



Osteoporosis And Vitamin D Deficiency

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Scope

- Background information:
 - Definitions
 - Causes
 - Prevalence
 - Risk factors
 - Complications (burden)
- Assessment:
 - Who
 - How
 - Differential diagnosis
 - FRAX correction

Scope

- Management
 - Conservative management
 - Alendronic acid
 - Denosumab
 - New drugs
- Vitamin D deficiency
 - Vitamin D correction
 - Vitamin D and Calcium supplement

Definitions

- **Osteoporosis:** disease characterized by low bone mass and structural deterioration of bone tissue.
- **Osteoporotic fracture:** fragility fracture occurring as a result of osteoporosis (more common in wrist, spine, and hip).
- **Fragility fracture:** fracture following a fall from standing height or less (vertebral fracture can occur spontaneously or from daily activities such as bending or lifting). Spine, hip, or 2 or more other fractures (KOPS).
- **DXA** stands for Dual-Energy-Xray absorptiometry.
- **BMD** stands for bone mineral density.

Causes

- Osteoporosis is the result of an imbalance in the normal process of bone remodeling by osteoclasts and osteoblasts.
- The age when osteoporosis becomes apparent depends on peak bone age which is depends predominantly on genetic factors but also levels of sex hormones (estrogen and testosterone), nutrition (calcium and vitamin d levels), and level of physical activity.
 - It is reached in the third decade and starts to decline in the fifth decade for men and women. In women, this decline accelerates after the menopause for a period of between 5 and 10 years.

Prevalence

- **Women** are at greater risk of osteoporosis due to the decrease in estrogen production at the menopause, which accelerates bone loss.
- The prevalence of osteoporosis increases markedly, from approximately **2%** at 50 years of age to almost **50%** at 80 years of age.

عبء هائل على العالم

 **1/3**

 **1/5**

عالمياً بعد
سن 50 سيعانون
من كسر بسبب
هشاشة العظام



+8.9

مليون كسر
سنوياً

كسر واحد
كل 3 ثواني

زيادة في كسور الورك

1990 → 2050

 **+310%**

 **+240%**



Risk Factors

- Divided into
 - Factors affecting bone strength that:
 - Reduce BMD
 - Do not reduce BMD
 - Have unestablished mechanisms
- Risk factors for falls

Risk factors reducing BMD

- **Endocrine:** diabetes mellitus, hyperthyroidism, hyperparathyroidism.
- **Gastrointestinal:** IBD, coeliac disease, chronic pancreatitis.
- **Chronic kidney / liver disease.**
- **Chronic obstructive pulmonary disease.**
- **Menopause.**
- **Immobility.**
- **BMI of less than 18.5 kg/m².**

Risk factors that do not reduce BMD

- **Age** — risk increases with age and is at least partly independent of BMD.
- **Oral corticosteroids** (dependent on the dose and duration of treatment).
- **Smoking.**
- **Alcohol** (3 or more units daily).
- **Previous fragility fracture** (risk increases with increasing number of fractures). Risk is highest for previous hip fractures and lowest for previous vertebral fractures.
- **Rheumatological conditions**, such as Rheumatoid arthritis, and other inflammatory arthropathies.
- **Parental history of hip fracture.**

Risk factors with unestablished mechanism

- **Selective serotonin reuptake inhibitors.**
- **Proton pump inhibitors.**
- **Anticonvulsant drugs**, in particular enzyme-inducing drugs, such as carbamazepine.

Risk factors for falls

- Impaired vision.
- Neuromuscular weakness and incoordination.
- Cognitive impairment.
- The use of alcohol and sedative drugs.

Burden of fragility fracture

- **Hip fracture:**
 - Almost always requires hospitalization
 - Mortality 20%, permanent disability 50%, 10-fold increased relative mortality risk in the year following fracture.
- **Vertebral fracture: 50-70 % silent**
 - Back pain (about one third of vertebral fractures present with acute and severe pain at the site of the fracture), loss of height, kyphosis, and difficulties activities of daily living.
 - 4.4-fold increased relative mortality risk in the year following fracture.
- **Forearm fracture**
 - Can cause significant pain and disability and affect a person's independence and quality of life.

