

Weekly Science Review

March 3rd – 17th, 2021

This weekly science review is a snapshot of the new and emerging scientific evidence related to COVID-19 during the period specified. It is a review of important topics and articles, not a guide for policy or program implementation. **The findings captured are subject to change as new information is made available.** We welcome comments and feedback at covid19-eiu@vitalstrategies.org.

COVID-19 in Brazil: Developments, Warnings and Lessons

Main message: Brazil is being hit hard by the COVID-19 pandemic again. After experiencing a large first wave of cases and deaths nine months ago, Brazil is now in the throes of a second wave that is overwhelming its health care system. The epidemic in Brazil has displayed a devastating synergy: weak mitigation measures fueled the emergence and spread of a more transmissible variant of SARS-CoV-2, the virus that causes COVID-19. COVID-19 vaccines are now available, but the rollout in Brazil has been slow. The full range of available mitigation measures, including vaccines and both individual and societal public health and social measures (PHSMs), is necessary to control the epidemic and limit its local and global impact.

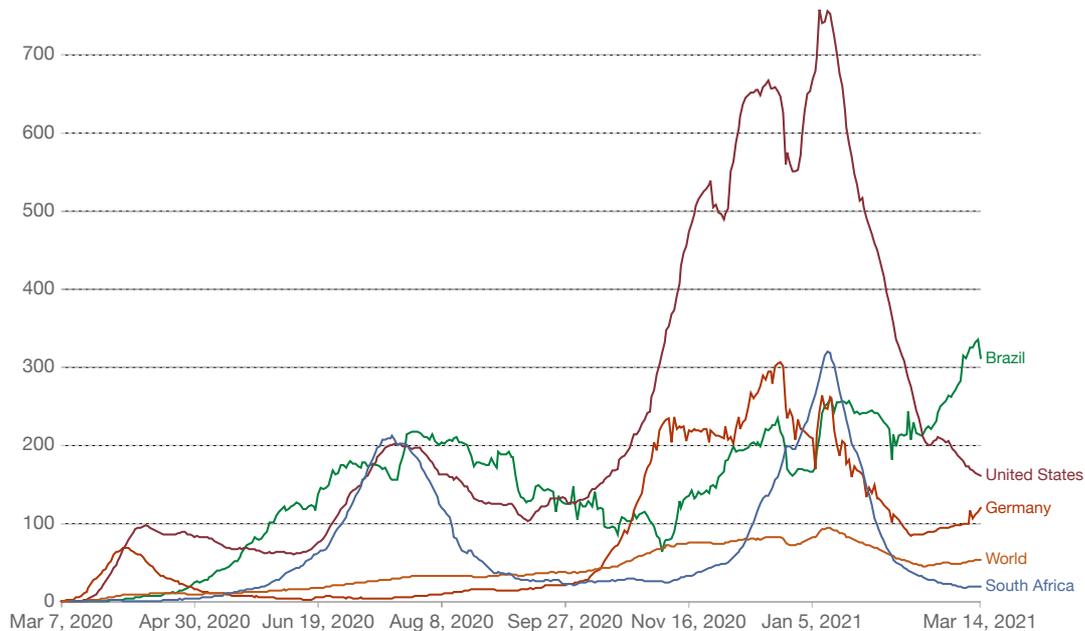
The COVID-19 epidemic in Brazil

Brazil was the first country in Latin America to confirm a case of COVID-19, when a man who had traveled to Italy tested positive for SARS-CoV-2 in Sao Paulo on Feb 25, 2020. In the first half of 2020, COVID-19 spread throughout the country. During April-May 2020, Brazil experienced a surge in cases and deaths. Rates of transmission were estimated to be higher than in other seriously affected countries. By the end of May 2020, Brazil had more than 500,000 confirmed COVID-19 cases and nearly 30,000 COVID-19 deaths, a significant proportion of the 6 million cases and 375,000 deaths reported globally up to that time. The number of reported deaths due to COVID-19 in Brazil corresponded to a rate of 138 deaths per million population. By the same date, the US had confirmed 325 deaths per million, Europe 230 deaths per million, South America 93 deaths per million and the world 48 deaths per million. It is likely that many unreported deaths due to COVID-19 occurred in Brazil and that the pandemic contributed to an increase in deaths from other causes. Between March 15 and June 6, 2020 in Brazil, there were approximately 62,000 deaths in excess of what was expected to occur during that time period.

Brazil has been experiencing a second wave of cases and deaths since late 2020. Although the surges observed in many countries during the same period were in decline by March 2021, a similar decrease has not been observed in Brazil. Daily new case counts continue to be high, and March 2021 has seen the highest daily death counts of the pandemic in Brazil, as shown in the figure below.

Daily new confirmed COVID-19 cases per million people

Shown is the rolling 7-day average. The number of confirmed cases is lower than the number of actual cases; the main reason for that is limited testing.



