

Preventing osteoporosis: outcomes of the Australian Fracture Prevention Summit

Cosponsored by Osteoporosis Australia and the National Prescribing Service

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Abbreviations

BMD	bone mineral density
DEXA	dual energy x-ray absorptiometry
DOES	Dubbo Osteoporosis Epidemiology Study
GOS	Geelong Osteoporosis Study
HRT	hormone replacement therapy
MBS	Medicare Benefits Schedule
NHMRC	National Health and Medical Research Council
NNT	number needed to treat
PBS	Pharmaceutical Benefits Scheme
PTH	parathyroid hormone
RCT	randomised controlled trial
RR	relative risk
TASOAC	Tasmanian Older Adult Cohort

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Cover

A Swedish woman at the age of 20 years and the same woman at the age of 59, showing the devastating effects of osteoporosis. She has suffered multiple fractures and has lost 22 cm in height. The diagnosis of osteoporosis was not made until long after the first osteoporotic fracture. (Original photographs taken by Mr Lennart Lundegaardh. Copyright: Inger Lundegaardh.)

Preamble: the burden of osteoporosis in Australia

The clinical manifestations of osteoporosis affect nearly two million Australians.¹ In the absence of interventions, the prevalence of osteoporosis-related conditions is predicted to increase over the next two decades from 10% of the population currently to 13.2% by 2021.¹ The incidence of osteoporotic fractures is also predicted to increase, from one every 8.1 minutes in 2001 to one every 3.7 minutes in 2021.

Total costs relating to osteoporosis are currently estimated at \$7.4 billion per annum, of which \$1.9 billion are direct costs. Its disease burden can be expressed in terms of premature mortality and disability, which together represented over 25 000 healthy years of life lost to Australians in the financial year 2000–01.¹

In Australia there are three ongoing prospective cohort studies of fracture epidemiology:

- The Dubbo Osteoporosis Epidemiology Study (DOES) of a cohort of about 1600 men and 2100 women aged over 60 years with pre-fracture assessments;²
- The Geelong Osteoporosis Study (GOS) of about 109 900 men and women aged over 35 years;³ and
- The Tasmanian Older Adult Cohort (TASOAC) study of about 229 600 men and women of all ages.⁴

The participants in these studies were selected because their age and sex distribution were considered to reflect the Australian population. Importantly, each study used substantially the same method for capturing “events”, namely x-ray reports containing the word “fracture” in radiology service records in each region.

These studies provide different estimates of the number of fractures occurring in Australia. DOES reported 306 fractures in 3.25 years (1989–1992), giving an estimated residual lifetime fracture risk of 29% for men and 56% for women aged over 60.⁵ TASOAC reported 2140 fractures over two years (1997–1999), with an estimated residual lifetime fracture risk of 27% for men and 44% for women aged over 50.⁴ GOS reported 2184 fractures over two years (1994–1996), with an estimated lifetime risk of fracture of 42% in women aged over 50³ (the estimate for men is not yet available). From these studies, the total number of fractures each year among Australians aged over 60 has been estimated at 73 000 (DOES), 57 000 (TASOAC) and 51 000 (GOS). Using a different methodology, Access Economics has estimated there were 65 000 osteoporotic fractures in Australia in 2001.¹ Using the GOS estimates, it is calculated that the total number of hip fractures in Australia will increase from 15 000 in 1996 to 21 000 by 2006.⁶

In 1996, the Pharmaceutical Benefits Advisory Committee of the Commonwealth Department of Health and Family Services sponsored a Consensus Conference on Osteoporosis. Since then there have been advances in our understanding of the epidemiology, pathogenesis, diagnosis and treatment of osteoporosis. Accordingly, Osteoporosis Australia and the National Prescribing Service convened a Fracture Prevention Summit in September 2001. The aims were to estimate the size of the problem of osteoporosis and to formulate appropriate practice in primary care, with

special emphasis, where possible, on evidence-based guidelines for the treatment of osteoporosis.

The National Health and Medical Research Council (NHMRC) levels of evidence (see Box, this page) are a useful guide for defining the quality of available data on the treatment of osteoporosis. The most important criteria for a high-quality trial include randomisation, placebo controls, double-blinding, large sample sizes, prolonged observation, low dropout rates, preplanned intention-to-treat analyses, and replication. Replication and internal consistency are particularly important, as low event rates will often result in wide confidence intervals and type 2 errors (ie, failing to detect a difference when it is really present).

Meta-analyses should be done to adequately define the point estimate of outcomes such as fracture risk reduction. Uncritical acceptance of reported “significant” results when a study is poorly designed and executed creates uncertainty and is not useful in decision-making in clinical practice. Lack of rigorous design in a drug trial does not mean a drug is necessarily ineffective, only that there is not good evidence to support the hypothesis that it is effective. Whether one drug has better antifracture efficacy than another can not currently be determined, as there have been no comparator trials using antifracture efficacy as an endpoint. Most trials compare a group treated with a single drug with a control group receiving a placebo (calcium).

Rating of the evidence for recommendations

Evidence is graded according to the level-of-evidence classifications endorsed by the National Health and Medical Research Council (NHMRC) in 1995.*

E1 Level I: Evidence obtained from a systematic review of all relevant randomised controlled trials.

E2 Level II: Evidence obtained from at least one properly designed randomised controlled trial.

E3 Level III: Evidence obtained from all well designed controlled trials without randomisation; well designed cohort or case-control analytic studies, preferably from more than one centre or research group; or from multiple time series with or without intervention.

E4 Level IV: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

* A guide to the development, implementation and evaluation of clinical practice guidelines. Canberra: National Health and Medical Research Council, 1995.

Summary of key recommendations

Diagnosis

Measurement of bone mineral density (BMD) of the hip and spine should be used to diagnose osteoporosis and for monitoring response to interventions.

Wider availability of Medicare Benefits Schedule (MBS) rebates for bone densitometry items, particularly for older people and those with a family history of osteoporosis, is recommended.

Biochemical markers of bone turnover provide additional information to assess fracture risk. The finding of an elevated bone resorption marker in addition to low BMD strengthens the case for treatment in an individual. In selected patients, biochemical markers may have a role in assessing therapeutic response and enhancing compliance.

Initiation of treatment

The presence of a spinal fracture is an indication that treatment should be given, provided that BMD is in the range for "osteoporosis" (T-score < -2.5) or "osteopenia" (T-score between -1 and -2.5) (see Box 1). If a non-spinal fracture is present, treatment should be considered if BMD is in the osteoporosis range (T-score < -2.5). However, prospective studies evaluating the antifracture efficacy of drugs in patients with osteoporosis and non-spinal fractures at baseline are not available.

Women with osteoporosis (T-score < -2.5), with or without fractures, should be investigated and considered for treatment. Evidence in men is limited, and recommendations must await further research.

First-line drug therapies for postmenopausal women with osteoporosis

The potent bisphosphonates alendronate and risedronate are the first-line agents for treating postmenopausal osteoporosis. For women with osteoporosis and one or more baseline spinal fractures, treatment with these bisphosphonates reduces the relative risk of subsequent spinal fractures by approximately 50% (E1). It also reduces the risk of non-spinal fractures, including hip fractures. These potent bisphosphonates can reduce bed-day use and healthcare costs (E2).

Treatment with raloxifene is an alternative first-line approach to prevent spinal fractures, but not non-spinal fractures. A dose of 60 mg daily is associated with a 36% reduction in the relative risk of spinal fractures (but not non-spinal fractures) over four years (E1).