كسر الورك

فقدان القدرة على العمل و الاعتماد على النفس عند الناجين

لا يستطيعون
الحركة بشكل
مستقل

40%

يحتاجون
لمساعدة
بعد سنة

60%

33%
يعتمدون على
الآخرين و مقيمين
في مصحات طبية
بعد سنة



الوفيات

تصل إلى 20-24%
في اول سنة
بعد كسر الورك

50%
من الافراد المصابون بكسر واحد
نتيجة الهشاشة سيصابون بكسر اخر



Differential diagnosis

- **Non-osteoporotic causes for fragility fractures include:**
 - **Metastatic bone disease** — suggested by bone pain, history of cancer (especially lung, thyroid, prostate, kidney, or breast cancer), or symptoms of undiagnosed cancer (for example unexplained general malaise or weight loss).
 - **Multiple myeloma** — suggested by bone pain, anemia, recurrent infections, bleeding, symptoms of hypercalcemia, or kidney disease.
 - **Osteomalacia** — suggested by bone pain, muscle pain, or proximal muscle weakness.
 - **Paget's disease** — suggested by bone pain or deformity

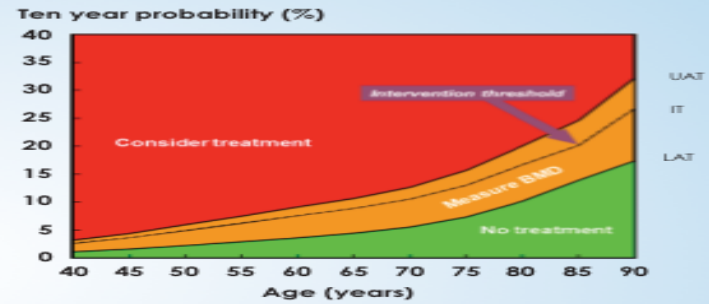
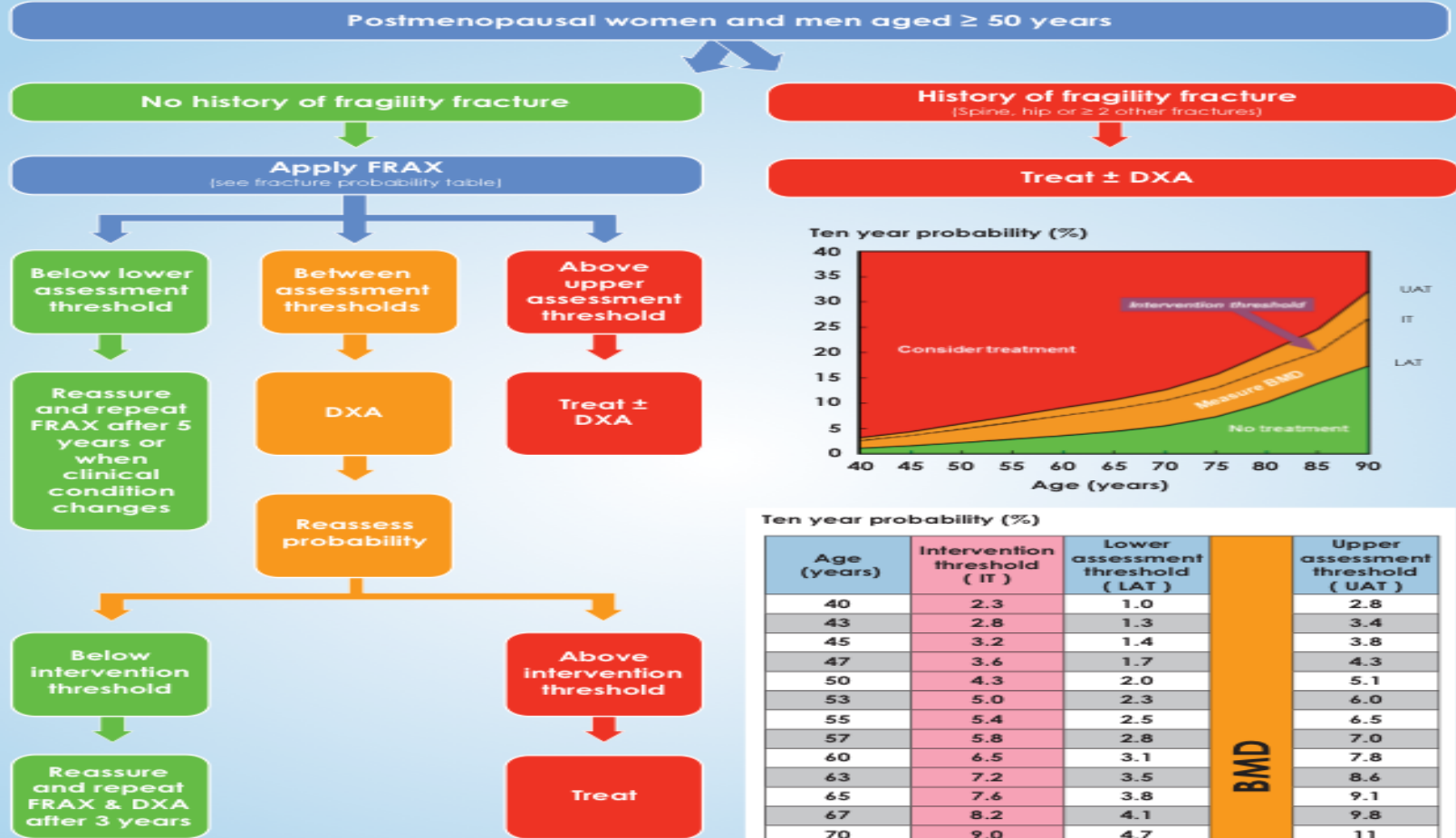
Interesting to know

