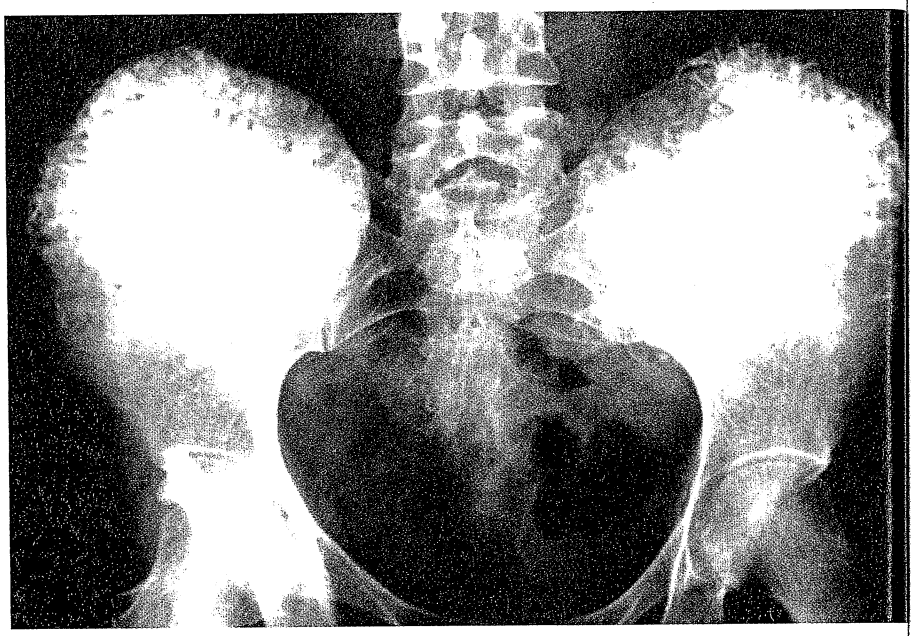
Deborah Franklin is based in San Francisco and has reported on science and medicine for NPR, the *New York Times*, *Fortune* and *Health Magazine*.

Cracks in the Bone Test

Current screens for osteoporosis are flawed, but doctors are repairing their methods

Hip fractures kill and cripple far too many elderly women and men. Every year roughly 350,000 people in the U.S. shatter their hips and end up in the hospital, where more than 14,000 of them die. Another 24 percent die within a year of the injury; half lose their ability to walk. Most of these fractures, which cost about $17 billion in medical care annually, result from a withering of the skeleton known as osteoporosis.

Physicians have long used x-rays to estimate the density of bone minerals—a rough indicator of bone strength. In 2011 the influential U.S. Preventive Services Task Force, which sets testing standards that Medicare and other health insurers tend to follow, began urging all women to get an enhanced x-ray—known as a DXA (*d*ual-energy *x*-ray *a*bsorptiometry) scan—of the hip or lower spine to check for small fractures or worn spots at age 65. The National Osteoporosis Foundation suggests that all men have the same screening scan by age 70.



X-RAY alone is not enough to accurately assess risk for osteoporosis.

Although everyone benefits from such baseline bone scans, most healthy people do not need screens every two years. "Repeat bone density testing has been oversold as a screening tool," says Steven R. Cummings, a bone researcher at the University of California, San Francisco. Evidence shows many doctors focus too narrowly on reduced bone density, particularly in younger women, confusing one sign of osteoporosis risk with the disease itself. A better measure of skeletal health, Cummings suggests, puts bone density in a broader context, taking into account smoking status, drug interactions and history of prior fractures. Together these factors more accurately predict the risk of serious bone breaks, offering a better a guide to who should start taking fracture-preventing drugs and who should not.

THE ROOTS OF OSTEOPOROSIS

FOR CENTURIES doctors assumed frail bones and stooped postures were just irreversible aspects of aging. In the 18th century, however, investigators began to uncover hints in experiments with animals that bones undergo continual remodeling throughout life.

Eventually scientists identified the key members of the bone construction crew: three types of specialized cells. Osteoclasts excavate small pits in old or cracked bone, whereas osteoblasts extrude into those pits a blend of soft collagen and other proteins, which they subsequently harden with calcium phosphate and other minerals. A third group of cells, the osteocytes, helps to coordinate skeletal repair via chemical signals to the demolition and construction crews. By overhauling about a million scattered, tiny patches of bone at a time, the adult human body renews its entire skeleton approximately every 10 years.

A remodeled chassis might seem like an automatic upgrade, but cross-sectional views of hips and vertebrae reveal that new bone is not as well crafted as the original. The honeycombed interior of freshly laid trabecular (from the Latin for "small beam") bone surrounding the marrow has fewer cross-struts to lend it strength and elasticity. Even though the hard outer shell, or cortical bone, grows thicker in some spots over time, autopsies show that these thickened sections are often riddled with holes.

The consequences of this lopsided bone repair—more destruction than construction of the adult skeleton over time—hit women harder and earlier in life than men. In the late 1930s endocrinologist Fuller Albright finally began to puzzle out why. Based partly on the bone-building benefits of estrogen in animal experiments, Albright surmised that the back and hip pain and collapsed vertebrae of his osteoporotic female patients might be related to the sudden drop of estrogen in menopause. He gave

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some of his patients estrogen, and, sure enough, many reported pain relief. Blood and urine tests for calcium and other bone metabolites confirmed that as long as they were taking the estrogen, they lost less bone.

