Plain Language Summary of Publication

Journal of Comparative Effectiveness Research

Semaglutide treatment for obesity in teenagers: a plain language summary of the STEP TEENS research study

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Summary

What is this summary about?
This is a plain language summary of the STEP TEENS research study, which was originally published in the *New England Journal of Medicine*. As more **teenagers** are living with **obesity** than ever before, researchers are searching for new treatments. This was the first study looking at how well the medicine semaglutide works as a treatment for obesity in teenagers.

What were the results?
In this study, researchers looked at the effect of semaglutide on **body mass index (BMI)** and weight loss compared to a dummy medicine (**placebo**). A 17% decrease in BMI was reported for teenagers treated with semaglutide compared with placebo. For weight loss, an 18 kg decrease was seen when comparing semaglutide with placebo. Researchers found that there were more teenagers who had weight loss of 5%, 10%, 15%, and 20% or more in the group given semaglutide compared with the group given placebo. Improvements were also seen with semaglutide treatment for some **risk factors** for other diseases caused by obesity. Semaglutide was generally well tolerated by the teenagers with obesity in this study, and serious medication **side effects** did not happen very often.

What do the results mean?
The results from this study showed that there were no safety issues with semaglutide in teenagers with obesity, and that semaglutide can be used to help them lose weight.

Where can I find the original article on which this summary is based?

The original article 'Once-Weekly Semaglutide in Adolescents with Obesity' was published in the *New England Journal of Medicine*. You can read the full article for free at: https://www.nejm.org/doi/10.1056/NEJMoa2208601

Who is this article for?

This summary was written by some of the authors of the original article. The aim of the summary is to help teenagers living with obesity and their **caregivers** understand the results of the STEP TEENS research study. This study looked at how well semaglutide works as a treatment for obesity in teenagers. The summary may also be helpful to **healthcare professionals** looking for a treatment option for teenagers with obesity.

A **Glossary** of terms and their definitions used throughout this summary can be found at the end of this article.

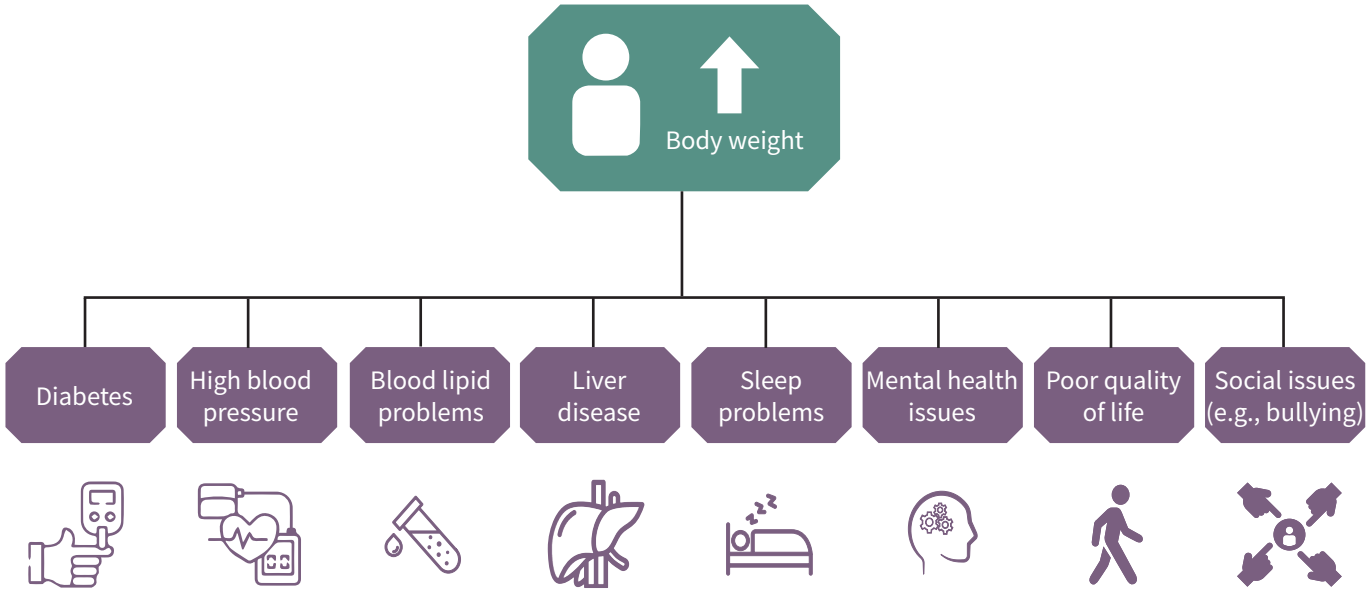
Becaris PUBLISHING

Why was the study carried out?

What is obesity?

Obesity means having too much stored body fat, which can lead to health problems. Obesity is a complicated disease caused by a lot of factors related to how our bodies work and the environment. It is not the result of being lazy or not trying hard enough to be healthy. Our bodies often make it hard to lose weight and keep it off, which means even if you lose weight, it can come back. People with obesity sometimes need help with weight loss and it can be difficult, particularly for teenagers, to get the right care. Obesity is a long-term disease and many children and teenagers with obesity will continue to have the disease as adults. In other words, it is rare to grow out of obesity.

Obesity can increase people's chances of developing other diseases (examples are shown in the figure below) and impact people's mental health, school and social life, and ability to do their daily activities. Losing weight can lower the risk of these diseases and improve wellbeing.

