

JUST THE FACTS¹

54 MILLION

American adults have osteoporosis or low bone mass

**1 IN 2 WOMEN
AND 1 IN 4 MEN**

age 50 and older will break a bone due to osteoporosis

2 MILLION

broken bones each year due to osteoporosis

\$19 BILLION

annual cost of osteoporosis in the United States



IN PARTNERSHIP WITH



MEDICINES IN DEVELOPMENT FOR OSTEOPOROSIS

A REPORT ON OSTEOPOROSIS

Advances in Diagnosis and Biopharmaceutical Research Bring Hope to Osteoporosis Patients

Nearly 54 million adults in the United States have either osteoporosis or low bone density, according to the National Osteoporosis Foundation. Osteoporosis causes loss of bone mass and deterioration of bone structure, leading to fragile and easily fractured bones. Although osteoporosis mainly affects women, men are also at risk for the disease. In fact, half of women and a quarter of men over the age of 50 will break a bone due to osteoporosis.¹

As the aging population increases in the United States, the incidence of osteoporosis is expected to rise as well. In 2010, it was estimated that 12 million people already had osteoporosis. Experts predict that number will increase to 14 million by 2020 if additional efforts are not made to prevent and effectively treat the disease, which may be largely prevented with lifestyle changes and appropriate treatment.¹ By 2025, it is predicted that osteoporosis will cause about three million bone fractures and cost the health care system more than \$25 billion each year.¹

However, it is not only the lost quality of life or the fear of breaking a bone that plagues patients. Today, about 20 percent of people age 50 and older who suffer a hip fracture due to

osteoporosis die within one year of the break.¹ And as many as 75 percent of older women who suffer their first fracture due to osteoporosis do not receive drug therapy for prevention of future fractures during the first year post-fracture.²

Not long ago, osteoporosis was only diagnosed when someone broke a bone, but new screening methods have helped diagnose the disease earlier and advances in science have supported researchers exploring new pathways for the prevention and treatment of the disease.

New research is turning our old understanding of osteoporosis on its head and there is hope that these advances in science will lead to game-changing osteoporosis treatments. Today, biopharmaceutical research companies are developing nine medicines³ for the treatment of osteoporosis, all of which are in clinical trials or undergoing regulatory review by the U.S. Food and Drug Administration. Osteoporosis treatments are being studied in 34 clinical trials across the United States.⁴ Of these, 16 are actively recruiting patients, and 18 are active but no longer recruiting patients.

For a complete list of the nine medicines in development, please visit <http://phrma.org/sites/default/files/pdf/medicines-in-development-drug-list-osteoporosis.pdf>

Closing the Gap in Osteoporosis Treatment: National Osteoporosis Foundation

“MY MOTHER AND AUNT WERE DIAGNOSED WITH SEVERE OSTEOPOROSIS AND FRACTURES, AND I LEARNED THAT I, TOO, WAS AT HIGH RISK FOR FRACTURE. AFTER ACTIVE TREATMENT FOR THE PAST 15 YEARS, I AM CONFIDENT THAT I WILL BE ABLE TO PARTICIPATE IN PHYSICALLY DEMANDING ACTIVITIES FOR YEARS TO COME.”

C. BERDON LAWRENCE
NATIONAL OSTEOPOROSIS
FOUNDATION TRUSTEE
AND OSTEOPOROSIS PATIENT

Established in 1984, the National Osteoporosis Foundation (NOF) is the leading health organization dedicated to preventing osteoporosis and broken bones, promoting strong bones for life and reducing human suffering through programs of public and clinician awareness, education, advocacy and research.

NOF is focused on a single, unifying goal: protecting Americans from the pain, disability and loss of independence millions suffer every year as the result of broken bones. Osteoporosis causes two million broken bones every year in the United States, yet more than 70 percent of older women who fracture a bone are never tested or treated for osteoporosis. If left untreated, patients who break a bone are twice as likely to break another.

The solution to this 70 percent care gap is the widespread implementation of Fracture Liaison Service (FLS) care coordination programs. NOF is working with its partners to implement a comprehensive Fracture Prevention Initiative, providing the training, tools and resources health care professionals need to spark implementation of FLS programs across the country.

Fractures are deadly for older Americans. At least 20 percent of older women and a higher percentage of older men who sustain a hip fracture die within one year. One in five hip fracture survivors end up in an assisted care facility, losing precious independence. The costs of caring for these fractures, particularly the

300,000 hip fractures that occur annually, are in excess of \$12 billion a year.

