NICE advice

Bindex for investigating suspected osteoporosis

Medtech innovation briefing
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Summary

- The **technology** described in this briefing is Bindex, a portable pulse-echo ultrasound device used to help make decisions on the investigation and treatment of osteoporosis.
- The **innovative aspects** are that it is pocket sized and can be connected to and used with any laptop or desktop computer's USB socket. Unlike other quantitative ultrasound that measures sound speed and attenuation in the heel, Bindex makes measurements of the tibia applying thresholds of 90% sensitivity and specificity compared with axial dual-energy X-ray absorptiometry (DXA), to help with decisions on further tests and treatment for osteoporosis.
- The intended **place in therapy** would be to use Bindex alongside current algorithmic fracture risk assessment tools (FRAX or QFracture). If these suggest an intermediate or high risk of osteoporosis fracture, Bindex could be used to determine whether referral for DXA scan is needed (in the case of confirmed intermediate risk) or not (if low risk). Treatment could be considered for those at high fracture risk or high risk for osteoporosis as measured with Bindex.

- The **main points from the evidence** summarised in this briefing are from 2 diagnostic accuracy studies (1 US and 1 Finnish), including a total of 1,127 women in primary care. The studies show reasonable agreement for osteoporosis risk when determined in women with intermediate risk using FRAX and Bindex compared with FRAX and DXA.
- **Key uncertainties** around the evidence are that there are no prospective studies showing the effect of Bindex on the need for DXA scans, and limited data on the correlation between tibial bone thickness and femoral bone mineral density. Also, the Bindex density index threshold values are only validated in women of white European family origin, which may limit the generalisability of the results.
- The **cost** of Bindex is based on the software licensing needed. This includes buying the device itself. A licence per computer varies by number of analyses needed: £4,000 for 300 analyses, £6,000 for 500 analyses and £10,000 for 1,000 analyses.

The technology

Bindex (Bone Index Finland OY) is a pulse-echo ultrasound tool for the screening and diagnosis of osteoporosis. The device measures cortical bone thickness at the upper shaft of the tibia and calculates a density index from this measure alongside other clinical risk factors or patient characteristics. The density index is an estimate of hip bone mineral density (BMD). Bindex provides a way to stratify the risk of osteoporosis using thresholds for diagnosis recommended by the International Society for Clinical Densitometry (ISCD) and National Osteoporosis Society.

The handheld Bindex device is a transducer that can be connected to a computer or Windows tablet, through a USB cable. A custom ruler is used to measure to a point one third of the length of the proximal tibia from the knee joint, where the Bindex ultrasound measurement will be taken. Ultrasound gel is applied to the measurement site and the hardware is calibrated using the Bindex software. To take a measurement, the transducer is moved over the measurement site for a few minutes. Cortical thickness is estimated by multiplying the speed of sound by the time lag between ultrasound echoes from the front and back surfaces of the cortical bone layer. The transducer collects the sound waves reflected from the bone and transmits the signal to the connected computer, which immediately displays the results using the Bindex software. The Bindex measurement typically takes under 15 minutes to do.

Bindex software uses the cortical thickness measurement plus age, weight and height of

the person being measured, to calculate the density index. These values are displayed alongside pre-determined density index thresholds that estimate the probability of osteoporosis. Results are displayed using a 'traffic light' colour bar; green shows a low probability of osteoporosis and a low need for further investigation, yellow shows that more investigations are needed, and red shows a high risk of osteoporosis and a need for treatment without dual-energy X-ray absorptiometry (DXA). Results are saved in the Bindex database on the computer and can be exported in a PDF format.

Innovations

Bindex is a pocket-sized ultrasound that can be connected and used with any laptop or desktop computer's USB socket. Unlike other quantitative ultrasound that measures sound speed and attenuation in the heel, Bindex measures the tibia, and applies thresholds of 90% sensitivity and specificity compared with axial DXA, which are designed to guide further tests and treatment for osteoporosis.