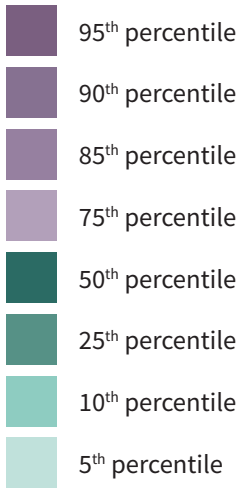


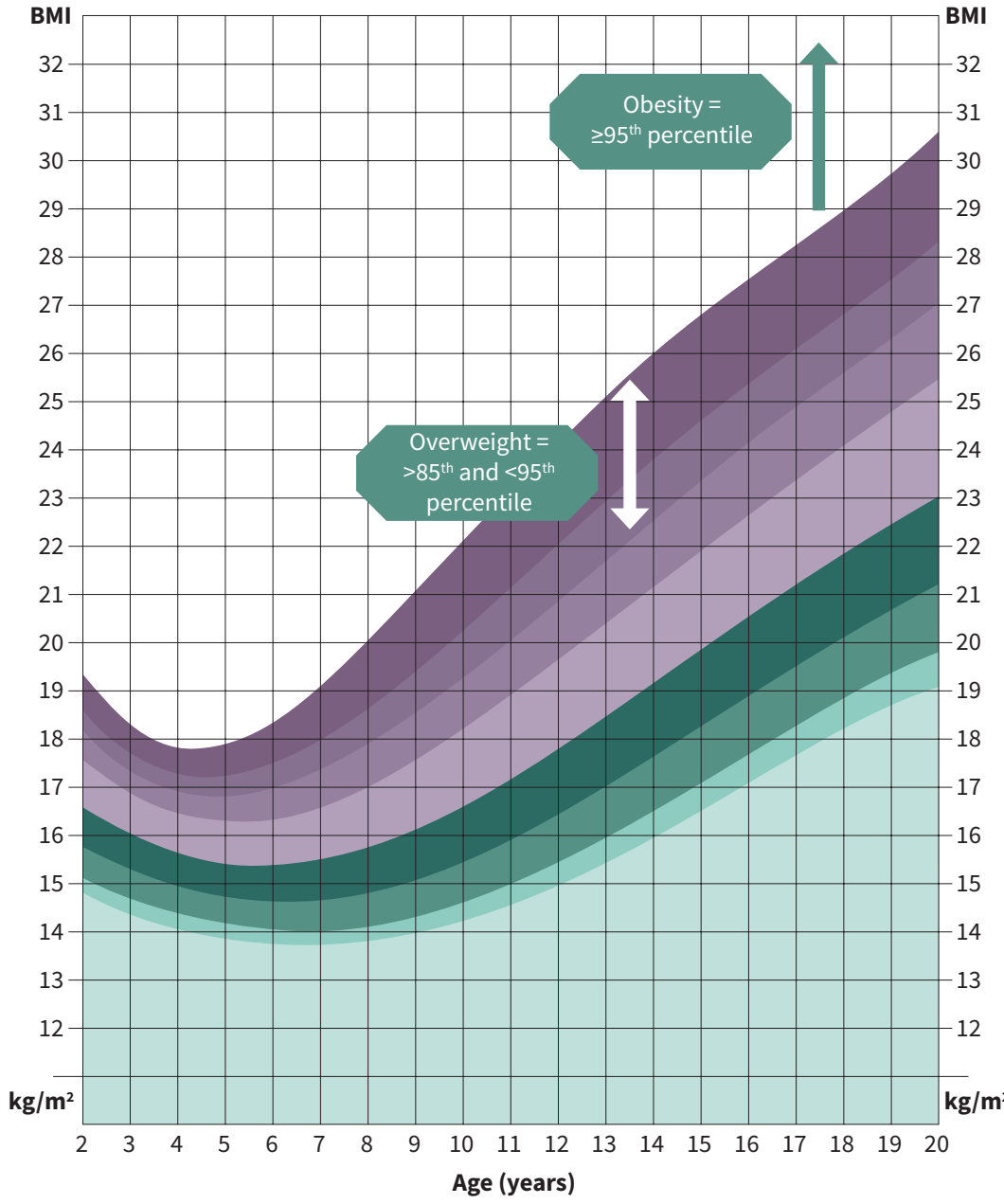
As obesity is a long-term or chronic disease, teenagers who have it will need ongoing support from caregivers and healthcare professionals to help them achieve and maintain weight loss.

Body Mass Index (which is also known as BMI) is the most common method used by healthcare professionals to check for obesity. It uses your weight and height to calculate if your weight is healthy. As you grow, your BMI changes. For children and teenagers, a normal BMI for their age can be found using growth charts (examples for girls and boys based on the charts developed by the USA Centers for Disease Control and Prevention are shown below). Based on these charts, a child or teenager is considered to have obesity if their BMI is in the 95th **percentile** or higher for their age and sex. If their BMI falls between the 85th and 95th percentile they are classed as overweight.

BMI-for-age percentiles:

