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Original Research

The 1st year of the COVID-19 epidemic in Estonia: a population-based nationwide sequential/consecutive cross-sectional study



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ABSTRACT

Objectives: The objective of this study was to assess the population prevalence of SARS-CoV-2 and changes in the prevalence in the adult general population in Estonia during the 1st year of COVID-19 epidemic.

Study design: This was a population-based nationwide sequential/consecutive cross-sectional study.

Methods: Using standardised methodology (population-based, random stratified sampling), 11 cross-sectional studies were conducted from April 2020 to February 2021. Data from nasopharyngeal testing and questionnaires were used to estimate the SARS-CoV-2 RNA prevalence and factors associated with test positivity.

Results: Between April 23, 2020, and February 2, 2021, results were available from 34,915 individuals and 27,870 samples from 11 consecutive studies. The percentage of people testing positive for SARS-CoV-2 decreased from 0.27% (95% confidence interval [CI] = 0.10%–0.59%) in April to 0.04% (95% CI = 0.00%–0.22%) by the end of May and remained very low (0.01%, 95% CI = 0.00%–0.17%) until the end of August, followed by an increase since November (0.37%, 95% CI = 0.18%–0.68%) that escalated to 2.69% (95% CI = 2.08%–2.69%) in January 2021. In addition to substantial change in time, an increasing number of household members (for one additional odds ratio [OR] = 1.15, 95% CI = 1.02–1.29), reporting current symptoms of COVID-19 (OR = 2.21, 95% CI = 1.59–3.09) and completing questionnaire in the Russian language (OR 1.85, 95% CI 1.15–2.99) were associated with increased odds for SARS-CoV-2 RNA positivity.

Conclusions: SARS-CoV-2 population prevalence needs to be carefully monitored as vaccine programmes are rolled out to inform containment decisions.

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Introduction

During the 1st year of COVID-19 pandemic,^{1,2} control measures (non-pharmaceutical interventions, including business and school closures, restrictions on movement, total lockdowns, social distancing) were widely implemented to contain the spread of

SARS-CoV-2 and have been effective in curbing the COVID-19 epidemic, but they do not represent desirable long-term strategies. The future trajectory of the COVID-19 pandemic hinges on the dynamics of both viral evolution and population immunity against SARS-CoV-2.

Understanding the future trajectory of this disease requires knowledge of the population-level landscape of immunity, generated by the life histories of the SARS-CoV-2 infection or vaccination among individual hosts.³ The drivers of future COVID-19 dynamics are complex. However, characterisation of the prevaccination

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prevalence, the change of active infections and development of immunity in the population are vital data elements for adequately projecting the future course of the SARS-CoV-2 epidemic and the effect of containment measures.

In Estonia, as of January 31, 2021, 785,333 SARS-CoV-2 (RNA) tests (58,967 per 100,000 population) were undertaken, and a total of 44,208 (3326 per 100,000) COVID-19 cases were confirmed^{4,5} (Fig. 1). The confirmed SARS-CoV-2 case rate was the highest among people aged 15–24 years (4120/100,000), followed by the age group 45–54 years (4053/100,000), and lowest among children younger than 10 years (522 and 1279 per 100,000 among 0- to 4-year olds and 5- to 9-year olds, respectively). By January 31, 2021, of all the confirmed COVID-19 cases, 5.6% ($n = 2471$) had been hospitalised for treatment and 0.9% ($n = 419$) had died.⁶

The first case of COVID-19 was confirmed in Estonia on February 26, 2020.⁴ A special digital referral system was developed in mid-March 2020 to simplify the referral process.⁶ Individuals who were deemed to be at a high risk for the SARS-CoV-2 infection (symptomatic patients referred by family physicians) and frontline staff members (health care, nursing home, social workers, police, border guard officers with a referral letter from their employer) were all eligible for testing. Testing eligibility was relaxed by July 2020.

On March 13, 2020, a set of lockdown rules was implemented—people were allowed to leave their homes at any time so long as they observed social distancing. By June 2020, the restrictions were gradually eased, but physical distancing requirements, that is, the 2 + 2 rule (up to two people can be in a public place together and at least a 2-m distance must be kept from others⁷), have remained in force. In response to the increase of new case notifications since the last week of July 2020, and attributing the new cases to visiting nightclubs and bars, the Police and Border Guard Board imposed bans on night-time alcohol sales from August 7 (in two counties),⁸ and since September 25, a nationwide restriction on the sale of alcohol has been in force. Since the beginning of November 2020, additional measures on the workplace (recommendation to work remotely and cancelling all joint events), in public places and in transport (mandatory mask wearing) were implemented.⁹ COVID-19 vaccination started in January 2021.¹⁰

The evidence of the first year of the COVID-19 epidemic is frequently based on the data from symptomatic patients,^{11,12} seroepidemiological studies¹³ and modelling.^{14,15} Most studies are based on small or selected population samples (e.g., hospital admissions) providing data not representative of the community. To the best of our knowledge, large population-based studies needed

