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Zurich Coronavirus Vaccination Cohort: an observational study to assess longer-term immune responses and health status after coronavirus (COVID-19) vaccination in Zurich, Switzerland

Submission date
17/03/2021

Recruitment status
No longer recruiting

Registration date
19/03/2021

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
In late December 2020 and early January 2021, two SARS-CoV-2 vaccines were approved in Switzerland and are in the process of being delivered to cantons. Since early January, the Epidemiology, Biostatistics and Prevention Institute (EBPI) at the University of Zurich (UZH) serves as the reference vaccine center for the Canton of Zurich. Its roles include the development of standards for a vaccine center as well as for decentralized vaccination strategies (such as in general practitioner (GP) practices, nursing homes and hospitals), the provision of vaccinations for the general population according to the regulations by the Federal Office of Public Health (FOPH) and the Canton of Zurich, as well as offering training to other vaccine centers, GPs, nursing homes and hospitals.
While large randomized trials have demonstrated the short-term development of humoral and cellular immunity up to approximately three months, it is currently unclear how long this immunity persists and whether it results not only in a reduction in the risk for severe SARS-CoV-2 infection but also transmission. The aim of this study is to assess the development of vaccine-induced short-, mid- and long-term immunity in individuals receiving any of the SARS-CoV-2 vaccines approved in Switzerland at the Corona Center of the UZH. Our setting as a reference vaccine center provides a unique opportunity to compare vaccine- versus infection-induced (wild contagion) immunity.

Who can participate?
Individuals receiving any of the SARS-CoV-2 vaccines approved in Switzerland at the Corona Center of the UZH are randomly selected and invited for study participation.

What does the study involve?
1. Questionnaires
All participants will be asked to fill out a self-administered electronic questionnaire at enrolment

(baseline; usually day of first vaccine dose), and 3-4 weeks, 6 weeks, 3 months, 6 months, 9 months and 12 months after baseline. Those consenting to further participation in the study will receive up to four additional questionnaires at 18 months, 24 months, 30 months, and 36 months after baseline. The questionnaires can be filled before or during the study visits and will collect the following information:

- Sociodemographic information
- Medical and smoking history
- SARS-CoV-2 related information (e.g. infection, symptoms, doctor visits and hospitalizations, and treatment)
- Vaccination-related information (e.g. type of SARS-CoV-2 vaccine received, vaccine-related adverse effects)
- Information regarding SARS-CoV-2 exposure (e.g. contacts with an infected person, professional exposure, receipt of a SwissCovid app warning)

Participants identified to have breakthrough SARS-CoV-2 infections after vaccination and consenting to participate in the additional assessments will receive two additional brief questionnaires at 3 and 6 months after the infection, in which we will gather data on the presence of symptoms and severity of the breakthrough infection.

2. Collection of biological material

Participants will be invited for a total of six study visits during which blood samples are collected. The collection of blood samples will be conducted at baseline before receipt of the first vaccine, and at 3-4 weeks, 6 weeks, 3 months, 6 months and 12 months after baseline. Those consenting to further participation in the study will be invited for up to four additional study visits at 18 months, 24 months, 30 months, and 36 months after baseline. Participants identified to have breakthrough SARS-CoV-2 infections after vaccination and consenting to participate in the additional assessments will be invited for two visits at 3 and 6 months after the infection. The study visits will take place at the Corona Center of the UZH and are expected to take 20-30 minutes during which:

- Study personnel will check the clinical follow-up questionnaires and will provide assistance to participants if incomplete.
- Trained personnel will collect two peripheral venous blood samples in EDTA tubes by venipuncture (total 30 ml)
- Participants will be given an information sheet explaining how to interpret serological test results (i.e., possibility of false positive or false negative results, uncertainty of the extent of protection against (re)infection).

Blood samples will subsequently be tested for SARS-CoV-2 antibodies. Participants will receive their test result by postal mail and will be called by the study personnel if no antibodies are detected after one month, or if antibody levels decline below the detection threshold with time.

