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# Zurich Coronavirus Cohort: an observational study to determine long-term clinical outcomes and immune responses after coronavirus infection (COVID-19), assess the influence of virus genetics, and examine the spread of the coronavirus in the population of the Canton of Zurich, Switzerland

**Submission date**
19/07/2020

**Recruitment status**
No longer recruiting

**Registration date**
22/07/2020

**Overall study status**
Completed

**Last Edited**
14/05/2024

**Condition category**
Infections and Infestations

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

## Plain English summary of protocol

Background and study aims
The ongoing pandemic with the novel coronavirus (SARS-CoV-2) is an unprecedented global challenge with an enormous impact on public health, economies and societies worldwide. Despite intensive research efforts, more information about is needed about the effects of an infection with the coronavirus and its transmission in the population, in order to make well-informed policy decisions to control the spread of the coronavirus and prevent further waves of infection.

It is unclear how the coronavirus infection affects health-related quality of life and what its complications are in the longer term. Furthermore, more knowledge is needed on the spectrum and durability of immune responses and how these relate to immunity against the coronavirus. Moreover, the relation between virus genetics and the severity of disease courses, immune responses and the transmission of the virus in the population are not known. And last, more knowledge is needed about the transmission pathways in the current stage of the pandemic and about what factors are most related to increased transmission.

The aim of this study is to study the long-term clinical outcomes, immune responses, transmission pathways and viral genetics in a representative, population-based cohort of persons infected with the coronavirus and their close contacts in the Canton of Zurich, Switzerland. The findings of this study will be highly important to guide future public health strategies for controlling the spread of the Coronavirus both in Switzerland and worldwide.

Who can participate?
Persons that are infected with the Coronavirus in the Canton of Zurich (so called index cases), as well as their close contacts will be invited to participate in this study.

What does the study involve?
Index cases will be followed up with electronic questionnaires over a total of 3 years. Participants will receive the first questionnaire at enrollment and then again after 2 weeks, 1 month, 3 months, 6 months, 9 months and 12 months. Those consenting to further participation in the study will receive up to six additional questionnaires at 18 months, 24 months, 30 months, 36 months, 42 months, and 48 months after baseline. Questions will be related to the acute illness (COVID-19), quality of life and mental health, clinical outcomes, medical history, details on the contact that led to the infection, protective and risk behaviors, as well as experiences and issues with isolation. A selection of the index cases will additionally be invited for the collection of blood and saliva samples to examine their immune responses, e.g. through antibody and T-cell testing. Blood and saliva collection will take place on seven occasions (after 2 weeks, 1 month, 3 months, 6 months, 12 months, 18 months, 24 months, 30 months, 36 months, 42 months, and 48 months).

Close contacts will be followed up with electronic questionnaires over approximately 2 weeks. Participants will receive the first questionnaire at enrollment and then again at the end of quarantine. The questions will be related to COVID-19 symptoms, details on their contact with the index case, protective and risk behaviors, as well as experiences and issues with quarantine. All close contacts will receive a coronavirus test as early as possible and a selection of close contacts that are tested negative in the first test will be tested again at the end of quarantine. Close contacts that are tested positive for the coronavirus will be invited to participate in the study as index cases.

The study plan additionally involved an analysis of the virus genes from samples obtained through coronavirus testing together with information from contact tracing, to analyze the transmission networks of the coronavirus in the Canton of Zurich and to study the association of virus genetics with disease severity, immune responses and transmissibility. This part of the project could not be realized due to logistical issues arising from the important increase in case numbers in fall 2020.

How does the study adapt to the changing demands of the pandemic? In the face of breakthrough infections, emerging variants of concern, and to examine the effects of (booster) COVID-19 vaccinations, the study follow-up was extended up to 4 years. In addition, index cases reporting a Coronavirus breakthrough infection over the course of the study (after primary infection and COVID-19 vaccination) will be invited for additional assessments with questionnaires and study visits following the reinfection.

What are the possible benefits and risks of participating?
This research project will help to better understand the effects of the coronavirus infection and its spread in the population. This information will be highly relevant for public health decision-makers and patients both locally in Switzerland and internationally. The risks of participating in this study are minimal.

