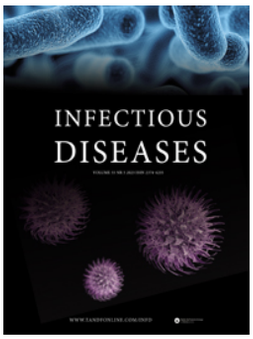

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ORIGINAL ARTICLE

COVID-19: seroprevalence and adherence to preventive measures in Arkhangelsk, Northwest Russia

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ABSTRACT

Background: The published estimates of SARS-CoV-2 seroprevalence in Russia are few. The study aimed to assess the SARS-CoV-2 seroprevalence in Arkhangelsk (Northwest Russia), in a year after the start of the pandemic, to evaluate the population adherence to non-pharmaceutical interventions (NPIs), and to investigate characteristics associated with COVID-19 seropositive status.

Methods: We conducted a SARS-CoV-2 seroprevalence study between 24 February and 30 June 2021 involving 1332 adults aged 40–74 years. Logistic regression models were fit to identify factors associated with seropositive status and with adherence to NPIs.

Results: Less than half (48.9%) of study participants adhered all recommended NPIs. Male sex (odds ratio [OR] 1.7, 95% confidence intervals [CI] 1.3; 2.3), regular employment (OR 1.8, 95% CI 1.3; 2.5) and low confidence in the efficiency of the NPIs (OR 1.9, 95% CI 1.5; 2.5) were associated with low adherence to internationally recommended NPIs. The SARS-CoV-2 seroprevalence rate was 65.1% (95% CI: 62.5; 67.6) and increased to 73.0% (95% CI: 67.1; 85.7) after adjustment for test performance. Regular employment (OR 2.0, 95% CI 1.5; 2.8) and current smoking (OR 0.4, 95% CI 0.2; 0.5) were associated with being seropositive due to the infection.

Conclusions: Two third of the study population were seropositive in a year after the onset of the pandemic in Arkhangelsk. Individuals with infection-acquired immunity were more likely to have regular work and less likely to be smokers. The adherence to NPIs was not found associated with getting the virus during the first year of the pandemic.

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Background

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in China in December 2019 and through the first half of 2020 developed into a global pandemic of coronavirus disease 2019 (COVID-19). The spectrum of infection varied from being asymptomatic to severe with hospitalization and death. The tendency of those who were asymptomatic or had only mild symptoms not to self-isolate will have contributed to further spread of infection [1].

The true cumulative incidence of COVID-19 in most populations remains uncertain and exceeds the number of reported cases [2]. Seroprevalence surveys of the general population can provide a less biased assessment of the extent of COVID-19 infection compared to those based on the number of positive tests reported by the health service. This is because the latter will differentially tend to exclude asymptomatic and mild cases and will also be a function of availability of testing facilities [2].

Several random population antibody surveys were performed during the first year of the COVID-19 pandemic. At the beginning of 2021, 34.6% of the population sample in England tested positive for antibodies against SARS-CoV-2, while the estimated seroprevalence in Norway was 0.9% [3,4]. In Russia, only a few serologic studies had been conducted by the middle of 2021 [5–7]. In June-December 2020, the average SARS-CoV-2 seroprevalence in Russia was estimated as 19.2% with variation between regions [7].

In the first year of the pandemic, studies tended to find seroprevalence to be associated with sociodemographic and behavioral characteristics. Male gender was shown to be positively associated with testing positive [8]. Having public-facing jobs, living in overcrowded households, using public transport, or having high social interaction for other reasons were also associated with testing positive for SARS-CoV-2 antibodies [9,10]. Lower seroprevalence has been reported in older populations and in people with chronic diseases who may have shielded themselves to reduce risks of getting infected [3,5,11–15].

Non-pharmaceutical interventions (NPIs), such as laws or regulations restricting face-to-face interactions, can significantly decrease the rate of viral transmission [16,17]. The varying speed of the infection spread in different countries depends on the public compliance with the related guidelines rather than the timeliness of implementing COVID-19 NPIs [10,18]. The level of adherence to COVID-19 restrictive measures can be influenced by public confidence in government and the information available to guide preventive behaviors [19]. Higher compliance with NPIs has been demonstrated in the elderly, women, those with higher educational level and income, non-smokers, people living alone and those having chronic diseases [1,20,21]. There is some evidence that some people who thought that they had had COVID-19 were less likely to adhere to NPIs due to their belief that this gave them protection from further infection [22].

In the Arkhangelsk Region in Northwest Russia (population 1.1 million in January 2021) [23], the first case of COVID-19 was registered on 17 March 2020 [24]. The period from 19 March to 2 July 2020 was associated with the first wave in the region, and the period from 20 September 2020 to 27 February 2021 was associated with the second wave of COVID-19 [24].

The vaccination campaign in the Arkhangelsk Region started in November 2020, mainly with Russian Sputnik V. As in other countries, therefore, levels of population immunity during the first year were driven largely by the spread of the infection.

