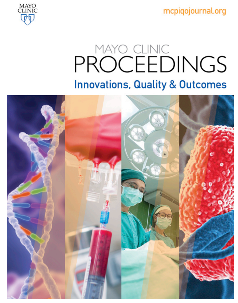

Rates of Asymptomatic COVID-19 Infection and Associated Factors in Olmsted County, MN in the Pre-Vaccination Era

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Rates of Asymptomatic COVID-19 Infection and Associated Factors in Olmsted County, MN in the Pre-Vaccination Era

Running Head: Asymptomatic COVID-19 in Olmsted County, MN

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ABSTRACT

Objective: To estimate rates and identify factors associated with asymptomatic COVID-19 in the population of Olmsted County during the pre-vaccination era.

Patients and Methods: We screened first responders (N=191) and Olmsted County employees (N=564) for antibodies to SARS-CoV-2 from November 2020 to February 2021 to estimate seroprevalence and asymptomatic infection. Second, we retrieved all PCR confirmed COVID-19 diagnoses in Olmsted County from March 2020 through January 2021, abstracted symptom information, estimated rates of asymptomatic infection and examined related factors.

Results: Twenty (10.5%; 95%CI: 6.9%-15.6%) first responders and thirty-eight (6.7%; 95% CI: 5.0%-9.1%) county employees had positive antibodies; an additional 5 (2.6%) and 10 (1.8%) had prior positive PCR tests per self-report or medical record, but no antibodies detected. Of persons with symptom information, 4/20, (20%, 95% CI: 3.0%-37.0%) of first responders and 10/39 (26%, 95% CI: 12.6%-40.0%) county employees, were asymptomatic. Of 6,020 positive PCR tests in Olmsted County with symptom information between March 1, 2020, and January 31, 2021, 6% (n=385; 95% CI: 5.8%-7.1%) were asymptomatic. Factors associated with asymptomatic disease included age [0-18 years (OR=2.3, 95% CI: 1.7-3.1) and 65+ years (OR=1.40, 95% CI: 1.0-2.0) compared to ages 19-44 years], body-mass-index [overweight OR=0.58, 95% CI: 0.44-0.77) or obese (OR=0.48, 95% CI: 0.57-0.62) compared to normal or underweight] and tests after November 20, 2020 [(OR=1.35; 95% CI: 1.13-1.71) compared to prior dates].

Conclusion: Asymptomatic rates in Olmsted County prior to vaccine rollout ranged from 6-25%, and younger age, normal weight, and later tests dates were associated with asymptomatic infection.

ABBREVIATIONS

BMI = body mass index

PCR = polymerase chain reaction

REP = Rochester Epidemiology Project

RT-PCR = reverse transcriptase-polymerase chain reaction

SES = socioeconomic status

INTRODUCTION

Globally, infection with the SARS-CoV-2 virus has caused over 383 million infections and 5.6 million deaths through February 2022.[1] Since the beginning of the pandemic, it has been clear that there is substantial variability in severity of disease, with some SARS-CoV-2-infected persons developing severe symptoms and progressing to hospitalization and death, whereas others may be completely asymptomatic. Asymptomatic infections refer to the positive detection of nucleic acid of SARS-CoV-2 in patient samples by reverse transcriptase-polymerase chain reaction (RT-PCR) among persons with no clinical symptoms or signs. Detection of antibodies to SARS-CoV-2 also provides evidence of prior infection. It is important to understand asymptomatic infection because even asymptomatic infection confers a level of natural immunity,[2-7] and failure to account for such infections will underestimate population-level immunity. In addition, asymptomatic persons may unknowingly transmit the virus to close contacts[8-10] albeit be less infectious than symptomatic persons.[11] Defining the characteristics of persons who are most likely to be asymptomatic can also help target public health recommendations (e.g. mask wearing, social distancing) toward persons who are most likely to unknowingly transmit the virus.

Estimates of asymptomatic SARS-CoV-2 infection among positive cases has ranged from 1.6-56% ; however, these estimates are frequently derived from studies with small samples sizes, selective inclusion criteria, and low participation rates.[12-16] Many of these studies are also biased by lack of sufficient follow-up for development of symptoms and/or ascertained only a limited number of symptoms. A recent meta-analysis of over 350 studies published through March 2021 estimated 35.1% infections as truly asymptomatic, that is, cases did not develop symptoms[12] over at least a 7-day period after a positive PCR test. The wide range in estimates of asymptomatic

SARS-CoV-2 infection underscores the difficulty of obtaining accurate estimates of persons who had asymptomatic infections within a defined population.[17] Ascertaining precise estimates of asymptomatic SARS-CoV-2 infection would require routine testing of everyone in a population and active follow-up to determine whether a given infection is truly asymptomatic or is just early in the course of the disease (presymptomatic). Such studies are challenging and to date, quite limited, particularly those of a truly population-based nature. [12, 13]

To address this critical evidence gap, we studied asymptomatic infection among persons residing in Olmsted County, MN between March 1, 2020, and January 31, 2021. Olmsted County is a well-characterized population with high testing rates, high access to medical care, and high interest in community-based research.[18, 19] Specifically, we used complementary data from two studies: 1) prospective antibody sampling and symptom information from county employees and first responders, and 2) symptom information abstracted from medical records in a records linkage system at time of positive PCR test for SARS-CoV-2. We also examined demographic and clinical factors associated with asymptomatic status. We focused on three main time periods that reflected varying mitigation efforts in the community, including two lockdown periods, from March to June 2020 and end of November to January 2021. Our findings reflect asymptomatic infection during circulation of the wildtype and alpha variant, which were the dominant strains circulating over the time-period of this study[20] and may inform asymptomatic status with other COVID-19 variants in this pandemic as well as targeted groups to be tested in future pandemics.

