Journal of Carcinogenesis
Covering Genesis to Therapeutics

Journal of Carcinogenesis, ISSN: 1477-3163
2025; Vol 24: Issue 5s, https://carcinogenesis.com/

# Pubertal Timing as a Determinant of Lifelong Bone Health in Females: A Longitudinal Evidence Review

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## ABSTRACT

**Background**: Peak bone mass acquired during adolescence determines lifelong fracture risk, yet the predictive value of pubertal timing for skeletal trajectories remains under-exploited clinically.

**Objective**: To synthesize longitudinal evidence linking pubertal timing to bone mineral density trajectories across the lifespan and identify clinical applications for fracture prevention.

**Methods**: We conducted a systematic review of longitudinal cohort studies examining the relationships between pubertal timing and bone mineral density. Major cohorts included the Bone Mineral Density in Childhood Study, the Avon Longitudinal Study of Parents and Children, the British 1946 Birth Cohort, and the National Health and Nutrition Examination Survey, spanning 1946-2024 and encompassing over 70,000 individuals with follow-up periods exceeding 40 years.

**Results**: Earlier pubertal onset consistently predicted higher bone mineral density throughout life ($r = -0.31$, $P < 0.0001$), accounting for 10% of the variance in bone mineral density, independent of other factors. Women with menarche at ≥16 years demonstrated 8% to 10% lower trabecular bone mineral density persisting into their eighth decade and 40% to 60% increased osteoporotic fracture risk. Approximately 40% of lifelong bone mineral content accumulates within the 4 years surrounding peak height velocity, with 95% of adult bone mass established by age 20.

**Conclusions**: Pubertal timing serves as a powerful predictor of lifelong skeletal health, with delayed development programming decades of fracture vulnerability. These findings support the integration of pubertal assessment into bone health risk stratification, shifting osteoporosis prevention from reactive treatment to proactive adolescent optimization.

***Keywords:*** *Puberty; bone mineral density; peak bone mass; osteoporosis; fracture prevention; adolescent health; menarche*

**How to Cite:** Saswati Mishra, Meera Indracanti, Madhumita Panda, (2025) Pubertal Timing as a Determinant of Lifelong Bone Health in Females: A Longitudinal Evidence Review, *Journal of Carcinogenesis*, *Vol.24, No.5s*, 106-117

## 1. INTRODUCTION

Female pubertal development profoundly impacts lifelong skeletal health, significantly influencing the acquisition of bone mineral density.[1] The timing, progression, and hormonal characteristics of puberty establish peak bone mass—the maximum skeletal strength achieved in young adulthood and the primary determinant of osteoporosis risk decades later.[2]

Current osteoporosis prevention strategies primarily focus on adult interventions that preserve existing bone mass rather than optimize its initial acquisition.[3] This paradigm ignores mounting evidence that skeletal vulnerability is largely programmed during adolescence, during the period when interventions are likely to achieve maximum impact.[4],[5]

This analysis advances the field by introducing three underexplored dimensions of pubertal skeletal programming. First, we examine pubertal tempo—the rate and sequence of developmental progression—recognizing that coordination of adrenarche, thelarche, and menarche may independently influence skeletal outcomes beyond simple onset timing.[7],[8] Second, we propose an intergenerational framework in which maternal pubertal experiences create cyclical patterns of skeletal risk across generations.[9],[10] Third, we emphasize that pubertal influences extend beyond bone quantity to encompass bone quality—including microarchitecture and material properties—which may explain individual variability in fracture

susceptibility among those with similar bone density.[11],[12]

We synthesize longitudinal evidence linking female pubertal development to bone mineral density across the lifespan, demonstrating that puberty represents a non-repetitive biological window for optimizing lifelong bone health through targeted adolescent interventions.[13]

