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WORKING GROUP ON PRIMARY AND COMMUNITY CARE PURCHASING

THE PREVENTION OF OSTEOPOROTIC FRACTURE IN WOMEN IN A PRIMARY CARE SETTING

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Table 1 is taken from Cummings SR, Nevitt MC, Brownes WS et al. New England Journal of Medicine 332, 776-773, 1995 with permission from the publishers.

ABOUT THE TRENT INSTITUTE FOR HEALTH SERVICES RESEARCH

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- undertakes Health Services Research (HSR), adding value to the research through the networks created by the Institute;
- provides advice and support to NHS staff on undertaking HSR;
- provides training in HSR for career researchers and for health service professionals;
- provides educational support to NHS staff in the application of the results of research;
- disseminates the results of research to influence the provision of health care.

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FOREWORD

Recent years have seen the emergence of evidence-based medicine, evidence-based commissioning and, to an extent, evidence-based policy. All GP practices in Trent and their Health Authorities face a range of similar issues. As decisions become more evidence-based, then the scope for sharing that evidence increases.

Following the establishment in Trent of the Working Group on Acute Purchasing, a similar group was set up to consider issues of importance to purchasers and providers of primary and community health care services.

The Department of General Practice at the University of Nottingham and the Nottingham Unit of the Trent Institute facilitate the Working Group on Primary and Community Care Purchasing. The first set of topics for consideration was suggested at an initial meeting in 1996 of representatives from purchasing authorities, from primary and community care and from academic departments. More recently, topics were suggested by a survey of general practitioners in the Trent Region. A list of topics was submitted to the Trent Development & Evaluation Committee (DEC) and osteoporosis was one of three selected as priorities for the Working Group. Final reports are also submitted to the DEC prior to publication.

CONTENTS Page

EXECUTIVE SUMMARY

Aim

The purpose of this study was to provide advice on the cost-effectiveness of interventions for the prevention of osteoporotic fracture in women in a primary care setting.

Background

Osteoporosis is a systemic disease characterised by abnormalities in the amount and architectural arrangement of bone. These changes lead to a reduction in skeletal strength and susceptibility to fractures. Osteoporosis is defined by the World Health Organisation as a bone mineral density (BMD) 2.5 standard deviations below that of a normal population aged 30-40[1]. Risk of osteoporosis increases with age and is more prevalent among women than men because of accelerated bone loss after the menopause. Osteoporosis affects 50% of women over 80. Alone it is a poor predictor of fracture risk. Osteoporosis is generally asymptomatic until it causes a fracture and this complicates the development of preventative strategies aimed at arresting its progression. When combined with other partially independent risk factors such as a previous fracture and with risk factors for falls, those most at risk are more easily identified. The estimated lifetime risk for a 50 year old woman of a fracture of the hip is approximately 17.5%, while for the forearm and vertebrae the figures are 16% and 15.6% respectively. For men the corresponding figures for the hip, forearm and vertebrae are 6.0%, 2.5% and 5.0% respectively.

Fractures represent the main effect of osteoporosis and are a significant burden to the NHS, costing in excess of £1 billion per annum. There is evidence to suggest that the incidence of fractures is increasing which together with the ageing of the population, implies that the disease will place an increasing burden upon health service budgets in the future.

Interventions

Interventions can be divided into population based strategies or high risk strategies. Population based strategies include lifestyle interventions (diet, smoking cessation and exercise) and environmental interventions (mainly around reducing the risk of falls).

For those at high risk of osteoporotic fracture four drug interventions are currently available for the treatment of osteoporosis: hormone replacement therapy (HRT); bisphosphonates; calcium and vitamin D therapy; and calcitriol. Of these only HRT was until recently licensed as a preventative measure. A selective estrogen receptor modulator (SERM) was introduced during the writing of this report but published data are not yet available.

There is high quality evidence to suggest that HRT and alendronate are effective in the prevention of osteoporotic fractures. There is some evidence suggesting that etidronate, calcitriol and dietary supplements may also be effective.

HRT is the cheapest pharmacological intervention. A simulation exercise suggested that even this needs to be targeted very specifically at those most at risk to be cost-effective in the prevention of osteoporotic fracture. The simulations make a number of restrictive assumptions.

Recommendations

General Population

Promote exercise, appropriate diet, and smoking cessation among all general practice patients as and when the opportunity occurs.

High Risk Population

1. Identify high risk women opportunistically:
   a) by using selected risk factors from Cummings et al [20] (Table 20);
   b) aged over 65 and with a prevalent fracture or radiographic osteopenia.

2. Recommend those at high risk for Dual Energy X-ray Absorptiometry (DEXA), and if osteopenic or osteoporotic:
   a) If on HRT, counsel to increase compliance;
   b) If not on HRT but suitable, prescribe HRT with counselling as above;
   c) Otherwise, if at high risk consider bisphosphonates (alendronate or etidronate).

Institutionalised, Housebound Or Over 80, With A Poor Diet

Offer combination therapy with calcium (1g per day) plus Vitamin D (25 mg per day). Hip protector use should be considered in frail elderly ambulatory patients in residential settings.

Sub-recommendations

An audit of appropriate prescribing should be encouraged. Guidelines on the use of DEXA's should be considered.

Conclusion

Approximately two thirds of fractures do not occur in the highest risk population (in whom risk strategies are cost-effective). We do not know how effective population strategies might be. It is unlikely that implementing our recommendations would reduce the incidence of hip fracture by more than 15%.

1. INTRODUCTION

Osteoporosis is a systemic disease characterized by abnormalities in the amount and architectural arrangement of bone tissue. These changes reduce skeletal strength leading to susceptibility to fractures. Bone mineral density (generally measured at lumbar spine or hip) is central to the definition and diagnosis of the disease. The World Health Organisation defines osteoporosis as a bone mineral density (BMD) 2.5 standard deviations below that of a normal population aged 30-40[1]. A BMD of between 1 and 2.5 standard deviations below the young normal mean defines osteopenia - often a precursor to osteoporosis.

Bone is maintained by a dynamic process of bone resorption by osteoclasts and formation by osteoblasts. Osteoporosis is caused by an imbalance between the rates of resorption and formation. From age 35 onwards in both men and women resorption tends to exceed formation with consequent weakening of the bone. In general, women have less bone mass than men and experience an accelerated period of bone loss (1-2% per year) during the decade immediately following the menopause. They are, therefore, more susceptible to osteoporosis and its effects, including fracture, than men. Much of the literature on osteoporosis relates to the disease as it affects postmenopausal women.

It is estimated that in England and Wales there are approximately 2.66 million people suffering from osteoporosis. Of this number 82% are women and around 81% are over the age of 65 years (ScHARR unpublished). Precise estimation of the prevalence or incidence is hampered by the often asymptomatic nature of the disease. The disease is usually only detected after the occurrence of an osteoporotic fracture.

