2006. Information on hip fractures was obtained from hospital records during follow-up until 2012.
- Higher milk intake was positively correlated with greater volumetric bone mineral density, showing an adjusted difference of 8.95 mg/cm<sup>3</sup> between the highest and lowest intake categories.
- During the follow-up period, 7.4% of participants experienced a hip fracture.
- The analysis revealed a decreased risk of hip fractures in those with the highest milk intake, with a hazard ratio of 0.69 (95% CI: 0.47-0.99) compared to those with the lowest intake.

	Frequency of milk consumption/day	Participants/cases	HR (95% confidence interval)	<i>P</i> -value
Model 1	< 0.5	n=651/55	Ref	Ref
	0.5-0.9	n=622/54	0.99 (0.68–1.43)	0.936
	1.0-1.4	n = 1438/109	0.83 (0.60-1.14)	0.250
	1.5-1.9	n=874/61	0.76 (0.53-1.10)	0.144
	≥2	n = 1029/63	0.63 (0.44-0.91)	0.013
Model 2	< 0.5		Ref	Ref
	0.5-0.9		0.98 (0.67-1.43)	0.914
	1.0-1.4		0.84 (0.60-1.16)	0.288
	1.5-1.9		0.78 (0.54-1.13)	0.186
	$\geq 2$		0.63 (0.44-0.90)	0.012
Model 3	< 0.5		Ref	Ref
	0.5-0.9		1.02 (0.69–1.49)	0.940
	1.0-1.4		0.89 (0.64–1.24)	0.488
	1.5-1.9		0.89 (0.62-1.30)	0.550
	≥2		0.69 (0.47-0.99)	0.045

\*Based on Cox regression; *P*-value for linear trend (based on group medians) for model 1, P = 0.004; for model 2, P = 0.004; and for model 3, P = 0.025

Model 1, corrected for age and sex; model 2, additionally corrected for education, marital status, smoking, alcohol, physical activity, number of medications, TUG, balance; model 3, additionally corrected for 25(OH)D and vBMD of femoral neck

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Skuladottir SS, Hjaltadottir I, Launer L, Cotch MF, Siggeirsdottir K, Gudnason V, Sigurdsson G, Steingrimsdottir L, Halldorsson T, Ramel A. Milk intake and hip fracture incidence in communitydwelling old Icelandic adults. Osteoporos Int. 2023 Nov;34(11):1951-1959.

# Types Of Dairy Foods And Risk Of Fragility Fracture In The Prospective Nurses' Health Study Cohort

- Consuming two or more servings of total dairy per day was associated with a significantly lower fracture risk (hazard ratio [HR]: 0.74) compared to those consuming less than one serving per day.
- Milk Consumption: More than two servings of milk per day also correlated with reduced fracture risk (HR: 0.85).
- Yogurt Intake: No significant association was found between yogurt consumption and fracture risk.
- Cheese Intake: A weak association was observed, with one or more servings of cheese per day linked to lower fracture risk (HR: 0.89).

	Total dairy intake						
	<1 servings/d	$\geq 1$ servings/d	<1 servings/d	$\geq 1$ servings/d			
	Cases		HR (95% CI) <sup>2</sup>				
N-D calcium							
Low (<500 mg/d)	1244	2039	1.00 (Ref)	0.87 (0.81, 0.94)			
High ( $\geq$ 500 mg/d)	703	1509	0.96 (0.87, 1.05)	0.87 (0.80, 0.94)			
N-D Vit D				21 D.			
Low ( $<6 \mu g/d$ )	1188	1881	1.00 (Ref)	0.88 (0.81, 0.94)			
High ( $\geq 6 \mu g/d$ )	759	1667	1.00 (0.91, 1.09)	0.89 (0.82, 0.97)			
N-D protein							
Low (<60 g/d)	1197	1617	1.00 (Ref)	0.88 (0.81, 0.95)			
High $(\geq 60 \text{ g/d})$	750	1931	1.01 (0.91, 1.12)	0.91 (0.83, 1.00)			
AHEI scores			10 M 10 M	57 S S			
Low (<50)	1010	1850	1.00 (Ref)	0.90 (0.83, 0.97)			
High $(\geq 50)$	937	1698	1.02 (0.93, 1.12)	0.88 (0.81, 0.96)			

Possible effect modification of dairy foods intakes by other dietary factors on fracture risk in women<sup>1</sup>

Yuan M, Hu FB, Li Y, Cabral HJ, Das SK, Deeney JT, Zhou X, Paik JM, Moore LL. Types of dairy foods and risk of fragility fracture in the prospective Nurses' Health Study cohort. Am J Clin Nutr. 2023 Dec;118(6):1172-1181.

# Cheese Consumption And Multiple Health Outcomes: An Umbrella Review And Updated Meta-analysis Of Prospective Studies

- The study concludes that cheese consumption may offer neutral to moderate health benefits, particularly in reducing risks related to mortality, cardiovascular diseases, fractures, and certain cancers. The evidence quality was rated as moderate according to the NutriGrade scoring system.
- Overall, this umbrella review highlights the potential positive impacts of cheese on various health outcomes while suggesting further research is needed for conclusive evidence on specific conditions.

