Police officer COVID-19 Seroprevalence Survey in the Canton of Bern, Switzerland

Research legislation:	Ordinance on human research with the exception of Clinical trials (HRO) [1].
Type of Research Project:	Research project involving human subjects
Risk Categorisation:	Category A (minimal risk for study participants)
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PROTOCOL SIGNATURE FORM

Study Title	Police officer COVID-19 seroprevalence survey in the Canton of Bern, Switzerland

The project leader has approved the protocol version **8.1 (dated 01.04.2021)**, and confirms hereby to conduct the project according to the protocol, the Swiss legal requirements [1, 2], current version of the World Medical Association Declaration of Helsinki [3] and the principles and procedures for integrity in scientific research involving human beings.

Project leader and Sponsor:

Site: Institute for Infectious Diseases (IFIK), University of Bern, Bern, Switzerland

Name: Prof. Dr. med. Parham Sendi

Date: _____ Signature: _____

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GLOSSARY OF ABBREVATIONS

BASEC	*Business Administration System for Ethical Committees*
CI	*Confidence Interval*
CRF	*Case report form*
CTU	*Clinical Trial Unit*
EDC	*Electronic Data Capture*
EU	*European Union*
FAIR	*Findable Accessible Interoperable Reusable*
FOPH	*Federal Office of Public Health*
HRA	*Human Research Act*
HRO	*Ordinance on Human*
IFIK	*Institute for Infectious Diseases*
PFU	*Plaque Forming Unit*
PI	*Principal Investigator*
RT-PCR	*Reverse Transcriptase Polymerase Chain Reaction*
TLS	*Transport Layer Security*
WHO	*World Health Organization*

1 BACKGROUND AND PROJECT RATIONALE

1.1 Background

Knowledge of diagnostic tests for SARS-CoV-2 is still evolving, and their correct use and an understanding of the results is important for both clinical and epidemiological studies. Two types of diagnostic tests commonly in use for SARS-CoV-2 infections are reverse transcriptase polymerase chain reaction (RT-PCR) and anti-SARS-CoV-2-antibodies [5]. Although SARS-CoV-2 is an antigenically variable pathogen, serological surveys provide powerful evidence during a pandemic. Serological testing has an increasing role in identifying convalescent cases and persons with nonspecific mild respiratory symptoms or no symptoms who have recovered from SARS-CoV-2 without being diagnosed [6]. The current prediction is that approximately 80% to 90% of people are undocumented or asymptomatic, hence facilitating the rapid spread of the virus [7]. Because serological surveys are able to identify both asymptomatic and symptomatic cases that have passed the acute phase of COVID-19, they are paramount to generating key data on the epidemiology of SARS-CoV-2 [8,9].

The Centers for Disease Control and Prevention and others have clearly indicated the importance of seroprevalence surveys on COVID-19 [8]. Recently, several institutions have performed different types of serological surveys [10]. Results from Geneva, Switzerland, indicate a seroprevalence of 3.1% to 9.7% over 3 weeks testing [11]. Nonetheless, there are considerable differences of COVID-19 seroprevalence both within a country and between countries. A direct comparison of results is difficult because of different study types, different population selections and hence potential bias, and the use of different (mostly not validated) tests. Epidemiological antibody studies are typically categorized as (i) large-scale geographic, (ii) community-level, and (iii) special population seroprevalence surveys [8]. This project is a special population seroprevalence survey.

While the majority of exposed workers are employed in healthcare sectors, other occupational sectors also have high proportions of exposed workers [12]. A recent study suggested that protective services (e.g., police officers and others) are the third most common exposed group, after healthcare support workers and healthcare practitioners. Approximately 30% of protective services personnel are exposed to COVID-19 risk at least once per week [12].

SARS-CoV-2 is transmitted by droplets and contact (and possibly by aerosols), particularly when contact occurs over a prolonged period and in close congregation, thus providing opportunity for disease spread through droplets or fomites. For police officers who do field work, social distancing is not always possible. Police activity includes close interrogation and close contacts with various degrees of physical defence. In contrast to healthcare workers, police officers have no information on the disease condition of the other party. Previous studies have clearly shown aerosol emission of contagious organisms during speech and an increase in emission with voice loudness [13-16]. These data underscore that police officers are potentially exposed to SARS-CoV-2 during field work. This notion is even more important considering that the COVID-19 pandemic has led to social collateral effects, including domestic violence [17-20]. EU states recently reported a 60% rise in emergency calls because of domestic violence [21]. However, apart from two case reports, no data are available on COVID-19 epidemiology in protective services occupations [22,23].