As the disease can be asymptomatic and due to low access to testing, the true proportion of the Arkhangelsk population with immunity to COVID-19 acquired during the first year of the pandemic remains unknown. Beyond that, the lack of knowledge of the factors associated with the COVID-19 infection was an obstacle to preventing the further spread of COVID-19 and controlling other similar future pandemics.

This study aimed to assess the seroprevalence of SARS-CoV-2 in Arkhangelsk, a city in Northwest Russia, in a year after the start of the pandemic, to estimate the population adherence to NPIs during the first year, and to investigate socioeconomic, behavioral and health-related characteristics associated with infection-acquired antibodies against SARS-CoV-2 as well as with adherence to NPIs.

Materials and methods

Study design and participants

A cross-sectional study of SARS-CoV-2 seroprevalence was conducted in Arkhangelsk between 24 February and 30 June 2021 (50% of participants were enrolled by 5 April 2021). This was a sub-study of the third multi-center survey 'Epidemiology of Cardiovascular Diseases and their Risk Factors in Regions of the Russian Federation' (ESSE-RF3) [25]. The ESSE-RF study aimed to recruit a sample that was representative of the population of

Russia. In Arkhangelsk, this was done by inviting participants involved in an earlier study of cardiovascular diseases, Know Your Heart (KYH), which was conducted in 2015–2017 and included a random sample of Arkhangelsk population aged 35–74 years [26]. The KYH study participants were recruited from four districts of Arkhangelsk with an anonymized list of addresses of residents with compulsory medically insurance used as the sampling frame. The address list was provided by the regional health insurance fund, with each address supplemented by age and sex of the insured resident. Trained interviewers visited randomly selected addresses to invite persons of the corresponding age and sex to take part in the study. The participation rate was 68% out of the total invitees.

Of 2380 KYH study participants, we invited 2258 to ESSE-RF3. The exclusions ($N = 122$) were for the following reasons: 56 KYH participants had not consented to be contacted with invitations to other studies, 61 had died prior to the launch of ESSE-RF3 (4 of 61 deaths were related to COVID-19), and 5 had become older than the maximum age (74 years). Most of the participants in the KYH study were aged 40 years or older at the time of the seroprevalence survey. Of those invited, 1348 KYH study participants (60%) aged 40–74 years took part, all with signed informed consent.

The study procedure included a health check, blood sample collection (for biochemical assays and for SARS-CoV-2 antibodies) and an interview at the outpatient clinic of Northern State Medical University (NSMU), Arkhangelsk. Two participants who did not complete the questionnaire and 14 participants who had an equivocal serological test result were excluded from the seroprevalence sub-study sample. Therefore, the final analytic sample comprised 1332 participants.

Ethical considerations

All participants included in the seroprevalence study provided written informed consent to participate. The study was conducted in compliance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments. Ethical approval for the original KYH study was given by the ethics committees of London School of Hygiene & Tropical Medicine (approval number 8808 received 24 February 2015) and NSMU, Arkhangelsk (approval number 01/01-15 received 27 January 2015). Ethical approval for ESSE-RF-3 was obtained from the Ethics Committee of the National Research Centre for Therapy and Preventive Medicine, Moscow, Russia (approval number №01-01/20 received 04 February 2020) and the Ethics Committee of NSMU, Arkhangelsk, Russia (approval number 01/02-21 received 17 February 2021). Ethical approval for the sub-study on COVID-19 and health-related factors was received from the Ethics Committee of NSMU, Arkhangelsk, Russia (approval number 01/02-21 received 17 February 2021). All study procedures were approved by the Regional Committees for Medical and Health Research Ethics (REK) in Norway (approval number 339397 received 7 December 2021).

Measurements

Laboratory methods

Blood samples were tested for SARS-CoV-2 IgG antibodies using a Vector Best ELISA assay (D-5501 SARS-CoV-2-IgG-EIA-BEST) [27,28]. The assay is an enzyme linked immunosorbent assay (ELISA) test-systems (Russia) for the semi-quantitative detection of antibodies to the spike (S) protein of SARS-CoV-2 in human blood serum [27]. The sensitivity of this assay has been reported to be 72% within the first 12 days following the infection and close to 100% at a later stage [27]. An independent test-performance study has shown the assay sensitivity of 89% and the specificity of 100% based on the comparisons of test results in pre-pandemic samples (negative controls) and polymerase chain reaction positive samples for SARS-CoV-2 [28].

Questionnaire

Every participant completed an interviewer-administered questionnaire capturing data on demographics, health-related characteristics, history of COVID-19 symptoms and self-reported protective behaviors. The questionnaire on COVID-19 was developed by the ESSE-RF3 team at the National Research Centre for Therapy and Preventive Medicine, Moscow [25]. Additional questions were asked in Arkhangelsk to collect data on vaccination against COVID-19. The original Russian version and the English translation of the COVID-19 questionnaire are provided in Appendix A.

Adherence to NPIs estimates were based on respondents' self-reports with respect to five COVID-19 NPIs: self-isolation, social distancing, wearing facemasks in public settings or transport, wearing gloves, and use of hand sanitizers [29]. The use of gloves for the prevention of SARS-CoV-2 transmission was not implemented globally, while in Russia wearing gloves was

recommended by the Federal service on customers' rights protection and human well-being surveillance (Rospotrebnadzor) until 4 February 2022 [30,31].