Fractures are the major sources of morbidity and mortality attributable to osteoporosis[2]. It is estimated in the UK that osteoporosis is responsible for approximately 60,000 hip fractures each year, 50,000 wrist fractures and 40,000 clinically diagnosed vertebral fractures[3]. (The latter is likely to be an underestimate given that vertebral fractures are often asymptomatic.[4]) It has also been estimated that the fracture related costs of osteoporosis to the NHS are around £1 billion per annum[5].

Health and social care costs associated with a hip fracture in the year following its occurrence are approximately £12,000 per patient[5]. Costs for a wrist or vertebral fracture over the same period are £428 and £479, respectively[5]. These three types of fracture are most commonly associated with osteoporosis[6] but, because the costs associated with hip fracture are so high, the cost-effectiveness analysis presented here is restricted to hip fractures.

Need for this Report

There is evidence that the age specific incidence of fractures is rising[7]. Given the relationship between prevalence of the disease and age, and the ageing of the population, it seems inevitable that fractures due to osteoporosis will represent an increasing burden to the health and social services.

A number of guidelines have been published on the management of osteoporosis[3,8,9,38]. Only one, however, has sought to examine the cost-effectiveness of treatment[8] (this moreover is confined to just one treatment). Given the range and cost of treatment[10,11] a more comprehensive cost-effectiveness analysis has been carried out.

A multi-disciplinary group comprising clinicians (medicine, surgery, public health and general practice), health authority representatives, an epidemiologist, statistician and economist was formed to report on cost-effectiveness in the prevention of osteoporotic fractures in women. The group would, based on current evidence relating to the burden of the disease in Trent and the available treatments, advise on a strategy for general practitioners dealing with the disease in the community.

2. BRIEF LITERATURE REVIEW

Following the menopause bone loss occurs at a rate of about 15% every ten years[12] and this is reflected in an increasing prevalence of osteoporosis and its effects. However, it is important to remember that, while BMD is used to define osteoporosis and can be used to identify those with an increased risk of fracture, low BMD is only a moderate predictor of fracture at an individual level. While, for example, it is known that a T-score (number of standard deviations above or below the mean BMD for healthy young women) of -1 is associated with an approximate doubling of the risk of hip fracture[13], it cannot confidently be predicted which individuals will suffer fractures. By the same token, attempts to determine what causes some women to develop osteoporosis has had limited success[14,15,16].

A large number of studies have examined risk factors for low BMD, particularly since the introduction of Dual Energy X-ray Absorptiometry (DEXA) technology in 1987. The largest study that has investigated BMD at the femoral neck (the Study of Osteoporotic Fractures[17]) included 7,963 women aged 65 or older. The main findings were that weight, quadriceps strength, age at menopause, calcium intake (from milk at ages 18-50 years), alcohol intake, physical activity (number of times engaged in high activity at age 50 and number of times active in last year), diuretic use and postmenopausal estrogen use were independently associated with high femoral neck BMD. Age, a maternal fracture after age 50 and a wrist fracture in a sister after age 50 were independently associated with low BMD. Of these variables, body weight was clearly the strongest predictor of femoral neck BMD[17].

2.1 Risk Factors for Hip Fracture

These come under four main headings.

1. Low BMD – A one standard deviation reduction in BMD approximately doubles the risk of a hip fracture[13]. One study found that BMD measured at the femoral neck was a better predictor of hip fracture than BMD measured at other sites[19].
2. Previous fracture – a previous wrist fracture[20,21] and a prevalent vertebral fracture[20,22] have both been shown to double the risk of a future hip fracture and this effect is at least partly independent of BMD.

3. Other bone-related factors have also been shown to predict hip fracture risk independently of BMD and include hip axis length and markers of bone turnover[23,24].

4. Fall-related factors affect the risk of hip fracture, as most hip fractures in the elderly occur as a result of a fall from standing height or less. There is an extensive literature on risk factors for falls in elderly men and women[25] and, as with risk factors for low BMD, these would also logically be risk factors for hip fracture. Dargent-Molina et al[26] specifically examined a number of fall related variables to see which predicted hip fracture risk in a prospective study of 7,575 women aged 75 years or over from France. They found that slow gait speed, difficulty in doing tandem walk, reduced visual acuity and small calf circumference were independently associated with the risk of a hip fracture.

A prospective analysis to investigate factors that predict a woman's risk of hip fracture was reported by Cummings et al[20] (who also used data from the Study of Osteoporotic Fractures[17]) A total of 9,516 women were followed up for an average of 4.1 years and factors that were found to be independently associated with hip fracture risk are listed below (Table 1). As the aim of this study was to investigate the effect of easily ascertainable risk factors on hip fracture risk, those mentioned in point 3 above were not examined in this analysis.

Table 1
MULTIVARIABLE MODELS OF RISK FACTORS FOR HIP FRACTURE WITH AND WITHOUT ADJUSTMENT FOR FRACTURES AND CALCANEAL BONE DENSITY AMONG 9,516 WOMEN

Measurement (Comparison unit)*	Relative risk of hip fracture (95% confidence interval)	
	Unadjusted ⅄	Adjusted for fractures and bone density
Age (per 5 year)	1.5 (1.3 - 1.7)	1.4 (1.2 - 1.6)
History of maternal hip fracture vs. none	2.0 (1.4 – 2.9)	1.8 (1.2 – 2.7)
Increase in weight since age 25 (per 20%)	0.6 (0.5 – 0.7)	0.8 (0.6 – 0.9)
Height at age 25 (per 6cm)	1.2 (1.1 – 1.4)	1.3 (1.1 – 1.5)
Self-rated health (per 1-point decrease) ⅄⅄	1.7 (1.3 – 2.2)	1.6 (1.2 - 2.1)
Previous hyperthyroidism (vs. none)	1.8 (1.2 – 2.6)	1.7 (1.2 – 2.5)
Current use of long acting benzodiazepines (vs no current use)	1.6 (1.1 – 2.4)	1.6 (1.1 – 2.4)
Current use of anticonvulsant drugs (vs. no current use)	2.8 (1.2 – 6.3)	2.0 (0.8 – 4.9)
Current caffeine intake (per 190 mg/day)	1.3 (1.0 – 1.5)	1.2 (1.0 – 1.5)
Walking for exercise (vs. not)	0.7 (0.5 – 0.9)	0.7 (0.5 – 1.0)
On feet ≤ 4 hr/day vs.> 4hr/day	1.7 (1.2 – 2.4)	1.7 (1.2 – 2.4)
Inability to rise from chair (vs. no inability)	2.1 (1.3 – 3.2)	1.7 (1.1 – 2.7)
Lowest quartile for distant depth perception (vs. other three)	1.5 (1.1 – 2.0)	1.4 (1.0 – 1.9)
Low frequency contrast sensitivity (per 1 SD decrease) a measure of visual acuity	1.2 (1.0 – 1.5)	1.2 (1.0 – 1.5)
Resting pulse rate > 80 beats/min (vs. ≤80 beats min)	1.8 (1.3 – 2.5)	1.7 (1.2 – 2.4)
Any fracture since age 50 (vs. none)		1.5 (1.1 – 2.0)
Calcaneal bone density (per 1 SD decrease)		1.6 (1.3 – 1.9)

* For continuous variables the relative risks are expressed as a change in risk for each specified change in the risk factor.
⅄Unadjusted model values are based on proportional-hazards analysis with backward stepwise elimination. Best subsets models yielded similar sets of risk factors, including the number of steps in a 360 -degree turn and the functional-status score; some did not include low-frequency contrast sensitivity, long-acting benzodiazepine therapy, or walking for exercise.
⅄⅄Health was rated as poor (1 point) fair (2 points) or good to excellent (3 points)

2.2 Risk Factors for Wrist and Vertebral Fracture

One study found that risk factors for fractures of the distal forearm were somewhat different to those for hip fractures[27]. Patients with a fracture of the forearm tended to be younger and more mobile than those with hip fractures.

