Turning point in COVID-19 severity and fatality during the pandemic: a national cohort study in Qatar

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ABSTRACT

Objective To assess the evolution of COVID-19 severity and fatality in a unique setting that consistently applied, throughout the pandemic, rigorous and standardised criteria for defining severe COVID-19 outcomes.

Methods and analysis We conducted a national cohort study on 312,109 Qatari citizens to investigate incidence of severe, critical or fatal COVID-19 classified according to the WHO criteria between 28 February 2020 and 21 April 2023. Incidence rates for severe, critical or fatal COVID-19 were estimated during the pre-omicron phase, first omicron wave, combined phases and throughout the pandemic.

Results Cumulative incidence of severe, critical or fatal COVID-19 after 3.14 years of follow-up was 0.45% (95% CI 0.43% to 0.47%). Incidence rate for severe, critical or fatal COVID-19 throughout the pandemic was 1.43% (95% CI 1.35 to 1.50) per 1000 person years. In the pre-omicron phase, first omicron wave, and combined phases, it was 2.01 (95% CI 1.90 to 2.13), 3.70 (95% CI 3.25 to 4.22) and 2.18 (95% CI 2.07 to 2.30) per 1000 person years, respectively. The post-first omicron phase saw a drastic drop to 0.10 (95% CI 0.08 to 0.14) per 1000 person years, a 95.4% reduction. Among all severe, critical and fatal cases, 99.5% occurred during the primary infection. Cumulative incidence of fatal COVID-19 was 0.042% (95% CI 0.036% to 0.050%), with an incidence rate of 0.13 (95% CI 0.11 to 0.16) per 1000 person years. In the post-first omicron phase, incidence rate of fatal COVID-19 decreased by 90.0% compared with earlier stages. Both severity and fatality exhibited an exponential increase with age and a linear increase with the number of coexisting conditions.

Conclusion The conclusion of the first omicron wave was a turning point in the severity of the pandemic. While vaccination and enhanced case management reduced severity gradually, the rapid accumulation of natural immunity during the first omicron wave appears to have played a critical role in driving this shift in severity.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ COVID-19 severity varied during the pandemic in response to subsequent waves of infection, increasing population immunity, and emergence of new viral variants. However, no study investigated evolution of COVID-19 severity from the start of the pandemic to the present time in a national population cohort using rigorous and standardised criteria applied throughout the pandemic.

⇒ Qatar appears to be the only country to consistently implement the standardised WHO classification to assess the severity of COVID-19 cases throughout the pandemic.

WHAT THIS STUDY ADDS

⇒ Based on a national population-based cohort study in Qatar, we found that the end of the first omicron wave marked a turning point in the pandemic, with a 95% drop in incidence rate of severe, critical or fatal COVID-19 compared with earlier stages.

⇒ Vaccinations and advancements in case management reduced severity gradually over time, but the end of the first omicron wave served as the central turning point. By the end of this wave, severity rates reached very low levels not seen since the onset of the pandemic, and these levels have been sustained since then, despite the occurrence of several immune-evasive omicron subvariant waves.

⇒ The rapid build-up of natural immunity during the first omicron wave appears to have played a pivotal role in driving this shift in severity levels.

INTRODUCTION

The COVID-19 pandemic, caused by the SARS-CoV-2, has resulted in significant morbidity and mortality globally.1–4 The pandemic has also caused extensive economic losses and societal disruptions due to the necessary implementation of social and physical distancing measures.
aimed at reducing virus transmission. The need for future public health interventions and restrictions will depend on the ongoing evolution of the virus, its disease severity and the effectiveness of current and future interventions.