The term 'self-isolation' was not described in the questionnaire, but was primarily considered as a measure required for those who were confirmed cases or had contacts with confirmed cases as well as those who were older than 65 years or had chronic diseases [32,33]. Besides, staying at home was recommended to everyone during paid non-working days (from March 30 to April 4, from April 4 to April 30, May 6 to May 8) established by the Presidential Decrees in 2020 [34–36].

The answer 'yes' to the question about adherence to NPIs during the pandemic was counted as 1 for each of the five interventions whereas the answer 'no' was counted as 0. The total gave a scale ranging from 0 to 5, which was dichotomized by combining scale values 0–3 (low adherence) and values 4–5 (high adherence). The threshold was chosen taking into account the median number of NPIs adhered, which is equal to 4.

The study participants assessed the efficiency of the five above-mentioned NPIs using a Likert scale (not effective at all = 0 to very effective = 5) (Appendix A). For each participant, we summed score assessments for all NPIs and this gave composite assessment score of NPIs ranging from 0 to 25. Values 0–19 were coded 1 (low confidence in the efficiency) and values 20–25 (at least 4 points for each assessment) were coded 0 (high confidence in the efficiency).

In order to identify factors associated with low adherence to NPIs and to investigate associations of the seroprevalence status with socioeconomic, behavioral and health-related characteristics, we used the questionnaire-based data on the following covariates: sex, age, education, marital status, number of persons in household, occupation, income, smoking, alcohol consumption and self-reported chronic non-communicable diseases (hypertension, diabetes mellitus, chronic pulmonary diseases, coronary heart diseases).

Age was categorized as: 40–54 years, 55–64 years and 65–74 years. The classification of educational levels was as follows: secondary or lower, specialized secondary and higher. Marital status was defined as single (including widowed and divorced) and married or living with partner. The number of persons in a household was analyzed as discreet variable. Living with children (<18 years) was categorized as yes or no. Occupation was classified as being in regular employment, or not. According to income categorization by the Federal State Statistics Service of Russia, participants earning less than 40,000 Rub a month were considered low-income, those earning between 40,000 and 100,000 Rub a month – middle income, and those earning more than 100,000 Rub a month – high-income [37,38]. With respect to tobacco smoking, the respondents were divided into three groups: never smokers, former smokers and current smokers. According to the definition of 'Heavy Episodic Drinking' suggested by the World Health Organization, heavy drinkers were defined as consumers of 60 or more grams of pure alcohol on a single occasion [39]. The frequency of heavy drinking was ascertained for previous 12 months and was classified as never, once a week or less often, and twice a week or more often.

Data on participant-reported chronic health conditions were collected in the ESSE-RF3 survey and included hypertension, diabetes mellitus, chronic pulmonary diseases and coronary heart diseases. Hypertension was defined as self-reported prior diagnosis and/or intake of antihypertensive drugs. Diabetes mellitus was defined as self-reported prior diagnosis of diabetes and/or diabetes medication use, chronic pulmonary disease – self-reported prior diagnosis of chronic bronchitis or bronchial asthma, coronary heart disease – prior diagnosis of angina pectoris and/or myocardial infarction and/or antianginal medication use.

Self-reports of vaccination against COVID-19 were used to classify participants either as those unvaccinated or those who had received one or two doses. Participants were classified as having COVID-19 during the first year of pandemic based on the answer to the question: 'Did you have COVID-19 during the last 12 months?' without further specification of symptoms or test results.

Study participants who reported having a positive test for COVID-19 but reported that they had had no symptoms of the infection as well as those who were tested positive for SARS-CoV2 antibodies but reported no COVID-19 infection were considered asymptomatic.

Statistical analysis

Continuous variables were summarized using descriptive statistics in terms of mean and standard deviation (SD). Seroprevalence was estimated as the number of SARS-CoV-2 IgG positive participants divided by the number of tested participants and reported in percentages. Confidence intervals (CIs) for unadjusted seroprevalence were calculated using Wilson's procedure. Seroprevalence adjusted for test performance (89%

sensitivity, 100% specificity) was estimated to improve comparability of the study findings with other studies as shown elsewhere [40,41]. The adjustment was performed using the equation: (crude prevalence + test specificity − 1)/(sensitivity + specificity − 1) [42]. The 95% CIs for the adjusted estimates of seroprevalence were calculated by bootstrapping procedure using R package bootComb (version 4.1.1) [43].

The unadjusted and adjusted seroprevalence of SARS-CoV-2 in subgroups were compared using 95% CIs. The Pearson Chi-squared test was used to analyze categorical data. Cronbach's alpha coefficient was used to measure the internal coherence/reliability of composite score for adherence to COVID-19 NPIs.

Binary logistic regression was used to investigate factors associated with low adherence to COVID-19 NPIs (1 – low adherence (0–3 NPIs), 0 – high adherence (4–5 NPIs)). Sex, age, education, occupation, income, smoking and drinking habits, chronic health conditions, vaccination against COVID-19 were introduced in regression model using enter option. Crude and adjusted odds ratios (ORs) with 95% CIs were calculated. Since wearing of gloves was not an international recommendation, we repeated the multivariable analysis with exclusion of the gloves wearing to ensure comparability of the results. In this analysis, the scoring for adherence was as follows: 1 – low adherence (0 to 3 NPIs), 0 – high adherence (4 NPIs).