- Most fractures happen in osteopenia range.
- Accumulation of risk factors increase future fracture risk.
- 50% of those with one fragility fracture will have a second one.

https://kops-kw.org/uploads/frax_guidelines_2018.pdf



FRAX Based Kuwait Osteoporosis Guidelines - 2018



Ten year probability (%)

Age (years)	Intervention threshold (IT)	Lower assessment threshold (LAT)	BMD	Upper assessment threshold (UAT)
40	2.3	1.0		2.8
43	2.8	1.3		3.4
45	3.2	1.4		3.8
47	3.6	1.7		4.3
50	4.3	2.0		5.1
53	5.0	2.3		6.0
55	5.4	2.5		6.5
57	5.8	2.8		7.0
60	6.5	3.1		7.8
63	7.2	3.5		8.6
65	7.6	3.8		9.1
67	8.2	4.1		9.8
70	9.0	4.7		11
73	10	5.5		12
75	11	6.2		13
77	12	7.0		14
80	14	8.5		17
83	17	10		20
85	19	12		23
87	20	13		24
90	23	14		27

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40	2.3	1.0		2.8
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63	7.2	3.5		8.6
65	7.6	3.8		9.1
67	8.2	4.1		9.8
70	9.0	4.7		11
73	10	5.5		12
75	11	6.2		13
77	12	7.0		14
80	14	8.5		17
83	17	10		20
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FRAX Based Kuwait Osteoporosis Guidelines - 2018

Fracture risk elevated based on FRAX assessment ± DXA scan

History of fragility fracture (Spine, hip or ≥ 2 other fractures)

NON PHARMACOLOGICAL:

- 1) Discontinue/limit smoking, alcohol, excess caffeine.
- 2) Weight-bearing exercises 30 minutes/day (walking, jogging, dancing, strength/resistance training).
- 3) Measures to reduce the risk of falling.
- 4) Use hip protectors in individuals with high risk of falling.

PHARMACOLOGICAL:

- 1) Treat vitamin D deficiency if present & maintain on 50,000 IU/month or equivalent dose to achieve Serum 25-OH vitamin D level between 75-150 nmol/L.
- 2) Maintain on calcium 1200 mg/day (preferably through diet, if not then through supplements).
- 3) One-Alfa should only be used in cases of chronic renal impairment and hypoparathyroidism.

