NHS FORTH VALLEY

Guidelines for Management of Osteoporosis in Patients aged 50 or over presenting with Fragility Fracture, and in Patients on Aromatase Inhibitors.

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Consultation and Change Record – for ALL documents

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Guidelines for Management of Osteoporosis in Patients aged 50 or over presenting with Fragility Fracture and in Patients on Aromatase Inhibitors.

This guideline is tailored to the limited osteoporosis service in FVRH, and therefore it is not accordance with the current SIGN 142 guidelines for management of osteoporosis and prevention of fragility fractures.

The recommendations in the guideline should be used to aid management decisions but do not replace the need for clinical judgement in the care of individual patients in clinical practice.

Introduction:-

Osteoporosis is the most common disease of bone characterized by reduced bone mass and increased risk of low trauma fractures.

Risk of osteoporotic and hip fractures increases steadily with age, and more steeply after the age of 65 in women and 75 in men [(1)]. People below age of 50 are likely to be at low risk of fracture in absence of other risk factors [(1)]. A number of retrospective studies have indicated that previous fractures increase the risk of subsequent fractures by 2-3 fold. Identification and referring these patients for DXA is recommended to evaluate the need for antiresorptive therapy to reduce risk of further fractures [(1)].

A fragility fracture or low trauma fracture is defined as a fracture caused by falling from standing height, which would not be expected to cause a fracture in healthy bone. This also includes vertebral fractures which may result following no or only minimal trauma.

Vertebral compression fracture is the most common osteoporotic fracture, more commonly occurs in the lower thoracic and lumbar spine. Having a previous vertebral compression fracture is a very good predictor of the fracture risk, and considered to be the hallmark of osteoporosis [(2)]. Although osteoporosis is the most likely underlying pathology, other causes of vertebral fractures should be considered and excluded, especially in younger adults; following severe trauma, or vertebral destruction from metastatic cancer. Further investigation is therefore indicated in these cases, which include; specific laboratory tests and further imaging, such as; CT scan, MRI or bone scans.

Prevalence of vertebral fracture is an indication for referral for DXA scan, and in some situations, an indication to start antiresorptive treatment, irrespective of the bone mineral density (BMD) values [(3)].

The World Health Organisation (WHO) definition of osteoporosis:-

It is defined as a BMD T score at or below 2.5 standard deviations below normal peak values of young adults.

DEXA BMD Values	Definition
T- score > -1.0 S.D	Normal bone mineral density
T- score between –1.0 and –2.5 SD	Osteopenia
T- score < - 2.5 SD	Osteoporosis
T- score < - 2.5 SD with 1 or more fragility fractures	Severe osteoporosis

Z-score compares the patient's BMD with that of adults of the same age and sex. Z-score of –2.0 SD or lower are defined as "below the expected range for age", and should trigger investigations to exclude secondary osteoporosis.

Diagnosis of osteoporosis (Diagnostic Criteria):-

- T- score at hip or lumbar spine < -2.5.

  OR
- Multiple low trauma vertebral fractures (≥2) in the absence of Myeloma or metastatic disease.

DXA referral criteria at FVRH:-

The referral must meet either of the following criteria:

- Men and women between 50 and 75 years of age with a fragility fracture at any skeletal site (exclude high trauma fracture, RTA or skull fracture).
- Any patient on or commencing adjuvant Aromatase Inhibitors for breast cancer treatment (letrozole/Femara; anastrazole/Arimidex; exemestane/Aromasin) requiring a baseline DXA scan at time of commencement or within 2-3 months of start of treatment.

Patients outside these criteria; such as patients with no previous fracture but with coexisting disease or on medications associated with bone loss (e.g. oral steroid, Rheumatoid arthritis ...etc), please ask their GP to refer for DXA at Golden Jubilee National Hospital (GJNH).

Patients over the age of 75 with a good clinical history of fragility fracture are very likely to have osteoporosis, and referral for DXA is unlikely to alter management.

Clinical risk factors for osteoporosis:-

- Low body mass index (BMI ≤ 20kg/m2)
- Previous fragility fracture, particularly of the hip, wrist and spine
- Parental history of hip fracture
- History of early menopause (below age of 45)
- Testosterone deficiency states
- Current glucocorticoid treatment (any dose, by mouth for 3 months or more)
- Aromatase inhibitors
- Current smoking
- Alcohol intake ≥ 4 units daily
- **Secondary causes of osteoporosis** including: -
  - Rheumatoid arthritis
  - Hyperparathyroidism
  - Untreated hypogonadism in men and women
  - Prolonged immobility
  - Hyperthyroidism
  - Gastrointestinal disease causes malabsorption e.g. Crohn's, UC or coeliac
  - Chronic liver disease

Conditions when referral for DXA is not appropriate:-

- For patients aged 50 – 75 years, if the responsible clinician considers it to be clinically inappropriate as in terminally ill patients or very frail patients with life expectancy less than 12 month.
- Patients with advanced dementia who are unlikely to be cooperative with the instructions of taking oral bisphosphonates.