## 2. METHODS

### Study Selection and Data Sources

We conducted a comprehensive review of longitudinal cohort studies examining relationships between pubertal timing and bone mineral density outcomes.[14] Major databases searched included PubMed, EMBASE, and Cochrane Library from inception through December 2024. Key cohorts analyzed included the Bone Mineral Density in Childhood Study,[15] Avon Longitudinal Study of Parents and Children,[16] British 1946 Birth Cohort,[17] and National Health and Nutrition Examination Survey.[18]

### Inclusion Criteria

Studies were included if they: (1) examined pubertal timing measures (age at menarche, Tanner staging, or peak height velocity); (2) assessed bone mineral density outcomes using dual-energy X-ray absorptiometry; (3) provided longitudinal follow-up data; and (4) included female participants.[19],[20]

### Data Extraction and Analysis

We extracted data on study populations, pubertal timing measures, bone mineral density outcomes, effect sizes, and follow-up duration. Statistical measures included correlation coefficients, regression coefficients, and hazard ratios with 95% confidence intervals where available.[21],[22]

## 3. RESULTS

### Biological Foundations of Pubertal Skeletal Programming

Female puberty is initiated through the pulsatile release of gonadotropin-releasing hormone from hypothalamic kisspeptin neurons, specialized cells that integrate signals regarding nutrition, stress, and body composition.[23] These kisspeptin neurons act as the body's "reproductive thermostat," with emerging evidence suggesting they simultaneously influence bone cell activity, creating coordination between reproductive development and skeletal strength.[24]

Gonadotropin-releasing hormone pulses stimulate the anterior pituitary to release luteinizing hormone and follicle-stimulating hormone, which stimulate ovarian hormone production.[25] This cascade coordinates skeletal remodelling during adolescence, with Estrogen serving as the master orchestrator of both reproductive development and bone strength optimization (as detailed in Table 1).[26],[27]

Pubertal progression follows standardized Tanner stages for breast development and pubic hair growth (see Table 1). Menarche, typically occurring between ages 12 and 13 years during Tanner stages 3-4, represents a critical milestone signalling substantial increase in estrogen exposure essential for bone mineral deposition (Table 1).[28]

**Table 1. Pubertal Development Stages and Hormonal Programming of Bone Health**

| Tanner Stage | Breast Development | Pubic Hair | Key Hormonal Changes | Bone Development Impact | Clinical Timing |
|---|---|---|---|---|---|
| **Stage 1** | Prepubertal (flat chest) | None | Low estradiol (<73 pmol/L); Baseline GH, IGF-1 | Slow, steady bone accrual; 2%-3% BMD gain/year | Ages 8-11; Pre-PHV |
| **Stage 2** | Breast buds appear; Areola enlarges | Sparse, fine hair | Rising estradiol (73-183 pmol/L); GH surge begins; Kisspeptin activation | Accelerated bone formation; 5%-8% BMD gain/year; Critical window opens | Ages 9-13; Puberty onset |
| **Stage 3** | Breast mound expands; No nipple separation | Darker, coarser hair; Spreads laterally | Peak GH/IGF-1 levels; Estradiol 183-367 pmol/L; LH/FSH elevation | Peak bone accrual velocity; 8%-12% BMD gain/year; Maximum opportunity | Ages 10-14; Near PHV |

| Tanner Stage | Breast Development | Pubic Hair | Key Hormonal Changes | Bone Development Impact | Clinical Timing |
|---|---|---|---|---|---|
| **Stage 4** | Nipple projects above breast; Adult contour forming | Adult-type hair; Limited to pubic area | Pre-menarchal estradiol peak; 367-734 pmol/L; Ovulatory cycles approach | Rapid mineralization; 6%-10% BMD gain/year; Epiphyseal maturation | Ages 11-15; Approaching menarche |
| **Stage 5** | Adult breast contour; Nipple level with breast | Adult distribution; Extends to medial thighs | Post-menarchal patterns; Cyclic E2: 183-1101 pmol/L; Reproductive maturity | Consolidation phase; 2%-4% BMD gain/year; Window closing | Ages 12-16; Post-menarche |