Where is the study run from?
The study is run from the Epidemiology, Biostatistics and Prevention Institute (EBPI) at the University of Zurich, Switzerland.

When is the study starting and how long is it expected to run for?
May 2020 to February 2025

Who is funding the study?
1. Department of Health of the Canton of Zurich (Switzerland)
2. Swiss Federal Office of Public Health (SFOPH) (Switzerland)
3. University of Zurich (UZH) Foundation (Switzerland)
4. Horizon Europe (EU)

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# Additional identifiers

# Study information

## Scientific Title
Zurich SARS-CoV-2 Cohort: Towards a long-term control of SARS-CoV-2 transmission - Identifying the epidemiological, immunological and viral genetic drivers of SARS-CoV-2 transmission and pathogenesis in a representative population-based cohort

## Acronym
ZSAC

## Study objectives
The overall aim of this study is to establish a representative, population-based cohort of individuals infected with SARS-CoV-2 in the Canton of Zurich to characterize clinical outcomes and immunological responses and examine transmission patterns among index cases and their close contacts by combining routine contact tracing and viral genetic analyses.

The project is structured in five work packages (WP) with the following objectives:
WP1. Determine long-term clinical outcomes among SARS-CoV-2 positive individuals
WP2. Examine patterns of SARS-CoV-2 infection and transmission among infected index cases and their close contacts in the context of contact tracing
WP3. Infer the transmission network by combining information from routine contact tracing and genetic sequences of SARS-CoV-2
WP4. Characterize immune responses and the development of immunity among SARS-CoV-2 positive individuals
WP5. Determine and identify the impact of SARS-CoV-2 viral genetics on pathogenicity, transmissibility and immune responses

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
Approved 09/07/2020, Cantonal Ethics Committee Zurich (Stampfenbachstrasse 121, CH-8090 Zurich, Switzerland; +41 43 259 79 70; Info.KEK@kek.zh.ch), ref: 2020-01739.

## Primary study design
Observational

## Study design
Single-centre combined retrospective and prospective longitudinal cohort study and complementary prospective case-ascertained study

## Study type(s)
Other

## Health condition(s) or problem(s) studied
COVID-19 (SARS-CoV-2 infection)

## Interventions
Current intervention as of 13/05/2024:
Individuals diagnosed with SARS-CoV-2 infection (index cases) and their close contacts identified

via the contact tracing activities of the Department of Health of the Canton of Zurich will be asked to provide informed consent for study participation. The study procedures are different for index cases and close contacts and include the following:

Index cases will be followed up over one year using self-administered electronic questionnaires. Evaluations will take place at the time of enrollment (baseline; i.e., as early as possible after identification as an index case), as well as after 2 weeks, 1 month, 3 months, 6 months, 9 months and 12 months after identification as an index case. Participants will be asked for consent for further participation in the study yearly for up to 4 years. Those consenting to further participation will receive up to six additional questionnaires at 18 months, 24 months, 30 months, 36 months, 42 months, and 48 months after baseline. Collected data will include information related to the acute COVID-19 episode (e.g. symptoms, severity, treatment), health-related quality of life and mental health, clinical outcomes (e.g. complications and sequelae of the infection, further healthcare contacts, SARS-CoV-2 reinfection and infection by/reactivation of other pathogens), medical history, details on the relevant contact leading to infection (e.g. setting, timing, factors potentially influencing transmission), protective and risk behaviors, use of digital proximity tracing apps, experiences and issues with isolation, and sociodemographic information. Additional information on relevant medical events, such as potential complications of SARS-CoV-2 or reinfection, may be collected from the treating physicians.

A subsample of index cases (total 500 planned) will additionally be invited for the collection of blood and saliva samples for the determination of immune responses. Evaluations will take place 2 weeks, 1 month, 3 months, 6 months and 12 months after identification as an index case. Those consenting to further participation in the study will be invited to up to six additional evaluations at 18 months, 24 months, 30 months, 36 months, 42 months and 48 months after baseline. Blood samples will undergo a detailed analysis for humoral (antibody) and cellular (T cell) immune responses. This will include the measurement of IgM/IgA/IgG antibodies specific for SARS-CoV-2 (N, S1, RBD, S2 antigens) using the Luminex technology-based test developed by the University Hospital Lausanne (within the framework of the Corona Immunitas Program), SARS-CoV-2 neutralizing antibodies using a neutralization assay, T cell subsets and activation using flow cytometry, SARS-CoV-2 specific T cells using interferon (IFN)-gamma ELISpot assays, and immunodominant SARS-CoV-2 proteins/epitopes using T cell incubation. Saliva samples will be analyzed for saliva antibody responses and additionally be evaluated for SARS-CoV-2 persistence (i.e., shedding) and viral viability (if still present) after the end of the isolation period.