Boys, 2 to 20 years

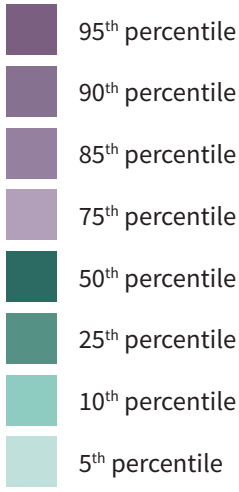


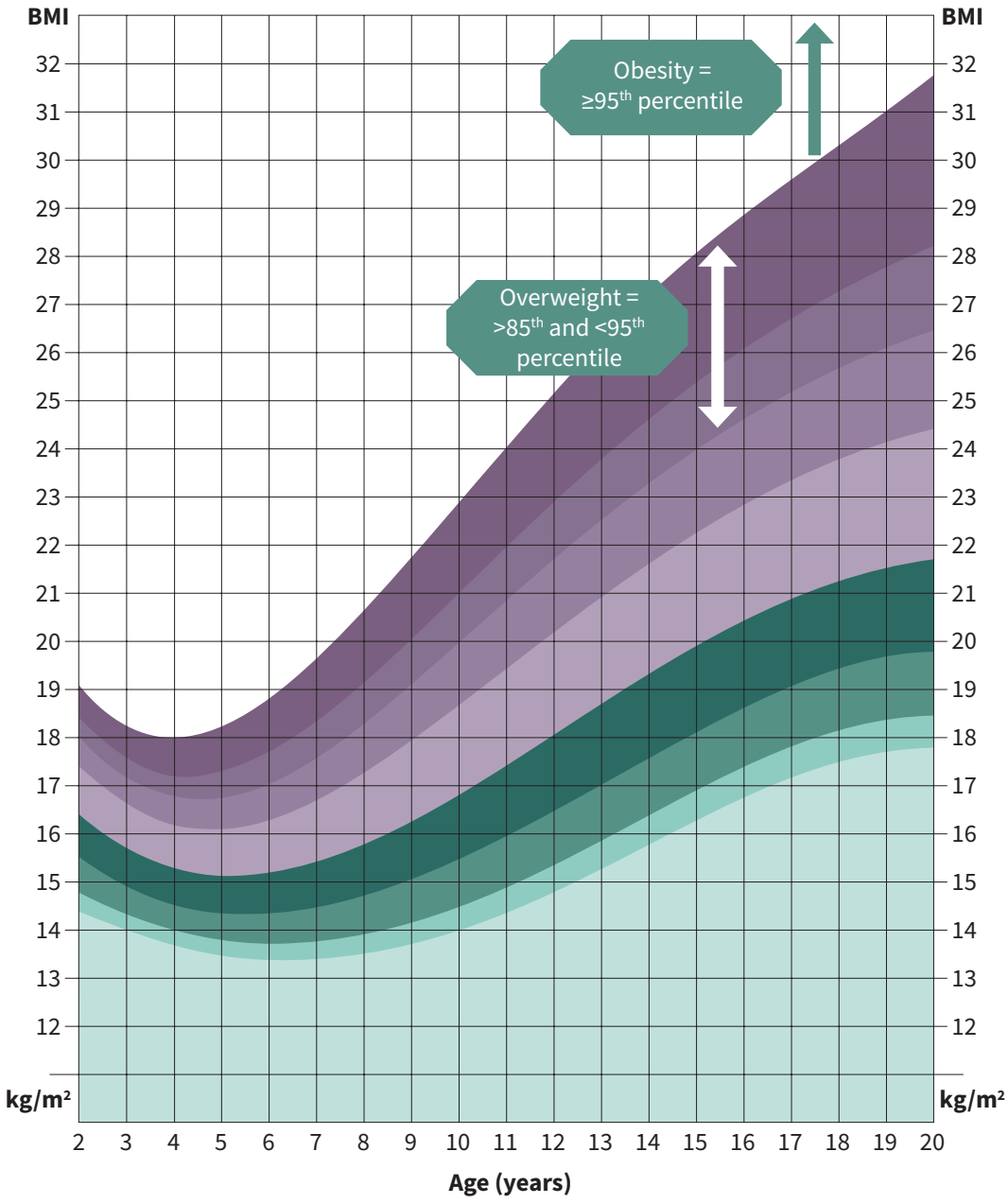


Weight status category	Underweight	Healthy weight	Overweight	Obesity
Percentile range	Less than 5th percentile	5th–85th percentile	85th–95th percentile	More than 95th percentile

BMI-for-age percentiles:

Girls, 2 to 20 years





Weight status category	Underweight	Healthy weight	Overweight	Obesity
Percentile range	Less than 5th percentile	5th–85th percentile	85th–95th percentile	More than 95th percentile

What are the current treatment options for obesity in teenagers?

Lifestyle changes, like eating healthily and exercising every day, are usually the first steps to treat obesity in teenagers. However, most people find it hard to lose weight and keep it off with lifestyle changes alone because the body will try hard to resist these efforts.

Medicines can be added to lifestyle changes to help with weight loss. Some medicines can make people feel less hungry and fuller after eating meals, and/or reduce cravings for certain types of unhealthy foods. Other medicines can stop the body from absorbing fat from meals. At the moment, there are not many medicines available for teenagers who have obesity.

What is semaglutide?

Semaglutide is a medicine that helps adults with obesity to lose weight. It is also used to treat type 2 diabetes, a disease that happens when you have too much **sugar** in your blood, which can be caused by excess weight gain or obesity.

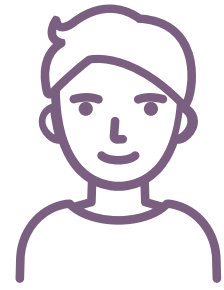
Semaglutide is similar to a **hormone** called glucagon-like peptide-1 (also known as GLP-1), which is made in the body. GLP-1 helps control the amount of sugar (glucose) in your blood and makes you feel less hungry and fuller after eating.

What did researchers want to find out?

More teenagers are living with obesity than ever before, and the numbers continue to rise. Researchers are searching for new medicines to help these teenagers lose weight.

The STEP TEENS research study looked at whether semaglutide could be a possible treatment for obesity in teenagers.

It is predicted that more than
250 million
children and teenagers
worldwide will have
obesity by 2030



How was the STEP TEENS study carried out?

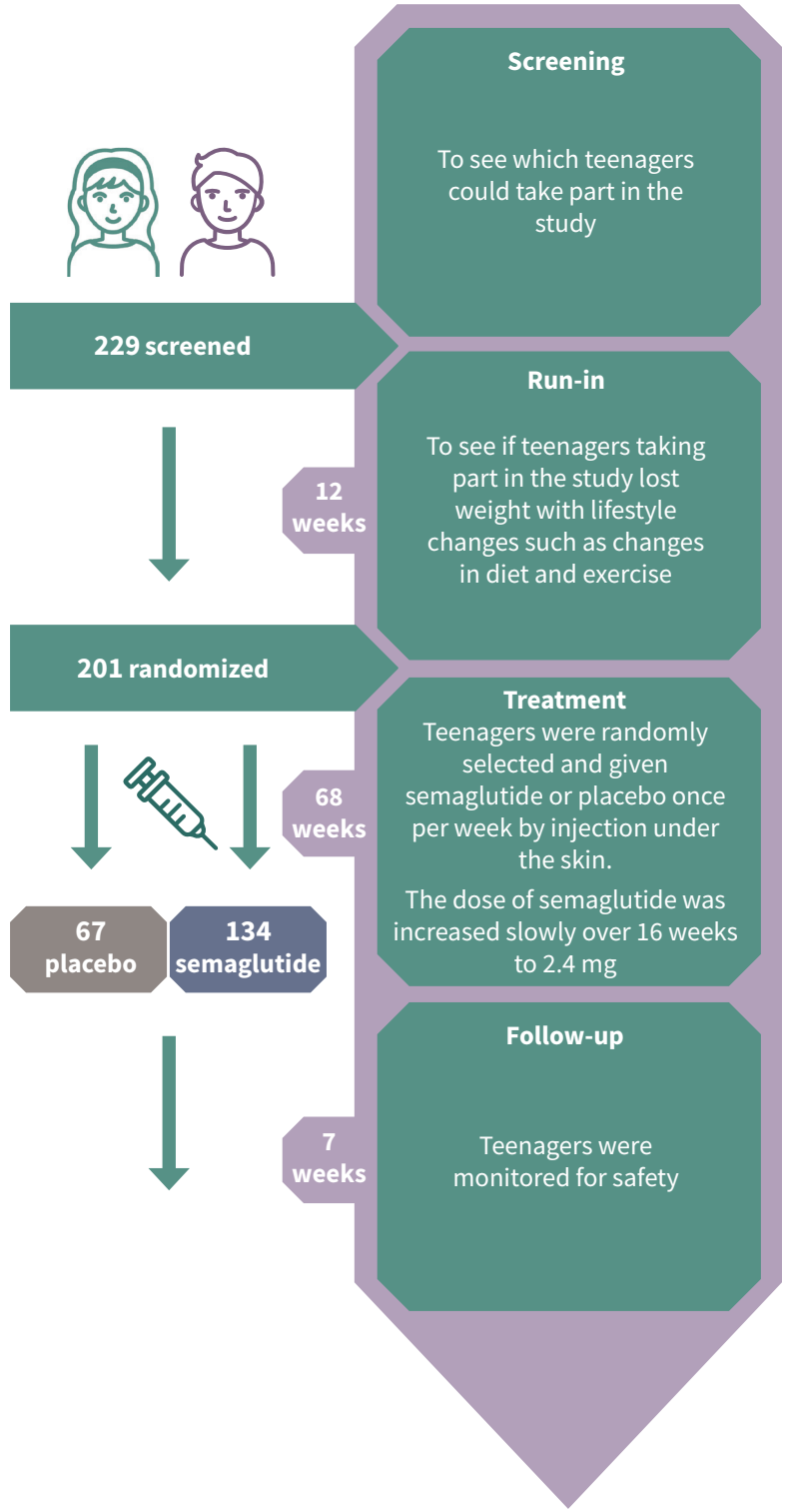
The STEP TEENS study included four parts:

1. **Screening**: During screening, teenagers who wanted to take part in the study were checked to make sure they met the entry requirements, for example, that they were the right age and had a high enough BMI. The teenagers who met all requirements moved on to the run-in period.

