**The Effectiveness of Vaccination on the COVID-19 Epidemic in California**

**Introduction**

COVID-19 is a respiratory disease with symptoms such as fever, cough, chest pain, sore throat, and rhinorrhea.1 The COVID-19 pandemic has spread around the world, causing massive disruption to educational, technological, financial, agricultural, and healthcare sectors.2 Several COVID-19 vaccines by different corporations were developed to prevent and mitigate the effects of the disease and have been shown to be extremely effective in doing so.3 To combat and limit the damage wreaked by pandemic, the United States Department of Defense and Department of Health and Human Resources launched Operation Warp Speed, which accelerated the development and manufacturing of the COVID-19 vaccine.4

This worldwide pandemic has impacted California heavily, manifested in the form of COVID-19 cases, COVID-related deaths, and COVID-related hospitalizations.5 These three outcomes are used as convenient measures of the spread and severity of the epidemic. COVID-19 cases are the most straightforward measure of the pandemic, but hospitalizations and deaths are a measure of the severity of the cases that occur in the pandemic.6 All three measures can help elucidate the impact of vaccinations on public health.7 The pandemic has seen many phases, and as SARS-CoV-2 virus has evolved, new strains such as the Delta strain and the Omicron strain has caused outbreaks during the pandemic.8 This study provides key metrics to determine the importance of COVID-19 vaccination, encouraging public policy that require proof of vaccination to enter public gatherings and events.

**Methods**

We designed a retrospective cohort study for the COVID-19 epidemic in California to investigate the differences in cases, deaths, and hospitalizations among vaccinated and unvaccinated individuals. COVID-19 cases, deaths, and hospitalizations in California was sourced from a dataset released publicly by the California Department of Public Health,9 using data collected from February 2021 to June 2022. The dataset contained information on vaccinated and unvaccinated populations, the number of cases, hospitalizations, and deaths according to the vaccination status, and the date of the outcome. COVID-19 cases were analyzed in three different periods: 1) the Pre-Delta Period ranging from March 2021 to April 2021, 2) the Delta Wave from July 2021 to September 2021, and 3) the Omicron Wave from December 2021 to February 2022. The exposed cohort group was composed of individuals that received a COVID-19 vaccine. Conversely, the unexposed cohort group was composed by individuals who did not receive a COVID-19 vaccine. We analyzed the number of COVID-19 cases, hospitalizations, and deaths in each group during the periods selected. The following parameters were calculated: the odds ratio (OR), incidence risk ratio(IRR), relative risk reduction (RRR), population prevented fraction (PPF), attributable risk reduction (ARR) and number needed to treat (NNT). χ2 tests were performed in R using the tidyverse and epiR packages. RStudio version 2022.12.0+353 was used for the purpose of this study. P-values < 0.05 were considered significant.

**Results**

Figure 1 shows the selected time periods between colored lines over the recorded time of the dataset. The Pre-Delta Period is shown between the green lines, the Delta Wave is shown between the blue lines, and the Omicron Wave is shown between the red lines.

All calculated statistics are shown on Table 2.

Table 3 contains all the raw numbers from each of the 2 by 2 tables used to calculate each statistic.

Incidence risk ratio describes the likelihood a person with the exposure is to experience an outcome compared to an individual who does not have the exposure, while the odds ratio describes the odds of an outcome in the exposed group versus the unexposed group.10 When evaluating the measures of association, every incidence risk ratio (Figure 1a) and odds ratio (Figure 1b) show a value much lower than 1, indicating that vaccinations are highly protective against COVID-19 cases, deaths, and hospitalizations in every time period analyzed in the general population of California. For the Delta and Omicron waves, incidence risk ratios and odds ratios decreased according to the increasing severity of the outcome, demonstrating the idea that vaccinations decrease severity of cases. Vaccinations vs. hospitalizations during the Pre-Delta Period had the highest overall incidence risk ratio [0.641 (95% CI 0.571, 0.720)] and odds ratio [0.641 (95% CI 0.571, 0.720)]. The lowest overall incidence risk ratios and odds ratio were consistently vaccinations vs. deaths across all time periods, the lowest being during the Delta Wave, with an incidence risk ratio of 0.0941 (95% CI 0.0879, 0.101) and an odds ratio of 0.0940 (0.0879, 0.101). χ2 testsfor every odds ratio showed p<0.001.

