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Severe Acute Respiratory Syndrome Coronavirus 2 Antibody Seroprevalence in Decedents Undergoing Forensic Postmortem Examination: Feasibility for Real-Time Pandemic Surveillance

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Background. Population-based seroprevalence studies offer comprehensive characterization of coronavirus disease 2019 (COVID-19) spread, but barriers exist and marginalized populations may not be captured. We assessed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibody seroprevalence among decedents in Maryland over 6 months in 2020.

Methods. Data were collected on decedents undergoing forensic postmortem examination in Maryland from 24 May through 30 November 2020 from whom a blood specimen could be collected. Those with available blood specimens were tested with the CoronaCHEK lateral flow antibody assay. We assessed monthly seroprevalence compared to the statewide estimated number of cases and proportion of positive test results (testing positivity). We used Poisson regression with robust variance to estimate adjusted prevalence ratios (aPRs) with 95% confidence intervals (CIs) for associations of demographic characteristics, homelessness, and manner of death with SARS-CoV-2 antibodies.

Results. Among 1906 decedents, 305 (16%) were positive for SARS-CoV-2 antibodies. Monthly seroprevalence increased from 11% to 22% over time and was consistently higher than state-level estimates of testing positivity. Hispanic ethnicity was associated with 2- to 3.2-fold higher seropositivity ($P < .05$) irrespective of sex. Deaths due to motor vehicle crash were associated with 62% increased seropositivity (aPR, 1.62 [95% CI, 1.15–2.28]) vs natural manner of death. Though seroprevalence was lower in decedents of illicit drug overdose vs nonoverdose in early months, this shifted, and seroprevalence was comparable by November 2020.

Conclusions. Decedents undergoing forensic postmortem examination, especially those dying due to motor vehicle trauma, may be a sentinel population for COVID-19 spread in the general population and merits exploration in other states/regions.

Keywords. decedents; drug overdose; motor vehicle crash; SARS-CoV-2 antibodies; seroprevalence.

Throughout the United States (US) severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) epidemic, scarce public health resources and overwhelmed healthcare systems have limited our ability to conduct studies that could rapidly inform our understanding of the spread of SARS-CoV-2. Seroprevalence surveys are one approach to measuring the spread of infectious agents by estimating the proportion of the population with evidence of antibody host response to the virus. This suggests prior exposure or infection at the time the serum specimen is collected from an individual. Such data have the potential to inform population-level immunity [1–3]. Seroprevalence studies are particularly important when (1) infected individuals can be asymptomatic or mildly symptomatic and may not seek healthcare and/or reportable molecular testing for their illness [4]; and (2) when there is differential access to nucleic acid amplification testing (NAAT) for coronavirus disease 2019 (COVID-19) diagnosis [5, 6]. Problematic interpretation of the results of an early high-profile SARS-CoV-2 seroprevalence study that was criticized for recruiting a biased study population [7, 8] should not overshadow seroprevalence studies with more rigorous sampling design [9, 10].

Seroprevalence surveys are often costly in terms of time and resources, and recruitment is challenging, especially during a pandemic. These studies (when not relying on residual biospecimens) recruit from a defined sampling frame, have target distributions of demographic characteristics in the study population to reflect the target population (to which results will be generalized), and incorporate weights for measurable factors that may influence the results [9, 10]. Marginalized populations, including homeless individuals and those of lower socioeconomic status, may be under-represented in seroprevalence studies [11]. There is a need to identify real-time, low-cost seroprevalence data sources that can be utilized to detect signals of potential infectious disease outbreaks and spread for SARS-CoV-2 and future agents.

An initial assessment of seroprevalence in decedents undergoing forensic postmortem examination by the Maryland Office of the Chief Medical Examiner (OCME) from 24 May 2020 to 30 June 2020 was completed [12]. This demonstrated the feasibility of such a study and the relevance of the results from this select group to the broader population of Maryland residents. It was estimated that 1 in 10 decedents examined was SARS-CoV-2 immunoglobulin M (IgM) or immunoglobulin G (IgG) antibody positive. There was a disproportionate burden of SARS-CoV-2 seropositivity among Hispanic (vs non-Hispanic) decedents, which was reflective of the burden observed in the larger Mid-Atlantic region [13, 14]. Decedents who died of motor vehicle crashes (vs natural death) had a 15% increase in seroprevalence, while decedents of an illicit drug overdose had significantly lower (71% decrease) seroprevalence compared to natural death [12].