METHODS

Seroprevalence Study

In collaboration with Olmsted County Public Health Services, we invited county employees and first responders (police, fire, sheriff) to participate in a seroprevalence study in November, 2020. First responders worked in person throughout the pandemic and were expected to be at higher risk of contracting COVID-19.[21] Olmsted County employees were expected to represent the general Olmsted County population because these employees had a mix of occupational and community interactions. For example, some worked from home through the study period, and others continued to work in community settings as essential workers, with masking and distancing restrictions. A small group of employees from Zumbro Valley Health Center were also invited and contributed to the county group. All employees were emailed an invitation letter through either the county or police/fire department.

Interested participants registered for an appointment at one of multiple testing events which took place between November 2020 and February 2021. Participants provided informed consent and a finger-stick blood sample for the antibody test. They also completed an online questionnaire about COVID symptoms and prior COVID-19 testing in addition to giving consent to access medical records. Testing for anti-SARS-CoV-2 antibodies was performed using dried blood spot extracts on the Luminex xMAP SARS-CoV-2 multi-antigen assay as described previously,[22] which measures IgG against three SARS-CoV-2 antigens–the nucleocapsid, the receptor binding domain and the spike glycoprotein S1 subunit. Compared to the Roche serology assay, the positive and negative percent agreement for the Luminex assay was 96.1% and 97.2%, respectively.[22] Remuneration for participation was provided. The Mayo Clinic IRB approved the study protocol and informed consent process.

Asymptomatic Status at Positive PCR Test

To define asymptomatic status at time of positive COVID-19 test and factors associated with asymptomatic COVID, we used the Rochester Epidemiology Project (REP) medical records-linkage system,[18, 19] that links medical records from local health care providers for 1.7 million persons who have lived in a 27-county Midwest region after January 1, 2010. For this study, we focused on persons living in Olmsted County, where the REP captures the majority (94.2%) of the population and their electronic medical record information.[18, 19] Health care data from all visits to each health care provider are coded and indexed electronically. Therefore, the REP includes demographic data and comprehensive information about medical diagnoses, hospital admissions, surgical procedures, drug prescriptions, laboratory test results, body mass index (BMI), and smoking status, etc.

We searched the REP electronic indexes to identify all persons who resided in Olmsted County and who had a positive nasopharyngeal polymerase chain reaction (PCR) test for COVID-19 between March 1, 2020 and January 31, 2021 (11 months). Persons who did not provide authorization to use their medical records for research were excluded (N=868, 9.9%). For multiple tests, the first positive test was considered. The full medical records of these persons were reviewed, and symptoms recorded at the time of the positive test (presenting symptoms) were abstracted by experienced nurse abstractors and study coordinators. Symptoms included dyspnea, chest pain or tightness, dizziness/lightheadedness, cough, fever, chills, myalgia, sore throat, headache, loss of taste or smell, runny or stuffy nose, congestion, rhinorrhea, nausea, vomiting, abdominal pain, diarrhea, skin changes or rash, or fatigue. If the records indicated that the person had no symptoms at the time of the positive PCR test, records were reviewed to determine if new symptoms developed over an additional 14 days following the test, given reported incubation period.[23]

BMI was extracted from the medical records closest to the date of the positive test result and categorized into 3 categories: under/normal weight (<25 kg/m^2), overweight (25-<30 kg/m^2), and obese (≥30 kg/m^2) for adults. For persons 18 years and younger, growth charts were used, and categories defined as under/normal weight (85th percentile and under), overweight (between 86th and 95th percentile), and obese (over 95th percentile).[24] International Classification of Diseases diagnosis codes (ICD-9 and ICD-10) for the 5 years prior to the positive test result were used to capture patient comorbidities and to define the Charlson Comorbidity index.[25]

Socioeconomic status (SES) was determined using HOUsing-based SocioEconomic Status (HOUSES) index which is a validated individual-level measure of socioeconomic status (SES) derived from real property data.[26] HOUSES is an aggregated z-score of housing value, number of bedrooms, area of living space, number of bathrooms, and bedrooms, with higher scores indicative of higher SES.[26] HOUSES was seen associated with lower test and higher positive rate of COVID-19 infection in Olmsted County, MN in March to October 2020 .[27] Addresses at the time of PCR-test were derived from the REP.

We also examined differences due to lockdown periods in Olmsted County. As described in Lopes et al (2022),[28] there were three major COVID-19 related state orders among residents of Olmsted County (Figure 1). First, a peacetime state of emergency was declared on March 12 with corresponding lockdown strategies, including closure of schools and pause in elective surgeries. Lockdown strategies began to lift on June 1 with re-opening of businesses, including restaurants which could resume outdoor dining, and elective medical procedures. Then, starting November 21, greater restrictions were again imposed on businesses as well as social gatherings outside of one's household. However, hospitals did not reduce or stop elective surgeries. Given that community testing was also limited in Olmsted County prior to June, we defined the three periods: First lockdown (March 12 to May 31), Between lockdowns (June 1 to November 20), and Second lockdown and after (November 21 to January 31) (Figure 1).

Statistical Analysis

For the prospective seroprevalence study, we calculated prevalence of antibodies in each risk group. This analysis included stratification by prior positive PCR COVID-19 test and further included estimated rates of SARS-CoV-2 seropositivity, rates of any evidence of infection, from either antibody or PCR tests, and the proportion who reported no prior COVID symptoms (asymptomatic). To estimate the precision of the estimates, 95% confidence intervals using the Wilson (score) binomial confidence intervals when a simple random sample was assumed or the hypergeometric confidence intervals with normal distribution when a finite population correction was needed. The small numbers of cases limited the examination of associations of asymptomatic status with other factors.

We next examined prevalence of asymptomatic vs. symptomatic COVID-19 among all positive PCR-tests in Olmsted County, over the entire time-period and by time intervals that reflected three lockdown periods in Minnesota as described above. We examined the association of demographic, clinical characteristics, HOUSES index, and comorbidities with asymptomatic status using logistic regression (odds ratios, 95% confidence intervals). Our models were adjusted for age and BMI as appropriate. The HOUSES index was analyzed both continuously (z-score) and in quartiles reflecting SES status.