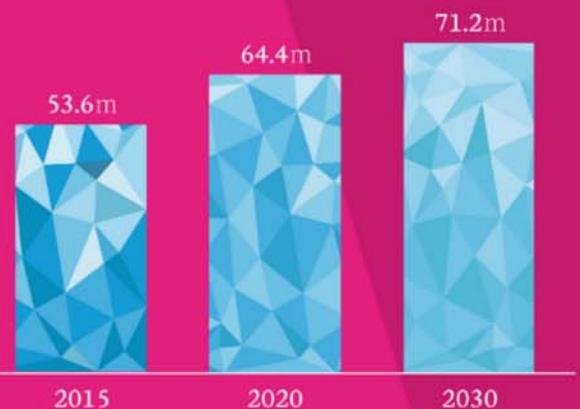
The good news is that therapies for osteoporosis are improving. Available therapies for osteoporosis are effective in preventing fractures and can reduce fracture risk by more than 50 percent. More importantly, new medicines in the pipeline may further increase bone mass and reduce fractures in older citizens.

“We hope and believe in a world where no older citizen has to experience an osteoporosis-related fracture and believe that with continued development of pharmacologic agents this will be possible,” said Robert F. Gagel, M.D., President of the National Osteoporosis Foundation.

As we look ahead to the challenges that remain and the new therapies being developed, NOF is confident and dedicated to changing the course of this disease. For more information, visit www.nof.org.

Need for New OSTEOPOROSIS TREATMENTS

The development of new treatments for osteoporosis will become even more important as prevalence of the disease and low bone mass in people over the age of 50 is expected to increase in the next 15 years. In 2015, an estimated 54 million American adults had osteoporosis or low bone mass, but that number could grow to 64 million in 2020 and 71 million in 2030.



EXPECTED GROWTH IN OSTEOPOROSIS PREVALENCE

Source: National Osteoporosis Foundation, Journal of Bone and Mineral Research, The Recent Prevalence of Osteoporosis and Low Bone Mass in the United States Based on Bone Mineral Density at the Femoral Neck or Lumbar Spine™ 2014

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Innovative Osteoporosis Treatments in the Pipeline

In patients with osteoporosis, bone loss occurs when bone resorption occurs at a faster rate than that of bone formation, resulting in decreased bone density. The medicines in the pipeline today take advantage of our increasing understanding of the disease, using novel approaches to correct this imbalance or investigating new ways to administer treatment. Among the nine medicines in development for treating osteoporosis are:

- An oral medicine in development that selectively inhibits cathepsin K, the primary enzyme on osteoclasts that digests proteins during bone resorption. Osteoclasts are cells that resorb bone and secrete signaling factors to stimulate osteoblasts, cells that form bone. Abnormal cathepsin activity may be involved in multiple bone disorders including osteoporosis.
 - A monoclonal antibody in development that binds to and inhibits the action of sclerostin, a protein encoded by the SOST gene. Mutations in sclerostin have been associated with abnormal bone growth. Inhibiting sclerostin may play a critical role in increasing bone formation and decreasing bone breakdown.
 - A synthetic analogue of human parathyroid hormone-related protein (hPTHrP) is in development for the treatment of postmenopausal osteoporosis. The protein hPTHrP is thought to be a critical cytokine for promoting new bone formation. The medicine is designed to build bone rapidly without inducing hypercalcemia
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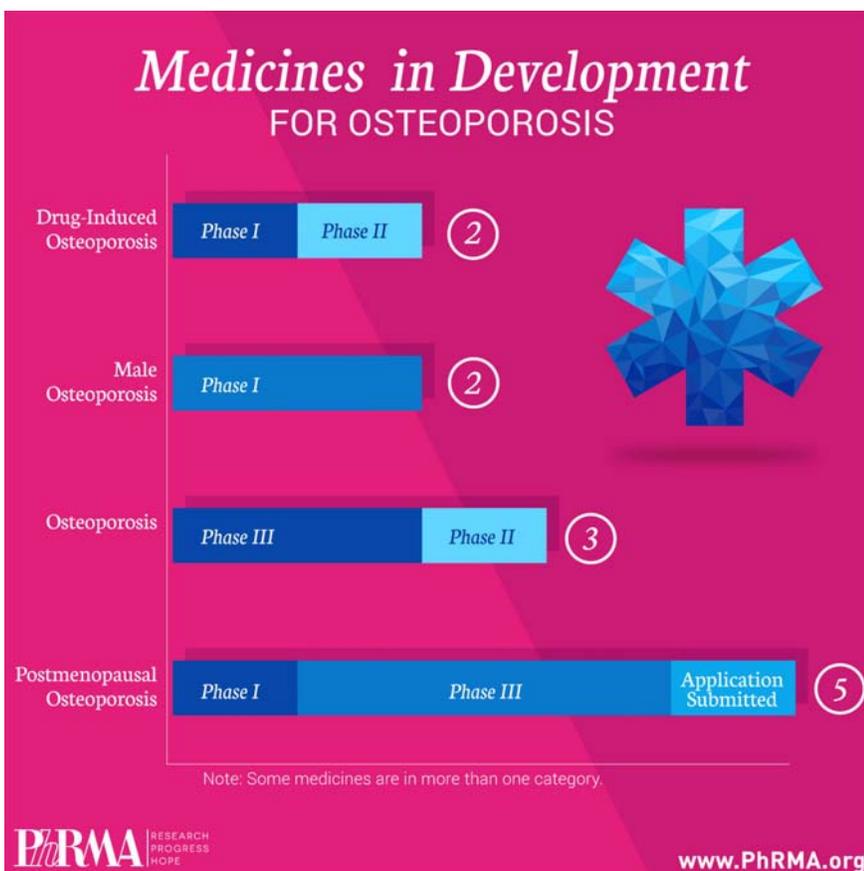
National Bone Health Alliance

