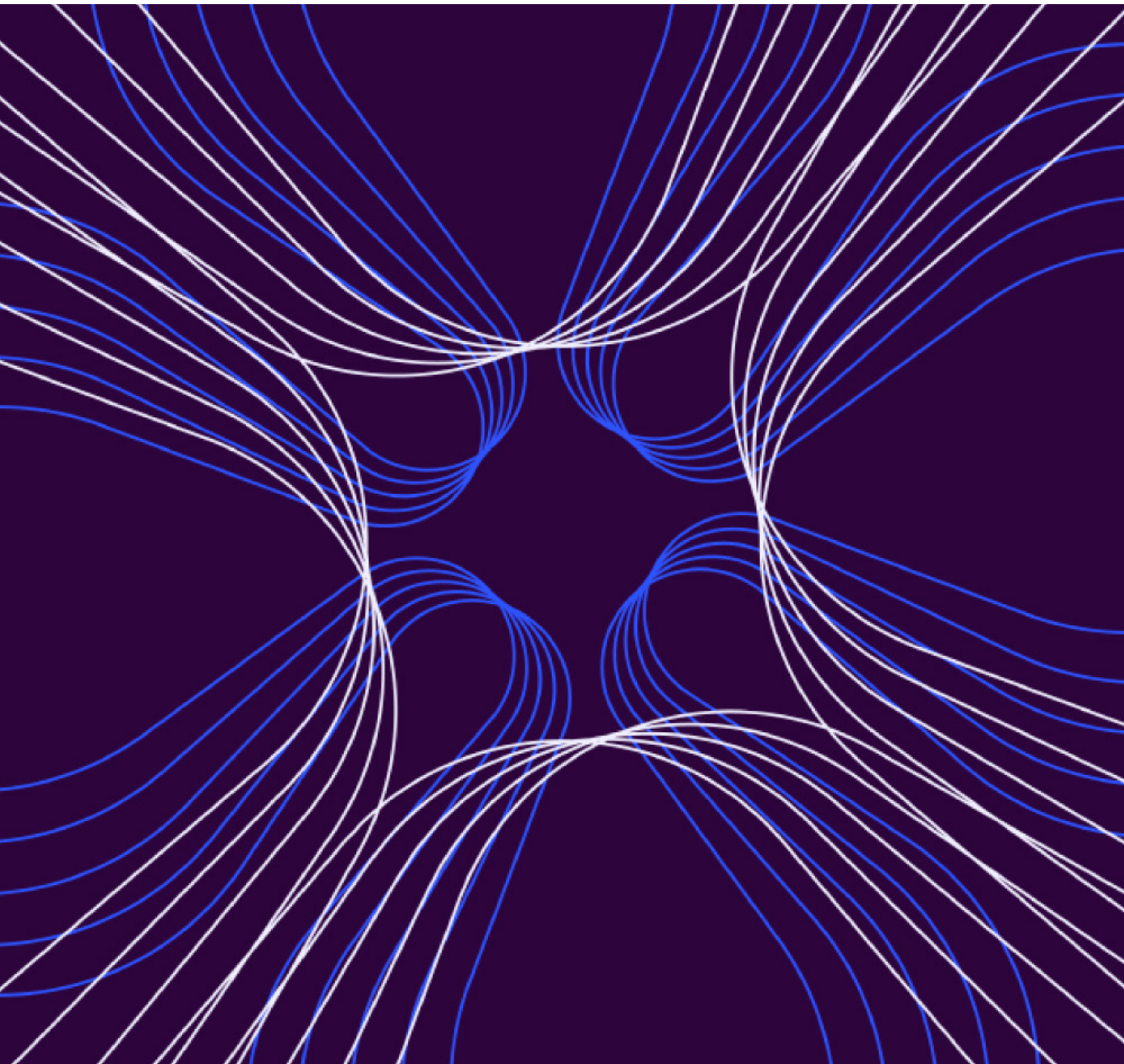
Clinical Oncology

National guideline of bone health management in patients with prostate cancer

FEBRUARY 2026

The Royal College of Radiologists



Contents

Key messages

1. One in five men over the age of 50 suffer from a fracture because of osteoporosis.[1] The majority of prostate cancer patients are over 70 years old and have an increased risk of **primary osteoporosis** and **fragility fracture (FF)**. This is often under-recognised and undermanaged in the UK.[2]
2. Prostate cancer patients receiving androgen deprivation therapy (ADT) with or without other combination systemic treatment concurrently or sequentially have significantly accelerated bone mineral loss and **secondary osteoporosis** and fragility fracture risk (FFR), in addition to their baseline risk.
3. Advanced prostate cancer patients also have a high incidence of bone metastases, leading to **skeletal-related events (SREs)** including fractures. The term 'pathological fracture' in this context refers to fractures caused by bone metastasis. However, radiologically it may be difficult to differentiate these from fragility (osteoporotic) fractures.
4. Despite longer overall cancer-specific survival due to advances in oncological therapeutic options, FFs and SREs in prostate cancer patients result in significant premature mortality, morbidity and socio-economic burden. 'If Disability Adjusted Life Years (DALYs) are used to calculate the disability burden of different diseases, osteoporosis has a greater impact than most types of cancer, with the exception of lung cancer.'[3]
5. The goals of bone health management in prostate cancer patients include **prevention, reduction and delaying both FFs and SREs**, in order to retain and maintain independence and promote optimal cancer survivorship.
6. Until now there has been limited consensus on how to optimise bone health in prostate cancer patients, despite growing evidence about the increased risk of FF associated with anticancer treatment.

The RCR guideline focuses on early identification of fracture risk, proactive general health promotion and pragmatic shared decision-making using risk stratification for pharmacological intervention.

Executive summary

With the advent of more effective treatments for advanced or metastatic prostate cancer, for many men and people with a prostate it has become a chronic illness that has seen significant improvements in overall survival. As we intensify the upfront treatment of our patients, we also place them at more risk of life-limiting toxicity, and so it is paramount that we, as a uro-oncology community, pay much more attention to the side-effects that we directly cause by our life-extending treatments.

Bone health in men and people with prostate cancer historically has been very poorly understood and managed, with even standard measurements of bone health underestimating the impact on patients. This consensus brings together stakeholders committed to ensuring that our patients' quality of life remains as good as possible, both because of and despite our treatments.

'Do the best you can until you know better. Then when you know better, do better.' Maya Angelou

Professor Alison Birtle

Foreword

Bone health guidelines in prostate cancer are essential to preserving quality of life, reducing treatment-related harm, and preventing avoidable fractures and skeletal complications in a growing population of long-term survivors.

Despite clear evidence of accelerated bone loss with ADT and the high prevalence of bone metastases in advanced disease, bone health assessment remains inconsistent. It is vital to ensure fracture risk evaluation and basic lifestyle and nutritional support, leading to preventable skeletal events. These guidelines promote a proactive strategy in which bone health is embedded as a routine, non-negotiable component of prostate cancer pathways rather than an optional add-on.

Optimising bone health is not solely about preventing fractures; it is about preserving mobility, autonomy and dignity throughout the prostate cancer journey. The RCR *National guideline of bone health management in patients with prostate cancer* is an important aspect in enabling optimal bone health, and British Uro-Oncology Group (BUG) is pleased to have supported this important guideline development.

Professor Amit Bahl, Chairperson, British Uro-Oncology Group

This consensus initiative is timely and strongly supported by the BAUS Section of Oncology. It provides an opportunity to standardise best practice, promote earlier identification of skeletal risk and embed proactive bone health management within prostate cancer care pathways. Improving outcomes must extend beyond survival alone to include preservation of long-term wellbeing. As our therapeutic capabilities advance, so too must our responsibility to minimise treatment-related harm and deliver truly holistic care.

Mr Vishwanath Hanchanale, Chair, BAUS Section of Oncology, British Association of Urological Surgeons

The Royal Osteoporosis Society welcomes this new national guideline, which addresses the urgent need for consistent, evidence-based bone health management in patients with prostate cancer. By focusing on early identification of fracture risk and proactive intervention, it will help prevent avoidable fractures and improve outcomes and quality of life for patients with prostate cancer.

The Royal Osteoporosis Society

The British Association of Urological Nurses (BAUN) welcomes and supports the Royal College of Radiologists' bone health guideline. These evidence-based recommendations provide a clear, consistent framework for improving the identification, assessment and management of treatment-related bone loss. As urology nurses, we recognise the significant impact of bone health on patient wellbeing and long-term outcomes, particularly for those undergoing androgen deprivation therapy. BAUN is committed to promoting best practice, and this guideline represents an important step in strengthening multidisciplinary care and enhancing patient safety across clinical pathways.

Emma Currant, President, British Association of Urological Nurses

Prostate Cancer Research is pleased to support the RCR *National guideline on bone health management in patients with prostate cancer*. People often live for many years on or after hormone therapy. They rightly expect to lead full and active lives, without the added fear of skeletal-related events or fragility fractures. This guideline will help ensure bone health becomes a priority in treatment planning and care, improving long-term quality of life for those treated with hormone therapy.

Prostate Cancer Research

Prostate Cancer UK welcomes the new *National guideline on bone health management in patients with prostate cancer*. This clear and evidence-based guideline provides recommendations and strategies that can prevent or minimise bone loss and protect bone health, for patients living with prostate cancer.

Essie Mac Eyeson, Policy & Health Influencing Manager and Lizzie Ellis, Senior Policy Officer, Prostate Cancer UK

BAUN
BRITISH ASSOCIATION of UROLOGICAL NURSES

The British Association of Urological Surgeons

BRITISH URO-ONCOLOGY GROUP
BUG

infopool
the prostate resource
theinfopool.co.uk

PROSTATE CANCER UK

ROYAL OSTEOPOROSIS SOCIETY
Better bone health for everybody

Lead authors and working group co-chairs

Dr Helen Killen, Consultant Clinical Oncologist, Barking, Havering and Redbridge University Hospitals NHS Trust

Dr Xue-Yan Jiang, Consultant Clinical Oncologist, The Newcastle Upon Tyne Hospitals NHS Foundation Trust

Lead authors

Dr Divya Manoharan, Specialty Registrar in Clinical Oncology, The Newcastle Upon Tyne Hospitals NHS Foundation Trust

Dr Carolina Navarro Rodriguez, Specialty Registrar in Clinical Oncology, The Newcastle Upon Tyne Hospitals NHS Foundation Trust

Thomas Chin, Senior Pharmacist, South Tyneside and Sunderland NHS Foundation Trust

Dr Timothy Hill, Specialty Registrar in Clinical Oncology, Barts Health NHS Trust

Authors

Dr Anum Azhar, Specialty Registrar in Clinical Oncology, Barking, Havering and Redbridge University Hospitals Trust

Professor Alison Birtle, Consultant Clinical Oncologist, Lancashire Teaching Hospitals NHS Foundation Trust

Professor Janet Brown, Professor of Translational Medical Oncology and Consultant Medical Oncologist, The University of Sheffield

Dr Amarnath Challapalli, Consultant Clinical Oncologist, University Hospitals Bristol and Weston NHS Foundation Trust, representing the British Uro-oncology Group (BUG)

Mr Conor Corbett, Senior PCN Pharmacist

Dr Hilary Glen, Consultant Medical Oncologist, Beatson West of Scotland Cancer Centre Glasgow, Ninewells Hospital Dundee

Mr Struan Gray, Urology Research Fellow and MD student, The Christie NHS Foundation Trust

Dr Craig Jones, Urology Research Fellow, The Christie NHS Foundation Trust

Professor Chris Parker, Consultant Clinical Oncologist, The Royal Marsden NHS Foundation Trust

Dr Delia Pudney, Consultant Clinical Oncologist, Swansea Bay University Health Board

Dr Ashwin Sachdeva, Academic Clinical Lecturer in Urology, The Christie NHS Foundation Trust, representing BAUS

Mr Kanagasabai Sahadevan, Consultant Urologist, South Tyneside and Sunderland NHS Foundation Trust

Dr Yousif Shanshal, Consultant Physician, Gateshead Health NHS Foundation Trust

Dr Helen Stancliffe, Specialist Oral Surgeon, The Newcastle Upon Tyne Hospitals NHS Foundation Trust

Mr William Thompson, Urology Registrar, Mersey and West Lancashire Teaching Hospitals NHS Trust

Dr Karen Tipples, Consultant Clinical Oncologist, Barts Health NHS Trust

Acknowledgements

Dr Petra Jankowska, The RCR Medical Director Professional Practice

Dr Nicky Thorp, The RCR Medical Director Professional Practice 2021–2024

Working group attendees and guideline contributors

Dr Terry Aspray, Consultant Physician, The Newcastle Upon Tyne Hospitals NHS Foundation Trust

Pauline Bagnall, British Association of Urological Nurses representative

Dr William Cross, Consultant Urologist, Leeds Teaching Hospitals NHS Trust

Dr Vishwanath Hanchanale, British Association of Urological Surgeons representative

Dr Nicola Hannaway, Medical Oncology SPR, NCCC, Freeman Hospital, Newcastle Hospitals NHS Trust

Professor Eugene McCloskey, Professor in Adult Bone Diseases at University of Sheffield

Dr Rhona McMenamin, Clinical Oncologist, NHS Grampian

Dr Ehiosa Charles Okuofo, Specialty Registrar in Clinical Oncology, James Cook University Hospital

Professor Joe O'Sullivan, Consultant Clinical Oncologist, Queen's University Belfast

Simon Rayner, patient representative

Stakeholders

British Association of Urological Nurses (BAUN)

British Association of Urological Surgeons (BAUS)

British Uro-oncology Group (BUG)

Prostate Cancer Research

Prostate Cancer UK (PCUK)

Royal Osteoporosis Society (ROS)

Brief description of sections

Section 1 defines bone health in prostate cancer and the purpose of the national guidance.

