



**ABTRACTS**  
**from selected cohort presentations at the**  
**Austrian Cohort Research Days**  
**25. - 26. April 2023**  
Hotel Regina, Rooseveltplatz 15, A-1090 Wien

### **The Vorarlberg Health Monitoring and Promotion Programme (VHM&PP)**

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The Vorarlberg Health Monitoring and Promotion Programme (VHM&PP) is a population-based risk factor surveillance programme in Vorarlberg,<sup>1</sup> in which 50%-60% of adult residents participated during 1985-2005, resulting in a cohort size of 185,000 individuals undergoing 716,000 health examinations. Routine examinations and data documentation were conducted and overseen by the Agency for Preventive and Social Medicine (Arbeitskreis für Vorsorge- und Sozialmedizin, aks gesundheit). Acquired parameters include age, sex, height, weight, blood pressure, smoking, blood glucose, total cholesterol, triglycerides, GGT, and uric acid. Owing to linkage with the national cancer and mortality registries, participants' follow-up is ongoing.

As of 2003, VHM&PP data have been applied copiously in epidemiological studies, oftentimes combined with other regional, national, and international data sources (e.g., Vorarlberg cancer registry, regional data on cardiovascular events and hip fractures, Austrian dialysis and transplant registry, transnational data on air pollution, several health surveillance cohorts from Scandinavia). Research has focused on metabolic parameters as risk factors for cardiovascular disease and cancer (total cholesterol inversely associated with cancer, and disparate, gender-related effects on cardiovascular risk), but lately also for hip fractures (uric acid, GGT) and dialysis (insulin resistance, blood pressure, and uric acid but not total cholesterol mediate BMI-related risk of kidney disease).<sup>2</sup>

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## Lifestyle-Intervention Studie: TirolGESUND, SUN-Tirol, LIFE-Tirol

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Substantial demographic changes (in the next 10-20 years, the distribution of > 65-year-olds will represent over 26% of the population) present us with enormous challenges. Known factors such as the absolute and relative increase in the elderly population, the proportion of people with chronic diseases and therefore an increase in the number of people requiring care commensurate with the number of carers falling, have effectively been overlooked by politicians thus far. This represents a dilemma as significant as problematic areas such as the environment and energy and there already exists a health emergency due to a lack of care. The Austrian health care system is one of the most expensive in Europe (10.9% of GDP), but Austria is in the bottom fifth of European countries in terms of healthy life years and spends only 2.1% of health care expenditure on prevention. Austria does not have a structured and comprehensive invitation-based prevention plan that is transparently documented, accessible to patients and doctors, and offered regionally. With a few exceptions (e.g., blood pressure), prevention generally lacks strategies that allow the risk of specific diseases to be assessed and the effectiveness of specific measures to be monitored.

We have therefore initiated 3 studies that should establish a basis that compensates for these deficits and contributes to establishing a sustainable, personalised prevention system in Austria:

1. **TirolGesund** (n=157; completed): Investigated how (i) smoking cessation or (ii) intermittent fasting +/- ketogenic supplementation affects various parameters (epigenome in various tissues, genome, microbiome, metabolome, lung function, vascular elasticity, skin composition, etc.) (at least 4 measurements over 6 – in some cases up to 18 – months).
2. **LIFE-Tirol** (n=600; fully recruited): Prospective randomised trial (stratified by BMI and physical activity level) to study the biological/medical effect of (i) intermittent fasting (“dinner cancellation”), (ii) structured exercise, (iii) stress-reducing exercise, or (iv) the combination of these measures, over a period of 8 months.
3. **SUN-Tirol** (n=200; 107 recruited to date): Prospective study in which smokers are randomised into a group with and a group without “biofeedback” (improvement of epigenetic smoking signatures) after established smoking cessation.

In all three studies, we have or are taking samples (blood, urine, stool, saliva, oral mucosal cells, and cervical smear) every 2 months and have asked the subjects to collect their own morning urine daily over an entire menstrual cycle or 3 times/month (depending on gender and menopausal status) at the beginning and end of the study (filter paper) and to measure ketone bodies three times per week after the fasting period has ended. Vascular elasticity, bioelectrical impedance, and physical condition are also evaluated every two months. A special SUN-LIFE app allows for the stringent documentation of lifestyle habits (incl. diet, exercise, etc.) and for communicating with the test persons and recording their quality of life.