The WHO has established a specific classification system for COVID-19 case severity, criticality and fatality. Qatar appears to be the only country to have consistently implemented this standardised WHO classification at a national level to assess the severity of COVID-19 cases from the pandemic onset to the present. Trained medical personnel evaluate the severity of COVID-19 cases using a national protocol that applies to every hospitalised patient with COVID-19. Importantly, COVID-19-associated hospitalisations are not used as a proxy for COVID-19 severity, as these have limitations in accurately capturing the true severity of COVID-19. This presents a special opportunity to investigate the evolution of COVID-19 severity from the start of the pandemic to the present time, using rigorous and standardised criteria in a national population cohort.

The objective of this study was to examine how COVID-19 severity changed over the course of the pandemic in response to subsequent waves of infection, increasing population immunity, and the emergence of new viral variants. The study analysed the incidence of COVID-19 acute-care hospitalisations, COVID-19 intensive care unit (ICU) hospitalisations, as well as the incidence of severe, critical and fatal COVID-19 cases, according to the WHO classification, in the national cohort of Qatari citizens.

Qatar’s population includes Qatars and a large expatriate workforce. A considerable proportion of the expatriate population consists of healthy men who are craft and manual workers aged 20–49, a population possibly affected by the healthy worker effect. As a result, they may not represent a natural national population. In contrast, Qatari citizens represent a typical national population, including both healthy and unhealthy individuals, making them relevant for assessing the severity of SARS-CoV-2 infections in this study.

**METHODS**

**Study population and data sources**

This study assessed the severity of COVID-19 in the national cohort of Qatari citizens from 28 February 2020, which marks the earliest record of a SARS-CoV-2-positive test in Qatar, to 21 April 2023. The study used the national, federated databases for COVID-19 laboratory testing, vaccination, hospitalisation and death, obtained from the integrated, nationwide, digital-health information platform (online supplemental section S1). The databases contain SARS-CoV-2-related data with no missing information since the pandemic’s onset, including all PCR tests and, from 5 January 2022, all medically supervised rapid antigen tests (online supplemental section S2).

SARS-CoV-2 testing in Qatar was conducted on a large scale, primarily for non-clinical reasons. The national mortality database was used to obtain data on all-cause mortality, including deaths occurring at healthcare facilities and elsewhere. Qatar launched its COVID-19 vaccination programme in December 2020 using the BNT162b2 and mRNA-1273 vaccines. Detailed descriptions of Qatar’s population and national databases have been previously reported.

**COVID-19 acute-care and ICU hospitalisations**

This study tracked COVID-19 hospitalisations based on a national protocol for COVID-19 case management administered at Hamad Medical Corporation, the national public healthcare provider, and the only authorised entity to provide COVID-19 healthcare in Qatar. A COVID-19 acute-care admission was defined as a record of an acute-care bed admission for an individual who had an active SARS-CoV-2 infection, irrespective of the clinical condition of the admitted individual. Initially, the duration of an active SARS-CoV-2 infection was defined to be 21 days following a SARS-CoV-2-positive test. However, this duration definition was subsequently reduced to 14 days on 1 July 2020 and then to 5 days on 17 October 2022, reflecting changes in policy guidelines in the country.

COVID-19 ICU admission was defined as an ICU bed admission for an individual with an active SARS-CoV-2 infection, and for which the ICU admission clinical team determined that the clinical condition could be related to COVID-19. If an ICU admission for an individual with an active SARS-CoV-2 infection was determined to be unrelated to COVID-19, it was classified as a COVID-19 acute-care admission according to the national protocol.

**Severe, critical and fatal COVID-19**

To ensure stringent and standardised assessment of COVID-19 infection severity, the national protocol for COVID-19 case management required that each hospitalised patient with COVID-19, in an acute-care or ICU bed, undergoes an infection severity assessment every 3 days using WHO guidelines until discharge or death. Trained medical personnel, independent of study investigators, performed the classification of cases into severe, critical or fatal COVID-19 categories using individual chart reviews (online supplemental section S3). This team of medical personnel operated independently from the clinical teams responsible directly for care of patient with
COVID-19, whether in acute care or ICU beds. Severe cases were typically hospitalised in acute-care beds, and sometimes in ICU beds out of precaution, while critical cases were always hospitalised in ICU beds.

