A randomised controlled study of the long-term effects of exercise training on mortality in elderly people: study protocol for the Generation 100 study

Dorthe Stensvold,1,2 Hallgeir Viken,1,2 Øivind Rognmo,1,2 Eirik Skogvoll,2,3 Sigurd Steinshamn,1,4 Lars J Vatten,1,5 Jeff S Coombes,6 Sigmund A Anderssen,7 Jon Magnussen,5 Jan Erik Ingebrigtsen,8 Maria A Fiatarone Singh,9,10,11 Arnulf Langhammer,5 Asbjørn Støyle,3,12 Jorunn L Helbostad,13,14 Ulrik Wisløff1

ABSTRACT

Introduction: Epidemiological studies suggest that exercise has a tremendous preventative effect on morbidity and premature death, but these findings need to be confirmed by randomised trials. Generation 100 is a randomised, controlled study where the primary aim is to evaluate the effects of 5 years of exercise training on mortality in an elderly population.

Methods and analysis: All men and women born in the years 1936–1942 (n=6966), who were residents of Trondheim, Norway, were invited to participate. Between August 2012 and June 2013, a total of 1567 participants (790 women) were included and randomised to either 5 years of two weekly sessions of high-intensity training (10 min warm-up followed by 4×4 min intervals at ∼90% of peak heart rate) or, moderate-intensity training (50 min of continuous work at ∼70% of peak heart rate), or to a control group that followed physical activity advice according to national recommendations. Clinical examinations, physical tests and questionnaires will be administered to all participants at baseline, and after 1, 3 and 5 years. Participants will also be followed up by linking to health registries until year 2035.

Ethics and dissemination: The study has been conducted according to the SPIRIT statement. All participants signed a written consent form, and the study has been approved by the Regional Committee for Medical Research Ethics, Norway. Projects such as this are warranted in the literature, and we expect that data from this study will result in numerous papers published in world-leading clinical journals; we will also present the results at international and national conferences.

Trial registration number: Clinical trial gov NCT01666340.

BACKGROUND

Owing to worldwide increasing longevity, the world population is rapidly ageing. It has been estimated that the proportion of people aged 60 years and older will double from about 11% in 2000 to 22% in 2050, and the age group 65 years and older will, for first time, outnumber children under the age of 5 by 2017. In Norway, life expectancy in women and men is predicted to increase by 10 years from 83 and 79 years, respectively, over the next 80 years. Future demands for healthcare services depend on illness and disability in the older population. Active ageing is a term used by WHO to describe “the process of optimizing opportunities for health, participation and security, in order to enhance quality of life and wellbeing as people age”, and includes delay of senescence and compression of morbidity and mortality. With societal expectances of an increasing older population, interventions that compress years with disability alongside increased life expectancy are warranted. The ageing process is characterised by functional and physiological changes, and includes a decline in activity, mobility,
maximal oxygen uptake (VO\textsubscript{2max})\textsuperscript{7} and muscle mass.\textsuperscript{8} In addition, the risk of most diseases, including type 2 diabetes,\textsuperscript{9} pulmonary diseases,\textsuperscript{10} cardiovascular diseases,\textsuperscript{11} cancer,\textsuperscript{12} and mental disorders such as depression and dementia,\textsuperscript{13} all increases with age.\textsuperscript{14} \textsuperscript{15} Physical activity and social engagement have been emphasised as important pathways to improve and maintain health in the elderly.\textsuperscript{16} \textsuperscript{17} It has been shown that older people who report being inactive reach a disability threshold (defined as needing help from another person to carry out several daily-life activities) 14 years earlier than those who report being highly active.\textsuperscript{18} Importantly, becoming physically active even in older age seems to provide health benefits.\textsuperscript{19} Randomised, controlled trials have shown that regular exercise training increases fitness\textsuperscript{20} \textsuperscript{21} and reduces several of the traditional risk factors for cardiovascular disease.\textsuperscript{22} \textsuperscript{23} It has also been shown that high-intensity exercise training has the potential to induce larger increases in VO\textsubscript{2max} and cardiovascular function than low-intensity or moderate-intensity training in healthy individuals,\textsuperscript{24} as well as in people with metabolic syndrome\textsuperscript{25} and in those with hypertension, and in patients with heart failure,\textsuperscript{26} intermittent claudication\textsuperscript{27} and coronary artery disease.\textsuperscript{28} \textsuperscript{29} However, reducing traditional risk factors for disease does not necessarily result in longer survival as it has been shown, exemplified by pharmacological interventions, that initial improvements in surrogate markers are not able to show corresponding effects on major end points.\textsuperscript{30} \textsuperscript{31} Multiple epidemiological studies have suggested that physical activity is associated with a reduced risk of premature death\textsuperscript{32} \textsuperscript{33} \textsuperscript{34} \textsuperscript{35} and that poor physical fitness is a strong predictor of mortality.\textsuperscript{36} \textsuperscript{37} \textsuperscript{38} Even a small difference in fitness appears to make a substantial impact on survival.\textsuperscript{39} Furthermore, epidemiological studies have suggested that physical activity is associated with lower risk for developing diabetes,\textsuperscript{40} hypertension,\textsuperscript{41} depression,\textsuperscript{42} dementia,\textsuperscript{43} breast cancer,\textsuperscript{44} colon cancer\textsuperscript{45} and of accidental falls.\textsuperscript{46} Although many reports suggest that high physical activity and fitness may have favourable health effects, there is a possibility that the level of physical activity is strongly correlated with a person’s state of health, and may not be the cause of it. Thus, there is a need for large randomised controlled studies that can test the long-term effects of exercise training on social participation, disability, disease and survival in the general population. The Generation 100 study will be the first large controlled randomised clinical trial where the primary aim is to study effects of exercise training on total mortality in an elderly population. The present paper describes the design and significance of the Generation 100 study.