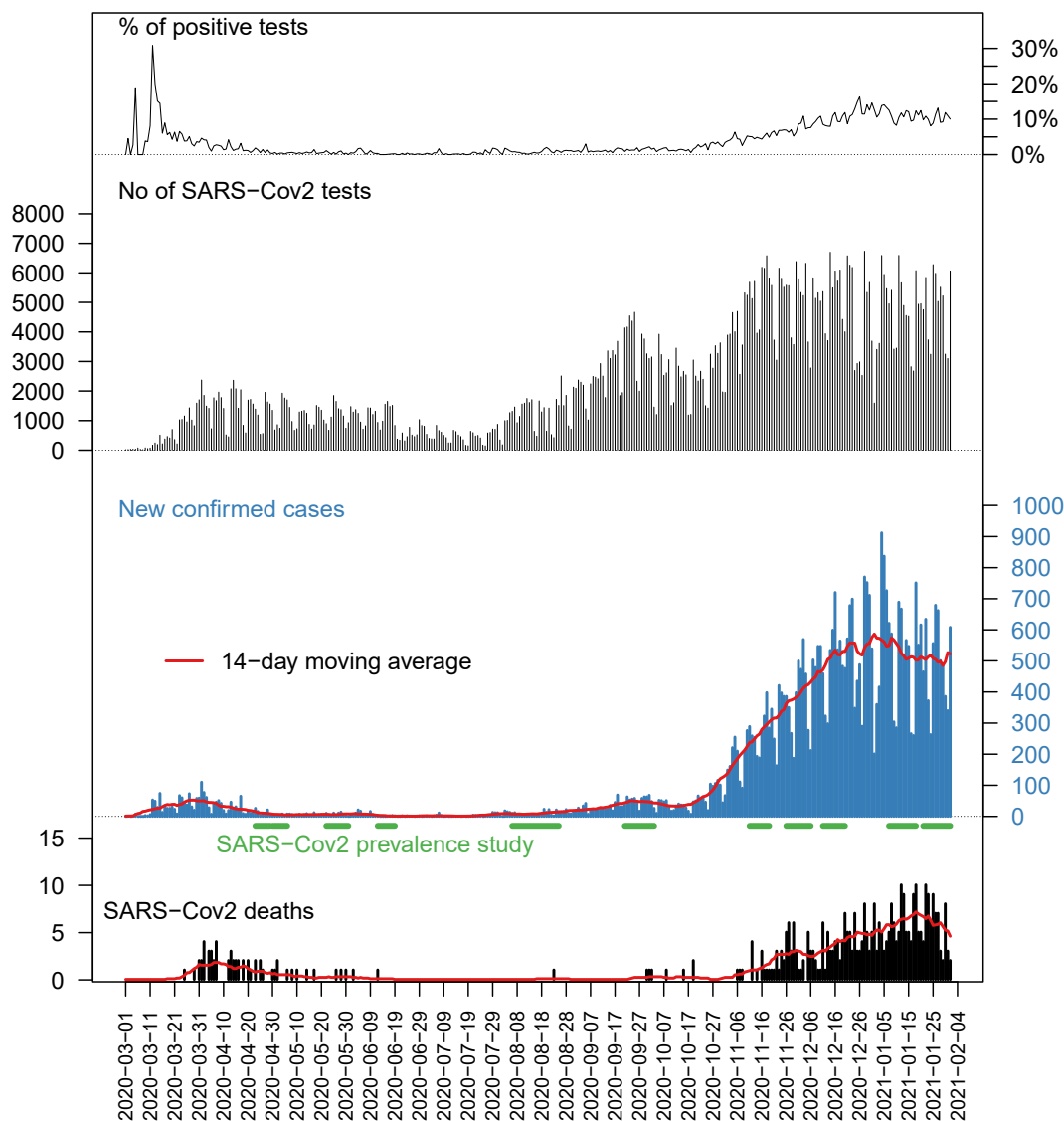


Fig. 1. The COVID-19 epidemic in Estonia: daily numbers of new confirmed cases, the number of tests, proportion of positive tests and the number of deaths, 2020–2021.

to understand risk factors and dynamics and delineate the pre-vaccination course of the COVID-19 pandemic are scarce.^{16,17}

In this study, we rely on a national survey designed to be representative of the target population to describe the course of the epidemic over the first year and risk factors for testing positive for SARS-CoV-2 in Estonia (until the end of January 2021).

Methods

Study design

A population-based nationwide sequential/consecutive cross-sectional study was conducted.

Source population

In 2020, the population of Estonia was estimated at 1,326,535 million people (equivalent to 0.02% of the total world population), with 68% of the population living in urban areas. The Estonian language is spoken by roughly 68% of the population, with approximately 28% of the population being Russian speakers.⁵ Historically, most of Russians-speaking population is settled in the capital, Tallinn, or the northeastern region of the country (Ida-Virumaa County).¹⁸

Data source: SARS-CoV-2 community prevalence studies

The data for this work originate from sequential/consecutive nationwide cross-sectional studies. This methodology was chosen on the premise that valid inferences of change in population values can be made on the basis of repeated cross sections within the single population.¹⁹

The listing of the Estonian Population Registry²⁰ was used as a sampling frame, and all individuals aged 18 years and older were eligible for study participation.

Using standardised methodology (population-based, random stratified sampling), 11 cross-sectional studies were conducted with data collection during April 23–29, April 30 – May 6, May 22–31, June 11–22, August 6–25, September 21 – October 3, November 11–19, November 26 – December 6 and December 11–20 in 2020 and during January 7–18 and January 21 – February 2 in 2021. For each study, multistage stratified random sampling was used. Primary sampling strata consisted of all counties ($n = 15$), and two most populated cities were considered separately from their respective counties. In each primary sampling stratum, stratified by gender and age (18–39, 40–64 and 65+ years), random samples ($n = 200$ in most regions, $n = 400$ in the three most populated areas) of civilian residents were recruited.

