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Research article

Impact of the COVID-19 vaccination campaigns in Argentina during 2021: An observational quantification of the death probability for confirmed cases in Buenos Aires province

Guillermo Durán [a,b,c], Manuel Durán [d], Andrés Farall [b], Jemina García [b,d], Daniela Parada [a,b,*], Ariel Salgado [b]

[a] *Departamento de Matemática, FCEN–UBA, Argentina*
[b] *Instituto de Cálculo, FCEN–UBA & CONICET, Argentina*
[c] *Departamento de Ingeniería Industrial, FCFM–Universidad de Chile, Chile*
[d] *Facultad de Ingeniería, UBA, Argentina*

ABSTRACT

Background: A SARS-CoV-2 (COVID-19) vaccination campaign was launched in Argentina in January 2021. The vaccines then available were administered to the population in several different schemes. This observational study presents a quantification of the impact of the different schemes on the probability of death for confirmed COVID-19 cases in Argentina's Buenos Aires Province. The results provide a local measure of the schemes' effectiveness that heretofore has been lacking.
Methods: The study's main source of information is the Integrated Health Information System database, which contains 1,538,113 records of confirmed SARS-CoV-2 (COVID-19) cases reported in 2021 in the Province. To assess the real-world effectiveness of the vaccination campaign, two categorical variables representing vaccination status were defined. Probability of death was formulated as a generalized linear model with a logistic link and includes variables for geography, a socio-economic level index, symptom onset, sex, and vaccination status. The effectiveness level was derived from the death probability estimates.
Findings: The study's findings indicated that the most effective vaccine was rAd26-rAd5 (Sputnik), with ChAdOx1-S (AZ/Covishield) and BBIBP-CorV (Sinopharm) following in efficacy, for both single and multiple doses. The effectiveness of a single dose was consistently below 50%, while it ranged from 50% to 90% for two or more doses. Notably, the analysis of variables such as the municipality of residence of the infected persons and the season of symptom onset yielded particularly intriguing insights. The socioeconomic level of a municipality emerged as a moderately strong predictor of the probability of death, which was marginally higher in municipalities with lower-income populations. Additionally, the data revealed an increased probability of death during the winter season.
Interpretation: The vaccination campaigns carried out in Buenos Aires Province in 2021 significantly contributed to reducing the number of deaths due to SARS-CoV-2 (COVID-19) among its population. However, the extent of this impact varied considerably depending on individual characteristics such as age, health status, and vaccination schedule adherence.

1. Introduction

Since the outbreak of the SARS-CoV-2 (COVID-19) pandemic, the world has witnessed not only the significance of studying this novel coronavirus due to its common respiratory symptoms and global impact, but also the unintended consequences it has had on the prevalence of other respiratory viral infections [1,2]. Before delving into the importance of vaccines, it is essential to acknowledge the

* Corresponding author.
E-mail address: dparada@dm.uba.ar (D. Parada).

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profound impact COVID-19 has had on public health, leading to a significant reduction in the prevalence of other respiratory infections before the pandemic.

Various studies have been conducted to measure the effectiveness of the vaccine schemes administered in low- and middle-income countries. Effectiveness in these analyses is typically estimated in terms of preventing infections, hospitalizations, or deaths. Some of the studies have employed observational methods including case-control and historical cohorts to determine the schemes' real-world effectiveness, in many cases using official data repositories. Although lacking some of the advantages of randomized controlled trials, these approaches to assessing the effectiveness of vaccine campaigns are invaluable in that they reflect the real-world challenges the campaigns face such as logistics, vaccination scheduling, and follow-up, and generally cover more diverse populations.

As of September 2021, the COVID-19 vaccines authorized for use in Argentina and widely administered in prioritized population groups were rAd26-rAd5, ChAdOx1-S and BBIBP-CorV (hereafter "Sputnik", "AZ/Covishield" and "Sinopharm", respectively) [3]. A test-negative, case-control, retrospective longitudinal study was carried out in the country using data from the National Surveillance System to assess the effectiveness of the three vaccines against SARS-CoV-2 infections and risk of death in persons with RT-PCR-confirmed COVID-19 [3]. Limited in coverage to people over the age of 60, the study found that the estimated effectiveness in preventing deaths among those who received one dose was 81.1% (95% CI 80.5–81.7) for AZ/Covishield, 83.1% (82.3–83.9) for Sputnik, and 70.4% (68.1–72.8) for Sinopharm. Among those receiving two doses the results for all three vaccines were better, the corresponding effectiveness levels being 93.1% (92.6–93.5), 93.7% (93.2–94.3), and 85.0% (84.0–86.0). In a similar study of the Sputnik vaccine alone, effectiveness levels in preventing infections, hospitalizations, and deaths were 79%, 88%, and 95%, respectively [4,5].

A historical cohort study on a target population of 1.8 million adults in southern Iran using 4-repository administrative data linkage showed a major reduction in mortality (at least 85%) in all age subgroups of the fully immunized population with Sinopharm, AZ/Covishield, Sputnik and the BIV1-CovIran vaccines [6].

In Israel, an observational study using national surveillance data to assess the real-world effectiveness of two doses of BNT162b2 (hereafter, "Pfizer") found that they were highly effective across all age groups in preventing COVID-19-related deaths [7]. The nationwide public-health impact of the widespread introduction of the vaccine was also evaluated. In England, a test-negative case-control study of the Pfizer vaccine in older adults estimated the real-world effectiveness against confirmed COVID-19 symptoms [8], concluding that a single dose was 85% effective in preventing deaths due COVID-19.

A prospective national cohort study was undertaken of the mass vaccination campaign in Chile to calculate the effectiveness in preventing COVID-19-related deaths of the CoronaVac vaccine [9]. Covering 10.2 million fully immunized persons who were vaccinated between February 2 and May 1, 2021, the study calculated that the adjusted vaccine effectiveness level was 86.3% (95% CI 84.5–87.9). Factors relating to socioeconomic status in Chile such as nationality, region of residence, and income were considered in the analysis as social determinants of health.

The 2021 vaccination campaign in Hungary, under which five different vaccines were administered, was the subject of an observational study to determine vaccine effectiveness against COVID-19-related mortality in 3.7 million vaccinated individuals [10]. It was estimated that two doses of either Pfizer, Sinopharm, Sputnik, AZ/Covishield or mRNA-1273 (hereafter "Moderna") had an adjusted effectiveness that varied between 87.8% and 97.5%.

As regards the present study, it uses the observational method to quantify the effects on probability of death (PD) due to COVID-19 of the vaccination campaigns conducted in 2021 in Buenos Aires Province, Argentina (hereafter "BAP"). Home to almost 40% of Argentina's inhabitants, BAP accounted for about 45% of the entire country's COVID-19 deaths that year. An analysis of the impact of vaccination campaigns in this large and populous region should therefore be of considerable interest.

The aim of the study was to quantify that impact in actual practice using observational data collected in the field, so the results obtained refer strictly to the population and combination of circumstances studied. The data employed relates only to COVID-19 cases confirmed either through testing or by epidemiological link that were recorded in BAP during the period from January 1 to December 31 of 2021.

2. Methods

2.1. Metrics

The metrics for vaccine impact used in the study were the probability of death (PD) reduction rate and effectiveness, calculated and estimated using two different modelling methodologies. The PD reduction rate was defined as the ratio of the PD for vaccinated individuals to unvaccinated individuals while effectiveness was defined as the complement of the PD reduction rate, that is, 1 minus that rate.

