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POSITION PAPER

Osteoporosis and osteoporosis therapies as determinants of implant fixation failure in arthroplasty and spinal fusion constructs: a position statement from the Fracture Working Group of the Council of Scientific Advisors of the International Osteoporosis Foundation

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Abstract

Summary This expert position statement reframes arthroplasty and spinal fusion complications under the unified endpoint of implant fixation failure, defined as loss of mechanical integrity of the bone–implant unit over time. It synthesizes mechanistic and clinical evidence and provides evidence-informed recommendations for peri-operative bone health optimization.

Background Osteoporosis is traditionally conceptualized as causing fragility fractures. However, compromised bone quality also affects the integrity of bone–implant constructs, influencing whether implants maintain fixation, interfaces remain stable, and fusion constructs consolidate.

Objective To synthesize mechanistic, translational, and clinical evidence on how osteoporosis and osteoporosis pharmacotherapies influence implant fixation failure across arthroplasty and spinal fusion, and to provide evidence-informed clinical recommendations for peri-operative bone health assessment and optimization within a unified construct-level framework.

Methods A position statement was developed following a structured literature search. Evidence was synthesized narratively by defining implant fixation failure as a construct-level outcome encompassing periprosthetic fracture, loosening, subsidence, pseudarthrosis, and junctional failure. Recommendations were categorized by strength (strong or conditional) and certainty of evidence (high, moderate, or low).

Results Low bone mineral density (BMD) is associated with implant fixation failure across arthroplasty and spinal fusion. In arthroplasty, randomized trials demonstrate preservation of periprosthetic BMD with bisphosphonates, while registry analyses suggest improved implant survival. In spinal fusion, antiresorptive and anabolic therapies influence fixation-related parameters, with anabolic agents showing the most consistent evidence for enhanced fusion mass and earlier union. Much of the literature relies on radiographic or biomechanical endpoints rather than definitive outcomes.

Conclusions Viewing arthroplasty and spinal fusion complications through a shared construct-level perspective provides a coherent link between osteoporosis and reconstructive durability. Systematic peri-operative bone health optimization may improve construct longevity, although more definitive outcome-driven trials are needed. Closer integration between orthopedic surgeons and osteoporosis specialists will be central to advancing peri-operative bone health care.

Keywords arthroplasty · cage subsidence · implant loosening · osteoporosis · periprosthetic fracture · pseudoarthrosis, osteoporosis treatment · screw fixation · spinal fusion

Extended author information available on the last page of the article

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Introduction

Osteoporosis has largely been conceptualized as a disease of fragility fractures and as a modifier of fracture healing. This paradigm has underpinned major advances in fracture prevention, post-fracture care, and pharmacological management. On the other hand, fracture-healing research has focused on biological processes operating at the tissue level, including inflammation, callus formation, endochondral and intramembranous ossification, and subsequent remodeling within a fracture gap [1].

Contemporary orthopedic practice, however, increasingly centers on surgical reconstruction using prostheses, fixation devices, and fusion procedures that fundamentally alter load transmission within the skeleton. In these settings, implants redistribute stress, introduce regions of stress concentration, and impose sustained mechanical demands on bone that may already be structurally compromised. While understanding of tissue-level healing biology remains essential, it does not fully explain the failure modes encountered in modern orthopedics, where adverse outcomes often arise not from impaired fracture repair per se, but from the inability of bone to maintain mechanical integrity following reconstruction.

As populations age and the number of arthroplasty, spinal instrumentation, and complex fixation procedures continues to rise, a growing proportion of adverse outcomes arise from the interaction between osteoporotic bone, orthopedic implants, and low-energy loading over time [2–4]. These outcomes are frequently catastrophic, costly, and associated with substantial morbidity and mortality, yet remain incompletely integrated into osteoporosis-focused paradigms.

In this manuscript, we deliberately shift the analytical scale upward, from tissue-level healing processes to the level at which orthopedic reconstruction interacts with surrounding bone. At this level, clinical outcomes reflect the interplay between a) bone quality, encompassing bone mass, microarchitecture, turnover, and material properties; b) orthopedic reconstruction, including prostheses, fixation devices, screws, cages, and fusion instrumentation; and c) repeated mechanical forces over time, that are redistributed and locally concentrated at specific bone-implant interfaces, influencing long-term stability.

Scope of the review and methodological approach

This expert position statement synthesizes and critically examines mechanistic, translational, and clinical evidence on how osteoporosis and osteoporosis therapies influence implant fixation failure in arthroplasty and spinal fusion constructs. While these two domains are unified by the shared mechanistic challenge of maintaining construct integrity under load, their specific clinical expressions differ. Consequently, we first establish this common framework before examining arthroplasty and spinal fusion separately; both sections utilize a parallel thematic structure encompassing pathophysiology, imaging assessment, and therapy to allow for a consistent evaluation across these two distinct orthopedic contexts. In addition, we also propose evidence-informed clinical recommendations for peri-operative bone health assessment and management aimed at reducing structural orthopedic failure; and identify key evidence gaps where targeted mechanistic studies and clinical trials are most urgently needed.

Approach to recommendation strength and evidence certainty

This document represents an expert position statement rather than a formal clinical practice guideline. Key recommendations are categorized using a simplified framework distinguishing certainty of evidence (High, Moderate, Low) - based on study design and directness of outcomes, and strength of recommendation (Strong or Conditional) - based on consistency of evidence and clinical applicability. This categorization was developed by the authors as a pragmatic framework to aid interpretation of the evidence and recommendations, and is not meant to be a formally validated one.

Literature search and study selection

This expert narrative review was informed by a structured literature search designed to identify studies relevant to perioperative bone health optimization in arthroplasty and spinal fusion.

PubMed/MEDLINE was searched from database inception through February 1, 2026, using combinations of terms related to the clinical setting (periprosthetic, arthroplasty, spinal fusion, implant fixation), bone health (osteoporosis, bone mineral density [BMD]), advanced skeletal imaging (dual-energy X-ray absorptiometry [DXA], opportunistic computed tomography [CT]-derived Hounsfield units [HU], quantitative computed tomography [QCT], high-resolution peripheral quantitative computed tomography [HR-pQCT]), biomechanical modeling (finite element analysis [FEA]), and commonly used osteoporosis pharmacotherapies (bisphosphonates, denosumab, teriparatide, abaloparatide, and romosozumab). Reference lists of key publications and prior reviews were also examined to ensure capture of influential studies.

Eligible studies included randomized controlled trials (RCTs), prospective and retrospective cohort studies,

registry analyses, systematic reviews, and meta-analyses reporting outcomes relevant to structural orthopedic integrity. These outcomes included periprosthetic fracture (PPF), revision or implant survival, component migration, periprosthetic BMD, spinal fusion rates, screw loosening, implant subsidence, DXA-derived areal BMD, CT-derived vertebral attenuation reported in Hounsfield Units (HU), volumetric BMD assessed by QCT, microarchitectural parameters measured by HR-pQCT, and FEA-derived estimates of construct stability or fixation strength.

Translational and preclinical studies were considered when experimental endpoints mapped directly to clinically relevant fixation, osseointegration, or fusion outcomes. Isolated case reports, small case series, and studies focused solely on short-term functional recovery or pain outcomes without structural correlates were excluded from the primary evidentiary base.

The evidence linking osteoporosis and osteoporosis therapies to reconstructive orthopedic outcomes varies substantially across domains. In spinal fusion and implant fixation, preclinical and biomechanical data complement a growing clinical evidence base. In contrast, PPF outcomes are predominantly informed by human observational studies, registry analyses, and epidemiologic data, with comparatively fewer translational models.

Given this heterogeneity, findings were synthesized narratively within a common conceptual framework. Preclinical and clinical evidence were integrated where biologically and methodologically appropriate, without imposing rigid symmetry across domains or outcome types.

Key orthopedic terms are briefly explained at their first occurrence in the text to support readability, with more detailed definitions and classifications provided within a ***Glossary in the Appendix*** *for readers who wish additional depth.*

The construct-level framework and the unifying endpoint of implant fixation failure

In this position statement, the term "construct" denotes the functional unit formed by an orthopedic implant and the surrounding host bone following surgical reconstruction. "Construct integrity" refers to the ability of this bone–implant unit to maintain stable structural support over time. We define "implant fixation failure" as loss of structural stability at the bone–implant interface due to inadequate mechanical support by the surrounding bone. This definition focuses specifically on mechanically mediated compromise of fixation, and not on patient-reported outcomes or early functional recovery. Clinically, fixation failure may be identified by imaging evidence such as fracture, loosening, migration, subsidence, non-union, or junctional failure. In many cases, these structural failures ultimately lead to revision surgery and are therefore reflected in revision rates in registry and clinical trial data.

Surgical technique, fixation strategy, and implant-related factors, including inadequate initial fixation, malposition, and material fatigue are recognized contributors to implant fixation failure [5–8]. Implant- and particle-associated inflammation and osteolysis, including chronic foreign-body responses that promote cytokine release and osteoclast activation with periprosthetic bone loss [6, 9, 10], may further reduce the mechanical margin of safety. However, these operator- and device-dependent mechanisms represent distinct pathways and lie outside the scope of the present position statement, which focuses specifically on bone-health-mediated determinants of construct durability.

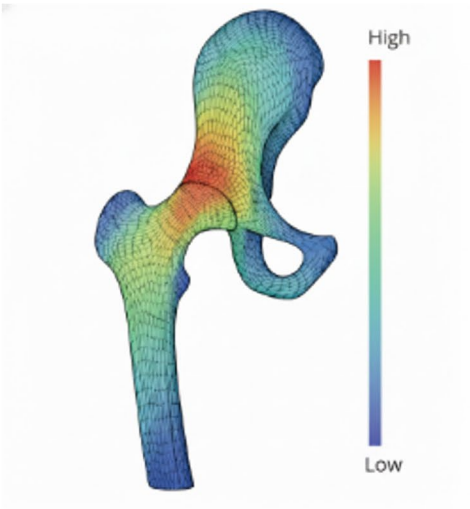
Arthroplasty context relevant to PPF risk

Arthroplasty is performed to restore joint function by replacing diseased articular surfaces with prosthetic components. *Total Hip Arthroplasty (THA)* replaces both the femoral head and acetabulum and is primarily performed for degenerative joint disease but is also used as primary or salvage treatment for displaced femoral neck fractures, failed internal fixation, or failed hemiarthroplasty in older adults. *Hemiarthroplasty* replaces only the femoral head and neck and is often selected for frail, low-demand older patients with hip fractures. *Bipolar designs* incorporate an additional internal articulation intended to distribute motion and reduce acetabular wear, although long-term acetabular degeneration may still occur [11].

Total knee arthroplasty (TKA) replaces the distal femur and proximal tibia of a diseased knee joint, with resurfacing of the patella performed selectively. It is most commonly undertaken for advanced knee osteoarthritis, but is also indicated for inflammatory arthritis, post-traumatic osteoarthritis, osteonecrosis, and severe deformity or instability refractory to non-operative management. TKA aims to relieve pain, restore alignment and stability, and improve function by replacing the diseased articular surfaces of the tibiofemoral and, where applicable, patellofemoral joints [12]. Although both hip and knee arthroplasty aim to restore joint function through replacement of diseased articular surfaces, the biomechanical pathways through which durable fixation is achieved differ between joints and vary according to implant design, patient factors, and regional practice patterns.

In THA, load transfer occurs predominantly through axial compression and bending along a long intramedullary stem, often resulting in proximal stress shielding; (a phenomenon discussed later), with relatively greater stress concentration distally. PPF patterns are therefore influenced by stem

a



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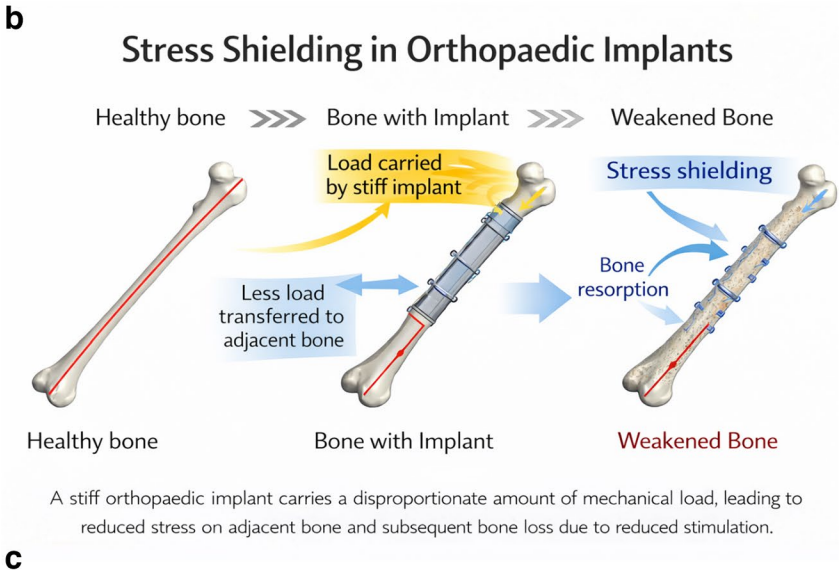
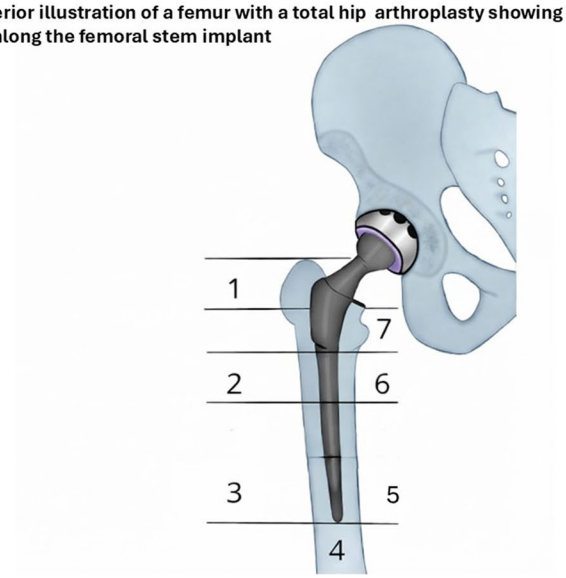


c

An anteroposterior illustration of a femur with a total hip arthroplasty showing the Gruen zone classification along the femoral stem implant



◀ **Fig. 1** **A**: A representative finite-element-style stress distribution of an intact (non-implanted) femur during routine weight bearing. Legend: In the native femur, load is transmitted from the femoral head through the femoral neck and calcar into the proximal medial cortex, with stress gradually distributed distally along the shaft. This native load pathway explains why the proximal medial and lateral regions (which correspond anatomically to Gruen zones 7 (calcar) and 1 (proximal lateral cortex) after stem implantation) normally experience higher strain, whereas more distal regions are relatively less loaded. Following stem implantation, load is partially redirected through the implant, resulting in relative unloading of proximal regions and greater stress transfer distally, providing a mechanistic basis for zone-specific stress shielding and bone remodeling observed after THA. Note: This panel is illustrative and intended to provide biomechanical context rather than quantitative stress values. **B**: Stress Shielding in Orthopedic Implants. **C** Gruen Zone Classification. **Legend:** The Gruen zone classification divides the proximal femur into seven standardized regions around the femoral stem on anteroposterior radiographs to localize patterns of periprosthetic bone remodeling and stress shielding following total hip arthroplasty. Zones 1 and 7 correspond to the proximal lateral and medial femur, respectively, including the greater trochanter and calcar femorale, regions that normally experience high compressive and bending loads. Zones 2 and 6 represent the mid-proximal femoral shaft, while zones 3 and 5 correspond to the distal stem region, and zone 4 represents the stem tip. *These figures were created by the authors using a generative AI-assisted image tool,

length, stiffness, and fixation strategy. In contrast, TKA transmits joint reaction forces across the distal femur and proximal tibia, with greater contributions from shear and torsional forces and typically without a long intramedullary femoral stem. Accordingly, fracture vulnerability in TKA relates more to metaphyseal bone loss and cortical thinning rather than stem-tip effects.