RESULTS

Seroprevalence Study

Overall, 564 (44%) of 1,284 county employees and 191 (63%) of 302 first responders invited to participate provided a blood sample. Median age for both risk groups was 44 years old but there was a higher percent of males (77%) in the first responders compared to county employees (42%). Thirty-eight (6.7%; 95% CI: 5.0%-9.1%) of the county employees and twenty (10.5%; 95%CI: 6.9%-15.6%) of the first responders had positive antibodies (Supplemental Table 1). After combining information from antibody testing and known prior infections reported in the EMR or questionnaire, there was a total of 48 (9%; 95% CI: 6.5%-11.1%) county employees and 25 (13%; 95% CI: 9.0%-18.6%) first responders with evidence of prior COVID. Among persons with questionnaire information, 10/39 (25.6%; 95% CI: 12.6%-40.0%) county employees and 4/20 (20%; 95% CI: 3.0%-37.0%) first responders reported no prior COVID symptoms at any time over the past year (Supplemental Table 1).

Asymptomatic COVID-19 among PCR-Positive Tests

We identified 8,730 persons in Olmsted County with a positive COVID-19 PCR test result between March 1, 2020, and January 31, 2021; 7,862 (90%) had provided authorization to use their medical records for research and were included in the study. We abstracted symptoms noted up to 14 days after the PCR test date for the majority of the study population (n=6,020; 69% of total). Persons with symptom information had similar demographic and clinical characteristics to the overall sample (Supplemental Table 2). The 23% without any symptom information in their medical records were more likely to be male, of younger age, of white race, with no comorbidities, and tested during the November-January time frame, compared to persons with symptom information (Supplemental Table 2).

Among persons with symptom information, 131 (2.2%) were asymptomatic at time of the PCR test but developed symptoms over the 14-day period. These people were considered presymptomatic at the time of the test and were subsequently classified as symptomatic. Persons not reporting any symptoms, n=385 (6%, 95% CI: 5.8%-7.1%) over the 14 days, formed the asymptomatic population. Figure 2 shows the rates of symptomatic and asymptomatic COVID across time (Figure 2A), highlighting relevant lockdown time periods in Olmsted County, overall and by age group (Figure 2B). The prevalence of asymptomatic infection was lowest in March-May (3%), which parallels the lowest rates of tests per day (151) and lowest rates of symptomatic COVID in Olmsted County (Figure 2A) as well as the first lockdown for the state. Higher rates were seen between lockdowns (June-November 2020; 6%) and in the time-period encompassing the second lockdown (November 2020-January 2021; 7.5%) (Figure 2A-B); rates of COVID testing during these periods were higher at 328 and 324, respectively. The older age group (65+) showed higher asymptomatic rates during the early period when testing was more frequent in this population, in particular nursing homes; but children, ages 0-18 years, had the highest asymptomatic rates across the June 2020-January 2021 time periods (Figure 2B).

Table 1 shows the distribution of clinical and demographic factors by symptom status at positive PCR test. Compared to ages 19-44 (reference group), there were over two-fold greater odds of asymptomatic positive test in children 0-18 years (OR=2.3, 95% CI: 1.7-3.1) and suggestive increase of asymptomatic infection in the 65+ age group (OR=1.4, 95% CI: 1.0-2.0) (Table 1). There were no significant differences for those aged 45-64 years. Positive COVID-19 cases who were overweight (OR=0.58, 95% CI: 0.44-0.77) or obese (OR=0.48, 95% CI: 0.57-

0.62) were less likely to be asymptomatic compared to those who were normal or underweight. Adjustment for age slightly attenuated findings (Table 1). Having a positive test after November 20, 2020 was associated with greater odds of asymptomatic COVID-19 (OR=1.39; 95% CI: 1.1-1.7) than a test before this date, likely reflecting the increased testing during this period. There were no statistically significant associations of asymptomatic infection with sex, race or ethnicity, number or type of comorbidities, education, or SES, even after adjustment for age and BMI (Table 1). In exploratory analyses where we examined individual conditions that form the Charlson comorbidity index (Supplemental Table 3), we found higher rates of dementia and lower rates of mild liver disease among persons with asymptomatic infection, but no differences for diabetes.

Symptoms by Age, Ethnicity, and Race

We also described presenting symptoms at time of COVID-19 test overall and by age, sex, race and ethnicity for the 6,020 positive tests with symptom information in the medical record (Supplemental Table 4). The most common symptoms were headache (45%) and cough (53%). Younger ages (18 or younger) were less likely to present with coughing, chills, or myalgia than middle or older age groups. The youngest cases (0-5 years) were most likely to present with fever. Older cases (65+) had lower percent of sore throat and headaches, but higher percent of fatigue (Supplemental Table 4). Fever was reported in 38% of Black cases, 27% of White and 30% of other races, whereas runny nose/congestion was 18% in Black and 28% in White cases. Prevalence of each of the symptoms was similar by ethnicity and sex.

DISCUSSION

Two complementary sampling strategies were used to add to the understanding of asymptomatic COVID-19 in Olmsted County prior to widespread introduction of vaccines. First, our prospective study of first responders and county employees found rates of prior infection from either SARS-CoV-2 antibody testing or prior positive COVID-19 tests to range from 9%-13%. Of these prior infections, 20-26% were asymptomatic. Second, our review of the medical records of all positive COVID-19 tests in the Olmsted County population over an 11-month period found 6% asymptomatic within the 14-day period after the positive test. Younger age (<18), normal BMI, and testing after November 2020 were associated with asymptomatic COVID-19 in this population.

