**Supplementary Appendix**

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# ***Section S1:* Further details on** **methods**

## **Population, data sources, and testing**

Qatar has a population of about 3 million people [1, 2]. The population is unusually young and diverse in that only 9% of its residents are ≥50 years of age, and 89% are expatriates from over 150 countries [1, 2]. The population is dynamic because the vast majority of Qatar’s residents come here because of employment and leave the country after end of employment [1]. Hosting of the World Cup 2022 and the years of infrastructure building that this has entailed contributed to a large surge and fluctuations in the population over the last few years. Nationality, age, and sex provide a powerful proxy for socio-economic status in this country [1, 3-6], as nationality is strongly associated with occupation in this population [1, 3, 5, 6].

The national, federated, mortality database is managed by the Hamad Medical Corporation (HMC) since the start of the year 2020. HMC is the national public healthcare provider in the country. The database includes all death records, including both deaths occurring at healthcare facilities and elsewhere. The database includes also forensic deaths investigated by Qatar’s Ministry of Interior. The number of deaths recorded in Qatar since 2020 averaged at about 2,300 deaths per year.

Qatar launched its coronavirus disease 2019 (COVID-19) vaccination program in December of 2020 using the BNT162b2 and mRNA-1273 vaccines [7]. Most of primary-series vaccination scale-up was implemented in 2021 [8, 9]. Most of booster vaccination scale-up was implemented in 2022 [10, 11]. Vaccination with the bivalent booster started towards the end of 2022, but it remains at low coverage. Nearly all individuals in the population were vaccinated free of charge in Qatar, rather than elsewhere.

Qatar’s national and universal public healthcare system uses the Cerner-system advanced digital health platform to track all electronic health record encounters of each individual in the country, including all citizens and residents registered in the national and universal public healthcare system. Registration in the public healthcare system is mandatory for citizens and residents.

The databases analyzed in this study are data-extract downloads from the Cerner-system that have been implemented on a regular (twice weekly) schedule since the onset of pandemic by the Business Intelligence Unit at HMC. At every download all tests, COVID-19 vaccinations, hospitalizations related to COVID-19, and all death records regardless of cause are provided to the authors through .csv files. These databases have been analyzed throughout the pandemic not only for study-related purposes, but also to provide policymakers with summary data and analytics to inform the national response.

Every health encounter in the Cerner-system is linked to a unique individual through the HMC Number that links all records for this individual at the national level. Databases were merged and analyzed using the HMC Number to link all records whether for testing, vaccinations, hospitalizations, and deaths. All deaths in Qatar are tracked by the public healthcare system. All COVID-19-related healthcare was provided only in the public healthcare system. No private entity was permitted to provide COVID-19-related healthcare. COVID-19 vaccination was also provided only through the public healthcare system. These health records were tracked throughout the COVID-19 pandemic using the Cerner system. This system has been implemented in 2013, before the onset of the pandemic. Therefore, we had all health records related to this study for the full national cohort of citizens and residents throughout the pandemic. This allowed us to follow each person over time.

Demographic details for every HMC Number (individual) such as sex, age, and nationality are collected upon issuing of the universal health card, based on the Qatar Identity Card, which is a mandatory requirement by the Ministry of Interior to every citizen and resident in the country.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) testing in Qatar is done at a mass scale where close to 5% of the population are tested every week [12, 9]. All SARS-CoV-2 testing in any facility in this country is tracked nationally in one database, the national testing database. This database covers all testing in all locations and facilities throughout the country, whether public or private. Every polymerase chain reaction (PCR) test and an increasing proportion of the facility-based rapid antigen tests conducted in Qatar, regardless of location or setting, are classified on the basis of symptoms and the reason for testing (clinical symptoms, contact tracing, surveys or random testing campaigns, individual requests, routine healthcare testing, pre-travel, at port of entry, or other). Based on the distribution of the reason for testing up to October 31, 2022, most of the tests that have been conducted in Qatar were conducted for routine reasons, such as being travel-related. Greater than 70% of those diagnosed are also diagnosed not because of appearance of symptoms, but because of routine testing (Table S2) [12, 9]. All testing results in the national testing database during follow-up in the present study were factored in the analyses of this study.

