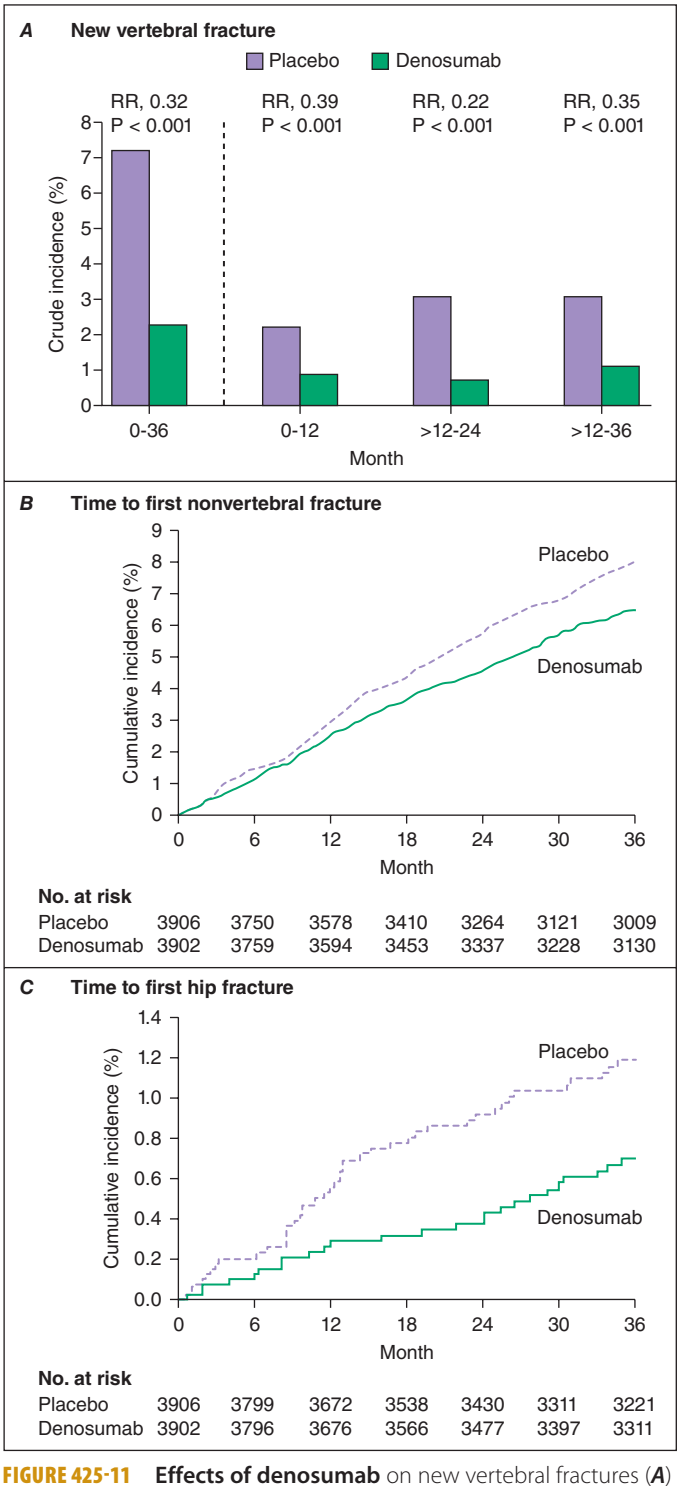

FIGURE 425-11 **Effects of denosumab** on new vertebral fractures (***A***) and times to nonvertebral and hip fracture (***B*** and ***C***). RR, relative risk. *(After SR Cummings et al: N Engl J Med 361:756, 2009.)*

