Impact of **Opioid Use** on **Bone Mineral Density**

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The prevalence of opioid use has reached alarming levels, particularly in the context of chronic pain management. Recent evidence indicates that approximately 3-4% of the adult population in the United States is prescribed opioids annually for chronic non-cancer pain, with nearly half of surgical patients having filled an opioid prescription in the preceding year (Zedler et al., 2014; Tang et al., 2020). This widespread use is often justified by the need for effective pain management, especially in populations with complex health needs, such as those with HIV or chronic pain conditions (Sharma et al., 2011). However, the increasing reliance on opioids has raised significant concerns regarding their long-term safety and efficacy, particularly in relation to bone health and the risk of fractures.

Bone health is critically important for maintaining structural integrity and reducing fracture risk, especially in populations that may already be vulnerable due to age or comorbid conditions. Bone mineral density (BMD) is a key indicator of bone health, and lower BMD is associated with an increased risk of fractures (Teng et al., 2015; Duarte et al., 2013). Opioids have been implicated in negatively affecting BMD, with evidence suggesting that chronic opioid use may lead to reductions in BMD and an increased risk of fractures (Teng et al., 2015; Duarte et al., 2013). For instance, a meta-analysis has shown that opioid use is significantly associated with a twofold increase in fracture risk, underlining the need for careful consideration of opioid prescribing practices (Teng et al., 2015). Furthermore, opioid-induced endocrine dysfunction, particularly opioid-induced androgen deficiency, has been proposed as a

mechanism linking opioid use to decreased BMD (Thompson, 2023; Fountas et al., 2018).

The biological mechanisms linking opioid use to bone health are multifaceted. Chronic opioid therapy can lead to hormonal changes that adversely affect bone metabolism. Specifically, opioids can inhibit the release of gonadotropin-releasing hormone (GnRH), leading to decreased levels of sex hormones such as testosterone and oestrogen, both of which are crucial for maintaining bone density (Thompson, 2023; , Fountas et al., 2018). Additionally, opioids may directly affect osteoblast and osteoclast activity, further contributing to bone loss (Duarte et al., 2013). The central nervous system effects of opioids, including sedation and dizziness, can also increase the risk of falls, which is a significant contributor to fracture risk in older adults (Duarte et al., 2013).

Current evidence on the impact of opioids on BMD and associated clinical outcomes is growing but remains complex. Studies have demonstrated that opioid users, particularly those on long-term therapy, exhibit significantly lower BMD compared to non-users (Sharma et al., 2011; Duarte et al., 2013). For instance, research involving HIV-infected women has shown that methadone use is associated with notable bone loss, highlighting the intersection of opioid use and specific health conditions (Sharma et al., 2011). Furthermore, the long-term consequences of opioid use extend beyond bone health, as persistent opioid use has been linked to increased mortality rates and adverse health outcomes following surgical procedures (Santosa et al., 2022).

The implications of these findings are profound, suggesting that while opioids may provide short-term relief for pain, their long-term use poses significant risks to bone health and overall well-being. This necessitates a re-evaluation of prescribing practices, particularly in populations at risk for osteoporosis and fractures. The integration of opioid-sparing strategies and alternative pain management modalities is essential to mitigate these risks while

still addressing the underlying pain conditions (Tournebize et al., 2015). Furthermore, ongoing education for healthcare providers regarding the risks associated with opioid therapy and the importance of monitoring BMD in at-risk populations is crucial for improving patient outcomes (Tournebize et al., 2015).

Bone Mineral Density

BMD is a critical measurement in the diagnosis of osteoporosis and the assessment of fracture risk. The World Health Organisation (WHO) defines osteoporosis based on BMD T-scores, where a T-score of -2.5 or lower indicates osteoporosis (Choi et al., 2016). This definition emphasises the importance of BMD as a predictor of fracture risk, as studies have shown that lower BMD correlates with a higher likelihood of sustaining osteoporotic fractures, particularly in older adults (Wu et al., 2020; Slevin et al., 2012). The clinical significance of BMD lies in its ability to identify individuals at increased risk of fractures, which can lead to severe health consequences, including morbidity and mortality (Wáng & Xiao, 2022).