**AIMS**

*Primary aim of Generation 100*

- To determine the effects of regular exercise training over a 5-year period on overall mortality in elderly people (70–76 years of age).

*Secondary aims of Generation 100*

- To evaluate the effect of high-intensity versus moderate-intensity training over a 3-year and 5-year period on traditional risk factors for cardiovascular disease, maximal oxygen uptake, physical activity level, pulmonary function, muscle strength, gait speed and characteristics, need for prescription medications, falls and fall-related injuries, dementia, depression, fatigue, rate of hospitalisation, and cost and use of healthcare services (general physician, nursing homes and home care).

- To increase the knowledge regarding genetic predisposition for fitness (VO\textsubscript{2max}) and cardiovascular diseases in order to facilitate prevention strategies before symptoms appear. We also intend to identify potential therapeutic targets by searching for blood-borne factors induced by training, using transcriptomics (messenger RNAs and microRNAs) and proteomics arrays.

**METHODS**

**Design**

This is a phase IIb clinical trial, where the participants are stratified by sex and marital status and randomised 1:1 into an exercise training group or to a control group (figure 1). The exercise training group was further randomised 1:1 into moderate-intensity or high-intensity training. Inclusion started August 2012 and ended in June 2013. The study will run until June 2018. The participants are tested at baseline (before randomisation) and at follow-up after 1, 3 and 5 years. The Unit for Applied Clinical Research at the Norwegian University of Science and Technology developed the randomisation procedure to ensure impartial assignments. After randomisation, participants received verbal and written information about their intervention. Participant data can be linked to the following registries until 2035: Cause of Death Registry, Statistics Norway, Norwegian Patient Register (NPR), National Injury Registry, Cancer Registry of Norway, Norwegian Myocardial Infarction Registry, National Population Register, GERICA (use of municipal care services) and the Norwegian Prescription Database. Generation 100 was registered in a clinical trials registry in August 2012 (ClinicalTrials.gov, Identifier: NCT01666340). All protocol modification must be approved by the Regional Committee for Medical Research Ethics, Norway. Participants are given a project-specific code. This project code is used during all analyses of the data. The procedures for data entry, coding and storage have been developed in close collaboration with the Norwegian Data Inspectorate and the Regional Committee for Medical Research Ethics, Norway. The participants gave informed, written consent to the main study and to receive invitations to...
Substudies. Participation in the main study is not influenced by willingness to participate in substudies. All substudies must have approval from the Regional Committee for Medical Research Ethics, and studies will not involve interventions that are in conflict with the main study.