Recommended routine investigations in patient with fragility fracture:-

- Blood tests: - FBC, ESR, U&Es, Bone profile, LFT & TFT.
- Arrange lateral X-rays of the thoracic-lumbar spine in suspicion of vertebral fractures (e.g. Spinal pain & tenderness, loss of height, or acquired kyphosis).
- **Further investigations as appropriate if secondary osteoporosis is suspected** [e.g Z-score < -2, particularly in premenopausal women and in men under 75 years of age]; Testosterone (men), Coeliac screening (anti-tTG), PTH, Myeloma screen.

- Further imaging should be discussed with the duty radiologist first (CT/MRI/Bone scan) to exclude metastatic bone cancer if high suspicion of underlying malignancy in presence of red flag features (e.g. weight loss, history of previous cancer).

Anti-resorptive treatments (in order of preference):-

1. **Oral Bisphosphonates (BP);**
   a. **Alendronic acid;** 1st line - 70mg Tablets once a week.
   Alendronic acid 70 mg once weekly effervescent tablets (**Binosto)** can be used in patients who are unable to swallow tablets where alendronic acid is the appropriate treatment choice.
   b. **Risedronate;** 2nd line - 35mg once a week, may be better tolerated by some patients who experienced minor GI symptoms (dyspepsia, nausea, constipation, etc) while on Alendronic Acid.

Prescribing:
Oral bisphosphonates should be taken at least 30 minutes before breakfast and any other medication, on the same day of each week.

Contraindications:
- Active dysphagia, oesophageal ulceration/ erosion/ stricture or achalasia.
- Unable to stand or sit upright for at least 30 minutes.
- Hypocalcaemia.
- Renal impairment; avoid if eGFR < 35 mL/min/1.73m^2 for alendronic acid, and < 30 mL/min/1.73m^2 for risedronate. In patients at both extremes of weight (BMI < 18.5 kg/m2 or > 30 kg/m2) Creatinine clearance should be calculated[4]. Avoid if Creatinine clearance <35 ml/min for alendronic acid, and < 30 ml/min for risedronate. **Creatinine Clearance calculator**
- Advanced dementia and no caregiver available to supervise administration.

Counselling:

Advise to swallow tablet whole first thing in the morning with a full glass of water on an empty stomach at least 30 minutes before breakfast (and any other oral medication). Remain upright for at least 30 minutes after taking tablet.
Patients should be instructed that if a dose is missed on their usual day the tablet should be taken on the day next remembered. Patients should then return to taking one tablet once a week on the day the tablet is normally taken. Two tablets should not be taken on the same day. Patients should be advised to stop taking the tablets and to seek medical attention if they develop symptoms of oesophageal irritation such as new or worsening heartburn, pain on swallowing or retrosternal pain. Due to the small risk of osteonecrosis of the jaw with bisphosphonates use, all patients should be advised to maintain good oral hygiene, receive routine dental check-ups, and report any oral symptoms. If dental treatment is required this should be performed before starting bisphosphonates treatment.

c. **Ibandronic acid (oral);** 150mg once a month may be suitable for patients who do not tolerate alendronic acid/risedronate and wish to take a monthly preparation to limit side effects. Should be taken at least 1 hour before breakfast. It is licensed for the treatment of osteoporosis in postmenopausal women to reduce the risk of vertebral fractures, however, its anti-fracture efficacy for hip fractures has not been adequately evaluated.
It is not licensed to use in men, although specialists might decide to prescribe it on an individual basis.

2. Other treatment options:- (Currently Not Available at FVRH)

Patients unable to tolerate oral bisphosphonates or unsuitable for oral BP should be referred to a specialist for consideration of alternative treatment such as; IV zoledronic acid, Denosumab (subcutaneous) or teriparatide (subcutaneous).

Treatment with calcium and vitamin D:-

- Calcium and vitamin D supplementation is widely recommended in older people who are housebound or living in care homes, where vitamin D deficiency and low dietary calcium intake are common [5].
- Should be considered for all patients over 50 years old with fragility fractures unless the clinician is satisfied that calcium and vitamin intake (daylight exposure) is sufficient. Consider Vitamin D only supplement if you are happy with patient's dietary calcium intake.