2. **Run-in period**: During the run-in, the teenagers and their caregivers were given advice on how to eat healthily and exercise more. The teenagers were asked to exercise and eat healthily for 12 weeks to see if they could lose weight with these activities alone. The teenagers who completed the run-in period but still had a high enough BMI started treatment.

3. **Treatment period**: During treatment, the teenagers were **randomized** and split into two groups. One group was given placebo once per week and the other group was given semaglutide once per week for a total of 68 weeks. The treatments in this study were given as an injection under the skin. Semaglutide was started with a low dose, which was slowly increased to higher doses over time. Semaglutide doses were increased until the maintenance dose (2.4 mg) was reached. The amount of placebo given was also increased so that the same amount as the semaglutide treatment was given, even though there was no active medicine in the placebo. As the teenagers were put in each group by chance (i.e., randomized), they and their caregivers did not know which treatment they were given. While they had treatment, the teenagers and their caregivers continued to be given advice on healthy eating and exercise. After 68 weeks, treatment was stopped, and the follow-up period started.

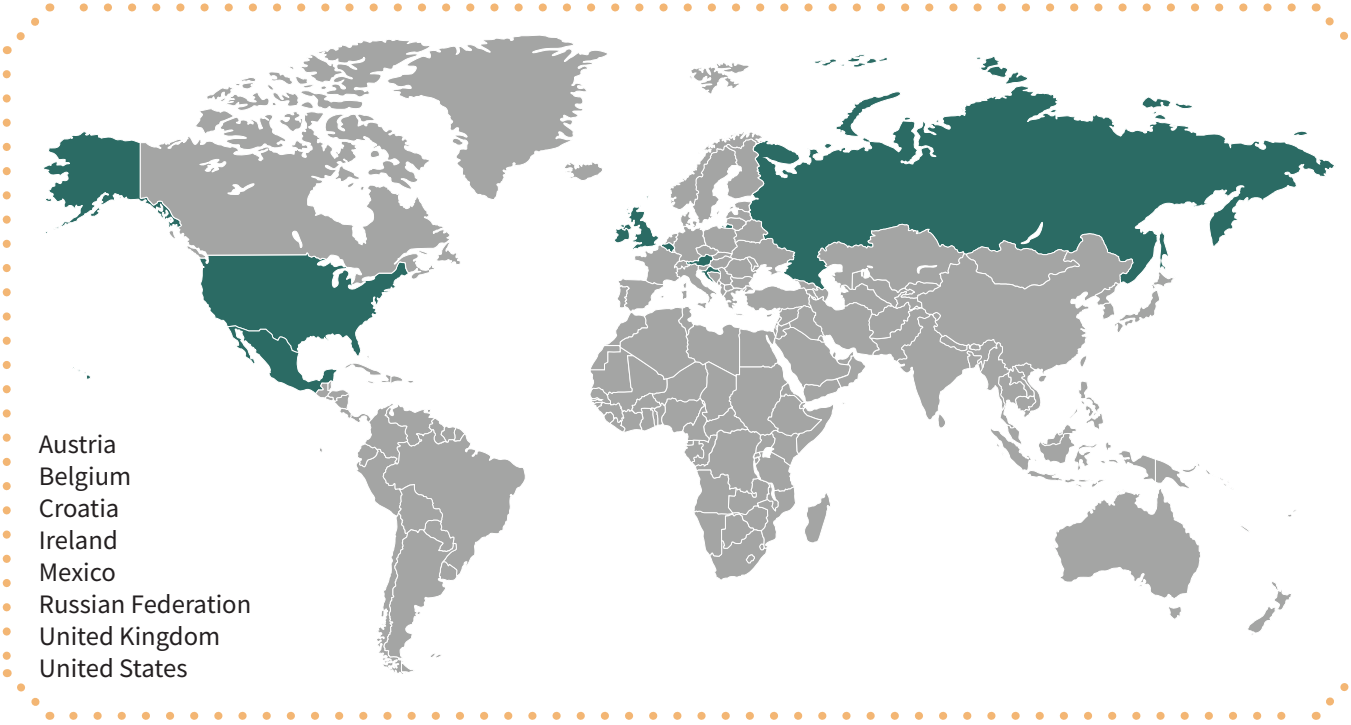
4. **Follow-up period**: During follow-up, each teenager was monitored for another 7 weeks to make sure they were okay after treatment.



In total, the STEP TEENS study was 75 weeks long and included a total of 201 teenagers. For every three teenagers who took part, two were randomly assigned to treatment with semaglutide, and one was randomly assigned to treatment with placebo.

Who took part in the study?

This was a global study and included participants from **37 study sites in 8 countries**.



People who could take part in the study were:

- Aged 12 or over, but less than 18 years old
- Boys and girls with a BMI well above the normal range (≥95th percentile) compared with other boys and girls of the same age and sex
- Boys and girls with a BMI slightly above the normal range (≥85th percentile) could also take part if they had weight-related health problems
- Not able to lose weight with diet and exercise
- Being treated with diet and exercise if they also had diabetes. They could also be using a diabetes medicine called metformin.

People who could not take part in the study were those:

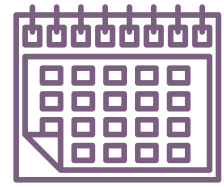
- Whose weight had increased or decreased by 5 kg (11 lbs) or more in the past 3 months
- Who had taken another medicine to treat their obesity in the past 3 months
- Who had had surgery to treat their obesity
- With other diseases such as thyroid problems, severe depression, severe mental health disorders, eating disorders, or attempts at suicide.

The age and proportion of boys and girls in the semaglutide and placebo treatment groups were similar, but body weight, BMI, and waist circumference were slightly higher in the semaglutide group at the start of the study.

Participant details	Sex	Average age	Ethnicity	Average body weight	Average BMI	Average waist size
	Boys: 37% Girls: 63%	15.5 years	White: 78% Black: 8% Asian: 2% Other: 12%	109.9 kg	37.7 kg/m^2	111.9 cm **Semaglutide group**
	Boys: 39% Girls: 61%	15.3 years	White: 82% Black: 7% Asian: 1% Other: 9%	102.6 kg	35.7 kg/m^2	107.3 cm **Placebo group**

Did all participants complete their study treatment?