Participants who have a breakthrough SARS-CoV-2 infection after primary infection and COVID-19 vaccination will be identified and asked for consent to participate in the additional assessments. Those consenting will be invited for two additional study visits for blood collection and asked to complete two additional brief questionnaires at 3 and 6 months after the reinfection event. In the additional assessments, we will gather data on the presence, severity and persistence of post-COVID-19 symptoms and immune responses after the breakthrough infection.

Close contacts will be followed up over approximately two weeks using self-administered electronic questionnaires. Evaluations will take place at the time of enrollment (baseline; i.e., as early as possible after identification as a close contact), as well as at the end of quarantine. Collected data will include information related to the presence of COVID-19-related symptoms, details on the relevant contact with the index case (e.g. setting, timing, factors potentially influencing transmission), protective and risk behaviors, use of digital proximity tracing apps, experiences and issues with quarantine, and sociodemographic information.

All close contacts will receive SARS-CoV-2 PCR testing as early as possible after identification as a close contact. A subsample of close contacts who tested negative on the first test (total 300 planned) will be retested at the end of quarantine. Close contacts who test positive for SARS-CoV-2 during study follow-up will be invited to participate in the study as index cases.

To construct the transmission networks of SARS-CoV-2 in the Canton of Zurich, we planned to sequence the available samples from SARS-CoV-2 PCR testing from index cases using full genome sequencing for phylogenetic analyses and to examine the association of viral genetics with disease severity, immune responses and transmissibility. Furthermore, we planned to retrieve pseudonymized information on the transmission networks from contact tracing and compare them with the network constructed through phylogenetic analyses. Work packages based on this information (WP3/WP5) could not be realized due to logistical issues arising from the important increase in case numbers in fall 2020.

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Previous intervention on 08/07/2022:
Individuals diagnosed with SARS-CoV-2 infection (index cases) and their close contacts identified via the contact tracing activities of the Department of Health of the Canton of Zurich will be asked to provide informed consent for study participation. The study procedures are different for index cases and close contacts and include the following:

Index cases will be followed up over one year using self-administered electronic questionnaires. Evaluations will take place at the time of enrollment (baseline; i.e., as early as possible after identification as an index case), as well as after 2 weeks, 1 month, 3 months, 6 months, 9 months and 12 months after identification as an index case. Participants will be asked for consent for further participation in the study after 1 and 2 years. Those consenting to further participation will receive up to four additional questionnaires at 18 months, 24 months, 30 months, and 36 months after baseline. Collected data will include information related to the acute COVID-19 episode (e.g. symptoms, severity, treatment), health-related quality of life and mental health, clinical outcomes (e.g. complications and sequelae of the infection, further healthcare contacts, SARS-CoV-2 reinfection and infection by/reactivation of other pathogens), medical history, details on the relevant contact leading to infection (e.g. setting, timing, factors potentially influencing transmission), protective and risk behaviors, use of digital proximity tracing apps, experiences and issues with isolation, and sociodemographic information. Additional information on relevant medical events, such as potential complications of SARS-CoV-2 or reinfection, may be collected from the treating physicians.

