Australian Government

Department of Health and Ageing

Australia and New Zealand Horizon Scanning Network

ANZHSN

AN INITIATIVE OF THE NATIONAL, STATE AND TERRITORY GOVERNMENTS OF AUSTRALIA AND THE GOVERNMENT OF NEW ZEALAND

National Horizon Scanning Unit
Horizon scanning prioritising summary

Volume 13, Number 4:

Vertebral assessment with DEXA: Screening for vertebral fracture during risk assessment for osteoporosis

June 2006

AHTA

Adelaide Health Technology Assessment

[add ISSN]
[add Publications Approval Number]

Electronic copies can be obtained from http://www.horizonscanning.gov.au

Enquiries about the content of this summary should be directed to:

HealthPACT Secretariat
Department of Health and Ageing
MDP 106
GPO Box 9848
Canberra ACT 2606
AUSTRALIA

The production of this *Horizon scanning prioritising summary* was overseen by the Health Policy Advisory Committee on Technology (HealthPACT), a sub-committee of the Medical Services Advisory Committee (MSAC). HealthPACT comprises representatives from health departments in all states and territories, the Australia and New Zealand governments; MSAC and ASERNIP-S. The Australian Health Ministers' Advisory Council (AHMAC) supports HealthPACT through funding.

This *Horizon scanning prioritising summary* was prepared by Tom Sullivan and Janet Hiller from the National Horizon Scanning Unit, Adelaide Health Technology Assessment, Discipline of Public Health, Mail Drop 511, University of Adelaide, South Australia, 5005.

PRIORITISING SUMMARY

REGISTER ID: **000209**

NAME OF TECHNOLOGY: **VERTEBRAL ASSESSMENT WITH DEXA**

PURPOSE AND TARGET GROUP: **SCREENING FOR VERTEBRAL FRACTURE DURING RISK ASSESSMENT FOR OSTEOPOROSIS**

STAGE OF DEVELOPMENT (IN AUSTRALIA):

- ☐ Yet to emerge
- ☐ Experimental
- ☐ Investigational
- ☐ Nearly established
- ☐ Established
- ☒ Established *but* changed indication or modification of technique
- ☐ Should be taken out of use

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

- ☐ Yes — ARTG number
- ☒ No
- ☐ Not applicable

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
United States	✓		
United Kingdom	✓		

IMPACT SUMMARY:

This prioritising summary investigates the effectiveness of dual energy X-ray absorptiometry (DEXA) in diagnosing vertebral fracture. The summary also investigates the health benefits of screening for vertebral fracture during risk assessment for osteoporosis.

BACKGROUND

Vertebral fracture is a serious health issue amongst the elderly with the condition associated with increased morbidity and mortality. The most notable risk factor for vertebral fracture is osteoporosis, a disease of the bone in which bone mineral density (BMD) is significantly diminished. The World Health Organization defines osteoporosis as a BMD measurement of 2.5 or more standard deviations below the mean BMD of healthy young adults (expressed as a T-score), as measured by DEXA. The presence of a vertebral fracture, independent of BMD, has also been shown to be predictive of future fracture risk (Klotzbuecher et al 2000). The identification of vertebral fracture in patients without osteoporosis, as defined by their T-score, may help to target additional individuals who will benefit from anti-fracture therapy. Unfortunately, it has been estimated that less than a third of vertebral fractures are diagnosed and

treated by medical practitioners (Cooper et al 1992). A large proportion of vertebral fractures go unnoticed because the symptoms are often not strong enough to warrant clinical investigation.

The standard method for diagnosing vertebral fractures is through the visual assessment of spinal lateral X-rays (produced using radiography) by either a radiologist or appropriately trained clinician. X-rays are assessed using one of a variety of grading systems, the most common being the semiquantitative method described by Genant (1993). There are three grades of vertebral deformity in the system, all related to the ratio of the anterior/posterior (AH/PH) and median/posterior (MH/PH) height. Grade one represents a 20 to 25 per cent reduction in any one ratio, grade two a 25 to 40 per cent reduction, and grade three a reduction of 40 per cent or more in any one ratio. The system allows for rapid assessment in the clinical setting, and unlike fully quantitative approaches, is capable of identifying false-positive vertebral fracture resulting from artefacts such as Sheuermann's disease (Duboeuf et al 2005). Despite being considered as a gold standard in the diagnosis of vertebral fracture, spinal lateral X-rays have not been recommended as a regular component of risk assessment for fracture. The primary reasons for this are the high costs and significant radiation dosages associated with radiography. It is typically reserved for patients either diagnosed with osteoporosis or reporting symptoms highly suggestive of vertebral fracture.