First choice (alphabetical order)

	Vertebral	Nonvertebral	Hip	Men
- Alendronate (Fosamax)	↓	↓	↓	✓
- Denosumab (Prolia) ⁽¹⁾	↓	↓	↓	✓
- Zoledronic Acid (Aclasta) ⁽²⁾	↓	↓	↓	✓

Second choice (alphabetical order)

- Ibandronate (Bonviva)	↓	↓ ⁽³⁾	NAE	NAE
- Raloxifene (Evista) ⁽⁴⁾	↓	NAE	NAE	NAE

After 5 yrs of Alendronate and Ibandronate use or 3 yrs of Zoledronic acid use:

- Patients with low fracture risk: consider drug holiday, monitor for BMD decline and reassess risk every 1-2 years, consider retreatment if indicated.
- Patients with high fracture risk: continue for up to 10 years if on alendronate or ibandronate and up to 6 years if on zoledronic acid, reassess risk and if still high then shift to other drug class.

NAE: Not Adequately Evaluated
⁽¹⁾ Preferred drug in renal insufficiency (Cl_{cr} < 35 ml/min)
⁽²⁾ Preferred drug after hip fracture
⁽³⁾ Post-hoc analysis
⁽⁴⁾ Preferred drug in women with strong family history of breast malignancy

Combination therapy is not advised

TREATMENT MONITORING

- Repeat DXA every 2 years on same machine & if possible with same technologist.
- Monitor changes at lumbar spine, total hip BMD. Compare BMDs and not T-scores.

TREATMENT ASSESSMENT

TREATMENT FAILURE

- 1) Declining BMD
- 2) Occurrence of >1 fragility fracture

Rule out:

- Non adherence
- Secondary causes including medications

Teriparatide (Forteo)

20 mcg s/c daily for 18 - 24 months (once in a lifetime)

Evidence for Fracture Risk Reduction				
Vertebral	Nonvertebral	Hip	Men	
↓	↓	↓	NAE	✓
NAE: Not Adequately Evaluated				

Contraindication to PTH:

- Hypercalcemia
- Hyperparathyroidism
- Skeletal malignancy
- Paget's disease
- Radiation therapy

Treatment should be followed by an antiresorptive agent



<u>First choice (alphabetical order)</u>	Evidence for Fracture Risk Reduction by Randomized Trials			
	<u>Vertebral</u>	<u>Nonvertebral</u>	<u>Hip</u>	<u>Men</u>
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- Denosumab (Prolia) ⁽¹⁾	↓	↓	↓	✓
- Zoledronic Acid (Aclasta) ⁽²⁾	↓	↓	↓	✓
 <u>Second choice (alphabetical order)</u>				
- Ibandronate (Bonviva)	↓	↓ ⁽³⁾	NAE	NAE
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↓

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TREATMENT ASSESSMENT

TREATMENT FAILURE

- 1) Declining BMD
- 2) Occurrence of >1 fragility fracture

Rule out:

- Non adherence
- Secondary causes including medications

TREATMENT SUCCESS

- 1) Stable or increasing BMD
- 2) Absence of fragility fractures

Duration of antiresorptive agents regimen

- Alendronate : Treat 5 – 10 years and reassess
 - Low risk = drug holiday
 - High risk = anabolic agent
- Zoledronate: treat for 3 – 6 years and reassess
 - Low risk = drug holiday
 - High risk = anabolic agent
- Denosumab: continue until the patient is no longer high risk and ensure transition into another antiresorptive

INDICATIONS FOR VERTEBRAL IMAGING

Consider vertebral imaging tests, by **Vertebral Fracture Assessment (VFA)** or lateral thoracic and lumbar spine x-ray, in the following individuals:

- In all women age 70 and older and all men age 80 and older.
- In women and men age >50 with specific risk factors:
 - Low trauma fracture
 - Historical height loss of 4 cm or more
 - Prospective height loss of 2 cm or more
 - Recent or ongoing long term glucocorticoid treatment

Adopted from the National Osteoporosis Federation 2013

Assessment

- Who should be assessed?
 - Kuwait osteoporosis guideline – 2018
 - Assess vitamin D and calcium levels.
 - People **younger than 50 years of age** with any of the following risk factors:
 - Current or frequent use of oral corticosteroids.
 - Untreated premature menopause.
 - A previous fragility fracture.
 - People **younger than 40 years of age** with any of the following risk factors:
 - Current or recent use of high-dose oral corticosteroids equivalent to, or more than, 7.5 mg prednisolone daily for 3 months or more.
 - Previous fragility fracture of the spine, hip, forearm, or proximal humerus.
 - History of multiple fragility fractures.