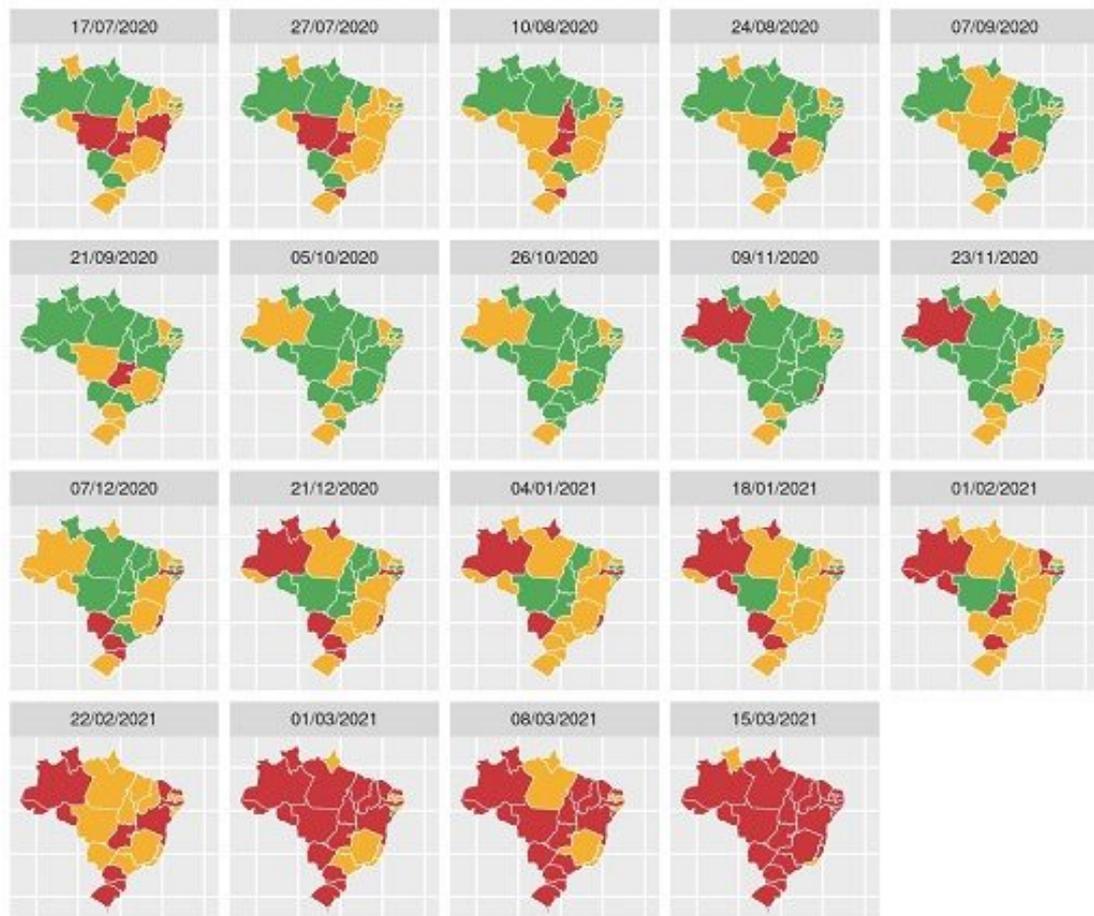
Source: Johns Hopkins University CSSE COVID-19 Data

CC BY

Source: ourworldindata.org

Brazil's second wave has been even larger than the first wave, overwhelming health care systems in almost all states simultaneously. This has likely increased the rate of death as supplies such as oxygen have run out and patients have been turned away from hospitals. Intensive care units are now over critical capacity across Brazil, as can be seen in these maps from the end of September 2020 (top left square) through March 15, 2021 (bottom right square).

Taxa de ocupação (%) de leitos de UTI Covid-19 para adultos



Alerta ■ Baixo ■ Médio ■ Crítico

Observatório Covid-19 | Fiocruz

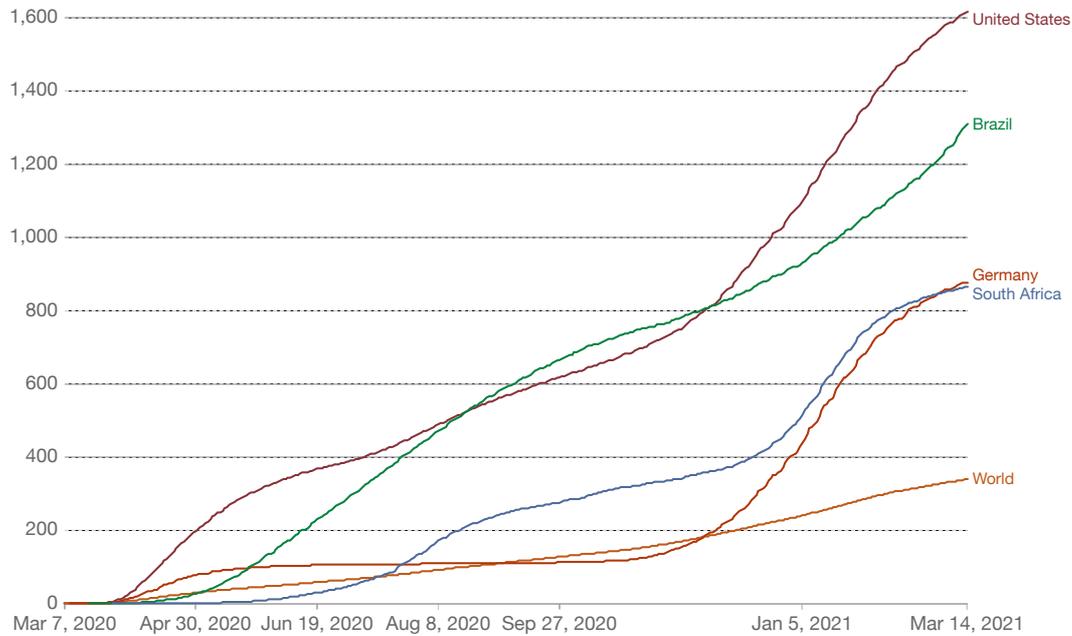
Adult intensive care unit (ICU) capacity alert level in Brazil, September 2020 - March 2021. (Green = Low; Yellow = Medium; Red = Critical).

Adapted from: agencia.fiocruz.br

As of March 16, 2021, Brazil has confirmed more than 11.5 million COVID-19 cases and nearly 280,000 COVID-19 deaths. This constitutes 10% of the world's cases and deaths, despite Brazil having less than 3% of the world's population.

Cumulative confirmed COVID-19 deaths per million people

Limited testing and challenges in the attribution of the cause of death means that the number of confirmed deaths may not be an accurate count of the true number of deaths from COVID-19.



