Better4All
– A study on digital support for overweight individuals

Participant information

To those who wish to participate in Better4All trial, conducted by researchers at Karolinska Institutet (KI)

Before you decide to participate in the study, it is important that you understand why it is being conducted and what it means for you to participate. Therefore, please take the time to read the information below and ask the research team any questions you may have if anything is unclear. Once you feel that you have received answers to your questions about the study and your participation, you can decide whether or not you want to participate. If you decide to participate, we will ask you to sign an informed consent form digitally. You can withdraw from the study at any time without giving a reason and without any consequences.

What is the purpose of the study?

Overweight and obesity are increasingly common and represent a significant public health challenge. They arise from a combination of factors, including genetic influences, the body's natural adaptations, lifestyle and behavioural patterns, and environmental conditions, which together make long-term weight management challenging. Artificial Intelligence (AI) may play an important role in future weight management, as AI can analyse large amounts of data about an individual and thus better predict how an individual will respond to various changes in their lifestyle. By finding patterns and tailoring support to each individual, AI can improve treatment, increase compliance and thus the chances of lasting results.

The BETTER4U project (Preventing obesity through Biologically and **bE**haviorally **T**ailored in**TER**ventions **for you**) is funded by the European Union (EU) and is an international collaboration with 28 partners in Europe, Israel and Australia. Karolinska Institute is the principal investigator for the project in Sweden. The research principal refers to the organisation responsible for the project. The research has been approved by the Swedish Ethical Review Authority, reference numbers Dnr: 2025-06172-01 and 2025-09015-02.

The project started in November 2023 and will run until October 2027. The aim of BETTER4U is to use digital tools and machine learning (AI) to develop an intervention

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that can be tailored to each individual, thereby improving the treatment of overweight and obesity.

The main purpose of the current study, Better4All, is to evaluate the effect of a personalized weight management program for adults who are overweight or obese. The intervention will be delivered through digital tools and individual consultations with a health coach, trained healthcare professionals/experts in nutrition and health, who, if necessary, will adapt the AI-based lifestyle recommendations together with the participants and set appropriate goals. The digital tools (an app and a smartwatch) enable both the participant and the health coach to monitor and adjust the set goals during the course of the study as needed.

The Better4All study is being conducted simultaneously at seven European universities. In addition to KI, the following universities are participating: Harokopio University (HUA), Greece, University of Navarra (UNAV), Spain, SWPS University (SWPS), Poland, Centre for Studies and Research in Social Dynamics and Health (CEIDSS), Portugal, University of Cyprus (UCY), Cyprus, and Centre de Recherche en Nutrition Humaine Rhone-Alpes (CRNH RA), France. Participants will be recruited from all these locations, and the data will be combined and analyzed together.

Who can participate in the study?

We are recruiting 146 adults (aged 18–65) who are overweight or obese according to their body mass index (BMI), i.e. ≥25. You can calculate your BMI by dividing your weight in kilograms by your height in meters squared. To participate, you need to be otherwise healthy (physically and mentally) and not be undergoing weight treatment or taking medication that affects your weight. You also need to be able to speak and understand Swedish or English well enough to be able to complete the study.

To participate, you also need to have an Android mobile phone.

How does the study work?

You will participate in the study for 12 months. The intervention will last for 6 months, during which we will meet on 5 occasions. You will also be invited to a follow-up visit after a further 6 months.

Before we meet for a physical visit, we will ask you to sign a consent form and then send you a link so that you can answer some questions about yourself in a questionnaire. The questions are about who you are (age, gender, country of birth, level of education, family) and questions about your health, food and drink habits, physical activity, smoking, sleep, and mental health.

After you have completed the online questionnaire, we will book an appointment for you at Karolinska Institutet. Below, we describe what will happen during the study's six visits.

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Visit 1: During the visit, we will measure your weight, height, and waist circumference. We will also take your blood pressure, and a trained nurse will take blood samples to examine your metabolic health and DNA (see Fact Sheet on Polygenic Risk Scores (PRS) below). We will also send you a small kit so that you can easily take a stool sample at home and bring it with you to your next scheduled visit with us. This sample will be analyzed and provide us with results about your gut flora.

