



Obesity, Treatment, and Key Stakeholders

A MARKET OVERVIEW

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The Current Landscape

Causes of obesity and key current facts





OVERVIEW

Obesity is defined by the World Health Organization (WHO) as an excessive accumulation and storage of fat cells in the body¹. Nearly one third of the world's population is currently overweight or obese. Rising rates of obesity are leading to the increase of comorbidities, such as cardiovascular diseases, type 2 diabetes, obstructive sleep apnea, certain types of cancers, osteoarthritis and depression, and high blood pressure².

Obesity is a global epidemic that poses a serious threat to public health worldwide.

The Demographics of Obesity

Overall Global Obesity Statistics and Trends

Key facts and figures¹:

- Worldwide obesity has nearly tripled since 1975.
- In 2016, more than 1.9 billion adults (18 years and older) were considered to be overweight and, of the 1.9 billion, 650 million were classified as obese.
- In the same year, over 216 million children and adolescents aged 5-19 were overweight and 124 million were obese, representing 6% of girls and 8% of boys.
- Obesity is on the rise in low- and middle-income countries.

Obesity rates are much higher in developed countries than in developing ones due to factors such as differences in lifestyle, resources, and environments.

Age-Based Trends

TRENDS IN THE ADULT POPULATION

Obesity rates among adults have been increasing in every country around the world, with the obesity rate almost doubling between 1980 and 2014. The two countries with the highest level of adult obesity are the United States of America and Saudi Arabia. In 2016, 36.2% of the United

¹ Obesity, [WHO](#)

² Obesity, [Institute for Health Metrics and Evaluation](#)



States' adult population and 35.4% of the adult Saudi Arabian population were classified as obese.³

TRENDS IN CHILDHOOD OBESITY

In 2014, approximately half of the population of overweight children younger than the age of 5 resided in Asia and another quarter lived in Africa⁴. In Africa, the number of overweight children has doubled in the last two decades⁴. Lower-middle-income countries have experienced a growth in the rate of overweight children from 1990 (7.5 million) to 2014 (15.5 million)⁴.

Between 1972 and 2009, the prevalence of childhood obesity has almost tripled in the U.S., and this trend is amplified amongst children from socioeconomically disadvantaged backgrounds⁵.

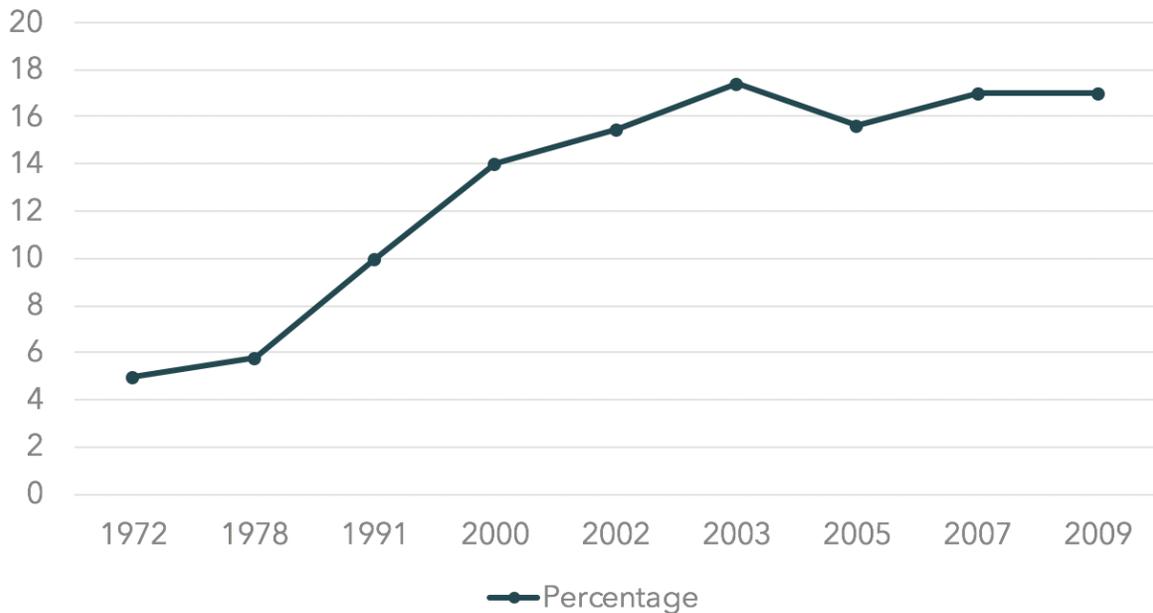
³ Obesity & BMI, [Our World in Data](#)

⁴ Global Trends in Overweight and Obesity, [IARC Publications](#)

⁵ Childhood Obesity, [National Center for Biotechnology Information](#)



Exhibit A: Prevalence of Obesity in Children Ages 2-19 in the United States



SOURCE: Literature Review from [National Center for Biotechnology Information](#)

There is also evidence that suggests childhood obesity leads to an increased probability of adult obesity⁵. Additionally, there is a higher rate of comorbidities associated with childhood obesity than adult obesity; for example, type 1 diabetes and hyperlipidemia are more heavily correlated with childhood obesity.

It is important to identify risk factors for childhood obesity early on, including but not limited to: birth weight, early insulin levels, antenatal maternal diet, early nutritional habits, genetic factors such as monogenic obesity and genetic variants, and weight gain during infancy⁵.

Gender-Based Trends

Gender has been shown to be correlated to obesity prevalence: in many countries including the United States, women are more likely to be obese than men^{1,6}.

⁶ Adult Obesity Rates Rise in 6 States, [American Medical Association](#)



TRENDS AMONG THE FEMALE POPULATION

In line with trends across the aggregate adult population, the two countries with the highest rates of obesity in the female adult population are the United States and Saudi Arabia. South Africa, Turkey, Libya, and Egypt also have high (>35%) rates of obesity in their female population. The rate of adult female obesity in 2016 was 37.0% in the United States of America, 42.3% in Saudi Arabia, 39.6% in South Africa, 39.2% in Turkey, and 41.1% in Egypt³.

TRENDS AMONG THE MALE POPULATION

In contrast, only the United States has a relatively high rate of obese men in the population (35.5%)⁷. Saudi Arabia follows behind the United States with a percentage of 30.8% of all adult males being obese in 2016⁷.

Country-Based Trends

Another pertinent factor is the income level of the country of residence; the rate of obesity in high-income and upper-middle-income class countries is more than double that of low-income countries⁴.

FACTORS OF OBESITY IN DEVELOPED COUNTRIES

Diet patterns and the availability of food options are the biggest factors affecting the obesity rate and explain the difference in obesity rates between low- and high-income countries.

“Rapidly growing, developing, or transitional economies face the globalization of food markets, fast food chains, and the increasing availability of street vendors who offer products at very competitive value to economic acquisition of inputs such as raw and processed foods.”⁸ On the other hand, better dieting can lead to lower rates of obesity and is much easier to access within high socioeconomic environments and countries. In richer areas of the world, there are distinct differences in the diet quality because of the ability to access fresher, higher quality food items such as fresh fruits, vegetables, and fish while still being able to afford the higher costs that come with these fresh foods⁸. In poorer countries, people often resort to food that is cheaper and usually less healthy. This is because cheaper food items are made from more unhealthy ingredients such as cheap vegetable oils, energy-dense carbohydrates, and trans-fats⁸.

⁷ Obesity & BMI, [Our World in Data](#)

⁸ Overweight and Obesity Epidemic in Developing Countries, [National Institutes of Health](#)



Another major factor that affects obesity rates within different countries is physical activity level. A big contributor to decreased physical activity level within many parts of the world is increased screen time; watching television is linked to high cholesterol levels and unhealthy diets⁸.

SHIFTING ATTENTION TO DEVELOPING COUNTRIES

In developing countries, there are many different factors to consider that have both positive and negative effects in developing obesity. Economic development is a main factor to consider when studying obesity trends in developing countries. Higher poverty levels result in fewer available nutritious foods, lower income, and lower work capacity. However, an interesting observation has been made by researchers that is still being explored—people who are poorer often live in more rural areas, and the level of physical activity is typically higher in rural areas than in urban areas which can help decrease obesity rates⁸.

Obesity also poses as a pressure to developing countries as a burden in which health systems must account for. “Historically, health care systems in developing countries have been designed to treat and manage only acute diseases, such as diarrhea or minor infections”⁹. Because money is often tight, health care systems must use means in which they can treat the most amount of people with the minimal amount of funds. Obesity-related diseases may act as a burden for these countries to accommodate within their health care systems and there are strong implications that poor countries will have trouble treating obesity as its rate increases⁹.

Economic Implications of Obesity

Cost to Patients

The cost of obesity has been rising in tandem with its prevalence. The United States Medical Expenditure Panel Survey (MEPS) found that in 1998, obesity was responsible for about 6% of all medical costs, but that by 2006, that number had risen to 10%, and by 2012, 20.6%**Error! Bookmark not defined.** In other countries, the percentage of spending on obesity is lower because of lower average drug prices and rates of obesity.

⁹ Obesity in Developing Countries: Causes and Implications, [David Hoffman](#)



Exhibit B: Proportion of Spending on Obesity as a Percentage of Total National Medical Expenditures

Country	Obesity-Related Costs (% of total spending on health care)	Publication Year
Brazil	3.0-5.8	2007
China	3.4	2008
Canada	2.9	2001
France	0.7-1.5	2000
Japan	3.2	2007
Sweden	2.3	2005
U.S.	20.6	2012

SOURCE: Literature Review from [Journal of Health Economics](#)

INCREASE IN TREATMENT COSTS

For any given condition, being obese increases treatment costs compared to a non-obese patient. Healthcare costs are 42% higher for obese individuals than their non-obese counterparts, which amounts to approximately \$1,429 per year¹⁰. This is due in part to the increased probability of treatment complications for other conditions. For example, the cost for treating chest pain in the emergency room is 41% higher for severely obese patients and 28% higher for obese patients compared to healthy weight patients¹¹. One reason for this difference is that obesity is associated with many comorbidities, which also require costly treatment.

LOSS OF PRODUCTIVITY AND SALARY

Beyond the direct treatment costs associated with obesity, there are also many indirect costs which drive up the effective cost of obesity. These indirect costs include lost productivity for companies from missing work, higher health and life insurance costs for employers and employees, and lower wages for individuals with obesity¹². In a cross-sectional study of 8000 participants conducted in Germany, researchers found that obese women and obese men had 5.19 and 3.48 extra sick leave days in 2009, respectively compared to their healthy weight

¹⁰ The Healthcare Costs of Obesity, [The State of Obesity](#)

¹¹ The medical care costs of obesity: an instrumental variables approach, [Journal of Health Economics](#)

¹² Economic Cost of Obesity,



peers. While the impact may appear marginal, in the aggregate the effects on the productivity level of the workforce are significant¹³.

Economic Impacts on the Developing World

Although the obesity epidemic has affected every country, there is a noticeable lack of research into economic impacts on the developing world¹⁴. The major difference between obesity in developing versus developed countries is concerning how obesity rates correlate with different socioeconomic status groups *within* the country.

Most developed countries experience a negative correlation between socioeconomic status and obesity, as cheaper foods in developed countries have less nutritional value. In developing countries, however, the association is positive, as higher socioeconomic status individuals have higher rates of obesity. In coming years, developing countries are projected to follow the same trend.

Specific examples of lifestyle changes in developed countries that contribute to obesity include decreases in jobs that have high levels of physical activity (such as farming and forestry) and increases in sedentary activities (such as sitting in front of a computer). Educational disparities also impact obesity, as knowledge about diet, nutrition, and food purchasing dissuade poor diet quality.

As depicted in Exhibit C, the proportion of individuals with obesity is currently much higher in developed countries, but as developing countries go through development and their accompanying “nutritional transition”, it’s likely that their obesity rates in developing countries will surpass that of developed countries.

