

# The prevention of fractures in adults

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## ABSTRACT

### Background

General practitioners (GPs) encounter patients who have suffered a fracture or are at an increased risk. Fragility fractures cost Europe 32 billion Euros per year. Recognizing this challenge and understanding its management allows GPs to engage in primary and secondary prevention of fragility fractures.

### Aim

To illustrate lifestyle and pharmacological management options offered by a general practitioner to an adult at increased risk of fractures or low bone mineral density (BMD). The National Osteoporosis Guideline Group (NOGG, 2016), World Health Organisation (WHO), International Osteoporosis Foundation (IOF, 2012), Kidney Disease Improving Global Outcomes (KDIGO, 2009), Scottish Intercollegiate Guidelines Network (SIGN) and National Institute for Health and Care Excellence (NICE) management guidelines are discussed in this regard.

### Objectives

- To provide key definitions in the management of osteoporosis.
- To identify groups at risk of developing low BMD, vitamin D deficiency and fragility fractures.
- To illustrate the current management options for an adult at increased risk of fractures or low bone mass by a general practitioner.
- To discuss current methods of investigation and measurement of low BMD, fracture risk assessment and vitamin D deficiency.
- To address dietary requirements of calcium and vitamin D and local formulations available.

### Method

A literature search was conducted using Pubmed and Google search engines. Keywords included: osteoporosis;

low bone mineral density; vitamin D; fragility fracture; postmenopausal. The NOGG (2016), WHO, IOF (2012), KDIGO (2009), SIGN and NICE management guidelines were included directly. Treatments ranging from fall prevention, dietary modification, anti-resorptive therapy and tailoring in subgroups were reviewed.

### Conclusion

Guidelines can close the gap between physicians in primary and secondary care, institutions and private practice providing a multifaceted approach for the proper identification, prevention and management of fragility fractures.

### Key words

Osteoporosis, risk assessment, bone density conservation agents.

## INTRODUCTION

General practitioners (GPs) encounter patients who have suffered a fracture or are at an increased risk. Post-fracture management models of care (IOF, 2012) have been developed to better identify those at risk. Nine million fragility fractures occur annually globally. Thirty-two billion Euros per year are spent in Europe. Recognising this challenge and understanding its management allows GPs to engage patients at primary and secondary prevention before a fracture career sets in.

### Aim

To illustrate the management options that could be offered by a general practitioner for an adult at increased risk of fractures or low bone mineral density. The NOGG - National Osteoporosis Guideline Group (2016), WHO - World Health Organisation, IOF - International Osteoporosis Foundation (2012), KDIGO - Kidney Disease Improving Global Outcomes (2009), SIGN - Scottish Intercollegiate Guidelines Network, and NICE - National Institute for Health and Care



Figure 1: Fall management exercise.

Excellence management guidelines are discussed in this regard. Treatments ranging from fall prevention, dietary modification, anti-resorptive therapy and tailoring of treatment in subgroups were reviewed.

### Objectives

- To provide key definitions in the management of osteoporosis, fracture prevention and vitamin D physiology.
- To identify those at risk of developing osteoporosis and vitamin D deficiency.
- To discuss methods of measurement and investigation of low bone mineral density (BMD), fracture risk assessment and vitamin D deficiency.
- To address the dietary requirements of calcium and vitamin D and local formulations available.
- To discuss the recommended treatments for low bone mass, osteoporosis and persons at high risk of fragility fractures.

### METHOD

A literature search was conducted using Pubmed and Google search engines. Keywords in searches included:

osteoporosis; low bone mass; vitamin D; fragility fracture; postmenopausal. Sources directly included were the Kidney Disease Improving Global Outcomes (KDIGO, 2009), International Osteoporosis Foundation (IOF, 2012), National Osteoporosis Society (England) (NOS, 2013), International Society for Clinical Densitometry (ISCD, 2015), the National Osteoporosis Guideline Group (UK) (NOGG, 2016), the Scottish Intercollegiate Guidelines Network (SIGN), the National Institute for Health and Care Excellence (NICE, UK) and the 71st edition of the British National Formulary.

### Ethical aspects

Photos included in this article of patients at Karen Grech Hospital were attained after permission was granted by the hospital's data protection officer and chief executive officer, and written informed consent was obtained from the patients.

