**SUPPLEMENTARY MATERIAL**

## Institutional review board approbals

The SEMI-COVID-19 Registry and the COVID registries of 12 de Octubre and the Costa del Sol hospitals have been approved by the Provincial Research Ethics Committee of Málaga (Spain; C.I.F. number: 0–9150013-B and Hospital 12 de Octubre Clinical Research Ethics Committee [reference 20/117]). Institutional review boards gave approval for each participating site in the Argentinian COVID-19 Network study (approval numbers: 1575, 5562, and 5606).

## Variables

Data regarding demographic, clinical, vaccination status and date of vaccination, COVID therapies, and clinical outcomes during hospitalization was captured. Clinical variables were retrieved based on ICD-10 codes for current or previous hospital visits, including hypertension, chronic obstructive pulmonary disease, coronary disease, peripheral arterial disease, asthma, heart failure, immunosuppression, cancer, chronic kidney disease, and diabetes. In-hospital treatments included steroids, and life-supporting therapies (invasive and noninvasive mechanical ventilation). Admission to critical care units was also recorded (see eTable 2). Data regarding the infecting SARS-CoV-2 variant for each patient was not available in the present study because it is not routinely collected in the participating centers. Nonetheless, infection with the Omicron variant was of special interest for this study. This variant has been proposed to present with both lower intrinsic severity among unvaccinated patients and with an inherited ability to reduce vaccine effectiveness among vaccinated ones.[18] Thus we estimated Omicron infection using data regarding circulating variants to define time intervals in which Omicron was responsible for most cases in Argentina and Spain.[19,20] From the first week of January 2022 until the end of the study period Omicron was isolated in over 80% of infections for both countries and therefore patients hospitalized in that time interval were considered as exposed to the Omicron variant in our study.

**eTable 1**. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline checklist.

| | Item No | Recommendation | Page No |
|---|---|---|---|
| Title and abstract | 1 | (a) Indicate the study's design with a commonly used term in the title or the abstract<br>(b) Provide in the abstract an informative and balanced summary of what was done and what was found | 1-2 |
| Introduction | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | 3 |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | 3-4 |
| Methods | | | |
| Study design | 4 | Present key elements of study design early in the paper | 4 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 4 |
| Participants | 6 | (a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br>(b) For matched studies, give matching criteria and number of exposed and unexposed | 4 |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 4-5 |
| Data sources/ measurement | 8 | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 4-5 |
| Bias | 9 | Describe any efforts to address potential sources of bias | 6 |
| Study size | 10 | Explain how the study size was arrived at | 6 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 6 |
| Statistical methods | 12 | (a) Describe all statistical methods, including those used to control for confounding<br>(b) Describe any methods used to examine subgroups and interactions<br>(c) Explain how missing data were addressed<br>(d) If applicable, explain how loss to follow-up was addressed<br>(e) Describe any sensitivity analyses | 6 |
| Results | | | |
| Participants | 13 | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed<br>(b) Give reasons for non-participation at each stage<br>(c) Consider use of a flow diagram | 6 |
| Descriptive data | 14 | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders<br>(b) Indicate number of participants with missing data for each variable of interest | 6-7 |

| | | | |
|---|---|---|---|
| | | (c) Summarize follow-up time (eg, average and total amount) | |
| Outcome data | 15 | Report numbers of outcome events or summary measures over time | 7 |
| Main results | 16 | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included<br>(b) Report category boundaries when continuous variables were categorized<br>(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | 7-8 |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | 7-8 |
| Discussion | | | |
| Key results | 18 | Summarize key results with reference to study objectives | 8 |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision.<br>Discuss both direction and magnitude of any potential bias | 8-9 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 8-9 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | 9 |
| Other information | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 6 |

