Peripheral X-ray absorptiometry in the management of osteoporosis
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This practical guide applies to all types of X-ray absorptiometry measurements made in the peripheral skeleton (principally sites in the forearm, heel and hand). It is based on the expert opinion and clinical experience of the author, informed by the existing evidence base including research papers published in peer-reviewed journals.

Axial (hip and spine) dual energy X-ray absorptiometry (DXA) has become an important diagnostic investigation to identify those individuals who have low bone mineral density (BMD) in the skeleton at these sites, and so are at an increased risk of fracture. DXA may also be used to measure BMD at sites on the peripheral skeleton such as the forearm, hand and heel. Using data for a reference population of young, healthy people, BMD may be expressed as a quantity known as a T-score. The World Health Organisation (WHO) has defined osteoporosis in terms of the T-score when BMD is measured by DXA at the hip, spine or distal forearm. This definition does not apply to other bone densitometry methods such as quantitative computed tomography (QCT) or quantitative ultrasound (QUS), or to other anatomical sites in the skeleton such as the heel and hand.

Because of the perceived high cost of DXA for axial measurements and the need for patients to be referred to hospital-based facilities, the use of less expensive, smaller and portable equipment providing more convenient methods of evaluating BMD is appealing. A variety of X-ray devices for measuring peripheral sites in the skeleton are currently in use in the UK. For the results of peripheral X-ray absorptiometry measurements to be correctly interpreted, and so to avoid patients being wrongly classified as ‘osteoporotic’, and perhaps being inappropriately treated or not treated, the BMD values that most closely relate to those defined by the WHO for DXA of the hip and spine as indicating osteoporosis have to be specifically determined for each type of peripheral X-ray absorptiometry scanner. This document emphasises the preferable use of axial DXA, but the appropriate use and proper operation of peripheral scanners are outlined for where peripheral scanners are available, and a method to define the machine and site-specific BMD values at which to treat osteoporosis is described.

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Key recommendations

1. The current ‘gold standard’ for the diagnosis of osteoporosis is a dual energy X-ray absorptiometry (DXA) measurement of bone mineral density (BMD) at the hip (femoral neck and total hip) interpreted according to the World Health Organisation (WHO) definition of osteoporosis of a T-score of –2.5 or below. Measurements of lumbar spine BMD can also be used to diagnose osteoporosis, but in older patients the presence of degenerative disease may make the results difficult to interpret.

2. Clinical trials of bisphosphonate treatments show that they are only proven to be effective at preventing hip fractures in patients with osteoporosis at the hip or spine.

3. Measurements of BMD at sites in the peripheral skeleton (forearm, heel or hand) can be used to predict fracture risk.

4. Peripheral BMD measurements cannot be used with the WHO fracture risk assessment tool (FRAX).

5. The use of peripheral BMD measurements to diagnose osteoporosis and make decisions about patient treatment in a ‘stand alone’ capacity without the ability to refer patients for a hip and spine BMD examination is complicated by:
   • The poor correlation of peripheral measurements with hip and spine BMD
   • The different age dependence of T-scores at different skeletal sites.
   • The lack of evidence to show that fracture prevention therapy is effective in patients treated on the basis of a peripheral measurement.

   In view of these limitations peripheral BMD measurements alone should not be used for making treatment decisions and should only be used to select patients for treatment in accordance with Key Recommendation 6.

6. It is recommended that in centres where peripheral BMD measurements are used for performing clinical examinations they are interpreted using a triage approach. In this approach, device-specific upper and lower thresholds are chosen to have 90% sensitivity and 90% specificity for identifying patients with osteoporosis at the hip or spine. This means that 90% of patients who have a T-score of –2.5 or below at either the hip or spine have a peripheral measurement below the upper threshold, and 90% of patients who have T-scores of greater than –2.5 at both central sites have a peripheral measurement above the lower threshold. Based on these thresholds, therapeutic intervention is recommended as follows:

   a) If the peripheral measurement is below the lower threshold, treatment is recommended, especially if other major risk factors for osteoporosis and/or fractures are present.
b) If the peripheral measurement lies between the upper and lower thresholds, hip and spine BMD measurements should be performed to obtain a definitive assessment.

c) If the peripheral measurement is above the upper threshold, and no low trauma fracture is present, no further treatment is required and the patient should be reassured that their risk of fracture is low.

In practice it will be necessary for approximately 40% of patients to be referred for BMD measurements of the hip and spine.

7. Suitable thresholds for triage have been defined for some of the more common types of peripheral device and are presented in Appendix 2. If suitable device-specific thresholds are not available in peer-reviewed literature, it is recommended that local studies are conducted to establish these thresholds. Details of an appropriate methodology are also included with these guidelines in Appendix 2.

