



cause they had to go to get their OAT medication once a week up to daily.

These assessments led to the facilities and institutions involved in the care of OAT patients taking far-reaching resource-intensive protective measures at the beginning of and throughout the corona pandemic to prevent transmission and detect possible infections early [9]. Home-delivery of OAT medication as well as home visits have been offered to allow OAT patients to stay at home as requested by the health authorities. For the same reason, the maximum take-home prescription has been extended from 1 to 7 days for diacetylmorphine and from 7 to 28 days for all other OAT substances. Every patient entering the centre was asked for symptoms and were tested if indicated. Supervised consumption rooms were enlarged to allow distancing rules. A temporary quarantine and isolation ward for people living in supervised facilities was established during the first wave of the pandemic.

The aim of this study was to assess the SARS-CoV-2 seroprevalence among OAT patients, to explore whether the antibody positive group differed from the antibody negative group and to compare the SARS-CoV-2 seroprevalence among OAT patients with the prevalence in the regional general population.

## Material and methods

### Study design, setting and participants

Corona Immunitas is a national research programme that investigates the extent and nature of infection with SARS-CoV-2 in 40 different seroprevalence studies [10]. In addition to general population-based random samples, various subpopulations have been studied [11]. Eleven universities and institutes are involved in this research programme.

In this cross-sectional substudy, we enrolled a subsample of OAT patients ( $n = 122$ ) who were recruited between the beginning of July and mid October 2020. This period corresponds to the phase between the end of the first corona pandemic wave and the beginning of the second wave in Switzerland. Recruitment took place at the outpatient clinic called Arud Centre for Addiction Medicine in Switzerland, located in Zurich. Arud takes care of around 2500 patients with any kind of addiction disorder. A total 1014 patients were in OAT during the recruitment period and therefore eligible for the study. We compared this subsample to the Corona Immunitas population-based random sample of 20- to 64-year-old inhabitants of the canton of Zurich ( $n = 472$ ), provided by the Federal Office of Statistics (FSO), recruited between the end of June and beginning of September 2020. The Ethics Committee of the Canton of Zurich (BASEC 2020-01247) approved the study.

### Procedures and measurements

Recruitment of the OAT patients took place on the one hand through advertisements in the centre. Interested patients could register at the reception desk to participate in the study. On the other hand, peer staff and therapists approached patients for possible participation in the study when they showed up in the centre or by phone. After giving written consent to the study, participants completed the

Corona Immunitas baseline questionnaire on-site alone or with the support of staff. The nursing staff then took 10 ml of venous blood from the participants for antibody determination. Participants were compensated with CHF 20 for their travel expenses.

The Corona Immunitas baseline questionnaire collected the following information: participant characteristics, health data, COVID-19-specific information such as symptoms, polymerase chain reaction (PCR) test results and use of the SwissCovid App, risk behaviour and exposure, and health-related quality of life (EQ-5D-5L scale).

### Laboratory analysis / serological testing

As antibody test, the Sensitive Anti-SARS-CoV-2 Spike Trimer Immunoglobulin Serological (SenASTrIS) assay developed by the Vaud Central University Hospital (CHUV), the Swiss Federal Institute of Technology in Lausanne (EPFL) and the Swiss Vaccine Center was used for all Corona Immunitas studies [12]. The test provides IgG and IgA antibody results. The specificity is 99.7% and the sensitivity 96.6% (15 days after infection). Presence of either IgG and/or IgA antibodies was counted as a positive test result.

### Statistical analysis

We used mean  $\pm$  standard deviation (SD) to show descriptive statistics of continuous variables, and count / valid percent for categorical ones. For the former, we applied two-sided t-test to assess statistical significance of mean differences between independent groups, and for the later, chi-square of cross tabulated cell frequencies, both at the 5% alpha-level. We calculated 95% confidence intervals (95% CIs) and prevalence ratio using a substitution method [13], calculated with SciStat online.

## Results

The characteristics of the two populations (OAT and general population) are presented in table 1.

OAT patients differed significantly from the general population in almost all of the studied characteristics. The proportion of men was higher; the level of education was lower; they lived with fewer people in the same household. They were more likely to be smokers, to be diagnosed with chronic conditions, and had more health-related limitations; they had travelled less outside the country; and they were more likely to have already been tested for SARS-CoV-2. The SARS-CoV-2 seroprevalence in the general population was 3.5% (95% CI 2.2–4.8%) vs 9.8% (5.1–17.2%) in the OAT population, corresponding to a prevalence ratio of 2.9 (95% CI 1.37–5.94;  $p = 0.004$ ). Table 2 shows the SARS-CoV-2-seroprevalence rates in the OAT patients and the general population sample by characteristics.