Current NHS pathway

NICE guidance on osteoporosis recommends that fracture risk should be assessed using the World Health Organisation's fracture risk assessment tool (FRAX) or the QFracture questionnaire, which is a web calculator designed to calculate the risk of developing an osteoporotic fracture. People whose fracture risk assessment result is above a threshold for intervention should have their BMD (typically hip and lower spine [NHS Choices 2016]) measured using DXA. The BMD value can be used to recalculate FRAX to get an absolute risk value.

The intervention threshold for a proposed treatment is based on other guidelines, such as ISCD's guidelines for peripheral dual-energy X-ray absorptiometry in the management of osteoporosis.

If adopted into the current NHS pathway, Bindex could be used after FRAX or QFracture assessment, in people with suspected osteoporosis. People with a high or intermediate risk classification based on FRAX would be scanned using Bindex. People whose Bindex scan gave a density index value that showed a high risk of osteoporosis would then be referred for osteoporosis treatment, without needing a DXA scan. Only people whose Bindex scan gave a density index value indicating an intermediate risk of osteoporosis would be referred for a DXA scan.

NICE is aware of 1 CE-marked device (and 5 similar devices in development) that appear to fulfil a similar function as Bindex:

- OsCare Sono (Oscare Medical Oy).

Population, setting and intended user

Bindex is designed to help guide further investigations and treatment in people who may have osteoporosis. It could be used in the primary, secondary or home care setting (for example, on a home visit). Bindex would be used by a trained healthcare professional, likely to include GP practice nurses in primary care and community nurses. Training is needed before using the device.

Costs

Technology costs

The cost of the Bindex device is based on the software licence and varies depending on the number of analyses needed. Table 1 shows the cost per measurement, based on the manufacturer's estimated lifespan of the equipment of 5 years.

Table 1 Cost by licence type

Type of licence	Cost	Cost per diagnostic session
300 analyses	£4,000	£13.30
500 analyses	£6,000	£12.00
1,000 analyses	£10,000	£10.00

Assuming that the Bindex would be used by a community nurse specialist (band 6) or a GP practice nurse, the cost of a 15-minute appointment would be about £16 and £9, respectively (Personal Social Services Research Unit 2016).

Costs of standard care

In cases of suspected osteoporosis (NHS Choices 2016), a GP uses a free online or paper-

based risk assessment tool such as FRAX or QFracture; they may also refer the patient for a DXA scan. The resource use associated with a community nurse specialist or GP contact for an hour is valued at £65 and £236 respectively (Personal Social Services Research Unit 2016). Therefore, the cost of a 15-minute appointment would be £16 (with a community nurse specialist) or £59 (with a GP). The average unit cost of a DXA scan is about £61 (code RD50Z, NHS reference costs 2015).

Resource consequences

Bindex does not need servicing or regular maintenance, as long as it passes self-calibration, which is done as a part of each analysis. No extra equipment is needed other than a working computer and standard ultrasound gel. No other practical difficulties have been identified in using or adopting the technology.

A poster presentation of a model-based cost-effectiveness analysis comparing a diagnostic strategy with Bindex to one without (Asseburg et al. 2013) was found during the systematic review of economic evidence. A Finnish societal perspective was used and the model duration was 10 years. The theoretical model was evaluated for 5 patient cohorts: women with a BMI of 24, aged 65 years with previous fracture, and aged 75 years or 85 years with and without previous fracture. Fractures included wrist, vertebral, hip and other fractures.

Two strategies were compared. First, a standard of care strategy: FRAX and BMI assessment, followed by no treatment or DXA scan and then treatment or no treatment. This was compared with a second 'using Bindex' strategy: FRAX with BMI assessment, followed by no treatment or Bindex (and after Bindex: no treatment, DXA scan and treatment, or DXA scan and no treatment). Differences in cost effectiveness could be the result of differences in technology costs and the differences of specificity and sensitivity in the diagnostic pathways.