Risk factors for vertebral fracture have received considerable attention in the literature[28]. One study found that women with a low BMD and two or more prevalent vertebral fractures at baseline, had a 75-fold increase in the risk of a new vertebral fracture at follow-up when compared with women with high BMD and no prevalent vertebral fractures[29].

2.3 Usefulness of Risk Factors in Predicting Low BMD and Fracture

Studies investigating risk factors for low BMD have found that, despite the large number of risk factors identified (Table 2), they have limited value in predicting which women have a low BMD[14,15,16]. Studies where the outcome is hip fracture suggest that using information on both BMD and risk factors may have some use in predicting fracture risk. In particular, Cummings et al[20] found that the 6% of women who reported five or more risk factors (listed in Table 1) and had low calcaneal bone density, comprised 32% of all hip fractures. Similarly, other large prospective studies have found that risk factors were useful when it came to predicting which subjects sustained a hip fracture during follow-up.

Table 2
RISK FACTORS FOR OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN[18]

Genetic First-degree relative with low-trauma fracture	**Environmental** Cigarette smoking Alcohol abuse Physical inactivity Thin habitus Diet low in calcium Little exposure to sunlight	**Menstrual status** Early menopause (before age of 45 years) Previous amenorrhea (e.g. due to anorexia nervosa, hyperprolactinaemia)
Drug Therapy Glucocorticoids (7.5mg/day or more of prednisone for more than 6 months) Antiepileptic drugs (e.g. phenytoin) Excessive substitution therapy (e.g. thyroxine, hydrocortisone) Anticoagulant drugs (e.g. heparin, warfarin)	**Endocrine diseases** Primary hyperparathyroidism Thyrotoxicosis Cushings' syndrome Addisons' disease	**Hematologic diseases** Multiple myeloma Systemic mastocytosis Lymphoma, leukemia Pernicious anemia
Rheumatologic diseases Rheumatoid arthritis Ankylosing spondylitis	**Gastrointestinal diseases** Malabsorption syndromes (e.g. celiac disease, Crohn's disease, surgery for peptic ulcer). Chronic liver disease (e.g. primary biliary cirrhosis	

As well as BMD, there are other factors (some related to the probability of a person falling) that increase the probability of a fracture. These include history of maternal hip fracture[20], current use of long acting benzodiazepines[20], current use of anti-convulsant drugs[20], use of corticosteriods[30] and lack of load bearing exercise. At an individual level, a BMD measurement is not a particularly good predictor of a fracture, but combined with information on other risk factors those most at risk are more likely to be identified. For example, previous wrist fracture[20,21] and a prevalent vertebral fracture[20,22] have both been shown to double the risk of a hip fracture at least partly independently of BMD. This may be helpful when targeting interventions so as to maximize cost-effectiveness.

2.4 Ethnicity

Most studies on risk factors for low BMD and fracture risk have been carried out in Caucasian or Asian women. Osteoporotic fractures are much less common in Caribbean and African women and in men and as a consequence these groups have received less attention in the literature.

2.5 BMD and Dual Energy X-ray Absorptiometry (DEXA)

DEXA is the current gold standard in the assessment of BMD of the hip and spine[31,32]. The use of DEXA continues to evolve and new techniques, such as peripheral DEXA, which are portable, may provide a means of predicting osteoporosis at the femur in a community setting.

2.6 Osteoporosis and Fractures in Trent Region

Table 3
PREVALENCE OF OSTEOPOROSIS IN WOMEN IN TRENT REGION

Age Range	Prevalence of Osteoporosis (T-score <-2.5)	Female Population	Estimated number of women with osteoporosis
50-59	7.0%	269,578	18,870
60-69	22.8%	235,780	53,758
70-79	32.0%	203,634	65,163
80+	56.2%	130,564	73,377
Total 50 +	25.1%	839,556	211,168

(Source: estimates based on prevalence of osteoporosis from Petley G, Cotton A, Murrills A et al. Reference ranges of bone mineral density for women in southern England: the impact of local data on the diagnosis of osteoporosis. British Journal of Radiology. 1996; 69:655-660. And population estimates from the Census)[33]

In Table 3 the number of women with osteoporosis in Trent Region is estimated from age-specific prevalence rates found elsewhere[33]. In Table 4 the incidence of fractured neck of femur by age group for the Trent Region is shown. Fractures increase dramatically from the age of 55 upwards and are far more numerous in women. The incidence of wrist and vertebral fractures follows a similar age related pattern, although these tend to peak at a somewhat earlier age.[34]

Table 4
NUMBER (INCIDENCE PER 10,000) OF HIP FRACTURES IN TRENT REGION (EXCLUDING SOUTH HUMBER) 1996/97

Age Range	Female Fractures	Female popn.	Male Fractures	Male popn.
45-49	27 (1.60)	168,789	9 (0.52)	172,346
50-54	31 (2.14)	144,944	28 (1.91)	146,551
55-59	55 (4.41)	124,634	28 (2.25)	124,303
60-64	84 (7.10)	118,243	36 (3.16)	113,967
65-69	168 (14.29)	117,537	70 (6.62)	105,757
70-74	401 (35.54)	112,839	151 (16.04)	94,112
75-79	617 (67.69)	90,795	167 (26.12)	63,935
80-84	882 (129.02)	68,364	215 (57.64)	37,302
85+	1494 (240.19)	62,200	229 (103.62)	22,099

(Source ONS and Patient Information System; with thanks to Fiona Sampson, operational research analyst ScHARR)

Fractures in Trent

The incidence rates reported in Table 4 are similar to those reported elsewhere[8]. The lifetime risk for a 50 year old woman of a fracture of the hip is estimated to be approximately 17.5%, while for the forearm and vertebrae the figures are 16.0% and 15.6% respectively. For men, the corresponding figures for the hip, forearm and vertebrae are 6.0%, 2.5% and 5.0% respectively[35]

2.7 Conclusion

Low BMD alone is a poor predictor of fracture at an individual level. Combining low BMD with other risk factors, such as previous fractures, provides more accurate prediction of future fractures. This combined approach might be able to identify the 6% of women at most risk of hip fracture in whom 32% of all fractures occur.