8. Spine BMD is the most sensitive bone mass measurement for monitoring response to treatment. In general, sites in the peripheral skeleton are not suitable for monitoring change.

9. Little, or no, information is available about the interpretation of peripheral BMD measurements in pre-menopausal women, men and children. It is recommended that at the present time the clinical use of peripheral X-ray absorptiometry is restricted to post-menopausal Caucasian women.

10. The use of any type of peripheral X-ray device must comply with the requirements of the Ionising Radiations Regulations (1999) and the Ionising Radiation (Medical Exposure) Regulations (2000). Equipment should be operated by a registered healthcare professional who has received appropriate training. Adequate attention must be paid to instrument quality control. The recommendation of any therapeutic intervention should only be made by a registered medical practitioner with specific knowledge of osteoporosis and its management.
**Introduction**

**Background**

Osteoporosis is recognised as one of the most serious problems in public health. Growing awareness of the impact of fractures on the lives of older people\(^1\), the consequent costs of healthcare\(^2\), and the development of new treatments for preventing fractures\(^3-6\) have all contributed to a growth in the demand for bone densitometry services. Today, scans to measure bone mineral density (BMD) have an essential role in the evaluation of patients at risk of osteoporosis\(^7-8\). In many osteoporosis clinics in the United Kingdom, the preferred method of investigation is to measure hip and spine BMD using dual energy X-ray absorptiometry (DXA)\(^8-10\). The reasons for this choice include the fact that hip BMD is the best predictor of hip fracture risk\(^11-12\); the use of spine BMD for monitoring treatment\(^13\); and the widespread consensus that spine and hip BMD results should be interpreted using the World Health Organisation (WHO) definition of osteoporosis of a T-score of –2.5 or below\(^10,14\). Of the two measurements, hip (femoral neck and total hip) BMD is often regarded as the preferred site for the diagnosis of osteoporosis\(^15\). This is because of the priority given to the prevention of hip fractures; the availability of reliable reference data for interpreting hip BMD results from the NHANES III study\(^16\); and the difficulty of interpreting spine BMD results in many older patients due to the presence of degenerative disease\(^17\).

Axial DXA systems that measure spine and hip BMD can also be used to assess BMD at peripheral sites such as the forearm. In addition to axial DXA scanners, a variety of different types of dedicated X-ray devices for measuring sites in the peripheral skeleton are also available\(^18\). These include peripheral DXA (pDXA) systems for measurements in the forearm, heel or hand, as well as radiographic absorptiometry and radiogrammetry methods for quantifying BMD from radiographs of the hand\(^19\). Guidance relating to the use of peripheral quantitative computed tomography (pQCT) is not included, as this technique is largely confined to research studies and is not used in clinical practice\(^20\). An alternative type of peripheral measurement, quantitative ultrasound (QUS), is the subject of separate National Osteoporosis Society guidance\(^21\). Because of the perceived high cost of DXA for axial measurements and the need for patients to be referred to hospital-based facilities, there continues to be an interest in small, low-cost X-ray absorptiometry devices dedicated to scanning the peripheral skeleton.

Historically, peripheral measurements were the first to be developed for the assessment of bone density\(^22\). In the 1960s, Cameron et al.\(^23\), introduced the technique of single photon absorptiometry (SPA), which used a radionuclide source to make measurements in the forearm. With the introduction of the first spine and hip DXA systems in the late 1980s, the same X-ray technology was used to improve the performance of SPA equipment by replacing the radionuclide source with a low dose X-ray tube. Today there is a variety of different commercial peripheral DXA equipment available for measurements in the forearm, heel (calcaneus) and hand. Technical advances have also improved the older methods of radiographic absorptiometry and radiogrammetry so that radiographs of the
hand and forearm can be scanned into a computer and the images processed to measure BMD\textsuperscript{24,25}. The ratio of cortical to trabecular bone varies according to the measurement site (Figure 1). In the mid-shaft of the radius there is only cortical bone, but the percentage of trabecular bone increases in more distal sites and reaches a maximum at the ultra-distal site. In contrast, the heel is mostly trabecular bone. With peripheral equipment there is a choice of measuring the right or left side of the body. Unless there is a contraindication such as a previous fracture at the measurement site, the usual convention is to measure the non-dominant limb.