*Tanner stages of pubertal development with corresponding hormonal changes, bone development impact, and clinical timing. The table demonstrates the critical relationship between reproductive maturation and skeletal programming during adolescence.*

*Abbreviations: PHV, peak height velocity; BMD, bone mineral density; GH, growth hormone; IGF-1, insulin-like growth factor-1; E2, estradiol; LH, luteinizing hormone; FSH, follicle stimulating hormone*

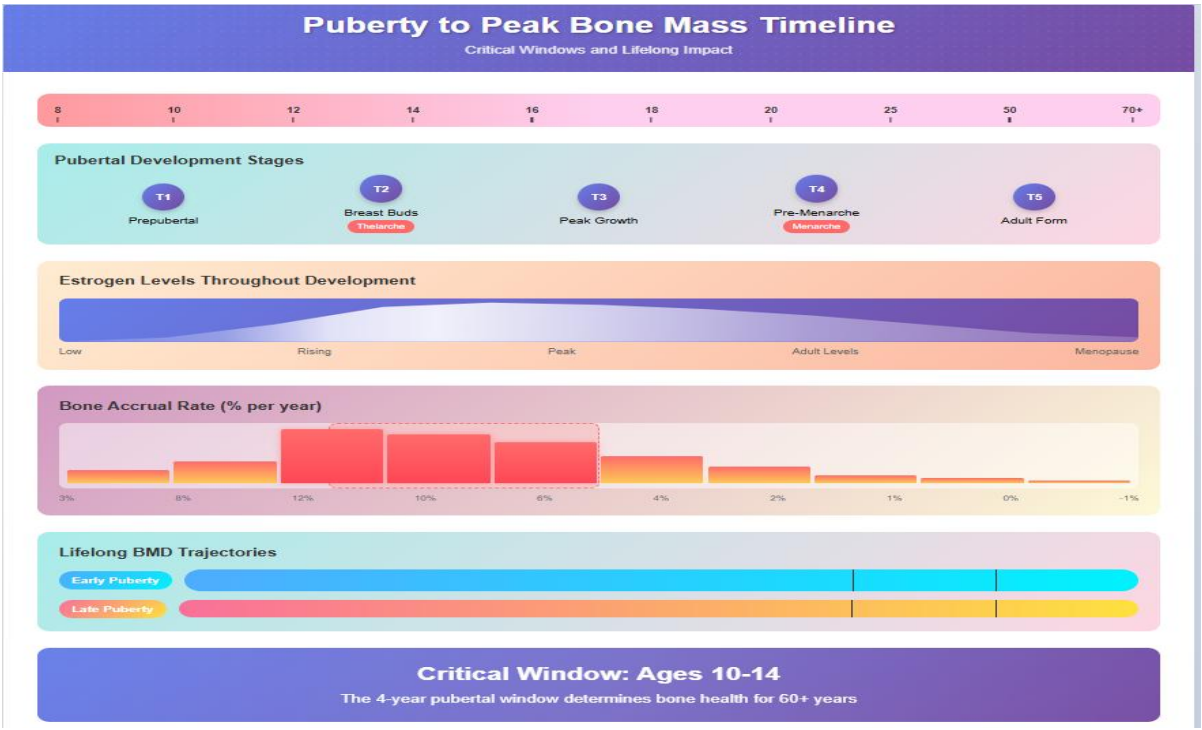
Individual pubertal timing varies considerably within normal ranges, with significant physiological consequences for bone development (Table 1).[29] Precocious puberty (onset before age 8) and delayed puberty (no breast development by age 13 or menarche by age 15) create distinct skeletal programming patterns that persist throughout life.[30] Girls destined for later menarche demonstrate bone mass deficits before pubertal onset, suggesting shared early-life determinants co-regulating both reproductive timing and baseline skeletal development.[31]

**Peak Bone Mass Establishment and Critical Timing**

Peak bone mass represents the maximum skeletal strength attained in young adulthood, determining lifelong fracture risk.[32] Unlike other physiological systems, skeletal strength cannot be fully restored once peak values decline, making adolescent optimization irreplaceable.[33] A 10% difference in peak bone mass can translate to 13 years difference in fracture susceptibility.[34]