The relative risk reduction, also known as the preventive fraction among the unexposed (Figure 1c), represents the percentage of positive cases, deaths, or hospitalizations among the unvaccinated that could have been prevented had this unexposed cohort been vaccinated.11 The Delta Wave had the largest percentages of preventable cases [80.3%(95% CI 80.2, 80.4)], hospitalizations [89.5%(95% CI 89.2, 89.8)], and deaths [90.6%(95% CI 89.9, 91.2)] among the unexposed. The values also tend to increase based on severity of outcome, with highest preventive fractions associated with vaccinations vs. deaths [Omicron 88.4% (95% CI 88.0, 88.9)], then vaccinations vs. hospitalizations [Omicron 83.7%(95% CI 83.4, 84.0)], and finally followed by vaccinations vs. cases [Omicron 68.4%(95% CI 68.3, 68.5)]**.**

The population prevented fraction (Figure 1d) is the percentage of positive cases, deaths, or hospitalizations that could have been prevented in the population through vaccination.12,13 The lowest population prevented fraction was during the Omicron Wave, for vaccinations vs. cases [33.9% (95% CI 33.8, 34.0)]. The highest population prevented fraction was during the Pre-Delta Period, as the vaccinations vs. deaths had a fraction of 84.1% (95% CI 76.3, 89.3). The highest population prevented fractions consistently were vaccinations vs. deaths across all periods. The population prevented fraction again follows severity of outcome, with vaccinations vs. deaths having the highest proportion, followed by hospitalizations, then cases.

The absolute risk reduction (Figure 1e) describes the number of outcomes that have been reduced because of the exposure.14 In this case, this statistic measures the number of individuals who do not develop a case of COVID-19, are not admitted to the hospital, or do not die as a result of receiving the COVID-19 vaccine. The effect is most pronounced in preventing cases, as 3.14 cases per 100 individuals were prevented during Omicron Wave, and 1.28 cases per 100 individuals during the Delta Wave. The lowest value was the Pre-Delta Period vaccinations vs. deaths, with 0.0072 deaths prevented per 100 individuals (95% CI 0.0066, 0.0079).

The number needed to treat is the number of individuals that need to be treated before one benefits.15 Only one in eight individuals were needed to prevent a case during the Omicron Wave. However, during the Pre-Delta Period, one in 10,500 would experience a benefit from prevention of hospitalization and one in 13,000 to experience a prevention from death due to COVID-19. The highest number needed to treat was 1 in 13,000 individuals (95% CI 12000, 14200) for vaccinations vs. deaths during the Pre-Delta Wave.