Several factors influence BMD, including age, gender, lifestyle, and genetic predispositions. Age is a significant determinant, as BMD typically peaks in early adulthood and declines with advancing age, particularly in postmenopausal women due to hormonal changes (Lv et al., 2022; Lim et al., 2018). Gender differences also play a role; women generally have lower BMD than men, and the risk of osteoporosis increases significantly after menopause (Rezaei & Dragomir-Daescu, 2015; Bleicher et al., 2010). Lifestyle factors such as physical activity, dietary intake (especially calcium and vitamin D), and body weight are crucial in maintaining healthy BMD levels. For instance, higher physical activity levels have been associated with better BMD outcomes, while sedentary lifestyles contribute to bone density loss (Tervo, 2011; Sommer et al., 2012; Gourlay et al., 2014). Additionally, obesity and body composition can influence BMD, with higher body mass indices often

correlating with increased BMD, although the relationship can be complex due to factors like fat distribution and inflammation (Jang et al., 2016; Chantler et al., 2011).

Socioeconomic factors also impact BMD, as individuals with lower socioeconomic status may have reduced access to nutritious food and healthcare, leading to poorer bone health (Mer, 2024; Garg et al., 2018). Furthermore, genetic factors account for a significant portion of the variability in BMD, with studies indicating that approximately 50-70% of the variation in bone mass can be attributed to genetic influences (Tervo, 2011; Funakoshi et al., 2010). Understanding these multifaceted influences on BMD is essential for developing effective prevention and treatment strategies for osteoporosis and related fractures.

Mechanisms of Opioid Impact on Bone

The use of opioids in pain management has been associated with significant alterations in the hypothalamic-pituitary-gonadal (HPG) axis, leading to a condition known as opioid-induced hypogonadism (OIH). This phenomenon is characterised by reduced levels of sex hormones, particularly testosterone in males and oestradiol in females, which can have profound implications for reproductive health and overall well-being. The mechanisms underlying OIH are multifaceted, involving both central and peripheral pathways. Chronic opioid exposure has been shown to suppress the pulsatile release of GnRH from the hypothalamus, which in turn leads to decreased secretion of luteinising hormone (LH) and follicle-stimulating hormone (FSH) from the pituitary gland, ultimately resulting in diminished testosterone synthesis in the testes and oestradiol production in the ovaries (Reddy et al., 2010; Bawor et al., 2014; Coluzzi et al., 2015).

Research indicates that the effects of opioids on the HPG axis can occur rapidly, with evidence suggesting that significant suppression of hormone levels can be observed within hours of opioid administration (Gudin et al., 2015). For instance, a study

highlighted that intrathecal opioid administration can lead to rapid suppression of the HPG axis, with changes in hormone levels becoming evident within a week (Gudin et al., 2015). Furthermore, the chronic use of opioids has been linked to alterations in the levels of other hormones, such as prolactin, which may also contribute to the endocrine dysfunction observed in patients undergoing long-term opioid therapy (Duarte et al., 2013; Merdin et al., 2016). The impact of opioids on the HPG axis is not only limited to hormone levels but also extends to the regulation of sexual function and libido, with many patients reporting diminished sexual desire and performance (Seyfried & Hester, 2012).

The influence of opioids extends beyond the HPG axis to encompass calcium metabolism and vitamin D levels, which are critical for maintaining bone health. Opioids have been implicated in the disruption of calcium homeostasis, potentially leading to altered bone turnover and increased risk of osteoporosis. The endocrine effects of opioids, particularly hypogonadism, can exacerbate these issues by diminishing the levels of sex hormones that play a protective role in bone density (Coluzzi et al., 2015; Merdin et al., 2016). Testosterone and oestradiol are known to promote osteoblast activity while inhibiting osteoclast formation; thus, their deficiency can lead to an imbalance in bone remodelling processes, resulting in decreased BMD (Duarte et al., 2013; Coluzzi et al., 2015). Furthermore, opioids may interfere with the metabolism of vitamin D, further complicating the maintenance of bone health and increasing the risk of fractures in opioid-dependent individuals (Coluzzi et al., 2015).

The potential for opioid-induced hypogonadism to affect bone turnover is a significant concern, particularly in populations that may already be at risk for osteoporosis, such as older adults and individuals with chronic pain conditions. Studies have demonstrated that patients on long-term opioid therapy exhibit lower BMD and higher rates of fractures compared to those not

receiving opioids (Duarte et al., 2013; Coluzzi et al., 2015). The relationship between hypogonadism and bone health highlights the need for monitoring hormone levels in patients undergoing chronic opioid treatment, as timely intervention may mitigate some of the adverse effects on bone metabolism (Merdin et al., 2016; Coluzzi et al., 2015). Furthermore, the reversibility of these endocrine changes upon discontinuation of opioid therapy highlights the need for healthcare providers to consider alternative pain management strategies that minimise the risk of hypogonadism and its downstream effects on bone health (Gudin et al., 2015; Coluzzi et al., 2015).

