screening in women over 65 years, based on cost-effectiveness analysis.[4] In addition, treatment of women with risk factors other than a prior fracture is cost-effective after the age of 65 years according to the European guidance.[5] Therefore, we have investigated the validity of the Dutch guidelines in women, after changing the original model: in the original guidelines, 1 risk point is given for the age 60–70 years and 2 points for the age of ≥70 years. Instead, we now gave 1 risk point for the age of ≥65 years. The original and adapted guidelines are shown in Table 2. Sensitivity, specificity, and predictive values of the adjusted guidelines for women are summarised in Table 3. Values were slightly higher if WHO criteria were used to define osteoporosis instead of the Dutch criteria. Furthermore, Table 3 shows that, when using a cut-off of 1, there is little benefit if age is increased from 60 to 65 years. However, instead of 60 (original), the use of 65 years (adapted) as a risk factor is recommended when taking into account cost-effectiveness.[5]

We showed that the clinical performance of the Dutch case finding instrument majorly improves with alternative use; sensitivity largely increases from 18% to 84%. Instead of missing five patients for each patient that is found with osteoporosis,[2] only one patient is missed for each six patients that are found. This implies that the majority of patients with osteoporosis will be referred for DXA and hence are properly diagnosed. However, PPV and specificity remain low. Low PPV can be explained by the low prevalence of osteoporosis in our relatively young population. Moreover, as we discussed in our previous paper,[2] an instrument with high sensitivity can be of great practical interest in primary care, even if PPV is low.

So far, there is no universal policy on case finding in Europe. We suggest that the Dutch College of General Practitioners revises its policy on prevention and case finding for osteoporosis.

Table 2. The original and adjusted Dutch osteoporosis guidelines for women.

Risk factor	Original score	Adjusted score
Established vertebral fracture	4	1
Long-term use of high dose of corticosteroids (>3 months; >7.5 mg/day)	2	1
Fracture after age of 50 years	2	1
Age >60 years	1	–
Age ≥65 years	–	1
Age >70 years	2	–
Hip fracture in first-degree family member	1	1
Weight <60 kg	1	1
Severe immobility	1	1

Table 3. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the adjusted Dutch osteoporosis guidelines in 345 women.

Cut-off	Criteria[a]	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV[b], % (95% CI)	NPV[b], % (95% CI)
1	WHO	85 (73–97)	51 (45–56)	15 (10–21)	97 (94–99)
	Dutch	79 (63–95)	49 (44–55)	10 (6–15)	97 (94–99)
2	WHO	48 (31–66)	84 (80–88)	24 (14–35)	94 (88–100)
	Dutch	46 (26–66)	83 (79–87)	17 (8–26)	95 (90–100)
3	WHO	24 (10–39)	89 (86–93)	19 (7–31)	91 (83–100)
	Dutch	25 (8–42)	89 (85–92)	14 (4–25)	94 (87–101)
4	WHO	21 (7–35)	91 (88–94)	19 (7–32)	92 (83–101)
	Dutch	21 (5–37)	90 (87–94)	14 (3–25)	94 (9–102)

[a]*WHO-criteria: DXA outcome is always based on T-scores. Dutch-criteria: DXA outcome is based on T-scores if age<70 years and on Z-scores of age ≥70 years.*

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A fractured service: will NOGG mend it?

Alun Cooper rightly points out the burdens of fragility fractures and the

difficulties that arise if we focus on the risk factor (osteoporosis) and not the end organ damage (the fracture).[1] The slow evolution of meaningful guidance from the National Institute for Health and Clinical Excellence (NICE) has attracted criticism as has its restrictive health economic model.

The suggestion that a solution presents itself in the new FRAX® algorithm[3] allied to new rival guidance from the National Osteoporosis Guidelines Group (NOGG) should be critically appraised.

Generic alendronate is now £20/year or about one-tenth of its cost when NICE first formulated their relevant technology appraisal, and cost-effectiveness arguments may now make it affordable for many more patients even if NICE may alter the model constantly. The suggestion by the NOGG authors however, that treatment should be considered in 24% of 50-year-old women and 47% of 80 year olds[1] may raise alarm bells for a number of reasons. How long should we treat these younger women with a 10-year fracture risk which is about four times lower than that needed to justify intervention in women of their mothers' age? The health economic model that underpins both NICE and NOGG assumes a 10-year cycle with 5 years' treatment and a 5-year offset of effect. Should we adopt that into clinical practice? No guideline or expert opinion has yet come out to support that over a potential 30-year time span until the modal age of hip fracture incidence. Do we know enough about the risks of long-term treatment with bisphosphonates? Do they all have the same offset of effect? It is, of course, in the adoption of an age-dependent risk gradient for intervention thresholds that NOGG differs significantly from practice in cardiovascular disease.

At the younger age margins, the 7.5% risk of 'major' osteoporotic fracture corresponds to an approximately 98% chance of not sustaining a hip fracture in the next 10 years. This may influence the decision of the patient and the physician to accept or recommend treatment. This uncovers the concern about the concept of 'major osteoporotic fracture: a forearm, humeral, hip, or clinical vertebral fracture. This is a very different morbid process in a 50 year old who is more likely to face a forearm fracture than an 80 year old at risk of hip or clinical vertebral fracture. Alendronate has not shown efficacy against forearm fractures in randomised controlled trials[3] or observational studies in the UK GPRD.[4] Do we know enough, on the other hand, about clinical efficacy in patients who may have a fragility fracture but not osteoporosis? In one of the pivotal alendronate studies there was no reduction in hip fracture risk among those with femoral neck bone mineral density (BMD) not in the osteoporotic range.[3] A recent re-analysis of the Fraction Intervention Trial data was not able to confirm that women identified on the basis of prior non-vertebral fracture after the age of 45 years with a mean age of just over 64 years and osteopenia had a reduced incidence of subsequent non-vertebral fracture.[5] The evidence cited[2] to support interventions in patients not selected on the basis of low BMD, as well as clinical risk factors, depends on studies in older people with a bisphosphonate not licensed for the treatment of osteoporosis, in studies involving patients at risk of glucocorticoid-induced osteoporosis or those not being treated with bisphosphonates at all.

FRAX® aims to inform treatment decisions on the basis of absolute risk and does this as well as can possibly be done at present in a way that is much more usable than the fearsomely complex iterations of NICE. However, the logical consequences of NOGG would be that 79% of those eligible for treatment according to the authors would be selected 'irrespective of fracture probability'.[2] This is because efficacy, effectiveness, and clinically appropriate treatment is assumed to exist for patients with a fragility fracture irrespective of their BMD. This does not put absolute fracture risk prediction, let alone reasonably sensible numbers needed to treat, at the centre of fracture prevention. NICE may have failed to adopt FRAX® and offer a potentially unethical approach to second line therapies, but it has the great virtue of insisting on the presence of osteoporosis alongside clinical risk factors before recommending treatment and this is where the best evidence-base lies. We have wasted several years arguing about the fine detail of NICE while making no progress in implementing what none of us disagree about: the secondary prevention of osteoporosis-related fragility fractures through a systematic approach, such as fracture liaison services backed up by primary care identifying the prior fracture population. Three national audits[6–8] and one primary care study in 3.4 million patients in a general practice setting[9] tell the same story: the care gap is wide and not getting any narrower.

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