Outcome	Studies, n	Cases, n	Participants, n		RR(95% CI)	P value	12(%)	Туре
Mortality								
All-cause mortality	14	119,402	764,664		0.98(0.96, 1.00)	0.027	60	updated
Cancer mortality	10	26,229	766,967	-	0.99(0.99, 1.00)	0.10	0	updated
Cardiovascular mortality	12	34,844	696,622	1	0.96(0.93, 0.99)	0.02	42	updated
Coronary heart disease mortality	5	4,415	222,138		1.00(0.96, 1.03)	0.81	34	updated
Stroke mortality	4	1,508	197,664	<	0.78(0.53, 1.13)	0.19	76	updated
Cardiovascular disease								
Overall CVD	10	28,651	1,072,452	HB .	0.97(0.95, 0.98)	<0.0001	7	updated
Coronary heart disease	7	11,430	552,606		0.96(0.93, 0.98)	0.0013	0	updated
Stroke	5	16,488	550,526		0.97(0.95, 0.99)	0.0023	0	updated
Hypertension	6	28,986	788,627		1.00(0.96, 1.04)	0.99	50	updated
Cancer								
Overall cancer	24	37,358	4,273,999	1-1-1-C	1.00(0.97, 1.04)	0.79	29	updated
Prostate cancer	7	12,195	730,897		1.06(1.00, 1.11)	0.051	0	updated
Colorectal cancer	4	8,502	1,028,991		1.00(0.90, 1.10)	0.94	30	updated
Breast cancer	5	8,901	407,338	i	0.96(0.87, 1.07)	0.48	49	updated
Metabolic disease								
Type 2 diabetes	18	35,449	394,508		1.00(0.95, 1.06)	0.91	57	updated
Perdiabetes	2	1,949	9,032		0.96(0.80, 1.15)	0.65	83	updated
Aging-related disease								
Total fracture	4	25,463	230,678		0.95(0.93, 0.97)	<0.0001	0	updated
Hip fracture	4	8,257	230,678	·=	0.86(0.82, 0.91)	<0.001	0	updated
Fall	2	1,002	11,908		0.99(0.97, 1.02)	0.67	0	de novo

FIGURE 4. Association between cheese consumption (per 30-g/d intake level) and mortality and multiple disease incidence.

# Vitamin D Supplementation And Muscle Power, Strength And Physical Performance In Older Adults: A Randomized Controlled Trial

- The vitamin D group showed a significant increase in 25(OH)D levels from a baseline of approximately 19.4 ng/mL to 28.6 ng/mL after 12 months, compared to minimal change in the placebo group.
- Despite the increase in vitamin D levels, there were no significant improvements in leg power, strength, SPPB scores, TUG times, or other measures of physical performance between the vitamin D and placebo groups over the study period.
- There were also no notable changes in muscle fiber composition or contractile properties after supplementation.
- These findings suggest that while vitamin D is important for overall health, its supplementation alone may not enhance muscle function in this population.
   Adjusted change in muscle power and strength and physical performance over 12 mo by intervention group and the difference in 12-mo change between intervention groups<sup>1</sup>

	Vitamin D		Placebo	)	Difference in change (vitamin D – placebo)	<i>P</i> value for difference in	
	$N^2$	LS Means $\pm$ SE	$N^2$	LS Means $\pm$ SE	LS Means $\pm$ SE	change by group	
Muscle power and strength							
Leg power, watts	61	$-11.96 \pm 3.75$	61	$-7.97 \pm 3.77$	$-4.00 \pm 5.26$	0.45	
Leg power quality, watts/kg	61	$-0.13 \pm 0.04$	61	$-0.10 \pm 0.04$	$-0.03 \pm 0.06$	0.63	
Knee extensor strength, Nm	45	$-8.09 \pm 1.75$	50	$-3.84 \pm 1.66$	$-4.25 \pm 2.37$	0.08	
Knee extensor quality, Nm/kg	45	$-0.09 \pm 0.02$	50	$-0.04 \pm 0.02$	$-0.04 \pm 0.03$	0.15	
Grip strength, kg	56	$-1.54\pm0.50$	64	$-1.39 \pm 0.48$	$-0.15 \pm 0.69$	0.82	
Physical performance							
SPPB score (0–12)	60	$1.64 \pm 0.22$	63	$1.83 \pm 0.22$	$-0.18 \pm 0.29$	0.53	
Health ABC PPB score (0-4)	54	$0.19 \pm 0.04$	51	$0.17 \pm 0.04$	$0.02\pm0.06$	0.75	
Balance time, s	59	$1.32 \pm 1.98$	57	$3.06 \pm 2.02$	$-1.74 \pm 2.58$	0.50	
4-meter usual gait speed, meters/s	60	$0.07 \pm 0.02$	61	$0.08\pm0.02$	$0.00 \pm 0.02$	0.83	
Chair stand times, s	56	$-3.12 \pm 0.53$	54	$-3.04 \pm 0.53$	$-0.08 \pm 0.59$	0.89	
Timed Up and Go, s	58	$1.01 \pm 0.21$	59	$0.98 \pm 0.21$	$0.03 \pm 0.27$	0.92	
4 stair climb, s	60	$0.41 \pm 0.07$	61	$0.32\pm0.07$	$0.09\pm0.10$	0.35	

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Houston, Denise K et al. "Vitamin D Supplementation and Muscle Power, Strength and Physical Performance in Older Adults: A Randomized Controlled Trial." The American journal of clinical nutrition vol. 117,6 (2023): 1086-1095.