FRAX

<https://www.sheffield.ac.uk/FRAX/>

Calculation tools

Middle east and Africa

kuwait

Correction of frax

If difference between hip T score and L1-4 T score is more than 1 SD

MOF x 1.(difference)

FRAX vs QFracture

- **KOPS** recommends FRAX, **SIGN** recommends Qfracture, **nice** recommends either methods.
 - FRAX can be recalculated considering BMD measurements while Qfracture can not.
 - FRAX underestimates the 10-year fracture risk in people over 75 years of age compared with Qfracture.
 - Qfracture Takes into account many more variables than FRAX.

Primary Health Care Information System - Doctor Examination Screen

Qurtuba Clinic
Al Assima

Room No : 15 LAYAL MOHAMED ALMENOFI

Get Patients No. Waiting Patients Transfer Patients

Civil ID: _____ Name: _____

Nationality: _____ Blood Group: _____ Age: _____ Gender: _____

Area: _____ Mobile: _____ Tel. No: _____ Reason for visit: _____

Medical Conditions
Chronic Diseases
Asthma
Diabetes Mellitus (Type 2)
Hyperlipidemia
Hypertension

Medication List

Allergy: Yes/No

Clinical Findings Management Investigations Referral Leaves **Appointment** Medical Reports Reports

Suicidal Risk Assessment Metabolic Risk Assessment...

Complain

Complain	Details

Diagnosis

Diagnosis	Remarks

Signs

Signs	Details

Spo2 Temp in C 37.5 Pulse Height (Cms) Weight (Kgs) BMI Blood Pressure

Notes

To enter a Complain / Sign / Diagnosis, click on the list button.

Visits Delivered...
Visits History...
Hospital History
Summary
Workable Diseases
Well Baby Clinic
NCD
Screening
VAIR
DAIR



Management

Conservative Management

- Exercise should be weight bearing hence swimming not counted as beneficial in protecting against osteoporosis.
- Measures to reduce risk of falling:
 1. rooms in ground floor, good lightening, avoid putting furniture at the Centre of the room, avoid pieces of carpets.
 2. avoid unnecessary medications that cause drowsiness e.g antihistamine , muscle relaxants.
 3. wear sensible foot wear avoid wearing floppy slippers or shoes with slick soles that can cause slipping.
 4. adding rails and grab bars to slippery areas e.g showers.

Fosamax (Alendronate)

- Absorbed into hydroxyapatite crystals of bone to reduce rate of bone turnover.
- Correct calcium and vitamin D and do dental check up before initiation.
- S/E: nausea, dyspepsia, mild gastritis
bone/ joint muscle pain, osteonecrosis of jaw
atypical stress fracture.
- C/I: pregnant/lactating, hypercalcemia, severe CKD(eGFR less than 35), cant set upright 30 minutes.
- Advice: take 30 mins. Before breakfast
swallow with a glass of water (200 ml), don't suck or chew
take in upright position and remain for 30 minutes
if missed dose not take 2 tablets together
Dental check up before and after initiation.

Fosamax (Alendronate)

- Drug interactions:
 - Calcium and PPI: at least 30 minutes in between.
 - Food and drinks: at least 30 minutes in between.
 - NSAID: use with caution in conjunction.
- Advice on missed dose of weekly alendronate:
 - To take the missed tablet on the day that it is remembered.
 - To continue taking one tablet once a week, on the day the tablet is normally taken.
 - That two tablets should not be taken on the same day.

Prolia (denosumab)

- Human monoclonal antibodies that inhibit osteoclasts formation, function, and survival; thereby decreasing bone resorption.
- Correct calcium and vitamin D before initiating treatment
- Consider dental check up and carry out invasive procedures before initiation of treatment.
- Preferred option in renal impaired patient.(increased risk of hypocalcemia if eGFR less than 30 therefore monitor calcium if that's the case)
- Avoid in pregnant/breastfeeding females.
- S/E: constipation, UTI, URTI, rash, cataracts, sciatica, pain in extremities.
- Dose: 60 mg SC every 6 months