Sample size

The required total sample size for individual SARS-CoV-2 RNA testing studies was estimated based on the upper Clopper-Pearson confidence limit under the assumption of no positive test results. The sample size of 2000 was derived at a 5% level of significance with an upper confidence limit of 0.184%.

Study procedures

Participants were contacted by e-mail (original invitation and up to two reminders) or telephone (for those aged 65 years or older) for completion of a screening questionnaire regarding previous SARS-CoV-2 testing and symptoms of COVID-19. Respondents could take a phone interview in case of any problems with accessing the web questionnaire. A structured questionnaire (based on the instrument

recommended by World Health Organization²¹) was used to elicit respondent sociodemographic data, data on the size and age structure of the household, health status and social- and work-related contacts within two weeks before the study.

Referral and registration for SARS-CoV-2 testing at state drive-in sites or home visit by the testing station team (for those study participants unable to access drive-in stations) was undertaken by the study team.

SARS-CoV-2 testing

The nasopharyngeal samples collected were tested for SARS-CoV-2 RNA by quantitative reverse-transcriptase–polymerase-chain-reaction (RT-PCR) at the SYNLAB Laboratory, a private medical laboratory company (SolGent DiaPlexQT Novel Coronavirus (2019-nCoV) Detection Kit CE-IVD). Viral RNA from all samples was isolated within 24 h.

All SARS-CoV-2 test results were entered into the state E-Health service system and communicated back to participants by the authorised staff member of the testing stations. Participants who tested positive for SARS-CoV-2 were required to self-isolate for 14 days since developing symptoms. All those who tested positive were monitored by their own family doctor until recovery.

Statistical analysis

Descriptive statistics (i.e., proportions and means) are presented. SARS-CoV-2 prevalence (the proportion of testing positive) and 95% Clopper-Pearson confidence interval (CI) were calculated, taking into account the sample design. Prevalence rates were calculated using the Estonian population at the beginning of 2020 as a denominator.¹⁷

A survey-adjusted logistic regression model was applied to explore associations between data collection timing (study round), age, gender, preferred language, region of residence, size and age structure of the household, pre-existing physician diagnosed chronic conditions, body mass index, number of contacts within two weeks before the study and having COVID-19–specific symptoms at the time of study with the SARS-CoV-2 RNA test positivity. Variables identified as statistically significant predictors with a significance level of $P < 0.05$ were inserted into a multivariable logistic model.

We present adjusted odds ratios (ORs) together with the 95% confident estimates. Since the observed prevalence is relatively low (<3%),²² the ORs found in the logistic regression model approximate the risk ratios reasonably well.

We used the R statistical programming language for the analyses.²³

The study is registered with the ISRCTN Registry, ISRCTN10182320.

Results

SARS-CoV-2 community prevalence over the first year of the epidemic

A total of 34,915 individuals, including 15,203 males and 19,712 females, participated in the series of cross-sectional studies from April 2020 to February 2021. The age of the study participants ranged from 18 to 96 years (average age = 48.1 years); 85.5% filled the survey in Estonian and 14.2% in Russian language. The average household size among the study participants was 2.7. SARS-CoV-2 prevalence declined at the beginning of the observation period (in April: 0.27%, 95% CI = 0.10%–0.59%; June 2020: 0.00%, 95% CI = 0.00%–0.12%) and remained low until the end of September 2020

Table 1
Characteristics of the population-based SARS-CoV-2 prevalence studies and respective study participants, Estonia, 2020–2021.