This necessitated further investigation to clarify if differences in SARS-CoV-2 seropositivity were maintained over time. If a high proportion of SARS-CoV-2 antibodies is consistently observed among decedents of motor vehicle crashes, data on such populations may be a uniquely poised opportunity for timely, feasible, and inexpensive sentinel surveillance. Studies have demonstrated that the SARS-CoV-2 epidemic has exacerbated an already staggering opioid overdose epidemic that, prior to the epidemic, showed a signal of improvement [15–18]. Whether illicit drug users have a differential proportion of SARS-CoV-2 antibodies can also potentially be studied among decedents.

The objectives of this study were to (1) estimate SARS-CoV-2 antibody seroprevalence among those undergoing forensic postmortem examination by the Maryland OCME over 6 months prior to the availability of vaccine; and (2) determine if the increased SARS-CoV-2 antibody seroprevalence associated with motor vehicle crashes and decreased seroprevalence associated with illicit drug overdose persisted through 30 November 2020.

METHODS

Study Population

Data collection and study population information have been previously described [12]. Maryland state statutes mandate that those who die suddenly and unexpectedly, from nonnatural causes (including suspected illicit drug intoxication), in police custody or with suspicious activity, with no physician attendant, and those who are homeless at death, undergo medicolegal death investigation and forensic postmortem examination by the OCME. All decedents who underwent forensic postmortem examination by the Maryland OCME between 24 May 2020 through 30 November 2020 were eligible for inclusion if 5 mL of whole blood could be collected. Blood was collected in clean plastic cups via cardiac puncture and then transferred to a red top tube and refrigerated. Both the Johns Hopkins Bloomberg School of Public Health and Maryland Department of Health institutional review boards determined this was not human subjects research.

Individuals were included in our sample if they had viable blood specimens for the lateral flow assay to detect SARS-CoV-2 antibodies. As of April 2020, the Maryland OCME established a new protocol that included questioning living relatives/friends regarding whether the decedent had any COVID-19 symptoms or was recently exposed to anyone who was COVID-19 infected prior to death. If the decedent was suspected to be SARS-CoV-2–infected, reverse-transcription polymerase chain reaction (RT-PCR) testing on a nasopharyngeal sample was performed by the Maryland Department of Health Laboratory.

Laboratory Measurements

We detected SARS-CoV-2 IgM and IgG antibodies using the CoronaCHEK serologic lateral flow assay (purchased from CLIAwaived Inc and made by Hangzhou Biotest Bioctech Co, Ltd). Previous studies of this assay on positive and negative control specimens in Maryland demonstrated good sensitivity (95% [95% confidence interval {CI}, 83%–99%] in convalescent plasma donors >28 days after symptom onset; 100% [95% CI, 89%–100%] in COVID-19–confirmed hospitalized individuals 15 days after symptom onset) and specificity (100% [95% CI, 94%–100%] in patients infected with rhinoviruses and other coronaviruses before the COVID-19 pandemic) [19]. A further study of 532 prepandemic samples from emergency room patients of Johns Hopkins Hospital showed a specificity of 99.3% (95% CI, 98.1%–99.8%) [20]. The performance of this assay was formally tested on whole capillary blood specimens. Given the hemolyzation of specimens collected from decedents, ad hoc experiments were conducted in which negative samples were spiked with positive concentrations and tested with CoronaCHEK. These experiments indicated that antibody sensitivity was at levels equivalent to what was seen in standard serum or plasma samples (data not shown).

We prioritized maximizing sensitivity for this analysis, given our goal of identifying a potential sentinel surveillance source. Accordingly, decedents were classified as antibody positive if they were positive for either IgM or IgG antibodies, or both. IgM antibodies appear first upon infection and decrease around 3 weeks following symptom onset, whereas IgG antibodies appear later in infection [21, 22]. Decedents were classified as antibody negative if they were negative for both antibodies or had indeterminate results due to hemolysis of the sample (n = 22).