### RESULTS

#### Definition and diagnosis of osteoporosis

In 1994 the World Health Organization (cited by NOGG, 2016) described osteoporosis as a 'progressive systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture'. 'Osteoporosis' is defined operationally as a value for BMD that is 2.5 standard deviations (SD) or less below the young adult mean value (T-score  $\leq -2.5$  SD). Lorentzon and Cummings (2015) however concluded that no perfect definition yet exists that can ascribe to the properties of fragile bone measured in terms of bone strength, risk factors and prior fractures. 'Severe osteoporosis' refers to the above and an additional



Figure 2: Lower limb proprioception exercise.



Figure 3: Stepping exercise.

documented fragility fracture. A higher threshold describes 'low bone mass' as a T-score that lies between  $-1$  and  $-2.5$  SD (NOGG, 2016).

#### Assessment of fracture risk

The NOGG (2016) and ISCD (2015) recommend the use of FRAX<sup>®</sup> as the preferred fracture risk score assessment tool in calculating the 10-year probability of major osteoporotic and hip fractures. FRAX<sup>®</sup> was modelled on population-based cohorts where the femoral neck BMD was used. The latter is therefore preferred when calculating risk, especially in the elderly where arthrosis and arthritis are established in the spine (University of Sheffield, 2011). Outcomes and follow up of treatment favour scores of the lumbar spine. The lower of the two T-scores should be used in diagnosing osteoporosis. Z-scores should be used in adults under 50 years of age with values  $< -2$  being below the expected range (ISCD, 2015).

#### Strategies in the prevention of osteoporosis

The NOGG (2016) endorses a group of strategies in high-risk groups to prevent fragility fractures globally. The main message is that of increasing mobility and calcium intake, stopping smoking, reducing alcohol consumption (less than 3 units a day), undertaking fall prevention programmes, weight bearing and balance exercises (Figures 1-5). Other indirect interventions,

such as the correction of visual acuity and the adjustment of medication that could affect alertness, have also been promoted.

#### Vitamin D

A serum level of 25-hydroxyvitamin D (25-(OH)D) (calcifediol) below 25nmol/L (i.e.  $<10$ ng/mL) is considered as 'vitamin D deficiency' and may lead to mineralization defects. 'Vitamin D insufficiency' occurs between 25nmol/L and 50nmol/L (i.e.  $<20$ ng/mL) and can lead to increased bone turnover and parathyroid hormone anomalies. The NOS (2013) states that half the patients with levels of vitamin D between 20-30nmol/L are vitamin D sufficient but all those above 50nmol/L are practically sufficient. The sufficiency of vitamin D on individuals varies according to the response on parathyroid hormone. Adverse effects may occur with levels above 125nmol/L and annual high dose vitamin D (500,000 IU) is associated with greater incidences of falls and fractures (NOGG, 2016). On the other hand Rizzoli et al. (2013) as part of the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal diseases and the NOS (2013) recommend vitamin D levels to be at least above 60nmol/L in the general population and ideally 75nmol/L in frail elderly patients who are at risk of falls or fracture for skeletal and extra-skeletal benefits.

Ross et al. (2013) recommend an intake of 800IU of vitamin D daily. Simple deficiency can be treated by administering 400 units (10ug) of ergocalciferol or colecalciferol twice daily. In those with little exposure to sunlight or have a limited diet, 800 units is recommended. Higher doses of 40,000 units (1mg) daily are appropriate in intestinal malabsorption and chronic liver disease states. Severe deficiency ( $<8$ ng/ml) may even require 50,000 units daily for one to three weeks (JFC, 2016). In cases of mild to severe deficiency (8-25ng/ml) 50,000 IU weekly for 8 weeks can be offered, followed by a maintenance dose of 800-2000 IU vitamin D orally daily for one month (NOS, 2013; Płudowski, et al., 2013). Serum calcium must be checked one month after the last loading dose to unmask hyperparathyroid states, and vitamin D measured 3-6 months after treatment has been terminated as levels reach a steady state after this period (NOS, 2013). Routine monitoring is not recommended but may be appropriate in patients with malabsorption syndromes and poor compliance (Kennel, Drake and Hurley, 2010; Ross, et al., 2011).