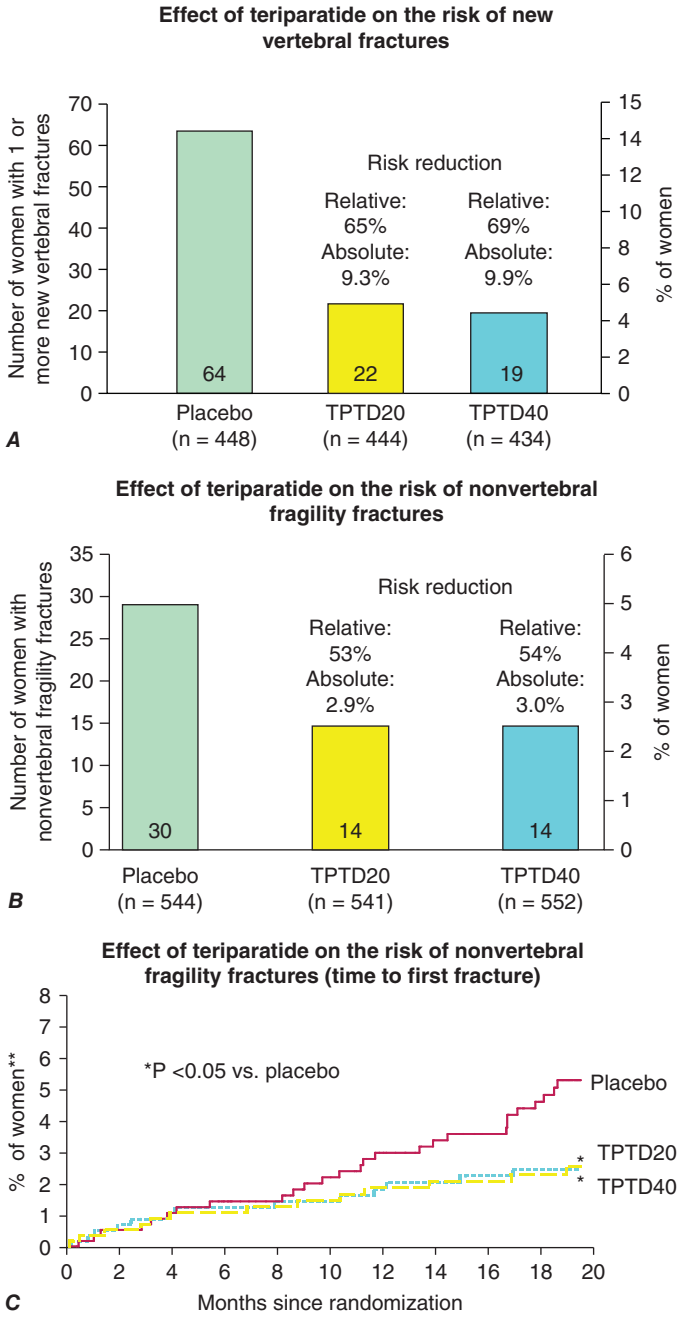

FIGURE 425-12 **Effects of teriparatide (TPTD)** on new vertebral fractures (***A***) and nonvertebral fragility fractures (***B*** and ***C***). *(After RM Neer et al: N Engl J Med 344:1434, 2001.)*

If denosumab is stopped, bone will be lost rapidly if another agent is not used.

Parathyroid Hormone Endogenous PTH is an 84-amino-acid peptide that is largely responsible for calcium homeostasis **(Chap. 424)**. Although chronic elevation of PTH, as occurs in hyperparathyroidism, is associated with bone loss (particularly cortical bone), PTH when given exogenously as a daily injection exerts anabolic effects on bone. Teriparatide (1-34hPTH) is approved for the treatment of osteoporosis in both men and women at high risk for fracture. In a pivotal study (median time of treatment, 19 months' duration), 20 μg of teriparatide daily by SC injection reduced vertebral fractures by 65% and nonvertebral fractures by 45% **(Fig. 425-12)**. Treatment is administered as a single daily injection given for a maximum of 2 years. Teriparatide produces increases in bone mass and mediates architectural improvements in skeletal structure. These effects are lower when patients have been exposed previously to bisphosphonates, possibly in proportion to the potency of the antiresorptive effect. When teriparatide is being considered for treatment-naive patients, it is best administered as monotherapy and followed by an antiresorptive agent such as a bisphosphonate. If teriparatide treatment is not followed by an antiresorptive agent, the bone gained is rapidly lost.

Side effects of teriparatide are generally mild and can include leg cramps, muscle pain, weakness, dizziness, headache, and nausea. Rodents given prolonged treatment with PTH in relatively high doses developed osteogenic sarcomas. Long-term surveillance studies suggest no association between 2 years of teriparatide administration and osteosarcoma risk in humans.

PTH use may be limited by its mode of administration; alternative modes of delivery are being investigated. The optimal frequency of administration also remains to be established, and it is possible that