The Omicron wave in Mexico: vaccine protection against progression to severe Covid-19 in SARS-CoV-2-infected workers

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Abstract

Objective. To assess the effectiveness of seven Covid-19 vaccines in preventing disease progression (DP) using data from national private sector workers during the Omicron wave in Mexico from January 2 to March 5, 2022. **Materials and methods.** This study employed an administrative retrospective cohort design, analyzing DP (hospitalization or death due to respiratory disease) among workers who filed a respiratory short-term disability claim and tested positive for SARS-CoV-2. Risk ratios (RRadj) were estimated using Poisson regression models adjusted for various factors. **Results.** Vaccinated individuals had a lower risk of hospitalization and death compared with unvaccinated individuals. The overall RRadj for hospitalization and death were 0.36 (95%CI 0.32, 0.41) and 0.24 (0.17, 0.33), respectively. When evaluating

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Resumen

Objetivo. Evaluar la protección de siete vacunas Covid-19 contra la progresión de la enfermedad (PE) utilizando datos de trabajadores del sector privado durante el pico de transmisión Omicron del 2 de enero al 5 de marzo de 2022 en México. **Material y métodos.** Cohorte administrativa retrospectiva, analizando PE (hospitalización o muerte por enfermedad respiratoria) entre trabajadores que registraron una incapacidad temporal de trabajo por enfermedad respiratoria y fueron positivos a SARS-CoV-2. Se estimaron razones de riesgo (RRadj) mediante modelos de regresión de Poisson ajustados. **Resultados.** Los individuos vacunados tuvieron menor riesgo de hospitalización y muerte en comparación con los no vacunados. Los RRadj globales de hospitalización y muerte fueron 0.36 (IC95% 0.32,0.41) y 0.24 (0.17,0.33),

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vaccines individually, the RRadj for hospitalization were as follows Pfizer BioNTech 0.27 (95%CI 0.22, 0.33), Moderna 0.29 (95%CI 0.15, 0.57), Sinovac 0.32 (95%CI 0.25, 0.41), AstraZeneca 0.39 (95%CI 0.34, 0.46), Sputnik 0.39 (95%CI 0.28, 0.53), CanSino 0.41 (95%CI 0.24, 0.7), and Janssen 0.53 (95%CI 0.39, 0.72). The RRadj for death were as follows: Pfizer BioNTech 0.12 (95%CI 0.07, 0.19), Sputnik 0.15 (95%CI 0.06, 0.38), Sinovac 0.29 (95%CI 0.16, 0.53), AstraZeneca 0.30 (95%CI 0.20, 0.44), CanSino 0.38 (95%CI 0.1, 1.4), and Janssen 0.50 (95%CI 0.26, 0.97). **Conclusion.** Covid-19 vaccines significantly reduced the risk of severe disease during the Omicron wave in Mexico.

Keywords: Covid-19; Omicron (B.1.1.529); vaccine protection; workers; Mexico

respectivamente. Por vacuna, RRadj de hospitalización: Pfizer BioNTech 0.27 (IC95% 0.22,0.33), Moderna 0.29 (IC95% 0.15,0.57), Sinovac 0.32 (IC95% 0.25,0.41), AstraZeneca 0.39 (IC95% 0.34,0.46), Sputnik 0.39 (IC95% 0.28,0.53), CanSino 0.41 (IC95% 0.24,0.7), Janssen 0.53 (IC95% 0.39,0.72). RRadj de muerte: Pfizer BioNTech 0.12 (IC95% 0.07,0.19), Sputnik 0.15 (IC95% 0.06,0.38), Sinovac 0.29 (IC95% 0.16,0.53), AstraZeneca 0.30 (IC95% 0.20,0.44), CanSino 0.38 (IC95% 0.1,1.4), Janssen 0.50 (IC95% 0.26,0.97). **Conclusión.** Las vacunas Covid-19 redujeron significativamente el riesgo de enfermedad grave durante el pico de transmisión Omicron en México.

Palabras clave: Covid-19; Omicron (B.1.1.529); protección vacunal; trabajadores; Mexico

While the effectiveness of products like the AstraZeneca, Pfizer, and Moderna Covid-19 vaccines is well documented in high-income countries, little is known about effectiveness of other Covid-19 vaccines and schedules against new variants, especially from low- and middle-income countries, which often used understudied vaccine products.[1]

SARS-CoV-2, the cause of the current coronavirus disease (Covid-19) pandemic, has had profound socioeconomic and health impacts across Latin America.[2] Globally, this region had one of the highest numbers of reported Covid-19 deaths.[3] Mexico suffered a grievous toll, with more than 5.6 million laboratory-confirmed Covid-19 cases and 660 000 excess deaths during 2020-2021.[4,5]

To mitigate Covid-19 impact, the Mexican government approved 10 Covid-19 vaccine products under emergency-use authorization, although only seven were included in the National Vaccination Strategy that reached 81.9 million Mexicans aged ≥18 years during December 2020 to December 2021.[6]