Covariates

Demographic and clinical factors were abstracted from the Maryland OCME electronic database at the time of death. We assessed age at death (10-year categories), homelessness at the time of death (yes, no), sex at birth (male, female), and race/ethnicity (Hispanic, non-Hispanic White, non-Hispanic Black, or other/unknown [including Asian, other, unknown]). Sex and race/ethnicity groups are presented due to the differences in seroprevalence in these groups. Manner of death was determined by the medical examiner and can include the following categories: natural, homicide, suicide, accidental, and undetermined. Undetermined is a classification used by the medical examiner when the cause of death is unknown or there is insufficient information per investigation and/or autopsy examination to definitively determine the manner of death. At the time of publication, 1 case was still under investigation and was classified as undetermined. For this study we defined overdose death as an overdose due to illicit drug intoxication irrespective of manner of death. Manner of death was categorized as natural, homicide, suicide, accidental (due to motor vehicle trauma), accidental (all other, excluding overdose), illicit drug overdose, or undetermined (excluding overdose).

Statistical Analyses

Covariates were compared by SARS-CoV-2 antibody status using χ^2 tests to test for differences in proportions and Student t tests for means as appropriate. To assess trends, the prevalence of SARS-CoV-2 antibodies was estimated for monthly from 24 May 2020 through 30 November 2020. Alongside trends in SARS-CoV-2 antibody prevalence in decedents, Maryland state data (compiled by the Johns Hopkins Centers for Civic Impact for the Coronavirus Resource Center [23]) was used to plot the total number of confirmed COVID-19 cases (via PCR and/or NAAT positive result) and the average proportion of these tests that were positive (ie, test positivity), by month. This plot visualizes waves in statewide Maryland COVID-19 transmission among living individuals and the SARS-CoV-2 antibody seroprevalence in decedents. Monthly seroprevalence among decedents was also plotted and stratified by whether the cause of death was considered an illicit drug overdose vs nonoverdose.

Seroprevalence among decedents was calculated within each category for all covariates with 95% CIs. We assessed

associations of covariates and SARS-CoV-2 antibody status using Poisson regression with robust variance to estimate unadjusted and adjusted prevalence ratios (aPRs) with 95% CIs. Covariates of interest included age, interaction of race/ethnicity and sex, homelessness at the time of death, and manner of death.

Assays are generally less specific for IgM antibodies, potentially leading to differentially higher false positives for this class of antibodies. Given this, sensitivity analyses were conducted reclassifying those who were IgM positive only to seronegative.

RESULTS

Of 2597 decedents who died within the state of Maryland, 1906 (73%) had viable whole blood specimens and were included in our study population. There was a greater proportion of non-Hispanic Black and Hispanic individuals and of those aged 18–64 years among decedents compared to the living general population of Maryland (Supplementary Table 1).

Three hundred five decedents (16%) were seropositive for either IgG or IgM SARS-CoV-2 antibodies from May through November 2020. Of the 305 seropositive decedents, 103 were IgM-only positive, 46 were IgG-only positive, and 156 were positive for both. Twenty-three of the decedents were identified as RT-PCR positive for SARS-CoV-2 antibodies through the OCME protocol, 14 of whom had COVID-19 listed as the cause of death. Among the 23 decedents, 15 (65%) were positive for both IgM and IgG antibodies, 1 was positive for IgM only, and 3 were positive for IgG antibodies only. There were no significant differences by age, sex, or homelessness (Table 1). Decedents who died of an illicit drug overdose were less likely to be seropositive (46% vs 39%, $P = .03$). Most overdose deaths were due to heroin/fentanyl (91%, alone or combined with other substances).

Seroprevalence was calculated by age group, race/ethnicity and sex, homelessness, and manner of death (Table 2). The prevalence of SARS-CoV-2 antibodies was much higher in Hispanic men (33%) and women (50%) compared to their Black and White counterparts (15% and 13%; 16% and 15%, for men and women, respectively). Seroprevalence was 20% among persons experiencing homelessness at death compared to 16% among those not experiencing homelessness. Seroprevalence was highest among those dying in a motor vehicle crash (25%), followed by homicide (18%), suicide (16%), and "other" accidental manners of death (17%) (Table 2).