**Settings and participants**

This study is conducted in Trondheim, the third-most populous municipality in Norway, with a population of 176,348 on January 1, 2012. Healthcare is provided predominantly by a public system, financed through general taxes, with no or nominal charge. All men and women born from January 1, 1936, to December 31, 1942, with a permanent address in the municipality of Trondheim (6966 people, 3721 women) were invited to participate (Figure 1). Potential participants were identified through the National Population Register. An invitation letter consisting of an informational brochure about the study, a health-related questionnaire and a response sheet with a consent form was sent to potential participants. All individuals were asked to return the response sheet with the consent form and the questionnaire independent of willingness to meet at baseline examinations. Inclusion and exclusion criteria are given in box 1. In total, 46% (3212) responded, 1422 were not interested while 1790 consented to participate. Of the 1790 people who initially said they were interested, 49 persons were excluded, and 174 actively withdrew or did not show up for testing. Thus, 1567 people, 777 men (72.5±2.1 years) and 790 women (72.5±2.1 years) were included (Figure 1). Sample characteristics, based on the questionnaire (see online supplementary file 1) sent out with the invitation letter are shown in Table 1. The portion of sedentary behaviour is lower in the participants included in our study compared with those who did not participate. Interestingly, 26% of those who did not want to participate reported to be highly active (almost every day), while the corresponding number among the participants was 22%. In the non-participating group, 32% reported to have higher education (college/university), which is the same percentage as for those who are 67 years and older in the general Norwegian population. In the participating group, 50% reported to have higher education. In total, 87% of the included participants and 66% in the non-participating group reported to have good health. Thus, the participants in our study are more active, have higher education and better health compared with the non-participating group.
of retirement is 67 years, thus we wanted to include people shortly after their working career ended. Initially, people born between 1938 and 1942 (inclusive) were invited. However, acceptance was lower than expected and fewer than 1500 participants were enrolled in the study. Therefore, in order to increase the sample size according to power calculations (see below), we additionally included those born in 1936 and 1937.

## Ethics

The risk of exercise is considered very small; however, the risk of complications/death is higher during and immediately following training/testing. Nevertheless, the health benefits from exercise training are sufficiently high and are considered less harmful than inactivity. The control group will not have access to supervised exercise training. However, they will be advised to follow current national guidelines for physical activity and will not take part in guided training. This reflects the ‘treatment’ currently offered to the public. Providing sufficient clear information is a high priority, so that participants feel that they know what consenting entails.

## Examinations

Figure 2 shows the physical test battery and examinations performed at baseline after 1, 3 and 5 years in all groups. All test personnel were blinded for intervention. Briefly, four different questionnaires are used in this study: Questionnaire 1 was sent out together with the invitation letter, thus those who wanted to participate and those who did not want to participate were both asked to fill out this questionnaire containing 21 health-related questions. Questionnaire 2 consisted of more detailed questions about specific aspects of health, lifestyle, social environment and family medical history. The short form health survey SF-8 (1-week recall version) is used to describe quality of life and chronic pain (Q3). The questions from Q1, Q2 and Q3 have

