

***Overdosed America* by John Abramson, M.D.**
[Excerpts From Chapter 13](#)

In 1995, Fosamax, the brand name for alendronate, was the first of the new generation of drugs approved by the FDA for the treatment of osteoporosis. Fosamax works by attaching itself to the surface of bone, interposed between the osteoclasts and the bone the osteoclasts are trying to absorb. Randomized clinical trials of Fosamax published in medical journals show dramatic reductions in the relative risk of hip fracture for women with osteoporosis. In a study published in JAMA in 1998, for example, women with an average age of 68 and a T score of - 2.5 or less who took Fosamax for four years were 56 percent less likely to suffer a hip fracture than women in the control group.

This sounds like very good news for women with osteoporosis, but how many hip fractures were really prevented? With no drug therapy at all, women with osteoporosis had a 99.5 percent chance of making it through each year without a hip fracture -- pretty good odds. With drug therapy, their odds improved to 99.8 percent. In other words, taking the drugs decreased their risk of hip fracture from 0.5 percent per year to 0.2 percent per year. This tiny decrease in absolute risk translates into the study's reported 56 percent reduction in relative risk. The bottom line is that 81 women with osteoporosis have to take Fosamax for 4.2 years, at a cost of more than \$300,000, to prevent one hip fracture. (This benefit does not include a reduction of less serious fractures, including wrist and vertebral fractures. Most vertebral fractures cause no symptoms.)

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What about using these drugs to prevent osteoporosis? Fosamax and Actonel were approved by the FDA to treat women with osteopenia based on studies that showed that they significantly increase the bone density of these women. It is important to remember, however, that bone density is only a surrogate end point; the real reason for taking these drugs is to reduce fractures, and hip fractures in particular. The study of Fosamax published in JAMA in 1998 (mentioned earlier) also included women with osteopenia. Did Fosamax reduce their risk of fracture? The results show that the risk of hip fractures actually went up 84 percent with Fosamax treatment.* The risk of wrist fractures increased by about 50 percent (that figure may be statistically significant -- but this can't be determined from the data as presented in the article).

How can it be that drugs approved for the prevention and treatment of osteoporosis succeed in increasing bone density but have such limited impact on reducing hip fractures? The answer can only inspire awe at Mother Nature's elegance. There are two types of bone. Eighty percent of the body's bone is made up of the hard and dense outer layer called cortical bone. In some areas of the body, bones also have an internal structure of trabecular bone, which works like an organic three-dimensional geodesic dome, providing additional strength in the areas of the skeleton most vulnerable to

fracture, such as the hips, wrists, and spine.

The lacelike structure of trabecular bone creates a much greater surface area than the densely packed cortical bone and therefore allows the former to be more metabolically active when the body needs calcium. Its greater metabolic activity also makes trabecular bone more vulnerable than cortical bone to the changed balance between osteoclast and osteoblast activity. As a result, when bone mass starts to decline in women, trabecular bone is lost more quickly than is cortical bone. Once the architecture of these internal struts is lost, there is no structure left onto which calcium can be added. (See Figure 13-1.) The new bone, formed as a result of taking the osteoporosis drugs, is then formed primarily on the outer part of the bone, the cortical bone. This increases the score on the bone density test but does not necessarily contribute proportionately to fracture resistance.