In order to proceed to the next visit, all baseline data must be collected.

After this screening visit, we will **randomly assign you to one of the study's two groups, the intervention group or the control group**. Both groups will use digital tools and have individual visits with a health coach during the study. The difference between the groups is that the recommendations given to the intervention group are based on collected data and have been developed using AI.

Visit 2: During this visit, you will have your first health consultation with a trained health coach. The coach will help you set achievable goals to improve your health based on your current situation—for example, your eating habits, physical activity, and sedentary lifestyle.

To get the best possible support, we ask you to bring the results of your most recent blood tests, if you have had any taken in the last 12 months. We also ask you to bring the stool sample that you were instructed to collect during your first visit.

During the visit, you will also receive a smartwatch that connects to your mobile phone via Bluetooth. You will also have access to a mobile app called BETTER4U, where you can track your lifestyle and habits yourself. During the visit, we will show you how to use the smartwatch and the BETTER4U app during the 6 months of the study.

Visit 3 (in person OR remotely): One month after visit 2, we will schedule visit 3. During this visit, you will meet with your health coach, and if it is an in-person visit, your weight will be measured. If the visit is remote, we will ask you to measure and report your weight yourself.

Visit 4: Three months after visit 1, it's time for visit 4 (halfway point). Before the visit, we'll send you a link so you can fill out some surveys (you can also do this in person). We'll also check your weight, height, waist measurement, and blood pressure. After the measurements, you'll have a meeting with your health coach. You will also receive a stool sample collection kit to bring with you to your next visit.

Visit 5: After six months, the intervention ends. During this visit, we will measure your weight, height, waist circumference, and blood pressure, and we will also collect blood samples and a stool sample. Before the visit, we will send you a link so that you can answer the questionnaires (you can also fill these in on site).

During this visit, you will also be asked to answer some questions about your experience of the app and your participation. To find out how you experienced your participation in

the study and the tools we have used, you may be asked to participate in a telephone interview. Participation in the interviews is entirely voluntary.

We conclude the visit by scheduling a follow-up visit six months later. Until then, we encourage you to continue with the lifestyle changes you have made and stick to the goals you have set. You are also encouraged to continue using the watch and app to keep track of your habits.

Visit 6: After six months (12 months after the start of the study), you will have your final visit. Before the visit, we will send you a link so that you can complete the final questionnaires (you can also fill these in on site). During the visit, we will measure your weight, height, waist circumference, and blood pressure. You will also return the smartwatch you have used during the study period, and your account in the Better4All app will be closed.

Benefits of participating

By participating in the study, you will contribute to important knowledge about how we can best design and implement individually tailored interventions to treat overweight and obesity in adults in the future. We hope that through your participation, you will also receive valuable support and information (such as weight status, feedback on metabolic health such as blood sugar, insulin, blood lipids) about your own health and habits in a way that is beneficial to you.

What are the risks of participating in the study?

The study complies with ethical rules and laws as well as international guidelines for conducting research studies, known as the Declaration of Helsinki and Good Clinical Practice (GCP). There is no obvious risk involved in participating in this study, but participants may find it unpleasant to have blood samples taken or to be weighed. However, experienced staff who are used to performing these measurements will participate in the project and will ask you how you are feeling before the measurements are taken.

What does your participation mean?

During the study period, you will participate in a total of six visits, five at KI and one digital visit. You will be asked to complete questionnaires prior to four of these visits and provide blood and stool samples on two occasions. We will also measure and weigh you, take your waist measurement and blood pressure, and ask you about your health on five occasions.

In addition to the questionnaires and measurements described above, you will wear a smartwatch daily for 12 months on your dominant hand, for at least 10 waking hours and while you sleep.

