

The impact of the Covid-19 vaccination policy in Mexico. A quasi-experimental effectiveness evaluation of a multi-vaccine strategy

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Abstract

Objective. To assess the impact of a vaccination campaign that administered five different technologies in a middle-income country with one of the largest Covid-19 epidemics. **Materials and methods.** Using data from Mexico's Epidemiological Surveillance System for Viral Respiratory Disease (Sisver) and the design of the vaccine policy in Mexico as a natural experiment, we applied difference-in-differences econometric methods to assess the strategy's effectiveness on transmission, hospitalizations, and mortality rates among adults 60 to 64 years old in Mexico between April and June 2021. **Results.** We estimated average effectiveness levels of 60.9% against confirmed cases of Covid-19. Vaccination also decreased hospitalizations and deaths by 62.7 and 62.6%, respectively. After adjusting for vaccination coverage, we found an impact of 79.1, 80.9, and 81.3% reduction in new cases, hospitalizations, and deaths among the vaccinated. **Conclusion.** Despite the significant progress in our knowledge of Covid-19 vaccination effectiveness, the available evidence relies mostly on experiences from high-income countries. This study contributes to the scientific literature of Covid-19 vaccination effectiveness in a middle-income country with a multi-vaccine scheme.

Keywords: Covid-19; vaccination; effectiveness; Mexico

Resumen

Objetivo. Evaluar el impacto de una campaña de vacunación que administró cinco tecnologías diferentes en un país de ingresos medios con una de las mayores epidemias de Covid-19. **Material y métodos.** Se utilizaron datos del Sistema de Vigilancia Epidemiológica de Enfermedades Respiratorias Virales (Sisver) de México y el diseño de la política de vacunación en México como un experimento natural. Se aplicaron métodos econométricos de diferencia en diferencias para evaluar la efectividad que tuvo la estrategia en las tasas de transmisión, hospitalizaciones y mortalidad entre adultos de 60 a 64 años en México entre abril y junio de 2021. **Resultados.** Se estimaron niveles promedio de efectividad de 60.9% contra casos confirmados de Covid-19. La vacunación también disminuyó, las hospitalizaciones y muertes en 62.7 y 62.6%, respectivamente. Después de ajustar la cobertura de vacunación, se encontró una reducción de 79.1, 80.9 y 81.3% de nuevos casos, hospitalizaciones y muertes entre las personas vacunadas. **Conclusión.** A pesar de los importantes avances en el conocimiento de la eficacia de la vacunación con Covid-19, la evidencia disponible se basa principalmente en experiencias de países de ingresos altos. Este estudio contribuye a la literatura científica sobre la efectividad de la vacunación con Covid-19 en un país de ingresos medios con esquemas de vacunación múltiple.

Palabras clave: Covid-19; vacunación; eficacia; México

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During 2021, the second year of the pandemic, Covid-19 vaccination coverage advanced rapidly in high-income countries. Early analyses showed that vaccines prevent infection and reduce hospitalization and deaths.¹⁻³ At the population level, a 2022 World Health Organization (WHO) report summarized the results of 18 observational studies on the effectiveness of the Covid-19 vaccines worldwide. Overall, evaluations found a 65 to 95% reduction in transmission (cases), 57 to 97% in hospitalizations, and 86 to 96% in mortality.⁴ Yet, the WHO estimates were based on mRNA-1273 (Moderna), BNT162b2 (Pfizer-BioNTech), and ChAdOx1-S (Oxford-AstraZeneca), the dominant vaccines in high-income countries.