The STEP TEENS study took place between **October 2019 and March 2022**.



The study compared BMI between teenagers who were given semaglutide and teenagers who were given placebo. Both treatments were given for **68 weeks**.

The study went as planned. Almost all of the teenagers (90%) completed their treatment. All of the teenagers started on a low dose and increased to a maintenance dose. For those who could not tolerate the maintenance dose, lower doses were used instead to continue treatment.

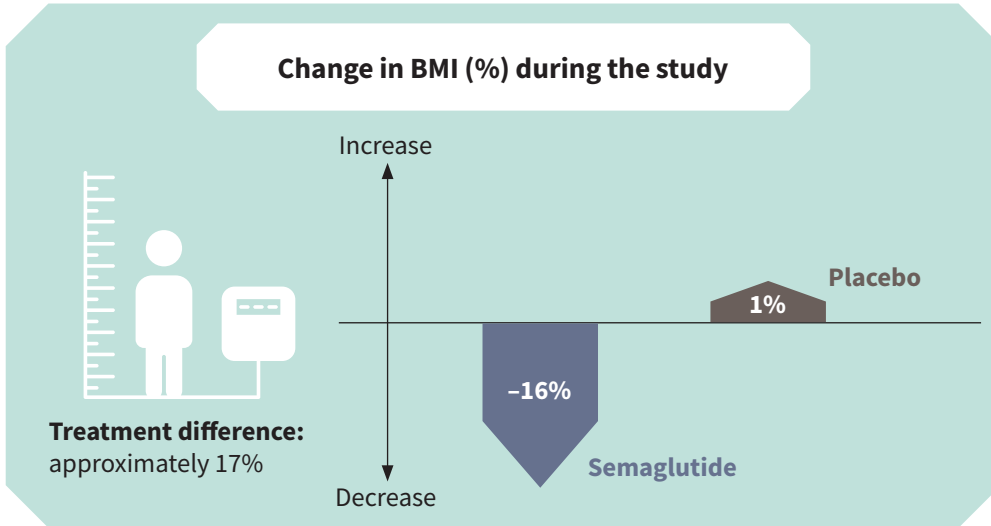
What were the overall results from this study?

1 BMI and body weight decreased in teenagers who were given semaglutide

After 68 weeks of treatment, the researchers measured the BMI of each teenager.
They found that the average BMI had:

Increased in teenagers given placebo by around 1% since the start of the study

Decreased in teenagers given semaglutide by around 16% since the start of the study



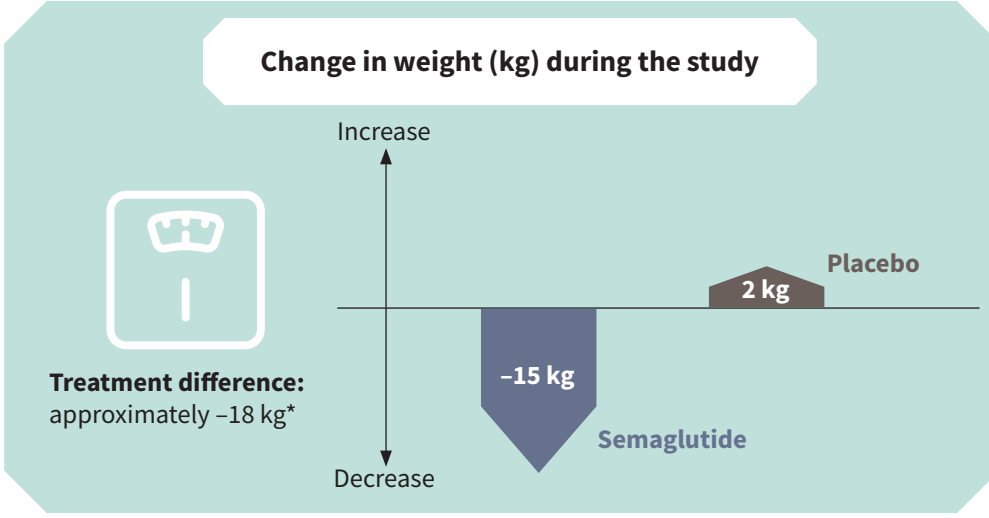
The **treatment difference** for BMI between **semaglutide** and **placebo** was therefore reported to be around –17%.

As well as BMI, the researchers wanted to see how the teenagers' weight had changed after treatment.

They found that:

Teenagers given placebo gained an average of 2 kg (4.4 lbs)

Teenagers given semaglutide lost an average of 15 kg (33 lbs) of weight

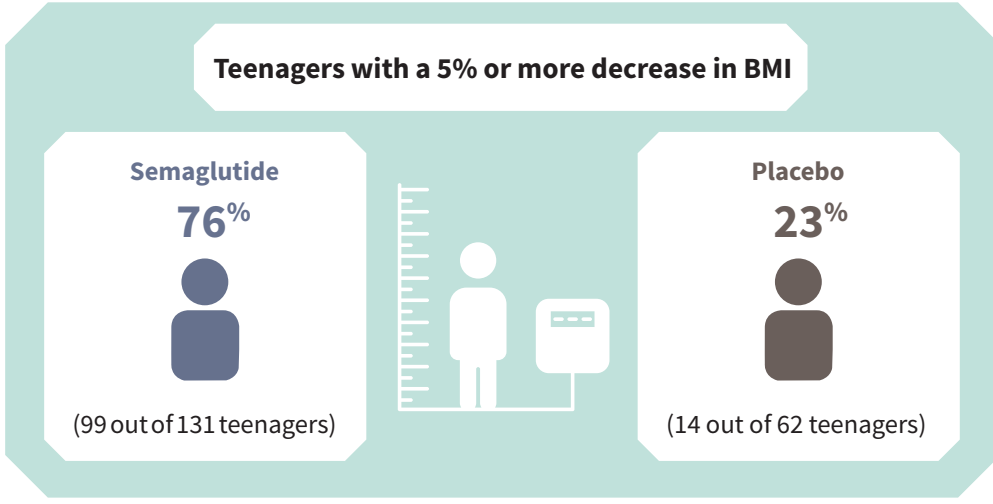


*Even though there was a 15 kg decrease in weight in the semaglutide group and a 2 kg increase in weight in the placebo group, the treatment difference is 18 kg rather than 17 kg because the numbers have been rounded up or down to the nearest whole number.

The treatment difference for weight between the **semaglutide** and **placebo** groups was around –18 kg (40 lb).