The incidence of severe COVID-19 cases was defined as the first assessment indicating severe COVID-19 for a given individual during their hospitalisation. Similarly, the incidence of critical and fatal COVID-19 cases were defined based on the first assessment indicating critical or fatal COVID-19 during hospitalisation. Additionally, if a severe or critical assessment for a newly admitted patient with COVID-19 occurred ≥30 days after discharge from the hospital, it was considered a new diagnosis that is independent of the first one.

Cohort study of incidence of severe, critical or fatal COVID-19
In addition to examining the link between hospitalisation and severity, a national retrospective cohort study was conducted to investigate the incidence of severe, critical or fatal COVID-19 cases among Qatari citizens between 28 February 2020 and 21 April 2023. The study cohort included all Qatars alive on 28 February 2020, who had at least one record of a SARS-CoV-2 test during the pandemic, which served as a proxy for their presence in Qatar during the study period.

Considering the various testing mandates implemented throughout the pandemic and large-scale routine testing (online supplemental section S1), it is unlikely that any Qatari residing in Qatar did not undergo at least one SARS-CoV-2 test. In total, 2,915,088 SARS-CoV-2 tests were conducted among this cohort of 312,109 Qatars from the onset of the pandemic until 21 April 2023, with an average rate of 9.5 tests per person. With this volume of testing, this cohort is expected to represent virtually the entire Qatari population, a stable affluent population. The size of the cohort is also consistent with the figures reported in the Qatar Census 2020.

We retrieved COVID-19 severity, criticality and fatality records for every documented SARS-CoV-2 infection or reinfection since the pandemic onset. SARS-CoV-2 reinfection was defined as a documented infection that occurred ≥90 days after an earlier infection, to avoid misclassifying prolonged SARS-CoV-2 positivity as reinfection. Patients who progressed to severe, critical or fatal COVID-19 after a documented infection (or reinfection) were classified based on the worst assessment outcome related to that infection (or reinfection), starting with death, followed by critical disease, and then severe disease (online supplemental section S3). The date of incidence of the outcome in this analysis was set as the day of the positive SARS-CoV-2 test that documented the infection that progressed into the severe forms of COVID-19.

All individuals were followed from the study start date (28 February 2020) until any of the following events: documented infection/reinfection associated with fatal COVID-19, or non-COVID-19-related death, or administrative end of follow-up (21 April 2023). The pandemic was categorised into distinct phases based on the level of SARS-CoV-2 infection and the predominant variant (online supplemental section S4).

Statistical analysis
The national cohort was characterised by calculating frequency distributions and measures of central tendency. The cumulative incidence of severe, critical or fatal COVID-19 was defined as the proportion of individuals at risk (that is members of this national cohort) who had at least one episode of severe, critical or fatal COVID-19 and was estimated using the Kaplan-Meier estimator method. Likewise, the cumulative incidence of fatal COVID-19 was estimated.

The incidence rate of any severe, critical or fatal COVID-19 outcome was determined by dividing the number of episodes by the total person years contributed by all individuals in the cohort. To estimate the incidence rate, we employed a Poisson log-likelihood regression model with the Stata 17.0 stptime command, which provided both the incidence rate and its corresponding 95% CI.

The hazard rate for any severe, critical or fatal COVID-19 outcome was also calculated and its estimates were smoothed by applying kernel-density weighting. The hazard rate quantifies the instantaneous probability at a specific point in time of an individual in the observed cohort experiencing an event (in this case, severe, critical or fatal COVID-19) per unit interval of time, assuming that this individual has survived up to that moment.

Using the same approach, we also estimated the incidence rate of a fatal COVID-19 outcome and the hazard rate for a fatal COVID-19 outcome. The incidence rates were assessed for the entire follow-up period as well as for different phases of the pandemic to investigate temporal trends.