The screening cost saved in the Bindex strategy averaged €230 per patient (about £179 after adjusting for inflation and converting to pound sterling) across all cohorts. The Bindex strategy was relatively cost saving in all cohorts compared with the standard of care.

Regulatory information

Bindex was CE marked as a class IIa device in July 2013.

A search of the Medicines and Healthcare products Regulatory Agency website revealed that no manufacturer field safety notices or medical device alerts have been issued for this technology.

Equality considerations

NICE is committed to promoting equality, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. In producing guidance and advice, NICE aims to comply fully with all legal obligations to: promote race and disability equality and equality of opportunity between men and women, eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, marriage and civil partnership, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief (these are protected characteristics under the Equality Act 2010).

Women are at higher risk than men of developing osteoporosis, and particularly women who are older and post-menopausal. Women of Asian or European family origin are at a higher risk for osteoporosis than those of other ethnicities. Age, sex, and race are protected characteristics under the Equality Act 2010.

Clinical and technical evidence

A literature search was done for this briefing in accordance with the interim process and methods statement. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

Two studies including 1,127 people are summarised in this briefing. One study (Karjalainen et al. 2016) examined the association between dual-energy X-ray absorptiometry (DXA)

measurements at the proximal femur and Bindex (measured at the tibia), using a diagnostic threshold for the density index based on International Society for Clinical Densitometry (ISCD) and National Osteoporosis Society guidelines. The study by Schousboe et al. (2017) estimated the diagnostic accuracy of Bindex using the threshold density index from the Karjalainen et al. (2016) study.

Table 2 summarises the clinical evidence as well as its strengths and limitations.

Overall assessment of the evidence

The evidence comes from 2 large diagnostic accuracy studies with participants recruited in the USA and Finland. No UK studies were found. The current evidence shows reasonable agreement for osteoporosis risk when determined using FRAX and Bindex compared with FRAX and DXA, which is a relevant outcome for the NHS. Both studies include authors affiliated to and in receipt of funding from the manufacturer.

The relationship of cortical thickness and density index may vary in populations of differing ethnicities. Therefore the density index thresholds need to be validated in a wider population (including women and men of differing ethnicities). Additional prospective validation studies to explore if using Bindex would decrease the number of DXA referrals and increase diagnosis using the thresholds defined by Karjalainen et al. (2016) would also be useful.

Table 2 Summary of evidence

Karjalainen et al. (2016)	
Study size, design and location	572 women of white European family origin (aged 20 to 91 years). Diagnostic accuracy study, but it is unclear if the study was prospective or retrospective. Set in Finland.
Intervention and comparator(s)	Bindex compared with DXA; FRAX and Bindex compared with FRAX and DXA.

Key outcomes	The FRAX followed by Bindex approach showed 85% sensitivity and 79% specificity for treatment decisions based on the Finnish standard criteria, when compared with treatment decisions obtained by FRAX and DXA. The false negative rate of the FRAX followed by Bindex approach was 14.6%. Using the FRAX followed by Bindex approach, 84% (of the total number of women) avoided DXA tests with the Bindex approach. Reproducibility between Bindex operators was good.
Strengths and limitations	The comparator was similar to UK standard care, so some of the study results may be generalisable to the NHS. However, the study did not take into account the use of DXA for baseline measurements to monitor treatment efficacy. The same population was used to develop and validate the density index thresholds, so the results do not validate the performance of Bindex.
Schousboe et al. (2017)	
Study size, design and location	555 post-menopausal women (43% with hip osteoporosis, 57% without hip osteoporosis), to investigate diagnostic accuracy (recruited by mail from the local bone densitometry database), based in the USA.
Intervention and comparator(s)	Bindex compared with DXA.
Key outcomes	Using single- or multi-site density index measures (taken from the proximal and distal tibia and radius) could decrease the number of follow-up DXA by about 70% in post-menopausal women who were screened for hip osteoporosis. Multi-site and single-site density index measures were shown to have good sensitivity and specificity (80–82%).
Strengths and limitations	The study is from an American centre, so the results may not be generalisable to the NHS. Recruitment by mail has an effect on the participation of frail individuals with hip osteoporosis who could not travel to the clinic. The manufacturer states that measurements should be taken from the upper shaft of the tibia, but measurements were taken from other bones in this study.