A public-private partnership that brings together expertise and resources to collectively promote bone health and prevent disease; improve diagnosis and treatment of bone disease; and enhance bone research, surveillance and evaluation.

The Alliance's 52 member organizations, including several PhRMA member companies, are working with key regulatory agencies to bring about a shared vision: to improve the overall health and quality of life of all Americans by enhancing their bone health.

One project of the National Bone Health Alliance is focused on the standardization of the use of bone turnover markers in osteoporosis research.

For more information on the Alliance, visit www.nbha.org.



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- (too much calcium in the blood) or significant bone resorption.
- Transdermal patches are in development to administer the active pharmaceutical ingredient from previously approved injectable treatments for

osteoporosis. Transdermal systems use biodegradable microneedles administered via a patch. Transdermal patches are expected to combine the convenience of a transdermal patch formulation with the speed of a standard injection.

Then, Now and Tomorrow: Treating Osteoporosis

Osteoporosis has affected people since the beginning of time. Egyptian mummies from more than 4,000 years ago have been found to have the revealing “osteoporosis hump” and the disease has been depicted in older women in Renaissance paintings. It wasn’t until the 19th century that osteoporosis was used to describe “porous bone,” when French pathologist Jean Lobstein coined the term from observations in autopsies. In the 1930s, Fuller Albright, M.D. made the first connection between menopause and frail bones, giving the condition a new name—“menopausal osteoporosis.”

THEN

The first treatment for women with osteoporosis was menopausal hormone therapy (MHT)—estrogen or a combination of estrogen and progestin.

NOW

Since those early days, new medicines have been developed and approved for treating osteoporosis that are helping target the underlying causes of the disease. Current treatments for osteoporosis are either anti-resorptive medicines that inhibit the breakdown of bone tissue, or anabolic drugs that increase the rate of new bone formation. While these treatments represent significant therapeutic advances, many of them entail strict methods for administering them, which can have serious side effects if taken incorrectly.

WHAT’S NEXT?

Researchers are exploring new approaches to attacking the disease based on scientific discoveries that have changed the way they fundamentally look at osteoporosis. Some recent discoveries that are informing research include: the identification of a high bone mass gene and its signaling pathway; the understanding that excess remodeling (the process of bone resorption and bone formation) plays a key role in making bones fragile; and the discovery of biomarkers for the rate of bone remodeling, which can help identify who is at greatest risk from osteoporosis.

Footnotes:

1. National Osteoporosis Foundation
2. A. Wilk, Osteoporosis International, August 2014
3. Number of medicines obtained through public, government and industry sources, and the Springer “Adis Insight” database. Current as of February 4, 2016
4. U.S. National Institutes of Health, www.clinicaltrials.gov. Search criteria: osteoporosis, United States only, Phase 0, 1, 2, 3. Search performed February 8, 2016