<u>Original Paper</u>

The Effectiveness of Pfizer-BioNTech and Oxford-AstraZeneca Vaccines to Prevent Severe COVID-19 in Costa Rica: Nationwide, Ecological Study of Hospitalization Prevalence

Luis Rosero-Bixby, MPH, PhD

Centro Centroamericano de Población, Universidad de Costa Rica, San Pedro, Costa Rica

Corresponding Author:

Luis Rosero-Bixby, MPH, PhD
Centro Centroamericano de Población
Universidad de Costa Rica
Ciudad Universitaria Rodrigo Facio
San Pedro, 11501
Costa Rica
Phone: 506 25111452
Email: roserobixby@gmail.com

Abstract

Background: The Costa Rican COVID-19 vaccination program has used Pfizer-BioNTech and Oxford-AstraZeneca vaccines. Real-world estimates of the effectiveness of these vaccines to prevent hospitalizations range from 90%-98% for two doses and from 70%-91% for a single dose. Almost all of these estimates predate the Delta variant.

Objective: The aim of this study is to estimate the dose-dependent effectiveness of COVID-19 vaccines to prevent severe illness in real-world conditions in Costa Rica, after the Delta variant became dominant.

Methods: This observational study is a secondary analysis of hospitalization prevalence. The sample is all 3.67 million adult residents living in Costa Rica by mid-2021. The study is based on public aggregated data of 5978 COVID-19–related hospital records from September 14, 2021, to October 20, 2021, and 6.1 million vaccination doses administered to determine hospitalization prevalence by dose-specific vaccination status. The intervention retrospectively evaluated is vaccination with Pfizer-BioNTech (78%) and Oxford-AstraZeneca (22%). The main outcome studied is being hospitalized.

Results: Vaccine effectiveness against hospitalization (VEH) was estimated as 93.4% (95% CI 93.0-93.9) for complete vaccination and 76.7% (95% CI 75.0-78.3) for single-dose vaccination among adults of all ages. VEH was lower and more uncertain among older adults aged ≥58 years: 92% (95% CI 91%-93%) for those who had received full vaccination and 64% (95% CI 58%-69%) for those who had received partial vaccination. Single-dose VEH declined over time during the study period, especially in the older age group. Estimates were sensitive to possible errors in the population count used to determine the residual number of unvaccinated people when vaccine coverage is high.

Conclusions: The Costa Rican COVID-19 vaccination program that administered Pfizer-BioNTech and Oxford-AstraZeneca vaccines seems to be highly effective at preventing COVID-19–related hospitalization after the Delta variant became dominant. Even a single dose seems to provide some degree of protection, which is good news for people whose second dose of the Pfizer-BioNTech vaccine was postponed several weeks to more rapidly increase the number of people vaccinated with a first dose. Timely monitoring of vaccine effectiveness is important to detect eventual failures and motivate the public to get vaccinated by providing information regarding the effectiveness of the vaccines.

KEYWORDS

XSL·FO
RenderX

Introduction

Concerns regarding the possible lack of effectiveness of a single dose of COVID-19 vaccine arose with the emergence of the Delta variant, a more contagious variant of COVID-19. In Costa Rica, COVID-19 cases caused by the Delta variant increased from 11% of new infections in the last week of June 2021 to 55% of new infections in the first week of August and to 100% in the last week of September 2021 (Instituto Costarricense de Investigación y Enseñanza en Nutrición y Salud [INCIENSA], unpublished data). In the same period, the incidence of COVID-19 increased from 288 to 445 daily cases per million population, despite the rapid increase in the proportion of vaccinated people from 32% on June 28, 2021, to 66% on September 27, 2021 [1].

