Cuban Abdala vaccine: Effectiveness in preventing severe disease and death from COVID-19 in Havana, Cuba; A cohort study

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Summary

Background COVID-19 vaccines have proven safe and efficacious in reducing severe illness and death. Cuban protein subunit vaccine Abdala has shown safety, tolerability and efficacy (92.3% [95% CI: 85.7–95.8]) against SARS-CoV-2 in clinical trials. This study aimed to estimate Abdala’s real-world vaccine effectiveness (VE).

Methods This retrospective cohort study in Havana analyzed Cuban Ministry of Public Health databases (May 12–August 31, 2021) to assess VE in preventing severe illness and death from COVID-19 (primary outcomes). Cox models accounting for time-varying vaccination status and adjusting by demographics were used to estimate hazard ratios. A subgroup analysis by age group and a sensitivity analysis including a subgroup of tested persons (qRT-PCR) were conducted. Daily cases and deaths were modelled accounting for different VE.

Findings The study included 1,355,638 persons (Mean age: 49.5 years [SD: 18.2]; 704,932 female [52.0%]; ethnicity data unavailable): 1,324 vaccinated (partially/fully) and 31,433 unvaccinated. Estimated VE against severe illness was 93.3% (95% CI: 92.1–94.3) in partially-vaccinated and 98.2% (95% CI: 97.9–98.5) in fully-vaccinated and against death was 94.1% (95% CI: 92.5–95.4) in partially-vaccinated and 98.7% (95% CI: 98.3–99.1) in fully-vaccinated. VE exceeded 92.0% in all age groups. Daily cases and deaths during the study period corresponded to a VE above 90%, as predicted by models.

Interpretation The Cuban Abdala protein subunit vaccine was highly effective in preventing severe illness and death from COVID-19 under real-life conditions.

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Introduction

The coronavirus disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has resulted in a massive global disease burden. Non-pharmacological interventions have been the main public health strategies and policies implemented. Likewise, several COVID-19 vaccines have been rapidly developed and approved for emergency use to tackle the prolonged pandemic, and mass
vaccination campaigns have been implemented in many countries. However, these achievements have not been made available equitably, and huge access asymmetries remain between rich and poor countries. In Cuba, the first COVID-19 cases were detected on March 11, 2020. Since then, the infection has reached epidemic levels, with thousands of cases and deaths, constituting the country’s main health problem. From the start of the epidemic, Havana accounted for the majority of cases and the highest incidence, despite the population being subject to non-pharmacological interventions established by the Ministry of Public Health (MINSAP). By July 9, 2021, there were 608 confirmed cases (284.4 per 1 000 000 population) and 3 deaths (1.4 per 1 000 000 population) in Havana, which increased notably, reaching a peak of 1994 cases (932.7 per 1 000 000 population) on July 30 and 10 deaths (4.7 per 1 000 000 population) on August 1. There was higher transmission in municipalities with higher population densities and more appreciable transmission in paediatric age groups. Of the circulating SARS-CoV-2 variants, Delta was detected in Cuba at the end of April, spread rapidly nationwide and replaced other variants by July, resulting in high disease transmission and dispersion.

Cuba’s strategy to address the pandemic’s challenges was to develop its own vaccine, taking advantage of biotechnological institutions with over three decades’ experience. By March 2021, Cuba had developed five vaccine candidates, all based on the protein subunit technological platform: Abdala, Mambisa, and Soberana 01, 02, and Plus.

Abdala is a recombinant protein subunit vaccine developed by the Genetic Engineering and Biotechnology Centre (CIGB) that uses the yeast Pichia pastoris as the microorganism for expression. Its formulation includes SARS-CoV-2’s recombinant protein receptor binding domain (RBD), with aluminium hydroxide gel as an adjuvant. Abdala’s complete vaccination schedule (per manufacturer guidelines, CIGB, Havana, Cuba), consists of three doses of 0.5 mL, administered intramuscularly (IM) in the deltoid region on days 0-14-28. It may be used as a booster or combined with other vaccines. Abdala’s clinical trials (RPCEC00000346, RPCEC00000359, RPCEC00000363), assessing safety, immunogenicity and efficacy, showed that it was well-tolerated, and no severe adverse events were reported. In a phase 1/2, randomized, double-blind, placebo-controlled trial carried out in “Saturnino Lora” Hospital, Santiago de Cuba, Abdala vaccine was safe, well tolerated, and induced humoral immune responses against SARS-CoV-2 with a 50 mg dose, applied in a 0-14-28 days schedule. In a multi-centre, randomized, double-blind placebo-controlled phase 3 study in 48 290 adult volunteers, Abdala demonstrated an efficacy of 92.3% (95% CI: 85.7–95.8), but, so far, peer-reviewed manuscript of phase 3 randomized clinical trials from Abdala are still unpublished.