1.2 Aims and Rationale

We aim to determine the immune status of the employees of the cantonal police of Bern against SARS-CoV-2 over a period of 1 year, and to investigate the risk profile of the study participants and their risk of SARS-CoV-2 exposure in their working and private environments, as well as to evaluate the use of personal protective equipment at potential exposure instances. This type of survey can help to answer important questions about risk factors for disease (person's age, location, underlying health conditions), risk of infection, and prevention of COVID-19 within this specific population. Because the age distribution of the working population may be mirrored in

this occupation, senior police officers are at risk [22]. Individuals may acquire the infection during their working hours or in the private environment, and transmit it to their colleagues at work while being asymptomatic. A police department may be further weakened by absence of personnel because of quarantine after contact with a SARS-CoV-2-PCR-positive colleague or self-isolation in the case of proven COVID-19 [22]. The acquisition of these data is paramount for future work and personnel planning of the police department. Determining how long anti-SARS-CoV-2-antibodies persist in serum following infection and which antibody titre levels are protective against reinfection will provide valuable information for the “Shield Immunity” strategy [9].

2 PROJECT OBJECTIVES AND DESIGN

2.1 Objectives and Hypothesis

i) To determine the extent of infection in the special population of police officers of the canton Bern. We hypothesize that the COVID-19 seroprevalence within the police department will be between 1% and 2% at the beginning of the study. We further hypothesize that the seroprevalence will increase during the study period by 8% (i.e., from 2% to 10%). The rationale for this increase proportion derives from the Geneva study, and the ongoing COVID-19 pandemic till the end of study period [11].

ii) To determine risk factors for infection by comparing the proportion of seropositivity (infected versus noninfected individuals). We hypothesize that police officers with fieldwork activity will have a higher seroprevalence than will office and administration personnel. We hypothesize that working in the city of Bern will be associated with a higher seroprevalence than will working in other geographic areas of the canton (i.e. rural area).

iii) To monitor COVID-19 antibody titres and neutralizing capacity over time and to associate them with reinfection rates and infection-free intervals in police officers after accidental contact with a proven COVID-19 case. We hypothesize that in seropositive individuals, there will be a decreasing dynamic of antibody titres over the one-year study period, and hence, a decrease of neutralizing capacity.

2.2 Primary and secondary endpoints

Primary endpoint: The variable of primary interest is **COVID-19 seropositivity**. This variable is measured at five time points over the one-year study period. The following baseline factors may have an influence on the primary endpoint and will be obtained: (i) pre-existing comorbidities, (ii) rural versus city distribution of working place, and (iii) office work versus field work.

Secondary endpoints: We will assess the proportion of symptomatic and asymptomatic cases among seropositive participants. We will calculate the attack rate in different subgroup. These include (i) study participants with health-related risk factors (age>50 and age>60 years, diabetes, arterial hypertension, cardiovascular disease, chronic pulmonary disease, immune-compromised status due to host diseases, medical treatment, cancer, obesity), (ii) activity-related subgroups (i.e. fieldwork vs office activity), (iii) geography-related subgroups (i.e. city vs rural areas). In follow-up visits, the antibody titers (i.e. dynamic) and the neutralization capacity will be assessed. Thereby we will determine the change in serum levels of SARS-CoV-2 antibodies over time in seropositive participants.

2.3 Project design:

This is a single center special population (i.e. police officers of the canton of Bern) seroprevalence survey. It is a repeated cross-sectional investigation in the canton of Bern combined with a longitudinal cohort study with serial sampling of the included study participants. The protocol is aligned with the one of seroprevalence studies recommend by the WHO [25].

3 PROJECT POPULATION AND STUDY PROCEDURES

3.1 Project population, inclusion and exclusion criteria

The project population consists of employees working for the police department of the canton. In 2019, the police department of the canton of Bern listed 2'491 full-time equivalents [24]. In an anonymous pre-study survey performed with the police department in September 2020, 927 individuals confirmed their interest to participate to this study. Hence, we calculate with 1’000 study participants.

Inclusion criteria include all police officers of the cantonal police of Bern volunteering to participate in the study. In addition, study participants must have a valid e-mail address.

Exclusion criteria include refusal or inability to give informed consent or contraindication to venepuncture.

3.2 Recruitment, screening and informed consent procedure

Recruitment: The study will be announced through internal communication channels from the directive committee of the cantonal police of Bern (see point 11 in the BASEC application: “other documents handed over to study participants”). Within this internal communication, there will be contact details to members of the study group. In the announcement, it will be stressed that participation is voluntary. In the announcement, volunteers have the possibility to download study information and patient consent sheet. We make use of electronic media to convey the information, because the number of study participants is very high (i.e.; approximately 1'000). In addition, the study participants are not selected because of a particular disease. The majority of them will be healthy volunteers and the study purpose does not consist of sensitive health-related issues. Considering these arguments, we feel that it is justified to convey the study information electronically, and that it is unfeasible to provide the study information personally to each single study participant. The computerized system is validated within the police department (intranet). Study volunteers have the possibility to contact personally (via e-mail, telephone, zoom or skype) the study team to clarify questions or unclear issues.