Despite these joint-specific differences in implant geometry and force distribution, both procedures ultimately create a bone-implant system that alters the physiological transfer of load through the native joint. Across these arthroplasty sites, common principles govern periprosthetic bone loss and fracture risk, with redistribution of mechanical forces, region-specific bone adaptation, and interaction with underlying osteoporosis, having implications on structural stability. For this reason, the present paper is framed at the level of construct behavior rather than joint-specific surgical technique. Although similar biomechanical principles apply to other joint replacements, including shoulder arthroplasty, the present position statement focuses primarily on THA and TKA, where the majority of PPF data and bone-health literature are concentrated.

Biomechanics of load transfer, fixation strategy, and bone quality

As illustrated in Fig. 1 Panel A, in the native femur, load is transmitted from the femoral head through the calcar and medial cortex, with adaptive remodeling maintaining structural integrity under habitual or low-energy external forces over time.

Stress shielding occurs when a relatively stiff implant assumes a disproportionate share of mechanical load, reducing stress transmission to adjacent bone [13]. In accordance with *Wolff's law,* reduced mechanical loading leads to adaptive or increased bone resorption and local weakening over time [14] (Fig. 1: Panel B). The magnitude and spatial distribution of stress shielding are influenced by implant stiffness, geometry, and fixation methods. The consequences of stress shielding include localized periprosthetic bone loss, increased susceptibility to PPF, implant loosening, and greater technical difficulty during revision surgery. These biomechanical effects are central to understanding why PPFs occur preferentially at specific anatomical locations.

Against this biomechanical backdrop, proximal femoral morphology and bone quality are commonly described using the *Dorr classification* (Appendix-Glossary of Terms), which categorizes femora into Type A (thick cortices, narrow canal), Type B (intermediate morphology), and Type C ("stovepipe" femora with thin cortices and a wide canal) [15]. This system was developed to guide the choice between *cemented* and *cementless* femoral fixation. *Cementless fixation* relies on press-fit mechanics and subsequent osseointegration, generating radial hoop stresses within the surrounding cortex. In osteoporotic bone, particularly Dorr Type C femora, thin cortices may be unable to tolerate these stresses, increasing the risk of intra-operative or early postoperative PPFs. *Cemented fixation* distributes load through a cement mantle and may reduce fracture risk in poor-quality bone [16, 17]. Similar principles apply in TKA, where altered load transfer can result in regional stress shielding and periprosthetic bone loss in the distal femur and proximal tibia, with implications for later fracture risk and fixation failure [18].

Periprosthetic fractures (PPFs)

Clinical significance and epidemiology

PPFs are among the most serious complications following joint arthroplasty and are associated with substantial morbidity, mortality, healthcare utilization, and cost. Population-based registry data demonstrate that the incidence of PPFs after total hip arthroplasty has increased steadily over the past two decades, with reported rates rising from approximately 0.1–0.4% in early postoperative periods to substantially higher rates over longer follow-up**,** largely paralleling growth in primary and revision arthroplasty in aging populations [3, 19]. Importantly, periprosthetic femoral fractures after THA are associated with 1-year mortality rates of

11–18%, similar to those observed after native hip fractures in older adults [20]. These events should therefore not be regarded as isolated technical complications, but as major adverse orthopedic events with systemic and prognostic consequences, particularly in older patients. In registry-based datasets, the typical age at primary THA is around 69 years [21]. Many patients therefore live for at least a decade with the primary implant in situ [22, 23], while age-related cortical thinning and systemic bone loss continue. Progressive reductions in cortical thickness and BMD may increase susceptibility to PPFs over time, even when the initial reconstruction was technically sound.

The number of TKAs performed per year also has been increasing annually. For example, in the USA, it is estimated that by 2030, 3.48 million TKAs will be performed per year [24]. Following TKA, the PPF incidence is reported between 0.3% and 2.5% for primary implants, escalating to 5–10% in revision settings [25]. These injuries carry a severe prognosis; population-based data indicate a 1-year mortality rate for periprosthetic distal femur fractures of 18.6%, with the vast majority of deaths occurring within the first three months postfracture [26].

PPFs as a biomechanically distinct failure entity

Although classified as fractures, PPFs differ from classic fragility fractures in their mechanical etiology and biological context, arising in bone whose mechanical behavior has been altered by orthopedic reconstruction. Failure occurs at anatomically predictable sites created by implant-related biomechanics, altered load transfer, and stress concentration, most commonly at transition zones such as the stem tip or implant–bone junction [27]. These characteristic failure patterns have been consistently demonstrated across hip, knee, and shoulder arthroplasty and are not specific to any single joint [28–30]. The fractures can occur across a wide range of BMD values, including individuals with DXA values in the normal range, reflecting the limitations of BMD in capturing bone strength, cortical thickness, bone geometry, and microarchitectural integrity. Reduced bone strength, whether reflected by low BMD or by deficits not captured by DXA lowers the threshold for fracture around an implant. However, a PPF is defined by its occurrence adjacent to a prosthesis and by the mechanical stresses created by that prosthesis; BMD increases susceptibility but does not dictate how or where the fracture occurs.

Classification of PPFs

Bone stock and implant stability are the core mechanistic variables governing PPF behavior and management. These variables also represent the principal pathways through which osteoporosis influences fracture risk at the bone-implant interface. Contemporary classification systems therefore explicitly encode residual bone quality and implant fixation, distinguishing whether failure is driven predominantly by compromised bone, implant instability, or a combination of both.

For post THA femoral fractures, the *Vancouver classification* stratifies fractures by anatomical location, femoral stem stability, and bone stock, with each category mapping directly to surgical strategy and reflecting the integrity of load transfer across the bone–implant interface [31]. (Appendix Glossary of Terms). PPFs around TKA are similarly classified according to fracture location and component stability, including systems for distal femoral and proximal tibial fractures [32, 33]. The *Unified Classification System* extends these principles across joints and implant types, providing a consistent descriptive framework while preserving the central importance of bone stock and implant fixation [34] (Appendix Glossary of Terms).

Role of osteoporosis in PPF risk

Low BMD and compromised bone quality are highly prevalent in patients undergoing THA and TKA [35]. Cross-sectional and cohort studies demonstrate that between 60–80% of patients presenting for TKA have osteopenia or osteoporosis, which remains substantially underdiagnosed and undertreated pre-operatively [36, 37]. In elderly patients undergoing THA, 18% meet densitometric criteria for osteoporosis and a further 41% for osteopenia, with nearly three-quarters of osteoporotic patients undiagnosed pre-operatively [36].

Osteoporosis contributes to PPF risk not only through reductions in bone mass, but also via deterioration of cortical thickness, trabecular microarchitecture, and material properties [38, 39], which together may reduce mechanical competence of bone at the implant interface and lower the threshold for failure. Periprosthetic regions experience different combinations of compression, tension and bending, hence, the mechanical consequences of bone loss are also mode-dependent: mineralization contributes strongly to stiffness and compressive load bearing [40], whereas collagen integrity is critical for post-yield behavior or toughness and resistance to failure under bending or tensile loading [41, 42]. Accordingly, local changes in matrix composition and microstructure can disproportionately reduce the 'margin of safety' in regions where tensile/bending strains predominate, even when areal BMD is not dramatically low.

Apart from affecting longevity of the primary reconstruction, reduced bone stock presents serious problems for revision surgery [43]. Bone remodeling commonly associated with implant loosening may require revision total hip replacement (THR) when there is substantial proximal femoral bone loss [44]. Additionally, the surgical exposure

required to remove primary implants may alter the proximal femur's structure. As a result, in many revision hip situations, the proximal femur provides compromised support for the revision femoral component. Femoral components without proper proximal support experience higher loading and the risk of fatigue fracture of the stem is increased. In revision THR, efforts directed toward proximal femoral bone restoration and use of larger prostheses may contribute to avoiding prostheses fatigue fracture [44]. Implant-related factors, including stem geometry, fixation method, and stiffness mismatch interact with bone quality to further influence PPF risk.

Arthroplasty itself induces region-specific bone loss. A systematic review and meta-analysis of longitudinal DXA studies demonstrated a rapid ~ 15% reduction in distal femoral BMD within 6 months of TKA, with the nadir reached by 12 months and no recovery by 24 months, consistent with stress shielding and altered load transfer [45]. However, the included studies were heterogeneous in quality and methodology, and some relied on small or variably defined regions of interest, which may influence estimates of the magnitude of change. Accordingly, while the direction of effect appears consistent, the extent of periprosthetic bone loss remains variable across studies, underscoring that the magnitude of periprosthetic bone loss after TKA remains incompletely defined and warrants further high-quality study. Similar patterns of periprosthetic bone loss have been documented following THA, particularly in Gruen zone 7 [46]—Fig. 1 Panel C.

In osteoporotic bone, uncemented femoral stems are associated with a higher risk of early PPF compared with cemented fixation, consistent with reduced initial mechanical stability and diminished cortical support [47]. In an analysis of 437,629 primary THA procedures from the Nordic Arthroplasty Register Association, revision for periprosthetic femoral fracture within the first two postoperative years was uncommon overall but substantially more frequent after uncemented than cemented stem fixation (0.47% vs. 0.07%; relative risk 8.72), highlighting fixation strategy as an important determinant of early fracture risk [48].

Registry data from the American Joint Replacement Registry similarly demonstrate marked reduction in early revision for PPF with cemented fixation in patients over 65 years of age, but also report higher short-term mortality associated with cemented stems compared with cementless fixation [49]. These findings underscore the complex risk–benefit trade-offs inherent in fixation strategy selection. Interpretation of all such registry-based observations should account for confounding by indication, as fixation choice is not randomized and reflects surgical judgment influenced by femoral morphology, frailty, fall risk, physiological reserve, and comorbidities, factors incompletely captured in arthroplasty registries. In addition, not all PPF lead to revision and may therefore be under-ascertained, while changes in implant design, surgical technique, and fixation preferences over time further influence observed risks.

Registry data also have consistently demonstrated higher rates of PPF among patients with osteoporosis or osteopenia compared with those with normal BMD. The Hip Arthroplasty Registry study mentioned earlier showed a significantly increased risk of early postoperative periprosthetic femoral fracture, particularly within the first two years, consistent with the likely vulnerability of the early fixation/implant–bone construct [48]. This heightened biological vulnerability must be interpreted alongside exposure to external mechanical load. Falls are common after total joint replacement, and most postoperative periprosthetic femoral fractures follow low-energy falls from standing or sitting height [50–52], highlighting falls as a major external precipitant of construct failure in this age group.

Risk factors for poor bone quality relevant to PPFs

Poor bone quality is common and frequently underdiagnosed in patients undergoing arthroplasty and spinal fusion, and is a major contributor to PPF and implant fixation failure [53]. Key patient-level risk factors that should prompt preoperative bone health evaluation include prior fragility fracture, known low BMD, chronic glucocorticoid exposure, and smoking [54]. In addition, meta-analytic data have identified other contributors including uncemented stems (Odds Ratio [OR]: 3.36, 95% Confidence Interval [95% CI]: 3.02–3.74), female gender (OR: 1.60, [95% CI]: 1.43–1.78), morbid obesity (OR: 1.44, [95% CI]: 1.01–2.16), major comorbidity burden with higher Deyo-Charlson index (OR: 1.44, [95% CI]: 1.18–1.77), rheumatoid arthritis (OR: 1.89, [95% CI]: 1.16–3.06), femoral Dorr type C (OR: 4.23, [95% CI]: 2.82–6.33), age > 70 years (OR: 1.67, [95% CI]: 1.19–2.34), revision hip arthroplasty (OR: 2.60, [95% CI]: 1.59–4.27 (the latter specifically for THA) [55] as well as anterior femoral notching and neurological disease (e.g., Parkinson's) - the latter two noted for TKA [56].

Importantly, intraoperative surgeon concern about poor bone quality during TKA and THA correlates with distal femur and overall DXA-measured BMD, supporting its use as a "safety-net" prompt to initiate formal bone health assessment when pre-operative evaluation was incomplete [57, 58].

Detection of periprosthetic bone loss: imaging modalities and clinical relevance

DXA

DXA remains the most widely used modality for evaluating peri-prosthetic BMD due to low radiation exposure, cost,

and availability. It can be adapted to assess regional stress-shielding patterns adjacent to implants and prosthesis stability. However, DXA is vulnerable to real-world sources of error including interference from metal artifacts, calcifications, degenerative change, soft-tissue thickness, and positioning, which may over- or underestimate BMD [59]. Limb rotation and knee flexion can significantly affect measurement precision, underscoring the need for standardized acquisition protocols, especially when performing region-specific peri-prosthetic assessments. It must also be remembered that, as a two-dimensional areal technique, DXA cannot distinguish cortical from trabecular compartments or account for geometric changes [60].

Periprosthetic bone loss after arthroplasty is highly regional and dependent on implant design and altered load transfer, rendering routine central hip or spine DXA alone insufficient for characterization of regional periprosthetic remodeling. Reproducibility is region dependent. After TKA, precision errors (Coefficient of Variations/CVs) for periprosthetic DXA measurements are approximately 2.9% in tibial Regions of Interest (ROIs) and 3.1% in femoral ROIs, comparable to control knees, indicating good reproducibility of these measurements. The highest reproducibility is observed in the femoral diaphysis above the implant (CV ~ 1.3%), likely reflecting reduced metallic interference and more consistent positioning, whereas the patella demonstrates poorer reproducibility (CV ~ 6.9%) due to its smaller size, variable positioning, and prosthesis-related artifact [61]. After THA, reproducibility likewise varies regionally, with proximal Gruen zones demonstrating higher variability (CVs ~ 5.0–5.3%) than distal regions (~ 2.8%), likely due to complex proximal geometry and metal-related artifact. Importantly, a change > 0.16 g/cm2 is considered reliably detectable. Smaller changes may simply reflect positioning differences, machine noise or measurement error [62]. The principal utility of periprosthetic DXA lies in longitudinal monitoring of regional bone remodeling and implant-related bone loss rather than osteoporosis diagnosis alone.

Blaty et al. demonstrated that distal femoral BMD at 15 and 25% of femoral length above the joint line was ~ 10% lower in the operated limb versus contralateral femur, with smaller differences in BMD observed proximally [63]. A reproducible method uses a standardized "stacking" ROI technique based on femur length, in which the femur is divided into sequential percentage-based segments and BMD is sampled at 5% increments proximally from the intercondylar notch. Very distal ROIs (5 and 10%) are avoided due to prosthesis or patellar interference [64]. Based on BMD distribution and fracture location, 15 and 25% femur-length ROIs are proposed as standard distal femoral monitoring sites after TKA [64]. For TKA assessment, PA projections generally demonstrate better reproducibility than lateral views, particularly in shaft regions, as lateral measurements are more susceptible to positioning variability and fibular overlap [54].