Prescribe; 1 - 1.2 g elemental calcium and 800IU (20mcg) vitamin D supplements.

Recommended preparations;

The following are the formulary products of choice:

1. Adcal D3 Caplets or Chewable Tablets: The products have different dosing instructions to ensure equivalent dose (1200mg elemental Calcium and 800IU Colecalciferol per day). Caplets are the most cost-effective product at the time of writing. The choice of caplets or chewable tablets will be guided by patient choice.
   Caplets dosage: Two caplets twice daily.
   Chewable tablets dosage: One tablet twice daily.

2. Where swallowing tablets is a problem and the patient does not like the taste of the chewable tablets: Calfovit D3 Sachet, 1 sachet per day.

Contraindications;

- Hypercalcaemia/hypercalciuria.
- Severe renal impairment.
- History of renal calculus.

Non-compliance with calcium and vitamin D preparations, especially in patient on bisphosphonates;

- Replace with alternative calcium and vitamin D preparation, such as caplets.
- Check vitamin D level. If > 50 nmol/l, replacement may not be required but ensure high calcium diet.

- **When to measure Vitamin D level:-**

1) Patients with low corrected serum calcium (<2.1 mmol/L) and/or where blood results suggest possible osteomalacia.
2) Patients with malabsorption syndromes.

Vitamin D only:-

Vitamin D only can be considered for patients with good dietary calcium intake.

- Colecalciferol 800IU daily.

For further details see NHS Forth Valley guidance for Investigation & Treatment of Vitamin D deficiency in Adults[(6)].

Lifestyle Advice:-

- Stop smoking.
- Reduce alcohol consumption (Men <21 unit; Women < 14 units per week).
- Ensure adequate daily intake of calcium and vitamin D.
- Regular weight bearing and progressive strengthening exercise programmes appropriate to general health.
- Maintain a healthy body weight.
- Patients with high risk of falling; consider referral for falls assessments & prevention (Review medications; avoid poly-pharmacy, visual assessment, etc).

Information about how to refer to local services to promote these lifestyle choices can be found on the NHS Forth Valley fracture liaison intranet .

Fracture risk assessment tools:-

SIGN recommends that "fracture-risk assessment should be carried out, preferably using QFracture (rather than FRAX), prior to DXA in patients with clinical risk factors for osteoporosis and in whom antiosteoporosis treatment is being considered" [(1)].

A. FRAX:- [(7)]

Individuals with T-score in the osteopenic range (-1.0 to -2.5) and with additional clinical risk factors may still have a high fracture risk, and treatment may be indicated. The FRAX score may help here to determine 10 year fracture risk and inform clinical decision making. Caution is advised in using the NOGG intervention threshold linked to FRAX as it may lead to over-treatment of younger individuals and under treatment of older individuals. **FRAX Calculator**.

B. QFracture- 10 years fracture risk assessment:- [(8)]

QFracture is an online fracture risk scoring tool, developed in the UK, which can be used to predict the absolute risk of hip fracture and of major osteoporotic fractures (spine, wrist, hip or shoulder) over timeframes of one to ten years. It is applicable to people aged 30–99 years.
QFracrure was found to be more accurate than FRAX tool in predicting fracture risk (including hip fracture) in older people up to the age of 85 [1, 9].

Men aged 76 – 80 who has no access to DXA; who is relatively fit, mobile and had a fragility fracture other than hip or vertebral fractures, with no risk factors for osteoporosis (apart from age) consider calculating fracture risk using QFracture to help with treatment decision. **QFracture calculator**.

Guidance for Bone Protection in association with Aromatase Inhibitors:-

Aromatase inhibitors are highly potent inhibitors of oestrogen production that suppress circulating oestradiol levels to almost undetectable levels, beyond what is achieved by natural menopause, thereby leading to accelerated bone loss [10]. **See algorithm page 15.**

There are three Aromatase inhibitors used;-

1- Letrozole
2- Anastrozole
3- Exemestane

Management of Glucocorticoid-induced Osteoporosis in Men and Women:-

Glucocorticoid therapy is strongly associated with the development of osteoporosis and fragility fractures in both men and women. The increased risk of fracture is dependent on glucocorticoid dose and duration of therapy. The increased risk is seen even at daily doses of prednisolone less than 7.5 mg [11]. There is evidence to suggest that fractures occur at higher levels of BMD in patients on glucocorticoids as compared with non-glucocorticoid-treated patients [1]. Fracture risk increases rapidly after the onset of treatment and declines rapidly after stopping therapy. Medications that can be used for glucocorticoid induced osteoporosis are; Alendronate, risedronate, zoledronate and teriparatide. Management recommendation is based on the Royal college of Physicians guidelines for Glucocorticoid-induced Osteoporosis, 2002 [11]. Available at;- https://nos.org.uk/media/98023/glucocorticoid-guidelines-concise.pdf