The SARS-CoV-2 B.1.1.529 variant (Omicron) emerged in Mexico during November 2021 and by the end of December 2021, it accounted for 88% of sequenced lineages.[7] Before Omicron was detected in Mexico, population immunity against Covid-19 was high, and a significant majority of adults likely to have protective immunity through infection, reinfection, or vaccination. This is suggested by the high Covid-19-related mortality observed during 2020-2021[4,5] since mortality is linked to the percentage of the population infected on one side, on the other side, by three national seroprevalence surveys that documented an increasing prevalence of SARS-CoV-2 antibodies: 26% in November 2020,[8,9] 33.5% in December 2020,[10] and 74% in November 2021.[11] An additional seroprevalence study conducted in December 2021 in a random sample of essential private-sector workers showed a 96% seroprevalence of SARS-CoV-2 antibodies.[12] Despite such high seroprevalence, emerging data from South Africa and the UK suggested that prior population immunity to previous SARS-CoV-2 variants might not effectively protect against the Omicron variant.[13,14]

In Mexico, by law employers in the private sector must enroll employees to the Mexican Institute of Social Security (IMSS) for the provision of health insurance. Through IMSS, workers have access to medical care based on need and free at the point of delivery at IMSS hospitals and medical offices across the country, as well as short-term disability pay (sick leave pay) that protect workers to take time off for health need, among other benefits. Within IMSS, all SARS-CoV-2 tests, Covid-19-related diagnoses, hospitalizations, sick-leave compensation, and deaths are registered. By linking these data, we aimed to describe the impact of Omicron on the Mexican private-sector workforce and to assess the real-world effect of complete vaccination, with either of seven authorized vaccines, on the risk of progression to severe Covid-19 (hospitalization or death) during the Omicron wave.