The monthly seroprevalence for SARS-CoV-2 antibodies among decedents ranged from 11% (95% CI, 7%–15%) to 22% (95% CI, 19%–24%) from the last week of May 2020 through 30 November 2020 (Figure 1). There was a bimodal wave in the seroprevalence of SARS-CoV-2 antibodies, peaking in August 2020 at 20% and November 2020 at 22%; reclassifying decedents with SARS-CoV-2 IgM-only antibodies to seronegative

Table 1. Characteristics of Decedents Undergoing Forensic Postmortem Examination by the Maryland Office of the Chief Medical Examiner With Viable Whole Blood Specimens (N = 1906)

Characteristic	Antibody Negative (n = 1601)		Antibody Positive (n = 305)		
	No.	(%)	No.	(%)	P Value
Age, y, mean (SD)	44.5	(16.7)	43.7	(16)	.42
Female sex	449	(28)	80	(26)	.52
Race/ethnicity[a]					**<.01**
Men					
Non-Hispanic White	510	(32)	95	(31)	
Non-Hispanic Black	572	(36)	99	(32)	
Hispanic	56	(**3**)	28	(**9**)	
Other or unknown	14	(1)	3	(1)	
Women					
Non-Hispanic White	243	(15)	42	(14)	
Non-Hispanic Black	189	(12)	29	(10)	
Hispanic	7	(0)	7	(2)	
Other or unknown	10	(1)	2	(1)	
Homeless at death	185	(12)	45	(15)	.12
Manner or cause of death					**.02**
Natural	334	(21)	59	(19)	
Homicide	180	(11)	40	(13)	
Suicide	68	(4)	13	(4)	
Illicit drug overdose[b]	730	(**46**)	119	(**39**)	
Accident (MVT)	145	(**9**)	48	(**16**)	
Accident (other)[c]	111	(7)	22	(7)	
Undetermined	33	(2)	4	(1)	

P values were calculated using χ^2 test for proportions or Student t test for means comparing antibody positive to negative. Differences in distributions of ≥5 percentage points were a priori deemed to have public health significance. Statistically significant and public health significant results are shown in bold. Decedents with an indeterminant CoronaCHEK result were classified as negative (n = 22). This includes 1 decedent with manner of death pending.

Abbreviations: MVT, motor vehicle trauma; SD, standard deviation.

[a]The sex-specific "Other or unknown" race/ethnicity groups included 11 Asian, 14 of other race, and 5 of unknown race.

[b]χ^2 test indicates that seropositive decedents were less likely to die from overdose compared to antibody-negative decedents ($P < .05$).

[c]Not including illicit drug overdoses.

further highlighted the first mode (Supplementary Figure 1). Data from the state of Maryland showed the average monthly test positivity (the proportion of PCR/NAAT tests that were positive) began at 9% in the last week of May 2020, declined to 3% in October 2020, and increased to 5% in November 2020; the total number of PCR/NAAT-confirmed cases in the state of Maryland was <700 per month from June to October and then more than doubled in November 2020 (Figure 1).

Monthly SARS-CoV-2 antibody seroprevalence estimates were stratified by overdose vs nonoverdose deaths. Seroprevalence among those with illicit drug overdose as the cause of death was initially lower than those with nonoverdose deaths in May–July 2020 (Figure 2). This trend reversed in August 2020, with decedents from overdose having higher antibody seroprevalence. In October and November 2020, seroprevalence by overdose status was comparable.

In regression analyses assessing risk factors for SARS-CoV-2 antibodies, Hispanic ethnicity was associated with increased likelihood of antibodies irrespective of sex (Table 2). For Hispanic men, antibody seroprevalence was 2.1 times higher (aPR, 2.12 [95% CI, 1.49–3.03]) when compared to non-Hispanic White men. For Hispanic women, antibody seroprevalence was 3.2 times higher compared to non-Hispanic White men (aPR, 3.23 [95% CI, 1.84–5.664]). There were no associations between age at death, or whether decedents were experiencing homelessness at their time of death, with SARS-CoV-2 antibodies. With respect to manner of death, motor vehicle trauma was associated with a 62% increase in SARS-CoV-2 antibodies as compared to natural manner of death (aPR, 1.62 [95% CI, 1.15–2.28]). There was no association comparing seroprevalence among those dying due to overdose to decedents dying from natural manners of death (aPR, 0.93 [95% CI, .70–1.25]). In the sensitivity analyses, reclassifying those who were IgM positive only to seronegative (ie, assessing IgG antibodies as the outcome), findings for Hispanic race were comparable, though the association with motor vehicle deaths was attenuated and did not reach the threshold for statistical significance (aPR, 1.30 [95% CI, .83–2.03]; Supplementary Table 2).

