Chapter 30
Smoking, Alcohol, and Bone Health

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Key Points

- Smoking and alcohol consumption are two lifestyle factors that have important contributions to skeletal health.
- Deleterious effects of smoking on the skeleton have been recognized for several decades. Smoking adversely affects bone density and increases hip fracture risk in postmenopausal women. In men emerging evidence is suggestive for similar associations but the evidence is not conclusive.
- The evidence is inadequate to infer a causal relationship between smoking and reduced bone density before menopause in women and in younger men.
- Previously, the role of alcohol on skeletal health was not as well studied as that of smoking, and results from those studies suggested both beneficial as well as deleterious effects on the skeleton. However, recent studies on the role of alcohol on the skeleton suggest a "J"-shaped curve. Moderate ingestion of alcohol may offer some degree of benefit to the skeleton.
- Ongoing research further suggests that both ethanol and non-ethanol components of alcohol containing beverages affect skeletal heath.

Keywords Smoking • Alcohol • Bone mineral density • Fracture

30.1 Introduction

Smoking and alcohol consumption are two lifestyle factors that have important contributions to skeletal health. Deleterious effects of smoking on the skeleton have been recognized for several decades. The 2004 Surgeon General's Report on Bone Health and Osteoporosis [1] recognized smoking and heavy alcohol use as significant contributors to reduced bone mass and increased fracture risk. The 2004 Surgeon General's Report on Women and Smoking [2] concluded that smoking adversely affects bone density and increases hip fracture risk in postmenopausal women while the association in men is suggestive but not conclusive. The evidence is inadequate to infer a causal relationship between smoking and reduced bone density before menopause in women and in younger men. Recent studies

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on the role of alcohol on skeletal health suggest a "J"-shaped curve. Moderate ingestion of alcohol may offer some degree of benefit to the skeleton. Ongoing research further suggests that both ethanol and non-ethanol components of alcohol affect skeletal heath.

30.2 Smoking and Bone Health

30.2.1 Smoking Effects on the Skeleton

There are potential direct and indirect effects of smoking on skeletal health and fracture risk. Direct toxic effects of smoking on bone cells may be related to nicotine effects [3, 4] or possibly to toxic chemicals in tobacco products such as cadmium [5]. Smoking has direct effects on osteogenesis including alteration in the RANK–RANKL–OPG system [6, 7], collagen metabolism [8], and bone angiogenesis [9] (Fig. 30.1). Indirect effects of smoking on bone may result from decreased intestinal calcium absorption [10], dysregulation in sex hormone production and metabolism [11], alterations in metabolism of adrenal cortical and gonadal hormones [12–14], calciotropic hormones [15] such as 25-hydroxy-vitamin D [11, 16] and parathyroid hormone [11]. These effects may account for the generally observed decrease in markers of bone formation, such as osteocalcin, in smokers [16, 17].

Smoking may also indirectly influence bone density and the risk of fractures through reductions in body weight. Body weight tends to be lower for smokers than for nonsmokers, and this weight difference may itself lead to lower bone density and increased risk for fracture [18, 19]. Finally, smokers may be less physically active, which itself may reduce bone density [20] and increase fracture risk [21]. In several analyses involving women, weight explains part of the increased risk of low bone