The first large omicron wave that peaked in January of 2022 was massive and strained the testing capacity in the country [12, 13]. Accordingly, rapid antigen testing was introduced to relieve the pressure on PCR testing. Implementation of this change in testing occurred quickly precluding incorporation of reason for testing in a proportion of the rapid antigen tests for several months. While the reason for testing is available for all PCR tests, it is not available for all rapid antigen tests.

Rapid antigen test kits are available for purchase in pharmacies in Qatar, but outcome of home-based testing is not reported nor documented in the national databases. Since SARS-CoV-2-test outcomes are linked to specific public health measures, restrictions, and privileges, testing policy and guidelines stress medically supervised testing as the core testing mechanism in the population. While medically supervised testing is provided free of charge or at low subsidized costs, depending on the reason for testing, home-based rapid antigen testing is de-emphasized and not supported as part of national policy. There is no reason to believe that home-based testing could have differentially affected the followed matched cohorts to affect our results.

Further descriptions of the study population and these national databases were reported previously [1, 10, 12, 14, 9].

## **Comorbidity classification**

Comorbidities were ascertained and classified based on the ICD-10 codes for chronic conditions as recorded in the electronic health record encounters of each individual in the Cerner-system national database that includes all citizens and residents registered in the national and universal public healthcare system. The public healthcare system provides healthcare to the entire resident population of Qatar free of charge or at heavily subsidized costs, including prescription drugs.

All encounters for each individual were analyzed to determine the comorbidity classification for that individual, as part of a recent national analysis to assess healthcare needs and resource allocation. The Cerner-system national database includes encounters starting from 2013, after this system was launched in Qatar. As long as each individual had at least one encounter with a specific comorbidity diagnosis since 2013, this person was classified with this comorbidity.

Individuals who have comorbidities but never sought care in the public healthcare system, or seek care exclusively in private healthcare facilities, were classified as individuals with no comorbidity due to absence of recorded encounters for them. This misclassification bias is not likely to affect the study results. The results for those more clinically vulnerable will not be affected, as this misclassification bias would have only resulted in a smaller cohort of these persons. This cohort was large enough for precise estimation of outcomes. As for those less clinically vulnerable, the misclassification bias could imply that some of them may have been more clinically vulnerable. However, this proportion is likely to be very small compared to the proportion of those with one or no comorbidity in the young population of Qatar. The effect on study outcomes is thus likely to be negligible.

## **Classification of COVID-19 death**

Classification of COVID-19 death followed World Health Organization (WHO) guidelines.[15] Assessments were made by trained medical personnel independent of study investigators and using individual chart reviews, as part of a national protocol applied to every deceased patient since pandemic onset.

COVID-19 death was defined per WHO classification as “a death resulting from a clinically compatible illness, in a probable or confirmed COVID-19 case, unless there was a clear alternative cause of death that could not be related to COVID-19 disease (e.g. trauma), and there was no period of complete recovery between the COVID-19 illness and death. A death due to COVID-19 could not be attributed to another disease (e.g. cancer) and was counted independently of preexisting conditions suspected of triggering or increasing the risk of a severe course of COVID-19”. Detailed WHO criteria for classifying COVID-19 deaths can be found in the WHO technical report [15].

# ***Section S2:* Laboratory methods and variant ascertainment**

## **Real-time reverse-transcription polymerase chain reaction testing**

Nasopharyngeal and/or oropharyngeal swabs were collected for polymerase chain reaction (PCR) testing and placed in Universal Transport Medium (UTM). Aliquots of UTM were: 1) extracted on KingFisher Flex (Thermo Fisher Scientific, USA), MGISP-960 (MGI, China), or ExiPrep 96 Lite (Bioneer, South Korea) followed by testing with real-time reverse-transcription PCR (RT-qPCR) using TaqPath COVID-19 Combo Kits (Thermo Fisher Scientific, USA) on an ABI 7500 FAST (Thermo Fisher Scientific, USA); 2) tested directly on the Cepheid GeneXpert system using the Xpert Xpress SARS-CoV-2 (Cepheid, USA); or 3) loaded directly into a Roche cobas 6800 system and assayed with the cobas SARS-CoV-2 Test (Roche, Switzerland). The first assay targets the viral S, N, and ORF1ab gene regions. The second targets the viral N and E-gene regions, and the third targets the ORF1ab and E-gene regions.