Before each visit to us, we will ask you to record your food intake for three days prior to the scheduled visit. The recording is done by photographing all your meals (food and

drink) using the app and answer additional questions. You will also be asked questions about your perceived appetite at each meal. Throughout the study period, data will be collected continuously via the BETTER4U app, both passively and actively.

Before visits where blood samples are taken, you need to fast for at least 12 hours prior to the visit. This means that you should not eat or drink anything (except water) during that time, in order for the test results to be as accurate as possible.

How is your information and collected data handled and stored?

The data collected from you will be processed, analyzed, and stored confidentially and used solely for research purposes. Karolinska Institutet is responsible for your personal data. Your data will be processed in accordance with the EU General Data Protection Regulation (GDPR), and your responses and results will be handled in such a way that unauthorized persons cannot access them. Only people involved in recruitment, data collection, and analysis will have access to your data. In addition, all identities will be coded so that they can only be traced back to you as a person using a code key. The code key is stored on Karolinska Institutet's server and separately from the data material. Only researchers at Karolinska Institutet who are participating in the project have access to it. When the results of the study are presented, it will not be possible to identify you as an individual.

As the project is a collaboration between several partners, the collected data will also be handled by researchers outside Europe. The data shared with our partners will be stored on a password-protected server at Aristotle University in Thessaloniki and Harokopio University in Athens, Greece. Researchers at the University of Bern, Switzerland, and WINGS ICT Solutions in Greece will also have access to pseudonymized data. These researchers are experts in their field and need access to data relevant to their tasks within the study, i.e., developing digital tools and analyzing data. No unauthorized person will have access to your data.

The data will be stored for at least 10 years after the last publication in accordance with the Karolinska Institute's rules for archiving research data. In the future, your data may be used for other related research and development of algorithms in accordance with the EU's Open Data Directive for publicly funded research. It will then be completely anonymous and cannot be linked to you as a person. The Karolinska Institute (Karolinska Institutet Huddinge, 08-524 80 00) is responsible for processing the data.

Under the EU's General Data Protection Regulation, you have the right to access the data about you that is processed in the study free of charge. If necessary, you can have any errors corrected. If you choose to discontinue your participation in the study, no further data will be collected, but we have the right to retain the data that has already been collected. In this case, this data will be anonymized so that it cannot be traced back to you in any way.

If you would like to access the data, please contact the project manager (Anna Ek, anna.ek@ki.se). If you have any questions about how your personal data is processed, please contact Karolinska Institutet's data protection officer (dataskyddsombud@ki.se).

If you are dissatisfied with how your personal data is processed, you have the right to lodge a complaint with the Swedish Data Protection Authority, which is the supervisory authority.

What happens to my samples?

From the blood samples we collect, we analyze your DNA, gene expression (RNA), hormones, metabolic markers such as blood sugar, blood lipids, bacteria in the gut, and so-called metabolites, substances that are formed when the body breaks down food and drugs, for example, or when the body breaks down its own tissue. It is important to note that your DNA and RNA are not analyzed in a way that can reveal your identity. This means that the samples cannot be directly linked to you as a person. Your data will be handled in such a way that your identity is protected (pseudonymized data).

The collected biological samples (blood and stool samples) will be sent to Harokopio University in Athens, Greece, for storage and onward transport to relevant partners for analysis, namely: Weizmann Institute of Science (WIS) in Israel for microbiome analysis, Università degli Studi di Cagliari (UNICA) in Italy for metabolome analysis, and Bioclinica SA in Romania for biochemical analysis, Helmholtz Zentrum München – German Research Center for Environmental Health (HMGU) in Germany for genetic analysis (genotyping), and Pirkanmaan Hyvinvointialue, Tampere University Hospital (TAUH) in Finland for biomarker analysis (adipokines and lipidomics). Your samples will be stored in two locations: the central biobank at Harokopio University in Athens (HUA Biobank) and, in smaller quantities, at the KI Biobank.

The samples we keep at KI will be used to analyze how the circadian rhythm is affected by the intervention by looking at gene expression (RNA), hormones, and metabolites in the blood. The researcher responsible for these analyses is Paul Petrus, associate professor at the Department of Medicine, Huddinge (MedH) and the Department of Physiology and Pharmacology at KI.