¹³ Sick Leave Days and Costs Associated With Overweight and Obesity in Germany, [Journal of Occupational Environmental Medicine](#)

¹⁴ Overweight and Obesity Epidemic in Developing Countries: A Problem with Diet, Physical Activity, or Socioeconomic Status?, [Scientific World Journal](#)



Exhibit C: Percent of Individuals in Income Group with Obesity

Income group	Male	Female	Both Sexes
Low-Income	2.6	5.1	3.9
Lower-middle income	4.7	8.4	6.5
Upper-middle income	19.5	28.9	24.5
High income	21.8	21.6	21.7

SOURCE: Literature Review from [Epidemiologic Reviews](#)

Potential Solutions

There are a few proposed methods to reduce obesity-related costs. Many of these solutions target the root lifestyle causes of obesity in the hopes of avoiding the expensive costs associated with treatment of comorbidities. In a 2008 study, the Urban Institute found that a mere \$10 per person investment into community programs aimed at improving exercise and nutrition and reducing alcohol and tobacco use would save the U.S. \$16 billion annually in healthcare costs and other obesity related expenditures¹⁰. This equates to a \$5.60 return on investment for every \$1 invested¹⁰.

Current Global Initiatives

The primary way in which the obesity epidemic has been addressed on a large scale has been through public policy initiatives. Historically, efforts to combat obesity have been led by influential health organizations. These organizations tend to use a “personal responsibility” framework in their work that considers poor diet and lifestyle choices to be the main drivers of obesity.¹⁵

International Efforts

INTERNATIONAL FOOD AND BEVERAGE ALLIANCE

¹⁵ The Increasing Weight of Regulation, [Georgetown Law](#)



In collaboration with WHO, The International Food and Beverage Alliance (IFBA), established in 2008, has outlined a set of five global public commitments in their efforts against obesity:

1. Continue to reformulate products and create new products that support goals of improving diets.
2. Provide clear and fact-based nutrition information to consumers.
3. Advertise and market products responsibly to children world-wide.
4. Raise awareness on balanced diets and increased levels of activity.
5. Seek and promote public-private partnerships that support the WHO *Global Strategy on Diet, Physical Activity and Health*.

Government Policies and Regulations

UNITED STATES

Many of the anti-obesity initiatives in the United States take place at the state, local, or school district level. State and local based initiatives are mainly focused on the following:

1. Including more nutritional food for children and more opportunities to be physically active.
2. Introducing taxes policies geared at changing the food and beverage diet tendencies of consumers.
3. Reforming health care industries to offer better weight management counseling and programming.
4. Restricting messaging and marketing of unhealthy food options, especially towards children.
5. Increasing physical activity of citizens through community efforts, recreational networks, and school programs.
6. Implementing initiatives at schools to educate children on obesity and its prevention¹⁶.

The United States Department of Agriculture has created a general framework for healthy eating, called the “My Plate” initiative. The initiative educates people about how to portion their meals by food group, giving consumers control of their diets in accordance with national suggestions.¹⁷ Additional school-oriented initiatives for healthy eating include the Hunger-Free Kids Act of 2010 that put guidelines in place for many programs, such as the National School Lunch Program and School Breakfast Program¹⁸. In terms of food labeling guidelines, companies can opt-in to a voluntary “Facts Up Front” system. Moreover, more than 40 states and some cities have enacted sugar-sweetened beverage (SSB) taxes.

¹⁶ Obesity Prevention Policies in US States and Localities, [NCBI](#)

¹⁷ MyPlate, [USDA](#)

¹⁸ School Meals, [USDA](#)



CHINA

China's Ministry of Health released in 2010 the Nutrition Improvement Work Management Approach to promote national nutrition initiatives and promote the health of Chinese citizens. The Management Approach includes nutrition surveillance, education, guidance, and intervention. The Ministry of Health also established fitness regulations in 2009.

In the twelfth Five-Year Plan for National Economic and Social Development, the Chinese government has tried to prevent chronic diseases such as obesity and increase health education. One of the goals was to reduce the prevalence of obesity to less than 12 percent in adults and less than 8 percent in children.¹⁹ However, recent studies have shown that Coca-Cola's ties with Chinese health authorities have focused anti-obesity policies on physical activity rather than regulation of the food and beverage industry.²⁰

UNITED KINGDOM

Building off on calorie labelling on restaurant menus, the United Kingdom has undertaken a traffic light labelling system to improve the dietary intake of consumers. Traffic light labels are a front-of-pack (FOP) nutrition rating system that provide information on the number of calories and selected nutrients found within a specified amount of food. The UK uses this system to label foods as "high", "medium", or "low" with the colors red, yellow and green in nutrients such as salt, sugar and fat. Studies have shown that such labeling mechanisms can reduce the number of "red" items sold²¹.

Healthy Weight, Healthy Lives is a national strategy adopted in 2008 to promote a healthy diet and is aimed at creating cross-government strategies to tackle the obesity epidemic, including the establishment of nutritional guidelines and initiatives to increase physical activity. The United Kingdom also has mandatory nutritional standards for school food and a voluntary food guideline system for preschools.

Ultimately, many initiatives across the globe are not nationally enforced, creating discrepancies in the efficacy of policies.

¹⁹ Programs and Policy Options for Preventing Obesity in China, [NCBI](#)

²⁰ Claims Coca-Cola Shaped Chinese Anti-Obesity Policies, [Food Navigator Asia](#)

²¹ Traffic-light labels, [NCBI](#)

The Current Market for Obesity

Major players, their roles, and market share





Treatment Overview

TREATMENT BACKGROUND

There are many different factors in how to approach and treat obesity. Before treatment is prescribed, the diagnosis procedure includes²²:

1. A comprehensive health screening, including patient history, reviewing information about past weight loss efforts, exercise habits, eating patterns, and other existing medical conditions and medications. Special attention to increased risk of predisposed conditions.
2. Perform a general physical exam, including taking vital signs such as heart rate, blood pressure, temperature, and pulmonary and cardiovascular health.
3. BMI (Body Mass Index) calculation will be performed to determine patient obesity risk and guide treatment selection.
4. Measurements of visceral and abdominal fat, which are good predictors for diabetes and heart disease. Depending on the severity of a patient's current health risks, blood tests may also be used.

TREATMENT OBJECTIVES

In order to reach and maintain a healthy body weight, treatment plans often involve multiple specialists such as a dietician, behavior counselor, and bariatrician²³. Treatment plans can consist of any combination of: dietary changes, exercise and physical activity, behavior change, prescription weight loss medications, and weight loss surgery²³.

²² Obesity, [Mayo Clinic](#)

²³ Hungering for Obesity Treatments, [National Institutes of Health](#)



DRUG TARGETS

Active ingredients in the earliest weight loss medications included either dinitrophenol or sibutramine²³.

Dinitrophenol (DNP)

Dinitrophenol is a combination of chemical compounds that dramatically increases metabolism rates, which results in rapid weight loss. After its introduction in 1933, it was publicly marketed for weight loss in the US. It was eventually pulled from the market by the FSA in 1938 after the discovery that it is highly toxic and can result in death²⁴.

Sibutramine

Sibutramine is a serotonin and norepinephrine reuptake inhibitor within the body that had a similar story to dinitrophenol. Originally, it was used as both a short term and long-term therapy for obesity because it appeared to cause a decrease in appetite and reduced caloric intake. From 1997 to 2010, it was marketed as an obesity treatment drug. However, in 2010 it was withdrawn by the FDA because of its dangerous side effects such as insomnia, headache, increased blood pressure and heart rate, and increased risk of myocardial infarction and stroke²⁵.

CURRENT DRUGS

Leptin and Ghrelin

Discovered in 1994, leptin is a hormone secreted by fat cells that maintains body weight by suppressing appetite²⁶. Researchers have found that obese patients have high levels of leptin because they have a higher percentage of body fat, but this leptin is ineffective at suppressing appetite²⁶. Leptin resistance can cause weight gain and vice versa²⁶.

Ghrelin, discovered six years after leptin, is a peptide secreted by the stomach²⁶. It increases in concentration directly before meals to boost appetite, promote fat storage, protect the cardiovascular system, and stimulate the release of growth hormones to aid in breaking down fats²⁶.

Treatments that target leptin and ghrelin have proven to be ineffective²⁶. Scientists are instead attempting to develop drugs that target neurotransmitters, neuropeptides, and neurons that respond to leptin or ghrelin²⁶. These drugs have been demonstrated to be more successful, affecting the whole appetite pathway instead of only targeting one part of the system²⁶.

²⁴ Warnings Issued Over Deadly DNP 'Diet Drug', [NHS](#)

²⁵ Drug Record: Sibutramine, [NIH](#)

²⁶ Leptin, Ghrelin, and Weight Loss, [PrecisionNutrition](#)



Pharmaceutical Companies and Therapeutics

Current Types of Therapeutics

In the broadest sense, therapeutics refers to the treatment of a disease or disorder²⁷. The therapeutics currently used for obesity treatment can be decomposed into three major categories by their mechanism of action on the body²⁸.

REDUCTION IN FOOD INTAKE

Therapeutics can successfully decrease food intake by activating the α_1 - and β_2 -adrenoceptors²⁹. Adrenoceptors are an important class of receptors that control the actions of two key neurotransmitters, norepinephrine and epinephrine. Through their modulation of these two neurotransmitters, adrenoceptors play an important role in many key bodily functions, including blood pressure and various metabolic functions²⁹.

ALTERATION OF METABOLISM

Alteration of metabolism is achieved through two main methods: inhibiting the digestion of fat and making post-digestion modifications to the way fat is handled in the body³⁰. Orlistat, marketed as Xenical by Roche Pharmaceuticals, is an example of a therapeutic that inhibits digestion of fat³⁰. There are several post-digestion modifications that can be made to fat. One is lipolysis, which is the biochemical pathway that converts fat into fatty acids that can be used for energy³⁰. Another is changing whether fat is stored as subcutaneous (less metabolically active) or visceral fat (more metabolically active) in the body³⁰.

INCREASE IN THERMOGENESIS

The area of increasing thermogenesis, or increasing heat production in the body to burn fat more rapidly, is a relatively unexplored area with no approved therapeutics. The combination

²⁷ Therapeutics, [Encyclopedia Britannica](#)

²⁸ A Concise Review on the Therapeutics of Obesity, [Nutrition](#)

²⁹ Adrenoceptors, [Guide to Pharmacology](#)

³⁰ Lipolysis, [Progress in Lipid Research](#)



of ephedrine and caffeine (which are both FDA approved, but not for obesity) is the only treatment that's been tested²⁸.

INSIGHT: COMMON THREAD OF OBESITY THERAPEUTICS ON THE MARKET

In general, the goal is to develop therapeutics that mimic exercise, producing the same physiologic consequences in the body as exercise.

Market Overview

The aggregate market for pharmaceutical companies is expanding in part due to the high cost of treatment for individuals with obesity, which totals \$210 billion in healthcare costs in the United States per year³¹. There are six major pharmaceutical companies in the obesity space.

Exhibit D: Table of major pharmaceutical with global networks or obesity treatments available on the market.

Company	Market Cap (52 week high) (B)	Revenue (in 2018)	Net Income (in 2018)	YoY Growth (2017-2018)	Spending on R&D as a % of Revenue
Pfizer	257.991	53,647,000,000	11,153,000,000	2.1%	14.8%
Roche	245.021	58,308,844,000	10,290,315,000	6.73%	18.8%
Novo Nordisk	125.818	16,709,117,034	5,771,293,000	.12%	13.2%
Bayer	122.711	44,168,475,360	1,891,026,000	13%	12.3%
Teva	28.361	10,892,000,000*	-16,265,000,000*	2.2%*	8.3%

*2017 Data

SOURCE: Yahoo Finance

³¹ Healthcare Costs of Obesity, StateofObesity.org



Pfizer

Founded in 1849 in New York, Pfizer is one of the largest pharmaceutical companies in the world. Pfizer manufactures vaccines for a range of medical practices, antibiotics, and other products such as Viagra.

OBESITY MEDICATIONS

In 2006, Pfizer had four CB-1-receptor antagonists at various stages of pre-trial development³². Pfizer halted their research following the failure of a rival CB-1-receptor antagonist drug, Rimonabant, which was developed and sold through Sanofi-Aventis. Rimonabant was withdrawn from the worldwide market due to high rates of depressive and suicidal tendencies in patients taking the medication.

COMORBIDITIES: RELATED MEDICATIONS

Since their failed CB-1 venture, Pfizer has not had any obesity products on the market or in clinical trials.