Duration of bisphosphonate treatment & drug holiday:-

Due to their chemical structure, bisphosphonates bind to bone mineral and exert inhibitory effects on osteoclastic bone resorption which can extend for years after treatment has been stopped. Furthermore, long-term bisphosphonate therapy has been linked to the development of skeletal adverse effects including atypical subtrochanteric fractures and Osteonecrosis of the jaw (ONJ). This has led to the suggestion that patients on bisphosphonates may benefit from a ‘drug holiday’.

Defining the optimal duration of bisphosphonate treatment is therefore relevant to weigh up the risks and benefits of treatment. The same comments apply to other anti-osteoporosis medications (denosumab), although the effects of these wear off much more quickly when treatment is stopped [1].

Bisphosphonates therapy should be evaluated every 5 years (every 3 years if IV zoledronic acid) to determine if the benefits in continuing therapy outweigh potential risks [1].

Drug holiday period [5];

No randomised controlled trials have evaluated the effectiveness of treatment breaks, termed "drug holidays" in reducing bisphosphonate associated adverse effects [12].
The suggested drug holiday as follow; 2 to 3 years for patients on Alendronic acid, 1 to 2 years for Risedronate and Ibandronate, and at least 3 years for IV Zoledronic acid.

Actions after 5 years of bisphosphonates treatment:- [5, 12]

- Treatment review should be performed after 5 years for alendronate, risedronate or ibandronate and after 3 years for zoledronic acid.
  Re-assessment of fracture risk in treated patients can be performed using FRAX with femoral neck BMD. The National Osteoporosis Guideline Group (NOGG) intervention threshold can then be used to guide the decision as to whether treatment can be stopped for a period of time[13]:- **(see algorithm page 13)**

  - If no fracture **but** deemed high risk with FRAX and NOGG, **or** total hip or FN BMD T-score is ≤ -2.5 SD, continuation of treatment should generally be advised.

  - If no fracture and deemed low risk with FRAX and NOGG **and** total hip or FN BMD T-score is > -2.5 SD, then a drug holiday can be considered. If treatment is discontinued a DXA scan is recommended after a new fracture regardless of when this occurs, or after two years (If no new fracture occurs).

- Continuation of treatment without the need for further assessment can generally be recommended in the following group:-

  - High-risk patients, for example:

    - Patients aged ≥ 75 years
    - Patients with previous hip or vertebral fracture.
    - Patients on continuous oral glucocorticoids in a dose of ≥ 7.5mg/day prednisolone or equivalent.

- Patients who sustain one or more fragility fractures while on treatment, after exclusion of poor adherence to treatment, (e.g. < 80% of treatment has been taken) and after causes of secondary osteoporosis have been excluded. In such cases the treatment option should be re-evaluated.

Actions after 10 years of oral bisphosphonates:- [14] (see algorithm page 14)

Patient should be re-assessed by receiving a clinical review and a DXA scan (unless >80 years and frail).

Clinical review (by a primary care or secondary care physician) involves looking at; frailty, indications of treatment, previous and recent fractures (fracture while on treatment), adherence with treatment, renal function and any adverse effects of therapy.

