For and against

Bone densitometry is not a good predictor of hip fracture

Bone densitometry is widely used in osteoporosis clinics to identify people at increased risk of fracture. Terence Wilkin and Devasenan Devendra believe that evidence for the efficacy of bone densitometry is weak, but Jan Dequeker and Frank P Luyten argue that their interpretation of the evidence is too narrow and that screening high risk patients is cost effective

FOR The World Health Organization defines osteoporosis as a “progressive systemic skeletal disease characterised by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture.”¹ The low bone mass used to define osteoporosis is arbitrarily fixed at 2.5 standard deviations or more below the mean bone density for premenopausal women. Assessment of bone density provides a precise figure to which doctors and patients feel able to relate with confidence. We believe this confidence is unjustified.

By one definition, osteoporosis is an arbitrary point on a scale. By another, it is a pathological process of microarchitectural deterioration in which the unconstrained activity of bone osteoclasts accelerates bone resorption. The two definitions are fundamentally different. Accelerated bone resorption exists throughout postmenopausal life, whereas osteoporosis does not—and may never. Bone densitometry measures bone density, not bone turnover or bone stability. We have argued previously that bone turnover, rather than bone density, is the responsive element in treatments for preventing fractures.² The pathology of osteoporosis is one of uncontrolled bone resorption and the treatment (whether hormone replacement therapy or bisphosphonates) antiresorptive. We present five evidence based reasons why the results of bone densitometry may not predict postmenopausal fracture of the hip in the way that many believe it to.

Hip fracture is rare before age 65

The purpose of measuring bone density is to direct preventive treatments towards those who would most benefit. Drug treatment is principally antiresorptive and it clearly reduces fractures. The 10 year chance of hip fracture in women age 50 who are already at twice the random risk is reportedly 1.4%.³ Antiresorptive drugs can halve the risk of fracture, but the cost-benefit of treating the group at risk, of whom only 0.7% will benefit from 10 years' treatment, is questionable. Furthermore, the cost of detecting everyone who is at twice the random risk of fracture by bone densitometry would be prohibitive. There is no evidence that

measurement of bone density in perimenopausal women can direct antiresorptive treatment cost effectively. Benefits are inevitably limited when large sums of money are targeted at the prevention of a rare event.

Fracture protection and bone mass gained are poorly related

Antiresorptive drugs have long been marketed for their ability to restore lost bone. The argument linking bone gain to protection from fracture is intuitive. Bone density rises in people taking these drugs, and treatment reduces fractures. In reality, however, cause and effect are far from established. The three most recently published multicentre fracture prevention trials—for alendronate,⁴ risedronate,⁵ and raloxifene⁶—report similar rates of fracture prevention (40-50%) for very different gains in bone density (2.4-8.2%). What characterises all three trials, however, is a reduction in the markers of resorptive activity by 30% or more within six months. Furthermore, 12 month data, which were available only for risedronate,⁴ showed that the risk of fracture had fallen well before bone density peaked.

The pathology in osteoporosis is one of high bone resorption, not one of low bone density, which is a variable consequence. The evidence suggests that the strength of bone lies with the integrity of its architecture and with its level of turnover, not merely with its mass. High turnover of bone seems to be intrinsically unstable, whereas low density bone need be weak only if its low mineral content results from chronically high bone turnover. Postmenopausal Chinese women, for example, have significantly lower hip bone mineral density than white women and are classified at higher risk, but in fact they have fewer fractures.^{7,8} Their rate of bone loss is reportedly slower, suggesting a lower rate of turnover.

The prevention trials suggest that antiresorptive drugs can halve the risk of fracture in the most osteoporotic bones without restoring significant density. Although change in bone mineral density may relate to reduction in risk of vertebral fracture,^{9,10} the evidence is weak for the hip. In many instances, the

Department of
Medicine,
Postgraduate
Medical School,
Derriford Hospital,
Plymouth PL6 8DH
Terence J Wilkin
professor of medicine
Devasenan
Devendra
specialist registrar

Correspondence to:
T J Wilkin
TWilkin@
plymouth.ac.uk

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modest gain in bone density after antiresorptive treatment is insufficient even to reclassify the patient, whose bones remain osteoporotic despite a significant reduction in their risk of fracture.

Fall in bone density with age contributes little to rise in fracture risk

A Dutch study of 5800 healthy men and women over the age of 55 years observed a 13-fold increase in the risk of femoral neck fracture between the ages of 60 and 80 years.¹¹ Multiple regression analysis was used to determine the contribution to the rise in risk of fracture made by the corresponding fall in density of bone. In women, the loss of bone density associated with age contributed only 1.9 (95% confidence interval 1.5 to 2.4) and in men 1.6 (1.3 to 1.8). Thus, 85% of the rise in risk of fracture in ageing women is attributable to something other than the loss of bone density. This study was cross sectional and should be evaluated with this in mind. It was, nevertheless, statistically powerful and involved merely observation of an unselected general population.