## Table 1 Descriptive statistics of people included in the study and those who did not want to participate

<table>
<thead>
<tr>
<th></th>
<th>Included</th>
<th>Not participating</th>
<th>p Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of participants</td>
<td>1567</td>
<td>1361</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Age (years)</td>
<td>72</td>
<td>73</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>172 (9)</td>
<td>171 (9)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>75 (13)</td>
<td>76 (14)</td>
<td>NS</td>
</tr>
<tr>
<td>College/university education (%) (SD)</td>
<td>50</td>
<td>32</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>9</td>
<td>12</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Self-reported health (%)</td>
<td></td>
<td></td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Poor</td>
<td>13</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>87</td>
<td>66</td>
<td></td>
</tr>
<tr>
<td>Self-reported diseases (%)</td>
<td></td>
<td></td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>5</td>
<td>11</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Angina pectoris</td>
<td>3</td>
<td>7</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Heart failure</td>
<td>0.7</td>
<td>3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>6</td>
<td>12</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>5</td>
<td>11</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Cancer</td>
<td>16</td>
<td>19</td>
<td>NS</td>
</tr>
<tr>
<td>Mental health problems</td>
<td>9</td>
<td>11</td>
<td>NS</td>
</tr>
<tr>
<td>Living condition, percentage of participants</td>
<td></td>
<td></td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Per cent living alone</td>
<td>25</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>Per cent living with others</td>
<td></td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>PA, percentage of participants</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>9</td>
<td>16</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Moderate</td>
<td>69</td>
<td>58</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>High</td>
<td>22</td>
<td>26</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

High, almost every day; low, less than once a week; moderate, 1–3 times per week; NS, non-significant (>0.05); PA, physical activity.

---

many of the same questions that have been used in the Nord-Trøndelag Health Study (HUNT). In addition, the participants are also asked to fill out a diet form. Only those who were included in the study fill out questionnaire Q2–Q4. Blood samples are obtained from an arm vein. Serum triglycerides, glucose, high-density lipoprotein, total cholesterol, C reactive protein, glycosylated haemoglobin (HbA1c) and c-peptide are measured immediately using standard procedures at St Olav's Hospital, Trondheim, Norway. Serum and EDTA-treated plasma are centrifuged at 3000 rpm for 10 min at 20°C. Aliquots are stored at −80°C, in case new blood markers will be analysed later. In addition, full blood from EDTA is taken and stored (at Regional Biobank) at −80°C for later DNA analysis. Blood pressure is taken in fasting state at rest and immediately after exercise testing. Testing of VO2max is performed on a treadmill identical to that used in previous studies in our group, and participants with previous heart diseases are tested under ECG monitoring, and the American College of Cardiology/American Heart Association (ACC/AHA) guidelines for exercise testing of patients with known cardiovascular disease is followed. Body composition and weight are measured using bioelectrical impedance (Inbody 720, BIOSPACE, Seoul, Korea). Gait characteristics are measured by the GAITRite electronic gait mat (CIR Systems Inc, Havertown, Pennsylvania, USA). Grip and leg strength were measured by the JAMAR Hydraulic Hand Dynamometer (Lafayette Instrument Company, USA) and a leg press machine (FCM 5540 Leg Press Rehab Standard, Helsinki University of Research, HUR, Finland), respectively. Objectively measured physical activity is assessed by SenseWear Armband activity monitor (BodyMedia 7, Pittsburgh, Pennsylvania, USA) or by Actigraph (GT3X, Manufacturing Technology Inc, Florida, USA). After the clinical test at the hospital, all participants are given either SenseWear or Actigraph monitor. The participants are instructed to wear it for 7 days continuously (24 h), except when in contact with water (shower/bath/swim). The lung function tests are performed with the Sensormedics Vmax22 Encore (CareFusion, San Diego, California, USA) in accordance with the American Thoracic Society/European Respiratory Society (ATS/ERS) recommendations. Cognitive function and brain structure were tested using a combination of questionnaires and MRI of the brain using 3 T with 32 channel head coil and the following protocol: three-dimensional T1-weighted ADNI, Flair, T2 and SWI volumes, and diffusion tensor imaging. Novel genetic biomarkers (serum, plasma, DNA, RNA) will be analysed using high-throughput OMICS technology (genotyping or exome sequencing, DNA methylation, RNA sequencing, microRNA screening, mass spectrometry-based proteomics and MR metabolomics) using validated methods established at Norwegian University of Science and Technology’s Genomics, Proteomics and Metabolomics Core Facilities. Health economic analysis will be calculated as the sum of hospital cost (inpatient, day care and outpatient care), use of general physician and primary healthcare (rehabilitation, nursing homes, home care, etc).

