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CALIFORNIA HEALTHCARE INSTITUTE

COMBATING OBESITY

ADVANCES IN TREATMENT OPTIONS & ACCESS TO CARE

The Biology of Obesity

Human bodies are not designed for plenty. For thousands of years, people lived as hunter gatherers, often facing severe famine and hunger. Even after civilizations arose, the food supply was often tenuous. As a result, the body preserves energy stores for hard times.

However, in the United States, there are no shortages; people have access to as much food as they can afford and must self-limit. For those contending with obesity, this is easier said than done.

A number of studies have shown that obesity actually rewires hormonal circuits to defeat weight loss. Leptin, a hormone produced by fat cells, tells the brain it is okay to stop eating. However, when a person is losing weight, fat cells stop secreting leptin, telling the brain to eat more. Mice without leptin grow enormous; they are missing the hormonal signal that tells them they have stored enough fat.

There are other hormones that manage the complex interrelationship between hunger and satisfaction, which makes maintaining weight loss even more challenging. In addition, a 2011 study in the New England Journal of Medicine found that hormones don't readjust after the weight is lost. In fact, they maintain obesity levels for at least a year.

This hormonal reprogramming can have severe consequences for people trying to maintain weight loss. They often feel as if they are starving, even when they have eaten a healthy meal. The body simply wants to store fat for lean times.

Sources: Genome News Network, New England Journal of Medicine.

THE OBESITY EPIDEMIC

Obesity has become a major public health issue. Around 35 percent of adults in the United States are obese. Many others are overweight and may soon be contending with obesity. Unfortunately, anyone who is significantly overweight or obese can face severe health consequences. Obesity is linked to heart disease, stroke, cancer, type 2 diabetes, high blood pressure, dyslipidemia (too much fat in the blood), joint issues, sleep apnea and many other conditions.

The economic costs are enormous. Americans spend more than $190 billion each year on obesity-related medical expenses, and that number is growing.

Beyond the health risks and societal costs, obesity carries significant stigma. Many view overweight/obese people as lazy or believe they are not trying to lose the extra pounds. Weight prejudice can have a profound impact on quality of life, social acceptance, employment and even medical care.

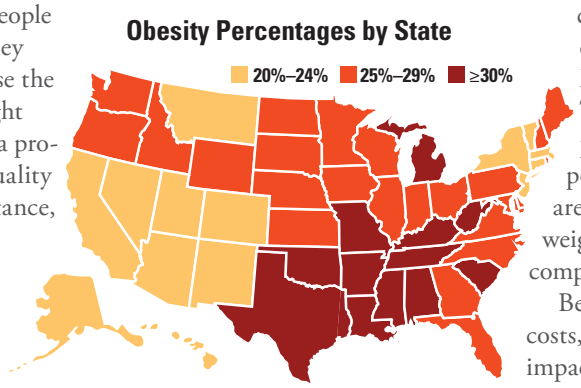
Tragically, these biases ignore an important fact: obesity is a medical condition. In 2013, the American Medical Association declared that obesity is a disease.

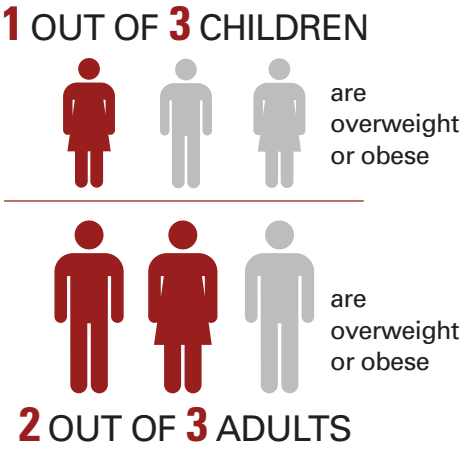
Given obesity's many consequences, people have a strong incentive to lose weight through diet, exercise and other lifestyle modifications. While these efforts may succeed in the short-term, many people have trouble maintaining their losses with diet and exercise alone. This weight loss rollercoaster is not a function of will, but rather a function of biology. Obesity restructures how the body responds to food *(see sidebar: The Biology of Obesity)*. Hormonal imbalances instruct the brain to perceive intense hunger.

Sometimes, extreme measures are required. Bariatric surgeries, which remove large portions of the stomach and small intestine, have helped many people achieve significant weight loss. More recently, pharmaceutical companies have developed a new generation of weight loss drugs. More are in the pipeline.