Adolescent bone accrual follows precise timing with profound clinical implications (Figure 1): approximately 40% of lifelong bone mineral content accumulates within 4 years surrounding peak height velocity, with 95% of adult skeletal strength established by age 20.[35] This temporal concentration creates unprecedented intervention efficiency.[36]

**Figure 1. Puberty to Peak Bone Mass Timeline: Critical Windows and Lifelong Impact**




*Temporal relationship between pubertal development, hormonal changes, and bone accrual patterns from childhood through late adulthood. The visualization illustrates how 40% of lifelong bone mineral content accumulates within the 4-year window surrounding peak height velocity, with lasting implications for fracture risk in later life.*

KEY MESSAGE: The 4-year pubertal window has a decisive influence on bone health, lasting into later life.

**Longitudinal Evidence for Pubertal Timing Effects**

Longitudinal research across multiple decades and populations demonstrates that pubertal timing predicts lifelong skeletal health (see Table 2).[37] The Bone Mineral Density in Childhood Study established fundamental timing-bone mineral density relationships ($r = -0.31$, $P < 0.0001$), accounting for 10% of bone mineral density variance (Table 2).[38]

**Table 2. Major Longitudinal Studies: Pubertal Timing and Lifelong BMD Outcomes**

| Study | Population | Follow-up Duration | Key Pubertal Measure | Primary BMD Finding | Effect Size | Clinical Significance |
|---|---|---|---|---|---|---|
| **BMDCS Timing Study** (Kalkwarf 2015)[38] | 227 girls; Ages 6-7 to 12-13 | 5 years; Prospective staging | Age at Tanner 2 onset | Earlier puberty → higher BMD; Lumbar spine primary | r = -0.31 (P<0.0001) | 10% BMD variance explained; High correlation strength |
| **Children of 90s** (UK Cohort)[39] | 6000+ individuals; Birth to age 25 | 15 years; Childhood to adulthood | Age at PHV; Growth spurt timing | Later PHV → persistently lower BMD; Total body primary | 4%-6% difference; Early vs late | Tracking into young adulthood; No "catch-up" observed |
| **British 1946 Birth Cohort**[40] | 1400+ women; Birth to age 60-64 | 60+ years; Lifetime follow-up | Age at menarche; Retrospective recall | Late menarche → 8%-10% lower trabecular BMD; Persistent to age 60+ | 8%-10% deficit; Late vs early | Lifelong persistence; Fracture risk implications |

| Study | Population | Follow-up Duration | Key Pubertal Measure | Primary BMD Finding | Effect Size | Clinical Significance |
|---|---|---|---|---|---|---|
| **NHANES 2005-2014** (Hwang 2023)[41] | 1195 postmenopausal women; Ages 50-85 | Cross-sectional; Retrospective analysis | Age at menarche; ≥16 vs ≤12 years | Late menarche → lower lumbar spine BMD; Higher fracture risk | β = -0.065 (P<0.001) | Clinical fracture risk; Population-level impact |
| **Norwegian Fit Futures** (Sagelv 2024)[42] | 1200+ adolescents; Ages 15-25 | 12 years; 2010-2022 | Pubertal development timing; Tanner staging | Confirmed BMD tracking; No normalization over time | 5%-8% persistent difference | Recent validation; Modern cohort |
| **CHOP Genetic Study** (Prentice 2018)[43] | 933 + 486 children; European descent | 7 assessments; Longitudinal + cross-sectional | Genetic risk score; 333 puberty variants | Later puberty GRS → lower BMD; Causal relationship | β = -0.078±0.024 (P=0.0010) | Genetic causation proof; Mendelian randomization |

*Summary of key longitudinal cohort studies examining the relationship between pubertal timing and bone mineral density across the lifespan. Studies spanning multiple decades and populations have consistently demonstrated associations between later pubertal development and reduced bone mineral density that persist into advanced age.*