Rates of asymptomatic COVID-19 varied substantially between our two studies, from 6% to 26%. Asymptomatic rates reported by Olmsted County Public Health during this same period were approximately 14.5% of PCR-positive tests but they lacked symptom data on up to 40% of positive cases (Personal communication, Olmsted County Public Health Department). The lower proportion of asymptomatic COVID in our REP study may reflect a few factors. First, in the REP study, we were able to review symptom information over a 14-day period instead of just at time of positive test, which identified additional individuals with symptoms that arose after initial testing (presymptomatic). Next, we lacked symptom information on over 30% of positives in Olmsted County over this time-period. These persons were more likely to be younger and to have a test after November 2020; both characteristics are associated with increased asymptomatic rates. Our higher rates of asymptomatic COVID-19 in the first responders and county employees (20-26%) compared to the general population were not surprising given the difference in study designs and testing. Screening for antibodies is more likely to identify evidence of asymptomatic virus while PCR testing is more likely to be performed due to symptomatic illness. Also, the prospective study is prone to selection bias as those who had greater concern about having a prior COVID infection may have been more likely to participate, thereby overestimating seroprevalence. Recall bias is also a problem for defining asymptomatic status in the prospective study, given the long time period for recalling symptoms and potential for differential recall by concern over having had a prior infection. Finally, our prospective screening studies are relatively small.. However ,these higher asymptomatic rates are consistent with several reports in the literature as noted below.[12]

Access to COVID testing likely impacted our findings for the REP study, given the increased trend in asymptomatic rates across the time period, with greatest rates after Nov 20th, where testing was widespread. In fact, 20% of Olmsted County residents had at least one COVID test by October 2020, illustrating the high testing rates in this community. Before June, testing was limited to symptomatic patients, nursing home surveillance and non-elective procedures, and the high asymptomatic rates among those ages 65 and older reflect the targeted testing.

Several reviews have been conducted to summarize prevalence of asymptomatic COVID-19 across multiple populations. In a systematic review and meta-analysis of 79 studies through June 2020, Buitrago-Garcia et al noted that an estimated 20% (95% CI, 17%-25%) of people infected with SARS CoV-2 remain asymptomatic**.** In a subset of seven studies in defined populations who were screened and followed to account for presymptomatic cases, this estimate increased to 31% (26%-37%).[13] The largest review to date, of over 350 studies between January 2020 and April 2021, which correspond with the time frame of our study, estimated rates of asymptomatic disease at time of PCR testing after removing index cases thought to inflate estimates of symptomatic disease.[12] They found overall rates of 35.1% in persons with at least 7 days of follow-up and noted as truly asymptomatic. Importantly, the review included over 45 studies of at least 50 cases or more in a community setting, involving population-surveillance and cohort studies. The average prevalence of silent infection in these communities was 29.8%, and for the few that were able to correctly classify presymptomatic COVID-19, the average of asymptomatic prevalence was similar, 32.3%.[12]

Even with the many studies of asymptomatic infection, few studies have specifically examined clinical factors associated with this milder presentation. Most prior studies found an inverse trend of asymptomatic rates with age,[29-31] with highest rates in children.[12, 32] Our findings support higher prevalence of asymptomatic illness in children, and are also suggestive of increases among the elderly which has not been seen in the majority of studies to date.[12] However, one of the largest studies of asymptomatic COVID-19, a nationwide cohort in South Korea, also showed a U-shape distribution with age.[33] Our findings in older ages groups may reflect widespread testing that occurred in long term care facilities in Olmsted County, resulting in greater detection of asymptomatic illness. In fact, one prior review showed higher rates of asymptomatic COVID-19 in aged care (20%) than in non-aged care (16%).[34] Also, pre-procedural COVID testing was likely prevalent in Olmsted County, in particular at older ages. Of our 327 asymptomatic cases identified at Mayo Clinic, only 16 (5%) had tests prior to procedures, so this didn't appear to be driving our findings.

Comorbidities are one of the most consistent factors associated with lower asymptomatic rates.[12, 30, 31] Although our data did not show statistical significance, the odds of asymptomatic COVID-19 were less than one in those with 1 (OR=0.90) or 2 or more comorbidities (OR=0.89) compared to none. Interestingly, adjustment for BMI resulted in attenuating the comorbidity association (OR=0.99 for 1 and OR=1.01 for 2+ comorbidities) underscoring the relative importance of BMI in asymptomatic COVID-19 and the suggestion that BMI may be on the same pathway or a confounder of these previously reported associations of comorbidities and symptomaticity. In fact, the few studies that examined the association of BMI with asymptomatic COVID-19 found stronger associations of overweight and obesity with symptomatic COVID-19[32] which mirror the positive associations of BMI or obesity with increased risk of severe COVID-19.[35-37,38] Regarding the exploratory findings of higher rates of dementia among persons with asymptomatic infection, we hypothesize that higher asymptomaticity may be due to inaccurate recall or underreporting of symptoms. The suggestive association with mild liver disease is provocative in light of at least two prior studies that found differences in liver function between asymptomatic and symptomatic patients.[29, 39] We found no evidence for differences in asymptomatic COVID-19 by race or ethnicity in Olmsted County, and access to testing was widespread, with approximately 47% of the Olmsted County population having at least one COVID test by 06/18/2021, which may partially explain our findings compared to other populations.[40, 41]

Some of the heterogeneity in findings across studies is likely due to the accuracy of the tests administered, which has improved over the pandemic. Our nasopharyngeal PCR test used to define positive COVID-19 in Olmsted County over most of this period is considered a gold standard with generally good accuracy.[42] Further, our screening study used dried blood spots for ease of serology testing off site, which has shown high concordance (96.9%) with serum assays using the Roche Diagnostics Elecsys anti-SARS-CoV-2 ECLIA or the Euroimmun anti-SARS-CoV-2 IgG ELISA.[22] However, IgG testing alone may miss some past infections, and including antibodies to IgA as part of serologic surveys may improve retrospective identification of asymptomatic infection.[43] Similar to ours, most of the early first-responder surveys were based on testing exclusively for IgG, and they may have significantly underestimated the rate of SARS-

CoV-2 exposure and infection. Dried blood spot testing is a feasible method for informing community seroprevalence rates as it can be done at a low cost, is easy to collect and store, and can be readily transported and distributed. Methods like these will be important in making testing more available, to help increase the identification of past infection, in particular, asymptomatic COVID, and to increase our understanding of factors that contribute to the development of asymptomatic infection.