2.2. Data

The primary data source for this study was the 2021 BAP data from the Integrated Health Information System database, overseen by Argentina's National Ministry of Health. This database comprehensively records all confirmed COVID-19 cases, either through diagnostic testing or via 'epidemiological link,' a term denoting symptomatic cases confirmed due to close contact with a test-confirmed individual [11]. Each case entry in the database includes the person's vaccination history and, if applicable, the date of death, with an explicit confirmation that the death was due to COVID-19.

To ensure privacy and confidentiality, the data underwent a rigorous anonymization process. The Buenos Aires Province Ministry of Health initially used personal identification numbers to cross-reference follow-up data with vaccination records. Subsequently, these personal identifiers were removed, and each individual was assigned a unique identification reference number. This reference number, devoid of any personal information, was utilized as the identifier in the database provided to us for this study. This method ensured the integrity of the data while strictly adhering to privacy standards.

In 2021, the database documented 1,538,113 confirmed COVID-19 cases. Each case, including repeat confirmations for the same individual, was logged as a separate record. However, repeat confirmations comprised only 4.08% of the total, leading us to focus our analysis solely on the initial 1,475,380 confirmations. These records detailed the date of symptom onset or the date of test confirmation, vaccine type, dose schedule, and, if it occurred, the date of death. Additionally, each record specifies the individual's municipality of residence. A limitation of this dataset is the absence of information about the specific COVID-19 variants involved.

We excluded 9120 records that showed a second vaccine dose without a prior recorded first dose, likely indicating the first dose was administered in another province. Other variables recorded included age at symptom onset and biological sex. Records of individuals younger than 3 or older than 99 years (9103 records) and those with non-binary sex designations (12,157 records) were omitted.

While the database also includes data on hospitalizations and comorbidities, a discrepancy in the proportions of these cases compared to national comorbidity data from the latest National Risk Factor Survey suggests potential under-registration in the survey [12]. This was also observed in hospitalization data, where non-admitted cases showed higher mortality rates than admitted ones. Consequently, we did not include these variables in our analysis.

After filtering the raw data, our study comprised 1,445,874 records, with 30,058 deaths reported, indicating a crude mortality rate of 2.08%.

2.3. Covariates and descriptive analysis

To quantify the real-world effectiveness of the BAP vaccination program for both descriptive and statistical analysis purposes, we defined two categorical variables representing vaccination status. The first variable, denoted *vaccination state*, is the simpler of the two and classifies individuals into three vaccination state categories: *unvaccinated*, *one dose* and *two or more doses*. Since widespread administration of the third dose did not begin until late in 2021, cases of three doses accounted for only 6% of all database records and thus were included in the ''two or more'' category, hereafter simply denoted ''two''. In assigning cases to these categories, a person was considered to have received one dose if at least 14 days had passed between receiving that dose and symptom onset. Similarly, a person was deemed to have received two doses if, having already received a first dose, at least 14 days had passed between receiving the second dose and symptom onset. This 14-day period between vaccination and symptom is the threshold routinely adopted in epidemiological studies given that it is considered to typify the amount of time required for vaccines to generate the immunization process in the recipient [13–15]. Nevertheless, we conducted a sensitivity study of the threshold on the effectiveness of the vaccines in the population under study, which confirmed that the 14-day threshold was a good empirical compromise between effectiveness and amount of data.

The second variable, denoted vaccine group, disaggregates and categorizes cases by the combination of vaccine type (Sputnik, Sinopharm, or AZ/Covishield) and the number of doses administered. Only the most frequent combinations were considered. This decision was made due to the relatively low percentages of heterologous vaccine cases in the data (less than 1%), which were not sufficient for detailed analysis. The two categorizations thus differ in that vaccine group distinguishes between the various types of vaccines.

Counting as vaccinated only those for whom symptom onset occurred at least 14 days after vaccine administration, the distribution of persons by vaccination state was as follows: unvaccinated, 78.31% (7831/10000); one dose, 10.83% (1083/10000); two doses, 10.86% (1086/10000). As regards vaccine type and dose combination, the cases were distributed as follows: unvaccinated, 78.31% (7831/10000); one dose of AZ/Covishield, 3.47% (347/1000); one dose of Sinopharm, 2.76% (276/1000); one dose of Sputnik, 4.46% (446/1000); two doses of AZ/Covishield (Covi-Covi), 2.94% (294/1000); two doses of Sinopharm (Sino-Sino), 4.31% (431/1000); two

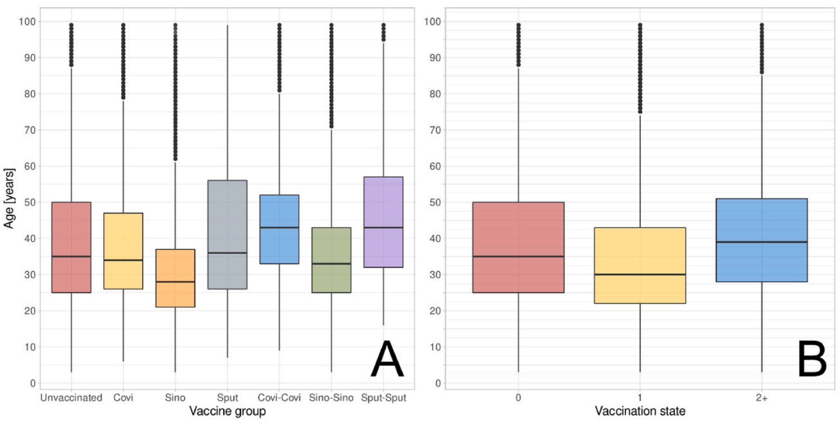

Fig. 1. Boxplot of the age variable by vaccine group (A) and vaccination state (B).

doses of Sputnik (Sput-Sput), 2.75% (275/1000). As previously stated, the number of cases involving heterologous vaccines was minimal (0.997%) and therefore not included in the detailed analysis.

The distributions broken down by age and sex are shown in Figs. 1 and 2. Tables S1 and S2 present statistical data to evaluate the significant age differences across vaccination states and vaccine groups, respectively. The temporal distribution of symptom onset dates is shown in Fig. 3. The numbers of confirmed cases and deaths by BAP municipality for the 30 municipalities that reported the most cases (accounting for 74.87% of the total) are displayed in Fig. 4.

To capture the effect on PD of socio-economic level, the unsatisfied basic needs index (UBNI) was included in the study [16]. The index values for the 30 municipalities that reported the most cases are set out in Table S3 [17].

The number of persons exposed, number of deaths, and proportions of deaths by sex and age range are all displayed in Table S4. The same indicators broken down by vaccination state are set out in Tables S5–S7. The same information is also shown in Fig. 5 which illustrates the proportions of deaths across different age ranges, vaccination states, and sexes. The empirical effectiveness of vaccination by age range, sex and number of doses is presented in Table S8.

2.4. Statistical analysis

Two different modelling methodologies were used to quantify the effectiveness of individuals' vaccination status based on the two categorical variables described earlier, that is, the three vaccination state categories (unvaccinated, one dose, two doses) and the seven vaccine group categories for the main vaccine type and dose combinations. Several control covariates were considered.