**eTable 2.** Variable definition

| **Demographic data** | **Variable characteristics** |
|---|---|
| Age | Age in years, continuous variable. Range 18 to 120 |
| Female sex | 1 = Female sex<br>0 = Male sex |
| Omicron Variant | 1 = patient hospitalized after 1/1/2022<br>0 = patient hospitalized before 1/1/2022 |
| High income countrie | 1 = patient from Spain<br>0 = patient from Argentina |
| **Medical History** | |
| Hypertension | 1 = Hypertension<br>0 = non Hypertension |
| Diabetes | 1 = Diabetes<br>0 = non Diabetes |
| Immunosuppression | 1 = Immunosuppression<br>0 = non Immunosuppression |
| CHD or Peripheral artery disease Arteriopathy | 1 = CHD or Peripheral artery disease Arteriopathy<br>0 = non CHD or Peripheral artery disease Arteriopathy |
| Heart failure | 1 = Heart failure<br>0 = non Heart failure |
| COPD | 1 = COPD<br>0 = non COPD |
| Asthma | 1 = Asthma<br>0 = non Asthma |
| Stroke | 1 = Stroke<br>0 = non Stroke |
| CKD | 1 = CKD<br>0 = non CKD |
| Active or past cancer | 1 = Active or past cancer<br>0 = non Active or past cancer |
| **Vaccinated status** | |
| COVID-19 Vaccine doses | 0 = any COVID-19 vaccine<br>1 = 1 COVID-19 vaccine doses<br>2 = 2 COVID-19 vaccine doses |
| Date of first vaccine | Date of first vaccine |
| Date of 2nd vaccine | Date of second vaccine |
| mRNA BNT162b2 (Pfizer) | 1 = received Pfizer vaccine<br>0 = did not received Pfizer vaccine |
| ChAdOx1 nCoV-19 (AstraZeneca) | 1 = received AstraZeneca vaccine<br>0 = did not received AstraZeneca vaccine |

| | |
|---|---|
| mRNA-1273 (Moderna) | 1 = received Moderna vaccine<br>0 = did not received Moderna vaccine |
| Gam-COVID-Vac (Sputnik) | 1 = received Sputnik vaccine<br>0 = did not received Sputnik vaccine |
| BIBP-CorV (Sinopharm) | 1 = received Sinopharm vaccine<br>0 = did not received Sinopharm vaccine |
| **Treatment during hospitalization** | |
| Corticosteroid treatment | 1 = received corticosteroid systemic therapy during hospitalization<br>0 = did not received corticosteroid systemic therapy during hospitalization |
| Oxygen requirement | 1 = received supplemental Oxygen during hospitalization<br>0 = did not receive supplemental Oxygen during hospitalization |
| **In-hospital Outcomes** | |
| In-hospital mortality | 1 = in-hospital death<br>0 = survivor to the hospitalization |

COPD: Chronic obstructive pulmonary disease; CHD: Coronary Heart Disease; CKD: Chronic kidney disease

**eTable 3**. Differences between patients vaccinated with 1 dose and with 2 vaccine doses.

| | All (N=717) | 1 vaccine dose (N=338) | 2 vaccine doses (N=379) | p, overall |
|---|---|---|---|---|
| **Demographics** | | | | |
| Age - mean (SD) | 60.7 (15.8) | 56.5 (16.2) | 64.2 (14.6) | <0.001* |
| Female sex - n (%) | 311 (43.4%) | 153 (45.3%) | 158 (41.7%) | 0.374 |
| Omicron Variant - n (%) | 221 (30.9%) | 42 (12.5%) | 179 (47.4%) | <0.001* |
| High income - n (%) | 318 (44.4%) | 54 (16.0%) | 264 (69.7%) | <0.001* |
| **Medical History** | | | | |
| Hypertension - n (%) | 339 (47.5%) | 156 (46.6%) | 183 (48.3%) | 0.701 |
| Diabetes - n (%) | 149 (20.9%) | 80 (23.8%) | 69 (18.3%) | 0.083 |
| Immunosuppression - n (%) | 92 (13.5%) | 28 (9.15%) | 64 (17.1%) | 0.004* |
| CHD or Peripheral artery disease Arteriopathy - n (%) | 54 (7.55%) | 18 (5.36%) | 36 (9.50%) | 0.051* |
| Heart failure - n (%) | 58 (8.12%) | 32 (9.55%) | 26 (6.86%) | 0.239 |
| COPD - n (%) | 75 (10.5%) | 23 (6.85%) | 52 (13.8%) | 0.004* |
| Asthma - n (%) | 39 (5.45%) | 19 (5.65%) | 20 (5.28%) | 0.955 |
| Stroke - n (%) | 22 (3.14%) | 11 (3.36%) | 11 (2.95%) | 0.923 |
| CKD - n (%) | 55 (7.77%) | 21 (6.36%) | 34 (8.99%) | 0.244 |
| Cancer - n (%) | 150 (21.0%) | 49 (14.6%) | 101 (26.6%) | <0.001* |
| **Treatment during hospitalization** | | | | |
| Corticosteroids - n (%) | 513 (76.8%) | 264 (85.7%) | 249 (69.2%) | <0.001* |

