Full title

The COVID-19 health equity twindemic: Statewide epidemiologic trends of SARS-CoV-2 outcomes among racial minorities and in rural America

Short title

COVID-19 epidemiologic trends among minority and rural populations

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Abstract

Background: Early studies on COVID-19 identified unequal patterns in hospitalization and mortality in urban environments for racial and ethnic minorities. These studies were primarily single center observational studies conducted within the first few weeks or months of the pandemic. We sought to examine trends in COVID-19 morbidity and mortality over time for minority and rural populations, especially during the U.S. fall surge.

Methods: Statewide cohort of all adult residents in Indiana tested for SARS-CoV-2 infection between March 1 and December 31, 2020, linked to electronic health records. Primary measures were per capita rates of infection, hospitalization, and death. Age adjusted rates were calculated for multiple time periods corresponding to public health mitigation efforts.

Results: Morbidity and mortality increased over time with notable differences among sub-populations. Initially, per capita hospitalizations among racial minorities were 3-4 times higher than whites, and per capita deaths among urban residents were twice those of rural residents. By fall 2020, per capita hospitalizations and deaths in rural areas surpassed those of urban areas, and gaps between black/brown and white populations narrowed. Cumulative morbidity and mortality were highest among minority groups and in rural communities.

Conclusions: Burden of COVID-19 morbidity and mortality shifted over time, creating a twindemic involving disparities in outcomes based on race and geography. Health officials should explicitly measure disparities and adjust mitigation and vaccination strategies to protect vulnerable sub-populations with greater disease burden.

Introduction

The rapid spread of coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, has challenged health systems. As of January 31, 2021, more than 102 million individuals were infected, and over 2.2 million individuals have died from COVID-19 globally.[1] In the United States, there are over 26 million cases, 131,384 hospitalizations, and 440,000 deaths associated with COVID-19. At the end of 2020, the US Centers for Disease Control and Prevention (CDC) reported a COVID-19-associated hospitalization rate of 326.7 per 100,000 population.[2]

Data from China, Italy, the US, and other nations suggest that hospitalization and mortality are associated with age as well as gender, in which older and male populations are at higher risk of severe outcomes including death.[3-5] Moreover, early evidence in the US identified unequal patterns in hospitalization and mortality from COVID-19 in dense urban environments with respect to race and ethnicity.[6, 7] Existing studies, however, are limited with respect to both scope and temporality. Early evidence largely comes from single, urban center studies or regional data during the first wave[8, 9] of the COVID-19 pandemic. Subsequent waves, or surges, have not been examined. For example, it is unclear whether the same populations were impacted in fall versus the spring 2020. Furthermore, most studies examine patients after inpatient admission. There are limited studies on individuals with COVID-19 in community settings. For example, early data suggested that testing rates per capita were unequal in the US with respect to race and ethnicity,[10] yet it is unclear how these rates have changed over time.

There further exists little evidence on individuals in rural communities, and few studies that compare rural patients to those in urban settings. Nearly 1-in-5 Americans live in a rural county,[11] which are often labeled as medically underserved areas. Using data from CDC gathered two years before the pandemic, Kaufman et al.[12] estimate rural residents to be at increased risk of hospitalization and death from COVID-19. In a single site study in rural Georgia, individuals hospitalized with COVID-19 from March to May 2020 found that, despite a higher burden of comorbid conditions, both critical care and in-hospital mortality was lower than in New York City, as well as China and Italy.[13] Given limited data from rural communities, more study is warranted.

No studies to date examine the resurgence of COVID-19 infections within the US during the fall, and little is known about shifts in morbidity and mortality over time from COVID-19. This study examines the epidemiologic trends in COVID-19 infection, hospitalization, and death in Indiana with a focus on health equity. The study examines a large, statewide cohort, including individuals tested by local and state health departments. It further examines care delivered at a wide array of settings, including critical access hospitals and rural county hospitals. Per capita rates, when stratified by age, race, sex, and geography, can shed light on changes in morbidity and mortality over time, as well as within and among sub-populations. Understanding patterns of COVID-19 morbidity and mortality beyond individual health systems and major metropolitan areas can inform national strategies to mitigate the ongoing spread of COVID-19, including vaccination strategies that seek to immunize based primarily on age.

Methods

Setting

The setting for this study is the State of Indiana, which is the 16th largest state in the US with respect to population density and 38th by area. The state has a growing population of 6,732,219 individuals, of which 5,063,133 (75.2%) are adults. Approximately 21.7% of residents reside in a rural county.