Section 2 describes the impact of oncological prostate cancer treatments on bone health including both systemic and localised treatments.

Section 3 addresses the practicalities of fragility fracture risk (FFR) assessment, looking at **who** should be assessed, **how** and **when** this should be undertaken, and **by whom**.

Section 4 addresses how FFR should be managed with regard to lifestyle changes and pharmacological approaches.

Section 5 summarises the key recommendations, including in visual and tabular form, to improve the management of bone health in men and people with prostate cancer.

Section 6 highlights the important role of staff education, clinical research, and audit and service development in supporting optimal management of bone health in this group.

Section 7 appendices include detailed pharmacological advice as well as useful patient resources and model letters to primary care settings.

01 Introduction

1.1 For whom is this guidance written?

This guideline aims to provide evidence-based recommendations to aid clinicians in the management of bone health in patients with prostate cancer. This is a bespoke guideline focusing on prevention and treatment of prostate cancer therapy-induced **osteoporotic fragility fracture (FF)** and **skeletal-related event (SRE)** prevention and delaying. This document represents the considered judgement of a multidisciplinary group of experts including clinical and medical oncologists, urologists, metabolic bone experts, dental surgeon, pharmacists, rheumatologist, orthogeriatrician, specialist nurses and patient representative.

1.2 What is bone health in prostate cancer?

Prostate cancer is the most common cancer[4] in the UK, affecting 1 in 8 men and people with a prostate. Approximately 1 in 4 black men are affected. Androgen deprivation therapy (ADT) is the mainstay of medical treatment for patients with high-risk localised and metastatic prostate cancer as it significantly improves overall survival. When measuring bone mineral density (BMD), this guideline refers to dual-energy X-ray absorptiometry (DEXA) as the gold standard, using areal BMD. Suppression of circulating androgens leads to disruption of bone remodelling, resulting in loss of BMD.[5,6] BMD loss and alterations in bone microarchitecture occur most rapidly within the first 6–12 months of commencing ADT (5–10%). This process continues throughout the duration of treatment, contributing to an increased risk of FF.[7,8,9,10,11] In addition, bone is the most common metastatic site, with bone metastases present in approximately 80% of patients presenting with metastatic prostate cancer.[12] Patients with prostate cancer and bone metastases are at risk of pain, skeletal complications including pathological fractures (fracture at a site of metastatic disease) and spinal cord compression. These complications frequently significantly impact morbidity and decrease quality of life.[13] The term ‘skeletal-related event’ encompasses pathological fractures as well as metastatic spinal cord compression, surgery to bone, radiation to bone and/or a change in systemic anticancer therapy due to bony pain. Data from the National Prostate Cancer Audit highlight the high cumulative incidence of clinical SREs at five years, which is approximately 44% for patients with metastatic disease.[14]

01
Introduction

Osteoporosis is defined by low BMD and micro-deterioration of bone tissue leading to fragile bone with an increased risk of FFs.[15] The prevalence of osteoporosis increases with advancing age, affecting 10–25% of men and people with a prostate aged 60 and over, and 50% of men and people with a prostate in their eighties. Osteoporosis is usually asymptomatic until fractures occur. The most common site of osteoporotic fracture is the vertebra, accounting for around 25% of FFs.[16,17] Although osteoporosis is closely associated with FFs, most patients who sustain a fracture do not have osteoporosis.[18] In the UK, there are approximately half a million FFs each year.[19] FFs, in particular hip fractures, are associated with increased mortality and can cause pain, disability and reduced quality of life. In the UK, the cost of FFs to the National Health Service (NHS) exceeds £4.7 billion per annum.[20] Targeted and coordinated fracture prevention has been shown to be highly cost-effective; for every £1 spent on active fracture prevention, over £3.20 is saved in return.[21]

The past decade has seen significant improvements in overall survival through earlier treatment sequencing in patients with high-risk non-metastatic and metastatic hormone-sensitive prostate cancer. Doublet therapy with androgen receptor pathway inhibitor (ARPI) alongside ADT is now the gold standard firstline treatment. Patients are therefore living longer on treatment with potential for greater exposure to the toxicities and side-effects of treatment. Furthermore, patients with advanced prostate cancer prior to ADT have higher rates of osteoporosis and osteopenia than age-matched controls: 42% and 27% respectively.[22] A meta-analysis of adverse event data on fractures and falls from randomised controlled trials highlighted a significantly increased risk with the addition of ARPIs to ADT.[23] Secondline therapies, including the addition of radium-223 alongside ARPIs, further increase the risk of fractures but can be mitigated with use of appropriate bone protection.[24,25] For the first time in prostate cancer studies, the PEACE-3 subgroup analysis also demonstrated overall survival benefit (of 17 months, HR 0.56, 95% CI 0.37–0.86) with bone protection agents (BPAs) compared with no BPAs. These are the only data to date in prostate cancer trials demonstrating a survival advantage of BPAs. We note that this is from a subgroup analysis and is contrary to the results of the STAMPEDE study looking at docetaxel and zoledronic acid.[26]

1.3 What is the current evidence and available recommendations?

There is widespread variation in the assessment of bone health and the use of BPAs.[27,28] In addition, fracture risk predictions using FRAX and other tools currently recommended within international guidelines were not developed in men and people with prostate cancer, and they may therefore have a limited role in this patient population.[29] BPAs (bisphosphonates and receptor activator of nuclear factor kappa-B ligand [RANKL] inhibitors such as denosumab) can be used to help preserve BMD in men and people with prostate cancer treated with ADT.

Both the STAMPEDE and LATITUDE trials have within recent years demonstrated a significant reduction in fracture-related hospitalisations with the addition of BPAs to those receiving ADT or ARPI, respectively.[30] These studies support the need for BPAs in patients with newly diagnosed metastatic prostate cancer commencing lifelong ADT. The updated European Association of Urology (EAU) guideline (March 2025) has recommended ‘offer bone protection to avoid fractures in patients receiving combination treatment. Offer calcium and vitamin D supplementation when prescribing either denosumab or bisphosphonate and monitor serum calcium’.[31]

01
Introduction

Case illustration

Fragility fracture in a patient receiving multimodality treatment for metastatic castration-resistant prostate cancer (mCRPC).

Mr A was a 69-year-old man who had a clinical diagnosis of metastatic prostate cancer – T3 N0 M1 with a presenting PSA 194 ng/ml in 2016. He had a medical history of hypertension and chronic obstructive pulmonary disease (COPD). His medications included amlodipine, atorvastatin and inhalers (salbutamol and beclomethasone). He lived with his wife in a house with stairs. He was an ex-smoker of 40 pack years. He drank two pints of beer every night (4 units/day). Functionally he was fit and active, walking unaided. His clinical frailty was scale 2 and performance status was 1.

He started on lifelong ADT mono treatment in 2016. In 2019 he developed castration-resistant disease with symptomatic disease progression in the bone. He started on abiraterone 1 g daily and prednisolone 10 mg daily. He had an excellent durable biochemical response.

In 2020 he received palliative radiotherapy to T11 with a single 8 Gy fraction and achieved good pain control. He had re-treatment at the same level of the spine (T10–T12) six months later due to the development of recurrent pain. Unfortunately, his pain worsened after radiotherapy. It was a constant ache and worsened by movement. There were no neurological symptoms.

Examination showed significant new kyphosis with a tender lower thoracic spine on percussion and reduced range of movement. A magnetic resonance imaging (MRI) whole-spine scan showed no spinal cord compression but compression fractures at T10 and T12 (levels above and below T11, which was the target vertebra with bone metastases). See Figure 1.

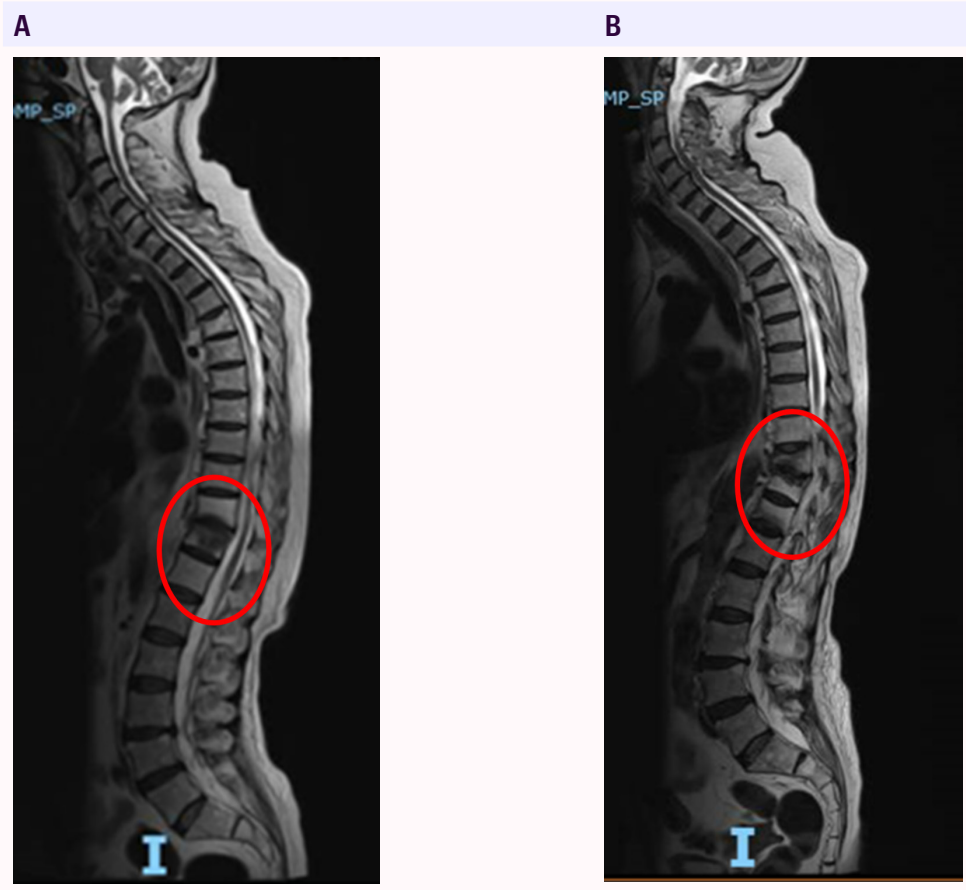


Figure 1. (A) MRI whole spine showing compression fractures at T10 and T12; (B) compared with baseline three months since palliative radiotherapy to T11 bone metastasis (which included T10 and T12 as standard margins).