The universal public health care system of Costa Rica, which is provided by the Costa Rican Social Security Fund (CCSS, acronym in the Spanish language), has been the single source of COVID-19 vaccination in the country. The CCSS uses two vaccines, the messenger RNA vaccine from Pfizer-BioNTech and the adenovirus vector vaccine from Oxford-AstraZeneca. By October 20, 2021, approximately 85% of the 3.7 million adult residents had been vaccinated with at least one dose and 59% with two doses [2]. Older adults aged ≥58 years received only the Pfizer-BioNTech vaccine; among older adults, 87% received the two doses with a 3-week interval and 13% with an 8- to 12-week interval. Among adults <58 years of age, 77% received the Pfizer-BioNTech vaccine and 23% received the Oxford-AstraZeneca vaccine, mostly with an 8- to 12-week interval between doses. The Costa Rican vaccination program had a strong initial focus on older adults (aged ≥58 years, as defined by the government). By June 1, 2021, more than 80% of the population in this age group had been vaccinated compared to 17% in the 40-57 years age group and 7% in the 20-39 years age group. Due to this initial focus on older adults, the proportion of older adults with more than a 6-month period after their second dose was growing rapidly during the study period, from 2% on September 14, 2021, to 24% on October 20, 2021.

At the time of this study, the literature reported the following real-world estimates (based on observational studies rather than randomized trials) of COVID-19 vaccine effectiveness against hospitalization (VEH). The 2-dose Pfizer-BioNTech VEH was 97% in Israel [3], 98% in Ontario, Canada, in a vaccination program that had primarily allocated Pfizer-BioNTech vaccine (77%) [4], 91% in the United States in the first 4 months after full vaccination [5], 90% in California when 93% of COVID-19 cases were caused by the Delta variant [6], and 90% in Qatar according to a preprint study on only Delta variant cases [7]. The highest VEH estimates (in Israel and Ontario) were obtained before the emergence of the Delta variant.

Single-dose VEH estimates were 70% in the Ontario vaccination program, which mostly used the Pfizer-BioNTech vaccine [4], 80% in England for both Pfizer-BioNTech and Oxford-AstraZeneca vaccines [8], and 91% and 88% in Scotland for Pfizer-BioNTech and Oxford-AstraZeneca vaccines, respectively [9]. All these estimates predated the Delta variant.

The objective of this study was to estimate the dose-dependent effectiveness of COVID-19 vaccines to prevent severe cases of COVID-19, as measured by the prevalence of hospitalizations, in a middle-income country (Costa Rica). These estimates were based on secondary analysis of COVID-19–related hospitalized individuals from September 14 to October 20, 2021.

Methods

Study Design

This observational, nationwide study used a cross-sectional prevalence design. The study performed secondary analysis of official statistics and reports. It compared the COVID-19–related hospitalization prevalence among the unvaccinated population with the prevalence among the semivaccinated and fully vaccinated populations at 6 time points, each 1 week apart, from September 14 to October 20, 2021.

Data

The VEH estimates used three sources of data:

1. A series of weekly reports presented by the Department of Health Statistics to the Board of Directors of the CCSS (unpublished data), which is the most important information. These reports show the distribution by vaccination status of COVID-19–related hospitalizations by the ages of patients. CCSS officers linked the databases of hospitalizations and vaccinations to determine the vaccination status of hospitalized individuals and some demographic characteristics such as age and sex. For 2% of the hospital records, the vaccination status was not established.

2. The time series of the number of first and second doses of the COVID-19 vaccines administered (6.1 million by October 20, 2021) according to population age groups as reported weekly by the CCSS [2]. These data were used to estimate the nationwide populations of semivaccinated and fully vaccinated individuals by age group at the 6 time points of the study. No adjustments were made for changes in demographics (no vaccinated individual died, out-migrated, or changed age bracket) in these populations since the impact of these changes is small considering the short study period.

3. The mid-2021 nationwide population estimate by the National Institute of Statistics and Censuses (INEC) [10]. This estimate was used to determine the residual group of unvaccinated individuals, who represented the control group in the analysis. It was assumed that there were no changes in the population from the date of the estimate to the study dates.

Variables

The outcome variable was "being hospitalized due to COVID-19."