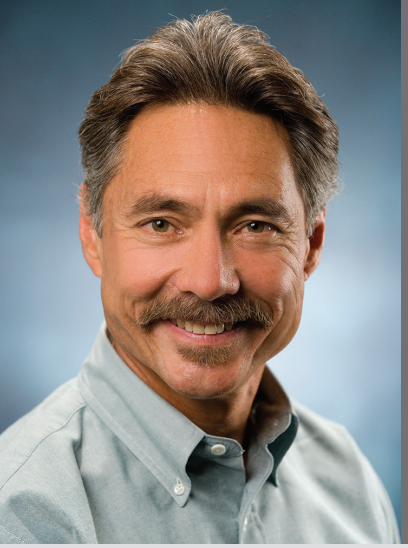
While weight loss options have increased, barriers remain. Though private health insurance policies are beginning to include coverage for anti-obesity drugs, Medicare does not. This may put many patients in a difficult position. While they are motivated to lose weight, they lack the complete means to do so.

Between the human costs, the budgetary impact and the burden on our healthcare system, obesity is a significant problem in the United States. We must develop creative solutions to meet the challenge.





Sources: Centers for Disease Control, National Institutes of Health, Journal of Health Economics, American Journal of Public Health, American Medical Association.



Q & A WITH DR. KEN FUJIOKA

Ken Fujioka, M.D., is director of the Nutrition and Metabolic Research Center and a member of the Division of Diabetes and Endocrinology at Scripps Clinic in La Jolla, California. Dr. Fujioka has spent his career helping people with obesity and obesity-related conditions, treating thousands of patients and contributing to numerous papers and clinical trials.

Is obesity a disease?
Yes it is. No matter how a person becomes obese, the body changes hormones and metabolism to maintain that higher weight. That's what makes obesity a disease *(see The Biology of Obesity on page 1).*

Let's say a guy weighs 150 pounds but has back problems or has to take prednisone. While being inactive for a few months, he goes from 150 to 200. However, after losing about 10 percent of his weight, the hormones associated with weight control shift towards regaining those pounds. His brain thinks his body is underweight. The metabolic rate drops, he doesn't feel full, and he's always hungry. So it is no surprise he can't keep the weight off.

What are the health risks for people who are overweight or obese?
For Caucasians or African Americans, about 70 percent run into serious health problems, such as heart disease, cancer, or type 2 diabetes. For Asians and Hispanics, that rate rises to around 90 percent.

Also, genetics play a huge role. It is kind of like a gun. The genetics are the loaded gun but it is the environment that pulls the trigger. The combination of low activity and almost unlimited access to food can be the environmental trigger that generates these health problems.

How do you treat obese patients?
First, we try to determine why they are overweight. Is it inactivity? Overeating? Hormonal issues? Prescriptions drugs, such as beta blockers or prednisone?

The treatment is based on the cause. Unfortunately it is usually multiple factors, including behavior, inactivity and genetics.

I also look at the disease progression. While stage 1 isn't too bad, in stage II patients may be developing type 2 diabetes. By stage III, they are morbidly obese and in pretty bad shape.

We try to treat the weight issue, as well as the effects of that added weight, such as type 2 diabetes. Usually I prescribe a low carb diet plus exercise. No matter what I tell them, they still have to diet and exercise.

Can anti-obesity drugs help?
These are incredibly well-tested agents and very welcome. In addition, the FDA has refined how we prescribe these drugs. For example, we don't give them to non-responders. If a patient doesn't lose 3 to 5 percent of their body weight in three months,* we stop the drug because it is just not going to work.

We've also adopted strategies to ensure these drugs are not used inappropriately. Patients must be fully aware of the side effects and other risks.

What can primary care physicians do to provide better care for obese patients?
There are so many overweight and obese patients; we have to bring it to the primary care level. These providers need to understand obesity—that it is more than calories in and calories out.

No matter how a person becomes obese, the body changes hormones and metabolism to maintain that higher weight. That's what makes obesity a disease.

Obesity is complicated by changing genetics, metabolic rates, hormones. It *is* rocket science.

Also, physicians need to understand their biases. Even doctors who treat this condition on a regular basis are sometimes prejudiced against obese patients. They may not even know it, but those biases are there.

They also need to be more aggressive. If someone is overweight, with type 2 diabetes or other comorbidities, they should treat it with diet and exercise, and they shouldn't wait to prescribe anti-obesity drugs. In fact, the American Association of Clinical Endocrinologists has issued guidelines encouraging physicians to prescribe these drugs earlier, rather than after a failed diet attempt. Some patients need the extra help on day one.

**These drugs are designed to help patients lose 5 to 10 percent of their body weight over a year.*

ADVANCING NEW THERAPIES

Because of obesity's unique biology, there is an urgent need to find effective therapies. A number of companies have developed, or are developing, drugs that can help obese patients lose weight.