On the other hand, middle- and low-income countries struggled to acquire vaccines, relying on multiple brands and platforms depending on affordability and availability. For example, Mexico started vaccinating health personnel in December 2021 using BNT162b2. In March 2021, the population vaccination campaign started vaccinating people 60 years and older, followed by the rest of the population by decade, downwardly. Vaccine types were allocated by municipality and age group and included BNT162b2, ChAdOx1-S, CoronaVac (Sinovac), Convidecia (CanSino), and Sputnik V. Recent studies suggest that the effectiveness of the vaccines could be different, yielding an unknown collective effectiveness.^{3,5-9}

In this paper, we used the design of the vaccination policy in Mexico as a natural experiment to assess the strategy's effectiveness. Specifically, we compare the transmission, hospitalization, and mortality rates among adults 60 to 64 to those observed in adults 55 to 59 between April and June 2021. The programmatic design of the vaccination campaign in Mexico provides exogenous variation in vaccine coverage independent of population characteristics other than age. We used this source of variation to estimate the impact of the strategy, with a difference-in-differences approach coupled with an event-study analysis to assess the impact of the Covid-19 vaccination policy.

Materials and methods

Natural experiment setting

The Mexican vaccination campaign for people 60 years old and older was undertaken from February to May 2021. State governments phased the strategy at the municipality level, and most eligible people within age groups at each municipality received the same type of vaccine (supplementary table S1).¹⁰ The decision on which vaccine to apply in each municipality

was based mainly on availability. However, since local governments used different types of vaccines across neighboring municipalities, anecdotal information suggests that an unknown - albeit negligible - proportion of the population traveled across municipalities to gain early access or to receive a different vaccine than that used in their localities.

The vaccination of the following eligible group - 50 to 59 years old - started 12 weeks after those 60 and older, between May and July 2021. We took advantage of the eligibility criteria and the fact that people closer in age are more comparable concerning their risk of infection, hospitalization, and death. Thus, we defined the intervention group as individuals 60-64 years old and the comparison group as individuals 55-59. To further improve comparability among treatment and control groups, we collapsed vaccination coverage data and health outcomes at the state level and compared individuals within the same state, which ensures that contextual factors are the same for both groups.

Data and variables

Infection, hospitalization, and deaths

We used data from Mexico's Epidemiological Surveillance System for Viral Respiratory Disease (Sisver, in Spanish). Sisver contains data on all individuals suspected of Covid-19 infection, i.e., with at least one primary symptom (cough, fever, dyspnea, or headache) and a minor symptom (myalgia, arthralgia, odynophagia, chills, chest pain, rhinorrhea, anosmia, dysgeusia, conjunctivitis).¹¹ Medical care units uploaded daily individual-level data linked to the Covid-19 tests performed and their results. The dataset contains Covid-19 diagnosis, symptoms, hospitalizations, deaths, self-reported comorbidities, sex, and age. We retrieved data from all patients with confirmed Covid-19 diagnoses between January 2020 and August 2021. We estimated rates of cases, hospitalizations, and mortality per 100 000 inhabitants, using population data from the National Population Council (Conapo, in Spanish).

Vaccination coverage at the municipal level

We used administrative data from the National Welfare Institute, in charge of the Covid-19 vaccination rollout, on vaccination coverage at the municipal level. The dataset included the number of doses applied daily in each municipality by age groups (60 and older, 50-59, 40-49, 30-39, and the rest of the population). Using population estimates from Conapo, we estimated the proportion of immunized people with full and partial

vaccination schemes (1 dose only). We aggregated the data set at the state level for the analyses and organized it chronologically by two-week periods.

Statistical analysis

Specifically, we used a difference-in-differences (DiD) identification strategy, a quasi-experimental method commonly used to estimate the causal effects of policies that affect different groups at different times.¹² This econometric approach compares the outcome variable's trends among four "objects" or groups; three of them in the absence of the intervention (the treatment group before, the comparison group before, and the comparison group after) and one in the presence of the intervention (the treatment group after).

For this strategy to be valid, three key assumptions must hold. The most important is that before the intervention, the trajectories of the outcomes must be similar between the intervention and comparison groups. Second, the composition of the two groups must be stable over time - before and after the intervention. Third, there should be no "spillover" effects, i.e., the intervention group receiving the vaccine should not change the trajectory of the outcomes in the comparison group.