The same group compared the predictive value for hip fracture of combining anthropometry (a measure of thinness) and a risk score with and without bone densitometry.¹² The area under the receiver operating characteristic curve, indicating discriminatory power, was good in both cases, but not significantly different (0.83 and 0.88 respectively). Bone densitometry added little to a questionnaire in the prediction of hip fracture.

Relation between bone density and fracture risk is age sensitive

The widespread use of T scores to infer risk of fracture from bone density is based on the concept of fracture threshold. Postmenopausal bone density measurements are referred to the young adult norm in the densitometer's software and expressed as standard deviation scores of the young adult mean. The fracture threshold, the WHO definition of osteopenia, is set arbitrarily at -1 standard deviation score, which reflects an absolute bone density. There is no evidence, however, that the risk of fracture relates to the same bone density throughout life. Indeed, Hui and colleagues cross classified incident fractures with age and bone mass and found age to be a better predictor of hip fracture than radial bone density.¹³ De Laet et al confirmed the independent contribution that age makes to risk of hip fracture using dual energy x ray absorptiometry.¹¹ A fracture threshold has little meaning when the risk of fracture to hips of the same bone density varies several fold over the postmenopausal age range.

Age is itself a robust predictor of risk of fracture, irrespective of previous treatment with antiresorptive drugs. The belief that taking antiresorptive drugs in middle age is an investment against fracture risk later on, seems ill founded. Protection against fracture is demonstrable within a few months of starting treatment but is lost again within five years of stopping it.¹⁴ There seems to be no age beyond which antiresorptive drugs are ineffective but no point in starting them earlier than the emergence of fracture risk.¹

Screen shot of densitometry scan of osteoporotic hip

Epidemiological argument is flawed

Randomised controlled trials show that antiresorptive drugs reduce the risk of fracture. The rate of fracture could be reduced by either treating the whole population or targeting those at highest risk. Universal treatment, even if workable, is wasteful and expensive. Use of bone density to target treatment at high risk patients has therefore been widely advocated. Even though the cost of bone densitometry represents a tiny fraction (perhaps 0.1%) of the treatment that may ensue, screening with bone densitometry has long been deemed uneconomic in the United Kingdom, and use of clinical guidelines to select appropriate cases is encouraged.¹⁵

All of this, however, neglects flaws in the way epidemiological evidence is applied to support bone densitometry. Firstly, the evidence that bone density predicts fracture is based on studies of large populations. Clinicians, on the other hand, treat individuals and, although each person must by the nature of randomisation own some part of the population risk, the confidence with which bone density can be used to predict fracture in the individual is arguably negligible. Only if treatment is offered to a population can the outcome be expected to reflect the generality of population based data.

The statistic so often quoted in support of bone densitometry comes from epidemiology. It suggests that for each standard deviation decrease in femoral neck bone density, there is a 2.6 times increase in the age adjusted risk of hip fracture (95% confidence interval 1.9 to 3.6).¹⁶ Women with bone density in the lowest quarter had an 8.5-fold greater risk of hip fracture than those in the highest quarter. The data seem impressive but are based on just 65 women who sustained a frac-

ture out of 8134 observed. Treatment of the entire 8000 with an antiresorptive drug (assuming acceptance, compliance, and a budget) could be expected to save a maximum 33 fractures (a generous estimate as the 50% reduction in fractures claimed for bisphosphonates is based on populations already selected for low bone density or existing fracture). Alternatively, 8000 scans to classify the 2000 women in the lowest quarter of bone density would, according to the trial data, identify only 34 of the 65 who suffered fractures,¹⁶ and only half (or 17) of these fractures could be prevented by drugs. Bone densitometry can tell us about populations, but the chances of predicting a preventable fracture by bone densitometry in an osteoporosis clinic of largely self referred individuals must be close to random.

