



A pragmatic proposal for triaging DXA testing during the COVID-19 global pandemic

H.R. Sapkota¹ · A. Nune² · J. Bateman¹ · S. Venkatachalam¹

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Abstract

The COVID-19 pandemic has resulted in huge disruption to healthcare provision, including to dual-energy X-ray absorptiometry (DXA) imaging. Increased waiting lists for DXA from the pandemic mean potential long and uncertain delays in treatment for osteoporosis. To address these increased waiting lists, we propose a rapid, simple, one-stop algorithm incorporating medication use (aromatase inhibitor, corticosteroid) and clinical risk stratification supplementing a standard FRAX assessment. Our pragmatic algorithm produces a recommendation to treat empirically, image with DXA, or observe. If applied, we model a significant reduction in DXA scan requirements with a corresponding reduction in treatment delays for those awaiting DXA. We estimate this will reduce DXA scan numbers by about 50%, whilst pragmatically ensuring those with the highest clinical need correctly receive treatment without delay. This algorithm will help many clinicians including general practitioners/family physicians prioritise DXA when they may not always have the expertise to make this judgement based on clinical information alone. Although we have used UK guidelines as an example, this approach is flexible enough for adaptation by other countries based on their local guidelines, licensing, prescribing requirements, and DXA waiting list times. There are some limitations to our proposal. However, it represents one way of managing the uncertainty of the current COVID-19 pandemic.

Keywords BMD · COVID-19 · DXA · FRAX · Osteoporosis

Introduction

Significant healthcare disruptions due to the COVID-19 pandemic may continue for several months or even years. In the UK, routine outpatient appointments and investigations have been delayed due to the COVID-19 pandemic. Consequently, there is a prolonged wait for DXA scans due to the coronavirus restrictions in the UK. DXA is an important investigation

in the management of patients with osteoporosis but it is not essential for the diagnosis [1]. In December 2019 in England, 29,972 patients were waiting for a DXA, whereas after the lockdown in June 2020, this number had gone up by 50% to 45,072. Compared to June 2019, 73% fewer DXA scans were carried out in June 2020, which illustrates the scale of disruption caused by the COVID-19 pandemic [2]. The extent of disruption in delivering the DXA service may vary in different countries depending on the local prevalence of COVID-19 and healthcare delivery. We anticipate that DXA services could take several months to catch up with the backlog. Locally, in our hospital, covering a population of 750,000 across two sites, we perform 4700 DXA scans annually. We had 680 patients waiting for DXA at the beginning of the UK lockdown on 23 March 2020. Our planned capacity currently has reduced to 50% due to stringent infection prevention measures and social distancing.

In light of the significant reduction in capacity due to the COVID-19 pandemic, prioritising DXA for patients who need it most is one way to manage the demand. A model, where only selected patients based on their fracture risk and clinical parameters are scanned, could minimise COVID-19

✉ H.R. Sapkota
hem.sapkota@nhs.net

A. Nune
arvind.nune@nhs.net

J. Bateman
jamesbateman@nhs.net

S. Venkatachalam
s.venkatachalam@nhs.net

¹ The Royal Wolverhampton NHS Trust, Wolverhampton Road, Wolverhampton WV10 0QP, UK

² Southport and Ormskirk NHS Trust, Southport PR8 6PN, UK

transmission, protect patients, and prioritise those with the highest clinical need. The Royal College of Radiologists (RCR), UK, has recently published guidelines on the safe resumption of imaging services [3]. Their advice was to reserve the radiological investigations during the pandemic for patients based on clinical urgency. Prioritising DXA is different from other diagnostic cross-sectional imaging such as computed tomography (CT) or magnetic resonance imaging (MRI), as patients at high risk of a fragility fracture require treatment irrespective of imaging findings. We have produced a standard operating procedure (SOP) to prioritise DXA based on the probability of fracture risk and to effectively manage our backlog. Based on this, we outline a pragmatic approach in triaging DXA referrals and clinical decision-making which varies from the UK Royal Osteoporosis Society (ROS) DXA restoration toolkit published in June 2020 [4]. We believe this will benefit clinicians in primary and secondary care to make treatment decisions for patients with osteoporosis without a DXA during the current crisis.

Prioritising DXA based on fracture risk stratification over the telephone

All patients should have a telephone consultation to complete the web-based FRAX (Fracture Risk Assessment Tool) questionnaire preferably at the time of the DXA referral or upon receipt of the DXA referral during the COVID-19 pandemic [5]. Patients' age, gender, weight, height, and clinical risk factors obtained during the telephone consultation are used to calculate the 10-year probability of fracture risk using FRAX specific for the UK. Patients are then classified into low-, intermediate-, or high-risk groups as per the UK NOGG (National Osteoporosis Guideline Group) recommendations (Fig. 1). NOGG intervention threshold is age-dependent up to the age of 70 and a fixed threshold thereafter (20% major fracture and 5.4% hip fracture risk).