01
Introduction

Despite maximal analgesia, oral BPAs with calcichew D3 Forte two tablets daily and alendronic acid 70 mg weekly, and physiotherapy, Mr A was unable to recover to his baseline functional status. He became housebound and was dependent on a wheeled walking frame for mobilisation. Unfortunately, he died of a chest infection a year later.

This is likely a case of FF with a multifactorial cause or pre-existing risk factors including:

- Age
- Smoking history
- Alcohol (>3 units/day)
- Glucocorticoid treatment (inhaler and prednisolone) and
- Lifelong ADT
- Abiraterone
- Radiotherapy
- The presence of bone metastases.

Questions

1. Should he have had a primary osteoporosis assessment at primary care, such as a Wellman clinic, based on his multiple risk factors independent of his cancer diagnosis?
2. Should he have had a bone health assessment when he was diagnosed with prostate cancer and when starting ADT?
3. Would earlier use of BPAs at the time of commencing ADT have prevented or delayed his fracture?
4. Would parenteral bone strengthening agents have been more effective in his case?

02 ADT, SACT and radiotherapy in prostate cancer and their impact on bone health

2.1 ADT and secondary osteoporosis and FF

The intended therapeutic effect of ADT is hypogonadism, which causes a rapid reduction in circulating androgens and oestrogens.[32,33] Hypogonadism causes a disruption in bone remodelling by increasing bone osteoclast activity, decreasing osteoclast apoptosis and increasing osteoblast apoptosis, with a net increase in bone resorption.[32,33,34,35] A retrospective large study by Shahinian *et al* looking at claims data for more than 50,000 patients demonstrated that ADT for prostate cancer increases the risk of fracture.[11] In data from the Surveillance, Epidemiology, and End Results Medicare (SEER-Medicare) database, patients on ADT were four times more likely to suffer from significant bone mass loss, and for those surviving five years after prostate cancer diagnosis, fracture incidence increased from 12% to 19.4% ($p<0.001$).[11,33]

Bone health complications cause significant morbidity and all-cause mortality. Annual loss of BMD in older men and people with a prostate ranges from 0.5% to 1% compared with 1% to 2% in women.[34] However, BMD in men and people with a prostate receiving ADT rapidly declines within the first 12 months of therapy. The rate of bone loss ranges from 2% to 8% in the lumbar spine and 1.8% to 6.5% in the femoral neck. BMD continues to fall with ADT treatment beyond 12 months.

ADT also causes muscle loss due to changes in body composition. ADT causes a substantial increase in adiposity and decrease in lean body mass within 3–12 months of initiation. This ADT-induced sarcopenia compounds the risk of falls, fractures and loss of independence.[35]

2.2 ARPI and secondary osteoporosis and FF

ADT was the cornerstone treatment for prostate cancer for many decades. Over the past decade, there has been a significant improvement in overall survival due to the early use of ARPI alongside ADT in both the high-risk non-metastatic and metastatic prostate cancer settings in both hormone-sensitive and castrate-resistant disease.[36,37]

As discussed earlier, the addition of ARPI to standard ADT has showed an improvement in the survival outcomes in patients with advanced prostate cancer. This has been evidenced in a recent large systematic review and meta-analysis of 23 randomised controlled trials, including many of the cornerstone trials.[38,39,40,41,42,43,44,45,46,47,48,49,50,51,52]

Abiraterone irreversibly inhibits androgen production in the tumour cells, testes and adrenal glands. Abiraterone requires steroid use alongside treatment (usually prednisolone 5 mg twice a day) to overcome secondary cortisol insufficiency and prevent overproduction of adrenocorticotrophic hormone (ACTH) and mineralocorticoids.

02
ADT, SACT and radiotherapy

Since 2015, the STAMPEDE and LATITUDE phase III trials have led to the widespread use of abiraterone in combination with ADT in the UK, demonstrating survival advantage in comparison with ADT alone. Abiraterone can be used in newly diagnosed mHSPC and metastatic castration-resistant prostate cancer (mCRPC), as well as in the high-risk non-metastatic setting.[36,37] Recent phase III trials have shown the efficacy of enzalutamide,[46,48,49,50] apalutamide[51,52] and darolutamide[43] in combination with ADT, demonstrating survival advantage in comparison with ADT alone.

Real-world data further reinforce these findings. A SEER-Medicare cohort study[53] revealed that fracture risk after ARPI initiation was as high as 25% within three years for patients with no history of previous fracture and exceeded 50% for those with prior fracture. History of previous fracture was the strongest predictor of future fracture. In the 37% of patients who received BPAs, their use was insufficient to mitigate risk in high-risk individuals. This underscores the importance of early bone health assessment and proactive use of BPAs in clinical practice.

2.3 Glucocorticoids and bone loss

Glucocorticoids are commonly prescribed in prostate cancer treatment. They have an independent, negative effect on bone health and increase the risk of fracture in patients with prostate cancer. They are often used long term and are a well-established and common cause of iatrogenic and secondary osteoporosis. The risk of hip and vertebral fractures increases with docetaxel and abiraterone up to 7-fold and 17-fold, respectively, with doses as low as 10–12 mg prednisolone given in combination with these agents for as little as three months.[35] Glucocorticoid monotherapy has been shown to increase the risk of fracture, with doses of prednisolone as low as 2.5 mg per day.[54]

2.4 Radium-223 radionuclides

The ERA223 trial in 2019 concluded that the addition of radium-223 to abiraterone plus prednisolone or prednisolone alone did not improve symptomatic SRE-free survival in patients with castration-resistant prostate cancer and bone metastases and was associated with an increased frequency of bone fractures compared with placebo.[55] Recent evidence from the PEACE-3 trial supports a new firstline mCRPC treatment option of combining radium-223 with enzalutamide for some patients.[56]

Both trials have unequivocally demonstrated higher fracture rate in those receiving these combinations, highlighting the importance of mandatory bone protection in these patients.[55,56]

02
ADT, SACT and radiotherapy

The guideline group agrees that radium-223 patients should be classified as the very high risk group for SREs and FFs with parallel parenteral BPAs preferred if possible.

Recommendation
The guideline group agrees that radium-223 patients should be classified as the very high risk group for SREs and FFs with parenteral BPAs preferred if feasible, especially during the duration of radium-223 treatment. For patients already established on oral agents, a switch may not be required; however, escalation to parenteral agents (more potent) can be considered if SREs or FFs occur while on oral agents.

2.5 Radiotherapy

Radiotherapy has been shown in cell culture and animal models to affect osteoblasts and osteoclasts leading to reduced bone formation.[57] In clinical practice, pelvic radiotherapy increases risk of fractures. However, the association between pelvic radiotherapy and an increased risk of hip fractures has not been formally established as an independent contributing factor. It remains unclear whether pelvic radiotherapy causes any independent deterioration in BMD or increases the risk of clinically meaningful fractures.[58]

2.6 The impact of systemic anticancer therapy (SACT) in prostate cancer on frailty and falls

Patients with advanced prostate cancer have a higher incidence of osteoporosis with loss of BMD that is 10-fold higher than for patients without prostate cancer of the same age (5%, compared with 0.5% for age-matched controls).[59] One study showed a deterioration in physical performance and strength and an increase in frailty with as little as 12 months of androgen deprivation. This highlights the importance of ongoing frailty assessment in people having prostate cancer treatment.[60]

A recent large meta-analysis in 2024, which included 23 randomised controlled trials (n=21,260 patients), looked at the risk of fractures and falls in patients with advanced or metastatic prostate cancer receiving ADT and ARPI. It demonstrated that the overall fracture incidence of any grade fracture was 8.3% with the addition of an ARPI in comparison with 3.2% in the control group. ARPI use was also associated with an increase in the overall incidence of any grade falls at 11.1% in comparison with the control group at 4.6%.[23,60]

02
ADT, SACT and radiotherapy

2.7 The role of BPAs in advanced prostate cancer therapy

STAMPEDE compared ADT ± docetaxel ± zoledronic acid (ZA) in M0 and M1 hormone-sensitive prostate cancer patients. ZA showed no evidence of overall survival improvement in 2016 and did not become part of the standard of care.[26] A 2023 post hoc analysis of this trial population (n=2,145 patients) on falls and fracture rates demonstrated that patients with advanced prostate cancer have a high incidence of clinical fractures. This was substantially reduced in participants allocated to ZA, with the five-year fracture incidence in the ZA arm and the non-ZA arm being 4.5% and 12.9%, respectively.[61]

A separate post hoc analysis in Japan demonstrated that bone-modifying agent use (bisphosphonates or denosumab) was associated with a longer time to SREs in patients with high-risk mCSPC treated with ADT, both with or without abiraterone (and prednisolone).[30]

The aforementioned PEACE-3 phase III trial demonstrated that mandatory use of BPAs significantly reduced fracture risk when radium-223 was combined with enzalutamide. This contrasts sharply with ERA-223, where the absence of mandated BPAs led to an increased fracture incidence when radium-223 was combined with abiraterone. These results underscore that BPAs are not optional but essential for mitigating skeletal toxicity in advanced prostate cancer treatment combinations.[55,56]

Recommendation

Given the significantly increased risk of both fractures and falls, it is important to appropriately consider and assess the frailty status and falls history in our patients. Please see the RCR frailty guidelines for further information including falls prevention strategies.[62]

03 Fragility fracture risk assessment in patients with prostate cancer: who, how and when?

3.1 Who should be assessed?

FFs are preventable and are becoming more common in our aging population. One in five men over the age of 50 suffer from a fracture because of osteoporosis.[1]

Prostate cancer is predominantly a disease of older people, with more than 50% of cases diagnosed in the UK in those aged 70 years and older.[4] The American Society of Clinical Oncology (ASCO) recommends that patients with prostate cancer and **any** risk factor in Table 1 be assessed for short- or long-term risk of osteoporotic fracture.[63] This therefore affects nearly **all** prostate cancer patients. Please see Section 3.3 for information on how FFR should be assessed.

Recommendation

Everyone with prostate cancer should have their bone health assessed.

The following criteria should be considered a high risk for developing fractures (Table 1). It is important to remember that anticancer therapies in combination or sequence may have cumulative or synergetic effects in increasing fracture risk in the short and the long term.

Table 1. Factors that increase risk of osteoporotic fractures in patients with prostate cancer

1.	Advanced age (>50 years)
2.	Current cigarette smoking and vaping
3.	Excessive alcohol consumption (>20 units/week)
4.	Previous fragility fracture, including morphometric vertebral fracture
5.	Hypogonadism
6.	Impaired mobility
7.	Increased risk of falls
8.	Long-term exposure to glucocorticoids
9.	Low body weight (BMI <19)
10.	Parental history of hip fracture
11.	Anticancer treatment

Adapted from ASCO[63] and National Osteoporosis Guideline Group (NOGG) 2022[64]

03
FFR assessment

3.2 Who should perform FFR assessments?

Bone health management is everyone's business. Bone health can be assessed at any point in the prostate cancer pathway but should be assessed as early as possible. Performing FFR assessments requires a multidisciplinary approach.

Assessments should be documented and updated by any qualified member of the healthcare team, including GPs, specialist nurses, pharmacists, therapeutic radiographers, dietitians, physiotherapists, occupational therapists and healthcare assistants as well as urologists and oncologists. The assessing professional may differ depending on the service set-up, the training of the professional and the stage the patient is at in the care pathway.

Incidental findings of fracture on radiological investigations should be managed using the high risk category pathway in Figure 2.