There are several strengths of our study, including the population-based investigation of asymptomatic COVID-19 in the REP, the partnership with Olmsted County Public Health, and the use of PCR and serology tests which had both high sensitivity and specificity. Furthermore, we were able to examine rates both among persons at high risk because of their occupation and in the general population. However, we acknowledge the small sample sizes for the seroprevalence study. In addition, the observed prevalence of antibodies depends on the durability of the antibody response after infection and the time elapsed since infection, resulting in possibility of underestimating seroprevalence. We also recognize that our findings are specific to Olmsted County during the period of observation and reflect mitigation strategies during this time period. The wild type SARS-CoV-2 was predominant through the majority of the study, with potential for some involvement of the alpha variant in the final month; we know that later strains, in particular the omicron, has been associated with less severe symptomatic disease and higher rates of asymptomatic infection.[44] Our study was also conducted before SARS-CoV-2 vaccines were available. Vaccination is known to reduce disease severity and consequently, rates of asymptomatic disease in vaccinated populations are likely to be higher.[45] However, we expect that age and BMI will continue to be important factors for severity of infection across all variants and could inform targeted vaccination and prevention strategies.

CRedIT statement

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REFERENCES

1. Johns Hopkins University & Medicine. Coronavirus Resource Center. Accessed at https://coronavirus.jhu.edu/ January 10, 2022.
2. Sekine T, Perez-Potti A, Rivera-Ballesteros O, et al. Robust T cell immunity in convalescent individuals with asymptomatic or mild COVID-19. *Cell*. 2020;183(1):158-68 e14 doi:10.1016/j.cell.2020.08.017.

3. Wajnberg A, Amanat F, Firpo A, et al. Robust neutralizing antibodies to SARS-CoV-2 infection persist for months. *Science*. 2020;370(6521):1227-30 doi:10.1126/science.abd7728.

4. Gaebler C, Wang Z, Lorenzi JCC, et al. Evolution of antibody immunity to SARS-CoV-2. *Nature*. 2021;591(7851):639-44 doi:10.1038/s41586-021-03207-w.

5. Chen C, Zhu C, Yan D, et al. The epidemiological and radiographical characteristics of asymptomatic infections with the novel coronavirus (COVID-19): A systematic review and meta-analysis. *Int J Infect Dis*. 2021;104:458-64 doi:10.1016/j.ijid.2021.01.017.

6. Boyton RJ, Altmann DM. The immunology of asymptomatic SARS-CoV-2 infection: what are the key questions? *Nat Rev Immunol*. 2021;21(12):762-8 doi:10.1038/s41577-021-00631-x.

7. Cohen KW, Linderman SL, Moodie Z, et al. Longitudinal analysis shows durable and broad immune memory after SARS-CoV-2 infection with persisting antibody responses and memory B and T cells. *Cell Rep Med*. 2021;2(7):100354 doi:10.1016/j.xcrm.2021.100354.

8. Singanayagam A, Hakki S, Dunning J, et al. Community transmission and viral load kinetics of the SARS-CoV-2 delta (B.1.617.2) variant in vaccinated and unvaccinated individuals in the UK: a prospective, longitudinal, cohort study. *The Lancet Infectious Diseases*. 2021 doi:https://doi.org/10.1016/S1473-3099(21)00648-4.

9. Zou L, Ruan F, Huang M, et al. SARS-CoV-2 viral load in upper respiratory specimens of infected patients. *N Engl J Med*. 2020;382(12):1177-9 doi:10.1056/NEJMc2001737.

10. He X, Lau EHY, Wu P, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nat Med*. 2020;26(5):672-5 doi:10.1038/s41591-020-0869-5.

11. 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 doi:10.1016/S0140-6736(20)32651-9.

12. Sah P, Fitzpatrick MC, Zimmer CF, et al. Asymptomatic SARS-CoV-2 infection: A systematic review and meta-analysis. *Proc Natl Acad Sci U S A*. 2021;118(34) doi:10.1073/pnas.2109229118.

13. Buitrago-Garcia D, Egli-Gany D, Counotte MJ, et al. Occurrence and transmission potential of asymptomatic and presymptomatic SARS-CoV-2 infections: A living systematic review and meta-analysis. *PLoS Med*. 2020;17(9):e1003346 doi:10.1371/journal.pmed.1003346.

14. Lai CC, Wang JH, Hsueh PR. Population-based seroprevalence surveys of anti-SARS-CoV-2 antibody: An up-to-date review. *Int J Infect Dis*. 2020;101:314-22 doi:10.1016/j.ijid.2020.10.011.

15. Oran DP, Topol EJ. The Proportion of SARS-CoV-2 Infections that are asymptomatic: A systematic review. *Ann Intern Med*. 2021;174(5):655-62 doi:10.7326/M20-6976.

16. Barboza JJ, Chambergo-Michilot D, Velasquez-Sotomayor M, et al. Assessment and management of asymptomatic COVID-19 infection: A systematic review. *Travel Med Infect Dis*. 2021;41:102058 doi:10.1016/j.tmaid.2021.102058.

17. Meyerowitz EA, Richterman A, Bogoch, II, Low N, Cevik M. Towards an accurate and systematic characterisation of persistently asymptomatic infection with SARS-CoV-2. *Lancet Infect Dis*. 2021;21(6):e163-e9 doi:10.1016/S1473-3099(20)30837-9.

18. St Sauver JL, Grossardt BR, Yawn BP, et al. Data resource profile: the Rochester Epidemiology Project (REP) medical records-linkage system. *Int J Epidemiol*. 2012;41(6):1614-24 doi:10.1093/ije/dys195.