For the methodology described fully in the present article, PD was formulated as a generalized linear model (GLM) with a logistic link. This model includes the vaccination status variables as well as age, sex, and municipality of residence. It also includes the UBNI by municipality and the time of year (calendar date) at symptom onset, the former being a proxy of socio-economic level and the latter to account for variability in the incidence of mortality that may reflect an annual cycle or other time-related tendencies. A variant of this model incorporates the interaction between the vaccination state and vaccine group variables. The continuous UBNI and time of year variables were introduced as second-degree natural splines, while for the age variable, a first-degree spline was used. Municipality was introduced as a categorical variable.

The other modelling strategy, based on Cox's proportional hazards model of time to death, was formulated such that the vaccination state and vaccine group co-variables act multiplicatively on the basal risk of death. This model estimated the risk of death as a function of elapsed time (in days) from symptom onset, allowing the predictor variables to modify the risk multiplicatively through the factors estimated by the model. The partial effects of the two vaccination status categorical variables were thus determined simply by estimating these multiplicative risk factors. Both details and results for this model can be found in the Supplementary Material.

3. Results

The temporal distribution of symptom onset dates shown in Fig. 3 clearly depicts the successive waves of contagion over the course of 2021, especially during April and May. The numbers of confirmed cases and deaths by BAP municipality for the 30 municipalities in Fig. 4 reflects the variations in their respective populations. A noteworthy aspect is the observed variability in mortality rates among these municipalities, with some, like Pilar, exhibiting notably lower rates. This disparity suggests the influence of various local factors, including public health responses and community characteristics, on the pandemic's impact.

To further enhance our study, we incorporated the Unsatisfied Basic Needs Index (UBNI) as a key variable. This index serves as an

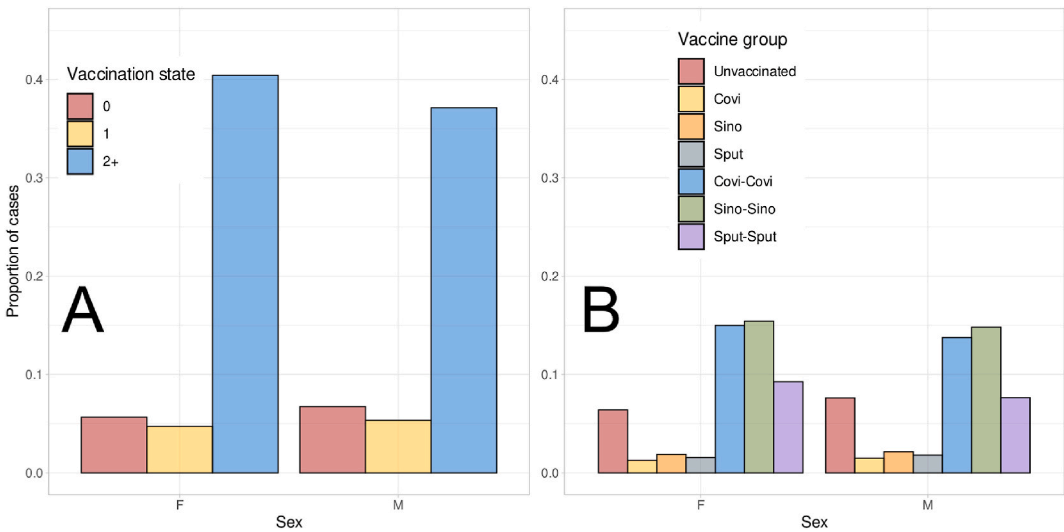

Fig. 2. Proportion of cases by sex and vaccination state (A) and by sex and vaccine group (B).

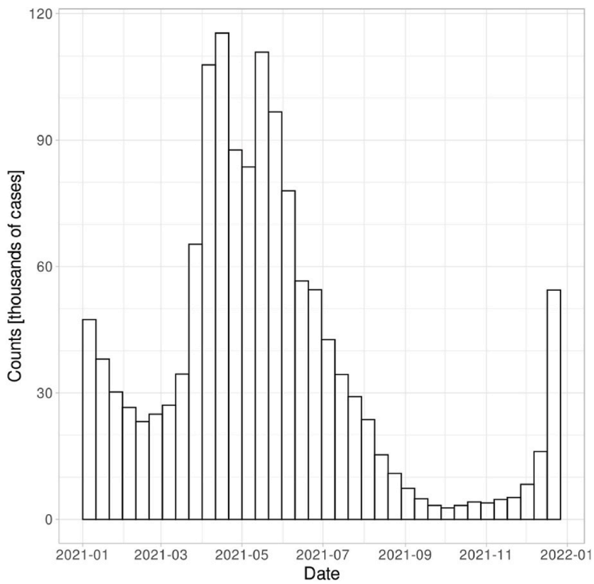

Fig. 3. Temporal distribution of symptom onset dates. This correlates with the successive waves of contagion over the course of 2021, especially during April and May.

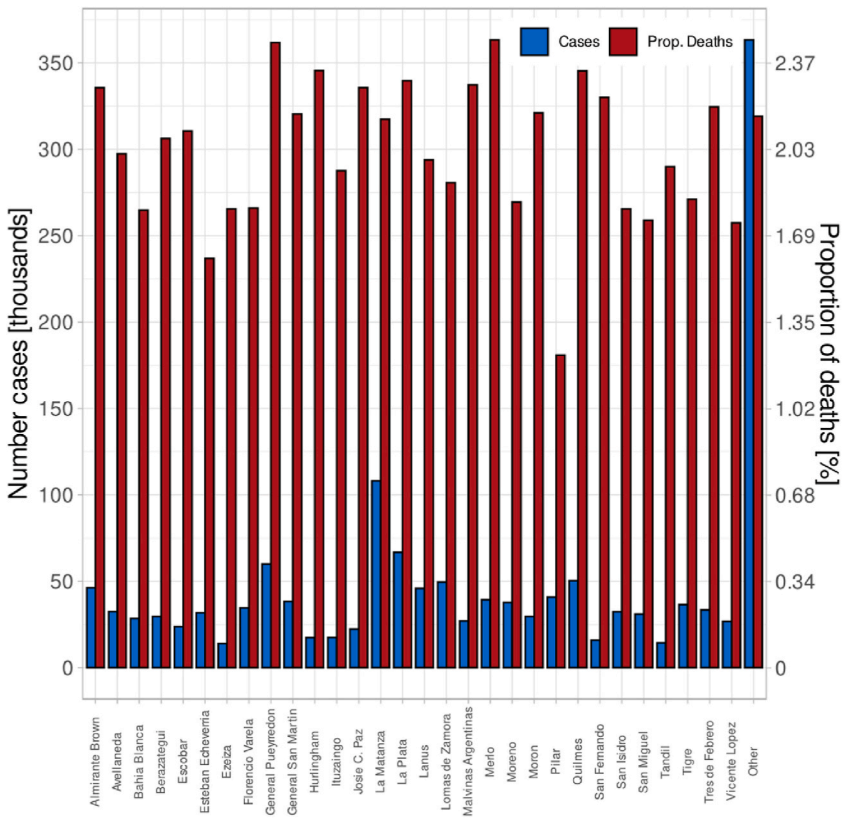

Fig. 4. Number of cases by municipality in blue; percentage of deaths by municipality in red. The bar labelled "Other" represents the 105 BAP municipalities other than the 30 with the most cases, shown individually. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