Screening: Individuals fulfilling inclusion criteria are eligible for the study. This includes having a valid e-mail address.

Consent procedure: Study information and the informed consent sheet can be downloaded from the announcement on the intranet. Study participants have the possibility to contact the study team via telephone, skype or zoom to give the possibility to ask questions prior to signing the consent. Participants will also be asked to consent to store their samples in our biobank for future use (further use). The subject’s consent will be documented on paper with a hand-written signature of both the patient and the investigator. Hence, patient consent sheets for participation to this study and for further use must be printed out by study volunteers, signed and sent to the study team with regular mail. The investigator will sign the consent sheets, make a copy, save the original in a folder, and send the copy back to the study participant with regular mail. No mailing costs will be burdened to study participants. The employer will be unaware of who and how many of his or her employees are participating at the time point of recruitment. No compensation or payments will be given to the project participants. Because the employer is helping to organize blood sampling, the employer will know who participated *after* study participants have been recruited. Considering the high burden of logistics, the organization for blood sampling time points by the police is needed. However, study participants have the possibility to organize the blood sampling via the study team (and not via the police), if they wish. The employer will not be aware of any individual result.

Efforts to ascertain voluntary participation: In the (i) pre-study survey, (ii) announcement, and (iii) study information, it will be stressed that participation in the investigation is voluntary and that the participant is free to withdraw (without justification) from the investigation at any time without consequences and without affecting professional responsibilities. The directors of

the police department are only authorized to view high-level summary information about the survey results, but will not be able to track an individual's result or decision to participate in or withdraw from the study. Study participants can choose the location for blood sampling when making an appointment in the given time frame, i.e., police station versus Interregionale Blutspende SRK. Similarly, the study participation requires a computer with internet access to fill out the questionnaire. Participants can fulfill this task at a location of their choice.

3.3 Study procedures

The overall project will span an 18-month period. We anticipate starting the study in December 2020, with a baseline visit and first sampling in January 2021. Sample collection will be terminated in February/March 2022. Hence, the project duration for each study participant will be 1 year.

The study protocol is aligned with that of the WHO for population-based age-stratified sero-epidemiological investigations. We adapted the protocol for our specific population and for the geographic region of the canton of Bern [25]. Data and serum results will be collected in a standardized format according to the questionnaires and tools in the WHO protocol to assist with data harmonization and comparison of results.

Upon signed consent, each study participant will be assigned a study identification number (code) for the labelling of questionnaires and serum specimens.

Each participant recruited for the investigation will be asked to complete an online questionnaire at their convenience within time frame of 2 to 3 weeks, which covers information on demographics and possible COVID-19 exposure or infection (see point 5 in the BASEC application: "CASE REPORT FORM"). Returned questionnaires will be reviewed for completeness and responses electronically stored in a database (REDCap).

A serum sample will be collected from each participant upon recruitment into the investigation (visit 1, baseline). According to the study participant's preference, the study team will conduct police station visits to collect specimens OR study participants will visit the Interregionale Blutspende SRK for blood sampling. Serial sampling is then to be conducted every 3 months (i.e., five sampling time points over 1 year), meaning that each participant will be asked to attend a total of 4 follow-up visits.

Figure 1 describes when data and specimens will be collected according to the study plan permitted timeframe for each visit. A visit corresponds to one blood sampling appointment. A visit is defined as a time frame between 2 and a maximum of 3 weeks. Dates for appointments will be randomly alternated between police stations in cities and those in rural areas to preserve equal temporal distribution of visits between these areas. Results from microbiological analyses will be entered into REDCap. A schedule of assessments is also illustrated in appendix 1.