Three of the 12 OAT patients (25%) with positive SARS-CoV-2-serology reported no COVID-symptoms since the beginning of the pandemic in January 2020. This was comparable the positive tested individuals in the general population where 4 of the 19 positive tested individuals (21%) had no of these symptoms during the first wave of the pandemic. The prevalence of the symptoms are show in table 3. The most frequent symptoms among the twelve pos-

itive tested OAT patients were cough with expectoration (50.0%), runny or blocked nose (50.0%) and body temperature of 38° or higher (41.7%). In the OAT sample, we found no significant differences between seropositive and seronegative individuals regarding socio-economic status, risk behaviour, or comorbidity. None of the reported symptoms did differ significantly between positive and negative tested OAT patients (Table 3). None of the positive tested OAT patients had a severe course of COVID-19.

## Discussion

In this study, we found an almost threefold increased seroprevalence for SARS-CoV-2 in OAT patients compared with the general population, indicating that the assessment made at the start of the pandemic that the OAT population is at increased risk of contracting coronavirus is correct. The comparatively high seroprevalence in the OAT pop-

ulation occurred despite the specific protective measures taken. On the other hand, the concern that OAT patients infected with SARS-CoV-2 are at high risk of severe COVID-19 was not verified by our data.

In contrast to our study, a large US retrospective case-control study found recent and lifetime substance use disorder to be associated with increased COVID-19 hospitalisation and mortality rate, mainly in African Americans. The authors explained their finding mainly by higher prevalence of kidney, pulmonary, liver, cardiovascular, metabolic, and immune-related disorders among individuals with substance use disorder [4]. This was not the case in our OAT sample. Although the OAT patients suffered from significantly more comorbidities than persons from the general population, they were not at higher risk for severe COVID-19.

In the same study by Wang et al., opioid use disorder was associated with a higher rate of COVID-19 diagnosis, irre-