Results of these studies should be incorporated into the optimisation of personalised prevention and supported by a prevention file.



## Combining evidence from multiple cohorts: Individual-participant-data meta-analyses

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Combined analysis of participant-level data from multiple cohorts requires sophisticated methods in data management and statistics. I will provide an overview of such projects I have been coordinating and – as an example – will present details on the Proof-ATHERO consortium.

This consortium involves 74 studies and 106,846 participants with repeat carotid ultrasound and risk factor measurements. Mean age at baseline was 59 years (standard deviation 10); 50 % of participants were female. Over a total of 830,619 person-years of follow-up, the studies recorded 17,270 incident cardiovascular events and 13,270 deaths. In one analysis within the Proof-ATHERO consortium, we evaluated whether carotid intima-media thickness (cIMT) would be a useful surrogate marker for cardiovascular risk in randomised controlled trials. We estimated that interventions reducing the yearly cIMT progression by 10, 20, 30, or 40  $\mu\text{m}$  would yield relative risks of 0.84 (95 % confidence interval 0.75-0.93), 0.76 (0.67-0.85), 0.69 (0.59-0.79), or 0.63 (0.52-0.74), respectively. Results were similar across types of intervention and in a primary vs. a secondary prevention context. Using cIMT progression as a surrogate marker in future cardiovascular outcome trials may therefore facilitate and speed up development and licensing of new therapies.

This research has been funded by the FWF Austrian Science Fund.



## Paracelsus 10,000: A prospective cohort study on the health status of the population of Salzburg, Austria.

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**Background:** Paracelsus 10,000 is a cohort study with the objective to investigate the health status of the population of Salzburg. The focus lies on common non-communicable diseases, mainly cardiovascular, cerebrovascular, and metabolic diseases, and their risk factors. The aim of the study is to establish a large database enabling to study associations between life style, genetic factors and development of common diseases.

**Methods:** Inhabitants of the city of Salzburg and the surrounding area were randomly selected and underwent a detailed investigation: The program included medical examinations, as well as assessments on mental disorders and life style including nutrition and physical activity. From all study participants biological samples were stored in a biobank at -80°C enabling future investigations of biomarkers and utilization of the whole spectrum of multi-omics.

**Results:** Between the years 2013 and 2020, 10,044 participants, 5,176 women and 4,868 men aged between 40 and 77 years, completed a baseline assessment. Special emphasis was put on participants between 50 and 59 years old, representing an age group especially prone to changes in health status.

**Conclusion:** The Paracelsus 10,000 study has the potential to gain new insight into the role of associations between genetic predisposition and life style factors for disease development in the Salzburg population.

**Outlook:** The first follow-up phase of the study started in 2020 aiming to observe the progression of the cohort's health status and the correlation with life style and genetic factors.



## COPLANT – a multicenter cohort study

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Plant-based diets (PBD) are becoming increasingly popular for health, ethical, and environmental reasons. However, high-quality cohorts to evaluate PBD in relation to individual and planetary health outcomes are lacking.

COPLANT was initiated as a multicentre cohort across seven German study centers in 2023 to investigate a broad range of health aspects of plant-based diets. The study is coordinated at the German Federal Institute for Risk Assessment (BfR), Berlin. In 2024, COPLANT-Vienna will join the COPLANT consortium as the eighth study center. At each site, a minimum of 800 adults aged 18-69 years (~50% females) will be recruited. Participants will be sampled by exposure status, i.e. the population will consist of four equally large groups of vegans, vegetarians, pescetarians, and omnivores. The study is launched as a cross-sectional study with a main focus on diet quality, nutrient status, cardio-metabolic health, bone health, exposure to contaminants, and environmental footprints among other topics. Study participants will undergo detailed examinations including biosample collections (blood, urine, fecal samples, saliva). A comprehensive dietary assessment is central to the study. Further assessments include accelerometry and body composition measurements. After baseline between 2024 and 2026 the study will continue as a prospective cohort with online and onsite follow-ups.