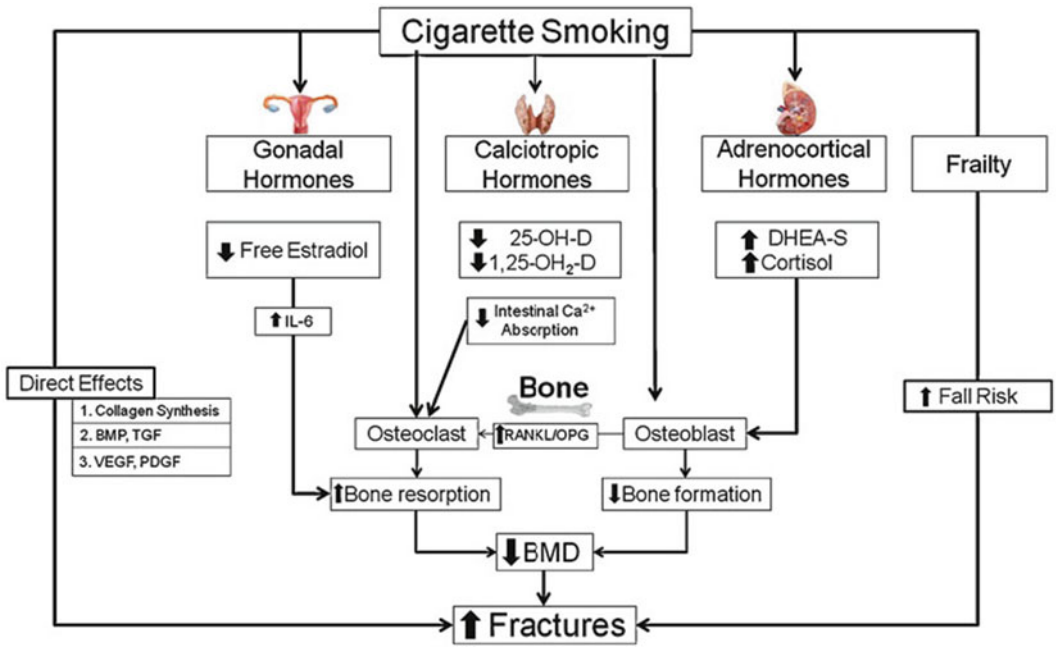

Fig. 30.1 Pathophysiologic mechanisms due to cigarette smoking that lead to decreased bone mineral density and increased fracture risk. Tobacco use increases risk through bone mineral density-dependent factors, as well as through direct effects that are independent of BMD [15]

mineral density (BMD) associated with smoking [22]; however, there are differences in BMD and fracture between smokers and nonsmokers, even after adjusting for weight differences [17, 23–25]. The lower weight in smokers compared to nonsmokers may increase the risk of fractures, such as hip fractures, through several mechanisms: reduced soft tissue mass overlying the trochanter, resulting in less energy absorption from a fall on the hip; or even reduced conversion of adrenal steroids into sex steroids in the adipose tissue. The anti-estrogenic effect of smoking may also contribute to osteoporosis in women [26, 27]. Interestingly, although estrogen appears to be a critical hormone for male skeletal health [28], smoking does not appear to attenuate the association between estradiol levels and bone density in men [29]. Finally, smoking may increase the risk of fracture through a reduction in physical performance capacity, which itself may increase the risk of falls [30].

30.2.2 Smoking and Bone Density

30.2.2.1 Skeletal Change Over the Lifespan

In adults, bone mass is dependent on the level achieved at the peak, and on losses due to aging and other factors. The skeleton grows rapidly in infancy, slows during childhood, and then accelerates during puberty, such that by age 20–30 years of age, peak skeletal mass is attained [31, 32]. Gains in BMD continue into the third decade and then BMD declines over the remaining decades of life [33, 34]. After menopause, bone loss accelerates compared with premenopausal years. These rates continue or actually increase with aging [35] and similar changes are observed in men [36, 37]. Because of these age-related patterns, smoking influences on bone density may be observed in the attainment of peak bone mass, in premenopausal women, and in men.

30.2.2.2 Smoking and Attainment of Peak Bone Mass

Data are actually somewhat limited with regard to the negative effects of smoking on the attainment of peak bone mass because less is known about the skeletal effects of smoking around the time of puberty [38–40]. A study from Belgium examined 12,446 men aged 25–45 years and reported that smoking at a young age was associated with unfavorable bone geometry and density and was associated with increased fracture prevalence, providing arguments for a disturbed acquisition of peak bone mass during puberty by smoking, possibly owing to an interaction with sex steroid action [38]. Another study of healthy military male recruits ages 16–19, reported that smoking was associated with preserved bone geometry, but worse BMD and Quantitative Ultrasound (QUS) characteristics [41].

Few data are available on the role of smoking in the attainment of peak bone mass because of the relatively rare exposure at very young ages. Some studies have been performed in premenopausal women initially suggesting that bone density does not differ between smokers and nonsmokers up to the time of menopause in women. Another study conducted in 1,061 Swedish women, all exactly 25 years of age, reported that among current smokers, negative effects were observed for BMD at the hip but not at other sites, and it was related to the amount of cigarettes smoked in a dose-dependent manner. Furthermore, young women with a long history of smoking had a higher BMI suggesting that attainment of peak bone mass is adversely associated with smoking in young women. Previous studies in young men suggested no real differences in bone density between young male smokers and nonsmokers. However, a recent study from the United Kingdom reported that smoking appeared to be detrimental to BMD and quantitative bone ultrasound measures, but not proximal femoral geometry in 723 healthy Caucasian male military recruits (age range 16–18 years) [41].

30.2.2.3 Smoking and Bone Density in Mid- and Late Life

In contrast to the results for younger persons, bone density studies performed in populations well beyond the years of peak bone mass demonstrate significant differences between smokers and non-smokers (Table 30.1). Previous data from longitudinal studies in men and women suggest there may be a causal relationship between smoking and bone loss in older women and men and that smoking cessation may slow, or partially reverse, the accelerated bone loss caused by years of smoking. However, it was unclear if there were sex differences related to smoking effect.