The State of Indiana reported its first case of COVID-19 on March 6, 2020. Similar to many locations, Indiana implemented public health interventions, including a stay-at-home order, to mitigate spread of COVID-19. On May 1, 2020, following declining rates of hospitalization for COVID-19, the Governor ended the stay-at-home order and initiated a phased re-opening plan.[14] New cases increased while hospitalizations declined into the summer, flattening until a second wave began following Labor Day. The second wave consisted of steady increases in new cases as well as hospitalizations and deaths, all of which climbed through the holidays before leveling off towards the end of the year.

Data and Sources

We use data from multiple sources integrated into the Regenstrief Institute COVID-19 Dashboard,[15] a data visualization tool developed in response to the pandemic that leverages clinical and administrative health data from the Indiana Network for Patient Care (INPC).[16] The INPC is one of the nation's largest health information networks, which includes 38 distinct health systems representing more than 100 hospitals, commercial laboratories, and physician practices across Indiana.[17] The INPC further includes COVID-19 test results from the Indiana

Department of Health (IDOH), which receives test results from large commercial labs contracted for pandemic response as well as local health departments which perform strategic testing in communities identified as high risk, such as nursing homes, prisons, and homeless shelters. All testing data, regardless of source, are linked to hospitalization data as well as death records from IDOH. The combined data represent >95% of the 5 million adult residents who interact with the state's health system.

We extracted data on all adults (age ≥18 years) tested for COVID-19 in the health system or community, as well as those diagnosed with COVID-19 during a clinical encounter. For each individual, we queried the following information from the INPC: COVID-19 test results, age, sex, race, hospitalizations up to 21 days before or after a positive COVID-19 test, and geography associated with home address. Hospitalizations before positive diagnosis were included due to delays in testing, especially at the start of the epidemic. During March and April 2020, most patients infected with the SARS-CoV-2 virus were admitted with COVID-like symptoms before testing positive. All positive cases were identified using RT-PCR tests recorded in medical records or reported to the public health department, including community-based testing efforts statewide by public health authorities. Individuals testing positive were only counted once, during the period of their first positive result. All patient addresses were geocoded using an established method[18] with rurality determined by a classification system developed by Purdue University for Indiana's geography based on ZIP Code.[19]

Data Analysis

We used epidemiological methods to calculate descriptive statistics, including rates per 100,000 population, also known as per capita rates. These rates provide an objective method for comparing population characteristics when communities or groups vary in size. Denominator data for calculating per capita rates came from 2018 U.S. Census estimates. All rates were age-adjusted using American Community Survey estimates.

Statistics were calculated overall and for multiple time periods corresponding to the state's initial lockdown and subsequent re-opening plan. We examined data from the start of the Indiana epidemic (March 6, 2020) thru the end of the stay-at-home order (April 30, 2020), referred to as Phase 1. Following the stay-at-home order, Indiana initiated a staged reopening. Each subsequent stage reopened additional sectors of the economy or expanded capacity in a given sector. Full details of each stage can be found on the Governor's Back on Track website.[14] The reopening occurred from May 1, 2020 through September 7, 2020 (Labor Day), when the only remaining restrictions included a statewide mask ordinance and a restriction on gatherings larger than 250 people. This is referred to as Phase 2. Finally, we examined data from September 8, 2020 through December 31, 2020, referred to as Phase 3. Institutional review board approval for the study was obtained from Indiana University.

Results

Through December 31, 2020, a total of 1,833,218 unique, adult Indiana residents were tested for COVID-19, which accounts for 36.2% of the statewide adult population. Of those tested, 354,539 (19.3%) unique individuals tested positive for COVID-19 infection. Among those

infected, 31,352 (8.8%) were hospitalized. A total of 8,104 (0.2% of infected individuals) died either during their hospital course or at home following COVID-19 infection.

Overall COVID-19 Infection and Burden

Characteristics, as well as morbidity and mortality, of individuals tested for COVID-19 in Indiana are summarized in **Table 1**. More women than men per capita were tested and positive for COVID-19, yet men had higher hospitalizations and mortality per capita compared to women. With respect to age, testing and morbidity were highest in the younger (0-29) and older (80+) groups. Hospitalization and mortality per capita increased with age, with older (70+) populations possessing significantly higher hospitalizations and deaths per capita. With respect to race, morbidity, hospitalization, and mortality rates per capita were higher among racial minority groups, especially Native Hawaiian/Pacific Islanders, American Indian/Native Alaskans, and African Americans respectively. Individuals who did not report their race during testing or hospitalization also possessed high rates of morbidity and mortality. With respect to geography, urban residents were tested more frequently. However, per capita morbidity, hospitalization, and mortality were highest among rural populations.