3.3 How should FFR be assessed?

A dynamic and systematic approach to FFR assessment should include the following:

1. **Medical history:** Assessment of specific risk factors, as per Table 1.
2. **Physical examination:** Height and weight measurement. Assessment of BMI and appropriate referral. Loss of height or changes in posture (kyphosis) may indicate clinical manifestations of FFs.
3. **Laboratory testing:** As per NOGG guidelines includes:[64]
    - Full blood cell count
    - Erythrocyte sedimentation rate or C-reactive protein
    - Renal function
    - Bone profile
    - Liver function
    - Serum 25-hydroxyvitamin D*
    - Thyroid function tests.
4. **Fracture risk assessment tools and BMD testing:** Risk assessment tools (eg FRAX, QFracture) and BMD testing with DEXA have limitations in many clinical situations and have not specifically been developed for the prostate cancer population. They should be interpreted using clinical judgement but provide a useful baseline to inform clinical decision-making. For example, FRAX score needs to be adjusted upward when there is a recent FF (within the past two years) depending on the type of FF and age of the patient in line with FRAX Plus software and the most recent NOGG 2024 guidelines.[65,35] DEXA scanning allows monitoring of bone mineral loss over time and the efficacy of interventions.[65] Where available in a timely way** consider baseline DEXA in non-metastatic patients.

* Mandatory when starting parenteral antiresorptive agents.

**The guideline working group recognises that there is significant variation in access to DEXA across the UK. DEXA primarily focuses on BMD and does not provide qualitative information on other factors such as bone quality or microarchitecture. Therefore, we recommend commencing BPAs treatment empirically based on clinical judgement (see Section 5) and the use of DEXA is not mandated.

03
FFR assessment

3.4 When should FFR be assessed?

Assessment of FFR should be done proactively and at the earliest opportunity. This could happen as early as at the time of diagnosis and should remain under review throughout the diagnostic and treatment pathway. The assessment should ideally be prior to or at the start of ADT or any other systemic anticancer agents. This stratifying of patients into low (green), medium (amber) and high (red) fracture risk categories (the traffic light system, see Section 5) will guide ongoing management and timing of future assessments.

04 Management of FF risks in patients with advanced prostate cancer

4.1 Lifestyle interventions

There is good evidence for lifestyle interventions to improve or maintain BMD and reduce risk of fractures. However, lifestyle interventions alone are not enough in patients on ADT to maintain BMD and reduce fracture risk.

4.1.1 Smoking and alcohol

Smoking, vaping and excessive alcohol intake are risk factors for fracture in older people. Moderate-to-heavy smoking (>20 pack years), especially with low body weight, increases the risk of bone loss. Smoking cessation should be advised to all patients and referral to local smoking cessation services considered.

There is a dose-dependent relationship with bone loss and alcohol use. Increased bone loss is associated with heavy alcohol use, particularly having a significant effect on BMD in men and people with prostate cancer on ADT.[66,67] The UK NOGG guideline[64] has indicated that in men with previous alcohol dependence, BMD is significantly lower but improves following three to four years of abstinence.

Recommendation

Lifestyle modifications should be recommended to all patients with the aim to encourage an active lifestyle, stop smoking and minimise alcohol consumption.

4.1.2 Diet, calcium and vitamin D supplementation

Meta-analyses have reported that the combination of calcium and vitamin D supplements can reduce hip and non-vertebral fractures, and possibly also vertebral fractures. Overall, there is little evidence that vitamin D supplementation alone reduces fracture incidence, although it may reduce falls risk. Regardless, it is important for patients taking antiresorptive osteoporosis drug therapies to be vitamin D replete.[64]

The Scientific Advisory Committee on Nutrition (SACN) recommends a reference nutrition intake (RNI) of 400 IU daily of vitamin D for adults of all ages. In the context of osteoporosis, higher levels, specifically 800 IU to 2,000 IU daily, may be appropriate.[66,67] A healthy, varied diet should be recommended to all patients commencing ADT. For patients who would only receive ≤ six months of ADT, dietary modification to include foods high in calcium is recommended.

Recommendation

Please see the flow chart in Section 5 for a risk-stratified pharmacological intervention approach.

04
Management of FF risks

4.1.3 Exercise and falls prevention

A combination of BMD reduction and sarcopenia increases the risk of fractures in men and patients with prostate cancer receiving ADT. The gradual loss of lean muscle mass or sarcopenia and muscle function, particularly in the lower extremities, leads to poor muscle strength and poor physical function, resulting in falls and fractures. ADT-associated metabolic syndrome is also linked with increased cardiovascular morbidity.[68,69] ADT with or without additional ARPI is also known to exacerbate cognitive impairment.[62] An active lifestyle and exercise, especially in the form of weight-bearing aerobic or resistance exercises, should be an essential component in the management of bone health.[66,67]

Combined exercise protocols including resistance training, aerobic exercises and impact exercises, totalling at least three hours per week, should be recommended to patients with a high risk of falls who are initiating ADT, as part of their holistic care and survivorship programme. Home safety interventions (best delivered by an occupational therapist) have been shown to reduce the risk of falls in people living in the community.[64]

Recommendation

Advise patients to combine weight-bearing exercise with impact on most days, with 20–30 minutes of muscle-strengthening exercise that targets the legs, spine and arms, on two to three (non-consecutive) days of the week. For further reference see Appendix Section 7.5.

The guideline working group references the Royal Osteoporosis Society *Strong, steady and straight expert consensus statement*, which offers advice on intensity and duration with linked patient information videos and factsheets.[70] Please see Table 2 for a summary of recommendations for non-pharmacological lifestyle interventions.

Table 2. National Osteoporosis Guideline Group (NOGG)[64] recommendations

1.	A healthy, nutrient-rich balanced diet **(strong recommendation).**
2.	An adequate intake of calcium (minimum 700 mg daily) preferably achieved through dietary intake or otherwise by supplementation **(strong recommendation)**.
3.	To consume vitamin D from foods or be prescribed vitamin D supplements of at least 800 IU–1,000 IU a day if they have identified vitamin D insufficiency or risk factors for vitamin D insufficiency. Those who are either housebound or living in residential or nursing care are more likely to require calcium and vitamin D supplementation to achieve recommended levels of intake **(strong recommendation).**
4.	A combination of regular weight-bearing and muscle-strengthening exercise, tailored according to the individual patient's needs and ability **(strong recommendation)**.
5.	Advice about smoking cessation if an individual is a smoker **(strong recommendation)**.
6.	Advice to restrict alcohol intake to ≤ 2 units/day **(strong recommendation)**.
7.	A falls assessment should be undertaken in all patients with osteoporosis and fragility fractures; those at risk should be offered exercise programmes to improve balance and/or that contain a combined exercise protocol **(strong recommendation)**.

04
Management of FF risks

4.2 Pharmacological management

4.2.1 Antiresorptive agents

All patients should be risk stratified using the traffic light system in Section 5.

There is a significant increase in fracture risk in patients with prostate cancer in the five years following the initiation of ADT when compared with those not receiving ADT. Antiresorptive agents are effective drug treatments for preventing BMD loss in those on ADT; exercise programmes are insufficient in isolation. Upfront intervention with selected antiresorptive agents in combination with calcium and vitamin D are recommended (NOGG strong recommendation) and are referred to as BPAs in this guideline.[64]

Oral or intravenous bisphosphonates are the most cost-effective interventions, although this may change with the upcoming availability of denosumab biosimilars. Where these are not tolerated, denosumab is an approved option for the treatment of men with increased FFR. Denosumab is given as a subcutaneous injection of 60 mg every six months for osteoporosis or 120 mg four-weekly for SRE prevention. The discontinuation of denosumab is associated with profound increase in bone turnover ('rebound phenomenon'). Stopping denosumab should be followed by two doses of IV zoledronic acid six months apart.

Adults who have been taking bisphosphonates for five years should have a review of the need for continuing treatment. Please see the Appendix Section 7.2 for information on the toxicities of antiresorptive agents and their management (including gastrointestinal and renal toxicity, hypocalcaemia, medication-related osteonecrosis of the jaw [MRONJ] and atypical fracture).

Recommendation

The guideline recommends treatment with empirical antiresorptive agents for the red group unless contraindicated. See Section 5 for the traffic light system.

Table 3. Summary of pharmacological treatment recommendations

(Please also see Appendix Section 7.1.3 for more details.)

Recommendation	Presence of bone metastasis	Indication/criteria	Frequency/ duration	Notes/references
Oral bisphosphonates (alendronate 70 mg weekly or risedronate 35 mg weekly) See Table 8	Any	Option for all patients unless contraindicated.	≥5 years. or ≥10 years for high risk patients.	NOGG strong recommendation. Avoid if Barrett's oesophagus, gastrointestinal symptoms. See Section 7.1.2
IV zoledronic acid 5 mg See Table 9	**No**	Patient/clinician preference or Oral bisphosphates contraindicated or poorly tolerated (eg Barret's oesophagus, troublesome gastrointestinal symptoms).	12–18* monthly for 3 years.	Contraindicated if CrCl <35 ml/min.[71] NOGG recommendation 12 monthly.
IV zoledronic acid 4 mg See Table 9	Yes	Can be considered as firstline or escalation after oral if: 1. A hip fracture (strong recommendation) or 2. SRE occurred while on oral bisphosphonate 3. Patient has severe bone pain from bone metastases or 4. For patients at **very high risk**: • Radium-223 treatment (current or previous) • 1 vertebral fracture within the past 2 years • ≥2 vertebral fractures at any time • BMD T-score ≤–3.5 • Treatment with high-dose glucocorticoids (≥7.5 mg/day of prednisolone or equivalent over ≥3 months). Multiple clinical risk factors (eg smoking, alcohol consumption), particularly with a recent FF.	Every 3–4 weeks (eg very high risk). or 3 monthly.	As per STAMPEDE and PEACE-3 criteria red group.[72,73] (Can be stepped down to oral for balance of quality of life in less mobile patients if appropriate.) Ongoing until clinically no longer appropriate.[74]

Recommendation	Presence of bone metastasis	Indication/criteria	Frequency/ duration	Notes/references
Sc denosumab See Table 9	Yes	As above.	60 mg SC injection 6-monthly. or 120 mg SC injection every 4 weeks. (**Zoledronic acid** recommended 3–6 months **after the last injection of denosumab**.)	• Increased vertebral fracture risk. • Check vitamin D before initiation. Higher risk of hypocalcaemia if eGFR <30 ml/min or having dialysis. As per PEACE-3 trial.[72,73] **Avoid unplanned cessation or delay** without discussion with a specialist healthcare professional (NOGG strong recommendation). **If denosumab therapy is stopped, at least two consolidation doses of intravenous zoledronate are recommended 3–6 months after the last injection of denosumab.
Calcium and vitamin D See Table 7	Any	As an adjunct to anti-osteoporosis drug treatment, or if dietary calcium is low and/or vitamin D insufficiency is a risk, respectively.	Continuous until clinically no longer appropriate.	NOGG strong recommendation. Check vitamin D level and treat vitamin D deficiency and insufficiency prior to initiation of parenteral antiresorptive agent treatment for 5–7 weeks (see Tables 5 and 6), and alongside initiation of oral anti-osteoporosis drug treatment.