Recent studies examined the impact of smoking characteristics in older men and women. A Co-Twin Study of 146 female twin pairs (aged 30–65 years) by MacInnis et al. reported that a discordance of

Table 30.1 Studies of BMD and bone loss according to smoking status in women and men

Study	Sample, age (year)	Smoking status	Measurement/site	Principal finding
BMD				
Tanaka et al. [83]	325 men aged ≥50 years	10 % current smokers	BMD femoral neck	Current smokers at higher risk of developing osteoporosis (OR = 6.43).
Tamaki et al. [44]	1,576 men aged ≥65 years	17.6 % current smokers; 59.2 % former smokers	BMD lumbar spine and total hip	Longer duration of smoking years was associated with lower BMD.
Szulc et al. [46]	719 men aged 51–84 years	11.5 % current smokers; 56.3 % former smokers	BMD spine, hip, distal forearm, ultra distal radius	Compared to never smokers, current and former smokers had lower BMD at most sites.
Supervia et al. [11]	74 men and women; mean age 32.2 years	29.7 % current smokers	BMD lumbar spine, femoral neck and total femur	In men smokers had lower BMD compared to never smokers.
Muraki et al. [84]	632 women aged ≥60 years	20.0 % smokers	BMD lumbar spine	Ever-smokers had lower BMD compared to never smokers.
MacInnis et al. [42]	146 women twin pairs aged 30–65 years	Pre-menopausal women: 47 % ever smokers (8.6 mean pack-years of smoking); post-menopausal women: 32 % ever smokers (14.1 mean pack-years of smoking)	BMD spine, total hip and forearm	10 pack-years smoking related to 2.3–3.3 % lower BMD at all sites except forearm. Effect more pronounced in post-menopausal women.
Izumotani et al. [85]	686 Japanese men aged 40–59 years	Mean smoking (pack-years) among normal men: 18.9 ± 20.0; osteopenic men: 19.1 ± 21.1 and osteoporotic men: 27.7 ± 29.4	Spine BMD	Pack-years of smoking was associated with lower BMD
Forsmo et al. [86]	1,652 Norwegian pre- and post-menopausal women aged 50–59 years	Mean smoking (pack-years) was 13.9 (95 % CI: 13.1–14.7); mean number of daily cigarettes was 10.8 (95 % CI: 10.3–11.3)	BMD distal and ultradistal radius	Pack-years of smoking were associated with lower distal radius BMD but not ultradistal radius BMD. Marginally significant interaction for smoking*coffee ($P = 0.09$).

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Table 30.1 (continued)

Study	Sample, age (year)	Smoking status	Measurement/site	Principal finding
Gerdham et al. [25]	1,032 Swedish women aged 75 years	14 % current smokers; 20 % former smokers; 66 % never smokers	BMD total body, spine and hip, bone mass assessed by ultrasound of the calcaneus and phalanges	Hip and total body BMD was low in current vs. never smokers. This difference was not detected by ultrasound measurements. No difference between former vs. never smokers at any bone site.
Baheiraei et al. [47]	90 Iranian women aged ≥35 years	Current smokers 8 % (pre-menopausal women); 8 % post-menopausal women	BMD spine and femoral neck	Smoking status associated with lower BMD. Current smokers had lower BMD compared to non-smokers.
Williams et al. [87]	46 pair of monozygotic twins discordant for alcohol consumption	Current smokers vs. former smokers	BMD hip and lumbar spine	Current smoking was negatively associated with BMD.
Muraki et al. [84]	632 women aged ≥60 years	Smokers (20.6 %) vs. non-smoker	BMD lumbar spine	Smoking was negatively associated with BMD.
Kuo et al. [43]	837 Taiwanese men aged 46–64 years	30.8 % current smokers; 5.6 % former smokers	BMD spine and femoral neck	Smoking status and duration of smoking were deleterious for spine BMD. The effect was cumulative with duration and quantity.
BMD loss				
Elgán et al. [88]	152 Swedish women (aged 18–26); average follow-up 2 years	18.5 % daily smokers; 18.5 % "party" smokers; 63 % non-smokers at the follow-up time	BMD heel bone (calcaneus)	Baseline smoking associated with lower BMD at the follow-up after adjusting for baseline BMD.
Bakhireva et al. [80]	507 community-dwelling men aged 45–92 years	Current smokers aged: 45–64 years (14.6 %); 65–74 years (7.5 %); 75–92 years (2.2 %)	BMD hip and lumbar spine	Compared to former smokers, % BMD loss in current smokers was increased at the total hip and femoral neck.

BMD bone mineral density

10 pack-years of smoking was related to a 2.3–3.3 % (SE, 0.8–1.0) lower lumbar spine BMD, total hip BMD and total body BMC but not the forearm BMD, with effects more evident in postmenopausal women [42]. Studies in older Asian men have reported a 3.8 % lower lumbar spine BMD in heavy smoking (≥20 cigarette/day) [43]. The Fujiwara-kyp Osteoporosis Risk in Men (FORMEN) study reported that the negative impact of smoking on bone status is mainly associated with the number of years of smoking in older men [44]. The Male Osteoporosis Study from Hong Kong, a longitudinal study, reported that in older men, current smokers had a 2.0 % decrease in hip BMD (95 % CI: −3.8, −0.1) while past smokers had a 1.3 % decrease in hip BMD (95 % CI: −2.5, −0.2) compared to never smokers [45]. However, some studies report no bone mass differences between former and never-smokers [25, 46]. It has also been suggested that former smokers may not lose or regain BMD after cessation of smoking [46].