# Fracture Risk Reduction And Safety By Osteoporosis Treatment compared With Placebo Or Active Comparator In Postmenopausal Women

- The results of this study showed: Bone anabolic treatments (e.g., romosozumab and parathyroid hormone receptor agonists) demonstrated superior efficacy compared to bisphosphonates in preventing clinical and vertebral fractures.
- Compared to placebo, all treatments showed significant protective effects against clinical fractures.
- Denosumab was less effective than parathyroid hormone receptor agonists and romosozumab for reducing clinical fractures.
- The effectiveness of antiresorptive treatments increased with the age of participants.

		Odds ratio (95% Cl)	Odds ratio (95% Cl)	Major osteoporotic fractures Bisphosphonates v denosumab				•	_			0.71 (0.30 to 1.66
ction and vith placebo nen: I meta- s." BMJ	Clinical fractures Bisphosphonates v denosumab Bisphosphonates v placebo Bisphosphonates v PTHR Bisphosphonates v romosozumab Bisphosphonates v SERM Denosumab v placebo Denosumab v PTHR Denosumab v romosozumab Denosumab v SERM Placebo v PTHR Placebo v romosozumab Placebo v SERM PTHR v romosozumab PTHR v SERM Romosozumab v SERM		0.81 (0.57 to 1.15) 0.79 (0.70 to 0.89) 1.49 (1.12 to 2.00) 1.26 (0.99 to 1.60) 1.40 (0.72 to 2.71) 0.98 (0.68 to 1.41) 1.85 (1.18 to 2.92) 1.56 (1.02 to 2.39) 1.74 (0.82 to 3.66) 1.90 (1.41 to 2.55) 1.60 (1.24 to 2.05) 1.78 (0.91 to 3.47) 0.84 (0.59 to 1.21) 0.94 (0.46 to 1.93) 1.11 (0.55 to 2.25)	Bisphosphonates v placebo Bisphosphonates v PTHR Bisphosphonates v romosozumab Bisphosphonates v SERM Denosumab v placebo Denosumab v PTHR Denosumab v SERM Placebo v PTHR Placebo v VSERM Placebo v SERM PTHR v romosozumab PIAR v SERM Romosozumab v SERM	0.1 Favo	0.2	0.5		2	-	- 10 700urs	0.66 (0.46 to 0.94 1.29 (0.69 to 2.42 1.28 (0.84 to 1.95 1.18 (0.33 to 4.27 0.93 (0.38 to 2.26 1.82 (0.65 to 5.07 1.81 (0.71 to 4.60 1.66 (0.37 to 7.56 1.96 (1.15 to 3.33 1.95 (1.26 to 3.04 1.79 (0.52 to 6.21 1.00 (0.50 to 1.98 0.92 (0.24 to 3.52 0.92 (0.25 to 3.42
y. 2023						reatme	ent		2nd	treat		

Händel, Mina Nicole et al. "Fracture risk reduction and safety by osteoporosis treatment compared with placebo or active comparator in postmenopausal women: systematic review, network meta-analysis, and metaregression analysis of randomised clinical trials." BMJ (Clinical research ed.) vol. 381 e068033. 2 May. 2023

## Efficacy Of Osteoporosis Pharmacological Treatments In Men: A Systematic Review And Meta-analysis

The findings of this study indicate that pharmacological treatments for osteoporosis are effective in increasing BMD and reducing fracture risk in men, similar to their benefits observed in women. The authors suggest that management algorithms for osteoporosis in men could align closely with those recommended for women.