Low risk

These patients are unlikely to need intervention for osteoporosis, and therefore DXA is not indicated. If it is still clinically felt that a baseline DXA is useful, it could be deferred for several months depending on local healthcare facilities and the COVID-19 pandemic status.

Intermediate risk

In this group, treatment decisions need to be made based on bone mineral density (BMD). Therefore, these patients will benefit the most from a DXA which should be carried out with stringent infection prevention measures in place. Even in this group, understanding the limitations of FRAX for example, in

patients on high-dose steroids, reviewing previous imaging, if available, to evaluate for the presence of osteoporotic vertebral fractures will aid treatment decision without a need for an immediate DXA.

High risk

These patients are at high risk for fragility fractures and therefore should be treated without a DXA. DXA could be carried out once it is safe and appropriate to do so as it will be useful to have a baseline BMD to monitor or plan treatment changes in future. Osteoporosis treatment can be commenced without a need for DXA in postmenopausal women above the age of 65 years with a prior fragility fracture [6].22

Special situations

Aromatase inhibitor-associated bone loss

In total, 8.5% of patients referred for a DXA locally were on an aromatase inhibitor (AI) in the last year. Some of these patients may miss treatment for their osteoporosis if we solely rely on FRAX. FRAX is not designed to assess the fracture risk of women taking AI for breast cancer [7]. The FRAX estimates fracture risk substantially lower than would be expected when AI is grouped under 'secondary osteoporosis'. Our local guidance includes this important group of patients who are at high risk for osteoporotic fractures. According to the international joint position statement on aromatase inhibitor-induced bone loss published in April 2017, women on AI therapy with two or more of the following risk factors could be considered for treatment without a BMD: age over 65 years; current or past history of smoking; BMI < 20 kg/m²; family history of hip fracture; a personal history of fragility fracture > 50 years; and oral glucocorticoid use for > 6 months [7]. Of the 400 patients on AI referred for DXA locally, 40% satisfied the threshold for intervention with two clinical risk factors without a BMD. Women started on AI therapy should be considered for a DXA within 3 months of initiation of treatment [8]. We recommend a DXA as soon as it is safe and practical to do so as it may be difficult to achieve the 3-month target during the COVID-19 pandemic.

Glucocorticoid-induced osteoporosis

BMD loss is an immediate consequence of glucocorticoid (GC) therapy. Postmenopausal women taking GC therapy have considerably higher fracture risk as compared to women not on GC therapy for similar BMD values [9]. GC therapy is included in the FRAX tool as a dichotomous variable and does not take into account the dose effect on fracture risk. A simple adjustment to FRAX-derived fracture risk probability is