DISCUSSION

Among decedents undergoing forensic postmortem examination with viable blood samples in Maryland, the seroprevalence of SARS-CoV-2 antibodies ranged from 11% to

Table 2. Predictors of Coronavirus Disease 2019 Antibody-Positive Test Results at Death Among Decedents Examined by Maryland Office of the Chief Medical Examiner, 24 May–30 November 2020 (N = 1906)

Characteristic	Seroprevalence, %[a] (95% CI)	Univariable		Multivariable	
		PR	(95% CI)	aPR	(95% CI)
Age, y					
<20	17 (9–27)	1.11	(.65–1.92)	0.89	(.51–1.56)
20–29	17 (13–21)	1.11	(.80–1.55)	1.00	(.72–1.39)
30–39	15 (12–19)	ref	…	ref	…
40–49	16 (12–20)	1.04	(.75–1.45)	1.07	(.77–1.49)
50–59	17 (14–22)	1.14	(.84–1.56)	1.24	(.90–1.70)
60–69	16 (11–21)	1.04	(.71–1.52)	1.16	(.78–1.72)
70–79	15 (8–24)	0.98	(.57–1.70)	0.94	(.53–1.64)
≥80	9 (2–21)	0.57	(.22–1.50)	0.51	(.19–1.38)
Race/ethnicity					
Men					
Hispanic	33 (23–45)	**2.12**	**(1.49–3.03)**	**2.09**	**(1.45–3.01)**
Non-Hispanic Black	15 (12–18)	0.94	(.73–1.22)	0.85	(.65–1.12)
Non-Hispanic White	16 (13–19)	ref	…	ref	…
Other/unknown	18 (4–43)	1.12	(.40–3.19)	1.08	(.36–3.18)
Women					
Hispanic	50 (23–77)	**3.18**	**(1.85–5.55)**	**3.23**	**(1.84–5.66)**
Non-Hispanic Black	13 (9–19)	0.85	(.58–1.25)	0.81	(.55–1.20)
Non-Hispanic White	15 (11–19)	0.94	(.67–1.31)	0.98	(.70–1.36)
Other/unknown	17 (2–48)	1.06	(.30–3.81)	0.91	(.25–3.32)
Homeless					
No	16 (14–17)	ref	…	ref	…
Yes	20 (15–25)	1.26	(.95–1.68)	1.24	(.94–1.65)
Manner or cause of death					
Natural	15 (12–19)	ref	…	ref	…
Homicide	18 (13–24)	1.21	(.84–1.75)	1.36	(.91–2.02)
Suicide	16 (9–26)	1.07	(.62–1.85)	1.12	(.65–1.93)
Illicit drug overdose	14 (12–17)	0.93	(.70–1.25)	0.93	(.70–1.25)
Accidental (MVT)	25 (19–36)	**1.66**	**(1.18–2.33)**	**1.62**	**(1.15–2.28)**
Accidental (other)[b]	17 (11–24)	1.10	(.70–1.73)	1.10	(.70–1.74)
Undetermined[b]	11 (3–25)	0.72	(.28–1.87)	0.66	(.26–1.64)

Statistically significant estimates are shown in bold.

Abbreviations: aPR, adjusted prevalence ratio; CI, confidence interval; MVT, motor vehicle trauma; PR, prevalence ratio.

[a]Estimates the number of decedents who were seropositive within the row total.

[b]Not including illicit drug overdoses.

22% from 24 May through 30 November 2020 and increased over time. Seroprevalence of SARS-CoV-2 antibodies was bimodal, uncovering a peak in August 2020 that was not detected via the state of Maryland total confirmed cases or test positivity indicator. In August 2020, the lower seroprevalence in those dying from overdose diminished and there was no significant association with seropositivity comparing those dying of overdose to nonoverdose deaths from August through November 2020. The large proportion of deaths due to illicit drug overdose (45%) is alarming and is a harbinger of the worsening opioid epidemic, as 91% of overdose deaths were at least partly attributed to heroin or fentanyl. As we observed in our prior analysis, Hispanic ethnicity (for both men and women) and dying in a motor vehicle crash were significantly associated with SARS-CoV-2 antibody seropositivity.