Certain factors such as higher body mass index [47], and higher calcium intake [48] have been reported to attenuate the smoking associations with bone. Smoking may also interfere with the treatment of osteoporosis in women using estrogen replacement therapy (ERT), as levels of estradiol are lower in smokers taking estrogen than in nonsmokers taking estrogen [49], and bone density values in women taking estrogen are lower in smokers than in nonsmokers [23].

These effects on bone density are significant in mid and late life, since for every 10-year increase in age, the bone density of smokers falls below that of nonsmokers by about 0.14 SD, or 2 % of the average bone density at the time of the menopause. Because a 1.0-SD decrease in bone density doubles the risk of fracture, and because fracture incidence increases with age, the proportion of all fractures attributable to smoking would be expected to increase as smokers continue smoking into old age. Attempts to decrease smoking as early in life as possible are likely to reduce fractures that occur in old age among smokers.

Taken together, cigarette smoking (both dosage and duration of smoking) is associated with lower BMD and increased bone loss in older men and women. Limited studies have examined if the deleterious effects of smoking on bone health may be reversible. Furthermore, smoking effects on bone may not be limited to BMD but may extend to other aspects of bone strength such as bone architecture and bone geometry, an area that has received little attention.

30.2.3 Smoking and Fracture Risk

Hip fractures, the most frequently studied fractures in relation to smoking, account for a significant proportion of the morbidity and mortality attributed to osteoporosis. Previous studies suggested that smoking appeared to increase the risk of hip fracture; however, there were fewer studies of smoking and fracture risk at other skeletal sites. Because the risk of hip fractures in smokers increases with age, and hip fracture incidence also increases with age, the proportion of hip fractures attributable to smoking increases with age.

A meta-analysis by Kanis et al. [50] included 59,232 men and women from ten prospective cohorts from across the world. This study reported that a smoking history was associated with a significantly increased risk of fracture compared with individuals with no smoking history. The highest risk was observed for hip fracture (84 % increased risk, 95 % CI: 1.52–2.22) while the risk of osteoporotic fractures considered as a group was marginally higher (29 % increased risk, 95 % CI: 1.13–1.28). The authors concluded that a history of smoking results in fracture risk that is substantially greater than that explained by the risk of lower BMD. A study by Olofsson et al. using data from the Uppsala Longitudinal Study of Adult men [51] supported these findings, and further clarified that the risk of fracture in older men depends both on recency of smoking and on the daily amount of tobacco smoked, rather than smoking duration (Table 30.2). However, Samelson et al. reported no significant associations of smoking (number of cigarettes/day compared to never smokers) and 25-year cumulative incidence of radiographic vertebral fracture in men and women [52].

Interventions aimed at helping smokers quit are likely to result in a significantly reduced number of hip fractures. Although hip fractures carry the greatest risk of mortality, morbidity, and cost, other fractures also contribute significantly to these outcomes. Further research is necessary to quantify the risk of these fractures in smokers.

Table 30.2 Studies of smoking and relative risk of fractures of the hip and other sites

Type of fracture/study	Study design	Sample	Results
Hip fracture			
Lau et al. [89]	Case–control	451 Asian men and 725 Asian women with hip fracture; aged 50 and older (mean, 72.0 for men, 73.7 for women) 1,162 healthy controls (456 men, 706 women) without hip fracture; mean age, 70.8 for men, 72.7 for women	Current smoking: Men, RR = 0.7 (95 %, CI, 0.5–1.0); women, RR = 0.5 (95 %, CI, 0.3–0.7) Former smoking: Men, RR = 2.1 (95 % CI, 1.5–2.9); women, RR = 1.4 (95 % CI, 0.9–2.0)
Baron et al. [82]	Age-matched, case–control	1,328 Swedish postmenopausal women with hip fracture; aged 50–81 years (mean, 72.5) 3,312 Swedish postmenopausal without hip fracture; mean age, 70.5	Current smokers had increased risk of fracture, OR = 1.35 (95 % CI, 1.12–1.64); Duration of smoking, particularly postmenopausal smoking was more important than the amount smoked
Du et al. [90]	Cross-sectional study	703 community-dwelling Chinese men and women (226 men, 467 women) aged ≥90 years (mean, 93.5)	Current or former smoking had no association
Porthouse et al. [91]	Prospective cohort study	703 community-dwelling English women aged ≥70 years (mean, 76.9)	Current smoking not related to fracture risk
Olofsson et al. [51]	Prospective cohort study	2,322 community-dwelling Swedish men aged 49–51 years	Current smoking (RR = 3.03; 95 % CI 1.02–3.44), former smoking (RR = 1.87; 95 % CI 1.02–3.44); ever smoking (RR = 2.12; 95 % CI 1.18–3.81) were associated with hip fracture
Jutberger et al. [92]	Prospective cohort study	3,003 men aged 69–80 years from the Swedish MrOs Study (n = 209 incident fractures over a follow-up of 3.32 years)	Current smokers had an increased risk of hip fractures (HR: 3.16, 95 % CI 1.44–6.95)
Vertebral fracture			
Jutberger et al. [92]	Prospective cohort study	3,003 men aged 69–80 years from the Swedish MrOs Study (n = 209 incident fractures over a follow-up of 3.32 years)	Current smokers had an increased risk of clinical and radiographic vertebral fractures (HR: 2.53, 95 % CI 1.37–4.65)
Klift et al. [93]	Prospective cohort study	3,001 men and women aged ≥55 years with 6.3 years of follow-up; 157 vertebral fractures (men, 44; women, 113)	Current smoking was associated with incident vertebral in women (RR = 2.1; 95 % CI 1.2–3.5)
Samelson et al. [52]	Prospective cohort study	Community-dwelling American men (252); women (452) aged 47–72 years; 92 (women) and 20 (men) new radiographic vertebral fractures occurred over 25 years follow-up	Smoking was not associated with 25-years cumulative incidence of radiographic vertebral fracture
Ankle fracture			
Valtola et al. [94]	Prospective cohort study	11,798 Finnish women aged 47–56 years with 5 years of follow-up; 194 malleolar fractures	Smoking had a dose–response effect with HR: 1.73 (95 % CI 1.11–2.71) in those smoking 1–19 cigarettes/day, and 2.94 (95 % CI 1.53–5.62) in those smoking ≥20 cigarettes/day