Considering these results, the Cuban regulatory agency (Centre for State Control of Medicines, Equipment and Medical Devices, CECMED, Spanish) issued an emergency use authorization (EUA) for Abdala on July 9, 2021. The complex epidemiological situation previously described increased the burden on healthcare services.

Research in context

Evidence before this study

We searched PubMed and preprint archives (MedRxiv) for articles published in English and Spanish between December 1st, 2021 and February 28, 2022, using the keywords “COVID-19”, “SARS-CoV-2”, “vaccine”, “vaccination”, “effectiveness”, “real world” and “cohort study”. We selected articles containing information about COVID-19 vaccine effectiveness in the real world. Our search returned 268 studies, 31 of which were relevant to this topic. Previous studies have mainly focused on the effectiveness conferred by messenger RNA, viral-vector and inactivated virus vaccines in high and middle-income countries, but data about the effectiveness conferred by protein subunit vaccines in low-income countries are limited. To our knowledge, there is no previous real-world effectiveness assessment of the Cuban Abdala vaccine.

Added value of this study

The analysis of the effectiveness of the Abdala protein subunit vaccine in real-world conditions is the first carried out in Cuba and is similar to others carried out in the world. Demonstrates its high protective effect against severe forms and death from SARS-CoV-2 infection, with a complete schedule of three doses (0-14-28 days), in a scenario with a clear predominance of the variant of concern Delta. Likewise, it shows that implemented vaccination strategy, with a reduced scheme, accelerated and massive application in the population, provided satisfactory results against severe disease and fatal outcomes in adults and may be viable in a low-income country.

Implications of all the available evidence

Data from this study, compared with others in different countries, support the benefit of vaccines against COVID-19 as public health measures and suggest that their rapid, organized and massive use is a correct strategy to control pandemic, always considering the health system’s characteristics. The inability of the available COVID-19 vaccines to effectively prevent infection, their potential effectiveness against the different variants of concern, the duration of their long-term protection and the need for booster doses are issues that require further attention.
in Havana, prompting the accelerated application of the Abdala vaccine, reaching a vaccination coverage of 88.4% in the adult population by August 31, 2021.

This study’s objective was to estimate Abdala’s real-world effectiveness in preventing severe illness and death from COVID-19 in fully and partially vaccinated adult persons in Havana, Cuba, compared to those who were unvaccinated. Estimates obtained for Abdala’s effectiveness were contrasted with vaccine effectiveness forecasts made, considering a 70% vaccine effectiveness; 90% vaccine effectiveness; and no vaccination for Abdala vaccine sufficient doses were available for the entire Havana adult population. The vaccine was administered free of charge in stages in each of the city’s municipalities, using both personnel and vaccination sites that were duly accredited by CECMED and MINSAP.

For the purpose of this study, persons were considered fully vaccinated if they had received the complete vaccination schedule and were ≥14 days past their third dose and partially vaccinated if they had received 1-2 doses or 3 doses and less than 14 days past their third dose. Those who did not meet this criterion were included in the unvaccinated group.

A short follow-up study of the cohort was carried out for 111 days (from May 12 through August 31, 2021) via surveillance mechanisms implemented by MINSAP.

Methods
Study context
The study was carried out in Havana, Cuba, which is comprised of 15 municipalities with an estimated population of 2,137,916 inhabitants as of June 30, 2021, according to the National Statistics and Information Office (ONEI; www.onei.gob.cu).

From the start of the epidemic, Havana’s population was subject to the general measures established by the Ministry of Public Health (MINSAP) including mandatory masking, social distancing, restrictions on movement, and isolation of positive cases. These conditions and guidelines were maintained throughout the study period.