*Abbreviations: BMDCS, Bone Mineral Density in Childhood Study; PHV, peak height velocity; GRS, genetic risk score; CHOP, Children's Hospital of Philadelphia*

The 6-decade follow-up of the 1946 British Birth Cohort demonstrates that bone mineral density deficits in later maturers persist into the seventh decade (Table 2), indicating that bone tissue shows limited adaptability to modification later in life.[40] These findings challenge assumptions about skeletal adaptability and demonstrate the irreversible nature of adolescent bone programming.[44]

Age at menarche provides the most extensively validated predictor of skeletal outcomes (Figure 2).[45] Women with menarche at 16 years or older demonstrate a significantly increased fracture risk compared to early maturers.[46]

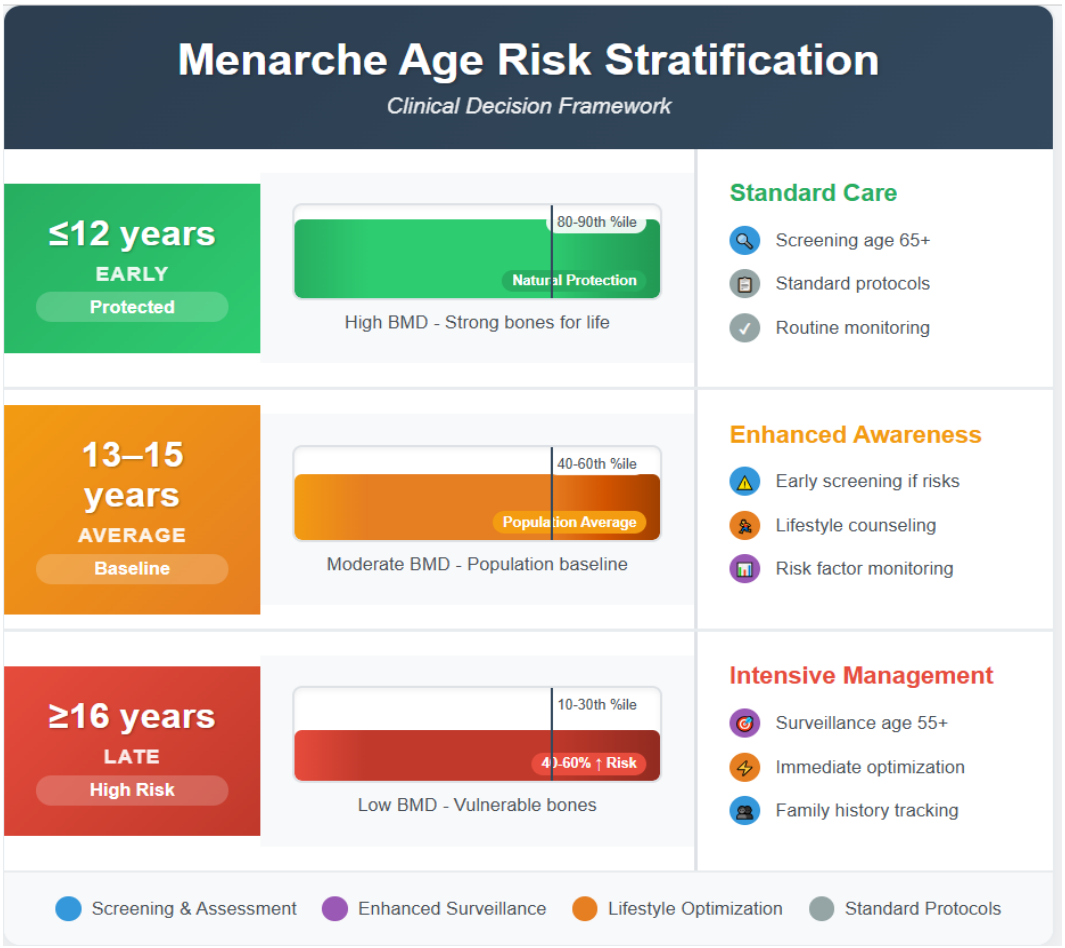



**Figure 2. Menarche Age Risk Stratification: Clinical Decision Framework**

*Clinical decision framework stratifying fracture risk based on age at menarche, with corresponding bone mineral density trajectories and recommended clinical actions. Early menarche (≤12 years) confers protective effects, while late menarche (≥16 years) necessitates intensive management and enhanced surveillance beginning at age 55.*