One of the largest clinical investigations to use peripheral equipment was the National Osteoporosis Risk Assessment (NORA) study, which included 200,000 post-menopausal women who were measured with one of four different devices\textsuperscript{26,27}. Peripheral measurements are frequently used in centres providing a hip and spine DXA service since they offer an alternative measurement site in patients in whom one or the other central measurement is not diagnostic due to technical factors such as bilateral hip replacement, degenerative spinal disease or excessive weight (scanner tables have a weight limit). Forearm BMD measurements at the distal or one-third (33\%) sites (Figure 1) are used to measure cortical bone loss in patients with hyperparathyroidism\textsuperscript{28}. The one-third (33\%) site, for which the WHO definition of osteoporosis is applicable, is also the forearm BMD site recommended by the International Society for Clinical Densitometry (ISCD)\textsuperscript{29}.

\textbf{Figure 1} The percentages of trabecular and cortical bone at different BMD measurement sites.
Limitations

All types of DXA and pDXA equipment suffer from a number of technical limitations. Firstly, the resulting scan image is a two-dimensional (2D) projection of the true three-dimensional (3D) object. The BMD values are measurements of ‘areal’ density (bone mineral content (BMC) divided by projected area (units: g/cm$^2$)) rather than true density (bone mineral content (BMC) divided by volume (units: g/cm$^3$)). The measurements therefore reflect both bone size and true density, and this is a particular problem for interpreting results in children$^{30}$. A second limitation is that the algorithms used to calculate BMD from the high-energy and low-energy X-ray transmission parameters assume that soft tissue has a homogeneous composition. In reality, soft tissue is composed of lean and adipose tissue in varying proportions and with different X-ray attenuations. As a result, DXA and pDXA measurements of BMD are subject to accuracy errors whose magnitudes are assessed from *in vitro* studies$^{31}$.

Reference data and quality assurance

The availability of accurate and appropriate reference data is important in enabling the BMD results to be interpreted as T-scores and Z-scores$^{10}$. The need for reliable reference data has been a source of controversy in the past, when comparisons between T-score results in the hip for the two principal DXA manufacturers have shown clinically significant differences$^{32}$. This problem was solved by the manufacturers agreeing to use the NHANES III study hip reference data$^{16}$. Unfortunately, for many types of peripheral device there is no independent data to confirm the reliability of reference ranges provided by manufacturers. Another requirement is regular instrument quality control (QC) scans using a phantom. Many devices include an internal phantom that is used to calibrate every patient study. However, it is good practice to perform regular scans of an appropriate external phantom as an independent QC check. This should be done at least once a week and preferably every day that patient studies are performed.

Radiation safety

The radiation dose to patients from all types of pDXA equipment is very small, with effective doses below 0.1 $\mu$Sv$^{33}$. Correspondingly, the radiation hazard to staff operating equipment is also very low with the controlled area confined to the immediate area of the scanning field. Nevertheless, the use of any type of peripheral X-ray device must comply with the requirements of the Ionising Radiations Regulations (1999)$^{34}$ and the Ionising Radiation (Medical Exposure) Regulations (2000)$^{35}$. Equipment should be operated by a registered healthcare professional who has received appropriate training. Adequate attention should be paid to instrument QC. All requests for patient investigations must be justified by a practitioner entitled to act in this capacity by the employer. The recommendation of any therapeutic intervention should only be made by a registered medical practitioner with specific knowledge of osteoporosis and its management. Further information is given in Appendix 1.
Can peripheral X-ray absorptiometry predict the risk of future fracture?

Fundamental to the clinical role of BMD scans is the ability to assess a patient’s risk of fracture. The most reliable way of evaluating the effectiveness of any bone densitometry technique is through prospective studies of incident fractures\textsuperscript{11,12}. Such studies are analysed using a proportional hazards model in which the findings are expressed as the relative risk (RR), defined as the increased risk of fracture for a 1 standard deviation (SD) decrease in BMD\textsuperscript{11}. This relationship means that there is a continuous gradient of risk, with fracture risk increasing progressively as BMD decreases. As a consequence there is no value of bone density at which the fracture risk is zero and a significant percentage of all fractures occur in patients with osteopenia rather than osteoporosis (Table 1, p13)\textsuperscript{12,26}.

Figure 2 The relative risk (RR), defined as the increased risk of fracture for a 1 SD decrease in BMD, is an important factor that determines how effective a BMD measurement is at identifying patients at risk of fracture. (A) When BMD measurements are converted into Z-scores, the distribution of the general population is a bell-shaped curve with its peak at \( Z = 0 \). The curve for patients who will fracture has a similar shape but with its peak at \( Z = -\beta \), where \( \beta = \ln(\text{RR}) \). Values of \( \beta \) and RR are listed in the figure. (B) By integrating the two curves in (A), the percentage of fracture patients and the percentage of the general population whose BMD lies below any chosen threshold can be used to plot ROC curves that show the true positive cases (percentage of patients that sustain a fracture who were correctly identified as being at risk) against the false positive cases (percentage of patients identified as being at risk but who never have a fracture).