Emerging research has begun to explore the role of opioid receptors in bone tissue, suggesting that opioids may have direct effects on bone cells. Opioid receptors, particularly the mu-opioid receptor (MOR), are expressed in osteoblasts and osteoclasts, indicating a potential role in regulating bone remodelling (Coluzzi et al., 2015; Gonzales et al., 2011). Studies have shown that activation of these receptors can influence the activity of osteoblasts and osteoclasts, thereby affecting bone formation and resorption (Coluzzi et al., 2015). This interaction suggests that opioids may not only exert their effects through hormonal pathways but also through direct actions on bone cells, which could have implications for understanding the full spectrum of opioid effects on skeletal health (Coluzzi et al., 2015; Gonzales et al., 2011).

The interaction between opioids, sex hormones, and bone metabolism is multifaceted and necessitates further investigation to elucidate the underlying mechanisms. Understanding how opioids affect the HPG axis, calcium metabolism, and bone turnover will be critical for developing strategies to prevent and manage the adverse effects associated with long-term opioid use. Clinicians should remain vigilant in monitoring hormone levels and bone health in patients receiving opioid therapy, as early identification of hypogonadism and related complications can lead to more effective management and improved patient

outcomes (Merdin et al., 2016; Coluzzi et al., 2015; Hochberg et al., 2018).

Epidemiological Evidence

Cross-Sectional Studies

Cross-sectional studies have increasingly focused on the association between opioid use and BMD, revealing significant insights into the populations most affected, particularly older adults and women. Research indicates that opioid use is correlated with lower BMD, particularly in specific demographics such as older adults and women. For instance, a study by Yoshida et al. highlights that while the longitudinal effects of opioids on fractures are well-documented, the cross-sectional association with lower BMD has been less explored, emphasising the need for further investigation into this aspect (Yoshida et al., 2017). This is particularly relevant for older adults, who are already at a higher risk for osteoporosis and fractures due to age-related bone density loss. The study underlines that opioid use may exacerbate these risks, leading to a greater prevalence of osteoporotic fractures in this population.

In addition to age, gender plays a critical role in the relationship between opioid use and BMD. Duarte et al. found that among male patients undergoing long-term oral opioid therapy, a significant proportion exhibited osteopenia, although the study did not assess the presence of hypogonadism, which is known to affect bone health (Duarte et al., 2013). This finding suggests that men on opioids may be at increased risk for reduced BMD, but the absence of hormonal assessments limits the understanding of the underlying mechanisms. Conversely, women, particularly those who are postmenopausal, may experience compounded risks due to the dual effects of hormonal changes and opioid use. Studies have shown that opioids can suppress the production of sex hormones, which are crucial for maintaining bone density (Saunders et al., 2010).

The impact of opioid use on BMD is further complicated by the presence of comorbid conditions. For example, Sharma et al. noted that middle-aged women infected with HIV who used methadone exhibited significant bone loss, highlighting the intersection of opioid use, chronic illness, and bone health (Sharma et al., 2011). This demographic is particularly vulnerable, as both HIV and opioid use can independently contribute to decreased BMD, suggesting a synergistic effect that warrants further exploration.

Furthermore, the effects of opioids on bone metabolism are not solely limited to hormonal suppression. Research indicates that opioids may directly impair osteoblast function, which is essential for bone formation. Carvalho et al. demonstrated that sustained morphine exposure negatively impacted bone formation rates in animal models, suggesting that opioids could have direct deleterious effects on bone cells (Carvalho et al., 2022). This finding is critical, as it implies that the relationship between opioid use and BMD is not merely a consequence of hormonal changes but may also involve direct biochemical pathways affecting bone health.

The risk of fractures associated with opioid use is also influenced by the side effects of these medications, such as sedation and dizziness, which can lead to falls. Saunders et al. posited that these side effects increase the likelihood of falls, thereby raising the risk of fractures among chronic pain patients using opioids (Saunders et al., 2010). This is particularly concerning for older adults, who may already have compromised balance and coordination. The cumulative effect of opioid-related side effects and the inherent risks of aging can create a precarious situation for this population.