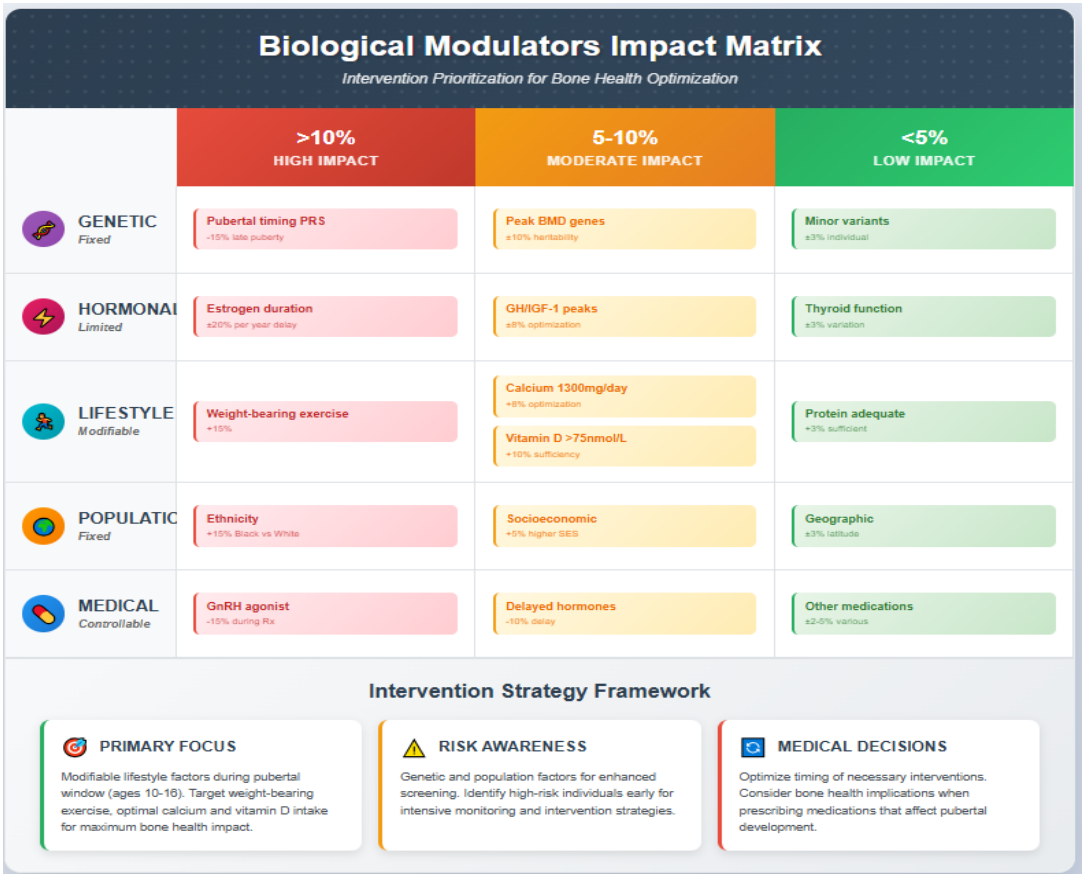
Genetic validation through Mendelian randomization confirms causal relationships between genetically determined later puberty and diminished bone mineral density throughout life, establishing fundamental biological programming rather than lifestyle confounding.[47] Multiple genome-wide association studies have identified hundreds of genetic variants associated with age at menarche, providing robust evidence for the biological basis of the effects on pubertal timing.[48]