In addition to trabecular loss, cortical thinning has been demonstrated in operated limbs [65]. Radiographic cortical thickness index correlates strongly with femoral neck BMD and osteoporosis in adults over 50 ($r = -0.7$, $p < 0.001$) [66], reinforcing that central DXA alone may miss clinically relevant periprosthetic deterioration.

Longitudinal periprosthetic DXA using Gruen zones has identified significant bone loss after cementless THA, greatest in proximal medial femur (zone 7), the region most susceptible to stress shielding [67]. In a retrospective cohort of 427 patients, Fu et al. reported early, region-specific bone loss in 61–63% of patients within the first postoperative year. In this study, baseline BMD in the affected Gruen zone and primary diagnosis predicted subsequent loss [68], suggesting potential for targeted early intervention. *These Gruen ROIs replicate the original radiographic zones and are implemented using metal-removal software, with the femoral stem as reference and ROIs positioned medially and laterally in proximal, mid, distal segments, plus distal to the stem tip* [69]. *Clinically, scans are obtained 1–3 months postoperatively to establish baseline, with follow-up at 6–24 months. Interpretation is based on percentage change exceeding facility-specific least significant change (LSC), rather than absolute thresholds.*

The International Society for Clinical Densitometry (ISCD) has concluded that femoral and proximal tibial BMD measurements are reliable and valid in the presence of orthopedic implants and can provide meaningful information regarding peri-implant remodeling and loosening [54]. Despite this endorsement, periprosthetic DXA is not yet routinely integrated into orthopedic practice, and standardized acquisition and interpretation protocols remain needed.

Quantitative computed tomography (QCT) for periprosthetic bone assessment

QCT provides three-dimensional, volumetric assessment of BMD with the ability to distinguish cortical from trabecular compartments, a theoretical advantage in the arthroplasty setting where cortical thinning, stress shielding, and altered load transfer predominate. In contrast to areal DXA, QCT enables regional volumetric analysis of periprosthetic bone adjacent to implants, which may enhance understanding of fixation integrity and failure risk after THA and TKA [60, 70, 71].

However, direct clinical validation of QCT for routine periprosthetic BMD assessment after THA or TKA remains limited. The literature supporting QCT-derived periprosthetic BMD measurements after arthroplasty is heterogeneous and inconclusive, with concerns relating to radiation exposure, reproducibility, metal artifact interference, and

lack of standardized protocols, limiting widespread clinical adoption. Consequently, while QCT offers important mechanistic and research value, its role in routine peri-operative bone health assessment for THA/TKA and PPF risk remains adjunctive rather than primary, pending further outcome-linked validation studies.

In parallel, advances in conventional (non-quantitative) CT imaging have focused on improving visualization at the bone-implant interface rather than on densitometric quantification. For example, Kasparek et al. demonstrated that dual-energy CT acquisition combined with titanium or ceramic prostheses significantly reduces metal artifacts and improves image quality around TKA implants [72]. While dual-energy CT does not provide calibrated volumetric BMD in the manner of QCT, it enhances structural assessment of the periprosthetic region and supports the feasibility of CT-based morphological evaluation in the presence of implants.

High-resolution peripheral quantitative computed tomography (HR-pQCT)

HR-pQCT enables in vivo, three-dimensional assessment of cortical and trabecular bone microarchitecture at a resolution far exceeding DXA or conventional QCT, allowing direct visualization of microstructural bone loss. Although its restricted field of view precludes routine assessment of periprosthetic bone at hip or knee arthroplasty sites, HR-pQCT has provided important mechanistic insights in selected reconstructive settings, including demonstration of trabecular ingrowth and microstructural integration at bone–implant interfaces in revision THA, supporting its role as a research-grade tool for elucidating pathways of implant fixation failure. [73].

Biomechanical and intra-operative evaluation of bone quality

Finite-element analyses (FEA) of cemented THA have demonstrated that proximal bone support and cement are critical for load transfer and construct stability, and when proximal bone support is reduced, the stem becomes less stable, leading to greater micromotion and bending forces that may promote fatigue failure [74]. Such stress amplification is likely to be clinically relevant in osteoporotic bone, where thinner and weaker cortices are particularly vulnerable to repeated bending and pulling forces generated by the implant, rather than compressive loading alone, leading to increased micromotion and fatigue-related failure. Intra-operative assessment of trabecular bone quality during THA has been explored using torque-based measurement devices. In a prospective clinical study, Klotz et al. demonstrated that trabecular peak torque measured in the femoral head and neck correlated significantly with areal BMD assessed by DXA, as well as with high-resolution micro-CT-derived structural parameters and monoaxial compressive strength [75]. These findings suggest that intra-operative trabecular torque measurements provide a feasible surrogate of local bone quality during THA, although further validation is required before routine clinical adoption [76].

Integrated perspective on peri operative imaging for periprosthetic bone loss

Assessment of periprosthetic bone health is best approached using a tiered imaging strategy that balances clinical feasibility with biomechanical insight. Region-specific DXA is the pragmatic first-line tool for longitudinal monitoring, as it captures spatial patterns of stress shielding and implant-related bone loss that are not apparent on conventional hip or spine DXA. Standardized approaches such as Gruen-zone analysis after THA are recognized in international densitometry guidance, including ISCD Official Positions [54]. However, implementation of region-specific periprosthetic DXA requires appropriate analysis software, standardized acquisition protocols, and trained operators, and is therefore not uniformly available worldwide.

Where region-specific periprosthetic DXA is not feasible, assessment should emphasize longitudinal change at standard clinical DXA sites (e.g., lumbar spine, contralateral hip, or forearm where indicated), comparing baseline and follow-up measurements within the same patient, rather than reliance on single absolute BMD values, together with routine radiographic follow-up to detect cortical thinning, radiolucency, or implant migration. Integration of imaging findings with biomechanical modeling and intraoperative measures reinforces that local bone quality is a primary determinant of implant stability and fatigue failure risk. Three-dimensional modalities such as QCT and HR-pQCT provide important mechanistic insight by distinguishing cortical from trabecular deterioration and microstructural failure pathways but remain adjunctive due to practical and validation constraints. Accordingly, routine surveillance should prioritize longitudinal, region-specific DXA where expertise and infrastructure permit, reserving advanced imaging and biomechanical assessment for selected high-risk or revision settings.

Osteoporosis therapies

Robust translational animal models examining pharmacologic modification of periprosthetic bone loss are sparse [77]. Consequently, evidence relating osteoporosis therapies to PPF outcomes is derived predominantly from human observational studies, registry analyses, and surrogate endpoints, rather than direct fracture-reduction trials. This evidence asymmetry necessitates cautious interpretation and underscores

the importance of evaluating osteoporosis therapies in the periprosthetic setting.

Antiresorptive therapy and periprosthetic outcomes

Bisphosphonates

The evidence supporting bisphosphonate use in arthroplasty spans animal models, randomized trials, registry cohorts, and meta-analyses [77–87] (Table 1).

Across study designs, bisphosphonates particularly the more potent ones and especially when administered during the early postoperative period, consistently have been shown to preserve peri-implant bone stock and attenuate early periprosthetic bone loss (Table 1). RCTs [82–84, 86] demonstrate preservation of periprosthetic BMD, while large observational cohorts suggest improved implant survival and reduced revision risk [79, 80], supporting a construct-level effect mediated through maintenance of peri-implant structural support rather than alteration of early mechanical fixation or migration. Evidence for reduction in PPF, early migration, or cementless fixation micromotion is limited and heterogeneous, and frequently confounded by indication. Thus, preservation of periprosthetic bone mass does not equate to uniform protection across all PPF phenotypes. Observational signals of an increased fracture risk reported in some bisphosphonate therapy settings likely reflect confounding, variation in fracture mechanisms, and timing of therapy relative to surgery rather than a direct adverse effect on fixation [87]. Taken together, the totality of evidence supports bisphosphonates as agents that stabilize the peri-implant environment and potentially enhance long-term construct durability, while highlighting the importance of context, timing, and fracture phenotype in interpreting fracture-related outcomes. *They should not be considered universal prophylaxis against all forms of arthroplasty failure.*

Denosumab

Denosumab consistently preserves early periprosthetic BMD after arthroplasty [88–91] (Table 2), but has not been shown to reduce early stem migration in randomized trials. Apparent differences noted compared to the studies employing bisphosphonates largely reflect endpoints assessed: denosumab trials emphasize early BMD and migration metrics, whereas bisphosphonate benefits are more often inferred from longer-term structural outcomes such as revision, loosening, or subsidence.

Anabolic and dual-action therapies

Teriparatide

As a synthetic human parathyroid hormone, teriparatide acts as an anabolic agent to enhance osteoblast function and bone formation. Teriparatide may be a reasonable treatment option for osteoporotic patients to preserve or improve periprosthetic BMD after TKA. In a prospective study that involved 17 patients, there was a significant increase in specific ROI BMD of the knee at 6 months and at 12 months [92]. The study group had a higher adjusted mean BMD in all regions than did the control group at 6 and 12 months. In THA, teriparatide was found to be equally as effective as alendronate for preserving periprosthetic BMD, achieving gains of up to $12.7 \pm 7.1\%$ at one year in one RCT [93].

Abaloparatide

There are no direct human outcomes trials showing that abaloparatide reduces PPFs**,** aseptic loosening**,** or the need for revision after THA/TKA. However, a post hoc analysis evaluated DXA hip scans from 500 randomly selected postmenopausal women with osteoporosis from the Phase-3 Abaloparatide Comparator Trial in Vertebral Endpoints (ACTIVE, NCT01343004) study after 0, 6, and 18 months of abaloparatide or placebo [94]. The DXA scans of these patients were subjected to 3-dimensional (3D) modeling using 3D-Shaper-a validated 3D-DXA reconstruction technique that derives volumetric BMD, cortical thickness, and geometric parameters of the proximal femur from standard two-dimensional hip DXA images [95]. Virtual resection of the proximal femur and simulated placement of a tapered, flat-wedge hip stem were then performed to delineate Gruen zones. Integral, cortical, and trabecular volumetric BMD, cortical thickness, and cortical surface BMD (the product of cortical volumetric BMD and cortical thickness) were determined for each zone. Compared with placebo, the abaloparatide group showed greater increases in integral volumetric BMD in all zones at months 6 and 18; cortical surface BMD in zones 1, 6, and 7 at month 6; cortical thickness, cortical volumetric BMD, and cortical surface BMD in all zones at month 18; and trabecular volumetric BMD in zones 1 and 7 at months 6 and 18. The conclusion of the study was that abaloparatide increases BMD in proximal femoral regions that interact with and support femoral stems, suggesting that abaloparatide may have value for pre-operative or potentially peri-operative bone health optimization in patients with osteoporosis undergoing THA.

Romosozumab

Romosozumab exerts a dual effect by binding sclerostin to promote bone formation while simultaneously reducing bone resorption. While its efficacy in primary osteoporosis populations has been well documented, there is currently a lack of specific research regarding its impact on periprosthetic BMD and clinical outcomes after arthroplasty.

Table 1 Bisphosphonates and periprosthetic outcomes: summary of evidence

Author (Year)	Study Type/Population	Agent	Timing & Dose	Primary Outcome(s)	Key Findings
Jakobsen et al. (2007) [77]	Large animal uncemented implant model	Zoledronic acid (local)	Local application at implantation	Peri-implant bone resorption, micromotion	Zoledronic acid significantly reduced micromotion-induced bone resorption and osteoclastic activity at the bone–implant interface, preserving peri-implant bone volume under load
Jaroma et al. (2006) [78]	Prospective clinical study, TKA patients	Alendronate	Post-op oral therapy	Tibial plateau BMD	Significant increase in lateral tibial plateau BMD vs calcium-only controls after TKA
(Prieto-Alhambra et al. 2011**)** [79]	National retrospective cohort, THA/TKA	Mixed bisphosphonates	Postoperative use	Revision risk	Bisphosphonate use is associated with lower revision risk and longer implant survival (HR 0.54)
Prieto-Alhambra et al., (2014) [80]	Nationwide cohort	Mixed bisphosphonates	Initiated post-op	Revision risk	Reduced revision risk, strongest when bisphosphonates were started postoperatively
Shi et al. (2018) [81]	Systematic review & meta-analysis (14 trials, n = 620)	Multiple bisphosphonates	Variable	Periprosthetic BMD	Significant preservation of periprosthetic BMD at 1 year (MD 0.06 (95% CI [0.03–0.081], *p*,0.001) 2–4 years (MD 0.04 (95% CI [0.01–0.07], $p = 0.02$, and > 5 years (MD 0.08 (95% CI [0.06–0.11], $p < 0.001$) post-THA; greater effect with third-generation agents
Huang et al. (2009) [82]	Prospective RCT, cementless THA	Zoledronic acid	Single IV infusion post-op	Bone turnover markers, Periprosthetic BMD	Restored suppressed bone turnover and significantly reduced periprosthetic BMD loss (+6.8% vs −11–17% in controls, $p < 0.001$) at 2 years
Liu et al. (2021) [83]	Meta analysis of 6 RCTs involving 307 patients	Zoledronic acid	Single IV infusion ranging from 2 days before operation to 2 weeks after	Periprosthetic BMD	Significantly less periprosthetic BMD loss at 3 months (MD = 4.03%, [95% CI:0.29–7.76%], $p = 0.03$), 6 months (MD = 7.04%, [95% CI: 2.12–11.96%], $p = 0.005$) and 12 months (MD = 7.12%, [95% CI: 0.33–13.92%], $p = 0.04$)

Table 1 (continued)

Author (Year)	Study Type/Population	Agent	Timing & Dose	Primary Outcome(s)	Key Findings
Scott et al. (2013) [84]	RCT, cementless THA	Zoledronic acid	Single IV dose post-op	Periprosthetic BMD, migration	Significant preservation of BMD in Gruen zone 1 (+13.8% vs +1.4%, $p=0.0065$), in zone 7(−8.4% vs 25.4%, p,0.0001) across all zones (+0.80% vs −6.03%, $p<0.0001$) at 12 months; no effect on early stem migration
Wang et al. (2018) [85]	Systematic review/meta-analysis	Risedronate	Oral, post-op	Periprosthetic BMD	Significant reduction in post-operative bone resorption and improved periprosthetic BMD after cementless THA
Muren et al. (2015) [86])	5-year single-center RCT, THA	Risedronate	35 mg weekly × 6 months	BMD, stem migration	Early BMD preservation in Gruen zones 1 & 7, but accelerated bone loss after discontinuation; no long-term difference at 4 years
Serino et al. (2024) [87]	National database, osteoporotic THA patients	Pre-op bisphosphonates	Chronic pre-op exposure	Periprosthetic fracture	Higher 2-year PPF risk (OR 1.29); no difference in loosening or infection, likely reflecting residual confounding and severity of skeletal fragility

Table 2 Denosumab and periprosthetic outcomes

Author (Year)	Study Type/Population	Agent	Timing & Dose	Primary Outcome(s)	Key Findings
Murahashi et al. (2020) [88]	Observational modeling, TKA	Denosumab	Postoperative	Periprosthetic tibial metaphyseal BMD	Denosumab significantly reduces early postoperative bone loss around implants after TKA
Nyström et al. (2020) [89]	RCT, 64 patients undergoing uncemented THA	Denosumab	60 mg at 1–3 days post-op and at 6 months post-op	Periprosthetic BMD (Gruen zones), bone turnover markers	At 12 months: BMD 32% (95% CI 22–44) higher in Gruen zone 7, and 11% (95% CI 8–15) higher across zones 1–7 vs placebo. At 24 months: 15% (95% CI 4–27) higher in zone 7 and 4% (95% CI 0–8) across zones 1–7. Bone turnover markers suppressed during treatment; rebound above baseline after 24 months
Aro et al. (2019) [90]	Randomized, double-blind trial, 65 postmenopausal women (Dorr A/B femora), cementless THA	Denosumab	Initiated preoperatively	Change in proximal femoral BMD (Gruen zone 7); stem subsidence via radiostereometric analysis	Significantly preserved BMD in Gruen zones 7 at 48 weeks, did not reduce early femoral stem migration. All stems achieved osseointegration indicating that denosumab improves periprosthetic bone density without influencing early implant migration
Nakura et al. (2023) [91]	Randomized comparative trial after THA	Denosumab vs weekly risedronate	Postoperative	Periprosthetic BMD (Gruen zones 1, 2, 6, 7)	Denosumab preserved proximal femoral periprosthetic BMD more effectively than weekly risedronate across Gruen zones 1, 2, 6, and 7 over 2 years

Nutritional, rehabilitation, falls prevention, and economic considerations

Adequate calcium and vitamin D status should be ensured peri-operatively, as deficiency is common in arthroplasty populations and has been associated with poorer postoperative outcomes In a retrospective study, knee osteoarthritis patients with vitamin D deficiency demonstrated worse preoperative function compared with vitamin D–sufficient patients; however, when deficiency was corrected beginning on postoperative day 14 for 4 weeks, 3-month functional recovery was comparable to vitamin D-sufficient individuals [96] suggesting that timely recognition and correction of deficiency may mitigate adverse effects on early postoperative recovery.