Source: Johns Hopkins University CSSE COVID-19 Data

CC BY

Source: ourworldindata.org

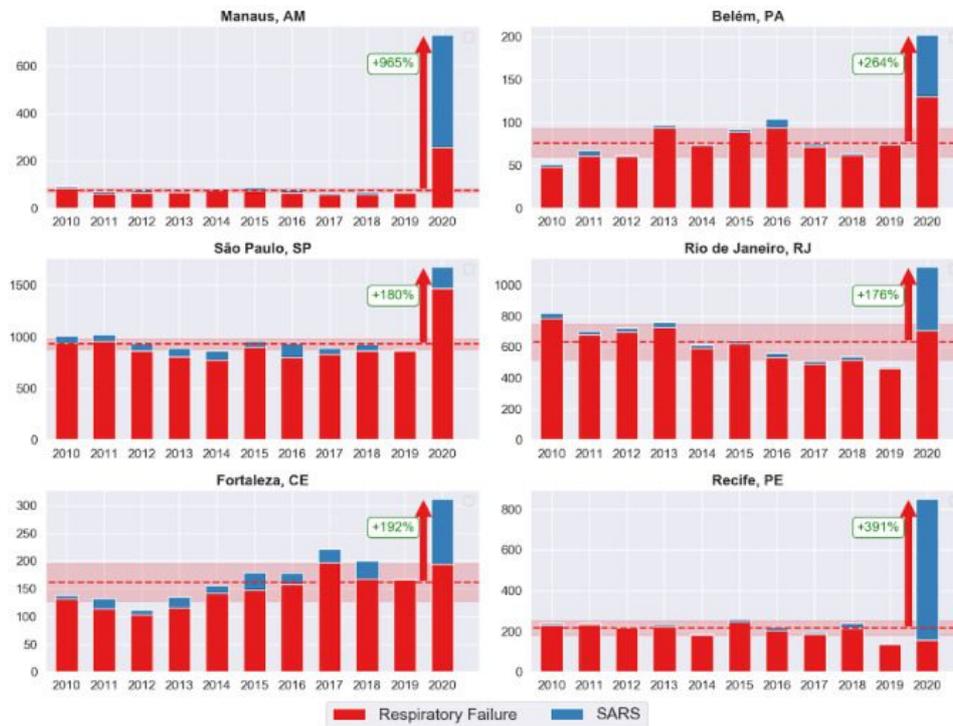
The COVID-19 epidemic in the State of Amazonas

Although all of Brazil has been affected by COVID-19, the situation in the northern state of Amazonas is notable. It has been particularly hard-hit during the first and second COVID-19 waves and may be the place of origin of a new SARS-CoV-2 variant known as the P.1 variant.

Amazonas is the largest of Brazil's 26 states, covering approximately 1.5 million of Brazil's 8.6 million square kilometers. The state is home to approximately four million people, or about 2% of Brazil's population, nearly half of whom live in the capital city of Manaus. The first case of COVID-19 in Amazonas was **detected in Manaus on March 13, 2020**. This was followed by an explosive epidemic that peaked in May, **overwhelming the fragile local health care system**. By May 31, **more than 41,000 cases and 2,000 deaths**

had been reported in Amazonas. However, the true number of infections and deaths due to COVID-19 was likely much higher, due in part to limited access to testing.

To better estimate the true prevalence of infection in Manaus, scientists tested blood donors for antibodies against SARS-CoV-2 during February-October 2020. In June, 44% of Manaus donors that were sampled tested positive for antibodies, suggesting they had previously had COVID-19. Scientists then adjusted for the accuracy of the antibody test used, the decline in antibodies that may occur over time and the age and sex of those sampled in relation to the general population. Accounting for these adjustments, the study authors estimated that by October, 76% of the Manaus population had previously had COVID-19. The reliability of that estimate depends on the validity of the antibody tests and adjustment methods and whether blood donors are representative of the general population, though scientists have noted that these estimates appear relatively consistent with the observed increase in deaths. One analysis of mortality data from Manaus found that during March-April 2020, the overall mortality rate was nearly five times what was observed during the same period in 2019. An analysis of deaths attributed to severe acute respiratory syndrome and other causes in Brazilian cities during January-June, 2020, suggested that COVID-19 deaths were under-reported by an average of 41%, and that the highest rate of COVID-19 death underreporting, 63%, occurred in Manaus. The figure below shows the number of deaths attributed to respiratory failure and severe acute respiratory syndrome in six Brazilian cities during 2020 and the ten years prior.



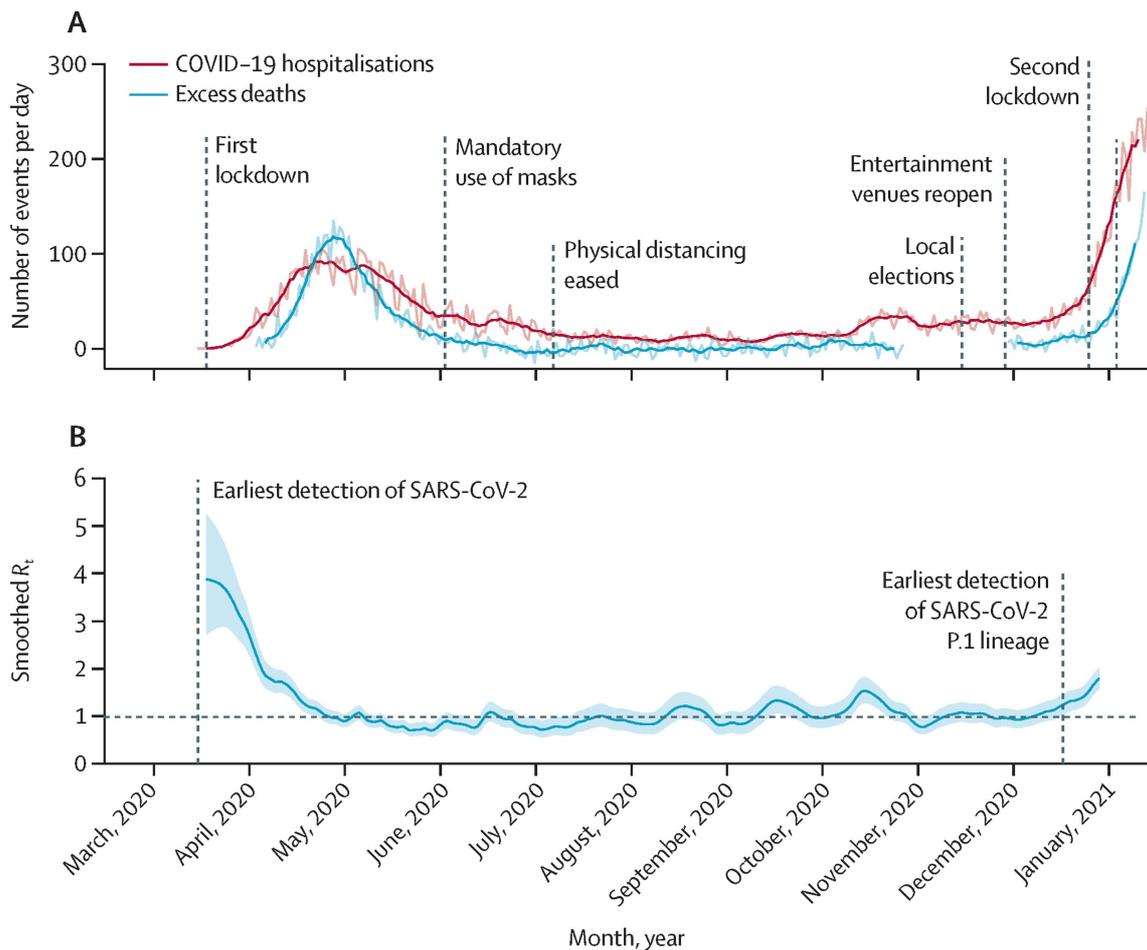
The number of deaths attributed to respiratory failure (red) and severe acute respiratory syndrome (blue, abbreviated “SARS”) in Manaus (top left-hand corner) and five other Brazilian cities during 2020 and the prior ten years. Each green box shows the percentage change between the number of deaths reported in 2020 and the average from the previous ten years.