3. CURRENT GUIDELINES AND THEIR EVIDENCE BASE

Published guidelines [3,8,9,36,37,38] and reviews published in academic journals[10,11] were identified (Tables 5 & 6). No attempt was made to determine how closely guidelines were being followed in practice (other than by reference to prescribing behaviour in two health authorities) nor what would happen in their absence.

Table 5
SUMMARY OF GUIDELINES

Strategy	Guidelines	Published Evidence
HRT	• **Use around the time of the menopause**; • Premarin 0.625 mgs daily • Oestradiol (oral) 1-2 mgs daily • Transdermal oestrogen 50 micrograms daily • Oestradiol implant 50 mgs • The addition of a progestogen given 12 days each cycle, is necessary in women with a uterus[9] • **Use for the treatment of osteoporosis up to age of 70 in those with a low bone mass with or without a fracture**. Consider its use in women "at risk" 15 years post menopause. Maintain use for 10 years for maximum effect and provide counseling to maximize compliance. Oestriol, oestradiol, oestrone and conjugated equine oestrogens are recommended. For women more than two years post menopause continuous regimes (e.g. Kliofem) may be the most convenient[3]. • The addition of a progestogen given 12 days each cycle, is necessary in women with an intact uterus[9]	• The use of estrogens at between 0.625 and 1.25mg per day[43] has been shown to be effective. A review of evidence[10] recommends commencing use at around age 60-65. • Effect decreases after withdrawal and may be negligible 10 years after cessation[71].
Alendronate	• Alendronate (Fosamax) used according to manufacturers instructions for the treatment of established osteoporosis. 10 mg p.o. once a day taken approximately 30 minutes before breakfast.[3,8]	• Vertebral, hip,wrist fracture reduced by 50% . Non vertebral clinical fractures reduced by 28%.
Etidronate	• Etidronate (Didronel PMO) Taken on a 90 day cycle: 400mg etidronate disodium daily for the first 14 days followed by 500mg calcium supplement (Calcit) for the next 76 days. The cycle is then repeated.[3,8]	• Vertebral fractures reduced by 50%. No effect on appendicular fracture incidence.

Calcium and Vitamin D	• 1000 mg per adult for postmenopausal women and 1200 mg for adolescents to maintain as RDA.[9] • Vitamin D (25mg per day) in the very elderly and in particular for those in a nursing home environment is advised. Many preparations are available[3]	
Exercise	• Children, adults and the elderly are advised to increase weight bearing exercise though the manner of this is unspecified[3,9]. These measures are recommended only as part of an overall programme. Exercise is not considered to be effective on its own.	• Studies have assessed exercise in different ways. One suggests up hill walking at least once a day[70]. • Another recommends at least five hours weight bearing exercise per week[39]. • At least one hour weight bearing exercise per day[72]. • One study recommends low impact group exercise such as Tai Chi as a way of reducing the risk of falls and maintaining BMD[73].
Miscellaneous	• Removal of indoor environmental hazards likely to increase the risk of falls[3,9] • Advice to stop smoking.[3,9] • Advice to reduce alcohol intake[3,9] • Advice to avoid overuse of sedative medication.[3,9]	• The advice offered in guidelines appears to be based on studies or reviews such as those by Paganini-Hill[74] and Eastall[18] respectively.

Table 6
SUMMARY OF ROYAL COLLEGE OF PHYSICIANS' RECOMMENDATIONS[38]

Intervention	Recommendation	Strength of evidence
Diagnosis BMD measurement by DEXA	For case-finding rather than population screening	B
Further assessment	To exclude diseases that mimic osteoporosis	C
Prevention Population-based strategies	Not recommended	
HRT	At time of ovarian failure	BMD-A. Vertebral and hip # -B
Tibolone	Where HRT is unacceptable 2nd line	BMD-A
Raloxifene	2nd line	BMD & vertebral #- A
Bisphosphonates	2nd line	BMD-A
Treatment Calcium supplements	≥ 1g daily	BMD & vertebral # -A, hip # -B
HRT	Oestrogen with or without progestogen	BMD & vertebral # -A, hip # -B
Alendronate		BMD, vertebral & hip # -A
Etidronate		BMD & vertebral # -A, hip # -B
Calcitonin		BMD & vertebral # -A, hip # -B
Anabolic steroids	In the elderly	BMD –A, hip # -B
Calcitriol		BMD –A, hip # -C
Exercise regimens	For well-being, muscle strength and postural stability	# -C Muscle strength etc –B
Hip protectors	In the elderly	# -A
Parenteral vitamin D ± calcium	In frail elderly women	#- A

Footnotes

- fracture. BMD – bone mineral density. Strength of evidence: A – evidence from at least one RCT or from a meta analysis of cohort studies where appropriate; B – from at least one controlled non- randomised trial or well designed quasi experimental or descriptive study; C – from expert committee reports or opinions etc

Most of the strategies had two strands: *population based strategies* – essentially the promotion of particular dietary and life style practices – and; *strategies for those at high risk* – essentially drug based clinical interventions.

3.1 Population Based Strategies

These are based on associations between life-style factors and osteoporosis/fractures. They assume causality. Evidence of the effectiveness of interventions to change lifestyle is often poor.[3, 8,9,37,38]

Exercise

A number of studies have demonstrated a relationship between exercise and the risk of hip fracture[20,39]. This relationship may be explained by a positive correlation between peak bone mass and exercise in earlier years, the maintenance of bone mass through exercise in later years, and through the maintenance of agility in later years thereby reducing risk of falls. A number of guidelines recommend regular weight bearing exercise and the elimination of indoor environmental hazards as a way of reducing the risk of fracture associated with osteoporosis[3,9] **Despite incomplete evidence, it is difficult to resist the conclusion that population based interventions should form part of any overall strategy aimed at reducing the risk of fractures. Any advice would have to be tailored to the capabilities of the patient. Low impact exercise, such as an hour walking per day, where appropriate should be recommended.**

Diet

While it is known that consumption of calcium and vitamin D will not prevent bone loss, it is recognized that, in the absence of sufficient consumption, bone loss may be accelerated[40,41,42] Among those with poor diets or little exposure to sunlight[40] (those who are housebound), calcium and vitamin D combination therapy may significantly decrease the risk of osteoporotic fractures. **While the change in relative risks may not be as great as those associated with HRT[40], calcium and vitamin D combination therapy is relatively safe and inexpensive.**

Guidelines recommend daily calcium intake of 1,000 mg per adult, 1,500 mg for postmenopausal women (not taking HRT) and 1,200 mg for adolescents and 25mg vitamin D. Vitamin D is particularly appropriate for the elderly who are housebound. Preparations are available which cost approximately £60 - £120 per annum and provide the recommended amounts of both vitamin D and calcium. **While advice on diet may be adequate for the general population, combinations of calcium and vitamin D may be worth considering for at risk groups such as the housebound and frail elderly (over 80).**

A number of guidelines also draw attention to the role of smoking, alcohol (a particularly important factor in male osteoporosis), poor vision and the use of sedatives as factors contributing to the risk of osteoporotic fractures.