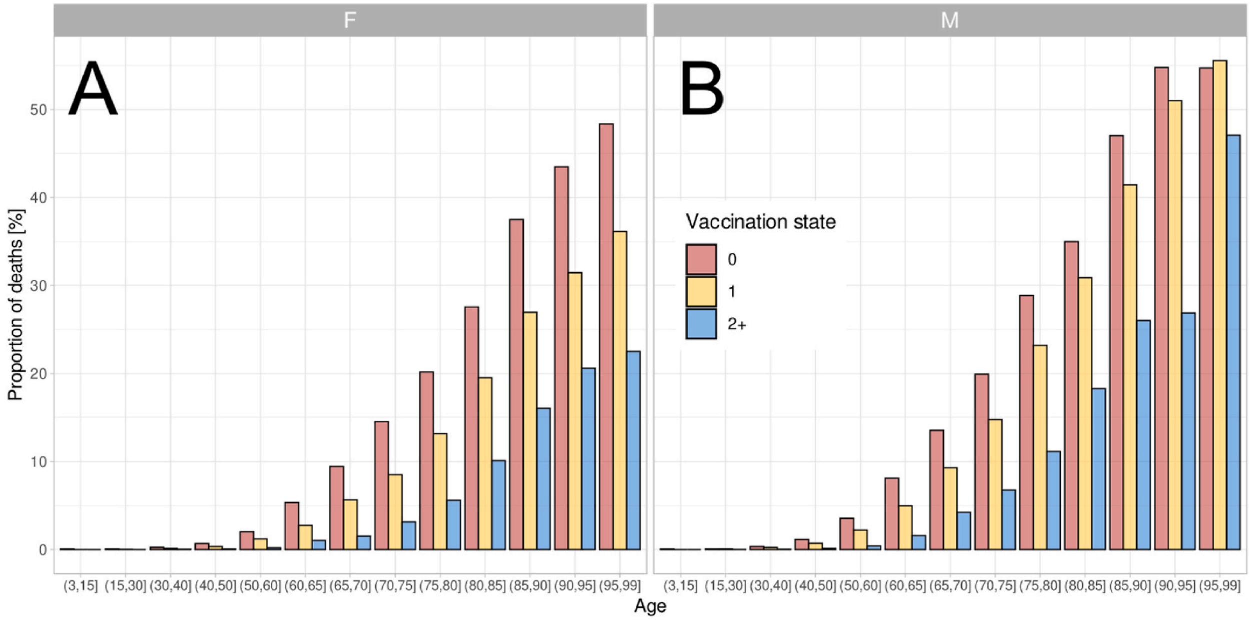

Fig. 5. Proportion of deaths as a function of age range, vaccination state and sex: female (A), male (B).

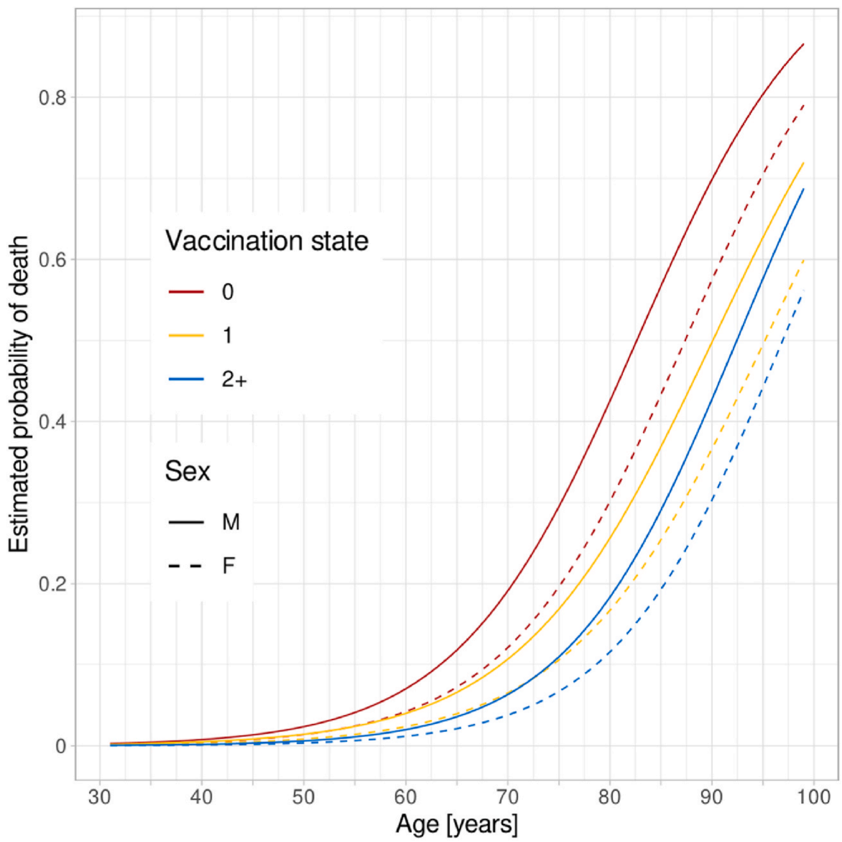

Fig. 6. Estimated curves for probability of death (PD) as a function of age, sex, and vaccination state.

effective proxy for gauging the socio-economic level of each individual's municipality of residence, with a lower UBNI indicating a higher socio-economic status. The inclusion of UBNI allows us to examine the interaction between socio-economic factors and health outcomes, particularly in terms of PD due to COVID-19.

Tables S4–S7 shows that mortality rates grew rapidly with age and were noticeably higher for men. A comparison of these tables reveals in descriptive terms the effect of vaccination in reducing mortality rates. This is also shown in Fig. 5 and displays a clear depiction of how mortality rates varied across these categories. Table S8 illustrates the empirical effectiveness of vaccination, stratified by age range, sex, and number of doses. It reveals the expected trend: the empirical effectiveness generally increases with the number of doses administered across all age groups, and this increase notably differs between males and females. For both one and two doses, higher effectiveness is observed in younger age groups (30–40 years), particularly among females. For instance, in the 30–40 age group, effectiveness is 46.52% for females and 34.15% for males with one dose, which significantly increases to 89.56% for females and 93.53% for males with two doses. This pattern of increasing effectiveness with additional doses continues across all age ranges, but the margin of increase diminishes in older age groups.

PD curves in our study were fitted using logistic regression, considering variables such as age ($p < 2e\text{-}16$), sex ($p < 2e\text{-}16$), and vaccination state ($p < 2e\text{-}16$). The derived estimates from this model are exhibited in Fig. 6. This estimated curves for the probability of death as a function of age, sex, and vaccination state exhibit variations in PD across different ages and sexes. Consistent with our descriptive analysis, the model showed a pronounced increase in PD with advancing age and higher PD levels in men compared to women. Importantly, the effect of vaccination was markedly evident, with a notable reduction in death probability following the administration of the second vaccine dose. This effect was especially pronounced in older age groups. To exemplify, we consider the estimate PD for an average 80-year-old man decreased from 44% when unvaccinated to 19% with two doses, as depicted in Fig. 6. This calculation involved estimating PD by fixing age and sex and altering the vaccination status from 'unvaccinated' to 'two doses'.

