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# TirolGESUND: General Exercise, Smoking Undone, and Nutrition Diet

**Submission date**
16/12/2022

**Recruitment status**
No longer recruiting

**Registration date**
28/12/2022

**Overall study status**
Completed

**Last Edited**
11/09/2024

**Condition category**
Other

[_] Prospectively registered
[_] Protocol
[X] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

## Plain English summary of protocol

Background and study aims
Smoking and diet are known risk factors for many diseases, including cancer, cardiovascular diseases, or metabolic disorders, and may promote premature cellular ageing. TirolGESUND investigates the effect of two lifestyle interventions, namely smoking cessation or intermittent fasting (both with additional optional exercise), over 6 months for the promotion of health and reduction of disease risk, focusing on women's cancers. We have recently described molecular (epigenetic markers) for risk of being diagnosed, or developing future, women's cancers, hence in this study we are only including female participants. Our primary endpoints are epigenetic markers of cellular ageing and disease risk. Additionally we will explore the impact of other biomarkers of health and disease over the time of the intervention.

Who can participate?
Healthy women aged 30-60 years in the Tirol region of Austria that have elevated disease risk due to heavy smoking (≥10 cigarettes a day for at least 5 years) or elevated body mass index (25-35 kg/m²) are able to participate. Participants should not have prior malignancies or major cardiovascular disorders as the study is primarily aimed to investigate primary prevention of diseases, i.e. prevention of disease occurrence.

What does the study involve?
Depending on participant characteristics, participants will either be guided to stop smoking or undergo intermittent fasting, i.e. eat food only over a window of 8 h per day, for 6 months. Participants are invited to sample collection at baseline and every two months thereafter. Collected samples include cheek swabs, blood samples, cervical samples, as well as fecal, saliva, and urine samples. At baseline and at the main timepoint (6 months), additional clinical tests to determine health status will be conducted, such as lung function and vascular health. Participants are also invited to optionally return at month 12 and month 18 after study initiation to donate follow-up samples.

What are the possible benefits and risks of participating?
Participants will receive support in implementing (putative) health-promoting interventions, including giving up smoking and intermittent fasting over 6 months, and are hence expected to personally benefit from participation. Risks are expected to be minimal as the study involves

only a behavioural/lifestyle change, but can include e.g. development of haematoma after blood sampling, mood swings due to smoking cessation, or hunger at the initiation of intermittent fasting.

Where is the study run from?
The study is run by the European Translational Oncology Prevention and Screening Institute at the University of Innsbruck, and participants are invited to the research clinic every 2 months. Additional study visitations at baseline and 6 months are at other clinical sites.

When is the study starting and how long is it expected to run for?
May 2020 to August 2022

Who is funding the study?
The study is funded by the European Translational Oncology Prevention and Screening Institute at the University of Innsbruck (Austria) and has received funding from the European Union under the Horizon 2020 framework programme, the Land Tirol, and the European Research Council.

Who is the main contact?
Prof. Martin Widschwendter (martin.widschwendter@uibk.ac.at)
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# Contact information

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Principal investigator

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# Additional identifiers

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

### ClinicalTrials.gov (NCT)
Nil known

### Protocol serial number
Innsbruck Clinical Trial Center (CTC) 20210420-2560

# Study information

### Scientific Title
TirolGESUND: Baseline-controlled comparison of the effects of fasting dietary intervention or smoking cessation combined with exercise in healthy female Tyrolean volunteers aged 30-60 on epigenetic and multi-omic biomarkers of health, ageing, and disease

### Acronym
TirolGESUND

### Study objectives
Dietary intervention or smoking cessation result in a modulation of epigenetic biomarker scores of age, environmental exposure and cancer risk compared to baseline over 6 months.

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
Approved 03/12/2020, Ethics Committee of the Medical University of Innsbruck (Anichstraße 35, A-6020 Innsbruck, Austria; +43 (0)50 504-22293; ethikkommission@i-med.ac.at), ref: 1391/2020

### Study design
Single-centre non-randomized baseline-controlled interventional study

### Primary study design
Interventional

### Study type(s)
Other

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

Monitoring of the response of epigenetic and other (multi-omic) biomarkers of ageing, exposure and disease risk to dietary or smoking cessation intervention, with the aim of piloting epigenetic and multi-omic biomarkers as surrogate endpoints for monitoring the prevention of age-associated diseases and cancer in healthy volunteers.

## Interventions
Allocation to intervention depends on participant baseline characteristics (smoking versus non-smoking and elevated BMI).

The dietary intervention encompasses induction (1 month) and maintenance (5 months) of a 16:8 intermittent fasting regime (time-restricted eating to 8 h a day, fasting for remaining 16 h). During the introductory month, participants will only maintain a 14:10 intermittent fasting regime. Within the dietary intervention arm, participants are randomised to receive ketogenic supplement (MCT oil) or not.

Smoking cessation encompasses three guided smoking cessation group therapy sessions (6-12 participants per session) followed by smoking cessation (occuring in the second session).

All study participants, regardless of intervention (dietary or smoking) receive an additional optional exercise programme and motivational coaching over the duration of the study.

For each participant, the main study duration is 6 months with optional follow-up visitations at months 12 and 18.