However, they do produce a range of products for comorbidities of obesity. Key products which will have an increase in demand along with the projected global increase in obesity are:

- Lipitor, which manages high cholesterol
- Norvasc, which treats high blood pressure
- Steglatro, Steglujan and Segluromet, which treat diabetes

INSIGHT: CURRENT SITUATION AND OUTLOOK

Despite the lack of obesity-specific therapeutics on the market, Pfizer's global presence alone is enough to make them a potential risk for the obesity medication market. To date, Pfizer sells its products to 125 different countries with actual operations being undertaken in 90 of them. Should they decide to venture back into the development of weight-loss medications or acquire an existing patent/product, Pfizer would have the ability to market and promote their products throughout the world in a very short period of time. Independent of any decision to pursue obesity-specific therapeutics, Pfizer will most definitely profit from the increased obesity rates worldwide thanks to its sale of drugs treating related conditions.

³² Diabetes and Obesity: the twin epidemics, [Nature Medicine](#)



Roche

Founded in 1896 in Switzerland, F. Hoffman-La Roche AG is a pharmaceutical company that is considered the most valuable pharmaceutical brand as of 2019³³. Roche focuses on both therapeutics and diagnostics and is labeled as the world's largest biotech company with 17 biopharmaceuticals on the market³⁴.

OBESITY MEDICATION: XENICAL (ORLISTAT)

Introduced to the market in 1998, Orlistat is a potent irreversible inhibitor of pancreatic lipases. The inhibition prevents absorption of up to one third of all dietary fat – both promoting weight loss and preventing weight gain in obese patients³⁵.

Orlistat has been approved by the FDA for up to two years of continuous use. However, the discontinuation rate of the drug is relatively high due to gastrointestinal side effects relating to fat malabsorption. On the other hand, one study showed that a combination of lifestyle interventions and the use of Orlistat treatment for four years delayed the onset of type 2 diabetes in obese subjects by 37 percent — attributable to the weight loss associated with Orlistat³⁶.

Until 2012, Orlistat was the only FDA-approved anti-obesity drug, creating a unique environment for Roche in the obesity market. The median cost-effectiveness ratio of Orlistat was 16,000 euros (~17,900 USD) per quality-adjusted life year (QALY)³⁷. The price range for Orlistat 120 mg is \$0.48 - \$1.50 per pill or unit.

³³ Brand Value of Pharmaceutical Brands, [Statista](#)

³⁴ About Roche, [Roche](#)

³⁵ Pharmaceutical Quality of Nine Generic Orlistat Products Compared with Xenical®, [Obesity Facts](#)

³⁶ Orlistat, Clinical Lipidology [Science Direct](#)

³⁷ Clinical and economic considerations of anti-obesity treatment: a review of orlistat, [PMC](#)

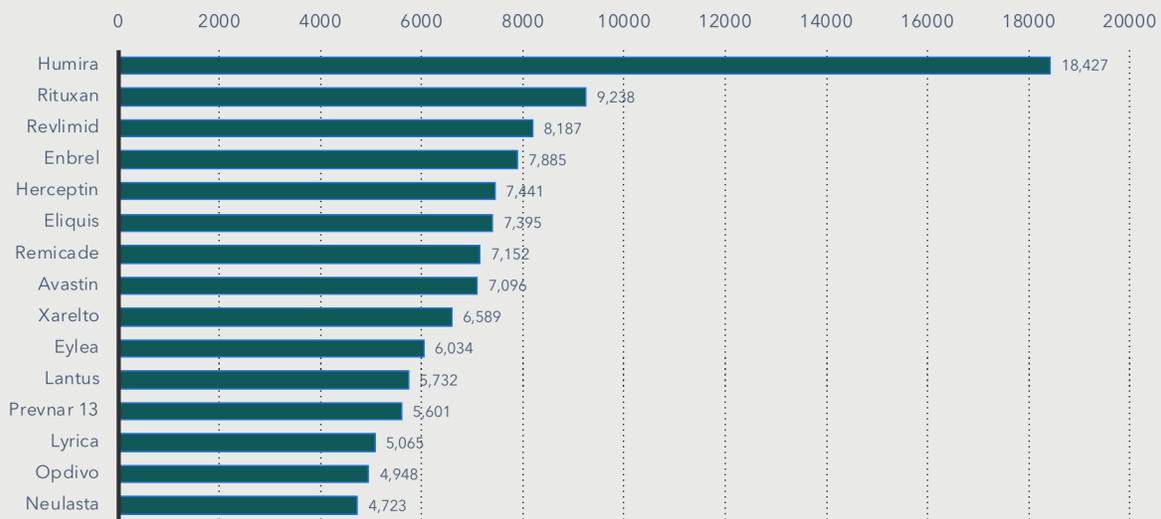


INSIGHT: ROCHE NOT EMPHASIZING XENICAL

Although Roche offered the first anti-obesity medication to the market and was able to profit off this unique market, in 2010 and 2011, Xenical sales accounted for only 1% of Roche's total pharmaceutical sales, indicating that its emphasis on this drug is decreasing as competition for anti-obesity drugs continues to increase.

Of the fifteen globally top selling drugs of 2017, Roche claims many (Rituxan, Enbrel, Herceptin and Avastin) that focus on cancer and autoimmune therapies, straying from the early success seen with Xenical (although the drug is still on the market)¹.

Top 15 Pharmaceutical Products by Sales Worldwide in 2017 (millions of USD)²



¹[Roche Finance Report 2011](#) ²[Statista](#)

COMORBIDITIES: DIABETES CARE PLATFORM

Currently, Roche offers “Roche Diabetes Care,” a platform providing a personalized approach utilize glucose monitoring systems to track and deliver insulin³⁸. Roche Diabetes Care falls under the Accu-Chek brand, which offers data management solutions coupled with flexible insulin pump therapy and lancing devices that minimize painful testing³⁸.

³⁸ Roche Diabetes Care, [Roche](#)



PIPELINE

Currently, Roche has a few different drugs in their pipeline, one of which is targeted towards type 2 diabetes, specifically related to obesity, and is in Phase 1b as of 2018. Results for anti-FGFR1/KLB (anti-Fibroblast Growth Factor Receptor 1/ β Klotho) is an antibody designed to mimic the metabolic hormone FGF21³⁹ -- a key mediator of lipid metabolism⁴⁰.

Novo Nordisk

Founded in 1923 in Denmark, Novo Nordisk is a pharmaceutical company which markets its products in 180 countries and employs over 40,000 people worldwide. Novo Nordisk's primary areas of focus are diabetes and hormonal treatments, marketing their products as brand name drugs.

OBESITY MEDICATION: SAXENDA (LIRAGLUTIDE)

Patients prescribed Saxenda take weekly injections with gradually higher doses for the first month and then continue to use the full dose for a year⁴¹. Saxenda causes patients to lose their appetites which subsequently lowers their caloric intake⁴¹.

Saxenda shares the same active ingredient as Novo Nordisk's diabetes treatment product, Victoza⁴¹. However, it does not help treat diabetes and cannot be taken with its counterpart, forcing patients inflicted with both symptoms to choose which medication they would like to take. This could put a ceiling on Novo Nordisk's profits from its obesity and obesity-related medication sales since it is unable to market all of its products to the same individuals.

TREND: DUEL LIFESTYLE-THERAPEUTIC TREATMENTS

Novo Nordisk offers Saxenda Care along with their Saxenda medication, which puts clients into contact with coaches and dietary planners¹. It also allows clients to access extra features on popular fitness apps.

Saxenda Care is marketed as personal support on top of medication. It's advertised that with both Saxenda Plus and Saxenda, patients can lose up to 2.5x more weight than a comparative group that only had a placebo medication².

¹ Chronic Weight Management, [Novo Nordisk](#)

² Saxena (liraglutide [rDNA origin] injection), [Center Watch](#)

³⁹ Roche Pipeline, [Roche](#)

⁴⁰ Obesity Is a Fibroblast Growth Factor 21 (FGF21)-Resistant State, [American Diabetes Association](#)

⁴¹Saxenda (liraglutide [rDNA origin] injection), [Center Watch](#)



PIPELINE

Novo Nordisk is currently testing semaglutide, which lowers blood sugar levels rather than acting on hormones and was originally developed for the treatment of type 2 diabetes⁴². This would be advantageous for Novo Nordisk as it would be able to treat both diabetes and obesity in the same medication. Semaglutide would also eliminate many of the risks and side effects associated with Saxenda, such as pancreatitis and thyroid cancer⁴².

Bayer

Founded in 1863 in Germany, Bayer is a pharmaceutical company that also has consumer health, crop science, and animal health divisions⁴³, and brought in 39.6 billion euros of revenue in 2018⁴⁴. With its decision to enter China in the early 2000s, Bayer has been able to tap into a lucrative obesity market that is only growing⁴⁵.

OBESITY MEDICATION: GLUCOBAY (ACARBOSE)

Glucobay was developed by Bayer in 1975 and first launched in Switzerland in 1986. It delays the breakdown of sugars and starches in the gut and their absorption into the bloodstream, preventing the rise in blood glucose that normally occurs after eating⁴⁶. This medication is taken with meals to inhibit enzymes that break down carbohydrates, reducing their absorption into the blood stream. Studies have shown that Glucobay has significantly decreased BMI, body weight, and skinfold thickness⁴⁷.

Glucobay was the first FDA-approved alpha-glycosidase inhibitor, which was considered particularly suitable for the Asian market due to the high levels of carbohydrates in the Asian diet/cuisine. Glucobay first entered China in 1994 and is now recommended as the first-line drug for type 2 diabetes. Since it is difficult to imitate Glucobay, China's Glucobay market is dominated by Bayer. However, the market share of Bayer's Glucobay is declining in China as the market share of domestic contemporaries rise. In 2017, the market size of Glucobay in China was CNY 1.09 billion and Bayer's market share was 66.4 percent, showing a continued

⁴² Chronic Weight Management, [Novo Nordisk](#)

⁴³ Bayer Divisions, [Bayer](#)

⁴⁴ Bayer Dossier, [Statista](#)

⁴⁵ Bayer: A Multinational Committed to China, [Springer](#)

⁴⁶ Glucobay, [Diabetes Community UK](#)

⁴⁷ Acarbose Treatment in Obesity, [Eating and Weight Disorders](#)



momentum of decline⁴⁸. Still, Glucobay is Bayer's seventh most popular pharmaceutical product, bringing in 443 million euros of revenue in 2018⁴⁹.

PIPELINE

Bayer currently has two pharmaceuticals in the pipeline that are associated with treatment of pulmonary hypertension and diabetic kidney diseases, which are both comorbidities of obesity. Targeting pulmonary hypertension, Bayer is developing a sGC Activator (soluble guanylate cyclase), which, as of February 2019, is in Phase I trials in Germany. Targeting diabetic kidney disease, Bayer is developing an MR antagonist named Finerenone, which, as of February 2019, is in Phase III trials⁵⁰.

⁴⁸ China's Acarbose (Bayer) Market Report, 2018-2022, [Research and Markets](#)

⁴⁹ Bayer AG's top pharmaceutical products from 2014 to 2018, [Statista](#)

⁵⁰ Bayer Drug Profile, [Adis Insight](#)



Teva

OVERVIEW

Founded in 1901 in Israel, Teva Pharmaceutical Industries is the largest producer of generic drugs in the world, but also produces proprietary pharmaceuticals. With 17 billion dollars in revenue, Teva is one of the fifteen largest pharmaceutical firms worldwide.

OBESITY MEDICATION: BELVIQ

In 2014 Teva struck a deal with Arena to market their obesity drug, Belviq, in Israel rather than deal with the costs of developing its own obesity medications. Following Arena's sale of Belviq to their marketing partner Eisai in late 2016, Teva's role was unchanged in Israel.

While Teva avoids hefty R&D costs by marketing another company's medication, it is also limited in market size due to the fact that it only has the rights to sell Belviq in Israel.

THE ISRAELI OBESITY MARKET

The Israeli obesity market should be very profitable on its own. What sets Israel apart from other markets is its population growth rate, rising faster than most other developed countries at approximately 2% per year⁵¹. The combination of wealth, high spending on healthcare and a rapidly growing population makes Israel an ideal market for obesity treatment medications. The OECD reported in 2015 that, 50.9% of the Israeli population was overweight or obese⁵².

Other available obesity medications in Israel include Saxenda (Novo Nordisk) and Xenical (Roche). Therefore, Teva does need to compete with Roche and Novo Nordisk for market share in Israel. This could be difficult considering that both of these firms have more resources and name brand compared to Teva.

⁵¹ Israel Population 2019, [World Population Review](#)

⁵² OECD Country statistical profile, [OECD iLibrary](#)



Surgical Techniques

Traditional Bariatric Surgeries

Similar to therapeutics, there are also a wide array of bariatric, or weight loss, surgeries available to obese patients. There are two main categories of bariatric surgery: restriction and malabsorption. Restriction physically constrains the stomach in order to reduce the amount of food that it can hold. Malabsorption effectively reduces the amount of calories that a patient consumes by adapting the digestive tract⁵³.

