Supplementary Material

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Section S1. Study population and data sources

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 onset of the pandemic by the Business Intelligence Unit at Hamad Medical Corporation. Hamad Medical Corporation is the national public healthcare provider in Qatar. At every download all tests, coronavirus disease 2019 (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 hospitalization. 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 Qataris 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. Data extraction from the Qatar Identity Card to the digital health platform is performed electronically through scanning techniques.

All severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) testing in any facility in Qatar 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 a 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).

Before November 1, 2022, SARS-CoV-2 testing in Qatar was done at a mass scale where about 5% of the population were tested every week.\textsuperscript{1,2} Based on the distribution of the reason for testing up to November 1, 2022, most of the tests in Qatar were conducted for routine reasons, such as being travel-related, and about 75% of cases were diagnosed not because of appearance of symptoms, but because of routine testing.\textsuperscript{1,2}

Starting from November 1, 2022, SARS-CoV-2 testing was substantially reduced, but still about 1% of the population are tested every week.\textsuperscript{3} 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.\textsuperscript{1-6} Accordingly, rapid antigen testing was introduced to relieve the pressure on PCR testing. Implementation of this change in testing policy occurred quickly precluding incorporation of reason for testing in a large 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. Availability of reason for testing for the rapid antigen tests also varied with time.

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 were linked to specific public health measures, restrictions, and privileges, testing policy and guidelines stress facility-based testing as the core testing mechanism in the population. While facility-based 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.

Further descriptions of the study population and the national databases were reported previously.\textsuperscript{1,2,5,7-10}
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.

**Classification of infections by variant type**

Surveillance for SARS-CoV-2 variants in Qatar is based on viral genome sequencing and multiplex RT-qPCR variant screening\(^{11}\) of random positive clinical samples,\(^{2\text{-}16}\) complemented by deep sequencing of wastewater samples.\(^{14\text{-}17\text{,}18}\) Further details on the viral genome sequencing and multiplex RT-qPCR variant screening throughout the SARS-CoV-2 waves in Qatar can be found in previous publications.\(^{1\text{-}2\text{,}4\text{-}8\text{,}12\text{-}16\text{,}19\text{-}23}\)
Section S3. COVID-19 severity, criticality, and fatality classification

Classification of Coronavirus Disease 2019 (COVID-19) case severity (acute-care hospitalizations), criticality (intensive-care-unit hospitalizations), and fatality followed World Health Organization (WHO) guidelines. 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 hospitalized COVID-19 patient. Each hospitalized COVID-19 patient underwent an infection severity assessment every three days until discharge or death.

Severe COVID-19

Severe COVID-19 disease was defined per WHO classification as a SARS-CoV-2 infected person with “oxygen saturation of <90% on room air, and/or respiratory rate of >30 breaths/minute in adults and children >5 years old (or ≥60 breaths/minute in children <2 months old or ≥50 breaths/minute in children 2-11 months old or ≥40 breaths/minute in children 1–5 years old), and/or signs of severe respiratory distress (accessory muscle use and inability to complete full sentences, and, in children, very severe chest wall indrawing, grunting, central cyanosis, or presence of any other general danger signs)”.

Critical COVID-19

Critical COVID-19 disease was defined per WHO classification as a SARS-CoV-2 infected person with “acute respiratory distress syndrome, sepsis, septic shock, or other conditions that would normally require the provision of life sustaining therapies such as mechanical ventilation
(invasive or non-invasive) or vasopressor therapy”. Detailed WHO criteria for classifying SARS-CoV-2 infection criticality can be found in the WHO technical report.

**Fatal COVID-19**

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 is a clear alternative cause of death that cannot be related to COVID-19 disease (e.g. trauma). There should be no period of complete recovery from COVID-19 between illness and death. A death due to COVID-19 may not be attributed to another disease (e.g. cancer) and should be counted independently of preexisting conditions that are suspected of triggering a severe course of COVID-19”. Detailed WHO criteria for classifying COVID-19 death can be found in the WHO technical report.
Section S4. Phases of the COVID-19 pandemic

The pandemic was categorized into distinct phases based on the level of SARS-CoV-2 incidence and the predominant variant. These phases included the ancestral virus wave (February 28, 2020 - July 31, 2020), a prolonged low incidence phase with the ancestral virus (August 1, 2020 - January 17, 2021), the alpha wave (January 18, 2021 - March 7, 2021), the beta wave (March 8, 2021 - May 31, 2021), a prolonged low incidence delta phase (June 1, 2021 - December 18, 2021), the first (BA.1 & BA.2) omicron wave (December 19, 2021 - February 28, 2022), the omicron BA.4 & BA.5 wave (March 1, 2022 - September 9, 2022), and the omicron BA.2.75 & XBB waves (September 10, 2022 - April 21, 2023).
Section S5. Comorbidity classification

Comorbidities were ascertained and classified based on the ICD-10 codes 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.
Table S1. STROBE checklist for cohort studies.