More recently, spinal imaging using DEXA has become available. Like radiography, the X-rays produced by DEXA can be assessed using a number of grading systems, including the semiquantitative method. Although the image quality is inferior, DEXA offers a number of advantages over standard radiography, including lower costs and radiation exposure (less than 40 μSv compared to 800 μSv from a spinal lateral x-ray), and greater convenience since the imaging can be performed at the same time as BMD measurement. For these reasons, many have recommended vertebral assessment by DEXA be performed in conjunction with the measurement of BMD as part of a standard fracture risk assessment. In clinical practice, such an approach may be particularly valuable in identifying fractures in patients with osteopenia or low bone mineral density (BMD T-score between -1 and -2.5) who otherwise would not be considered for anti-fracture therapy.

CLINICAL NEED AND BURDEN OF DISEASE

Osteoporosis is often referred to as a silent disease. Gradual loss of bone mass and deterioration of bone microarchitecture results in an increased susceptibility to fracture, often with little or no symptoms until the fracture occurs. Approximately 300,000 Australians have been diagnosed with osteoporosis, although many more have the condition without knowing it (DHA 2005). In 2001 it was estimated that more than 1.9 million Australians were suffering from osteoporosis and that this number would rise to three million by 2021 (Access 2001). In all age groups the prevalence of osteoporosis is higher in females than in males (Access 2001).

Studies have shown that fracture incidence rates increase exponentially with age, an occurrence attributable to age-related decreases in BMD and increases in the number of falls (Cummings & Melton 2002). Of those Australians aged 60 years and over, more than 50 per cent of women and 30 per cent of men suffer a fracture due to osteoporosis (DHA 2005). The total number of fractures sustained each year by Australians aged 60 years and over has been estimated to be between 51,000 and 73,000 (Sambrook et al 2002). Of all diagnosed osteoporotic fractures, 46 per cent are in the vertebral region (Access 2001).

A number of studies have demonstrated that the existence of a prevalent vertebral deformity increases the risk of further fracture two- to fivefold, independent of BMD (e.g. Klotzbuecher et

al 2000). It has also been estimated that 20 per cent of patients who suffer a vertebral fracture experience a subsequent fracture within a year of the first (Brown & Josse 2002). In addition to further fracture, vertebral fractures have been associated with loss of stature, kyphosis, back pain, functional impairment, depression and higher morality rates (Cummings & Melton 2002). Despite these adverse outcomes, it has been estimated that less than a third of vertebral fractures come to the attention of medical practitioners (Cooper et al 1992).

DIFFUSION

DEXA is used extensively in clinical practice for the assessment of BMD. To perform vertebral fracture assessment on the various DEXA devices, additional software is required. To date, no DEXA devices have received marketing approval from the TGA for the purposes of vertebral fracture assessment. In the United States, DEXA devices that have received FDA approval for fracture assessment include GE LUNAR Corporation's Dual Energy Vertebral Assessment (DVA™) and Hologic's Instant Vertebral Assessment™

COMPARATORS

Radiography is currently considered the gold standard for the assessment of vertebral fracture. Although radiography offers superior image quality over DEXA, it is not a candidate for routine fracture risk assessment due to the high costs and radiation dosages involved. At present, fracture risk assessment is achieved using BMD measurements alone (Sambrook et al 2002).

EFFECTIVENESS AND SAFETY ISSUES

The most significant limitation of DEXA in screening for vertebral fracture is the poor image quality of the upper thoracic vertebrae. Visualisation of vertebral bodies in the T4 to T6 region is severely diminished due to the presence of ribs and increased X-ray spill over attributable to lung tissue in the area (Duboeuf et al 2005). As a result, fractures in this region often go undetected. In studies investigating the diagnostic qualities of DEXA, between 5 and 15 per cent of vertebrae are generally excluded from analysis due to poor image quality. A recent study by Binkley et al (2005) (level III-2 diagnostic evidence) of 80 postmenopausal women found that while 95 per cent of vertebrae from T7 to L4 were evaluable, a majority of vertebrae in the T4 to T6 region (66%) were not adequately visualised. Although the exclusion of poorly visualised vertebrae should be taken into account when assessing the diagnostic value of DEXA, it is worth noting that vertebral fractures in the T4 to T6 region are relatively uncommon (Melton et al 1989).