Design
To estimate the real-world effectiveness of the Abdala vaccine, we conducted an observational retrospective cohort study including persons aged ≥19, residing in Havana, and unvaccinated at the start of the study, which received subsequently the vaccine during a massive vaccination campaign. From this population, and after considering eligibility criteria, study cohorts were formed according to vaccination status: unvaccinated and vaccinated (partially and fully), and followed for 111 days. Inclusion in the three groups was dynamic throughout the study period; participants who did not receive vaccination were initially counted in the unvaccinated group until they had received their first dose, after which they were transitioned into the partially vaccinated group, where they stayed until received the third dose and 14 days elapsed, then they were moved to the fully vaccinated cohort. Havana’s primary health-care system covers the resident population regardless of socioeconomic, political or cultural status, gender, race or ethnicity. Primary care data from family doctors’ office records were linked to laboratory test results, vaccination registries, patients’ clinical histories and epidemiological survey forms.

Exposure
Abdala vaccine sufficient doses were available for the entire Havana adult population. The vaccine was
Provincial Hygiene, Epidemiology and Microbiology Centre via real-time reverse transcriptase polymerase chain reaction (qRT-PCR, STAT-NAT COVID-19 MULTI, Italy) using nasopharyngeal swab samples, according to World Health Organization (WHO) guidelines for qRT-PCR,17 applied free of charge for the general population, including all participants in this study.

Participants
For the purpose of this study, we considered inclusion criteria to be 19 years of age or older, not having been diagnosed with SARS-CoV-2 infection (qRT-PCR test+) prior to the start of the study, being residents of Havana, and having complete and accurate data.

Eligible for the study were 1 733 607 persons aged ≥19 years whose data were available and correctly registered. Of these, 377 969 were excluded: 52 260 whose qRT-PCR tests confirmed SARS-CoV-2 infection prior to study start; 83 400 who received a COVID-19 vaccine other than Abdala; and 242 309 who had inaccurate data.

Study inclusion criteria were met by 1 355 638 persons who were divided into two cohorts: 1 324 205 individuals in the vaccinated cohort (1 223 350 fully vaccinated and 100 855 partially vaccinated), and 31 433 in the unvaccinated cohort (Figure 1).

Variables
In both cohorts, the COVID-19 outcomes measured included severe disease, defined by MINSAP’s COVID-19 National Action Protocol,18 and death according to WHO.19 All cases included in the study were confirmed positive for COVID-19 by qRT-PCR.

The following criteria were considered for variables:

- Age: four groups were established (19–40, 41–60, 61–80, >80 years).

![Figure 1](https://example.com/figure1.png)

**Figure 1.** Abdala vaccine effectiveness study participants: eligibility, exposure and outcomes. Havana, Cuba, May 12–August 31, 2021.
• SARS-CoV-2 infection: an individual with or without characteristic COVID-19 symptoms, with a positive qRT-PCR test from a nasopharyngeal swab sample taken at a healthcare institution.
• Severe clinical illness due to COVID-19: patients with fever, cough, polyneuropenia, infiltrate/condensation in radiological examination or lung ultrasound, oxygen saturation <90%, or who required mechanical ventilation.
• Death from COVID-19: a person who died as a result of confirmed COVID-19, with symptoms clinically compatible with the disease.

Statistical methods
We estimated the vaccine effectiveness with Cox proportional hazards models, using vaccine status as a time-varying covariate for all individuals included. Primary outcomes of interest were severe disease and death. We right-censored individuals at the time of an event (Intensive Care Units [ICU] admission or death associated with COVID-19) and at the end of the follow-up period (31st of August). Exposure was specified according to vaccination status (fully-vaccinated, partially-vaccinated or unvaccinated). The same cohort contributed person-time at risk to unvaccinated and vaccinated exposure categories, with all individuals starting in the unvaccinated state and sequentially transitioning through vaccinated exposure states until the outcome of interest or being censored at the point of the follow-up period. Hazard ratio (HR) estimates were obtained with 95% confidence intervals (95% CI).

For crude vaccine effectiveness estimates, we only used vaccine status as a time-varying covariate with no adjustments for covariates. The adjustment was made using stratification by age, sex and municipality in the survival R package. To estimate specific vaccine effectiveness for age groups we implemented independent Cox models still adjusting for the remaining covariates. The adjustment was made using stratification by age, sex and municipality in the survival R package. To estimate specific vaccine effectiveness; 90% vaccine effectiveness; and no vaccine effectiveness. Data was analysed with R (4.1.1), Foundation for Statistical Computing, Vienna, Austria. Forecasting cases were estimated with MATLAB and Statistics Toolbox Release 2018b software, The MathWorks, Inc., Natick, Massachusetts, United States.