The intervention variables were the two vaccination statuses as defined by the CCSS:

1. Partially or semivaccinated individuals: 15 or more days after the first dose and either less than 15 days after the second dose or no second dose.

XSL•FO
RenderX

2. Fully vaccinated individuals: 15 or more days since the second dose.

All analyses were stratified according to three age groups: 20-39, 40-57, and ≥58 years. These age brackets were defined in the priority calendar of the national vaccination program.

Statistical Methods

VEH is an epidemiological measure of relative risk reduction. Therefore, it was estimated as one minus the hospitalization prevalence ratio of vaccinated to unvaccinated populations.

Given the strong confounding effects of age, the Mantel-Haenzel technique was used to aggregate the age-specific estimates into a summary indicator for the entire adult population [11]. No imputations were made for the 2% of hospitalizations that had missing data, which were assumed to be randomly distributed. Estimates were obtained using Stata 17 statistical software (version 17; StataCorp LLC) and its "epitab" commands [12].

Although the number of vaccinated persons is a direct count of administered vaccines, the number of unvaccinated persons was an indirect estimate of the residual: population minus the number of vaccinated people. Errors in the population estimate would therefore overestimate or underestimate the number of unvaccinated individuals. A sensitivity analysis was performed to assess the impact of this potential error on the VEH.

Ethics Statement

This study is a secondary analysis of aggregated public data and as such does not need clearance or permissions from an ethics committee.

Results

Participants

Overall, the study included data of 3.67 million individuals, the entire adult population of Costa Rica. Of this population, 47% were in the younger group, 31% in the intermediate group, and 22% in the older group. The number of hospital records assessed in the 6 time periods was 5978, excluding 138 records with missing information. Table 1 shows the data used in the study, namely the number of participants (the population) and COVID-19–related hospitalizations. The table also shows the resulting prevalence proportions.

The highest rates of hospitalization occurred among older unvaccinated individuals, with a prevalence of 3537-4765 per million people. The lowest rates of hospitalization occurred among fully vaccinated younger adults, with prevalence ranging from 7-32 per million people, approximately 400 times lower than unvaccinated older adults. Hospitalization prevalence increased with age and was substantially higher among unvaccinated individuals. Over time, the prevalence proportions reflected the fact that COVID-19 cases in Costa Rica had reached their peak at the beginning of September, followed by a peak in hospitalizations 2 weeks later [13].

Table 1. Population, number of COVID-19–related hospitalized people, and hospitalization prevalence by vaccination status and age at 6 points in time, using data from Costa Rica.

Date and vaccination status	Age 20-39 years			Age 40-57 years			Age ≥58 years		
	N-pop[a]	N-hosp[b]	Prev[c]	N-pop	N-hosp	Prev	N-pop	N-hosp	Prev
September 14, 2021									
Total	1,732,200	249	144	1,124,100	476	423	817,400	476	582
No	602,453	189	314	243,809	302	1239	63,883	302	4727
Semi	944,645	54	57	593,039	147	248	20,660	147	7115
Fully	185,102	6	32	287,252	27	94	732,857	27	37
September 22, 2021									
Total	1,732,200	255	147	1,124,100	428	381	817,400	428	524
No	596,169	204	342	240,656	302	1255	63,374	302	4765
Semi	824,275	42	51	458,855	91	198	16,322	91	5575
Fully	311,756	9	29	424,589	35	82	737,704	35	47
September 29, 2021									
Total	1,732,200	239	138	1,124,100	409	364	817,400	409	500
No	551,141	180	327	224,643	287	1278	62,052	287	4625
Semi	790,324	54	68	355,344	84	236	14,192	84	5919
Fully	390,735	5	13	544,113	38	70	741,156	38	51
October 6, 2021									
Total	1,732,200	233	135	1,124,100	377	335	817,400	377	461
No	469,731	165	351	195,425	250	1279	58,864	250	4247
Semi	740,414	57	77	263,446	80	304	14,829	80	5395
Fully	522,055	11	21	665,229	47	71	743,707	47	63
October 13, 2021									
Total	1,732,200	196	113	1,124,100	312	278	817,400	312	382
No	387,924	130	335	164,113	194	1182	53,971	194	3595
Semi	724,720	57	79	227,889	79	347	17,645	79	4477
Fully	619,556	9	15	732,098	39	53	745,784	39	52
October 20, 2021									
Total	1,732,200	159	92	1,124,100	232	206	817,400	416	509
No	354,165	108	305	150,857	146	968	51,176	181	3537
Semi	704,530	46	65	208,980	52	249	18,588	31	1668
Fully	673,505	5	7	764,263	34	44	747,636	204	273
Pooled (averages)									
Total	1,732,200	222	128	1,124,100	372	331	817,400	403	493
No	493,597	163	330	203,251	247	1214	58,887	253	4291
Semi	788,151	52	66	351,259	89	253	17,039	85	5008
Fully	450,452	8	17	569,591	37	64	741,474	65	88