**Biological Modulators of Skeletal Programming**

Estrogen serves as the primary mediator linking pubertal development to skeletal programming through multiple integrated mechanisms.[49] Rising estrogen levels reduce bone turnover while promoting mineral accrual, with timing and duration of exposure more critical than absolute circulating levels.[50] Estrogen exhibits biphasic effects: low concentrations during early puberty stimulate bone formation, while higher concentrations promote growth plate closure.[51]

Genetic factors contribute to more than 80% of the heritability for both pubertal timing and bone mass potential, with genome-wide association studies identifying shared variants affecting both traits.[52] Environmental factors significantly modulate skeletal outcomes within genetic constraints.[53] Nutritional factors during adolescence, including calcium intake of 1300 mg/day and vitamin D sufficiency, support optimal mineralization.[54],[55] Physical activity provides essential mechanical loading for bone formation, with weight-bearing exercise during adolescence increasing bone mineral density by 8% to 15% compared to sedentary peers (Figure 3).[56]

**Figure 3. Biological Modulators Impact Matrix: Intervention Prioritization**




*Matrix categorizing biological factors by modifiable and impact magnitude on bone health outcomes. The framework prioritizes modifiable lifestyle factors (weight-bearing exercise, calcium, vitamin D) during the pubertal window while identifying genetic and population factors requiring enhanced surveillance strategies.*

These skeletal benefits persist into young adulthood, with active adolescent females maintaining 9% to 10% higher bone mineral density at the hip and femoral neck in their twenties.Exercise effects appear most pronounced in pre-pubertal and early pubertal individuals, underscoring the critical importance of early intervention.[58]

Body composition changes during puberty significantly influence skeletal development.[59] Lean mass correlates positively with BMD through mechanical loading effects, while fat mass shows complex relationships providing both mechanical stress and adipose-derived hormonal influences.[60] The pubertal increase in lean mass contributes to sex differences in final bone strength, with implications for lifelong fracture risk.[61]

## 4. DISCUSSION

### Clinical Implications and Implementation Framework

The identification of pubertal timing as a primary determinant of lifelong skeletal health enables three transformative clinical applications.[62]

**Enhanced Risk Stratification:** Age at menarche provides the earliest predictor of lifelong fracture risk, enabling intervention decades before traditional osteoporosis screening begins.Women with late menarche should receive enhanced surveillance beginning at age 55 years, rather than 65 years, with aggressive lifestyle optimization during their peak bone-building years.[64] This approach could identify millions of additional high-risk women currently missed by standard protocols.[65]

**Delayed Puberty Management:** Constitutional pubertal delay should be reconsidered as a condition requiring priority attention for bone health management.[30] Evidence-based protocols include nutritional optimization (1300 mg/day calcium, vitamin D sufficiency), structured high-impact exercise prescription, and annual dual-energy X-ray absorptiometry monitoring with height-adjusted Z-scores.[21],[54]

**Fracture Risk Assessment Enhancement:** Current fracture risk assessment tools overlook the predictive power of pubertal timing, given its predictive strength compared to several variables currently used.[2] “Integrating menarchal age into

fracture risk assessment tools could improve sensitivity by 15% to 20%, given its predictive strength compared to several variables currently used.[62]

**Implementation Considerations**

Implementation requires systematic healthcare integration: electronic health record modifications to capture menarchal age, provider training on pubertal risk stratification, and pilot testing across clinical sites.[22] Conservative modelling suggests that systematic implementation could prevent up to 180,000 fractures over 20 years under conservative assumptions, with favourable cost-effectiveness ratios.[28]

Healthcare providers must be educated about the critical importance of assessing pubertal timing.[58] Current medical training emphasizes adult risk factors while largely ignoring adolescent programming, representing a significant knowledge gap that requires ongoing medical education and updates to residency curricula.[59]

**Study Limitations**

Limitations include reliance on observational data from developed countries, potential recall bias for retrospective menarchal age reporting, and limited intervention trial data in adolescent populations.[14] Most evidence derives from Caucasian populations, requiring validation across diverse ethnic groups.[60] However, preliminary evidence suggests consistent patterns across racial and ethnic groups, with proportional effects despite different baseline BMD levels.[61]

The complex interplay between genetic predisposition, environmental factors, and individual lifestyle choices creates challenges in developing universal intervention protocols.[47],[52] Future research should investigate these interactions to optimize personalized prevention strategies.