Materials and methods

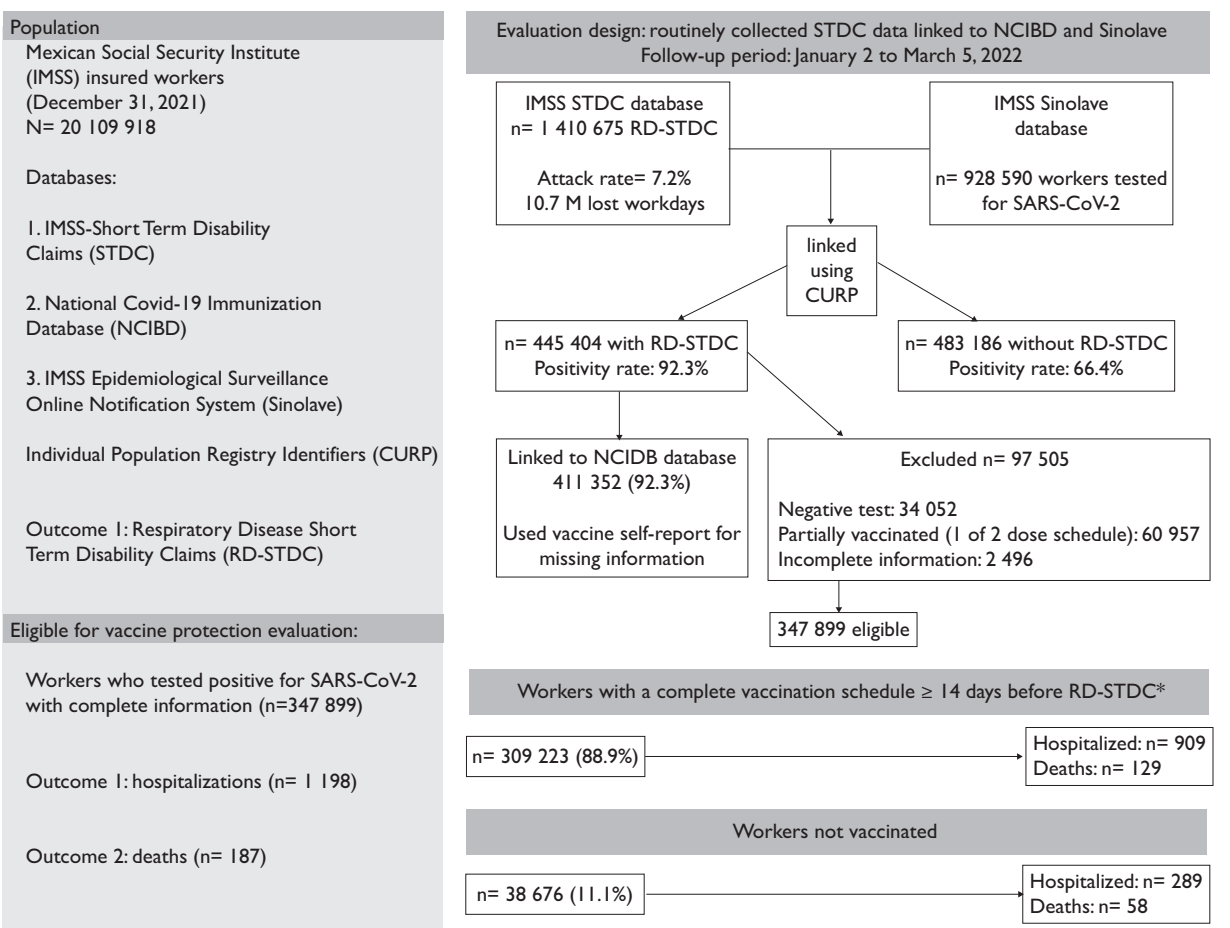
Population identification

The evaluation population comprises 1 410 675 of the 20.1 million workers from the Mexican private sector that were insured by IMSS (December 31, 2021) and filed for a short-term disability claim (STDC) for respiratory disease (RD-STDC) between January 2 and March 5, 2022.

In Mexico, population access to health care is segmented and fragmented. In this context, IMSS provides medical care and social security benefits to retired work-

ers and to registered salaried workers (≥16 year-old) from the private sector and to their families, through a national network of 1 530 primary health care units and 251 secondary care and 25 tertiary care hospitals nationwide. Among other social security benefits, active workers have access to universal temporary disease/injury protection for workers, including a subsidy for paid sick leave. To be eligible for paid sick leave, workers must have an IMSS physician authorization that includes a diagnosis and the number of authorized days, which is registered and coded using the International Classification of Disease Codes (ICD)-10. This authorization is used to notify employers and provide the wage replacement (60% of registered salary starting at day-4 if not work related or 100% of wage starting day-1 if work related). Depending on the cause, sick leave is registered during the first days after onset of symptoms causing work impairment and prompting the visit to an IMSS medical facility. Our data shows that for Covid-19 there were an average of 1.8 days (IQR: 1-3 days) between symptoms occurrence and STDC authorization. All IMSS-authorized STDC are registered starting from day 1 of authorization.

To identify evaluation participants (figure 1), using workers' Individual Population Registry Identifiers (*Clave Única de Registro de Población*, CURP, in Spanish), we first selected all respiratory-disease STDCs (RD-STDCs) authorized from January 2 to March 5, 2022 (n= 1 410 675) from the IMSS STDC database under specific ICD-10: Covid-19 [U070, U071, U072, U07E, U07S, B342, B972], acute respiratory diseases [J01, J04-J06, J20, J21], influenza [J10, J11], pneumonia [J12-J18], and other [J029, J00X, J02X, J039, J22X].[15,16] We then linked the CURP to the IMSS Epidemiological Surveillance Online Notification System (*Sistema de Notificación en Línea para la Vigilancia Epidemiológica*, Sinolave, in Spanish) database



* Complete vaccination for seven vaccines of one dose (Ad26.COV2.S or Ad5-nCoV) or two doses (ChAdOxInCoV-19, BNT162b2, CoronaVac, SputnikV, Spikevax)

FIGURE 1. POPULATION AND DATA SOURCE DESCRIPTION

to identify workers with a SARS-CoV-2 test and their information (i.e., sex, age, salary group, state of residency), date of RD-STDC authorization, previous RD-STDCs during 2020-2021, and ICD10 diagnosis (*n*= 928 590). Thirty-one percent of workers with a RD-STDC were tested for SARS-CoV-2 (1.7% RT-PCR and 98.3% antigen tests) at IMSS facilities; 92.3% tested positive for SARS-CoV-2. After excluding those who tested negative (*n*= 34 052), were partially vaccinated (i.e. 1 of 2 doses vaccine schedule *n*= 60 957) or had incomplete information (*n*= 2 496), *n*= 347 899 (70.4%) were included in the cohort to assess the protective effect of a complete vaccination schedule (i.e. 1 or 2 dose) against SARS-CoV-2 in preventing Covid-19-associated hospitalization and death. Finally, we linked these workers to the National Covid-19 Immunization Database- NCIDB (n= 411 352). The NCIDB was used as the primary source for Covid-19 vaccination information and Sinolave (self-reported information) as the secondary source. The NCIDB registered only the primary series of Covid-19 vaccines administered in Mexico, no booster information was available at the time of the study. For our analyses, the Ministry of Health provided NCIDB vaccination information for IMSS registered workers that filed an RD-STDC, which included vaccine product receipt, number of doses received, and dates of vaccination. If information was unavailable in NCIDB, we used self-reported vaccination status information from Sinolave.