In general, bariatric surgery costs anywhere from \$20,000 to \$25,000, with the price determined by the type of surgery, the fee that one's specific surgeon charges, and where the surgery is conducted¹¹. Fortunately, many insurance plans cover bariatric surgery, as many states mandate that bariatric surgery is included under health insurance plans⁵⁴. Prior to receiving surgery, individuals will be required to undergo a diet program as surgery is seen as a last resort invasive treatment.

FOUR MAIN TYPES OF BARRIATRIC SURGERY

Laparoscopic adjustable gastric banding (LAGB):

- An inflatable balloon is placed near the entrance of the stomach, reducing its capacity⁸.
- The balloon can be adjusted depending on desired intake, regulating how much food the individual is capable of eating⁵⁵.
- In addition to being an invasive procedure, there is also a risk of the tube puncturing the stomach.
- For two to three weeks after the surgery, patients must maintain a strict diet of liquids and easily digestible foods. Vitamin supplements are recommended in order to make up for the lack of certain nutrients.
- In order to render the procedure as successful as possible, patients should increase physical activity and maintain a balanced diet.

⁵³ Gastric Bypass Surgery, [Mayo Clinic](#)

⁵⁴ Financing Weight Loss Surgery, [WebMD](#)

⁵⁵ Laparoscopic Adjustable Gastric Banding, [Johns Hopkins Medicine](#)



Gastric bypass surgery

- Based on the most common type of gastric bypass, a pouch is created at the top of the stomach and is attached to the small intestine, effectively replacing or “bypassing” the stomach⁸.
- Through this modification, the stomach can comfortably hold less food, leading to the loss of 60-80% of excess weight and a change in composition of the gut to favor hormones that reduce an individual’s appetite⁵⁶.
- Complications include excessive bleeding, infection, or adverse reactions to anesthesia.

Sleeve Gastrectomy

- Part of the stomach is extracted from the body, turning what remains into a tube-like structure.
- This reduces the size of the patient’s stomach, resulting in a loss of appetite.
- This loss of appetite is exacerbated by a decrease in the stomachs production of ghrelin.
- Unlike gastric bypass surgery however, sleeve gastrectomy does not reduce the absorption of calories.

Biliopancreatic Division with Duodenal Switch

- About 80% of the stomach is removed, leaving a smaller tube shaped stomach, in addition to the valve that releases food to the small intestine (pyloric valve) along with the portion of the small intestine that normally connects to the stomach (duodenum).
- The end portion of the intestine is then connected to the duodenum near the stomach, bypassing the majority of the small intestine and limiting absorption of calories and nutrients.

While the specific procedures for each of these surgeries can be vastly different, there are some commonalities across the different kinds of bariatric surgery, particularly in the pre-operation and post-operation phases. Ahead of the procedure, the surgeon will enroll patients in an education program to inform individuals of what to expect post-surgery, provide nutritional counseling, a psychological evaluation, and physical exams. Certain high risks behaviors/factors such as smoking and blood thinning medications will have to stop months before the abovementioned surgeries.

⁵⁶ Roux-en-Y Gastric Bypass, [PeaceHealth](#)



Endoscopic Bariatric Techniques

The development of endoscopic bariatric techniques is the newest trend in obesity treatments, especially for patients who do not meet surgical requirements or are unwilling to undergo more invasive, traditional bariatric operations.

Exhibit E: Table of Definitions, Advantages, Disadvantages, and Weight Loss Expectations For 5 Endoscopic Bariatric Techniques

Procedure	Device Explanation	Advantages	Disadvantages	Excess Weight Loss
Space Occupying Devices	Balloons made of silicon and filled with fluid or air occupy space in the stomach normally occupied by food.	Easily placed endoscopically; restrict food consumption; well tolerated; can be removed	Balloon may deflate over long time; can migrate, leading to perforation; FDA required removal after 6 mo. with poor results	39% at 1 year after removal
Restrictive Procedures	Reduce gastric volume via suturing, stapling, or tissue anchors	Permanently reduces stomach capacity; effective; well tolerated	Not easily reversible; folding durability varies with device	Up to 54% at 1 year
Bypass Liner	A sleeve that is implanted into the duodenal bulb and extends into the small bowel; allows food to bypass the duodenum and proximal jejunum.	Secretions can still travel along the sleeve, as opposed to surgical bypass	High risk of hepatic abscesses; not currently available in the U.S.	Up to 36% at 1 year
Aspiration Therapy	Manually aspirate approximately 30% of the meal after consumption	Patients can continue to eat normal diet	Potential to be abused and can promote poor eating habits and eating disorders	41% after 6 months
Gastric Stimulation	Electrical stimulator is placed in the abdomen to block nerve activity between the brain and stomach	Easily placed; Decrease caloric intake	Risk associated with electrical stimulation	N/A

SOURCE: Literature Review from [European Journal of Radiology](#), [FDA](#)



Lifestyle Interventions

Tackling Childhood Obesity

Efforts to address childhood obesity generally focus on combatting poor nutrition and inactivity. Because lifestyle behaviors are significantly influenced by one's environment, the following interventions are categorized by setting.⁵⁷

EARLY CARE AND EDUCATION (ECE)

ECE settings help shape childhood habits into later life behaviors. Successful ECE center-based interventions employ a multi-prong approach to nutrition, exercise, and parental involvement. ECEs are often considered an untapped opportunity for early childhood interventions.

SCHOOL

Physical education (PE) classes and the federal school meal program are two primary targets of wellness-centered policy changes (i.e.: advocating for daily PE classes during the entire school year). These programs are often coupled with district wellness policies.

HEALTH CARE

Clinicians are recommended to screen children aged 6 years or older for obesity and refer them to comprehensive, intensive behavioral intervention to promote improvement in weight status.⁵⁸ Treatment involves BMI assessment, counseling, providing a structured weight-management plan, and using a comprehensive intervention delivered by multidisciplinary teams.⁵⁹

COMMUNITY

In the effort to shape environmental and cultural practices, community-based interventions are designed to support obesity-prevention behaviors through increased access to healthy foods, media campaigns, and other policy strategies. Additionally, population-based environment approaches aim to encourage physical activity (i.e.: sidewalks, safe parks, bike paths). This strategy in particular can aid the overall health of underserved communities.

HOME AND FAMILY

⁵⁷ Population-Level Intervention Strategies and Examples for Obesity Prevention in Children, [Annual Review of Nutrition](#)

⁵⁸ Obesity in Children and Adolescents: Screening, [U.S. Preventive Services Task Force](#)

⁵⁹ Expert committee recommendations regarding the prevention, assessment, and treatment of child and adolescent overweight and obesity: summary report, [Pediatrics](#)



Home-based interventions recommend family meals and authoritative parenting from caretakers to enforce portion control and physical activity. This approach is unique in its key focus on honing parenting skills and shaping the home environment.

INSIGHT: INTERVENTION EFFICACY

While studies have analyzed the efficacy of childhood obesity intervention and prevention programs, most have focused on individual interventions with relatively limited pools of data. However, a few meta-analyses have compared across several different intervention methods:

Wang et al: School-based interventions are moderately effective; physical activity interventions in a school-based setting with a family component or a diet and physical activity intervention in a school-based setting with home and community components have the most evidence for effectiveness. Studies based in school-only, school-home, home-only, primary care, childcare, and community were reviewed¹.

Home-based interventions recommend family meals and authoritative parenting from the caretaker to enforce portion control and physical activity. This approach is unique in its key focus on honing parenting skills and shaping the home environment.

¹ Childhood Obesity Prevention Programs: Comparative Effectiveness Review and Meta-Analysis, [Comparative Effectiveness Reviews](#)

INSIGHT: Up-and-Coming Obesity Treatment Markets

The major areas of growth in the obesity treatment market are solutions that target millennials and childhood obesity. Kurbo is a growing initiative that helps children and teenagers develop healthy eating and exercise habits. Conversely, the structured food plan market is on the decline¹.

¹Interview with Sean G. Eldridge, founder of Gain Life



Dietary Changes and Eating Habits

Beyond setting-based intervention programs focused on education and habit formation, support systems for healthy decision-making exist in other ways. The most common form of lifestyle intervention is centered around patients' diets and eating habits. Strong lifestyle modification programs are the first step in losing weight for many patients and in terms of eating, the four most common diets that can be chosen by a doctor and the patient as a lifestyle plan are low-carbohydrate, low fat, Mediterranean, and portioned diets.

LOW CARBOHYDRATE DIETS

Low carbohydrate diets tend to be much higher in proteins, fats, and vegetables which often lead to higher sense of satiety. This helps patients maintain their dietary goals.⁶⁰ Though there are no restrictions in the amount of food that one can consume when on a low-carbohydrate diet, consumption of grains, breads, pastas, rice, starchy root vegetables, and sugar sweetened beverages are highly restricted or often eliminated altogether.

Low-carbohydrate diets help obese patients lose weight through the manipulation of insulin levels within the body. Carbohydrates, or sugars, is the body's primary source of immediate energy which is used after consumption. However, if one consumes too many carbohydrates and there is excess sugars left within the body, the body converts this sugar into fat. The reduction of intake of carbohydrates is significant because there is a direct relationship between carbohydrate intake with insulin secretion within the body. If one lowers the amount of carbohydrates eaten, the insulin levels within the body also decrease. As a result of lower insulin levels, body fat storage decreases and the fat already stored begins to be utilized^{Error! Bookmark not defined.}. Over time, this results in weight loss and healthier eating habits overall.

LOW FAT DIETS

Low fat diets consist of 10%-20% of calories coming from fat while the rest are based on low-fat foods such as grains, fruits, and vegetables. The goal of this diet is to ensure the patient has a low-energy-density diet while still feeling full because of the sheer amount of low-energy foods they consume⁶⁰.

When choosing which diet to go on, patients often choose between either low-fat diets or low-carb diets. Though low-fat diets are effective in reducing weight by reducing calorie intake, the ultimate long-term effects of both low-carb or low-fat diets result in the same amount of

⁶⁰ Lifestyle Modification for Obesity, [National Institutes of Health](#)



weight loss⁶¹. However, in obese adults, low-carb diets are seen to have better effects overall as they are more conducive to leading a healthier lifestyle and promoting healthier eating habits overall⁶¹.

A MEDITERRANEAN DIET

Mediterranean diets consist of a high intake of unsaturated fats, which are found in foods such as: olive oil, nuts, fish, fruits, vegetables, and whole grains. Mediterranean diets limit red meat and butter-based foods as those are high in saturated fat content⁶⁰. Unlike other discussed strategies, the Mediterranean diet is a traditional diet that is embedded with historical significance.

The Mediterranean diet can help lower risk of cardiovascular disease, while promoting increased longevity and healthier weight, and also lowering the risk of Alzheimer's disease and even certain cancers.⁶² Following this diet has been shown to allow for better overall control of lipid levels and blood sugar control than those in the other dieting groups⁶².

Changing Meal Delivery

PORTIONED MEALS

Portioned meals consist of a set amount of food for every meal. They usually take the form of high-protein, liquid diets, which allows the patient to know exactly how many calories they are consuming and fixes the amount of food they receive to a constant.

MEAL KITS

Meal kits, which advertise nutritious, portion-controlled food options, generated \$1 billion in revenue worldwide in 2015; the market is projected to hit \$10 billion by 2020.⁶³ In the U.S., 9% of consumers (or 10.5 million households) have purchased a meal kit in the last six months. Moreover, 25% of consumers (or 30.1 million households) reported interest in trying a meal kit in the next six months.⁶⁴

However, as major players like Walmart and Amazon enter the meal delivery market, smaller, healthier companies are pushed to the margins.

⁶¹ Do Low Fat Diets Really Work?, [Healthline](#)

⁶² The Mediterranean Diet, [Obesity Medicine Association](#)

⁶³ Direct-to-door meal kit service market revenue worldwide, [Statista](#)

⁶⁴ Meal Kit Mania: Innovation for Foodies, [Nielsen](#)



Physical Activity and Weight Loss

The other major component that general lifestyle interventions focus on is physical activity. Physical activity is not only important for losing body weight, but also making sure the patient maintains a consistent healthy weight and lifestyle after the weight is loss. Physical activity has been proven to benefit the body in many ways including, but not limited to: improving cardiovascular health in all individuals, reduction in blood pressure, lipids, and visceral fat, and improved glucose tolerance⁶⁰. However, physical activity plans are rarely conducted by themselves. They are often paired with other forms of lifestyle intervention programs such as dieting.