New drugs

- Abaloparatide (Tymlos) approved April 2017
 - Parathyroid hormone related peptide
 - 86% reduction in vertebral fracture
 - Daily Subcutaneous injection for 2 years
- Romosozumab (Evenity) approved April 2019
 - Monoclonal antibody against sclerostin
 - Subcutaneous injection monthly for 12 months

Referral

- Severe osteoporosis
- Age less than 50
- Treatment failure, intolerance to oral tx
- Conditions that complicate management (hyperparathyroidism, CKD, malabsorption)
- Repeated fractures with normal BMD

Vitamin D deficiency

- vitamin D is derived from skin exposure to ultraviolet B radiation from sunlight, with the remaining 10–20% being derived from dietary sources.
- Deficiency is defined as a serum 25-hydroxyvitamin D level of less than 50 nmol/l, and insufficiency is defined as a serum 25-hydroxyvitamin D level of 50 - 75 nmol/L).
- Risk factors:
 - Aged 65 years and over.
 - People with low or no exposure to the sun, for example those who cover their skin; who are housebound or confined indoors for long periods.
 - People with darker skin pigmentation.
 - Malabsorption disorder or following weight loss surgery.
 - Severe liver or end-stage chronic kidney disease.
 - Pregnant or breastfeeding.
 - Obesity.

Vitamin d correction

- Natural source:
 - salmon, sardines, egg yolk, meat, some breakfast cereals, margarines, and milk formulas
 - exposure to sun (30 minutes before 10 am or after 3 pm exposing head , neck, chest and arm 1-2 times aweek), prolonged exposure to strong sunlight and sunbeds are ineffective.
- Maintenance:
 - day 1 – 18 years 400-800 IU of D₃/day
 - above 18 years old (inc. pregnant and lactating) 400/800 IU /day orally, or 10,000 IU/wk, or 30,000-50,000 IU/month, or 200,000-300,000 IU/6m IM
- Treatment:
 - day 1-18 years only with documented rickets and severe deficiency 2,000-4,000 iu/day for 6-8 weeks with calcium intake for 2 weeks
 - above 18 years 50,000 IU/wk or 200,000-300,000 iu/m im for 2 months

Vitamin d and Calcium Supplements

- Adverse effects:
 - Calcium: GI (constipation, flatulence, abdominal pain, nausea), hypercalciuria, hypersensitivity reactions.
 - Vitamin D: occasional skin rashes.
- Contraindications:
 - Severe CKD stage 4 or 5, conditions that cause hypercalcemia or hypercalciuria, hypervitaminosis D, renal stone disease, hyperparathyroidism.
- Cautions:
 - Mild – moderate CKD (stage2- 3B), a history of renal stone disease.

Vitamin d and Calcium Supplements

- **Drug interactions**
 - **Oral bisphosphonates** — leave a gap of at least 30 minutes.
 - **Quinolones and tetracyclines** —Quinolones should be taken at least 2 hours before taking a calcium supplement. Tetracyclines should be taken at least 2–3 hours before taking a calcium supplement.
 - **Levothyroxine, iron, and zinc** —These drugs should be taken at least 2 hours before taking a calcium supplement.
 - **Digoxin** — increased effects of digoxin. monitoring an ECG and renal function is recommended during long-term calcium supplementation, to check for cardiac arrhythmias.
 - **Thiazide diuretics** — reduced urinary calcium excretion. Monitor serum calcium levels regularly during concomitant use of thiazide diuretics with calcium and vitamin D preparations.
 - **Oral corticosteroids** — reduced calcium absorption. It may be necessary to increase the dose of the calcium and vitamin D preparations.
 - **Phenytoin or barbiturates (long-term use)** — there have been a few reports of decreased effects of vitamin D (due to an increase in its metabolism). Consider monitoring for vitamin D deficiency as a higher dose of vitamin D may be required.

References

- Kuwait osteoporosis guidelines 2018
- NICE guidelines 2017
 - Osteoporosis: assessing the risk of fragility fracture
- Sign guidelines 2020
 - Management of osteoporosis and the prevention of fragility fracture
- National osteoporosis guideline group 2019
 - Clinical guideline for the prevention and treatment of osteoporosis
- American family physician 2009
 - Recognition and management of vitamin D deficiency

Thank you 😊