We considered workers vaccinated if they had received the second of a two-dose Covid-19 vaccine series or a single dose of a one-dose product ≥14 days before a positive SARS-CoV-2 test result. Two-dose products included AstraZeneca (ChAdOx1nCoV-19), Pfizer BioNTech (BNT162b2), Sinovac (CoronaVac), Sputnik (Sputnik V), and Moderna (Spikevax); one-dose products were Janssen (JNJ-78436735) and CanSino (Ad5-nCoV). Workers without documented receipt of a Covid-19 vaccine in NCIDB or Sinolave before the test date were considered unvaccinated.

Sinolave contains individual-level data from all Covid-19 tests (polymerase chain reaction [PCR] or antigen detection) performed within IMSS testing sites and medical facilities, including testing dates, results, and self-reported information on Covid-19 symptoms, for some chronic comorbidities, and for Covid-19 vaccination (self-reported information was used to reclassify those workers not found in the vaccination registry). Although home and pharmacy testing were available, only tests performed at IMSS were accepted as valid at the IMSS clinics. Sinolave also has real-time information about hospitalizations and deaths associated with Covid-19 that occurred within IMSS. Hospitalizations and deaths that occurred outside IMSS medical facilities were not recorded or included in this study. From Sinolave, we retrieved information for *n*= 928 590 workers with SARS-CoV-2 laboratory testing information (RT-PCR or rapid antigen, test dates, results). We then extracted information from those workers that had a RD-STDC (*n*= 445 404) for hospitalizations, deaths, self-reported comorbidities (i.e., obesity, diabetes mellitus, chronic obstructive pulmonary disease, human immunodeficiency virus, hypertension, cardiovascular disease, asthma, chronic kidney disease, hepatic disease, and neurologic disease), and self-reported history of vaccination (unvaccinated or vaccinated: vaccine brand, doses received, and immunization dates). Hospitalization or deaths for evaluation participants with an RD-STDC and a positive SARS-CoV-2 result were attributed to Covid-19. These events had to meet two criteria 1) date of SARS-CoV-2 testing was between two days before and until 14 days after symptoms onset, and 2) the start of the RD-STDC was between five days before and 10 days after symptoms onset.

Statistical analyses

First, we described the RD-STDC Omicron outbreak at population level estimating the RD-STDC attack rate (AR) during Omicron's wave, and compared this estimate to previous RD-STDC AR observed during Mexico's Alpha, Beta, Kappa and Delta waves. Variant proportion was obtained through the Global Initiative on Sharing All Influenza Data (GISAID) initiative.[17,18] We used the total amount of authorized days of absence in the RD-STDC to estimate the lost work days during the Omicron wave.

Workers who filed an RD-STDC were eligible for the Omicron vaccine protection analyses if they had a positive test result (PCR or antigen) with a specimen collection date between January 2 and March 5, 2022. We retrieved information on prior RD-STDC during 2020 and 2021 and included this information as a surrogate of workers having a history of Covid-19.

We modeled outcomes assuming a fixed cohort design where all workers who tested positive were assumed to be at risk for progression to hospitalization or death during Epidemiological Weeks (EWs) 1 to 9. We calculated both outcomes as a rate per 1 000 workers who tested positive. The crude RR (overall and by vaccine brand) was estimated by dividing the cumulative incidence in the vaccinated group by that in the unvaccinated group. Partially vaccinated persons (i.e. with only one dose of a 2 dose vaccine) were excluded from this analysis.

We used two approaches to explore waning vaccine protection. We defined three-time intervals: 15-149 days,

150-199 days, and ≥200 days based on existing studies on waning intervals after the final dose.[19]

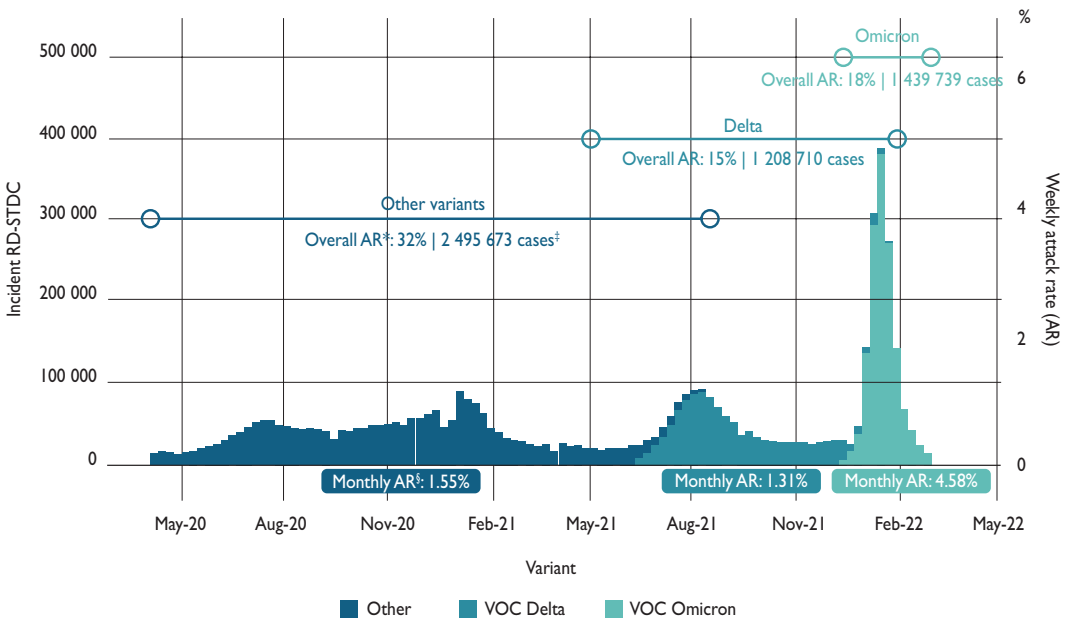
We used Poisson multivariable regression to compare risk of hospitalization or death by vaccination status or time since vaccination, adjusting by age group (≤29 years old [reference category], 30-49, 50-59, ≥60), sex, prior RD-STDC, salary quartile, comorbidities (obesity, diabetes, hypertension, or other comorbidities), state of residency, and EW.[20,21] We used Stata version 17.0 (https://www.stata.com) and R version 4.1.2 (2021-11-01) for all graphical and statistical analyses.