Behavior Therapy

Behavioral therapy is a process in which patients work directly with many medical professionals to set realistic goals that will induce a behavior change in their everyday lives. More general than dieting and physical activity plans, behavior therapy targets a wide variety of factors that contribute to weight gain/loss, helping patients modify their eating, activity, and thinking habits⁶⁰.

Behavior therapy was first introduced in 1967 and has since evolved into a method that involves several different factors such as stimulus control, problem solving, cognitive restructuring, self-monitoring, exercise, and diet⁶⁰. The most important part of behavior therapy is the capacity for self-monitoring coupled with accountability; patients review their own food intake, physical activity, and body weight so they can discuss, review, and identify areas of success and areas that require improvement with their doctors⁶⁰.

FDA Approval

What is FDA Approval?

According to the FDA website, the FDA (U.S. Food and Drug Administration) “provides scientific and regulatory advice needed to bring new therapies to market... with its understanding of the science used to create new products, testing and manufacturing procedures, and the diseases and conditions that new products are designed to treat”⁶⁵.

⁶⁵Novel Drug Approvals for 2019, FDA, [FDA](#)



The Process

A COMMON GOAL

The FDA website clearly lays out a set of general guidelines when approving products⁶⁶:

“At the heart of all FDA's medical product evaluation decisions is a judgment about whether a new product's benefits to users will outweigh its risks.”

“FDA will allow a product to present more of a risk when its potential benefit is great — especially for products used to treat serious, life-threatening conditions.”

“FDA reviews the results of laboratory, animal and human clinical testing done by companies to determine if the product they want to put on the market is safe and effective. FDA does not develop or test products itself”

The FDA has different pathways to approval for drugs and for devices.

PATHWAY TO DRUG APPROVAL

The FDA's main priorities when approving new drugs are safety and effectiveness of the drug both in the short-term and long-term. Over the last ten years, the time to approve new drugs has halved and the approval rate for new drugs has tripled⁶⁷. Lifesaving drugs may have an expedited approval time. The accelerated approval time was likely caused by the Prescription Drug User Fee Act (PDUFA), passed in 1992 which allowed the FDA to charge drug companies for reviewing applications⁶⁷.

Additionally, “in 2017, the FDA set an all-time record for generic drug approvals and for more novel drugs than any year since 1996.⁶⁸” This positive transformation can be accredited to Scott Gottlieb, FDA Commissioner, who has taken steps to make the approvals process more transparent and more predictable⁶⁸.

PATHWAY TO DEVICE APPROVAL

For devices, the approvals process is detailed on the FDA website, but the main priority is to ensure that products are up to performance standards both in the short-term and long-term. The timeline for device approval is significantly different than the one for drugs. Since there is

⁶⁶ About FDA Product Approval, FDA, [FDA](#)

⁶⁷ The FDA Has Regulated Drug Approvals Over The Past Decade, Mother Jones, [Mother Jones](#)

⁶⁸ Trump's FDA Pick is Speeding Up New Drug Approvals, Newsweek, [Newsweek](#)



so much variation in devices and usage of devices, the FDA first classifies devices into three classes: I, II, and III, based on the level of control needed to provide reasonable assurance of safety and effectiveness, with Class III requiring the most regulation⁶⁹. Differing control levels produce great variety in approval timeframe; while successful drugs usually take 2-2.5 years to obtain FDA approval, it is much harder to estimate a timeframe for a devices' pathway to approval.

Stages of Drug Development

STAGE 1

In a laboratory, researchers with grants undertake basic research to understand processes behind a disease and locate a target. They then look for compounds that act on this target, which normally come from plants but are now being created by computers.

STAGE 2

These molecules are then confirmed to be safe and effective through clinical trials with models with computers, cells, and animals. There are multiple stages in this process, testing varying doses and patient groups.

STAGE 3

For drugs that make it this far, marketing is crucial. Companies are granted a license through a submission with data on testing information, toxicity and pharmacology, results, and proposed labelling.

STAGE 4

Pharmaceutical companies then look to patent their products. Patents last up to 20 years from the FDA, but more research and development occurs after the patent is obtained. It can be up to eight years after the patent is obtained until marketing and usage of the drug by patients can occur⁷⁰.

Examples

On the next page is a list of FDA approved drugs and devices.

⁶⁹ Step 1: Device Discovery and Concept, FDA, [FDA](#)

⁷⁰ Drug Development: The Journey Of A Medicine From Lab To Shelf, *The Pharmaceutical Journal*, [The Pharmaceutical Journal](#)



Exhibit F: List of FDA-approved therapeutics, their mechanism of action, side effects, and listed warnings.

Name	Target	How It Works	Common Side Effects	Warnings
Orlistat (Xenical)	Adults and children aged 12 and older	Works in the gut to reduce the amount of fat the body absorbs	Diarrhea, gas, leakage of oily stools, stomach pain	Rare cases of severe liver injury, recommended to take a multivitamin pill to compensate for reduced nutrient absorption
Belviq (Lorcaserin)	Adults	Acts on the serotonin receptors in your brain; may help patients feel full after eating smaller amounts of food	Constipation, cough, dizziness, dry mouth, feeling tired, headaches, nausea	Caution with taking antidepressants or migraine medications at the same time
Qsymia (Phentermine-topiramate)	Adults	A mix of two medications: phentermine, which lessens appetite, and topiramate, which is used to treat seizures or migraine headaches; Makes patients less hungry/ feel full sooner	Constipation, dizziness, dry mouth, taste changes, tingling of hands/feet, trouble sleeping	Refrain from use if afflicted with glaucoma or hyperthyroidism, may lead to birth defects
Contrave (Naltrexone-bupropion)	Adults	A mix of two medications: naltrexone, which is used to treat alcohol and drug dependence, and bupropion, which is used to treat depression or help people quit smoking	Constipation, dizziness, dry mouth, diarrhea, headache, increased blood pressure and heart rate, insomnia, liver damage, nausea	Refrain from use if afflicted with uncontrolled high blood pressure, seizures or a history of anorexia or bulimia nervosa or if taking bupropion (Wellbutrin, Zyban), may increase suicidal thoughts or actions.
Saxenda (Liraglutide)	Adults	May make you feel less hungry or full sooner. At a lower dose under a different name, Victoza, FDA-approved to treat type 2 diabetes.	- Constipation, diarrhea, headache, increased pulse, abdominal pain, nausea	May increase the chance of developing pancreatitis, has been found to cause a rare type of thyroid tumor in animals.

SOURCE: Literature Review from NIDDK



FDA APPROVED DEVICES⁷¹

There are currently four types of FDA-approved devices on the market for obesity treatment:

- 1) Gastric Band
 - a. Bands placed around the top portion of the stomach leaving only a small portion available for food
 - b. Ex. Lap-Band Adjustable Gastric Banding System
- 2) Electrical Stimulation Systems
 - a. Electric stimulator is placed in the abdomen to block nerve activity between the brain and stomach
 - b. Ex. Maestro Rechargeable System
- 3) Gastric Balloon Systems
 - a. Inflatable balloons are placed in the stomach to take up space
 - b. Ex. ReShape Integrated Dual Balloon, ORBERA IntraGastric Balloon System, Obalon Balloon System
- 4) Gastric Emptying Systems
 - a. A tube is inserted between the stomach and outside of abdomen to drain food after eating
 - b. Ex. AspireA

The Pricing Model

A Mutual Agreement

The pharmaceutical industry follows a “two-level” pricing system based off of brand of the drug, similar to the way many supermarkets price the “supermarket brand” for much cheaper than other name brands⁷². Serious questions remain however, because with the pharmaceutical industry, the price difference can be several hundred-fold. In addition, the high price of brand name drugs seems to be unique to the US, as pharmaceutical companies in 2011 made 45% of their revenue from the US⁷². The data in Exhibit G illustrates specific examples of pricing disparities.

⁷¹ Obesity Treatment Devices, FDA, [FDA](#)

⁷² *The Pharmaceutical Industry*, [The True Cost of Healthcare](#)



Exhibit G: Pricing differences in common medications between the United States and Canada.

Medication and Dose	Price in the US	Price in Canada
Brilinta 90 mg	\$5.99 per pill	\$1.67 per pill
Gilenya 0.5 mg	\$265.03 per capsule	\$91.30 per capsule
Humalog Insulin 100 units/ml	\$26.14 per ml	\$2.78 per ml
Pradaxa 150 mg	\$6.92 per capsule	\$1.78 per capsule
Spiriva 18 mcg	\$13.72 per capsule	\$1.91 per capsule
Xarelto 20 mg	\$14.37 per pill	\$3.07 per pill

SOURCE: Data table [The True Cost of Healthcare](#)

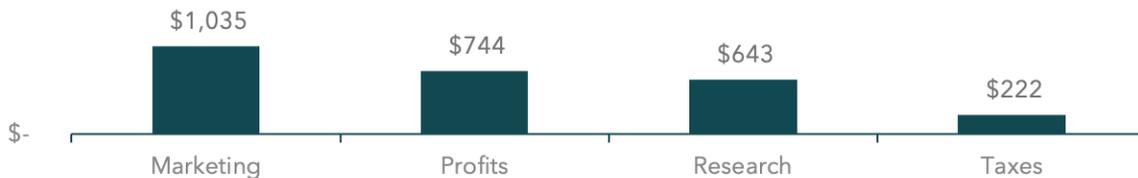
Pharmaceutical companies justify these high prices, claiming that the money is necessary to fund research towards new cures¹. Essentially, the United States is funding more than its share of the portion of the cost for pharmaceutical innovation.

In reality, while research and development is a large expense for pharmaceutical companies, much more of their revenues are directed towards marketing. The 13 major pharmaceutical companies (AbbVie, Amgen, AstraZeneca, Bristol-Myer Squibb, Eli Lilly, Gilead Sciences, GlaxoSmithKline, Johnson&Johnson, Merck Novartis, Pfizer, Roche, and Sanofi) spent \$1.04 trillion on marketing, 60% more than what they spent on research in 2011⁷².



Exhibit H: Spending on different areas by the 13 biggest pharmaceutical companies

Total Amounts Spent by All Companies (Billions of USD)



SOURCE: Graph [The True Cost of Healthcare](#)

Despite the large amount of money spent on research, more is still kept as profit, and even more is spent on marketing. In addition, half of new drug innovations in the US in the period spanning 1998 and 2007 came from academic and biotech research, not from work done by pharmaceutical companies⁷³. Clearly, the high price of drugs in the US isn't just for research and development, and something is still not adding up with the pricing model that drug companies have.

The bottom line is this: Pharmaceutical Companies Ask for Ultra High Prices, and Hospitals Comply because they rely on the companies for new innovations, which won't exist without the revenue.

Why are Drugs so Much More Costly in the United States?

Unlike other countries, the US Government does not bargain with pharmaceutical companies for lower prices because it is illegal for the government to do so.

Individual patients have little to no bargaining power because they no control over what the doctor prescribes them and, when their lives are at stake, they have no choice but to pay a higher price. Internationally, foreign governments bargain with pharmaceutical companies on

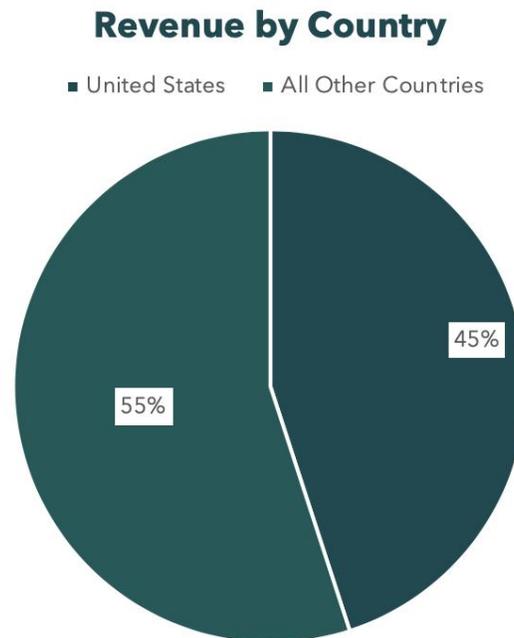
⁷³ *Negotiating for Lower Drug Costs in Medicare Part D*, [National Committee to Preserve Social Security & Medicare](#)



behalf of their citizens, because pharmaceutical companies would rather sell their product for cheaper in a given country than not have a market in that country at all, they reduce their prices significantly.