Secondly, the epidemiological data relating bone density to fracture risk is derived mainly from short term studies, which are by their nature limited to association, not prediction. Individuals lose bone density at different rates throughout later life, so that even the epidemiological relation between current bone mineral density and future fracture risk breaks up progressively with time.¹⁷

Finally, epidemiological studies tend to compare the bone densities of people in a large cohort who have had fractures with the densities of people who have not. In order to do so, they correct the bone density measurements for age with a z score but do not correct the other age related factors that contribute to risk of fracture. In the study by Cummings et al, the mean age of people who had a fracture (76.4 years) was significantly greater than the age of people who did not (73.2 years).¹⁶ Bone density was corrected for the age difference, but nothing else was. The omission is important because some 85% of the contribution to the rise in fracture risk with age is unrelated to bone density. It will overestimate the contribution which bone density makes to risk of fracture, perhaps seriously, by attributing to bone density other (more powerful) factors that are independent of it. Epidemiology provides data on the burden of disease. It is for the medical community to apply the data appropriately, but in the case of bone densitometry it clearly is not doing so.

Conclusion

The ability of bone densitometry to predict future fracture is overstated, and the data on which such claims

are based are overinterpreted. Bone densitometry is a major industry (an estimated 34 000 densitometry machines were in existence worldwide in 2000), and much of the research into osteoporosis depends on it. Clinical trials test efficaciousness (can it work?) in selected groups. The clinician is concerned with effectiveness (does it work?) in unselected individuals. The challenge is to show the latter.—Terence J Wilkin, Devasenan Devendra

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AGAINST We do not argue against the need for more correct use and interpretation of bone densitometry. Indeed, the current practice of relying on a T score definition to diagnose osteoporosis at the individual level is a major concern.¹ But let it be clear that the World Health Organization T score criteria were proposed for use in epidemiological studies, for comparison between populations all over the world, and for defining some thresholds for including subjects in clinical trial. They were not intended for diagnosis or treatment decisions in individual cases.

The value of bone densitometry as a diagnostic test lies in its ability to provide objective information of

practical relevance in clinical management. Bone densitometry is at present the best validated method for predicting fragility fractures, with lumbar bone mineral density predicting spinal fractures and proximal femur density predicting hip fracture. As with all measurements influenced by ageing, race, and sex, there is no clear cut-off between "organ failure and reduction in organ reserves." Therefore, the bone density results have to be interpreted in relation to the individual clinical findings.

There are many other risk factors for fragility fracture. These are less strong but add, in a cumulative way, important information to the overall decision making

Department of Rheumatology, Universitaire Ziekenhuizen K U Leuven, B-3000 Leuven, Belgium
Jan Dequeker
professor emeritus
Frank P Luyten
professor

Correspondence to:
J Dequeker
jan.dequeker@med.kuleuven.ac.be

Cumulative effect of independent risk factors on fracture rate (%) among women in different spinal bone mineral density thirds. Independent risk factors were previous fracture, no hormone replacement therapy, or ≥ 3 chronic diseases. Reproduced with permission²

process to start prevention or treatment of osteoporosis. This has been clearly shown in a recent prospective study of 3068 women aged 47-56 years over 3.6 years in Finland (figure).² Although being in the lowest third of bone mineral density of the spine predicted occurrence of fracture better than presence of three independent risk factors, having both these features increased the predictive value of spinal bone mineral density by 250% and of three independent risk factors by 360%.

Fractures other than hip should be considered

Although hip fractures before the age of 65 are rare, other fractures are not. In the European vertebral osteoporosis population study, 33% of the participants over the age of 50 years had a hip fracture.³ Hip fractures are more related to ageing than vertebral, wrist, and other fragility fractures (rib, humerus, etc). Men have fractures at a younger age than women, and corticosteroid induced fractures are not rare in any age group.

The WHO task force on osteoporosis management agrees that screening by densitometry before the age of 65 is not cost effective. But screening of high risk patients (case finding through education) is thought to be cost effective, in particular at age 70 in people who already have a low bone mass together with other risk factors such as low body weight, previous fracture, or family history.⁴

Osteoporosis is not always postmenopausal

Osteoporosis is the end stage of a number of pathophysiological processes and is not always postmenopausal. To concentrate only on bone resorption, leaving out bone formation, is shortsighted and without scientific basis.

Bisphosphonates and hormone replacement therapy are not the only treatments for prevention or management of osteoporosis. Much cheaper treatments include thiazides, vitamin D, dairy products such as milk (calcium at night), hip protectors, and physiotherapy. There is evidence based data that these

treatments all prevent fracture.⁵⁻⁷ A relatively expensive but effective intervention with substantial non-compliance may prevent fewer fractures than an inexpensive, safe, and somewhat less effective intervention with a higher compliance.

