

# Impact of Different Statin Potencies on Bone Health in Patients with Chronic Kidney Disease Stages 3–5

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**INTRODUCTION:** Patients with chronic kidney disease (CKD) have elevated cardiovascular risk and often require statin therapy. However, the impact of different statin potencies on bone health outcomes in CKD patients remains controversial. This study aimed to compare the effects of high-potency versus low-potency statins on osteoporosis incidence, anti-osteoporotic medication use, and fracture risk in patients with CKD stages 3-5.

**METHODS:** This retrospective cohort study utilized the TriNetX global federated health research network, encompassing electronic medical records from 68 healthcare organizations. The study included patients aged  $\geq 18$  years with diagnosed CKD stage 3 (ICD-10-CM: N18.3) or stage 5 (ICD-10-CM: N18.5) and estimated glomerular filtration rate  $\leq 60$  mL/min/1.73m<sup>2</sup>. High-potency statin group received atorvastatin 40-80mg or rosuvastatin 20-40mg; low-potency statin group received pravastatin, lovastatin, cerivastatin, pitavastatin, simvastatin, or fluvastatin. Statin therapy was initiated between January 1, 2014, and December 31, 2018. Patients using fibrates, other lipid-modifying agents, or those with kidney transplant, dialysis, or end-stage renal disease were excluded. Primary outcomes included osteoporosis incidence (ICD-10-CM: M80, M81), anti-osteoporotic medication use (bisphosphonates, denosumab, raloxifene, estrogen therapy, teriparatide, parathyroid hormone, romosozumab), and fracture incidence. Propensity score matching (PSM) was used to balance baseline characteristics with 12-month follow-up. Statistical analysis employed survival analysis with hazard ratios and 95% confidence intervals.

**RESULTS SECTION:** The study initially included 244,036 patients in the high-potency statin group and 275,699 patients in the low-potency statin group. After propensity score matching, 222,260 patients were included in each group for analysis. Following PSM, both groups achieved balance in baseline characteristics including age, gender, and CKD severity. High-potency statin group demonstrated significantly lower osteoporosis incidence compared to low-potency group (HR: 0.832, 95% CI: 0.816-0.849,  $p < 0.001$ ). Patients in the high-potency group had reduced likelihood of requiring anti-osteoporotic medications (HR: 0.804, 95% CI: 0.784-0.825,  $p < 0.001$ ). However, the high-potency statin group showed slightly increased fracture risk (HR: 1.046, 95% CI: 1.025-1.067,  $p < 0.001$ ).

**DISCUSSION:** This large-scale real-world evidence study demonstrates that high-potency statin therapy in CKD patients is associated with reduced osteoporosis incidence and decreased need for anti-osteoporotic medications compared to low-potency statins. The observed reduction in osteoporosis diagnosis and treatment requirements suggests potential pleiotropic effects of high-potency statins beyond cardiovascular benefits. However, a modest increase in fracture risk was observed, which warrants careful monitoring and individualized assessment. Study limitations include the inherent limitations of retrospective observational design, potential unmeasured confounding variables, and reliance on electronic medical record coding accuracy. These findings provide important evidence for clinical decision-making when balancing cardiovascular protection and bone health considerations in CKD patients.

**SIGNIFICANCE/CLINICAL RELEVANCE:** This study provides the first large-scale comparative analysis of statin potency effects on bone health in CKD patients, offering evidence-based guidance for personalized treatment strategies that consider both cardiovascular and skeletal outcomes in this high-risk population.

IMAGES AND TABLES:

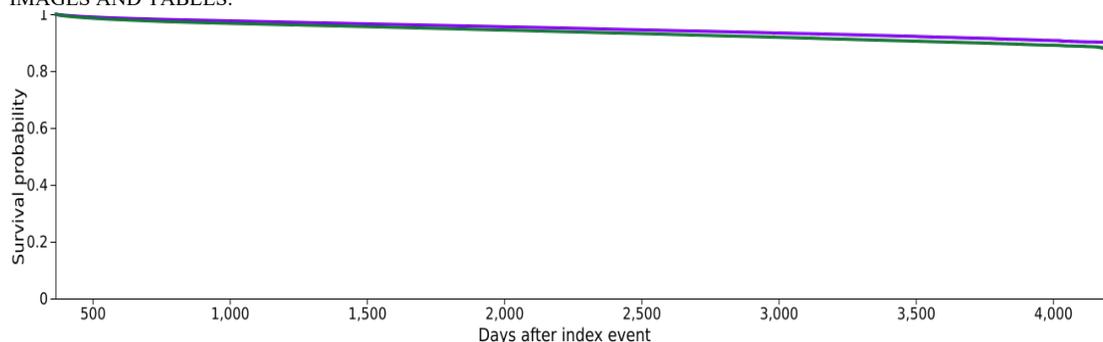


Figure 1. Kaplan-Meier survival analysis of osteoporosis between high-potency and low-potency statin groups with chronic kidney disease.