**Bisphosphonates** 

Study	Total	Experi Mean	mental SD	Total	Mean	Control SD		Mean	Difference		MD	98	5%-CI	Weigh
Bisphosphonate = Aler	ndrona	ate							1					
Gonnelli, 2003	39	8.80	6.2400	38	-1.20	6,1600					10.00	[7.23;	12.771	8.79
Hwang, 2010	23	5.50	3,3600	23	2.00	3.3600						[1.56:		
Miller, 2004	109	4.28	4,5000	58	1.45	4.1000						[1.48]		
Orwoll, 2000	146	7.10	3.6200	95	1.80	4.8700						[4.16]		
Shimon, 2005			6 6 3 0 0			3 3200						[0.72]		
Random effects model	328			225						F.		[2.76:		
Heterogeneity: $I^2 = 83\%$ , $\tau^2$			0.01											
Bisphosphonate = Rise	edrona	ate												
Boonen, 2009	191	5.70	5.5300	93	1.20	5.7900					4.50	[3.09;	5.91]	12.29
Ringe, 2009	158	6.50	5.5300	158	2.20	5.5300					4.30	[3.08;	5.52]	12.79
Random effects model	349			251					+		4.39	[3.46;	5.31]	24.9%
Heterogeneity: $I^2 = 0\%$ , $\tau^2$	= 0, p =	= 0.83												
Bisphosphonate = Zole	droni	c Acid												
Boonen, 2012	588	7.70	9.7000	611	1.60	9.9000			+		6.10	[4.99;	7.21]	12.99
Bisphosphonate = Ibar														
Orwoll, 2010	85	3.52	4.5000	47	0.95	4.1000					2.57	[1.06;	4.08]	12.09
Random effects model				1134					-		4.75	[3.45;	6.05]	100.0%
Heterogeneity: $I^2 = 79\%$ , $\tau^2$	<sup>c</sup> = 3.09	926, p <	0.01				1		1					
Test for overall effect: $z = 7$							-10	-5	0 5	10				
Test for subgroup difference	es: x3	= 14.33,	df = 3 (	0.0 > 0	1)									

Beaudart, Charlotte et al. "Efficacy of osteoporosis pharmacological treatments in men: a systematic review and meta-analysis." Aging clinical and experimental research vol. 35,9 (2023): 1789-1806.

#### Denosumab

Experimental Control Mean Difference MD Study Total Mean SD Total Mean SD 95%-Cl Weight 23 7.35 3.3800 24 0.17 3.7020 Nakamura, 2014 7.18 [5.15; 9.21] 42.1% Orwoll, 2012 121 5.70 3.0900 121 0.90 3.3700 4.80 [3.99; 5.61] 57.9% 5.80 [3.50; 8.11] 100.0% Random effects model 144 Heterogeneity:  $l^2 = 78\%$ ,  $\tau^2 = 2.2119$ , p = 0.03Test for overall effect: z = 4.94 (p < 0.01) -5 (A) Experimental Control Total Mean Mean Difference Study SD Total Mean SD MD 95%-CI Weight 23 2.07 3.5400 24 0.24 5.8500 Nakamura, 2014 1.83 [-0.92, 4.58] 9.4% Orwoll 2012 121 2.10 3.6500 121 0.00 3.3800 2.10 [1.21; 2.99] 90.6% Random effects model 144 2.07 [1.23; 2.92] 100.0% Heterogeneity:  $l^2 = 0\%$ ,  $\tau^2 = 0$ , p = 0.85Test for overall effect: z = 4.82 (p < 0.01) -4 -2 0 2 4 (B) Experimental Control Study Total Mean SD Total Mean SD Mean Difference 95%-CI Weigh Nakamura 2014 23 249 29800 24 -0.65 3.1900 3.14 [1.38; 4.90] 16.9% Orwoll 2012 121 240 25200 121 0 30 2 2400 2.10 [1.50; 2.70] 83.1% Random effects model 144 2.28 [1.51; 3.04] 100.0% Heterogeneity:  $I^2 = 16\%$ ,  $\tau^2 = 0.0888$ , p = 0.27Test for overall effect: z = 5.84 (p < 0.01) -4 -2 0 2

#### Teriparatide

		Expe	rimental			Control										
Study	Total	Mean		Total	Mean	SD		Me	an D	Diffe	renc	e		MD	95%-CI	Weight
Kurland, 2000	13	13.50	10.8000	10	0.75	6.3000					4	18		12.75	[5.70; 19.80]	38.4%
Drwoll, 2003	151	5.87	4.5000	147	0.52	3.9000								5.35	[4.39; 6.31]	61.6%
Random effects model leterogeneity: $I^2 = 76\%$ , $\tau^2$		906 p =	0.04	157				-		-	_	7		8.19	[1.14; 15.25]	100.0%
est for overall effect: z = 2	.28 (p	= 0.02)						-10		0		10				
Study	Total	Mean	imental SD	Total	Mean	Control SD		Me	ean	Diffe	eren	ce		MD	95%-CI	Weight
Kurland, 2000	13	2 00	5.4000	10	0.50	4,7400				1	rs -	<u>.</u>		- 3.40	[-0.75; 7.55]	5.1%
Drwoll, 2003	151		3.9500			4.1000				4	÷				[0.31; 2.13]	94.9%
Random effects model Heterogeneity: $l^2 = 1\%$ , $\tau^2$			0.32	157			1	81	- 1	-	-	-		1.33	[ 0.39; 2.27]	100.0%
incerogeneity. i into, i	2.79 (p	< 0.01)	)				-6	-4	-2	0	2	4	6			
Test for overall effect: z =																
Test for overall effect: z =																