All PCR testing was conducted at the Hamad Medical Corporation Central Laboratory or Sidra Medicine Laboratory, following standardized protocols.

## **Rapid antigen testing**

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antigen tests were performed on nasopharyngeal swabs using one of the following lateral flow antigen tests: Panbio COVID-19 Ag Rapid Test Device (Abbott, USA); SARS-CoV-2 Rapid Antigen Test (Roche, Switzerland); Standard Q COVID-19 Antigen Test (SD Biosensor, Korea); or CareStart COVID-19 Antigen Test (Access Bio, USA). All antigen tests were performed point-of-care according to each manufacturer’s instructions at public or private hospitals and clinics throughout Qatar with prior authorization and training by the Ministry of Public Health (MOPH). Antigen test results were electronically reported to the MOPH in real time using the Antigen Test Management System which is integrated with the national Coronavirus Disease 2019 (COVID-19) database.

# ***Table S1:* STROBE checklist for cohort studies.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Item No | Recommendation | Main Text page |
| **Title and abstract** | 1 | (*a*) Indicate the study’s design with a commonly used term in the title or the abstract | Abstract |
| (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | Abstract |
| Introduction | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | Introduction |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | Introduction |
| Methods | | | |
| Study design | 4 | Present key elements of study design early in the paper | Methods (‘Study design and cohorts’ & ‘Cohorts’ matching and eligibility’, & ‘Cohorts’ follow-up’) |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | Methods (‘Study design and cohorts’ & ‘Cohorts’ matching and eligibility’, ‘Cohorts’ follow-up’, ‘Classification of COVID-19 death’, & ‘Clinical vulnerability status’), & Figure S1 & Sections S1-S2 in Supplementary Appendix |
| Participants | 6 | (*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up | Methods (‘Study population and data sources’, ‘Study design and cohorts’, ‘Cohorts’ matching and eligibility’, & ‘Cohorts’ follow-up’), & Figure S1 in Supplementary Appendix |
| (*b*)For matched studies, give matching criteria and number of exposed and unexposed |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | Methods (‘Study design and cohorts’ & ‘Cohorts’ matching and eligibility’, ‘Cohorts’ follow-up’, ‘Classification of COVID-19 death’, & ‘Clinical vulnerability status’), Table S2, & Figure S1 & Sections S1-S2 in Supplementary Appendix. |
| 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 | Methods (‘Study population and data sources’ & ‘Statistical analysis’, paragraph 1), Table S2, & Sections S1-S2 in Supplementary Appendix |
| Bias | 9 | Describe any efforts to address potential sources of bias | Methods (‘Cohorts’ matching and eligibility’, ‘Cohorts’ follow-up’, & ‘Statistical analysis’) |
| Study size | 10 | Explain how the study size was arrived at | Figure S1 in Supplementary Appendix |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | Methods (‘Cohorts’ matching and eligibility’ & ‘Cohorts’ follow-up’) & Table S2 |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding | Methods (‘Statistical analysis’) |
| (*b*) Describe any methods used to examine subgroups and interactions | Methods (‘Statistical analysis’) |
| (*c*) Explain how missing data were addressed | Not applicable, see Methods (‘Study population and data sources’) |
| (*d*) If applicable, explain how loss to follow-up was addressed | Not applicable, see Methods (‘Study population and data sources’) |
| (*e*) Describe any sensitivity analyses | Methods (‘Statistical analysis’) |
| 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 analysed | Figure S1 in Supplementary Appendix |
| (b) Give reasons for non-participation at each stage |
| (c) Consider use of a flow diagram |
| Descriptive data | 14 | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | Results (paragraph 1), & Table S2 in Supplementary Appendix. |
| (b) Indicate number of participants with missing data for each variable of interest | Not applicable, see Methods (‘Study population and data sources’) |
| (c) Summarise follow-up time (eg, average and total amount) | Results (‘Acute SARS-CoV-2 Infection Mortality Analysis, paragraph 1 & ‘Post-acute SARS-CoV-2 Infection Mortality Analysis’, paragraph 1), Figures 1 & 4, & Table 1 |
| Outcome data | 15 | Report numbers of outcome events or summary measures over time | Results (‘Acute SARS-CoV-2 Infection Mortality Analysis, paragraph 1 & ‘Post-acute SARS-CoV-2 Infection Mortality Analysis, paragraph 1), Figures 1 & 4, Table 1, & Figure S1 in Supplementary Appendix |
| 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 | Results (Unvaccinated population ‘Acute SARS-CoV-2 Infection Mortality Analysis, paragraph 2 & ‘Post-acute SARS-CoV-2 Infection Mortality Analysis, paragraph 2, & ‘Combined Acute and Post-acute SARS-CoV-2 Infection Mortality Analysis’, & Vaccinated population), Figures 2-3, & Table 1 & Tables S3 & S4 in Supplementary Appendix |
| (b) Report category boundaries when continuous variables were categorized | Table S2 in Supplementary Appendix |
| (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | Not applicable |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | Results (‘Additional and sensitivity analyses), & Table S5 in Supplementary Appendix |
| Discussion | | | |
| Key results | 18 | Summarise key results with reference to study objectives | Discussion, paragraphs 1-6 |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | Discussion, paragraphs 7-15 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | Discussion, paragraph 16 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | Discussion, paragraph 14 |
| 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 | Funding |