The associations between sex, age, marital status, number of persons in household, living with children (<18 years), education, occupation, income, adherence to NPI, smoking and drinking habits, chronic health conditions (later referred as selected factors) and the seropositive status (1 – seropositive, 0 – seronegative) were investigated using binary logistic regression, with some analyses being stratified by vaccination status. The independent variables were grouped into two hierarchical blocks in relation to the dependent variable. Block 1 included socio-demographic characteristics (sex, age, marital status, number of persons in household, living with children (<18 years), education, occupation, income). Block 2 included behavioral factors (adherence to COVID-19 NPIs, smoking, heavy alcohol drinking) and chronic health conditions. The blocks of variables were introduced in the regression model in a stepwise manner. The independent variables associated with seropositive status after the exclusion of vaccinated individuals were interpreted as factors associated with infection-acquired immunity.

We calculated the statistical power of a binary logistic regression model to identify factors associated with seropositive status in a sample of 1332 observations. Calculations have shown that the sample gives a statistical power of ≥80% to identify factors which increase or reduce odds of the outcome by 1.5 times for all combinations of the outcome prevalence in the range from 25% to 70% and predictor prevalence in the range from 30% to 70%.

Results

The mean age of the study participants was 57 (SD 9.6) years. Women made up 59.7% of the sample (Table 1). Overall, 867 of the total 1332 participants were tested positive for SARS-CoV-2 IgG antibody corresponding to a seroprevalence rate of 65.1% (95% CI: 62.5; 67.6). Seroprevalence adjusted for test performance was 73.0% (95% CI: 67.1; 85.7).

Only 61.7% of 47 individuals who had received one dose of the vaccine were seropositive whereas 99.5% of 195 participants who had received two doses were seropositive. Among 339 participants who self-reported having had COVID-19, 95.0% were seropositive.

Among those unvaccinated ($N = 1090$), 335 (30.7%) did not report having had COVID-19 but were seropositive. In addition, seven of eight unvaccinated individuals who reported having had COVID-19 asymptomatically were also seropositive. Overall, the proportion of asymptomatic cases among unvaccinated study participants was 31.4% (342/1090).

Adjusted seroprevalence was lower in current smokers and was higher in vaccinated individuals and those who self-reported having COVID-19 (Table 1).

Almost all participants reported wearing facemasks in public settings or transport during the pandemic period (98.6%), maintaining social distancing (92.9%) and using hand sanitizers (91.5%). Over 90.0% of retired or unemployed study participants and 72.0% of regularly employed participants followed self-isolation guidelines during the COVID-19 pandemic, which may include not mixing socially during lockdowns, $p < .001$. More than half (59.6%) reported wearing gloves. The use of gloves was adhered by 55.7% of participants aged 40–54 years, 62.1% of those aged 55–64 years and 63.2% individuals older than 65 years, $p = .036$. In total, 48.9% adhered all five NPIs. The Cronbach alpha reliability coefficient for the composite adherence scale (0.67) was considered acceptable. The low-adherent participants were less

Table 1. Unadjusted and adjusted SARS-CoV-2 seroprevalence by selected participant characteristics, Arkhangelsk, Russia.