## Characteristics of patients and samples of the biobanked cohort from PsoRA (Psoriasis Registry Austria)

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Psoriasis is a systemic inflammatory disease that mechanistically increases life-shortening comorbidity and decreases patient quality of life. To improve patient care, the Austrian Psoriasis Registry (PsoRA), per capita one of the largest population-based registries in the world, was established in 2010. PsoRA is enriched with a wealth of clinical data including short-, mid- and long-term response to treatment, comorbidities, and routine clinical haematology. To pave the way for research in personalised medicine, the collection of cross-sectional blood samples, which are stored in the Biobank of the Medical University of Graz, was started in 2016. To date, the PsoRA biobank cohort contains 733 samples from 560 individuals (~65% male) covering all time points, from treatment naïve to long-term treatment, mostly with different biologics such as IL-17, IL-23 and TNF $\alpha$  inhibitors. The median age of the cohort currently is 46 years and its median BMI 27.4 kg/m<sup>2</sup>. The majority of patients had an excellent response to treatment, with 39% achieving complete remission and another 38% achieving >75% PASI (Psoriasis Area and Severity Index) reduction. In conclusion, the PsoRA biobank cohort in Graz is a valuable resource for research to improve the understanding of psoriasis and support the development of new treatment strategies.



## Successfully building up a broadly usable cohort - example COVID-19 convalescents

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Biobank Graz in cooperation with six divisions took the initiative to collect, process and store biospecimens from COVID-19 convalescents in a longitudinal cohort study.

Between April 2020 and February 2021 more than 360 volunteering COVID-19 convalescents (age:  $\geq 18$ ; avg. age 41 years) were included into the COVID-19 Convalescent Cohort. During the initial visit and four follow-up visits, which took place 1, 2, 5 and 12 months after the first visit, participants donated blood, saliva, serum, plasma, buffy coat and an oral or nasal swab and aliquots were stored at  $-80^{\circ}\text{C}$ . Buffy coat was used for automated isolation of genomic DNA. Data on symptom characteristics, clinical history, lifestyle and pre-history were collected via a questionnaire. All participants signed a broad informed consent. The participating departments filled the collected data points into a shared cohort database (RDA tool) and are using the cohort extensively for very diverse research projects (current usage rate 12%). So far, six papers have been published in peer reviewed journals (1-6).

This "demand-based" biobanking approach is a use-case how Biobanks – as trusted partner between study participants and the scientific community - and associated divisions join forces to efficiently set up highly standardized, well-characterized cohorts of high scientific impact.

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## Long-COVID cohort of the Dept. Cardiology, Medical University of Vienna

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The purpose of our on-going prospective POSTCOV registry is to investigate the clinical presentation and progression of long COVID syndrome and to reveal disease-specific biomarkers for diagnosis, prevention or outcome prediction of Long-COVID syndrome.

Patients with a confirmed COVID-19 infection and symptoms present after 12 weeks who visited the cardiology outpatient clinic are included in this registry, if they had no acute or chronic inflammatory disease (EC: 1008/2021, <https://clinicaltrials.gov> NCT05398952), Institutional registry: <https://innere-med-2.meduniwien.ac.at/kardiologie/wissenschaft-forschung/forschungsprojekte/postcov/>

As of March 2023 we have included 400 individuals in our long-COVID cohort. The median age our cohort is 44.5 (IQR: 33.7–54.9) years and the majority of patients are female (70.1 %).

After registry inclusion, detailed anamnesis, electrocardiogram (ECG), physical exam with blood pressure and heart rate registration, echocardiogram and laboratory investigations are performed. Additional investigations are upon medical indications, such as chest x-ray, lung function, cardiac magnetic resonance imaging, thorax computed tomography or ventilation- perfusion lung scintigraphy. All data are recorded in the MUW specific scientific database (RDA, Research Documentation and Analysis). Blood samples are stored in the Biobank of the MUW, containing RNA-tubes, cfDNA tubes, isolated peripheral blood mononuclear cells, plasma and serum tubes, aliquoted.

The POSTCOV project is supported by the Austrian Science Fund and Bürgermeisterfond der Stadt Wien.