**Discussion**

Measures of association and of public health risk showed significant variation among the three different time periods. Omicron Wave incidence risk ratios (Cases IRR: 0.316, Deaths IRR: 0.116, Hospitalizations IRR: 0.163) were always somewhat higher than the Delta Wave values (Cases IRR: 0.197, Deaths IRR: 0.0941, Hospitalizations IRR: 0.105), with similar values for odds ratios. Between the two waves, the percentage of preventable cases among the population were higher during the Delta Wave (80.3%) compared to the Omicron Wave (68.4%), as were deaths (Delta: 90.6% vs Omicron: 88.4%) and hospitalizations (Delta: 89.5% vs Omicron: 83.7%). There were also more preventable cases in the population during the Delta Wave (59.4%) compared to during the Omicron Wave (33.9%), as well as for deaths (Delta 77.5% vs. Omicron 64.4%) and hospitalizations (Delta 75.4% vs. Omicron 54.8%). This could mean that vaccinations were more effective in a small to moderately sized outbreak such as the Delta Wave versus a larger outbreak such as the Omicron Wave, or that vaccines were less effective at targeting the Omicron viral variant as compared to the Delta variant. Research has shown that Omicron variant was much more transmissible but less deadly than the Delta variant, causing a larger spike in cases but a lower mortality rate in comparison.16 Surprisingly, the Delta Wave had a higher mortality than the Omicron Wave across the United States,17,18 despite our finding that the vaccine was more effective during the Delta Wave in California. Taken together, vaccines seemed to have prevented somewhat fewer outcomes in a more contagious, less deadly wave. One explanation is that the population of California, by the time of the Omicron Wave, were more successful in employing other public health measures, such as hand-washing, masking, and increased social distancing. Increased awareness of these other methods may have increased their effectiveness while mitigating that of vaccines. According to their(CDPH) data, approximately 100,000 more people were vaccinated between the beginning of the Delta Wave to the beginning of the Omicron Wave, but it is possible that the approximately 20 million people who were already vaccinated in California had begun to lose their immunity from their vaccines by the time of the Omicron Wave and had not received boosters.

Across the three periods, the Pre-Delta Period consistently had higher incidence risk ratios and odds ratios as well as lower preventive fractions among the unexposed compared to the Delta and Omicron wave periods. The incidence risk ratio for cases is 0.472, 0.151 for deaths, and 0.641 for hospitalizations, with similar values for odds ratios. No value for the Delta Wave or Omicron Wave exceeds these respective values. With the exception of a population prevented fraction for cases (51.4%) greater than that of the Omicron Wave, all other preventive fractions among the unexposed and population preventable fractions were lower for the Pre-Delta Period compared to the wave periods. This may be due to vaccinations having a greater effect against adverse outcomes when transmission is higher during wave periods. Alternatively, the Pre-Delta Period is when many people first began receiving vaccines. Many people may have lost their precaution they exhibited when they had not received a vaccine, believing they were now “safe” from adverse outcomes, which ironically may have led to cases, hospitalizations, and deaths. However, many individuals may have returned to their careful habits after seeing the ravaging of the Delta and Omicron Waves on the population of California, as well as many other populations around the world. In addition, vaccines were later produced that targeted the Delta and Omicron variants in particular, and this may have contributed to the relative effectiveness for these strains compared to strains before them.

An unusual finding was that the Pre-Delta Period did not follow the trend of decreasing incidence risk ratios and odds ratios for worse outcomes. The incidence risk ratio (0.641) and odds ratio (0.641) were higher for hospitalizations than they were for cases or deaths. The preventive fraction of the unexposed (35.9%) and the population prevented fraction (34.5%) were also lower for hospitalizations than they were for cases or deaths. A possible reason could be that the particular strain of virus during this period was more virulent and caused more hospitalizations in breakthrough cases. Alternatively, the vaccine, while effective in preventing cases and deaths, may not have been as effective in moderate to moderately severe cases of COVID-19, causing this phenomenon.

The attributable risk reduction and number needed to treat show results that are not as dramatic compared to the findings from other statistics. Only cases during the Delta Wave (1.28 per 100) and Omicron Wave (3.14 per 100) are above 1 outcome per 100 individuals prevented; attributable risk reduction for cases during the Pre-Delta Period were 0.201 per 100 individuals, and for hospitalizations, they were 0.0089 per 100 individuals. Similarly, the number to treat for cases during the Delta Wave (1 in 8) and during the Omicron Wave (1 in 28) are relatively high, while others are much lower—deaths were 1 in 2130 had a prevented death during the Delta Wave and 1 in 863 during the Omicron Wave. Because of these modest results, it would appear that vaccinations to do not reduce risk of outcomes by much, and there needs to be an enormous number of vaccinations that need to be administered before seeing a prevented outcome. However, this is attributed to the low baseline risk of hospitalization19 and extremely low baseline risk of death from COVID-19.20 There is significant benefit from vaccination against all outcomes of COVID-19, but because risk of these outcomes before vaccinations, aside from that of cases, is already incredibly low, the attributable risk reduction and number needed to treat appear to have relatively minor effect sizes.