(continued)

Table 30.2 (continued)

Type of fracture/study	Study design	Sample	Results
Wrist fracture			
Porthouse et al. [91]	Prospective cohort study	703 community-dwelling English women aged ≥70 years (mean, 76.9)	Current smoking not related to fracture risk
Any nonvertebral fracture			
Porthouse et al. [91]	Prospective cohort study	703 community-dwelling English women aged ≥70 years (mean, 76.9)	Current smoking not related to fracture risk
Jutberger et al. [92]	Prospective cohort study	3,003 men aged 69–80 years from the Swedish MrOs Study (nonvertebral fractures defined as humerus, radius, pelvis, and hip fractures over a follow-up of 3.32 years)	Current smokers had an increased risk of nonvertebral osteoporotic fractures (HR: 2.14, 95 % CI 1.18–3.88)
Any fracture			
Jutberger et al. [92]	Prospective cohort study	3,003 men aged 69–80 years from the Swedish MrOs Study (nonvertebral fractures defined as humerus, radius, pelvis, and hip fractures over a follow-up of 3.32 years)	Current smokers had an increased risk of all new fractures (HR: 1.76, 95 % CI 1.19–2.61)

30.3 Alcohol and Bone Health

30.3.1 Alcohol Effects on the Skeleton

The mechanisms by which alcohol acts on the skeleton are poorly understood. This is due to the following factors: *First*, it is difficult to isolate the specific contribution of alcohol from other comorbidity factors known to influence bone health [53]. *Second*, it is difficult to isolate ethanol effects from other nutritional factors within alcoholic beverages, which usually differ by beverage type (for example silicon present as orthosilicic acid in beer and resveratrol in wine). *Third*, methods of assessing exposure to alcohol are inconsistent, especially in observational studies in humans. Additionally, the definition for moderate alcohol is not clear and the guidelines on acceptable intakes of alcoholic beverages is different between nations [54]. *Fourth*, the effect of alcohol on fracture outcomes is complicated, as it may be influenced by other factors such as age, drinking patterns, and alcohol effect on falls [55]. *Fifth*, ethanol-related health effects vary between populations because genetic background greatly influence the metabolism of alcohol [54].

Nevertheless, the direct effects of alcohol on bone and mineral metabolism have been described in both rats and in humans. Studies of chronic alcohol consumption in growing male and female rats have indicated that bone growth is suppressed, leading to a failure to acquire a normal peak bone mass [56]. Bone loss in adult rats fed ad libitum a liquid diet containing increasing concentrations of ethanol until receiving the appropriate percentage of total caloric intake, resulted in a dose-dependent decrease in trabecular thickness, bone turnover, and bone formation rate [57]. When equated to humans, the doses used in the adult rat experiments ranged from the low end of moderate (3 % of caloric intake) to alcoholic levels comprising 35 % of caloric intake. These findings in rats suggest that even moderate levels of alcoholic beverage consumption in humans may have the potential to reduce bone turnover and possibly to have deleterious effects on the skeleton. In rats fed ethanol over long periods, Peng et al. reported a greater risk of tibial fractures and a decrease in trabecular bone volume and bone strength [58]. Turner et al. reported that alcohol-consuming rats had decreased bone turnover after 4 months of treatment. Furthermore, an imbalance between bone formation and bone resorption at higher levels of alcohol consumption resulted in trabecular thinning [57].