NICE (2016) determined that persons at risk of vitamin D deficiency include:

- infants and children aged under 5 years;
- pregnant and breastfeeding women, particularly teenagers and young women;
- people over 65 of age;
- persons with little or no exposure to the sun, for example persons who remain indoors for long periods or have a large surface of their body covered due to cultural reasons;
- people with darker skin.

### Vitamin D in Chronic Kidney Disease

As Figure 6 demonstrates, renal function plays a part in the conversion of 25-(OH)D to the active form 1,25-(OH)<sub>2</sub>D. This ability diminishes at an estimated glomerular filtration rate (eGFR) <30ml/min/1.73m<sup>2</sup> and leads to impaired hydroxylation of vitamin D. Secondary effects include: raised parathyroid hormone (PTH) levels, reduced intestinal calcium absorption, reduced phosphaturia, and reduced calcium urinary reabsorption. PTH, calcium and phosphate should be measured to reflect this deficiency. The cardiovascular, biochemical, endocrine and bone mineral disorders that develop secondary to renal impairment were coined 'Chronic Kidney Disease-Mineral and Bone Disorder'. 'Renal osteodystrophy' is restricted to describing an alteration



Figure 4: Parallel bars for walking and gait training.

of bone morphology which is confirmed by bone biopsy in those with chronic kidney disease (KDIGO, 2009a). Alfacalcidol, a hydroxylated form of vitamin D, can be used as an alternative. It will not influence 25-(OH)D plasma concentrations and cannot be directly measured. Alfacalcidol can be prescribed at 1ug daily in adults and 0.5ug daily in the elderly. Calcium and phosphate levels serve as rough indicators to whether one is overtreating (JFC, 2016).

Table 1: Local preparations of combined calcium and vitamin D

Formulation	Calcium salt per single unit	Percentage of elemental calcium per salt	Elemental calcium per tablet	Cholecalciferol	Comments
Tablet	1250mg calcium carbonate	40%	500mg	400IU	
Tablet	Not available.		400mg	400IU	Magnesium, zinc, copper, manganese, selenium and boron included
Effervescent tablet	Not available.		400mg	100IU	
Syrup	Not available.		600mg per 20ml	300IU per 20ml	
Tablet	300mg calcium lactate	13%	39mg		25 tablets daily would be recommended for adequate elemental calcium intake.
Tablet	600mg calcium hydrogen phosphate	23%	138mg	500IU	4-5 tablets needed to attain the recommended dose of elemental calcium; however the intake of vitamin D would be high.

Sources: Globalrph, 1993; Ross, et al., 2011.

## Calcium

The Institute of Medicine (IOM, US) Committee to Review Dietary Reference Intakes for Vitamin D and Calcium recommends 1gr. of elemental calcium per day after meals (IOM, 2011). The low pH improves absorption and halving the dose into a twice daily regimen prevents saturation of the gastrointestinal tract. Thiazide diurectics, lithium and low sodium diets will enhance renal excretion of calcium and losses (WHO, 2004; Kennel, Drake and Hurley, 2010; SIGN, 2015).

Calcium supplements contain different amounts of elemental calcium. The supplements facts panel of a product can be used to calculate the amount of elemental calcium available. There are online calculators that can determine this (Institute of Genetics and Molecular Medicine, 2016). Table 1 presents local combined preparations of calcium and vitamin D and the percentage of elemental calcium per salt.

## Identifying cases of osteoporosis and low bone mineral density

A study by Gourlay et al. (2012) followed the time needed to reach a T-score of -2.5 on BMD in almost 6,000 predominantly white women over 65 years of age, who were ambulatory and did not suffer a prior hip or vertebral fracture. The study included co-variables for age, smoking, glucocorticoid use, oestrogen use and self-reported rheumatoid arthritis. The outcomes for recommended follow up DXA scanning for osteopenia was shown to depend on the severity as illustrated in Table 2. The global risk still needs to be considered when following up patients, as well as the onset of new diseases such as diabetes, immobility, etc. This study was criticized on these grounds as risk for fracture is not attributable to T-scores alone. Apart from this a clinically

significant change in BMD was appreciable after a minimum of 2 years according to the National Clinical Guideline Centre (2012). Women were not given lifestyle advice or started on supplementation in the study, which could influence the rate of deterioration in BMD.