## Comparisons Between Different Anti-osteoporosis Medications On Post Fracture Mortality: A Population-based Study

- Compared to raloxifene and bazedoxifene, the following medications were associated with significantly lower mortality rates: Alendronate/Risedronate: HR = 0.83, Denosumab: HR = 0.86, Zoledronic Acid: HR = 0.78
- Patients receiving long-acting zoledronic acid exhibited the lowest mortality rates, particularly in subanalyses stratified by sex and among those over 65 years old.
- This real-world evidence highlights the importance of medication choice in managing osteoporosis-related fractures and associated mortality risks.
  Table 2. Multivariate Cox proportional hazard analyses of the association between fracture sites and all-cause mortality

	Total fracture	Hip fracture	Vertebral fracture	Nonhip/nonvertebral fracture
Gender (ref. male)	1.00	1.00	1.00	1.00
Female	0.61 (0.59-0.63)**	0.65 (0.61-0.68)**	0.61 (0.57-0.64)**	0.52 (0.47-0.58)**
Age	1.08 (1.08-1.08)**	1.07 (1.07-1.08)**	1.08 (1.07-1.08)**	1.08 (1.07-1.09)**
CCI	1.13 (1.13-1.14)**	1.12 (1.10-1.13)**	1.14 (1.12-1.15)**	1.18 (1.16-1.20)**
Type of osteoporosis medications				
Raloxifene/bazedoxifene (ref.)	1.00	1.00	1.00	1.00
Alendronate/risedronate	0.83 (0.79-0.88)**	0.78 (0.72-0.83)**	0.88 (0.81-0.95)**	0.88 (0.79-0.99)**
Ibandronate	0.96 (0.88-1.05)	0.91 (0.79-1.04)	0.99 (0.85-1.14)	1.05 (0.85-1.29)
Denosumab	0.86 (0.81-0.91)**	0.79 (0.73-0.86)**	0.89 (0.81-0.98)**	0.96 (0.84-1.10)
Zoledronic acid	0.78 (0.73-0.84)**	0.78 (0.70-0.86)**	0.76 (0.67-0.86)**	0.81 (0.68-0.97)**

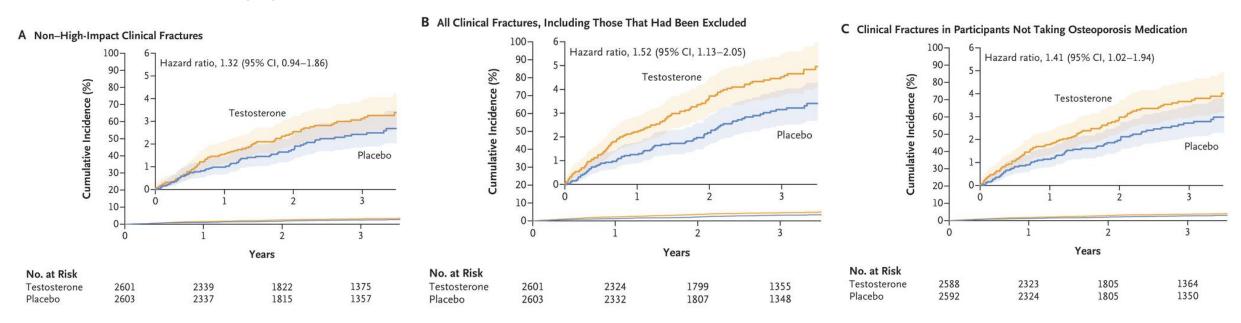
Data presented as adjusted hazard ratios (95% CI), adjusted with immortal time bias. Abbreviation: CCI, Charlson Comorbidity Index.

\*\*P < 0.05.

Wu, Chih-Hsing et al. "Comparisons Between Different Anti-osteoporosis Medications on Postfracture Mortality: A Population-Based Study." The Journal of clinical endocrinology and metabolism vol. 108,4 (2023): 827-833.

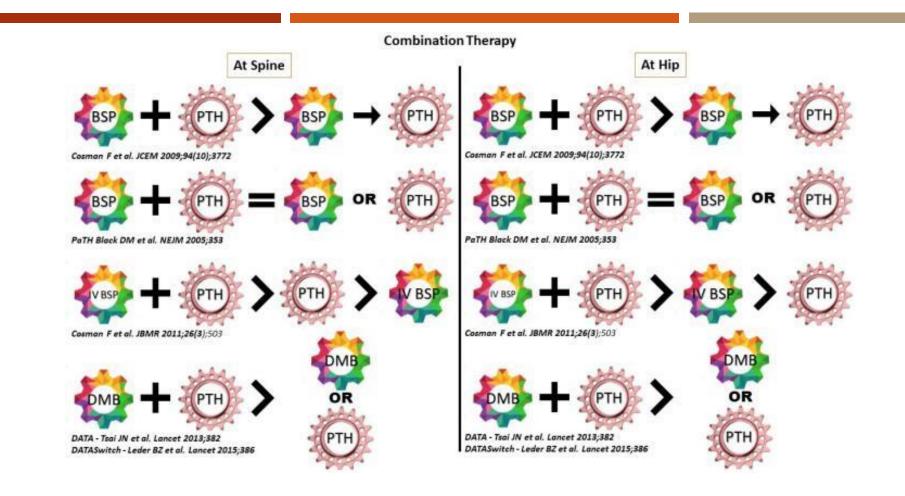
#### Testosterone Treatment And Fractures In Men With Hypogonadism

This study showed that although testosterone therapy can enhance bone density in men with hypogonadism, it does not lead to a significant reduction in fracture risk over one year. These findings suggest that while testosterone treatment may have benefits for bone health, additional strategies may be necessary to prevent fractures in this population.