Sample size and statistics

Overall mortality was selected as the primary outcome for the sample size calculation. For this purpose, the exercise intervention groups (moderate and high intensity) will be pooled and compared with the control group. Epidemiological studies have reported a 50% lower death rate after 14–16 years of follow-up in people who are active compared with those who are inactive. In Trondheim (2010), 2% of the population between 70 and 77 years old died, and the expected mortality rate after 5 years will be approximately 10%. With a power of 90%, about 600 participants are needed in each group to detect a 50% reduction in mortality (ie, from 10% to 5%). We aimed to include 1500 participants to allow for up to 20% of dropouts. It is unknown, however, whether exercise has an effect on mortality. We therefore focus...
on the precision of the estimated absolute mortality group difference in terms of the expected width of the resulting CI for the true difference. With 750 participants in each group, the expected 95% CI width will be between 0.05 and 0.06 depending on the observed mortality in the intervention group (figure 3). We think this precision is acceptable and emphasise that it does not depend on whether the result is statistically significant or not. The comparisons of change between the groups will be made by the intention-to-treat principle. Thus, data will be analysed according to the group that participants are assigned to, regardless of possible crossover and/or adherence to the intervention. In addition, we will perform a per protocol analysis, based on adherence to the intervention. The analysis will be made based on whether participants have followed the prescribed intervention or not. Non-adherence will be defined as having performed less than 50% of the prescribed training sessions over the 5 years. Survival and morbidity analysis will be carried out by performing \( \chi^2 \) and log-rank tests. Cox regression analyses will be used to compute HRs of all-cause mortality and onset of new diseases between the groups. The precision of the estimates will be assessed by 95% CIs. All statistical tests will be two-sided.

**Interventions**

**High-intensity training**

Participants randomised to high-intensity training are asked to complete two weekly ∼40 min long workouts. The participants are instructed to use a Borg 6–20 scale (rating of perceived exertion) as guidance for exercise intensity.59 They are supervised to perform a light 10 min warm-up, followed by 4 min working periods (intervals) interspersed by 3 min active breaks. The intensity during the intervals should be 85–95% of peak heart rate, corresponding to approximately 16 on the Borg scale.59 60 Breaks consist of working at an intensity corresponding to ∼12 on the Borg scale (60–70% of peak heart rate). Every sixth week the participants meet for a supervised spinning session (ergometer cycling) where they exercise with a heart rate monitor, to ensure that they exercise at the recommended intensity, as described above. In addition, organised training is offered twice per week in different walking areas around Trondheim. Attendance to these activities is voluntary, and participants may choose to perform their exercise training individually. The activity type performed will vary between seasons of the year and includes indoor and outdoor activities such as: walking/running, cross-country skiing and aerobics.

**Moderate-intensity training**

To obtain isocaloric exercise, participants randomised to moderate-intensity training are asked to complete 50 min of continuous moderate-intensity exercise corresponding to 70% of peak heart rate (‘talking pace’) twice a week.27 61 The participants are instructed to use the Borg scale as guidance for exercise intensity, and the exercise intensity should be perceived as approximately 13 on the Borg scale.59 60 The protocol regarding frequency and type of exercise was the same as for the high-intensity group.

**Control group**

The control group will be instructed to follow current recommendations for physical activity in Norway,62 meaning 30 min of moderate-level physical activity every day. No further supervision is given.