A subsample of index cases (total 500 planned) will additionally be invited for the collection of blood and saliva samples for the determination of immune responses. Evaluations will take place 2 weeks, 1 month, 3 months, 6 months and 12 months after identification as an index case. Those consenting to further participation in the study will be invited to up to four additional evaluations at 18 months, 24 months, 30 months, and 36 months after baseline. Blood samples will undergo a detailed analysis for humoral (antibody) and cellular (T cell) immune responses. This will include the measurement of IgM/IgA/IgG antibodies specific for SARS-CoV-2 (N, S1, RBD, S2 antigens) using the Luminex technology-based test developed by the University Hospital Lausanne (within the framework of the Corona Immunitas Program), SARS-CoV-2 neutralizing antibodies using a neutralization assay, T cell subsets and activation using flow cytometry, SARS-CoV-2 specific T cells using interferon (IFN)-gamma ELISpot assays, and immunodominant SARS-CoV-2 proteins/epitopes using T cell incubation. Saliva samples will be analyzed for saliva antibody responses and additionally be evaluated for SARS-CoV-2 persistence (i.e., shedding) and viral viability (if still present) after the end of the isolation period.

Participants that have a breakthrough SARS-CoV-2 infection after primary infection and COVID-19 vaccination will be identified and asked for consent to participate in the additional assessments. Those consenting will be invited for two additional study visits for blood collection and asked to complete two additional brief questionnaires at 3 and 6 months after the reinfection event. In the additional assessments, we will gather data on the presence, severity and persistence of post-COVID-19 symptoms and immune responses after the breakthrough infection.

Close contacts will be followed up over approximately two weeks using self-administered electronic questionnaires. Evaluations will take place at the time of enrollment (baseline; i.e., as early as possible after identification as a close contact), as well as at the end of quarantine. Collected data will include information related to the presence of COVID-19 related symptoms, details on the relevant contact with the index case (e.g. setting, timing, factors potentially influencing transmission), protective and risk behaviors, use of digital proximity tracing apps, experiences and issues with quarantine, and sociodemographic information.

All close contacts will receive SARS-CoV-2 PCR testing as early as possible after identification as a close contact. A subsample of close contacts tested negative on the first test (total 300 planned) will be retested at the end of quarantine. Close contacts that are tested positive for SARS-CoV-2 during study follow-up will be invited to participate in the study as index cases.

To construct the transmission networks of SARS-CoV-2 in the Canton of Zurich, we planned to sequence the available samples from SARS-CoV-2 PCR testing from index cases using full genome sequencing for phylogenetic analyses and to examine the association of viral genetics with disease severity, immune responses and transmissibility. Furthermore, we planned to retrieve pseudonymized information on the transmission networks from contact tracing and compare them with the network constructed through phylogenetic analyses. Work packages based on this information (WP3/WP5) could not be realized due to logistical issues arising from the important increase in case numbers in fall 2020.

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Previous intervention:
Individuals diagnosed with SARS-CoV-2 infection (index cases) and their close contacts identified via the contact tracing activities of the Health Directorate of the Canton of Zurich will be asked to provide informed consent for study participation. The study procedures are different for index cases and close contacts and include the following:

Index cases will be followed up over one year using self-administered electronic questionnaires. Evaluations will take place at the time of enrollment (baseline; i.e., as early as possible after identification as an index case), as well as after 2 weeks, 1 month, 3 months, 6 months, 9 months and 12 months after identification as an index case. Collected data will include information related to the acute COVID-19 episode (e.g. symptoms, severity, treatment), health-related quality of life and mental health, clinical outcomes (e.g. complications and sequelae of the infection, further healthcare contacts, SARS-CoV-2 reinfection and infection by/reactivation of other pathogens), medical history, details on the relevant contact leading to infection (e.g. setting, timing, factors potentially influencing transmission), protective and risk behaviors, use of digital proximity tracing apps, experiences and issues with isolation, and sociodemographic information. Additional information on relevant medical events, such as potential complications of SARS-CoV-2 or reinfection, may be collected from the treating physicians.

A subsample of index cases (total 500 planned) will additionally be invited for the collection of blood and saliva samples for the determination of immune responses. Evaluations will take place 2 weeks, 1 month, 3 months, 6 months and 12 months after identification as an index case. Blood samples will undergo a detailed analysis for humoral (antibody) and cellular (T cell) immune responses. This will include the measurement of IgM/IgA/IgG antibodies specific for SARS-CoV-2 (N, S1, RBD, S2 antigens) using the ABCORA test developed by the Institute for Medical Virology at the University of Zurich, SARS-CoV-2 neutralizing antibodies using a neutralization assay, T cell subsets and activation using flow cytometry, SARS-CoV-2 specific T cells using interferon (IFN)-gamma ELISpot assays, and immunodominant SARS-CoV-2 proteins/epitopes using T cell incubation. Saliva samples will be analyzed for saliva antibody responses and additionally be evaluated for SARS-CoV-2 persistence (i.e., shedding) and viral viability (if still present) after the end of the isolation period.