[a]N-pop: population.

[b]N-hosp: number of COVID-19–related hospitalized people.

[c]Prev: hospitalization prevalence per 1 million population.

Vaccine Effectiveness

As stated previously, VEH was estimated by comparing the prevalence of COVID-19 hospitalizations in the partially or fully vaccinated group to that in the unvaccinated group. Figure 1 shows all VEH estimates with 95% CIs.

The VEH for full vaccination ranges between 0.90 and 0.98 in the 3 age groups and 6 time points, with a statistically significant ascending time trend in the youngest group. In contrast, the VEH for partial vaccination significantly declined during the study period, especially in the older age group. The average weekly decline is 0.01, 0.02, and 0.05 in the 3 age groups, respectively. The partial vaccination effectiveness estimates ranged from 0.52-0.77 among older adults and from 0.71-0.84 among the other adult groups. Estimates of VEH for partial vaccination are substantially less precise than that for full

vaccination, as shown by the wider confidence interval, especially in the older adult group.

Table 2 shows the summary indicators of VEH obtained after pooling the data from the 6 observed time periods. These estimates represent the status of the COVID-19 vaccination effort in early October 2021 in Costa Rica. The age-adjusted estimates for all adults suggest a VEH of 93.4% (95% CI 93.0-93.9) for the full vaccination schedule of 2 doses and 77% (95% CI 75.0-78.3) for partial vaccination with 1 dose. Older adults showed slightly lower VEH for full vaccination (92%, 95% CI 91.4-92.5) and substantially lower VEH for partial vaccination (64%, 95% CI 57.5-69.4) compared to the other age groups. The majority of the COVID-19 hospitalizations were probably caused by the Delta variant, which was dominant at the time of the study according to the Costa Rican genomic tracking system of the variants of concern (INCIENSA, unpublished data).

Figure 1. COVID-19 VEH estimates and their 95% CIs by age group and cross-section date, in Costa Rica, September and October 2021. VEH: vaccine effectiveness against hospitalization.
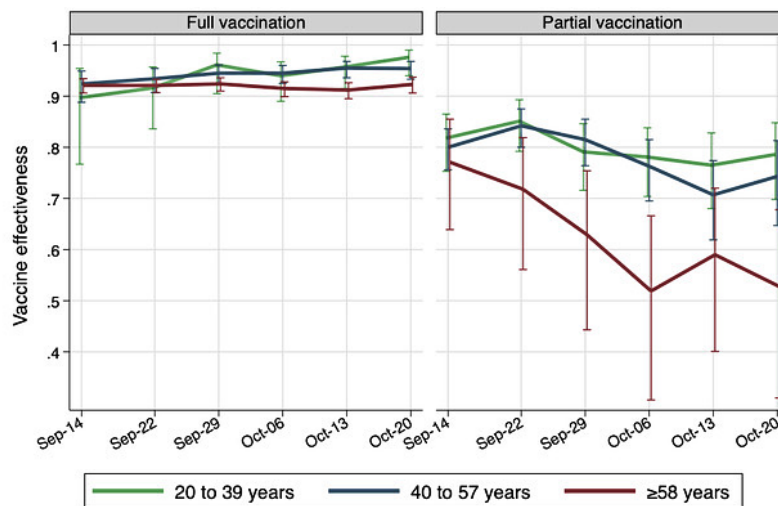

Table 2. Vaccine effectiveness against hospitalization for full and partial COVID-19 vaccination and relative risk of the unvaccinated being hospitalized by age group in Costa Rica in October 2021.