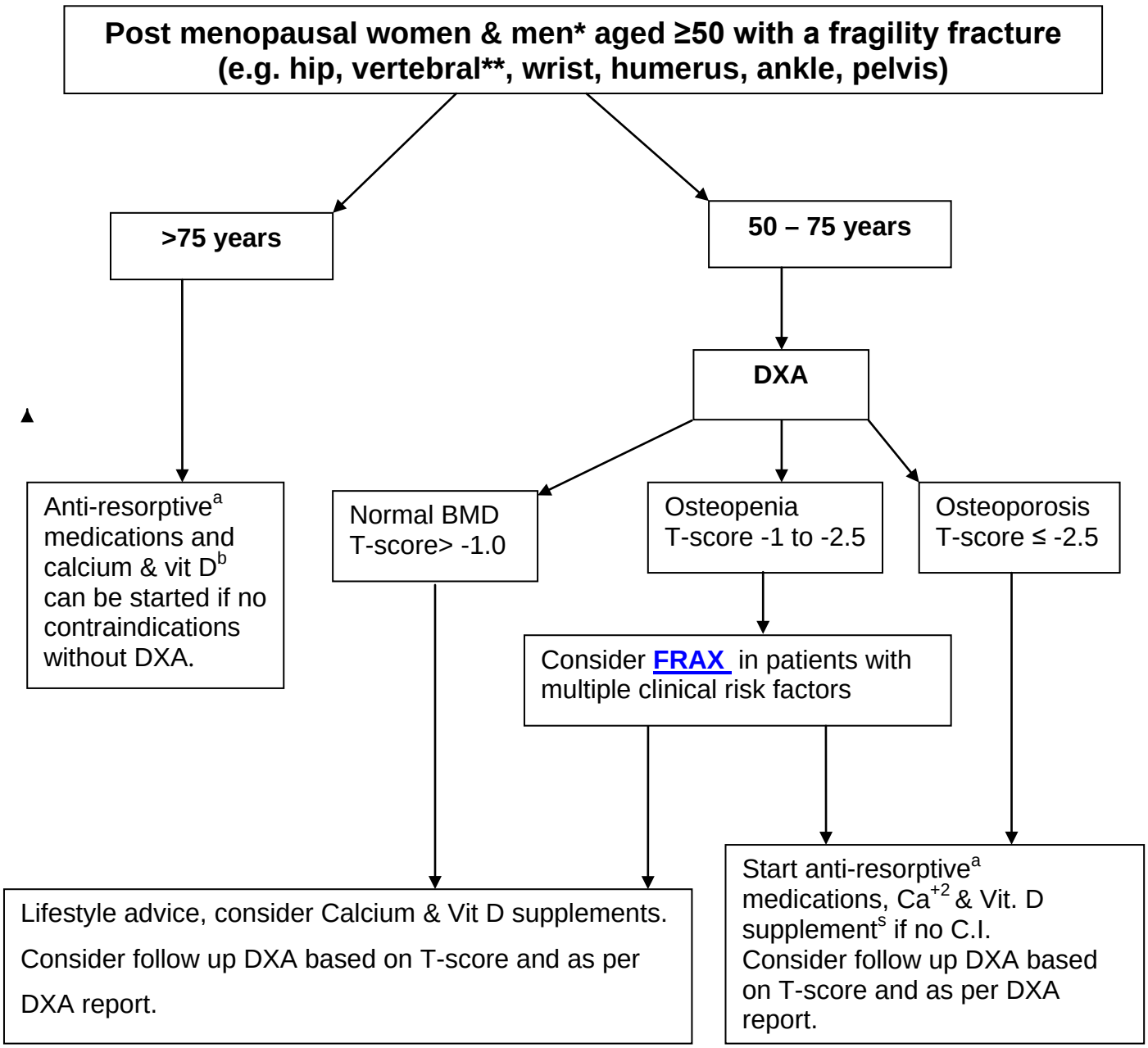
The decision then can be made either to;

- Stop treatment and repeat DXA after 5 years **[if T-score >-2.5 and no further fractures or FRAX <20%]**.
- Drug holiday; alendronic acid for 2 years, risedronate for 1 year then restart treatment **[if T-score <-2.5 or FRAX 20-30% but no further fractures]**.
- Continue treatment; (**alternative therapy may be considered)** [**if T-score <-3.5 or FRAX >30% or further fractures or >80 years old and frail]**.

If the decision has been made to continue bisphosphonates, patient should be made aware of the small risk of **atypical fracture of the femur** associated with prolonged use of oral bisphosphonates, and should be advised to report any thigh, hip, or groin pain which may be due to atypical fracture requiring referral for X-ray.
Atypical femoral fractures are often bilateral.
Discontinuation of BPs therapy in patients suspected to have an atypical femur fracture should be considered.

Fracture Liaison Service;

This service is new in Forth Valley and it is continuing to develop. The plan is that as the Fracture Liaison Service develops all individuals sustaining a low trauma fracture will be assessed.
Further information on the service can be found on the intranet
http://staffnet.fv.scot.nhs.uk/a-z/fracture-liaison-service/



a) **Anti-resorptive Medications ;-**
1st line; Alendronic acid 70mg once weekly, **2nd line**; Risedronate 35mg once weekly.