Seroprevalence among decedents undergoing forensic postmortem examination was higher than what has been observed in other antibody seroprevalence studies conducted in Maryland and the US more broadly within similar timeframes [2, 24, 25]. Differences could be due to calendar time of observation (particularly when comparing to the US more broadly due to the heterogeneity in timing of COVID-19 transmission waves across the US), assays used, or the source populations used to derive study populations. Those dying unexpectedly or from nonnatural causes and examined by the Maryland OCME differ demographically from the living general population Maryland by age, race, and ethnicity. Higher seroprevalence among our study population of decedents could be due to a higher prevalence of structural risk factors for nonnatural causes of death that are also associated with COVID-19 infection relative to the Maryland general population. Lower
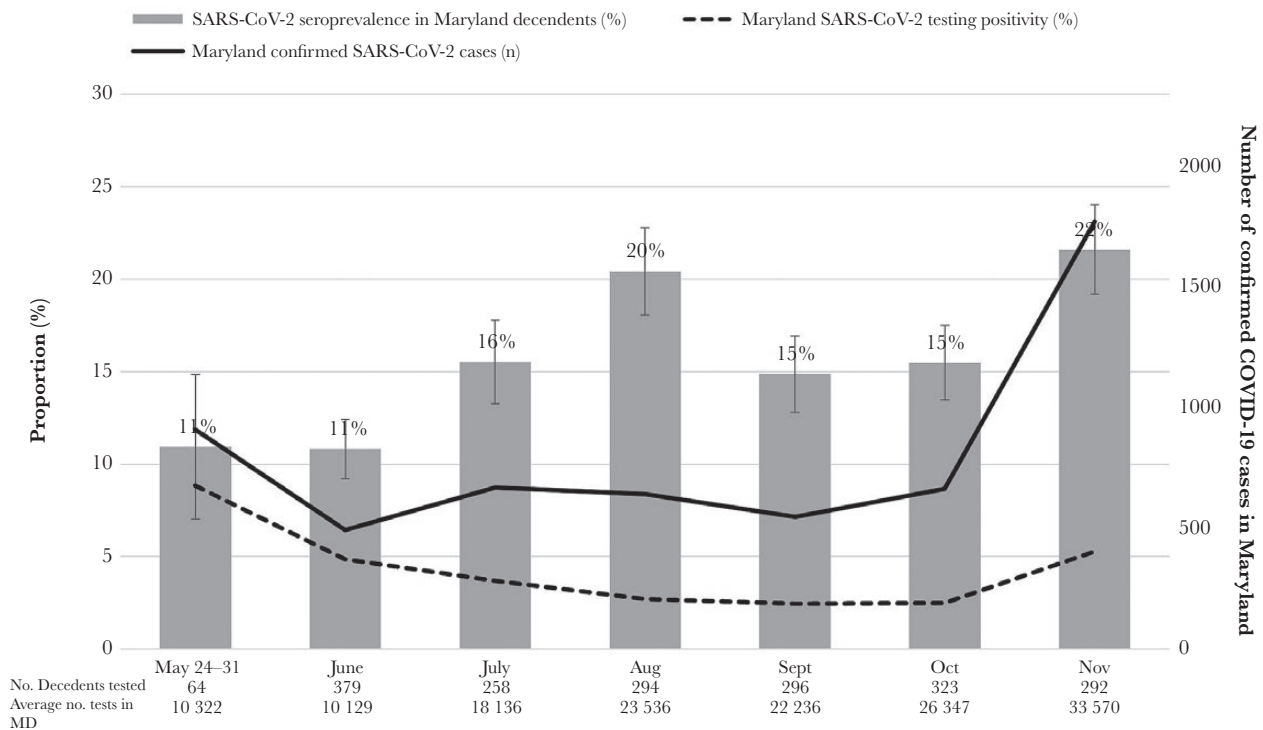
Figure 1. Seroprevalence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibodies in decedents (primary y-axis) and estimated statewide number of confirmed coronavirus disease 2019 (COVID-19) cases (secondary y-axis) and SARS-CoV-2 test positivity (primary y-axis) in Maryland (MD) from 24 May 2020 to 30 November 2020 (N = 1906). MD state data (compiled by the Johns Hopkins Centers for Civic Impact for the Coronavirus Resource Center) were used to plot the total number of confirmed COVID-19 cases (defined as polymerase chain reaction– and/or nucleic acid amplification test–positive result) and the average proportion of these tests that were positive (ie, test positivity), by month.

socioeconomic status and race/ethnicity have been associated with increased COVID-19 infection [14, 26–36] and higher burden of nonnatural causes of death including motor vehicle crashes and illicit drug overdoses [37–40]. The increase in seroprevalence could indicate ongoing transmission and infection over time within the community, or high risk for multiple exposures (ie, those who undergo forensic postmortem examinations are exposed to more infected individuals over time).