We tested the double differences evaluation strategy's main assumption by comparing outcomes trends between control and treatment groups and found no differences in the observed trends before the implementation of the vaccination campaign. Specifically, we tested the comparability of outcome trends between 60-64-year-olds and 55-59 from April 22, 2020, to March 12, 2021. Then, we empirically determined the time window for estimating the vaccine effectiveness using "event study" modeling. Briefly, the event study analysis identifies the moment in which vaccine coverage in the intervention group was high enough to observe changes in the outcomes, and the coverage of the comparison group was low enough to remain valid as a control group.¹³ Event study analyses were conducted under the following specification:

$$Y_{Et} = \sum_{\omega=55\omega=0}^{20} \square \theta_{\omega} Age \times 1 (WEP = \omega) + \delta Age + \phi Sex$$

Where Y_{Et} represents the outcome in time t (two-week periods). Age is a dummy variable equal to 1 for the 60-64 years group and 0 for the 55-59 group. Sex indicates the sex of the participant, and WEP represents dichotomous variables for each two-week period to control for the trends of the epidemic in the analysis period.

We considered that the three outcomes naturally occur successively and allowed for two-week time lags

between them. This assumption was confirmed using event study models. Thus, to estimate the effect of the vaccines, we compared the changes in cases between March 12 and May 7, hospitalizations between March 12 and May 21, and deaths between March 12 and June 4, 2021. Within the analysis period, we observed 144 763 Covid-19 cases, 56 220 hospitalizations, and 32 235 deaths among adults 60-64 years old. The corresponding figures among the population 55-59 were 190 322, 55 534, and 27 800.

Once the specific dates were determined using the event study analysis, we used an OLS approach to estimate a difference-in-difference model under the following model specification:

$$Y_{Et} = \beta_0 + \lambda Vac_t + \delta Age + \beta_1 Vac_t * Age + \phi Sex + \lambda WEP + \epsilon_{Et}$$

Where Y_{Et} represents the outcome of interest, Vac_t is a dummy variable indicating the before (=0), and after (=1) periods (determined by the two weeks when coverage among the intervention group reached 23.5%) age is a dummy variable equal to 1 for the 60-64 years group, and 0 for the 55-59 group. Sex indicates the sex of the participant, and WEP indicates dichotomous variables every two weeks in the analysis period. We tested different specifications changing the control variables to assess the robustness of our results. In our primary estimations, we used the logarithm of the outcomes to interpret the results in percentage changes.

Finally, we tested the robustness of our strategy using a falsification test in which we explored the impact of Covid-19 vaccination on hospitalizations and mortality among Covid-19-negative people in Sisver.

Results

Mexico has over 4.8 million people between 60 and 64 years of age and 5.9 million between 55 and 59. In the group 60-64, 422 municipalities in the country used Pfizer, 662 AstraZeneca, 790 Sinovac, and 502 Sputnik V. For the group 55 to 59, 545 municipalities used Pfizer, 524 AstraZeneca, 437 Sinovac, and 870 Sputnik V.

Figure 1 shows the trends in new Covid-19 cases, hospitalizations, and deaths before and after the vaccination campaign among the intervention and comparison groups. This figure also shows vaccination coverage in the analysis period. Before vaccination, the intervention and comparison groups exhibited similar trends in new cases, hospitalizations, and death rates, as required by the DiD strategy. After the coverage of the intervention group reached 23.5%, the curves declined more rapidly among the vaccinated than for the comparison group.

The “event study” models formally test for differences in trends between intervention and comparison groups biweekly throughout the analysis period. We found no statistically significant differences in the rate trends of new cases, hospitalizations, or deaths before the Covid-19 vaccine program in Mexico. However, we observed a significant decline in the three outcomes once the vaccination coverage reached 23.5% in the intervention group. The maximum observed impact within the evaluation period was a reduction of 60% (95% CI -0.75,0.45), 61% (95% CI -0.86,0.37), and 59% (95% CI -0.89,0.30) in rates of cases, hospitalizations, and deaths respectively (figure 2).