Additionally, the implications of opioid use extend beyond individual health to public health concerns. The increasing prevalence of opioid prescriptions among older adults raises questions about the long-term management of chronic pain and its consequences on bone health. A systematic review by Ramli et al. highlighted that while opioid substitution therapy is common,

the long-term effects on BMD remain inadequately understood, particularly in populations with chronic conditions (Ramli et al., 2021). This gap in knowledge highlights the need for comprehensive assessments of bone health in patients receiving long-term opioid therapy.

Longitudinal Studies

Longitudinal studies examining the relationship between opioid use and BMD have provided valuable insights into the long-term effects of opioid analgesics on skeletal health. Opioids, commonly prescribed for pain management, have been associated with various adverse effects, including the potential for decreased BMD and increased fracture risk. The evidence suggests that opioid use may lead to a reduction in BMD over time, particularly in vulnerable populations such as older adults and individuals with chronic pain conditions.

Confounding factors such as underlying health conditions and concurrent medications must be carefully considered when interpreting the effects of opioid use on BMD. For instance, Brogly et al. emphasised the necessity of adjusting for comorbidities and medication use when evaluating the safety of prenatal opioid agonist therapy, as these factors can significantly influence health outcomes (Brogly et al., 2015). Similarly, the findings of Gotthardt et al. indicated that low testosterone levels, prevalent among opioid-dependent men, were associated with decreased lumbar spine BMD, further complicating the relationship between opioid use and bone health (Gotthardt et al., 2016). This interaction of hormonal status and opioid use necessitates a comprehensive approach to understanding BMD changes.

Furthermore, Lee et al. pointed out that various confounding factors, including age and pre-existing health conditions, can obscure the relationship between BMD and opioid use (Lee et al., 2016). Their study illustrated that the assessment of BMD using dual-energy X-ray absorptiometry (DXA) could be influenced by

factors such as vertebral collapse and osteophyte formation, which are common in older populations. This highlights the importance of considering the broader context of health when evaluating the impact of opioids on bone density.

In addition, the meta-analysis by Teng et al. synthesised data from multiple cohort studies, reinforcing the notion that opioid use is associated with an increased risk of fractures, particularly among older adults (Teng et al., 2015). This finding aligns with the work of Miller et al., who noted that the risk of fractures escalated with higher opioid doses and prolonged use (Miller et al., 2011). These studies collectively emphasise the critical need for ongoing monitoring of BMD in patients receiving opioid therapy, particularly in those with additional risk factors for osteoporosis.

The potential for opioid use to contribute to long-term skeletal health issues is further complicated by the presence of other medications. For example, concurrent use of selective serotonin reuptake inhibitors (SSRIs) has been linked to an increased risk of fractures, suggesting that the interaction between opioids and other pharmacological agents may exacerbate the risk of bone density loss (Teng et al., 2015). This interaction of medications necessitates a careful evaluation of treatment regimens in patients requiring opioid analgesics.

Clinical Implications

Fracture Risk in Opioid Use

The relationship between opioid use and increased fracture risk has garnered significant attention in clinical research, particularly given the rising prevalence of opioid prescriptions for pain management. Numerous studies have established a clear association between opioid use and heightened fracture risk, with evidence suggesting that opioid users face a significantly higher risk of sustaining fractures compared to non-users (Teng et al., 2015). This increased risk is particularly pronounced in specific

populations, such as older adults and those with pre-existing conditions like arthritis, where the interchange of opioid pharmacology and patient vulnerability can lead to adverse outcomes (Miller et al., 2011).

The mechanisms underlying the increased fracture risk in opioid users are multifaceted. Opioids are known to impair cognitive function, balance, and coordination, which are critical factors in preventing falls, one of the primary causes of fractures (Carbone et al., 2013; Silverman et al., 2022). The sedative effects of opioids can lead to decreased vigilance and slower reaction times, thereby increasing the likelihood of falls, especially in elderly populations (Rolita et al., 2013). Furthermore, the long-term use of opioids can lead to physical dependence and opioid-induced hyperalgesia, complicating pain management and potentially leading to prolonged opioid use, which further exacerbates the risk of falls and fractures (Oelreich et al., 2020).