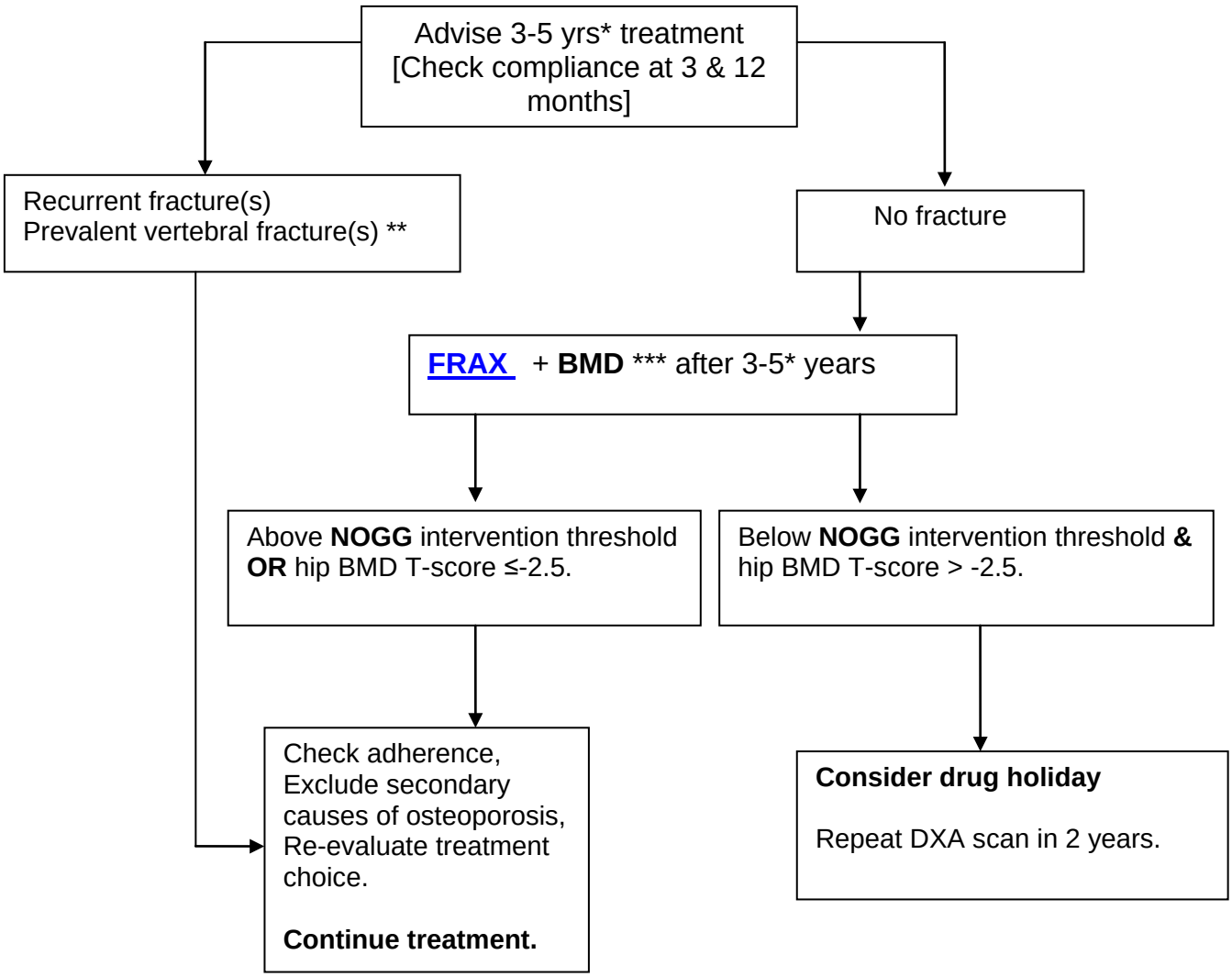
b) **Calcium & vitamin D supplements;**
1 - 1.2 g elemental calcium and 800IU (20mcg) vitamin D/day. e.g. Adcal D3 one tablet twice a day.

(*) Men aged 76 – 80 who has no access to DXA; who is relatively fit, mobile and had a fragility fracture other than hip or vertebral fractures, with no risk factors for osteoporosis consider calculating Qfracture to help with treatment decision.

(**) Prevalence of 2 or more vertebral fractures is an indication to start antiresorptive medications regardless to the BMD values, if not due to major trauma, after excluding non-osteoporotic causes (multiple myeloma/metastatic).