156 **Table 1**. Characteristics and rates for Indiana residents tested for, infected with, hospitalized with, and death following infection

157 from COVID-19 through December 31, 2020; State of Indiana.

Characteristics	Individuals Tested for COVID-19			COVID-19 Cases			COVID-19 Hospitalizations			COVID-19 Deaths		
	N	%	rate per capita*	N	%	rate per capita*	N	%	rate per capita*	N	%	rate per capita*
Total	1833218		36207.2	354539		7002.4	31352		619.2	8104		160.1
Gender												
Female	1031547	56.3%	39709.7	190632	53.8%	7338.4	15890	50.7%	611.7	4008	49.5%	154.3
Male	790687	43.1%	32071.2	162363	45.8%	6585.6	15459	49.3%	627.0	4073	50.3%	165.2
Age Category												
18-19	73702	4.0%	39707.1	14169	4.0%	7633.6	130	0.4%	70.0	2	0.0%	1.1
20-29	357306	19.5%	39038.2	70064	19.8%	7655.0	1472	4.7%	160.8	38	0.5%	4.2
30-39	312253	17.0%	37227.7	58867	16.6%	7018.3	1950	6.2%	232.5	75	0.9%	8.9
40-49	284677	15.5%	34644.3	59479	16.8%	7238.4	2771	8.8%	337.2	154	1.9%	18.7
50-59	294838	16.1%	32976.5	58540	16.5%	6547.5	4731	15.1%	529.1	408	5.0%	45.6

60-69	258639	14.1%	34580.4	46261	13.0%	6185.2	6756	21.5%	903.3	1244	15.4%	166.3
70-79	157831	8.6%	38123.8	27605	7.8%	6667.9	7241	23.1%	1749.1	2038	25.1%	492.3
80+	93972	5.1%	38238.7	19554	5.5%	7956.8	6301	20.1%	2564.0	4145	51.1%	1686.7
Race												
White	1420211	77.5%	32772.9	272622	76.9%	6291.1	24140	77.0%	557.1	6538	80.7%	150.9
African American	164730	9.0%	37075.1	31596	8.9%	7111.2	4922	15.7%	1107.8	952	11.7%	214.3
Asian	29043	1.6%	23872.1	5638	1.6%	4634.2	353	1.1%	290.2	54	0.7%	44.4
American Indian / Native Alaskan	3961	0.2%	35423.0	1193	0.3%	10668.9	69	0.2%	617.1	4	0.0%	35.8
Native Hawaiian / Pacific Islander	3057	0.2%	142783.7	783	0.2%	36571.7	79	0.3%	3689.9	19	0.2%	887.4
Other or Unknown	212216	11.6%	194470.6	42707	12.0%	39135.9	1789	5.7%	1639.4	537	6.6%	492.1
Geography												
Rural	379567	20.7%	34585.2	82276	23.2%	7496.8	6962	22.2%	634.4	1890	23.3%	172.2
Urban	1453651	79.3%	36656.1	272263	76.8%	6865.5	24390	77.8%	615.0	6214	76.7%	156.7

158 *Rate per capita adjusted for age

Comparison of infection, hospitalization, and death over time

Table 2 summarizes per capita testing, infections, hospitalizations, and deaths during the three phases of the COVID-19 epidemic in Indiana through the end of 2020. Testing, infection, hospitalization, and death per capita all increased over time. Furthermore, there are notable differences among sub-populations.

Testing and morbidity for women was higher in each phase. Hospitalization and death due to COVID-19 was higher for women only in Phase 2. Men experienced worse outcomes even though women experienced higher morbidity per capita.

At the beginning of the pandemic, testing rates were highest in adults 70 years and above. During Phase 2 and Phase 3, per capita testing increased among all groups, but the highest rates were observed in young adults and older adults (70+). Morbidity, hospitalization, and death increased with age and increased across phases for all groups. No deaths occurred among adults aged 18-19 years during the first two phases; there were 0.2 deaths per 100,000 population for this age group in Phase 3. Deaths among those 70-79 years and those 80+ years doubled over time, and these rates were 2-10 times higher than younger age groups.

175 **Table 2**. Comparison of per capita rates for COVID-19 infection, hospitalization and death for residents across three phases of the

176 epidemic; State of Indiana.