Close contacts will be followed up over approximately two weeks using self-administered electronic questionnaires. Evaluations will take place at the time of enrollment (baseline; i.e., as early as possible after identification as a close contact), as well as at the end of quarantine. Collected data will include information related to the presence of COVID-19 related symptoms, details on the relevant contact with the index case (e.g. setting, timing, factors potentially influencing transmission), protective and risk behaviors, use of digital proximity tracing apps, experiences and issues with quarantine, and sociodemographic information.

All close contacts will receive SARS-CoV-2 PCR testing as early as possible after identification as a close contact. A subsample of close contacts tested negative on the first test (total 300 planned) will be retested at the end of quarantine. Close contacts that are tested positive for SARS-CoV-2 during study follow-up will be invited to participate in the study as index cases.

To construct the transmission networks of SARS-CoV-2 in the Canton of Zurich, the available samples from SARS-CoV-2 PCR testing from index cases will be sequenced using full genome sequencing for phylogenetic analyses and to examine the association of viral genetics with disease severity, immune responses and transmissibility. Furthermore, pseudonymized information on the transmission networks from contact tracing will be retrieved and compared with the network constructed through phylogenetic analyses.

## Intervention Type
Other

## Primary outcome(s)
Current primary outcome measures as of 08/07/2022:
WP1. Proportion of SARS-CoV-2 infected individuals developing long-term symptoms or complications related to COVID-19, measured through participant questionnaires and clinical file review up to 36 months
WP2. Secondary infection rate and secondary clinical attack rate among close contacts of SARS-CoV-2 infected index cases, measured through participant questionnaires and SARS-CoV-2 PCR testing at enrollment and at the end of quarantine
WP3. Transmission networks constructed via routine contact tracing data.
WP4.1. Proportion of SARS-CoV-2 infected individuals with measurable anti-SARS-CoV-2 IgA and IgG antibodies, measured using Luminex technology-based antibody testing at 2 weeks, 1 month, 3 months, 6 months, 12 months, 18 months, 24 months, 30 months and 36 months after laboratory confirmation of SARS-CoV-2 infection
WP4.2. Proportion of SARS-CoV-2 infected individuals with SARS-CoV-2 antigen-specific T cells, measured using IFN-gamma assays at 2 weeks, 1 month, 3 months, 6 months, 12 months, 18

months, 24 months, 30 months and 36 months after laboratory confirmation of SARS-CoV-2 infection

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Previous primary outcome measures:
WP1. Proportion of SARS-CoV-2 infected individuals developing long-term complications related to COVID-19, measured through participant questionnaires and clinical file review at 12 months
WP2. Secondary infection rate and secondary clinical attack rate among close contacts of SARS-CoV-2 infected index cases, measured through participant questionnaires and SARS-CoV-2 PCR testing at enrollment and at the end of quarantine
WP3. Transmission network constructed via routine contact tracing data and via phylogenetic analyses of SARS-CoV-2 sequences as determined at the end of follow-up
WP4.1. Proportion of SARS-CoV-2 infected individuals with measurable anti-SARS-CoV-2 IgM, IgA and IgG antibodies, measured using ABCORA testing at 2 weeks, 1 month, 3 months, 6 months and 12 months after laboratory confirmation of SARS-CoV-2 infection
WP4.2. Proportion of SARS-CoV-2 infected individuals with SARS-CoV-2 antigen-specific T cells, measured using IFN-gamma assays at 2 weeks, 1 month, 3 months, 6 months and 12 months after laboratory confirmation of SARS-CoV-2 infection
WP5. Extent of association of viral genetics with pathogenicity or transmissibility of SARS-CoV-2, or immune responses against SARS-CoV-2, measured using phylogenetic mixed-effects models and/or other phylogenetic comparative approaches as determined at the end of follow-up