**Table 1:** Characteristics of the study participants compared with the population-based sample.

|                                                                                                                           |                                      | Population sample<br>n = 472 | OAT sample<br>n = 122 | p-value |
|---------------------------------------------------------------------------------------------------------------------------|--------------------------------------|------------------------------|-----------------------|---------|
| Age (mean ± SD) years (Population: 20 to 64 y., OAT: 18 to 72 y.)                                                         |                                      | 44.7 ± 11.7                  | 44.3 ± 9.4            | 0.727   |
| Male gender                                                                                                               |                                      | 47.9 (226)                   | 69.7 (85)             | <0.001  |
| BMI (mean ± SD) kg/m <sup>2</sup>                                                                                         |                                      | 24.9 ± 4.9                   | 24.5 ± 4.1            | 0.407   |
| Swiss citizenship                                                                                                         |                                      | 75.8 (358)                   | 80.3 (98)             | 0.300   |
| Education level                                                                                                           | Primary                              | 2.8 (13)                     | 26.2 (32)             | <0.001  |
|                                                                                                                           | Secondary                            | 39.2 (185)                   | 52.5 (64)             | 0.008   |
|                                                                                                                           | Tertiary                             | 56.8 (268)                   | 9.0 (11)              | <0.001  |
| Household size                                                                                                            | Single person                        | 15.0 (70)                    | 45.1 (55)             | <0.001  |
|                                                                                                                           | Two persons                          | 37.6 (176)                   | 27.0 (33)             | 0.029   |
|                                                                                                                           | Three persons or more                | 47.4 (144)                   | 22.1 (27)             | <0.001  |
| Chronic conditions*                                                                                                       | No chronic condition                 | 80.3 (378)                   | 47.5 (58)             | <0.001  |
|                                                                                                                           | At least one chronic condition       | 19.7 (93)                    | 52.5 (64)             |         |
| Smoking status                                                                                                            | Current smoker                       | 24.8 (117)                   | 86.1 (105)            | <0.001  |
|                                                                                                                           | Ex-smoker                            | 53.5 (252)                   | 8.2 (10)              |         |
|                                                                                                                           | Never smoker                         | 21.7 (102)                   | 4.1 (5)               |         |
| Presence of health-related quality of life limitations (Eq5d-5l dichotomised: 1 = no; 2 to 5 = yes)                       | Walking around problems              | 9.5 (45)                     | 24.6 (30)             | <0.001  |
|                                                                                                                           | Self-care problems                   | 1.1 (5)                      | 9.8 (12)              | <0.001  |
|                                                                                                                           | Problems performing daily activities | 7.6 (36)                     | 28.7 (35)             | <0.001  |
|                                                                                                                           | Pain or physical discomfort          | 28.4 (117)                   | 51.6 (63)             | <0.001  |
|                                                                                                                           | Anxiety or depression                | 24.8 (117)                   | 45.0 (55)             | <0.001  |
| Self-rating (mean ± SD) of current health status (EQ VAS: 0 = worst to 100 = best)                                        |                                      | 85.3 ± 11.6                  | 69.1 ± 18.8           | <0.001  |
| Episodes of symptoms for at least 3 days in 2020                                                                          | No episode                           | 40.3 (190)                   | 63.9 (78)             | <0.001  |
|                                                                                                                           | One or more episodes                 | 59.7 (285)                   | 36.1 (44)             |         |
| Self-reported adherence to recommended precaution measures in past 7 days (5-point Likert-scale: 1 = never to 5 = always) | Distancing (mean ± SD)               | 4.1 ± 0.7                    | 3.8 ± 1.3             | <0.001  |
|                                                                                                                           | Stay at home (mean ± SD)             | 3.2 ± 1.1                    | 3.2 ± 1.4             | 1.000   |
|                                                                                                                           | Wearing face mask (mean ± SD)        | 3.0 ± 1.2                    | 3.8 ± 1.2             | <0.001  |
|                                                                                                                           | Hygiene measures (mean ± SD)         | 4.6 ± 0.6                    | 4.4 ± 0.8             | 0.003   |
| Previous SARS-CoV-2 test results                                                                                          | Tested positive                      | 0.0 (0)                      | 0.8 (1)               | 0.052   |
|                                                                                                                           | Tested negative                      | 8.7 (41)                     | 23.8 (29)             | <0.001  |
|                                                                                                                           | No test done                         | 91.1 (429)                   | 72.1 (88)             | <0.001  |
| SARS-CoV-2 in immediate environment                                                                                       | No people previously tested positive | 89.8 (424)                   | 93.4 (114)            | 0.226   |
|                                                                                                                           | One person tested positive           | 3.6 (17)                     | 2.5 (3)               | 0.549   |
|                                                                                                                           | Two or more people tested positive   | 6.6 (31)                     | 4.1 (5)               | 0.304   |
| Trips taken outside the country since January 2020                                                                        | No trips                             | 53.2 (251)                   | 89.3 (109)            | <0.001  |
|                                                                                                                           | One trip                             | 23.3 (110)                   | 6.6 (8)               |         |
|                                                                                                                           | Two or more trips                    | 23.5 (111)                   | 4.1 (5)               |         |

Unless otherwise stated, all figures are given as % (n). In all statistical analyses, the fraction denominator is the total number of cases with valid information for the respective variable (valid percent); p-value = significance of two-sided test: chi square for categorical variables, independent samples t-test for continuous variables.

\* Excluding allergies

n: number of participants; OAT: opioid-agonist therapy; SD: standard deviation; BMI: body mass index; EQ5D-5L: five-level version of the EuroQol Instrument; EQ VAS: EuroQol visual analogue scale; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2 infection

spective of its severity. The SARS-CoV-2 seroprevalence was not assessed in this paper.

A recent published study assessed during the first pandemic wave the SARS-CoV-2 seroprevalence, Covid-19 symptoms, and comorbidity among OAT patients from one addiction outpatient unit in Dublin, Ireland. The study included 103 individuals with a median age of 39.5 years

and showed a seroprevalence of 1.9%. Among the few persons who tested positive, there was no severe course of COVID-19 or death.