Mechanical loading is similarly biologically relevant. Immobilization accelerates bone loss (disuse osteoporosis) [97], supporting the importance of progressive rehabilitation rather than prolonged inactivity after arthroplasty. Conversely, excessive early activity THA may accelerate remodeling and aggravate stress shielding without clear functional benefit [98]. Rehabilitation should therefore be structured and graduated rather than accelerated indiscriminately. Given the high incidence of falls after total joint replacement [99, 100] and the established effectiveness of structured fall-prevention interventions in older adults, fall-risk assessment and mitigation strategies should be incorporated into peri-operative care pathways for arthroplasty patients.

Health-economic evidence specific to PPF prevention remains limited but is emerging. A 2024 break-even analysis conducted in the USA, estimated the minimum absolute PPF risk reduction required for osteoporosis medications to be cost-effective following hip arthroplasty for femoral neck fracture [101]. Using 3-year medication costs (oral bisphosphonates, estrogen therapy, IV bisphosphonates, denosumab, teriparatide, abaloparatide), costs of PPF care, and observed fracture rates in untreated patients, the analysis demonstrated that oral bisphosphonate therapy would be economically justified if it prevented 1 in 56 PPFs (absolute risk reduction 1.8%). The authors concluded that intravenous bisphosphonates and newer agents would require substantial cost reduction to achieve comparable economic viability [101].

Spinal fusion as a structural orthopedic outcome

Definition

Spinal fusion (arthrodesis) is a surgical procedure intended to achieve permanent osseous continuity between two or more vertebral segments in order to eliminate pathological intervertebral motion, restore mechanical stability, and maintain or correct spinal alignment [102]. Initially developed for the treatment of instability and deformity due to tuberculosis, scoliosis, and traumatic injury, today spinal fusion is most commonly performed for conditions (Table 3) in which abnormal motion or loss of structural

Table 3 Indications for spinal fusion surgery

Indication category for spinal fusion	Clinical context/explanation
Spondylolisthesis	Vertebral slippage caused either by age-related degeneration of the intervertebral disc and facet joints, or by an isthmic defect, in which a stress fracture or non-union of a small posterior bony bridge of the vertebra (the pars interarticularis) reduces resistance to shear forces, allowing one vertebra to slip relative to another
Spinal deformity	Structural abnormalities such as scoliosis or kyphosis that compromise alignment, load distribution, or long-term mechanical stability
Mechanical instability	Excessive or abnormal motion at a spinal segment, present pre-operatively or created following decompression surgery, where bone or ligament is removed to relieve neural compression, thereby reducing intrinsic stability
Painful pathological motion	Persistent pain attributed to abnormal segmental motion that has failed appropriate non-operative management, including physical therapy, analgesia, or injections
Trauma	Acute fractures or ligamentous injuries in which the spinal column cannot safely withstand routine weight bearing and movement without surgical stabilization
Tumor	Neoplastic processes causing structural weakening, collapse, or instability requiring restoration of mechanical integrity
Infection	Destructive spinal infections (e.g., spondylodiscitis) leading to bone loss or instability that necessitate surgical stabilization
Revision surgery	Failure of prior spinal surgery resulting in instability, deformity, or loss of load-bearing capacity requiring reconstruction

stability is believed to drive symptoms or progression [103].

Spinal fusion numbers have risen over recent decades and appear to be increasing across multiple health systems worldwide, with one U.S. analysis reporting more than ~ 217,000 lumbar spinal fusion surgeries from 2004 through to 2021 with rates generally increasing through 2019 [104]. Reoperation and revision surgery following fusion are also well documented, with reoperation rates reported between approximately 10% and nearly 20% for lumbar degenerative fusion cohorts depending on follow-up duration and definitions of reoperation [105].

Clinically, implant fixation failure in the setting of spinal fusion is most often manifested by *pseudoarthrosis or non-union,* i.e., the failure to achieve solid bony fusion with persistent motion at the intended fusion site, and mechanical implant complications such as screw loosening, rod fracture, hardware breakage, or progressive deformity that necessitate revision [106]. Implant fixation failure is determined by *why* instability occurs, not simply by what it looks like radiographically. The failure is driven by factors such as fatigue-induced rod fractures, progressive screw loosening, or the gradual progression of a deformity due to poor load sharing in osteoporotic bone. It is important to distinguish this from failures driven by outside factors where the construct itself was not the primary issue. For instance, if an infection causes bone destruction leading to secondary loosening, or if a tumor erodes the bony substrate until the implant loses its foundation, these do not qualify as construct-level failures. Similarly, failure resulting from high-energy trauma is excluded, as the external forces in those cases far exceed the standard design assumptions of the hardware.

Mechanical environment of spinal fusion: relative stability

While fusion is indicated because excessive or abnormal motion is harmful, successful arthrodesis does not require complete rigidity. Instrumentation limits gross motion but allows small degrees of micromotion at the fusion site. This biomechanical environment contrasts with the absolute stability required for primary (direct) fracture healing.

Pedicle screw-rod constructs, interbody cages, and supplemental fixation provide sufficient stability to permit bone formation while allowing controlled strain. Consequently, healing occurs through secondary (indirect) bone repair. This process moves from an initial inflammatory phase to a reparative phase, where cells differentiate along osteogenic or chondrogenic lineages and finally to a prolonged remodeling phase where woven bone is replaced by load-bearing lamellar bone [1].

Spatial heterogeneity in ossification pathways

Spinal fusion is not a single, uniform healing process. Instead, the ossification pathways involved are spatially heterogeneous and determined by the local biological and mechanical environment. In well-vascularized posterolateral beds that have been decorticated, i.e., where the superficial cortical bone has been surgically removed to expose bleeding cancellous bone, fusion proceeds predominantly through intramembranous ossification**,** characterized by direct osteoblast-driven bone formation. This surgical preparation is critical because it transforms an otherwise biologically inert surface into a metabolically active fusion bed by enhancing vascular access and permitting ingress of osteogenic cells [107].

In contrast, when the recipient environment is less biologically favorable such as in non-decorticated, relatively hypovascular, or higher-strain regions, tissue differentiation shifts toward endochondral ossification**,** in which bone forms via a cartilage intermediate [108]. This spatial heterogeneity is particularly evident in interbody fusion environments, where higher mechanical demands, altered oxygen tension, and local strain conditions favor endochondral pathways. Experimental and mechanobiological models demonstrate that differences in local strain and biological milieu can activate different ossification pathways within the same fusion construct, rather than a single uniform mechanism of bone formation [102, 109]. Evidence for anatomically distinct skeletal stem cell populations, including vertebral skeletal stem cells that differ from long-bone stem cells in gene expression and functional contribution to bone formation further highlights that skeletal repair and ossification vary by anatomical site and local cellular milieu [110].

Fusion techniques and structural context

Spinal fusion techniques differ primarily in their surgical approach; posterior, transforaminal, anterior, lateral, or oblique, and in their biomechanical strategy, including whether fusion is achieved through posterolateral grafting without disc removal, interbody cage placement for anterior column support, or combined approaches with unilateral or bilateral instrumentation. Successful fusion ultimately depends on optimizing both biological fusion potential and mechanical stability. Figure 2 is an illustration of some of the commonly performed fusion techniques and Fig. 3 is an illustration of some examples of fusion failures.

Osteoporosis and risk of fusion failure

Osteoporosis is a major risk factor for spinal fusion failure, with consistently higher rates of pseudoarthrosis, implant loosening, and revision surgery reported in osteoporotic

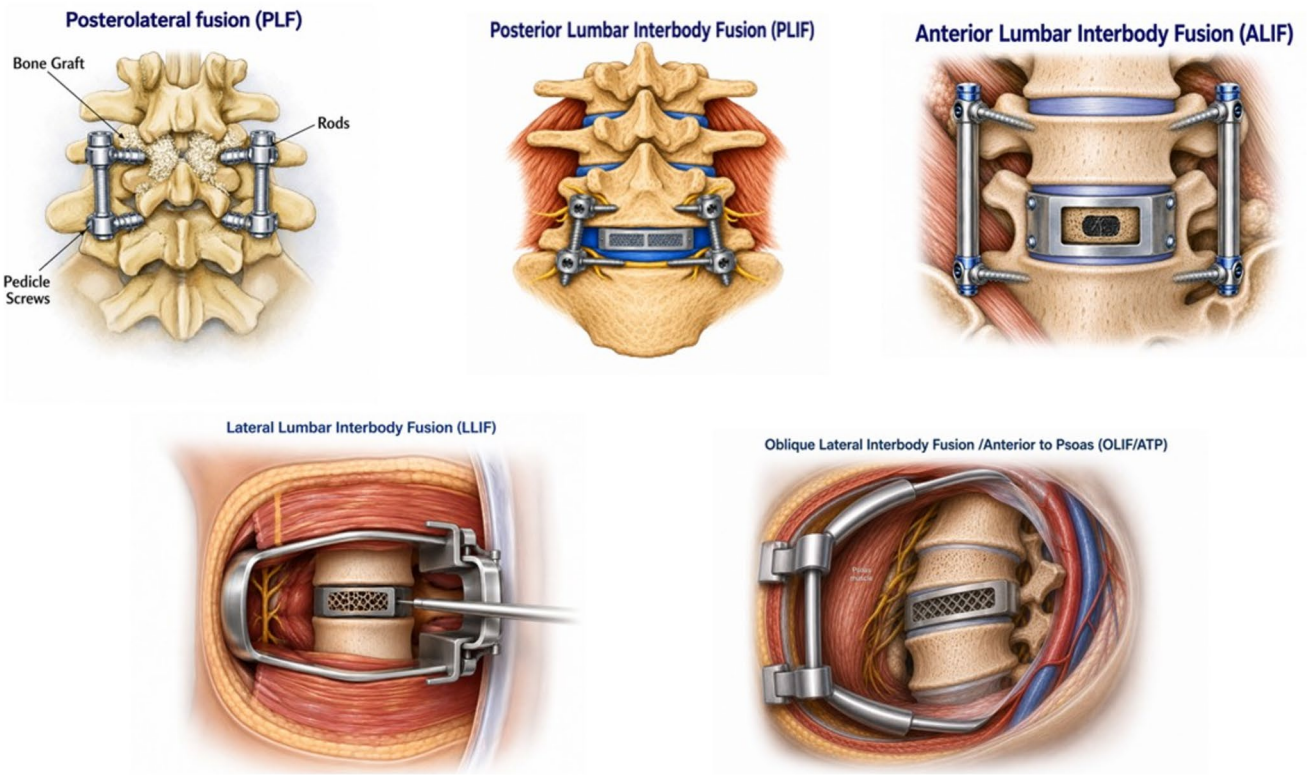


Fig. 2 Fusion techniques and structural context in lumbar spine surgery. Legend: This figure illustrates some of the posterior and interbody spinal fusion techniques used to achieve lumbar arthrodesis, highlighting their anatomical targets and surgical approaches. **Posterolateral fusion (PLF)** relies on new bone formation between the transverse processes and posterior elements of adjacent vertebrae. *Bone graft material is placed in the posterolateral gutter*s. Fusion success depends on the biological quality of the posterior fusion bed as well as mechanical stability provided by posterior instrumentation, typically pedicle screws and rods. No intervertebral disc space is entered in PLF. **Interbody fusion techniques** achieve fusion through the intervertebral disc space by removing disc material and inserting an interbody cage or graft to promote anterior column support and fusion. Interbody techniques may be performed with or without supplemental posterior instrumentation depending on construct design. ● **Posterior lumbar interbody fusion (PLIF)** *accesses the disc space through a midline posterior approach with bilateral neural retraction*. ● **Oblique lumbar interbody fusion/anterior-to-psoas (OLIF/ATP)** *approaches the disc space through an oblique retroperitoneal corridor anterior to the psoas muscle*. This avoids direct psoas traversal. ● **Lateral lumbar interbody fusion (LLIF)** *accesses the disc space* via *a true lateral transpsoas approach*. This provides wide disc access and indirect decompression. ● **Anterior lumbar interbody fusion (ALIF)** *approaches the disc space from an anterior retroperitoneal or transperitoneal route*. This allows placement of large interbody implants while preserving posterior structures. ● **Transforaminal lumbar interbody fusion (TLIF)** *uses a unilateral posterior-lateral approach through the neural foramen*. This reduces dural and neural element manipulation. *These figures were created by the authors using a generative AI–assisted image tool. *The figures presented are purely schematic, conceptual renderings designed to visually convey the underlying biomechanical concepts and surgical approaches discussed in the text. They are not intended to represent precise and correct anatomical detail, operative technique, or actual clinical imaging

patients [111]. In a systematic review and meta-analysis of 71 studies comprising 12,278 patients, low BMD was not only associated with higher rates of implant failure such as cage subsidence, screw loosening with consequent pseudoarthrosis, but also was a significant risk factor for proximal junctional kyphosis (PJK) due to fracture [112]. In patients with osteoporosis, compromised vertebral strength, decreased endplate failure load and increased stress concentrations within the surgical segment all contribute to failure at the cage end plate interface. One study reported significantly prolonged time to fusion in patients with low BMD following TLIF [113]. Consistent with the biological importance of bone quality, meta-analyses of randomized and comparative studies have demonstrated that osteoporosis therapies, including bisphosphonates and teriparatide, are associated with improved fusion rates after thoracolumbar instrumentation [114, 115]. Osteoporosis acts as a "double-edged sword" that undermines the biological and mechanical pillars of fusion, with reduced cellular activity and signaling impairing the progression of secondary bone repair and reduced trabecular and cortical strength diminishing pedicle screw purchase. This leads to increased micromotion at the fusion site, precisely the condition that shifts the biological environment toward pseudoarthrosis rather than

