



## Project description

### Title

Utilising the Danish PCR test dataset from 2020 to estimate the level of protection against repeat infection with SARS-CoV-2 following a first infection.

### Aims

1. To compute a measure of the likelihood among Danish residents of testing positive for SARS-CoV-2 more than once relative to a single positive test.
2. Using the measure developed under point (1), to estimate the degree of protection (i.e. observed immunity) against re-infection.
3. If possible, to extend the analysis to investigate effects of age and sex, and the longevity of protection.

### Background

The degree to which SARS-CoV-2 infection protects against a new infection in the same individual is still largely unknown. However, knowledge hereof is important to our understanding of the epidemic and how it will develop in the future. Forecasts of the epidemiological trajectory are hugely dependent on the level of immunity resulting from a first infection, e.g. whether a strong and long-lasting immune response can be assumed, or a much weaker and temporary effect, and is of importance to considerations around herd immunity and whether this can be achieved through natural infection in various populations. It is also possible that different age groups are affected differently. The strategy of ending the epidemic through vaccination of a large proportion of the population are based on the notion that vaccinations induce protection of a certain duration in the population, and context and relevant evidence are needed to further qualify such considerations, e.g. through studies of immunity following natural infection.

Infection with other endemic coronaviruses strains that cause the common cold is known to not result in long-lasting immunity against new infections, although protection generally seem to last a couple of seasons. Results are beginning to appear from a longitudinal serological studies investigating immunological parameters (particularly antibodies) relating to SARS-CoV-2 infection and appear to show detectable antibodies lasting beyond six months. This suggests some degree of durable protection against new infection. Similarly, there is limited evidence to suggest that repeat infections occur frequently, because most reports of repeat infections are in the form of individual case-reports. Consistent with a general hypothesis that the majority of people who are infected develop immunity for some period of time (of unknown length), it seems that repeat infections occur only rarely. Furthermore, it is often unclear whether a seemingly repeat infection is the result of an immunologically new infection with the virus or



simply a recurrence/re-detection of existing lingering virus from a first infection that is still detectable by the highly sensitive PCR test.

A large proportion of the Danish population has been tested in 2020 and many have been tested several times. The aim of this project is therefore to utilise the National Danish PCR test database to determine the likelihood of a second positive PCR test some months after a first confirmed infection, and in this way to estimate the level of protection (natural immunity) against repeat infection.

## Data

Data for the analysis will be extracted from the COVID-19 electronic surveillance system at SSI and will comprise all PCR tests carried out in Denmark in 2020, i.e. from 1 January to 31 December 2020. The database contains details of all PCR tests carried out on Danish residents, whether tested through the healthcare system (*sundhedssporet*) or the parallel public clinics (*samfundssporet*). The data contains information on test result, test date, civil registry number (of the person tested), birthday, sex, council of residency, date of death (if applicable), profession, and more. Analyses are conducted on a pseudo-anonymised dataset.

## Analysis

A cohort will be created of all individuals who have had a PCR test performed in 2020. Individuals enter the cohort at the time of their first test and are followed up until a future positive test result, death, or the end of follow-up. Those with an initial positive test result will be compared with people in the cohort who have not previously tested positive. Rates of infection will be compared across those with and without a previous positive PCR test.

As it is possible for traces of viral material to remain detectable for some time after infection, repeat positive tests may actually derive from the same round of infection. For this reason, we will exclude from the analysis any repeat positive tests that are close in time. A gap of 60 or 90 days between repeat tests should be applied. The analysis will be controlled for potential confounders, including age and sex. It will be possible to derive the relative protection from the rates of infection. It will also be possible to contrast infections during the first wave of infection with those occurring during the autumn wave, leaving out any infections occurring over the summer period. Sub-group analyses will also be relevant, especially sub-analyses with individuals who are frequently tested as they might contribute additional information. Analysis models using either Cox regression or Poisson regression may be used – the details will be determined at the analysis stage. Further analyses may be conducted as appropriate, e.g. sensitivity and supplementary analyses, analysis of age effects, etc.

On the basis of the ratio effect measure that is derived from the analysis models, it will be possible to compute a measure of protection (observed immunity in the population) similar to the derivation of vaccine efficacy.



### **Legal/Ethical considerations**

According to the SSI Compliance department, this project is part of the disease surveillance remit of the SSI and does not require registration with the Danish Data Protection agency. Findings stemming from the project may be disseminated (*added later*: confirmed by SSI Compliance 1 Feb 2021); the presentation of findings shall be done in a GDPR compliant manner.

### **Project team**

The proposed project team consists of: Steen Ethelberg, Christian Holm Hansen (Dept. of Infectious Disease Epidemiology & Prevention), Daniela Michlmayr (Dept of Bacteria, Parasites & Fungi), Kåre Mølbak (Infectious Disease Preparedness) and Sophie Gubbels (secretariat for Data Analysis and Integration), all from the SSI. Additional staff may be included.

### **Timeline**

The analyses can start in December 2020 and are expected to be completed in the course of approx. one month. Results of the project are expected in the beginning of 2021.

### **Dissemination of results:**

Findings are to be shared with the Danish health authorities and are expected to form part of the SSI covid-19 epidemic surveillance and management activities. It is likely that results obtained from the study will be of general interest in which case we should seek to prepare them for publication in a scientific journal.

*SSI, November/December 2020*

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