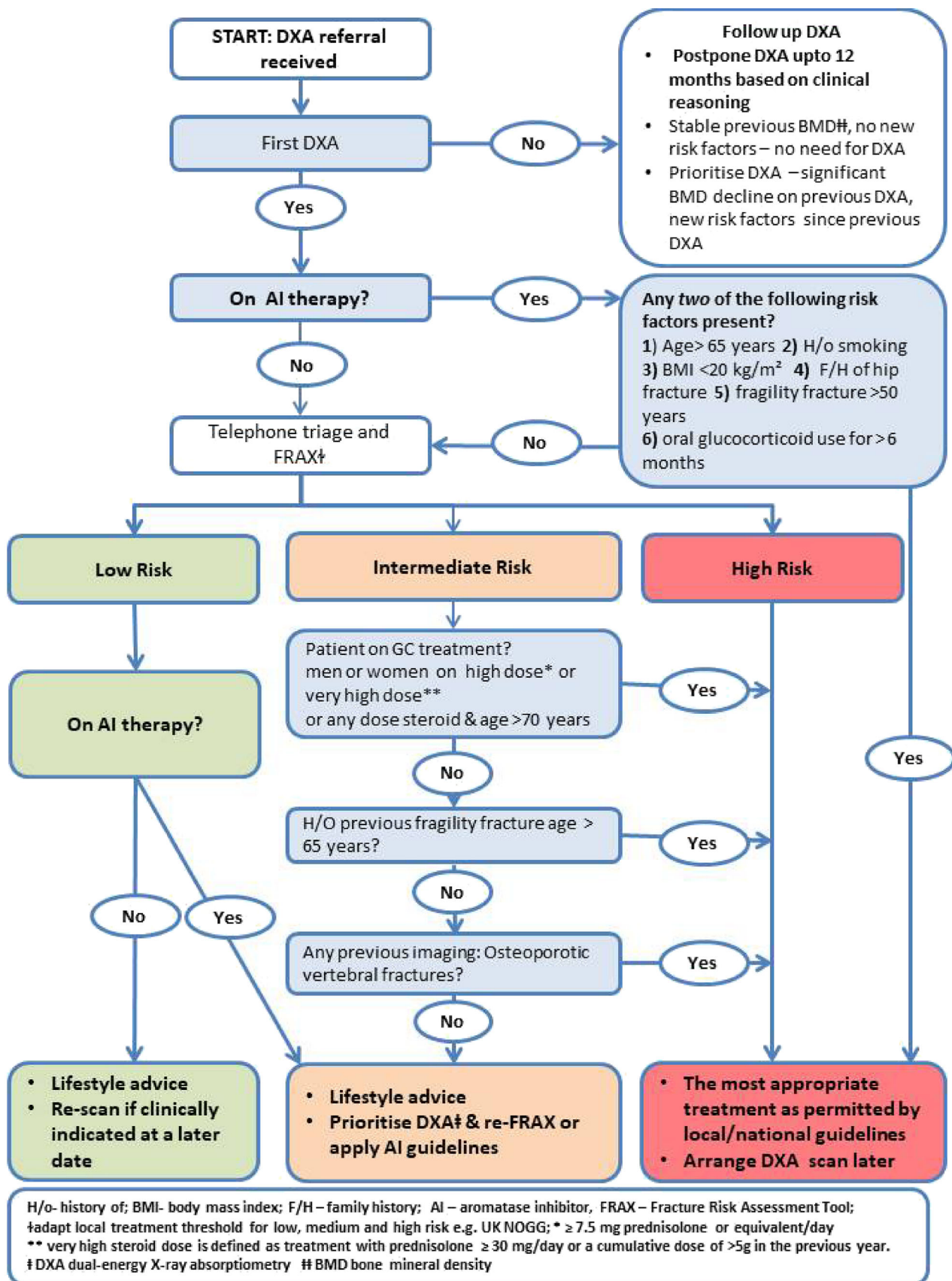


Fig. 1 Prioritising DXA scan based on fracture risk stratification

available for GC dose of < 2.5 mg, 2.5–7.5 mg, and > 7.5 mg daily [10]. Greater upward adjustment of fracture probability has been suggested for taking a higher dose of GC but no further details are available regarding adjustment factor [11]. The FRAX algorithm also does not take into account the duration of GC therapy and the cumulative dose. Hence, FRAX will underestimate actual fracture risk for patients taking high-dose GC therapy. NOGG guidelines recommend bone protective therapy for both men and women who are taking high doses of GC (≥ 7.5 mg prednisolone or equivalent/day) [12]. Current American College of Rheumatology (ACR) guidelines, for the treatment of glucocorticoid-induced osteoporosis, recommend anti-resorptive therapy for any patient over the age of 40 years starting on very high-dose steroids and the expected duration of treatment is 3 months or more, or anybody with high fracture risk (GC-adjusted FRAX 10-year major osteoporotic fracture risk $\geq 20\%$, hip fracture $\geq 3\%$) or moderate fracture risk (GC-adjusted FRAX 10-year major osteoporotic fracture risk 10–19%, hip fracture risk 1–3%). Very high steroid dose is defined as treatment with prednisolone ≥ 30 mg/day and a cumulative dose of > 5 g in the previous year [13]. We acknowledge that other countries may have different thresholds. We have incorporated high GC therapy into the algorithm enabling further reduction on DXA testing during the pandemic.

Evidence of osteoporosis based on other clinical risk factors or radiological investigations

Review of previous imaging such as CT, MRI, and X-rays, if available, may provide valuable clues to the presence of osteoporotic fractures. If identified, treatment could be started and DXA could be deferred. All other available clinical information, particularly risk factors for osteoporosis that are not included in the FRAX tool, should be taken into account which may push these patients into the higher risk category.

Prioritising follow-up DXA

The majority of DXAs could be delayed in this group of patients depending on the indications for DXA, previous serial BMD readings, and duration of osteoporosis treatment. The information provided on the DXA request or obtained from the telephone consultation is used to calculate the fracture risk based on FRAX and treatment recommended as per local/national guidelines. DXA requests made for monitoring purpose, for example patients with hyperparathyroidism or coeliac disease without any new osteoporotic risk factors, can be deferred. DXA should be prioritised if the previous DXA had shown a significant decline in the BMD, new risk factors have

occurred since the last scan, or new therapy has been commenced either for treatment of osteoporosis or having potential for significant bone loss.