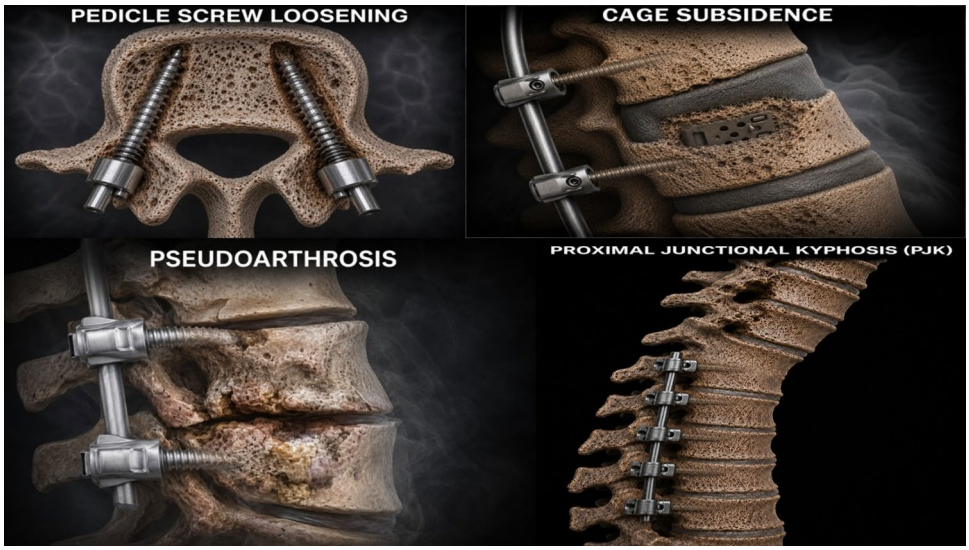


Fig. 3 Examples of spinal fusion failures. **Key visual indicators of Pedicle Screw Loosening**. ● A clear lucent zone surrounds the screw threads, breaking the bone-metal continuity with a radiolucent halo around the screw (classically ≥ 1 mm). ● Loss of intimate bone-thread contact. Sometimes subtle screw toggling or backing out (late finding). ● No solid trabecular continuity around threads. ● The screws remain *within* the pedicle. ● The bone appears osteopenic and granular rather than dense and interlocked. ● The construct alignment may still look intact reinforcing that loosening precedes gross failure. **Key visual indicators of Cage Subsidence.** ● Cage remains centered in the disc space and embedded into the vertebral body. ● Superior and/or inferior endplates show crushing and indentation. ● Loss of disc height or segmental lordosis. ● Posterior instrumentation is intact. **Key visual indicators of Proximal Junctional Kyphosis (PJK) with vertebral body proximal junctional failure (PJF) phenotype.** ● The rod-screw construct ends abruptly. Above it, Sharp kyphotic angulation at (Upper instrumented Vertebra) UIV + 11. ● Fusion construct itself remains rigid. ● Adjacent vertebra shows collapse, wedge fracture, or ligamentous failure. ● The deformity is above, not within the instrumented levels. **Key visual indicators of Psuedoarthrosis.** ● Lack of bridging trabecular bone i.e. a non-union gap across the intended fusion site. ● Persistent disc space or cleft. ● Sclerosis at fusion margins. ● No mature fusion mass is present. ● Instrumentation bears load→ stress shielding. *These figures were created by the authors using a generative AI-assisted image tool. The figures presented are purely schematic, conceptual renderings designed to visually convey the underlying biomechanical concepts discussed in the text. They are not intended to represent precise and correct anatomical detail, operative technique, or actual clinical imaging

bridging through mature bone. Pre-existing kyphosis due to osteoporotic vertebral fracture represents an additional, alignment-related risk factor that compounds the effects of low BMD. Beyond compromised bone quality, kyphotic deformity increases anterior column loading and stress at the cage–endplate interface and contributes to junctional failure. In this sense, osteoporotic kyphosis and low BMD act synergistically to increase the risk of implant failure, pseudoarthrosis, and PJK [116]. Ultimately, because osteoporosis impairs both the "living bed" (biology) and the "anchor" (mechanics), patients with low BMD face significantly higher rates of implant loosening, rod fatigue, and revision surgery [111].

Risk modifiers of spinal fusion failure in patients with osteopenia and osteoporosis

While low BMD is a primary determinant of spinal fusion failure, outcomes in osteoporotic and osteopenic patients are further modified by a limited number of well-established patient-level and surgical factors that influence fusion biology and construct mechanics. Active cigarette smoking is one of the most consistently identified and modifiable risk modifiers, with strong experimental and clinical evidence demonstrating impaired osteogenesis, reduced graft incorporation, and higher rates of non-union following lumbar fusion [117]. Advanced age, independent of measured BMD, is associated with higher rates of fusion failure and revision surgery, reflecting age-related impairments in bone turnover, vascularity, and repair capacity [118]. From a surgical perspective, a greater number of fused levels substantially elevates the risk of implant fixation failure, likely reflecting greater construct length, increased lever arms, and higher cumulative mechanical demand on compromised bone [118]. In the setting of surgery for osteoporotic vertebral collapse, long rigid constructs with extension to the sacrum further predispose to PJK [119], underscoring the interaction between alignment, construct stiffness, and poor bone quality. Vitamin D deficiency has also been associated with poorer postoperative functional outcomes following spinal fusion in meta-analytic data, although a consistent association with radiographic non-union has not been demonstrated [120]. Repeated epidural steroid injections (ESIs), commonly administered in patients with degenerative lumbar

disease prior to fusion surgery, may represent an under-recognized contributor to impaired vertebral bone quality at planned fixation levels. Using quantitative CT, Liu et al. demonstrated significantly lower volumetric BMD across multiple lumbar vertebral levels in patients with prior ESIs compared with matched controls, with cumulative steroid exposure correlating inversely with vertebral density [121], potentially further compromising pedicle screw fixation and endplate strength in osteoporotic fusion constructs.

Pre-operative imaging assessment of bone health before lumbar spine surgery

Osteoporosis is frequently under-recognized in spine surgery candidates. Importantly, in degenerative spine disease, lumbar DXA measurements may substantially overestimate true vertebral strength because the trabecular compartment actually being instrumented may be considerably more compromised than suggested by areal BMD alone. Therefore, a structured pre-operative imaging assessment should combine standard DXA with opportunistic CT-based bone evaluation *when* CT is already part of surgical planning. *Opportunistic measurement of vertebral trabecular attenuation, expressed in Hounsfield units (HU), on routine lumbar CT provides a practical, level-specific surrogate of bone strength at regions subjected to fixation and load transfer.* Mean trabecular HU obtained from a region of interest within the vertebral body correlates with DXA-defined BMD, enabling osteoporosis risk stratification without additional radiation, cost, or dedicated imaging. Schreiber et al. demonstrated that lumbar vertebral trabecular HU derived from CT discriminates osteoporosis and correlates with DXA, supporting HU as an accessible, imaging-embedded screening tool when DXA is unavailable or delayed [122]. *L1 is commonly selected because it is frequently included on chest, abdominal, and lumbar CT scans and is often less affected by degenerative change, improving interpretability.*

ROI placement should target the mid-vertebral body trabecular bone, including as much cancellous bone as possible while avoiding the cortical shell and focal heterogeneous areas (e.g., posterior venous plexus, sclerosis/bone islands, compressed bone), and can be averaged across axial/sagittal/coronal views for robustness [122–124]. *Commonly cited diagnostic cut-points at L1 include < 110 HU (high specificity) and < 160 HU (high sensitivity) for osteoporosis defined by DXA/vertebral fracture criteria, with some authors recommending a more conservative "abnormally low" threshold around < 100 HU to account for scanner/calibration variability* [123].

Importantly, HU-based stratification has also demonstrated construct-level clinical relevance. Narayanan et al. defined osteoporosis as L1 HU ≤ 110 in adults undergoing 1–3 level PLF or TLIF and found that the osteoporotic HU group had a significantly higher incidence of pedicle screw loosening and less improvement in back-pain Visual Analogue Scale (VAS) on multivariable analysis, despite no clear differences in early readmissions/complications [125]. These findings extend HU assessment beyond diagnostic concordance with DXA and link level-specific attenuation values to fixation-related outcomes.

In practice, DXA remains the reference standard for diagnosing osteoporosis, while CT-HU-based opportunistic screening, when performed using transparent methodology and predefined thresholds, provides surgically relevant, level-specific risk stratification for fixation failure and longer-term outcomes, particularly when CT has already been obtained for navigation, morphology, or deformity planning.

Trabecular Bone Score (TBS) has been explored as an adjunctive skeletal assessment tool in spinal fusion candidates, particularly because degenerative spinal changes may artifactually elevate lumbar DXA BMD. In spine surgery populations, TBS and CT-derived Hounsfield Units (HU) appear to be less influenced by degenerative change than areal BMD alone, potentially allowing better characterization of underlying trabecular bone quality in surgical candidates [126]. Accordingly, several peri-operative bone health assessment frameworks have incorporated TBS alongside DXA, vertebral fracture assessment, FRAX, and opportunistic CT HU evaluation as part of multimodal skeletal risk assessment prior to spinal instrumentation [127, 128]. However, evidence supporting TBS specifically as a predictor of construct-level fusion outcomes remains limited. In a prospective lumbar fusion cohort, early postoperative complications were more strongly associated with abnormal HR-pQCT-derived microarchitectural parameters than with either TBS or areal BMD alone [129]. Accordingly, TBS is probably best viewed as an adjunctive rather than standalone tool in pre-operative spinal fusion assessment. The 2019 ISCD Official Position on bone health evaluation in orthopedic surgery also recommends TBS measurement in patients with diabetes, if available, recognizing that patients with T2DM may have increased fracture risk despite preserved or higher BMD, likely reflecting impaired bone quality and microarchitectural deterioration not captured by areal BMD alone [123].

Effect of osteoporosis medications on spinal fusion

Antiresorptives

Bisphosphonates

Early concerns regarding bisphosphonate use in spinal fusion arose primarily from preclinical studies, in which suppression

of osteoclastic remodeling variably altered fusion strength. This has not been borne out in human studies. Preclinical models showed dose- and species-dependent modulation of fusion biology, with supratherapeutic dosing enhancing fusion metrics but clinical-equivalent dosing producing largely neutral effects [130–134]. Human meta-analyses demonstrate reduced vertebral fractures and cage subsidence but inconsistent fusion-rate enhancement [135–137]. Overall, bisphosphonates appear to stabilize construct integrity rather than directly augment fusion biology.

Denosumab

Prospective data suggest improved vertebral strength and pedicle screw fixation with denosumab, with enhanced early fusion when combined with teriparatide [138, 139]. Effects appear primarily mediated through improved bone quality and fixation strength rather than direct osteogenic stimulation.

A summary of the studies of bisphosphonates and Denosumab on spinal fusion outcomes is provided in Table 4.

Anabolic therapies

Teriparatide and spinal fusion outcomes: a construct-level framework

Teriparatide has the most robust and clinically interpretable evidence among pharmacologic options studied in spinal fusion [114, 115, 138, 140–148] (Table 5). Animal models demonstrate that intermittent teriparatide reliably increases fusion mass volume and bone formation, although gains in biomechanical stiffness may plateau in biologically intact environments, suggesting a ceiling effect when baseline-healing capacity is preserved. These observations provide a mechanistic basis for the preferential benefit of teriparatide in compromised bone rather than healthy fusion beds.

In clinical practice, failures after fusion rarely occur because the fusion mass in the middle of the construct is inadequate; rather, they occur at mechanically stressed interfaces, the bone-screw interface, the cage-endplate interface, and the junctional vertebrae adjacent to long constructs. Across clinical studies and meta-analyses, teriparatide is consistently associated with higher and earlier fusion rates and lower rates of implant-related complications, particularly pedicle screw loosening and fracture-related junctional failure. These benefits are best understood as improvements in local bone quality, where fixation and stress concentration matter most, rather than simply producing more bone overall.

The dosage regimen associated with benefit is relatively consistent across studies. Teriparatide is typically started preoperatively, most often at least one month before surgery, and continued postoperatively for 6 to 12 months. Both daily dosing (20 µg) and weekly dosing (56.5 µg) have demonstrated clinical benefit, including acceleration of early fusion, with no clear signal that one regimen is superior in this setting. This allows flexibility in dosing based on patient preference, adherence, and local practice. In urgent or neurologically compromised cases, therapy initiation in the early postoperative period is reasonable and supported by similar mechanistic logic, and surgery should not be delayed solely to initiate and complete a pre-operative anabolic course.

Several studies have also examined combination therapy of teriparatide with denosumab. This approach has been associated with higher early fusion rates compared with teriparatide alone in selected high-risk populations. While not required for most patients, combination therapy may be considered in individuals at particularly high risk of fixation failure, such as those with severe osteoporosis or undergoing long-segment deformity correction.

It must be noted that most available trials using teriparatide in this setting are modest in size, rely on radiographic or biomechanical surrogate endpoints (e.g., fusion mass volume, screw loosening, cage subsidence), and are heterogeneous in surgical technique and patient selection. Therefore, although pre-operative initiation is biologically plausible and supported by mechanistic rationale, it should therefore be considered a conditional strategy supported by moderate-certainty evidence for surrogate improvement rather than definitive reduction in revision or failure across all fusion contexts. Accordingly, the evidence supports a selective role for teriparatide in spinal fusion, favoring its use in high-risk osteoporotic patients rather than routine application across all fusion procedures.

As in arthroplasty and PPFs, health economic evaluations in the realm of spinal fusion surgeries are rare. An exception is a 2022 cost utility analysis study which showed that neoadjuvant teriparatide for osteopenic patients undergoing adult spinal deformity surgery is economically attractive, with a mean incremental net monetary benefit of USD 3,948 and dominance over no-treatment in 82% of model iterations, driven largely by reductions in pseudarthrosis and proximal junctional failure [149].