The anabolic agent parathyroid hormone (PTH) is associated with a 65% reduction in the relative risk of spinal fractures in women who have osteoporosis and one or more baseline spinal fractures (E2). It also reduces the relative risk of non-spinal fractures. Although not yet available in Australia or elsewhere, it is likely to become first-line therapy in patients with severe osteoporosis given its marked effect on bone structure.

Other drug therapies for postmenopausal women with osteoporosis

Other, less rigorously evaluated agents include etidronate, a less potent bisphosphonate, and hormone replacement therapy (HRT). Both agents are likely to reduce the risk of spinal fractures (E3). A reduction in non-spinal fractures is not well established.

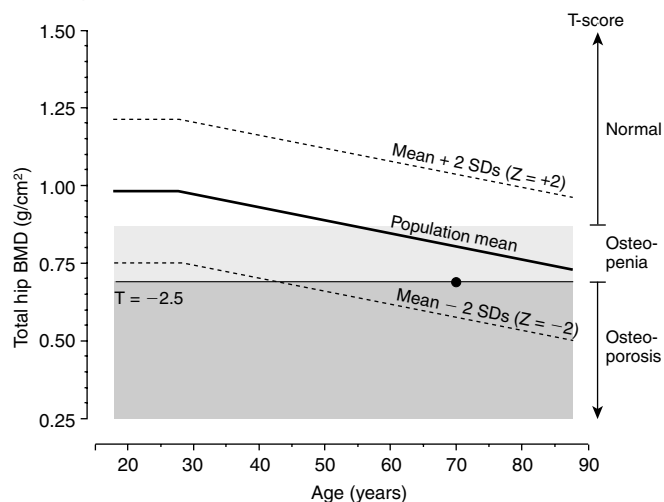
There is weak evidence for the efficacy of calcitriol in reducing fracture risk in women with postmenopausal osteoporosis (E3). There are no randomised controlled trial (RCT) data to support a role for anabolic steroids such as nandrolone in reducing the risk of fractures.

Calcium and vitamin D

Dairy products are the largest source of calcium in the diet. Increased calcium intake, from dietary sources or supplementation, should always be adjunctive therapy in the treatment of postmenopausal osteoporosis (E4). Studies suggest that calcium monotherapy has a modest effect in reducing fracture incidence.

Vitamin D, alone or in combination with calcium, reduces the risk of non-spinal fractures in institutionalised elderly

1: Explanation of T- and Z-scores, with World Health Organization thresholds



Relationship between hip bone mineral density (BMD) and age in women, showing the difference between:

(i) Z-score (number of SDs from population mean for age).

Z = -2.0 to $+2.0$ is the reference range; and

(ii) T-score (number of SDs from mean for a young, healthy population). A T-score of -2.5 is defined as the threshold for osteoporosis.

• Indicates a woman aged 70 years with a BMD Z-score of -1 , which is within the reference range for age. However, this Z-score means the woman has double the risk of fracture compared with a 70-year-old woman with mean BMD for age. Further, her T-score is -2.5 , indicating her BMD is at the threshold for osteoporosis (adapted from Prince⁷).

people (E2), among whom there is generally a high prevalence of vitamin D deficiency. A calcium–vitamin D combination is recommended for such people.

Exercise

Engaging in regular exercise, to maximise peak bone mass and prevent age-related and menopause-related bone loss, is a potentially important approach to reducing fracture risk (E4). However, there is currently no RCT evidence supporting the efficacy of exercise in preventing fractures at any specific site. Exercise increases muscle strength and may improve coordination and balance and reduce the risk of falls. Evidence that the reduction in falls leads to fewer fractures is not currently available.

Fall-prevention strategies and hip protectors

Fall-prevention programs that involve balance training and environmental modifications reduce the risk of falls (E2). Hip protectors prevent hip fractures in people at high risk of falls, but compliance remains an issue (E1).

Therapies for osteoporosis in men

Alendronate or etidronate are the drugs of choice for men with primary osteoporosis (E2). Testosterone replacement therapy is indicated in men with hypogonadism (E3). There is no evidence to support the use of calcitriol for osteoporosis in men. Men with osteoporosis should be considered for investigation and treatment.

Diagnosis

Use of densitometry

Dual-energy x-ray absorptiometry (DEXA) is the current “gold standard” for the diagnosis of osteoporosis. BMD predicts fracture risk. Each standard deviation reduction in femoral-neck BMD increases the age-adjusted risk of hip fracture by a factor of about two (range, 2.0–3.5) and the risk of any atraumatic fracture by almost the same amount (range, 1.7–2.4).⁸ Similarly, each SD reduction in lumbar spine BMD increases the risk of spinal fracture by a factor of about 2.3 (range, 1.9–2.8). Proximal femur BMD appears to be the best overall predictor of fracture risk, particularly as it is unaffected by osteoarthritis, which can spuriously elevate spine BMD values.

DEXA is reliable, with a reported precision of about 1%. However, these precision data are obtained under idealised conditions — in clinical practice such values are rarely achieved. At a realistic clinical precision of 2%, a change of at least 5.6% between measurements is necessary to be 90% confident the change is real. In postmenopausal women, the rate of bone loss is generally 1%–2% per annum, and hence, in most patients, an interval of two years between scans is

Therapies for glucocorticoid-induced osteoporosis

Postmenopausal women and older men receiving glucocorticoids are at the greatest risk of spinal fracture and should be considered for prophylaxis, usually with a bisphosphonate plus calcium as the first choice (E1). Adjunctive therapy with some form of vitamin D should also be considered.

Other strategies to reduce the fracture burden

As the risk of fracture increases after the first fracture and the initial osteoporotic fracture often goes undiagnosed and untreated, education and awareness programs are one key strategy to increase rates of treatment in people who have already sustained an osteoporotic fracture.

Liaison with orthopaedic units to ensure patients with fractures are adequately investigated and treated is recommended. Secondary prevention by special clinics in teaching hospitals or initiatives in primary care are another strategy that may increase treatment rates in people who have sustained their first osteoporotic fracture.

Specific programs are needed to address the high prevalence of vitamin D deficiency in elderly people in both residential care and the general community.

Public health prevention strategies, including increasing dietary calcium intake from dairy sources and promoting exercise for people of all ages, are recommended.

Wider availability of drugs under the Pharmaceutical Benefits Scheme (PBS) for subgroups at high risk of fracture, such as people with very low BMD or those using glucocorticoids, is recommended.

satisfactory, unless there is an accelerated rate of bone loss (eg, as a result of glucocorticoid medication), in which case yearly measurements may be warranted.

BMD is expressed in terms of a “T-score”, representing the number of SDs from the young normal mean BMD. Diagnosis based on bone densitometry, measured by DEXA and the T-score, provides a normal distribution of values as defined by a working group for the World Health Organization (see Box 1):⁹

- Normal bone density: T-score greater than –1;
- Osteopenia (low bone mass): T-score between –1 and –2.5;
- Osteoporosis: T-score less than –2.5.

Population screening is inappropriate

Population screening is a seemingly simple solution to the problem of fractures. Screening may appear to be justifiable: fractures are a public health problem, densitometry is a safe screening tool, BMD measurements identify high-risk indi-

viduals, and drugs are available that reduce fracture rates. So why not screen, and treat those at high risk?