Risk vs benefit strategy

We propose that the clinical vulnerability of patients should be taken into account and those patients who are at high risk for COVID-19 because of their age, comorbidity, or immunosuppression should not be routinely invited for a DXA [14]. Treatment for osteoporosis can be started in this group of patients if appropriate as outlined above, and they can be reassessed at a later date. The short-term use of oral bisphosphonates generally does not pose significant harm, provided patients have no contraindications. Hence, we feel that the benefits of taking bisphosphonates outweigh the risks and favour their use in high-risk patients without a DXA during the pandemic.

Discussion

The proposed algorithm outlined in this paper is a pragmatic, evidence-based approach accommodating important international guidelines alongside the practical restrictions in DXA scanning. We have used NOGG guidelines to classify fracture risk into low-, intermediate-, and high-risk groups after calculating fracture risk using UK FRAX. Our model can be adapted across the world with country-specific FRAX scores and intervention thresholds. For example, Canada uses FRAX-derived fixed intervention threshold and major fracture risk probability over 20% as ‘high risk’, 10–20% ‘moderate risk’, and less than 10% ‘low risk’ [15].

There are several clinical scenarios that a referring clinician could take into account before treating a patient without a DXA. In our hospital, 8.5% of total referrals were sent by clinicians for AI use. From our experience, 40% of these patients could be started on treatment without a need for an immediate DXA. Further fracture risk is significantly high immediately after the first fracture and reduces progressively over time, which is not factored into FRAX [16]. The fracture risk following a recent clinically apparent vertebral fracture is much higher than for a woman of the same age with a history of a previous vertebral fracture of uncertain age [17]. A probability ratio can be used to quantitatively adjust FRAX 10-year fracture probability for hip and major fractures based on the fracture site within the past 2 years for women and men [18]. Even though the intermediate-risk group comprises up to 60% of DXA referrals, we believe our algorithm will be able to reduce the need for DXA by 50% with potential for further reductions based on the clinical information as detailed above [19, 20].

Many guidelines recommend a DXA scan within 3–6 months from starting treatment [7, 13]. Guidelines during the beginning of the pandemic had suggested that there will be no adverse outcomes delaying DXA for 3–6 months until after treatment is commenced [21, 22]. It may not be possible to meet these targets as the course of the COVID-19 pandemic remains uncertain. Depending on the demand and capacity at the local level, our pragmatic guidance could be used until such time a DXA is available.

Pharmacological treatment of the patient with osteoporosis during the era of COVID-19 has been widely published [23]. We recommend oral bisphosphonates as the first-line therapy based on UK guidelines and our experience in treating patients with osteoporosis. Bisphosphonates are inexpensive drugs, allowing their use globally even in the developing world with financial constraints in the era of COVID-19. However, we recommend using the most appropriate treatment for each patient, depending on local policy and availability. For example, adjuvant bisphosphonates reduce breast cancer bone recurrence in postmenopausal women and adjuvant denosumab treatment improves disease-free survival in postmenopausal women with hormone receptor-positive early breast cancer receiving aromatase inhibitor [24, 25]. The ARCH and VERO trials have provided data suggesting anabolic agents such as romosozumab and teriparatide have a greater reduction in fracture risk than anti-resorptive agents [26, 27]. Despite the evidence from the VERO study of greater efficacy, the high cost of teriparatide largely restricts its use to those at very high risk, particularly for vertebral fractures [12]. Romosozumab is not yet available in the National Health Service in the UK. In health economies with direct access to anabolic agents, such as the USA, these drugs could be considered first-line for very high-risk patients. We have implemented denosumab ‘self-injections’ during the pandemic as did some other regions in the UK but it is not yet widely practised.

We do appreciate that healthcare delivery systems worldwide are different and various countries are in different stages of the evolving COVID-19 pandemic. Our proposed algorithm presents a pragmatic approach in the face of limited clinical data, evidence, and DXA resources. The algorithm can be adapted as per the local or national guidelines and depending on the prevalence of COVID-19. These recommendations will require further review as and when normal access to DXA scanning resumes.

Conclusion

The COVID-19 pandemic has disrupted DXA services, and it remains unclear what impact this will have in the coming 12 months. DXA has an important role to play in the diagnosis and treatment of patients with osteoporosis. However, in the

current operating conditions of reduced DXA capacity, our pragmatic algorithm can help ensure DXA is offered to the most appropriate patients, without delaying treatment in those with a clinical need. Although we have mainly used UK guidelines as an example, we support and encourage others to adapt it to their national requirements. This approach may help all clinicians conduct shared decision-making when considering DXA scanning, risk-benefit analyses, and primary and secondary prevention of osteoporosis.

Data availability Not applicable

Compliance with ethical standards

Conflicts of interest None.

Code availability Not applicable

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