Table I shows the results of the multivariate DiD models. Specifications I to IV used variations in the control variables sex, vaccination coverage, and time. All specifications yielded consistent results. We observed average treatment effectiveness (ATE) of 60.9% (95% CI -0.92,-0.30) in new cases, 62.7% (95% CI -0.92,-

0.33) in hospitalizations, and 62.6% (95% CI -0.94,-0.31) in deaths.

Table II presents the ATE interpreted in two ways. The coefficients of the DiD models (column I) estimate the average decline in cases, hospitalizations, and deaths, among the entire population of 60-64 years old, compared to those 55-59. However, the maximum coverage reached among the intervention group in the analysis period was 78%. Therefore, we adjust the estimates by coverage in column II and present the ATE among the vaccinated. Thus, we found an impact of 79.1, 80.9, and 81.3% reduction in cases, hospitalizations, and deaths among the vaccinated (column II). Such levels of effectiveness imply that the Covid-19 vaccination strategy averted 274 507 cases, 141 658 hospitalizations, and 92 808 deaths among the 60+ age group within the analysis period between March 12 and June 4, 2021. Additional robustness and sensitivity analysis can be found in the supplementary material.¹⁰

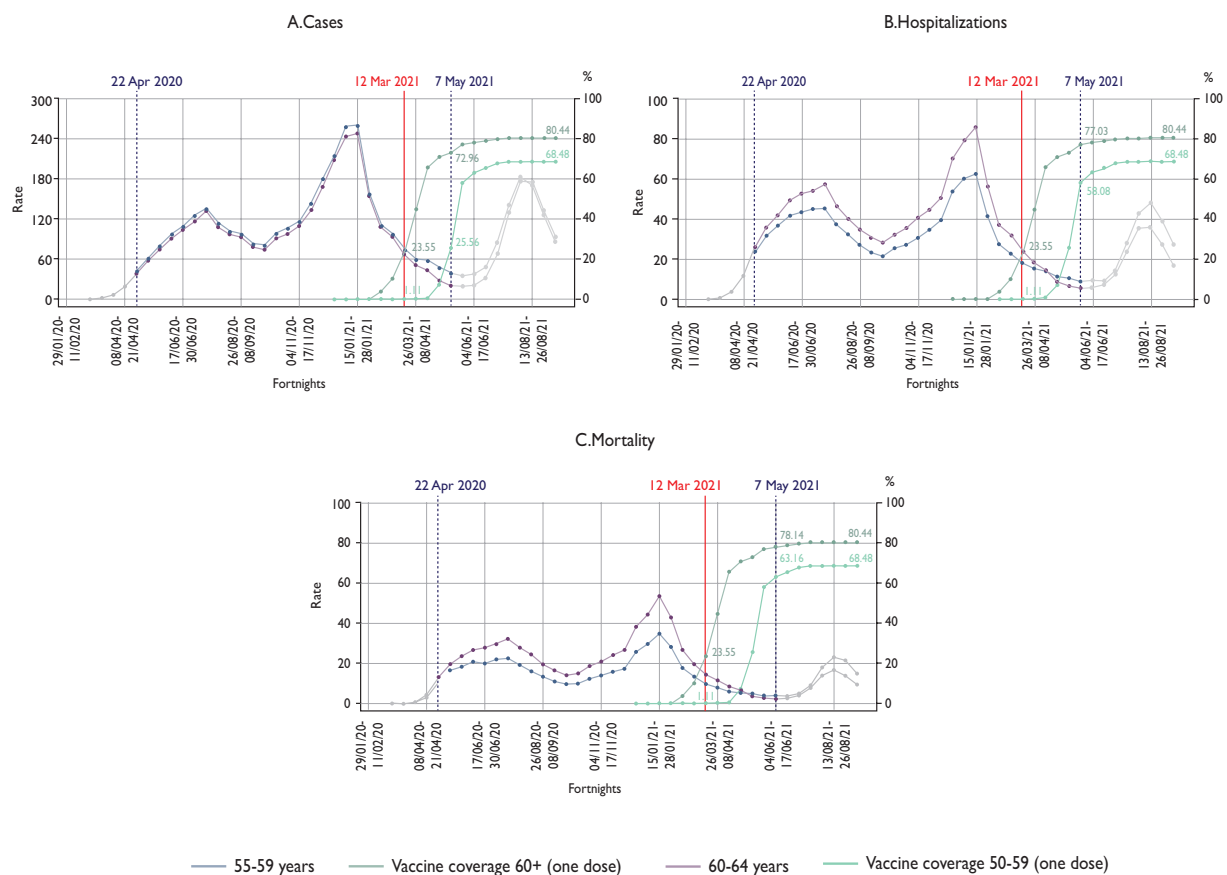


FIGURE 1. TRENDS IN RATES OF COVID-19 CASES, HOSPITALIZATIONS, AND DEATHS PER 100 000 POPULATION, AMONG 60-64 AND 55-59 ADULTS, MEXICO’S EPIDEMIOLOGICAL SURVEILLANCE SYSTEM FOR VIRAL RESPIRATORY DISEASE (SISVER). 2021