Variables	N (%)	Unadjusted seroprevalence[a] % (95% CI)	Seroprevalence[a] adjusted for test performance % (95% CI)
Sex			
Male	537 (40.3)	66.1 (62.0; 70.0)	74.2 (64.9; 85.4)
Female	795 (59.7)	64.4 (61.0; 67.7)	72.3 (63.7; 83.0)
Age			
40–54 years	575 (43.2)	66.3 (62.3; 70.0)	74.3 (65.2; 85.5)
55–64 years	420 (31.5)	60.7 (56.0; 65.3)	68.1 (58.7; 79.1)
65–74 years	337 (25.3)	68.6 (63.4; 73.3)	76.9 (66.9; 89.0)
Marital status			
Single (including widowed and divorced)	464 (34.8)	60.3 (55.8; 64.7)	67.7 (58.4; 78.4)
Married or living with partner	868 (65.2)	67.6 (64.5; 70.7)	75.9 (67.3; 87.0)
Number of persons in household			
1 (alone)	240 (18.0)	61.3 (55.0; 67.2)	68.7 (57.8; 80.6)
2–3	882 (66.2)	64.3 (61.1; 67.4)	72.1 (63.6; 82.7)
≥4	210 (15.8)	72.9 (66.5; 78.4)	81.7 (70.9; 94.5)
Living with children (<18 years)			
No	1019 (76.5)	63.7 (60.7; 66.6)	71.4 (63.0; 81.8)
Yes	313 (23.5)	69.7 (64.3; 74.4)	78.1 (67.9; 90.4)
Education			
Higher	563 (42.3)	64.3 (60.3; 68.2)	72.1 (63.0; 83.1)
Specialized secondary	661 (49.6)	66.0 (62.3; 69.5)	74.0 (65.1; 85.0)
Secondary or lower	108 (8.1)	63.9 (54.5; 72.3)	71.7 (57.9; 86.4)
Occupation			
Retired or unemployed	542 (40.7)	60.2 (56.0; 64.2)	67.5 (58.5; 78.0)
Regular employment	790 (59.3)	68.5 (65.2; 71.6)	76.8 (68.1; 88.0)
Income			
High	175 (13.1)	69.1 (61.9; 75.5)	77.6 (65.8; 90.8)
Middle	764 (57.4)	66.4 (62.9; 69.6)	74.4 (65.6; 85.3)
Low	393 (29.5)	60.8 (55.9; 65.5)	68.2 (58.5; 79.2)
Smoking			
Never smoker	742 (55.7)	67.8 (64.3; 71.1)	76.1 (67.2; 87.2)
Former smoker	366 (27.5)	67.8 (62.8; 72.3)	76.0 (66.3; 88.0)
Current smoker	224 (16.8)	51.8 (45.3; 58.3)	58.1 (47.2; 69.1)
Frequency of heavy drinking			
Never	825 (61.9)	66.2 (62.9; 69.3)	74.6 (65.6; 85.2)
Once a week or less often	453 (34.0)	64.5 (60.0; 68.7)	72.3 (62.9; 83.6)
Twice a week or more often	54 (4.1)	53.7 (40.6; 66.3)	72.3 (62.9; 83.6)
Chronic health conditions			
No	393 (29.5)	63.4 (58.5; 68.0)	71.1 (61.4; 82.4)
Yes	939 (70.5)	65.8 (62.7; 68.8)	73.8 (65.4; 84.7)
Self-reported having had COVID-19			
No	993 (74.5)	54.9 (51.8; 58.0)	61.6 (53.4; 70.7)
Yes	339 (25.5)	95.0 (92.1; 96.0)	100.0 (95.9; 100.0)
Vaccinated against COVID-19			
No	1090 (81.8)	59.1 (56.1; 62.0)	66.3 (58.1; 76.0)
1 dose	47 (3.5)	61.7 (47.4; 74.2)	69.2 (50.1; 88.3)
2 doses	195 (14.6)	99.5 (97.2; 99.9)	100.0 (97.2; 100.0)
Adherence to NPIs[b]			
High (4–5)	1082 (81.2)	65.3 (62.5; 68.1)	73.3 (65.0; 84.0)
Low (0–3)	250 (18.8)	64.0 (57.9; 69.7)	71.8 (60.9; 83.9)
Total	1332 (100.0)	65.1 (62.5; 67.6)	73.0 (64.9; 83.5)

CI: confidence interval; COVID-19: coronavirus disease 2019; NPI: non-pharmaceutical interventions.
[a]Including vaccinated individuals.
[b]The total number of NPIs adhered.

likely to have high confidence in NPIs (53.8%) compared to those who were highly adherent (77.2%), $p < .001$.

In the crude analysis, male sex, age 40–54 years compared to age 65–74 years, secondary or lower education compared to higher education, regular employment, smoking, heavy alcohol drinking, being unvaccinated and having low confidence in the efficiency of NPIs were associated with low adherence to COVID-19 NPIs. Those who were vaccinated were more likely to have high adherence (Table 2). Multivariable analysis showed that male sex, low income compared to high income, low confidence in the efficiency of NPIs and heavy drinking twice a week or more often were associated with low adherence to NPI. After exclusion of wearing gloves from the analysis, low income and frequency of heavy drinking were no longer associated with low adherence to COVID-19 NPIs. Male sex, regular employment and low confidence in the efficiency of NPIs were associated with low adherence to NPIs recommended globally.

Among those unvaccinated, being in regular employment was associated with higher odds of being seropositive due to the infection (Table 3, Model 1). After

Table 2. Variables associated with low adherence to COVID-19 non-pharmaceutical interventions, Arkhangelsk, Russia (binary logistic regression analysis).