The influence of the time of year ($p < 2e\text{-}16$) on symptom onset is captured in the estimated curves shown in Fig. 7. These curves clearly demonstrate a seasonal increase in PD during the southern hemisphere winter months (June through August). Additionally, Fig. 8 illustrates the relationship between UBNI ($p < 2e\text{-}16$) and PD, highlighting how socio-economic factors interplay with the pandemic's impact across various ages and vaccination statuses. To exemplify this relationship, Fig. 9 shows the PD of a 70-year-old unvaccinated man in relation to UBNI for each of the 30 municipalities with the highest case counts. This figure strikingly contrasts municipalities like Pilar ($p < 3.38e\text{-}07$), where PD is significantly lower than expected based on UBNI, with others like Malvinas Argentinas ($p < 2.32e\text{-}07$), where PD is considerably higher. These results are also shown numerically in Table S9, where the predicted PD for the main municipalities is compared with the expected PD regarding the other municipalities. A difference column is also added to ease the identification of outstanding cases.

In Fig. 10, we present the estimated PD curves based on vaccine group (covi: $p < 1.30e\text{-}07$, sino: $p < 1.27e\text{-}06$, sput: $p < 1.85e\text{-}10$), age ($p < 2e\text{-}16$), and sex ($p < 2e\text{-}16$). These curves underscore the superior mortality reduction associated with the second dose of vaccines, particularly with the Sputnik vaccine, which showed the most favorable outcomes. We also observed distinctions in vaccine effectiveness between females and males. These differences are particularly notable when comparing the effectiveness of different vaccines schemes. For instance, while the Sputnik vaccine exhibited the most favorable outcomes overall, the reduction in PD and the

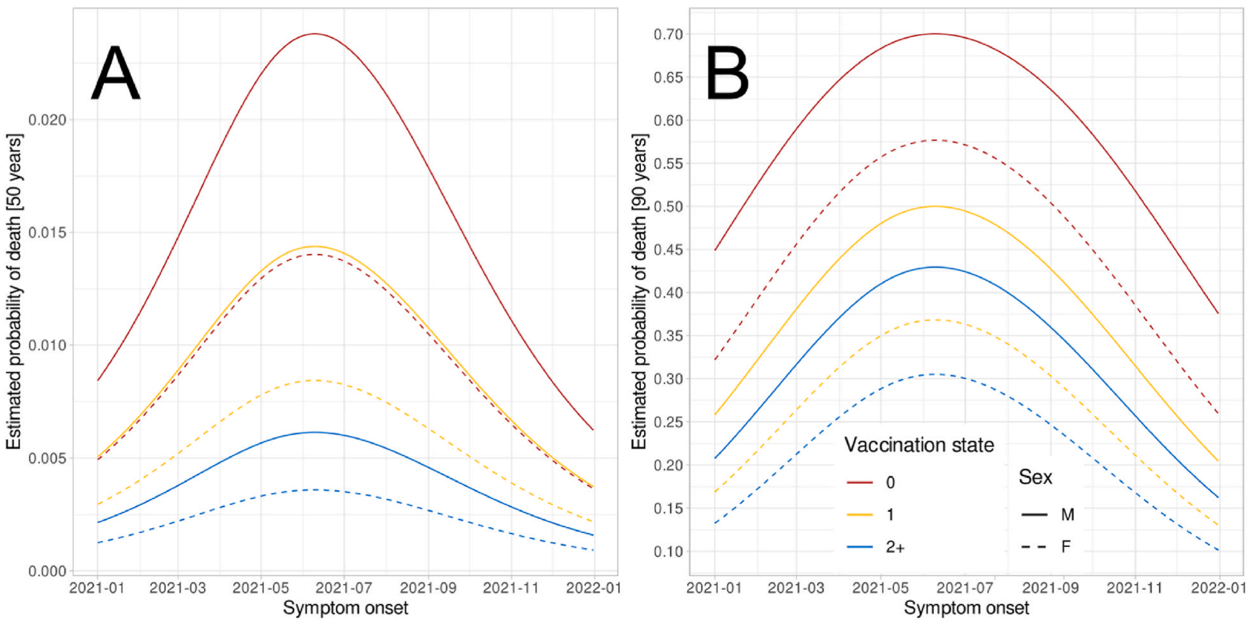

Fig. 7. Estimated curves for death probability as a function of time of year (calendar date), for persons aged 50 (A) and 90 (B). The solid lines are for men and the dotted lines are for women. Unvaccinated, one-dose, and two-dose curves are shown in red, yellow, and blue, respectively. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

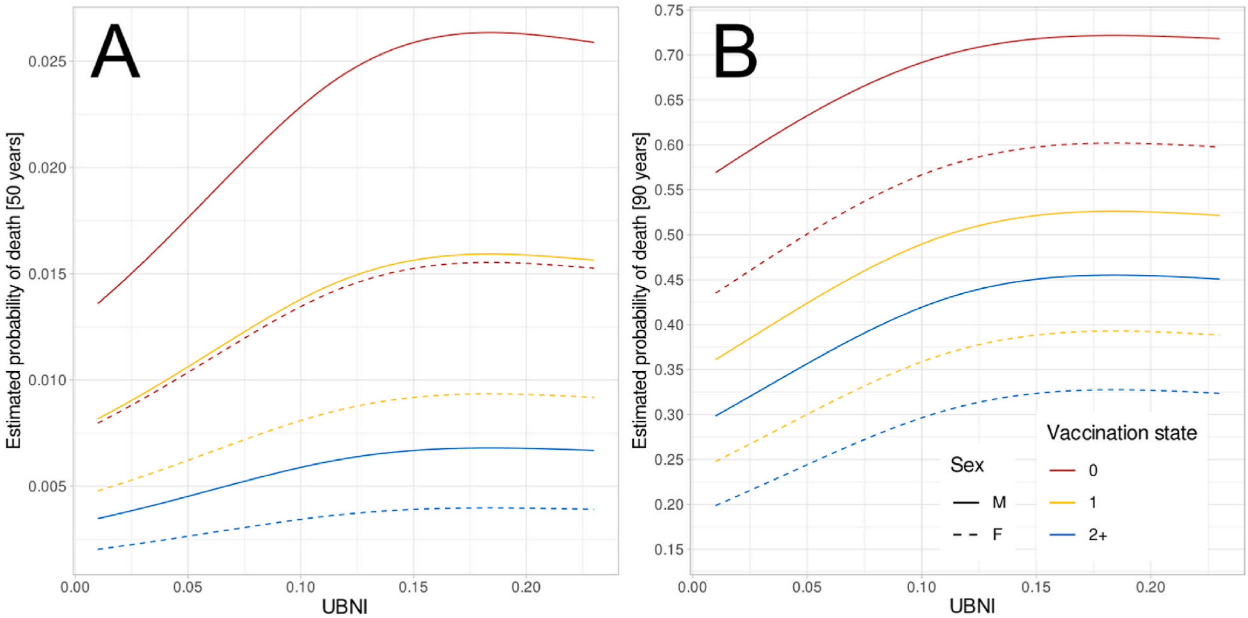

Fig. 8. Estimated curves for death probability as a function of UBNI, for persons aged 50 (A) and 90 (B). The solid lines are for men and the dotted lines are for women. Unvaccinated, one-dose, and two-dose curves are shown in red, yellow, and blue, respectively. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