A number of studies have assessed the diagnostic accuracy and inter-rater reliability of DEXA scans for detecting vertebral fracture. Rea et al (2000) (level III-2 diagnostic evidence) compared DEXA scans to conventional spinal lateral radiographs in a group of 161 postmenopausal women, including those with normal BMD and those with multiple vertebral deformities. According to their DEXA scan, participants were divided into normal, equivocal and definite deformity groups. DEXA and radiography demonstrated good agreement (96.3%, $\kappa = 0.79$) in classifying vertebrae as either normal or deformed. DEXA also demonstrated good sensitivity (91.9%) in identifying moderate/severe vertebral deformities as shown by radiography, and an excellent negative predictive value (98%) when used to identify subjects without vertebral deformity. In another study, Schousboe and Debold (2006) (level III-2 diagnostic evidence) compared DEXA scans to radiography in a group of 205 women aged 65 years and over. In the study, the authors were interested in assessing the diagnostic qualities of DEXA and whether they would be affected by the presence of disc space osteoarthritis, a condition common amongst the elderly. Excluding participants with scoliosis, the sensitivity and specificity of DEXA in detecting participants with one or more grade 2-3 deformities, as detected by radiography, was 87-93 and 93-94 per cent

respectively. Although osteoarthritis was not shown to affect sensitivity, it did have a substantial impact on reliability. Using the entire sample, the inter-rater reliability for detecting a grade 2-3 deformity was acceptable for both radiography ($\kappa = 0.73$) and DEXA ($\kappa = 0.64$). After excluding participants with disc space osteoarthritis, the inter-rater reliability improved for both radiography ($\kappa = 0.76 – 0.82$) and DEXA scans ($\kappa = 0.70 – 0.78$).

Ferrar et al (2000) (level III-2 diagnostic evidence) compared DEXA scans to radiography in a group of 327 women, including 83 who had been diagnosed with osteoporosis. Using the entire sample, inter-rater reliability was moderate to poor for both radiography ($\kappa = 0.59$) and DEXA ($\kappa = 0.47$). In the osteoporotic group however, inter-rater reliability improved for both radiography ($\kappa = 0.86$) and DEXA ($\kappa = 0.79$). Treating radiography as the gold standard, DEXA demonstrated reasonable sensitivity (72 to 82%) and negative predictive value (90%) in the osteoporotic patients. The sensitivity dropped considerably however when the entire sample was considered (54 to 58%). Across this and a number of other studies, the diagnostic qualities of DEXA have been noted to vary according to the prior probability of fracture in the studied population (Duboeuf et al 2005). In general, the lower the probability of fracture in the studied population, the lower the sensitivity of the test is likely to be. Given that screening tests require high levels of sensitivity in order to rule out a positive diagnosis, it is likely that DEXA will only be appropriate for routine screening in subgroups which have a higher likelihood of fracture (Duboeuf et al 2005).

In addition to requiring satisfactory diagnostic qualities, a program of routine screening with DEXA as an adjunct to BMD measurement should be capable of identifying additional patients at risk of future fracture who would otherwise not be considered for anti-fracture therapy. Several studies have addressed this issue. Greenspan et al (2001) (level IV diagnostic evidence) investigated the prevalence of vertebral fracture, as measured by DEXA, in 482 asymptomatic postmenopausal women being screened for an osteoporosis study. Vertebral fractures were discovered in 18.3 per cent of women in the study. In the absence of DEXA scans, between 11 and 19 per cent of clinically osteoporotic patients (defined by a T-score of less than -2.5 or the presence of a low impact fracture) would have been classified as normal using BMD measurements alone. In a similar study, Vokes et al (2003) (level III-2 diagnostic evidence) obtained DEXA scans and measured BMD in a sample of 297 participants (272 women). Evidence of vertebral fracture was found in 55 subjects, of which only 56 per cent would have met the criteria for osteoporosis using BMD measurements alone. The results indicate that DEXA screening is a useful adjunct in the identification of clinical osteoporosis, providing a more comprehensive fracture risk assessment than would be afforded by the measurement of BMD alone.

COST IMPACT

At this stage, DEXA devices have not received marketing approval from the TGA to be used for the purpose of vertebral fracture assessment. As a result, the cost of the relevant software is currently unknown.

The cost impact of a routine program of vertebral fracture assessment in a high-risk population is currently unknown. It is possible however, that the additional costs associated with vertebral fracture assessment would be outweighed by a reduction in the number of spinal lateral X-rays required and cost savings associated with the prevention of future fractures.

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No issues were identified/raised in the sources examined.

OTHER ISSUES

An important issue in evaluating the effectiveness of a program of vertebral assessment using DEXA is the benefit associated with treating osteopenia patients (BMD T-score between -1 and -2.5) diagnosed with one or more vertebral fractures. Presumably it would be this group of patients and not patients with osteoporosis who would benefit from a routine screening program for vertebral fracture. Therapies currently available for the prevention of osteoporotic fractures include calcium and vitamin D supplementation, fall prevention education and antiresorptive drugs such as bisphosphonates (Access 2001). At present however, it is unclear whether any of these preventative strategies are effective in patients with BMD T-scores between –1 and –2.5. While a number of large-scale trials on bisphosphonates have included patients with low BMD and prevalent vertebral deformities (e.g. Ettinger et al 1999), separate results for this subgroup have not been reported.