Specific fracture sites commonly associated with opioid use include the hip, wrist, and spine. Hip fractures, in particular, are a significant concern, as they are often associated with high morbidity and mortality rates in older adults (Yoo et al., 2021). Studies have shown that opioid use prior to hip fracture surgery is linked to higher rates of postoperative complications and prolonged opioid dependence (Simoni et al., 2019). Similarly, wrist fractures, which are prevalent among older adults, have been associated with opioid use, particularly in those who may already be at risk due to osteoporosis or other underlying conditions (Weiss et al., 2012). The spine is another critical area, as opioid use has been linked to increased risk of vertebral fractures, particularly in patients with chronic pain conditions (Nathan et al., 2020).

The implications of these findings are profound, necessitating a re-evaluation of opioid prescribing practices, particularly in vulnerable populations. Clinicians must weigh the benefits of pain relief against the potential risks of fractures and other adverse

events associated with opioid use. Strategies to mitigate these risks include careful patient selection, monitoring for signs of opioid dependence, and considering alternative pain management strategies that may pose less risk to bone health (Chen et al., 2013; Kim et al., 2017). Additionally, educating patients about the risks associated with opioid use, particularly regarding falls and fractures, is essential in promoting safer pain management practices (Kingston et al., 2023).

Risk Assessment and Monitoring

To identify individuals at high risk for opioid-related bone loss, several factors must be considered. First, the duration and dosage of opioid therapy are critical indicators. Long-term opioid use has been associated with decreased BMD and increased fracture risk, particularly in populations such as postmenopausal women and older adults (Duarte et al., 2013; Chrastil et al., 2013). For instance, studies have shown that chronic opioid use can lead to hypogonadism, which is a significant risk factor for low BMD and fractures (Campana et al., 2022). Additionally, the presence of other comorbidities, such as obesity and low oestrogen levels, further exacerbates the risk of osteoporosis in these patients (Paneri et al., 2014).

Furthermore, the assessment of opioid misuse history is vital in identifying at-risk individuals. Tools such as the Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R) and the Opioid Risk Tool have been developed to evaluate the potential for opioid misuse and associated risks (Butler et al., 2013; Cheatle et al., 2019). These tools incorporate various factors, including previous substance use history, psychological conditions, and demographic variables, to stratify patients into low, moderate, or high-risk categories for opioid dependence (Brenton et al., 2017; Brenton et al., 2018).

In addition to these assessment tools, healthcare providers should consider the impact of concurrent medications on bone health.

The use of proton-pump inhibitors, for example, has been shown to increase fracture risk, particularly in patients who are also using opioids (Inacio et al., 2016). This highlights the importance of a comprehensive medication review as part of the risk assessment process.

Monitoring BMD in long-term opioid users is essential for early detection and intervention of osteoporosis. The National Osteoporosis Foundation recommends that individuals at high risk for osteoporosis undergo regular BMD testing, particularly those who have been on long-term opioid therapy (Duarte et al., 2013). Dual-energy X-ray absorptiometry (DEXA) scans are the gold standard for assessing BMD and should be performed at baseline and periodically thereafter, depending on the initial results and the patient's risk factors (Paneri et al., 2014).

Furthermore, clinicians should be vigilant about the signs of bone loss, such as unexplained fractures or changes in mobility, which may indicate a decline in bone health (Chrastil et al., 2013; White et al., 2021). It is also advisable to implement lifestyle modifications and pharmacological interventions aimed at improving bone density. For instance, weight-bearing exercises and adequate calcium and vitamin D intake can help mitigate bone loss in patients on long-term opioid therapy (Paneri et al., 2014).

In cases where BMD is found to be low, bisphosphonates or other osteoporosis treatments may be warranted. The decision to initiate treatment should be based on a thorough evaluation of the patient's overall health status, risk factors, and preferences (Paneri et al., 2014).

Additionally, the role of patient education cannot be overstated. Patients should be informed about the potential risks associated with long-term opioid use, including the impact on bone health. Providing education on the importance of adherence to prescribed osteoporosis medications and lifestyle changes can

allow patients to take an active role in their health management (Marie, 2019).

Knowledge Gaps and Future Directions

Despite the growing body of literature, significant knowledge gaps remain, particularly concerning the long-term effects of opioids on bone density and fracture risk. Current studies often suffer from limitations such as small sample sizes and a lack of diverse populations, which hinder the generalisability of findings. Furthermore, there is a pressing need for longitudinal studies and randomised controlled trials to establish causality between opioid use and adverse bone health outcomes.