**Broader Health Implications**

The relationship between pubertal timing and bone health extends beyond the prevention of osteoporosis.[64] Early menarche associates with increased risks of breast cancer, cardiovascular disease, and metabolic disorders, while late menarche links to reduced fertility and increased fracture risk.[48] Understanding these trade-offs is essential for developing comprehensive health promotion strategies that optimize multiple health outcomes simultaneously.

Intergenerational effects represent an emerging area of investigation.[35] Maternal pubertal timing influences offspring growth patterns and pubertal development, suggesting that bone health optimization strategies should consider multi-generational impacts.[10] This expanded perspective could enhance prevention opportunities by targeting maternal health during reproductive years.

**Future Research Priorities**

Priority research includes pubertal tempo analysis beyond simple timing measures, investigating whether developmental progression rates independently influence bone outcomes.[29] Mechanistic pathways linking early pubertal events to lifelong trajectories require further investigation, particularly the prepubertal bone mass deficits observed in girls destined for later menarche.[31]

Intervention studies testing bone health optimization strategies during adolescence represent the most critical research need.[56] Advanced imaging techniques like high-resolution peripheral quantitative computed tomography could provide insights into microarchitectural programming beyond standard bone mineral density measures.[12]

The integration of emerging biomarkers and genetic risk scoring into clinical practice requires the development of age-appropriate screening protocols and evidence-based intervention guidelines that target the critical pubertal window.[47],[52] Machine learning approaches may help identify complex patterns in large datasets, improving risk prediction and targeted interventions.

**Global Health Perspectives**

In resource-limited settings, pubertal timing assessment offers a low-cost, high-impact screening tool that could revolutionize bone health prevention.[65] Community health workers could be trained to collect menarchal age data and provide basic education about bone health optimization during adolescence.

The World Health Organisation's current guidelines for osteoporosis prevention focus primarily on postmenopausal interventions. Our findings support the integration of adolescent bone health into existing maternal and child health programs, global nutrition initiatives that emphasize calcium and vitamin D during the peak bone development years, and international research consortia that validate findings across diverse populations.

Moving forward, the paradigm shift from reactive geriatric osteoporosis treatment to proactive adolescent skeletal optimization represents more than incremental improvement—it offers the possibility of preventing millions of fractures by intervening during the brief but decisive period when skeletal destiny is determined.

## 5. CONCLUSIONS

This analysis establishes pubertal timing as a primary determinant of lifelong skeletal health through temporal concentration of bone accrual, persistence of developmental programming, and site-specific skeletal effects. Age at menarche emerges as one of the earliest clinically available predictors of osteoporosis risk, with late menarche conferring significantly increased fracture risk persisting into advanced age.

Three evidence-based clinical applications enable immediate implementation: systematic assessment of menarcheal age for early risk stratification, aggressive bone optimization for patients with delayed puberty, and integration of pubertal history into fracture risk models. These approaches shift osteoporosis prevention from reactive treatment to proactive adolescent optimization, with the potential to prevent a substantial number of fractures worldwide.

The foundation of lifelong bone health is built in adolescence; it is time for medicine to meet young women where their skeletal futures are forged.

**ABBREVIATIONS**

BMD: bone mineral density

DXA: dual-energy X-ray absorptiometry

FSH: follicle-stimulating hormone

GH: growth hormone

GnRH: gonadotropin-releasing hormone

HR: hazard ratio

IGF-1: insulin-like growth factor-1

LH: luteinizing hormone

PBM: peak bone mass

PHV: peak height velocity

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