Ethics
The study protocol was approved by the Research Ethics Committee of the Pedro Kouri Tropical Medicine Institute (IPK)—CEI-IPK protocol 31-21, November 2021. The study complies with the bioethical framework for this type of medical research. Data for the study come from records of the MINSAP entity responsible for collecting infectious disease notifications, as well as for epidemiological population health surveillance and management, and thus their use does not require informed consent. This information is protected, and the confidentiality of all participants is preserved. Demonstrating the effectiveness of the Abdala vaccine against COVID-19 provides essential information and is the benefit of this study.

Role of the funding source
The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results
Throughout the study period of May 12 through August 31, 2021, 1,355,638 persons met the inclusion criteria. Of these, 1,223,350 were fully-vaccinated, 106,855 were partially-vaccinated, and 31,433 were unvaccinated. The mean age was 49.5 years (SD: 18.2), thus most individuals were aged 19-40 years (469,383/1,355,638 [34.6%]) and 41-60 years (307,362/1,355,638 [37.4%]). Overall, there were more females (52.0%) than males and most participants inhabited Boyeros (10.8%) and Arroyo Naranjo (10.0%) municipalities. More than 70.6% of severe disease cases (946/1347 [70.3%]) and deaths (441/579 [70.4%]) were observed in individuals >60 years and males predominated in both outcomes (738/1347 [54.8%] and 312/570 [54.7%], respectively. The highest numbers of severe disease cases and deaths were observed in municipalities Diez de Octubre and Plaza (Table 1).
During follow-up, COVID-19 severe disease occurred among 181 fully-vaccinated individuals, 228 partially-vaccinated individuals and 938 unvaccinated individuals, with incidence rates per 10,000 person-years of 0.03, 0.04 and 0.23, respectively (Table 2). All participants received specialized medical care in Havana hospitals’ ICU. Death from COVID-19 was reported in 76 patients who had been fully-accinated, 128 patients partially-vaccinated and 366 who were unvaccinated. Among COVID-19 fatalities, lower incidence densities were observed in fully-vaccinated (0.01 per 10,000 person-years) and partially-vaccinated (0.02 per 10,000 person-years), compared to unvaccinated individuals (0.09 per 10,000 person-years) (Table 2).

The overall estimated effectiveness against severe disease reached 93.3% (95% CI: 92.1-94.3) in partially-vaccinated and 98.2% (95% CI: 97.9-98.5) in fully-vaccinated (Table 2), with the highest numbers in

| Outcome | Total person-time, days | Number of event | Incidence density per 10,000 person-days | Unadjusted hazard ratio (95% CI) | Adjusted hazard ratio (95% CI) | Vaccine effectiveness (95% CI) |
|---------|-------------------------|-----------------|------------------------------------------|--------------------------------|-------------------------------|--------------------------------|
| **Severe disease** | | | | | | |
| Unvaccinated | 40 550 127 | 938 | 0.23 | - | - | - |
| Partially vaccinated | 58 783 518 | 228 | 0.04 | 0.07 (0.06-0.08) | 0.06 (0.05-0.07) | 93.3 (92.1-94.3) |
| Fully vaccinated | 51 071 360 | 181 | 0.03 | 0.02 (0.01-0.02) | 0.01 (0.01-0.02) | 98.2 (97.9-98.5) |
| **Deaths** | | | | | | |
| Unvaccinated | 40 550 363 | 366 | 0.09 | - | - | - |
| Partially vaccinated | 58 783 994 | 128 | 0.02 | 0.08 (0.06-0.10) | 0.06 (0.05-0.08) | 94.1 (92.5-95.4) |
| Fully vaccinated | 51 071 345 | 76 | 0.01 | 0.02 (0.01-0.03) | 0.01 (0.01-0.02) | 98.7 (98.3-99.0) |

Table 2: Abdala vaccine effectiveness in preventing severe disease and death from COVID-19. Havana, Cuba, May 12-August 31 2021.

* Adjusted by Age, Sex and Resident Area (Municipality).