Although the study shows that vaccinations have been extremely beneficial to the population of California, the effectiveness of vaccination may vary in other states or nations, and the continued evolution of the SARS-CoV-2 virus21 may present new and unforeseen challenges to vaccination as a public health intervention. New developments in vaccine development and new virus strains may also influence the effectiveness of vaccinations against the COVID-19 pandemic.

Include the time period of the third wave.

Discussion: why we have less deaths and more contagious people

This study is vulnerable to limitations suffered by all cohort studies. One major limitation is variation of measurement of exposure. Our dataset simply indicates vaccination status of each individual, but the brand of vaccine, number of doses, and time of vaccine inoculation are not recorded, which could potentially have had an impact on the outcomes of interest. In addition, the measurement of the outcomes may not be completely accurate. Many COVID-19 cases may have gone unreported, affected the resulting statistics. Finally, confounding variables may impact both the exposure and the outcomes, potentially influencing the relationship between vaccination and COVID-19 cases, deaths, and hospitalizations.

Vaccination has been shown to be an excellent way of preventing adverse outcomes of COVID-19, but the best vaccine of all may be education. A good understanding of COVID-19 will spur people and communities to engage in mask-wearing, covering their coughs, and having awareness of other individuals after knowing how disease is spread. A vaccination campaign without educating the public as to why it is important is doomed to fail, as people would not know why they need to be vaccinated. Before vaccinating individuals, it is important to remember that informing the public as to what the vaccine can do for them, as well as any precautions and risks they should consider, will greatly increase the acceptance of vaccines within communities.

**Conclusion**

From this study, we conclude that vaccinations in California achieved their greatest effect during the Delta Wave, followed by Omicron Wave, followed by the Pre-Delta Period. In addition, vaccinations significantly decreased cases but had an even greater reduction in hospitalizations, and the greatest reduction on deaths. Therefore, we encourage state and local governing bodies to create and enact legislation that encourage or enforce the vaccination against COVID-19 among the general populace of California. Similar policies can be enacted by any organization in California requiring one to have been vaccinated to enter parties, gatherings, and other social functions. Vaccination should be widely adopted by the people of California to curtail further ongoing effects of the COVID-19 epidemic in the state.

**References**

1. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020;395(10223):507-513. doi:10.1016/S0140-6736(20)30211-7

2. Nicola M, Alsafi Z, Sohrabi C, et al. The socio-economic implications of the coronavirus pandemic (COVID-19): A review. *Int J Surg*. 2020;78:185-193. doi:10.1016/J.IJSU.2020.04.018

3. Chirico F, Silva JAT da, Tsigaris P, Sharun K. Safety & effectiveness of COVID-19 vaccines: A narrative review. *Indian J Med Res*. 2022;155(1):91. doi:10.4103/IJMR.IJMR\_474\_21

4. A Timeline of COVID-19 Vaccine Developments in 2021. Accessed September 4, 2022. https://www.ajmc.com/view/a-timeline-of-covid-19-vaccine-developments-in-2021

5. Tracking COVID-19 in California - Coronavirus COVID-19 Response. Accessed September 24, 2023. https://covid19.ca.gov/state-dashboard/#county-statewide

6. Martins-Filho PR, de Souza Araújo AA, Quintans-Júnior LJ, et al. Dynamics of hospitalizations and in-hospital deaths from COVID-19 in northeast Brazil: a retrospective analysis based on the circulation of SARS-CoV-2 variants and vaccination coverage. *Epidemiol Health*. 2022;44. doi:10.4178/EPIH.E2022036