3.2 Strategies for Those at Risk

Hormone Replacement Therapy (HRT)

All of the guidelines reviewed, as well as the published scientific evidence, identify HRT as the most cost-effective primary prevention strategy for reducing the risk of fracture among those perceived to be at high risk, providing that they continue treatment. HRT is suitable (because of its low cost) for primary prevention and its role in the prevention of fractures is supported by case control studies but few RCTs.

HRT may also reduce the risk of cardio-vascular disease[44,45] . Prolonged use of HRT may, however, have adverse effects[45,46] including endometrial and breast cancer though some studies suggest that these risks are small relative to the benefits gained[45,47,48].

HRT has been shown to reduce the risk of hip fracture by approximately half compared to those not receiving HRT when other factors are controlled for [10,11]. These benefits are attributable to reduced/arrested postmenopausal bone loss[49,50]. The effectiveness of HRT appears to last as long as the treatment is taken[49,51,52] but compliance has been found to be variable[53,54]. Most individuals take the treatment for menopausal symptoms[55] and cease before it is likely to offer effective protection against osteoporotic fractures. In one study of women taking HRT for menopausal symptoms compliance fell to 73% within one year of starting treatment[56], while in another study of osteoporosis prevention the compliance after one year was 72%[57].

Assuming the recorded decline in compliance continued at the same rate (28% per annum), only 5% of women starting HRT would still be continuing treatment at 10 years and, thus, be protected from bone loss. This low level of compliance has prompted some to argue that HRT use as a preventative treatment should be more effectively targeted (specifically at those well past the menopause[58,59]) and should be accompanied by pre-treatment counselling[47]. Compliance represents a major issue when considering HRT as a strategy aimed at reducing fractures on a population-wide scale.

Advice on who should take HRT is mixed. One set of guidelines recommends that women who have undergone a premature menopause and those with clinical risk factors should take HRT for at least 10 years[3]. HRT has been shown to be effective in osteoporosis prevention/treatment up to age 70 and it may also be effective in older women. Initiation of HRT, therefore, has been recommended in women up to 15 years after the menopause. In contrast, other guidelines[9,36] argue for the introduction of HRT at the time of the menopause (because of increased uptake) continuing for 5-10 years.

The guidelines agree that before prescribing HRT, blood pressure measurement, breast and pelvic examination should be performed. The cost of a no-bleed preparation – likely to maximize compliance - is approximately £120 per annum (similar to that for vitamin D and calcium supplements). Women with breast cancer, endometrial cancer, active liver disease, severe renal disease or porphyria are not suitable for HRT and alternatives (where fracture risk is high and a clinical response to the risk of fracture is deemed appropriate) may be considered.

Bisphosphonates

Bisphosphonates work by inhibiting the resorptive activity of osteoclasts without impairing osteoblastic bone formation. Two bisphosphonates are licensed for the treatment of osteoporosis in the UK - Alendronate (Fosamax) and Etidronate (Didronel PMO) - the former currently only for postmenopausal women, the latter for both men and women.

Alendronate

A number of studies have shown Alendronate to be effective in reducing the risk of hip, vertebral and Colles fractures[4,60,61,62] by 50% and non-vertebral clinical fractures by 28%. Currently there is no recommended limit on the duration of treatment with Alendronate and some have argued for prolonged treatment, given that bone resorption will resume after treatment is withdrawn[63] However, the treatment is significantly more expensive than HRT (£340 per annum per patient) and in one set of guidelines it is asserted that Alendronate "..does not offer good value for money unless patients at high risk of fracture can be identified".[8] The Royal College of Physicians recommends Alendronate for the treatment of osteoporosis but only as a second line agent for prevention.[38]

Data from Leicestershire and the Wessex study[8] (Tables 7 and 8) show the current use of Alendronate compared to other drugs which may be used for the prevention and treatment of osteoporosis. The data for HRT do not distinguish between HRT used in the prevention and treatment of osteoporosis from that used for other (mainly symptomatic) reasons. The relative use of the two bisphosphonates may reflect the longer availability of Etidronate relative to Alendronate. It is also worth noting that there is evidence[64] that Alendronate may be effective in the primary prevention of bone loss and that it is licensed for this purpose in the USA.

Table 7
PRESCRIBING DATA: LEICESTERSHIRE HEALTH AUTHORITY APRIL 1997 - MARCH 1998

Drug	Number of Prescriptions	Total Cost £	% of prescriptions
HRT preparations	94,447	1,757,467	92.4
Alendronate (a relatively new bone specific treatment)	1,969	67,463	1.9
Etidronate (a relatively older bone specific treatment)	5,498	211,260	5.4
Calcitriol	308	4,822	0.03
Total	102,222	2,041,012	100.0

Percentages need not add to 100% due to rounding. (Source Leicestershire Health Authority)

Table 8
PRESCRIBING DATA: ONE HEALTH AUTHORITY IN THE SOUTH AND WEST REGION APRIL 1997 - JUNE 1998[8]

Drug	Number of Prescriptions	Total Cost £	% of prescriptions
HRT preparations	20,082	353,548	90.1
Alendronate	647	22,577	2.9
Etidronate	1,544	60,338	6.9
Calcitonin	3	365	0.0
Total	22,276	436,828	100

Percentages need not add to 100% due to rounding.

Etidronate

Evidence suggests that Etidronate is effective in reducing the risk of fractures[65,66,67]. Evidence in relation to non-vertebral fractures is weaker[68] than that relating to vertebral fractures. Whilst Etidronate is cheaper than Alendronate (costing approximately £160 per patient per annum) its use for the prevention of non-spine fractures is not evidence based.

Other: Calcitriol and Calcitonin

Both Calcitriol and Calcitonin are licensed for use in the treatment of osteoporosis in the UK. The costs of the two treatments are respectively £150 per annum and approximately £500 per annum. Evidence of their effectiveness is poor and, therefore, they are not considered as first line agents in the treatment of osteoporosis.

Hip Protectors

There is some evidence that hip protectors may reduce the risk of fracture in frail, elderly, ambulatory patients in residential settings[75].

4. COST-EFFECTIVENESS OF DRUG TREATMENT FOR PREVENTION OF HIP FRACTURE IN WOMEN: A SIMULATION

4.1 A Population Based Strategy with Limited Selectivity

Of the strategies available for preventing hip fracture, HRT is as cheap and at least as effective in reducing the risk of fracture based on current evidence as other more expensive strategies. As discussed in Chapter 3, it is the most likely candidate for a cost-effective intervention on a wide scale but in practice long term compliance will substantially reduce its impact on fracture reduction.