Characteristics	Crude OR (95% CI)[a] Low 0–3 / high 4–5	Adjusted[b] OR (95% CI) Low 0–3 / high 4–5[a]	Adjusted[b] OR (95% CI)[c] Low 0–3 / high 4[c]
Sex			
Female	Reference	Reference	Reference
Male	2.3 (1.8; 3.1)	2.2 (1.5; 3.1)	1.7 (1.3; 2.3)
Age			
40–54 years	1.9 (1.2; 2.7)	1.3 (0.8; 2.1)	1.3 (0.9; 2.0)
55–64 years	1.5 (1.0; 2.3)	1.2 (0.7; 1.9)	1.1 (0.7; 1.6)
65–74 years	Reference	Reference	Reference
Marital status			
Single (including widowed and divorced)	Reference	Reference	Reference
Married or living with partner	1.0 (0.8; 1.3)	0.9 (0.6; 1.2)	1.0 (0.7; 1.4)
Education			
Higher	Reference	Reference	Reference
Specialized secondary	1.3 (1.0; 1.7)	1.3 (0.9; 1.8)	1.1 (0.8; 1.5)
Secondary or lower	1.7 (1.1; 2.8)	1.6 (0.9; 2.8)	1.3 (0.8; 2.1)
Occupation			
Retired or unemployed	Reference	Reference	Reference
Regular employment	1.6 (1.2; 2.2)	1.4 (1.0; 2.0)	1.8 (1.3; 2.5)
Income			
High	Reference	Reference	Reference
Middle	1.4 (0.9; 2.2)	1.6 (1.0; 2.7)	1.3 (0.8; 1.9)
Low	1.5 (0.9; 2.5)	2.2 (1.2; 4.1)	1.7 (1.0; 2.8)
Smoking			
Never smoker	Reference	Reference	Reference
Former smoker	1.4 (1.0; 1.9)	0.9 (0.6; 1.3)	0.9 (0.7; 1.2)
Current smoker	1.8 (1.3; 2.6)	1.0 (0.7; 1.5)	1.1 (0.8; 1.6)
Frequency of heavy drinking			
Never	Reference	Reference	Reference
Once a week or less often	1.8 (1.4; 2.5)	1.3 (0.9; 1.8)	1.1 (0.8; 1.5)
Twice a week a week or more often	4.0 (2.3; 7.2)	2.5 (1.3; 4.9)	1.7 (0.9; 3.3)
Chronic health conditions			
No	Reference	Reference	Reference
Yes	1.0 (0.7; 1.3)	1.0 (0.7; 1.4)	1.1 (0.8; 1.7)
Confidence in the efficiency of NPIs			
Yes	Reference	Reference	Reference
No	2.9 (2.2; 3.8)	2.7 (2.0; 3.7)	1.9 (1.5; 2.5)
Vaccinated against COVID-19			
Yes	Reference	Reference	Reference
No	1.7 (1.1; 2.6)	1.4 (0.9; 2.1)	1.2 (0.8; 1.7)

Note: CI: confidence interval; COVID-19: coronavirus disease 2019; NPI: non-pharmaceutical interventions; OR: odds ratio.
[a]Low adherence meant to adhere 3 or less NPIs out of maximum 5 (self-isolation, social distancing, wearing facemasks in public places or transport, wearing gloves, and use of hand sanitizers).
[b]Adjusted for all independent variables included in the model.
[c]Wearing gloves was excluded from the analysis. Low adherence meant to adhere 3 or less NPIs out of maximum 4.

introducing behavioral factors and chronic health conditions, regular employment was associated with higher odds of being seropositive, while current smoking was associated with lower odds (Table 3, Model 2). The same analysis performed after including vaccinated individuals ($N = 242$) showed that regular employment and smoking had similar associations with seropositive status regardless of whether it was obtained *via* infection or *via* vaccination (Supplementary table 1, Appendix B).

Discussion

The SARS-CoV-2 seroprevalence 12–16 months after the beginning of the pandemic in Arkhangelsk was 65.1% (95% CI: 62.5; 67.6) and increased to 73.0% (95% CI: 67.1; 85.7) after adjustment for test performance. The individuals having regular employment had higher probability to be seropositive to SARS-CoV-2, while smokers were less likely to be seropositive. Low adherence to NPIs recommended globally during the first year of the pandemic was associated with male sex, regular employment and low confidence in the efficiency of NPIs.

SARS-CoV-2 seroprevalence

The SARS-CoV-2 seroprevalence in Arkhangelsk a year after the start of the pandemic was higher than found in other cities of Russia for which data had been reported [5–7,44]. Asymptomatic cases comprised 31.4% of unvaccinated participants. This percentage was twice as high as the asymptomatic proportion found in meta-analysis of COVID-19 studies [1,45]. This could be partly explained by the possibility of misdiagnosis or missed diagnosis of patients with COVID-19 due to limited capacity of testing and the pressure on the healthcare system in Arkhangelsk. People could

Table 3. Variables associated with being SARS-CoV-2 seropositive among those not immunized, Arkhangelsk, Russia (binary logistic regression).

Variables	Model 1 Adjusted[a] OR (95% CI)	Model 2 Adjusted[b] OR (95% CI)
Sex		
Female	Reference	
Male	0.8 (0.7; 1.1)	1.1 (0.8; 1.6)
Age		
40–54 years	0.8 (0.5; 1.2)	1.0 (0.7; 1.6)
55–64 years	0.8 (0.5; 1.1)	0.9 (0.6; 1.3)
65–74 years	Reference	Reference
Marital status		
Single	Reference	Reference
Married	1.2 (0.8; 1.6)	1.1 (0.8; 1.5)
Number of persons in household	1.2 (1.0; 1.4)	1.2 (1.0; 1.5)
Living with children (<18 years)		
No	Reference	Reference
Yes	1.0 (0.7; 1.6)	1.0 (0.6; 1.5)
Education		
Higher	Reference	Reference
Specialized secondary	1.1 (0.9; 1.6)	1.3 (1.0; 1.8)
Secondary or lower	1.1 (0.7; 1.8)	1.2 (0.7; 1.9)
Occupation		
Retired or unemployed	Reference	Reference
Regular employment	2.0 (1.5; 2.7)	2.0 (1.5; 2.8)
Income		
High	Reference	Reference
Middle	1.0 (0.7; 1.5)	1.0 (0.7; 1.5)
Low	1.0 (0.6; 1.6)	1.0 (0.6; 1.7)
Adherence to NPI[c]	–	
High (4–5)	–	Reference
Low (0–3)	–	1.0 (0.7; 1.4)
Smoking		
Never smoker	–	Reference
Former smoker	–	0.8 (0.6; 1.1)
Current smoker	–	0.4 (0.2; 0.5)
Frequency of heavy drinking		
Never	–	Reference
Once a week or less often	–	0.9 (0.7; 1.3)
Twice a week or more often	–	0.5 (0.3; 1.0)
Chronic health conditions		
No	–	Reference
Yes	–	1.1 (0.8; 1.4)