Arena Pharmaceuticals

Arena is focused on developing innovative drugs that address a number of unmet medical needs, including obesity. Belviq® (lorcaserin HCl) tablets CIV, the first new chemical entity approved by the FDA for weight management in more than a decade, was launched in the United States in June 2013. Belviq is believed to decrease food consumption and promote satiety by selectively activating serotonin receptors in the brain. When activated, these receptors may help patients eat less and feel fuller after eating smaller amounts of food.

Eisai

There are many diseases with no effective treatments. A global pharmaceutical company, Eisai seeks to address these needs. In July 2010, Eisai entered into a collaboration with Arena Pharmaceuticals to market Belviq in the United States. Belviq is used in conjunction with diet and exercise to support weight loss in individuals with BMIs above 30 or those with BMIs above 27 who also suffer from at least one obesity-related complication.

Orexigen Therapeutics

Orexigen Therapeutics is a biopharmaceutical company focused on treating obesity. The company's lead product candidate is NB-32, which combines bupropion and naltrexone. NB-32 is believed to increase the level of dopamine activity at specific receptors in the brain, leading to a reduction in appetite and an increase in energy expenditure. In addition, NB-32 may regulate activity in the brain's dopamine reward system, helping control food cravings and overeating. If approved, Takeda Pharmaceuticals will commercialize NB-32 in the United States.

Takeda Pharmaceutical Company

Based in Deerfield, Ill., Takeda Pharmaceuticals U.S.A., Inc., and Takeda Global Research & Development Center, Inc., are subsidiaries of Takeda Pharmaceutical Company Limited, the largest pharmaceutical company in Japan. These companies market oral diabetes, insomnia, rheumatology and gastroenterology treatments and seek to bring innovative products to patients through a pipeline that includes compounds in development for metabolic and cardiovascular disease, gastroenterology, neurology and other conditions.

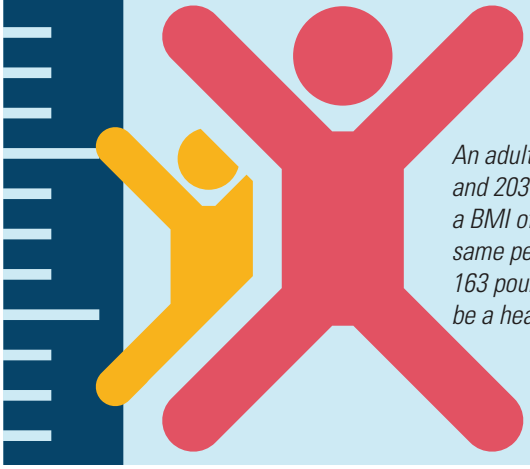
Vivus, Inc.

Vivus is a biopharmaceutical company that develops therapies to address obesity and sexual health. The company's obesity drug, Qsymia® (phentermine and topiramate extended-release) capsules CIV combines phentermine, which is believed to reduce appetite and decrease food consumption, and topiramate extended release, an anti-seizure medication that may address cravings, helps patients feel full and could influence other metabolic effects. Approved by the FDA in summer 2012, Qsymia is used as an adjunct to diet and exercise to support weight loss in individuals who have BMIs above 30 or those with BMIs above 27 who also suffer from at least one obesity-related complication.

