CHRIS Covid-19 Study

Biochemical traits

Version 1.0

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Authors: MG

1. Introduction

This module stores the results of the serological SARS-CoV-2 antibody (anti-Ncapsid) tests and the nasopharyngeal swab RT-PCR tests of the CHRIS COVID-19 study participants, as well as anti-Spike measurements, measured since December 2020 to assess the vaccination status and its response.

The CHRIS COVID-19 study was designed to estimate the distribution of SARS-CoV-2 infection cases in Val Venosta/Vinschgau since 1 February 2020, as well as the proportion of asymptomatic individuals among positive cases, to characterize transmission within households, to assess the relationship between antibody response and disease severity, to observe the evolution of antibody response over time, to identify environmental, molecular and genetic risk factors, to identify long-term sequelae.

The CHRIS COVID-19 study was organized in three stages:

Stage 1: A stratified random sample of 1812 CHRIS study participants was selected to represent the adult population of the Val Venosta/Vinschgau district. Out of this sample, 845 CHRIS participants replied to an online or paper questionnaire, underwent a molecular test based on a nasopharyngeal swab and a serum antibody test.

Stage 2: All 13,393 CHRIS study participants and their consenting cohabitants were invited to fill in an online questionnaire on their past and current health status, and on SARS-CoV-2 (potential) exposure and testing. Each CHRIS participant received ten access tokens to let them and their cohabitants register online. A shorter questionnaire was then sent repeatedly to all participants every 4 weeks for an update on their symptoms, COVID-19 exposure, and testing. All individuals at risk of positivity to SARS-CoV-2 infection and their cohabitants have been invited for a nasopharyngeal swab molecular test and a serum antibody test at the CHRIS study center.

Stage 3: To trace and monitor antibody response over time, all individuals testing positive to either the nasopharyngeal or the serum test in Stages 1 or 2 have been invited to repeat the serum antibody test every three months for a year, since their first measurement.

Every time study participants came to the CHRIS study center either as part of the random sample (stage 1) or as potentially infected individuals (stage 2) or to monitor their antibody count (stage 3), their swab and/or serum samples were then shipped to Bolzano/Bozen hospital and analyzed by the hospital laboratory within 24 hours. It is possible that a participant has more than 5 serological measurements and more than one swab RT-PCR measurement, if they once visited the CHRIS study center (either as part of the random sample or as potentially infected) and resulted negative. In that case, they kept filling in the monthly online questionnaire as long as they had another potential positivity, and therefore visited again the study center.

2. History version changes

Lipaemic index (cclp82b), Hemolytic index (cclp83b), and Icteric index (cclp84b): measured since October 20th, 2020.

Maglumi SARS-CoV-2 IgM/IgG (cclp91a, cclp91b): measured until November 3rd, 2020.

Elecsys Anti-SARS-CoV-2 anti-Spike (cclp90a, cclp90b): measured since December 1st, 2020.

3. Data cleaning

1. The CHRIS COVID-19 biochemical traits dataset was loaded in Stata.
2. Entries without serological antibody tests were deleted.
3. For the Elecsys Anti-SARS-CoV-2 (anti-Ncapsid) traits:
    a. Missing values of the quantitative trait cclp89a were set to "Sample not received" (-125) if this was the value of the categorical trait cclp89b;
    b. Missing values were set to "Unexpected missing" (-89), otherwise;
    c. Value 2 of the categorical trait cclp89b was transformed to "Non-reactive" (0).
4. For the Elecsys Anti-SARS-CoV-2 S (anti-Spike) traits:
    a. Missing values of the quantitative trait cclp90a were set to ">250" (-2012), ">2500" (-2011), and "<0.4" (-1020) if this was the value of the categorical trait cclp90b;
    b. Missing values of the quantitative trait cclp90a and of the categorical trait cclp90b were set to "Not in use" (-98) for tests performed before December 1st, 2020;
    c. Missing values were set to "Unexpected missing" (-89), otherwise;
    d. Values -1020 and 2 of the categorical trait cclp90b were transformed to "Negative" (0) and values -2012 and -2011 were transformed to "Positive" (1).
5. For the Maglumi SARS-CoV-2 IgM/IgG traits cclp91a and cclp91b:
    a. Missing values were set to "Not in use" (-98) for tests performed since November 3rd, 2020;
    b. Missing values were set to "Missing by design" (-99) if the Elecsys Anti-SARS-CoV-2 (anti-Ncapsid) categorical trait cclp89b was 0 or -125;
    c. Missing values were set to "Unexpected missing" (-89), otherwise.
6. For the lipaemic index cclp82b, the hemolytic index cclp83b, and the icteric index, cclp84b:
    a. Missing values were set to "Not in use" (-98) for tests performed before October 20th, 2020;
    b. Missing values were set to "Unexpected missing" (-89), otherwise.
7. For the swab SARS-CoV-2 RT-PCR test cclp92, all missing values were set to "Missing by design" (-99).
8. The counter of serological antibody tests cc_tcount was created to distinguish the various serological antibody tests performed for each participant. For serological antibody tests at the random sample examination, the counter was set to 0.
9. The counter of serological antibody tests performed since the first positive test cc_tpcount was created to distinguish between the various follow-up serological antibody tests performed for each participant after the initial positive test (baseline). For the initial positive test, the counter was set to 0; for previous negative tests, the counter was set to "Missing by design" (-99).
10. The biochemical traits dataset was saved.