	Round 1	Round 2	Round 3	Round 4	Round 5	Round 6	Round 7	Round 8	Round 9	Round 10	Round 11
	April 23–29, 2020	April 30–May 6, 2020	May 22–31, 2020	June 11–22, 2020	Aug 6–25, 2020	Sept 21–Oct 3, 2020	Nov 11–19, 2020	Nov 26–Dec 6, 2020	Dec 11–20, 2020	Jan 7–18, 2021	Jan 21–Feb 2, 2021
<i>Study characteristics</i>											
Total sample	10,209	12,020	21,830	28,034	25,998	22,900	23,187	20,032	23,921	21,063	25,135
Non-contacts (n)	4119	6113	12,869	20,133	19,467	15,460	16,322	14,296	17,900	14,957	18,042
Refusals (n)	2060	1791	2923	2414	1546	3024	2623	2211	2294	2583	2816
Other non-response (n)	1141	981	2538	1615	1813	983	893	688	749	732	1318
Participants (n)	2889	3135	3500	3872	3172	3433	3349	2837	2978	2791	2959
SARS-CoV-2 tested (n)	2306	2666	2579	2983	2335	2532	2726	2381	2522	2370	2470
<i>Participants characteristics</i>											
Men (n, %)	1254, 43.4%	1377, 43.9%	1627, 46.5%	1657, 42.8%	1413, 44.6%	1504, 43.8%	1388, 41.5%	1189, 41.9%	1297, 43.6%	1202, 43.1%	1295, 43.8%
Age (mean, SD, range)	47.7, 15.8, 18-94	46.7, 15.6, 18-94	49.6, 16.7, 18-93	47.5, 15.6, 18-92	47.2, 15.9, 18-94	48.2, 15.8, 18-95	48.7, 15.9, 18-96	49.9, 16.2, 18-94	47.0, 15.8, 18-91	48.1, 16.1, 18-93	48.6, 16.0, 18-93
Size of the household (mean, SD)	2.77, 1.42	2.79, 1.42	2.70, 1.41	2.75, 1.41	2.77, 1.43	2.68, 1.36	2.62, 1.36	2.63, 1.36	2.68, 1.37	2.66, 1.36	2.67, 1.38
Respondent language Russian (yes; n, %)	396, 13.7%	432, 13.8%	513, 14.7%	554, 14.3%	380, 12.0%	482, 14.0%	565, 16.9%	411, 14.5%	388, 13.0%	406, 14.6%	428, 14.5%
Smoking (yes; n, %)	685, 23.7%	709, 22.6%	762, 21.8%	789, 20.4%	706, 22.3%	681, 19.9%	652, 19.5%	520, 18.3%	600, 20.2%	555, 19.9%	553, 18.7%
Pre-existing chronic disease (yes; n, %)	1138, 39.4%	1217, 38.8%	1493, 42.7%	1532, 39.6%	1224, 38.6%	1375, 40.1%	1345, 40.2%	1176, 41.2%	1120, 37.6%	1123, 40.2%	1192, 40.3%
Self-reported COVID-19 symptoms (yes; n, %)	1079, 37.4%	1132, 36.1%	1110, 31.7%	1142, 29.5%	1047, 33.0%	1234, 36.0%	1159, 34.6%	1005, 35.4%	1987, 36.5%	939, 33.6%	945, 31.9%
Previous SARS-CoV-2 testing (yes; n, %)	143, 4.95%	159, 5.07%	318, 9.09%	308, 7.95%	363, 11.4%	810, 23.6%	1107, 33.1%	1061, 37.4%	1268, 42.6%	1341, 48.1%	1475, 49.9%
Previously tested positive for SARS-CoV-2 RNA (n, %)	12, 8.39%	11, 6.92%	16, 5.03%	15, 4.87%	6, 1.65%	14, 1.73%	19, 1.72%	31, 2.92%	43, 3.39%	75, 5.59%	82, 5.56%
<i>SARS-CoV-2 positivity and estimated prevalence</i>											
No of test positives	4	8	2	0	1	5	10	30	31	55	42
Prevalence (%; 95% CI)	0.27% (0.10%–0.59%)	0.17% (0.05%–0.41%)	0.04% (0.00%–0.22%)	0.00% (0.00%–0.12%)	0.01% (0.00%–0.17%)	0.22% (0.08%–0.49%)	0.37% (0.18%–0.68%)	1.34% (0.92%–1.89%)	1.27% (0.87%–1.79%)	2.69% (2.08%–2.69%)	2.05% (1.53%–2.69%)

CI, confidence interval; SD, standard deviation.

Table 2
Risk factors for testing positive for SARS-CoV-2, population-based SARS-CoV-2 prevalence studies, Estonia, 2020–2021.

Variables	Odds ratio (OR)	Lower confidence limit (2.5%)	Upper confidence limit (97.5%)	P-value ^a
<i>Data collection timing</i>				
April 23–29, 2020 (base)	1			
April 30–May 6, 2020	0.63	0.13	3.10	
May 22–31, 2020	0.67	0.08	5.39	
June 11–22, 2020	0.00	0.00	0.00	***
Aug 6–25, 2020	0.02	0.00	0.22	**
Sept 21–Oct 3, 2020	0.84	0.16	4.43	
Nov 11–19, 2020	1.44	0.30	6.84	
Nov 26–Dec 6, 2020	5.35	1.25	22.93	*
Dec 11–20, 2020	5.12	1.21	21.73	*
Jan 7–18, 2021	11.07	2.65	46.32	***
Jan 21–Feb 2, 2021	8.48	2.03	35.43	**
<i>Participant Language</i>				
Estonian (base)	1.00			
Russian	1.85	1.15	2.99	*
<i>Size of the household (number of individuals)</i>				
	1.15	1.02	1.29	*
<i>Reporting symptoms^b at the time of study</i>				
No	1.00			
Yes	2.21	1.59	3.08	***
<i>Region of the country</i>				
Harju County w/o Tallinn (base)	1.00			
Hiiu County	0.91	0.32	2.60	
Ida-Viru County	3.06	1.67	5.59	***
Jõgeva County	0.14	0.02	1.03	
Järva County	0.54	0.14	2.05	
Lääne-Viru County	1.08	0.38	3.04	
Lääne County	0.24	0.05	1.06	
Põlva County	0.13	0.02	1.00	
Pärnu County	0.86	0.37	1.99	
Rapla County	0.38	0.11	1.32	
Saare County	0.93	0.38	2.27	
Tallinn city	1.32	0.74	2.34	
Tartu city	0.87	0.36	2.11	
Tartu County w/o city	0.50	0.17	1.52	
Valga County	0.83	0.19	3.60	
Viljandi County	2.20	0.95	5.12	
Võru County	1.71	0.74	3.91	

^a ****P* < 0.001; ***P* < 0.01; **P* < 0.05.