Our finding of a higher number of decedents that were IgM only seropositive is intriguing. This is unlikely due to differential specificity for IgG vs IgM antibodies, as a recent evaluation of this assay indicated high specificity irrespective of antibody type [20]. Rather, higher sensitivity for IgM antibodies vs IgG antibodies <14 days after infection may have led to differentially higher detection of IgM antibodies if we were capturing more recent infections. That said, the sensitivity and specificity of this assay could have been impacted by the hemolyzation of these samples, leading to higher than expected IgM positivity. Our study population includes a higher proportion of individuals who use illicit drugs relative to the general population, who are generally at a higher risk of death. It is possible we captured a higher proportion of recent SARS-CoV-2 infection during months when there was substantial SARS-CoV-2 transmission in this population at higher risk of death.

Our observation that Hispanic ethnicity was associated with higher seroprevalence of SARS-CoV-2 antibodies has been noted previously [14, 25]. This analysis confirmed our prior findings that motor vehicle crash deaths were associated with a higher prevalence of SARS-CoV-2 antibody positivity [12]. These findings could be attributed to occupational exposure, as Hispanics were overrepresented in essential work, and essential workers continued driving to commute, but requires further examination. This builds on the evidence from our prior analysis that this could be a potential sentinel surveillance population in cases of new emerging infectious pathogens.

In the earlier study on this population, overdose death was inversely associated with seropositivity for SARS-CoV-2 antibodies as compared to those dying of a natural manner of death [12]. In the present work, there was no association between illicit drug overdose and SARS-CoV-2 antibody seroprevalence in regression analyses. Though there was lower antibody seroprevalence among overdose deaths as compared to nonoverdose deaths, once estimates were stratified by calendar month, seroprevalence shifted over time and was comparable by November 2020. Initial lower seroprevalence may be explained by longer postmortem intervals and decomposition time for overdose deaths vs other causes of death. Individuals dying from illicit drug overdoses who may be isolated are often found many days
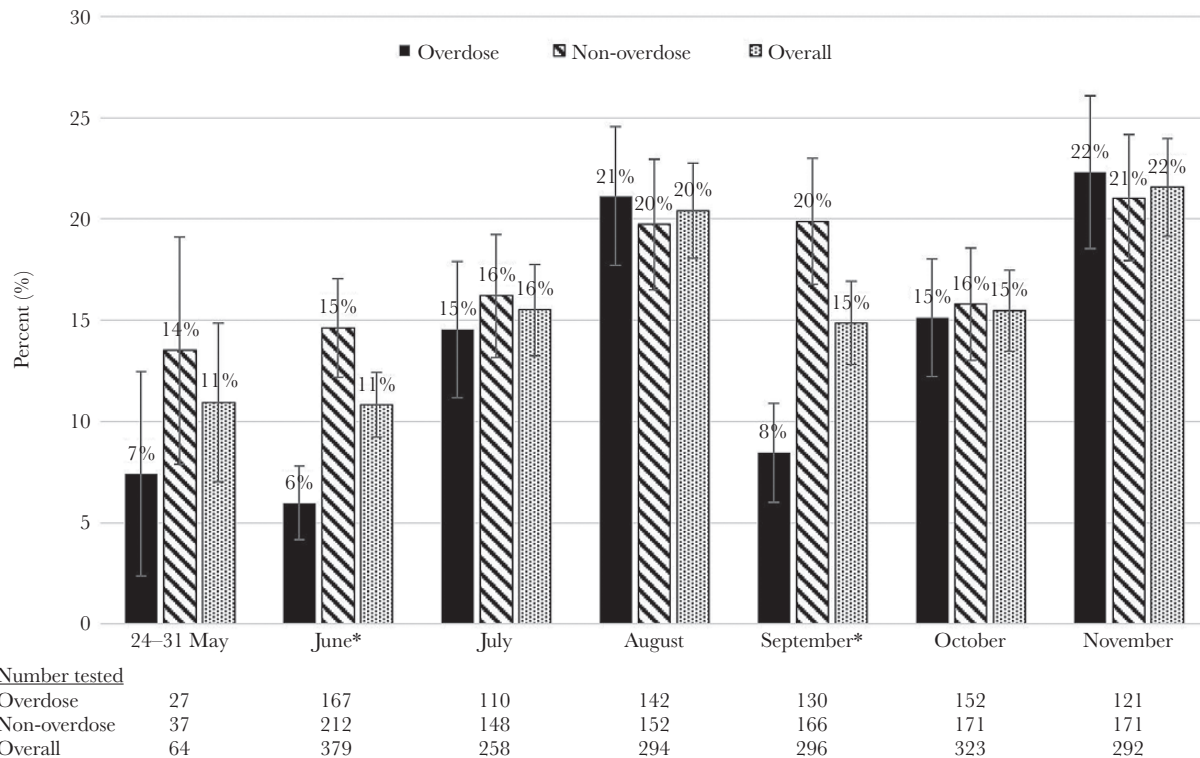
Figure 2. Seroprevalence of severe acute respiratory syndrome coronavirus 2 antibodies by overdose as the cause of death among Marylanders, 24 May–30 November 2020 (N = 1906). *There is no overlap in the 95% confidence intervals for seroprevalence among overdose and nonoverdose deaths in the months of June and September 2020.