NOGG (2016) identifies the secondary causes of osteoporosis as:

- chronic obstructive pulmonary disease,
- rheumatoid arthritis,
- untreated hypogonadism in men and women,
- prolonged immobility,
- organ transplantation,
- type I diabetes,
- hyperthyroidism,
- gastrointestinal disease,
- chronic liver disease.

Investigations to exclude secondary sources may be indicated were appropriate. Serum total calcium, total protein and albumin for a corrected calcium level (or ionized calcium), phosphate, alkaline phosphatase levels for Paget's disease, creatinine for eGFR and PTH are to be assessed if calcium levels are deranged. A full blood panel and erythrocyte sedimentation rate would screen for inflammatory processes while serum protein electrophoresis would assess for free light chains indicative of multiple myeloma. Thyroid function tests are advised in suspected thyrotoxicosis, serum testosterone for hypogonadism, coeliac serology for related malabsorption and an overnight dexamethasone suppression test to exclude Cushing's disease (Lee and Vasikaran, 2012).

## Types of fractures

The NOGG (2016) defines the different types of clinically relevant fractures. A major osteoporotic fracture is a clinical spine, hip, forearm or humerus fracture; however multiple major fractures carry a higher risk than the adding up of each individual risk. Vertebral fractures carry a two-fold higher risk than other types of fractures. A fragility fracture follows a fall from standing height or less. Fragility fractures may be consequential to osteoporosis or other more serious conditions affecting bone such as metastatic bone cancer or myeloma.

## Pharmacological interventions in osteoporosis

There are conflicting recommendations when it comes to starting treatments. The NOGG (2016) deemed treatment be considered in those above the intervention threshold



Figure 5: Training stairs used for lower body co-ordination and balance.