^b Participants reporting at least one of the three major symptoms (cough, fever, dyspnoea) or at least two of minor symptoms (fatigue, sputum production, muscle or joint aches, headache, new loss of taste or smell, sore throat, congestion or runny nose, nausea or vomiting, diarrhoea, irritability or confusion).

(0.01%, 95% CI = 0.00%–0.17%) (Fig. 2). Since then, SARS-CoV-2 positivity rates have been increasing from 0.22% (95% CI = 0.08%–0.49%) in September to 1.27% (95% CI = 0.18%–0.68%) in November 2020 and then reaching an all-time high at 2.69% (95% CI = 2.08%–2.69%) by mid-January, 2021. About 34% of individuals (*n* = 11 879) self-reported experiencing COVID-19 symptoms at study participation (34.8% of participants testing negative, and 52.1% testing positive). Of all people tested for SARS-CoV-2, 190 were RNA-positive (Table 1).

Modelling confirms significant changes in SARS-CoV-2 prevalence over the first year of the epidemic. In comparison to the first survey round (April 23–29, 2020), SARS-CoV-2 RNA prevalence was significantly lower in rounds four (June 11–22: OR = 0.00, 95% CI =

0.00–0.00) and five (August 6–25: OR = 0.02, 95% CI = 0.00–0.22) and started to increase from round 8 (Nov 26 – Dec 6, 2020: OR = 5.35, 95% CI = 1.25–22.9) onward to round 11 (Jan 21 – Feb 2, 2021: OR = 8.48, 95% CI = 2.03–35.4). Furthermore, regions of the country (Ida-Viru County OR = 3.05, 95% CI = 1.67–5.59), increasing number of household members (for one additional OR = 1.15, 95% CI = 1.02–1.29), reporting symptoms of COVID-19 (OR = 2.21, 95% CI = 1.59–3.09) and completion of the survey in Russian (OR = 1.85, 95% CI = 1.15–2.99) were all associated with higher SARS-CoV-2 RNA positivity (Table 2).

Discussion

The nationwide study documents substantial changes in the population prevalence of SARS-CoV-2 RNA in Estonia during the 1st year of the COVID-19 epidemic, with an initial decrease between April and June, 2020. The findings of the post-1st wave of COVID-19 prevalence and decline are in perfect agreement with a community-based SARS-CoV-2 study from England for the period of April to June 2020.¹⁶ In their study, SARS-CoV-2 community prevalence of 0.32% (95% credible interval 0.19%–0.52%) in April 2020 declined to a very low level by the end of June 2020 (0.08%, 95% credible interval 0.05%–0.12%). In Estonia, the short period of very low SARS-CoV-2 prevalence over the summer of 2020 was followed by an initially slow (in September and October) and then escalating increase since November 2020.

This study documents a clear decline in the prevalence of SARS-CoV-2 following the implementation of the nationwide non-pharmacological intervention (NPI) at the beginning of the epidemic. SARS-CoV-2 prevalence remained extremely low for a short period after lifting NPI measures. In the face of mitigation (slowing down transmission) rather than suppression (stopping SARS-CoV-2 community spread) of containment, an exponential increase of new COVID-19 cases occurred at the verge of the 2nd year of the epidemic.

These findings allow us to speculate that, until now, this is a very unforgiving virus. While rigorous and comprehensive NPI measures are clearly effective in stopping transmission, lifting the measures or less stringent implementation will lead to new and sizable outbreaks.

Second, findings from Estonia should be interpreted in the context of the high SARS-CoV-2 testing rate (80,630/100,000),²⁴ a very low COVID-19 case fatality rate of 0.8% (both, as of March 18, 2021) and no significant excess (all cause) deaths over the first year of the epidemic.²⁵

We saw that those with a larger household size were at a higher risk of SARS-CoV-2 infection with no attributable risk either from the age of the individual or from the age structure of the household (very similar to the results of the study from the UK²⁶). Ongoing household transmission with occasional spill over to other households could act as an important driver for ongoing transmission²⁷ and is estimated to be responsible for roughly 70% of SARS-CoV-2 transmission when widespread community control measures are in place.²⁸

Our findings of higher SARS-CoV-2 risk among those reporting symptoms characteristic to COVID-19 are clearly not new. Yet, it highlights the need to focus on symptomatic cases rather than mass-testing in the face of resource constraints or competing resource needs (i.e., vaccination). Focus on symptomatic COVID-19 cases has a solid evidence base—the majority of COVID-19 cases are symptomatic (~60–80%)²⁹ and are significantly more likely to infect their close contacts than their asymptomatic counterparts.³⁰

Last but not least, we saw regional and ethnic (main language spoken) differences in SARS-CoV-2 positivity. Disproportionately affected racial and ethnic minority groups have been reported elsewhere (United States,³¹ UK,³²). In Estonia, ethnic disparities are not unique to COVID-19 outcomes.³³ The reasons for ethnic disparities in COVID-19 outcomes are multilayered³² and underline