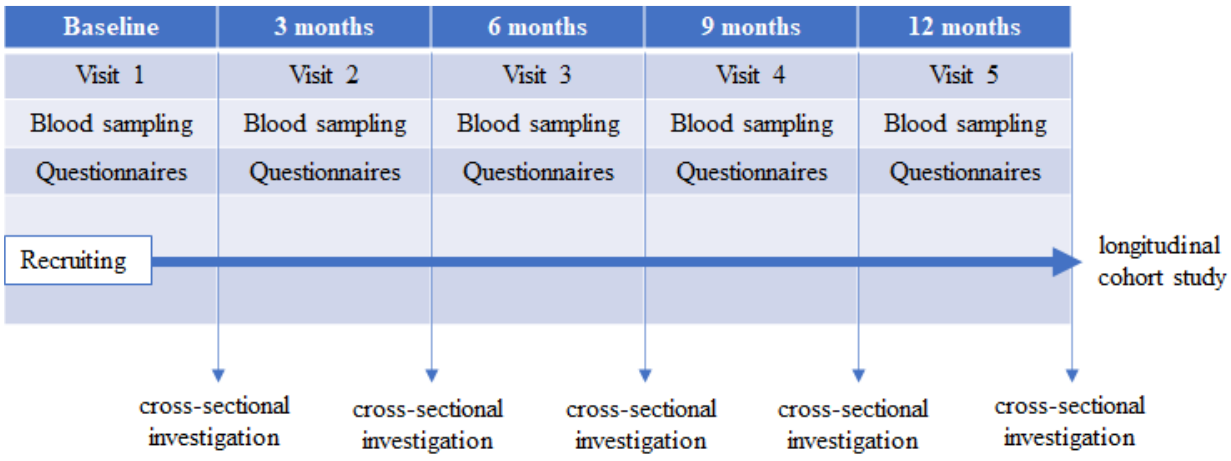

Figure 1: Schematic overview of the study procedure

Each sample will be labelled with the study participant's code immediately prior to blood withdrawal. For each serum sample collected, the time of collection, the conditions for transportation, and the time of arrival at the study laboratory will be recorded. Given the efficient means of transport in the canton of Bern, we anticipate that serum samples will reach the laboratory within the same day after collection. They will be aliquoted and stored at our at the Interregionale Blutspende SRK (-30°C), for coordinated analysis of batches. The diagnostic laboratories of both the Interregionale Blutspende SRK and the IFIK have the required government permits to operate a diagnostic service for clinical specimens of human origin, including storage of such specimens; furthermore, they are accredited to the ISO/IEC 17025 Standard.

On each sample two commercially available SARS-CoV-2 serological assays will be performed (Elecsys® Anti-SARS-CoV-2-Test). According to the manufacture's information, the specificity is 99.81 % (95% CI 99.65 – 99.91 %) and sensitivity 100 % (88.1 – 100 %), respectively. The rationale for using this particular test includes a performance evaluation at the Interregionale Blutspende SRK that demonstrated a high specificity (Riester et al. medRxiv 2020.08.07.20169987). Overall specificities for the Elecsys Anti-SARS-CoV-2 immunoassay in 9575 samples from blood donors (n = 6714) and routine diagnostic testing specimens (n = 2861) were 99.82% (95% CI 99.69-99.91) and 99.93% (95% CI 99.75-99.99), respectively. In addition, the test will be purchased to a reasonable price. The rational for choosing two commercially available SARS-CoV-2 serological assays is the following. One test detects anti-nucleocapsid antibodies, while the other detects anti-spikeprotein antibodies. Anti-nucleocapsid antibodies detect antibodies derived from natural infection but do not detect antibodies derived from mRNA-vaccination. It is important for both the investigator and the study participant to identify antibodies derived from vaccination. Therefore, we complement the tests for anti-nucleocapsid antibodies with tests for anti-spike-protein antibodies. Testing will be carried out at the Interregionale Blutspende SRK.

In serum samples with positive antibody test, quantification of neutralizing antibodies will be performed at the IFIK. They will be measured by pre-incubating serial dilutions of baseline and convalescent serum with 200 to 400 plaque forming units (PFU) of SARS-CoV-2, after which a PFU reduction assay will be performed on Vero-E6 cells. After 2 days, cells will be fixed and stained with crystal violet to analyse the neutralizing capacity of antibodies generated towards SARS-CoV-2, as previously described [26].

The results of Anti-SARS-CoV-2-Test of will be communicated to study participant via e-mail within 2 weeks of blood sampling. The results of neutralization capacity will be communicated at the end of the study period. This experimental assay will be performed in the research laboratory with all positive samples during one month, at the end of the study period.

Seropositive participants or participants with a positive SARS-CoV-2 test in the past (PCR or antigen test) will be asked to complete an additional questionnaire that investigates possible contacts (i.e., working versus private environment) and sources of transmission (see point 5 in the BASEC application: "CASE REPORT FORM").

Seropositive participants or vaccinated participants will contacted by the study team within 4 weeks after laboratory result, for one additional blood sampling that investigates neutralization capacity. Seropositive participants with vaccination will be contacted twice. Figure 2 illustrates the sampling scheme.

Antibodies	Vaccine	No. of blood sampling in 1 year	
negative	no	5	baseline + every 3 months
positive	no	6	baseline + every 3 months + 1 sampling
negative	yes	6	baseline + every 3 months + 1 sampling
positive	yes	7	baseline + every 3 months + 2 samplings

Figure 2: Schematic overview of the blood sampling over one year

Measures taken to reduce expected biases: If study participants reveal anti-SARS-CoV-2-antibodies at baseline or reveal seroconversion during the study year, additional investigations will be performed. Serum sampling will be repeated 2 and 4 weeks after the first positive antibody test result to confirm seropositivity and to exclude false positive results. It is possible that among the study participants, scientifically motivated persons or individuals keen to know their serostatus will in particular volunteer to donate samples. Such a scenario points towards a convenience sampling, and has a higher uncertainty bias in comparison to random samples. We will try to counterbalance this potential bias by including a large sample size (i.e., high proportion of the total number of employees) and by monitoring the age distribution during recruitment. Another potential bias includes the social pressure from superiors or peers to participate. We have included the following counter measures: First, there is no possibility for superiors to identify participating employees at the time of recruitment if study volunteers sign consent in their private area. Second, the online questionnaire will directly ask participants. Third, study participants can choose the location for blood sampling when making an appointment in the given time frame, i.e., police station versus Interregionale Blutspende SRK. In the latter location, privacy can be guaranteed, whereas in the former location, working colleagues will be aware of blood sampling, and hence, study participation.

