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High SARS-CoV-2 seroprevalence but no severe course of COVID-19 disease among people on opioid agonist treatment in Zurich: a cross-sectional study

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Summary

BACKGROUND AND AIMS: Among people on opioid agonist treatment (OAT), social-environmental and behavioural risk factors may promote the spread of SARS-CoV-2, and somatic comorbidities are highly prevalent. Thus, this population is considered at elevated risk for being infected as well as for developing a more severe course of COVID-19 disease. The aim was to assess the SARS-CoV-2 seroprevalence among people in ongoing OAT, 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.

METHODS: The nationwide Corona Immunitas study assessed the participants' Sars-CoV-2 antibody status, social characteristics and behavioural data after the first wave of the corona pandemic in Switzerland, between the end of June and beginning of September 2020. We analysed the subsample of OAT patients (n = 122) and the subsample from the general population of the canton of Zurich (n = 472).

RESULTS: SARS-CoV-2 seroprevalence in the general population (mean age ± standard deviation 44.7 ± 11.7 years; 50.9% female) was 3.5% (95% confidence interval [CI] 2.2–4.8%) vs 9.8% (5.1–17.2%) in the OAT population age 44.3 ± 9.4 years; 30.3% female), corresponding to a prevalence ratio of 2.9 (95% CI 1.37–5.94; p = 0.004). OAT patients had a significantly worse health status than the general population. In the OAT group, we found no significant difference between seropositive and seronegative individuals regarding socioeconomic status, risk behaviour, COVID-19-related symptoms or comorbidity. None of the OAT patients who tested positive had a severe course of COVID-19.

CONCLUSION: The 3-fold higher seroprevalence suggests a higher than average viral exposure in the OAT group. Nevertheless, no severe COVID-19 course occurred, although the number of study participants was relatively small. One possible reason for this could be possible cross-immunity to SARS-CoV-2 due to frequent viral contacts in OAT patients.

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Introduction

In Switzerland, around 18,400 people with opioid dependency are on opioid agonist therapy (OAT) with morphine, methadone, codeine, buprenorphine or diacetylmorphine [1, 2]. OAT patients together make up around 0.2% of the Swiss population. The population entering treatment for opioid addiction consists of 75% men and is on average 41 years old [3].

Various comorbidities that are clustered in people in OAT increase the risk for severe disease progression of COVID-19 [4]. Cardiovascular, pulmonary and hepatic diseases are more frequent in this population than the general population of the same age [5, 6]. The prevalence of chronic obstructive pulmonary disease (COPD) among people in OAT is 30% and 2.5 times higher than in the general population [7]. Thus, OAT patients are considered at elevated risk for developing more a severe course of COVID-19 disease. Immunosuppressive effects of long-term opioid intake could be an additional reason for an elevated risk for severe COVID-19 disease among people on OAT [8].

Furthermore, OAT patients are at increased risk of contracting the SARS-CoV-2 virus due to their housing situation, their limited economic opportunities and the frequent contacts with the healthcare system in the context of OAT delivery. Many OAT patients live in assisted living facilities or other living situations that do not allow for social distancing or consistent quarantine or isolation. During the first lockdown, a number OAT patients were unable to comply with the authorities' request to stay at home be-

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 ± 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 38º 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 population 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 n = 472	OAT sample 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^2		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 people 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 EuroQuol Instrument; EQ VAS: EuroQuol 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 seroprevalance 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^2		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 people 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 = 12/122 (9.8%)	AB negative n = 110/122 (90.2%)	Diff. pos. – 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^2)	<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 ± SD) of reported symptoms (0–21)	4.8 ± 5.1	5.3 ± 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 ± SD)	1.2 ± 0.4	1.4 ± 0.9	–0.2	0.61	3
	Self-care problems (mean ± SD)	1.1 ± 0.3	1.1 ± 0.4	0.0	0.77	3
	Problems performing daily activities (mean ± SD)	1.1 ± 0.3	1.5 ± 0.9	–0.4	0.15	3
	Pain or physical discomfort (mean ± SD)	2.0 ±1.2	2.0 ± 1.2	0.0	0.93	3
	Anxiety or depression (mean ± SD)	1.6 ± 1.0	1.8 ± 1.1	–0.2	0.60	3
	Level sum-score (5 = best to 25 = worst	7.0 ± 2.2	7.8 ± 3.4	–0.8	0.93	3
	Self-rating (mean ± SD) of current health status (VAS: 0 = worst to 10 = best)	7.4 ± 1.3	7.0 ± 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 multicentre 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 supressing 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 studies 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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References

1. Gmel G, Labhart F, Maffli E. Heroingestützte Behandlung in der Schweiz – Resultate der Erhebung 2018 (Forschungsbericht Nr. 108). Lausanne: Sucht Schweiz; 2019.