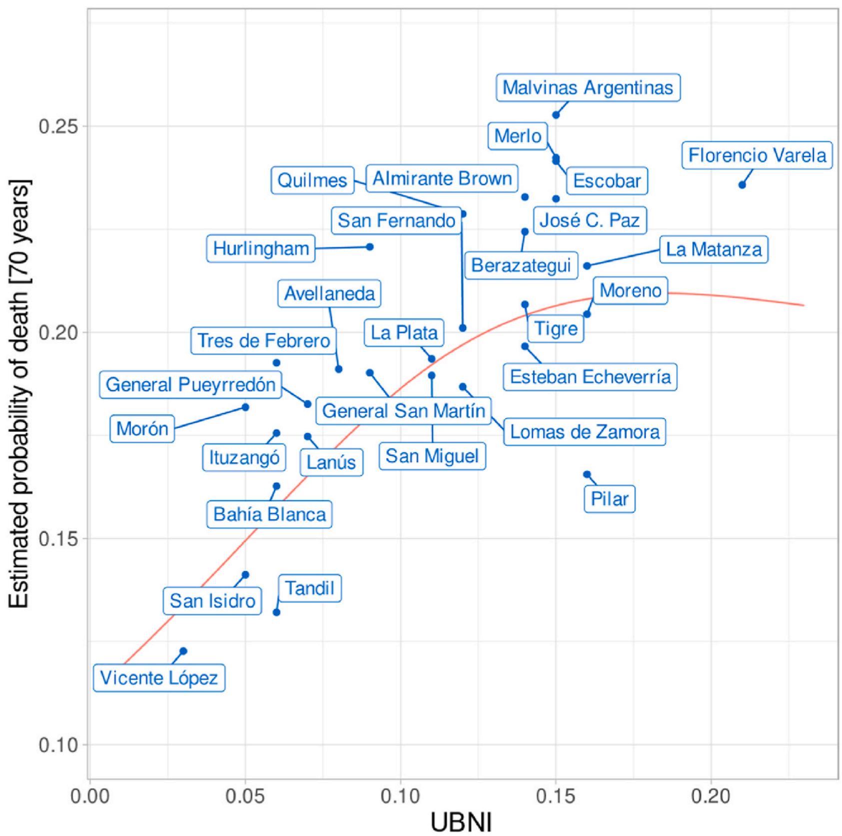

Fig. 9. Probability of death curve for a 70-year-old unvaccinated man as a function of UBNI. The blue dots are the individual probabilities for the 30 municipalities with the most cases while the red curve is the corresponding probability for the other 105 municipalities combined. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

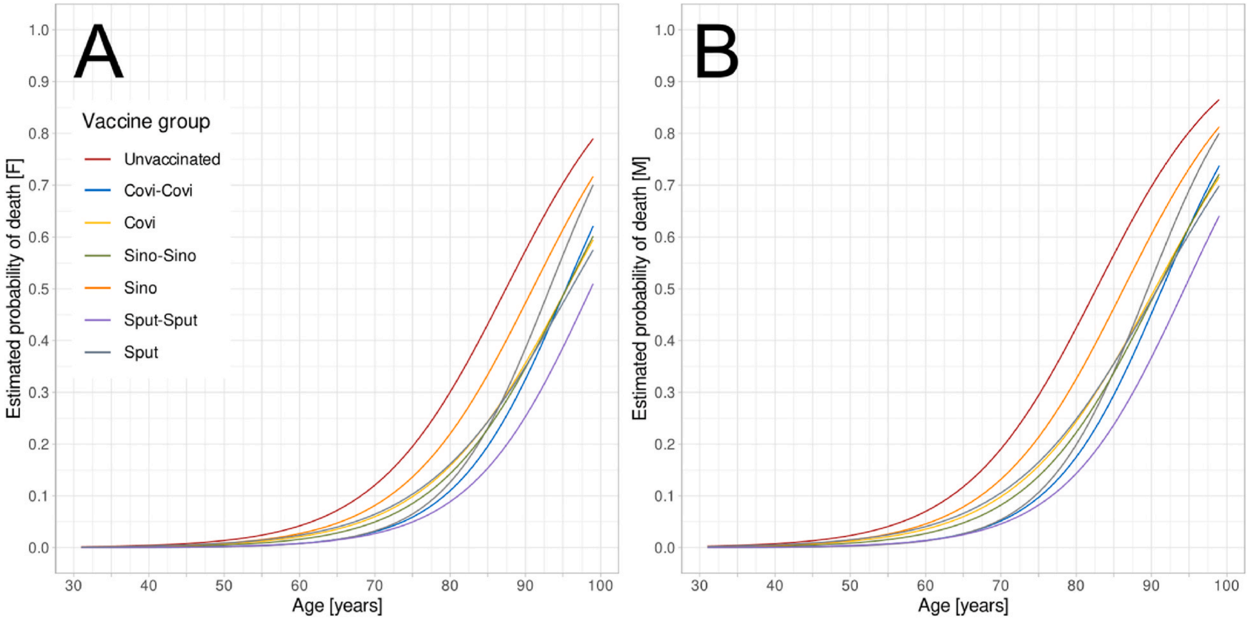

Fig. 10. Probability of death curves estimated for vaccine group by age and sex, for women (A) and men (B).

resultant effectiveness varied between males and females. Specifically, for a 70-year-old man initially unvaccinated the estimated PD decreased from 20% to 5% after receiving two doses of Sputnik, indicating a reduction of 20 pp in PD and an effectiveness of 75%, as depicted in Fig. 10. Similar patterns were observed for other vaccines, but the magnitude of effectiveness varied between sexes, with some schemes showing more pronounced benefits in either males or females.

Fig. 11 provides a detailed examination of vaccine effectiveness as influenced by sex and vaccination status. The curves clearly demonstrate that the effectiveness for individuals who received two doses generally stayed above the 50% mark, highlighting a robust response to the full vaccination schedule. Notably, this trend was consistent across both sexes, though a marked decrease in effectiveness was observed in individuals over the age of 80. Conversely, for those who received only a single dose, the effectiveness rarely met or exceeded the 50% threshold, suggesting a significantly diminished protective effect compared to the complete course.

Fig. 12 extends this analysis to include age and vaccine group, presenting a nuanced view of how these factors interact. It's evident that two doses of certain vaccines, specifically Sputnik (Sput-Sput) and AZ/Covishield (Covi-Covi), were highly effective, exceeding

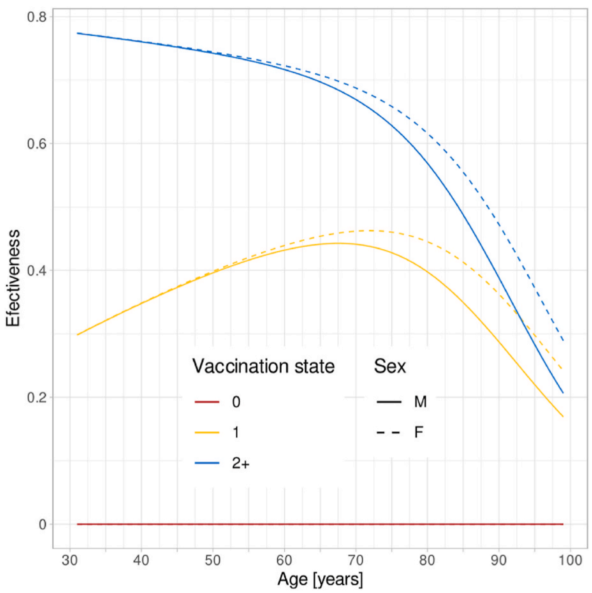

Fig. 11. Effectiveness curves estimated as a function of age, sex, and vaccination state.