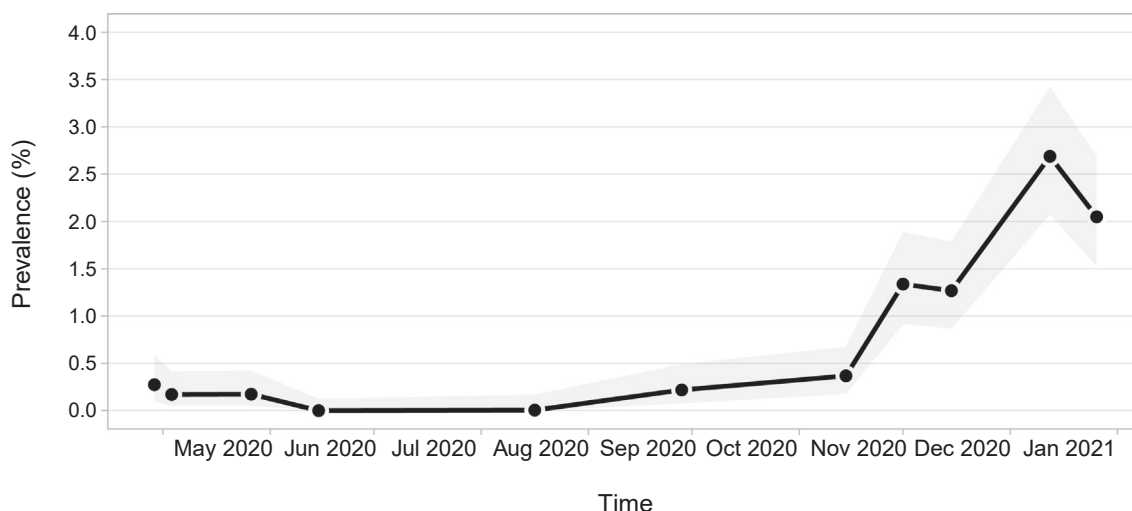


Fig. 2. Percentage of population testing positive for SARS-CoV-2 over time in Estonia during the 1st year of the COVID-19 epidemic 2020–2021. The grey area indicates 95% confidence intervals.

the regional differences in Estonia. Ida-Viru County is in the northeastern part of Estonia bordering the Russian Federation. The overwhelming majority (82%) of residents are Russian speaking. It is important to note that nearly 75% of Russian speakers in Estonia regularly follow TV channels and online media originating from the Russian Federation³⁴ and are more likely to trust Russian than domestic (Estonian) or EU media.³⁵ Whether the Russian Federation's pandemic-related disinformation campaign³⁶ has had some effect on the beliefs and behaviours of the Russian-speaking population in Estonia (and other neighbouring countries with sizable Russian speaking minorities) is unknown at this stage. There are anecdotal reports from Ida-Viru County on residents of declining state-provided COVID-19 vaccines and demands to be vaccinated with the Russian Sputnik vaccine.³⁷ There is a risk that COVID-19 vaccine uptake will be lower among minority ethnic groups in Estonia, thereby widening the health gap further. COVID-19 risk communication and community engagement is a priority for information provision and to counter misinformation.

In conclusion, a rather limited number of studies have assessed the prevalence of SARS-CoV-2 infection in the general population (seroprevalence,^{38,39} SARS-CoV-2 RNA^{10,40,41}). Population-based studies assessing temporal changes in SARS-CoV-2 prevalence, either via repeated cross-sectional studies⁴² or following subjects longitudinally,⁹ are, to our best knowledge, exceedingly rare. It is critically important to create a knowledge base to inform future strategies, and a range of real-life COVID-19 epidemic scenarios over extended periods needs to be documented to assist in understanding the infection risk factors at the individual and population levels. Analyses based on patients in need of hospital treatment, and/or with comorbidities reported during the early phases of the COVID-19 epidemic, were unable to disentangle infection from virulence risks. Yet, primary prevention operates through the control of (the true) infection risk factors.

Our study has several limitations. The degree to which the study is representative of the larger population is influenced by the low response rate and potential selective factors associated with responses. To minimise non-response bias, the prevalence estimates were weighted (age, gender and region) to ensure representativeness of the source population. Yet, there could be other factors for which we did not have detailed information about population distributions which are also associated with testing positive for SARS-CoV-2. The number of people testing SARS-CoV-2 RNA

positive in the cross-sectional studies is low, leading to relatively large uncertainty around estimates.

We see the long period of observation and population-based nationwide study design as strengths of our work. Interpretation of changes in SARS-CoV-2 incidence and positivity rates originating from case notification or clinical cases is likely to be confounded by substantial changes in testing practice over time. Our study is based on a series of cross-sectional studies with a standardised methodology and is thereby very unlikely to be influenced by the testing practice. As this evaluation is based upon observing a single population over time, we speculate that selection bias or unmeasured confounders would operate rather uniformly over the period of observation, though presenting a less-threatening trend of SARS-CoV-2 prevalence and analysis of factors associated with SARS-CoV-2 positivity.

Conclusions

The population-based effect of the novel vaccines against SARS-CoV-2 is highly contingent on the infection-blocking (or transmission-blocking) action of the vaccine and population uptake.⁸ SARS-CoV-2 population prevalence needs to be carefully monitored to inform containment decisions as vaccine programmes are rolled out.

Author statements

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Ethical approval

Ethical approval for the study was obtained from the Research Ethics Committee of the University of Tartu.

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Competing interests

The authors report no competing of interest.