The importance of the RR value of a bone densitometry technique is apparent when the results of fracture studies are expressed using receiver operating characteristic (ROC) curves (Figure 2). The greater the value of RR for a given type of measurement, the more effective the technique is at identifying those patients who will subsequently suffer a fracture.
Results from fracture studies and meta-analyses provide important evidence for the effectiveness of peripheral BMD measurements for predicting fracture risk\(^{11,36}\). One such study, the Study of Osteoporotic Fractures (SOF), is especially useful because it allows a direct comparison of RR values for hip, spine, forearm and heel BMD measurements in a large group of Caucasian women aged 65 years and over\(^{12}\). Fracture studies are intended to verify fracture discrimination by showing that the RR value is significantly greater than 1.0. However, they often lacked the statistical power to compare the effectiveness of different types of measurement. The situation improved with the publication of the results of the SOF 10-year follow-up study (Figure 3)\(^{12}\). With several hundred fractures recorded at each of the principal sites (hip, wrist and spine), the statistical errors in the RR values are significantly smaller than in previous studies and allow improved comparison between the different types of measurement.

The new data:

- Strongly support the ability of peripheral BMD measurements to predict 10-year fracture risk.
- Confirm, with much greater reliability than previously, that hip BMD is the most effective way of predicting hip fracture risk.
- Show that, for predicting fracture risk at any skeletal site, different BMD measurement sites are equally effective.

The importance of the RR value for the clinical effectiveness of BMD measurements is evident from the ROC curves plotted in Figure 2B. However, the exact operating point on the ROC curve is set by other considerations such as the choice of a particular diagnostic threshold, for example the WHO definition of osteoporosis as a T-score of −2.5 or below.
Can peripheral X-ray absorptiometry be used with the WHO Fracture Risk Assessment Tool (FRAX)?

FRAX offers a new approach to the use of BMD scans that seeks to improve decisions made about treatment by basing them on the 10-year probability of the patient sustaining an osteoporotic fracture. This has a number of advantages, including the targeting of osteoporosis treatment according to the patient’s risk of fracture and the incorporation of additional clinical risk factors, such as a history of previous fracture, to refine the algorithm for estimating fracture probability. Although combining BMD with clinical risk factors predicts fracture risk better than BMD or risk factors alone, the FRAX algorithm was developed solely using hip BMD measurements and does not permit the use of BMD data measured at peripheral skeletal sites.

Can peripheral X-ray absorptiometry be used for the diagnosis of osteoporosis?

In 2000 a Consensus Conference defined osteoporosis as a skeletal disorder characterised by compromised bone strength predisposing to an increased risk of fracture. Bone strength reflects both bone density, bone size and shape and bone quality, where quality is determined by factors such as architecture, turnover, microfractures and mineralisation. The definition of osteoporosis therefore retains BMD as one of several factors that contribute to overall skeletal integrity and together determine patients’ risk of fracture.

The current practice in bone densitometry is to express BMD measurements as T-scores and base their clinical interpretation on the WHO study group definition of osteoporosis. T-scores are calculated by taking the difference between a patient’s measured BMD and the mean BMD in healthy young adults matched for gender and ethnic group and expressing the difference relative to the young adult population SD:

\[
T\text{-score} = \frac{\text{Measured BMD} - \text{Young adult mean BMD}}{\text{Young adult standard deviation}}
\]

A T-score indicates the difference between the patient’s measured BMD and the mean BMD achieved by young adults. A negative T-score means either that the patient failed to achieve the optimum BMD as a young adult or has subsequently lost bone tissue due to the effects of ageing, disease or both. The WHO report classifies a patient as having osteoporosis if the T-score is –2.5 or below at the hip, spine or distal forearm (Table 1). A T-score greater than –1 is regarded as normal, while an intermediate state of osteopenia is defined by a T-score between –2.5 and –1. A state of established osteoporosis denotes osteoporosis as defined above but in the presence of one or more fragility fractures.
**WHO Category** | **T-score**  
---|---  
Normal | Above –1.0  
Osteopenia | Between –1.0 and –2.5  
Osteoporosis | Below –2.5  
Established osteoporosis | Below –2.5 with fragility fracture  