2. Labhart FK, Maffli E. Nationale Statistik der Substitutionsbehandlungen mit Opioid-Agonisten – Ergebnisse 2018. Lausanne: Sucht Schweiz; 2019.
3. Maffli EE, Delgrande Jordan M, Labhart F, Gmel G, Kretschmann A. act-info Jahresbericht 2018: Suchtberatung und Suchtbehandlung in der Schweiz. Ergebnisse des Monitoringsystems. Bern: Bundesamt für Gesundheit; 2020.
4. Wang QQ, Kaelber DC, Xu R, Volkow ND. COVID-19 risk and outcomes in patients with substance use disorders: analyses from electronic health records in the United States. Mol Psychiatry. 2021 Jan;26(1):30–9. http://dx.doi.org/10.1038/s41380-020-00880-7. PubMed. 1476-5578
5. Bech AB, Clausen T, Waal H, Šaltytė Benth J, Skeie I. Mortality and causes of death among patients with opioid use disorder receiving opioid agonist treatment: a national register study. BMC Health Serv Res. 2019 Jul;19(1):440. http://dx.doi.org/10.1186/s12913-019-4282-z. PubMed. 1472-6963
6. Wittchen HU, Rehm J, Soyka M, Träder A, Mark K, Trautmann S. Der Verlauf und Ausgang von Substitutionspatienten unter den aktuellen Bedingungen der deutschen Substitutionsversorgung nach 6 Jahren. Suchtmed. 2011;13(5):232–46.
7. Grischott T, Falcato L, Senn O, Puhan MA, Bruggmann P. Chronic obstructive pulmonary disease (COPD) among opioid-dependent patients in agonist treatment. A diagnostic study. Addiction. 2019 May;114(5):868–76. http://dx.doi.org/10.1111/add.14559. PubMed. 1360-0443
8. Lambert DG. Opioids and the COVID-19 pandemic: does chronic opioid use or misuse increase clinical vulnerability? Br J Anaesth. 2020 Oct;125(4):e382–3. http://dx.doi.org/10.1016/j.bja.2020.07.004. PubMed. 1471-6771
9. Bruggmann PK, Meyer F, Bäni S, Beck T. Massnahmen zur COVID-19-Prävention in suchtmedizinischen Einrichtungen in Zürich. Suchtmed. 2020;22(4):182–6.
10. West EA, Anker D, Amati R, Richard A, Wisniak A, Butty A, et al.; Corona Immunitas Research Group. Corona Immunitas: study protocol of a nationwide program of SARS-CoV-2 seroprevalence and seroepidemiologic studies in Switzerland. Int J Public Health. 2020 Dec;65(9):1529–48. http://dx.doi.org/10.1007/s00038-020-01494-0. PubMed. 1661-8564
11. Health SSoP. What is Corona Immunitas? 2020Available from: https://www.corona-immunitas.ch/en/program/research-program/
12. Fenwick C, Croxatto A, Coste AT, Pojer F, André C, Pellaton C, et al. Changes in SARS-CoV-2 Antibody Responses Impact the Estimates of Infections in Population-Based Seroprevalence Studies. medRxiv. 2020:2020.07.14.20153536. http://dx.doi.org/10.1101/2020.07.14.20153536.
13. Daly LE. Confidence limits made easy: interval estimation using a substitution method. Am J Epidemiol. 1998 Apr;147(8):783–90. http://dx.doi.org/10.1093/oxfordjournals.aje.a009523. PubMed. 0002-9262
14. Eagleton M, Stokes S, Fenton F, Keenan E. Does opioid substitution treatment have a protective effect on the clinical manifestations of COVID-19? Comment on Br J Anaesth 2020; 125: e382-3. Br J Anaesth. 2021 Mar;126(3):e114–6. http://dx.doi.org/10.1016/j.bja.2020.11.027. PubMed. 1471-6771