In the United States, this is not possible because of laws pushed for by drug lobbies that prohibit the government from actively negotiating for prices of drugs. The reasoning behind these kinds of laws is that the “free market” for drugs should be preserved. This has resulted in statistics such as the one displayed in the graph below, with almost half of the revenue of the big pharmaceutical companies coming from the United States despite a significantly smaller share of real sales occurring there.

Exhibit I: Revenue of the 13 biggest pharmaceutical companies, U.S. versus the rest of the world



SOURCE: Graph [The True Cost of Healthcare](#)

Emerging Trends and Global Insights

Anticipated changes in the market that will be relevant for treatment and gaining market share





Novel Therapeutic Approaches and Targets

Therapeutic Peptides: Antag Therapeutics

THE COMPANY

Founded in 2017, Antag Therapeutics aims to develop therapeutic peptides for the treatment of dietary-related metabolic diseases. The scope of this company's research extends beyond obesity to diseases such as type 2 diabetes and fatty liver disease⁷⁴. As a research-intensive company, Antag bases their drug development on the finding of an effective antagonist of the GIP receptor.

THE POTENTIAL

In the past few years, an increasing number of studies have shown that therapeutic peptides as well as peptide conjugates may very well be a key to solving the problem of obesity. It holds great potential when it comes to fat turnover and fat storage and breakdown, which could be one of the roots of obesity⁷⁵. Currently, there are no predecessors and competitors in the market for therapeutic peptides with the purpose of treating obesity, so Antag has the space to develop when it can.

Novo Nordisk invested \$3 million in Antag in 2017⁷⁶. Antag's drug is promising because it can easily be used in conjunction or combined with other therapeutics such as Novo Nordisk GLP-1 to improve treatment of other diseases.

⁷⁴ Antag Therapeutics, [Antag Therapeutics](#)

⁷⁵ Therapeutic Peptide for Obesity and Diabetes, [Ohio University Research](#)

⁷⁶ Antag Therapeutics raises 3M USD in a Series A investment from Novo Seeds, [Accelerace News](#)



Fat Tissue Target: Adipo Therapeutics

THE COMPANY

Founded by Purdue University assistant professor Meng Deng, Adipo Therapeutics is developing a disruptive nanotherapeutic platform that safely acts on fat tissue by converting “bad fat” to “good fat.”⁷⁷ The therapeutic treatment is based on two platforms. The first platform uses Deng’s discovery of adipocyte browning, the conversion of energy-storing fat cells into energy-burning fat cells, to induce browning and burn off fat cells. The second platform is uses a polymer-based nanoparticle delivery system with Notch signaling to control how much browning happens safely and effectively⁷⁸.

This research is supplemented by another Purdue University study showing that Notch signaling plays an important role in combatting the onset of obesity and Type 2 diabetes by breaking down fat tissue and testing signaling on mice⁷⁹.

THE POTENTIAL

Currently, Adipo is seeking funding and partnerships with other firms. The company is currently a small player in the obesity market as it is more research-focused than commercially-driven. Adipo is still in its infancy but has a high growth potential.

⁷⁷ Startup developing nanotherapeutic technology that could safely, effectively convert bad fat to good fat, treat obesity, [Purdue University](#)

⁷⁸ Feel the burn: Researcher converts bad fat to good using technology, *The Exponent*, [The Exponent](#)

⁷⁹ Cell signaling pathway linked to obesity, Type 2 diabetes, *Purdue University*, [Purdue University](#)



Duel Obesity-Diabetes Target: Eisai

THE COMPANY

Founded in 1941 in Japan, Eisai Co. is a pharmaceutical company that has seen recent growth as a member of the Topix 100 and the Nikkei 225 stock indices. Their key areas of focus are in neurology, oncology, and metabolic diseases.

Eisai's main and only obesity drug is Belviq, a drug bought fully from creator Arena Therapeutics. Belviq is a lorcaserin hydrochloride drug that targets chronic weight management issues in adults. By activating the serotonin 2C receptors, Belviq promotes satiety and decreases consumption of food⁸⁰.

In 2012, the FDA approved Belviq usage as an “adjunctive therapy combined with reduced-calorie diet and increased exercise in obese (BMI of 30 kg/m² or greater) patients, or those who are overweight (BMI 27 kg/m²) and have a weight-related comorbid condition”⁸¹. Belviq was launched in the U.S. in 2013, approved in Mexico in 2016 and Brazil later the same year, and currently, Belviq is formulating a once-daily pill that has already been approved.

THE MARKET ADVANTAGE OF BELVIQ

Belviq reduces diabetes risk. Specifically, Belviq can be used to prevent initial and reoccurrence of type 2 diabetes. Analysis of treatment showed 19% improvement in reducing risk of incident and 7.1% increased rate of remission of hyperglycemia⁸². In addition, Belviq does not increase combined incidence of heart attack, stroke, and cardiovascular death in obese patients⁸². These results make Eisai the only maker of obesity drugs able to market heart safety as a competitive edge⁸².

Three prescription weight loss rivals of importance are Qysmia by Vivus, Contrave by Nalpropion, and Saxenda by Novo Nordisk. Like Belviq, Qysmia was FDA approved in 2012, and the latter two were approved in 2014.

⁸⁰ R&D Pipeline, [Eisai](#)

⁸¹ Arena, Eisai Win FDA Okay for Obesity Drug, [GenEngNews](#)

⁸² Eisai Obesity Drug Belviq May Have An Edge To The With New Heart-Safety Data – But To What End? [FiercePharma](#)



Exhibit J: Competitive Landscape for 4 Important Obesity Drugs on the Market



SOURCE: CBE Analysis, Literature Review from [LA Times](#), [Elle](#)

Of the four, Qysmia made the most revenue, though it has faltered in recent years. Saxenda remains the only drug seeing increasing revenue.

Additionally, the weight loss advantage differentials amongst the four drugs is significant. A report from the LATimes tells us that “On average, participants who took Qsymia lost 8.8 kilograms — just short of 20 pounds — after a year...the average weight loss was 5.3 kilograms (about 11.5 pounds) for those on Saxenda, 5 kilograms (about 11 pounds) for those on Contrave, 3.2 kilograms (about 7 pounds) for those on Belviq”⁸³. For safety, Ken Fukioka, MD from San Diego’s Scripps Clinic, tells Elle that “ironically, Belviq offers the best safety profile and the lowest average weight loss...but for the patient who doesn't need to lose a tremendous amount that's a trade-off I'll take any day”⁸⁴. Qysmia, on the other hand, has more limitations; if the patient has any cardiovascular issues, the central nervous system stimulant can be extremely dangerous⁸⁴.

⁸³ Experts Rated Weight-Loss Drugs And Qysmia Came Out On Top, [Los Angeles Times](#)

⁸⁴ Are The New Generation of Diet Drugs Safe? [Elle](#)



Overall, this analysis reveals that Belviq, positioned against other weight-loss drugs, does not a significant advantage and faces greatest competition from both Qysmia and Saxenda. It may want to remarket itself as a drug to those who desire safety over greater effects.

INSIGHT: Commonalities and Trends

For many major pharmaceutical companies, obesity-specific medications do not seem to be of the highest priority, although some medications do seem to be in the pipeline (such is the case for Novo Nordisk). Even pharmaceuticals that offer obesity medications such as Roche, which created the first obesity specific medication, are moving into even larger markets; where pharmaceuticals seem to be focusing are treatments for comorbidities (i.e. diabetes, high cholesterol, hypertension) which not only act as effective treatments for individuals with obesity, but also directly target patients afflicted with these conditions. Thus, emphasizing the treatment of comorbidities offers pharmaceuticals greater consumer reach.¹

¹CBE Insight

THE POTENTIAL

Currently, Eisai’s positioning is not the strongest. Arena, Belviq’s original maker and at least half the force running Belviq’s production, left Belviq to Eisai for \$23 million with more than \$80 million in cost savings. The report cited previously states that “the drug hasn't exactly soared since then; it brought in just \$3.6 million in Eisai's fiscal 2017, which ended this March⁸².” From the company’s perspective, this is a huge hurdle.



Exhibit K: ROI for Belvii over time

	1-2 years	5 years	10 years	> 10 years	Overall Return
Originally: With Arena	×	×	×	×	×
Currently: Arena's Exit	×	×	×	+	×
Ideal Future: Solely Eisai	×	×	+	+	+

Key: + High return + Moderate return × No return

SOURCE: CBE Analysis

Arena had accumulated costs at a faster rate than Belvii was making revenue, and with Arena's exit, Eisai has a lot of cleanup to do. Ideally, with internal restructuring, Eisai has the potential to grow and obtain profits, but we can see that it will take a long-term change to obtain moderate to high returns.

Emerging Surgical Treatments

Gastric Balloons: Allurion

THE COMPANY

Allurion's main device is the Ellipse Balloon. Allurion, a startup, markets the balloon as a non-invasive and pain-reduced method of weight loss. In the past decade, most solutions for gastric bypass have been surgical, and implanting devices in patients is a lifechanging move. Allurion's Ellipse Balloon sidesteps that process by introducing a pill that takes around 15 minutes to inflate in the stomach⁸⁵. The gastric balloon stays in the stomach for a few months, allowing the

⁸⁵ Gastric bypass surgery in a pill startup Allurion gets \$27 million as it pursues FDA approval, *TechCrunch*, [TechCrunch](#)



patient to lose a significant amount of fat before they are able to excrete the balloon when the balloon pops.

THE POTENTIAL

Approval has been gained for the Ellipse balloon in parts of Europe and the Middle East, but the device is not yet FDA approved⁸⁶. The company has gained around \$27 million in funding from Romulus Capital. Allurion also offers diet training and nutrition coaches in preparation for gastric bypass surgery⁸⁶. In May of 2017, Allurion won the Emerging Technology Innovation Award from the Society of American Gastrointestinal and Endoscopic Surgeons⁸⁶.

OBALON BALLOON SYSTEM

Obalon, another balloon device company, went public in 2016 and markets itself to be the “first and only” swallowable pill⁸⁷. More importantly, it *is* FDA-approved, and has proven results of weight loss. Obalon Balloon System requires an invasive endoscopic process to remove the balloon after six months⁸⁷.

Skipping Gastric Bypass: Xeno Biosciences

THE COMPANY

Founded in 2015, Xeno Biosciences boasts its lead product candidate in XEN-101, an oral-pill formula designed to deliver molecular oxygen to the lower gut. This triggers the microbiome shift and weight loss normally induced by the Roux-en-Y Gastric Bypass (RYGB) surgery, saving the need for surgery⁸⁸.

THE POTENTIAL

Xeno, with its XEN-101, mimics RYGB through the Air Hypothesis. The Air Hypothesis is a mechanism that allows extra air and oxygen to alter the gut microbiome, leading to weight loss⁸⁸. Although many papers have been written about this mechanism, there is no substantial proof to support the hypothesis; as of now, there are many more prevalent factors leading to obesity. It is an innovative hypothesis but has a long way to go until FDA approval.

⁸⁶ Another startup hoping to tackle obesity using a device raises \$19 million, *MedCity News*, [MedCity News](#)

⁸⁷ Obalon, [Obalon](#)

⁸⁸ Approach, *Xeno Biosciences*, [Xeno Biosciences](#)



Emerging Avenues for Lifestyle Interventions

A number of startups focused on lifestyle changes have gained success amongst patients and physicians alike. These startups focus on a variety of different elements, from ensuring patients visit their physicians to motivating patients by integrating education programs, meal preparation services, and fitness programs.