The main strength of our work lies in the possibility to compare identically collected data on seroprevalence, symptoms, behaviour and comorbidities of a well-defined

**Table 2:**  
SARS-CoV-2-antibody prevalence in OAT-patients and in the general population sample.

|                                                                                                                           | Population sample                    |             |                   | OAT sample  |             |                   |            |
|---------------------------------------------------------------------------------------------------------------------------|--------------------------------------|-------------|-------------------|-------------|-------------|-------------------|------------|
|                                                                                                                           | Total n                              | n AB neg.   | n (%) AB positive | Total n     | n AB neg.   | n (%) AB positive |            |
| Total participants                                                                                                        | 472                                  | 453         | 19 (3.5%*)        | 122         | 110         | 12 (9.8%)         |            |
| Asymptomatic                                                                                                              | 18                                   | 14          | 4 (22.2%)         | 35          | 32          | 3 (8.6%)          |            |
| Age (mean ± SD) years (population: 20 to 64 y., OAT: 18 to 72 y.)                                                         | 44.7 ± 11.7                          | 44.6 ± 11.7 | 46.2 ± 11.0       | 44.3 ± 9.4  | 43.8 ± 9.3  | 48.8 ± 9.8        |            |
| Sex                                                                                                                       | Female                               | 246         | 239               | 7 (2.8%)    | 37          | 34                | 3 (8.1%)   |
|                                                                                                                           | Male                                 | 226         | 214               | 12 (5.3%)   | 85          | 76                | 9 (10.6%)  |
| BMI (mean ± SD) kg/m <sup>2</sup>                                                                                         | 24.9 ± 4.9                           | 25.0 ± 4.9  | 23.1 ± 3.8        | 24.5 ± 4.1  | 24.4 ± 4.1  | 25.3 ± 4.3        |            |
| Citizenship                                                                                                               | Swiss                                | 358         | 342               | 16 (4.5%)   | 98          | 89                | 9 (9.2%)   |
|                                                                                                                           | Other                                | 114         | 111               | 3 (2.6%)    | 24          | 21                | 3 (12.5%)  |
| Education                                                                                                                 | Primary                              | 13          | 12                | 1 (7.7%)    | 32          | 29                | 3 (9.4%)   |
|                                                                                                                           | Secondary                            | 185         | 179               | 6 (3.2%)    | 64          | 59                | 5 (7.8%)   |
|                                                                                                                           | Tertiary                             | 268         | 256               | 12 (4.5%)   | 11          | 10                | 1 (9.1%)   |
| Household size                                                                                                            | Single person                        | 70          | 68                | 2 (2.9%)    | 55          | 50                | 5 (9.1%)   |
|                                                                                                                           | Two persons                          | 176         | 167               | 9 (5.1%)    | 33          | 32                | 1 (3.0%)   |
|                                                                                                                           | Three persons or more                | 222         | 214               | 8 (3.6%)    | 27          | 23                | 4 (14.8%)  |
| Chronic conditions**                                                                                                      | No chronic condition                 | 378         | 364               | 14 (3.7%)   | 58          | 55                | 3 (5.2)    |
|                                                                                                                           | At least one chronic condition       | 93          | 88                | 5 (5.4%)    | 64          | 55                | 9 (14.1)   |
| Smoking status                                                                                                            | Current smoker                       | 102         | 95                | 7 (6.9%)    | 105         | 95                | 10 (9.5%)  |
|                                                                                                                           | Ex-smoker                            | 117         | 112               | 5 (4.3%)    | 10          | 10                | 0 (0.0%)   |
|                                                                                                                           | Never smoker                         | 252         | 245               | 7 (2.8%)    | 5           | 4                 | 1 (20.0%)  |
| Presence of health-related quality of life limitations (EQ5D-5L dichotomised: 1 = no; 2 to 5 = yes)                       | Walking around problems              | 45          | 42                | 3 (6.7%)    | 26          | 24                | 2 (7.7%)   |
|                                                                                                                           | Self-care problems                   | 5           | 5                 | 0 (0.0%)    | 8           | 7                 | 1 (12.5%)  |
|                                                                                                                           | Problems performing daily activities | 36          | 35                | 1 (2.9%)    | 31          | 30                | 1 (3.2%)   |
|                                                                                                                           | Pain or physical discomfort          | 134         | 128               | 6 (4.5%)    | 57          | 52                | 5 (8.8%)   |
| Anxiety or depression                                                                                                     | 117                                  | 109         | 8 (6.8%)          | 51          | 47          | 4 (7.8%)          |            |
| Self-rating (mean ± SD) of current health status (EQ VAS: 0 = worst to 100 = best)                                        | 85.3 ± 11.6                          | 85.2 ± 11.6 | 86.3 ± 11.8       | 69.1 ± 18.0 | 68.8 ± 18.5 | 72.8 ± 12.2       |            |
| Episodes of symptoms for at least 3 days in 2020                                                                          | No episode                           | 190         | 185               | 5 (2.6%)    | 78          | 70                | 8 (10.3%)  |
|                                                                                                                           | One or more episodes                 | 282         | 268               | 14 (5.2%)   | 44          | 40                | 4 (9.1%)   |
| Self-reported adherence to recommended precaution measures in past 7 days (5-point Likert-scale: 1 = never to 5 = always) | Distancing (mean ± SD)               | 4.1 ± 0.7   | 4.1 ± 0.8         | 4.2 ± 0.5   | 3.8 ± 1.2   | 3.7 ± 1.3         | 4.1 ± 1.0  |
|                                                                                                                           | Stay at home (mean ± SD)             | 3.2 ± 1.1   | 3.2 ± 1.1         | 3.3 ± 1.1   | 3.1 ± 1.4   | 3.1 ± 1.4         | 3.3 ± 1.4  |
|                                                                                                                           | Wearing face mask (mean ± SD)        | 3.0 ± 1.2   | 3.0 ± 1.2         | 2.9 ± 1.1   | 3.8 ± 1.2   | 3.8 ± 1.2         | 3.8 ± 1.4  |
|                                                                                                                           | Hygiene measures (mean ± SD)         | 4.6 ± 0.6   | 4.6 ± 0.6         | 4.6 ± 0.6   | 4.4 ± 0.7   | 4.4 ± 0.7         | 4.7 ± 0.5  |
| Previous SARS-CoV-2 test results                                                                                          | Tested positive                      | 0           | 0                 | 0 (0.0%)    | 1           | 0                 | 1 (100.0%) |
|                                                                                                                           | Tested negative                      | 40          | 38                | 2 (5.0%)    | 29          | 27                | 2 (6.9%)   |
|                                                                                                                           | No test done                         | 429         | 412               | 17 (4.0%)   | 88          | 81                | 7 (8.0%)   |
| SARS-CoV-2 in immediate environment                                                                                       | No people previously tested positive | 424         | 407               | 17 (4.0%)   | 114         | 104               | 10 (8.8%)  |
|                                                                                                                           | One person tested positive           | 17          | 16                | 1 (5.9%)    | 3           | 1                 | 2 (66.7%)  |
|                                                                                                                           | Two or more people tested positive   | 31          | 30                | 1 (3.2%)    | 5           | 5                 | 0 (0.0%)   |
| Trips taken outside the country since January 2020                                                                        | No trips                             | 251         | 242               | 9 (3.6%)    | 109         | 97                | 12 (11.0%) |
|                                                                                                                           | One trip                             | 110         | 107               | 3 (2.7%)    | 8           | 8                 | 0 (0.0%)   |
|                                                                                                                           | Two or more trips                    | 111         | 104               | 7 (6.3%)    | 5           | 5                 | 0 (0.0%)   |