This evaluation was based on routine observational data collected by IMSS and deemed IRB-exempt public health surveillance. Procedures were instituted to protect confidentiality, and all staff with access to personal data were bound by a signed confidentiality agreement. A predefined set of data elements was extracted from each database using a customized, secure computerized data transfer protocol.

Results

Between April 1 2020, and March 4 2022, a total of 5 144 122 RD-STDC were registered among IMSS-insured workers. Of these, 1 439 739 (28%) were attributed to Omicron (first reported by EW 46 of year 2021, W-46-2021 and becoming predominant by W-51-2021). The maximum number of RD-STDC per week (n= 388 002) was registered during EW-3-2022 during Omicron predominance (figure 2). In contrast, the second maximum (EW-32-2021 *n*= 92 728) was registered during Delta predominance period. During the study period 7.2% of registered workers at IMSS filed for a RD-STDC, which accounted for 10.7 million workdays lost.

A greater percentage of workers in the analytical sample were vaccinated when compared to all workers with RD-STDC (88.9 vs. 83.6%, p<0.01), but otherwise were of similar age, sex, and salary (supplementary table S1).[22] Workers in the analytic sample had a mean age of 35.9 years (interquartile range [IQR] 27-44 years) and 46.7% were male, 88.9% were fully vaccinated and 11.1% were unvaccinated. Demographic characteristics such as age and state of residence differed by vaccine brand received (supplementary table S2).[22] Workers 50 years-old and older were more likely to receive the Pfizer (BNT162b2) vaccine whereas younger workers received AstraZeneca (ChAdOx1 nCoV-19). In the state of Baja California 61.1% received a Janssen (JNJ-78436735) vaccine. AstraZeneca (ChAdOx1 nCoV-19), Pfizer (BNT162b2) and Sinovac (CoronaVac) were the most widely distributed vaccines among the other states



* AR: Attack rate considering a population of 7 866 418 workers affiliated to IMSS by March 31st 2022; ‡ Cumulative cases attributable to each variant are defined as: weekly proportion of the variant x Total RD-STDC of the week. Variant information comes from GISAID-EpiCov; § Monthly attack rates represent the variant's average (weekly) attack rate x 4; RD-STDC : respiratory-disease short-termdisability claim
VOC: variant of concern

FIGURE 2. WEEKLY RESPIRATORY DISEASE SHORT TERM DISABILITY CLAIMS REGISTERED AT THE MEXICAN SOCIAL SECURITY INSTITUTE (IMSS) AND ATTACK RATE PER SARS-COV-2 VARIANT

with varying proportions. Sputnik V (Gam-COVID-Vac) was mostly used in Mexico City and the State of Mexico. CanSino (Ad5-nCoV) use was more prevalent in Chiapas, Oaxaca, and Veracruz, while Nuevo Leon and Jalisco states had the highest percentage of Moderna (Spikevax).

In the cohort sample, a total of 1 198 workers were hospitalized and 187 died (table I). Among unvaccinated workers who filed for an RD-STDC, 7.4 per 1 000 were hospitalized and 1.5 per 1 000 died. In contrast, among vaccinated workers with RD-STDC, the proportion hospitalized was significantly lower at 2.9 hospitalizations per 1 000 (RR 0.40; 95%CI 0.35,0.45) and proportion who died was also significantly lower at 0.42 deaths per 1 000 workers (RR 0.28; 95%CI 0.20,0.38).

Significant predictors for hospitalization / death were age, sex, diabetes, obesity, hypertension, and other comorbidities, salary, history of RD-STDC during years 2020 or 2021, state of residency, and epidemiological week (supplementary table S3).[22]

Having received any of the evaluated vaccines within the recommended schedule significantly reduced the risk of progression to hospitalization or death (table II).