**Adherence**

Different strategies are used to improve and evaluate adherence to exercise training. Participants in the exercise groups are asked to fill in exercise logs immediately after each exercise session and send all the logs to the research centre either in prepaid envelopes monthly, or to use internet-based forms following each exercise session.63 The procedures for reporting were prepared after consulting the Regional Committee for Medical and Health Research Ethics and the Data Inspectorate of Norway. To increase motivation, spouses are randomised to the same intervention group. The control group reported their physical activity level once a year, using a questionnaire. All participants are invited to an information meeting once a year, and newsletters are sent out twice a year. The participants can contact the administration of the study by phone or email, and they can find all necessary information about the study and the different interventions on the study’s homepage.64 An adherence committee was initiated after 1 year. The committee will be responsible for implementing measures that increase adherence in the exercise groups, such as arranging different activity events.
Organisation
The steering committee of Generation 100 has developed the study protocol and is responsible for data collection, management, publications and the final data set. All major scientific and ethical questions will be resolved by majority vote. The committee is responsible for finding solutions to unforeseen questions/problems that arise in the course of the study. In addition, a Safety committee, consisting of two physicians, will continuously monitor the safety of the study and the study progression. The first 300 included in the study filled out a safety report 1 month after the initiation of the study. In addition, participants fill out a safety report every year after the initiation of the training. The participants should report if there has been: no special events, worsening of disease, newly diagnosed disease, or if they have been in the hospital. In addition, participants are asked to classify the cause of the event to different diseases/incidents. Furthermore, the Norwegian population registry is checked every year to uncover unreported mortality. Five times during the study, the safety committee will evaluate if there are any differences in the number of events between the groups (1 month, 1 year, 2 year, 3 year and 4 year), and continuously evaluate if it is ethically justifiable to let the study continue. Adverse events during training and testing will be reported to the safety department at the university. The study has one physician (medical director), who will take care of those participants suffering from harm related to participation in the study.

Dissemination
Participants will receive their test result immediately after the test. In addition, participants will be invited to an annual meeting where general and new information will be given. Providing sufficient information to the participants is a high priority. It is anticipated that Generation 100 will garner widespread interest and media attention, and will have results in a series of articles that will be published in highly ranked international scientific journals.

DISCUSSION
To our knowledge, Generation 100 will be the first study with the primary aim of examining whether exercise has an effect on mortality in an older population. Generation 100 is unique because of the large sample size, because the entire population is invited and because of the long intervention period. The descriptive data demonstrate that a larger portion of those who were randomised reported better health, higher education and less heart disease compared with those who did not participate. However, the study consists of a diverse group of elderly people, as healthy people and people with many different diseases are both included. The heart failure-action (HF-action) study was the first large (n=2331, average age 59 years, 661 females) randomised study with the primary aim of evaluating the effect of exercise alone on all-cause mortality and all-cause hospitalisation.65 In contrast to Generation 100, HF-action only included patients with heart failure. After adjusting for highly prognostic predictors, exercise training was associated with a significant, but modest, reduction in mortality and hospitalisation.66 However, the intervention in that study included only 36 supervised exercise sessions, followed by home-based exercise, and, importantly, only 38% of the participants in the exercise group fully adhered to exercise after 1 year.67 Exercise training with high intensity has previously shown to induce greater cardioproteective effect compared with moderate exercise.22 27 47 68 To our knowledge, Generation 100 will be the first study to evaluate the long-term effect of both high-intensity training and moderate intensity on how people age. Longevity seems to be an important health goal for most western countries, and improved health, increased self-reliance and preventing diseases are highlighted as important strategies to reduce the anticipated financial burden of an ageing population.1 15

Data from Generation 100 will contribute to an improved understanding and provide solutions on how to achieve active ageing. Further, our data will demonstrate if exercise can be used as a preventive intervention for disease and functional decline, and give more and healthier years to those who are systematically physically active. If proven beneficial, exercise as medicine will be a relatively cheap, accessible and available treatment, with few negative, but a large number of positive side effects that can be offered systematically to a large ageing population. The use of exercise as prevention and treatment will potentially benefit a large proportion of the population, and may give a significant economic benefit both at an individual level and from a societal perspective. In conclusion, Generation 100 will give new knowledge to whether exercise has an impact on morbidity and mortality in elderly people, and further if exercise training has an impact on several major health issues that affect the elderly population. In light of the ageing population, our data will hopefully contribute to a better understanding of ageing, and serve as an example of how to implement large health initiatives in the future.