Further data sources

Collection of supplementary medical information

The vaccination cards of participants will be scanned and archived as a medical record of the SARS-CoV-2 vaccination, as well as further vaccinations received during child- and adulthood. The participants' treating physicians may be contacted for more detailed information regarding relevant clinical outcomes and/or medical consequences for all participants reporting a health care contact at the follow-up evaluations.

Study extension

In the face of breakthrough infections, emerging variants of concern and to examine the effects of booster vaccinations, the study follow-up will be extended up to three years after baseline.

What are the possible benefits and risks of participating?
This research project will significantly advance our understanding of how immunity develops with the SARS-COV-2 vaccines both in terms of humoral and cellular response. Also, it will allow a unique comparison between vaccine- and infection-induced immunity, as assessed in the Zurich SARS-CoV-2 Cohort study. This information will be highly relevant for public health decision-makers and patients both locally in Switzerland and internationally. Participants directly benefit from information about their antibody responses. Minimal risk to participants is anticipated during biological sample collection. Possible complications occurring during biological sample collection will be minimized by adopting standard sample collection protocols and working with trained personnel.

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

When is the study starting and how long is it expected to run for?
February 2021 until December 2025

Who is funding the study?
The Uniscientia Foundation (Switzerland) and Swiss School of Public Health (SSPH+) (Switzerland) in the frame of Corona Immunitas

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
Zurich SARS-CoV-2 Vaccine Cohort (ZVAC): Development of immunity after SARS-CoV-2 vaccination

Acronym
ZVAC

Study objectives
Current hypothesis as of 30/05/2022:
The overall aim of this prospective and population-based cohort study is to assess the development of vaccine-induced short-, mid- and long-term immunity. The primary and secondary objectives are the following:

Primary objectives:
1. Characterize the presence, dynamics and persistence of antibodies produced in response to the different SARS-CoV-2 vaccines over time
2. Assess the presence and durability of SARS-CoV-2 specific T cell responses, as well as antigen specificity and phenotype in response to the different SARS-CoV-2 vaccines over time

Secondary objectives:
3. Assess the relationship between antibody and T cell immune responses against SARS-CoV-2 induced by different SARS-CoV-2 vaccines
4. Evaluate the occurrence and severity of SARS-CoV-2 infections among individuals who received a SARS-CoV-2 vaccine
5. Evaluate the occurrence and severity of adverse effects among individuals who received a SARS-CoV-2 vaccine
6. Compare the humoral and cellular immune response between individuals with SARS-CoV-2 infection and those who received a SARS-COV-2 vaccine
7. Compare the humoral and cellular immune response to different SARS-CoV-2 vaccines with immune responses to other common vaccines

Over the course of the project, the following objectives were added to the study:
8. Assess whether hematological parameters of iron status prior vaccination predict the development and maintenance of humoral and cellular immune responses to SARS-CoV-2 vaccines

9. Assess the occurrence of new SARS-CoV-2 infection (breakthrough infection) after vaccination and determine its association with SARS-CoV-2 binding and neutralizing antibodies and T cell responses.

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Previous hypothesis:
The overall aim of this prospective and population-based cohort study is to assess the development of vaccine-induced short-, mid- and long-term immunity. The primary and secondary objectives are the following:
Primary objectives:
1. Characterize the presence, dynamics and persistence of antibodies produced in response to the different SARS-CoV-2 vaccines over time
2. Assess the presence and durability of SARS-CoV-2 specific T cell responses, as well as antigen specificity and phenotype in response to the different SARS-CoV-2 vaccines over time
Secondary objectives:
3. Assess the relationship between antibody and T cell immune responses against SARS-CoV-2 induced by different SARS-CoV-2 vaccines
4. Evaluate the occurrence and severity of SARS-CoV-2 infections among individuals who received a SARS-CoV-2 vaccine
5. Evaluate the occurrence and severity of adverse effects among individuals who received a SARS-CoV-2 vaccine
6. Compare the humoral and cellular immune response between individuals with SARS-CoV-2 infection and those who received a SARS-COV-2 vaccine
7. Compare the humoral and cellular immune response to different SARS-CoV-2 vaccines with immune responses to other common vaccines