Multivariable Poisson regression models comparing vaccinated to unvaccinated workers suggest a significant reduction in the risk of hospitalization (RR_{adj} 0.36; 95%CI 0.32,0.41) and death (RR_{adj} 0.24; 95%CI 0.17,0.33). Stratification by vaccine product showed similar results, the RR_{adj} for hospitalization and death was lowest for Pfizer BioNTech 0.27 (95%CI 0.22,0.33) and 0.12 (95%CI 0.07,0.19, respectively (table II).

Stratifying by time since vaccination, the RR_{adj} for hospitalization among vaccinated vs. unvaccinated workers was 0.37 (95%CI 0.32,0.41) for days 15-149, 0.32 (95%CI 0.31,0.43) for days 150-199, and 0.32 (95%CI 0.27,0.39) for days ≥200 from vaccination. Similarly, estimates were observed across time periods for individual vaccine products (figure 3).

Discussion

Our results add to the body of knowledge on the epidemiology of SARS-CoV-2 variants and the evaluation of national immunization programs which have used a combination of various vaccine types. Despite a high protective immunity against Covid-19 either by natural or vaccine acquired antibodies, we observed an overwhelming impact of the Omicron surge in the Mexican workforce.

We documented a 7.1% AR of RD-STDCs among 20.1 million workers insured by IMSS during the 9 weeks duration of the Omicron surge; representing a substantial burden of unplanned absences and lost productivity (10.7 million lost work days) a higher economic impact than previously reported in Mexico during 2020 and 2021.[15] In contrast, hospitalization rates during the Omicron wave were well below those reported during previous waves (3.8 vs. 28.4 per 1 000 SARS-CoV-2-positive workers).[16] Our results agree with observations suggesting that Omicron breakthrough infections were frequent among vaccinated populations but generally associated with less severe disease.[13,23-27]

Table I

Risk ratios for progression to hospitalization or death associated with full vaccination among private-sector workers insured by the Mexican Social Security Institute who filed a respiratory-disease short-term disability claim (RD-STDC) and tested positive for SARS-CoV-2 (RT-PCR or antigen). Mexico, January 4-March 5, 2022

Vaccination status	*Workers (n= 347 899)*	*Hospitalizations*		*Deaths*	
		Total (n= 1 198)	*Risk ratio (RR) (95%CI)*	*Total (n= 187)*	*Risk ratio (RR) (95%CI)*
Not vaccinated	38 676	289	Ref. group	58	Ref. group
Complete vaccination of 1 or 2 dose schedules	309 223	909	0.36 (0.32,0.41)	129	0.24 (0.17,0.33)
15-149 days	207 387	456	0.37 (0.31,0.43)	35	0.2 (0.13,0.33)
150-199 days	61 109	241	0.32 (0.27,0.39)	50	0.29 (0.19,0.43)
≥200 days	40 727	212	0.32 (0.26,0.4)	44	0.19 (0.13,0.3)

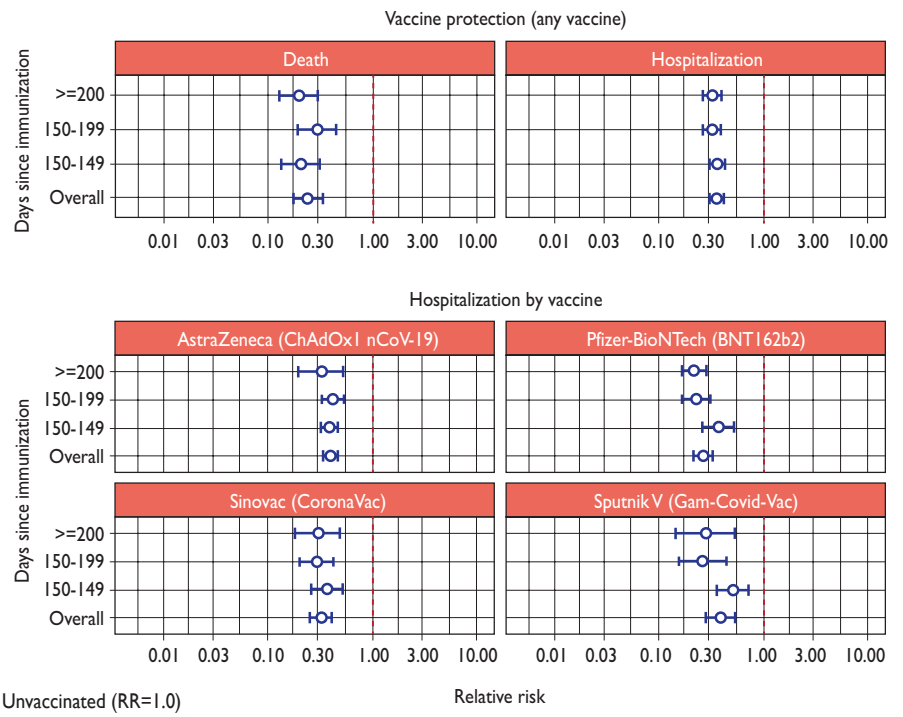
Models adjusted by age group (≤29 years old [reference category], 30-49, 50-59, ≥60), sex, prior RD-STDC, salary quartile, comorbidities (obesity, diabetes, hypertension, or other comorbidity), state of residency, and epidemiological week