A BMD measurement should only be done if the decision to treat (or not to treat) is influenced by the result of the test. Thus, it is a valid and essential investigation in patients at high risk of osteoporotic fracture who seek medical advice, but not justified for screening a population of healthy people. At present, the decision to measure BMD in patients is supported by a Medicare rebate for certain high-risk categories only.¹⁰ The usefulness of population screening also depends on the prevalence of the disease and cost of the screening test. Screening of unselected populations (eg, using ultrasound in pharmacies) is not recommended by any authoritative group in the field of bone biology.

Moreover, the definition of osteoporosis is not without problems. The BMD cut-off of -2.5 SD below the young normal mean used to define osteoporosis was developed to apply to DEXA measurements of BMD at the spine or hip. This cut-off value, when applied to other techniques such as ultrasound, quantitative computed tomography or forearm measurements, does not identify the same number or the same proportion of individuals.^{11,12} Moreover, reference ranges may differ between people of different ethnic origin.

In summary, measurement of BMD by DEXA of hip and spine is the current gold standard for diagnosing osteoporosis and monitoring response to lifestyle interventions or pharmacological treatments. It should be used as part of patient care rather than screening.

Biochemical markers of bone remodelling

Several biochemical markers of bone turnover can be measured in serum and urine. Although measuring the levels of biochemical bone markers can not quantify total skeletal bone mass, it can provide additional information to assess fracture risk and may have a clinical role in measuring a patient's compliance and response to therapy. Serum and urine levels of several biochemical markers of bone resorption and formation have been used as surrogate endpoints for gauging drug efficacy. In women aged 75 years or older, urine C-telopeptide and free deoxypyridinoline crosslinks of type I collagen have been shown to be independent predictors of an increased risk of hip fracture, and their combination with low BMD is an even stronger predictor.¹³ Two other prospective studies, one of hip fractures in elderly women and the other of spinal and peripheral fractures in women closer to the menopause, have confirmed these observations.^{14,15} An elevated bone resorption marker in addition to low BMD strengthens the case for treatment in an individual. In clinical trials of HRT or bisphosphonates, the percentage decrease in bone turnover markers correlates with the change in BMD at two years.^{16,17} There is no good evidence that reduced levels of bone-turnover markers in response to therapy predict fracture-risk reduction.

Treatment of osteoporosis in postmenopausal women

The purpose of treatment is to reduce morbidity and mortality associated with the first fracture and all subsequent fractures. Treatment of osteoporosis is needed because (i) fractures are associated with significant morbidity and mortality; (ii) bone loss and fracture risk accelerate with advancing age; and (iii) treatments are available to prevent accelerated bone loss, slow the deterioration of microarchitecture and reduce the risk of fractures.

Who to treat and when

1. Women with osteoporosis or osteopenia and fractures — treat

Perhaps the single most easily recognised risk factor for osteoporotic fracture is the presence of any spinal¹⁸ or non-spinal fragility fracture. The risk for further spinal fractures increases 3–5-fold as the number or severity of prevalent deformities increases, rising to an 11-fold increase if three or more fractures are present. The risk of hip fracture increases after one or more spinal fractures. The risk of forearm fracture is higher if there has been a previous forearm fracture: of patients who had had a distal forearm fracture, 46% of women and 30% of men suffered further fractures over the following seven years.¹⁹

Moreover, in people having an incident fracture (with or without a prevalent [pre-existing] fracture at baseline), the

risk of a further fracture is increased by 30%–40% within three years. Thus, if a spinal fracture is present, treatment should be given, provided that BMD is in the “osteoporosis” range (T-score < -2.5) or should be strongly considered if BMD is in the “osteopenia” range (T-score between -1 and -2.5). Values in the osteopenia range should not deter the clinician from proceeding with assessment and treatment — the lower the BMD, the greater the imperative to treat. If the T-score is above -1 , assessment and investigation should proceed with a high index of suspicion that the fracture may be due to trauma or local pathology rather than bone fragility.

Although there have been no RCTs of prevention of fracture in patients with non-spinal fractures and osteoporosis, it is likely that treatment would reduce future fracture rates. This is an area in need of further research, and studies designed to examine this are under way.

2. Women with osteoporosis without fractures — treat

The aim of treatment is to prevent the first and all subsequent fractures safely and cost-effectively, reducing total morbidity and mortality. Women aged over 50 years with a T-score below -2.5 are already at increased risk for fracture. Even though the absolute risk of fracture in the ensuing five years may be low, menopause-related oestrogen deficiency will increase bone remodelling, prolong osteoclast life span, reduce osteoblast life span and increase the negative bone

balance, thus accelerating bone loss and further increasing the risk. There is evidence that existing treatments can reduce the risk of fracture in these women.

Trials of alendronate and raloxifene have been carried out in women who have osteoporosis but no prevalent fracture. Treatment reduces spinal fracture rates and, at least with bisphosphonates, the reduction in fracture rate is seen within 12–18 months.^{20,21}

Data from alendronate studies indicate that a BMD T-score below –2.5 indicates a level of fracture risk comparable to that associated with a pre-existing low-trauma fracture.^{21,22} The number needed to treat (NNT) to prevent a spinal fracture was 15 in women with a prior spinal fracture and 35 in women with low BMD without a prior fracture; for hip fracture, the NNTs were 81 and 90, respectively. Women with osteoporosis, even if they have no fractures, should be treated.

3. Women with osteopenia or normal BMD — defer treatment

Should women with BMD T-scores between –1 and –2.5 but no prevalent fracture be treated? The issue in this group is that it comprises such a large proportion of women in the general population (estimated to be about 50% of all women over 50 years). In the Geelong Osteoporosis Study, 80% of the fractures occurred in women over 60 years; of the women under 60 years who had fractures, about 40% had osteoporosis and about 60% had normal BMD or BMD in the osteopenic range.³

As the majority of fractures occur after 60 years of age, it is difficult to justify treating large numbers of 50–60-year-old women with osteopenia, as the modest deficit in BMD and younger age confer only a low absolute risk of fracture over the following five years. When absolute risk is low, the NNT to prevent one fracture is large. Thus, large numbers of people would be exposed to the inconvenience of treatment, side effects and costs without likelihood of benefit. Early treatment may maintain or increase BMD, but most 50–60-year-old women are at low risk of an event, even if they have not received therapy.

Few data are available on the antifracture efficacy of drugs in women with osteopenia, as most trials have been carried out in women with osteoporosis. For this reason alone, making recommendations for treatment of women with osteopenia is difficult and not evidence-based, and making recommendations about universal treatment of large sectors of the population at modest risk for fracture is inappropriate. In RCTs, bisphosphonates have been shown to reduce by about 50% the risk of spinal fractures in women with BMD T-scores between –1 and –2.5, but this was not statistically significant, as event rates were low.²⁰

Although antiresorptive drugs (oestrogen, bisphosphonates, raloxifene) prevent bone loss, lifelong treatment of women from the age of 50 onwards can not be recommended except for those with osteoporosis. Drugs have not been shown to reduce fracture rates in women with normal BMD or in women with osteopenia but no fracture.

4. Women with other clinical risk factors for bone loss and falls — more data needed

Risk factors are used in the clinical decision-making process, but there is limited evidence that women selected solely on the basis of risk factors for osteoporotic fractures or falls benefit from drug treatment.

Risk factors that are common and have a large effect may be important for both the individual and the population. For example, suboptimal dietary calcium intake and vitamin D deficiency are important public health problems in Australia.