<table>
<thead>
<tr>
<th>Item No.</th>
<th>Recommendation</th>
<th>Main Text page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(a) Indicate the study’s design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found</td>
<td>Title and Abstract</td>
</tr>
<tr>
<td>2</td>
<td>Explain the scientific background and rationale for the investigation being reported</td>
<td>Introduction</td>
</tr>
<tr>
<td>3</td>
<td>State specific objectives, including any prespecified hypotheses</td>
<td>Introduction</td>
</tr>
<tr>
<td>4</td>
<td>Present key elements of study design early in the paper</td>
<td>Methods ('Cohort study of incidence of severe, critical, or fatal COVID-19')</td>
</tr>
<tr>
<td>5</td>
<td>Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection</td>
<td>Methods ('Study population and data sources' &amp; 'Cohort study of incidence of severe, critical, or fatal COVID-19') &amp; Sections S1 &amp; S4 in Supplementary Material</td>
</tr>
<tr>
<td>6</td>
<td>(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed</td>
<td>Methods ('Study population and data sources', 'COVID-19 acute-care and ICU hospitalizations', 'Severe, critical, and fatal COVID-19' &amp; 'Cohort study of incidence of severe, critical, or fatal COVID-19') &amp; Section S1 in Supplementary Material</td>
</tr>
<tr>
<td>7</td>
<td>Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable</td>
<td>Methods ('COVID-19 acute-care and ICU hospitalizations', 'Severe, critical, and fatal COVID-19', 'Cohort study of incidence of severe, critical, or fatal COVID-19', &amp; 'Statistical analysis'), &amp; Sections S1-S5 in Supplementary Material</td>
</tr>
<tr>
<td>8*</td>
<td>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</td>
<td>Methods, Table 1, &amp; Sections S1-S5 in Supplementary Material</td>
</tr>
<tr>
<td>9</td>
<td>Describe any efforts to address potential sources of bias</td>
<td>Methods ('Statistical analysis')</td>
</tr>
<tr>
<td>10</td>
<td>Explain how the study size was arrived at</td>
<td>Methods ('Cohort study of incidence of severe, critical, or fatal COVID-19')</td>
</tr>
<tr>
<td>11</td>
<td>Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why</td>
<td>Methods ('Statistical analysis') &amp; Table 1</td>
</tr>
<tr>
<td>12</td>
<td>(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses</td>
<td>Methods ('Statistical analysis') Not applicable, see Methods ('Study population and data sources') &amp; Section S1 in Supplementary Material Not applicable, see Methods ('Cohort study of incidence of severe, critical, or fatal COVID-19') Not applicable</td>
</tr>
<tr>
<td>13*</td>
<td>(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 (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram</td>
<td>Table 1 &amp; Figure 4</td>
</tr>
</tbody>
</table>
| 14       | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | Results ('Acute-care hospitalizations and severe cases', 'ICU hospitalizations and critical cases', & 'All-cause and COVID-
<table>
<thead>
<tr>
<th>Table 1:</th>
<th>Figures 1-2 &amp; 4, &amp; Figure S2 in Supplementary Material</th>
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<tbody>
<tr>
<td>(b) Indicate number of participants with missing data for each variable of interest</td>
<td>19 deaths'), Table 1, Figures 1-2 &amp; 4, &amp; Figure S2 in Supplementary Material</td>
</tr>
<tr>
<td>(c) Summarise follow-up time (eg, average and total amount)</td>
<td>Results ('Incidence rate of severe, critical, or fatal COVID-19', paragraph 2) &amp; Figure 4</td>
</tr>
<tr>
<td>Outcome data</td>
<td>Table 1</td>
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<tr>
<td>15</td>
<td>Report numbers of outcome events or summary measures over time</td>
</tr>
<tr>
<td>16</td>
<td>(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</td>
</tr>
<tr>
<td>Main results</td>
<td>Results ('Incidence rate of severe, critical, or fatal COVID-19', paragraphs 1-2, &amp; ‘Incidence rate of fatal COVID-19’, paragraph 1) &amp; Figures 3-5</td>
</tr>
<tr>
<td>(b) Report category boundaries when continuous variables were categorized</td>
<td>Table 1</td>
</tr>
<tr>
<td>(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Other analyses</td>
<td>Results ('Incidence rate of severe, critical, or fatal COVID-19', paragraphs 3-5, ‘Incidence rate of fatal COVID-19’, paragraphs 2-4, &amp; ‘Associations with severe and fatal COVID-19’), Figures 3-6, &amp; Figure S1 in Supplementary Material</td>
</tr>
<tr>
<td>17</td>
<td>Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses</td>
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<tr>
<td>Discussion</td>
<td>Discussion, paragraphs 1-4</td>
</tr>
<tr>
<td>Key results</td>
<td>Discussion, paragraphs 5-8</td>
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<tr>
<td>Limitations</td>
<td>Discussion, paragraphs 5-8</td>
</tr>
<tr>
<td>Interpretation</td>
<td>Discussion, paragraph 9</td>
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<tr>
<td>Generalisability</td>
<td>Discussion, paragraphs 7-8</td>
</tr>
<tr>
<td>Other information</td>
<td>Funding</td>
</tr>
<tr>
<td>Funding</td>
<td>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</td>
</tr>
</tbody>
</table>
Figure S1. The hazard rate for A) severe, critical, or fatal COVID-19 and B) fatal COVID-19 since the onset of the pandemic.
Figure S2. Scale-up of A) primary-series and B) booster vaccination in the national study cohort.

*The y-axis scale in both A and B was standardized to emphasize the contrast between uptake of primary-series and booster vaccinations, with a lower uptake of booster vaccination.*
References