Sc: subcutaneous; IV: intravenous; CrCl: creatinine clearance; BMD: bone mineral density; NOGG: National Osteoporosis Guideline Group[64]

*Can be used every 18 months for osteopenia www.nejm.org/doi/full/10.1056/NEJMoa1808082

**www.nejm.org/doi/full/10.1056/NEJMoa0809003 and https://academic.oup.com/jcem/article/106/1/264/5939974

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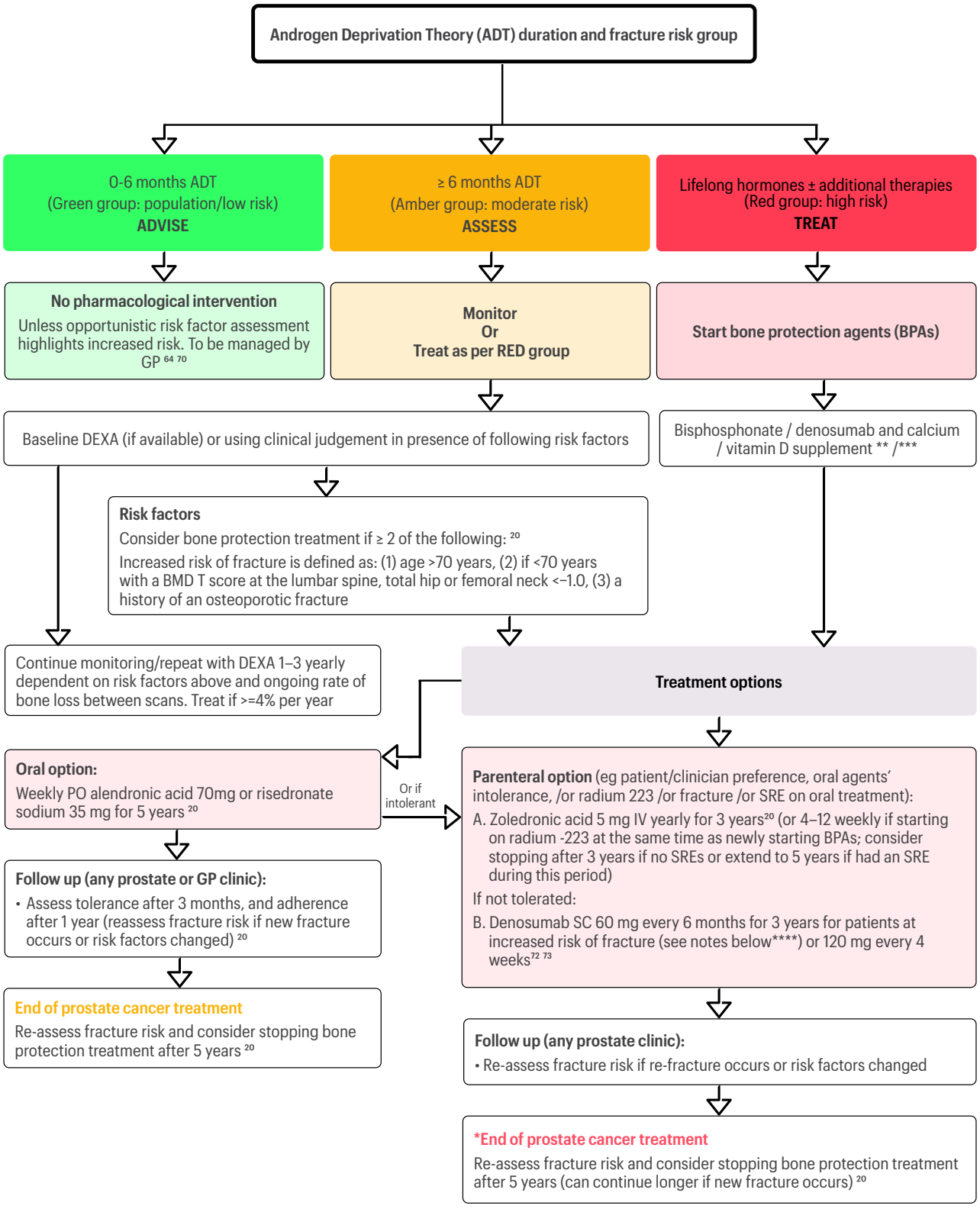
Figure 2. Summary of traffic light system for treatment decision-making[75]



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RCR recommendations

Notes for Figure 2

*Oral prednisolone ≥7.5 mg/day or equivalent.[20]

**Vitamin D level should be measured and deficiency (<25 nmol/L) corrected with loading regimen if patient is symptomatic (eg bone pain, lower back pain, muscle pain or weakness) or before starting IV zoledronic acid or SC denosumab. Vitamin D level is not routinely required in asymptomatic patients starting oral bisphosphonates.[76]

***Consider use concomitantly if receiving radium-223 and step down to oral or continuous after completing radium-223 depending on patient fitness, preference and logistics on shared decision-making.

****Increased risk of fracture is defined as >70 years, or <70 years with a BMD Tscore at the lumbar spine, total hip or femoral neck <–1.0 or a history of an osteoporotic fracture.[77]

Table 4. Summary of prostate cancer patient groups, fracture risk stratification and treatment recommendation

	Green group (low risk: M0, Stage I–II): ADVISE	Amber group (moderate risk: M0, Stage III): ASSESS	Red group (high risk: M1 or M0 advanced disease): TREAT
Patient group	**M0:** Non-metastatic low- or intermediate-risk prostate cancer at population fracture risk.	**M0:** Non-metastatic high-risk prostate cancer at increased but variable fracture risk.	1. **M0:** Non-metastatic hormone-sensitive prostate cancer (nmHSPC) (**STAMPEDE high risk group***). 2. **M1:** Metastatic hormone-sensitive prostate cancer (mHSPC). 3. **M1 and M0:** Metastatic and non-metastatic castration-resistant prostate cancer (**mCRPC/ nmCRPC**).
Oncological treatment	Surgery (radical or salvage) or radiotherapy with 0–6 months of ADT.	Radical or salvage radiotherapy with **≥6–36 months ADT**.	Lifelong ADT with or without additional treatment.
Bone health management	**Goal:** Primary osteoporosis prevention. No additional intervention required unless opportunistic identification of multiple fracture risk factors. • Communicate to primary care for further management.	**Goal:** Osteoporosis and FF risk reduction. 1. Lifestyle advice and general health promotion. 2. Consider FRAX score and/or baseline DEXA ± follow-up (see flow chart amber group). 3. Thresholds for treatment-based clinical judgement (see flow chart amber group +NOGG).[65] 4. If **BMD ≤–2.5** (osteoporotic) or **clinically high risk** (≥2 risk factors) **treat**: • Oral bisphosphonate (see red group ii A or • IV zolendronic acid 5 mg once yearly or • Denosomab 60 mg every 6 months.	**Goal:** SRE prevention, delaying and/or prevention/treatment for osteoporosis and FF. 1. Lifestyle advice and general health promotion. 2. Upfront pharmacological intervention (**i+ii**): i. Calcium and vitamin D: At least 1 g elemental calcium + 800 IU colecalciferol daily and ii. An anti-resorptive agent: A. **Oral** bisphosphonate alendronic acid 70 mg weekly or risendronate 35 mg weekly for 5 years or B. **Parenteral** options for **very high risk** group (**radium-223 or NOGG definition**[64]) • Zoledronic acid IV 5 mg annually or 3–4 weekly or 3 monthly[71] or • Denosumab SC 60 mg every 6 months or 120 mg 4 weekly. 3. Monitor tolerability and risk of hypocalcaemia with IV/SC therapies.
Comments	Managed as per general population risk (primary care-led) as per NICE[75] and NOGG guideline.[64]	Pathways may vary (eg primary care-led or specialist-led based on local arrangements).	Managed under oncology pathway (parenteral BPAs given by oncology where bone metastases are present). Consider seeking advice from osteoporosis specialist for very high-risk patients (eg those with recurrent FFs), for assessment and management of FF risk.[65]

*STAMPEDE prostate cancer high risk group definition: node-positive (N1) or, if node-negative, at least two of the following criteria: (1) clinical stage cT3–T4, (2) Gleason score 8–10, (3) PSA ≥ 40 ng/ml.

06 Education, research, audit and service improvement

6.1 Education

Patient education should begin with an understanding of how ADT affects bone health and increases fracture risk. Patients should be informed of symptoms such as bone pain, loss of height or sudden fractures, which may indicate underlying osteoporosis or metastatic involvement. Preventive strategies (calcium and vitamin D supplementation, regular weight-bearing and resistance exercises), lifestyle changes (smoking cessation, moderation of alcohol intake) and fall prevention are endorsed by major guidelines.[78,79] Interventions to increase BMD and reduce SREs (bisphosphonates, denosumab), particularly in patients with bone metastases,[80] should be considered in men with high fracture risk or confirmed osteoporosis. Patients should have a conversation about the importance of evaluation of dental health prior to initiation and maintaining oral health to reduce the risk of osteonecrosis of the jaw.

The assessment of bone health should become second nature to healthcare professionals caring for patients with prostate cancer. Optimisation of bone health can and should start at the earliest possible opportunity. This requires good education for teams about the assessment and management of bone health. This guideline is a good starting point for current best practice, but it is crucial to keep knowledge among teams up to date to allow optimal bone health management. A collaborative approach with patients to manage their bone health, including discussions regarding the risks and benefits of treatment, should be established to allow patients to take an active role in managing their own risk of fracture with regard to lifestyle and treatment compliance. Interdisciplinary collaboration across professions and specialties could potentially improve the effectiveness of bone health management.

Educational tools such as printed materials, videos, workshops and digital apps can improve awareness and adherence to bone health guidelines. There should be particular emphasis on early intervention and continuous monitoring, which can significantly reduce SREs in patients with prostate cancer undergoing ADT.

6.2 Audit

The following audit aspects are designed to evaluate and improve clinical practice related to bone health in this patient population.

1. Baseline evaluation

- DEXA scan: Was a baseline BMD assessment performed prior to or within six months of starting ADT?
- Fracture risk assessment: Was a risk score tool (eg FRAX) used to stratify patients?
- Calcium and vitamin D levels: Were these checked and actioned before initiating therapy?

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Education, research, audit

2. Risk factor identification

- Osteoporosis or prior fracture history: Is there documented evidence of past fragility fractures?
- Patient age: Is older age documented as a risk factor?
- Bone metastases: Was bone imaging performed to identify skeletal involvement?

3. Preventive measures

- Supplementation: Were calcium and vitamin D supplements prescribed?
- Lifestyle counselling: Is there documented advice on smoking cessation, alcohol moderation, fall prevention and exercise?
- Fall risk: Has this been assessed, especially in older or frail patients?

4. Pharmacologic interventions

- Bone-modifying agents: Were these appropriately prescribed (eg bisphosphonates or denosumab) for high-risk patients?
- Dental review: Was this conducted prior to initiating antiresorptive therapy?
- Monitoring for adverse events: Was the patient monitored for side-effects like jaw osteonecrosis or hypocalcaemia?

5. Follow-up and monitoring

- Adherence review: Was there ongoing documentation of adherence to supplements and medications?
- Fracture surveillance: Were any new fractures identified and managed?

6. Documentation and communication

- Multidisciplinary involvement: Was there evidence of referrals (eg endocrinology, geriatrics)?
- Patient education: Were risks, benefits and self-care strategies explained and documented?

7. Audit metrics

- % with baseline bone health assessment within 6 months of ADT start [Target 90–100%]
- % with FRAX/DEXA documented (where available/appropriate) [Target 90–100%]
- % with vitamin D checked prior to IV/SC antiresorptives [Target 90–100%]
- % with dental review before IV/SC [Target 90–100%]
- % of high-risk (Red) patients started on BPA
- Time to BPA from the start of ADT [Target <= 6 months]
- Adherence checks documented at 3 and 12 months [Target 90–100%]
- Fracture-related hospitalisations [improvement in rate, locally defined target as dependent on local population factors]
- New fragility fractures at 12/24 months [improvement in rate, locally defined target as dependent on local population factors]
- SRE incidence at 12/24 months [improvement in rate, locally defined target as dependent on local population factors]

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Education, research, audit

Audit checklist: bone health in prostate cancer

How to use in clinic (quick flow)

1. **At diagnosis or pre-ADT**: complete patient details, baseline risks, start ADT/SACT.
2. **Assign traffic-light risk** in risk investigations; order DEXA (if available/timely) and labs; arrange dental assessment if considering IV/SC antiresorptives.
3. **Record interventions**: lifestyle, Ca/vitamin D and BPA (oral vs IV/SC per risk, tolerance and presence of bone mets/radium-223).
4. **Track process outcomes** for timeliness, adherence, monitoring and communication.
5. **At each review, update clinical outcomes** (fractures, SREs, admissions, adverse events) and repeat BMD/labs as indicated.