Source: Adapted from: ncbi.nlm.nih.gov

What fueled the second wave in Amazonas and across Brazil?

As we [previously wrote](#), the “effective reproduction number” (R_t) describes transmission dynamics during an epidemic. R_t is defined as the number of secondary cases generated by a typical infectious person. If R_t is less than 1, an epidemic will eventually stop because, on average, each case generates less than one new case. The R_t may change over time due to the influence of several factors, including: development of protective immunity across the population through exposure to the disease; changes in the causative pathogen that alter transmissibility; and mitigation measures that limit the risk of transmission. Changes in all three of these factors preceded Brazil’s second wave. As described above, widespread transmission in some parts of Brazil during the first wave suggests that there should be at least some immunologic protection from COVID-19 in the population. However, this was juxtaposed against two factors further discussed below: 1) the emergence of a

more transmissible variant of SARS-CoV-2 that appears to evade the immunologic protection from prior infection, the P.1 variant, and 2) the failure of mitigation measures to sufficiently suppress transmission. The figure below shows a timeline of: COVID-19 hospitalizations, excess deaths and implementation of PHSMs (A); and the SARS-CoV-2 effective reproductive number and emergence of the P.1 variant in Manaus (B).



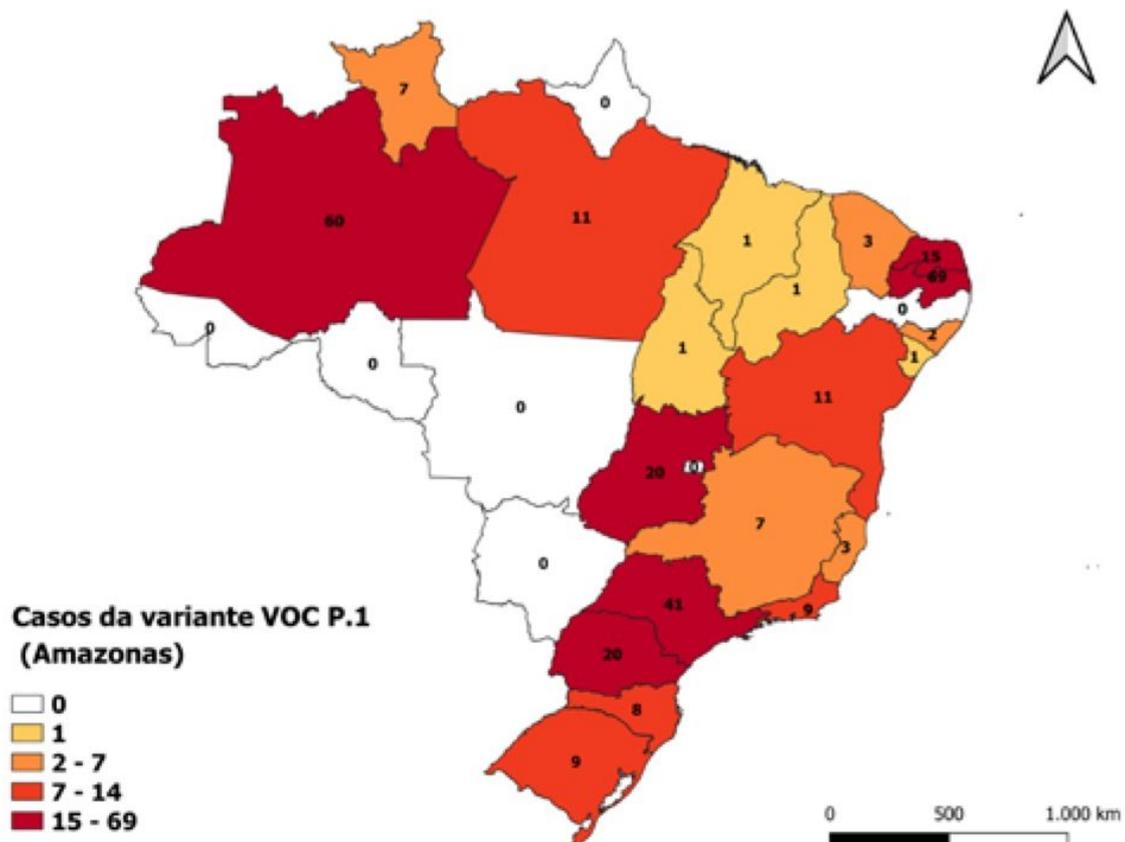
COVID-19 hospitalizations, excess deaths and the effective reproductive number (R_t) in Manaus, Brazil, 2020–21.

Source: [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00183-5/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00183-5/fulltext)

1. The emergence of the P.1 variant

In early January 2021, four travelers returning to Japan from Amazonas, Brazil, were found to be infected with a new SARS-CoV-2 variant. This variant, subsequently named P.1, has 21 lineage-defining mutations in its genetic code. Two mutations thought to be of particular importance (N501Y and E484K) are also present in variant B.1.351 (initially identified in South

Africa). The N501Y mutation is also present in variant B.1.1.7 (initially identified in the U.K.). These mutations are all in the viral genes that encode for the spike protein, the part of the SARS-CoV-2 virus that attaches to human cells to gain entry. The N501Y mutation is associated with increased transmissibility: it has been shown to increase affinity of the viral spike protein for the ACE2 receptor on human cells. A preprint analysis of genomic and mortality data from Manaus suggests that the P.1 variant may be as much as 2.2 times more transmissible than non-P.1 lineages. A study of SARS-CoV-2 isolates from 142 COVID-19 patients in Manaus during March 2020-January 2021 found no evidence of the P.1 variant during March-November 2020. However, in December, 52% (n=35/67) of genotyped isolates were the P.1 variant, and in January, the frequency of P.1 isolates increased to 85% (n=41/48). A second variant, P.2, initially detected in Rio de Janeiro, carries the E484K mutation discussed below, but not the N501Y mutation. In contrast with the P.1 variant, the P.2 variant was detected in Manaus at a relatively low and constant frequency (4%-11%) during November 2020-January 2021. The P.1 variant has now spread across Brazil. The figure below, from the Brazilian Ministry of Health, shows the number of P.1 variant cases confirmed from Jan. 9 to Feb. 27, 2021, by state.