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 16/02/2021, Cantonal Ethics Committee Zurich (Stampfenbachstrasse 121, CH-8090 Zurich, Switzerland; +41 43 259 79 70; Info.KEK@kek.zh.ch), ref: BASEC 2021-00273

Study design
Observational prospective longitudinal cohort study

Primary study design
Observational

Study type(s)
Prevention

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

Interventions
Current intervention as of 30/05/2022:
Individuals receiving any of the SARS-CoV-2 vaccines approved in Switzerland at the Corona

Center of the UZH, who are randomly selected and invited for study participation will be asked to provide informed consent for study participation. The study procedures are the same for all different vaccines and include the following:

1. Questionnaires
All participants will be asked to fill out a self-administered electronic questionnaire at enrolment (baseline; usually day of first vaccine dose), and 3-4 weeks, 6 weeks, 3 months, 6 months, 9 months and 12 months after baseline. Those consenting to further participation in the study will receive up to four additional questionnaires at 18 months, 24 months, 30 months, and 36 months after baseline. The questionnaires can be filled before or during the study visits (see below) and will collect the following information:
1.1. Sociodemographic information
1.2. Medical and smoking history
1.3. SARS-CoV-2 related information (e.g. infection, symptoms, doctor visits and hospitalizations, and treatment)
1.4. Vaccination-related information (e.g. type of SARS-CoV-2 vaccine received, vaccine-related adverse effects)
1.5. Information regarding SARS-CoV-2 exposure (e.g. contacts with an infected person, professional exposure, receipt of a SwissCovid app warning)
Participants identified to have breakthrough SARS-CoV-2 infections after vaccination and consenting to participate in the additional assessments will receive two additional brief questionnaires at 3 and 6 months after the infection, in which we will gather data on the presence of symptoms and severity of the breakthrough infection.

2. Collection of biological material
Participants will be invited for a total of six study visits during which blood samples are collected. The collection of blood samples will be conducted at baseline before receipt of the first vaccine, and at 3-4 weeks, 6 weeks, 3 months, 6 months and 12 months after baseline. Those consenting to further participation in the study will be invited for up to four additional study visits at 18 months, 24 months, 30 months, and 36 months after baseline. Participants identified to have breakthrough SARS-CoV-2 infections after vaccination and consenting to participate in the additional assessments will be invited for two visits at 3 and 6 months after the infection. The study visits will take place at the Corona Center of the UZH and are expected to take 20-30 minutes during which:
2.1. Study personnel will check the clinical follow-up questionnaires and will provide assistance to participants if incomplete.
2.2. Trained personnel will collect two peripheral venous blood samples in EDTA tubes by venipuncture (total 30 ml)
2.3. Participants will be given an information sheet explaining how to interpret serological test results (i.e., possibility of false positive or false negative results, uncertainty of the extent of protection against (re)infection).
Blood samples will subsequently be tested for SARS-CoV-2 antibodies. Participants will receive their test result by postal mail and will be called by the study personnel if no antibodies are detected after 1 month, or if antibody levels decline below the detection threshold with time.

Further data sources - Collection of supplementary medical information
The vaccination cards of participants will be scanned and archived as a medical record of the SARS-CoV-2 vaccination, as well as further vaccinations received during childhood and adulthood. The participants' treating physicians may be contacted for more detailed information regarding relevant clinical outcomes and/or medical consequences for all participants reporting a health care contact at the follow-up evaluations.

Study extension
In the face of breakthrough infections, emerging variants of concern and to examine the effects of booster vaccinations, the study follow-up will be extended up to 3 years after baseline. Study participants reaching the 12-month follow-up will be informed about the prolongation of the study by email and will provide written informed consent for the continued participation during the 12-month study visit.