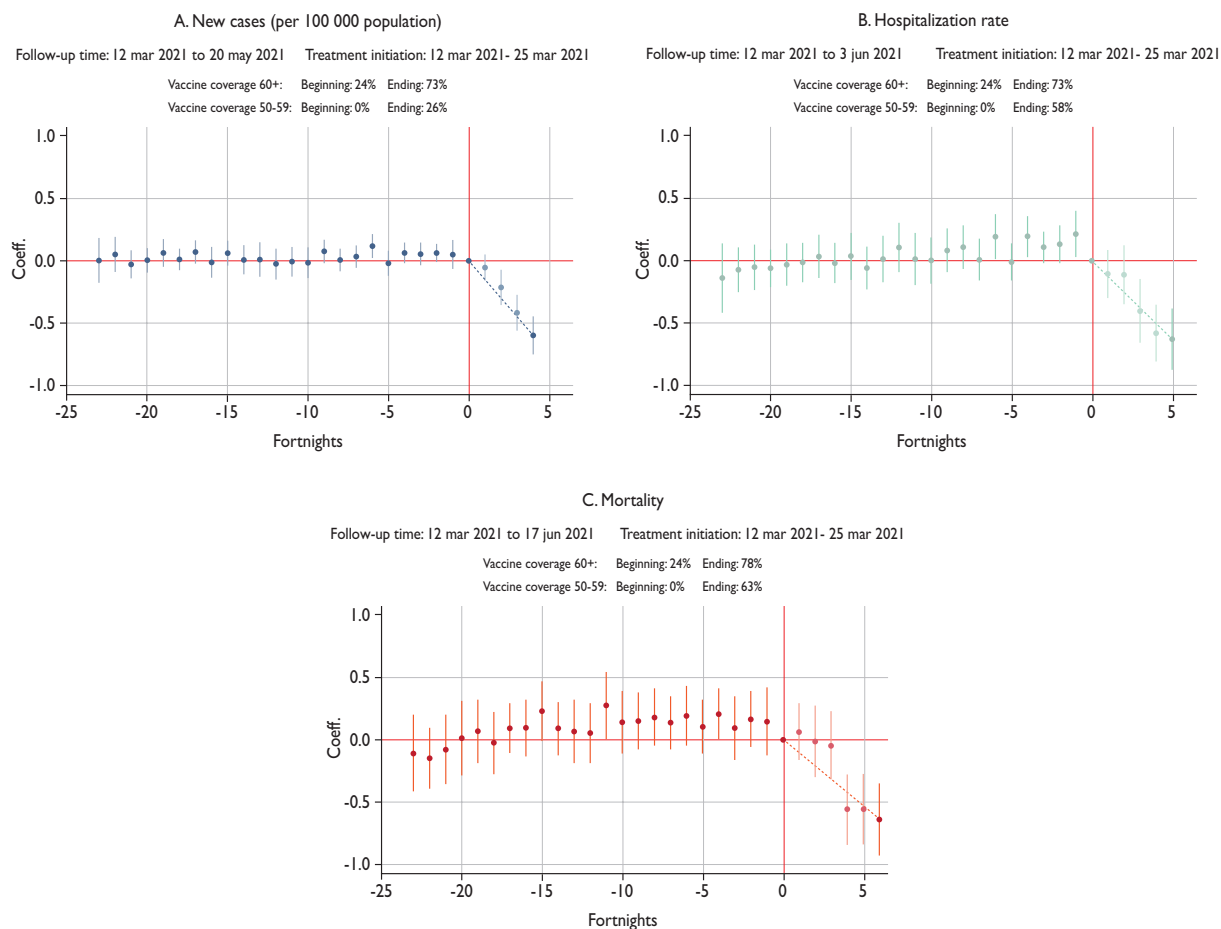


FIGURE 2. EVENT STUDY MODELS FOR CASES, HOSPITALIZATIONS, AND DEATHS PER 100 000 POPULATION, MEXICO'S EPIDEMIOLOGICAL SURVEILLANCE SYSTEM FOR VIRAL RESPIRATORY DISEASE (SISVER). 2021

Table I
AVERAGE TREATMENT EFFECT (ATE) OF COVID-19 VACCINATION ON CASES, HOSPITALIZATIONS, AND DEATHS. MEXICO 2020-2021

	Specification			
	I	II	III	IV
Panel A. Cases				
ATE	-0.608*	-0.606*	-0.599*	-0.609*
	(-0.93,-0.28)	(-0.93,-0.28)	(-0.92,-0.28)	(-0.92,-0.30)
Panel B. Hospitalizations				
ATE	-0.643*	-0.637*	-0.633*	-0.627*
	(-0.95,-0.33)	(-0.93,-0.34)	(-0.93,-0.34)	(-0.92,-0.33)
Panel C. Mortality				
ATE	-0.649*	-0.642*	-0.643*	-0.626*
	(-0.99,-0.31)	(-0.96,-0.32)	(-0.96,-0.32)	(-0.94,-0.31)
Controls				
Sex	No	Yes	Yes	Yes
Coverage	No	No	Yes	Yes
Week	No	No	No	Yes

* p<0.01

Table II
AVERAGE TREATMENT EFFECTS (ATE) OF COVID-19 VACCINATION OBSERVED ON RATES OF CASES, HOSPITALIZATIONS, AND DEATHS. MEXICO 2020-2021

	I	II	III
	Average treatment effectiveness	Average treatment effectiveness among vaccinated %	Averted cases/hospitalizations/deaths within the analysis period
Panel A. Cases			
Effectiveness	-0.609*	79.1	274 507
	(-0.92,-0.30)		
Panel B. Hospitalization			
Effectiveness	-0.627*	80.9	141 658
	(-0.92,-0.33)		
Panel C. Mortality			
Effectiveness	-0.626*	81.3	92 808
	(-0.94,-0.31)		

* p<0.01

Discussion

This study provides evidence of the effectiveness of the Covid-19 vaccination strategy against transmission, hospital admissions, and mortality among adults 60 years old and older in Mexico. We estimated average effectiveness levels of 60.9% against confirmed cases of Covid-19. Vaccination also decreased hospitalizations and deaths by 62.7 and 62.6%, respectively. After adjusting for vaccination coverage, the average treatment effect on the vaccinated was 79.1, 80.9, and 81.3% on new cases, hospitalizations, and deaths. These figures translate into roughly 274 500 cases, 141 600 hospitalizations, and 92 800 deaths averted among the 60+ age group within the analysis period of almost three months.

Former studies assessed the impact of Covid-19 vaccines in Latin America. Previously, researchers found a 65% reduction in cases, 87.5% in hospitalizations, and 86.3% in deaths in Chile.¹ Another study estimated a reduction of 69.9% in hospitalizations, 79.4% in deaths after hospitalization, and 74.5% in death without hospitalization in Colombia.¹⁴

Unlike estimates from Chile and Colombia, our paper relies on quasi-experimental methods to assess the population-level impact of a national strategy. Like the program in Colombia, the strategy in Mexico administered multiple vaccines, including some not recommended by WHO at the time of the campaign (CanSino and Sputnik V).