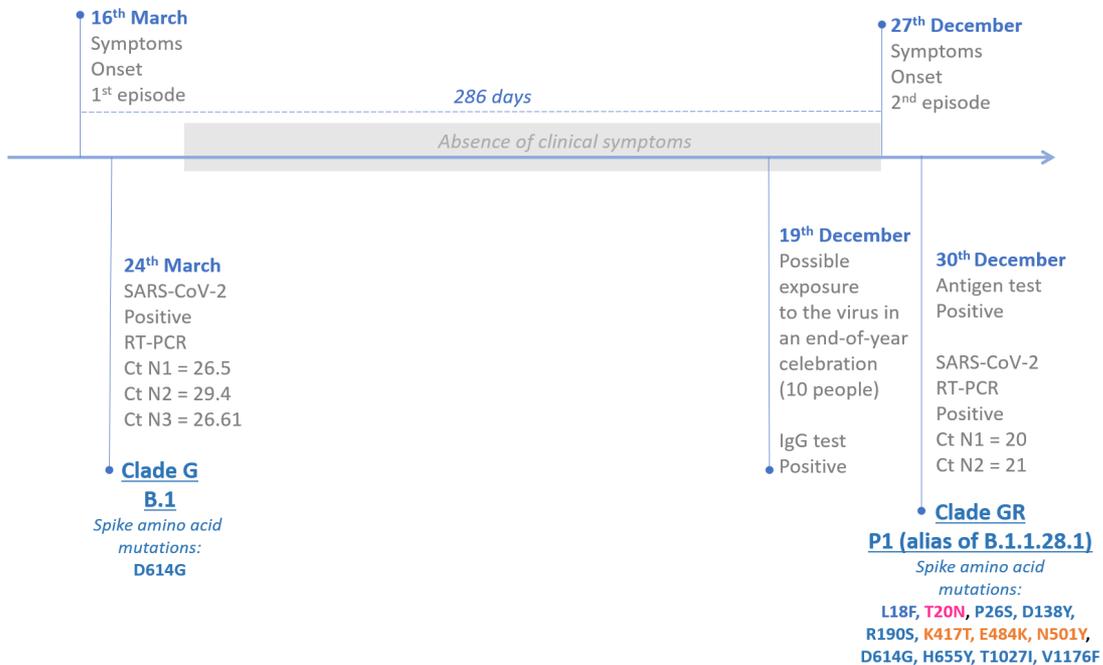
Number of P.1 variant cases confirmed in each state in Brazil, Jan. 9 to Feb. 27, 2021.

Source: gov.br

In addition to increased transmissibility, another factor contributing to the spread of new variants may be susceptibility to new variants among people previously infected with other variants. The second wave of COVID-19 cases and deaths in Manaus occurred despite high estimated levels of previous population exposure to SARS-CoV-2. As we [previously wrote](#), infection with SARS-CoV-2 generally provides some degree of protection against future reinfection, though reinfection may occur as a consequence of either waning immunity or the virus evading existing immunity. The [E484K mutation, which is found in the P.1 and P.2 variants, has been associated with resistance to neutralization by the antibodies in convalescent plasma.](#)

This suggests that people who were previously infected with SARS-CoV-2 may not be protected from reinfection with a variant carrying the E484K mutation. In an analysis available as a preprint, [researchers took serum samples from 19 Brazilians who had COVID-19 before the P.1 variant was widespread and tested them against P.1 and non-P.1 variants in the lab.](#) They found that antibodies in the serum samples did not neutralize the P.1 variant as effectively as they neutralized a non-P.1 variant virus, again suggesting that the P.1 variant may evade immunity induced by other SARS-CoV-2 variants. The potential contribution of other mutations to immune escape is not yet known, and the clinical significance of reduced antibody neutralization in the lab must be validated by real-world data.

There have now been several reports of reinfections with the P.1 and P.2 variants (both of which carry the E484K mutation) among Brazilians who previously had COVID-19. The [first reported reinfection with the P.1 variant was in a 29-year-old woman living in Amazonas state.](#) She was first ill with COVID-19 in March 2020, prior to the emergence of the P.1 variant, as shown on the figure below. Eight months later, on Dec. 19, she tested positive for antibodies to SARS-CoV-2. Then, just eight days after her positive antibody test, she developed symptoms and tested positive for COVID-19. Genomic sequencing showed that the second infection was caused by the P.1 variant. This case suggests that reinfection may occur even when measurable anti-SARS-CoV-2 antibodies are present, in concordance with the findings of the aforementioned laboratory study.



Timeline of the epidemiologic, clinical and laboratory events in a case of reinfection with the P.1 variant in Manaus, Brazil, 2020.

Source: Adapted from: virological.org

At least two other cases of reinfection in Brazil with SARS-CoV-2 variants carrying the E484K mutation have been reported in manuscripts that have not yet been peer-reviewed. One case was in a health care worker initially infected in June 2020, who recovered and tested negative in September before being diagnosed a second time in October. The second case was in a woman diagnosed with COVID-19 in May and October 2020. In all three of these cases, the patients were otherwise healthy adults who experienced symptomatic disease during both their initial infections and their reinfections. Although these are just three cases of the millions of cases that have occurred in Brazil, it is likely that reinfection occurs more often than reported because confirmation of reinfection requires genetic sequencing of isolates from the first and second infections.

What can we learn from the experience in Manaus about how widespread natural infection may contribute to pandemic control? First, it is difficult to determine the precise degree of population exposure to SARS-CoV-2. Second, the degree and duration of protection offered by natural infection is unknown, particularly in the setting of newly emergent SARS-CoV-2 variants. Third, two waves of uncontrolled spread of COVID-19 have caused enormous suffering. Thus, whether the above-cited 76% seroprevalence estimate from Manaus is correct (and prior infection was not protective) or incorrect (and a

higher level of population immunity is needed for protection), it is clear that relying on the development of herd immunity through natural infection is not an appropriate COVID-19 control strategy.