## Intervention Type
Behavioural

## Primary outcome(s)
Epigenetic biomarkers of ageing and disease risk are measured at baseline and at 6 months using Illumina Human MethylationEPIC array on the samples, to obtain epigenetic WID disease risk and exposure scores

## Key secondary outcome(s))
1. Description of general study characteristics relating to participation and dropout: sign-up rate, drop-out rate, compliance
2. Molecular endpoints (1): Evaluation of temporal and tissue-specific dynamics of epigenetic markers of ageing, disease risk, and exposure (e.g. smoking)
3. Molecular endpoints (2): Evaluation of microbial dynamics in fecal and saliva samples, including changes in overall diversity and proportions of certain beneficial or harmful microbial species in fecal microbiome depending on the intervention, distinction of health and lean individuals using microbiome, distinction of smokers and non-smokers using microbiome, shift in dominant types and association with weight loss and potential changes in functional prediction
4. Molecular endpoints (3): Exploratory investigation of metabolomic alterations in urine and saliva over 6 months of intervention.
5. Molecular endpoints (4): Exploratory investigation of cellular and humoral inflammatory dynamics over 6 months of intervention.
6. Clinical endpoints (1): changes in BMI and body composition (muscle, fat, water, abdominal fat composition) (diet arm of the study).
7. Clinical endpoints (2): changes in smoking status (smoking cessation arm of the study).
8. Clinical endpoints (3): Vascular health, including pulse wave velocity, intima-media thickness, and plaque score before and after intervention.

9. Clinical endpoints (4): Physical activity and health, including activity status measured using the international physical activity questionnaire (IPAQ), sports examination (VO2max), and fitnesstracker (daily steps, active minutes, floors climbed); additionally measuring heart rate variability and resting heart rate
10. Clinical endpoints (5): Pulmonary health before and after intervention as measured by spirometry.
10. Psychological endpoints (1): Health-related quality of life (EuroQoL) before and after 6 months of intervention.

### Completion date
30/08/2022

## Eligibility

### Key inclusion criteria
1. Women aged 30 to 60 years
2. Motivated to change their lifestyle
Smoking cessation intervention:
3.1. Smoking cessation: ≥10 cigarettes per day for at least the last five years
Dietary intervention:
3.2. Dietary intervention: BMI between 25 and 35 kg/m²
NB, should 3a and 3b apply, participants will be allocated to the smoking cessation intervention.

### Participant type(s)
Healthy volunteer

### Healthy volunteers allowed
No

### Age group
Adult

### Lower age limit
30 years

### Upper age limit
60 years

### Sex
Female

### Total final enrolment
156

### Key exclusion criteria
1. Relevant underlying conditions:
1.1. Current or previous malignant tumour or cancer
1.2. Current or previous significant cardiovascular disorder [participants with elevated blood pressure are allowed to participate as long as it is well controlled under their current medication]
1.3. Current or previous metabolic disorder (e.g., diabetes type I or II) [in the dietary intervention

arm, participants with current hypothyroidism/Morbus Hashimoto will be excluded as the switch to intermittent fasting may require a adjustment of their medication]
1.4. Current or previous psychiatric disorder (e.g., eating disorder, depression)
2. Current pregnancy or lactation period
3. Total hysterectomy
4. Known current or previous premalignant lesion of the cervix uteri (CIN2/3)
5. Concurrent participation in another interventional trial

### Date of first enrolment
21/04/2021

### Date of final enrolment
08/02/2022

## Locations

### Countries of recruitment
Austria

### Study participating centre
**European Translational Oncology Prevention and Screening Institute, University of Innsbruck**
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## Sponsor information

### Organisation
Tirol Kliniken

### ROR
https://ror.org/028ze1052

### Organisation
Universität Innsbruck

### ROR
https://ror.org/054pv6659

## Funder(s)

**Funder type**
Government

**Funder Name**
Land Tirol

**Funder Name**
Horizon 2020 Framework Programme

**Alternative Name(s)**
EU Framework Programme for Research and Innovation H2020, Horizon 2020, Horizon 2020 Framework Programme (H2020), Rahmenprogramm Horizont 2020, Horizont 2020, Programa Marco Horizonte 2020, Horizonte 2020, Programme-cadre Horizon 2020, Orizzonte 2020, Programma quadro Orizzonte 2020, H2020

**Funding Body Type**
Government organisation

**Funding Body Subtype**
National government

**Location**

**Funder Name**
European Research Council - BRCA ERC Project

# Results and Publications

**Individual participant data (IPD) sharing plan**
Current IPD sharing plan as of 12/09/2023:
The datasets generated during and/or analysed during the current study, in particular epigenetic, metabolomic, and microbial will be made available either completely anonymised wherever possible, or under controlled access (EGA-European Genome Phenome Archive, https://ega-archive.org/ e.g., due to the sensitive nature of epigenetic data). All data will only be shared in a coded (pseudonymised) or completely anonymised format. Prior to use, any potential collaborators must sign a data access agreement and comply with the terms of data sharing. Some datasets (summary characteristics, or completely anonymised results) may additionally be published as a supplement to the results publications.
Data will be restricted for non-commercial research in the space of healthy ageing research. Sharing is restricted to certain geographical areas that have high GDPR standards.

Previous IPD sharing plan:
The datasets generated during and/or analysed during the current study, in particular epigenetic, metabolomic, and microbial will be stored in a publicly available but access-

controlled repository (EGA-European Genome Phenome Archive, https://ega-archive.org/, or similar), due to the sensitive nature of epigenetic data. All data will only be shared in a coded (pseudonymised) or completely anonymised format. Prior to use, any potential collaborators must sign a data access agreement and comply with the terms of data sharing.
Some datasets (summary characteristics, or completely anonymised results) may additionally be published as a supplement to the results publications.
Data will be restricted for non-commercial research in the space of healthy ageing research.
Sharing is restricted to certain geographical areas that have high GDPR standards.

## IPD sharing plan summary

Stored in publicly available repository, Published as a supplement to the results publication

## Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Participant information sheet | Participant information sheet | 11/11/2025 | 11/11/2025 | No | Yes |
| Statistical Analysis Plan | version 1.0 | 01/11/2022 | 22/12/2022 | No | No |