Characteristics	COVID-19 Cases			COVID-19 Related Hospitalization			COVID-19 Related Deaths		
	Phase 1 (rate per capita)	Phase 2 (rate per capita)	Phase 3 (rate per capita)	Phase 1 (rate per capita)	Phase 2 (rate per capita)	Phase 3 (rate per capita)	Phase 1 (rate per capita)	Phase 2 (rate per capita)	Phase 3 (rate per capita)
Total	402.8	1375.2	5224.4	84.6	133.3	402.5	41.5	41.1	77.5
Gender									
Female	419.4	1421.9	5497.2	80.3	134.5	398.2	39.8	41.9	72.6
Male	377.3	1308.1	4900.3	89.1	132.1	406.8	42.5	40.1	82.6
Age Category									
18-19	83.5	2003.1	5547.0	5.4	23.2	42.0	0.0	0.0	0.2
20-29	265.2	1858.7	5531.4	15.6	46.5	98.9	1.1	1.5	1.5

30-39	370.3	1377.3	5270.7	35.2	62.1	135.9	2.3	2.7	3.9
40-49	426.8	1379.4	5432.3	58.2	89.9	190.1	5.1	5.7	7.9
50-59	416.2	1144.5	4986.8	88.7	119.0	322.0	13.3	12.0	20.4
60-69	396.7	1016.1	4772.5	126.1	181.2	598.2	43.7	39.8	82.8
70-79	480.7	1084.1	5103.4	199.5	330.7	1221.0	116.9	125.4	250.0
80+	1026.6	1501.5	5428.7	323.5	502.1	1743.2	446.8	436.6	803.3
Race									
White	287.2	1068.1	4935.9	62.4	109.2	386.5	35.3	36.5	79.1
African American	926.4	1816.3	4368.5	285.8	287.6	536.1	89.1	63.0	62.1
Asian	433.2	922.2	3278.8	51.0	87.1	152.1	14.8	10.7	18.9
American Indian / Native Alaskan	3559.3	2012.2	5097.5	232.5	152.0	241.5	8.9	0.0	26.8
Native Hawaiian / Pacific Islander	2942.6	10462.4	23166.7	747.3	747.3	2195.2	186.8	280.2	420.4
Other or Unknown	2607.1	12557.2	23971.6	188.8	549.8	904.5	137.5	184.2	170.4

Geography									
Rural	355.9	1232.6	5908.2	51.6	124.5	459.7	24.7	43.7	103.8
Urban	415.8	1414.6	5035.2	93.7	135.8	386.6	46.1	40.4	70.2

Footnote: Phase 1 (March – April, 2020); Phase 2 (May 1, 2020 – September 7, 2020); Phase 3 (September 8, 2020 – December 31, 2020)

Testing, morbidity, hospitalization, and mortality generally increased for each racial group over time, with two exceptions. Morbidity, hospitalization, and deaths decreased between Phase 1 and 2 for American Indian/Native Alaskans. Per capita hospitalization and mortality decreased for African Americans, especially between Phase 2 and Phase 3. Comparing Whites with African Americans, however, reveals major disparities. Testing and morbidity per capita was higher for African Americans, except in Phase 3. Hospitalizations were higher for African Americans in all phases (**Figure 1**). Mortality was higher for African Americans in the first two phases.

Fig 1. Per capita rates for hospitalizations and deaths due to COVID-19 among adults in Indiana, stratified by race, during three distinct time periods between March 1 and December 31, 2020. State of Indiana.

In each phase, testing per capita was highest for urban residents. Morbidity and hospitalizations were also higher for urban populations during the first two phases. Deaths were higher among urban populations only in Phase 1. Over time, per capita morbidity (**Figure 2**) and negative outcomes, hospitalization and mortality (**Figure 3**), shifted to rural populations. Morbidity shifted in Phase 3 following the conclusion of the state's re-opening plan. Higher per capita hospitalization and mortality among rural populations began towards the end of Phase 2 then accelerated in Phase 3.

Fig 2. Weekly COVID-19 incidence, defined as cases per 100,000 population, among adults in Indiana, stratified by urban versus rural county of residence between March 1 and December 31, 2020. State of Indiana.

Fig 3. Weekly rates per capita for hospitalizations and deaths due to COVID-19 among adults in Indiana, stratified by urban versus rural county of residence between March 1 and December 31, 2020.

Discussion

Among a statewide cohort of individuals tested for COVID-19, we examined epidemiological trends in testing, infection, hospitalization, and death among three time periods corresponding to mitigation efforts by public health authorities. Infections due to the SARS-CoV-2 virus increased over time across the entire state, across the three phases, yet its impact was not even across sub-populations. Following the initial lockdown in the spring, testing, as well as morbidity, hospitalizations, and mortality, increased over time. During the summer months, the gap between White and African American morbidity and mortality narrowed, although burden remained higher among African American populations. As summer turned into fall, burden among rural communities increased and surpassed urban communities through the end of the year. These trends reveal a twindemic, not of influenza and COVID-19, but of race and geography. The twindemic has implications for continued mitigation of disease spread, as well as vaccination strategies.