7. Steele MK, Couture A, Reed C, et al. Estimated Number of COVID-19 Infections, Hospitalizations, and Deaths Prevented Among Vaccinated Persons in the US, December 2020 to September 2021. *JAMA Netw Open*. 2022;5(7):E2220385. doi:10.1001/JAMANETWORKOPEN.2022.20385

8. Doll MK, Waghmare A, Heit A, et al. Acute and Postacute COVID-19 Outcomes Among Immunologically Naive Adults During Delta vs Omicron Waves. *JAMA Netw Open*. 2023;6(2):e231181-e231181. doi:10.1001/JAMANETWORKOPEN.2023.1181

9. COVID-19 Post-Vaccination Infection Data (ARCHIVED) - Datasets - California Health and Human Services Open Data Portal. Accessed September 24, 2023. https://data.chhs.ca.gov/dataset/covid-19-post-vaccination-infection-data

10. Monaghan TF, Rahman SN, Agudelo CW, et al. Foundational Statistical Principles in Medical Research: A Tutorial on Odds Ratios, Relative Risk, Absolute Risk, and Number Needed to Treat. *Int J Environ Res Public Health*. 2021;18(11). doi:10.3390/IJERPH18115669

11. Yamada K, Kuroki M. Counterfactual-Based Prevented and Preventable Proportions. *J Causal Inference*. 2017;5(2). doi:10.1515/JCI-2016-0020

12. Prevented Fraction For The Population - Oxford Reference. Accessed September 26, 2023. https://www.oxfordreference.com/display/10.1093/acref/9780199976720.001.0001/acref-9780199976720-e-1492

13. 21.9: Prevented fraction of disease - Medicine LibreTexts. Accessed September 26, 2023. https://med.libretexts.org/Bookshelves/Nursing/Field\_Trials\_of\_Health\_Interventions\_-\_A\_Toolbox\_(Smith\_Morrow\_and\_Ross)/21%3A\_Methods\_of\_analysis/21.09%3A\_Prevented\_fraction\_of\_disease

14. Ranganathan P, Pramesh CS, Aggarwal R. Common pitfalls in statistical analysis: Absolute risk reduction, relative risk reduction, and number needed to treat. *Perspect Clin Res*. 2016;7(1):51. doi:10.4103/2229-3485.173773

15. Mendes D, Alves C, Batel-Marques F. Number needed to treat (NNT) in clinical literature: an appraisal. *BMC Med*. 2017;15(1). doi:10.1186/S12916-017-0875-8

16. Duong B V., Larpruenrudee P, Fang T, et al. Is the SARS CoV-2 Omicron Variant Deadlier and More Transmissible Than Delta Variant? *Int J Environ Res Public Health*. 2022;19(8). doi:10.3390/IJERPH19084586

17. Tabatabai M, Juarez PD, Matthews-Juarez P, et al. An Analysis of COVID-19 Mortality During the Dominancy of Alpha, Delta, and Omicron in the USA. *J Prim Care Community Health*. 2023;14. doi:10.1177/21501319231170164

18. Tabatabai M, Juarez PD, Matthews-Juarez P, et al. An Analysis of COVID-19 Mortality During the Dominancy of Alpha, Delta, and Omicron in the USA. *J Prim Care Community Health*. 2023;14. doi:10.1177/21501319231170164

19. Taylor CA, Patel K, Patton ME, et al. COVID-19–Associated Hospitalizations Among U.S. Adults Aged ≥65 Years — COVID-NET, 13 States, January–August 2023. *MMWR Morb Mortal Wkly Rep*. 2023;72(40):1089-1094. doi:10.15585/MMWR.MM7240A3

20. Risk of COVID-19-Related Mortality. Accessed October 9, 2023. https://www.cdc.gov/coronavirus/2019-ncov/science/data-review/risk.html

21. Markov P V., Ghafari M, Beer M, et al. The evolution of SARS-CoV-2. *Nature Reviews Microbiology 2023 21:6*. 2023;21(6):361-379. doi:10.1038/s41579-023-00878-2