Surveys of dietary calcium intake in Sydney, Dubbo and Geelong suggest that 75%–87% of premenopausal and postmenopausal women receive less than the recommended daily calcium intake of 800 mg/day (premenopausally) and 1000 mg/day (postmenopausally).^{23–25}

Among older people and those with low exposure to sunlight, there is a high prevalence of vitamin D deficiency. For example, vitamin D deficiency has been found to be remarkably high among residents of hostels and nursing homes in Sydney and Melbourne.

Whether calcium intake or vitamin D status can be altered in the whole population, and whether this would reduce the population burden of fractures, is unknown. However, on the basis of current evidence,²⁶ calcium and vitamin D supplementation is recommended for nursing-home residents in Australia.

How long should treatment continue?

In principle, drug therapy should be continued indefinitely, because stopping treatment results in increased remodeling, bone loss, progression of structural damage and increased fracture risk. Most of the increase in BMD that is observed occurs within the first two years of treatment, although continued increases have been reported with alendronate beyond that time. The longest study of bisphosphonates has been for seven years.²⁷ If BMD increases into the normal range, it may be reasonable to consider stopping treatment and monitoring bone turnover markers and rates of bone loss. However, further research is needed to address the optimal duration of therapy.

Barriers to identification and treatment and case-finding strategies

Although there are deficiencies in our knowledge of the barriers to identification and treatment of osteoporosis in primary care, some areas that have been identified include a doctor's knowledge, perception and interpretation of diagnostic methods. In a study on diagnosis and treatment of osteoporosis by primary care physicians compared with specialists, the records of 1743 patients who had undergone bone densitometry scans were reviewed. The study revealed that primary care physicians were less likely to recognise and treat osteoporosis than specialist endocrinologists or rheumatologists, as they had had less exposure to specific education about osteoporosis.²⁸

Despite evidence that the incidence of further fracture increases markedly after the first fracture, most people (over 80% in Australia) who present with their first osteoporotic fracture fail to be investigated or treated.²⁹ Initiatives to increase rates of treatment, such as specialised multidisciplinary hospital-based first-fracture clinics, in cooperation with Divisions of General Practice, are one approach to this problem. Orthopaedic surgeons should heighten their awareness of the need for secondary prevention after a fracture in people aged over 50 years.

Barriers to identification, treatment and prevention of osteoporosis include inaccessibility of bone densitometry testing facilities and limited availability of subsidised medication. Patients and their treating practitioners require physical and financial access to bone densitometry testing facilities for effective clinical management. Current indications for bone densitometry under Medicare restrict access to densitometry,¹⁰ and PBS guidelines restrict the use of some agents to patients who have already had an osteoporotic fracture.

Densitometry testing has been subsidised by the MBS for selected indications since 1994. This followed a comprehensive evaluation by the National Health Technology Advisory Panel, with input from the medical profession, mainly the Australian and New Zealand Bone and Mineral Society and the Australian Medical Association. In the year 2000, Medicare funded 110 737 densitometry services in Australia at a cost of \$7.6 million. There is a case for expanded indications for densitometry that might include patients at high risk of fracture, such as older patients, or people with a family history of spinal or hip fracture in a first-degree relative.³⁰

For over 50 years, Australia has had in operation a subsidised scheme for pharmaceuticals as part of a comprehensive national health cover for all residents. Of all pharmaceutical expenditure in Australia (including prescription and over-the-counter products), the PBS system pays about 50%. The cost-effectiveness of medications is relevant to whether they are PBS-listed. The relative risk reduction in the incidence of new spinal fractures associated with most anti-osteoporotic medications is fairly consistent at around 50%, regardless of baseline risk or history of fracture.

The NNT to prevent a fracture varies with the absolute difference in fracture rates between treatment and control groups and is higher in groups whose baseline fracture risk is lower. However, RCT data suggest that the cost-effectiveness is comparable between people with bone density T-

2: Major fracture-prevention randomised controlled trials with bisphosphonates in postmenopausal women with osteoporosis

(a) Trial details

Trial	Drug	Number of patients	Age (years)	Baseline BMD	Prior vertebral fracture (% of patients)	Duration (years)	Primary endpoint
Lieberman et al ³³	Alendronate	994	45–80	LS T < -2.5	> 50%	3	BMD
Black et al ²²	Alendronate	2027	55–81	FN T < -2.1	100%	3	Vertebral fractures
Cummings et al ²⁰	Alendronate	4432	54–81	FN T < -1.6	0	4.2	Clinical fractures
Harris et al ³⁴	Risedronate	2458	Postmenopausal up to 85	LS T < -2	100%	3	Vertebral fractures
Reginster et al ³⁵	Risedronate	1226	Postmenopausal up to 85	~-2.7f	100% (all had at least 2 fractures)	3	Vertebral fractures
McClung et al ³⁶	Risedronate	9331	> 70	~-3.7*	38%†	3	Hip fractures

(b) Outcomes

Trial	LS BMD (% change v placebo)	FN BMD (% change v placebo)	Vertebral fracture reduction	Non-vertebral fracture reduction	Hip fracture reduction
Lieberman et al ³³	8.8	5.9	48%	21%	—‡
Black et al ²²	6.2	4.1	47%	20%	51%
Cummings et al ²⁰	8.3	3.8	44%	12%*	21%
Harris et al ³⁴	5.4	1.6	41%	39%	—‡
Reginster et al ³⁵	5.9	3.1	49%	33%	—‡
McClung et al ³⁶	—‡	2.1*	40%†	—‡	30%

f = mean. * Not measured in all patients. † Not assessed in all patients. ‡ Not measured. BMD = bone mineral density. FN = femoral neck. LS = lumbar spine. T = T-score.

scores less than -2.5 and those with a pre-existing osteoporotic fracture.

As over 90% of hip fractures result from a fall, people found to be at high risk of falls are a group worthy of further investigation. Simple assessments for falls risk have been developed that discriminate (with sensitivities and specificities of 75%) between “faller” and “non-faller” groups living in the community and in institutions.^{31,32}

Evidence for specific therapies in postmenopausal women with osteoporosis

Bisphosphonates

Three bisphosphonates are available in Australia for the treatment of osteoporosis: alendronate, risedronate and etidronate. Alendronate has been reported to reduce the risk of single and multiple spinal fractures, asymptomatic (morphometric) and symptomatic spinal fractures in women with

osteoporosis and one or more baseline spinal fractures (E1).^{22,33} Risedronate has also been reported to reduce the risk of single and multiple spinal fractures and morphometric spinal fractures in women with osteoporosis and one or more baseline spinal fractures (E1) (see Box 2).^{34,35} Alendronate halves the risk of spinal fractures in women who have osteoporosis without a pre-existing spinal fracture.²⁰ No studies with risedronate in this population are available. Although the BMD response and the suppression of bone remodelling with alendronate 70 mg once weekly is no different from alendronate 10 mg daily,³⁸ there are no fracture studies with the latter formulation. Etidronate may also prevent spinal fractures (E2), but problems in design, execution, and analysis make the results of existing studies difficult to interpret.^{39,40}

The risk reduction with potent bisphosphonates is seen early, usually within 12 months. There is evidence that the reduction in spinal fracture risk with alendronate reduces bed-days, days of sickness and pain and healthcare costs.³⁶

Non-spinal fracture rates are also reduced with alendronate and risedronate in patients with a prevalent spinal fracture (E1).³³⁻³⁵ Data for anti-hip-fracture efficacy are also available. In the alendronate trials there was consistency in hip-fracture risk reduction, but event rates were low and hip fracture was not a primary endpoint.^{20,22} In one risedronate trial,³⁷ in which hip fractures were the primary endpoint and there were many events (232 hip fractures), there was a 40% reduction in hip-fracture risk among women aged 70–79 with a baseline femoral-neck T-score below –4 (or below –3 together with one non-skeletal risk factor for hip fracture) (E2). In women aged over 80 years and selected primarily on the basis of non-skeletal risk factors (such as poor gait or propensity to fall) but not low BMD, there was no significant reduction in hip-fracture risk overall. However, a recent analysis suggests that there was a reduction in intertrochanteric fractures in this group.⁴¹