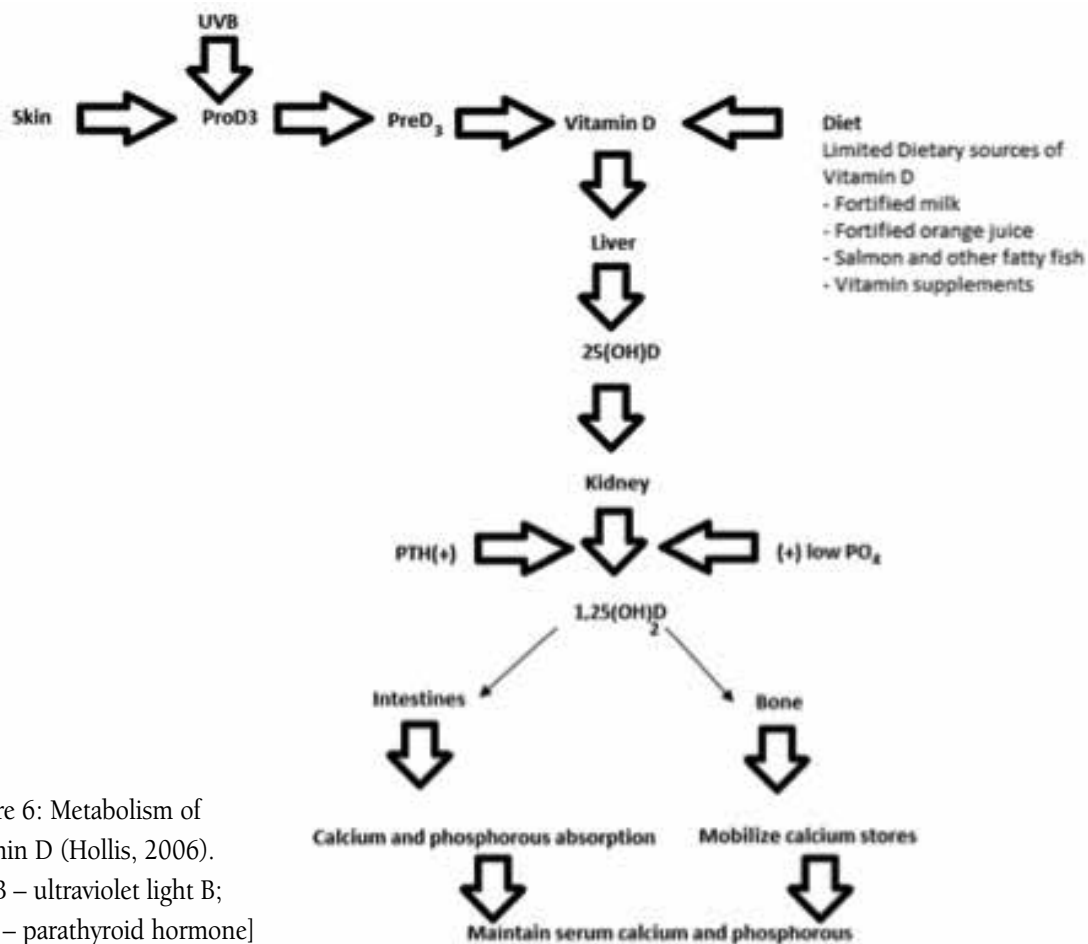


Figure 6: Metabolism of vitamin D (Hollis, 2006).  
 [UVB – ultraviolet light B;  
 PTH – parathyroid hormone]

calculated by FRAX® and started without prior BMD in:

- postmenopausal (PMP) women who have had a previous fragility fracture,
- people over 70 years of age who are taking large doses of oral corticosteroids,
- PMP women and men under 50 years of age who have had an osteoporotic fracture (specialist management is recommended in this group).

SIGN (2015) is more cautious and recommends measurements of BMD by DXA in those above the intervention threshold, with pharmacotherapy started in those with T-scores < -2.5. The group goes on to comment that therapy can be commenced in patients with prevalent vertebral fractures without undertaking BMD measurements if these are felt to be inappropriate or impractical, implying that skeletal imaging be performed as part of screening in certain cases. NICE does not comment with regards to the grey area incorporating those who are above the intervention threshold but have a femoral neck T-score > -2.5. Perhaps the intervention here lies in the global initiatives recommended by NOGG (2016) as the effect of alendronic acid, studied by Cummings et al. (1998) in the FITS trial, showed only

a statistically-significant reduction in clinical fractures in women with a femoral neck T-score < -2.5 after 4 years. Women treated with higher T-scores did not show an improvement in fracture rates.

Patients treated with anti-resorptive therapy will have a demonstrable improvement in BMD after three years of treatment and for this reason guidelines recommend repeat BMD testing after this period and not sooner as the within-person variations differ widely with DXA measurement after just one year of treatment (Sharma and Stevermer, 2009; Ott, 2013; Doshi, et al., 2016).

The preferred first line treatments offered by NICE are bisphosphonates. They act by inhibiting bone resorption by binding to hydroxyapatite crystals. Indications such as glucocorticoid induced osteoporosis or vertebral fractures make certain interventions more appealing than others (Table 3). To postmenopausal women who are unable to comply with the special instructions, have a contraindication or are intolerant to certain treatments, NICE gives the variables (e.g. BMD thresholds) and clinical scenarios against which other treatment options can be weighed.

Denosumab is a monoclonal antibody that inhibits osteoclast formation, function and survival. Its use is

recommended with caution in those with an eGFR < 30ml/min/1.73m<sup>2</sup> (NOGG, 2016) and is second-line to cases where there was an insufficient response, along with zoledronic acid. Strontium ranelate works by stimulating bone formation and reducing resorption. Raloxifene acts as a selective oestrogen receptor modulator that inhibits bone resorption and is only indicated in the secondary prevention of osteoporosis (JFC, 2016) (Table 3).

After three to five years of treatment, NOGG (2016) asks physicians to review BMD measurements and to offer patients to stop treatment if acceptable T-scores have been reached and no fractures have occurred. Follow up DXA scanning should take place after two years (three years in the case of zoledronic acid) and after a new fracture regardless of when this occurs.