Bisphosphonates: algorithm for actions after 3-5 years* of treatment [5]

*3 yrs for zoledronic acid
5 yrs for other BPs



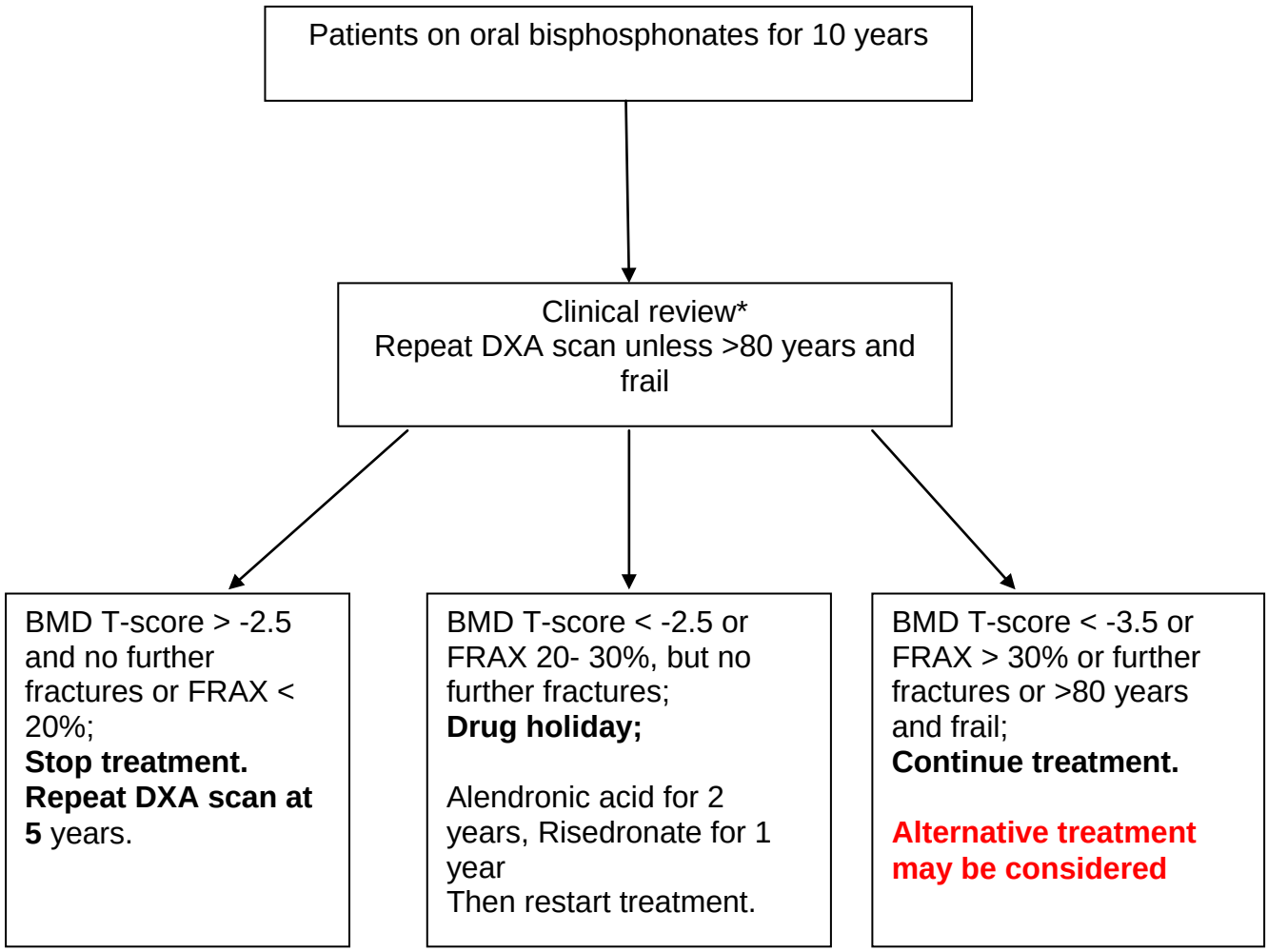
** In patients taking oral BPs consider continuation if;

- Age >75 yrs.
- Previous hip fracture or vertebral fracture
- Current oral glucocorticoid therapy equivalent to ≥ 7.5 mg/d prednisolone.