Selective oestrogen-receptor modulators

Selective oestrogen-receptor modulators (eg, raloxifene) are compounds that have oestrogen agonist activity at some sites and antagonist activity at others. RCTs of the effects of raloxifene have shown increases in bone density,⁴² but less than those reported with bisphosphonates or oestrogen. Despite this, in postmenopausal women with osteoporosis, raloxifene treatment has been found to be associated with a 36% reduction in the risk of one or more spinal fractures using a 60 mg daily dose for four years.²¹ Non-spinal fractures were not reduced, for reasons that are unclear. Raloxifene treatment is also associated with a 60%–70% reduction in risk of breast cancer⁴³ and with reduced low-density-lipoprotein cholesterol and total cholesterol (the latter being surrogate endpoints for cardioprotection).⁴²

An increased risk of venous thrombosis has been reported with raloxifene, similar to that seen with oestrogen. Raloxifene should be stopped if patients are immobilised for any prolonged period. Unlike oestrogen, raloxifene is not useful for control of menopausal symptoms, and indeed may worsen them. Raloxifene has also been shown to be effective in preventing postmenopausal bone loss,⁴⁴ and can be considered as an alternative in women unable to take

oestrogen for this indication. Currently, there are no RCTs with preplanned endpoints supporting the use of selective oestrogen-receptor modulators for the prevention of non-spinal fractures.

Hormone replacement therapy

Numerous RCTs have shown that oestrogen therapy can prevent bone loss in postmenopausal women (E1). Oestrogen is not only effective in preventing bone loss when given at or near menopause, but also continues to reduce bone loss for 10–15 years after menopause, with increases in bone density averaging 5% over three years.^{45,46}

However, the paucity of trials demonstrating antifracture efficacy of HRT has led to questions about its value in the treatment of osteoporosis. Two recent meta-analyses of the effects of HRT on spinal and non-spinal fractures have reviewed 22 controlled trials of at least one year's duration in which HRT was compared with either placebo, no treatment, calcium, or vitamin D.^{47,48} In the pooled analysis, the relative risk of non-spinal fracture in women randomly assigned to receive HRT was 0.73 (95% CI, 0.56–0.94; $P = 0.02$). For hip and wrist fractures alone, the relative risk was 0.60 (95% CI, 0.40–0.91; $P = 0.02$). Significant effects were seen only in women under the age of 60.⁴⁷ The finding that risk reduction was not significant in women over 60 was dependent on the inclusion of the HERS study,⁴⁹ which involved relatively obese older women with cardiovascular disease who may not have had osteoporosis. For spinal fractures, the relative risk in women randomised to receive HRT was 0.67 (95% CI, 0.45–0.98; $P = 0.04$) and the effect was not confined to women under 60 years.⁴⁸ Thus, although some positive data exist, there is a need for RCTs of the effect of HRT on spinal and non-spinal fractures.

Ideally, oestrogen therapy should be continuous, not cyclical, and long-term. Women with a uterus should take oestrogen in combination with progestogens to protect against endometrial cancer. Progestogens may be given cyclically for 10–14 days each month in perimenopausal women or as continuous therapy combined with oestrogen in postmenopausal women. The latter treatment is more suitable for women who are more than two years postmenopausal, to prevent the initial irregular bleeding (normally seen with this regimen) being unduly prolonged. Tibolone, a synthetic steroid reported to have activity through oestrogenic, progestogenic and androgenic receptors, can also improve bone density.⁵⁰ Moreover, it can be taken without unwanted progestogen-induced withdrawal bleeding. However, there are no data evaluating its antifracture efficacy.

Calcium

It is important to realise that most RCTs discussed so far have used calcium as adjunctive therapy and compared a single treatment (plus calcium) with a calcium control group. Dairy products or calcium-enriched soy drinks represent the best source of calcium in the diet. Although there are other dietary sources, dairy products are the primary dietary source for most people. Three or more servings of dairy products per day, combined with a normal diet, should allow most individuals to achieve their recommended daily intake.

Controlled trials of calcium as a monotherapy have found small but consistent effects of calcium on BMD (E1), averaging 1%–2% over two to three years and showing accumulation over time.^{51,52} Several studies have reported a significant beneficial effect of calcium monotherapy on fracture incidence.^{51,53–55} However, these findings should be interpreted with caution, as the studies were small and not powered to assess the effects of calcium supplementation on fractures. They may represent selective reporting of fracture results in that fracture data were probably recorded in other RCTs but not reported because no significant effect was found. The effect of this bias towards the reporting of positive results will only be addressed when adequately powered studies with fracture rate as the primary endpoint are undertaken.

Vitamin D

Vitamin D is better regarded as an endogenously produced pro-hormone than as an essential dietary constituent. It is produced in the skin as a result of sunlight exposure. With increasing age and frailty, vitamin D levels tend to decline, resulting in malabsorption of calcium and increased secretion of PTH, which in turn leads to accelerated bone loss. Physiological supplements of calciferol (eg, 400 IU/day) reduce PTH concentrations and lead to increases in BMD. Similar changes in biochemical endpoints can be achieved with regular sunlight exposure for 15–30 minutes daily. Two large studies have assessed the effect on fracture rates of calciferol supplementation alone. Lips et al⁵⁶ reported no change in fracture incidence among 2578 community-dwelling men and women aged over 70 years who were randomised to receive calciferol 400 IU/day or placebo, whereas Heikinheimo et al⁵⁷ reported that 150 000 IU/year of vitamin D reduced symptomatic fracture rates by 25% in a cohort of 800 elderly subjects in Finland.

Two other studies have reported the effects of calcium plus calciferol given to elderly people. Chapuy et al²⁶ reported a reduction of more than 25% in non-spinal and hip fracture rates in a cohort of 3000 elderly institutionalised women studied over three years. Dawson-Hughes et al⁵⁸ reported a reduction of more than 50% in non-spinal fracture rates among 400 older men and women randomised to receive calcium 500 mg/day plus 700 IU vitamin D per day, or placebo. It is not possible to determine whether the calcium, the vitamin D or the combination were the essential components in the success of these two studies. However, the studies point to the possibility that a safe and inexpensive intervention with calcium and vitamin D may reduce morbidity among institutionalised elderly patients.

Calcitriol

Evidence is less straightforward for the vitamin D metabolite calcitriol. There are a number of studies demonstrating both small beneficial and small detrimental effects on BMD and reports of both increased and decreased numbers of fractures.

A recent study of 489 postmenopausal women compared the effects of HRT and calcitriol over three years.⁵⁹ HRT increased BMD by 3% at the femoral neck ($P < 0.0001$) and by 4.4% at the spine compared with placebo

($P < 0.0001$). By comparison, calcitriol had no significant effect on BMD at the femoral neck (0.1% increase; $P = 0.57$), but significantly increased BMD at the spine (1.7% increase; $P = 0.01$).