19. St Sauver JL, Grossardt BR, Yawn BP, Melton LJ, 3rd, Rocca WA. Use of a medical records linkage system to enumerate a dynamic population over time: the Rochester epidemiology project. *Am J Epidemiol*. 2011;173(9):1059-68 doi:10.1093/aje/kwq482.

20. Situation Update for COVID-19. MN Department of Health. Access at https://www.health.state.mn.us/diseases/coronavirus/situation.html January 10, 2022.

21. Ellingson KD, Gerald JK, Sun X, et al. Incidence of SARS-CoV-2 infection among health care personnel, first responders, and other essential workers during a prevaccination COVID-19 surge in Arizona. *JAMA Health Forum*. 2021;2(10):e213318-e doi:10.1001/jamahealthforum.2021.3318.

22. Turgeon CT, Sanders KA, Rinaldo P, et al. Validation of a multiplex flow immunoassay for detection of IgG antibodies against SARS-CoV-2 in dried blood spots. *PLoS One*. 2021;16(5):e0252621 doi:10.1371/journal.pone.0252621.

23. Li Q, Guan X, Wu P, et al. Early Transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med*. 2020;382(13):1199-207 doi:10.1056/NEJMoa2001316.

24. Clinical growth charts. Centers for Disease Control and Prevention. National Center for Health Statistics. Accessed at https://www.cdc.gov/growthcharts/clinical_charts.htm January 11, 2022.

25. Austin SR, Wong YN, Uzzo RG, Beck JR, Egleston BL. Why summary comorbidity measures such as the Charlson comorbidity index and elixhauser score work. *Med Care*. 2015;53(9):e65-72 doi:10.1097/MLR.0b013e318297429c.

26. Juhn YJ, Beebe TJ, Finnie DM, et al. Development and initial testing of a new socioeconomic status measure based on housing data. *J Urban Health*. 2011;88(5):933-44 doi:10.1007/s11524-011-9572-7.

27. Juhn YJ, Wheeler P, Wi CI, et al. Role of geographic risk factors in COVID-19 Epidemiology: Longitudinal geospatial analysis. *Mayo Clin Proc Innov Qual Outcomes*. 2021;5(5):916-27 doi:10.1016/j.mayocpiqo.2021.06.011.

28. Lopes GS, Manemann SM, Weston SA, et al. Minnesota COVID-19 lockdowns: the effect on acute myocardial infarctions and revascularizations in the community. *Mayo Clinic Proceedings: Innovations, Quality & Outcomes*. 2022;6(1):77-85 doi:https://doi.org/10.1016/j.mayocpiqo.2021.12.002.

29. Leulseged TW, Alemahu DG, Hassen IS, et al. Factors associated with development of symptomatic disease in Ethiopian COVID-19 patients: a case-control study. *BMC Infect Dis*. 2021;21(1):759 doi:10.1186/s12879-021-06465-1.

30. Saurabh S, Verma MK, Gautam V, et al. Tobacco, alcohol use and other risk factors for developing symptomatic COVID-19 vs asymptomatic SARS-CoV-2 infection: a case-control study from western Rajasthan, India. *Trans R Soc Trop Med Hyg*. 2021;115(7):820-31 doi:10.1093/trstmh/traa172.

31. Al-Rifai RH, Acuna J, Al Hossany FI, et al. Epidemiological characterization of symptomatic and asymptomatic COVID-19 cases and positivity in subsequent RT-PCR

tests in the United Arab Emirates. *PLoS One*. 2021;16(2):e0246903 doi:10.1371/journal.pone.0246903.

32. Cheng WA, Turner L, Marentes Ruiz CJ, et al. Clinical manifestations of COVID-19 differ by age and obesity status. *Influenza Other Respir Viruses*. 2021 [Online ahead of print] doi:10.1111/irv.12918.

33. Jung CY, Park H, Kim DW, Choi YJ, Kim SW, Chang TI. Clinical Characteristics of asymptomatic patients with COVID-19: A nationwide cohort study in South Korea. *Int J Infect Dis*. 2020;99:266-8 doi:10.1016/j.ijid.2020.08.001.

34. Byambasuren O, Cardona M, Bell K, Clark J, McLaws M-L, Glasziou P. Estimating the extent of asymptomatic COVID-19 and its potential for community transmission: systematic review and meta-analysis. *Official Journal of the Association of Medical Microbiology and Infectious Disease Canada*. 2020;5(4):223-34 doi:10.3138/jammi-2020-0030.

35. Gao M, Piernas C, Astbury NM, et al. Associations between body-mass index and COVID-19 severity in 6.9 million people in England: a prospective, community-based, cohort study. *Lancet Diabetes Endocrinol*. 2021;9(6):350-9 doi:10.1016/S2213-8587(21)00089-9.

36. Jacob L, Koyanagi A, Smith L, Haro JM, Rohe AM, Kostev K. Prevalence of and factors associated with COVID-19 diagnosis in symptomatic patients followed in general practices in Germany between March 2020 and March 2021. *Int J Infect Dis*. 2021;111:37-42 doi:10.1016/j.ijid.2021.08.010.

37. Simonnet A, Chetboun M, Poissy J, et al. High prevalence of obesity in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) requiring invasive mechanical ventilation. *Obesity (Silver Spring)*. 2020;28(7):1195-9 doi:10.1002/oby.22831.

38. St Sauver JL, Lopes GS, Rocca WA, et al. Factors associated with severe COVID-19 infection among persons of different ages living in a defined midwestern US population. *Mayo Clin Proc*. 2021;96(10):2528-39 doi:10.1016/j.mayocp.2021.06.023.

39. Han H, Xu Z, Cheng X, et al. Descriptive, retrospective study of the clinical characteristics of asymptomatic COVID-19 patients. *mSphere*. 2020;5(5) doi:10.1128/mSphere.00922-20.