Table II

RISK RATIOS FOR PROGRESSION TO HOSPITALIZATION OR DEATH AMONG PRIVATE-SECTOR WORKERS INSURED BY THE MEXICAN SOCIAL SECURITY INSTITUTE WHO FILED A RESPIRATORY-DISEASE SHORT-TERM DISABILITY CLAIM (RD-STDC) AND TESTED POSITIVE FOR SARS-CoV-2 (RT-PCR OR ANTIGEN) ACCORDING TO TYPE AND BRAND OF VACCINE RECEIVED. MEXICO, JANUARY 4-MARCH 5, 2022

Vaccine status	*Workers (n= 347 899)*	*Average lag between last vaccine dose and start of RD-STDC (months)*	*Hospitalizations*		*Deaths*	
			Total (n= 1 198)	*Risk ratio (RR) (95%CI)*	*Total (n= 187)*	*Risk ratio (RR) (95%CI)*
Not vaccinated	38 676		289	Ref. group	58	Ref. group
AstraZeneca (ChAdOx1nCoV-19)	139 569	3.7	430	0.39 (0.34,0.46)	57	0.30 (0.2,0.44)
Pfizer BioNTech (BNT162b2)	61 841	5.4	190	0.27 (0.22,0.33)	29	0.12 (0.07,0.19)
Sinovac (CoronaVac)	49 062	4.9	106	0.32 (0.25,0.41)	19	0.29 (0.16,0.53)
Sputnik (Sputnik V)	21 719	3.8	87	0.39 (0.28,0.53)	7	0.15 (0.06,0.38)
CanSino (Ad5-nCoV)	12 256	6.4	30	0.41 (0.24,0.7)	4	0.38 (0.1,1.4)
Janssen (Ad26.COV2.S)	15 522	6.7	56	0.53 (0.39,0.72)	13	0.5 (0.26,0.97)
Moderna (Spikevax)	9 254	3.1	10	0.29 (0.15,0.57)	0	NE

NE: Non estimable due to small number of events
Models adjusted by: age group (≤29 years old [reference category], 30-49, 50-59, ≥60), sex, prior RD-STDC, salary quartile, comorbidities (obesity, diabetes, hypertension, or other comorbidity), state of residency, and epidemiological week



Reference category: Unvaccinated (RR=1.0)

FIGURE 3. OVERALL AND WANING OF VACCINE PROTECTION AGAINST PROGRESSION TO DEATH OR HOSPITALIZATION OF ANY VACCINE AND BY VACCINE TYPE

During the Omicron-predominant period, we documented that full vaccination with any of the seven vaccines evaluated was associated with a 2.7-fold reduction in the risk of Covid-19-related hospitalization and a 4.2-fold reduction in risk of death (table I). We observed protection against hospitalization for vaccine types: mRNA vaccines (RR_{adj}= 0.27 for Pfizer BioNTech and 0.29 for Moderna), two-dose inactivated or viral vector vaccines (RR_{adj}= 0.32 for Sinovac, RR_{adj}= 0.39 for Sputnik, and RR_{adj}= 0.39 for AstraZeneca), and one-dose viral vector vaccines (RR_{adj}= 0.41 for CanSino and 0.53 for Janssen) (table II). However, product-specific comparisons might be confounded by differences in time since vaccination which was not included in the model. For example, Janssen had a mean time from vaccination to illness of 6.9 months, while Pfizer BioNTech had a mean time of 5.4 months.

Results from recently published studies show that vaccination continues to provide a high level of protection against severe disease and hospitalization linked to the Omicron variant, which are similar to what we observed. Davies and colleagues (South Africa) reported that laboratory-confirmed Covid-19 patients, with a primary immunization with Janssen (one dose) or Pfizer BioNTech (two doses) had a reduced the risk of death (RR 0.24; 95%CI 0.10,0.58).[28] Lauring and colleagues (New York, U.S.) reported a lower protection level for primary vaccination with Pfizer BioNTech or Moderna (odds ratio [OR] 46%; 95%CI 12,67) for progression to invasive mechanical ventilation or death in patients hospitalized with Covid-19 than we observed,[29] however, confidence intervals overlapped with our estimates. Young-Xu and colleagues (Veterans' Health Administration, U.S.) reported a lower protective effect, vaccine efficacy of 24% (95%CI 1,43) against hospitalization and 59% (95%CI 25,77) against death among patients with a positive test who received for two doses of an mRNA vaccine during the Omicron period.[30] Their study population included US Veterans ≥ 65 years, which differed in age compared to the other studies including ours, possibly explaining the difference in results. However, a recent test-negative design study by our group in Mexican pensioners showed 75.3% (95%CI 73.4,77) VE against hospitalization and 79.8% (95%CI 78.1,81.4) against death.[31] Young-Xu and colleagues discuss that waning protection could explain the lower VE and highlight the protection of booster vaccines.