The samples stored can be kept for up to 15 years. This is done in order to be able to perform new analyses related to the study, now or in the future. When the samples are no longer needed, they will be destroyed. The code key to the samples is stored on KI's server and is processed so that unauthorized persons cannot access them.

You have the right to refuse to allow the samples to be stored without giving any explanation. If you consent to the samples being stored, you have the right to later withdraw (revoke) that consent without giving any explanation. In that case, your samples will be discarded or de-identified. If you wish to withdraw your consent, please contact the principal investigator with your address and telephone number.

The samples may only be used in the manner to which you have given your consent. If you agree to allow us to store and use your samples for future purposes, you must give your specific consent to this. If research that is not yet planned is added, the Ethical Review Authority will decide whether you should be asked again.

If you have any questions regarding the transfer of data to our partners, please contact the principal investigator, Dr. Ioannis Ioakeimidis (see contact details below).

How will I receive information about the results of the project?

The results of the study will only be reported at group level and cannot be traced back to you personally. The results will be presented in scientific journals, reports, at conferences, and posted on the study's website. The results may also be published and communicated in popular science contexts. Compiled data that cannot be linked to individual persons may thus become available to other researchers in order to support future research or the development of other technological solutions outside the current project.

Compensation

A symbolic compensation is paid in the form of a gift certificate (200 SEK/gift certificate) at visits 1, 5 and 6 as a thank you for participating in the study.

Participation in the study is voluntary

Your participation is, of course, voluntary, and you may choose to withdraw at any time without providing an explanation. However, we will need to meet with you again so that you can return the smartwatch you borrowed from us. If you wish to withdraw from the study, please contact project manager Anna Ek (see contact details below) with your name, address, and telephone number.

Thank you for your interest in BETTER4ALL!

If you have any questions, we will be happy to answer them.
Please contact us at B4U-medh@ki.se

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Fact sheet: What is the Polygenic Risk Score (PRS)?

As part of BETTER4ALL's intervention, we will calculate several **polygenic risk scores** (PRS) in order to provide more **personalised advice for weight loss**.
Below you will find clear information about what PRS are and how they are used in the project.

What is PRS and how should it be understood?

A **PRS is a value that shows how your genes can influence various behaviours and bodily functions**, such as weight, physical activity or sedentary behaviour.

The value is calculated by looking at many small differences in your genome (DNA). Your results do **not** predict your future, but they can show whether you have a **slightly higher or lower hereditary risk** compared to others.

Do all people have the same PRS?

No, everyone has different PRS values because each person has their own combination of genetic traits. This means that your PRS for, say, weight, physical activity or sedentary behaviour may be **higher, lower or about average** compared to others.

Why are researchers interested in these values?

Researchers want to understand **how genes and lifestyle are linked**.
In the BETTER4ALL project, we want to see if **personalised advice based on PRS** gives better results in weight loss than standard advice. In the future, this could help develop better ways to **prevent and treat overweight and obesity**.

How does this affect you as a person, and what can you do about it?

Your PRS will be used alongside other information about your health and lifestyle to provide you with **personalised** weight loss **recommendations**.

Important to know: **A high PRS does not mean that you will gain weight or become inactive.** It just means that you have **a slightly higher genetic tendency** to do so.
Regardless of your PRS value, you can positively influence your health through lifestyle changes and the right support.

How is my genetic information protected?

Your genetic data will be handled **very securely and in accordance with data protection regulations (GDPR, EU 2016/679)**. The data will **only** be used for the purposes stated in the consent form and information sheet.

Only **specially trained** experts will have access to the **original DNA files** (which are very large and technically difficult to interpret), and then only to calculate PRS values. Your data **will never be used to judge, discriminate against or negatively influence you**.

Can I see my PRS results?

You will **not** receive your PRS results directly in numerical form. However, they will be used **in your personal health profile in the BETTER4U programme** so that the advice you receive is better suited to you.

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