3.4 Withdrawal and discontinuation

Each participant will be informed that participation in the investigation is voluntary and that he or she is free to withdraw, without justification, from the investigation at any time without consequences and without affecting professional responsibilities. In case of participant(s) withdrawing their consent to participate in the study, their data and results of tests performed prior to withdrawal will be used by the study team, as stated in the study information provided at recruitment. After termination of the study, the data will be completely anonymized. Anonymization will be performed with a random number, not associated or related to any personal data or study protocol. The serum sample will be destroyed according to institutional biosafety disposal procedure. Data and samples of study participants who dropped out of the study (no show and no filling out of questionnaires at any follow-up visit) without withdrawing from the study will be used until the time point of drop out, as stated in the study information provided at recruitment, and then stored as described in 7.4.

4 STATISTICS AND METHODOLOGY

4.1. Statistical analysis plan

We consulted a statistician from the CTU Bern (Dr. B. Gahl), and we will conduct the study in collaboration with the department of statistics of the CTU Bern. In 2019, the police department of the canton of Bern listed 2'491 fulltime equivalents [24]. Nix et al. examined response rates to 497 police surveys reported in 390 articles published in 15 journals from 2008 to 2017, and found a mean response rate of 64.3% (St. Dev. 25.9) [27]. Because our survey includes serum sampling, we estimated a conservative voluntary study participation of 25% (i.e., approx. 625 individuals). We also performed a pre-study survey within the police department, and 927 individuals confirmed their interest to participate. Hence, this pre-study investigation corrects our sampling size estimate to 1’000 study participants.

For the primary endpoint, we hypothesize that the COVID-19 seroprevalence within the police department will be between 1% and 2% at the beginning of the study. We further hypothesize that the seroprevalence will increase during the study period by 8% (i.e., from 2% to 10%). A precision-based sample size calculation will be applied to reduce the margin of error. Considering the uncertainty from the serological survey and including our validation results and

the manufacturer's data, we calculate a sensitivity of 97% and a specificity of ≥99% for detecting SARS-CoV-2 antibodies in serum [28].

	CI width (%) for				
Proportion, %	800 Participants	1000 Participants	1200 Participants	1400 Participants	1600 Participants
1%	15	13	12	11	10
2%	20	18	16	15	14
3%	24	21	20	18	17
4%	27	24	22	21	19
5%	30	27	25	23	21
6%	33	30	27	25	23
7%	36	32	29	27	25
8%	38	34	31	28	27
9%	40	36	32	30	28
10%	42	37	34	31	29

Reading example: Including 1200 participants yields a CI 13.4 to 29.6%, given a true proportion of 2%.

The Table demonstrates sample size consideration to derive the precision (width of 95% confidence interval, CI) for a specific seroprevalence achieved when the corresponding number of policemen of Kanton Bern is included into the prospective cohort study using serological testing. The Wilson method was used to calculate CIs.

At every visit, we will first calculate the crude seroprevalence as the proportion of the seropositive samples among all collected samples. Second, we will adjust the seroprevalence for test characteristics (false positive and false negative rate). Third, we will calculate the weighted seroprevalence to adjust for sampling imbalances, with weighting factors based on the demographic structure of the police force (age, sex, rural vs. city distribution). We will furthermore analyze changes in seropositivity in a repeated-measures mixed-effects logistic regression model. In a second step, we will include health-related, activity-related and geography-related risk factors as covariates into the model to study effects of these factors and derive corresponding odds ratios. Change of risk factors over time will be accounted for. The change of antibody titres over time will also be analyzed using mixed models.

In addition to demographic characteristics, a descriptive analysis of health-related variables (i.e. diabetes, arterial hypertension, cardiovascular disease, chronic pulmonary disease, immunocompromised status because of host diseases or medical treatment, cancer, obesity), and activity-related data (i.e. fieldwork activity vs office and administration activity, working in cities or rural areas) will be performed. The categorization of variables is illustrated in appendix 2. Comparison of categorical and continuous variables will be performed with chi-square tests, t-tests, Wilcoxon-Mann-Whitney-Test, Kruskal-Wallis-Test and multivariate analysis, accordingly. The significance level will be two-sided $\alpha = 0.05$.

4.2. Handling of missing data

Questionnaires will be screened for completeness. In case of missing data, study participants will be contacted by the study team to verify missing data. In the final analysis, we will use all available data. Mixed models implicitly account for missing data as long as at least one measurement per participant is available.