An open-label trial of 622 women found a threefold reduction in new spinal fractures among women with postmenopausal osteoporosis treated with calcitriol compared with women receiving supplemental calcium⁶⁰ — fracture rates remained stable in calcitriol-treated patients but increased in the calcium-treated patients. This study suffered from several design flaws, making the results difficult to interpret (E3). In summary, the paucity of available data from well-designed, large-scale RCTs provides only weak evidence for the efficacy of calcitriol as a treatment for postmenopausal osteoporosis.

Parathyroid hormone

The possibility that PTH might have an anabolic effect on bone has been explored over many decades. Recently, RCTs have confirmed that PTH substantially increases bone density and reduces the incidence of spinal and non-spinal fractures (E2). It is well tolerated in human studies, but there remains some concern based on long-term animal toxicology results.

The largest study, involving 1637 postmenopausal women with prior spinal fractures, assigned participants randomly to receive placebo or one or two doses of subcutaneous recombinant human PTH over a median period of 19 months.⁶¹ New spinal fractures occurred in 14% of placebo-treated women versus 5% of women treated with 20 µg PTH. A 20 µg dose of PTH increased BMD by 9% (spine) and 3% (femoral neck) over and above the control group. Fracture-risk reduction with 20 µg PTH was 65% for spinal fractures and 55% for non-spinal fractures.

Other drugs

Androgenic steroids such as nandrolone have been widely used in Australia for management of osteoporosis. While there is some evidence of beneficial effects on bone density (E3),⁶² their antifracture efficacy is untested and there are no adequate safety data.

Recently, anabolic effects of statins on bone have been reported *in vitro* and in animal experiments. However, observational epidemiological studies of bone density and fracture rates among statin users are conflicting and may be confounded by the metabolic abnormalities that led to statin use in the first place. Two RCTs of statin use in non-osteoporotic populations have failed to demonstrate an effect of statins on fracture risk.^{63,64}

Plant constituents with a phenol structure similar to oestrogen are known as phyto-oestrogens. Epidemiological studies, primarily comparing Asian and Western populations, have been interpreted to indicate that a phyto-oestrogen-rich diet ameliorates oestrogen-deficiency symptoms in postmenopausal women and may protect against breast cancer, bone loss and cardiovascular disease. However, the interindividual diversity and complexity of dietary phyto-oestrogen absorption and metabolism make the bioactivity of these compounds unpredictable, and results of *in vitro* and *in vivo* studies are inconsistent.

There is a paucity of data on the effects of phyto-oestrogens on bone^{65,66} and no evidence that phyto-oestrogen supplements prevent bone loss. In one prospective, randomised, placebo-controlled study of 474 women treated with ipriflavone, no significant differences in BMD, biochemical bone markers or spinal fracture rates were observed after 36 months.⁶⁷

Fall-prevention strategies and hip protectors

Risk factors for falls include impairments of vision, sensation, strength and balance, and patient thinness and frailty. In the Dubbo Osteoporosis Epidemiology Study, quadriceps strength and postural sway were of similar importance to BMD in predicting fractures in both men and women.² Most fractures occur after falls, but not all falls result in fractures. Nevertheless, interventions that reduce falls risk may prevent fractures.

Several studies have examined single and multiple risk factors and the use of hip protectors. Of the single risk factor interventions, programs that involve balance training, such as home-based physiotherapy and tai chi, reduce the risk of falls (pooled relative risk [RR], 0.80; 95% CI, 0.66–0.98; and RR, 0.51; 95% CI, 0.36–0.75, respectively).^{68,69} Environmental modifications by occupational therapists (eg, removing mats, improving lighting) may reduce falls.⁷⁰ One study has reported that a reduction in psychoactive medications reduces the risk of falls (RR, 0.34; 95% CI, 0.16–0.74), but adoption and compliance rates in the study were low.⁷¹

Studies in nursing homes in Denmark and Sweden of the effect of hip protectors have reported reductions in hip fracture rates of 56% and 67%, respectively (E2).^{72,73} However, hip fractures did occur in the intervention subjects when not wearing their hip protectors, so that compliance remains an issue (one reason for non-compliance is that women believe it makes them look “fat” around the hips). Systematic reviews⁷⁴ suggest that hip protectors reduce the risk of hip fracture in high-risk populations (E1).

Exercise

Evidence that exercise reduces fractures is derived from retrospective and prospective observational cohort studies and case-control studies (E3). Maximising the attainment of peak bone mass and preventing age- and menopause-related bone loss by exercise, as well as attending to related risk factors (such as loss of muscle mass, poor gait and balance and depression), are potentially important approaches to reducing fracture risk in older people. However, no RCTs have examined the efficacy of exercise in preventing fractures at specific sites and this remains a gap in our knowledge.

Vigorous exercise undertaken by athletes during growth is well documented as increasing peak bone mass by biologically worthwhile amounts.^{75–77} The difference in bone density between athletes and sedentary controls ranges from 5% to 25%, depending on the sport and duration of participation. After retirement from intensive training, the effects appear to persist for many years, but whether the benefits are maintained into old age, when fractures and falls become common, is uncertain. The sparse data on 70–80-

year-old retired athletes suggest that the effects may be eroded in people who have substantially reduced training volumes. The same pattern is seen for other physiological adaptations to exercise, such as muscle hypertrophy, increased aerobic capacity, and increased insulin sensitivity.

Whether moderate exercise during growth produces benefits in terms of BMD and bone structure is less well established. There have been several exercise studies in school children in which loading (such as jumping and other sporting activity) is incorporated into the physical education program for 20–30 minutes three times weekly. The results are generally positive, with variable evidence of increased bone size, increased BMD and thickening of cortices.^{78–80} However, there are few data on whether the modest improvements in bone mass and structure are maintained after these exercise programs are stopped. There have been no long-term (> two years) exercise intervention studies using moderate exercise programs in normally active children.

Moderate- to high-intensity weight-bearing aerobic exercise, high-intensity progressive resistance training and high-impact loading (such as jumping) increase BMD by 1%–4% in pre- and postmenopausal women (E1).^{81–85} Excessive exercise carries some risk, especially in premenopausal women, in whom it may induce amenorrhoea. In studies of generally one year's duration, with sample sizes ranging from 30 to 150, exercise has been found to slow the rate of bone loss in older women by about 1.5% per year compared with sedentary controls (E1).⁸⁶ More robust exercise interventions appear to produce greater effects, but optimal prescriptive elements await further RCTs. Inclusion of weight-lifting and balance-training exercises should provide the widest range of benefits relevant to fracture protection, as well as reducing muscle weakness, falls risk and depression, and increasing muscle mass and mobility. Whether these benefits translate into fracture-risk reduction is currently unknown.

Pain management and rehabilitation after osteoporotic fracture

There is little evidence available regarding pain management after osteoporotic spinal fracture. The general principles of management of acute, subacute and chronic pain include use of non-pharmacological modalities and recognition of the potential for comorbid mood disorders, particularly in elderly people. Non-pharmacological, non-evidence-based modalities include physiotherapy and other physical modalities, transcutaneous electrical nerve stimulation, cognitive behaviour therapy, and procedures such as vertebroplasty, kyphoplasty and nerve blockade. Pharmacotherapy should employ a stepwise approach in the use of analgesics and other pain-modifying agents. Subcutaneous calcitonin has been reported to reduce the pain of acute spinal fractures in two small placebo-controlled trials (E2).^{87,88}

Rehabilitation to independent living is the primary goal after any fracture. Rehabilitation after hip fracture has been the most investigated. Systematic reviews of randomised and non-randomised trials^{89,90} have concluded that coordinated geriatric hip-fracture programs and early discharge (with support) for selected patients can significantly increase rates of returning home and reduce length of hospital stay and

costs (E1). No controlled trials are available to guide recommendations specifically for spinal fractures. Given the absence of evidence for this condition, strategies that

encourage independence and limitation of disability, together with interventions directed at secondary prevention of fractures, should be applied in clinical practice.