Author contributions

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References

- WHO. WHO Director-General's opening remarks at the media briefing on COVID-19 - 11. <https://www.who.int/dg/speeches/detail/>, March 2020. [Accessed 21 August 2020].
- COVID-19 situation update worldwide, as of week 49. Updated 16 December 2021, <https://www.ecdc.europa.eu/en/geographical-distribution-2019-ncov-cases>, 2021. [Accessed 21 December 2021].
- Saad-Roy CM, Wagner CE, Baker RE, Morris SE, Farrar J, Graham AL, et al. Immune life history, vaccination, and the dynamics of SARS-CoV-2 over the next 5 years. *Science* 2020;**370**(6518):811–8. <https://doi.org/10.1126/science.abd7343>.
- Koroonakaart. [Coronamap]. <https://koroonakaart.ee/en>, 2022. [Accessed 23 January 2022].
- Statistics Estonia. Population indicators and composition. <https://andmed.stat.ee/en/stat>, 2021. [Accessed 18 March 2021].
- COVID-19. Health system monitor. <https://www.covid19healthsystem.org/countries/estonia/livinghit.aspx?Section=1.5%20Testing&Type=Section>, 2021. [Accessed 18 March 2021].
- Estonian Government. The government specified the easing of restrictions after the emergency situation. 21.05.2020, <https://www.kriis.ee/en/news/government-specified-easing-restrictions-after-emergency-situation>, 2020. [Accessed 1 June 2020].
- Police and Border Guard Board. Restriction on alcohol sales in Tartu county. <https://www.politsei.ee/en/instructions/emergency-situation/restriction-on-alcohol-sales-in-tartu-county>. [Accessed 1 December 2020].
- Estonian Government. The government announced new measures to stop the spread of the coronavirus. 10.11.2020, <https://www.valitsus.ee/en/news/government-announced-new-measures-stop-spread-coronavirus>, 2020. [Accessed 1 December 2020].
- COVID-19 vaksineerimise plaan Sotsiaalministeerium. 19.01.2021, https://www.sm.ee/sites/default/files/news-related-files/covid-19_vaksineerimise_plaan_19.01_0.pdf, 2021. [Accessed 18 March 2021].
- Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020;**382**(18):1708–20. <https://doi.org/10.1056/NEJMoa2002032>.
- Doherty AB, Harrison EM, Green CA, et al. Features of 20133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. *BMJ* 2020;**369**. <https://doi.org/10.1136/bmj.m1985>.
- Hallal PC, Hartwig FP, Horta BL, et al. SARS-CoV-2 antibody prevalence in Brazil: results from two successive nationwide serological household surveys. *Lancet Global Health* 2020;**8**(11):e1390–8. [https://doi.org/10.1016/S2214-109X\(20\)30387-9](https://doi.org/10.1016/S2214-109X(20)30387-9).
- Adam D. Special report: the simulations driving the world's response to COVID-19. *Nature* 2020;**580**(7803):316–8. <https://doi.org/10.1038/d41586-020-01003-6>.
- Moore S, Hill EM, Tildesley MJ, Dyson L, Keeling MJ. Vaccination and non-pharmaceutical interventions for COVID-19: a mathematical modelling study. *Lancet Infect Dis* 2021;**21**(6):793–802. [https://doi.org/10.1016/S1473-3099\(21\)00143-2](https://doi.org/10.1016/S1473-3099(21)00143-2).
- Pouwels KB, House T, Pritchard E, Robotham JV, Birrell PJ, Gelman A, et al. Community prevalence of SARS-CoV-2 in England from April to November, 2020: results from the ONS coronavirus infection survey. *Lancet Public Health* 2021;**6**(1):e30–8. [https://doi.org/10.1016/S2468-2667\(20\)30282-6](https://doi.org/10.1016/S2468-2667(20)30282-6).
- Gudbjartsson DF, Helgason A, Jonsson H, Magnusson OT, Melsted P, Norddahl GL, et al. Spread of SARS-CoV-2 in the Icelandic population. *N Engl J Med* 2020;**382**(24):2302–15. <https://doi.org/10.1056/NEJMoa2006100>.
- Schellaars D. Integration of Russian-speaking minorities and stateless persons in Estonian society. Tallinn University of Technology; 2016. <https://digikogu.taltech.ee>. [Accessed 18 March 2021].
- Lopez Bernal J, Cummins S, Gasparrini A. The use of controls in interrupted time series studies of public health interventions. *Int J Epidemiol* 2018;**47**(6):2082–93. <https://doi.org/10.1093/ije/dyy135>.
- Estonian Population Registry. <https://www.rahvastikuregister.ee/>, 2021. [Accessed 18 March 2021].
- Survey tool and guidance COVID-19. WHO/EURO; 2020. 2020-696-40431-54222, https://www.euro.who.int/__data/assets/pdf_file/0007/436705/COVID-19-survey-tool-and-guidance.pdf. [Accessed 5 April 2020].
- Davies HT, Crombie IK, Tavakoli M. When can odds ratios mislead? *BMJ* 1998;**316**(7136):989–91. <https://doi.org/10.1136/bmj.316.7136.989>.
- Lumley L. Survey: analysis of complex survey samples. R package version 4.0; 2020.