2 More teenagers in the semaglutide group achieved a beneficial level of BMI reduction compared with the placebo group

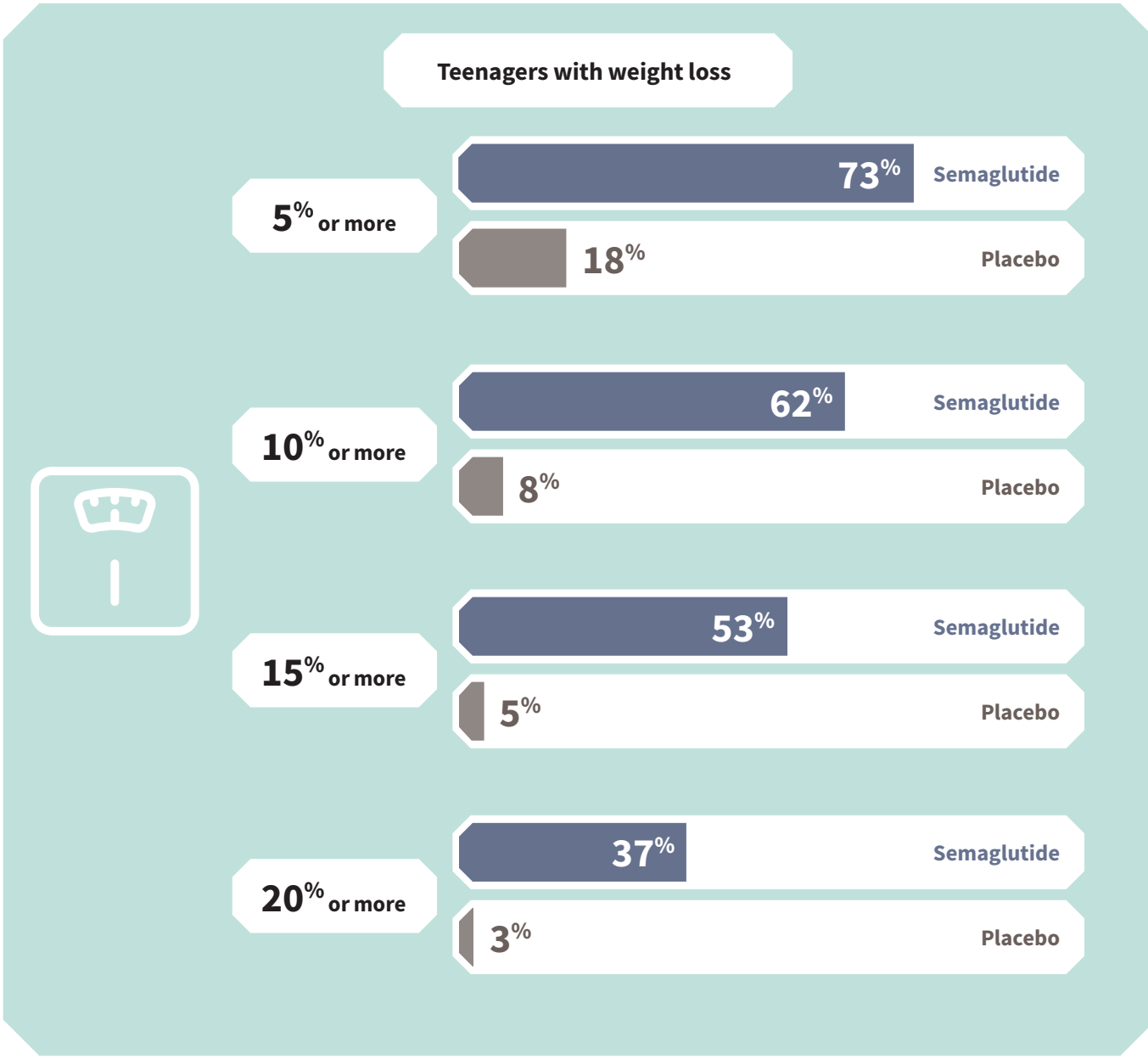
The researchers also looked at how many teenagers in each treatment group had a **decrease in their BMI of 5%** or more since the start of the treatment period. This level of BMI reduction is known to improve health. Many more teenagers in the **semaglutide** group had reached this level of decrease in their BMI compared with the **placebo** group.



The number of participants here might be different from the number of participants who started the study. This is because these numbers only include the participants who had a BMI measurement at both the start and the end of the study.

3 More teenagers in the semaglutide group reached different levels of weight loss than in the placebo group

They also considered how many teenagers in each treatment group had different levels of weight loss since the start of the study (5% or more, 10% or more, 15% or more, and 20% or more). Many more teenagers in the **semaglutide** group reached each level of weight loss than in the **placebo** group.



The number of participants here might be different from the number of participants who started the study. This is because these numbers only include the participants who had a body weight measurement at both the start and the end of the study.

4 Teenagers who were given semaglutide reported better results in other weight-related risk factors than teenagers given placebo

Researchers also looked at other risk factors that are related to diseases caused by obesity to see how they were affected by semaglutide.

Compared with **placebo**, **semaglutide**:

- Reduced the size of the teenagers' waists
- Reduced the levels of sugar in the teenagers' blood in those with and without diabetes
- Improved the levels of some types of lipids (fats) in the teenagers' blood
- Improved the results of a test that shows how well the liver is working.