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Previous intervention:
Individuals receiving any of the SARS-CoV-2 vaccines approved in Switzerland at the Corona Center of the UZH, who are randomly selected and invited for study participation will be asked to provide informed consent for study participation. The study procedures are the same for all different vaccines and include the following:

1. Questionnaires
All participants will be asked to fill out a self-administered electronic questionnaire at enrolment (baseline; usually day of first vaccine dose), and 3-4 weeks, 6 weeks, 3 months, 6 months, 9 months and 12 months after baseline. The questionnaires can be filled before or during the study visits (see below) and will collect the following information:
- Sociodemographic information
- Medical and smoking history
- SARS-CoV-2 related information (e.g. infection, symptoms, doctor visits and hospitalizations, and treatment)
- Vaccination-related information (e.g. type of SARS-CoV-2 vaccine received, vaccine-related adverse effects)
- Information regarding SARS-CoV-2 exposure (e.g. contacts with an infected person, professional exposure, receipt of a SwissCovid app warning)

2. Collection of biological material
Participants will be invited for a total of six study visits during which blood samples are collected. The collection of blood samples will be conducted at baseline before receipt of the first vaccine, and at 3-4 weeks, 6 weeks, 3 months, 6 months and 12 months after baseline. The study visits will take place at the Corona Center of the UZH and are expected to take 20-30 minutes during which:
- Study personnel will check the clinical follow-up questionnaires and will provide assistance to participants if incomplete.
- Trained personnel will collect two peripheral venous blood samples in EDTA tubes by venipuncture (total 20 ml).
- Participants will be given an information sheet explaining how to interpret serological test results (i.e., possibility of false positive or false negative results, uncertainty of the extent of protection against (re)infection).

Blood samples will subsequently be tested for SARS-CoV-2 antibodies. Participants will receive their test result by postal mail and will be called by the study personnel if no antibodies are detected after one month, or if antibody levels decline below the detection threshold with time.

Further data sources - Collection of supplementary medical information
The vaccination cards of participants will be scanned and archived as a medical record of the SARS-CoV-2 vaccination, as well as further vaccinations received during child- and adulthood.

The participants' treating physicians may be contacted for more detailed information regarding relevant clinical outcomes and/or medical consequences for all participants reporting a health care contact at the follow-up evaluations.

Intervention Type
Other

Primary outcome(s)
Current primary outcome measures as of 08/06/2022:
Measured using blood samples:
1. Presence of anti-SARS-CoV-2 IgG antibodies before receiving the first dose of a vaccine (baseline) and at 3-4 weeks, 6 weeks, 3 months, 6 months, 12 months, and every 6 months up to 3 years after baseline
2. Presence of SARS-CoV-2 antigen-specific T cells before receiving the first dose of a vaccine (baseline) and at 3-4 weeks, 6 weeks, 3 months, 6 months, 12 months, and every 6 months up to 3 years after baseline

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Previous primary outcome measures:
Measured using blood samples:
1. Presence of anti-SARS-CoV-2 IgG antibodies before receiving the first dose of a vaccine (baseline), at 3-4 weeks, at 6 weeks, and at 3, 6 and 12 months after baseline
2. Presence of SARS-CoV-2 antigen-specific T cells before receiving the first dose of a vaccine (baseline), and at 3-4 weeks, at 6 weeks, and at 3, 6 and 12 months after baseline

Key secondary outcome(s))
Current secondary outcome measures as of 17/06/2022:
1. Proportion of individuals with neutralizing antibodies measured using blood test before receiving the first dose of a vaccine (baseline) and at 3-4 weeks, 6 weeks, 3 months, 6 months, 12 months, and every 6 months up to 3 years after baseline
2. Humoral (IgG antibodies) and cellular response (T cells) measured using blood test before receiving the first dose of a vaccine (baseline) and at 3-4 weeks, 6 weeks, 3 months, 6 months, 12 months, and every 6 months up to 3 years after baseline
3. Proportion of individuals who received a SARS-CoV-2 vaccine who experience a SARS-CoV-2 infection and determination of the severity of that infection measured using a questionnaire at baseline, and 3-4 weeks, 6 weeks, 3 months, 6 months, 9 months and 12 months, and every 6 months up to 3 years after baseline
4. Proportion of individuals who received a SARS-CoV-2 vaccine who experience adverse effects and determination of the severity and consequence of that adverse effect measured using a diary during the first 3 months after vaccination
5. Proportion of individuals who received a SARS-CoV-2 vaccine who are later exposed to SARS-CoV-2 and determination of the exposure context measured using a questionnaire at baseline, and 3-4 weeks, 6 weeks, 3 months, 6 months, 9 months and 12 months, and every 6 months up to 3 years after baseline

