Prevention and treatment of osteoporosis

Clinical guidelines and new evidence

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Osteoporosis is a progressive systemic skeletal disease characterised by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture. In the United Kingdom, the disorder results in over 200,000 fractures each year, causing severe pain and disability to individual patients at an annual cost to the National Health Service of over £940 million. More than one third of adult women will sustain one or more osteoporotic fractures in their lifetime. Lifetime risk among men is less, but still substantial.

In 1999, guidelines on the prevention and treatment of osteoporosis were prepared under the auspices of the Royal College of Physicians, sponsored by the Department of Health[1]. The aim of the guidelines was not to provide a working document for clinical practice, but rather to produce a framework from which local management protocols could be developed. When they were released, the results of some important randomised controlled trials (RCTs) had been published; the ensuing 18 months have seen these supplemented by new clinical trial data both for existing and new pharmacological interventions[2–12]. An update of the guidelines has recently been prepared by the original writing group of the Royal College of Physicians in collaboration with the Bone and Tooth Society[13]. The main aims of this document were first, to supplement the evidence-based account of therapeutic interventions in the light of newly published trials, and second, to distil an algorithm (Fig 1) for the management of individual patients based on the evidence-based synthesis of the different pharmacological interventions.

Prevention and treatment of osteoporosis

The distinction between prevention and treatment that is used for regulatory purposes is less appropriate in clinical practice, since all agents currently in use act fundamentally in the same way, namely by inhibition of bone resorption. Furthermore, increasing evidence for a relatively rapid rate of onset and offset of treatment effect for these interventions has resulted in a shift away from long-term preventive strategies towards the use of shorter term intervention in high risk individuals. This latter approach is supported by the demonstration of significant reductions in vertebral and non-vertebral fracture rate in postmenopausal women with established osteoporosis after only one year of treatment[10,14,15].

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Summary guideline recommendations on the evidence for efficacy of different interventions

Using updated information from clinical trials, guideline recommendations on the evidence for efficacy of different interventions in the prevention of postmenopausal bone loss and fracture reduction are shown in Tables 1 and 2. The gradings of these recommendations refer solely to the level of evidence of efficacy, regardless of effect size; it should also be noted that for some agents there are inconsistencies between studies. Evidence for reduction in vertebral, all non-vertebral and hip fractures is considered separately in view of the lack (or differing levels) of evidence of efficacy, for some interventions, at all three sites. The grading of evidence base is derived as follows:

Grade A is awarded if there is evidence of efficacy from:
- meta-analysis of RCTs, or from at least one RCT

Grade B is awarded if there is evidence of efficacy from:
- at least one well-designed controlled study without randomisation
- at least one other type of well-designed quasi-experimental study
- well-designed non-experimental descriptive studies, eg comparative studies, correlation studies, case-control studies

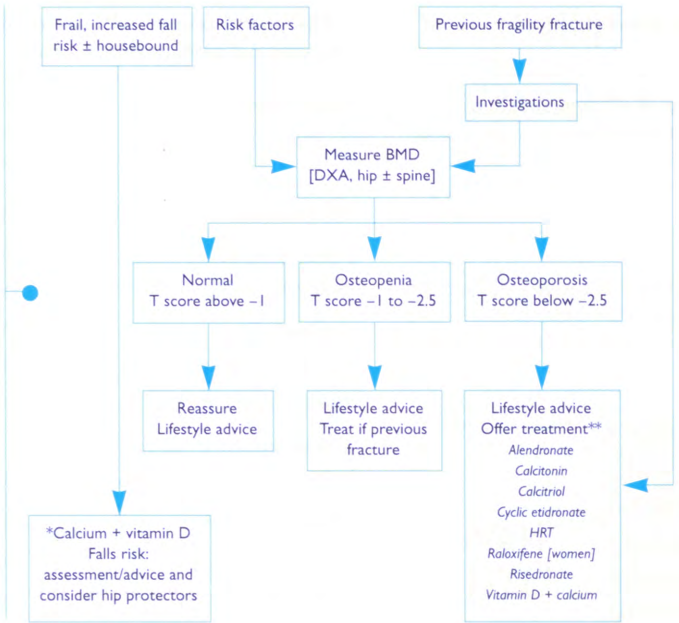
Grade C is awarded if there is evidence of efficacy from:
- expert committee reports/opinions and/or clinical experience of authorities

Diagnosis and risk assessment

Diagnosis

There is no evidence that population-based screening is effective in reducing fracture incidence, and the recommended approach towards management in clinical practice is that of selective case finding, in which individuals with risk factors for or evidence of osteoporosis are offered appropriate diagnostic and therapeutic intervention.

A variety of bone mass measurement techniques is predictive of fracture, including dual energy X-ray absorptiometry (DXA) and quantitative ultrasound. Measurements at the site of potential fracture are more predictive than assessments at other sites. Measurements undertaken at different sites or at the same site with different technologies in the same individual are not well correlated and accordingly a universal T score cut-off for the diagnosis of osteoporosis is inappropriate, since the proportion of individuals classified as having osteoporosis (a T score below −2.5) will vary substantially depending on the site and method of measurement.