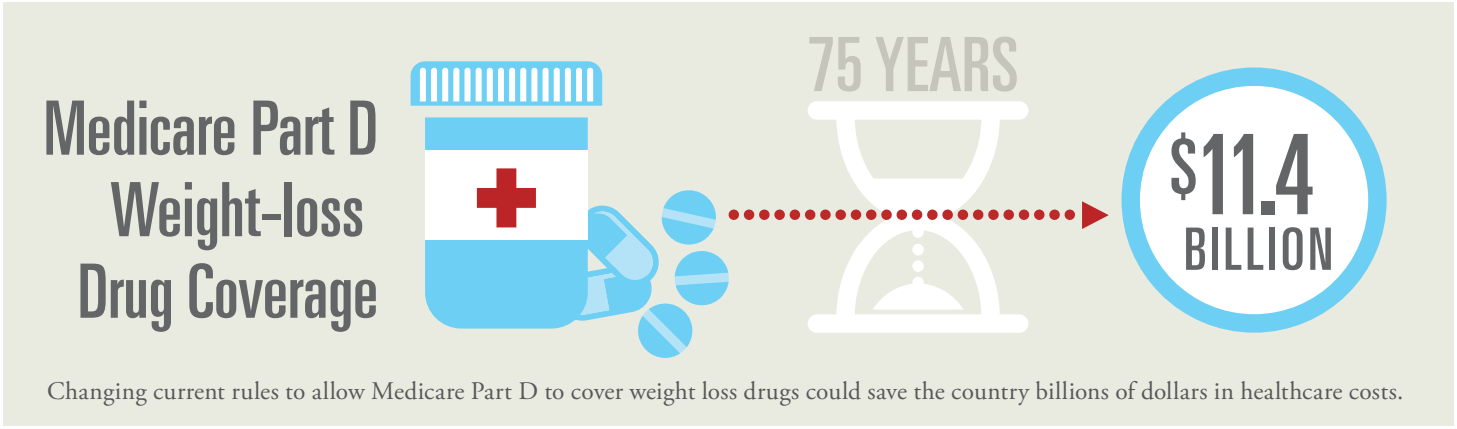
MEASURING OBESITY

Body mass index (BMI) is a screening tool to measure body fat based on a person's height and weight.

- People with a BMI below 18.5 are considered underweight.
- Those with a BMI between 18.5 and 24.9 are in a normal weight range.
- People with a BMI between 25 and 29.9 are considered overweight.
- People with a BMI above 30 are considered obese.



An adult who is 5' 9" and 203 pounds has a BMI of 30. The same person at 163 pounds would be a healthy 24.1.



Changing current rules to allow Medicare Part D to cover weight loss drugs could save the country billions of dollars in healthcare costs.

Source: The Long-Term Returns of Obesity Prevention Policies, Robert Wood Johnson Foundation

THE PRICE OF INACTION

The obesity epidemic is taking an enormous toll on the United States and other countries. Obesity is a gateway to heart disease, cancer, high blood pressure, type 2 diabetes and other conditions. In addition to human suffering and premature death, obesity places an enormous strain on the nation's healthcare infrastructure, costing more than $190 billion each year.

A number of important steps have been taken to control obesity. California and other states have removed high-sugar sodas from public schools. Governments have also made communities more walkable, installed bike lanes and endorsed other strategies to encourage physical activity. In addition, pharmaceutical companies have developed new drugs to help people lose excess weight.

While obesity drugs are being approved by the Food and Drug Administration (FDA), the people who need them most have trouble accessing them. Quite often, they are not covered by insurance. Private insurance coverage is spotty and government coverage is often non-existent. Medicare Part D does not cover these drugs, though some Medicare Advantage plans are starting to allow them.

As a result, many patients lack access to weight loss drugs that could prevent significant complications, such as heart disease, cancer and osteoarthritis. From a public policy standpoint, this is nonsensical, as these drugs could save billions of dollars now being spent on obesity-related complications.

In addition, government insurance programs rarely cover preventive behavioral therapy before type 2 diabetes and other complications set in. Covering consultations with dietitians, diabetes educators and other healthcare professionals could prevent many of the most serious complications.

Fortunately, there has been progress. The Office of Personnel Management recently issued guidelines encouraging insurers to cover weight loss medications for federal employees on the grounds that obesity is a disease, not a lifestyle. This is a great start, but more must be done.

We encourage federal and state representatives to act quickly to remedy these shortcomings. Preventive care is a proven lifesaver for obese patients. Both government and private insurance must cover it.

COMMUNITY RESOURCES

American Association of Clinical Endocrinologists
www.aace.com

American Public Health Association
www.apha.org/programs/resources/obesity

Campaign to End Obesity
www.obesitycampaign.org

Centers for Disease Control and Prevention
www.cdc.gov/obesity

National Institutes of Health Obesity Research
www.obesityresearch.nih.gov

Obesity Action Coalition
www.obesityaction.org

The Obesity Society
www.obesity.org

Stop Obesity Alliance
www.stopobesityalliance.org

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CHI-California Healthcare Institute is a non-profit public policy research organization for California's biomedical R&D industry. CHI represents more than 275 leading medical device, biotechnology, diagnostics and pharmaceutical companies and public and private academic biomedical research organizations. CHI's mission is to advance responsible public policies that foster medical innovation and promote scientific discovery. CHI's website is www.chi.org. Follow us on Twitter @calhealthcare, Facebook, LinkedIn and YouTube.

Headquarters
888 Prospect Street, Suite 220
La Jolla, California 92037
858-551-6677 | 858-551-6688 fax

Sacramento
1201 K Street, Suite 1840
Sacramento, California 95814
916-233-3497 | 916-233-3498 fax

Washington
1608 Rhode Island Ave. N.W., 2nd Floor
Washington, DC 20036
202-974-6313 | 202-974-6330 fax