Recent and ongoing studies

One ongoing trial was identified.

- Point-of-care osteoporosis diagnostics with Bindex pocket-size instrument and FRAX. ClinicalTrials.gov identifier: NCT01998737. Status: completed, waiting for results. Indication: osteoporosis. Devices: Bindex, DXA.

Specialist commentator comments

Comments on this technology were invited from clinical experts working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

Two out of 4 specialist commentators were familiar with this technology but none had used it before.

Level of innovation

Two specialists stated that this was a minor variation on existing technology. A third specialist said that the technology was novel, particularly because of its use as an initial assessment tool to complement FRAX and reduce dependence on dual-energy X-ray absorptiometry (DXA) imaging.

All 4 commentators agreed that users of Bindex would need some training, and 1 noted that if the device is used in a community setting (such as primary care centres and care homes), then a wide variety of allied health professionals would need training.

Potential patient impact

One specialist did not think the technology would benefit patients, in terms of treatment, patient experience or outcomes. Three specialists thought that Bindex may be useful for people who would have difficulties attending a hospital appointment for a DXA scan, such as people who are older, frail or have cognitive impairment. One specialist thought that Bindex would be useful for patients with intermediate FRAX risk.

One commentator noted that the available studies on Bindex only involved women of white

European family origin, and that this meant that this group of patients were likely to benefit most from this technology because its potential benefits had not been studied in other groups. Two specialist commentators stated that there is currently no prospective evidence showing Bindex can predict fracture risk, and that this evidence is essential for an investigative tool assessing osteoporosis because treatments are mainly aimed at reducing fracture risk.

Another specialist stated that Bindex would provide better patient experience in comparison with DXA, as well as reduced radiation exposure. However, 2 commentators noted that DXA imaging has very low radiation compared with other X-ray imaging and does not represent a significant risk.

Potential system impact

One specialist stated that Bindex would be most useful in a community bone health clinic setting, whereas another stated that it could be used by nurse specialists in primary or secondary care alongside FRAX as part of fracture liaison services. Using Bindex in a fracture liaison service could contribute to the reduction of future fractures.

The specialists did not believe any change in NHS infrastructure or facilities would be necessary for Bindex to be adopted in the NHS, but 1 commentator stated that this would depend on the services in the local area (for example, some areas manage bone health in a community setting).

One specialist did not think that the use of Bindex would result in cost savings for the NHS. Three of the specialist commentators agreed that using Bindex could result in fewer hospital visits for DXA scans, which are more expensive than Bindex and this could lead to cost savings. One specialist felt that savings are also likely to occur through reduced patient transport services (for example, elective ambulance journeys) attending these appointments. Reducing the demand for DXA scans could also reduce waiting lists in some centres with higher throughput.

One specialist stated that any costs saved by reducing the number of DXA scans would be countered by the cost of additional pre-screening using Bindex. They also said that the cost of treating hip fractures that might be missed by Bindex because of false negatives. They felt that its predictive value for hip bone mass density is only moderately good. Another commentator stated that the licensing options are restrictive, because a 'pay as you go' scheme would encourage adoption and pilot testing of the technology with less

financial risk.

General comments

One of the specialists stated that bone mass density measurements can vary between different anatomical sites, and there is not enough evidence to say whether the Bindex measurement at the tibia is comparable in predicting fracture risk to measurements at the hip or spine. This specialist also stated that more information on the concordance of Bindex with DXA and FRAX would be useful, particularly in understanding how BMD changes when it is measured with Bindex in comparison with DXA. More prospective studies on predicting fracture risk at non-spine and non-hip sites are needed, according to the specialist.