Relation between fracture protection and bone mass gained

The relation between protection against fracture and bone mass gained through treatment is debatable. However, evidence based data indicate that fracture protection is related to the gain in bone mass⁸ and that bone strength is more strongly correlated with areal and actual bone density than with architectural values.⁹ But it is still possible that quality differences in bone composition contribute to bone strength and can be altered by drugs such as vitamin D, oestrogens, and fluoride.¹⁰

The evidence at present is that bone strength lies in its bone mass, geometry, architecture, and composition. Lowering bone turnover over a long time with strong antiresorptive drugs such as bisphosphonates will induce hypermineralisation of osteons, which may result in microcracks.¹¹ The relative contribution of bone density to mechanical competence is also species dependent and relates to differences in bone composition.¹²

Effect of age

It cannot be argued that age is the main risk factor for fracture because physiological ageing is not equal for everyone. About 70% of the bone mass is genetically determined,¹³ and comorbidity, lifestyle, and use of corticosteroids over a lifetime will interfere with the physiological effects of ageing.

Nevertheless, the fall in bone density with age makes an important contribution to risk of fracture for at least some fragility fractures. The study by De Laet et al, which appears to show that this is not true for hip fractures, is a cross sectional study and therefore does not show a real fall in density.¹⁴ Cross sectional studies are subject to a cohort effect; participants could have already had a low bone mass from adult age. This together with lifestyle changes and falls might explain why differences in density did not explain the risk of fracture. It is not surprising that thinness and risk score may give important information in line with what bone density can measure. But measurement of bone mineral density can still be useful to select further high risk cases because the best reduction in fracture with drugs occurs in people in the lowest third of bone mineral density.¹⁵

The risk gradient for fracture roughly doubles for each decade's decrease in bone mineral density after age 50. The fracture threshold is set so that appropriate prevention is possible, but of course not everyone who is at risk will have a fracture. That ageing is an independent contributor is not surprising, because frailty increases with age, raising the risk of falls and failure of other organ systems. These are important elements for hip fracture. Because antiresorption drugs have to be given lifelong, they are now usually started close to the time when fractures occur or after the first fracture has occurred.

Interpreting the science

Although the chances of predicting a preventable fracture by bone densitometry may be small, it is also important that two thirds of patients can be reassured that fracture is less likely and therefore long term treatment is not needed. That there is overuse, overdiagnosis, and overtreatment for osteoporosis is due not to bone densitometry or to epidemiological reports but to various factors, including pressure of some competing pharmaceutical companies and the uncritical medical society relying more on technical instrumentation than on clinical skills and reasoning. As Wilkin and Devendra assert above, effectiveness is critical in daily clinical practice.—Jan Dequeker, Frank P Luyten

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Complexity science

Coping with complexity: educating for capability

Sarah W Fraser, Trisha Greenhalgh

Recent high profile scandals in the United Kingdom have highlighted the changing values by which the National Health Service is judged.¹ The public expects, and the government has promised to deliver, a health service that is ever safer, constantly up to date, and focused on patients' changing needs. Successful health services in the 21st century must aim not merely for change, improvement, and response, but for changeability, improvability, and responsiveness.

Educators are therefore challenged to enable not just competence, but also capability (box). Capability ensures that the delivery of health care keeps up with its ever changing context. Education providers must offer an environment and process that enables individuals to develop sustainable abilities appropriate for a continuously evolving organisation. Recent announcements in the United Kingdom of a "university for the NHS,"² a "national leadership programme,"³ and "workforce confederations"⁴ raise the question of what kind of education and training will help the NHS to deliver its goals

Capability is more than competence

Competence—what individuals know or are able to do in terms of knowledge, skills, attitude

Capability—extent to which individuals can adapt to change, generate new knowledge, and continue to improve their performance

Summary points

Traditional education and training largely focuses on enhancing competence (knowledge, skills, and attitudes)

In today's complex world, we must educate not merely for competence, but for capability (the ability to adapt to change, generate new knowledge, and continuously improve performance)

Capability is enhanced through feedback on performance, the challenge of unfamiliar contexts, and the use of non-linear methods such as story telling and small group, problem based learning

Education for capability must focus on process (supporting learners to construct their own learning goals, receive feedback, reflect, and consolidate) and avoid goals with rigid and prescriptive content

This is the last in a series of four articles

5 Cuddington Road, Dinton, Aylesbury, Buckinghamshire HP18 0AB

Sarah W Fraser
visiting professor,
Middlesex University

University College
London, London
N19 3UA

Trisha Greenhalgh
professor of primary
health care

Correspondence to:
S W Fraser
sfraser881@aol.com

Series editors:
Trisha Greenhalgh,
Paul Plsek

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The principles of complexity theory introduced earlier in this series (box) are explicitly or implicitly espoused in a series of NHS documents covering continuing professional development and lifelong learning⁵; learning networks⁶; quality improvement and organisa-