after death. Longer postmortem interval could lead to lower antibody detection. Exploring this hypothesis would require investigation into postmortem interval time by manner and cause of death, which was not available for this study.

Our findings on overdose deaths suggest that those using illicit drugs, especially opioids, are likely exposed to COVID-19 infection at a comparable level to those dying from other manners of death. The large proportion of overdose deaths we observed, especially due to opioids, is consistent with nationwide trends in increasing overdose deaths [41]. Although opioid deaths in Maryland had been improving prior to the pandemic, the downward trend in 2019 reversed upon the inception of the pandemic [42]. According to the Maryland OCME, compared to 2019, the number of overdose deaths in the first quarter of 2020 was 4.5% higher, and in the second quarter through the end of 2020 it was 20.8% in 2020 (results not shown). Continued efforts to reach people who use drugs with respect to overdose prevention are critical to curb overdose-related deaths.

There are limitations to our study. Only decedents with viable blood specimens were included; our findings may not be generalizable to all decedents undergoing forensic postmortem examination. Our seroprevalence estimates may not be generalizable to the living general population of Maryland due to the sociodemographic differences between our study

population and the general population. Our findings are not generalizable to the living general population of the US as COVID-19 transmission differed by geographic place and over time. Differential postmortem intervals and decomposition by manner of death could have led to higher detection of antibodies among victims of motor vehicle crashes as compared to natural manner of death, or overdose deaths. Though data were unavailable to explore this, the short postmortem interval for traffic deaths yielding higher detection of antibodies provides more support for this group as a population for sentinel surveillance. Comparing seroprevalence estimates from decedents to population-based seroprevalence estimates from the same living population from which the decedents come, and the same time period (not available to our knowledge from May to November 2020 in Maryland), would allow for the most rigorous examination of strengths and weaknesses of decedents as a sentinel surveillance population.

The lateral flow antibody test we employed has demonstrated high sensitivity and specificity; however, enzyme-linked immunosorbent assays (ELISAs) could have yielded different seroprevalence. Studies have demonstrated the comparability of this assay to ELISAs [19], and this assay is inexpensive and easier to perform, which is critical in the context of a pandemic. The use of a lateral flow assay in our study was at the beginning of the pandemic when information on spread was critical but

vaccination was not available. This assay was also examined as a diagnostic tool among symptomatic patients, which could miss subclinical infections. It is unlikely that subclinical vs clinical infection differed by manner of death in our study population undergoing forensic postmortem examination; nondifferential misclassification would attenuate our estimated association, suggesting the association with motor vehicle trauma is greater in magnitude.

Overall, our study demonstrates how readily available, cost-effective data can be leveraged in a systematic way to provide real-time information on potential signals of infectious disease spread. We add to the growing literature from serologic studies that help to identify population exposure to SARS-CoV-2 rather than relying on molecular testing alone. One such effort, SeroTracker, is a dashboard that synthesizes findings from SARS-CoV-2 serological studies from across the world and underscores the influence of study population characteristics, testing modalities, geographic location, and calendar time to understand differences in seroprevalence estimates [43]. We encourage further exploration of the applicability of our approach among decedents for potential sentinel surveillance to other states and regions in the US as COVID-19 and future pandemic preparedness remains an enduring public health priority, especially among marginalized individuals with poor access to testing and vaccination.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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