Age groups	Full vaccination	Partial vaccination
Vaccine effectiveness against hospitalization (95% CI)		
20-39 years	0.949 (0.932-0.963)	0.801 (0.774-0.825)
39-57 years	0.947 (0.939-0.954)	0.792 (0.770-0.811
≥58 years	0.920 (0.914-0.925)	0.639 (0.575-0.694
All ≥20 years, crude	0.806 (0.795-0.816)	0.835 (0.824-0.846)
All ≥20 years, age adjusted[a]	0.934 (0.930-0.939)	0.767 (0.750-0.783)
Relative risk of hospitalization of the unvaccinated (95% CI)		
20-39 years	19.8 (14.7-26.7)	5.0 (4.4-5.7)
39-57 years	18.9 (16.4-21.7)	4.8 (4.3-5.3)
≥58 years	12.5 (11.6-13.4)	2.8 (2.4-3.3)
All ≥20 years, crude	5.1 (4.9-5.4)	6.1 (5.7-6.5)
All ≥20 years, age adjusted[a]	15.3 (14.2-16.4)	4.3 (4.0-4.6)

[a]Mantel-Haenzel estimate.

Another metric for demonstrating vaccine effectiveness is by comparing the risk of being hospitalized between the unvaccinated and vaccinated, as reported in the second half of Table 2. These metrics may be more meaningful for laypeople. Table 2 shows that risk of hospitalization in the unvaccinated was 15.3 (95% CI 14.2-16.4) times higher than that in the fully vaccinated and 4.3 (95% CI 4.0-4.6) times higher than that in the partially vaccinated.

There were significant differences between the crude and age-adjusted estimates for the entire adult population (Table 2). Age was a significant confounder in these data. Older individuals had a much higher risk of being hospitalized and were more likely to be fully vaccinated than other adults. These two associations meant that for the all-age estimate, the crude VEH was substantially lower in the older adult group than in the other age groups and, thus, lower than its real magnitude, which was estimated by the simple method proposed by Mantel and Haenzel [11] in 1959 (ie, as a weighted average of

age-specific figures). The crude all-age VEH for full vaccination was 81% compared to 93% when the age was adjusted.

Sensitivity Analysis

Figure 2 summarizes the sensitivity of VEH estimates to possible errors in the population data used as input. Errors of plus or minus 1% in the population input would bias the VEH estimates by less than 0.01 except in partially vaccinated older adults, where a change of 0.05 would occur. Larger errors of plus or minus 5% in the population input would alter the VEH by 0.02 in the two younger groups and would strongly bias the estimate between 0.04 and 0.27 for the partially vaccinated. VEH estimates for older adults appear especially sensitive to errors in the population data, which originates from the very high vaccination coverage reached by this age group: approximately 90% fully and 3% partially vaccinated at the end of the study period. Small errors in population inputs substantially amplify the residual estimates of unvaccinated individuals when vaccine coverage is high.