## Combination Therapy In Osteoporosis

- Emerging evidence suggest that therapy should be initiated with an anabolic agent in patients who are at high risk to attain BMD gains quickly.
- Anabolic therapy after a potent antiresorptive such as alendronic acid is associated with an initial blunting in BMD response, however, reassuringly this does not seem to result in increased fracture risk.
- The effects of all anabolic agents appear to be reversible and the administration of an antiresorptive medication is needed after their discontinuation.

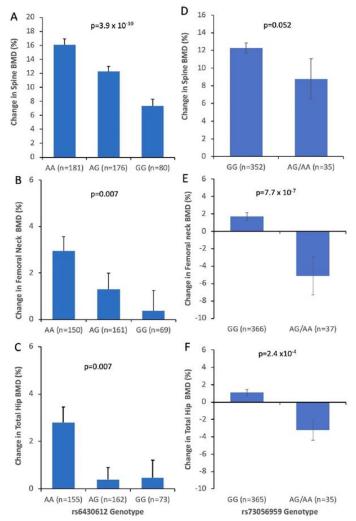


- The concomitant administration of denosumab with teriparatide has been shown to significantly increase areal BMD as well as to increase volumetric BMD
- A regimen in which a moderately potent antiresorptive is followed by a stronger one has the potential to be associated with a higher risk of adverse events such as atypical fractures and osteonecrosis of the jaw.

Chandran M. The why and how of sequential and combination therapy in osteoporosis. A review of the current evidence. Arch Endocrinol Metab. 2022 Nov

## Genome-wide Association Study Identifies Genetic Variants Which Predict The Response Of Bone Mineral Density To Teriparatide Therapy

- Several genetic variants were significantly associated with the change in BMD following teriparatide treatment.
- The findings suggest that genetic profiling may enhance personalized treatment approaches for osteoporosis, allowing for more tailored use of teriparatide based on individual genetic makeup.

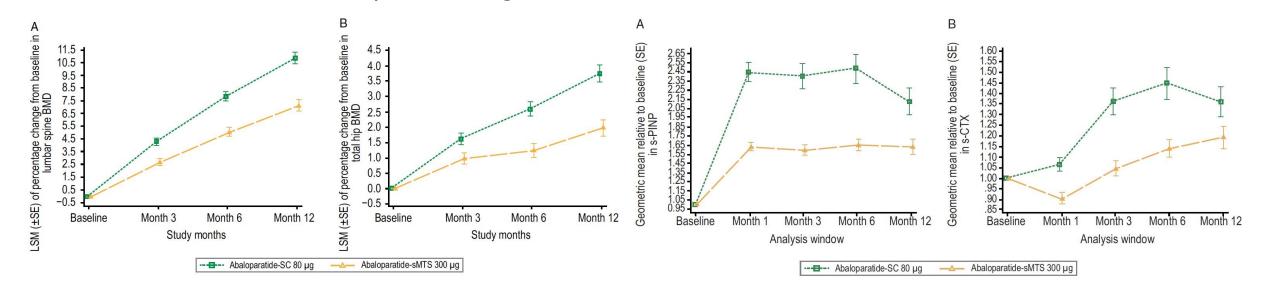


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Alonso, Nerea et al. "Genome-wide association study identifies genetic variants which predict the response of bone mineral density to teriparatide therapy." Annals of the rheumatic diseases vol. 82,7 (2023): 985-991

#### Efficacy And Safety Of Transdermal Abaloparatide In Postmenopausal Women With Osteoporosis: A Randomized Study

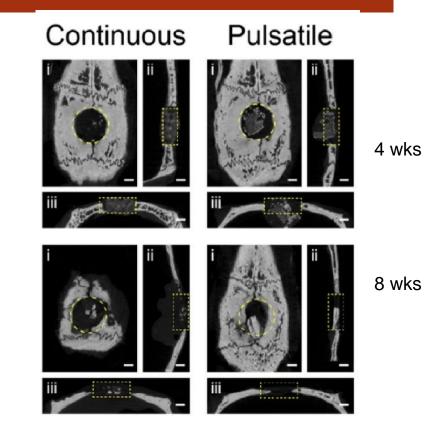
- Participants receiving transdermal abaloparatide showed significant improvements in BMD at key sites such as the lumbar spine and hip compared to those on placebo.
- The treatment was associated with a reduction in the risk of new vertebral fractures.
- The study demonstrates a favorable safety profile, suggesting that this formulation could be a viable alternative for osteoporosis management.