### Interventions in chronic kidney disease

Chronic kidney disease (CKD) stages 1-2 and stage 3 with a normal PTH range are recommended management as for the general population for osteoporosis and/or high risk of fracture. With abnormal biochemical markers at CKD stage 3 one should consider the degree and reversibility of the biochemical anomalies and a bone biopsy. In CKD stages 4-5D having biochemical anomalies of chronic kidney disease -mineral and bone disorder (CKD-MDB), low BMD or fragility fractures, a bone biopsy is suggested prior to therapy with anti-resorptive agents (KDIGO, 2009b). Table 4 illustrates the frequency of measurements of bone turnover markers.

### Treatment issues and counselling

Patients should be counselled about the following issues before and during anti-resorptive treatment:

- dental checkups should take place prior to treatment and on a regular basis. Invasive dental procedures should be avoided. Gum swelling and hypermobility of the teeth should be immediately reported.
- bisphosphonate tablets are to be swallowed whole with plenty of plain water only. Their use is cautioned or contraindicated in patients with gastric or duodenal ulcers, bedridden patients and those with eGFR<35ml/min/1.73m<sup>2</sup> (NOGG, 2016).
- calcium supplements are to be taken at least two hours before or after a bisphosphonate and should be taken during anti-resorptive treatment along with vitamin D.
- the length of time one should avoid food before and after taking a bisphosphonate should be consulted for every product according to the dose. Aldendronic acid should be taken 30 minutes before breakfast on an empty stomach. Thirty minutes must elapse before eating or taking other medications and lying down after taking alendronic acid.
- atypical fractures of subtrochanteric and diaphyseal regions of the femoral shaft should be reported to the prescriber.
- it is important to check serum calcium one week before and two weeks after administration of denosumab and monitor for the presence of hypocalcaemia.
- patients taking raloxifene should be counselled that discontinuation should take place at least 72 hours prior to and during prolonged immobilization as it confers a greater risk of stroke and venous thromboembolic events. It also confers a reduction in risk of breast cancer but can also procure hot flushes (JFC, 2016).

Bisphosphonates could be continued indefinitely in high-risk individuals who (NOGG, 2016):

- are aged 75 years or more;
- have sustained a hip or vertebral fracture;
- are taking continuous oral glucocorticoids at a dose of  $\geq 7.5$  mg/day prednisolone or equivalent;
- sustain a low trauma fracture during treatment, after exclusion of poor adherence to treatment (<80% of treatment) and causes of secondary osteoporosis have been excluded (in such cases treatment should be re-evaluated);
- have a total hip or femoral neck BMD T-score  $\leq -2.5$  SD.

Table 2: Time to develop osteoporosis in low bone mass in white women over 65 years of age, who were ambulatory and did not suffer a prior hip or vertebral fracture

Severity	T-Score Ranges	Time (years)
Mild	-1.00 to -1.49	15
Moderate	-1.5 to -2	5
Severe	-2 to -2.49	1

Source: Gourlay et al. (2012).

Table 3: Recommended anti-resorptive treatments

Choice	Drug	Indication			Duration	Frequency	Dose
		PMP Women	Glucocorticoid induced	Men			
First	Alendronate	Yes	Yes	Yes	5-10 years	daily	10mg
						weekly	70mg
	Risedronate	Yes <sup>1</sup>	Yes	Yes	5-7 years	daily	5mg
						weekly	35mg
First / Second	Zoledronic acid	Yes <sup>2</sup>	Yes	Yes	3 years	yearly	5mg
Second	Denosumab	Yes <sup>3</sup>			5 years	six months	60mg
	Teriparatide	Yes <sup>4</sup>			24 months	daily	20ug
Third	Strontium ranelate	Yes <sup>5,6</sup>		Yes	10 years	daily	2g
	Ibandronate	Yes			5 years	monthly	150mg
	Raloxifene	Yes			Until 50 years of age	daily	60mg

Source: NICE, 2008a; NICE, 2008b; JFC, 2016; NOGG, 2016; SIGN, 2015.

