

# The effect of physical exercise on markers of aging

<b>Submission date</b> 19/04/2022	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 25/04/2022	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 03/10/2023	<b>Condition category</b> Other	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

As we age the body functions deteriorate and the body is more susceptible to chronic diseases. That is why it is important to promote healthy aging in order to preserve independence and quality of life in old age. Healthy ageing can be advanced with regular physical activity and exercise. Physical activity is one of the most important ways to slow down the physical, mental and cognitive decline associated with aging. Aging is a complex process in which many different factors interact. There are different aging measures which try to describe the biological aging process. These measures can be used to assess if a treatment such as physical exercise is effective and advance healthy aging. Therefore, the aim of this study is to investigate the effect of the 6-month home-based exercise training on different biological aging measures and other markers of aging.

### Who can participate?

50-70-year old physically inactive adults who don't smoke and don't have major chronic diseases.

### What does the study involve?

Participants are allocated to one of two groups. Those in the exercise group train for 24 weeks according to a training program consisting of Nordic walking two or three times per week and resistance training with elastic bands two times per week. Participants are instructed three times before they start to exercise but otherwise they train independently at home and are contacted by phone and messages. Those in the control group continue their normal life. All participants take part in the same assessments and measurements before and after the 24-week study period. These include questionnaires and assessments done at rest, tests for functional capacity and physical performance, fasting blood samples and oral glucose tolerance tests. In addition, each participant will measure their physical activity and sleep at home for 7 days.

### What are the possible benefits and risks of participating?

All participants receive information about their health, functional capacity and physical performance. Participants in the exercise group receive three teaching sessions for the exercise training and a training program. This training program is given to all participants after the study, especially recommended if proven beneficial. Possible risks related to physical exercise include muscle soreness and pain and injuries e.g. in the ligaments but risks are estimated to be low

when starting easily enough at low or moderate intensity. Slight pain and bruises can emerge when drawing blood samples.

Where is the study run from?  
Samfundet Folkhälsan (Finland)

When is the study starting and how long is it expected to run for?  
June 2022 to December 2025

Who is funding the study?  
1. Samfundet Folkhälsan (Finland)  
2. Medicinska Understödsföreningen Liv och Hälsa (Finland)  
3. Finska Läkaresällskapet (Finland)

Who is the main contact?  
Niko Wasenius  
niko.wasenius@helsinki.fi

## Contact information

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## Additional identifiers

**Clinical Trials Information System (CTIS)**  
Nil known

**ClinicalTrials.gov (NCT)**  
Nil known

**Protocol serial number**  
HUS/467/2022

## Study information

**Scientific Title**  
The effect of physical eXercise on phenotypic AGE acceleration in adults approaching later life: a randomized controlled trial

**Acronym**  
XAGE

**Study objectives**  
The 24-week physical exercise intervention has a beneficial effect on phenotypic age and phenotypic age acceleration and other phenotypic markers of aging in people approaching later life.

**Ethics approval required**  
Old ethics approval format

**Ethics approval(s)**

Approved 12/04/2022, Helsingin ja Uudenmaan sairaanhoitopiirin alueellinen lääketieteellinen tutkimuseettinen toimikunta (The Ethics Committee of the Helsinki and Uusimaa Hospital District; PL 705, 00029 HUS, Finland / Biomedicum Helsinki 2C, 7. krs, Tukholmankatu 8 C, 00290 Helsinki, Finland; +358 (0)40 359 4618, eettiset.toimikunnat@hus.fi), ref: HUS/467/2022

## **Study design**

Single-centre interventional randomized controlled trial

## **Primary study design**

Interventional

## **Study type(s)**

Prevention

## **Health condition(s) or problem(s) studied**

Effects of physical exercise on markers of aging in physically inactive adults approaching later life

## **Interventions**

Participants are randomized 1:1 either to the control group or the exercise intervention group after all the baseline measurements. A computerized randomization sequence is used, stratified by sex and age with a 1:1 allocation using block sizes of 10–15.

Control group: Participants will receive the national physical activity guidelines.

Exercise intervention group: A 24-week Nordic walking and resistance training program where training load is planned to increase progressively. Nordic walking 2-3 times a week for 30-60 minutes at the relative intensity of 50-70 % of heart rate reserve and resistance training for the main muscle groups with elastic bands 2 times a week for 30 minutes. Training program and exercises are instructed to the participants before the intervention. Otherwise participants perform exercises at home without supervision but are contacted (calls/messages) according to the predetermined schedule.

## **Intervention Type**

Behavioural

## **Primary outcome(s)**

1. Phenotypic age measured using a fasting blood sample as a linear combination of chronological age and nine multisystem clinical chemistry biomarkers at baseline and 24 weeks
2. Phenotypic age acceleration measured using a fasting blood sample as a residual of phenotypic age after accounting for chronological age at baseline and 24 weeks

## **Key secondary outcome(s)**

1. (Relative) leucocyte telomere length is measured from whole blood leukocyte DNA using quantitative real-time polymerase chain reaction at baseline and 24 weeks
2. DNA methylation is measured from blood and saliva samples using techniques based on methylation arrays to compute b (% methylation) values for each CpG site at baseline and 24 weeks
3. Epigenetic clocks are measured from blood and buccal swab samples using the methylation information at baseline and 24 weeks  
(updated 04/05/2022, previously: Epigenetic clocks are measured from blood and saliva samples)

using the methylation information at baseline and 24 weeks)

4. Mitochondrial function is measured using near-infrared spectroscopy (NIRS) and markers of mitochondrial function from fasting blood samples at baseline and 24 weeks

5. Inflammatory markers (CRP, hs-CRP) are measured using fasting blood samples at baseline and 24 weeks

6. Lipid (total cholesterol, HDL-cholesterol, LDL-cholesterol, and triglycerides) and glucose (fasting plasma glucose, fasting plasma insulin, and hemoglobin A1c) metabolism markers are measured using fasting blood samples and oral glucose tolerance test at baseline and 24 weeks.