One of the primary limitations of existing research is the small sample sizes that are often employed. For instance, studies investigating the impact of opioids on BMD frequently include limited cohorts, which may not adequately represent the broader population of opioid users. This is particularly relevant in the context of chronic pain patients, where factors such as age, sex, and comorbidities can significantly influence bone health outcomes. For example, a study by Saunders et al. highlights the association between opioid use and fractures in older chronic pain patients, but the small sample size limits the robustness of the conclusions drawn (Saunders et al., 2010). Similarly, the research conducted by Chrastil et al. on opioid-induced androgen deficiency in an orthopaedic model also suffers from limited generalisability due to its specific animal model (Chrastil et al., 2014).

Furthermore, the lack of diverse populations in opioid research is a critical gap that needs addressing. Many studies do not account for racial, ethnic, or socioeconomic differences that may influence both opioid prescribing practices and bone health outcomes. For instance, Romanelli et al. discuss disparities in opioid prescribing for long bone fractures, indicating that implicit biases may affect treatment decisions (Romanelli et al., 2019). This lack of diversity

can lead to skewed results that do not accurately reflect the experiences of all opioid users, particularly marginalised communities who may face different risks and health challenges.

To address these limitations, there is a clear need for longitudinal studies and randomised controlled trials that can provide more definitive evidence regarding the causal relationships between opioid use and bone health. Longitudinal studies would allow researchers to track changes in bone density over time in opioid users compared to non-users, thereby providing insights into the long-term effects of opioid therapy. Randomised controlled trials could help isolate the effects of opioids on bone health from other confounding factors, such as lifestyle choices and comorbid conditions. For example, the study by Teng et al. conducted a meta-analysis of cohort studies, suggesting that opioids contribute to fracture risk, but the observational nature of these studies limits the ability to draw causal conclusions (Teng et al., 2015).

In addition to the need for more rigorous study designs, exploring the genetic and molecular mechanisms linking opioids to bone health is essential for understanding how these substances affect bone metabolism. Research has indicated that chronic opioid use may lead to hormonal changes that adversely impact bone health. For instance, chronic opioid use has been associated with opioid-induced androgen deficiency, which can lead to decreased bone density and increased fracture risk (Thompson, 2023). The mechanisms underlying these hormonal changes are not fully understood, but they may involve the inhibition of GnRH and subsequent reductions in sex steroid production (Thompson, 2023; Duarte et al., 2013).

Furthermore, the interaction between opioids and bone cells, particularly osteoblasts and osteoclasts, warrants further investigation. Studies have shown that opioids can directly affect bone remodelling processes, potentially leading to decreased

bone formation and increased resorption (Carvalho et al., 2022). For instance, the research by Carvalho et al. demonstrated that sustained morphine delivery suppresses bone formation and alters metabolic profiles in mice, indicating a direct impact on bone health (Carvalho et al., 2022). Understanding these molecular pathways could lead to the development of targeted interventions to mitigate the negative effects of opioids on bone health.

Additionally, the role of central nervous system effects of opioids, such as sedation and dizziness, in increasing the risk of falls and fractures cannot be overlooked. Opioids are known to impair balance and coordination, which may lead to an increased likelihood of falls, particularly in older adults (Saunders et al., 2010; Teng et al., 2015). This relationship highlights the importance of considering both direct and indirect effects of opioids on bone health when evaluating their overall impact on patients.

Conclusion

The evidence emphasises a compelling link between opioid use and decreased BMD, highlighting significant risks to bone health, including increased fracture susceptibility. While opioids remain a critical tool for managing pain, their long-term effects on bone metabolism and fracture risk necessitate a cautious and balanced approach to prescribing. The multifaceted mechanisms by which opioids influence bone health, ranging from hormonal disruptions to direct effects on bone cells, demand further investigation to fully elucidate their impact.

Healthcare providers must prioritise risk assessment, monitoring, and patient education to mitigate these adverse effects. Regular BMD evaluations, integration of opioid-sparing strategies, and the use of alternative pain management modalities are critical to reducing the burden of opioid-related bone health complications. Additionally, addressing gaps in research, such as conducting larger, more diverse longitudinal studies and exploring genetic

and molecular mechanisms, will enhance our understanding and inform better clinical practices.

Finally, a comprehensive approach that balances the benefits of pain relief with the risks to skeletal health is essential for improving patient outcomes and ensuring the long-term safety of opioid therapy.

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