Note: CI: confidence interval; NPI: non-pharmaceutical interventions; OR: odds ratio.
[a]Adjusted for all sociodemographic factors in model 1.
[b]Adjusted for the factors in model 1, behavioral factors (adherence to preventive measures, smoking, heavy alcohol drinking) and chronic health conditions (model 2).
[c]The total number of NPIs adhered.

have had symptoms but were not tested for SARS-CoV2. Therefore, they did not realize that their symptoms were due to COVID-19. At the beginning of the pandemic only people arriving in Arkhangelsk from abroad and close contacts of confirmed cases were required to be tested for COVID-19 using polymerase chain reaction. By the middle of 2020, healthcare-workers as well as all patients with community-acquired pneumonia or other respiratory infection considered by a doctor as suspected COVID-19 cases were tested free of charge [32]. Voluntary testing and obligatory testing of those arriving from abroad were not covered by compulsory health insurance. Some enterprises provided COVID-19 testing for their employees for free. The number of people tested in the Arkhangelsk Region during 2020 was 598,113 (690,209 tests), including voluntary testing in private clinics [24].

The proportion of fully vaccinated study participants (14.6%) was low as the vaccination campaign in Arkhangelsk, as in the rest of Russia, progressed slowly [5]. Nevertheless, the proportion of the study participants vaccinated against COVID-19 was higher than the officially reported percentage of vaccinated Arkhangelsk inhabitants, which varied during the study period from 3.3% in March 2021 to 13.6% in June 2021 [24]. The likely reason is that our study covered predominantly urban population with better access to vaccination. Another possible explanation is a higher willingness of vaccinated individuals to take part in the study.

We cannot exclude the possibility that participants who thought they had had COVID-19 were more likely to take part in the study. They might feel safer to 'go out' because of having recovered from the disease, while those who decided to avoid having a health check might be the people who had not had COVID-19 and preferred staying home because of fear of getting infected. Besides, those who refused to participate in the study and decided to avoid visiting the healthcare facility might have higher adherence to NPIs and higher probability to be seronegative.

Adherence to preventive measures

Less than half (48.9%) of study participants adhered all recommended NPIs, which corresponds to the results obtained by others [46,47]. In line with the results previously reported by other researchers, we found that people aged 65 years or older were more likely to have high adherence to NPIs as compared to a younger age group. After adjustment for all independent variables, adherence to NPIs was no longer different across age groups [48]. We did not find an association between smoking, chronic health conditions and adherence to COVID-19 NPIs [20,21,46]. Our results are in agreement with prior research, which has shown that males and heavy drinkers were less likely to comply with recommended NPIs [46,47,49,50]. Low confidence in NPIs could be associated with unwillingness to follow recommendations from the government.

Factors associated with SARS-CoV-2 seroprevalence

In unvaccinated individuals, seropositivity was associated with regular employment. These findings are in agreement with prior research, which has shown that

employed people had higher odds to be infected with SARS-CoV-2 [46,49].

In contrast with other studies, we did not find a negative association between adherence to COVID-19 NPIs and infection-acquired positive serological status of the participants [21]. This could be partly explained by common counterfeit compliance with NPIs (e.g. wearing facemask leaving nose exposed) which was reported as being adherent. This might lead to higher viral exposure compared to people who properly follow all restrictions [13,14]. Moreover, behaviors could have changed during the pandemic period, which may result in underestimated association between seroprevalence and adherence to NPIs due to non-differential misclassification of the adherence status.

In our study, adherence to NPIs was assessed as a composite variable made up of five variables (self-isolation, social distancing, wearing facemasks in public settings or transport, wearing gloves, and use of hand sanitizers) with acceptable reliability of 0.67. Since the term 'self-isolation' was not clearly defined in the questionnaire, the participants could consider staying at home during paid non-working days in March–May 2020 as being self-isolated. This could blur the positive association between self-isolation due to being a confirmed COVID-19 case or having contacts with confirmed cases and SARS-CoV-2 seroprevalence.