**Table 1** *WHO criteria using BMD T-scores to diagnose post-menopausal osteoporosis*

While there is a widespread consensus that DXA measurements of hip and spine BMD should be interpreted according to the WHO study group report\(^{10}\), the uncritical application of the WHO definitions of osteoporosis and osteopenia to other types and sites of measurement raises a number of serious difficulties. One of these is the relatively poor correlation between different types of measurement\(^{38,39}\), which leads to discordance in the classification of patients’ results as normal, osteopenic or osteoporotic when measurements made at different skeletal sites are compared. A second problem is that, even if discrepancies between individual patients are ignored, significant differences in the numbers of patients diagnosed with osteoporosis arise because of differences in the way in which the mean T-score changes with age at different measurement sites and between different measurement devices\(^{40}\). These issues will now be examined in turn.
The correlation between BMD measurements made at different skeletal sites is dependent on their distance apart in the skeleton. This is not unexpected, and taking into account the different composition and cortical/trabecular ratios in the various anatomical sites. Measurements made at closely related sites, for example adjacent regions of interest (ROI) in the hip, or the same ROI measured on the left and right sides of the body, correlate quite highly ($r = 0.8$ to $0.95$) (Figure 4A). For such measurements, the problem of discordant interpretation of T-scores is less serious and confined to cases close to the respective thresholds (Figure 4B). However, for measurements made at distant sites, for example the hip, spine, forearm and heel, the correlation is poorer and often lies in the range $r = 0.55$ to $0.65$ (Figure 4C). For such comparisons the problem of discordant T-scores is more serious since cases can arise in which patients classified as osteoporotic by one technique are found to be normal by another and vice-versa (Figure 4D). In evaluating the reasons for this discordance it should not be assumed that the peripheral measurement is always the one that is wrong. The problem is caused by unavoidable factors such as accuracy errors that affect all types of BMD measurements whether made at the hip, spine or a peripheral site. When evaluating discordant results in cases where there is no obvious technical explanation, it is important to bear in mind that the measurement with the higher RR value provides the better discrimination of fracture risk (Figure 2).
The second issue that arises from the comparison of results from different measurement sites is that the uncritical use of the WHO definition of osteoporosis can result in large differences in the percentage of patients diagnosed with osteoporosis. As applied to hip BMD, the WHO criterion of a T-score of –2.5 or below was intended to identify the 16% of post-menopausal women who will suffer a hip fracture. However, Lu et al., reported that, based on the WHO definition, the prevalence of osteoporosis in the SOF study population ranged from 3 to 60%, depending on the measurement site chosen. This problem was discussed in detail by Faulkner et al., who used reference data to plot the mean T-score as a function of age for different types of measurement. The age at which the mean T-score falls below –2.5 (when 50% of subjects are ‘osteoporotic’) varied from 55 to over 100. Figure 5 shows T-score graphs plotted using manufacturers’ reference data for forearm, heel and hand BMD for a number of different peripheral devices, which are shown compared with the NHANES III reference data for femoral neck and total hip T-score. It is clear that it is inappropriate to use the WHO T-score threshold of –2.5 to interpret the results from all types of measurement.

**Figure 5** Plots of mean T-score against age derived from manufacturers’ reference data for: (A) forearm BMD; (B) heel BMD; (C) hand BMD. In each plot the ‘gold standard’ curves for hip BMD (femoral neck and total hip sites) derived from the NHANES III study are shown for comparison.
Can peripheral X-ray absorptiometry be used to recommend treatment?

Women referred for hip and spine BMD measurements are often considered for treatment on the basis of the DXA results and other clinical considerations. Evidence for the effectiveness of several different types of treatment in preventing fractures has come from a number of large international trials for which subjects were enrolled using entry criteria that included a low baseline hip or spine BMD. Two of these studies, the Fracture Intervention Trial (FIT)\textsuperscript{42} and the Risedronate Hip Trial\textsuperscript{5}, reported that a statistically significant reduction in fracture risk was found only in those patients enrolled on the basis of a hip BMD T-score below –2.5 (Figure 6). More recently, studies of ibandronate and bazedoxifene showed benefits when patients were selected with a T-score below –3.0\textsuperscript{43,44}. Thus, the WHO definition of osteoporosis has achieved additional significance as a threshold for identifying those patients likely to respond to treatment. With the growing emphasis placed on evidence-based medicine, this finding has created a significant obstacle to the concept of treating patients on the basis of a ‘stand-alone’ peripheral measurement. For this reason, and taking into account the issues discussed in the preceding section, a ‘stand-alone’ approach in which peripheral measurements are used to make treatment decisions without reference to a patient’s hip and spine BMD is not recommended.