## Key secondary outcome(s)

Current secondary outcome measures as of 08/07/2022:
WP1.1. General and COVID-19 specific health-related quality of life, measured using the EQ-5D, DASS-21, Fatigue Assessment Scale and MRC dyspnea scale at 2 weeks, 1 month, 3 months, 6 months, 12 months, 18 months, 24 months, 30 months and 36 months after laboratory confirmation of SARS-CoV-2 infection
WP1.2. Proportion of individuals with severe disease courses, defined as requiring hospitalization or leading to death within 28 days of confirmation of SARS-CoV-2 infection, measured through participant questionnaires and clinical file review
WP1.3. Proportion of individuals diagnosed with SARS-CoV-2 reinfection within 36 months of confirmation of SARS-CoV-2 infection, measured using participant questionnaires and contact tracing data
WP1.4. Proportion of individuals diagnosed with a new infection or reactivation of a chronic infection by any pathogen within 36 months of laboratory confirmation of SARS-CoV-2 infection, measured through participant questionnaires and clinical file review
WP1.5. Proportion of individuals requiring hospitalization, ICU admission, mechanical ventilation or death (all cause and COVID-19 related) within 36 months after confirmation of SARS-CoV-2 infection, measured through participant questionnaires and clinical file review
WP1.6. Proportion of individuals with self-reported symptoms and/or known risk factors at time of SARS-CoV-2 testing, measured using participant questionnaires
WP1.7. Proportion of individuals that received treatment against SARS-CoV-2, measured through participant questionnaires and clinical file review at enrollment
WP2.1. Proportion of symptomatic and asymptomatic SARS-CoV-2 infected individuals among close contacts of index cases, measured using participant questionnaires and contact tracing data at enrollment and at the end of quarantine
WP2.2. Serial interval of SARS-CoV-2 infection, calculated based on data from participant questionnaires
WP2.3. Factors potentially influencing SARS-CoV-2 transmission between SARS-CoV-2 infected index cases and their close contacts, measured using participant questionnaires at enrollment

WP2.4. Barriers and facilitators, worries and personal burden related to adhering to quarantine measures among close contacts of SARS-CoV-2 infected index cases, measured using participant questionnaires at enrollment and at the end of quarantine
WP4.1. Proportion of individuals with neutralizing anti-SARS-CoV-2 antibodies, measured using neutralization assays at 2 weeks, 1 month, 3 months, 6 months, 12 months, 18 months, 24 months, 30 months and 36 months after laboratory confirmation of SARS-CoV-2 infection
WP4.2. Proportion of individuals with non-severe and severe COVID-19 that develop anti-SARS-CoV-2 antibody, neutralizing antibody, and/or T cell responses, based on the aforementioned measurements at 2 weeks, 1 month, 3 months, 6 months, 12 months, 18 months, 24 months, 30 months and 36 months
WP4.3. Level and durability of anti-SARS-CoV-2 antibody, neutralizing antibody, and/or T cell responses among SARS-CoV-2 infected individuals with non-severe and severe COVID-19, based on the aforementioned measurements at 2 weeks, 1 month, 3 months, 6 months, 12 months, 18 months, 24 months, 30 months and 36 months
WP4.4. Proportion of SARS-CoV-2 infected individuals with long-term virus persistence (shedding) and viral viability of virus specimen in such individuals, measured by using SARS-CoV-2 PCR testing of saliva samples and virus cultures at 2 weeks and thereafter in 2 weekly intervals until tested negative, stratified by different levels of immune responses
WP4.5. Level and durability of anti-SARS-CoV-2 antibody, neutralizing antibody, and/or T cell responses among SARS-CoV-2 infected individuals receiving a COVID-19 vaccination.
WP4.6. Proportion of SARS-CoV-2 infected or SARS-CoV-2 infected and COVID-19 vaccinated individuals experiencing a reinfection/breakthrough infection.
WP4.7. Level and durability of anti-SARS-CoV-2 antibody, neutralizing antibody, and/or T cell responses in SARS-CoV-2 infected and COVID-19 vaccinated individuals after breakthrough infection.