Table 1: Cohort socio-demographics characteristics. Havana, May 12-August 31 2021.

| Outcomes | Total person-time, days | Number of event | Incidence density per 10,000 person-years | Unadjusted hazard ratio (95% CI) | Adjusted hazard ratio (95% CI) |
|----------|-------------------------|-----------------|------------------------------------------|--------------------------------|-------------------------------|
| Severe disease | | | | | |
| Unvaccinated | n=31 433 | | | | |
| Partially vaccinated | n=100 855 | | | | |
| Fully vaccinated | n=223 350 | | | | |
| Total | n=355 638 | | | | |
| Deaths | | | | | |
| Unvaccinated | n=23,023 | | | | |
| Partially vaccinated | n=2,468 | | | | |
| Fully vaccinated | n=1,071 | | | | |

Table 2: Abdala vaccine effectiveness in preventing severe disease and death from COVID-19. Havana, Cuba, May 12-August 31 2021.
individuals 19-40 years (99.4 [95% CI: 98.2-99.8] and >80 years (99.1 [95% CI: 98.6-99.4]) fully-vaccinated (Table 3). Likewise, effectiveness in preventing death from COVID-19 was greater in fully-vaccinated 98.7% (95% CI: 98.3-99.0) than those partially-vaccinated 94.1% (95% CI: 92.5-95.4) (Table 2). Similarly, the highest figures were observed in persons fully-vaccinated 19-40 years (99.5 [95% CI: 98.2-100.0] and 61-80 years (98.8 [95% CI: 98.3-99.2]) (Table 3).

Sensitivity analyses of potential differences in access to health care services between vaccinated and unvaccinated by immunization status, adjusted by age group, sex and resident area including only individuals who took an qRT-PCR during the study period, showed vaccine effectiveness estimates against severe disease COVID-19 and death above 90.0% (Appendix, Tables S-I and S-II), similar to those of the main analysis; confirming that effectiveness in the vaccinated cohort was consistent. These results address the concern that the observed vaccine effectiveness might be affected by healthcare access because all individuals included in the analysis had demonstrated access to the Cuban healthcare system.

At the beginning of the study, daily cases and deaths reported by MINSAP agreed with forecasts that aligned with vaccine effectiveness of 90%, but by the study’s midpoint, when vaccination coverage was 75%–80%, cases and deaths began to steadily decrease. This was much more apparent in the last weeks of the study period, indicative of effectiveness above 90% and thus consistent with the estimated effectiveness (Figure 2).
Discussion
This study was conducted under real-world conditions amidst COVID-19 Delta variant transmission, in a middle-income country, and included a large segment of Cuba’s most populous city. The results validate the high effectiveness of the protein subunit Abdala vaccine in preventing severe COVID-19 disease and death, when measured from 14 days after administration of the full three-dose schedule (following the manufacturer’s recommended application at 0-14-28 days), achieving the desired effect in a relatively short time. In partially vaccinated individuals (1-2 doses or 3 doses and less than 14 days past their third dose), similar results were obtained for both outcomes (vaccine effectiveness 93.3% and 94.1% respectively).

Severe disease has important implications for public health and policy making, since it may not only lead to death but also long-lasting sequels, with substantial repercussions for populations and healthcare systems. Our results demonstrate that the Abdala vaccine provides substantial protection for older adult populations and adds to the knowledge base of real-world COVID-19 vaccine effectiveness. In both outcomes (preventing severe disease and death), the Abdala vaccine’s effectiveness was satisfactory (>90%) for all age groups, and the vaccine has received EUA in several other countries.

Similar results in preventing severe disease and death have been reported in other countries. Systematic reviews including a wide variety of study types and settings, including 107 real-world vaccine effectiveness studies in adults which covered eight vaccines across all vaccine platforms, demonstrated protection against COVID-19 severe infection or death in the general population of, at least, 60% and most often close to 100%. However, it should be noted that variations in estimated effectiveness reported in other studies could result from differing study designs, settings, testing protocols, study populations, types of vaccine, schedules and time intervals considered appropriate to best measure each vaccine’s immunological effects. More real-world effectiveness studies of longer durations are required in low-and middle-income countries since the majority of such research has been carried out in high-income nations.

A major unresolved issue regarding COVID-19 vaccines is their inability to effectively prevent infection. Additionally, authorizations for their use have been given via accelerated regulatory pathways, with limited supporting clinical data, making it imperative to continue research to provide additional, more robust information on their safety, efficacy, effectiveness, and long-term protection; all of which are important to consider risk, minimize damage and maintain public confidence over time.