Evidence for treatment of other populations

While there are multiple published RCTs assessing the benefits of different therapies for osteoporosis in postmenopausal women, studies of osteoporosis in other populations (such as men, glucocorticoid-treated patients, and frail older people) are relatively few. Here we attempt to summarise the evidence for treatments in these “neglected” populations, using the same NHMRC levels of evidence. Evidence and recommendations regarding children with osteoporosis and athletes with stress fractures can be found at the Osteoporosis Australia website (<<http://www.osteoporosis.org.au>>).

Treatment of osteoporosis in men

Osteoporotic fractures occur in about 28% of men aged over 60 years.⁵ While fractures tend to occur in elderly men with multiple comorbid disorders, secondary underlying causes of osteoporosis are common and need to be rigorously excluded. Up to 16% of men with spinal fractures have evidence of hypogonadism. Chronic smoking, excessive alcohol use, glucocorticoid therapy, malabsorption and

underlying bone-marrow malignancies are some of the important risk factors for osteoporosis that need to be identified.

Osteoporosis remains a neglected area in men's health, with less than 10% of men with osteoporotic fractures currently receiving antifracture therapy. RCTs of men with osteoporosis are generally of smaller sample size and lesser quality than in those involving postmenopausal women (see Box 3). The limited RCTs that have been conducted suggest that alendronate, followed by cyclical etidronate, are the drugs of choice for men with primary osteoporosis.^{91,92,94} The effects of risedronate have not yet been reported, except in men receiving corticosteroids, but its efficacy should be similar to that of alendronate and etidronate. Preliminary studies also suggest that subcutaneous PTH may be as effective in reducing fracture rates in men as it is in postmenopausal women.

Adequate supplementation with calcium and vitamin D (if required) is recommended for all men with osteoporosis. There are no RCTs assessing the role of calcium or vitamin

D₃ alone in men. In a single small RCT (20 treated subjects and 19 controls) in osteoporotic men with pre-existing fractures conducted over two years,⁹⁵ calcitriol was no better than calcium in reducing spinal fracture (E3).

Testosterone replacement therapy is indicated for men with hypogonadism (serum total testosterone concentration < 8 nmol/L), but there are no data to assess the antifracture efficacy of testosterone in men with osteoporosis. Testosterone therapy and its effect on BMD are largely dependent on the gonadal and growth status of the individual, the duration of pre-existing hypogonadism, the degree of osteopenia and the duration of testosterone therapy. Two RCTs (E2) have demonstrated the positive effects of testosterone therapy on both cortical and trabecular bone, with maximal responses occurring in men before epiphyseal closure.^{96,97} The results of studies of testosterone therapy in hypogonadal, osteoporotic eugonadal and normal elderly men are summarised in Box 3.⁹⁶⁻¹⁰⁰

Large, well designed RCTs with adequate power to demonstrate spinal and hip fracture prevention in men with osteoporosis are needed.

3: Summary of randomised trials in male osteoporosis

(a) Bisphosphonates

Trial	Drug	Number of patients	Age (years)	LS BMD (% change v placebo)	Vertebral fracture (% of patients)	Duration (years)
Orwoll et al ⁹¹	Alendronate	241	31–87	5.3%	7.1% v 0.8% (P = 0.02)	2
Ringe et al ⁹²	Alendronate*	134	~ 53	7.3%	7.4% v 21.2% (P = 0.05)	2
Combined†	Alendronate	625	—§	6%	—§	1–3
Combined‡	Etidronate	300	—§	3%–9%	—§	2–5

(b) Testosterone

Group	Route	Number of patients	Age (years)	LS BMD (% change v placebo)	Duration (months)
Men with acquired hypogonadism¶	IMI	73	19–53	5%–15%	18–24
Osteoporotic eugonadal men	IMI	21	34–73	5%	6
Normal elderly men**	IMI, sublingual or transdermal	76	> 65	1%–2%	3–36

BMD = bone mineral density. IMI = intramuscular injection. LS = lumbar spine. *Compared with alfacalcidol.

†Combined data from 6 randomised controlled trials (RCTs). ‡Combined data from 9 RCTs. §Not measured.

¶Combined data from 2 RCTs. **Combined data from 8 RCTs.⁹³

Glucocorticoid-induced osteoporosis

A number of RCTs of bisphosphonates, in which the primary efficacy endpoint was BMD, have shown a consistent reduction in spinal fracture risk in postmenopausal women taking glucocorticoids (E1).¹⁰¹⁻¹⁰⁵ In these studies, the risk of spinal fracture in control-group women taking glucocorticoids ranged from 13% to 22% over 12 months. For etidronate, alendronate and residronate, the number of postmenopausal women taking glucocorticoids who would need to be treated to prevent one fracture over 12 months was low. Treating these women would be more cost-effective than treating postmenopausal women with osteoporosis unrelated to glucocorticoid use.

A number of RCTs of active vitamin-D metabolites, such as calcitriol and alfacalcidol, have reported prevention of spinal bone loss in patients starting glucocorticoids.^{106,107} None of these studies were powered for fracture as an endpoint, and mild hypercalcaemia occurred in about 10%–20% of patients.

In trials in which calcium alone was used as the control therapy for patients starting glucocorticoids, calcium did not prevent rapid spinal bone loss.^{106,108} However, in patients receiving chronic low-dose glucocorticoids, treatment with calcium and simple vitamin D resulted in small increases in spine BMD.¹⁰⁹ Although none of these studies were powered for fracture as an endpoint, meta-analyses have concluded that adjunctive therapy with some form of vitamin D should be considered.¹¹⁰

There is limited evidence for the effects of HRT (either oestrogen or testosterone) on bone density (E2), and there are no data on the effectiveness of HRT in reducing fractures among people with glucocorticoid-induced osteoporosis. Nevertheless, HRT should probably be considered if hypogonadism is present.^{111,112}

Fracture risk with glucocorticoids is a function of multiple factors, including the severity of reduction in bone density and the duration of exposure to glucocorticoids. The available evidence suggests that postmenopausal women and older men receiving glucocorticoids are at the greatest risk

of spinal fracture and should be considered for prophylaxis, usually with a bisphosphonate as the first choice. Adjunctive therapy with some form of vitamin D should be considered. If an active vitamin D metabolite is used, calcium supplementation should be avoided, unless dietary calcium intake is low. In premenopausal women and young men who are taking glucocorticoids, the risk of spinal fracture is less clear but appears to be lower, so the decision to use anti-osteoporosis prophylaxis is less straightforward.

Osteoporosis in frail older people

About a third of older Australians with profound and severe disability are resident in nursing homes and hostels (which provide a total of around 150 000 beds), and there is evidence of undertreatment for osteoporosis in this group. In one study, 26% of hostel residents and 36% of nursing home residents were known to have previous osteoporotic fractures, but anti-osteoporosis therapy was prescribed for only 17% and 11% of residents, respectively (Leon Flicker, Professor of Geriatric Medicine, Royal Perth Hospital, personal communication).