Author affiliations
1KG Jebsen Center of Exercise in Medicine at Department of Circulation and Medical Imaging, Faculty of Medicine, Norwegian University of Science and Technology, Trondheim, Norway
2St Olav’s Hospital, Trondheim University Hospital, Trondheim, Norway
3Department of Circulation and Medical Imaging, Faculty of Medicine, Norwegian University of Science and Technology, Trondheim, Norway
4Department of Thoracic Medicine, St Olav’s Hospital, Trondheim University Hospital, Trondheim, Norway
5Department of Public Health and General Practice, Faculty of Medicine, Norwegian University of Science and Technology, Trondheim, Norway
6School of Human Movement Studies, University of Queensland, Queensland, Australia
7Department of Sports Medicine, The Norwegian School of Sport Sciences, Oslo, Norway
8Institute for Science in Sport, Norwegian University of Science and Technology, Trondheim, Norway


Open Access
Acknowledgements The authors thank the Clinical Research Facility at St Olavs Hospital for excellent assistance during the testing periods; all master and bachelor students who contributed to collection of data; and SIT (the student organisation in Trondheim), for helping out with locations for spinning sessions.

Contributors All authors meet the ICMJE criteria for authorship. UW and DS take responsibility for the integrity of the study. DS, HV, ØR, ES, SS, LJV, JSC, SAA, JM, JEI, MAFS, AL, AS, JLH and UW were involved in study concept and design. DS, HV, ØR, ES, SS, LJV, JSC, SAA, JM, JEI, MAFS, AL, AS, JLH and UW were involved in acquisition of data. DS, HV, ØR, ES, SS, LJV, JSC, SAA, JM, JEI, MAFS, AL, AS, JLH and UW were involved in drafting and revising the article critically for important intellectual content. DS, HV, ØR, ES, SS, LJV, JSC, SAA, JM, JEI, MAFS, AL, AS, JLH and UW were involved in final approval of the version to be published.

Funding This work was supported by the Norwegian University for Science and Technology (NTNU), Central Norway Regional Health Authority, St Olavs Hospital, Trondheim, Norway, and The KG Jebsen Foundation.

Competing interests None.

Ethics approval Regional Committee for Medical Research Ethics, Norway (REK 2012/381 B).

Provenance and peer review Not commissioned; internally peer reviewed.

Data sharing statement The authors have collected clinical data from the participants. Quality check needs to be performed on this data before it can be published.

Open Access This is an Open Access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

REFERENCES

1. WHO. Ageing and life-course. 28 March 2012.


A randomised controlled study of the long-term effects of exercise training on mortality in elderly people: study protocol for the Generation 100 study

Dorthe Stensvold, Hallgeir Viken, Øivind Rognmo, Eirik Skogvoll, Sigurd Steinshamn, Lars J Vatten, Jeff S Coombes, Sigmund A Anderssen, Jon Magnussen, Jan Erik Ingebrigtsen, Maria A Fiatarone Singh, Arnulf Langhammer, Asbjørn Støylen, Jorunn L Helbostad and Ulrik Wisløff


Updated information and services can be found at: http://bmjopen.bmj.com/content/5/2/e007519

These include:

Supplementary Material
Supplementary material can be found at: http://bmjopen.bmj.com/content/suppl/2015/02/12/bmjopen-2014-007519.DC1.html

References
This article cites 58 articles, 11 of which you can access for free at: http://bmjopen.bmj.com/content/5/2/e007519#BIBL

Open Access
This is an Open Access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections

Geriatric medicine (108)
Public health (963)
Sports and exercise medicine (107)

Notes

To request permissions go to: http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to: http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to: http://group.bmj.com/subscribe/