Lewiecki, E Michael et al. "Efficacy and Safety of Transdermal Abaloparatide in Postmenopausal Women with Osteoporosis: A Randomized Study." Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research vol. 38,10 (2023): 1404-1414.

## A Biomimetic And Bioactive Scaffold With Intelligently Pulsatile Teriparatide Delivery For Local And Systemic Osteoporosis Regeneration

- The scaffold is made from mesoporous bioglass and features a polydopamine coating that allows for near-infrared (NIR) light-triggered drug release.
- Teriparatide is encapsulated in thermosensitive liposomes within the scaffold, enabling localized and systemic effects. The release can be controlled by NIR light, which heats the scaffold and triggers the release of the drug.
- The pulsatile release of teriparatide significantly improves BMD and promotes osteogenic differentiation, leading to better healing of osteoporotic bone defects.
- In animal models, the scaffolds demonstrated effective bone regeneration capabilities, indicating their potential for clinical application in treating osteoporosis-related fractures.



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## International Organizations In The Treatment Of Osteoporosis And The Prevention Of Fragility Fractures

## Importance Of International Collaboration In Reducing Osteoporosis And Fragility Fractures

International collaboration is crucial in addressing the global challenge of osteoporosis and fragility fractures. These collaborations aim to enhance awareness, prevention, and treatment strategies on a global scale.

The International Osteoporosis Foundation (IOF), as the largest non-governmental organization focused on osteoporosis, plays a pivotal role in uniting stakeholders to share knowledge, research, and best practices.



## Key IOF Goals And Priorities



#### **IOF Board Members**





Morocco



Tunisia









India









JORGE LUIS ALBERTO MORALES TORRES Mexico







MICHAEL MCCLUNG United States of America United States of America

DANIEL PINTO United States of America

STUART SILVERMAN United States of America

#### Capture The Fracture (CTF)

- Capture the Fracture (CTF) is a global initiative launched by the IOF in 2012, aimed at improving secondary fracture prevention for individuals who have already experienced a fragility fracture. This initiative seeks to address the significant care gap that often leaves these patients at risk for future fractures.
- Objectives of Capture the Fracture
  - Global Standards: CTF establishes internationally endorsed standards for best practices in post-fracture care, primarily through the implementation of Fracture Liaison Services (FLS).
  - Best Practice Framework: The initiative includes a Best Practice Framework (BPF) that outlines essential components for effective FLS implementation. This framework serves as a benchmark for healthcare providers and allows them to gain recognition on the CTF Global Map of Best Practices.
  - Mentorship and Resources: CTF offers mentorship programs and a variety of resources to support the development and sustainability of FLS at local levels. This is crucial for healthcare systems aiming to enhance their fracture care services

IOF

**CAPTURE** the

FRACTURE

partnership

#### CTF Governance

#### Chair



#### Vice-Chairs



eve University Hospitals



#### **FLS Expert Members**





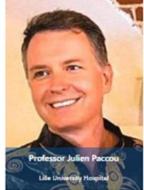












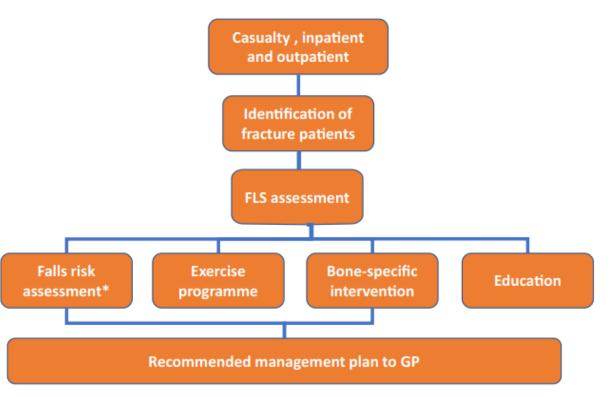
Tehran University of Medical Sciences



Doctor José Francisco Torres Naranjo President of Asociación Mexicana de Metabolismo Óseo y Mineral (AMMOM)

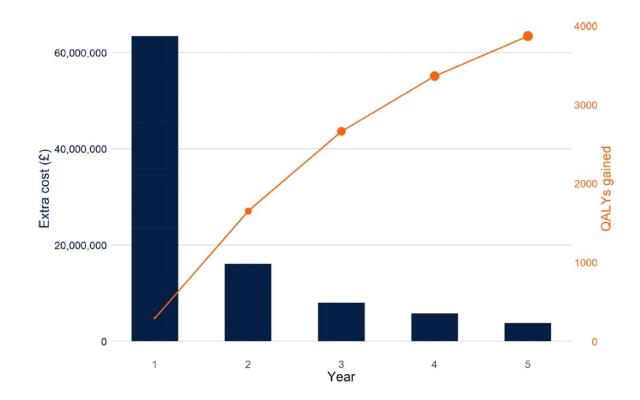
#### What Is Fracture Liaison Services

- Fracture Liaison Services (FLS) are specialized healthcare programs designed to provide secondary prevention for fragility fractures, particularly in older adults. These services aim to identify patients who have suffered a fragility fracture and assess their risk for future fractures, ensuring timely intervention and management.
- By providing comprehensive assessments, multidisciplinary care coordination, and targeted interventions, FLS effectively addresses the gaps in care for individuals who have sustained fragility fractures.