In humans, alcoholics have been shown to have low BMD that is due to an inhibition of bone remodeling by a mechanism independent of the calciotropic hormones [59, 60]. Others have compared alcoholics to controls and found that serum concentrations of 25-hydroxyvitamin D_3 and 1,25-dihydroxyvitamin D_3 were significantly reduced among the alcoholics as compared to the controls [61, 62]. These low levels have been suggested to be the result of a deficient diet, reduced exposure to sunlight, malabsorption of vitamin D, increased biliary excretion of 25-hydroxyvitamin D metabolites, or to be the result of reduced reserves of vitamin D owing to a reduction of adipose and muscle tissue in alcoholics [63]. Laitenen and colleagues demonstrated that the low serum levels of vitamin D metabolites in non-cirrhotic alcoholics were not because of nutritional deficiency, and hypothesized that there was increased degradation of vitamin D metabolites in the liver. However, they showed that high calcium intake could counteract the vitamin D abnormalities [64]. Alcohol may also have deleterious effects on bone homeostasis through increased excretion of calcium and magnesium [65]. Consistent with the observations of reduced bone formation in alcohol-fed rats, reductions in osteoblastic activity have been observed in acute alcohol intoxication and in moderate use over 3 weeks time in humans [66, 67].

On the other hand, recent studies have also focused on non-ethanol components of alcohol beverages such as silicon and resveratrol. Recent reviews by Jugdaohsingh [68] and more recently by Price et al. [69] have provided extensive research on silicon's effect on bone and connective tissue. While the exact mechanisms are still unclear, various mechanisms were suggested in these reviews. Silicon improves bone matrix quality, facilitates bone mineralization, and plays a role in collagen synthesis and/or its stabilization as well as in the utilization (i.e. gastrointestinal uptake and metabolism) of essential elements that are required for bone and collagen synthesis. Available epidemiological data also supports silicon's role in BMD [70, 71] in humans. Research on health effects of resveratrol is limited and primarily comes from studies of animals. One study in an ovariectomized rat model showed that rats treated with resveratrol had significantly greater BMD than those not treated [72] suggesting that resveratrol could play a role in protecting against bone loss induced by estrogen deficiency. A recent study of male rats showed that trans-resveratrol supplementation (12.5 mg/kg body weight/day) appeared to preserve the skeletal system during disuse and age-related bone loss [73].

30.3.2 Alcohol and Bone Density

Most studies investigating alcohol intake and bone health suggest a "J"-shaped curve such that the inflection point is at moderate ingestion, which offers maximum protection. Increased intake beyond this level shows negative effects on the skeleton. Wosje et al. reported bone beneficial effects of moderate alcohol consumption (measured as drinking occasions/month) using the data from the Third National Health and Nutrition Examination Survey (NHANES III, 1988–1994) [74]. This study reported that total hip BMD in men and FN-BMD in postmenopausal women were higher among those with >29 drinking occasions/month compared to abstainers. However, no associations were observed in premenopausal women or with binge drinking (Table 30.3). Results from the Cardiovascular Health Study (subgroup of 1,567 men and women with BMD measures) showed that alcohol intake (measured as drinks/week) was associated with hip BMD in a U-shaped relationship, with approximately 5 % higher BMD among participants with ≥14 drinks/week compared to abstainers [75].

Cawthon et al. examined the association of alcohol intake and problem drinking history with BMD in a cross-sectional study of 5,974 men (aged ≥65 years) [76]. Alcohol intake categories were defined as non/infrequent (<12 drinks/year, abstainers), light (≥12 drinks/year to <13 drinks/week), and moderate to heavy (≥14 drinks/week). Alcohol intake was positively associated with hip and spine BMD. Although the absolute differences in BMD levels across categories of alcohol were modest (3.5 % for total hip BMD). Men with problem drinking also had higher hip and spine BMD. The type of alcohol consumed was not ascertained.