5 REGULATORY ASPECTS AND SAFETY

5.1 Local regulations / Declaration of Helsinki

This research project will be conducted in accordance with the protocol, the Declaration of Helsinki [3], the principles of Good Clinical Practice, the Human Research Act (HRA) and the

Human Research Ordinance (HRO) [1] as well as other locally relevant regulations. The Project Leader acknowledges his responsibilities as both the Project Leader and the Sponsor.

5.2 Notification of safety and protective measures (HRO Art. 20)

The project leader is promptly notified (within 24 hours) if immediate safety and protective measures have to be taken during the conduct of the research project. The Ethics Committee will be notified via BASEC of these measures and of the circumstances necessitating them within 7 days.

5.3 Serious events (HRO Art. 21)

If a serious event occurs, the research project will be interrupted and the Ethics Committee notified on the circumstances via BASEC within 7 days according to HRO Art. 21[1].

5.4 Procedure for investigations involving radiation sources

Not applicable

5.5 Amendments

Substantial changes to the project set-up, the protocol and relevant project documents will be submitted to the Ethics Committee for approval according to HRO Art. 18 before implementation. Exceptions are measures that have to be taken immediately in order to protect the participants.

5.6 End of project

Upon project completion or discontinuation, the Ethics Committee is notified within 90 days. Biological material (serum samples) and data from the questionnaire will be kept for 10 years.

5.7 Insurance

In the event of project-related damage or injuries, the Sponsor will be liable, except for damages that are only slight and temporary; and for which the extent of the damage is no greater than would be expected in the current state of scientific knowledge (Art. 12 HRO).

6 FURTHER ASPECTS

6.1 Overall ethical considerations

Our study aims to generate robust epidemiological data on a special population that is at risk because of their occupation. Social distancing and contact avoidance rules may not be possible in the practice of policemen's work. Conversely, the risk of exposure in this population may be increased because of emergency calls for violence or because of actions against groups of people who ignore or demonstrate against lockdown measures [29-31]. Considering that 80% to 90% of individuals infected with SARS-CoV-2 are undocumented or asymptomatic, the risk of exposure of police officers when entering the scene is unknown. These arguments justify the necessity of a special population seroprevalence survey.

[1] A serious event is defined as any adverse event where it cannot be excluded, that the event is attributable to the sampling of biological material or the collection of health-related personal data, and which:
a. requires inpatient treatment not envisaged in the protocol or extends a current hospital stay;
b. results in permanent or significant incapacity or disability; or
c. is life-threatening or results in death.

Serological testing has a role in identifying people with milder disease who have been missed by other methods. Serological surveys address the problem of overfitting the trajectories of the epidemic curve based on the number of symptomatic infections instead of the total number of infections, which includes asymptomatic infections [9]. Our study will generate data while we conduct the investigation (at cross-sectional time points) and immediately after we end it (cohort data). Thus, epidemiological data will be readily available and will help refine epidemic trajectory models. Population immunity levels are required to inform disease control policies. The data will represent a measurement of those who are susceptible to infection, quantify the need for vaccination, and aid policies for decision making about vaccination strategies.

The seroprevalence survey will generate data that are useful for police departments in other cantons in Switzerland and in other countries. The methodology can be easily implemented in other institutions, and hence allows comparisons of preventive measures in association with seroprevalence results between cantons and nations.

The duration of both antibody persistence and neutralizing capacity over time is unknown. Because we are generating a cohort, we are able to monitor antibody levels over 1 year. Similarly, we are able to investigate the neutralizing capacity in study participants who repeatedly test positive for SARS-CoV-2. These data are important to evaluate possible immunity over time, both after virus exposure and – if available – after vaccination.

The burden and time effort for participants is minimal. We are not using genetic data, nor are we investigating a vulnerable patient population. Therefore, we are convinced that there is an overall fair balance for the study participant.

6.2 Risk-Benefit Assessment

This study poses minimal risk to participants, requiring the collection of one serum sample per visit (each tube has a volume of 9 mL). If there is a contraindication to venipuncture, the subject will not be recruited in the study. We have included means to counterbalance social pressure from superiors or peers to participate in the study.
There is no immediate benefit to the project participant. The data collected will help improve and guide efforts to understand the extent and risk of COVID-19 virus among police officers. In addition, it may be important for an individual to know whether they were exposed to SARS-CoV-2 prior to or during the study. The use of convalescent plasma has been proposed for the treatment of COVID-19, recently [32]. With our study strategy, potential antibody donors, and those with neutralizing antibody capacity can be identified. The study strategy may be transferred to large scale populations, and hence, generate a higher number of donors. Thus, the results of the project could benefit future patients.
It is anticipated that a vaccine will be available in the future. Study participants can compare the immune response and vaccine efficacy/synergism pre- and post-vaccination by using the stored serum sample from this study and a serum sample taken after vaccination. However, such a scenario will require a new research and ethic proposal.