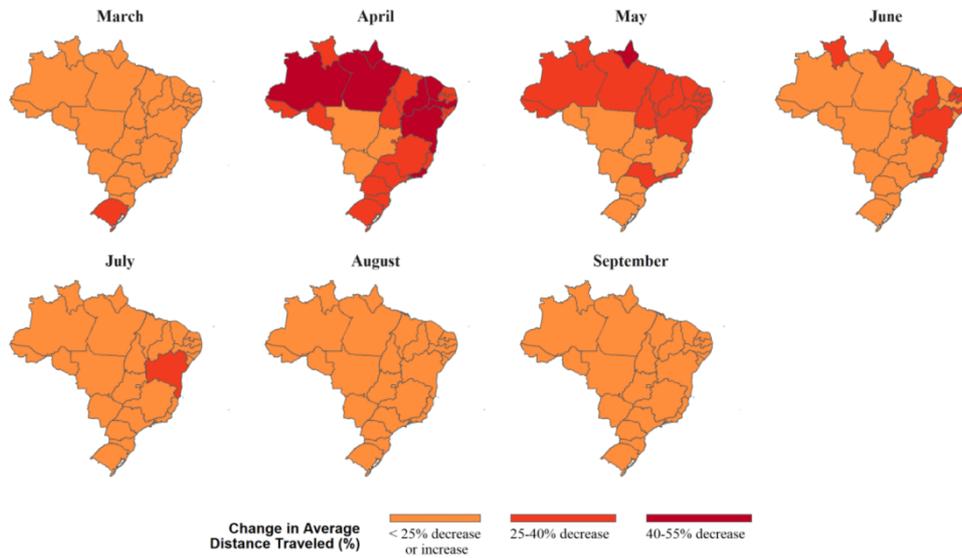
2. The failure of mitigation measures to sufficiently suppress transmission of SARS-CoV-2

Public health and social measures (PHSMs) are measures or actions by individuals, communities or governments to slow or stop the spread of a disease such as COVID-19. PHSMs encompass measures ranging from mask-wearing and physical distancing to closures of businesses and travel restrictions. PHSMs can prevent transmission and thus reduce hospitalizations and deaths. Unfortunately, the response to the epidemic in Brazil has been **characterized not just by the lack of a national pandemic mitigation strategy but also by federal obstruction of sub-national mitigation efforts.**

A research group that tracks implementation of PHSMs has **monitored state and federal policies and mobile phone mobility data and conducted two survey waves on COVID-19-related knowledge and practices in Brazil.** Their analysis shows that most policy responses to COVID-19 have occurred at the state (as opposed to national) level. Implementation of national-level policies was limited and chaotic. For example, in July 2020, wearing a mask in spaces “with public access” became a federal legal requirement with enforcement left to local authorities. Four days later, the President vetoed parts of the law but then, in August, the veto was overturned by the Supreme Court and Congress.

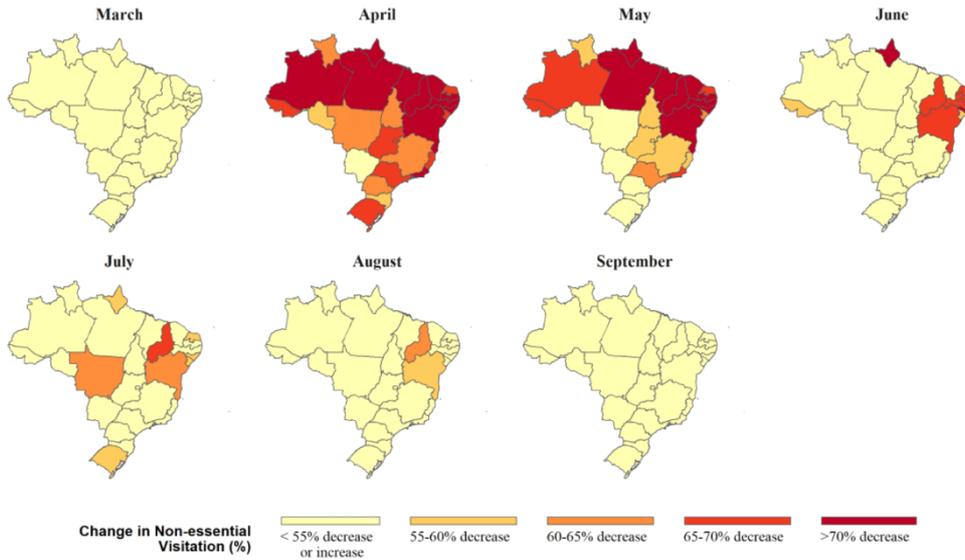
Despite these challenges, an **analysis of patterns of SARS-CoV-2 transmission in Brazil states during early months of the pandemic suggests transmission rates fell after implementation of PHSMs.** The research group tracking PHSMs observed **large decreases in daily distances traveled and non-essential trips in April and May,** using data from approximately 60 million smartphone users across Brazil. However, by June, the stringency of control measures in Brazil had begun declining and measures of mobility returned to near pre-pandemic levels in most states.

Figure 6. Daily distances travelled relative to baseline, averaged over each month



Source: Inloco

Figure 7. Daily number of non-essential trips made by smart phone users relative to baseline, averaged over each month.



Source: Inloco

Average number of kilometers travelled and the average number of non-essential trips, both relative to the first five weeks of 2020, observed in Brazil during March - September 2020.

Source: bsg.ox.ac.uk

In addition, comparison of policy stringency against mobility data suggested the phenomenon of “pandemic fatigue,” or less change in behavior in response to new policies as the pandemic progressed. Together with evidence of ongoing transmission, these data suggest that the degree of PHSM implementation and/or adherence was not sufficient to control transmission during the second half of 2020.

The synergistic effects of the emergence of the P.1 variant and insufficient mitigation measures

An analysis of SARS-CoV-2 samples collected in Amazonas municipalities during March 2020-January 2021 suggests that the first wave was driven mostly by one variant (B.1.195), which was gradually replaced by another variant (B.1.1.28), which then gave rise to variant P.1. Comparing the relative prevalence of different SARS-CoV-2 variants and adherence with physical distancing over time suggests that ongoing transmission allowed the establishment and local persistence of new viral lineages. Then the increased transmissibility of the P.1 variant further fueled the surge in cases and hospitalizations observed in Manaus. The top half of the figure below shows the relative prevalence of variant B.1.195 (green), variant B.1.1.28 (pink) and variant P.1 (blue) between February 2020 and February 2021. The bottom half of the figure shows the estimated reproductive number of each variant (colored bars) as well as the proportion of people who reported adhering with physical distancing recommendations over the same time period in Manaus (dashed line) and outside Manaus (solid line).