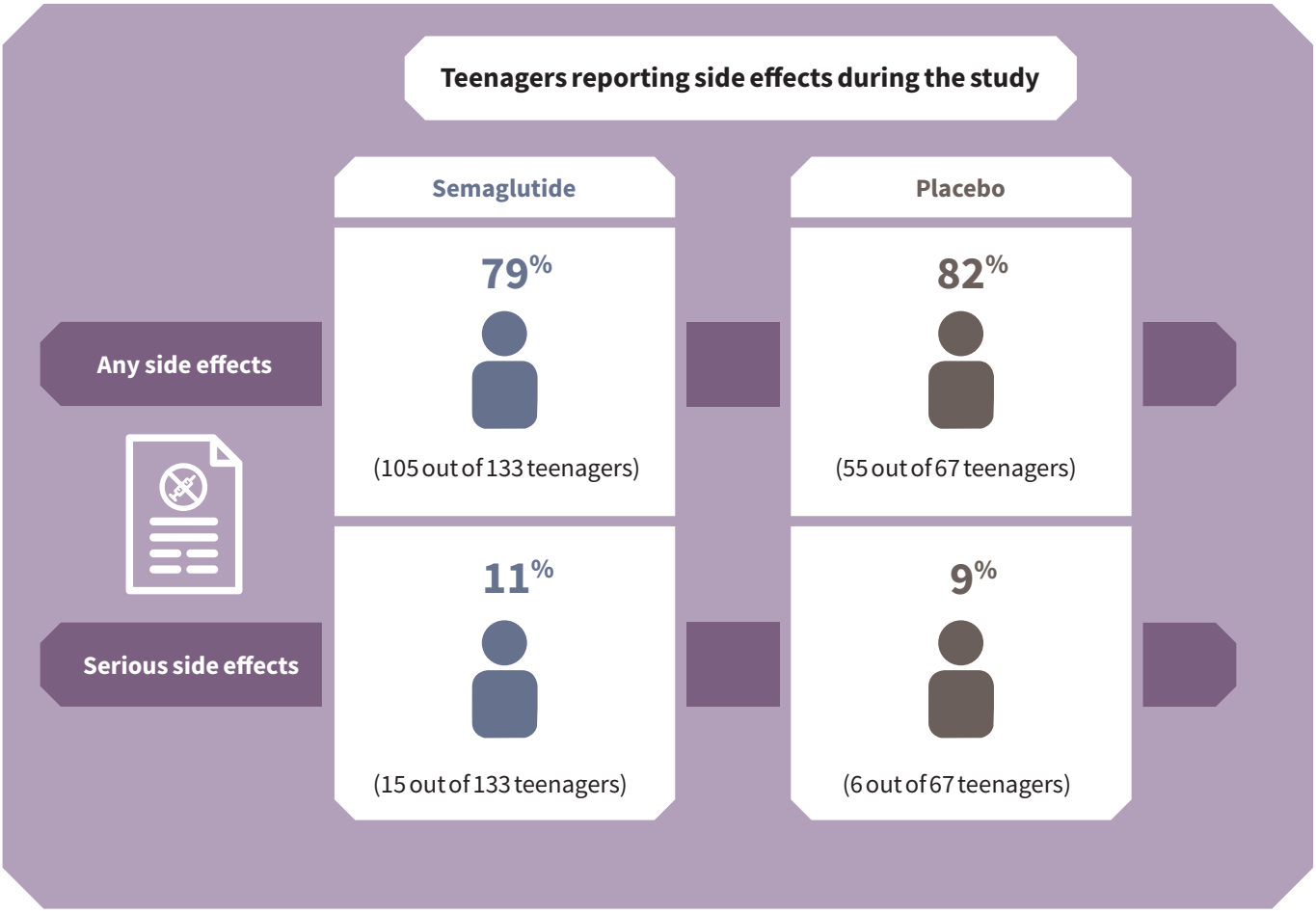
The teenagers who were given **semaglutide** also reported better scores than those given **placebo** on a questionnaire about how their weight affects their lives and how they feel about themselves.

Were there any side effects seen in this study?

1 There were no safety issues with semaglutide in teenagers with obesity

This study suggests that there were no safety issues with **semaglutide** in teenagers with obesity.

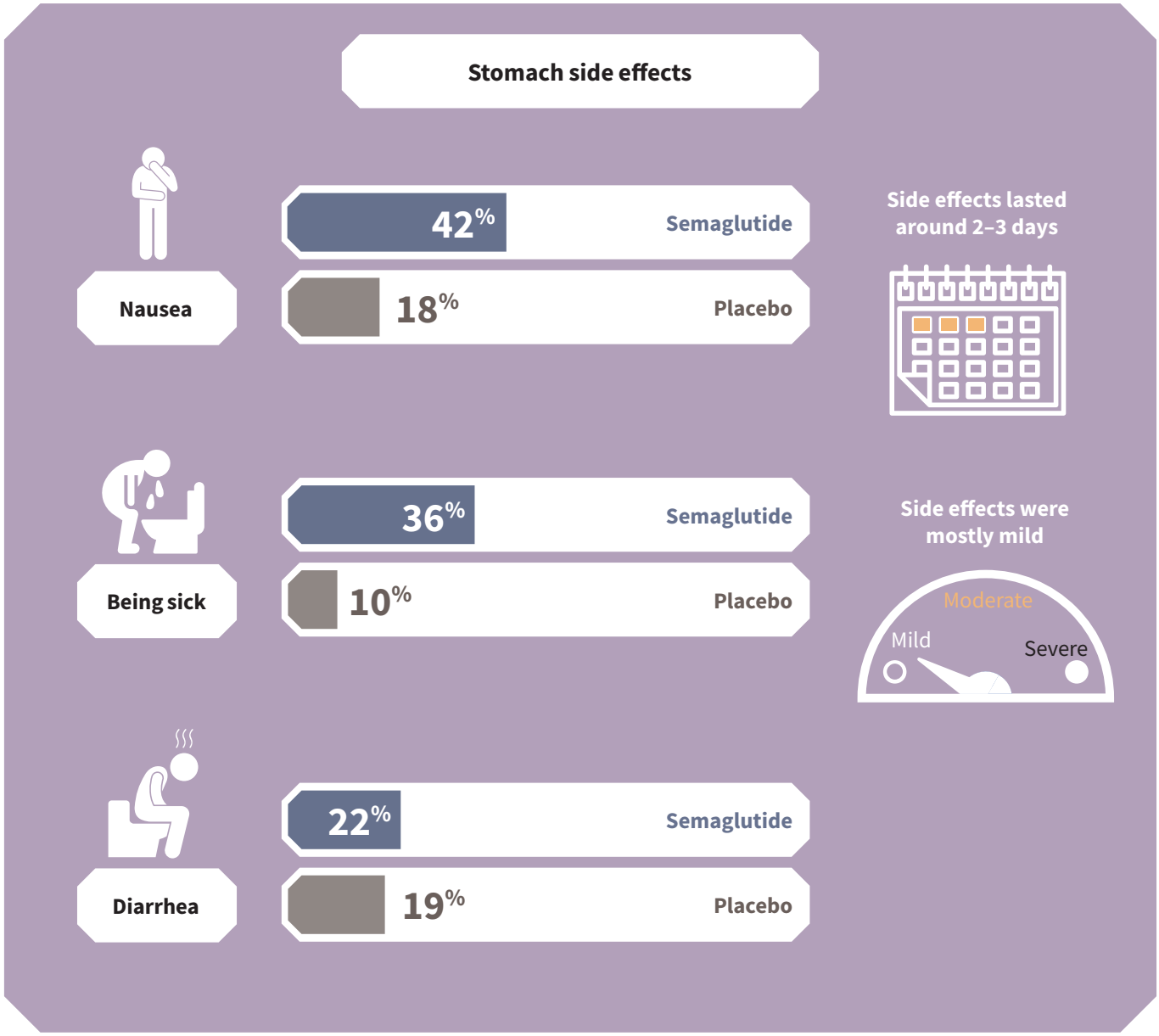
The number of teenagers reporting side effects with **semaglutide** was similar to the number reporting side effects with **placebo**. The most common serious side effect was gallstones, which did not happen very often. No deaths were reported in this study.



The number of participants here might be different from the number of participants who started the study. This is because these numbers only include the participants who received a dose of study treatment.