40. Kalish H, Klumpp-Thomas C, Hunsberger S, et al. Undiagnosed SARS-CoV-2 seropositivity during the first 6 months of the COVID-19 pandemic in the United States. *Sci Transl Med*. 2021;13(601) doi:10.1126/scitranslmed.abh3826.

41. Morozova O, Clouston SAP, Valentine J, Newman A, Carr M, Luft BJ. COVID-19 cumulative incidence, asymptomatic infections, and fatality in Long Island, NY, January-August 2020: A cohort of World Trade Center responders. *PLoS One*. 2021;16(7):e0254713 doi:10.1371/journal.pone.0254713.

42. Boger B, Fachi MM, Vilhena RO, Cobre AF, Tonin FS, Pontarolo R. Systematic review with meta-analysis of the accuracy of diagnostic tests for COVID-19. *Am J Infect Control*. 2021;49(1):21-9 doi:10.1016/j.ajic.2020.07.011.

43. Montague BT, Wipperman MF, Hooper AT, et al. Anti-SARS-CoV-2 IgA identifies asymptomatic infection in first responders. *J Infect Dis*. 2021 [Online ahead of print] doi:10.1093/infdis/jiab524.

44. High rate of asymptomatic carriage associated with variant strain omicron. medRxiv The Preprint Server for Health Sciences. Accessed at: https://www.medrxiv.org/content/10.1101/2021.12.20.21268130v1 April 13, 2022.

45. Hall V, Foulkes S, Insalata F, et al. Protection against SARS-CoV-2 after Covid-19 vaccination and previous infection. *N Engl J Med*. 2022;386(13):1207-20 doi:10.1056/NEJMoa2118691.

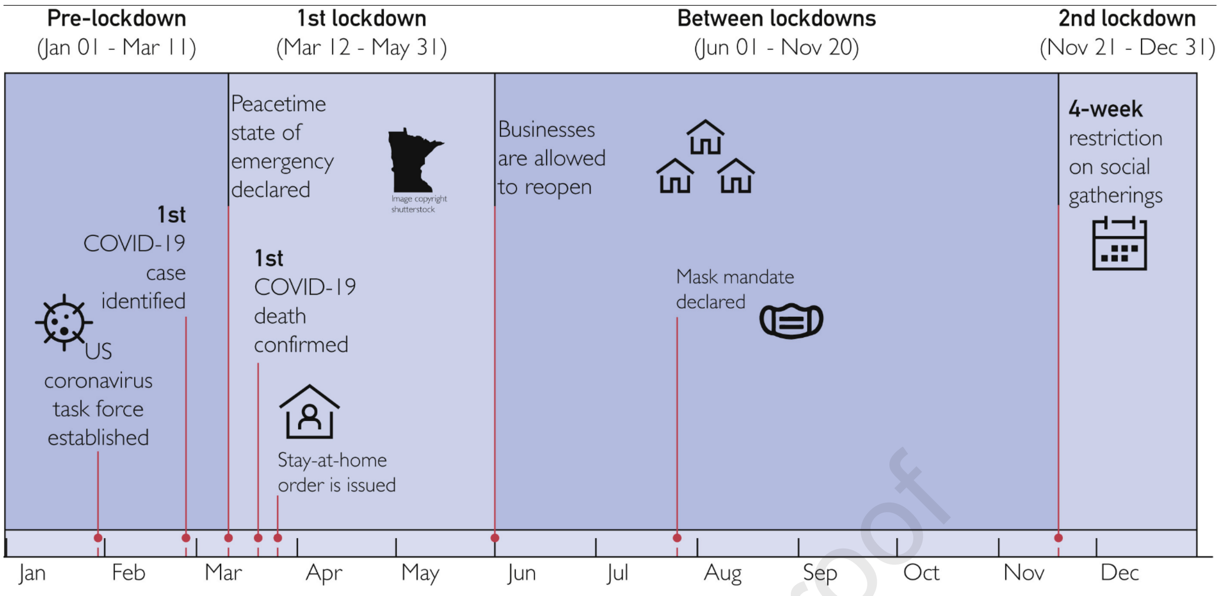
Figure 1. Relevant lockdown periods in Olmsted County, MN, from March through December, 2020. (Reprinted with permission from: Lopes GS, et. Al. Minnesota COVID-19 lockdowns: The effect on acute myocardial infarctions and revascularizations in the community. Mayo Clin Proc Inn Qual Out 2022;6(1):77-85).

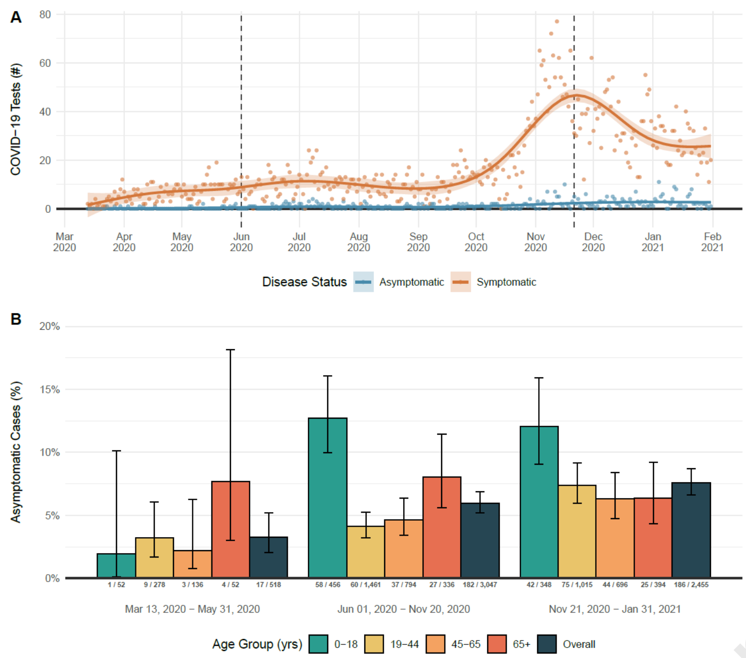
Figure 2. Symptomatic vs. asymptomatic status of PCR positive tests in Olmsted County. Panel A plots the number of positive tests by day stratified by asymptomatic and symptomatic status for the reasons of the test. The colored lines and shaded regions are the expected value and 95% confidence band, respectively, for a generalized additive models (GAM) fit over the data to help visualize the temporal trends. Three time periods are used to capture the first (March 2020 – May 2020) and second (November 2020 – January 2021) lockdown periods—separated by dashed lines in panel A and categorized in panel B. Panel B tabulates the percentage of positive test results in asymptomatic patients by age group and for all patients combined. Error bars in panel B are 95% Score confidence intervals.