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Previous secondary outcome measures as of 08/06/2022:
1. Proportion of individuals with neutralizing antibodies measured using blood test before receiving the first dose of a vaccine (baseline) and at 3-4 weeks, 6 weeks, 3 months, 6 months, 12 months, and every 6 months up to 3 years after baseline

2. Humoral (IgG antibodies) and cellular response (T cells) measured using blood test before receiving the first dose of a vaccine (baseline) and at 3-4 weeks, 6 weeks, 3 months, 6 months, 12 months, and every 6 months up to 3 years after baseline
3. Proportion of individuals who received a SARS-CoV-2 vaccine who experience a SARS-CoV-2 infection and determination of the severity of that infection measured using a questionnaire at baseline, and 3-4 weeks, 6 weeks, 3 months, 6 months, 9 months and 12 months after baseline
4. Proportion of individuals who received a SARS-CoV-2 vaccine who experience adverse effects and determination of the severity and consequence of that adverse effect measured using a questionnaire at baseline, and 3-4 weeks, 6 weeks, 3 months, 6 months, 9 months and 12 months after baseline
5. Proportion of individuals who received a SARS-CoV-2 vaccine who are later exposed to SARS-CoV-2 and determination of the exposure context measured using a questionnaire at baseline, and 3-4 weeks, 6 weeks, 3 months, 6 months, 9 months and 12 months after baseline

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Previous secondary outcome measures:
1. Proportion of individuals with neutralizing antibodies before receiving the first dose of a vaccine (baseline), and at 3-4 weeks, at 6 weeks, and at 3, 6 and 12 months after baseline measured using blood test
2. Humoral (IgG antibodies) and cellular response (T cells) before receiving the first dose of a vaccine (baseline), and at 3-4 weeks, at 6 weeks, and at 3, 6 and 12 months after baseline measured using blood test
Measured using a questionnaire at baseline, and 3-4 weeks, 6 weeks, 3 months, 6 months, 9 months and 12 months after baseline
3. Proportion of individuals who received a SARS-CoV-2 vaccine who experience a SARS-CoV-2 infection and determination of the severity of that infection
4. Proportion of individuals who received a SARS-CoV-2 vaccine who experience adverse effects and determination of the severity and consequence of that adverse effect
5. Proportion of individuals who received a SARS-CoV-2 vaccine who are later exposed to SARS-CoV-2 and determination of the exposure context

Completion date
31/12/2025

Eligibility

Key inclusion criteria
1. Individuals receiving any of the SARS-CoV-2 vaccines approved in Switzerland at the Corona Center of the UZH
2. Aged ≥18 years,
3. Able to follow the study procedures
4. Providing informed consent

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
575

Key exclusion criteria
1. Having insufficient knowledge of the German language
2. Individuals whose primary residence is outside of the Canton of Zurich
3. Previously received SARS-CoV-2 vaccine

Date of first enrolment
22/03/2021

Date of final enrolment
19/01/2022

Locations

Countries of recruitment
Switzerland

Study participating centre
University of Zurich (UZH)
Corona Center of the University of Zurich, Epidemiology, Biostatistics and Prevention Institute (EBPI)
Hirschengraben 84
Zurich
Switzerland
CH-8001

Sponsor information

Organisation
University of Zurich

ROR
https://ror.org/02crff812

Funder(s)

Funder type
Charity

Funder Name
Uniscientia Foundation

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Switzerland

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
Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		24/04/2023	14/05/2024	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes