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The effect of physical exercise on markers of aging

Submission date 19/04/2022	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 25/04/2022	**Overall study status** Completed	
Last Edited 03/10/2023	**Condition category** Other	

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?
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Additional identifiers

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

Primary study design
Interventional

Study design
Single-centre interventional randomized controlled trial

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_2max, 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 ≥1 year ago
2. Age 50–70 years
3. Body mass index ≥25 and <32 kg/m²
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.
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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?
Study website	Study website	11/11/2025	11/11/2025	No	Yes