- Rate of coronavirus (COVID-19) tests performed in the most impacted countries worldwide as of March 8, 2021 (per million population). <https://www.statista.com/statistics/1104645/covid19-testing-rate-select-countries-worldwide/>. [Accessed 18 March 2021].
- Euromomo. Graphs and maps (18.03.2021). <https://www.euromomo.eu/graphs-and-maps/#excess-mortality>, 2021. [Accessed 18 March 2021].
- Martin CA, Jenkins DR, Minhas JS, Gray LJ, Tang J, Williams C, et al. Socio-demographic heterogeneity in the prevalence of COVID-19 during lockdown is associated with ethnicity and household size: results from an observational cohort study. *EclinicalMedicine* 2020;**25**:100466. <https://doi.org/10.1016/j.eclinm.2020.100466>.
- Nande A, Adlam B, Sheen J, Levy MZ, Hill AL. Dynamics of COVID-19 under social distancing measures are driven by transmission network structure. *PLoS Comput Biol* 2021;**17**(2):e1008684. <https://doi.org/10.1371/journal.pcbi.1008684>.
- Shen M, Peng Z, Guo Y, Rong L, Li Y, Xiao Y, et al. Assessing the effects of metropolitan-wide quarantine on the spread of COVID-19 in public space and households. *Int J Infect Dis* 2020;**96**:503–5. <https://doi.org/10.1016/j.ijid.2020.05.019>.
- Byambasuren O, Cardon M, Bell K, Clark J, MvLaws ML, Glasziou P. Estimating the extent of asymptomatic COVID-19 and its potential for community transmission: systematic review and meta-analysis. *JAMMI* 2020;**5**(4):223–34. <https://doi.org/10.3138/jammi-2020-0030>.
- Sayampanathan AA, Heng CS, Pin PH, Pang J, Leong TY, Lee VJ. Infectivity of asymptomatic versus symptomatic COVID-19. *Lancet* 2021;**397**(10269):93–4. [https://doi.org/10.1016/S0140-6736\(20\)32651-9](https://doi.org/10.1016/S0140-6736(20)32651-9).
- Van Dyke ME, Mendoza MCB, Li W, Parker EM, Belay B, Davis EM, et al. Racial and ethnic disparities in COVID-19 incidence by age, sex, and period among persons aged <25 Years - 16 U.S. Jurisdictions, January 1-December 31, 2020. *Morb Mortal Wkly Rep* 2021;**70**(11):382–8. <https://doi.org/10.15585/mmwr.mm7011e1>.
- Razai MS, Kankam HKN, Majeed A, Esmail A, Williams DR. Mitigating ethnic disparities in covid-19 and beyond. *BMJ* 2021;**372**:m4921. <https://doi.org/10.1136/bmj.m4921>.
- Rahu K, Viiklepp P, Villand K, Pehme L, Rahu M. Respiratory tuberculosis incidence and mortality in Estonia: 30-year trends and sociodemographic determinants. *Int J Tubercul Lung Dis* 2019;**23**(1):112–8. <https://doi.org/10.5588/ijtld.18.0388>.
- Loit U, Harro-Loit H. Media Pluralism Monitor 2016. In: *Monitoring risks for media pluralism in the EU and beyond. Country report: Estonia*; 2021. <https://cmpf.eu/media-pluralism-monitor/mpm-2016-results/estonia/>. [Accessed 18 March 2021].
- Role of Russian Media in the Baltics and Moldova. <https://www.usagm.gov/wp-content/uploads/2016/02/BBG-Gallup-Russian-Media-pg2-02-04-164.pdf>, 2021. [Accessed 18 March 2021].
- Weits R. Assessing the Russian disinformation campaign during COVID-19. International Center for Defence and Security; 2020. 13.11.2020, <https://icds.ee/en/assessing-the-russian-disinformation-campaign-during-covid-19/>. [Accessed 18 March 2021].
- Eesmaa M. Sotsiaalministeerium hakkab Sputniku vaktsiini soovijaid ümber veenma. 10.02.2021, <https://www.delfi.ee/news/paevauudised/estii/video-sotsiaalministeerium-hakkab-sputniku-vaktsiini-soovijaid-umbers-veenma?id=92523421>, 2021. [Accessed 18 March 2021].
- Stefanelli P, Bella A, Fedele G, Pancheri S, Leone P, Vacca P, et al. Prevalence of SARS-CoV-2 IgG antibodies in an area of northeastern Italy with a high incidence of COVID-19 cases: a population-based study. *Clin Microbiol Infect* 2020. <https://doi.org/10.1016/j.cmi.2020.11.013>. S1198-743X(20)30709-6.
- Pollán M, Pérez-Gómez B, Pastor-Barruso R, Oteo J, Hernán MA, Pérez-Olmeda M, et al. Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study. *Lancet* 2020;**396**(10250):535–44. [https://doi.org/10.1016/S0140-6736\(20\)31483-5](https://doi.org/10.1016/S0140-6736(20)31483-5).
- Menachemi N, Yiannoutsos CT, Dixon BE, Duszynski TJ, Fadel WF, Woos-Kaloustian KK, et al. Population point prevalence of SARS-CoV-2 infection based on a statewide random sample - Indiana, April 25-29, 2020. *Morb Mortal Wkly Rep* 2020;**69**(29):960–4. <https://doi.org/10.15585/mmwr.mm6929e1>.
- Riley S, Ainslie KEC, Eales O, et al. High prevalence of SARS-CoV-2 swab positivity in England during September 2020: interim report of round 5 of REACT-1 study. *medRxiv* 2020. <https://doi.org/10.1101/2020.09.30.20204727>.
- Lavezzo E, Franchin E, Ciavarella C, et al. Suppression of a SARS-CoV-2 outbreak in the Italian municipality of Vo'. *Nature* 2020;**584**:425–9.