Table 30.3 Studies of bone density and bone loss according to alcohol use

Study	Sample, age (year)	Alcohol status	Measurement/site	Principal finding
BMD				
Wosje et al. [74]	14,646 men and women aged ≥20 years	Frequency of alcohol consumed in past 1 month	BMD total hip and femoral neck	Alcohol intake was positively associated with BMD in men and postmenopausal women but not in premenopausal women. No associations with binge drinking.
Williams et al. [87]	46 pair of monozygotic twins discordant for alcohol consumption	Units per week, defined as half a pint of beer; a glass of wine or one measure of spirits	BMD hip and lumbar spine	Alcohol consumption was positively associated with BMD.
Tucker et al. [77]	1,182 men, 1,289 postmenopausal women and 248 premenopausal women aged 29–86 years	Drinks/day, defined as 356 mL beer; 118 mL wine; 42 mL liquor	BMD Spine and hip	Moderate alcohol intake was positively associated with BMD in men and postmenopausal women but not premenopausal women.
Kouda et al. [78]	1,421 Japanese men aged ≥60 years	Grams of absolute ethanol per day calculated from current alcohol intake by beverage type	BMD Spine and hip	Alcohol intake <55 g/day was associated with higher BMD and intake of ≥55 g/day was associated with lower BMD.
Cauley et al. [95]	5,995 men aged ≥65 years	Drinks/week	BMD Spine and hip	A 1 SD (approximately seven drinks/week) increase in alcohol consumption was associated with a 1 % higher hip and spine BMD.
Muraki et al. [84]	632 women aged ≥60 years	Alcohol drinker vs. nondrinker	BMD lumbar spine	Alcohol consumption was positively associated with BMD.
BMD loss				
Macdonald et al. [79]	891 women aged 45–55 years	Alcohol intake in quartiles	BMD lumbar spine and femoral neck	Modest alcohol intake was associated with less bone loss.
Bakhireva et al. [80]	507 community-dwelling men aged 45–92	Frequency of alcohol consumption (drinking ≥3 vs. ≤2 days/week)	BMD lumbar spine, total hip and femoral neck	Moderate alcohol intake was associated with less bone loss.

BMD bone mineral density

Tucker et al. further attempted to identify the different classes of alcohol in relation with BMD in older men and women (1,182 men, 1,289 postmenopausal women, and 248 premenopausal women) from the Framingham Heart Study [77]. This study sample of predominantly beer-drinking men, and predominantly wine drinking women, supported the earlier findings that moderate consumption of alcohol is associated with higher BMD in men and postmenopausal women. This protective effect peaked at one to two drinks/day for men (the benefits declined with higher intakes). However, for unclear reasons and contrary to the current guidelines for women, this protective effect peaked at a higher limit (>2 drinks/day) in women. No associations were observed in premenopausal women, perhaps due to low power. Interestingly, men with high liquor intakes (>2 drinks/day) were associated with significantly lower BMD. The authors concluded that stronger associations with beer or wine, relative to liquor, suggest that other constituents (such as silicon in beer) rather than ethanol may contribute to bone health.

Using data from the baseline survey for the Fujiwara-kyo Osteoporosis Risk in Men (FORMEN) study, Kouda et al. reported a positive association between alcohol intake (g/day) and BMD as well as with bone markers (serum levels of osteocalcin and tartrate-resistant acid phosphatase 5b (TRACP5b) [78]. However, they reported an inflection point for the relation between alcohol intake and BMD as 55 g/day. Thus the range of positive association in this study was larger than the previous studies.

Only two longitudinal studies examined alcohol intakes with bone loss. One study from the Aberdeen Prospective Osteoporosis Screening Study examined the association of alcohol intake (in g/day) with recent bone loss around menopause in 891 women aged 45–44 years at the baseline and 50–59 years at the follow-up (5–7 years later) [79]. MacDonald et al. reported that participants in the highest quartile of alcohol intake (median intake of 13.6 g/day) had significantly lower bone loss (calculated as annual percentage change) at the lumbar spine bone loss compared to nonalcohol drinkers. These differences remained significant after adjustment for appropriate confounders and covariates. The other study from Rancho Bernardo in Southern California, examined 507 older men aged 45–92 years. This study reported moderate alcohol consumption of ≥3 times/week to be associated with less bone loss at femoral neck over 4 years [80].

30.3.3 Alcohol and Fracture Risk

Despite the suggestion from some of the above studies that alcohol may have beneficial effects on the skeleton, the vast majority of previous studies examining alcohol consumption and risk of fractures either showed no significant association, or in some cases, an increased risk of fracture among those men and women with high intakes of alcohol. Higher intakes may predispose to trauma-associated fracture outcomes. Finally, alcoholics appear to have low bone density and metabolic abnormalities that threaten bone health. However, recent studies suggest that moderate alcohol consumption may be protective against hip fracture risk [75] and one study on alcoholic showed that the increased lifetime prevalence of fractures among problem drinkers could be due to factors other than the acute intoxication [81].

Cawthon et al. examined the association of alcohol intake and problem drinking history with fracture risk in 5,974 men (aged ≥65 years, 256 nonvertebral fractures, and 46 hip fractures over 3.65-year follow-up) in a prospective cohort study of MrOs [76]. The authors reported no significant association between alcohol intake and risk of nonspine and hip fractures among older men (Table 30.4). There were however, weak protective trends for greater weekly alcohol intake and lower relative hazard of hip fracture. History of problem drinking, heavy drinking, or current episodic drinking were also not related to risk of nonspine or hip fractures. Similar weak inverse associations were also observed for alcohol intake and hip fracture risk from a case–control study in Swedish postmenopausal women [82].