There are many similarities in the Indiana trends with prior studies as well as national trends. Rates per capita for hospitalization and death increase with age.[4, 6, 20-22] Furthermore, hospitalization and death per capita was greater among men versus women,[21, 22] even though women experienced greater morbidity. Moreover, burden of COVID-19 within the African American community overall was much greater than its proportional composition of the

state's population.[7] Per capita hospitalization among African Americans grew and remained highest among all sub-populations throughout the pandemic. Burden among American Indian/Native Alaskan and Native Hawaiian/Pacific Islander populations were also among the highest overall and during most time periods, a trend observed nationally.

While the data in this study share much in common with prior studies, there are several unique characteristics that distinguish our work. First, the study uses a large repository of testing data linked to electronic medical records. Testing data includes results from hospital-based, commercial, and public health departments creating a comprehensive source measuring testing, as well as morbidity, per capita. Second, the study measures burden of disease and outcomes during the fall surge, something few studies to date have reported. Stratification by phase is also unique, allowing comparison of burden and outcomes over time. These methods would not be possible without a robust electronic data infrastructure in Indiana aided by a 16+ year health information exchange[23] that partnered with the state health department, county health departments, and health care systems in response to the COVID-19 pandemic.[16] This multi-sector approach aligns with the vision set forth by the Public Health 3.0 framework described by DeSalvo et al.[24, 25]

Although prior studies document racial disparities, especially during the initial phase of the pandemic, this study presents data on racial disparities in COVID-19 morbidity, hospitalization, and mortality over time. Rates, adjusted for population size, clearly show significant burden on African American populations during each phase of the pandemic. Although deaths per capita were lower than other racial groups in the fall surge, the cumulative mortality is 50% higher than mortality among White populations. Moreover, burden among Native Hawaiian/Pacific

Islander populations, albeit they account for a small percentage of the overall population, is nearly 10 times that of Whites. Among those who did not disclose or reported their race as 'Other,' is 3-4 times higher than Whites. It is not unreasonable to assume that many Hispanics may be in that group. Therefore, we conclude that while racial disparities narrowed later in the pandemic, especially as burden shifted from urban to rural communities, cumulative burden on racial minorities from COVID-19 are severe. The burden on minority populations exacerbates existing health disparities, necessitating action as the nation attempts to both mitigate further disease spread and protect vulnerable populations through vaccination.

Another distinguishing feature of this analysis is a focus on rural communities. A brief report on COVID-19 incidence thru October 2020 from the U.S. Centers for Disease Control and Prevention[26] revealed that morbidity was shifting nationally from urban to rural areas beginning in late summer. These trends are mirrored in this study. Yet this study further provides evidence on hospitalizations and mortality, which both surpassed urban rates per capita around the same time. Rural morbidity is of great concern, as many of these areas are medically underserved. Hospitals in rural areas may possess few ICU beds, and they may lack the staff necessary to handle an influx of COVID-19 cases.[27] During the fall surge, we observed several rural hospitals in Indiana reaching capacity quickly, necessitating transfers to urban centers, in many cases, more than 2 hours away from the resident's home. This placed additional burden on urban hospitals already managing increased workload and burden from local residents infected with COVID-19. The situation further caused a response from public health in which elective procedures were reduced by order of the Governor, placing financial strain on both rural and urban facilities. More attention is needed on the impact of COVID-19 in

rural areas, combined with reasonable policies to support rural mitigation strategies and equitable distribution of vaccines to rural populations.

Limitations

This observational study has several limitations worth noting. Observational clinical data (e.g., "real-world evidence"), from which much of our findings are derived, is known to have potential biases.[28] First, a significant number of race classifications were reported as Other or Unknown. Similarly, the dataset could not identify ethnicity, as these data are also missing for many patients. Medical records as well as other health information systems, must improve the capture rates for race and ethnicity to enable large scale measurement of health disparities so public health can work with health systems to ensure health for all persons.[29, 30] Second, these data represent hospitalizations and death among individuals from one state. The patterns observed in Indiana may not generalize to all geographic regions of the U.S. or other countries.

Public Health Implications

This study offers several implications for public health in the wake of the COVID-19 pandemic. First, trends demonstrate a flattening of the curve following the initial stay-at-home order from public health authorities. As the state re-opened, morbidity and mortality increased during subsequent phases. This suggests aggressive mitgation for a longer period of time may be necessary for stronger mitigation. Moreover, sub-population differences highlight the need for more nuanced mitigation policies, perhaps data-driven approaches, that can evolve as the pandemic unfolds.