Major risk factors

[other than previous fragility fracture] include the following:

1. Untreated hypogonadism [premature menopause, 2° amenorrhoea, 1° hypogonadism in women; 1° or 2° hypogonadism in men]
2. Glucocorticoids [7.5 mg per day prednisolone for 6 months or more][#]
3. Disease associated with increased prevalence of osteoporosis [eg gastrointestinal disease, chronic liver disease, hyperparathyroidism, hyperthyroidism]
4. Radiological osteopenia

Other risk factors in national and international guidelines include family history, low body weight, cigarette smoking, height loss, or low bone mass as assessed by other techniques.

Lifestyle advice

- Adequate nutrition especially with calcium and vitamin D
- Regular weight bearing exercise
- Avoidance of tobacco use and alcohol abuse

Previous fragility fracture

Defined as a fracture from standing height or less and includes prevalent vertebral deformity. A previous fragility fracture is a strong independent risk for further fracture and may be regarded as an indication for treatment without the need for BMD measurement when the clinical history is unequivocal.

Investigations

- FBC, ESR
- Bone and liver function tests [Ca, P, alk phos, albumin, AST/γGT]
- Serum creatinine
- Serum TSH

If indicated

- Lateral thoracic and lumbar spine X-rays
- Serum paraproteins and urine Bence Jones protein
- Isotope bone scan
- Serum FSH if hormonal status unclear [women]
- Serum testosterone, LH and SHBG [men]

For men aged less than 65 years, specialist referral should be considered.
*Recommended daily dose 0.5–1 g and 800 IU respectively.
#Refer to previously published guidelines.
**Treatments listed in alphabetical order. Vitamin D and calcium are generally regarded as adjuncts to treatment. HRT: oestrogen in women, testosterone in hypogonadal men.
BMD: bone mineral density
DXA: dual energy x-ray absorptiometry
HRT: hormone replacement therapy

Fig 1. Medical management of men and women aged over 45 years who have or are at risk of osteoporosis.

In order to avoid these variations in disease classification, it has been suggested that a gold standard be adopted for diagnostic purposes in terms of the site and method of measurement[16]. The most appropriate candidate is total hip bone mineral density measured by DXA, since this measurement is predictive of both cervical and trochanteric fractures, which collectively cause the highest morbidity, mortality and cost of all osteoporotic fractures. Furthermore, the precision error of measurements at this site is low and adequate reference data are available for Caucasian men and women.

Risk assessment

Assessment of the risk of fracture in an individual should ideally be expressed as absolute rather than relative risk and related to a relevant time interval, for example 10 years. This approach is likely to be used increasingly in the future to determine interventional, as opposed to diagnostic, thresholds. A variety of bone mass measurements at sites other than the hip and using different technologies is useful in risk assessment, including peripheral and spinal DXA measurements and ultrasound of the os calcis. Further improvement of fracture prediction can be achieved by the addition of risk factors for fracture that are independent of bone mineral density (BMD): for example, previous fragility fracture, maternal history of hip fracture, risk factors for falling, and increased levels of bone resorption markers.

Monitoring the response to treatment

Bone mineral density measurements may be used to monitor responses to treatment, the spine being the preferred site. In postmenopausal women with osteoporosis, significant treatment benefits can often be detected after two years of treatment with an anti-resorptive agent. Biochemical markers of bone turnover may have a place in monitoring the response to treatment; however, further research is recommended to evaluate their utility in clinical practice.

Osteoporosis in men

Up to 20% of symptomatic vertebral fractures and 30% of hip fractures occur in men. The World Health Organization (WHO) has defined osteoporosis as a BMD 2.5 standard deviations or more below the mean value for young adults (T score below −2.5), but this has only been established for women. Nevertheless, there is a similar relationship between absolute bone density values and fracture risk in both sexes[17,18]. As there is no established treatment for

Table 1. Effect of interventions on the prevention/reduction of postmenopausal bone loss.

Intervention	Grade of recommendations
Alendronate	A
Calcitonin	A
Calcitriol	A
Calcium	A
Cessation of smoking	B
Cyclic etidronate	A
Calcium and vitamin D	A
Hormone replacement therapy	A
Physical exercise	A
Raloxifene	A
Reduced alcohol consumption	C
Risedronate	A
Tibolone	A

Table 2. Anti-fracture efficacy of interventions in postmenopausal osteoporotic women.

Intervention	Grade of recommendations		
	Spine	Non-vertebral	Hip
Alendronate	A	A	A
Calcitonin	A	B	B
Calcitriol	A	A	ND
Calcium	A	B	B
Calcium and vitamin D	ND	A	A
Cyclic etidronate	A	B	B
Hip protectors			A
Hormone replacement therapy	A	A	B
Physical exercise	ND	B	B
Raloxifene	A	ND	ND
Risedronate	A	A	A
Tibolone	ND	ND	ND
Vitamin D	ND	B	B

ND = not demonstrated.

osteoporosis in men, consideration should be given to referral to a specialist centre, particularly for men aged below 65 years.

Conclusions

In the light of recently published clinical trial data, updated guideline recommendations have been produced for the assessment and treatment of osteoporosis in clinical practice[13]. The algorithm contained within them (Fig 1), which meets a need expressed by many practising clinicians, provides a protocol for the management of individual patients based on the framework provided by the Royal College of Physicians guidelines of 1999[1] and the updated information. By this means the update[13] seeks to maintain and extend the usefulness of the original guidelines, consistent with their spirit and methodology.

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