Older people are more likely to have several risk factors for fracture, including previous fractures. NNT analyses suggest that older people are more likely to derive greater benefit per year of anti-osteoporotic treatment than younger people.¹¹³ However, in frail older subjects, osteoporosis treatments must take account of the likelihood of comorbidity and the use of multiple other therapies. Calcium and vitamin D supplementation may have a special role in treating older frail people, particularly those in residential care. In Australia, 22% of women in low-level care and 45% of women in high-level care have frank vitamin D deficiency, and virtually all the remainder have a 25-hydroxy-vitamin-D level in the lower half of the reference range.¹¹⁴ Other factors that need special consideration in frail older people are the use of hip protectors and interventions to prevent falls.

Summary and recommendations

Osteoporosis represents a substantial health burden on the Australian community. In the financial year 2000–01, it led to an estimated 65 000 fractures. Total financial costs in 2001 were estimated at \$7.4 billion per annum, of which \$1.9 billion were direct healthcare system costs. If nothing is done, it is estimated that the number of Australians sustaining a fracture will increase from one every 8.1 minutes in 2001 to one every 3.7 minutes in 2021.

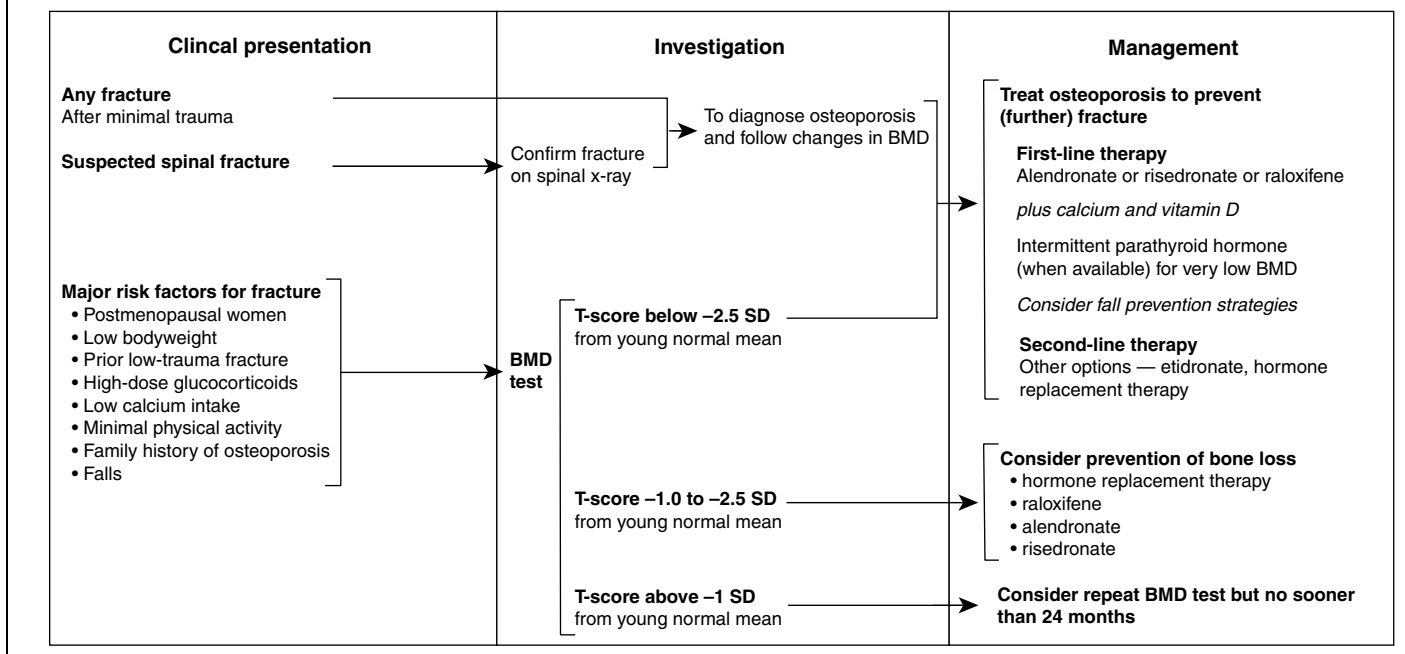
Relative to other diseases, management of osteoporosis is expensive — more costly in absolute terms than either diabetes or asthma, both of which are National Health Priority Areas. In terms of disease burden, more years of healthy life are lost in Australia due to osteoporosis than to Parkinson's disease, HIV/AIDs, rheumatoid arthritis or cervical cancer.

New strategies to reduce the fracture burden

Increased education and awareness programs

Education and awareness programs are a key strategy for reducing the fracture epidemic. Because the risk of fracture increases after the first fracture and the initial osteoporotic fracture often goes undiagnosed and untreated, increasing the rate of treatment in people who have already sustained an osteoporotic fracture is important. Despite the evidence, most people do not realise they are at risk of osteoporosis.

The role of lifestyle changes (including specific exercise regimens, changes in diet and quitting smoking) has not been evaluated adequately. Regardless of whether or not such strategies can reduce fracture risk, they are likely to have other major public health benefits.

4: Algorithm for treatment of osteoporosis in postmenopausal women**Wider use of effective treatments**

The most rigorously investigated drugs in the field of osteoporosis are the potent bisphosphonates alendronate and risedronate, and the selective oestrogen-receptor modulator raloxifene (see Box 4). Calcium, in combination with vitamin D, has been reported to reduce fracture risk in nursing-home residents and ambulant individuals.

Lower levels of evidence exist for the effectiveness of HRT and etidronate. Still weaker and contradictory evidence for anabolic steroids and calcitriol makes these drugs difficult to recommend.

Introduction of fall-prevention programs

Fall-prevention strategies and hip protectors are potentially effective in preventing fractures, particularly in elderly people, for whom treatment of vitamin D insufficiency is also vital.

A national strategy

The international Bone and Joint Decade (2001–2010), endorsed by the World Health Organization, provides an opportunity to launch a strategic plan against osteoporosis. In light of the enormous and growing prevalence, costs and disease burden of osteoporotic fractures in Australia, we make two recommendations:

- Osteoporosis should be adopted by the Federal Government as a National Health Priority Area, with commensurate funding; and
- The Federal Government should support a National Strategic Plan for urgent implementation during the international Bone and Joint Decade (see Box 5).

5: Components of a National Strategic Plan

- (a) Awareness programs implemented through State-based osteoporosis organisations with national coordination, including programs targeted at general practitioners.
- (b) Public health prevention strategies such as school-based programs to increase dietary calcium intake and exercise in young people.
- (c) Specific programs to address the high prevalence of vitamin D deficiency in elderly people, as well as fall-prevention programs and provision of hip protectors for older people in residential care and in the general community.
- (d) Secondary prevention strategies, such as special clinics in teaching hospitals or initiatives in general practice, to increase treatment rates in people who have sustained their first osteoporotic fracture.
- (e) Wider availability of Medicare Benefits Schedule rebates on bone densitometry items for elderly people and those with a family history of osteoporosis.
- (f) Wider availability of drugs under the Pharmaceutical Benefits Scheme to treat subgroups of people at high risk of suffering fractures (eg, people with very low bone mineral density [BMD] and glucocorticoid users). There is a need to identify a BMD level at which the cost-effectiveness of treatment is similar to that for a pre-existing fragility fracture.
- (g) Research initiatives in cooperation with the National Health and Medical Research Council and other funding agencies.
- (h) Monitoring and evaluation of fracture rates, the cost-effectiveness of treatments and the prevalence and burden of osteoporosis in Australia at specific time points over the next decade (eg, 2005 and 2010).
- (i) Liaison with orthopaedic units to ensure that patients with fractures are adequately investigated and treated.

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