1. Patient and visit details

Name/identifier:
Date of review:
Clinician/service:

2. Baseline demographics and risk factors

(All patients with prostate cancer should receive bone health assessment)

Age >70	☐ Yes	☐ No
BMI <19	☐ Yes	☐ No
Current smoker/vaping	☐ Yes	☐ No
Alcohol >20 units/week	☐ Yes	☐ No
Prior fragility fracture	☐ Yes	☐ No
Prior vertebral fracture	☐ Yes	☐ No
Parental hip fracture	☐ Yes	☐ No
Falls ≥1 in last 12 months	☐ Yes	☐ No
Impaired mobility/frailty	☐ Yes	☐ No
Glucocorticoid use (>3 months or ≥7.5 mg pred.)	☐ Yes	☐ No
Low dietary Ca/vitamin D symptoms	☐ Yes	☐ No

3. Cancer stage and treatment factors

(ADT, ARPI, steroids, pelvic RT, radium-223 all increase fracture/SRE risk)

Current disease state:	☐ Localised (M0)
	☐ High-risk M0
	☐ mHSPC
	☐ mCRPC
Treatments:	
ADT start date:	
ARPI (abiraterone/enzalutamide/ apalutamide/darolutamide)	☐ Yes
Steroids with cancer therapy	☐ Yes
Bone metastases	☐ Yes
Radium-223 (current/previous)	☐ Yes
Pelvic radiotherapy	☐ Yes

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Education, research, audit

4. Risk stratification (traffic-light classification)

(Use guideline thresholds)

Risk group:

☐ **Green** (0–6 months ADT; population risk)

☐ **Amber** (≥6 months ADT; moderate risk)

☐ **Red** (lifelong hormones ± ARPI/bone mets/**radium-223** [mandatory BPA])

Basis (tick all that apply):

☐ ADT duration ≥6 months

☐ High-risk cancer (STAMPEDE criteria)

☐ Bone metastases

☐ Radium-223

☐ Recurrent fragility fractures

☐ Multiple risk factors

5. Investigations

(DEXA useful but not mandatory; vitamin D mandatory before IV/SC BPA)

DEXA performed: ☐ Yes ☐ No

Lumbar T-score:

Total hip T-score:

Femoral neck T-score:

Labs:

eGFR:

Calcium/corrected Ca:

Vitamin D level:
(Mandatory before IV zoledronic acid or SC denosumab)

PTH/ALP (if available):

Dental assessment completed ☐ Yes ☐ No

(Mandatory before IV bisphosphonate or denosumab)

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Education, research, audit

6. Interventions

(Lifestyle + Ca/vitamin D for all; BPA for Red risk unless contraindicated)

Lifestyle

☐ Exercise plan (weight-bearing + resistance) explained
☐ Smoking cessation advice
☐ Alcohol reduction
☐ Falls risk addressed (OT referral if needed)

Calcium/vitamin D

☐ Prescribed Ca 1,000–1,200 mg/day
☐ Vitamin D 800–1,000 IU/day
☐ Vitamin D loading given if deficient (before IV/SC therapy)

Bone protection agent (BPA)

☐ **Not indicated** (Green without extra risk factors)
☐ **Oral bisphosphonate** (alendronic acid/risedronate)
☐ **IV zoledronic acid** (for intolerance, high-risk, bone mets, radium-223)
☐ **SC denosumab** (if bisphosphonate contraindicated)

BPA start date:
Dental clearance (for IV/SC): ☐ Yes
Monitoring plan established: ☐ Yes

7. Process outcomes (quality measures)

(Recommended audit metrics in the RCR guideline)

☐ Baseline bone assessment done within 6 months of ADT
☐ Vitamin D checked prior to IV/SC antiresorptive
☐ Dental review completed before IV/SC therapy
☐ FRAX/DEXA documented where applicable
☐ BPA indicated? ☐ Yes ☐ No
☐ BPA given if indicated
☐ 3-month adherence check completed
☐ 12-month adherence check completed
☐ Monitoring bloods prior to each IV/SC dose
☐ GP informed
☐ Patient information leaflet provided

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8. Clinical outcomes (follow-up documentation)

(Fragility vs pathological fractures; SREs)

New fragility fracture since last review: ☐ Yes ☐ No

Site:

Date:

Pathological fracture: ☐ Yes ☐ No

Morphometric vertebral fracture: ☐ Yes ☐ No

Any SRE (tick):

☐ Pathological fracture

☐ MSCC

☐ Radiation to bone

☐ Surgery to bone

☐ Systemic therapy change due to bone pain

Hospital admission: ☐ Yes ☐ No

LOS (days):

Adverse events:

☐ MRONJ

☐ Atypical femoral fracture

☐ Severe hypocalcaemia

Survival status: ☐ Alive ☐ Deceased

Date of death:

Cause:

Clinician summary

Overall ongoing risk: ☐ Low ☐ Moderate ☐ High

Next steps/follow-up plan:

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Education, research, audit

6.3 Research questions

1. Is FRAX score appropriate for assessing 10-year fracture probability for patients with prostate cancer on ADT?
2. Are oral bisphosphonates superior to intravenous bisphosphonates?
3. What is the optimal duration of bisphosphonates?
4. Projected health economic impact analysis of the intervention or guideline.
5. Evaluation of compliance of oral BPAs – consider addressing some well-known reasons:
    - Lack of motivation: since osteoporosis is often asymptomatic, many patients experience no obvious improvement.
    - Adverse effects associated with some treatments.
    - Safety concerns about treatments.
    - Inconvenient dosing, such as daily dosing and/or the need for fasting.
    - Simply forgetting to take medication as directed.
6. Frequency of DEXA monitoring if used in patients on ADT ± other agents.
7. A future trial of anabolic medications (eg Romosuzumab, Teriparatide) may be useful.
8. Service improvement – identifying and addressing some well-known challenges:
    - Undertreatment or overtreatment.
    - Failure to implement recommendations.
    - Poor coordination between primary and secondary care.
    - Lack of public awareness about osteoporosis and fragility fracture.
    - Lack of awareness among prostate cancer healthcare professionals about osteoporosis and fragility fracture.

07 Appendix

7.1 Bone health supplements and medications

7.1.1 Calcium and vitamin D supplementation

All patients should be screened for symptoms of vitamin D deficiency (eg generalised bone pain, lower back pain, muscle pain or weakness).[76] Serum vitamin D level is **not** routinely recommended in asymptomatic patients starting oral bisphosphonates.[81] If an oral antiresorptive agent is initiated, maintenance dosing of calcium and vitamin D supplements (refer to Table 5) should be co-prescribed.

Table 5. The recommended vitamin D thresholds in the UK with respect to bone health[76,81]

Serum vitamin D level (nmol/L)	Threshold	Action required
<25	Deficient	If symptomatic or starting IV zoledronic acid or SC denosumab: Loading regimen (refer to Table 6), followed by regular maintenance doses (refer to Table 7) a month later.
25–50	Insufficient	Regular maintenance doses (refer to Table 7).
>50	Sufficient	No action required.

Table 6. Suggested vitamin D loading regime in vitamin D deficiency

*The loading regimen should provide a total of approximately 300,000 IU of vitamin D, given as either separate weekly or daily doses over 5–7 weeks.
Several vitamin D loading dose treatment regimens are available: • 20,000 IU 3 times a week for 5 weeks (300,000 IU in total) • 50,000 IU once a week for 6 weeks (300,000 IU in total) • 40,000 IU once a week for 7 weeks (280,000 IU in total)

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Table 7. *Commonly used calcium and vitamin D supplements (aiming for daily intake of ≥1,000 mg calcium and ≥800–1,000 IU [20–25 micrograms] vitamin D)

Brand	Formulation	Elemental calcium (mg)	Vitamin D_3 (IU)	Suggested dose	Notes
Accrete D3[82]	Tablets	600	400	1 BD	-
Accrete D3 One a Day[83]	Chewable tablets	1,000	880	1 OD	Suitable for vegetarians and safe in peanut/soya allergy
Adcal-D3[84,85]	Caplets	300	200	2 BD	Suitable for vegetarians and safe in peanut/soya allergy
Adcal-D3[86]	Chewable tablets	600	400	1 BD	-
Adcal-D3 Dissolve[84,87]	Effervescent tablets	600	400	1 BD	Suitable for vegetarians and safe in peanut/soya allergy
Cacit D3[84,88]	Sachet	500	440	1 BD	Safe in peanut/soya allergy
Calceos[89]	Chewable tablets	500	400	1 BD	-
Calcichew-D3 Forte[84,90]	Chewable tablets	500	400	1 BD	Safe in peanut/soya allergy
Calcichew-D3 Once Daily[84,91]	Chewable tablets	1,000	800	1 OD	Safe in peanut/soya allergy
Evacal D3[84,92]	Chewable tablets	600	400	1 BD	Suitable for vegetarians and safe in peanut/soya allergy
Natecal D3[93]	Chewable tablets	600	400	1 BD	-
theiCal-D3[84,94]	Chewable tablets	1,000	880	1 OD	Suitable for vegetarians and safe in peanut/soya allergy

*The above information might change over time. Please always check the latest summary of product characteristics (SPC) or with the manufacturer before treatment initiation. Licensed colecalciferol preparation is currently unavailable for vegans due to the involvement of lanolin in the production process. However, unlicensed products are available for vegans using colecalciferol that is produced from lichen. Please check with your pharmacy team for more advice.

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Appendix

7.1.2 Oral bisphosphonates

Oral bisphosphonates are recommended as the firstline treatment option for patients in the amber or red groups, with the exception of patients receiving radium-223. They **should not be used in patients with** oesophageal disorders such as achalasia, oesophageal stricture, oesophageal varices or Barrett's oesophagus as these can increase the risk of oesophageal irritation or damage.[95,96]

There are two main oral bisphosphonates:

Table 8. Key Information for oral bisphosphonates

	Alendronic acid	Risedronate sodium
Recommended renal function	Creatinine clearance >35 ml/min [97,98,99,100]	Creatinine clearance >30 ml/min[101,102]
Dosing frequency	70 mg once weekly (same day every week)[97,98,99,100]	35 mg once weekly[101,102](same day every week)
Available formulation	Tablet,[97,98] effervescent tablet[97,99] liquid[97,100]	Tablet[101,102]
Administration method	1. Take first thing in the morning when stomach is empty at least half an hour before any food or drink (plain water is fine) or medications. Take calcium and vitamin D supplements at least 2 hours later.[97,98,99,100,103] **Tablet:** 2. Swallow the tablet whole (do not chew, suck or crush) with a full glass of water (≥200 ml).[97,98,103] **Effervescent tablet:** 2. Dissolve tablet completely in half a glass of water (≥120 ml) before administration. Another ≥30 ml of water should be taken afterwards.[99] **Liquid (70 mg or 100 ml):** 2. Take the 100 ml dose (1 bottle) as a single dose. Another ≥30 ml of water should be taken afterwards.[100] 3. Sit upright or stand for at least half an hour after taking alendronic acid.[97,98,99,100,103]	1. Take when stomach is empty at least half an hour before breakfast or drink (plain water is fine) or medications OR at least 2 hours before or after food or drink (plain water is fine) or medications if between meals OR at least 2 hours after evening meal or drink (plain water is fine) or medications. Take calcium or vitamin D supplements at least 2 hours later.[101,102,103] 2. Swallow the tablet whole (do not chew, suck or crush) with a full glass of water (≥200 ml[101,102,103] 3. Sit upright or stand for at least half an hour after taking risedronate sodium.[101,102,103]
Missed dose	Can still take it when you remember (eg the following morning), then return to your usual day every week. Do not take two doses on the same day.[98,99,100,102,103]	
Common side-effects	Upper gastrointestinal problems (eg heartburn or dyspepsia) – usually the first month and improve over time.[103]	
Red flag symptoms	New pain in the jaw, thigh, hip, groin, ear or when you are swallowing, discharge from ear, ear infection and swallowing difficulties.[97,98,99,100,103]	

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Appendix

7.1.3 Parenteral antiresorptive agents

Parenteral antiresorptive agents recommended in this guideline are zoledronic acid (bisphosphonate) and denosumab (fully human monoclonal antibody). They work differently in stopping the activity of osteoclasts but share some risks and side-effects. Table 9 summarises the key information for both agents.

Table 9. Key information for zoledronic acid and denosumab

	Zoledronic acid	Denosumab
Dosing schedule	**Option 1:** 5 mg IV infusion yearly.[104] OR **Option 2 (with bone metastases):** 4 mg IV infusion every 3–4 weeks[72,73] (as per STAMPEDE and PEACE-3 trial) or 3 monthly[74] (see Table 4).	**Option 1:** 60 mg SC injection 6-monthly.[105] OR **Option 2 (with bone metastases):** 120 mg SC injection every 4 weeks[72,73] (as per PEACE-3 trial).
Renal function	**Option 1:** Proceed if CrCl ≥35 ml/min; contraindicated if CrCl <35 ml/min.[71] **Option 2 (with bone metastases):** Refer to Table 10 for starting dose based on renal function. Withhold treatment if serum creatinine increases by 44 mol/L (baseline serum creatinine <124 mol/L) or 88 mol/L (baseline serum creatinine >124 mol/L). Resume at the same dose when serum creatinine returned to within 10% of the baseline value.[106]	Higher risk of hypocalcaemia if eGFR <30 ml/min or having dialysis.[107]
Supplements [71,73,103,105,106]	Vitamin D deficiency must be treated with loading regimen (see Tables 5 and 6) and hypocalcaemia must be corrected beforehand. Maintenance doses of calcium and vitamin D supplements (see Table 7) should be taken alongside treatment.	
Monitoring [71,73,103,105,106]	• Baseline dental assessment and maintain good oral hygiene. • Osteonecrosis of the jaw. • Atypical femoral fractures. • Osteonecrosis of the external auditory canal. • Urea and electrolytes (particularly hypocalcaemia) before each dose. • Serum creatinine and renal function before each dose.	

Table 10. Zoledronic acid and creatinine clearance

Baseline creatinine clearance (ml/min)	Zoledronic acid starting dose (mg)
>60	4
50–60	3.5
40–49	3.3
30–39	3

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7.2 Antiresorptive agent toxicities and management

7.2.1 Gastrointestinal toxicity

Oral bisphosphonates (alendronic acid or risedronic acid) and intravenous zoledronic acid are recommended for use in prostate cancer patients.

- Alendronic acid is given 70 mg orally once weekly.
- Risedronate 35 mg orally once weekly.
- Zoledronic acid may be administered annually via intravenous infusion (5 mg over 15 minutes), particularly when oral bisphosphonates cause significant adverse effects, including upper gastrointestinal discomfort and bowel disturbances.[108]

Bisphosphonates may cause the following gastrointestinal adverse effects:

- Common: stomach pain, dyspepsia, constipation, diarrhoea, flatulence, oesophageal ulcer, dysphagia, abdominal distension, acid regurgitation.[109]
- Uncommon: nausea, vomiting, gastritis, oesophagitis, oesophageal erosions, melena.[109]
- Rare: oesophageal stricture, oropharyngeal ulceration, upper gastrointestinal perforation, ulcers, haemorrhage.[109]

Use with caution when prescribing bisphosphonates to individuals with:

- Upper gastrointestinal disorders, including dysphagia, oesophageal disease, gastritis, duodenitis and peptic ulceration.[108]
- A recent history (within the past 12 months) of significant gastrointestinal disease or upper gastrointestinal tract issues.[108]

Consider the pros as well as cons of treatment in patients with Barrett's oesophagus on a case-by-case basis.[108]

7.2.2 Hypocalcaemia

Antiresorptive agents may cause hypocalcaemia.

Recommendation

- Pre-existing hypocalcaemia must be addressed prior to initiating bisphosphonate therapy. Concurrent disorders of bone and mineral metabolism (eg parathyroid dysfunction, hypovitaminosis D) should be addressed upon initiation of bisphosphonate therapy.[71,110,111] Calcium supplements may be necessary to achieve 1,000–1,200 mg per day.[110]
- Vitamin D levels should be sustained with regular supplementation of vitamin D3, ranging from 800 to 2,000 IU per day. A loading dose should be given if indicated, as per Table 6.

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7.2.3 Renal impairment and bisphosphonates

Special consideration must be given to bisphosphonate dosing where there is renal impairment.

Recommendations

- Oral bisphosphonates and zoledronic acid are contraindicated in cases of severe renal impairment (creatinine clearance <30 ml/min). Alendronic acid should be avoided where eGFR is <35 ml/min.[110] Stepwise dose reductions of zoledronic acid are recommended for patients with a baseline creatinine clearance of 30–60 ml/min, depending on the renal function.[110]
- Check renal function before each administration of zoledronic acid.
  - In patients with bone metastases and mild to severe renal impairment (eGFR 30–60mls/min), it is advisable to dose reduce zoledronic acid at the start of treatment.
  - In patients who develop renal impairment during treatment, discontinue zoledronic acid. Zoledronic acid can be reinstated when serum creatinine levels revert to within 10% of baseline. Restart zoledronic acid at the dose used before the treatment break.[110]

7.3 Medication-related osteonecrosis of the jaw (MRONJ)

MRONJ is a rare but significant side-effect of antiresorptive and antiangiogenic agents. In patients with cancer, studies estimate an incidence of around 5%.[112] The incidence of MRONJ in patients with prostate cancer appears to be higher than in other cancers, but this may be related to the longevity of prostate cancer follow-up. Denosumab has been shown to increase the risk of MRONJ when compared with bisphosphonates.[113] A randomised controlled trial in 2012 noted a 5% risk of MRONJ in patients with non-metastatic castration-resistant prostate cancer who had received six months of ADT and intravenous denosumab.[114]

MRONJ is defined clinically as: (1) exposed bone, or bone that can be probed through an intra- or extraoral fistulae in the maxillofacial region, (2) persisting for greater than eight weeks, (3) in patients on antiresorptive and antiangiogenic agents, (4) with no history of radiation therapy to the jaws or metastatic disease to the jaws.[114]

A key risk factor is dentoalveolar and mucosal trauma, typically extraction of teeth, but it can also occur spontaneously. Pathophysiology is not fully understood, but hypotheses suggest necrosis secondary to suppression of bone remodelling inhibition, angiogenesis inhibition and toxic effects of soft-tissue inflammation infection.[115]

Additional risk factors include cumulative drug dose (linked to duration) and concurrent use of glucocorticoids.[115]

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The type of antiresorptive agent used can affect the risk of MRONJ. The incidence of MRONJ in osteoporotic patients taking denosumab has been reported as 0.3% after 10 years of follow-up.[112] This is higher than those taking oral and IV bisphosphonates. In patients with cancer the literature for both denosumab and IV zoledronate has reported rates <5% but with ranges of 0–6.9% and 0–18%, respectively.[112] A Cochrane review in 2016 reported risk of MRONJ specifically with long-term use and frequent IV dosing.[116]

To minimise the risk, dentoalveolar surgery (typically extraction of teeth with a poor prognosis) should ideally be carried out prior to starting antiresorptive or antiangiogenic agents. The prevention of dental disease is key, with oral health recommendations including twice daily brushing with a fluoride toothpaste, daily flossing, dietary advice to prevent tooth decay and regular dental review.

If a significant delay to dental treatment is anticipated, starting a patient on oral bisphosphonates at the same time as dental referral, given the low risk of MRONJ, could be considered. However, patients considered for IV bisphosphonates or denosumab therapy should ideally have a dental assessment and complete treatment prior to starting the medication. The MRONJ risk also increases with the duration of therapy, so early involvement of the dentist when prescribing these medications will reduce the risk.[112]

Recommendation

Patients should ideally have a dental assessment before starting BPAs. Where this is unavailable or significant delay to dental treatment is anticipated, oral bisphosphonates can be started and a dental referral done at the same time.

Management of MRONJ is led by secondary care oral surgery or special care dentistry teams. Antibiotics in conjunction with antibacterial mouthwashes and regular follow-up can be effective conservative management. However, in severe cases, debridement, extensive resection and surgical reconstruction may be indicated, causing severe patient morbidity.

7.4 Atypical fractures and rebound bone resorption with denosumab withdrawal

7.4.1 Atypical fractures

Atypical fractures are rare, typically involving the lateral cortex of the proximal femoral shaft and the subtrochanteric region.[117]

Bisphosphonates prevent normal bone remodelling; hence, microscopic damage can accumulate resulting in brittle bones likely to fracture during low-impact activity.[118]

Risk factors include longer duration of bisphosphonate treatment (particularly over five years), Asian ancestry, shorter height, higher weight and glucocorticoid use greater than one year.[119]

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Patients present with groin, hip or thigh pain. Atypical fractures are typically seen bilaterally, and imaging of the contralateral side is recommended if suspected.[117]

Urgent assessment by orthopaedics is required. Stopping bisphosphonates results in a rapid decline in risk of an atypical fracture but should be balanced against typical fracture risk.[119]

7.4.2 Rebound bone resorption

Discontinuing denosumab results in the rapid reversal of its inhibition of bone remodelling.

The relative risk of major osteoporotic fracture, including vertebral fracture, hip and other fractures, is significantly higher when denosumab is discontinued. Multiple vertebral fractures are more likely after stopping the medication, especially if the patient has a history of vertebral fracture prior to commencing therapy.[120]

Evidence suggests that vertebral fractures occur earlier and in higher numbers in longer durations of treatment, or if there is a history of osteoporosis prior to treatment.[119]

Discontinuing denosumab treatment therefore comes with risks. Extending denosumab beyond 10 years should be on an individual basis. If discontinuing, starting an oral bisphosphonate towards the end of therapy may reduce the incidence of rebound resorption.[120] In metastatic prostate cancer, continuing patients on denosumab for life seems sensible given their life expectancy and the risks of withdrawal. Where possible and commissioned, denosumab can be administered in the community. In the future this may be available for self-administration. When withdrawing denosumab, at least two infusions of zoledronic acid should be administered within 3–6 months.

7.5 Useful resources

At present there is no single resource addressing all aspects of bone health in this cohort of patients. Prostate Cancer UK has information on diet and physical activity for patients with prostate cancer.[121] Macmillan produces generic information on bone health and cancer ranging from detailed booklets to simple factsheets.[122] The Royal Osteoporosis Society (ROS) provides information on the risks of osteonecrosis of the jaw,[123] which can be provided to patients to facilitate discussions on dental care and hygiene while on bisphosphonates. The ROS has also produced a helpful guide to the strong, steady and straight[70] approach to physical exercise in the setting of osteoporosis, which can be incorporated into local practice. It is recommended that patients are referred to local exercise classes where available.

7.5.1 Dietary guidance

A list of the calcium content of different foods can be found on the website of the International Osteoporosis Foundation:

www.osteoporosis.foundation/sites/iofbonehealth/files/2021-09/Calcium Rich Food List_3007.pdf

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The Royal Osteoporosis Society has a calcium-rich food chooser. It has a list of calcium-rich foods by food groups and examples of how to add calcium to food as part of a balanced diet:

https://theros.org.uk/information-and-support/bone-health/nutrition-for-bones/calcium/calcium-rich-food-chooser

NOGG recommends the following:

- Recommend a healthy and balanced diet, moderation of alcohol consumption and avoidance of smoking.
- Ensure dietary calcium and vitamin D intake and supplement these as necessary.
- Encourage a combination of regular weight-bearing and muscle-strengthening exercise.

7.5.2 Exercise guides

Strong, steady and straight: physical activity and exercise for osteoporosis quick guide (for use in conjunction with the full expert consensus statement, Royal Osteoporosis Society):

https://theros.org.uk/media/0o5h1l53/ros-strong-steady-straight-quick-guide-february-2019.pdf

Strong, steady and straight: UK consensus statement on physical activity and exercise for osteoporosis. *British Journal of Sports Medicine*. https://bjsm.bmj.com/content/56/15/837

7.5.3 Patient information leaflets

Bisphosphonates. www.royalwolverhampton.nhs.uk/wp-content/uploads/2025/05/Bisphosphonates_for_Osteoporosis.pdf

BoneMed Online is a digital service from the Royal Osteoporosis Society for patients prescribed an osteoporosis medicine for the first time. https://theros.org.uk/bonemed-online

Osteoporosis drug treatments. Royal Osteoporosis Society. https://theros.org.uk/information-and-support/osteoporosis/treatment

7.5.4 General information on osteoporosis

Information for patients and the public on the prevention and treatment of osteoporosis in the NOGG Clinical Guideline.[64]

Royal Osteoporosis Society. www.theros.org.uk

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7.5.5 Dental letter: recommendations for patients

Patient information: medication-related osteonecrosis of the jaw (MROJ)

Some medicines used to strengthen your bones during prostate cancer treatment can very rarely cause a problem called **osteonecrosis of the jaw** (MRONJ). *Osteonecrosis* means 'bone death'. This happens when a small part of the jawbone does not heal properly. It often occurs after a tooth is taken out, an infection, an injury or if your mouth is not healthy. The bone may become exposed inside the mouth and can be slow to heal. This can cause pain, swelling or infection.