Abaloparatide

At present, evidence supporting the use of abaloparatide in spinal fusion is limited to preclinical animal models. Daily abaloparatide started 1 day post-PLF increased the bone formation marker osteocalcin, without increasing Tartrate Resistant Acid Phosphatase 5b (TRACP-5b), improved fusion-mass microarchitecture, and though it was reported as non-significant, a twofold higher bilateral fusion rate at

Table 4 Bisphosphonates, denosumab and spinal fusion outcomes

Author (Year)	Study Type/Population	Agent	Timing & Dose	Primary Outcome(s)	Key Findings
Babat et al. (2005) [130]	Rabbit posterolateral fusion model	Calcitonin, Pamidronate	Experimental	Fusion mass, manual palpation	Increased fusion-mass density but variable effects on manual fusion strength
Huang et al. (2005) [131]	Rat posterolateral fusion model	Alendronate	Experimental	Fusion rate	Alendronate inhibited fusion in this rat model
Koo et al. (2012) [132]	Rabbit lumbar fusion model	Alendronate	Experimental	Fusion mass density	Increased fusion-mass density; heterogeneous biomechanical outcomes
Lehman et al. (2004) [133]	Rabbit fusion model	Alendronate	Experimental	Fusion integrity	Variable effects on fusion strength
Yasen et al. (2015) [134]	Ovariectomized osteoporotic rat model	Zoledronic acid	Dose-dependent	Fusion metrics	Supratherapeutic dosing improved fusion metrics; clinical-equivalent doses largely neutral
Jin et al. (2025) [135]	Systematic review & meta-analysis	Various bisphosphonates	Post-operative	Vertebral fracture, cage subsidence, Oswestry Disability Index (ODI)	Reduced vertebral fractures (OR 0.29, 95% CI 0.09–0.81); reduced cage subsidence (OR 0.29, 95% CI 0.11–0.75); improved ODI (SMD − 0.75, 95% CI − 1.42 to − 0.08)
Mei et al. (2021) [136]	Meta-analysis (RCTs & comparative cohorts)	Postoperative bisphosphonates	Post-operative	Fusion rate, Vertebral Compression Fracture (VCF), cage subsidence	No clear improvement in fusion rate; but reduced VCF, cage subsidence, pedicle screw loosening
Fretes et al. (2020) [137]	Meta analysis of comparative studies	Bisphosphonates	Post-operative	Fusion rate, subsidence	Higher Fusion rate OR 2.2,95% CI 0.87–5.56, $p = 0.09$); decreased cage subsidence (OR 0.29, 95% CI 0.11–0.75, $p = 0.01$); reduced vertebral fractures (OR 0.18, 95% CI 0.07–0.48, $p = 0.007$), no difference in screw loosening rates (OR 0.45, 95% CI 0.14–1.48, $p = 0.19$)
Ide et al. (2018) [138]	Prospective clinical study, Posterior Lumbar Interbody Fusion (PLIF)	Teriparatide + Denosumab	TPT 20 mcg daily (1 month before to 12 months after surgery); Denosumab 60 mg at 2 & 8 months after surgery	CT-based fusion rate	6-month union: 82% combination vs 36% teriparatide alone ($p < 0.05$)

Table 4 (continued)

Author (Year)	Study Type/Population	Agent	Timing & Dose	Primary Outcome(s)	Key Findings
Tani et al. (2021) [139]	2-year prospective open-label study (21 postmenopausal women)	Denosumab	60 mg every 6 months	CT-based FEA, screw pullout strength	Increased pedicle screw pull-out strength and vertebral compression force at 12 & 24 months; stronger correlation with 3D QCT BMD ($r = 0.83$) at 24 months vs DXA ($r = 0.35$)

day 28 (50% vs 25%) [151]. In a randomized, placebo-controlled rabbit PLF model, daily abaloparatide produced a 100% fusion rate (10/10) vs 45% (5/11) in controls improved radiographic fusion scores, and more than doubled fusion-mass bone volume assessed through quantitative CT [152].

Collectively, the rat and rabbit PLF data support that abaloparatide can amplify the early osteoanabolic phase at the graft site, improve fusion-mass microarchitecture/volume, and in a larger model can materially increase fusion success which aligns with the concept that osteoporosis causes fusion failure through inadequate bone formation/remodeling under construct loading.

Romosozumab

Key preclinical and clinical studies evaluating romosozumab in the context of spinal fusion [153–157] are summarized in Table 6.

Animal studies in both non-osteoporosis and ovariectomized (osteoporotic) rat PLF models show that romosozumab increases fusion mass and bone union compared with controls [153, 155]. Human evidence remains limited and largely retrospective. Opportunistic CT analyses demonstrate significant increases in lumbar vertebral Hounsfield units following romosozumab therapy, consistent with improved vertebral bone density [154]. The most direct "fusion-related" clinical signal with romosozumab relates to junctional failure/PJK, where failure is commonly driven by fracture of the osteoporotic vertebra immediately adjacent to the construct rather than non-union of the fusion mass [156]. The data from this study suggests that fracture-related junctional complications after multilevel corrective fusion may be reduced when therapy is initiated pre-operatively. In a CT-based biomechanical modeling analysis using vertebrae from randomized osteoporosis trials, romosozumab significantly increased shear strength and reduced predicted failure volume around virtually implanted pedicle screws compared with placebo, teriparatide, or alendronate, indicating enhanced structural competence of bone adjacent to instrumentation [157]. As romosozumab is a time-limited therapy, its peri-operative use should be planned within an overall osteoporosis treatment strategy and should not be interpreted as a routine switch option in patients already stable on effective therapy.

Integrated synthesis and clinical implications

Arthroplasty and spinal fusion represent distinct surgical procedures, but they share a common biological-mechanical challenge: long-term maintenance of structural integrity in bone that has been permanently altered by instrumentation. In both settings, success depends on the ability of host bone

Table 5 Teriparatide and spinal fusion outcomes: animal and human studies

Author (Year)	Study Type/Population	Pre-Op Duration	Post -Op Duration	Dose/Regimen	Outcome/Measure	Key Findings
O'Loughlin et al. (2009) [140]	Rabbit posterolateral fusion model	N/A	8 weeks	PTH1-34 Intermittent	Fusion rate, fusion mass volume, mechanical strength	Significantly increased fusion mass volume, fusion rate, and biomechanical strength vs controls
Lina et al. (2014) [141]	Rabbit dorsolateral intertransverse fusion	N/A	8 weeks	PTH (1–34) ± rhBMP-2	Fusion mass volume, stiffness	Increased fusion mass volume but no additional biomechanical stiffness either when used alone or as adjunct to growth factors such as recombinant human Bone morphogenic protein (rhBMP-2), suggesting ceiling effect in healthy bone
Ohtori et al. (2012) [142]	Prospective Observational study Postmenopausal women with osteoporosis undergoing decompression and 1-or 2-level instrumented posterolateral fusion with a local bone graft	2 months	8 months	Teriparatide 20 mcg daily subcutaneously or Risedronate 17.5 mg weekly	Fusion rate, time to union	Higher fusion rate (82% vs 68%, $p = 0.02$) compared to Risedronate and faster time to union (8 ± 2.5 months) vs risedronate (9.7 ± 2 months), $p = 0.03$

Table 5 (continued)

Author (Year)	Study Type/Population	Pre-Op Duration	Post -Op Duration	Dose/Regimen	Outcome/Measure	Key Findings
Inoue et al. (2014) [143]	Retrospective comparative cohort study in spinal fusion surgery Postmenopausal women with osteoporosis	≥ 1 month (mean = 61 days)	N/A (i.e. not given post operatively)	Teriparatide 20 mcg daily subcutaneously or 56.5 mcg weekly subcutaneously	Pedicle screw insertional torque	Significantly higher insertional torque (1.28 ± 0.42 Nm vs controls (1.08 ± 0.52 Nm, $p < 0.01$). No significant difference between the daily and the weekly teriparatide groups (1.34 ± 0.50 Nm and 1.18 ± 0.43 Nm respectively ($p = 0.07$). Negligible correlation between insertional torque and duration of pre-operative teriparatide treatment indicating that teriparatide injections beginning at least 1 month prior to surgery are effective in increasing the insertional torque of pedicle screws i.e. maximizing the purchase of pedicle screws to the bone during surgery in patients with postmenopausal osteoporosis
Ebata et al. (2017) [144]	Multicenter RCT. In patients undergoing Posterior or TLIF for Osteoporosis-Associated Lumbar Degenerative Disorders	N/A	Starting at week one week after surgery for 6 months	Teriparatide 56.5 mcg weekly subcutaneously	Early fusion (CT)	Higher 6-month fusion rate (78% vs 45% placebo)
Yagi et al. (2016) [145]	Adult spinal deformity (long fusion). Prospective Cohort study	N/A	6–24 months	20 mcg subcutaneously daily	PJK type 2 incidence, BMD at UIV + 1	Increased BMD at UIV + 1 and reduced bony PJK at 2 years (4.6% vs 15.2%, $p = 0.02$) and improved UIV + 1 bone quality suggesting that teriparatide improves bone quality at a mechanically vulnerable junction

Table 5 (continued)

Author (Year)	Study Type/Population	Pre-Op Duration	Post -Op Duration	Dose/Regimen	Outcome/Measure	Key Findings
Ide et al. (2018) [138]	Randomized trial. Patients with Osteoporosis and lumbar spinal stenosis undergoing PLIF	1 month	12 months	20 mcg Teriparatide daily subcutaneously from 1 month before to 12 months after surgery or Teriparatide 20 mcg subcutaneously daily from 1 month before to 12 months after surgery with Denosumab 6 monthly subcutaneously administered at 2 and 8 months after surgery	Fusion rate (CT)	Combination therapy achieved faster and higher fusion at 6 months (82% vs 36%)
Stone et al. (2017) [146]	Systematic review. including 5 prospective studies, 4 retrospective studies and 2 RCTs Postmenopausal women undergoing PLF or PLIF or TLIF. All were short-segment fusions (1–3 levels)	2 months before surgery, or 3 months before surgery. Some studies started teriparatide only postoperatively	8–10 months post-surgery in most studies. Some compared: Short duration (< 6 months) vs Long duration (> 6 months, up to ~ 13 months)	20 mcg daily	Fusion rate, Pedicle screw loosening	Teriparatide improved fusion speed and reduced screw loosening (13%) vs bisphosphonates (26%) and controls (25%) suggesting that beyond fusion, teriparatide enhances the bone-screw interface to mitigate hardware failure

Table 5 (continued)

Author (Year)	Study Type/Population	Pre-Op Duration	Post -Op Duration	Dose/Regimen	Outcome/Measure	Key Findings
Buerba et al. (2018) [114]	Meta analysis of older adults majority women with osteoporosis undergoing Short-segment lumbar fusion Instrumented PLF →3 studies PLIF/TLIF, LIF→6 studies Long-segment fusion: Instrumented long posterior fusion (> 5 segments) →2 studies	Started preoperatively in most studies 2 months before surgery (multiple studies) 3 months before surgery (one study)	Some studies started teriparatide on the day of surgery One study initiated 1 week after surgery (weekly dosing study) Postoperative continuation ranged from: 6 months (weekly dosing study) 8–10 months 18 months Up to 21 months	**Teriparatide regimens** Teriparatide was used in 5 of the 9 studies Daily dosing: 20 µg subcutaneously Weekly dosing: 56.5 µg subcutaneously (one study only) **Bisphosphonate regimens** Used in 7 of the 9 studies Oral bisphosphonates: started 2–3 months preoperatively Continued 8–21 months postoperatively Risedronate Daily low-dose and Weekly dosing Alendronate Weekly dosing Zoledronic acid 5 mg IV Single dose 3 days post-op Single dose 2 weeks post-op Annual dosing in one study	Fusion rate (comparative	No statistically significant differences noted between bisphosphonates and control groups regarding fusion rate and risk of screw loosening (fusion: OR = 2.2, 95% CI: 0.87–5.56, $p = 0.09$; loosening: OR = 0.45, 95% CI: 0.14–1.48, $p = 0.19$). Teriparatide associated with higher fusion rates than bisphosphonates (OR = 2.3, 95% CI: 1.55–3.42, $p < 0.0001$). No statistically significant difference noted between teriparatide and bisphosphonates on screw loosening (OR = 0.37, 95% CI: 0.12–1.18, $p = 0.09$)., Bisphosphonate use associated with decreased odds of cage subsidence and vertebral fractures compared to controls (subsidence: OR = 0.29, 95% CI 0.11–0.75, $p = 0.01$; fracture: OR = 0.18, 95% CI 0.07–0.48, $P = 0.0007$)

Table 5 (continued)

Author (Year)	Study Type/Population	Pre-Op Duration	Post -Op Duration	Dose/Regimen	Outcome/Measure	Key Findings
He et al. (2023) [150]	Network meta-analysis of 13 RCTs. Predominantly older patients. Most cohorts were female predominant. Most patients had osteoporosis or low bone mass Short-segment lumbar fusion that included PLIF, TLIF, and PLF Long-segment fusion including PLIF	Variable from 3 months before surgery to up to 1 week after surgery	Variable 6–24 months	Variable Teriparatide 20 mcg daily. One trial used Teriparatide 56.5 mcg weekly Combination of teriparatide and denosumab only in one study	Fusion rate, ODI	Teriparatide only mono therapy shown to be significantly more effective than placebo increasing fusion rates (OR 3.2, 95% CI; 1.4–7.8). Combining Teriparatide with Denosumab achieved the highest surface under the cumulative ranking curve (SUCRA) for both fusion rate (90.9%) and improvement in Oswestry Disability Index (ODI) scores (90.8%)
Jordan et al. (2023) [147]	Systematic Review and Meta analysis of 14 studies including Prospective randomized trials, Prospective cohort studies and Retrospective observational studies, Adults with osteoporosis undergoing instrumented thoracolumbar spinal fusion, PLF, PLIF, TLIF, Multilevel lumbar fusion, Adult spinal deformity surgery, adjacent-level fracture prevention after vertebroplasty	1 month	Up to 12 months	Teriparatide vs bisphosphonates, or Teriparatide vs no drug/placebo Teriparatide + denosumab vs teriparatide alone (Only one study) Doses studied: Teriparatide 20 mcg daily and 56.5 mcg weekly	Fusion	Fusion rate reached 79.28% in 1 st 6 months (OR: 2.62; CI: 1.79–3.84) with 81.9% decrease in rate of screw loosening with teriparatide compared to controls

Table 5 (continued)

Author (Year)	Study Type/Population	Pre-Op Duration	Post -Op Duration	Dose/Regimen	Outcome/Measure	Key Findings
Cheng et al. (2020) [148]	Systematic review and network meta-analysis of 8 RCTs + 3 prospective comparative studies (n = 676) undergoing thoracic/lumbar spinal fusion; predominantly elderly, largely female. Indications included lumbar degenerative disease, spondylolisthesis, spinal stenosis	Variable across included trials; some studies initiated teriparatide pre-operatively, others post-operatively	Follow-up ranged 6–24 months depending on included study	Most trials: Teriparatide 20 µg SC daily; one trial: weekly teriparatide; comparator arms included bisphosphonates (alendronate, risedronate, zoledronic acid) and placebo; one study evaluated Teriparatide + Denosumab	Primary: ● Fusion rate (radiographic) Secondary: ● Oswestry Disability Index (ODI) ● Adverse events	Teriparatide significantly improved fusion rate vs placebo (RR 1.26, 95% CI 1.08–1.47); combination teriparatide + denosumab highest fusion rate (RR 2.84 vs placebo); bisphosphonates did not significantly improve fusion; no significant difference in ODI or adverse events

PTH 1–34 Parathyroid Hormone 1–34, *rhBMP-2* recombinant human Bone Morphogenic Protein-2, *HU* Hounsfield Unit, *CT* Computerized Tomography, *PJK* Proximal Junction Kyphosis, *UIV + 1* Vertebra immediately proximal to the upper-instrumented vertebra, *PLF* Posterolateral fusion, *PLIF* Posterior lumbar interbody fusion, *TLIF* Transforaminal Lumbar Interbody Fusion, *OR* Odds Ratio, *CI* Confidence Interval

to sustain altered load transfer, anchor fixation elements, and adapt to repetitive stress over time. osteoporosis compromises this process by reducing cortical thickness, trabecular connectivity, and material strength at precisely those regions where implants concentrate force, whether at the bone-stem interface in arthroplasty or at screw, cage, and junctional interfaces in spinal fusion. Failure therefore emerges not as an isolated biological event, but as a progressive loss of mechanical competence at predictable stress-concentrated sites, manifesting clinically as PPF, implant loosening, subsidence, non-union, or junctional collapse. Framing these outcomes as expressions of a shared, construct-level failure process provides a coherent basis for integrating bone health assessment and osteoporosis management into both arthroplasty and spinal fusion pathways, rather than treating them as unrelated complications or procedure-specific anomalies.