Results from the Cardiovascular Health Study (5,865 men and women, 412 cases of hip fracture over 12 years follow-up) showed a U-shaped relationship between alcohol intake (measured as drinks/week) and hip fracture. Compared with long-term abstainers, the hip fracture risk was 22 % lower (HR: 0.78; 95 % CI: 0.61–1.00) among consumers of up to 14 drinks/week and the risk was 18 % (HR: 1.18; 95 % CI: 0.77–1.81) higher among those with ≥14 drinks/week [75]. However, it was unclear if the increased fracture risk with higher alcohol intake was mediated through an increased risk for falls or other types of trauma. Increased vertebral fracture risk in men but not women was also reported in the Framingham Study where the increased risk was observed even at lower intakes of 1–4 oz/week (~1.5–6.5 drinks/week) and at higher intakes of ≥4 oz/week (≥6.5 drinks/week) [52].

Clark et al. examined the differences in self-reported lifetime fracture prevalence in Caucasian women ($n=834$, aged 18–70 years) in treatment for alcohol abuse, in recovery and nonalcohol-dependent women [81]. Women in treatment and recovery reported more fractures during childhood and adolescence than nonalcohol-dependent women. Women with histories of alcohol dependence

Table 30.4 Studies of alcohol and relative risk of fractures of the hip and other sites

Type of fracture/study	Study design	Sample	Results
Hip fracture			
Lau et al. [89]	Case–control	451 Asian men and 725 Asian women with hip fracture; aged 50 and older (mean, 72.0 for men, 73.7 for women) 1,162 healthy controls (456 men, 706 women) without hip fracture; mean age, 70.8 for men, 72.7 for women	Occasional alcohol consumption: associated with lower risk in women, RR = 0.5 (95 %, CI, 0.3–0.9) Daily alcohol consumption (7 days/week) associated with higher risk: men, RR = 2.0 (95 % CI, 1.3–3.1); women, RR = 2.1 (95 % CI, 1.0–4.7) Number of alcoholic drinks/week ≥14; RR = 2.9 (95 %, CI, 1.2–7.1)) and years of alcohol consumption ≥25; RR = 3.0 (95 %, CI, 1.7–5.2) was associated with higher risk in men
Baron et al. [82]	Age-matched, case–control	1,328 Swedish postmenopausal women with hip fracture; aged 50–81 years (mean, 72.5) 3,312 Swedish postmenopausal without hip fracture; mean age, 70.5	Drinkers had lower risk, OR = 0.70 (95 % CI, 0.60–0.82). All types of alcoholic beverages were protective except for light beer, which showed no association
Du et al. [90]	Cross-sectional study	703 community-dwelling Chinese men and women (226 men, 467 women) aged ≥90 years (mean, 93.5)	Former alcohol consumption was associated with higher hip fracture risk (OR = 2.5; 95 % CI 1.0–5.5)
Mukamal et al. [75]	Prospective cohort study	5,865 community-dwelling American men and women aged ≥65 years; 412 fractures occurred over 12 years follow-up	U-shaped relationship with lower risk among consumers of <14 drinks/week, HR: 0.78 (95 % CI, 0.61–1.00) and higher risk among consumers of ≥14 drinks/week, HR: 1.18 (95 % CI, 0.77–1.81)
Cawthon et al. [76]	Prospective cohort study	5,974 community-dwelling American men aged ≥65 years; 46 hip fractures occurred over 3.65 years follow-up	Alcohol not significantly associated with hip fracture
Osteoporotic fracture			
Clark et al. [81]	Cross-sectional study	831 Caucasian women aged 18–70 years	Percent osteoporotic fractures: Women in treatment for alcohol abuse: 25 % vs. non-alcohol abusers: 15 % ($P < 0.01$) Women in recovery and abstainer: 25 % vs. non-alcohol abusers: 15 % ($P < 0.01$)
Vertebral fracture			
Samelson et al. [52]	Prospective cohort study	Community-dwelling American men (252); women (452) aged 47–72 years; 92 (women) and 20 (men) new vertebral fractures occurred over 25 years follow-up	Alcohol consumption (≥4 oz/week) was associated with increased 25-years cumulative incidence of vertebral fracture
Non-vertebral fracture			
Cawthon et al. [76]	Prospective cohort study	5,974 community-dwelling American men aged ≥65 years; 256 non-vertebral fractures occurred over 3.65 years follow-up	Alcohol not significantly associated with hip fracture

RR relative risk, *CI* confidence interval, *OR* odds ratio, *HR* hazard ratio

had higher lifetime prevalence of fractures, including time periods before the onset of problem drinking and following abstinence, suggesting that factors other than the acute intoxication contributed to the greater fracture prevalence.

30.4 Conclusion

Smoking and alcohol consumption are two lifestyle factors that have important contributions to skeletal health. Smoking adversely affects bone density and increases hip fracture risk in postmenopausal women. However, the association in men is not conclusive while the evidence is inadequate for premenopausal women and younger men. The role of alcohol on skeletal health can be both beneficial as well as deleterious depending upon the level of intake. Recent studies on the role of alcohol on the skeleton suggest a "J"-shaped curve and report that moderate ingestion may offer benefits to the skeleton, and both ethanol and non-ethanol components of alcohol may be involved in affecting skeletal heath.

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