Figure 2. Sensitivity of estimates of vaccine effectiveness against hospitalization to possible errors in the population number used as input.
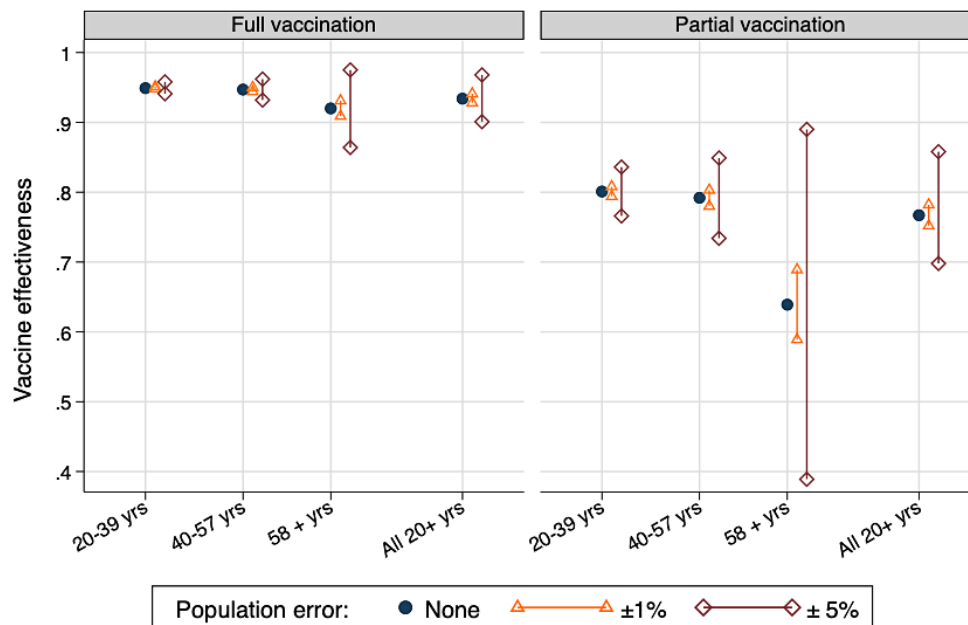
Discussion

Principal Findings

COVID-19 vaccine effectiveness to prevent severe illness, as identified by the prevalence of hospitalizations, is 93% for the complete vaccination scheme of 2 doses in the adult population of Costa Rica. Among the subgroup of adults aged ≥58 years, VEH was slightly lower (92%) than that in the other subgroups. The corresponding VEH estimates for 1 dose were 77% for all adults and 64% for the older subgroup. Costa Rica uses two COVID-19 vaccines, Pfizer-BioNTech (78% of the vaccines administered) and Oxford-AstraZeneca (22% of the vaccines administered) [2]. The estimates in this article largely reflect vaccine effectiveness against the Delta variant since it was the dominant variant in the country during the study period (INCIENSA, unpublished data).

The high VEH for the single dose showed a statistically significant decline in time trend by 0.01 or 0.02 per week in adults aged 20-57 years and 0.05 per week in the older age group. It is important to note that the decline in the VEH did not occur for full vaccination. If it was caused by the spread of the Delta variant or by depletion of the immunity provided by the vaccine, the decline should have also occurred among the fully vaccinated. A plausible explanation is that the partially vaccinated may have comprised two types of people: those who are in the group temporarily while waiting for the second shot and those who intentionally avoid the second shot and behave less carefully to avoid contagion. The VEH decline might reflect an increased share of the second subgroup as complete vaccination coverage approaches 100%.

Comparison With Prior Studies

This study's estimate of 93% VEH for 2 doses of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines is within

the 90%-98% range of previous real-world estimates obtained in Israel, Ontario, the United States, California, and Qatar [3-7]. Only the studies performed in California and Qatar reported that most of the sample population had the Delta variant, as reported in this study.

The 77% VEH for a single dose of the vaccines is also within the range of 70%-91% found by studies performed in Ontario, England, and Scotland [4,8,9]. However, these previous estimates predated the Delta variant. This Costa Rican estimate is thus the first study that has reported that the Delta variant did not substantially reduce the effectiveness of a single dose of either the Pfizer-BioNTech or Oxford-AstraZeneca vaccine to prevent hospitalization. Costa Rican adults aged ≥58 years received only the Pfizer-BioNTech vaccine, while the vaccine mix for the remaining adults was 77% Pfizer-BioNTech and 23% Oxford-AstraZeneca at the time of this study.