An observational study under real-world conditions is difficult to conduct without introducing bias, given the lack of vaccine randomization and of balance between vaccinated and unvaccinated persons with respect to the risk of contracting the disease. The main biases of concern for this study (the search for and access to healthcare, diagnosis confirmation, exclusion of persons with prior COVID-19 infection, and previous vaccine administration, among others) coincide with the bias described by WHO. Overall, our adjusted sensitivity analyses of qRT-PCR tested individuals by immunization status were qualitatively similar to those obtained by considering the complete cohort, and provides empirical evidence that they are unaffected by a potential differential health care access. Potential under-testing, under-diagnosis and under-notification bias cannot be ruled out and should be considered as a limitation. All three were minimized by performing confirmatory qRT-PCR tests on everyone with COVID-19 symptoms, as well as on their contacts, a practice established in the Cuban National COVID-19 Action Protocol (Version 1.6) and backed by the characteristics of the Cuban health system described previously.

To control for prior infection bias those who were confirmed positive for SARS-CoV-2 before the start of the study were excluded. During the study period, the number of tests was considerably expanded nationwide, increasing the number of qRT-PCR and antigen tests performed.

Selection biases and confounding effects due to possible imbalances caused by comorbidities associated with the disease were unavoidable potential limitations and should be considered when assessing our study. It was not possible either to fix propensity bias to get vaccinated, or propensity to get vaccinated early in the study period. Data on ethnicity were not collected either, considering that Cuba is a country with an important mix of race among the population and no particular ethnic groups share economic, cultural and social characteristics.

Outcome misclassification due to false negatives cannot be completely ruled out, even if a test with high SARS-CoV-2 specificity was used. Finally, although vaccination registries may have missed some vaccinated individuals within the Cuban healthcare system, automated data collection via the ANDariego.HIGia registry minimized this effect. Although genomic sequencing in Havana detected a switch from beta to delta as the main variant of concern with the highest circulation during the study period, we lack representative contextual data from that period.

The study period encompasses the most complex epidemiological situation of the COVID-19 epidemic in Havana. From our point of view, the accelerated and high coverage vaccination campaign carried out and including all population (regardless of age, sex, skin colour, economic status, religion or political trends), based on community participation and supported by governmental institutions, contributed decisively to a fast decline of cases, severe disease and deaths, allowing for the recovering of social and productive activities -
including the opening of airports - a few weeks later, which continued until today.

Our results contribute to a better understanding of Abdala’s effects on SARS-CoV-2 infection and highlight the importance of these studies in demonstrating vaccine protection against severe illness and death from COVID-19, and ratify the usefulness of vaccines as essential tools to control the disease and improve its outcomes. These data may also be useful to health policymakers for use in controlling COVID-19 in their respective settings.

Follow-up on these effectiveness values over time and the need to apply booster doses to maintain effective protection are pending tasks requiring further research. However, it merits repeating that vaccines alone will not solve the problems associated with the pandemic; success in meeting these challenges requires a health system capable of rapid and organized action. This was a great strength that contributed to our ability to achieve results in a comparatively short time.

The Abdala vaccine showed high effectiveness in preventing severe illness and death under real-world conditions. Future studies will make it possible to assess the duration of the vaccine’s protection over the long term, as well as the advisability of booster doses.

Contributors
PIM-B participated in the conceptualization and study design, data analysis and interpretation, conduct and supervision of research process, literature search, writing initial draft, critical review & editing of pre- or post-publication stages. FOD-M contributed in the conceptualization and study design. Data analysis and interpretation, supervision of research, literature search, figures, writing initial draft, critical review & editing of pre- or post-publication stages. KA-R participated in conceptualization and study design. Data/evidence management, collection, analysis, and interpretation. Statistical analysis. Visualization and data presentation. Writing the initial draft. Review of pre- or post-publication stages. Literature search. LS-V contributed in conceptualization and study design. Data management, collection, analysis, and interpretation. Statistical analysis and modelling. Literature search, writing initial draft, critical review & editing of pre- or post-publication stages. RGD performed data analysis and interpretation. Mathematical analysis and modelling. Writing the initial draft, critical review & editing or revision of pre- or post-publication stages and Figures. MV-L took part in the data/evidence collection and management. Critical review & revision of pre- or post-publication stages. SD-C, MP, FH-B, ML-F, G G-N, VLM-G AND MA-A contributed to study design. Data analysis and interpretation. Critical review & revision of pre- or post-publication stages.

Data sharing statement
Data on participant vaccination were obtained from the national online registry database which is limited to authorized users. Data on other related documents are also not available. Aggregate data on vaccination, incidence and mortality are publicly available at https://covid19cubadata.github.io/#cuba

Declaration of interests
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Supplementary materials
Supplementary material associated with this article can be found in the online version at doi:10.1016/j.lana.2022.100366.

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