Stata v16.1 was used for the data cleaning process. The do file is available at the LINK-TO-cr_03b_clean_concerto.do.

4. Data structure

The variables listed in table 1 constitute all the variables associated with the serological antibody test and the nasopharyngeal test. The variables listed in table 2 constitute all the variables needed to identify the different tests of the same participant.

Table 1. Biochemical traits variables list

Variable	Parameter	Unit	Coding	Reference values	Linearity range	Notes	Substrate	Machine	Kit/Test	Available	Derived
cclp82b	Lipaemic index	mg/dL	<integer>		10-2000 mg/dL	together with cclp89, cclp90	Serum	COBAS 8000 - module c 701/702	Serum Index Gen.2	Yes	No
cclp83b	Hemolytic index	mg/dL	<integer>		5-1200 mg/dL	together with cclp89, cclp90	Serum	COBAS 8000 - module c 701/702	Serum Index Gen.2	Yes	No
cclp84b	Icteric index	mg/dL	<integer>		0.5-60 mg/dL	together with cclp89, cclp90	Serum	COBAS 8000 - module c 701/702	Serum Index Gen.2	Yes	No
cclp89a	Elecsys Anti-SARS-CoV-2 (anti-Ncapsid) quantitative	-	<float>	COI < 1.0	N/A		Serum	COBAS 8000 - module e 801	Elecsys Anti SARS-CoV-2	Yes	No
cclp89b	Elecsys Anti-SARS-CoV-2 (anti-Ncapsid) categorical		0 Non-reactive 1 Reactive		N/A	0 if COI<1.0 1 if COI≥1	Serum	COBAS 8000 - module e 801	Elecsys Anti SARS-CoV-2	Yes	Yes
cclp90a	Elecsys Anti-SARS-CoV-2 S (anti-Spike) quantitative	U/mL	<float>	<0.80 U/mL	0.40-250 U/mL		Serum	COBAS 8000 - module e 801	Elecsys Anti SARS-CoV-2 S	Yes	No
cclp90b	Elecsys Anti-SARS-CoV-2 S (anti-Spike) categorical		0 Negative 1 Positive		0.40-250 U/mL		Serum	COBAS 8000 - module e 801	Elecsys Anti SARS-CoV-2 S	Yes	Yes
cclp91a	Maglumi SARS-CoV-2 IgG	AU/mL	<float>	<1.00 AU/mL	N/A	cclp89b=1	Serum	N/A	MAGLUMI 2019-nCoV IgM/IgG	Yes	No
cclp91b	Maglumi SARS-CoV-2 IgM	AU/mL	<float>	<1.00 AU/mL	N/A	cclp89b=1	Serum	N/A	MAGLUMI 2019-nCoV IgM/IgG	Yes	No
cclp92	Swab SARS-CoV-2 RT-PCR test		1 Detected 2 Not detected 3 Dubious		N/A		Nasopha-ryngeal swab	N/A	-	Yes	No

Table 2. Test identifier variables list

Variable	Description	Unit of reference	Coding	Filter	Notes	Version	Available	Derived
cc_examd	Date of sample collection		<date>				Yes	No
cc_tcount	Counter of serological tests		0 Random sample examination 1 First 2 Second, 3 Third 4 Fourth 5 Fifth 6 Sixth				Yes	Yes
cc_tpcount	Counter of serological antibody tests since first positive test		0 Baseline 1 First follow-up 2 Second follow-up 3 Third follow-up 4 Fourth follow-up 5 Fifth follow-up				Yes	Yes

5. Advices for the analysis

The structure of the dataset is by serological antibody test.

1241 distinct participants have had at least one RT-PCR test performed, for a total of 1261 tests. In total, 4962 valid Elecsys® Anti-SARS-CoV-2 tests were collected for 1673 participants, and 4881 Elecsys® Anti-SARS-CoV-2 S assays (anti-Spike) were measured for 1642 participants. Moreover, 14 participants had their IgG and IgM measured with the MAGLUMI assay.

Within the random sample, only one participant tested positive to the RT-PCR swab test and one sample was not received. Within the study period, 1161 participants were at one point reactive to SARS-CoV-2 N-capsid assay, and 1170 had a positive SARS-CoV-2 anti-Spike serological test.

Roche Elecsys® Anti-SARS-CoV-2 assay has 99.5% sensitivity at ≥14 days post RT-PCR confirmation and 99.8% specificity, as declared by its manufacturer. Post-market validation of these immunoassays has been assessed in numerous large studies.

6. References

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