Osteoporosis medications exert broadly consistent biological effects across these domains, yet their clinical impact is domain- and endpoint-specific. Antiresorptive therapies preserve bone mass and limit remodeling-mediated loss, thereby stabilizing peri-implant bone stock and the fusion environment, but do not reliably influence early mechanical fixation or construct migration. Anabolic therapies enhance bone formation and microarchitectural integrity and appear most relevant where new bone formation is rate-limiting, such as in fusion beds or compromised implant interfaces, although robust human data linking these effects to reduced revision or failure rates remain limited. Collectively, these observations underscore that osteoporosis in orthopedic surgery should not be reduced to "fracture risk" alone, but understood as a determinant of construct longevity, with adverse outcomes such as loosening, subsidence, pseudarthrosis, and PPF, reflecting predictable system-level failure when the load-bearing capacity of an osteoporotic bone-implant construct is exceeded.

The findings of this review support a proactive and integrated approach to bone health in patients undergoing orthopedic reconstruction

Pre-operative bone health assessment should be considered not only for fracture prevention, but also for prediction of construct survival in patients undergoing arthroplasty, spinal fusion, or complex fixation procedures.

The timing and selection of osteoporosis therapy should be aligned with the dominant construct-level failure mechanism anticipated. Preservation of peri-implant bone stock and screw purchase is best supported by antiresorptive therapy (bisphosphonates or denosumab), which may reduce stress-shielding-related bone loss and help maintain long-term fixation strength. Enhancement of fusion mass formation and consolidation is best supported by anabolic therapy (teriparatide) with or without

Table 6 Romosozumab and spinal fusion outcomes: animal and human studies

Author (Year)	Study Type/Population	Pre-Op Duration	Post -Op Duration	Dose/Regimen	Outcome/Measure	Key Findings
Kim et al. (2022) [153]	Rat posterolateral lumbar fusion (PLF) model; non-osteoporotic rats	N/A	Started at surgery; assessed through 8 weeks (CT every 2 weeks in the study)	Romosozumab 25 mg/kg SC twice weekly vs saline	Bone union rate; fusion mass volume; trabecular bone area (histology)	Higher mean bone union rates and fusion mass volumes vs controls from week 4 onward; greater increase rates at weeks 4 and 6; trabecular bone area ~ 1.7 × control by week 8 suggesting that romosozumab has the ability to trigger rapid bone formation on inactive surfaces i.e. this modelling based bone formation may lead to faster, more robust volume increase at the graft margins and transverse processes
Okuyama et al. (2024) [155]	Ovariectomized rat bilateral PLF model (osteoporotic model)	N/A	8 weeks (SC injections twice weekly for 8 weeks; CT every 2 weeks)	Romosozumab 25 mg/kg (R group) or 2.5 mg/kg (1/10R group) SC twice weekly vs saline for 8 weeks	Fusion volume (CT); trabecular bone area (histology)	Both doses had higher fusion volume vs control from week 4; trabecular bone area ~ 1.5 × control in both romosozumab groups; no significant difference between 25 mg/kg and 2.5 mg/kg suggesting dose saturation and Romosozumab stimulates bone growth at the graft site with similar effects achieved at 1/10 th the standard dose
Mikula et al. (2024) [154]	Retrospective analysis; 318 treated patients receiving osteoporosis medications;	Not procedure-specific	Mean duration of exposure: romosozumab 10.5 months; denosumab > 12 months; alendronate > 12 months; teriparatide > 12 months (mean 23 months)	Romosozumab	Opportunistic CT-derived lumbar density measured in Hounsfield Unit (HU) L1–L4	Romosozumab: + 26% HU (85 → 107; $p = 0.012$). Denosumab and alendronate: no significant HU change. Teriparatide: + 25% HU (106 → 132; $p = 0.039$) with longer mean exposure (23 months)

Table 6 (continued)

Author (Year)	Study Type/Population	Pre-Op Duration	Post -Op Duration	Dose/Regimen	Outcome/Measure	Key Findings
Sawada et al. (2025) [156]	Retrospective cohort: 111 patients aged > 50 years undergoing corrective fusion (> 2 vertebrae) for adult spinal deformity or vertebral compression fracture; included men and women	Typically started ~ 2 months pre-op	Assessed to 1 year post-op	Romosozumab administration vs no romosozumab (group n = 32 vs n = 79)	Incidence of PJK and fracture-type PJK (PJK-Fx); HU change at UIV + 1; osteoporosis-related complications; JOA and VAS	Romosozumab group: lower PJK (39.24% → 18.75%; p = 0.046), lower PJK-Fx (26.58% → 6.25%; $p = 0.019$), fewer osteoporosis-related complications (55.70% → 34.38%; $p = 0.011$); increased HU at UIV + 1 (− 1.22% vs + 13.60%; $p < 0.001$); protective in multivariable models (adjusted OR PJK 0.32; $p = 0.033$; adjusted OR PJK-Fx 0.15; $p = 0.018$)
Keaveny et al. (2025) [157]	Retrospective secondary imaging analysis of randomized clinical trials; postmenopausal women with low BMD or osteoporosis (Phase 2 and Phase 3 romosozumab trials). CT scan was used to create a finite element model for the L1 vertebra, which was then virtually implanted with pedicle screws and virtually loaded to failure in a "shear pullout" configuration	Not applicable since it was a virtual pedicle that was inserted; 6–12 months exposure (depending on trial phase)	Imaging follow-up at 12 months for the Phase 2 study and at 6, 12, and 24 months for Phase 3 study	In the Phase 2 study: Romosozumab 210 mg monthly for 12 months vs Placebo vs teriparatide In the Phase 3 study: Romomsozumab 210 mg monthly for 12 months followed by alendronate for 12 months vs alendronate alone for 24 months	Biomechanical CT (BCT)-derived percent change in: – Shear bone strength around virtually implanted pedicle screws – Volume of failed tissue – Periprosthetic BMD	Shear bone strength, peripros- thetic BMD, and amount of failed tissue were significantly improved over time after treatment with romosozumab compared to placebo, teriparatide, and alendronate. Effects reflect enhanced bone strength around instrumentation rather than direct evidence of accelerated fusion

Table 7 Expert recommendations on peri-operative bone health optimization

1. Who Should Be Assessed?

Recommendation: We recommend that bone health assessments be undertaken in patients undergoing arthroplasty or instrumented spinal fusion who meet any of the following:

• Age ≥65 years, or prior fragility fracture
The age threshold should not be interpreted as an absolute cutoff . It is intended as a pragmatic trigger for assessment in the context of increasing age related skeletal fragility. Bonehealth evaluation may be appropriate in younger individuals with relevant risk factors.

• Clinical risk factors: known or suspected osteoporosis, chronic glucocorticoid exposure, systemic inflammatory disorders (e.g., rheumatoid arthritis, inflammatory bowel disease), hypogonadism, malabsorption, or other secondary contributors to bone loss

• High mechanical demand constructs:

o Revision arthroplasty

o Long-segment spinal fusion

o Deformity correction

o Prior fixation or implant failure

Strength of Recommendation: Strong | Certainty of Evidence: Moderate

Rationale: Large registry analyses, observational surgical cohorts, and meta-analyses demonstrate higher rates of periprosthetic fracture, pseudarthrosis, cage subsidence, screw loosening, and revision in patients with low BMD and/or advanced age. There are no RCTs that have evaluated screening versus no screening; certainty is therefore based on consistent epidemiologic and cohort data rather than randomized evidence. Early identification allows targeted intervention.

2. Urgency of Assessment

Recommendation: In acute fracture or spinal fusion operative settings, surgery must not be delayed

Strength of Recommendation: Strong | Certainty of Evidence: Moderate

Recommendation: Bone health assessment should be initiated as early as possible peri-operatively

Strength of Recommendation: Conditional | Certainty of Evidence: Moderate

Rationale: Large registry data demonstrate increased morbidity and mortality associated with surgical delay in hip fracture and neurologically urgent spine conditions. There are no RCTs that have compared delayed versus immediate surgery. Observational and interventional osteoporosis studies demonstrate that peri-operative initiation of therapy does not impair fixation or fusion biology.

Table 7 (continued)

3. Baseline Biochemical Optimization

3a. Vitamin D

Recommendation: Target serum 25(OH)D at least ≥50 nmol/L (20 ng/ml) in patients with deficiency

Examples of correction regimens in situations of deficiency

The following regimens are illustrative examples only and should not be interpreted as preferred or universally applicable protocols. Vitamin D replacement should be individualized based on baseline vit D status, clinical context, local practice standards, available formulations, and country-specific guideline recommendations.

- o 50,000 IU Colecalciferol once–twice weekly for 8–12 weeks or
- o 8,000–10,000 IU Colecalciferol daily for 8–12 weeks, then reassess

• Maintenance 1,000–2,000 IU daily

Strength of Recommendation: Conditional | Certainty of Evidence: Low

Rationale: Vitamin D deficiency is common in arthroplasty and spinal fusion populations and has been associated with poorer postoperative functional outcomes in observational studies. Randomized trials in osteoporosis demonstrate improved mineralization with correction; however, no studies directly evaluate effects on periprosthetic fracture, fixation failure, or fusion outcomes. Certainty is therefore low for construct-level endpoints.

3b. Calcium

Recommendation: Total calcium intake of 1,000–1,200 mg/day, preferably through dietary sources, is recommended. Supplementation should be considered only where dietary intake is inadequate.

Strength of Recommendation: Conditional | Certainty of Evidence: Low

Rationale: Foundational bone physiology and large osteoporosis fracture-prevention RCTs support adequate calcium intake for mineralization. However, no RCTs or cohort studies directly evaluate calcium supplementation in relation to construct-level orthopedic outcomes.

4. Falls (External Load Driver) – Assessment and Mitigation

Recommendation: Assess falls risk and implement basic fall-prevention measures (falls history, medication review, vision/footwear, gait/balance assessment and targeted exercise/physiotherapy; home safety advice where relevant) in older/frail arthroplasty patients, particularly those with osteoporosis or prior fragility fracture.

Strength of Recommendation: Strong | Certainty of Evidence: Moderate

Rationale: Low-energy falls are frequent after THA/TKA and are repeatedly shown as the dominant mechanism for most postoperative periprosthetic femoral fractures (low-energy falls from standing/sitting height). Evidence that multifactorial/exercise-based interventions reduce falls in older adults is supported by systematic reviews, though PPF-specific prevention trials are lacking.

5. Arthroplasty (THA / TKA)

Table 7 (continued)

Primary Goal: Preserve periprosthetic bone stock and reduce construct failure risk.

5a. Imaging & Structural Assessment

Recommendation: Baseline skeletal assessment should include the following where clinically appropriate

• Baseline central/axial DXA

• 1/3 radius if hip/spine uninterpretable

• Periprosthetic DXA for longitudinal monitoring where available

-Gruen zone analysis (THA)

-Distal femoral ROIs (TKA)

• Radiographic surveillance

• QCT in selected complex cases

Strength of Recommendation: Conditional | Certainty of Evidence: Moderate

Rationale: Longitudinal DXA studies demonstrate early region-specific periprosthetic bone loss after THA and TKA. Cohort studies show correlation between regional bone loss and structural vulnerability. Evidence derives from observational imaging cohorts rather than randomized outcome trials.

5b. Pharmacotherapy (Selective, Risk-Stratified)

5b1• Bisphosphonates.

Recommendation: Standard osteoporosis bisphosphonate regimen initiated postoperatively (initiated 2-12 weeks after surgery) in patients with osteoporosis or high-risk bone phenotype (e.g. very low BMD, revision arthroplasty, Dorr C femur, elderly frail patients)

Strength of Recommendation: Strong | Certainty of Evidence: Moderate

Rationale: Multiple RCTs and meta-analyses demonstrate preservation of periprosthetic BMD with bisphosphonates. However, association with reduced revision risk has been demonstrated only in large registry studies, i.e., there are no RCTs proving reduction of periprosthetic fracture or proving reduction in revision with bisphosphonate treatment. Therefore the "strength" of the recommendation comes from consistency (multiple RCTs, meta-analysis showing periprosthetic BMD preservation and large population registry data, with implant survival association). The certainty remains "moderate" because the hard end points i.e. reduction in revision are observational.

5b2• Denosumab

Recommendation:

• Alternative if bisphosphonates contraindicated

• Must transition to bisphosphonate if stopped

Table 7 (continued)

Strength of Recommendation: Conditional | Certainty of Evidence: Moderate

Rationale: RCTs consistently demonstrate significant attenuation of early periprosthetic BMD loss with denosumab compared with placebo. These trials are methodologically robust but evaluate surrogate imaging endpoints rather than revision, migration, or long-term construct survival. Accordingly, certainty is moderate for preservation of peri-implant bone stock but low for hard construct-failure outcomes.

5b3• Anabolic Therapy

Recommendation

• Not routine

• Consider in severe osteoporosis or repeated fixation failure

Strength of Recommendation: Conditional | Certainty of Evidence: Low

Rationale: Small RCTs and modeling data suggest increased periprosthetic BMD. No robust RCTs or cohort studies demonstrate reduced revision or fracture endpoints.

6. Spinal Fusion

Primary Goal: Enhance fixation strength and reduce pseudoarthrosis and junctional failure.

6a. Imaging & Structural Assessment

Recommendation:

• Baseline DXA ± TBS

• Vertebral fracture assessment

• Opportunistic CT HU assessment if available

Strength of Recommendation: Strong | Certainty of Evidence: Moderate

Rationale: Large database and meta-analysis data demonstrate that low BMD is associated with higher pseudoarthrosis, cage subsidence, and screw loosening. L1 HU <110–160 correlates with osteoporosis and fixation failure risk.

6b. Pharmacotherapy (Selective, risk stratified)

6b1. Teriparatide

Recommendation: Prescribe if no contraindications in osteoporotic or low–bone-mass patients undergoing instrumented spinal fusion and /or in those who are at increased risk of construct-level fixation failure (e.g., multilevel constructs, prior fixation failure, poor bone quality on imaging, severe trabecular compromise). There is insufficient evidence to recommend teriparatide solely for peri-operative construct optimization in patients with normal BMD.

Strength of Recommendation: Strong | Certainty of Evidence: Moderate

Rationale: Randomized trials and meta-analyses consistently demonstrate increased

Table 7 (continued)

fusion mass volume, accelerated time to union, and reduced rates of pedicle screw loosening and cage subsidence. These effects align directly with the dominant mechanisms of construct failure in osteoporotic fusion. While definitive large-scale revision reduction trials remain limited, the consistency of fusion-related and fixation-interface benefits supports strong recommendation in appropriately selected high-risk patients.

Dosing and Duration of Teriparatide therapy

Recommendation:

• 20 µg daily (or 56.5 µg weekly where locally approved)

• Typically initiated ≥1 month preoperatively when feasible

• Continued postoperatively for 6–12 months to support early fusion consolidation

Strength of Recommendation: Conditional | Certainty of Evidence: Moderate

Rationale: Across clinical studies, regimens are relatively consistent, with initiation prior to surgery and continuation through the early fusion window associated with improved fusion-related metrics. However, no randomized trials directly compare alternative initiation windows or durations, and optimal timing has not been definitively established.

6b2• Romosozumab

Recommendation:

Romosozumab may be considered selectively in osteoporotic patients undergoing multilevel, deformity, or high-risk fusion constructs where fracture-related junctional failure is a concern.