# Expected Benefits And Budget Impact From A Microsimulation Model Support The Prioritization And Implementation Of Fracture Liaison Services

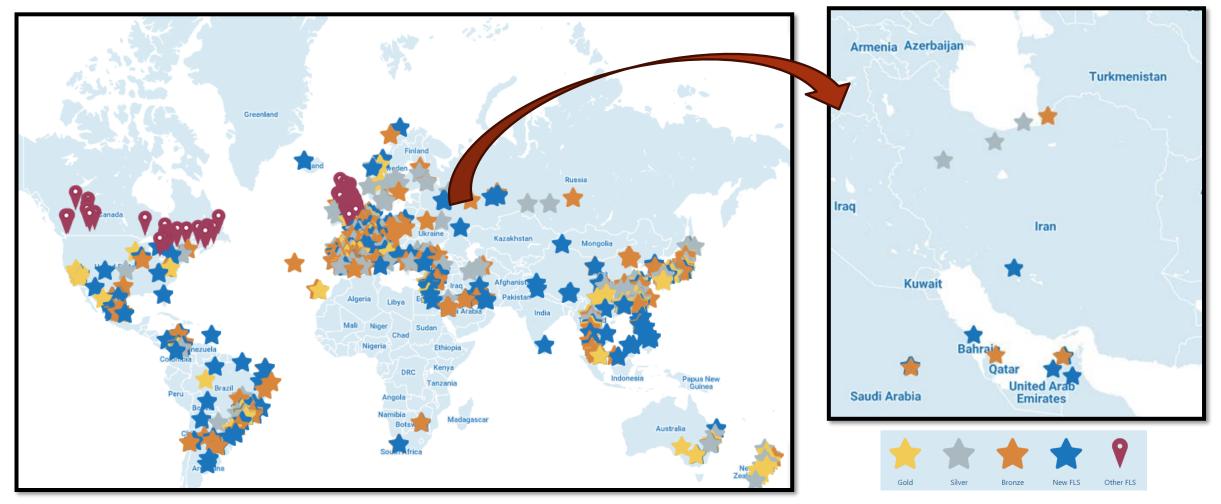
- This study showed that implementing FLS was projected to significantly reduce the incidence of subsequent fractures, leading to improved quality of life for patients.
- The analysis indicated that FLS could result in substantial cost savings for healthcare systems by preventing fractures and associated complications.
- The findings support the argument that investing in FLS is economically viable and beneficial for managing osteoporosis, ultimately leading to better patient outcomes and reduced healthcare costs.



Pinedo-Villanueva, Rafael et al. "Expected Benefits and Budget Impact From a Microsimulation Model Support the Prioritization and Implementation of Fracture Liaison Services." Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research vol. 38,4 (2023): 499-511.



#### Fracture Liaison Services: Map Of Best Practice



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در کلینیکهای استئوپاد چه میکنیم؟



#### پیگیریهای دورهای

پیگیریهای دورهای و منظم برای شروع درمان، پایبندی به درمان، اصلاح عوامل خطر زمینهای و ...



#### معاینه و درمان

بررسی سوابق خطر و سبک زندگی، ارزیابی خطر سقوط، مشاوره عمومی و آموزش، ارزیابی وضعیت پوکی استخوان، درمان پوکی استخوان و ...



شناسایی بیماران

شناسایی بیماران با شکستگی مهرهای و غیرمهرهای با ضربه خفیف در افراد بالای ۵۰ سال

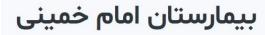




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مركز تحصصي فوق تحصصي بعثت جلان



🚯 اطلاعات بیشتر

بیمارستان شهید چمران

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Chamran Hospital

مرکز تخفیقات روماتولوژی

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بیمارستان ۵ آذر

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#### Future Directions For Osteoporosis Management

#### Personalized Management :New Horizons Of Diagnosis And Treatment



## PoC in-office device for identifying individuals at high risk of osteoporosis and osteoporotic fracture.

We believe it is possible to develop an in-office device capable of determining both the genetic predisposition and BTM values of osteoporosis from a single drop of blood at acceptable cost







# PoCOsteo

A PoC, in-office device for identifying individuals at high risk of osteoporosis and osteoporotic fracture

GENT



## Conclusions

- Osteoporosis is caused by many different factors
- Treatment of osteoporosis is a multifaceted approach that includes lifestyle modification, exercise, and medications
- Currently approved for the treatment of osteoporosis are generally divided into broad categories of antiresorptive and osteoanabolic medications
- Covid-19 pandemic has severely affected osteoporosis management in all countries, including Iran
- General approach to osteoporosis is **personalized** and designed for each individual patient.
- Future strategies against osteoporotic fractures should be multidisciplinary and inclusive of different strategies.