\textbf{Figure 6 Effectiveness of osteoporosis therapy shown as the relative risk of a new fracture for treated compared with untreated patients for: (Left): Any clinical fracture for patients in three ranges of femoral neck T-score\textsuperscript{41}; (Right): Hip fracture for patients selected on the basis of low femoral neck BMD and those selected on the basis of clinical risk factors\textsuperscript{5}. Only patients who fulfil the WHO definition of osteoporosis show a statistically significant response to treatment.}
The approach to the clinical use of peripheral measurements recommended by these guidelines is to integrate peripheral measurements with hip and spine DXA using a triage approach. In the triage approach, peripheral measurements are interpreted as normal, abnormal or equivocal, and patients with equivocal findings are sent for hip and spine measurements for a definitive diagnosis. To identify patients in the three groups it is recommended that device-specific upper and lower thresholds are set to achieve 90% sensitivity and 90% specificity for the identification of patients with osteoporosis at the hip and spine (i.e. 90% of patients with a T-score of −2.5 or below at the hip or spine are below the upper threshold and 90% of patients with T-scores greater than −2.5 at both central sites are above the lower threshold).

Based on these thresholds, therapeutic intervention is recommended as follows. If the peripheral measurement:

- Is below the lower threshold, treatment is recommended, especially if other major risk factors for osteoporosis and/or fractures are present.
- Lies between the upper and lower thresholds, then DXA hip and spine BMD measurements should be performed in order to obtain a definitive assessment
- Is above the upper threshold, and no low trauma fracture is present, then no further treatment is required and the patient should be reassured that her risk of fracture is low.

Although a triage approach for the interpretation of forearm BMD measurements using upper and lower thresholds of T = −1.0 and T = −2.5 has previously been recommended, the use of device-specific thresholds (defined by a set sensitivity and specificity) is preferred because it is an approach that can be applied to all types of peripheral measurement equipment and guarantees a reproducible level of diagnostic accuracy, irrespective of issues such as differences in the plot of mean T-score against age and the accuracy of the peripheral reference data. The method of setting the upper threshold is the same as that recommended by the International Society for Clinical Densitometry (ISCD), whose guidelines propose the use of a single upper threshold with 90% sensitivity.

In practice, for values of the correlation coefficient between peripheral and axial BMD in the range $r = 0.55$ to $0.65$ (Figure 4C), the triage approach with 90% sensitivity and specificity requires that around 40% of patients are sent for hip and spine DXA (see the Appendix 2). In clinical use, the triage approach will lead to some patients with osteoporosis at the hip or spine not receiving treatment, while other patients without osteoporosis are treated. However, these patients will tend to be those lying closely on either side to the hip and spine T-score threshold of −2.5 and so the use of the triage approach is unlikely to have any significant effect on the efficacy of treatment.

Suitable thresholds for triage based on 90% sensitivity and specificity have been defined for some of the more common types of peripheral device and are presented in Appendix 2. Where suitable device-specific thresholds are not available in peer-reviewed literature, it is recommended that local studies are conducted to establish them. An appropriate methodology is set out in Appendix 1.
Can peripheral X-ray absorptiometry be used to monitor response to treatment?

Most trials of bisphosphonate therapies have shown forearm BMD to be an insensitive site for monitoring response to treatment\(^5\). This is largely due to the distal measurement site being composed predominantly of cortical bone, which is some eight times less metabolically active than trabecular bone. However, a possible exception is the carefully defined forearm region of interest reported by Ravn \textit{et al.}\(^5\). This latter finding has not yet been confirmed by other independent studies.

With parathyroid hormone (PTH) treatment there is a paradoxical decrease in forearm BMD in response to therapy\(^6,54\). Treatment with strontium ranelate is known to increase BMD, an effect mainly resulting from the higher atomic number of strontium, which is taken up in bone and which attenuates X-rays more strongly than calcium\(^5\). However, there have been no studies reported yet of the size of the increase in forearm BMD following strontium treatment.

Little is known about the use of heel or hand BMD measurements for monitoring therapy, and until there is better evidence, no recommendation can be made about their use.

The results of many studies confirm that, taking into account both the magnitude of changes and the precision of the measurements, the best site for monitoring treatment is the spine\(^5\). Bone densitometry measurements should generally not be repeated at intervals of less than two years.

Can peripheral X-ray absorptiometry be used for clinical studies in pre-menopausal women, men and children?

The advice given in this guidance relates to the investigation of osteoporosis in post-menopausal Caucasian women. Little evidence is available on which to base equivalent recommendations for clinical use of peripheral measurements in pre-menopausal women and men. The effects of age, growth and pubertal status on BMD complicate the interpretation of results in children. The National Osteoporosis Society has issued a separate practical guide about the use of bone densitometry in children\(^30\).
Appendix 1:

Minimum standards for a peripheral X-ray absorptiometry service

**Organisation**

The service must comply with current regulations for the use of ionising radiation: the Ionising Radiations Regulations 1999[^34], the Ionising Radiation (Medical Exposure) Regulations 2000[^35] and the Ionising Radiation (Medical Exposure) (Amendment) Regulations 2006[^58]. The requirements include the need for a risk assessment, discussion with a Radiation Protection Adviser (RPA) and identification of duty holders.