6.3 Rationale for the inclusion of vulnerable participants

The study includes healthy volunteers, because the study focuses on employees of the cantonal police of Bern and not on individuals with a disease.

7 QUALITY CONTROL AND DATA PROTECTION

7.1 Quality measures

The study protocol is aligned with that of the WHO for population-based age-stratified sero-epidemiological investigations, adapted for the specific population and geographic region in our study [25]. Data and serum results will be collected in a standardized format according to the

questionnaires and tools in the WHO protocol to assist with data harmonization and comparison of results.

The study team consists of a collaborative consortium of the core research team, the Interregionale Blutspende SRK, the police department of the canton of Bern, and the Clinical Trial Unit (CTU) of Bern for data management and statistical analysis. In addition, highly qualified study nurses and serology laboratory technicians at our institution (IFIK) support our team. Members of the team are trained in the collection and transportation of serum specimens, safe handling practices, and spill decontamination procedures. They are also trained in infection prevention and control procedures (standard contact and droplet precautions) and in Good Clinical Practice.

Results of antibody testing will directly and automatically be transferred to the databank (REDCap) to avoid entry mistakes. Study participants will enter the response of the questionnaire into the REDCap system. A study nurse will verify data and contact study participants in case of entry mistakes or missing data. Hence, the study is accompanied by project personnel trained on all project related aspects.

7.2 Data recording and source data

Project data will be recorded in a central database (Research Electronic Data Capture, REDCap) hosted by our collaborator, the CTU of the University of Bern. The databases are highly secured and fulfil all requirements of the Swiss Human Research Act. Different data access privileges will be set for different user types (data clerks, data managers, PI). Study participants will be asked to complete an online questionnaire that covers information on demographics and possible COVID-19 exposure or infection. Questionnaires and database will be designed in order to minimize data capture errors, using drop-down menus, data range limits and data type protection where possible. Returned questionnaires will be reviewed for completeness and responses electronically stored in the REDCap database. Routine data checks will be performed. Also results from serology analyses will be automatically entered into REDCap. The PI is responsible for assuring that the data collected is complete, accurate and recorded in a timely manner. Security and back-up of data storage will be guaranteed by CTU, University of Bern. To access this source, user authentication and a password will be required. Data will be accessible according to Open Research Data and FAIR principles when corresponding manuscripts are published.

7.3 Confidentiality and coding

Project data will be handled with uttermost discretion and is only accessible to authorized personnel who require the data to fulfil their duties within the scope of the research project. Each study participant will be assigned a unique study identification number (barcode) for the labelling of questionnaires and serum specimens. This code will be coupled with a second code that indicates the visit number and the result assignment (serum sample or questionnaire, see below coding). On the CRFs and other project specific documents, participants are identified by the unique participant number (barcode). In the databank (REDCap), the study participant's email address is collected, too. Therefore, **the databank is not completely coded**, because study participants may be potentially identified if they use an e-mail address displaying their names. The use of e-mail addresses is required because online questionnaires will be distributed through an automated process. This is to avoid potential mistakes that are likely to be generated when using a manual system, due to the large number of participants recruited and followed up at each study visit. The CRFs in this trial are implemented electronically using a dedicated electronic data capturing (EDC) system (REDCap, https://www.project-redcap.org/). Questionnaires for patients will be prepared in electronic format and will be accessible through a personal link. The personal link will be sent to the patient’s email address. Patients’ email address will be therefore collected into REDCap but this field will be tagged as “Identifier field” and thus will be automatically removed from data exports. Considering that we expect 1'000 study participants and at least 5 visits for each study participant, there is a high risk of mistakes