It is very important to **look after your mouth and teeth** while you are having treatment. You should see a dentist regularly (every 6–12 months, even if you feel well) to lower your risk of problems. Avoid having teeth removed if possible, but if you do need a tooth taken out, your dentist will need to check you carefully afterwards to make sure you heal well.

Contact your doctor or dentist straight away if you notice:

- pain, swelling or redness of the gums
- a loose tooth that does not settle
- a mouth ulcer or sore that does not heal
- bone showing inside your mouth
- a heavy or numb feeling in your jaw

Keeping your mouth healthy

Tooth decay often happens when you eat or drink sugary things, especially between meals. Sugar feeds the bacteria that damage teeth. Try to have sugary foods and drinks only with meals. For snacks, choose sugar-free foods like cheese or vegetables. Drink only water or tea/coffee without sugar between meals.

Tooth wear can also occur from acidic foods and drinks. Drink plenty of water, and try to keep fizzy or acidic drinks to mealtimes, or avoid them if you can.

Avoid smoking and reduce alcohol, as both slow down healing and raise the risk of mouth problems.

Gum disease happens when plaque builds up around the teeth. Keeping your mouth clean, visiting the dentist for regular cleaning and not smoking can all help reduce this.

If you wear dentures, make sure they fit well and do not rub or cause sores. Clean them every day and remove them at night. If they start to feel loose or uncomfortable, see your dentist promptly.

How to keep your mouth clean

- Brush your teeth twice a day, morning and night, using a fluoride toothpaste.
- Brush for 2–3 minutes each time.
- Use a medium-bristled manual or electric toothbrush.
- Clean between your teeth with interdental brushes, floss or a water flosser (ask your dentist which is best).
- You may use an alcohol-free fluoride mouthwash after brushing to help protect your teeth and gums.

Dental check-ups

If possible, see a dentist **before** you start cancer treatment, so any problems can be treated early. If you need to start treatment quickly, see a dentist as soon as you can afterwards, so your mouth stays healthy during your cancer care.

If you develop any dental problems during treatment, you should get dental help straight away. Your oncologist can provide a letter to explain this to your dentist.

See Section 7.3 for information on medication -related osteonecrosis of the jaw (MRONJ).

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7.5.6 Bone health management letter templates

Letter 1. Sample letter to GP – amber group

Dear Dr [GP's name]

Recommendation of bone protection agents for patient with prostate cancer

[Patient name; NHS number] has a diagnosis of prostate cancer and requires long-term androgen deprivation therapy (ADT). ADT is known to reduce bone mineral density over time. A bone health assessment has been performed to manage the high cumulative risk of secondary osteoporosis and fragility fracture, along with provision of lifestyle advice. We recommend the following as per The Royal College of Radiologists *National guideline of bone health management in patients with prostate cancer*.

Please prescribe bone protection agents including:

- A Weekly bisphosphonate – alendronic acid 70 mg or risedronate sodium 35 mg) AND
- B Calcium and vitamin D3 supplement (eg evacal D3 chewable tablets 1 BD; aiming for daily intake of at least 1,000 mg elemental calcium and 800 units vitamin D3).

We would be grateful if you could add these to their repeat prescriptions. Please kindly review the renal function prior to commencing bisphosphonate therapy.

A dental check has been advised if there is a history of poor dentition prior to starting bisphosphate therapy. The patient has also been counselled on side-effects of bisphosphonate therapy, including oesophagitis and osteonecrosis of the jaw.

In the event of intolerance to **all** types of oral treatment, please contact us to consider an alternative route of administration.

Yours sincerely

Letter 2. Sample letter to GP – red group

Dear Dr [GP's name]

Recommendation of bone protection agents for patient with prostate cancer

[Patient name; NHS number] has a diagnosis of prostate cancer and requires long-term androgen deprivation therapy (ADT) and a new [additional system anticancer therapy] treatment. They are known to reduce bone mineral density over time. A bone health assessment has been performed to manage the high cumulative risk of secondary osteoporosis and fragility fracture, along with provision of lifestyle advice. We recommend the following as per The Royal College of Radiologists *National guideline of bone health management in patients with prostate cancer*.

Please prescribe bone protection agents including:

- A Weekly bisphosphonate – alendronic acid 70 mg or risedronate sodium 35 mg) AND
- B Calcium and vitamin D3 supplement (eg evacal D3 chewable tablets 1 BD; aiming for daily intake of at least 1,000 mg elemental calcium and 800 units vitamin D3).

We would be grateful if you could add these to their repeat prescriptions. Please kindly review the renal function prior to commencing bisphosphonate therapy.

A dental check has been advised if there is a history of poor dentition prior to starting bisphosphate therapy. The patient has also been counselled on side-effects of bisphosphonate therapy, including oesophagitis and osteonecrosis of the jaw.

In the event of intolerance to **all** types of oral treatment, please contact us to consider an alternative route of administration.

Yours sincerely

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Letter 3. Sample letter to dentist

Baseline dental assessment for risk of MRONJ

[Insert date]

Dear [name of dentist]

I would be grateful if you could make arrangements to carry out a dental assessment of [insert patient name] to ensure they are dentally fit prior to starting antiresorptive treatment as part of the management of their prostate cancer.

- Diagnosis: [add details]
- Proposed treatment and start date: [add details]
- Medical history: [add details]
- Medications: [add details]
- Allergies: [add details]

[insert patient name] [is/is not] aware of current dental problems. [Give details of any history of pain or infection from the mouth] They do not have access to a primary care dental practitioner and due to the risk of them developing osteonecrosis of the jaw as a result of their treatment, I would be grateful if you could provide an urgent dental assessment to help to minimise this risk.

Thank you for your help with their care.

Yours sincerely

08 Glossary of terms and abbreviations

A	
ADT (androgen deprivation therapy)	A hormone-based treatment that reduces androgen levels to slow or stop the growth of prostate cancer.
AHP (allied health professionals)	Healthcare workers such as pharmacists or physiotherapists (not doctors or dentists) who provide system-wide care across a variety of healthcare and social settings.
androgen	A steroid hormone. For the purposes of this guideline, the use of androgen will refer specifically to testosterone.
androgen receptors	Proteins found on the external cell surface that bind testosterone. Once activated these receptors promote downstream signalling essential for cell growth and survival. Prostate cancer cells are often dependent on androgens and are a common target in its treatment.
antiresorptive agents	A class of medication that slows or inhibits bone resorption by osteoclasts. These can also be referred to as bone-modifying agents.
ARPI (androgen receptor pathway inhibitor)	A class of drugs used to block androgens in the treatment of prostate cancer. They include abiraterone, apalutamide, darolutmide and enzalutamide.
ARSI (androgen receptor signalling inhibitor)	A class of drugs that block androgen receptors and prevent testosterone bonding. ARSIs disrupt signalling pathways that would otherwise promote cell growth and survival.
ARTA (androgen receptor targeted agent)	Drugs that interfere with androgen receptor activation, inhibiting cell growth and survival. Examples include enzalutamide or darolutamide.
B	
bisphosphonates	A class of drugs that slow bone breakdown and reduce the risk of fractures or conditions like osteoporosis. Bisphosphonates work by reducing the activity of osteoclasts, cells responsible for the breakdown or resorption of bone.
BMAs (bone-modifying agents)	Medications such as bisphosphonates and denosumab that alter normal bone metabolism to help protect bone health. Sometimes referred to as antiresorptive agents.
BMD (bone mineral density)	A measure of bone strength often helpful in assessing osteoporosis risk.
BPAs (bone protection agents)	An umbrella term referring to drugs, including antiresorptive agents, such as bisphosphonates and denosumab and calcium or vitamin D supplements.

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C	
CFS (clinical frailty scale)	A tool used to assess a patient's frailty level and risk of falls.
COPD (chronic obstructive pulmonary disease)	A lung disease that may be a co-morbidity in prostate cancer patients.
CRPC (castration-resistant prostate cancer)	A form of prostate cancer that continues to progress despite low testosterone levels.
D	
denosumab	A targeted drug (monoclonal antibody) treatment used to prevent bone loss and fractures in patients receiving hormone therapy.
DEXA (dual-energy X-ray absorptiometry)	A scan used to measure bone mineral density, useful in assessing conditions such as osteoporosis and risk of fragility fracture.
F	
FFR (fragility fracture risk)	A scoring system to assess the likelihood of a fracture due to weakened bones.
FRAX (fracture risk assessment tool)	A tool used to estimate the 10-year probability of a major osteoporotic fracture.
G	
glucocorticoids	A type of steroid medication that can contribute to bone loss when used long term.
GP (general practitioner)	A primary care physician responsible for managing general health and referrals.
H	
HSPC (hormone-sensitive prostate cancer)	Prostate cancer that responds to hormone therapy.
L	
LHRHa (luteinising hormone-releasing hormone agonist)	A drug that works on the pituitary gland to reduce testosterone levels, commonly prescribed in prostate cancer treatment.
M	
mCRPC (metastatic castration-resistant prostate cancer)	A stage of prostate cancer that has spread beyond the prostate and does not respond to hormonal therapy.
metastasis	The spread of cancer beyond the prostate to affect other parts of the body, such as bones.
mHSPC (metastatic hormone-sensitive prostate cancer)	Prostate cancer that has spread beyond the prostate but still responds to hormone therapy.
morphometric vertebral fracture	A vertebral fracture defined by a change in shape or size of the vertebra.
MRONJ (medication-related osteonecrosis of the jaw)	A rare but serious condition of the jawbone related to medication use and often characterised by pain, swelling or poor healing.
N	
NICE (National Institute for Health and Care Excellence)	A UK body that provides guidelines for healthcare treatment and management.
NOGG (National Osteoporosis Guideline Group)	A UK-based organisation providing recommendations for osteoporosis prevention and management.

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O	
osteopenia	A condition where bone mineral density is lower than average, but not sufficient to be classified as osteoporosis or to significantly increase the risk of fracture. For patients who have received DEXA imaging osteopenia is described as a T-score between –1 and –2.5.
osteoporosis	A condition that weakens bones, making them more prone to fractures, often without other noticeable symptoms. For patients who receive DEXA imaging osteoporosis is defined by a T-score of <–2.5. T-scores compare a patient's bone mineral density with that of a healthy young adult.
P	
prednisolone	A corticosteroid often prescribed alongside prostate cancer treatments or to manage treatment side-effects.
R	
radium-223	A radiopharmaceutical used to treat bone metastases in prostate cancer.
RANKL (receptor activator of nuclear factor kappa-B ligand)	A protein involved in bone metabolism, targeted by drugs like denosumab.
rebound bone resorption	A condition where bone density rapidly declines after stopping certain osteoporosis treatments, such as denosumab.
S	
SACT (systemic anticancer therapy)	Treatments such as chemotherapy or targeted therapy used to treat cancer throughout the body.
SRE (skeletal-related event)	A complication such as a fracture, spinal cord compression or bone pain caused by bone metastases.
T	
traffic light system	A risk stratification method categorising patients into low (green), moderate (amber) and high (red) risk for bone fractures.

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The Royal College of Radiologists
63 Lincoln's Inn Fields
London, WC2A 3JW, UK

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+44 020 7405 1282
enquiries@rcr.ac.uk
rcr.ac.uk

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