Albright's findings began to reframe osteoporosis as a treatable progressive disorder. His work launched a new wave of research into bone biology that continues today and has stimulated a lucrative market for drugs that either spur the creation of new bone or—in most cases—slow the loss of old bone. Hip fractures were the main concern because they are so deadly, but many other types of fractures significantly reduce quality of life. As scientists began testing the new drugs, they needed a machine that could detect subtler changes in bone than conventional x-rays. Eventually the DXA scan emerged as the clinical standard for measuring bone density: it compares how hard bone and soft tissue differentially absorb low-energy beams directed at the same spot in the skeleton. As DXA scanners became less expensive in the 1990s, the market for bone drugs soared.

Better Than a Bone Scan

A new online calculator called FRAX computes a 10-year probability of fractures based on many risk factors, including:

- **Age, gender, weight and height, all of which have complex relations to risk**
- **History of previous fractures in patient or parents**
- **Whether the patient smokes, which may weaken bone**
- **Alcohol consumption (more than three drinks a day may increase risk)**
- **Whether the patient takes glucocorticoid drugs, particularly oral medication, which may increase risk**
- **Whether the patient has lost bone to disease or trauma**
- **Bone mineral density, an indicator of bone strength**

RISK IS NOT DISEASE

BONE DENSITY TESTS quickly became a rite of passage for many postmenopausal women in their 50s. When doctors started scanning these women, however, a problem emerged, says Cummings, who has co-authored some of the largest studies of osteoporosis in the past three decades. Instead of regarding "low bone density" as one sign of risk, doctors equated it with full-blown osteoporosis. Even worse, under the banner of early detection and prevention, bone density that was slightly lower than average got its own medical label—osteopenia—and some doctors started treating that condition with drugs, too.

The conflation of disease with disease risk might not be so bad, Cummings says, if bone density tracked tightly with the incidence of serious fractures at every age, under every condition. But it does not. Among 16,000 postmenopausal women in Manitoba who received baseline bone scans at age 50 or older, for example, most of those who eventually suffered fractures had normal bone density, according to a 2007 study in the *Canadian Medical Association Journal*. As the studies piled up, Cummings notes, "it quickly became evident that in a group of people with the same bone mineral density, some got fractures and others didn't. Clearly, some other feature of bone plays an important role here."

That should not come as a surprise, says Markus Seibel, who studies bone metabolism at the University of Sydney. Much of modern medicine is about treating risk instead of symptoms, he notes. Doctors attempt to lower bad cholesterol in hopes of preventing a heart attack, for example. But relying strictly on numbers to predict health outcomes is tricky. "The more we move away from actual disease, the harder it is to predict what will happen in a particular patient," Seibel says.

So far, Seibel observes, scientists have not identified the underlying physiological features that make a bone resistant or prone to cracks. Large epidemiological studies, however, have revealed more characteristics of people that, when taken together with measurements of bone density, can help improve predictions about who will suffer a major fracture. In 2008 the World Health Organization integrated 12 of the most influential of these risk factors into an algorithm that is the basis for an easy-to-use online risk calculator known as FRAX.

BEYOND BONE DENSITY

FRAX RELIES ON a long list of variables that influence risk: age; sex; weight; height; previous fractures in patients and their parents; current smoking status; prior chronic treatment with glucocorticoids; a diagnosis of rheumatoid arthritis (not osteoarthritis); a diagnosis of secondary osteoporosis (bone loss from a trauma or illness); level of alcohol consumption (more than three daily glasses of wine, or the equivalent, increases the likelihood of a break); and low bone mineral density at the femoral neck (a frequent site of hip fracture, just below the bony knob of the upper thigh bone).

After patients fill out a simple online survey, the FRAX calculator weights the risk factors according to the most recent data and spits out two numbers—a 10-year probability of hip fracture and a 10-year probability of any major fracture of the hip, spine, forearm or shoulder. Those numbers are a rough guide, the WHO emphasizes, and should not substitute for a doctor's clinical judgment about a particular patient. Someone who smokes and binge drinks frequently and has already had a painful fractured hip, for example, is probably more likely to suffer another broken hip than a light smoker and drinker of the same age who has had a painless vertebral fracture that could barely be detected by x-ray. Even so, the FRAX calculator would give those two people the same score.

Despite FRAX's flaws, Cummings says the tool is an improvement in risk prediction because it puts bone density in proper context as "one factor—an important factor but just one factor—in your likelihood of fracture." Bone health experts currently recommend a baseline bone scan and FRAX calculation around age 65. And anyone—male or female—older than their mid-50s who fractures any bone in the absence of a car accident or similar trauma should be evaluated for osteoporosis and considered for bone-building drugs. Too many emergency room doctors today, Seibel says, are still just setting the broken arm or wrist and sending the patient home. After late middle age, experience and statistics confirm, there is no such thing as a simple fracture.

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