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Previous secondary outcome measures:
WP1.1. General and COVID-19 specific health-related quality of life, measured using the EQ-5D, DASS-21, Fatigue Assessment Scale and MRC dyspnoea scale at 2 weeks, 1 month, 3 months, 6 months, 9 months and 12 months after laboratory confirmation of SARS-CoV-2 infection
WP1.2. Proportion of individuals with severe disease courses, defined as requiring hospitalization or leading to death within 28 days of confirmation of SARS-CoV-2 infection, measured through participant questionnaires and clinical file review
WP1.3. Proportion of individuals diagnosed with SARS-CoV-2 reinfection within 12 months of confirmation of SARS-CoV-2 infection, measured using participant questionnaires and contact tracing data
WP1.4. Proportion of individuals diagnosed with a new infection or reactivation of a chronic infection by any pathogen within 12 months of laboratory confirmation of SARS-CoV-2 infection, measured through participant questionnaires and clinical file review
WP1.5. Proportion of individuals requiring hospitalization, ICU admission, mechanical ventilation or death (all cause and COVID-19 related) within 12 months after confirmation of SARS-CoV-2 infection, measured through participant questionnaires and clinical file review
WP1.6. Proportion of individuals with self-reported symptoms and/or known risk factors at time of SARS-CoV-2 testing, measured using participant questionnaires
WP1.7. Proportion of individuals that received treatment against SARS-CoV-2, measured through participant questionnaires and clinical file review at enrollment
WP2.1. Proportion of symptomatic and asymptomatic SARS-CoV-2 infected individuals among close contacts of index cases, measured using participant questionnaires and contact tracing data at enrollment and at the end of quarantine
WP2.2. Serial interval of SARS-CoV-2 infection, calculated based on data from participant

questionnaires
WP2.3. Factors potentially influencing SARS-CoV-2 transmission between SARS-CoV-2 infected index cases and their close contacts, measured using participant questionnaires at enrollment
WP2.4. Barriers and facilitators, worries and personal burden related to adhering to quarantine measures among close contacts of SARS-CoV-2 infected index cases, measured using participant questionnaires at enrollment and at the end of quarantine
WP3.1. The proportion of SARS-CoV-2 infected index cases with missing links in routine contact tracing that were identified via phylogenetic analyses as determined at the end of follow-up
WP3.2. The proportion of imported cases among SARS-CoV-2 infected index cases in the Canton of Zurich, as determined by phylogenetic analyses as determined at the end of follow-up
WP4.1. Proportion of individuals with neutralizing anti-SARS-CoV-2 antibodies, measured using neutralization assays at 2 weeks, 1 month, 3 months, 6 months and 12 months after laboratory confirmation of SARS-CoV-2 infection
WP4.2. Proportion of individuals with non-severe and severe COVID-19 that develop anti-SARS-CoV-2 antibody and/or T cell responses, based on the aforementioned measurements at 2 weeks, 1 month, 3 months, 6 months and 12 months
WP4.3. Level and durability of anti-SARS-CoV-2 antibody and/or T cell responses among SARS-CoV-2 infected individuals with non-severe and severe COVID-19, based on the aforementioned measurements at 2 weeks, 1 month, 3 months, 6 months and 12 months
WP4.4. Proportion of SARS-CoV-2 infected individuals with long-term virus persistence (shedding) and viral viability of virus specimen in such individuals, measured by using SARS-CoV-2 PCR testing of saliva samples and virus cultures at 2 weeks and thereafter in 2 weekly intervals until tested negative, stratified by different levels of immune responses
WP5.1. Viral strains associated with pathogenicity or transmissibility of SARS-CoV-2, or immune responses against SARS-CoV-2, identified using viral imprinting approaches based on phylogenetic viral clusters as determined at the end of follow-up
WP5.2. Viral genetic mutations associated with pathogenicity or transmissibility of SARS-CoV-2, or immune responses against SARS-CoV-2, identified using a viral genome wide association study (GWAS) methodology as determined at the end of follow-up

### Completion date
01/02/2025

# Eligibility

### Key inclusion criteria
Current participant inclusion criteria as of 08/07/2022:
Index cases:
1. Individuals newly diagnosed with SARS-CoV-2 infection in the Canton of Zurich from the start of the study (prospective index cases)
2. Individuals previously diagnosed with SARS-CoV-2 infection in the Canton of Zurich between February 2020 and the start of the study (retrospective index cases)