Information on the incidence of fractures by age cohort was obtained for the Trent Region (Table 4). Assuming that HRT will reduce the risk of a hip fracture for those taking the drug by 50% (for those continuing on treatment), the number of fractures prevented (under various compliance rates) are shown in Tables 9 - 11. Total costs of providing HRT under current conditions, expressed in present value terms, and assuming an annual cost per person of £120 are also shown. The benefits of HRT - calculated in terms of fracture costs avoided (£12,000 per fracture[5]), together with drug costs are used to estimate a ratio of benefits to costs (benefits also having been discounted at a rate of 6%). Thus, the value in column 4 of the Tables shows the magnitude by which the health service cost of avoiding a fracture exceeds the benefits (in terms of costs incurred). From this ratio, the value which must be attached to a prevented fracture for the intervention to be justified can be calculated. This equates to the present value of drug costs minus the present value of benefits divided by the number of fractures prevented. This value is shown in column 5 of the Tables. This value represents the cost of maintaining quality of life by preventing hip fracture - i.e. what the change in quality of life must be for the intervention to be worthwhile. It must be noted, however, that no allowance has been made in these calculations for benefits accruing from HRT use in terms of:

1. vertebral or Colles fractures avoided as a result of HRT use;
2. mortality avoided as the result of fracture prevention;
3. other benefits such as prevention of coronary heart disease.

The decision not to include mortality costs was deliberate. Thus, while as many as 20% of hip fracture patients will die within one year[36] many of these fractures will occur among the most elderly groups where potential years of life lost may well be small. Given the range of values attached to human life[69] any attempt to build such benefits into the analysis in monetary terms would be extremely difficult. One study[8] has estimated the QALY gain from a prevented hip fracture at 2.5 QALYs, although the accuracy of this figure cannot be assessed. Therefore, the values in column 6 of the Tables showing the implicit value which must be attached to a QALY gain for the intervention to be worthwhile should be treated with caution.

Table 9
COSTS AND BENEFITS FROM INTERVENING WITH HRT IN ALL WOMEN IN AGE COHORTS, ASSUMING A COMPLIANCE RATE DECLINING BY 28% PER ANNUM

Age Band at Which 10 Years of Treatment is Initiated	Fractures Avoided	Total Cost of HRT £	Ratio of Costs to Benefits	Implicit Value of One Avoided Fracture if HRT is Provided £	Cost per QALY £
50-59	11.95	10.41m	83.77	860,731	344,292
55-64	20.46	9.06m	42.25	432,334	172,934
60-69	33.43	8.64m	25.01	248,117	99,247
65-74	70.43	8.55m	11.87	111,170	44,468
70-79	149.42	8.05m	5.14	43,393	17,357
75-84	226.21	6.43m	2.71	17,936	7,174

Table 10
COSTS AND BENEFITS FROM INTERVENING WITH HRT ASSUMING A COMPLIANCE RATE DECLINING BY 14% PER ANNUM

Age Band at Which 10 Years of Treatment is Initiated	Fractures Avoided	Total Cost of HRT £	Ratio of Costs to Benefits	Implicit Value of One Avoided Fracture if HRT is Provided £	Cost per QALY £
50-59	21.54	15.59m	75.02	714,122	285,649
55-64	35.80	13.73m	39.33	373,768	149,507
60-69	61.74	13.18m	22.31	203,907	81,563
65-74	135.05	12.98m	10.18	86,671	34,668
70-79	261.81	11.96m	4.69	35,942	14,377
75-84	390.84	9.48m	2.45	14,355	5,742

Table 11
COSTS AND BENEFITS FROM INTERVENING WITH HRT ASSUMING A COMPLIANCE RATE DECLINING BY 7% PER ANNUM

Age Band at Which 10 Years of Treatment is Initiated	Fractures Avoided	Total Cost of HRT £	Ratio of Costs to Benefits	Implicit Value of One Avoided Fracture if HRT is Provided £	Cost per QALY £
50-59	30.12	19.70m	70.34	644,752	257,901
55-64	49.32	17.48m	37.71	345,021	138,008
60-69	87.36	16.84m	20.92	183,551	73,420
65-74	194.41	16.55m	9.35	76,025	30,410
70-79	360.99	15.03m	4.43	32,237	12,895
75-84	535.02	11.86m	2.35	12,734	5,094

Assumptions: Tables 9-11

1. The incidence of hip fractures by age band are as detailed in Table 4.
2. A non-bleed HRT preparation costing £120 p.a. is used and reduced the risk of fracture by 50% while in use.
3. The cost of treating a fracture is £12,000.

4.2 A Population Based Strategy with More Restrictive Selectivity

Treatment of osteoporosis. (Low BMD and prevalent fracture).

In Tables 12-14 a similar exercise has been completed where it is assumed that the female population is screened by DEXA prior to referral for HRT. Only those diagnosed as osteoporotic are offered HRT. (In practice and depending on the degree of osteoporosis, this may not be an effective strategy since, in established osteoporosis, HRT may not offer protection against fractures.)

Table 12
COSTS AND BENEFITS FROM INTERVENING WITH HRT ASSUMING ALL WOMEN IN AGE COHORTS RECEIVE A DEXA, THE RESULTS OF WHICH ARE USED TO TARGET THE INTERVENTION. A COMPLIANCE RATE DECLINING BY 28% PER ANNUM IS ASSUMED

Age Band at Which 10 Years of Treatment is Initiated	Fractures Avoided	Total Cost of HRT £	Total Cost of DEXA £	Total Cost of Intervention £	Ratio of Costs to Benefits	Implicit Value of One Avoided Fracture if HRT is Provided £	Cost per QALY £
50-59	11.95	0.56m	13.31m	13.87m	115.58	1,150,627	460,251
55-64	20.46	0.68m	11.70m	12.38m	58.95	594,819	237,928
60-69	33.43	0.94m	11.16m	12.10m	35.59	351,780	140,712
65-74	70.43	1.78m	10.25m	12.03m	16.71	160,586	64,234
70-79	149.42	2.39m	5.73m	8.12m	5.20	43,893	17,557
75-84	226.21	2.37m	5.94m	8.31m	3.49	26,210	10,484

Table 13
COSTS AND BENEFITS FROM INTERVENING WITH HRT ASSUMING ALL WOMEN IN AGE COHORTS RECEIVE A DEXA, THE RESULTS OF WHICH ARE USED TO TARGET THE INTERVENTION. A COMPLIANCE RATE DECLINING BY 14% PER ANNUM IS ASSUMED

Age Band at Which 10 Years of Treatment is Initiated	Fractures Avoided	Total Cost of HRT £	Total Cost of DEXA £	Total Cost of Intervention £	Ratio of Costs to Benefits	Implicit Value of One Avoided Fracture if HRT is Provided £	Cost per QALY £
50-59	21.54	0.78m	13.31m	14.09m	67.09	644,382	257,753
55-64	35.80	0.98m	11.70m	12.68m	36.23	344,414	137,766
60-69	61.74	1.30m	11.16m	12.46m	21.02	191,287	76,515
65-74	135.05	2.41m	10.25m	12.66m	9.97	84,340	33,736
70-79	261.81	3.46m	5.73m	9.19m	3.60	25,351	10,140
75-84	390.84	3.39m	5.94m	9.33m	2.44	14,088	5,635