As public health attempts to mitigate disease spread going forward, additional attention should be paid to racial minority and rural populations. Testing increased per capita among racial minority groups in Indiana, enabling better detection of morbidity. Equitable testing was not sufficient for stemming hospitalization due to COVID-19. Mortality decreased among minority groups in the latter phases, yet this might be attributable to improved clinical management rather than contact tracing and isolation which our data did not measure. With respect to rural populations, morbidity, hospitalization, and mortality steadily increased over time, suggesting perhaps rural county health departments struggled with mitigation strategies or rural populations ignored mask ordinances, restrictions on social gatherings, and/or other public health tactics. Anecdotally, we observed complaints from several rural county health officers that local authorities would not enforce ordinances and that residents overtly refused to comply with many policies. More research is necessary to confirm these observations and support the development of more robust mitigation policies.

Strategies to vaccinate against COVID-19 need to explicitly address racial disparities. Poorer health outcomes among racial minorities is often attributable to lack of health care access,[31] including preventative medicine and vaccination. In a majority White state, we achieved equity in testing. This means we can achieve equity in testing. However, current policies focus on age and comorbid conditions to drive decisions about which populations should receive vaccines first. While age places individuals at higher risk of hospitalization and death, this study demonstrates that racial minorities and rural populations also should be prioritized given their morbidity and mortality. If health departments are serious about addressing social determinants and racial disparities, they must factor these phenomena into vaccination plans.