The relative prevalence of three SARS-CoV-2 variants, their effective reproductive numbers and the level of adherence with social distancing during February 2020 - February 2021 in Amazonas, Brazil.

Source: [researchsquare.com](https://www.researchsquare.com)

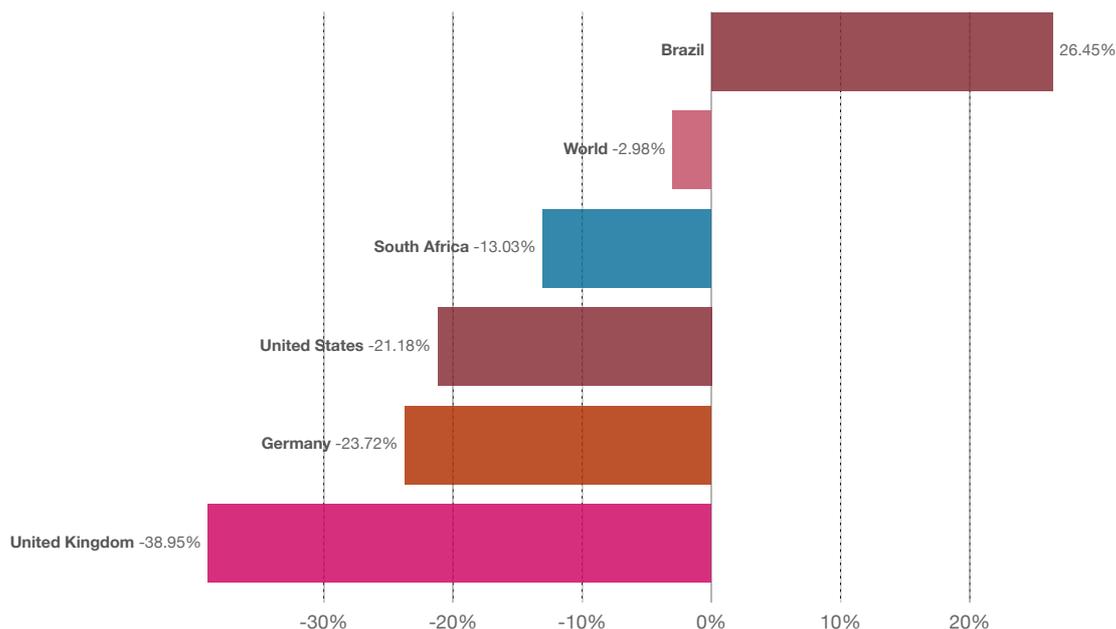
Given the current state of the COVID-19 epidemic in Brazil, what can be done?

Brazil has now surpassed 11 million confirmed cases and 270,000 deaths. And the epidemic remains uncontrolled, with some areas hit particularly hard. Data from the [Ministry of Health through Feb. 27, 2021](#), show that the cumulative number of deaths per capita in Amazonas was the highest recorded in any Brazilian state, at 257 per 100,000 people, compared with 120 per 100,000 in Brazil overall (and 155 per 100,000 in the United States). As mentioned above, the true count of cases and COVID-19 deaths is likely much higher. Despite this already massive toll, the number of confirmed COVID-19

deaths increased by 26% in Brazil during March 7-13 compared to the prior week, in contrast to the global trend of decreasing deaths, as shown in the figure below.

Week by week change of confirmed COVID-19 deaths, Mar 13, 2021

The weekly growth rate on any given date measures the percentage change in number of confirmed deaths over the last seven days relative to the number in the previous seven days.



Source: Johns Hopkins University CSSE COVID-19 Data

CC BY

Source: ourworldindata.org

In response to the burgeoning epidemic across Brazil, authorities in several states - **including Amazonas** - announced restrictions on movement and non-essential services in January 2021. Further restrictions have been announced more recently, such as **plans to restrict essential services in São Paulo from mid-March**. These **new measures have been met with protest** in some cities. Although the **potential economic, health and societal costs of PHSMs must be considered and mitigated**, such measures may be necessary to control the spread of COVID-19. In the **context of increased transmission due to a more transmissible variant in a largely unvaccinated population, models suggest that:** 1) restrictive PHSMs are particularly critical to reduce cases and deaths and 2) an accelerated vaccine rollout is unlikely to have a major impact on transmission in the near-term, but may be necessary to reduce transmission after the surge has peaked and to avert a resurgence when PHSMs are relaxed.

Brazil has approved the use of three COVID-19 vaccines: the Oxford-AstraZeneca (Oxford) vaccine developed in the U.K., the CoronaVac vaccine developed by the Sinovac company in China, and the Pfizer-BioNTech (Pfizer) vaccine developed in Germany and the United States. To date, only the Oxford and CoronaVac vaccines have been available in Brazil outside of clinical trials. All three vaccines were tested in Brazil. However, there is uncertainty about vaccine efficacy to protect from infection with the P.1 variant because the trials were conducted prior to widespread transmission of the variant.

The **Oxford vaccine** uses a viral vector to expose the immune system to the SARS-CoV-2 spike protein. Theoretically, the vaccine could be less protective against infection with SARS-CoV-2 variants that have mutations in the spike protein. The efficacy of the Oxford vaccine **did not differ between trial sites** in Brazil, South Africa and the United Kingdom but data were collected before new variants were widespread. Although data on protection against other variants should be extrapolated with caution, it is notable that in February, South Africa **halted the rollout of the Oxford vaccine** after a **small trial that enrolled participants aged 18-64** did not demonstrate efficacy against mild-to-moderate COVID-19 in the setting of widespread transmission of the B.1.351 variant, which shares some important mutations with the P.1 variant. This trial could not assess efficacy against severe COVID-19 because of the low frequency of severe disease in the study population. The World Health Organization currently **recommends use of the Oxford vaccine even in the presence of new variants.**

The **CoronaVac vaccine** is an inactivated virus vaccine which exposes the immune system to whole killed SARS-CoV-2 virus. Theoretically, because the vaccine includes many viral proteins, efficacy may be less affected by variants with spike protein mutations. The vaccine was tested in Brazil, Chile, Indonesia and Turkey. In January, Brazilian researchers **first announced that the vaccine is 78% effective against symptomatic COVID-19, the outcome used for most other vaccine efficacy trials, and announced an efficacy of 50.4% when “very mild infections” were included in the analysis.** Researchers also announced 100% efficacy against severe COVID-19. To date, **efficacy estimates for CoronaVac have only been announced in press releases;** data supporting these estimates have not been published nor have analyses been peer reviewed. Therefore, it is not clear how the clinical endpoints used to evaluate efficacy compare to other vaccine trials. There are

also no available data on the efficacy of the vaccine against the P.1 variant; most study participants were enrolled before the P.1 variant was widespread, so additional studies may be needed.