Unless otherwise stated, all figures are given as n (%). In all statistical analyses, the fraction denominator is the total number of cases with valid information for the respective variable (valid percent).

\* Prevalence estimate for population sample was calculated using a Bayesian logistic regression model and weighted for age, sex and sensitivity/specificity of the antibody test

\*\* Excluding allergies

OAT: Opioid-agonist treatment; n: number of participants; AB neg.: antibody negative; AB positive: antibody positive; SD: standard deviation; BMI: body mass index; EQ5D-5L: five-level version of the EuroQuol Instrument; EQ VAS: EuroQuol visual analogue scale; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2 infection

**Table 3:**  
Comparison of OAT patients' characteristics according to SARS-CoV-2 antibody-test result.

|                                                                                                                           |                                                       | AB positive n<br>= 12/122 (9.8%) | AB negative n<br>= 110/122<br>(90.2%) | Diff. pos. –<br>neg. | p-value | Sig. test |
|---------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|----------------------------------|---------------------------------------|----------------------|---------|-----------|
| Age (mean ± SD) years (range: 18 to 72 y.)                                                                                |                                                       | 48.8 ± 9.8                       | 43.8 ± 9.3                            | 5.0                  | 0.12    | 1         |
| Male gender                                                                                                               |                                                       | 75.0                             | 69.1                                  | 5.9                  | 1.00    | 2         |
| Swiss citizenship                                                                                                         |                                                       | 75.0                             | 81.7                                  | –6.7                 | 0.70    | 2         |
| Swiss or German mother tongue                                                                                             |                                                       | 91.7                             | 87.0                                  | 4.6                  | 0.71    | 2         |
| Economic situation                                                                                                        | Payed work                                            | 10.0                             | 21.5                                  | –11.5                | 0.69    | 2         |
|                                                                                                                           | Disability pension                                    | 33.3                             | 22.7                                  | 10.6                 | 0.48    | 2         |
|                                                                                                                           | Household income <3,000 CHF/month                     | 90.9                             | 69.9                                  | 21.0                 | 0.28    | 2         |
| Household size                                                                                                            | Single                                                | 50.0                             | 47.6                                  | 2.4                  | 0.30    | 2         |
|                                                                                                                           | Two to four persons                                   | 30.0                             | 44.8                                  | –14.8                |         |           |
|                                                                                                                           | > Four persons                                        | 20.0                             | 7.6                                   | 12.4                 |         |           |
| Household composition                                                                                                     | With children <7 years of age                         | 8.3                              | 2.7                                   | 5.6                  | 0.34    | 2         |
|                                                                                                                           | With children between 7 and 17 years                  | 0.0                              | 1.8                                   | –1.8                 | 1.00    | 2         |
|                                                                                                                           | With adults between 18 and 35 years                   | 8.3                              | 15.5                                  | –7.1                 | 1.00    | 2         |
|                                                                                                                           | With adults between 36 and 65 years                   | 41.7                             | 29.1                                  | 12.6                 | 0.51    | 2         |
|                                                                                                                           | With adults over 65 years of age                      | 8.3                              | 2.7                                   | 5.6                  | 0.34    | 2         |
| Mobility                                                                                                                  | Travel(s) to other countries                          | 0.0                              | 15.3                                  | –15.3                | 0.59    |           |
|                                                                                                                           | Buy groceries (mean ± SD)*                            | 3.4 ± 1.9                        | 3.4 ± 1.9                             | 0.1                  | 0.62    | 3         |
|                                                                                                                           | Outing (mean ± SD)*                                   | 3.1 ± 0.8                        | 6.2 ± 5.6                             | –3.0                 | 0.12    | 3         |
| Self-reported adherence to recommended precaution measures in past 7 days (5-point Likert-scale: 1 = never to 5 = always) | Distancing (mean ± SD)                                | 4.1 ± 1.0                        | 3.7 ± 1.3                             | 0.3                  | 0.44    | 4         |
|                                                                                                                           | Stay at home (mean ± SD)                              | 3.3 ± 1.5                        | 3.2 ± 1.4                             | 0.2                  | 0.64    | 4         |
|                                                                                                                           | Wearing face mask (mean ± SD)                         | 3.8 ± 1.4                        | 3.8 ± 1.2                             | 0.1                  | 0.67    | 4         |
|                                                                                                                           | Wearing gloves in public (mean ± SD)                  | 1.6 ± 1.1                        | 1.3 ± 0.8                             | 0.3                  | 0.25    | 4         |
|                                                                                                                           | Hygiene measures (mean ± SD)                          | 4.7 ± 0.5                        | 4.4 ± 0.8                             | 0.3                  | 0.28    | 4         |
| Body Mass -Index (kg/m <sup>2</sup> )                                                                                     | <20                                                   | 0.0                              | 9.2                                   | –9.2                 | 0.37    | 2         |
