

Table 15j. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Osteopenia and Osteoporosis (Last updated April 7, 2021; last reviewed April 7, 2021)

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
Osteopenia and Osteoporosis	Any ART regimen Specific Agents of Concern: • TDF, especially when used in a regimen that includes a boosting agent (i.e., RTV, COBI) • PIs	Onset: • Any age; decrease in BMD is usually seen soon after initiating ART. Presentation: • Usually asymptomatic • Rarely presents as osteoporosis, a clinical diagnosis defined by evidence of bone fragility (e.g., a fracture with minimal trauma).	BMD z-Score Less Than -2.0: • <10% in U.S. cohorts • Approximately 10% to 20% in international cohorts	Longer duration and greater severity of HIV disease Vitamin D insufficiency/deficiency Delayed growth or pubertal delay Low BMI Lipodystrophy Non-black race Smoking Prolonged systemic corticosteroid use Medroxyprogesterone use Lack of weight-bearing exercise	Prevention: • Ensure that the patient has sufficient intake and levels of both calcium and vitamin D. • Encourage weight-bearing exercise. • Minimize modifiable risk factors (e.g., smoking, low BMI, use of steroids or medroxyprogesterone). • Use TAF instead of TDF whenever possible. • Use TDF with EFV or an unboosted INSTI. • When using TDF in a regimen, consider supplementing with vitamin D3. Monitoring: • Assess nutritional intake (calcium, vitamin D, and total calories). • Strongly consider measuring serum 25-OH-vitamin D levels, particularly in patients who are taking ARV drugs of concern. ^a • DXA is rarely indicated. ^b	Same options as for prevention. Consider changing the ARV regimen (e.g., switching from TDF to TAF, and/or from LPV/r to EFV or an unboosted INSTI whenever possible). Treat patient with vitamin D3 to raise serum 25-OH-vitamin D concentrations to >30 ng/mL. There is no clear benefit to administering daily supplemental vitamin D3 doses that are >4,000 IU. If patients are receiving a daily dose of vitamin D3 that is >4,000 IU, consider monitoring levels of 25-OH-vitamin D. An increase in BMD was seen in one study that evaluated the use of alendronate in youth with HIV. However, the role of bisphosphonates in managing osteopenia and osteoporosis in children with HIV has not been established.

^a Some experts periodically measure 25-OH-vitamin D. This is especially important in children and adolescents with HIV who live in urban areas; the prevalence of vitamin D insufficiency is high in this population.

^b Until more data are available on the long-term effects of TDF on bone mineral acquisition in childhood, DXA scanning is not usually recommended for children who are being treated with TDF. DXA scanning could be considered for youth who are receiving TDF along with additional medications, which affect bone density and for children with indications that are not uniquely related to HIV infection (such as cerebral palsy).

Key: ART = antiretroviral therapy; ARV = antiretroviral; BMD = bone mineral density; BMI = body mass index; COBI = cobicistat; DXA = dual-energy x-ray absorptiometry; EFV = efavirenz; INSTI = integrase strand transfer inhibitor; IU = international unit; LPV/r = lopinavir/ritonavir; ng = nanogram; PI = protease inhibitor; RTV = ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

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