At installation, all X-ray absorptiometry equipment should be subject to radiation and electrical safety checks.

Referrals for X-ray absorptiometry measurements should comply with guidelines of good and appropriate practice. The referrer must supply sufficient clinical and other information about the patient.

Each measurement (exposure to ionising radiation) must be justified by a practitioner (as defined by IR(ME)R 2000) who has received appropriate training and is entitled by the employer to act in this capacity. Furthermore, each patient request must be authorised to indicate that the exposure is justified; this may be done by the practitioner or an operator acting under written guidelines from the practitioner.

Operators must be qualified healthcare professionals (such as a nurse, radiographer or clinical technologist) and should be registered with a professional body. Operators must have received clinical training in osteoporosis and the basic principles of peripheral X-ray absorptiometry, in addition to having a detailed knowledge of their specific equipment.

A peripheral X-ray absorptiometry service should not be linked to the sale of dietary supplements or other products.

**Procedures**

All measurements should be carried out according to the manufacturer’s standard operating procedure.

Equipment must be subject to a regular service (at least once a year) and quality control measurements of a phantom (at least once a week) using the procedure recommended by the manufacturer.

The equipment must be stored and used in a secure place that is acceptable to the Radiation Protection Adviser (RPA). In the event of a malfunction, the equipment must be immediately withdrawn from use and arrangements made for its repair.

The names of all patients who have had peripheral measurements of bone mineral density must be listed in an up-to-date register. Although for many types of equipment the software in the scanner computer can be used for this purpose, not all devices are capable of recording patients’ names. Back-up of patient records on computer should be carried out routinely in case of system failure. Copies of the scan data and results should be retrievable at any time.

[^34]: Ionising Radiations Regulations 1999
[^35]: Ionising Radiation (Medical Exposure) Regulations 2000
[^58]: Ionising Radiation (Medical Exposure) (Amendment) Regulations 2006
Interpretation of results

Measurements are only appropriate in peri- or post-menopausal women who are at risk of osteoporosis.

The measurement of BMD by any method is only part of the necessary diagnostic and clinical service for osteoporosis. The complete service requires an experienced registered medical practitioner and a multidisciplinary team with a good understanding of the disease and its management.

The results of BMD measurements should only be interpreted by an experienced medical practitioner with specific knowledge of osteoporosis and its management. A registered healthcare professional with training and expertise in the clinical use of X-ray absorptiometry may assist the patient’s understanding of the results and provide advice on lifestyle and therapeutic options as appropriate.

As with other BMD measurements, the results need to be judged within each individual patient’s clinical history (e.g. with consideration of the patient’s medical history and other potential risk factors such as previous low-trauma fractures) before making any recommendations for treatment.

The medical practitioner reporting the BMD measurements to the referring clinician should provide a relevant clinical interpretation to facilitate the patient’s further management.

The recommendation of any therapeutic intervention should only be made by a registered medical practitioner with specific knowledge of osteoporosis and its management. He/she must take other relevant risk factors for osteoporotic fracture into account when reaching a decision on treatment and further management.
Appendix 2:

A method for determining appropriate scanner and site specific BMD values for the treatment of osteoporosis.

This appendix describes a method to establish device-specific upper and lower thresholds so that the triage approach can be used to identify patients with osteoporosis at the hip and spine with 90% sensitivity and 90% specificity. This means that 90% of patients with a T-score of –2.5 or below at the hip or spine are below the upper threshold and 90% of patients with both T-scores greater than –2.5 are above the lower threshold.

Before starting the study the approval of the local research ethics committee should be obtained.

In order to achieve sufficient statistical power in setting the thresholds, it is necessary to include at least 70 subjects with osteoporosis (i.e. with a T-score of –2.5 or below at either the hip or spine) and 70 subjects without osteoporosis (i.e. with both T-scores greater than –2.5). These numbers are sufficient to ensure with 95% confidence that the true sensitivity and specificity do not fall below 80%.

Subjects should be Caucasian female patients who meet the normal referral criteria for the peripheral bone densitometry service.

To ensure that patients in the appropriate age range are studied, subjects should be between 55 and 70 years old. Both the osteoporotic and non-osteoporotic groups should include subjects throughout the entire age range and the mean age for both groups should lie in the range 60 to 65 years.

To avoid bias in setting the thresholds, subjects for inclusion in the study must be randomly selected without any prior knowledge of their hip, spine or peripheral BMD. To achieve this, subjects must be enrolled before any BMD measurements are made.