Strengths

A strength of this observational study is that it shows the effectiveness of COVID-19 vaccines in the real-world conditions of a middle-income country, which is beyond the hypercontrolled conditions of clinical trials. Further strengths include that this study reports on the vaccines' effectiveness after the Delta variant became dominant and on the dose-specific effectiveness of the vaccines.

The secondary analysis of existing aggregated data in this study is an inexpensive design that can be broadly used to produce quick estimates for timely monitoring of vaccine effectiveness.

Being a nationwide study based on the entire adult population, it is free of issues regarding sampling bias and random errors derived from small sample sizes.

The outcome variable used in this study, being hospitalized due to COVID-19–related conditions, is a definite count that is mostly free of classification errors. A threat to its validity as a measure of severe COVID-19 infections could occur if some people have poor access to hospital care. However, this is not the case in the universal health care system of Costa Rica.

The statistics of dose-specific vaccinated people are probably accurate since the sole provider of vaccines in the country digitally records real-time information of every single vaccine administered. The database for this information is also used for inventory control purposes and for providing digital vaccination certificates to the population. If there were widespread errors, they would certainly be noticed by these other uses of the data.

Limitations

This observational study has the well-known limitations of nonrandomized, nonblinded trials including selection biases,

such as the early vaccination of older people in Costa Rica (which biased the crude VEH estimates, as shown in this study), and other confounders such as the risk-taking behavior modification of some individuals after vaccination. The VEH estimates in this study should be interpreted as associations between vaccination status and hospitalization rather than the true causal effects of vaccination.

Being a study based on aggregated data, instead of microdata, it does not offer an opportunity to understand how differences at an individual level can contribute to VEH or can bias the VEH estimate. Potential errors derived from this limitation are sometimes called "ecological fallacy."

A more specific limitation of the method used in this study is that it requires high-quality data of the population count to obtain a valid estimate of the number of unvaccinated individuals. Errors in the population count affect the calculation of the number of people who have not been vaccinated, especially as the vaccination coverage approaches 100%, as is the case for older adults in Costa Rica. However, it must be noted that Costa Rica is considered to have accurate demographic data [14].

The lack of specific results for each brand of vaccine used in Costa Rica, as well as the lack of estimates of the vaccines' effectiveness at preventing COVID-19, may also be limitations of the interpretation of these study results.

Conclusions

The Costa Rican vaccination program, based on the Pfizer-BioNTech and Oxford-AstraZeneca vaccines, was highly effective at preventing COVID-19–related hospitalizations even after the Delta variant became dominant. Completing the 2-dose scheme clearly provides more protection than that provided by a single dose, and this result must always be the goal of vaccination policies. However, the data also show that even a single dose appears to provide some protection against the Delta variant, which is good news for people whose second dose of the Pfizer-BioNTech vaccine was postponed several weeks to more quickly increase the number of people who received a first dose.

Timely monitoring of vaccine effectiveness appears feasible with procedures that are analogous to those used in this study. It is important to continue the monitoring of vaccine effectiveness to detect eventual failures in the vaccination program and motivate the public by showing that vaccinations are having an impact.

Conflicts of Interest

None declared.

[XSL•FO]

RenderX

References

1. Our World in Data, COVID-19 dataset. GitHub. 2021. URL: https://raw.githubusercontent.com/owid/covid-19-data/master/public/data/owid-covid-data.csv [accessed 2022-05-10]

2. Vacunación contra COVID-19. Avance de vacunación por grupos de edad. CCSS. URL: https://www.ccss.sa.cr/web/coronavirus/vacunacion [accessed 2022-05-10]

3. Haas EJ, Angulo FJ, McLaughlin JM, Anis E, Singer SR, Khan F, et al. Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: an observational study using national surveillance data. Lancet 2021 May 15;397(10287):1819-1829 [FREE Full text] [doi: 10.1016/S0140-6736(21)00947-8] [Medline: 33964222]