CONCLUSION:

A program of screening for vertebral fracture using DEXA offers a number of potential health benefits. In an appropriate high risk subgroup, DEXA vertebral assessment may be particularly useful in identifying fractures in patients who would otherwise not have been considered for therapy. Advantages of DEXA include its convenience, low radiation dosage and low costs. In high-risk subgroups, DEXA has also exhibited high levels of sensitivity in the detection of vertebral fracture, an important property in any screening program. Despite the potential benefits of DEXA fracture assessment, a number of questions remain unanswered. In addition to uncertainty regarding the cost impact of vertebral fracture screening, it is not currently known whether anti-fracture therapy is beneficial for patients with low BMD. A further unresolved issue is precisely what population subgroup a screening program should apply to.

HEALTHPACT ACTION:

Given the uncertainties associated with this new use of DEXA, HealthPACT recommended that the technology be monitored.

SOURCES OF FURTHER INFORMATION:

Access (2001). *The Burden of Brittle Bones: Costing Osteoporosis in Australia*, Canberra.

Binkley, N., Krueger, D. et al (2005). 'Lateral vertebral assessment: a valuable technique to detect clinically significant vertebral fractures', *Osteoporos Int,* 16 (12), 1513-1518.

Brown, J. P. & Josse, R. G. (2002). '2002 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada', *Cmaj,* 167 (10 Suppl), S1-34.

Cooper, C., Atkinson, E. J. et al (1992). 'Incidence of clinically diagnosed vertebral fractures: a population-based study in Rochester, Minnesota, 1985-1989', *J Bone Miner Res,* 7 (2), 221-227.

Cummings, S. R. & Melton, L. J. (2002). 'Epidemiology and outcomes of osteoporotic fractures', *Lancet,* 359 (9319), 1761-1767.

DHA (2005). *Arthritis, Osteoporosis and Musculoskeletal Health* [Internet]. Department of Health and Ageing. Available from: http://www.health.gov.au/internet/wcms/publishing.nsf/Content/factsheet-arthritis.htm [Accessed 19th April].

Duboeuf, F., Bauer, D. C. et al (2005). 'Assessment of vertebral fracture using densitometric morphometry', *J Clin Densitom,* 8 (3), 362-368.

Ettinger, B., Black, D. M. et al (1999). 'Reduction of vertebral fracture risk in postmenopausal women with osteoporosis treated with raloxifene: results from a 3-year randomized clinical trial. Multiple Outcomes of Raloxifene Evaluation (MORE) Investigators', *Jama,* 282 (7), 637-645.

Ferrar, L., Jiang, G. et al (2000). 'Identification of vertebral deformities in women: comparison of radiological assessment and quantitative morphometry using morphometric radiography and morphometric X-ray absorptiometry', *J Bone Miner Res,* 15 (3), 575-585.
Genant, H. K., Wu, C. Y. et al (1993). 'Vertebral fracture assessment using a semiquantitative technique', *J Bone Miner Res,* 8 (9), 1137-1148.
Greenspan, S. L., von Stetten, E. et al (2001). 'Instant vertebral assessment: a noninvasive dual X-ray absorptiometry technique to avoid misclassification and clinical mismanagement of osteoporosis', *J Clin Densitom,* 4 (4), 373-380.
Klotzbuecher, C. M., Ross, P. D. et al (2000). 'Patients with prior fractures have an increased risk of future fractures: a summary of the literature and statistical synthesis', *J Bone Miner Res,* 15 (4), 721-739.
Melton, L. J., 3rd, Kan, S. H. et al (1989). 'Epidemiology of vertebral fractures in women', *Am J Epidemiol,* 129 (5), 1000-1011.
Rea, J. A., Li, J. et al (2000). 'Visual assessment of vertebral deformity by X-ray absorptiometry: a highly predictive method to exclude vertebral deformity', *Osteoporos Int,* 11 (8), 660-668.
Sambrook, P. N., Seeman, E. et al (2002). 'Preventing osteoporosis: outcomes of the Australian Fracture Prevention Summit', *Med J Aust,* 176 Suppl, S1-16.
Schousboe, J. T. & Debold, C. R. (2006). 'Reliability and accuracy of vertebral fracture assessment with densitometry compared to radiography in clinical practice', *Osteoporos Int,* 17 (2), 281-289.
Vokes, T. J., Dixon, L. B. & Favus, M. J. (2003). 'Clinical utility of dual-energy vertebral assessment (DVA)', *Osteoporos Int,* 14 (11), 871-878.

LIST OF STUDIES INCLUDED

Total number of studies	6
Level III-2 evidence	5
Level IV evidence	1

SEARCH CRITERIA TO BE USED:

Densitometry, X-Ray/methods
Thoracic Vertebrae/injuries/radiography
Bone Density
Absorptiometry, Photon/*methods
Lumbar Vertebrae/pathology/radiography/*radionuclide imaging