It is recommended that the hip and spine measurements are performed first, since these define into which of the two groups subjects fall. When the required number is reached for one group, enrolment should continue until the second group is also full.

When the complete data is obtained, plots should be drawn showing the distribution of the peripheral T-score results of the patients in the two groups (Figure A1.A).

- The upper triage threshold is the peripheral T-score below which 90% of the osteoporotic subjects lie.
- The lower triage threshold is the peripheral T-score above which 90% of the non-osteoporotic subjects lie.

When using the triage approach, the percentage of patients who fall into the equivocal group and require hip and spine measurements will vary with the correlation coefficient between the peripheral and central BMDs (Figure A1.B). For values of the correlation coefficient in the range $r = 0.55$ to 0.65, this is expected to be between 35 and 45%.

T-score thresholds for a number of peripheral DXA scanners are given in Table A1.
Figure A1  (A) Results of a study to establish the upper and lower thresholds for peripheral T-score to identify patients with osteoporosis at the hip or spine with 90% sensitivity and 90% specificity. One hundred osteoporotic and 100 non-osteoporotic patients aged between 55 and 70 years were included in the study. The mean age of the osteoporotic group was 63.7 years and that of the non-osteoporotic group was 62.4 years. The upper cut point (T = -1.4) was chosen so that 90 out of 100 osteoporotic patients lie below this threshold (sensitivity = 90%). The lower cut point (T = -2.6) was chosen so that 90 out of 100 non-osteoporotic patients would lie above this threshold (specificity = 90%) (data supplied by Rajesh Patel). (B) Results of mathematical modelling to estimate the percentage of patients aged 60 who will fall within the equivocal group and require hip and spine BMD measurements, as a function of the correlation coefficient between peripheral and central BMD. A triaxial gaussian model was assumed.

Table A1

<table>
<thead>
<tr>
<th>Peripheral Device</th>
<th>BMD site</th>
<th>Number of osteoporotic women</th>
<th>Number of non-osteoporotic women</th>
<th>Upper triage T-score</th>
<th>Lower triage T-score</th>
<th>Axial DXA device</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alara Metriscan</td>
<td>Hand</td>
<td>70</td>
<td>100</td>
<td>-0.6</td>
<td>-2.4</td>
<td>GE Lunar</td>
</tr>
<tr>
<td>Demetech DXL Calscan</td>
<td>Heel</td>
<td>70</td>
<td>70</td>
<td>-1.4</td>
<td>-2.7</td>
<td>GE Lunar</td>
</tr>
<tr>
<td>Lunar PIXI</td>
<td>Heel</td>
<td>98</td>
<td>73</td>
<td>-0.4</td>
<td>-1.5</td>
<td>GE Lunar</td>
</tr>
<tr>
<td>Osteometer DTX200</td>
<td>Forearm</td>
<td>100</td>
<td>100</td>
<td>-1.4</td>
<td>-2.6</td>
<td>Hologic</td>
</tr>
<tr>
<td>Schick AccuDEXA</td>
<td>Hand</td>
<td>80</td>
<td>220</td>
<td>+0.1</td>
<td>-1.6</td>
<td>Hologic</td>
</tr>
</tbody>
</table>

Device-specific thresholds established using the methodology described above for different peripheral X-ray absorptiometry systems in use in the United Kingdom. The studies on each device were based on measurements of white female patients aged 55 to 70 years referred for hip and spine BMD examination. At least 70 women with osteoporosis at the hip and spine and 70 patients without osteoporosis were included in each study\textsuperscript{47,48}. 
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About us

The National Osteoporosis Society is the only UK-wide charity dedicated to improving the diagnosis, prevention and treatment of osteoporosis. The charity works to:

- Influence government and campaign to improve and maintain essential services.
- Provide a range of information resources including leaflets on all aspects of osteoporosis for you and your patients, some of which can be ordered in quantities for you to use in healthcare settings.
- Provide a helpline staffed by nurses with specialist knowledge of osteoporosis and bone health.
- Raise money to fund important research.
- Host a major UK scientific conference on osteoporosis for health professionals

Professional membership

Professional membership of the National Osteoporosis Society can make your job easier if you support people with osteoporosis or fractures, or are involved in research connected with osteoporosis.

Your professional membership will mean you can stay up-to-date with new treatments, care and the latest news on research. It means you’ll have a deeper understanding of the condition.

You can also feel proud to be part of an organisation working hard to help those affected by osteoporosis.

To find out more about becoming a professional member, call our membership department on 01761 473287 or visit us at www.nos.org.uk/professionals