Close contacts:
1. Symptomatic and asymptomatic close contacts of prospective index cases as identified by routine contact tracing by the Department of Health of the Canton of Zurich

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Previous participant inclusion criteria:
Index cases:
1. Individuals newly diagnosed with SARS-CoV-2 infection in the Canton of Zurich from the start

of the study (prospective index cases)
2. Individuals previously diagnosed with SARS-CoV-2 infection in the Canton of Zurich between February 2020 and the start of the study (retrospective index cases)

Close contacts:
1. Symptomatic and asymptomatic close contacts of prospective index cases as identified by routine contact tracing by the Health Directorate of the Canton of Zurich

### Participant type(s)
All

### Healthy volunteers allowed
No

### Age group
Adult

### Sex
All

### Key exclusion criteria
1. Children and adolescents aged <18 years
2. Insufficient knowledge of the German language
3. Individuals with primary residence outside of the Canton of Zurich, Switzerland
4. Individuals that are unable to follow study procedures
5. Individuals that cannot be reached on maximum of 5 attempts
6. Individuals that do not provide informed consent

### Date of first enrolment
27/07/2020

### Date of final enrolment
30/04/2021

## Locations

### Countries of recruitment
Switzerland

### Study participating centre
**Epidemiology, Biostatistics and Prevention Institute (EBPI)**
University of Zurich
Hirschengraben 84
Zurich
Switzerland
CH-8001

# Sponsor information

**Organisation**
University of Zurich

**ROR**
https://ror.org/02crff812

# Funder(s)

**Funder type**
Government

**Funder Name**
Department of Health of the Canton of Zurich (Gesundheitsdirektion des Kantons Zürich)

**Funder Name**
University of Zurich Foundation (UZH Foundation)

**Funder Name**
Bundesamt für Gesundheit

**Alternative Name(s)**
Federal Office of Public Health, Office Fédéral de la Santé Publique, Ufficio Federale della Sanità Pubblica, Office fédéral de la santé publique, Confédération suisse, BAG, FOPH, OFSP, UFSP

**Funding Body Type**
Government organisation

**Funding Body Subtype**
National government

**Location**
Switzerland

**Funder Name**
HORIZON EUROPE Health

**Alternative Name(s)**

Health, Cluster 1: Health, Polo tematico 1: Salute, Salute, Cluster 1: Gesundheit, Gesundheit, Pôle 1: Santé, Santé, Zoskupenie 1: Zdravie, Zdravie

### Funding Body Type
Government organisation

### Funding Body Subtype
National government

### Location

# Results and Publications

### Individual participant data (IPD) sharing plan
Individual participant level data underlying the results reported in the publications will be made available at a later date directly from the authors or via an openly accessible repository.

### IPD sharing plan summary
Available on request

### Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Results article | Analysis of exposure notification cascade in the SwissCovid digital proximity tracing app | 01/05/2022 | 08/07/2022 | Yes | No |
| Results article | Burden of post-COVID syndrome | 12/07/2021 | 08/07/2022 | Yes | No |
| Results article | Effectiveness of digital proximity tracing app | 16/08/2021 | 08/07/2022 | Yes | No |
| Results article | Mental health of COVID-infected people during isolation | 16/03/2022 | 08/07/2022 | Yes | No |
| Results article | Heterogenous humoral and cellular immune responses | 18/08/2022 | 14/05/2024 | Yes | No |
| Results article | Recovery at 2 years | 31/05/2023 | 14/05/2024 | Yes | No |
| Results article | Work ability and occupational changes | 23/06/2023 | 14/05/2024 | Yes | No |
| Preprint results | non-peer-reviewed results of efficacy of a proximity tracing app in preprint | | 17/03/2021 | No | No |
| Preprint results | non-peer-reviewed results on long-term disease burden in preprint | 24/03/2021 | 17/03/2021 | No | No |
| Preprint results | Immunological analyses | 16/12/2021 | 08/07/2022 | No | No |
| Preprint results | Natural course of post-COVID syndrome | 22/06/2022 | 08/07/2022 | No | No |
| Study website | Study website | 11/11/2025 | 11/11/2025 | No | Yes |