7. Metabolomics measured with nuclear magnetic resonance (MNR) from fasting blood samples at baseline and 24 weeks

8. Gut microbiota are measured from stool samples with techniques based on the 16S-rRNA gene sequencing and separately Short Chain Fatty Acids (SCFA) content is determined from stool samples at baseline and 24 weeks

9. Advanced glycation end products (AGE) are measured using the AGE reader as skin autofluorescence at baseline and 24 weeks.

10. Body composition (lean body mass, fat mass, fat%) is measured using bioimpedance and anthropometrics (height, weight, body mass index, waist and hip circumference) at baseline and 24 weeks

11. Muscle strength is measured using the grip strength test, the upper body dynamic strength test and the repetitive squat test for the lower body at baseline and 24 weeks

12. Physical performance is measured using a spiroergometry test (VO<sub>2</sub>max, Pmax), a 6,1-meter walk test (normal and maximal walking speed) and a one-legged stance test (balance) at baseline and 24 weeks.

13. Sleep is measured using the ActiGraph wGT3X-BT-accelerometer at baseline, at the 8th week, at the 16th week and at the 24-week and using the Oura-ring at baseline, during the whole 24-week intervention and at 24 weeks

14. Physical activity is measured using the ActiGraph wGT3X-BT-accelerometer at baseline, at the 8th week, at the 16th week and at the 24-week and using the Oura-ring at baseline, during the whole 24-week intervention and at the 24-week. Leisure-time physical activity is also measured using an exercise diary and Polar Vantage M multisport watch during the whole 24-week intervention.

15. Health-related quality of life (HRQoL) is measured using the 36-Item Short Form Survey (SF-36) at baseline and 24 weeks

16. Depressive symptoms are measured using the Beck Depression Inventory (BDI) at baseline and 24 weeks

## **Completion date**

31/12/2025

## **Eligibility**

### **Key inclusion criteria**

1. Non-smoker or quit smoking  $\geq 1$  year ago

2. Age 50–70 years

3. Body mass index  $\geq 25$  and  $< 32$  kg/m<sup>2</sup>

4. Passed medical examination to participate

5. Not following a regular physical exercise regime or having a physically active lifestyle

6. Finnish or Swedish as a first language

### **Participant type(s)**

Healthy volunteer

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

50 years

**Upper age limit**

70 years

**Sex**

All

**Key exclusion criteria**

1. Pre-existing, or history of major cardiovascular disease (coronary artery disease, heart failure, stroke, peripheral vascular disease)
2. Type 1 diabetes
3. Type 2 diabetes
4. Cancer
5. Neurodegenerative disease (e.g. Alzheimer's disease, Parkinson's disease)
6. Rheumatoid arthritis
7. Chronic obstructive pulmonary disease (COPD)
8. Diagnosed moderate or severe depression
9. Use of metformin or other hyperglycemia medication
10. Scheduled to undergo major surgery in the next 6 months
11. Findings detected during spiroergometry that limit safe participation to the intervention according to the Finnish national guidelines

**Date of first enrolment**

01/08/2022

**Date of final enrolment**

01/04/2025

**Locations****Countries of recruitment**

Finland

**Study participating centre**

**Samfundet Folkhälsan i svenska Finland r.f.**

Topeliuksenkatu 20

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# Sponsor information

## Organisation

Folkhälsans Forskningscentrum

## ROR

<https://ror.org/05xznzw56>

## Funder(s)

### Funder type

Research organisation

### Funder Name

Samfundet Folkhälsan

### Alternative Name(s)

Folkhälsan Foundation, Folkhälsan

### Funding Body Type

Private sector organisation

### Funding Body Subtype

Other non-profit organizations

### Location

Finland

### Funder Name

Medicinska Understödsföreningen Liv och Hälsa

### Alternative Name(s)

Medicinska Understödsföreningen Liv och Hälsa r.f.

### Funding Body Type

Private sector organisation

### Funding Body Subtype

Associations and societies (private and public)

### Location

Finland

**Funder Name**

Finska Läkaresällskapet

**Alternative Name(s)**

Finnish Medical Society, Finnish Society of Physicians, Finnish Medical Association, Finska Läkaresällskapet r.f., FLS

**Funding Body Type**

Government organisation

**Funding Body Subtype**

Associations and societies (private and public)

**Location**

Finland

## Results and Publications

**Individual participant data (IPD) sharing plan**

The datasets generated and analysed during the current study will be available upon request from Niko Wasenius (niko.wasenius@helsinki.fi). Data will be shared in the EU/EEA region according to the general data protection regulations, Finnish national data protection act (1050/2018) and the act on the secondary use of health and social data (552/2019). Data will become available after the data collection has ended and the data has been cleaned and processed. Third-party usage requires a legal contract between the register holder and the third party. Data will be shared only for the original purpose of the study.

**IPD sharing plan summary**

Available on request

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes
<a href="#">Study website</a>	Study website	11/11/2025	11/11/2025	No	Yes