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# ***Figure S1:* Cohort selection for investigating the risk of all-cause mortality in the primary-infection cohort relative to the infection-naive cohort.**

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# ***Table S2:* Baseline characteristics of full and matched cohorts.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Characteristics** | **Full eligible cohorts** | | | **Matched cohorts\*** | | |
| **Primary-infection** | **Infection-naïve** | **SMD†** | **Primary-infection** | **Infection-naïve** | **SMD†** |
| **N=890,705** | **N=3,965,765** | **N=685,871** | **N=685,871** |
| Median age (IQR)—years | 33 (24-41) | 32 (25-40) | 0.01‡ | 32 (23-39) | 32 (23-39) | 0.00‡ |
| Age—years |  |  |  |  |  |  |
| 0-9 years | 86,986 (9.8) | 359,438 (9.1) | 0.13 | 73,165 (10.7) | 73,165 (10.7) | 0.00 |
| 10-19 years | 84,120 (9.4) | 272,855 (6.9) | 63,764 (9.3) | 63,764 (9.3) |
| 20-29 years | 183,616 (20.6) | 973,741 (24.6) | 151,561 (22.1) | 151,561 (22.1) |
| 30-39 years | 282,025 (31.7) | 1,280,464 (32.3) | 226,172 (33.0) | 226,172 (33.0) |
| 40-49 years | 158,757 (17.8) | 678,087 (17.1) | 116,971 (17.1) | 116,971 (17.1) |
| 50-59 years | 66,108 (7.4) | 277,233 (7.0) | 41,183 (6.0) | 41,183 (6.0) |
| 60-69 years | 21,514 (2.4) | 94,683 (2.4) | 10,418 (1.5) | 10,418 (1.5) |
| 70+ years | 7,579 (0.9) | 29,264 (0.7) | 2,637 (0.4) | 2,637 (0.4) |
| Sex |  |  |  |  |  |  |
| Male | 558,518 (62.7) | 2,805,558 (70.7) | 0.17 | 445,511 (65.0) | 445,511 (65.0) | 0.00 |
| Female | 332,187 (37.3) | 1,160,207 (29.3) | 240,360 (35.0) | 240,360 (35.0) |
| Nationality§ |  |  |  |  |  |  |
| Bangladeshi | 50,496 (5.7) | 289,261 (7.3) | 0.37 | 41,106 (6.0) | 41,106 (6.0) | 0.00 |
| Egyptian | 47,114 (5.3) | 190,814 (4.8) | 34,771 (5.1) | 34,771 (5.1) |
| Filipino | 88,481 (9.9) | 294,798 (7.4) | 70,056 (10.2) | 70,056 (10.2) |
| Indian | 200,810 (22.6) | 1,111,610 (28.0) | 175,997 (25.7) | 175,997 (25.7) |
| Nepalese | 61,707 (6.9) | 374,369 (9.4) | 50,905 (7.4) | 50,905 (7.4) |
| Pakistani | 37,770 (4.2) | 231,607 (5.8) | 29,990 (4.4) | 29,990 (4.4) |
| Qatari | 170,274 (19.1) | 319,522 (8.1) | 134,475 (19.6) | 134,475 (19.6) |
| Sri Lankan | 22,739 (2.6) | 131,015 (3.3) | 17,499 (2.6) | 17,499 (2.6) |
| Sudanese | 23,152 (2.6) | 81,538 (2.1) | 15,957 (2.3) | 15,957 (2.3) |