Initiatives Targeting Key Demographics

GAIN LIFE: TARGETING MALE CUSTOMERS

A mindset-based initiative, Gain Life offers users a weight-loss service focused on behavioral change, encouragement through in-app activities, and interaction with life health coaches. Gain Life is a Harvard-based startup aiming to not only offer nutritional and exercise advice, but also gender-specific therapy. According to the founders of Gain Life, weight loss programs directed specifically at men are not prevalent enough, despite the fact that men suffer from obesity at higher rates.⁸⁹ Thus, the Gain Life app features language that differs greatly between genders; men are offered a sports-themed app and women have a health and wellness-themed one. Gain Life also has specific initiatives targeted towards their male users such as ManUP Health, a 16-week mindset, exercise, and nutritional program guided by health coaches and reinforced by peers. ManUP Health delivers 14% weight loss in a year, compared to the Diabetes Prevention Program that achieves 6% weight loss. A similar program, PowerUP, is also offered through Gain Life that claims 12% weight loss in a year.⁹⁰

Members are personality-matched with a coach that keeps patients accountable through weekly check-ins, video calls, and phone calls. Gain Life has also gained traction with employers and offers a partnership with a gym chain, Global Fit, in which employer wellness programs can subsidize gym memberships. Partnering with employers can save companies \$853 per employee in annual medical care cost savings if an employee with a 35 BMI loses 10% of their weight, with more weight loss being associated with greater future savings.

⁸⁹Harvard-based weight loss startup combines tech, human coach, [Boston Business Journal](#)

⁹⁰ Harvard Startup Looks to Disrupt Employer Wellness Market , [HuffPost](#)



RETROFIT: TARGETING THE WEALTHY

Retrofit claims to offer a holistic weight-management solution that uses a combination of smart technology and coaching. It offers a personalized experience that encourages positive and sustainable behavioral changes.⁹¹

Retrofit is a 12-month program that aims to have users lose 10-15 percent of their body weight. The program costs \$249-\$349 a month, with users being assigned three personal trainers: a therapist which acts as the behavior coach, a dietician, and an exercise specialist aimed at keeping users accountable. Through the use of a Fitbit fitness tracker that clients receive as part of their package, the personal trainers are able to create specialized programs for users.

No workout regime is strictly enforced; however, clients are encouraged to take 10,000 steps a day. Also, instead of logging calories, users instead send short messages to their dietitians after eating a meal or having a snack. This is related to the mindset-focused initiative of the start-up. Retrofit has already been able to raise \$11 million.

INSIGHT: ROLE OF TECHNOLOGY

The implementation of electronic health record-based decision support and self-guided behavioral change support for parents is suggested to be more cost-effective than previous clinical interventions. However, it should be noted that in general, such strategies may be less cost-effective than other policies like school-based interventions and taxes.

Sharifi et al: A childhood obesity intervention involving electronic decision support in primary care improved BMI at a cost of \$119 per child and \$237 per BMI unit reduced. National implementation over 10 years could reach >2 million children and avert 43,000 obesity cases.¹

¹ Cost-Effectiveness of a Clinical Childhood Obesity Intervention, [Pediatrics](#)

⁹¹ Personalized, holistic weight management solutions that transform lives and workplaces, [Retrofit](#)



Emerging Integrative Approaches

Although solely therapeutic, device, and lifestyle interventions are effective, some of the most promising approaches combine or are applicable to multiple categories.

Integrative Care

ZILLION: GENERAL CARE BY GROUPING RELATED DISEASES INTO A SINGLE TREATMENT PLAN

Zillion, a Boston-based care management company, is geared toward patients dealing with obesity, diabetes, and similar chronic conditions. Zillion's digital engagement platform offers three types of programs: (1) preventative, in which weight loss is the main focus, especially for those who are pre-diabetic, (2) care dealing with chronic conditions such as obesity, and (3) procedural, such as prenatal, orthopedic, or bariatric care.

With its recent partnerships with UnitedHealth Group's Real Appeal program and Apollo Endosurgery, Zillion has been able to provide patients with real human interaction, educational programs, and lifestyle coaching.⁹²

Zillion aims to provide the necessary technology that healthcare organizations have not been able to create. The easy to use app has raised \$28 million in an effort to expand their digital technology capabilities.⁹³

HEALTHIMATION WHY WAIT: MEALS, EXERCISE, AND EDUCATION FOR RELATED DISEASES

Healthimation Why WAIT (Weight Achievement and Intensive Treatment) offers a clinically-proven weight loss program with weight loss preservation for up to five years. Healthimation Why WAIT has over 12 years of proven evidence in helping patients struggling with obesity and associated type 2 diabetes/pre-diabetes.

⁹² Keep Digital Health Innovations Simple, [Medtech Boston](#)

⁹³ Zillion raises \$28M for digital patient engagement platform, [MobiHealth News](#)



The program offers easily digestible meals and entertaining exercise and education plans, keeping users happy and engaged while on their specialized weight loss plan. The Why WAIT program, developed at the Joslin Clinic at Harvard, has a \$12 million research budget that has allowed 53% of patients to maintain 9% weight loss even after a period of 5 years.⁹⁴

This game-like digital platform is specifically designed to not look like a typical health care app to make it more engaging and unique. The program also offers a real (not virtual) personal health coach and support group.

⁹⁴ [Healthimation](#)



TREND: DATA ANALYTICS AND HIGH TECH

When combating a problem as prevalent and caustic as obesity, a combination of tactics are required. Through the use of technology (i.e. monitoring devices, programs used by healthcare companies and physicians to integrate patient data, etc.), patients dealing with obesity can gain deeper insight into their condition. Two startups jumping on this trend are detailed below.

OM1

OM1, is a health outcomes and technology company focused on combining standardized health information and artificial intelligence technology to provide patients with synthesized data on health outcomes. OM1 is a personalized health data compiler that allows quick research-grade information on the effectiveness of different treatment options. This increases patient engagement with their health and allows access to the right options for patients, taking into account personal factors¹.

With its recent \$21 million investment, OM1 is focused on continuing and advancing its cloud technology to connect patients with clinical trials and treatments².

Twine Health

Twine Health is a cloud-based collaborative care platform for chronic pain management based in the Greater Boston Area, built out of the MIT Media Lab. Twine Health allows a platform for users to build customized health action plans — including reminders to take medications and implement lifestyle changes. The platform tracks trends and progress towards goals, offering users key analytics. Patients have the option to work independently or with health coaches, healthcare providers, family, and friends, to develop the plan together, in order to monitor progress and accountability and provide much needed encouragement and support.

¹ [OM1](#)

² Health Outcomes & Technology Company OM1 Closes \$21 Million Series B Financing And Expands Product Offerings , [Cision PR Newswire](#)



TREND: DATA ANALYTICS AND HIGH TECH (CONTINUED)

In a case study at the Joslin Diabetes Center in Boston, patients using the platform combined with standard care saw a 3.2 percent drop in a key measure of blood sugar content (hemoglobin A1c) over a three-month period. Compared to a completely standard model of care, without the use of Twine, patients only see a 1 percent drop in a year. Other diabetes and hypertension management studies have shown similar positive results.

Now, Twine is transitioning to the workplace-health space; as of 2017, Twine has 65 workplace clients across the nation and over 100,000 employee users. A 2016 study in the *American Journal of Managed Care* showed that patients with diabetes, hypertension, and high cholesterol — all associated diseases with obesity — who began using Twine saw improved health outcomes and saved \$2,000-\$5,300 in medical costs for their employers³.

³ Coaching platform improves health outcomes, lowers medical costs , [MIT News](#)

Precision Medicine and Obesity

Precision medicine is an emerging approach for disease treatment and prevention that accounts for individual variability in genes, environment, and lifestyle for each person⁹⁵. Previous studies have indicated that the contribution of genetic heritability to the development of obesity may be as high as 70%, with key genes regulating processes such as food intake, nutrient preferences, and energy expenditure, among others⁹⁶. Indeed, a recent study found that adolescents with severe obesity responded heterogeneously to treatment, further highlighting the need for precision obesity treatment⁹⁷. Thus, the advent of big data and genomic information has catalyzed the transformation of traditional weight loss methods into precision medicine strategies. Compared to other conditions, precision medicine in obesity has been largely unexplored. The current treatment procedures and efficacy are summarized in Exhibit L.

⁹⁵ What is Precision Medicine?, [National Institutes of Health National Library of Medicine](#)

⁹⁶ Precision Medicine in Weight Loss and Healthy Living, [Progress in Cardiovascular Diseases](#)

⁹⁷ Heterogeneity in Response to Treatment of Adolescents with Severe Obesity: The Need for Precision Obesity Medicine, [Obesity](#)



Exhibit L: Current interventions fall under the categories of pharmacotherapy, device therapy, bariatric surgery, and lifestyle medication therapy.

Pharmacotherapy	Device Therapy	Bariatric Surgery	Lifestyle Modification Therapy
<ul style="list-style-type: none"> Weight loss efficacy ranging 3-5% Additional research required to evaluate long-term safety Four new medications in the pediatric pipeline: lorcaserin, phentermine plus extended-release topiramate, naltrexone extended-release plus bupropion extended-release, high dose liraglutide 	<ul style="list-style-type: none"> Devices include: intra-gastric balloon, vagal blockade, aspiration therapy More research required to determine obesity device safety for the pediatric population Barriers include many adverse side effects, ranging from abdominal discomfort to gastric ulcers 	<ul style="list-style-type: none"> Most effective weight loss intervention in adolescents with severe obesity Improves obesity-associated comorbidities Outcomes generally variable Barriers include long-term risks of micronutrient deficiency and alcohol use disorders 	<ul style="list-style-type: none"> Children over the age of 6 screened for obesity and offered at intensive behavioral interventions Generally associated with minimal to modest decreases in weight-related parameters in adolescents Less effective for older children and those with more severe obesity

Source: Literature Review from the [International Journal of Obesity](#)

CHALLENGES AND OPPORTUNITIES FOR PRECISION MEDICINE IN OBESITY

There are still significantly hurdles to overcome in obesity treatment. These include⁹⁸:

1. Developing valid and clinically meaningful BMI metrics for severe obesity
2. Developing valid and developmentally appropriate measures of phenotypes and predictors
3. Mechanisms and biopsychosocial predictors of developing severe obesity
4. Establishing a clinical context for the development and delivery of precision care

To solve some of these problems, the clearest way forward is collecting data. Exhibit M details methods to collect pertinent data.

⁹⁸ Working towards Precision Medicine Approaches to Treat Severe Obesity in Adolescents, [International Journal of Obesity](#)



Exhibit M: Potential sources of data for tailored nutritional advice in large-scale precision nutrition interventions⁹⁹.

Data	Aims of data collection	Methods to produce data
Eating behavior	To evaluate dietary intake and eating behavior	Dietary assessment on several days using: Online food diary Smartphone applications (self-description and quantification of consumed foods) Digital photography (semi-automatic identification and quantification of consumed foods)
Physical activity	To measure physical activity level To estimate energy expenditure	Accelerometry techniques using: Wearable/portable devices (e.g. wristband) Online questionnaire
Deep phenotyping	To assess body composition, nutritional status, other risk factors for diet-related diseases	Anthropometric measurements (e.g. weight, waist circumference, bone densitometry), clinical chemistry from various bio-samples to assess visceral fat distribution, insulin resistance, low-density lipoprotein cholesterol, nutrient deficiencies, etc.
Nutrigenomics	To look for genetic variants associated with diet-related diseases and/or responsive to dietary changes	DNA extraction and genotyping of selected loci from whole-blood samples
Microbiomics, metagenomics	To understand the interplay between diet and gut microbiota	Feces collection to sequence the microorganism present in the gut for microbial profiling and detection of dysbiosis
Metabolomics	To understand how the body metabolizes/uses nutrients	Complex chemical analyses from bio-samples (e.g. serum, plasma, urine) using: Nuclear magnetic resonance spectroscopy Mass spectrometry-based techniques

SOURCE: International Journal of Obesity

Power of Patient Perspective

The initial month of treatment is a determining factor when it comes to whether patients chose to stay on their medication. Patients may choose to stop because the medication's side effects become unbearable for the patient or, more often, the patient does not notice the rapid weight loss. The initial amount of weight lost is key: when patients reported upwards of 4 pounds lost in the first week, they were much more likely to continue their treatments despite the weight lost being mostly water weight. While they would often be disappointed by a decreased rate of weight loss (since one can only lose so much water weight), patients who experienced higher

⁹⁹ Precision Nutrition: hype or hope for public health interventions to reduce obesity?, [International Journal of Epidemiology](#)



initial loss were much more likely to stay on their medications than those who lost the same amount progressively.