Smoking status was negatively associated with being tested positive for antibodies to SARS-CoV-2. Some authors reported similar results [5,51,52]. These findings require further research and should be interpreted with caution. The mechanisms that might underline this association suggested by others are largely speculative [53]. It remains possible that smokers develop a lower antibody response after the infection [54]. Other researchers demonstrated a higher expression of angiotensin converting enzyme-2 in smokers that might lead to greater susceptibility to COVID-19 [55]. Although the high expression of the angiotensin converting enzyme-2 had an inhibitory effect on virus replication and smokers might be more likely to have asymptomatic infection [55]. In our study, we found no evidence that would confirm this statement.

Strengths and limitations

This is the first population-based study in Russia estimating SARS-CoV-2 seroprevalence and exploring factors associated with seroprevalence, including the adherence to NPIs, that could play an important role in the COVID-19 pandemic and should be considered in preventing similar epidemics in the future. A strength of our study is that we adjusted seroprevalence estimates for laboratory test performance characteristics to prevent the bias associated with imperfect test performance and improve the comparability of the results [56–58].

Our findings should be interpreted in the light of some limitations. The study was limited to citizens aged 40–74 years in Arkhangelsk, Northwest Russia. We invited participants of the previous random population study (Know Your Heart), who may not have been a fully representative sample of the population. However, we have compared the socio-demographic characteristics of the 1332 seroprevalence survey participants to the 2380 persons in the sampling frame. There were not any significant differences in sex, age or education distributions between them [59]. This, together with the emerging evidence that response rates may not be as strongly related to non-response bias, suggests that the sampling frame is likely to be representative of the adult population aged 40–74 years of Arkhangelsk.

We did not verify the self-reported data on having COVID-19 or vaccination status with medical records, so they may not be completely accurate. Therefore, an element of informational bias could not be excluded.

Most of the participants reported that they followed COVID-19 NPIs during the pandemic period and considered preventive measures to be highly effective. These data can be compromised by socially desirable answer to the question regarding COVID-19-related restrictions introduced by the local government. Due to the possible influence of social desirability bias, the reported rates of adherence to NPIs may be overestimated. To improve reliability of the adherence assessment, we used composite scale with an acceptable value of Cronbach's alpha coefficient (0.67). The questions about adherence to NPIs did not specify whether the individual adherence was careful and permanent throughout the pandemic period, or formal and sporadic. For this reason, we did not take into account how frequently and appropriately facemasks, gloves, and sanitizers were used. We also cannot exclude the possibility of improper wearing of facemasks (covering only the mouth and leaving the nose exposed, and reusing disposable masks), which could be useless for the prevention of the infection. The definition of 'self-isolation' in the questionnaire was ambiguous, which might also influence the results.

We collected blood samples during four months between 24 February and 30 June 2021, when the infection rates were relatively steady. Regardless of the

extended period of sample collection, we can still consider the seroprevalence to be the average estimate over the period studied.

Individual antibody levels are highly dependent on the timing after exposure to the infection or vaccine. The seroprevalence could be underestimated due to low test sensitivity within two weeks following the infection or immunity waning with time passing after the disease onset or getting vaccine [27]. We cannot be certain that seronegative individuals were not previously exposed to the virus; their antibody levels may have declined with time to an undetectable level.

The analyses of predictors were performed with no adjustments for the test performance. The imperfect test performance could have attenuated the ORs toward unity because of the non-differential misclassification of the outcome status.

Finally, given the cross-sectional study design, the directions of the revealed associations cannot be interpreted unambiguously. For this reason, it was impossible to be clear on causality. Relatively small sample sizes may also limit the interpretation of our findings.

Public health importance of the findings

Level of antibodies correlating with antiviral protection as well as the proportion of the population immune to SARS-CoV-2 required to reach the herd immunity remain unknown [60]. Due to the individual-level infection-acquired or vaccine-induced immunity is short-lived and wanes rapidly over time, herd immunity might never be reached [61]. By the middle of 2021, over 70% of the population of Arkhangelsk became seropositive to SARS-CoV-2. Regardless of that, the rate of new cases registered in Arkhangelsk is still high. It can be due to the new strains of SARS-CoV-2 regularly appearing, while immunity wanes after both the infection and immunization. Nevertheless, regular seroprevalence studies should continue to be conducted in order to reveal changes in the proportion of the susceptible population [62].

We found a high rate of asymptomatic infection among unvaccinated study participants, which may play an important role in the ongoing pandemic. Previous studies showed that the proportion of asymptomatic cases could be even higher in younger adults and in children [63]. To stop the virus transmission by asymptomatic individuals, it is necessary to obtain high population coverage with vaccines, including the pediatric population [64].

Conclusion

Two third of the study population were SARS-CoV-2 seropositive in a year after the start of the pandemic in Arkhangelsk, Russia. Regular employment was positively associated with seropositive status, while smokers were less likely to be seropositive. Factors associated with low adherence to NPIs were male sex, employment and low confidence in the efficiency of NPIs. Seropositivity was not associated with adherence to NPIs during the first year of the pandemic.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Data availability statement

Researchers may apply for access to KYH and ESSE-RF3 data. See KYH data access regulations and instructions at https://metadata.knowyourheart.science/. Inquiries concerning ESSE-RF3 data access are to be sent to esserf2020@gmail.com. All data requests will be guided by protecting of personal information, confidentiality agreement with participants, and their informed consents.

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