- (1) Risedronate is recommended as second line in the primary and secondary prevention of osteoporotic risk fractures in patients unable to tolerate alendronate against the variables provided by NICE (2008a; 2008b).
- (2) Zoledronic acid was shown to improve survival in hip fracture patients unable to tolerate oral osteoporosis treatment and is recommended as second line in such cases (SIGN, 2015) or if inadequate response to initial agents.
- (3) Denosumab is recommended as third line treatment in the primary and secondary prevention of osteoporotic fractures if alendronate and either risedronate or etidronate are not tolerated and against the variables recommended by NICE (2010) or if inadequate response to initial agents.
- (4) Teriparatide is indicated in severe spinal osteoporosis as second line to alendronate or risedronate.
- (5) NICE recommends that raloxifene and strontium ranelate are recommended as alternative treatment options for the secondary prevention of osteoporotic fragility fractures in PMP women who are unable to comply with the special instructions for the administration of alendronate and either risedronate or etidronate, or have a contraindication to or are intolerant of alendronate and either risedronate or etidronate against the variables recommended by NICE (2008a; 2008b).
- (6) Strontium ranelate is recommended as third line to alendronic acid, etidronate and risedronate when it comes to the prevention of osteoporotic fragility fractures in PMP women (NICE, 2008a; NICE, 2008b). Strontium ranelate is recommended in severe PMP osteoporosis to reduce the risk of vertebral and non-vertebral fractures in women without established cardiovascular disease when other treatments are contraindicated (SIGN, 2015).

Table 4: Frequency of measurement per respective bone turnover marker in chronic kidney disease

Stage	eGFR (ml/min/1.73m <sup>2</sup> )	Frequency of measurement (months)		
		Calcium and phosphate	Parathyroid hormone	Alkaline phosphatase
3	30-59	6-12	According to disease progression	
4	15-29	3-6	6-12	12 <sup>1</sup>
5	<15	1-3	3-6	

1. Stages 4–5D alkaline phosphatase activity measurement: every 12 months, or more frequently in the presence of elevated PTH.

Source: KDIGO, 2009a.



## Glucocorticoid-induced osteoporosis

Steroid doses greater than an equivalent of 7.5mg prednisolone daily for more than three months are considered significant. Daily doses of prednisolone higher or equal to 15mg however should need a higher adjustment of fracture probability (NOGG, 2016). Treatment should be started at the beginning of steroid therapy in patients considered at risk of fracture (JFC, 2016).

## Osteoporosis in men and women

Secondary causes are commoner amongst men and will need investigation (NOGG, 2016). Hormone replacement therapy (HRT) should be offered to women who have experienced premature menopause (before 45 years of age) to reduce the risk of fragility fractures and for the relief of menopausal symptoms. If the main concern is increased fracture risk, bisphosphonate therapy should be offered first line. HRT was shown to decrease fracture risk but benefits were lost shortly after stopping therapy. HRT should be continued up until 50 years of age and then stopped and the need for continuing treatment with an alternative drug considered (JFC, 2016).

## DISCUSSION

The different levels of Vitamin D for different ages is still a subject of debate. Ultimately the pathophysiology behind low bone mineral density reflects our investigation and management.

Secondary causes and risk factors should be looked out for pending a mandatory dental review along with proper counselling if bisphosphonates are considered. T-scores measured after a minimum 2 years of treatment with anti-resorptive agents accompanied by calcium and vitamin D supplementation should then be followed up. Earlier measurements can deceive GPs into perceiving that no improvement BMD deterioration has occurred as within-person variation confounds measurements. Those with an eGFR  $<30\text{ml}/1.73\text{m}^2$  should have bisphosphonate therapy stopped and be switched to alfacalcidol or another suitable vitamin D alternative. For those with BMD  $> -2.5$  bisphosphonates will not decrease fracture rates and prevention lies in managing other risk factors. Patients after a minimum three year period with an adequate BMD (T-score  $> -2.5$ ) should be counselled about stopping antiresorptive therapy and considered for follow up after 2 years. At the end of the spectrum recognising fragility fractures allows us to treat them as such, irrespective of the sex of the patient. Major osteoporotic fractures, especially spinal fractures, increase one's fracture probability further and should be accounted for when using prediction tools.

The authors look forward to the identification of other risk factors that could have a role in osteoporosis. Anti-resorptive treatments are currently limited by gastric side-effects and renal impairment. Safer alternatives are still needed in these groups.

## Limitations

This review does not include the management of secondary causes of osteoporosis and younger age groups.

## CONCLUSION

Guidelines can close the gap between physicians in primary and secondary care, institutions and private practice by providing a multifaceted approach for the proper identification, prevention and management of fragility fractures.

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