Exhibit N: Table of reviews and reported side effects of most popular US obesity medications

Product	Reviews within one Month	Reviews after one Month	Reported Weight loss vs proven	Reported Side Effects (in order of frequency)
Saxenda	Mixed	Positive	Reported>Proven	Fecal Incontinence, Dizziness
Xenical	Positive	Extremely Positive	Reported>Proven	Diarrhea (and orange coloration)
Belviq	Mixed	Positive	Reported>Proven	Frequent headaches (consensus), fatigue, heart palpitations
Phentermine	Positive	Positive	Reported>Proven	Dry Mouth
Tenuate	Mixed	Positive	Same as proven	No generalized reported side effects
Contrave	Mixed	Positive	Same as Proven	Mild Nausea, Sweats

SOURCE: CBE Research

TREND: Repeat Users

There was a near consensus in patients who chose to continue to take their medications after the first month that they were satisfied. Often, even if they were not simultaneously on a dietary plan or an exercise regiment, they would still report weight losses above those that their respective medications were found to provide in their trials.

CBE Research

Treatment Decision Process

When it comes to the choice of treatment, there does not seem to be one that is superior. For therapeutics, patients often made their choices based on how the drugs affected them and their insurance policies. Only Tenuate appeared to have no generalized reported side effects. Interestingly, reports on how well weight loss was maintained after treatment did not factor into the decision of patients.

Many patients had the expectation that they would most likely regain their lost weight and were happy to repeat the treatment when that occurred. This could prove immensely



profitable for pharmaceutical companies: if patients are only concerned with the weight they lose while on the medication, as long as the medications are effective in the short term, firms can profit from a variety of repeat clients.

Given the information about the various kinds of therapeutics and surgeries that are available, it is evident that there are many treatment options available. As a result, there are many important decisions to be made by both the healthcare provider and the patient regarding what the best course of action is for treatment. The two sections below outline two of the questions that need to be addressed.

Therapeutics versus Surgery

WHICH THERAPEUTIC TREATMENT?

In general, therapeutics are less invasive, and thus a treatment that would be tried before bariatric surgery is attempted. In deciding which treatment to recommend, physicians rely on patient BMI to make a general judgement of which treatment option is best. Dr. Judy Yang, a physician at Newton Wellesley Hospital who often sees obese patients had this to say about deciding whether a patient should choose bariatric surgery:

Medications are indicated for people with a BMI of 30 and above, and surgery for 40; unless they have medical comorbidities, then the numbers are 27 and 35¹⁰⁰.

Beyond these BMI metrics, however, lies a more complicated story with more factors to consider. Medication has many unavoidable side effects, and surgery carries risk of complication, which is not guaranteed, but is a risk nonetheless. In addition, neither of these treatments will be successful without accompanying changes in lifestyle, as an unhealthy lifestyle will reduce the effects of any physiological changes brought about by therapeutics¹⁰¹. Ultimately, if BMI requirements are met and less invasive methods such as dieting have been tried, it is up to the patient and the healthcare provider to come to a decision that is best for that individual patient.

WHICH TYPE OF SURGERY?

Like the previous question, there are no easy answers— tradeoffs exist with each type of bariatric surgery that is chosen. However, research suggests that gastric bypass surgery results in the greatest weight loss in both the short and long term, resulting in an average 31 percent loss in body weight one year after the surgery and an average 25 percent loss in body weight five years

¹⁰⁰ Interview with Dr. Judy Yang

¹⁰¹ Medications for Weight Loss: Indications and Usage, [JAMA](#)



after the surgery¹⁰². Gastric bypass surgery has more side effects, however. Again, statistics can provide general information, but treatment decisions boil down to a patient-by-patient basis.

Physicians and Prescription Drugs

RELATIONSHIP OVERVIEW

Literature clearly shows that the drugs physicians prescribe to their patients is heavily dependent on what kind of relationship exists between the pharmaceutical company and physician. In fact, some practitioners earn hundreds of thousands of dollars or more each year working with drug and device companies with a wide variation among states. When it comes to the proportion of prescribers who take industry money, Alabama, Nevada, Kentucky, and South Carolina have twice the number of prescribers involved with large pharmaceutical companies than Vermont, Minnesota, Wisconsin, and Maine¹⁰³.

Physicians with existing monetary relationships with pharmaceutical companies tend to more aggressively prescribe brand-name drugs. However, an important fact to note with this claim is that many of the studies done in order to come to this conclusion are observational studies where patients and physicians were not subject to random assignment, so only correlation can truly be proven (no causal relationships)¹⁰⁴.

Nonetheless, there is significant evidence that doctors who received industry payments were two to three times as likely to prescribe brand-name drugs at exceptionally high rates compared to others within their respective specialties¹⁰⁴. There appears to be a relationship such that the more money that physicians received from the industry the more brand-name medication they would prescribe. For example, for one study that was conducted, physicians who received no payments from pharmaceutical industries prescribed brand-name medications 20 percent of the time, while those who did receive money from pharmaceutical companies prescribed brand-name medications 30 percent of the time, representing a 10% increase. In 2014, doctors who received payments of more than \$5000 a year had the highest brand name prescribing percentages¹⁰³.

In 2014, nearly 9 in 10 cardiologists who wrote at least 1000 prescriptions for Medicare patients received payments from a drug or device company. Also, in 2014, 7 in 10 internists and family practitioners were seen to have been paid by industries. In a study released by ProPublica, five common medical specialties were examined to see if there were certain doctors in certain fields that prescribed brand-name drugs more. The five specialties

¹⁰² Which Weight Loss Surgery is Best?, [WebMD](#)

¹⁰³ Now There's Proof: Docs Who Get Company Cash Tend to Prescribe More Brand-Name Drugs, [ProPublica](#)

¹⁰⁴ Doctors Prescribe More Generics When Drug Reps are Kept at Bay, [NPR](#)



observed were psychiatry, cardiovascular disease, family medicine, internal medicine, and ophthalmology. In all five of these medical fields, there was found to be a strong, direct correlation between the amount of money

That the physicians receive and the amount of brand-name prescriptions. For the psychiatry sector, there was a 6.3 percent increase between psychiatrists who were not paid by the industries against to those who were paid over \$5k a year from the companies with the amount of prescriptions steadily increasing along the graph between \$0 and \$5k. For the cardiovascular disease sector, there was a 3.9 percent increase between physicians who were not paid to physicians who were paid over \$5k a year. For the family medicine sector, internal medicine sector, and the ophthalmology sector, there was a 7.1 percentage increase, 10.3 percentage increase, and 18.2 percentage increase in prescription rates, respectively¹⁰⁴.

FACTORS PHYSICIANS CONSIDER WHEN CHOOSING PRESCRIPTIONS

There are many different factors physicians consider when choosing prescriptions for patients. One of the main factors is the medical condition that the patient has. Unsurprisingly, there are many medical sectors in which doctors treat patients with conditions that have few non brand-name drugs available. An example of this would be HIV/ AIDS. Other patients may have complicated conditions where generic drugs no longer become useful¹⁰⁵. However, when the choice is available, some doctors still prescribe brand-name drugs over generic drugs. When questioned, many of the doctors who received money from brand-name companies responded with frustration and the retort that they are simply prescribing what they believe is best for the patient. However, due to the nature of interviews, we do not know if what they are claiming is genuinely true or if it is simply a cover up. What pharma companies want to establish is a mutually-beneficial relationship with physicians. In exchange for money, meals, sponsorships, and other commodities, pharma companies want physicians to prescribe their products more¹⁰⁵.

Another major factor is the relationship between the physician and the pharma companies. The extent of this effect can vary due to many different factors. In order to reach physicians and gain their favor, pharma companies use different strategies such as: face-to-face detailing, providing medicine samples, presenting written evidence of their drug's effectiveness, organizing meetings and medical launches, offering sponsorship, and providing gifts in the form of meals and money¹⁰⁵. Pharma companies usually change their tactics to better suit each physician, making their advertising and promotion strategies dynamic rather than static. In order to discourage the manipulation of physicians, some hospitals limit how much sales reps are allowed within hospitals. However, some companies do not have any policies and there is a

¹⁰⁵ Factors Influencing Prescribing Decisions of Physicians : A Review, [National Institute of Health](#)



drastic difference in the amount of brand-name prescription between the two.¹⁰⁶ Some ways hospitals limit the number of visits by sales representatives was by limiting access, limiting gifts, and enforcing punishments for those who broke the rules. Significant results were seen when tougher policies were enforced; a 1.67% decrease in market share for the average promoted brand-drug.¹⁰⁷

BRAND NAME VERSUS GENERIC DRUGS

According to many studies, there are no differences between brand-name drugs and generic drugs that are made for the same purpose that justify doctors to prescribe the brand-name drug. In reality, many of the drugs that are most aggressively promoted to doctors are not cures or even big medical breakthroughs. Brand names have been shown to be more expensive, yet when surveys were taken by patients that reported results and patient satisfaction, there was not much of a difference between brand-name and generic drugs¹⁰⁸. Both brand-name drugs, and the generic counterparts have the same active ingredients. Furthermore, due to rules set by the U.S. Food and Drug Administration (FDA), both need to pass the same manufacturing, packaging, and quality standards. The FDA also requires generic drugs to have the same performance and quality as brand name drugs, essentially making cost the only difference between brand-name and generic prescriptions¹⁰⁹.

However, the difference in cost comes with the competition involved in the drugs' respective industries. Brand-name drugs are well established among their users; however, generic manufacturers can compete on price. As a result of the direct price competition, price is driven down for consumers. Generic drugs have saved Americans \$1.67 trillion over the last decade¹⁰⁹.

Marketing Strategies

From a broad level, the marketing strategies that pharmaceutical companies use to sell their drugs can be divided into two categories: Push and Pull marketing¹¹⁰. Push marketing refers to marketing targeted at physicians, because physicians “push” the drugs to their patients. Pull marketing refers to marketing targeted at patients, because patients “pull” drugs from physicians. Together, physicians and patients have a push pull relationship that pharmaceutical companies seek to influence from both sides.

¹⁰⁶ Now There's Proof: Docs Who Get Company Cash Tend to Prescribe More Brand-Name Drugs, [ProPublica](#)

¹⁰⁷ Doctors Prescribe More Generics When Drug Reps are Kept at Bay, [NPR](#)

¹⁰⁸ Now There's Proof: Docs Who Get Company Cash Tend to Prescribe More Brand-Name Drugs, [ProPublica](#)

¹⁰⁹ Appropriate Prescribing Of Medications: An Eight-Step Approach, [Association for Accessible Medicines](#)

¹¹⁰ The Push and Pull of Pharma Marketing, [MedCrunch](#)



Push Strategies

Traditionally, push marketing has been the area of heaviest focus for pharmaceutical companies, as physicians are the ones who ultimately make the decision on whether or not to use a drug¹¹¹. After all, more prescriptions for a certain drug will mean more revenue for that drug. In 2003, \$13.2 billion dollars were invested by pharmaceutical salespeople in marketing drugs towards healthcare providers⁵.

One area of push marketing is social media, as many physicians utilize social media¹¹². This includes directly reaching out to physicians through services such as LinkedIn and online forums related to the treatment area of a given drug. Striking the right balance between promoting drugs and providing information relevant to understanding the drug is important to building a strong relationship with physicians so that they are confident in the drugs they are prescribing⁶.

Another push marketing tactic is giving free samples of a drug to a physician⁶. Physicians then can give out these free samples without much liability⁶. The downside to this method is that it raises some ethical questions of pharmaceutical marketers getting too close with healthcare providers⁶. Some healthcare networks have banned free samples as a result. These kinds of ethical concerns are becoming stronger, as the FDA over the past decade has developed a stricter set of guidelines regarding what is permissible for the marketing of pharmaceuticals. The full set of guidelines can be found [here](#). The main concern of pharmaceutical marketers now is that the marketing methods for legacy drugs, or drugs that were on the market before these new guidelines were adopted, do not abide by the new guidelines¹¹³.

Pull Strategies

While push strategies have traditionally been the area of focus for marketing pharmaceutical products, pull strategies have grown in popularity recently¹¹⁴. Pharmaceutical companies now directly reach consumers through promotions that market prescription and over the counter drugs¹¹⁵. This phenomenon calls into question whether pull strategies are creating market demand for drugs that have an actual medical need or are just well-advertised¹¹⁵.

¹¹¹ Pharmaceutical Drug Marketing Strategies and Tactics, [Taylor & Francis Online](#)

¹¹² Pharmaceutical Marketing Strategies and Tactics, [LinchpinSEO](#)

¹¹³ Strategies of Bringing Drug Product Marketing Applications to Meet Current Regulatory Standards, [American Association of Pharmaceutical Scientists](#)

¹¹⁴ CBE Analysis

¹¹⁵ Pharmaceutical Drug Marketing Strategies and Tactics, [Taylor & Francis Online](#)