| Other nationalities¶ | 188,162 (21.1) | 941,231 (23.7) | 115,115 (16.8) | 115,115 (16.8) |
| Coexisting conditions |  |  |  |  |  |  |
| None | 688,703 (77.3) | 3,483,150 (87.8) | 0.28 | 562,885 (82.1) | 562,885 (82.1) | 0.00 |
| 1 | 111,556 (12.5) | 274,952 (6.9) | 76,009 (11.1) | 76,009 (11.1) |
| 2 | 46,373 (5.2) | 108,253 (2.7) | 27,069 (4.0) | 27,069 (4.0) |
| 3 | 19,641 (2.2) | 45,366 (1.1) | 9,545 (1.4) | 9,545 (1.4) |
| 4 | 10,925 (1.2) | 25,145 (0.6) | 4,735 (0.7) | 4,735 (0.7) |
| 5 | 6,538 (0.7) | 14,363 (0.4) | 2,542 (0.4) | 2,542 (0.4) |
| 6+ | 6,969 (0.8) | 14,536 (0.4) | 3,086 (0.5) | 3,086 (0.5) |
| Vaccination status\*\* |  |  |  |  |  |  |
| Unvaccinated | 545,756 (61.3) | 2,665,308 (67.2) | 0.13 | 460,620 (67.2) | 460,620 (67.2) | 0.00 |
| 1 dose | 185,93 (2.1) | 53,244 (1.3) | 10,366 (1.5) | 10,366 (1.5) |
| 2 doses | 257,358 (28.9) | 1,006,540 (25.4) | 168,939 (24.6) | 168,939 (24.6) |
| 3 doses | 68,602 (7.7) | 238,708 (6.0) | 45,900 (6.7) | 45,900 (6.7) |
| 4 doses | 396 (0.04) | 1,965 (0.05) | 46 (0.01) | 46 (0.01) |
| Vaccine type |  |  |  |  |  |  |
| Unvaccinated | 545,756 (61.3) | 2,665,308 (67.2) | 0.19 | 460,620 (67.2) | 460,620 (67.2) | 0.00 |
| BNT162b2 | 251,345 (28.2) | 802,053 (20.2) | 165,657 (24.2) | 165,657 (24.2) |
| mRNA-1273 | 92,114 (10.3) | 487,864 (12.3) | 58,624 (8.6) | 58,624 (8.6) |
| Pediatric BNT162b2 | 1,490 (0.2) | 10,540 (0.3) | 970 (0.1) | 970 (0.1) |
| Testing method |  |  |  |  |  |  |
| PCR | 700,342 (78.6) | 2,889,278 (72.9) | 0.13 | 551,228 (80.4) | 551,228 (80.4) | 0.00 |
| Rapid antigen | 190,363 (21.4) | 1,076,487 (27.1) | 134,643 (19.6) | 134,643 (19.6) |
| Reason for testing |  |  |  |  |  |  |
| Clinical suspicion | 253,259 (28.4) | 290,431 (7.3) | 0.84 | 164,763 (24.0) | 164,787 (24.0) | 0.00 |
| Contact tracing | 131,087 (14.7) | 203,717 (5.1) | 104,321 (15.2) | 104,331 (15.2) |
| Survey | 89,513 (10.1) | 444,064 (11.2) | 77,090 (11.2) | 77,146 (11.3) |
| Individual request | 53,690 (6.0) | 282,014 (7.1) | 40,193 (5.9) | 40,168 (5.9) |
| Pre-travel | 92,031 (10.3) | 739,057 (18.6) | 76,575 (11.2) | 76,613 (11.2) |
| Port of entry | 96,420 (10.8) | 1,252,304 (31.6) | 91,876 (13.4) | 91,872 (13.4) |
| Healthcare routine testing | 31,715 (3.6) | 138,225 (3.5) | 24,505 (3.6) | 24,534 (3.6) |
| Other | 9,169 (1.0) | 36,721 (0.9) | 6,756 (1.0) | 6,758 (1.0) |
| Unspecified | 133,821 (15.0) | 579,232 (14.6) | 99,792 (14.6) | 99,542 (14.5) |