*Covariables with different distribution between vaccinated with 1 and 2 covid-19 vaccine doses. These covariables were adjusted in the Multivariable Cox regression analysis.
COPD: Chronic obstructive pulmonary disease; CHD: Coronary Heart Disease; CKD: Chronic kidney disease

**eTable 4**. Missing data proportion

| | All (N=21479) | Unvaccinated (N=20762) | Vaccinated (N=717) |
|---|---|---|---|
| Hospital admission date | 408 (1.90%) | 404 (1.95%) | 4 (0.57%) |
| Age | 1617 (7.51%) | 1605 (7.73%) | 0 (0%) |
| Female sex | 398 (1.90%) | 398 (1.92%) | 0 (0%) |
| Hypertension | 45 (0.20%) | 42 (0.2%) | 3 (0.43%) |
| Diabetes | 61 (0.32%) | 58 (0.28%) | 3 (0.43%) |
| Immunosuppression | 204 (10%) | 167 (0.8%) | 37 (5.25%) |
| CHD or Peripheral artery disease Arteriopathy | 23 (0.10%) | 21 (0.1%) | 2 (0.28%) |
| Heart failure | 52 (0.20%) | 49 (0.24%) | 3 (0.43%) |
| COPD | 54 (0.30%) | 51 (0.25%) | 3 (0.43%) |
| Asthma | 52 (0.20%) | 50 (0.24%) | 2 (0.28%) |
| Stroke | 285 (1.33%) | 268 (1.29%) | 16 (2.27%) |
| Chronic kidney disease | 96 (0.50%) | 87 (0.42%) | 9 (1.28%) |
| Active or cancer history | 52 (0.20%) | 50 (0.24%) | 2 (0.28%) |
| Systemic corticosteroids | 13416 (62.50%) | 13367 (64.38%) | 49 (6.95%) |
| Non invasive ventilatory support | 85 (0.41%) | 85 (0.41%) | 0 (0%) |
| Mechanical assistance | 83 (0.40%) | 83 (0.4%) | 0 (0%) |
| ICU admission | 8 (0%) | 8 (0.04%) | 0 (0%) |
| In-hospital death | 0 (0%) | 0 (0%) | 0 (0%) |
| Oxygen supply | 0 (0%) | 0 (0%) | 0 (0%) |
| COVID-19 Vaccine | 0 (0%) | 0 (0%) | 0 (0%) |
| Number of dosis | 0 (0%) | 0 (0%) | 0 (0%) |
| Date of COVID-19 diagnosis | 390 (1.80%) | 388 (1.87%) | 2 (0.28%) |
| Date of hospital discharge | 5341 (26.89%) | 5097 (26.61%) | 244 (34.61%) |
| Date of COVID-19 vaccine | 115 (0.50%) | 0 (0%) | 115 (17%) |
| Days of hospitalization | 5341 (26.89%) | 5097 (26.61%) | 244 (34.61%) |
| Vaccine type mRNA-1273 (Moderna) | 0 (0%) | 0 (0%) | 0 (0%) |
| Vaccine type ChAdOx1 nCoV-19 (AstraZeneca) | 0 (0%) | 0 (0%) | 0 (0%) |
| Vaccine type mRNA BNT162b2 (Pfizer) | 0 (0%) | 0 (0%) | 0 (0%) |
| Vaccine type BIBP-CorV (Sinopharm) | 0 (0%) | 0 (0%) | 0 (0%) |

| | | | |
|---|---|---|---|
| Vaccine type Gam-COVID-Vac (Sputnik) | 0 (0%) | 0 (0%) | 0 (0%) |
| High income countrie | 0 (0%) | 0 (0%) | 0 (0%) |
| Omicron Variant | 388 (1.80%) | 386 (1.87%) | 2 (0.2%) |

COPD: Chronic obstructive pulmonary disease; CHD: Coronary Heart Disease; CKD: Chronic kidney disease

**eTable 5**. Days between last doses and hospitalization depending on vaccine type

| | Days from last vaccine dose to hospitalization |
|---|---|
| mRNA BNT162b2 (Pfizer) - mean (SD) | 185 (85) |
| mRNA-1273 (Moderna) - mean (SD) | 150 (97) |
| ChAdOx1 nCoV-19 (AstraZeneca) - mean (SD) | 74 (79) |
| Gam-COVID-Vac (Sputnik)- mean (SD) | 70 (52) |
| BIBP-CorV (Sinopharm) - mean (SD) | 60 (53) |