if data are transferred manually. **After termination of the study, and confirmation of the completeness of the data set, the e-mail address will be removed from the data bank, to ascertain a completely coded databank.**
The server hosting the EDC system and the database is kept in a locked server-room at the CTU Bern. Only the system administrators have direct access to the server and back-up tapes. A role concept with personal passwords (site investigator, statistician, monitor, administrator) regulates permission for each user to use the system and database as he/she requires.
All data entered into the CRFs are transferred to the database using Transport Layer Security (TLS) encryption. Each data point has attributes attached to it identifying the user who entered it with the exact time and date. Retrospective alterations of data in the database are recorded in an audit table. Time, table, data field and altered value, and the person are recorded (audit trail). A multi-level back-up system is implemented. Back-ups of the whole system including the database are run internally several times per day and on external tapes once a day. The back-up tapes are stored in a secure place in a different building.
Coding: Each study participant will be assigned a unique study identification number (barcode) for the labelling of questionnaires and serum specimens. We will use a barcode system that allows scanning and printing out stickers. This barcode will be coupled with a second code that indicates the visit number and the result assignment. Study-related data of the patient will be collected in a coded manner. The names of the patients will not be disclosed. As outlined above, e-mail addresses provided by the study participants will be used. Depending on the provided e-mail address, the patient's names may be identifiable. After termination of the study, and confirmation of completeness of data, e-mail addresses will be removed, and only coded data used.
Biological material: Biological material (serum sample) is not identified by participant name but by a unique participant number (barcode, see paragraph above). Biological material (serum sample) is appropriately stored in a restricted area only accessible to authorized personnel. Serum samples will be stored at IFIK (-80°C) and at Interregionale Blutspende SRK (-30°C). The diagnostic and research laboratories of the IFIK and at Interregionale Blutspende SRK have the required government permits to operate a diagnostic service for clinical specimens of human origin, including storage of such clinical specimens; furthermore, they are accredited to the ISO/IEC 17025 Standard. All laboratory equipment throughout the entire Institute, including freezers and microbiological safety cabinets, is covered by contracts for planned preventative maintenance. Where appropriate, equipment is also monitored by laboratory staff in accordance with the comprehensive Quality Management and Safety Management systems in place at the Institute. All visitors, irrespective of their business, are required to sign a confidentiality agreement before being granted access to the building (they also sign when leaving the institute).

7.4 Retention and destruction of study data and biological material

At *interim* and final analyses, data files will be extracted from the database into statistical packages to be analyzed. After database lock, the status of the database is recorded in special archive tables. The sponsor (PI) will keep the Trial Master File, the extracted data, the meta data and *interim*/final reports for at least 10 years after project termination. Serum samples will be stored for at least 10 years after project termination. The storage of serum samples depends on the consent for further use (see 5.6). In line with the study information and consent form, study participants are invited to sign additional consent for further use of their serum samples. If there is no consent for further use or withdraw of consent during the study period, serum samples will be destroyed after termination of the project. If there is consent for further use, serum samples will be stored in our biobank for at least 10 years after project termination.

8 FUNDING / PUBLICATION / DECLARATION OF INTEREST

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Appendix 1: Schedule of assessments

Time (months)	**0-3**	**3-6**	**+0.5 & +1**	**6-9**	**+0.5 & +1**	**9-12**	**+0.5 & +1**	**12-15**	**+0.5 & +1**	**15-18**	**+0.5 & +1**
Visit	Study information & candidates registration	1st visit baseline		2nd visit		3rd visit		4th visit		5th visit	
Oral and written Information	+										
Candidates registration on study website	+										
Written consent		+									
Check inclusion-/ exclusion criteria		+									
Online Questionnaire		+		+		+		+		+	
Blood Sampling		+		+		+		+		+	
Procedures (serum testing)		+		+		+		+		+	
Additional questionnaire for seropositive participants			+		+		+		+		+
Confirmatory blood sampling			+		+		+		+		+
Procedures (confirmatory serum testing)			+		+		+		+		+

Appendix 2: The categorization of variables

Parameter	Definition	Source of data to calculate the parameters
Cumulative incidence	The proportion of individuals with seropositivity	Laboratory result
Age- and gender specific attack rate	The proportion of individuals per age and gender strata with seropositivity	Laboratory result Questionnaire
Symptomatic proportion of cases	The proportion of individuals with seropositivity who showed symptoms or signs of COVID-19 infection (+/- confirmed PCR result in the past)	Questionnaire
Asymptomatic proportion of cases	The proportion of individuals with seropositivity who showed no symptoms or signs of COVID-19	Questionnaire
Attack rate in risk group (health-related data) (Persons over 65 years are not included because retirement is expected at this age in the study population).	Study participants with one or more of the following risk factors: diabetes, arterial hypertension, cardiovascular disease, chronic pulmonary disease, immuno-compromised because of host diseases or because of medical treatment, cancer, obesity (BMI > 30 kg/m2)	Laboratory result Questionnaire
Activity related cumulative incidence	The proportion of individuals with seropositivity in the following 2 groups: Group 1: Police officers with fieldwork activity and frequent population contact. Group 2: office and administration occupation with low population contact.	Laboratory result Questionnaire
Geography related cumulative incidence	The proportion of individuals with seropositivity in the following 2 groups: Group 1: occupation in cities (Bern, Thun, Biel) Group 2: occupation in rural area of Bern or in cities but not belonging to group 1.	Laboratory result Questionnaire
Sub-study in seropositive study participants		
Parameter	**Definition**	**Source of data to calculate the parameters**
Serological response to infection	The change in serum level of specific antibodies to COVID-19 virus (increase in antibody titres)	Laboratory result over time
Seropositive result confirmation (specificity)	Seropositive result at baseline or seroconversion during the study year that will be confirmed with two additional serum samples, two and four weeks after the positive antibody result.	Laboratory result
Work or social environment-related exposure	Study participants perception of possible COVID-19 exposure	Questionnaire