The **Pfizer vaccine** uses an mRNA platform to expose the immune system to the viral spike protein. **The vaccine was observed to have 95% efficacy** in trials held in the US (76% of participants), Argentina (15%), Brazil (6%), and South Africa (2%). As was the case with the other vaccines, the trials took place before widespread transmission of the P.1 variant. In a recent lab study, **researchers tested 20 serum samples from 15 Pfizer vaccine trial participants against viruses with the same spike protein mutations carried by the P.1 variant.** Antibodies generated by vaccination with the Pfizer vaccine were found to neutralize the P.1 variant and a non-P.1 variant to a roughly equivalent degree. This laboratory evidence suggests that the vaccine may retain its effectiveness against the P.1 variant; however, real-world evidence is needed to confirm whether this is the case.

Despite some uncertainty about the protection offered by COVID-19 vaccines against the P.1 variant, it is likely that widespread vaccination would be the most effective way to ultimately control Brazil's COVID-19 epidemic. Unfortunately, despite Brazil's **historical proficiency at rolling out vaccination programs**, as of March 15 less than 5% of Brazil's population had received at least one dose of a COVID-19 vaccine. Vaccine **availability has been severely limited**; the government recently ordered **100 million doses of the Pfizer vaccine**, but it is anticipated that doses will not be available until later this year. Even if the pace of vaccine rollout picks up in Brazil, it is unlikely that coverage rates necessary to significantly reduce cases, hospitalizations and deaths will be achievable in the near future. **Modeled scenarios suggest** that priority populations (including health care workers, older adults and those with comorbidities) may not be fully vaccinated until as late as August, and that the general population may not be fully vaccinated this year.

Lessons may be learned from three countries—**Israel, South Africa** and the **U.K.**—that have documented high prevalences of more transmissible variants yet managed to reduce rates of cases and deaths. All three countries documented surges in hospitalizations and deaths in late 2020 and then implemented strict PHSMs which were lifted when cases and deaths dropped. The degree to which vaccination may have contributed to epidemic control likely varies between countries. In Israel, a lockdown in January 2021 was

associated with a decrease in cases, but there was a greater decrease among people aged 60 or older, 75% of whom had received at least one vaccine dose by early January.

In the U.K., a lockdown was implemented in the beginning of January 2021. As of January 10, approximately **3% of the total population**, including **30% of those over age 80**, had received at least one vaccine dose. During January and February, cases and deaths fell in the U.K., and the government began easing restrictions in early March. While vaccination of those most vulnerable to severe disease likely contributed to the decline in deaths, **it is likely that strict PHSMs played the biggest role** in reducing transmission and the burden of disease. In South Africa, cases and deaths fell after a lockdown was implemented at the end of December 2020, and restrictions were eased on March 1, 2021. The vaccine rollout did not begin until **mid-February** and **as of March 1, only 0.1% of the population had received at least one vaccine dose.** Vaccination has thus far played a limited role in controlling South Africa's epidemic.

Multiple coordinated and targeted strategies are needed to curb COVID-19 cases and deaths in Brazil. Rapid rollout of COVID-19 vaccines is necessary to protect the most vulnerable people as quickly as possible and to prevent future epidemic surges. At the subnational level, critical efforts are being made to mitigate the spread and impact of the epidemic. But more stringent, coordinated PHSMs targeted to areas with high levels of transmission may be necessary, at least in the short term. Ideally, financial and social support that allows the population to adhere to mitigation measures should come with those measures. If transmission is not reduced, it is not just Brazilians at risk: a surging epidemic poses a serious threat to both local and global populations. The **World Health Organization reports** that the P.1 variant has been found in 32 countries to date, and the U.S. CDC has reported at least **17 cases in 10 U.S. locations.** According to the **Director General of the World Health Organization**, "If Brazil is not serious, then it will continue to affect all of the neighborhood there – and beyond...This is not just about Brazil. It's about the whole Latin America, and even beyond."

Weekly Research Highlights

Effect of Ivermectin on Time to Resolution of Symptoms Among Adults With Mild COVID-19: A Randomized Clinical Trial

(JAMA, March 2021)

Main Message: Ivermectin is a widely prescribed drug used to treat several parasitic diseases. Multiple observational and clinical trials have assessed the use of ivermectin for prevention or treatment of COVID-19 with inconsistent results, as described in the most recent [Weekly Science Review](#). In this study, 398 participants with mild COVID-19 disease were randomized to receive ivermectin or placebo to evaluate if ivermectin reduced the time until resolution of symptoms. The study found that ivermectin was not associated with a statistically significant reduction in the time to resolution of symptoms, results that do not support the use of ivermectin for treatment of mild COVID-19.

- Researchers enrolled participants into a double-blind, placebo-controlled trial at a single facility in Colombia. Participants with mild COVID-19 who had been symptomatic for seven or fewer days were eligible to be enrolled. Participants were followed for 21 days to determine the date when symptoms resolved.
- Among those randomized to receive ivermectin, the median time to resolution of symptoms was 10 days compared to 12 days in the placebo group. This corresponded to a hazard ratio of 1.07 (95% CI 0.87 to 1.32) for resolution of symptoms.
- The authors evaluated several secondary clinical outcomes, though statistical power to evaluate these outcomes in this study was limited. They found no statistically significant association between ivermectin use and clinical deterioration (OR = 0.56, 95% CI 0.16 to 1.93), escalation of care (OR = 0.38, 95% CI 0.12 to 1.24) or developing fever (OR = 0.73, 95% CI 0.37 to 1.45).
- This study had several limitations. It may not have been adequately powered to detect a smaller but still clinically meaningful reduction in time until resolution of symptoms, and it was not designed with adequate sample size to detect clinical outcomes of disease progression. The study population was also relatively young, and results could differ among an older population.

Suggested citation: Cash-Goldwasser S, Jones SA, Bierrenbach AL, Bochner A and Frieden TR.. Weekly COVID-19 Science Review March 3rd - 17th, 2021. Resolve to Save Lives. 2021 March 18. Available from <https://preventepidemics.org/coronavirus/weekly-science-review/>