A second specialist commentator stated that anyone needing treatment should still have DXA imaging, even if Bindex is used. A third opinion was that including Bindex as a pre-screening tool would produce a less effective pathway overall. People who are found to be at high risk after an ultrasound but low risk after a DXA scan may raise anxiety and uncertainties about whether they need treatment. This specialist stated that there has extensive pathway redesign in recent years including significant increased capacity for DXA scans, and that the proposal to use Bindex would undermine existing NHS care pathways as well as having a negative effect on clinical and cost effectiveness.

Patient organisation comments

The National Osteoporosis Society gave the following comments.

Quantitative ultrasound technologies, such as Bindex, are quick and portable and have been used as a method of triaging patients for dual-energy X-ray absorptiometry (DXA). However, they noted that as quantitative ultrasound does not measure bone mass density, it cannot be used to diagnose osteoporosis as currently defined by bone mass density or bone mineral content. Online tools recommended in the NICE guideline on osteoporosis can incorporate measurements from DXA to improve fracture risk assessment, but the tool is not able to include quantitative ultrasound measurements.

They felt that Bindex would not streamline the diagnosis of osteoporosis, but instead would be an extra assessment and another appointment. People with a high-risk result from Bindex would still need a DXA scan to establish a baseline measurement to monitor

treatment efficacy. Bindex cannot measure changes in bone mass, and so people who are having treatment for osteoporosis after a high risk Bindex result, but do not have a baseline DXA scan, will have delayed treatment monitoring.

The patient organisation stated that some people may prefer Bindex to online fracture risk assessment tools and may see it as more rigorous. They said that information is shown in an aesthetically pleasing way on the screen, but it is unclear how easily the user or the patient would understand the results (for example, how risk thresholds are described by the tool).

The organisation recommended that Bindex is operated by staff trained in the use of quantitative ultrasound devices and that the results should be interpreted by a clinician with knowledge of osteoporosis management in healthcare settings (including community settings, care homes and home visits). They noted that the licensing is based on a cost per analysis, suggesting that Bindex would need to be done in dedicated clinics to be cost effective. This negates the advantage of being able to use Bindex in any setting.

They expressed concern about the lack of data for predicting fracture risk. Based on the proposed triage pathway, treatment management would be based on a measurement that has not been prospectively validated to predict fracture risk. Also, the data is limited because the intervention thresholds were taken from studies in Finnish women of white European family origin and cannot be extrapolated to other populations.

Bindex measurements correlate with DXA measurements, however the technology does not assess bone mass density and therefore the measurements cannot be assumed to be interchangeable. Further validation of the measurements in prospective fracture studies and wider populations are needed. According to the National Osteoporosis Society, Bindex does not add enough information or improvement to justify modification to the diagnosis pathway for osteoporosis.

Specialist commentators

The following clinicians contributed to this briefing:

- Dr Stephen Allsup, Consultant in Geriatrics and General Medicine, St Helens and Knowsley Teaching Hospitals NHS Trust. No conflicts of interest.

- Dr Simon Grint, Consultant in Orthogeriatrics and Geriatric Medicine, Wirral University Teaching Hospital NHS Foundation Trust. No conflicts of interest.
- Dr Rizwan Rajak, Consultant Rheumatologist, Croydon Health Service NHS Trust. No conflicts of interest.
- Professor Jon Tobias, Osteoporosis and Consultant Rheumatologist, Bristol NHS Foundation Trust. Professor Tobias has received speaker fees from pharmaceutical companies in the osteoporosis field (UCB, Eli Lilly).

Representatives from the following patient organisations contributed to this briefing:

- National Osteoporosis Society

Development of this briefing

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