IQR denotes interquartile range, SARS-CoV-2 severe acute respiratory syndrome coronavirus 2, and SMD standardized mean difference.

\*Cohorts were matched exactly one-to-one by sex, 10-year age group, nationality, number of coexisting conditions, vaccination status, vaccine type, SARS-CoV-2 testing method, reason for testing, and calendar week of testing.

†SMD is the difference in the mean of a covariate between groups divided by the pooled standard deviation. An SMD ≤0.1 indicates adequate matching.

‡SMD is for the mean difference between groups divided by the pooled standard deviation.

§Nationalities were chosen to represent the most populous groups in Qatar.

¶These comprise up to 183 other nationalities in the unmatched cohort and 144 other nationalities in the matched cohort.

\*\*Ascertained at the time of the SARS-CoV-2 test.

# ***Table S******3:* Adjusted hazard ratios for all-cause death by clinical vulnerability in the A) unvaccinated and B) vaccinated populations.**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Epidemiological measures** | | **Acute SARS-CoV-2 Infection Mortality Analysis** | | **Post-acute SARS-CoV-2 Infection Mortality Analysis** | | **Acute & Post-acute SARS-CoV-2 Infection Mortality Analysis** | |
| **Primary-infection cohort\*** | **Control cohort\*** | **Primary-infection cohort\*** | **Control cohort\*** | **Primary-infection cohort\*** | **Control cohort\*** |
| 1. **Unvaccinated population** | | | | | | | |
| **Less clinically vulnerable** | | | | | | | |
| Sample size | | 415,596 | 415,596 | 285,006 | 284,984 | 415,596 | 415,596 |
| Total follow-up time (person-years) | | 85,223 | 85,219 | 172,002 | 171,972 | 257,225 | 257,191 |
| Number of deaths during follow-up | | 105 | 111 | 33 | 41 | 138 | 152 |
| Incidence rate of death (per 1,000 person-years; 95% CI) | | 1.23 (1.02 to 1.49) | 1.30 (1.08 to 1.57) | 0.19 (0.14 to 0.27) | 0.24 (0.18 to 0.32) | 0.54 (0.45 to 0.63) | 0.59 (0.50 to 0.69) |
| Unadjusted hazard ratio for death (95% CI) | | 0.95 (0.73 to 1.25) | | 0.78 (0.49 to 1.24) | | 0.91 (0.72 to 1.14) | |
| Adjusted hazard ratiofor death(95% CI)† | | 0.94 (0.72 to 1.24) | | 0.77 (0.48 to 1.24) | | 0.90 (0.71 to 1.14) | |
| **More clinically vulnerable** | | | | | |  |  |
| Sample size | | 45,024 | 45,024 | 30,483 | 30,522 | 45,024 | 45,024 |
| Total follow-up time (person-years) | | 9,044 | 9,052 | 15,357 | 15,347 | 24,401 | 24,399 |