We examined whether vaccine protection waned and found no statistical difference in vaccine protection within a time frame of 200 days after vaccination. Such findings are consistent with a number of other evaluations both during and prior to Omicron predominance. Lewnard and colleagues (Kaiser Permanente, Southern California, U.S.) investigated vaccine efficacy of 2-dose Pfizer BioNTech or Moderna VE and estimated a RR 0.51 (95%CI 0.34,0.76) for hospital admission at ≤90 days, 0.43 (95%CI 0.32,0.56) at 91-180 days, and 0.52 (95%CI 0.44,0.61) at ≥180 days after vaccination.[32] Chemaitelly and colleagues (Qatar) did not identify vaccine efficacy waning against any severe, critical, or fatal disease for ≥7 months after the second dose of Pfizer BioNTech, but documented a 20% reduction for Moderna.[33] Other studies, however, have reported a significant waning effect and suggested the need for a booster; particularly with the emergence of novel SARS-CoV-2 variants of concern.[30,34]

Routinely collected surveillance data frequently experience delays and incompleteness. The strengths of our data, however, include the linkage of data across multiple surveillance systems via unique identifiers, and the fact that RD-STDC are collected in a standardized way across all IMSS-medical facilities. Furthermore, information from linked between Sinolave and STDC provide timely data and facilitate real-world evaluation of vaccination for public health response.

Our evaluation also has some limitations. First, vaccine booster data were not registered in the NCIDB, we used the available self-reported information in Sinolave in a sensitivity analysis. We excluded persons who reported receiving a booster dose (1.3% of the analytic sample) and this did not change estimations (results not shown); however, there might have been underreporting of Covid-19 vaccine boosting. Failure to adjust for Covid-19 vaccine boosting could create a false impression that there is less waning within 200 days of vaccination than in reality; our results must be interpreted within this context. Both timing of vaccination and receipt of booster doses were likely associated with age and with specific vaccine products, making it further difficult to isolate the effects of waning over time. In Mexico, older adults and persons with comorbidities were immunized earlier in the national vaccination rollout, so these groups may be overrepresented in categories with longer time since vaccination. Our results also documented that by the end of 2021, 83.6% of workers registered with IMSS were vaccinated, confirming the high vaccine take-up by this group. Second, we did not have access to sequencing for workers' individual results, and we used countrywide genomic surveillance to assume that a predominance of SARS-CoV-2 positive workers during the evaluation period were infected with Omicron. Third, we used routinely collected surveillance data and did not have access to clinical data to adjust for information about disease severity beyond

hospitalization and death status. Fourth most cases were diagnosed by rapid antigen tests (98.5%), which have lower sensitivity and specificity than RT-PCR assays and could have biased risk ratios towards the null if relatively mild infections were not detected.

Finally, RD-STDCs might have underestimated the real magnitude of the Omicron surge, because not all symptomatic workers claimed an STDC. Workers receive 60% of their wage starting on the fourth day, for the duration of the STDC which may bias claims to those with more severe clinical spectrum. In a recent study of IMSS-insured workers, only 26-40% with SARS-CoV-2 antibodies and symptoms compatible with Covid-19 sought an RD-STDC (personal communication by Barros-Sierra 2022), suggesting real symptomatic attack rates could be 3-4 times higher. In addition, not all workers might have sought care at IMSS facilities and thus severe outcomes could have been underreported, leading to possible underestimation of the risk of progression to severe disease. The 2020 National Survey of Health and Nutrition Covid-19 reported that over half of the IMSS affiliates with Covid-19 that were hospitalized were hospitalized at an IMSS hospital (60.1%), however, there is no evidence that hospitalization at non-IMSS facility, may be different for vaccination groups.[35]

Conclusions

This evaluation provides an assessment of seven vaccines used in Mexico's Covid-19 vaccination program (AstraZeneca (ChAdOx1nCoV-19), Pfizer BioNTech (BNT162b2), Sinovac (CoronaVac), Sputnik (Gam-COVID-Vac), CanSino (Ad5-nCoV), Janssen (Ad26.COV2.S), Moderna (Spikevax), which reduced risk of disease progression in workers during the Omicron wave. All vaccines protected against Covid-19 hospitalization and death. These results indicate the success of Mexico's national immunization program in protecting the country's workforce against Covid-19,[36-38] and can be used for further vaccine implementation and messaging in Mexico and other global settings.

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

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