Table 1. Factors associated with asymptomatic infection in Olmsted County, MN, Rochester Epidemiology Project (REP), March 2020-January 2021

	Cases	Controls	Univariate models		Age adjusted		Age and BMI adjusted	
	Asymptomatic	Symptomatic	Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval
Total	385	5635						
Age (years)								
0-18	113 (29.4%)	909 (16.1%)	2.3	1.7 - 3.1				
19-44	134 (34.8%)	2513 (44.6%)	0.97	0.73-1.3				
45-65	80 (20.8%)	1460 (25.9%)	(ref)	(ref)				
66+	58 (15.1%)	753 (13.4%)	1.4	0.99-2.0				
Sex								
Female	195 (50.8%)	3031 (53.8%)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
Male	189 (49.2%)	2603 (46.2%)	1.1	0.92-1.4	1.10	0.90 – 1.4	1.03	0.82-1.3
BMI								
Underweight/Normal	135 (40.5%)	1336(26.2%)	(ref)	(ref)	(ref)	(ref)		
Overweight	89 (26.7%)	1506 (29.6%)	0.58	0.44 - 0.77	0.73	0.54 – 0.98		
Obese	109 (32.7%)	2254 (44.2%)	0.48	0.37 - 0.62	0.59	0.44 – 0.79		
Race								
White	267 (69.4%)	3888 (69.0%)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
Black	49 (12.7%)	804 (14.3%)	0.89	0.60 - 1.2	0.84	0.60 – 1.1	0.905	0.64-1.2
Other/Unknown	69 (17.9%)	943 (16.7%)	1.07	0.81 - 1.4	1.04	0.78 – 1.4	0.92	0.66-1.3
Ethnicity								
Non-Hispanic	343 (89.1%)	5047 (89.6%)	(ref)	(ref)				
Hispanic	42 (10.9%)	588 (10.4%)	1.05	0.74 - 1.4	1.02	0.72 – 1.4	1.07	0.72-1.5
Comorbidities								
0	244 (63.4%)	3357 (59.6%)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
1	83 (21.6%)	1363 (24.2%)	0.84	0.64 - 1.1	0.90	0.69 – 1.2	0.99	0.75-1.3
2+	58 (6.0%)	915 (16.2%)	0.87	0.64 - 1.2	0.89	0.61 – 1.3	1.01	0.69-1.5
Education								
High School	63 (16.4%)	1003 (17.8%)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
Some College/2 yr degree	54 (14.0%)	1231 (21.8%)	0.70	0.48 - 1.0	0.72	0.49-1.04	0.80	0.68-1.4
4 yr. degree or More	82 (21.3%)	1445 (25.6%)	0.90	0.64 - 1.3	0.93	0.66-1.3	0.97	0.54-1.2

No Report or Too Young	186 (48.3%)	1956 (34.7%)	--	--	--	--	--	--		
HOUSES index Quartiles										
Q1 (lowest SES)	104 (30.8%)	1521 (29.1%)	1.2	0.88 – 1.6	1.2	0.90 – 1.7	1.30	0.94-1.8		
Q2	70 (20.7%)	1222 (23.4%)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)		
Q3	79 (23.4%)	1392 (26.6%)	0.99	0.71 – 1.4	0.99	0.71 – 1.4	1.00	0.71-1.4		
Q4	85 (25.1%)	1092 (20.9%)	1.4	0.98 – 1.9	1.3	0.94 – 1.8	1.22	0.86-1.7		
Date of Test										
March-November 20, 2020	199 (51.7%)	3366 (59.7%)	ref	ref	ref	ref	ref	ref		
November 21 - January 2021	186 (48.3%)	2269 (40.3%)	1.4	1.1 - 1.7	1.4	1.1 – 1.7	1.3	1.1-1.7		


Pre-lockdown
(Jan 01 - Mar 11)
1st lockdown
(Mar 12 - May 31)
Between lockdowns
(Jun 01 - Nov 20)
2nd lockdown
(Nov 21 - Dec 31)
Peacetime state of emergency declared
Image copyright shutterstock
Businesses are allowed to reopen
4-week restriction on social gatherings
1st COVID-19 case identified
1st COVID-19 death confirmed
Mask mandate declared
US coronavirus task force established
Stay-at-home order is issued
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
Dec


A
COVID−19 Tests (#)
80
60
40
20
0
Mar 2020
Apr 2020
May 2020
Jun 2020
Jul 2020
Aug 2020
Sep 2020
Oct 2020
Nov 2020
Dec 2020
Jan 2021
Feb 2021
Disease Status
Asymptomatic
Symptomatic
B
Asymptomatic Cases (%)
20%
15%
10%
5%
0%
1 / 52
9 / 278
3 / 136
4 / 52
17 / 518
58 / 456
60 / 1,461
37 / 794
27 / 336
182 / 3,047
42 / 348
75 / 1,015
44 / 696
25 / 394
186 / 2,455
Mar 13, 2020 − May 31, 2020
Jun 01, 2020 − Nov 20, 2020
Nov 21, 2020 − Jan 31, 2021
Age Group (yrs)
0−18
19−44
45−65
65+
Overall