2 The most common side effects with semaglutide were stomach problems

The most common side effects with semaglutide were stomach problems, such as nausea and vomiting (feeling sick or being sick to the stomach). These side effects were expected by the researchers, as similar side effects have also been seen in other studies with semaglutide and in studies of other similar medicines. Most of the side effects were mild and happened at the beginning of the study while the teenagers got used to the medicine. For most of the teenagers, these side effects went away after a few weeks.



What do the results of this study mean?

This study is the first to find out whether semaglutide can be used to treat obesity in teenagers aged 12 or over, but less than 18 years old.

In this study, researchers looked at the effect of the medicine semaglutide on BMI compared with placebo.

The researchers reported benefits in teenagers treated with semaglutide compared with placebo.
These included:

- A decrease in BMI of around 17%
- Weight loss of around 18 kg (40 lbs)
- More teenagers achieving weight losses of more than 5%, 10%, 15%, and 20% compared with the group given placebo
- Improvements in some risk factors for other diseases caused by obesity.

Semaglutide is already used to treat overweight (with underlying health issues) and obesity (with or without underlying health issues) in adults. The side effects reported for semaglutide in this study in teenagers were similar to the side effects of semaglutide in adults.

The results from this study show that semaglutide can be used to help teenagers with obesity to lose weight when it is used alongside healthy eating and exercise. These results are for this study only. Other studies with different types of people may show different results.

Glossary of terms used in this summary

Blinding: When people take part in a research study and they do not know which of the medicines being studied are being given to them, it is called "blinding". For research studies that use a placebo (a dummy medicine that has no effect on the body; see **Placebo**) in a blinded fashion, the people taking part do not know if they are given the placebo or the active medicine. This is because knowing you are taking a placebo can change how you behave in a study, which can in turn affect the results. This way researchers can see if the active medicine works as it was expected to.

Blood lipids: Your blood is the transport system used by your body to carry many things essential for life. These include red blood cells that carry oxygen and white blood cells that help the body fight off infections. Particles of fat are also present in the blood, which the body can use as energy. However, because fat does not dissolve in water, fats have to be carried around the body in special packages called lipids. Lipids can join with proteins in your blood to form lipoproteins, which are important to the cells in the body and are used for making energy. If the levels of lipids in the blood are too high, it can lead to problems with your heart and blood vessels.

Blood pressure: The pressure of the blood circulating in your body pushes against the walls of your veins and arteries. Most of the pressure comes from the heart pumping blood through the blood vessels.

Blood sugar: The level of sugar (called glucose) in the blood.

Body mass index: Often shortened to BMI. A measurement used to find out if you are a healthy weight for your height. A healthy BMI in children and teenagers depends on their age and sex. This is because their height, weight, and body fat are affected by growth and development. Most children and teenagers are considered a healthy weight if their BMI is above the 5th percentile and below the 85th percentile of a reference (i.e., similar) population of other people of the same age and sex (see **Percentile**).

Caregiver: The person who is caring for a child or teenager (for example a parent or guardian).

Healthcare professionals: A person trained to work in healthcare, such as a doctor, dietitian, nutritionist, nurse, weight specialist, psychologist, or psychiatrist.

Hormones: Chemicals that send messages around your body.

Obesity: A long-term disease in which too much body fat is stored, which can lead to health problems.

Percentage increase or decrease: Percentages can be used to show the relative change between an old value and a new one. For example, if someone weighs 90 kg and they lose 9 kg, their new weight would be 81 kg. The 9 kg change from 90 kg to 81 kg would be a 10% decrease (because 9 is 10% of 90). If they gained 9 kg, their new weight would be 99 kg, a 10% increase from their starting weight of 90 kg.

Percentile: Percentiles are used to help see whether children and teenagers are a healthy weight by comparing their BMI with the BMI of others of the same age and sex from a reference population. The range of BMI values for each age group and sex in the reference population are ordered from lowest to highest. The percentiles act as set cut points in this range to show you the highest BMI for different proportions of the reference population. You can then see how a child or teenager's BMI compares with the BMI in the reference population at the cut point. For example, if a 15-year-old boy's BMI is within the 85th percentile, it means that his BMI is lower than the highest BMI value seen in 85% of the 15-year-old boys in the reference population. He would therefore be considered a healthy weight (see **Body mass index**). However, if his BMI was above the 95th percentile, that would mean it was higher than the highest BMI value seen in 95% of the reference 15-year-old boys and he would be confirmed as having obesity.

Placebo: A placebo is not a medicine, but it looks like one. A placebo has no effect on the body.

Randomization: In some research studies, people are chosen by chance (or randomized) to be given either the active medicine or a placebo. The process of randomly putting people into treatment groups is called randomization (like flipping a coin, for instance). The people in the research study would not know which group they were randomly put in and so would not know which treatment they were given (this is called "blinding"; see **Blinding**).

Risk factor: Something that increases the chance of getting a disease.

Side effect: An unintended, often negative reaction to a drug or treatment. Side effects differ from person to person and can vary from minor problems (like a runny nose or headache) to serious issues (such as a heart attack or liver damage).

Teenager: A person between childhood and adulthood. In the STEP TEENS study, the people were aged 12 or over, but less than 18 years old.

Treatment difference: When measuring the effect of a medicine and a placebo in a research study, the difference between the two measurements (i.e., the measurement for the medicine and the measurement for the placebo) is known as the treatment difference. The treatment difference gives you an idea of how much better or worse the medicine was than the placebo.

Who sponsored this study?

The STEP TEENS study was sponsored by Novo Nordisk A/S.

Where can readers find more information on this study?

Original article
The original article this summary is based on, 'Once-Weekly Semaglutide in Adolescents with Obesity', was published in the *New England Journal of Medicine*

You can read the full article for free at: https://www.nejm.org/doi/10.1056/NEJMoa2208601

Trial registration site
You can read more about the STEP TEENS study at the following trial registration website:
https://clinicaltrials.gov/ct2/show/NCT04102189

Educational resources
European Association for the Study of Obesity [Patients]:
https://easo.org/patients/

Global Obesity Patient Alliance (GOPA):
https://www.gopa.org

Obesity Action Coalition (OAC) – Learn about Childhood/Adolescent Obesity:
https://www.obesityaction.org/education-support/learn-about-childhood-obesity

Obesity Action Coalition:
https://www.obesityaction.org/

The European Coalition for People Living with Obesity (EASO ECPO) – Education:
https://eurobesity.org/education

United Nations Children's Fund (UNICEF) – Prevention of Overweight and Obesity in Children and Adolescents: Advocacy Strategy and Guidance:
https://www.unicef.org/media/92331/file/Advocacy-Guidance-Overweight-Prevention.pdf

World Health Organization (WHO) – Fact Sheet on Obesity and Overweight:
https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight

World Obesity Federation (WOF):
https://www.worldobesity.org

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Financial & competing interests disclosure
Full disclosure information for the authors can be found in the original article, found at the link above.