|                                                                                                                           | 20 to 24                                              | 58.3                             | 50.5                                  | 7.9                  |         |           |
|                                                                                                                           | 25 to 29                                              | 16.7                             | 29.4                                  | –12.7                |         |           |
|                                                                                                                           | 30 to 34                                              | 25.0                             | 9.2                                   | 15.8                 |         |           |
|                                                                                                                           | 35+                                                   | 0.0                              | 1.8                                   | –1.8                 |         |           |
| Smoking status                                                                                                            | Daily cigarette smoker                                | 90.9                             | 86.2                                  | 4.7                  | 1.00    | 2         |
|                                                                                                                           | Average daily smoked cigarettes (mean ± SD)           | 21.1 ± 7.5                       | 18.5 ± 9.6                            | 2.6                  | 0.21    | 3         |
|                                                                                                                           | Use of other tobacco products                         | 18.2                             | 22.6                                  | –4.5                 | 1.00    | 2         |
|                                                                                                                           | E-cigarette user                                      | 0.0                              | 7.8                                   | –7.8                 | 1.00    | 2         |
| Self-reported pre-existing medical diagnoses                                                                              | Cancer                                                | 9.1                              | 1.8                                   | 7.3                  | 0.25    | 2         |
|                                                                                                                           | Diabetes                                              | 9.1                              | 3.6                                   | 5.5                  | 0.38    | 2         |
|                                                                                                                           | Disease or treatment that weakens the immune system   | 18.2                             | 16.7                                  | 1.5                  | 1.00    | 2         |
|                                                                                                                           | Hypertension                                          | 27.3                             | 12.0                                  | 15.2                 | 0.17    | 2         |
|                                                                                                                           | Cardiovascular diseases (CVD)                         | 9.1                              | 8.4                                   | 0.7                  | 1.00    | 2         |
|                                                                                                                           | Chronic respiratory diseases                          | 33.3                             | 20.6                                  | 12.8                 | 0.29    | 2         |
|                                                                                                                           | Pollen allergy / allergic coryza                      | 9.1                              | 19.3                                  | –10.2                | 0.68    | 2         |
|                                                                                                                           | other                                                 | 11.1                             | 23.4                                  | –12.3                | 0.68    | 2         |
|                                                                                                                           | Number (mean ± SD) of pre-existing diagnoses (0 to 8) | 1.2 ± 1.0                        | 1.0 ± 1.2                             | 0.1                  | 0.45    | 4         |
| One diagnosis or more reported                                                                                            | 75.0                                                  | 55.5                             | 19.5                                  | 0.23                 | 2       |           |
| Self-reported unspecific symptoms in recent past                                                                          | Fever feeling                                         | 33.3                             | 25.5                                  | 7.9                  | 0.51    | 2         |
|                                                                                                                           | Body temperature of 38°C or higher                    | 41.7                             | 16.8                                  | 24.8                 | 0.05    | 2         |
|                                                                                                                           | Dry cough                                             | 16.7                             | 24.5                                  | –7.9                 | 0.73    | 2         |
|                                                                                                                           | Cough with expectoration                              | 50.0                             | 31.8                                  | 18.2                 | 0.22    | 2         |
|                                                                                                                           | Bloody sputum                                         | 0.0                              | 3.6                                   | –3.6                 | 1.00    | 2         |
|                                                                                                                           | Runny or blocked nose                                 | 50.0                             | 37.3                                  | 12.7                 | 0.53    | 2         |
|                                                                                                                           | Sneezing                                              | 25.0                             | 30.0                                  | –5                   | 1.00    | 2         |
|                                                                                                                           | Sore throat                                           | 16.7                             | 21.8                                  | –5.2                 | 1.00    | 2         |
|                                                                                                                           | Shortness of breath                                   | 33.3                             | 22.7                                  | 10.6                 | 0.48    | 2         |
|                                                                                                                           | Breathing difficulties                                | 25.0                             | 34.5                                  | –9.5                 | 0.75    | 2         |
| Headache                                                                                                                  | 25.0                                                  | 34.5                             | –9.5                                  | 0.75                 | 2       |           |