Table 14
COSTS AND BENEFITS FROM INTERVENING WITH HRT ASSUMING ALL WOMEN IN AGE COHORTS RECEIVE A DEXA THE RESULTS OF WHICH ARE USED TO TARGET THE INTERVENTION. A COMPLIANCE RATE DECLINING BY 7% PER ANNUM IS ASSUMED

Age Band at Which 10 Years of Treatment is Initiated	Fractures Avoided	Total Cost of HRT £	Total Cost of DEXA £	Total Cost of Intervention £	Ratio of Costs to Benefits	Implicit Value of One Avoided Fracture if HRT is Provided £	Cost per QALY £
50-59	30.12	0.95m	13.31m	14.26m	50.93	464,144	185,658
55-64	49.32	1.20m	11.70m	12.90m	28.04	252,229	100,892
60-69	87.36	1.57m	11.16m	12.73m	15.91	136,560	54,624
65-74	194.41	2.87m	10.25m	13.12m	7.41	58,379	23,352
70-79	360.99	4.27m	5.73m	10.00m	2.95	18,311	7,324
75-84	535.02	4.16m	5.94m	10.10m	1.82	8,430	3,372

Assumptions: Tables 12-14

1. The incidence of hip fractures by age band are as detailed in Table 4.
2. A non-bleed HRT preparation costing £120 p.a. is used and reduces the risk of fracture by 50% while in use.
3. The cost of treating a fracture is £12,000.
4. A DEXA scan can identify osteoporosis with 100% accuracy.
5. The full cost of a DEXA scan is £65.

The prevalence of osteoporosis is used to determine the numbers eligible for treatment in each age cohort – estimated prevalence is based upon the figures presented in Table 3 and the cost of a DEXA is estimated at £65.

Tables 15-17 show the cost of intervention with HRT assuming that the Cummings et al[20] risk criteria are first used to screen the population for those most at risk of fracture before recommending DEXA measurement. It is assumed that such a screening exercise can be conducted at negligible cost and that the same risks will be found as in the Cummings et al[20] study.

Table 15

COSTS AND BENEFITS FROM INTERVENING WITH HRT ASSUMING THAT A SCREEN USING THE CUMMINGS CRITERIA IDENTIFIES 15% OF WOMEN IN AGE BANDS WHO THEN RECEIVE A DEXA, THE RESULTS OF WHICH ARE USED TO TARGET THE INTERVENTION. A COMPLIANCE RATE DECLINING BY 28% PER ANNUM IS ASSUMED.

Age Band at Which 10 Years of Treatment is Initiated	Fractures Avoided	Total Cost of HRT £	Total Cost of DEXA £	Total Cost of Intervention £	Ratio of Costs to Benefits	Implicit Value of One Avoided Fracture if HRT is Provided £	Cost per QALY £
50-59	11.95	0.56m	1.55m	2.11m	17.58	166,525	66,610
55-64	20.46	0.68m	1.17m	1.85m	8.81	80,157	32,063
60-69	33.43	0.94m	0.94m	1.88m	5.51	46,031	18,412
65-74	70.43	1.78m	0.63m	2.41m	3.35	24,004	9,602
70-79	149.42	2.39m	0.36m	2.75m	1.76	7,947	3,179
75-84	226.21	2.37m	0.26m	2.63m	1.10	1,057	423

Table 16

COSTS AND BENEFITS FROM INTERVENING WITH HRT ASSUMING THAT A SCREEN USING THE CUMMINGS CRITERIA IDENTIFIES 15% OF WOMEN IN AGE BANDS WHO THEN RECEIVE A DEXA, THE RESULTS OF WHICH ARE USED TO TARGET THE INTERVENTION. A COMPLIANCE RATE DECLINING BY 14% PER ANNUM IS ASSUMED

Age Band at Which 10 Years of Treatment is Initiated	Fractures Avoided	Total Cost of HRT £	Total Cost of DEXA £	Total Cost of Intervention £	Ratio of Costs to Benefits	Implicit Value of One Avoided Fracture if HRT is Provided £	Cost per QALY £
50-59	21.54	0.78m	1.55m	2.33m	11.09	98,417	39,367
55-64	35.80	0.98m	1.17m	2.15m	6.14	50,275	20,110
60-69	61.74	1.30m	0.94m	2.24m	3.80	26,733	10,693
65-74	135.05	2.41m	0.63m	3.04m	2.39	13,092	5,237
70-79	261.81	3.46m	0.36m	3.82m	1.50	4,864	1,946
75-84	390.84	3.39m	0.26m	3.65m	0.95	-491	

Table 17
COSTS AND BENEFITS OF INTERVENING WITH HRT ASSUMING THAT A SCREEN USING THE CUMMINGS CRITERIA IDENTIFIES 15% OF WOMEN IN AGE BANDS WHO THEN RECEIVE A DEXA, THE RESULTS OF WHICH ARE USED TO TARGET THE INTERVENTION. A COMPLIANCE RATE DECLINING BY 7% PER ANNUM IS ASSUMED

Age Band at Which 10 Years of Treatment is Initiated	Fractures Avoided	Total Cost of HRT £	Total Cost of DEXA £	Total Cost of Intervention £	Ratio of Costs to Benefits	Implicit Value of One Avoided Fracture if HRT is Provided £	Cost per QALY £
50-59	30.12	0.95m	1.55m	2.50m	8.93	73,707	29,483
55-64	49.32	1.20m	1.17m	2.37m	5.15	38,723	15,489
60-69	87.36	1.57m	0.94m	2.51m	3.14	19,581	7,832
65-74	194.41	2.87m	0.63m	3.50m	1.98	8,911	3,564
70-79	360.99	4.27m	0.36m	4.63m	1.37	3,464	1,385
75-84	535.02	4.16m	0.26m	4.42m	0.80	-2065	

Assumptions: Tables 15-17

1. The incidence of hip fractures by age band are as detailed in table 4.
2. A non-bleed HRT preparation costing £120 p.a. is used and reduces the risk of fracture by 50% while in use.
3. The cost of treating a fracture is £12,000.
4. A DEXA scan can identify osteoporosis with 100% accuracy.
5. The Full cost of a DEXA scan is £65.
6. Those with appropriate risk factors can be identified at no cost prior to DEXA screening.

In Table 18 a range of costs per QALY gain is presented[69] for illustrative purposes. From this the cost per QALY of this intervention can be compared with that of others – though it must be stressed that care is warranted in the interpretation of the results as not all studies have adopted identical methodologies.