4. Chung H, He S, Nasreen S, Sundaram M, Buchan S, Wilson S, Canadian Immunization Research Network (CIRN) Provincial Collaborative Network (PCN) Investigators. Effectiveness of BNT162b2 and mRNA-1273 covid-19 vaccines against symptomatic SARS-CoV-2 infection and severe covid-19 outcomes in Ontario, Canada: test negative design study. BMJ 2021 Aug 20;374:n1943 [FREE Full text] [doi: 10.1136/bmj.n1943] [Medline: 34417165]

5. Self WH, Tenforde MW, Rhoads JP, Gaglani M, Ginde AA, Douin DJ, et al. MMWR Morb Mortal Wkly Rep 2021 Sep 24;70(38):1337-1343 [FREE Full text] [doi: 10.15585/mmwr.mm7038e1] [Medline: 34555004]

6. Tartof SY, Slezak JM, Fischer H, Hong V, Ackerson BK, Ranasinghe ON, et al. Effectiveness of mRNA BNT162b2 COVID-19 vaccine up to 6 months in a large integrated health system in the USA: a retrospective cohort study. Lancet 2021 Oct 16;398(10309):1407-1416 [FREE Full text] [doi: 10.1016/S0140-6736(21)02183-8] [Medline: 34619098]

7. Tang P, Hasan MR, Chemaitelly H, Yassine HM, Benslimane FM, Al Khatib HA, et al. BNT162b2 and mRNA-1273 COVID-19 vaccine effectiveness against the SARS-CoV-2 Delta variant in Qatar. Nat Med 2021 Dec;27(12):2136-2143. [doi: 10.1038/s41591-021-01583-4] [Medline: 34728831]

8. Lopez Bernal J, Andrews N, Gower C, Robertson C, Stowe J, Tessier E, et al. Effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines on covid-19 related symptoms, hospital admissions, and mortality in older adults in England: test negative case-control study. BMJ 2021 May 13;373:n1088 [FREE Full text] [doi: 10.1136/bmj.n1088] [Medline: 33985964]

9. Vasileiou E, Simpson CR, Shi T, Kerr S, Agrawal U, Akbari A, et al. Interim findings from first-dose mass COVID-19 vaccination roll-out and COVID-19 hospital admissions in Scotland: a national prospective cohort study. Lancet 2021 May 01;397(10285):1646-1657 [FREE Full text] [doi: 10.1016/S0140-6736(21)00677-2] [Medline: 33901420]

10. Estimaciones y proyecciones de población por sexo y edad. 1950 - 2050. Instituto Nacional de Estadística y Censos (INEC). 2013. URL: https://www.inec.cr/sites/default/files/documentos/poblacion/estimaciones_y_proyecciones_de_poblacion/publicaciones/repoblacev1950-2050-01.pdf [accessed 2022-05-17]

11. Mantel N, Haenszel W. Statistical aspects of the analysis of data from retrospective studies of disease. Journal of the National Cancer Institute 1959;22(4):719-748. [doi: 10.1093/jnci/22.4.719]

12. Stata Statistical Software: Release 17. StataCorp. College Station, TX: StataCorp LLC; 2020. URL: https://www.stata.com/ [accessed 2022-05-10]

13. Rosero-Bixby L, Jiménez-Fontana P. Crónica de la pandemia de Covid-19 en Costa Rica. Programa Estado de la Nación (PEN), Repositorio Institucional CONARE. 2021. URL: https://tinyurl.com/mp5bmvwb [accessed 2022-05-10]

14. Glei D, Barbieri M, Santamaría-Ulloa C. Costa Rican mortality 1950 2013: An evaluation of data quality and trends compared with other countries. DemRes 2019 Apr 09;40:835-864. [doi: 10.4054/demres.2019.40.29]

Abbreviations

CCSS: Costa Rican Social Security Fund (Caja Costarricense de Seguro Social)
INCIENSA: Instituto Costarricense de Investigación y Enseñanza en Nutrición y Salud
INEC: National Institute of Statistics and Censuses (Instituto Nacional de Estadística y Censos)
RR: relative risk
VEH: vaccine effectiveness against hospitalization

XSL•FO

RenderX