| Number of deaths during follow-up | | 237 | 177 | 39 | 101 | 276 | 278 |
| Incidence rate of death (per 1,000 person-years; 95% CI) | | 26.21 (23.07 to 29.76) | 19.55 (16.88 to 22.66) | 2.54 (1.86 to 3.48) | 6.58 (5.41 to 8.00) | 11.31 (10.05 to 12.73) | 11.39 (10.13 to 12.82) |
| Unadjusted hazard ratio for death (95% CI) | | 1.31 (1.08 to 1.59) | | 0.39 (0.27 to 0.57) | | 0.99 (0.84 to 1.17) | |
| Adjusted hazard ratiofor death(95% CI)† | | 1.34 (1.11 to 1.63) | | 0.37 (0.25 to 0.54) | | 1.00 (0.85 to 1.19) | |
| 1. **Vaccinated population** | | | | | | | |
| **Less clinically vulnerable** | | | | | | | |
| Sample size | 186,894 | 186,894 | 109,504 | 109,500 | 186,894 | 186,894 | |
| Total follow-up time (person-years) | 33,603 | 33,602 | 47,288 | 47,286 | 80,891 | 80,888 | |
| Number of deaths during follow-up | 16 | 18 | 12 | 7 | 28 | 25 | |
| Incidence rate of death (per 1,000 person-years; 95% CI) | 0.48 (0.29 to 0.78) | 0.54 (0.34 to 0.85) | 0.25 (0.14 to 0.45) | 0.15 (0.07 to 0.31) | 0.35 (0.24 to 0.50) | 0.31 (0.21 to 0.46) | |
| Unadjusted hazard ratio for death (95% CI) | 0.89 (0.45 to 1.74) | | 1.71 (0.67 to 4.35) | | 1.12 (0.65 to 1.92) | | |
| Adjusted hazard ratiofor death(95% CI)† | 1.08 (0.51 to 2.29) | | 2.00 (0.68 to 5.84) | | 1.33 (0.72 to 2.46) | | |
| **More clinically vulnerable** | | | | | | | |
| Sample size | 38,357 | 38,357 | 22,456 | 22,442 | 38,357 | 38,357 | |
| Total follow-up time (person-years) | 6,823 | 6,821 | 9,233 | 9,223 | 16,056 | 16,044 | |
| Number of deaths during follow-up | 43 | 56 | 33 | 37 | 76 | 93 | |
| Incidence rate of death (per 1,000 person-years; 95% CI) | 6.30 (4.67 to 8.50) | 8.21 (6.32 to 10.67) | 3.57 (2.54 to 5.03) | 4.01 (2.91 to 5.54) | 4.73 (3.78 to 4.93) | 5.80 (4.73 to 7.10) | |
| Unadjusted hazard ratio for death (95% CI) | 0.77 (0.52 to 1.14) | | 0.89 (0.56 to 1.42) | | 0.82 (0.60 to 1.11) | | |
| Adjusted hazard ratiofor death(95% CI)† | 0.64 (0.41 to 1.02) | | 0.96 (0.56 to 1.66) | | 0.76 (0.53 to 1.07) | | |

CI denotes confidence interval.

\*Each person in the primary-infection cohort was matched exactly one-to-one by sex, 10-year age group, nationality, number of coexisting conditions, vaccination status, vaccine type, SARS-CoV-2 testing method, reason for testing, and calendar week of testing to a person with a SARS-CoV-2-negative test who was alive, infection free, and did not receive a new vaccine dose at the start of follow-up.