Table 18
QUALITY ADJUSTED LIFE YEARS OF COMPETING THERAPIES: SOME TENTATIVE ESTIMATES [69]

Treatment	Cost/QALY 1990 £
Cholesterol testing and diet therapy only (all adults, aged 40-69)	220
Neurosurgical intervention for head injury	240
GP advice to stop smoking	270
Neurosurgical intervention for subarachnoid haemorrhage	490
Anti-hypertensive therapy to prevent stroke (ages 45 – 64)	940
Pacemaker insertion	1,100
Hip replacement	1,180
Valve replacement aortic stenosis (narrowing)	1,410
Cholesterol testing and treatment	1,480
CABG (left main vessel disease, severe angina)	2,090
Kidney transplant	4,710
Breast cancer screening	5,780
Heart transplant	7,840
Cholesterol testing and treatment (incrementally) of all adults 25-39 years	14,150
Home haemodialysis	17,260
CABG (1 vessel disease, moderate angina)	18,830
CAPD	19,870
Hospital haemodialysis	21,970
Erythropoietin treatment for anaemia in dialysis patients (assuming 10% reduction in mortality)	54,380
Neurosurgical intervention for malignant brain tumors	107,780
Erythropoietin treatment for anaemia in dialysis patients (assuming no increase in survival)	126,290

Only when intervention is targeted at the 60 plus age group and is preceded by screening based on risk factor analysis and DEXA does it appear to be cost-effective. This is conditional upon DEXA being applied only to high risk cases and that no unnecessary DEXA costs are incurred. It is also assumed that pre-DEXA screening is 'free' and that HRT compliance rates can be improved. However, it should be noted that no additional fractures are assumed to be prevented once HRT is discontinued – which is somewhat pessimistic. This analysis also assumes that compliance in a targeted strategy with a non-bleed preparation will be higher than observed in past studies and this has not been prospectively tested. Other benefits associated with fracture prevention (such as reduced mortality, non-hip fractures prevented etc.) have not been included. If all these assumptions are shown to be valid then a strategy based on targeted HRT use preceded by screening should be cost-effective.

Many untested assumptions have been made in concluding that HRT would be a cost-effective strategy for the prevention of hip fracture in the presence of established osteoporosis. Bisphosphonates and Alendronate have been tested in prospective RCTs and shown to be effective in fracture prevention[4]. These large trials are free of the untested assumptions essential to make the case for HRT therapy. HRT has not been directly compared to a potent Bisphosphonate in a randomised trial in the treatment of established osteoporosis. These two agents have been compared in primary prevention where the effect on preservation of spine and hip BMD of cyclical HRT was substantial[64], as was the effect of Alendronate 5mg daily.

In Table 19, an analysis similar to those of Tables 9-11 is reported for Alendronate. The figures reported are based on assumed compliance rates of 70%, 80%, and 90% declining pro rata each year. The annual cost of Alendronate per person treated of £348, treatment confined to three years and delivered only to high risk groups - BMD 2.5 standard deviations below normal at spine or hip and/or this BMD and a prevalent fracture – is also assumed. High risk groups are assumed to have been identified using DEXA screening of all women in the age group at a cost of £65 per person screened. As can be seen from Table 19 the cost per fracture avoided is high and cost-effectiveness is uncertain.

Table 19
COSTS AND BENEFITS OF INTERVENING WITH ALENDRONATE ASSUMING ALL WOMEN IN AGE BANDS RECEIVE A DEXA, THE RESULTS OF WHICH ARE USED TO TARGET THE INTERVENTION. COMPLIANCE RATE DECLINING BY 10%, 20% AND 30% PER ANNUM

Age Band at Which 3 Years of Treatment is Initiated	Fractures Avoided	Total Cost of Alend. £	Total Cost of DEXA £	Total Cost of Intervention £	Ratio of Costs to Benefits	Implicit Value of One Avoided Fracture if Alend. is Provided £	Cost per QALY £
65-67[1]	45.53	4.79m	0.65m	5.44m	10.50	119,482	47,793
65-67[2]	40.99	4.33m	0.65m	4.98m	10.63	121,493	48,597
65-67[3]	36.79	3.91m	0.65m	4.56m	12.87	123,947	49,579

Assumptions
[1] 10% decline in compliance rate pa.
[2] 20% decline in compliance rate pa.
[3] 30% decline in compliance rate pa.

Other assumptions are as detailed in the text. All costs in all tables are expressed in terms of their present value.

Table 20
CHECK-LIST OF RISK FACTORS FOR HIP FRACTURE IN WOMEN AGED ≥65 YEARS

Women with five or more risk factors should be recommended for further screening.

1. Age ≥ 80 years
2. History of maternal hip fracture
3. Current weight less than at age 25
4. Height at age 25 ≥ 168 cm
5. Self-reported health rated as fair, poor or very poor as opposed to good or excellent
6. Previous hyperthyroidism
7. Current use of long-acting benzodiazepines
8. Current use of anticonvulsant drugs
9. Current caffeine intake equivalent to more than two cups of coffee a day
10. Does not walk for exercise
11. On feet ≤ 4 hours a day
12. Inability to rise from a chair without using arms
13. Lowest quartile of visual acuity[1]
14. Resting pulse > 80 beats/min
15. Any fracture since age 50

[1] Using whatever instrument is available to the practitioner for measuring either visual acuity, depth perception or contrast sensitivity. The cut-points for quartiles should be based on the distribution of measurements expected for women aged 65 and older.

Further details of these factors including an estimate of the magnitude of their effect on the risk of hip fracture can be found in Cummings et al [20].

5. THE STRATEGY

Population

Advice to increase exercise, improve diet and reduce risk factors such as smoking, opportunistically in primary care setting

High risk population

↓

Identify those at risk opportunistically using selected criteria (Table 20) from Cummings et al[20]

Or if age> 65 years + prevalent fracture or radiographic osteopenia

↓

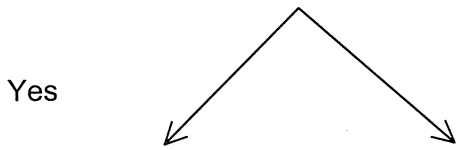
Recommend at risk individuals for DEXA

↓

Counsel those identified as osteopenic or osteoporotic on HRT

↓

Suitable for HRT ?



Receive HRT

Consider Alendronate or Etidronate if at substantial fracture risk

Intermediate risk population

Those who are housebound or over 80 with poor diet are offered calcium (1g per day) + vitamin D (25 mg per day) combination therapy. In residential care settings, frail elderly ambulatory patients may be offered hip protectors.

6. CONCLUSIONS

Fractured neck of femur is a major cause of morbidity and mortality. Treatment costs are high. Demographic change and the age related increase in incidence suggests that the burden will continue to rise.

Population measures could reduce the burden, but the effectiveness of interventions to change behaviour and, hence, reduce fracture incidence is uncertain.

Osteoporosis is common in elderly women and alone is a poor predictor of fractures. The presence of osteoporosis must be considered alongside other risk factors for fracture (such as propensity to fall) to better predict those at most risk of fracture. However, the cost and practicality of a screening programme to do this is highly uncertain.

HRT is the cheapest pharmacological intervention and most likely to be effective. However its acceptability amongst elderly women is uncertain. The more expensive bisphosphonates are less likely to be cost-effective.

All these uncertainties confirm that a screening programme cannot be recommended. Our results suggest that clinical osteoporosis services must focus on those most at risk to be cost-effective. Calcium and vitamin D in elderly housebound or institutionalised women with a poor diet is probably worthwhile.

Hip protectors may be cost-effective in frail, elderly, ambulatory patients in residential care settings.

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LIST OF TABLES