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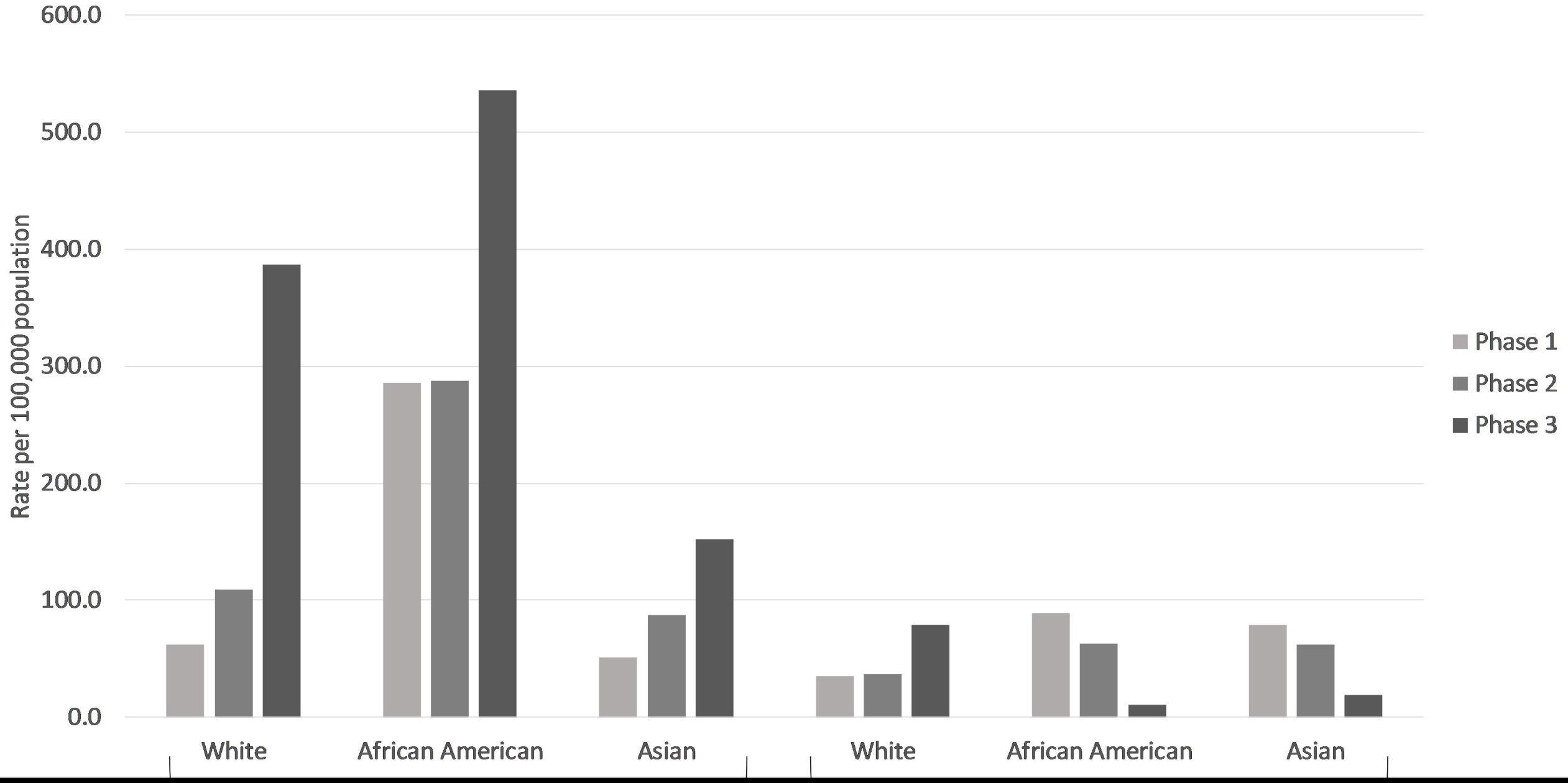
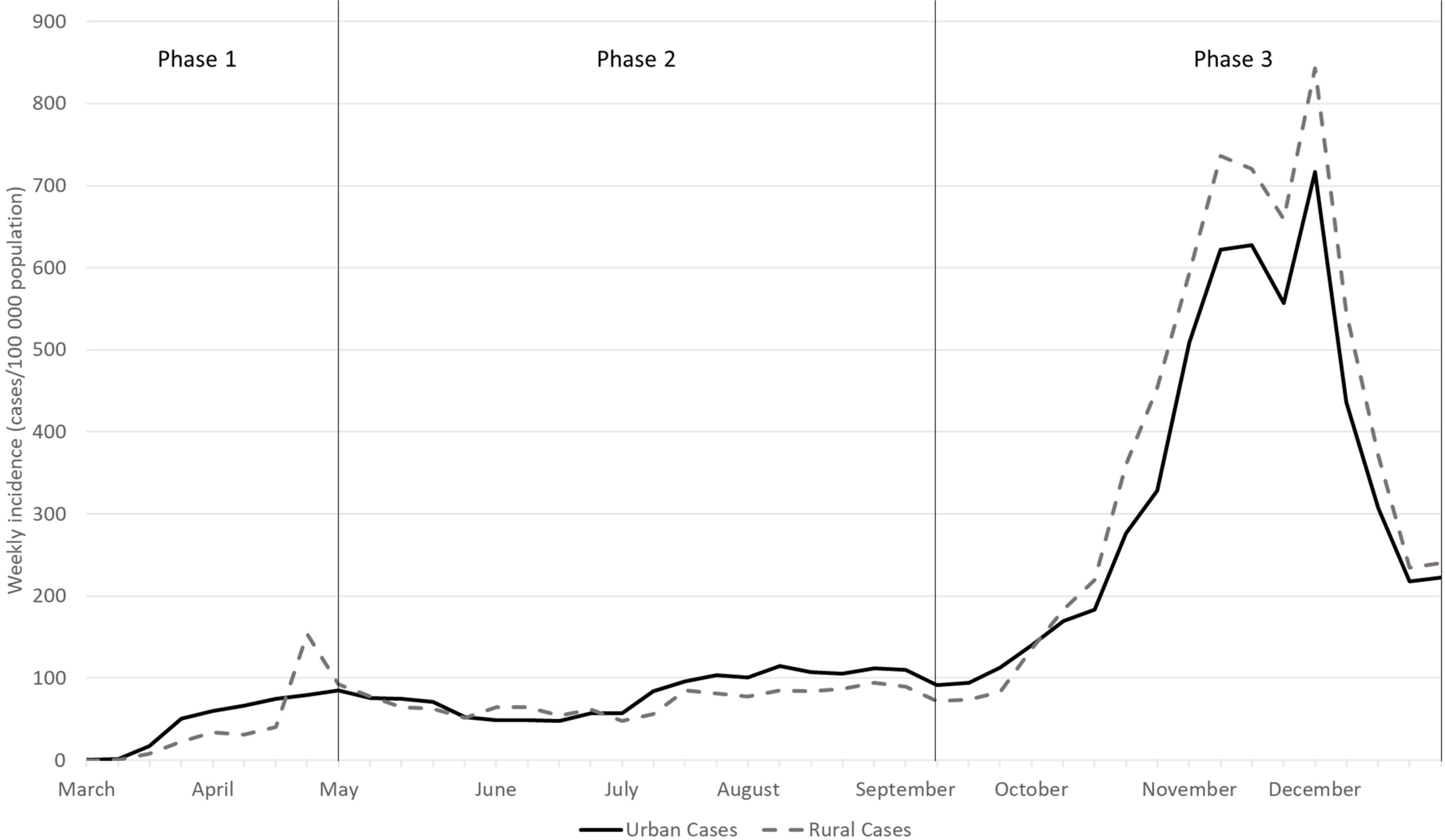
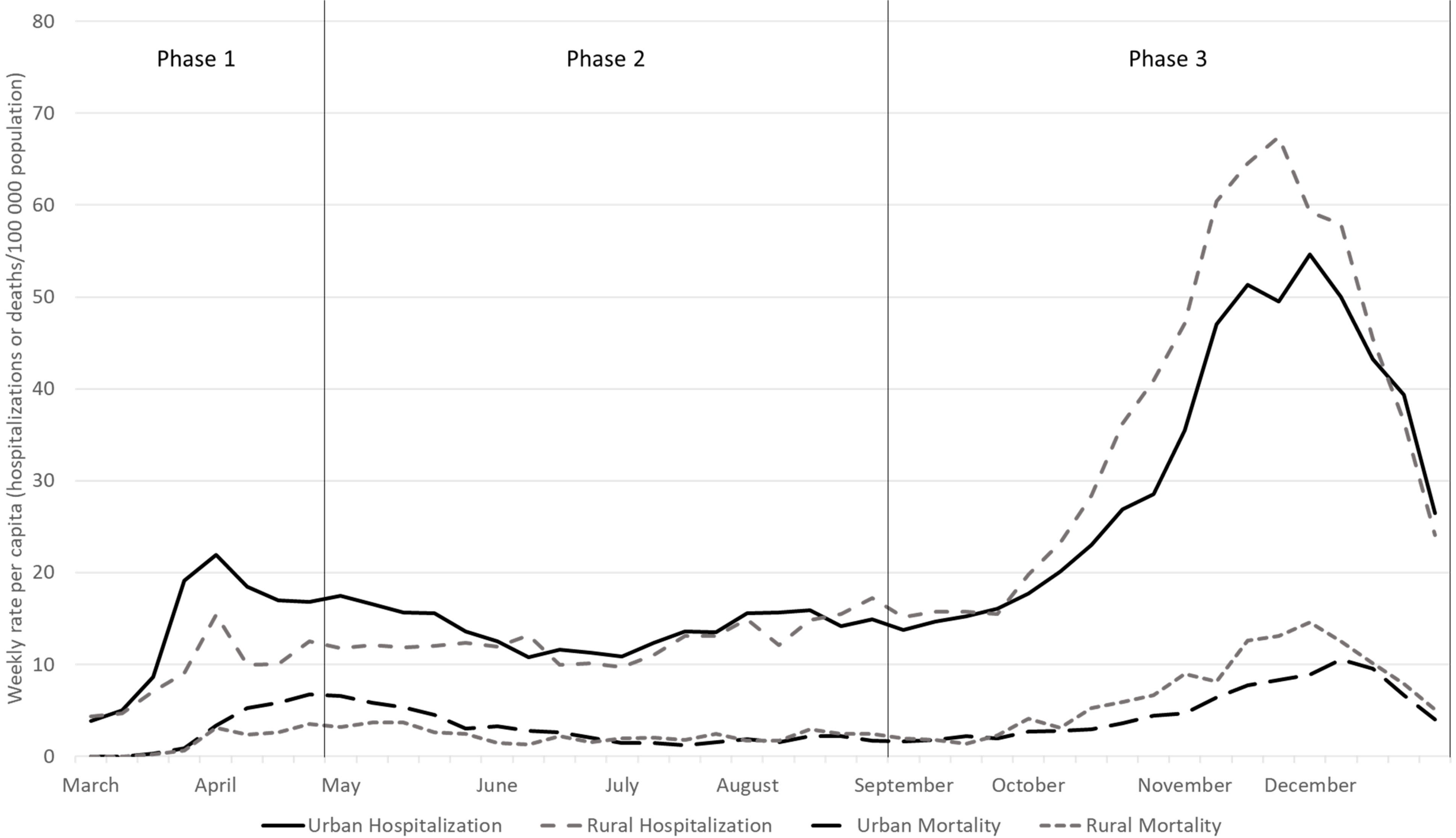

600.0
500.0
400.0
300.0
200.0
100.0
0.0
Rate per 100,000 population
White
African American
Asian
White
African American
Asian
Phase 1
Phase 2
Phase 3


Phase 1
Phase 2
Phase 3
Weekly incidence (cases/100 000 population)
900
800
700
600
500
400
300
200
100
0
March
April
May
June
July
August
September
October
November
December
Urban Cases
Rural Cases


Phase 1
Phase 2
Phase 3
Weekly rate per capita (hospitalizations or deaths/100 000 population)
80
70
60
50
40
30
20
10
0
March
April
May
June
July
August
September
October
November
December
Urban Hospitalization
Rural Hospitalization
Urban Mortality
Rural Mortality