Our results are consistent with previous studies on the population effectiveness of the Covid-19 vaccine. For example, one study in the United Kingdom found maximum effectiveness against symptomatic cases of 61 and 73% for the Pfizer-BioNTech and the Oxford-AstraZeneca vaccine, respectively. However, the same study showed a reduction in hospital admissions in the range of 37-43%, and the effectiveness against death after 14 days of vaccination was 51%.³ Overall, according to the "Landscape of observational study designs on the effectiveness of Covid-19 vaccination" by WHO,⁴ the effectiveness of the Covid-19 vaccine ranges from 65.9% (Chile) to 95.3% (Israel) in cases averted, 57% (UK) -97.2% (Israel) in hospitalizations, and 86.3% (Chile) -96.7% (Israel) in deaths.

Although most previous studies used cohort or case-control study designs, comparing vaccinated to unvaccinated people, other investigations used econometric, quasi-experimental approaches. For example, in the United States, McNamara and colleagues¹⁵ used a DiD approach to estimate the national-level impact of the initial phases of the US Covid-19 vaccination program on Covid-19 cases, emergency department visits, hospital admissions, and deaths among adults

aged 65 years and older. They found a 53% decline in the Covid-19 incidence ratio among adults aged 65 to 74 and a 62% reduction among those 75 years and older. Hospital admissions declined by 39 and 60%, respectively. However, the authors found limited evidence of the effectiveness against mortality -41 and 30%.¹⁵

Our study benefits from using a national public dataset (Sisver) containing all confirmed Covid-19 cases, hospitalizations, and deaths since the beginning of the epidemic in Mexico. Although it does not include undiagnosed cases or unconfirmed Covid-19 deaths, this rich source provides a large sample size covering Mexico's entire territory and the vast majority of Covid-19 cases. Our analyses applied regression models accounting for the trends before vaccine implementation in the country. Employing "event study" analyses, we formally validated our comparison group by statistically testing the chief assumptions of the DiD identification strategy.

Readers of our findings should interpret them in light of some limitations. Because we used a quasi-experimental approach, we identified the analysis period empirically. We relied on a relatively small window of time to measure the impact of the vaccination program, determined by the period within which we could observe statistically significant differences in outcome trends between the intervention and comparison groups. Two conditions had to be met simultaneously: high enough coverage among the former for the effects of the vaccine to be measurable and low enough coverage among the latter for the comparison group to remain valid as a counterfactual. This limitation most likely resulted in an underestimation of the vaccine's effectiveness.

One important implication of our study design is that the evaluation timeframe we used ended at the same time for the three outcomes - likely leading to underestimating the impact of the vaccination program on hospitalizations and deaths, since these events follow infections chronologically. It also probably underestimates each impact differently - likely, lower bias in hospitalizations than deaths.

Secondly, we cannot assess to what extent reductions in the number of cases in the 55-59 age group are associated with increased vaccination coverage among those 60+. i.e., we cannot rule out spillover effects, by which vaccination among the treatment group might have prevented cases among the comparison group. We do not have any evidence suggesting that this might have been significant; however, it would also lead to underestimating the vaccine impact.

Our approach also implies that we did not measure individual behaviors that might have changed differently among age groups over time, which affected the

likelihood of Covid-19 infection. It is uncertain to what extent this could have happened. However, given the short time we analyzed, it is unlikely to result in a significant bias in our results, even if it did. Finally, results from this study cannot be extrapolated to the current context in which several variants of SARS-CoV-2 coexist.

Despite significant progress in our knowledge of Covid-19 vaccination effectiveness, the available evidence overwhelmingly relies on experiences from rich countries. Multiple and complex factors explain the gap between randomized clinical trial efficacy and real-world effectiveness. This study contributes to the scientific literature by rigorously assessing the impact of a vaccination campaign that administered five different technologies in a middle-income country with one of the largest Covid-19 epidemics.

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Declaration of conflict of interests. The authors declare that they have no conflict of interests.

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