• If used, initiation prior to surgery or early post-operatively may be reasonable.

• Therapy is limited to 12 months and should be followed by antiresorptive consolidation

Strength of Recommendation: Conditional | Certainty of Evidence: Low

Rationale: Available evidence suggests potential improvement in vertebral strength and possible reduction in fracture-related junctional complications, but human data are limited and predominantly based on surrogate or retrospective findings, without definitive construct-failure trials.

6b3. Antiresorptives

Recommendation:

In osteoporotic or low–bone-mass patients undergoing instrumented spinal fusion:

• **Oral bisphosphonates (e.g., alendronate) or intravenous zoledronic acid** may be initiated peri-operatively (pre-operatively or early post-operatively) when anabolic therapy is not feasible.

Table 7 (continued)

• Therapy should generally be continued for at least 12 months, and thereafter according to underlying osteoporosis indications.

• **Denosumab** may be considered when bisphosphonates are contraindicated or not tolerated; if used, transition to a bisphosphonate is required upon discontinuation.

Strength of Recommendation: Conditional | Certainty of Evidence: Moderate

Rationale: Antiresorptives support vertebral strength and reduce vertebral fracture and cage subsidence risk after fusion. Effects on fusion rate itself are less consistent than with anabolic therapy, and high-quality construct-failure endpoint trials remain limited.

7. Sequential Therapy (Antiresorptive Consolidation after anabolic therapy)

Recommendation:

• In patients with underlying osteoporosis or persistent fracture risk, transition to antiresorptive therapy following completion of an anabolic course is appropriate to maintain skeletal gains.

Strength of Recommendation: Conditional | Certainty of Evidence: Low

Rationale: Anabolic therapy increases bone formation and improves bone mass and microarchitecture; however, these gains may partially regress after discontinuation in the absence of subsequent antiresorptive treatment. In general osteoporosis management, sequential antiresorptive therapy following anabolic therapy is recommended to preserve improvements in BMD and fracture protection. While this sequencing strategy is biologically plausible in the peri-operative spinal fusion setting, no randomized trials have specifically evaluated consolidation regimens after teriparatide used for construct-level optimization. Accordingly, recommendations regarding post-anabolic antiresorptive therapy in this context are extrapolated from established osteoporosis treatment paradigms rather than fusion-specific outcome data.

8. Global Principles

• 8a. Surgery should not be delayed solely for bone optimization

Strength of Recommendation: Strong | Certainty of Evidence: Moderate

• 8b. Medications support, not replace, surgical technique

Strength of Recommendation: Strong | Certainty of Evidence: Moderate

• 8c. Avoid abrupt discontinuation of denosumab without transition to further antiresorptive therapy, due to the risk of rebound bone turnover increase and vertebral fractures.

Strength of Recommendation: Strong | Certainty of Evidence: Moderate

• 8d. Multidisciplinary coordination between orthopedic surgeons and bone specialists is required

Strength of Recommendation: Strong | Certainty of Evidence: Moderate

Table 7 (continued)

• 8e. Orthopedic surgical patients with osteoporosis or high fracture risk should receive pharmacologic osteoporosis treatment to reduce future fracture risk, independent of the index surgical procedure. Strength of Recommendation: Strong | Certainty of Evidence: Moderate **Rationale:** Construct-level failure reflects the interaction between surgical mechanics (implant design, fixation strategy, alignment, load transfer) and host bone biology (bone mass, microarchitecture, turnover, mineralization). Registry, cohort, and fusion studies consistently demonstrate that low bone mass increases the risk of periprosthetic fracture, loosening, subsidence, and pseudarthrosis. Optimizing both mechanical and biological determinants therefore requires coordinated peri-operative evaluation and management across surgical and metabolic bone disciplines. **Approach to Strength of Recommendation and Certainty of Evidence** **Certainty of evidence (High, Moderate, Low)** reflects the predominant level and directness of the available evidence: **High**: consistent findings from multiple randomized controlled trials or high-quality systematic reviews/meta-analyses reporting clinically direct structural outcomes. **Moderate:** randomized trials reporting surrogate endpoints or consistent large observational cohort or registry studies. **Low:** limited, heterogeneous, indirect, mechanistic, or extrapolated data. **Strength of recommendation (Strong or Conditional)** reflects whether the recommendation represents consistent, practice-relevant guidance aligned with current clinical standards: **Strong recommendation:** The direction of effect is consistent across studies and aligns with current standard clinical practice; the recommendation is broadly applicable and unlikely to be reversed by future evidence. **Conditional recommendation:** The evidence base is limited, heterogeneous, indirect, or primarily based on surrogate endpoints; applicability may depend on clinical context or patient selection.

denosumab, which may accelerate bone formation, increase fusion mass volume, and reduce pseudarthrosis risk in osteoporotic bone. Optimization of bone-implant interface competence in high-demand or long constructs may require pre-operative or early peri-operative bone strengthening, preferentially with anabolic therapy in severe osteoporosis, combined with fixation strategies that reduce endplate and junctional overload.

Surgical strategy and pharmacologic management should therefore be integrated as coordinated components of construct preservation in patients with low bone mass, rather than viewed as alternative or competing approaches.

Table 7 provides expert recommendations on peri-operative bone health optimization.

Evidence gaps and future directions

Despite increasing use of osteoporosis therapies around orthopedic reconstruction, several gaps limit their effective translation into practice.

First, bone assessment remains poorly aligned with construct failure risk. Central DXA does not adequately capture the regional bone loss that predisposes to PPF or fixation failure. Emerging data suggest that simple structural surrogates such as femoral morphology (e.g., Dorr classification), TBS, and opportunistic CT-based measures may help identify patients with compromised load-bearing bone despite "acceptable" areal BMD. These

pragmatic tools require prospective validation against construct-relevant outcomes.

Second, most pharmacologic studies rely on surrogate endpoints (periprosthetic BMD, CT density, radiographic fusion) rather than revision surgery, mechanical failure, or clinically significant PPF. Future trials should be designed around orthopedic-failure endpoints, stratified by procedure type (arthroplasty vs spinal fusion) and construct demand.

Third, timing and sequencing of therapy remain undefined. Evidence suggests that early implant migration is mechanically driven, whereas longer-term fixation failure and junctional fracture are biologically modifiable. Studies defining the minimum effective pre-operative exposure, optimal postoperative duration, and sequencing of anabolic and antiresorptive therapies are needed to guide real-world decision-making.

Finally, implementation remains a major barrier. Bone health optimization is inconsistently applied, with wide variation in responsibility, assessment pathways, and treatment initiation. Research into integrated peri-operative models rather than new drugs alone will be critical to reducing preventable construct failure.

Conclusion

Across arthroplasty and spinal fusion, osteoporosis acts as a modifiable determinant of implant fixation failure, manifesting as periprosthetic fracture, loosening, subsidence, pseudarthrosis, and junctional failure. These outcomes reflect failure of the bone-implant system rather than of fracture healing alone.

The available evidence supports integrating bone health assessment and targeted osteoporosis therapy into peri-operative planning, with treatment selection guided by the dominant mechanical and biological failure risks of each construct. Progress will depend on moving beyond central DXA toward structurally relevant bone assessment, aligning therapy with procedure-specific demands, and embedding bone optimization into routine orthopedic pathways rather than treating it as an adjunct.

Appendix

Glossary A: Arthroplasty & periprosthetic fracture terms

Anterior femoral notching

An inadvertent cortical defect created in the anterior distal femur during total knee arthroplasty, which acts as a stress concentrator and increases the risk of periprosthetic femoral fracture.

Arthroplasty

Surgical replacement of a joint with prosthetic components to relieve pain and restore function. Arthroplasty fundamentally alters physiological load transmission across bone by introducing rigid implants that redistribute mechanical forces.

Bipolar hemiarthroplasty

A form of hemiarthroplasty in which the prosthesis incorporates two articulations: an inner articulation between the prosthetic head and shell, and an outer articulation between the shell and the native acetabulum. The design aims to distribute motion and reduce acetabular wear, although progressive acetabular degeneration may still occur over time.

Bone–implant construct

The integrated mechanical system formed by orthopedic implants and the surrounding host bone. Clinical outcomes depend on the ability of this construct to tolerate and adapt to repetitive physiological loading over time.

Cemented fixation

A method of implant fixation in which polymethylmethacrylate (bone cement) is used to anchor prosthetic components to host bone. Cemented fixation transfers load through a cement mantle rather than relying on direct bone-implant contact.

Cementless (uncemented) fixation

A fixation strategy in which implant stability is achieved without bone cement, relying instead on close initial implant-bone contact and subsequent biological fixation at the implant surface.

Dorr classification

A radiographic classification system describing proximal femoral morphology based on cortical thickness and canal shape:

- **Type A**: Thick cortices and a narrow medullary canal ("champagne-flute" femur).
- **Type B**: Intermediate cortical thickness and canal width.
- **Type C**: Thin cortices with a wide canal ("stovepipe" femur).

The Dorr classification is commonly used to characterize femoral structural support and is relevant to implant fixation behavior and fracture risk around femoral stems.

Gruen zones

A seven-zone radiographic classification used to localize periprosthetic bone changes around femoral stems following total hip arthroplasty:

- **Zones 1 and 7**: Proximal femur (lateral and medial, including the greater trochanter and calcar).
- **Zones 2 and 6**: Mid-proximal femoral shaft.
- **Zones 3 and 5**: Distal femoral shaft adjacent to the stem.
- **Zone 4**: Region surrounding the stem tip.

Gruen zones provide a standardized framework for describing stress shielding, bone loss, implant migration, and fracture patterns.

Hemiarthroplasty

Replacement of the femoral head and neck without replacement of the acetabulum. Hemiarthroplasty is commonly used in older or frail patients with hip fractures.

Hybrid fixation

A fixation strategy combining cemented and cementless components within the same reconstruction, most commonly a cemented femoral stem with a cementless acetabular component in total hip arthroplasty.

Implant loosening

Loss of stable fixation between an orthopedic implant and host bone, typically identified radiographically and reflecting failure of the bone-implant interface to maintain mechanical integrity under load.

Osseointegration

The direct structural and functional connection between living bone and the surface of an implant, resulting in biological fixation without intervening fibrous tissue.

Periprosthetic fracture

A fracture occurring in bone adjacent to an orthopedic implant. Periprosthetic fractures reflect failure of the bone-implant construct rather than isolated bone fragility alone.

Stress shielding

Reduction in physiological loading of bone adjacent to an implant due to preferential load transfer through the implant, which may lead to adaptive bone loss over time.

Subsidence

Progressive sinking or settling of an implant into surrounding bone, indicating insufficient mechanical support or failure of fixation.

Total hip arthroplasty (THA)

Replacement of both the femoral head and acetabulum with prosthetic components. THA is performed to restore joint function and alleviate pain in degenerative and fracture-related conditions.

Total knee arthroplasty (TKA)

Replacement of the distal femur and proximal tibia with prosthetic components, with optional resurfacing of the patella, to restore knee alignment, stability, and function.

Vancouver classification

A widely used classification system for **periprosthetic femoral fractures following total hip arthroplasty**, based on **fracture location, implant stability, and bone stock quality**. The system guides clinical decision-making by linking fracture patterns to construct stability.

- **Type A**: Fractures involving the trochanteric region
  - **AG**: Greater trochanter
  - **AL**: Lesser trochanter
- **Type B**: Fractures around or just distal to the femoral stem
  - **B1**: Stable femoral stem with adequate bone stock
  - **B2**: Loose femoral stem with adequate bone stock
  - **B3**: Loose femoral stem with poor bone stock
- **Type C**: Fractures well distal to the femoral stem tip, with the implant typically remaining stable

The Vancouver classification emphasizes the **interaction between fracture location and implant fixation**, rather than fracture morphology alone.

Unified Classification System (UCS)

An extension of the Vancouver classification designed to provide a **standardized framework for classifying periprosthetic fractures across all joints and fixation constructs**, including arthroplasty, internal fixation devices, and spinal implants.

The UCS incorporates:

- **Fracture location relative to the implant**
- **Implant stability**
- **Quality of surrounding bone**
- **Presence of multiple implants or complex constructs**

UCS fracture types include:

- **Type A**: Fractures involving apophyseal or periarticular bone (e.g., trochanters)
- **Type B**: Fractures around the implant or at the bone-implant interface
    - o **B1**: Stable implant
    - o **B2**: Loose implant
    - o **B3**: Loose implant with compromised bone stock
- **Type C**: Fractures distant from the implant
- **Type D**: Fractures occurring between two implants (interprosthetic fractures)
- **Type E**: Fractures involving multiple bones supporting a single implant
- **Type F**: Fractures involving a fixation device rather than a joint replacement

The Unified Classification System allows periprosthetic fractures to be conceptualized as **failures of an implant-bone construct**, enabling consistent classification across anatomical sites and surgical disciplines.

Glossary B: Spinal fusion & implant fixation failure terms

Arthrodesis

Surgical fusion of two or more skeletal segments to eliminate pathological motion and restore mechanical stability. In the spine, arthrodesis aims to achieve permanent osseous continuity between vertebral segments.

Cage subsidence

Progressive sinking of an interbody cage into the adjacent vertebral endplates following spinal fusion. Cage subsidence reflects inadequate structural support from the surrounding bone and may compromise alignment, fusion progression, or construct stability.

Construct-level fixation failure

Failure of a spinal reconstruction to maintain mechanical integrity under physiological loading over time. Construct-level fixation failure encompasses multiple manifestations, including pseudarthrosis, implant loosening, rod fracture, cage subsidence, and junctional failure.

Fusion mass

The newly formed bone bridges intended spinal segments following fusion surgery. The size, continuity, and structural quality of the fusion mass determine the long-term mechanical stability of the fused segment.

Junctional failure

Structural failure occurring at the transition zone between a fused spinal segment and adjacent mobile segments. Junctional failure may involve fracture, implant pullout, progressive deformity, or soft-tissue disruption at the ends of a fusion construct.

Pedicle screw loosening

Loss of stable fixation between a pedicle screw and the surrounding vertebral bone, typically identified radiographically. Pedicle screw loosening reflects inadequate bone-screw interface strength and may precede construct instability or failure.

Proximal junctional kyphosis (PJK)

A postoperative spinal deformity characterized by abnormal kyphotic angulation at the spinal segments immediately above the upper end of a fusion construct. PJK reflects failure of load transfer and structural adaptation at a mechanically vulnerable junction and may progress to fracture, instrumentation failure, or proximal junctional failure.

Pseudoarthrosis

Failure to achieve solid bony union following an intended spinal arthrodesis, resulting in persistent motion at the fusion site. Pseudoarthrosis increases mechanical demands on instrumentation and is a major contributor to construct failure and revision surgery.

Spinal fusion

A reconstructive surgical procedure intended to eliminate pathological intervertebral motion, restore mechanical stability, and maintain or correct spinal alignment by achieving permanent osseous continuity between vertebral segments.

Stress concentration

Local amplification of mechanical forces within specific regions of bone or instrumentation caused by altered load transmission following spinal reconstruction. Stress concentration contributes to failure at interfaces such as screw-bone junctions and junctional segments.

Subsidence

Progressive settling of spinal implants, such as interbody cages or vertebral body replacements, into adjacent bone. Subsidence reflects inadequate structural support and may compromise alignment, neural decompression, or fusion success.

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