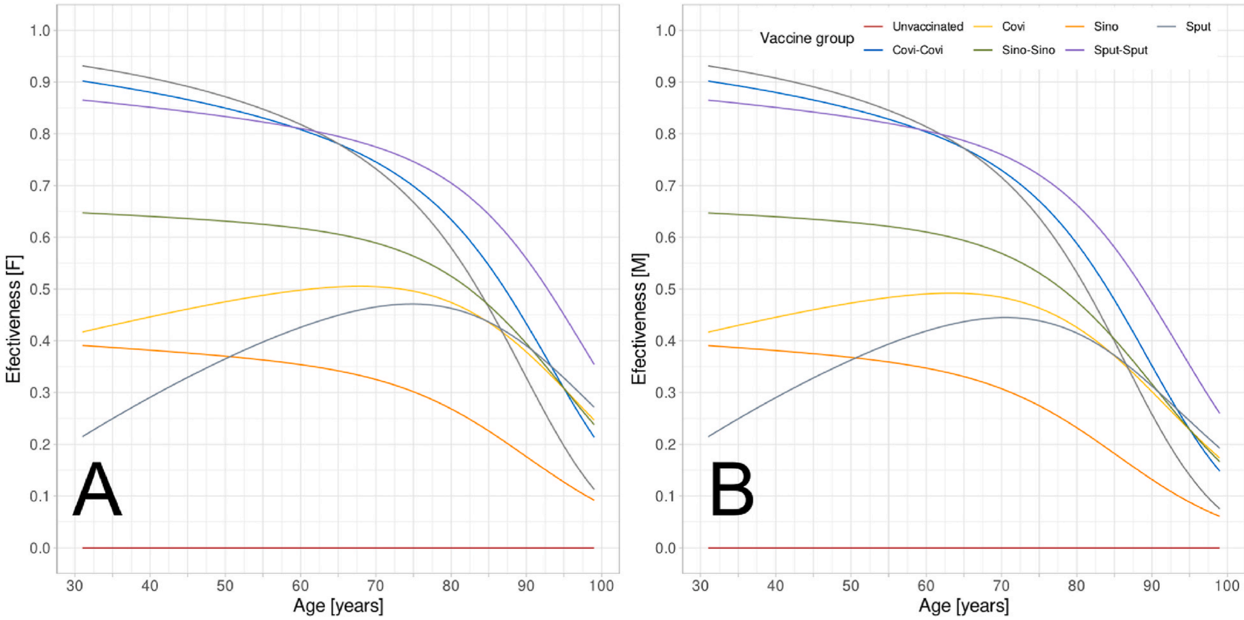

Fig. 12. Effectiveness curves estimated as a function of age, vaccine group and sex: female (A) and male (B).

80% effectiveness in individuals under 60. This high level of effectiveness, however, showed variations when considering different age groups and vaccines, indicating the importance of considering both age and vaccine type in assessing vaccine effectiveness.

Second modelling approach showed similar results, highlighting the notable influence of vaccination (state: $p < 2e\text{-}16$, group: $p < 0.000367$), age ($p < 2e\text{-}16$), sex ($p < 2e\text{-}16$), and socio-economic factors (UBNI: $p < 2e\text{-}16$) on COVID-19 mortality (see Figs. S1–S3). It also showed the enhanced effectiveness of two vaccine doses, particularly Sputnik and AZ/Covishield, in significantly reducing death risk. Women showed a lower risk compared to men. Seasonal trends influenced mortality rates, notably increasing in winter. Additionally, socio-economic status and municipality of residence were influential, as shown by variations across municipalities in Fig. S3. More detailed results are available in the Supplementary Material.

Finally, to assess the overall impact of the vaccination program during the study period, we sought to quantify the additional number and proportion of deaths that would likely have occurred if the entire population in our dataset had not been vaccinated. This calculation involved estimating the death probability for each individual case while maintaining all other co-variables at their actual observed values but altering the vaccination status to 'unvaccinated'. By doing so, we were able to simulate a scenario where vaccination was not a contributing factor. The critical step in this process was to compare the sum of these predicted probabilities against the actual number of deaths recorded. This comparison provided us with an estimate of the excess deaths that might have been expected had there been no vaccination intervention. For the Buenos Aires Province (BAP) during the year 2021, our analysis revealed that the absence of vaccination would have resulted in an additional 7610 deaths. This figure represents a significant excess of 25.4% over the actual number of deaths observed. This extrapolated increase in mortality, derived from our model, underscores the profound impact that the vaccination program had in mitigating the effects of COVID-19 within the studied population.

4. Discussion

This study presents an observational quantification of the impact on the probability of death due to COVID-19 of the vaccination campaigns conducted in 2021 in Buenos Aires Province, Argentina. The study population consists of all confirmed cases of the pandemic recorded in a database made available to the authors. To our knowledge, this is one of the first studies in Argentina that derives an observational quantification of the effect of a vaccination campaign, has comprehensive coverage of a large area and population, and includes variables for socio-economic level and municipality of residence in the analysis. These elements provide a nuanced understanding of the impact of vaccination campaigns in the region and represent a valuable contribution to the existing literature on this topic.

The results obtained reveal that the impact of the COVID-19 vaccination campaigns on the population's death probability was statistically and empirically significant, thus testifying to their effectiveness. Especially good results were achieved with persons receiving two or more doses, for whom effectiveness levels in some cases came close to 90%. This is more or less consistent with, although generally slightly below, what has been reported in similar studies [3–6,10]. The levels declined with age and were lower for men than for women, but generally remained above 50%. For a single dose, by contrast, effectiveness was considerably reduced, with levels reaching 50% at most and falling off rapidly for men of advanced age. As for the comparative effectiveness of the three widely administered vaccine types, the best performer was Sputnik. The results obtained with AZ/Covishield were somewhat less impressive, while for Sinopharm they were slightly worse both with one dose and two or more. Similar vaccine effectiveness trends are reported in the Hungarian study and the Argentinean study of over-60s cited earlier [3,10].

It is important to note that our analysis did not consider cases of heterologous vaccination due to their low representation in the dataset. This limitation precluded a detailed comparative analysis of the efficacy of heterologous vaccine combinations, that could have been of interest [20].

The estimate of the proportion of expected additional deaths that would have occurred had none of the persons in the study received vaccinations indicated an excess of 25.4% over the number of deaths actually observed. This value provides further perspective on the quantitative impact of the Buenos Aires Province vaccination campaigns. In global terms, the above findings suggest that they had a positive effect in preventing deaths due to COVID-19, consistent with and similar to the positive effect reported in the Hungarian case [10]. This calculation should not, however, be interpreted as a counterfactual estimate of the number of persons who would have died had they not been vaccinated, given that without vaccination the propagation dynamic over the course of the year would have been very different. Rather, it should be seen as one possible approach to quantifying the positive impact of the vaccination drives.

Two other factors included in the study that generated interesting results were the municipality of residence of infected persons and the time of year of symptom onset. In the former case, a municipality's socioeconomic level as measured by the unsatisfied basic needs index proved to be a moderately good predictor of death probability, which was slightly higher in municipalities with poorer populations. In the latter case, death probability was found to rise in the winter months.

It should also be noted that as an observational study, the analysis presented here may not be free of confounding factors such as individual risk factors or co-morbidities. The vaccinated population covered by the data could be expected to have an above-average prevalence of such factors given that the vaccination campaigns prioritized populations groups where this was the case [19,20]. The effectiveness estimates reported here may thus be considered as minimum levels.