†Cox regression analysis adjusted for sex, 10-year age group, 10 nationality groups, number of coexisting conditions, vaccination status, vaccine type, SARS-CoV-2 testing method, reason for testing, and calendar week of testing.

# ***Table S4:*** **Adjusted hazard ratio for all-cause death** **in the full matched primary-infection and infection-naïve cohorts, including both unvaccinated and vaccinated persons, over the entire time of follow-up, that is combining the acute and post-acute phases.**

|  |  |  |
| --- | --- | --- |
| **Epidemiological measures** | **Primary-infection cohort\*** | **Control cohort\*** |
| **SARS-CoV-2 Infection Mortality** | | |
| Sample size | 685,871 | 685,871 |
| Total follow-up time (person-years) | 378,573 | 378,523 |
| Number of deaths during follow-up | 518 | 548 |
| Incidence rate of death (per 1,000 person-years; 95% CI) | 1.37 (1.26 to 1.49) | 1.45 (1.33 to 1.57) |
| Unadjusted hazard ratio for death (95% CI) | 0.94 (0.84 to 1.06) | |
| Adjusted hazard ratiofor death(95% CI)† | 0.95 (0.84 to 1.07) | |

CI denotes confidence interval.

\*Each person in the primary-infection cohort was matched exactly one-to-one by sex, 10-year age group, nationality, number of coexisting conditions, vaccination status, vaccine type, SARS-CoV-2 testing method, reason for testing, and calendar week of testing to a person with a SARS-CoV-2-negative test who, by the start of the follow-up, was alive, infection free, and did not receive vaccine doses with different vaccines, or a new vaccine dose between the SARS-CoV-2-negative test and the start date of follow-up.

†Cox regression analysis adjusted for sex, 10-year age group, 10 nationality groups, number of coexisting conditions, vaccination status, vaccine type, SARS-CoV-2 testing method, reason for testing, and calendar week of testing.

# ***Table S5:*** **Adjusted hazard ratio for all-cause death** **in the matched\* primary-infection and infection-naïve cohorts for each of unvaccinated and vaccinated persons in A) the model including an interaction term between study cohorts and vaccination status and B) the main analysis restricted to Qataris only.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Adjusted hazard ratio for death in the primary infection cohort relative to the infection-naïve cohort (95% CI)** | **Unvaccinated** | | **Vaccinated** | |
| 1. **Model including an interaction term between study cohorts and vaccination status**† |  |  |  |  |
| Acute SARS-CoV-2 Infection Mortality Analysis | 1.19 (1.01 to 1.39) | | 0.74 (0.50 to 1.10) | |
| Post-acute SARS-CoV-2 Infection Mortality Analysis | 0.50 (0.37 to 0.67) | | 1.11 (0.69 to 1.78) | |
| 1. **Main analysis restricted to Qataris only**‡ |  | |  | |
| Acute SARS-CoV-2 Infection Mortality Analysis | 1.14 (0.83 to 1.56) | | 0.74 (0.44 to 1.27) | |
| Post-acute SARS-CoV-2 Infection Mortality Analysis | 0.46 (0.29 to 0.74) | | 1.52 (0.82 to 2.82) | |

CI denotes confidence interval.

\*Each person in the primary-infection cohort was matched exactly one-to-one by sex, 10-year age group, nationality, number of coexisting conditions, vaccination status, vaccine type, SARS-CoV-2 testing method, reason for testing, and calendar week of testing to a person with a SARS-CoV-2-negative test who, by the start of the follow-up, was alive, infection free, and did not receive vaccine doses with different vaccines, or a new vaccine dose between the SARS-CoV-2-negative test and the start date of follow-up.

†Cox regression analysis adjusted for sex, 10-year age group, 10 nationality groups, number of coexisting conditions, vaccine type, SARS-CoV-2 testing method, reason for testing, and calendar week of testing.

‡Cox regression analysis adjusted for sex, 10-year age group, number of coexisting conditions, vaccination status, vaccine type, SARS-CoV-2 testing method, reason for testing, and calendar week of testing.

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