*** Not for DXA if frail patient

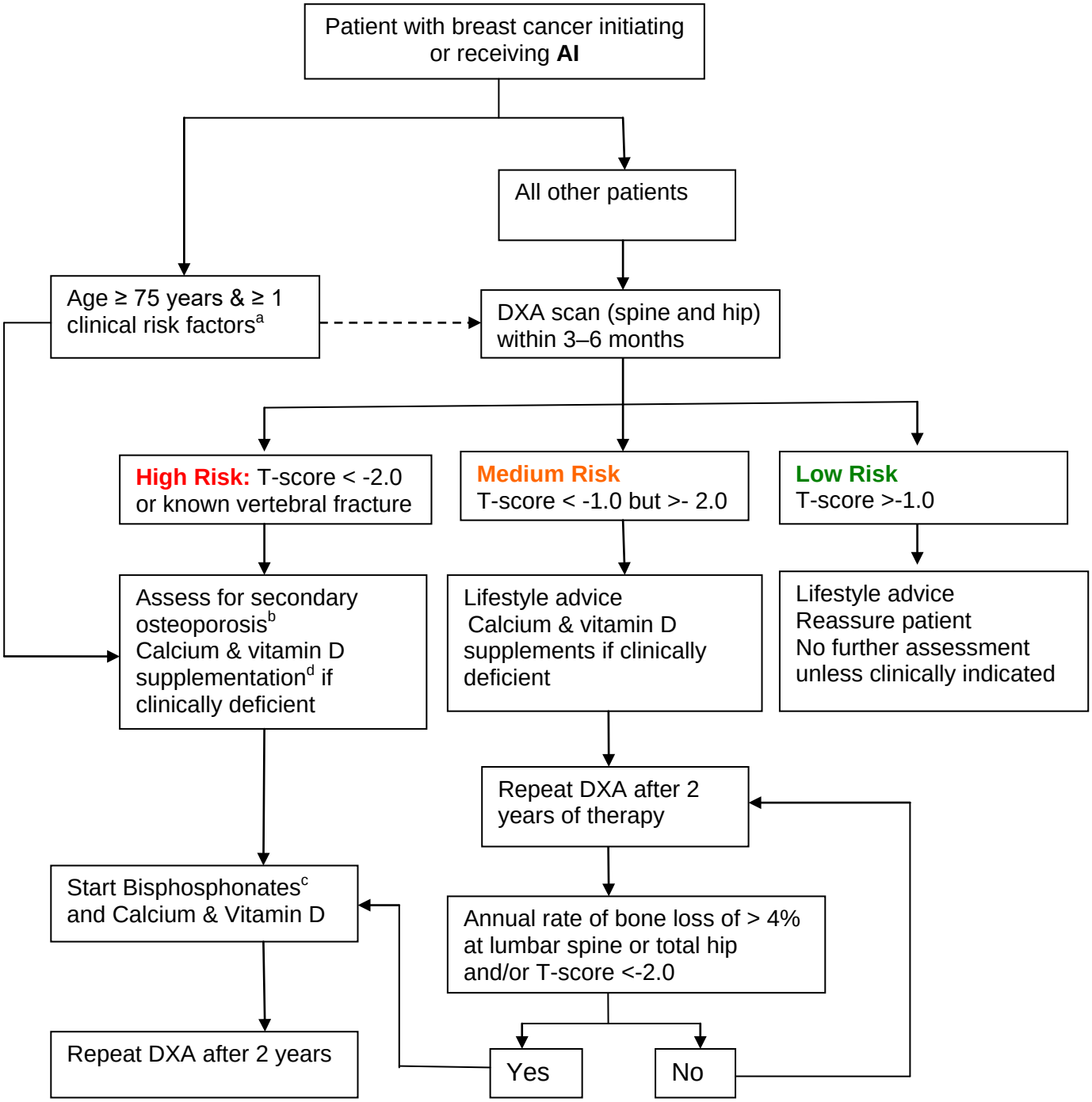
National Osteoporosis Guideline Group (NOGG). Osteoporosis: clinical guidelines for prevention and treatment; executive summary. London: NOGG, 2013.

Bisphosphonates: algorithm for actions after 10 years treatment [14]



Clinical review*:- Looking at; frailty, indications of treatment, previous and recent fractures (fracture while on treatment), adherence with treatment, renal function and any adverse effects of therapy.

Algorithm for managing bone health in women receiving AI therapy for breast cancer [15].



a. Risk factors:
Personal fragility fracture after age 50
Parental history of hip fracture
Diseases associated with 2ry osteoporosis
Prior corticosteroid use > 6months
Alcohol intake of ≥4units/day
Low BMI(<22).

b. ESR,FBC, Bone profile, LFT, U&Es, anti-tTg Ab. & TFT.

c. Alendronate 70mg /week, Risedronate 35mg/week, Ibandonates (150mg po monthly or 3mg iv 3 monthly), Zoledronic acid 4mg iv 6 monthly.

d. To be given as ≥ 1 g of calcium + ≥800 IU of vitamin D

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