This study's findings could be significantly improved by including reliable metrics for individuals' risk factors and pre-existing co-morbidities at the time of infection. Such information would assist in reducing potential biases that complicate the comparisons of effectiveness for different vaccine types and numbers of doses received. A further extension of interest would be to compare the different models' results with thresholds for the time elapsed between vaccination and symptom onset other than the 14 days considered here.

As regards other studies, despite certain similarities, most of them do not adjust for potential confounders relating to socioeconomic level so their results are not directly comparable with the present analysis [6,10]. An exception is the study done for Chile which did adjust for such factors, but the CoronaVac vaccine administered there was not used in Argentina [9].

Finally, we recall that our study population was limited to confirmed COVID-19 cases. Thus, it was not possible to draw any conclusions regarding the effectiveness of the vaccines in terms of their potential reduction of contagion or infection rates. In the latter case, an analysis could be performed by incorporating data on the percentage of the population by age and sex that was vaccinated at each date over the course of the year. The same limitations apply to the case of heterologous vaccination cases due to their low representation in the dataset. This prevented a detailed comparative analysis of the efficacy of mixed vaccine schedules, a topic that could be highly relevant given emerging global vaccination strategies [18].

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Research in context

For the present study, we looked in PubMed and medRxiv for observational studies published between January 1, 2021, and December 31, 2022, using the terms "COVID19 vaccine effect observational", "COVID19 vaccine effect real-world nation", or "COVID-19", "vaccine", "effectiveness", and "real-world effectiveness". Only articles with no language restrictions were selected. The search returned six studies, all of which were relevant in some regard to our research. In a test-negative, case-control, and retrospective longitudinal study conducted in Argentina on persons aged over 60, the effectiveness of the rAd26-rAd5 (Sputnik), ChAdOx1-S (AZ/Covishield), and BBIBP-CorV (Sinopharm) vaccines on SARS-CoV-2 infection and the risk of death in people with RT-PCR-confirmed COVID-19 was assessed using data from the National Surveillance System. The estimated vaccine effectiveness in preventing death due to COVID-19 among those who received one dose varied between 70.4% and 83.1%. Effectiveness was found to be higher among those who received two doses, ranging from 85.0% to 93.7%, with BBIBP-CorV (Sinopharm) being the least effective vaccine. An observational study in Israel using national surveillance data evaluated the nationwide public-health impact following the widespread introduction of BNT162b2 (Pfizer) vaccine by estimating real-world effectiveness of two doses of that vaccine. In England, a test-negative case-control study of older adults was conducted to estimate the real-world effectiveness of the BNT162b2 (Pfizer) vaccine against confirmed COVID-19 symptoms. Combined with the effect against symptomatic disease, a single dose was 85% effective at preventing death due to COVID-19, while a second dose was associated with further protection against symptomatic disease. Similarly, a national prospective cohort study in Scotland of first-dose mass COVID-19 vaccination with the BNT162b2 (Pfizer) and ChAdOx1-S

(AZ/Covishield) vaccines showed substantial reductions in the risk of hospital admission due to COVID-19. An historical cohort study on a target population of 1.8 million adults residing in southern Iran using 4-repository administrative data linkage showed that the implementation of a vaccination plan was associated with a significant reduction of deaths related to COVID-19. More precisely, the results showed a major reduction in mortality (at least 85%) in all age subgroups of the population fully immunized with the BBIBP-CorV (Sinopharm), ChAdOx1-S (AZ/Covishield), rAd26-rAd5 (Sputnik), and BIV1-CovIran (COVIran Barekat) vaccines. In Chile, a prospective national cohort study for the country's mass vaccination campaign with the CoronaVac (Sinovac) vaccine assessed the effectiveness in preventing Covid-19-related death. Covering approximately 10.2 million persons from February 2 through May 1, 2021, it included socio-economic variables such as income. Among persons who were fully immunized, the adjusted vaccine effectiveness in preventing Covid-19-related deaths was estimated to be above 86%. The vaccination campaign in Hungary, conducted with five different vaccines during 2021, was no exception to the above results. An observational study of 3.7 million individuals in that country receiving two doses of the BNT162b2 (Pfizer), BBIBP-CorV (Sinopharm), rAd26-rAd5 (Sputnik), ChAdOx1-S (AZ/Covishield), or mRNA-1273 (Moderna) vaccines estimated effectiveness against COVID-19-related mortality at 87.8%–97.5%.

Added value of this study

The present study in Argentina (Buenos Aires Province) provides valuable insights to the existing literature on the real-world effectiveness of national vaccine campaigns in low- and middle-income countries. Buenos Aires Province is home to almost 40% of Argentina's inhabitants and accounted for about 45% of the entire country's 2021 SARS-CoV-2 (COVID-19) deaths. Our analysis presents an observational quantification of the impact of vaccination campaigns on the probability of death due to COVID-19 using a dataset of nearly 1.5 million confirmed COVID-19 cases from Argentina's Integrated Health Information System database. Among its strengths are the comprehensive coverage of a large area and population, the observational quantification of the effect of vaccination campaigns considering the recipient's age and sex, and the inclusion as variables of socio-economic level and municipality of residence. These characteristics together provide a nuanced understanding of the impact of vaccination campaigns and represent a valuable contribution to the existing literature.

Implications of all the available evidence

The results reveal significant statistical and empirical impacts of the vaccination campaigns studied on the death probability of the population of confirmed SARS-CoV-2 (COVID-19) cases, thereby providing evidence of the campaigns' effectiveness. The effectiveness levels were always below 50% for a single dose and ranged from 50% to 90% for two or more doses, declined with increasing age, and were greater among women than men. A municipality's socioeconomic level proved to be a moderately good predictor of death probability, which was slightly higher in municipalities with poorer populations.

Data availability statement

The data associated with this study is not publicly available in a repository, and the authors do not have the permissions to share it. Data access can be obtained by approaching the Buenos Aires Province Ministry of Health directly.

This study was made possible thanks to the data provided under an agreement signed in 2020 between the Faculty of Exact and Natural Sciences at the University of Buenos Aires and the Buenos Aires Province Ministry of Health with a view to developing mathematical and computational tools to assist health authorities in decision-making and public policy analysis relating to the COVID-19 pandemic.

This study did not require ethical approval. This is because, according to Resolution 1480/11 of the Ministry of Health of the Argentine Nation, the following are exempt from the ethical evaluation:

(…)(b) when the intervention is limited to the study of health systems, official public health programs, or public health surveillance, provided that there is no possibility of identifying individuals. Public health surveillance includes official records or records made in accordance with the health authority of diseases and adverse drug effects already registered by the competent regulatory authority.

Also, the analysis of the database was conducted without any personal identification. The data were anonymized using the following procedure: the personal identification number was used by the Buenos Aires Province Ministry of Health to link the follow-up and vaccination databases. After this process, they removed the personal identification number and created an identification reference number for each individual. This reference number is not associated with any personal information and was the reference number given to us when they provided the database.

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Credit authorship contribution statement

Guillermo Durán: Supervision, Resources, Project administration, Investigation, Funding acquisition, Conceptualization. **Manuel Durán:** Data curation. **Andrés Farall:** Validation, Supervision, Project administration, Methodology, Formal analysis, Conceptualization. **Jemina García:** Visualization, Software, Methodology, Investigation, Formal analysis. **Daniela Parada:** Writing – review & editing, Writing – original draft, Validation, Supervision, Software, Formal analysis, Data curation. **Ariel Salgado:** Writing – review & editing, Visualization, Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e26310.

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