|                                                                                                                          |                                                                                    |               |               |       |      |   |
|--------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------|---------------|---------------|-------|------|---|
|                                                                                                                          | Muscle / limb pain                                                                 | 37.3          | 16.7          | 20.6  | 0.21 | 2 |
|                                                                                                                          | Pain in chest, thorax and/or sternum                                               | 18.2          | 17.3          | 0.9   | 1.00 | 2 |
|                                                                                                                          | Fatigue or exhaustion                                                              | 33.3          | 50.9          | -17.6 | 0.36 | 2 |
|                                                                                                                          | Loss of appetite                                                                   | 0.1           | 29.1          | -29.0 | 0.29 | 2 |
|                                                                                                                          | Nausea and/or vomiting                                                             | 19.1          | 16.7          | 2.4   | 1.00 | 2 |
|                                                                                                                          | Diarrhoea                                                                          | 16.7          | 23.6          | -7.0  | 0.73 | 2 |
|                                                                                                                          | Abdominal pain                                                                     | 33.3          | 22.7          | 10.6  | 0.48 | 2 |
|                                                                                                                          | Loss of smell and/or taste                                                         | 8.3           | 21.8          | -13.5 | 0.46 | 2 |
|                                                                                                                          | Irritated and/or watering eyes                                                     | 25.0          | 21.8          | -11.8 | 0.60 | 2 |
|                                                                                                                          | Other                                                                              | 0.0           | 11.8          | -11.8 | 0.60 | 2 |
|                                                                                                                          | Number (mean $\pm$ SD) of reported symptoms (0–21)                                 | 4.8 $\pm$ 5.1 | 5.3 $\pm$ 5.6 | -0.5  | 0.91 | 4 |
|                                                                                                                          | One symptom or more reported                                                       | 75.0          | 70.9          | 4.1   | 1.00 | 2 |
|                                                                                                                          | Hospitalisation due to reported symptoms                                           | 0.0           | 13.0          | -13.0 | 1.00 | 2 |
| Vaccination status                                                                                                       | Influenza, ever                                                                    | 33.3          | 44.5          | -11.2 | 0.55 | 2 |
|                                                                                                                          | Tuberculosis, ever                                                                 | 36.4          | 11.9          | 24.4  | 0.05 | 2 |
| Presence of health-related quality of life limitations (Eq5d-5l: 1 = No problems / not any to 5 = Not able to / extreme) | Problems walking around (mean $\pm$ SD)                                            | 1.2 $\pm$ 0.4 | 1.4 $\pm$ 0.9 | -0.2  | 0.61 | 3 |
|                                                                                                                          | Self-care problems (mean $\pm$ SD)                                                 | 1.1 $\pm$ 0.3 | 1.1 $\pm$ 0.4 | 0.0   | 0.77 | 3 |
|                                                                                                                          | Problems performing daily activities (mean $\pm$ SD)                               | 1.1 $\pm$ 0.3 | 1.5 $\pm$ 0.9 | -0.4  | 0.15 | 3 |
|                                                                                                                          | Pain or physical discomfort (mean $\pm$ SD)                                        | 2.0 $\pm$ 1.2 | 2.0 $\pm$ 1.2 | 0.0   | 0.93 | 3 |
|                                                                                                                          | Anxiety or depression (mean $\pm$ SD)                                              | 1.6 $\pm$ 1.0 | 1.8 $\pm$ 1.1 | -0.2  | 0.60 | 3 |
|                                                                                                                          | Level sum-score (5 = best to 25 = worst)                                           | 7.0 $\pm$ 2.2 | 7.8 $\pm$ 3.4 | -0.8  | 0.93 | 3 |
|                                                                                                                          | Self-rating (mean $\pm$ SD) of current health status (VAS: 0 = worst to 10 = best) | 7.4 $\pm$ 1.3 | 7.0 $\pm$ 1.9 | 0.4   | 0.49 | 3 |

