

Novo Nordisk's Revolutionary Obesity Drug

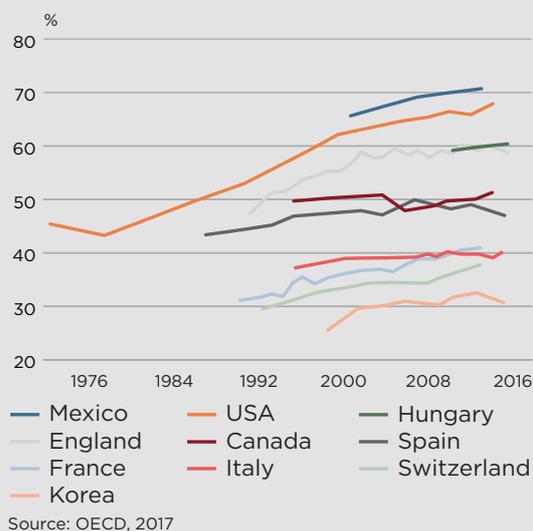
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Key Insights

- In 2016, the World Health Organization (WHO) concluded that overweight in humans had tripled since 1975, seeing that 1.9 billion adults aged 18 years or older were overweight, and of these about 650 million were obese.
- Obesity-related complications are not just a challenge to the individual – they represent a challenge to society in general.
- The development of a new ground-breaking drug will create attractive opportunities for Novo Nordisk.

**Figure 1: Rising Overweight among Adults
BMI >25**



In 2016, WHO concluded that overweight in humans had tripled since 1975. Worldwide, 1.9 billion adults aged 18 years or over were overweight; of these about 650 million were obese. This is a frightening trend for the world's adult population, see figure 1, and the situation is even worse for children and adolescents. The percentage of overweight/obese children/adolescents increased from 4% in 1975 to 18% in 2016 (Source: WHO as of Apr. 2020).

Overall, about 13% of the world's adult population was obese in 2016. In 2019, an estimated 38.3 million children under the age of 5 years were overweight or obese. Once considered a high-income country problem, overweight and obesity are now on the rise in low- to middle-income countries, particularly in urban settings. In Africa, the number of overweight children under 5 has increased by 24% since 2000. Almost half of the children under 5 who

were overweight or obese in 2019 lived in Asia. These are all facts from the latest WHO publication on obesity. So obesity is not only a problem in the Western World, like in the USA and the UK, but will become an even bigger problem for the developing countries in the future.

This trend is worrying as a rise in BMI (body mass index) indicates an increased risk of 1) cardiovascular disease such as stroke etc., 2) diabetes, 3) joint diseases such as osteoarthritis, and 4) certain types of cancer.

Complications of obesity are not just a challenge to the individual person – they represent a challenge to society in general as the derived costs, direct as well as indirect, are huge. A study by the US-based Milken Institute concluded in 2018 that the total cost of treatment of obesity, treatment of complications as well as lost economic productivity in the US attributed to overweight/obesity exceeded USD 1,700 billion annually, equivalent to 9.3% of GDP. This is based on an estimated prevalence of obesity in the US population of 36% in 2020.



Novo Nordisk has launched its first product, Saxenda, for the treatment of obesity. Saxenda sales totalled DKK 5.7 billion in 2019. Novo Nordisk expects revenue from their anti-obesity medications to double in 2025.

The traditional treatment of obesity has been a change of lifestyle with nutritional advice from a dietician to promote a healthier diet combined with increased physical activity. Medical treatment of obesity has also been attempted with medicines that either 1) suppress appetite, 2) increase energy conversion, or 3) reduce the absorption of nutrients from intestines, but they all have side effects such as nausea or diarrhoea. Today, medical treatment is combined with dietary and lifestyle changes. As this method has not been optimal for many people, an alternative method is surgery – a so-called “laparoscopic gastric bypass” – which involves reduction of the stomach.



Calculation of Body Mass Index (BMI)

Overweight and obesity levels are defined using the international concept, the body mass index, which is calculated as a person’s weight divided by the square of height (kg/m²).

Overweight is a BMI over 25, and obesity is a BMI over 30.

The results are a faster feeling of fullness and reduced nutritional absorption. The method has few side effects, including fatigue, loose stools, nausea and abdominal pain after ingestion of fatty foods.

Large unmet demand for a weight-loss drug with a few side effects

Novo Nordisk is currently the only company with an approved drug on the market for the treatment of obesity with a few side effects, i.e. glucagon-like peptide-1 (GLP-1).

This drug was developed in continuation of a discovery made in 1986 by Professor Jens Juul Holst and the department for endocrinological research of the Panum Institute at the University of Copenhagen. Professor Holst discovered that the GLP-1 hormone that promotes insulin secretion also inhibits the secretion of glucagon, thereby decreasing blood sugar levels. Also importantly, GLP-1 has an appetite suppressant effect. This ability was a significant change in the management of diabetes, as patients receiving traditional insulin treatment gain weight.

Professor Holst connected with Lise Heding, a researcher working at Novo Nordisk in the 1980s. Lise Heding had worked with the hormone glucagon, which, like insulin, is produced by the pancreas and which Novo Nordisk manufactured for use in persons with low blood sugar levels and in cardiac treatment. With the new discovery, Novo Nordisk began integrating this knowledge with their ongoing research and development of GLP-1 medications. They have since launched their first product, Saxenda, for the treatment of obesity. Saxenda sales totalled DKK 5.7 billion in 2019. Novo Nordisk expects revenue from their anti-obesity medications to double in 2025 (Source: Novo Nordisk, Capital Markets Day, as of Nov. 2019).

New convincing trials

Novo Nordisk recently published the results of the latest trials with its novel GLP-1 analogue, semaglutide 2.4 mg, for obesity treatment. The trials showed an average weight loss of 18% versus placebo. This product could likely be brought to market in the autumn of 2021. Novo Nordisk also published results of combination therapy with the hormone amylin (AM833) and semaglutide 2.4 mg in a Phase 1 trial. This combination therapy with two different hormones demonstrated a weight loss of 17% after only 20 weeks. AM833 affects the level of serotonin in the brain that regulates anxiety, happiness, mood and appetite. GLP-1 affects appetite through the hypothalamus,

which is the lower part of the midbrain with centres that control the autonomous nervous system regulating blood pressure, body temperature, appetite, thirst, among other things. Mads Krogsgaard Thomsen, Head of R&D and Chief Scientific Officer at Novo Nordisk, sees a good potential in this new combination therapy. He expects to see a potential weight loss of 25-35% in patients after twelve months of combination therapy. This combination therapy can compete with surgery of obesity without any significant side effects.

The joker in using GLP-1, which is difficult to quantify, is the use of GLP-1 in the treatment of Alzheimer's disease and other forms of dementia. In the UK, the use of the GLP-1 analogue liraglutide has shown a positive effect in patients with Alzheimer's disease. Dr. Paul Edison of Imperial College London started a trial with the assistance of Alzheimer's Society UK to evaluate the effects of GLP-1 in patients with Alzheimer's disease. The trial commenced in 2014, and the results will be published over the coming months. In Denmark, Professor Filip Knop of Gentofte Hospital in Copenhagen aims to demonstrate that GLP-1 not only prevents obesity and regulates insulin, but also prevents dementia. However, whether Alzheimer's disease and dementia are GLP-1 treatable conditions is still a major unknown. Obesity, on the other hand, represents a huge untapped potential with strong business opportunities for Novo Nordisk.

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