Unless otherwise stated, all figures are given as %. In all statistical analyses, the fraction denominator is the total number of cases with valid information for the respective variable (valid percent).

\* Mean of before, during and after shutdown, 0 to 30 days per month

OAT = opioid-agonist treatment; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2 infection; AB positive: antibody positive; AB negative: antibody negative; Diff. pos. – neg.: difference between value of antibody positive minus value of antibody negative group; p-value: Significance of two-sided test (see legend); Sig. test: test of statistical significance; n: number of participants; SD: standard deviation; EQ5D-5L: five-level version of the EuroQuol Instrument; VAS: visual analogue scale

Legend: Sig. test: 1 = t-test, 2 = Fisher's exact, 3 = Mann-Whitney-U, 4 = Kruskal-Wallis

cohort with a representative sample from the general population of the same region.

Limitations of our study are the relatively small number of OAT patients, which limits the significance of our study results. Furthermore, the OAT population was recruited at only one centre, albeit the largest in the country, which limits the generalisability of the findings. Within the OAT population, we cannot exclude a selection bias, as the data were assessed only for study participants at the addiction centre and there was no random selection in for this group. While we deem it likely that the seroprevalence estimate is applicable to the OAT population, it is possible that we missed OAT patients with severe COVID-19. Further studies are needed to determine how much OAT patients in Switzerland are actually at risk of severe COVID-19 progression.

If the results of our work can be confirmed in larger multi-centre studies, the question arises as to what the protective effects on severe COVID-19 in the OAT population might be. A protective effect of long-acting opioids by restoring immune function and suppressing oxidation is discussed in literature, but so far there is no evidence for such effects in relation to COVID-19 disease progression [14]. Since people in OAT might be more exposed to viral infections owing to their living situation, cross-immunity could also play a protective role. Confirmation of our results by other stud-

ies would also require a review of the necessity or extent of comprehensive protective measures taken for this population.

Until such possible protective effects are confirmed, the increased susceptibility of OAT patients to severe COVID-19 courses must continue to be assumed due to the frequent comorbidity with corona risk diseases, and the extensive protective measures taken must be maintained.

#### Potential competing interests

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflict of interest was disclosed.

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