Adjusted HRs (AHRs) were estimated to compare the incidence of severe, critical or fatal COVID-19 by sex, 10-year age group, number of coexisting medical conditions (0, 1, 2, 3, 4, 5, 6+; online supplemental section S5), and vaccination dose status (unvaccinated, 1 dose, 2 doses, 3+ doses). This analysis estimated associations using a multivariable Cox regression model to adjust simultaneously for the different factors. To account for changes in vaccination status over time, vaccination was included as a time-varying covariate. Standard errors were adjusted for clustering effects. Interactions were not investigated. Analogously, the same analysis was done for only fatal COVID-19. All statistical analyses were conducted using Stata/SE V.17.0 (StataCorp LLC).

Oversight
The study was reported following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (online supplemental table S1).
RESULTS

Acute-care hospitalisations and severe cases

Figure 1A presents the occurrence of COVID-19 acute-care hospitalisations and of severe COVID-19 cases among Qataris on a monthly basis since onset of the pandemic. The data include a total of 6742 acute-care admissions, with 4384 occurring during the pre-omicron phase, 843 during the first wave of the omicron variant (BA.1 and BA.2), and 1515 in the post-first omicron phase.

Out of the total acute-care admissions, 1362 cases met the criteria set by the WHO for severe COVID-19 (figure 1A). Among these severe cases, 1103 were reported during the pre-omicron phase, 228 during the first omicron wave and 31 in the post-first omicron phase.

The higher number of acute-care admissions compared with severe cases is attributed to admissions that did not meet the exact definition of severe COVID-19 and hospitalisations with COVID-19 rather than strictly because...
of COVID-19—incidental hospitalisations or hospitalisations for conditions that COVID-19 may have directly or indirectly worsened. In the very early stage of the pandemic, hospitalisation was also used for isolation purposes.

**ICU hospitalisations and critical cases**

**Figure 1B** presents the occurrence of COVID-19 ICU hospitalisations and of critical COVID-19 cases among Qataris. The data include a total of 641 ICU admissions, with 485 occurring during the pre-omicron phase, 121 during the first omicron wave and 35 in the post-first omicron phase.

Out of the total ICU admissions, 281 cases met the criteria set by the WHO for critical COVID-19 (**figure 1B**). Among these critical cases, 215 were reported during the pre-omicron phase, 54 during the first omicron wave, and 12 in the post-first omicron phase.
The number of ICU admissions surpassed the count of critical cases, although the difference was not as large as the gap observed between acute-care admissions and severe cases. The gap appears to be attributed to precautionary admissions not meeting the precise criteria for critical COVID-19, and some admissions being with COVID-19 rather than strictly because of COVID-19.

### All-cause and COVID-19 deaths

Figure 2 depicts the occurrence of all-cause deaths and fatal COVID-19 cases among Qataris. The data comprise a total of 2002 all-cause deaths, with 1045 occurring during the pre-omicron phase, 192 during the first omicron wave and 765 in the post-first omicron phase (figure 2A).

Among all-cause deaths, 131 cases met the WHO criteria for fatal COVID-19 (figure 2A). Out of these deaths, 86 were reported during the pre-omicron phase, 33 during the first omicron wave, and 12 in the post-first omicron phase. COVID-19 deaths comprised 6.5% of all-cause deaths. This proportion was highest during the first omicron wave at 17.2% and lowest during the post-first omicron phase at only 1.6% (figure 2B).

### Incidence rate of severe, critical or fatal COVID-19

Table 1 provides the baseline characteristics of the participants in the cohort study. Figure 3A visually represents the incidence of SARS-CoV-2 infection, including periods of dominance of various variants throughout the pandemic (dates are found in online supplemental section S4).

There were 1396 episodes of severe, critical or fatal COVID-19 during a total follow-up of 978041 person years. The median follow-up time was 3.14 years (IQR: 3.14–3.14 years). The majority of infected individuals (99.5%) progressed to severe, critical or fatal COVID-19 subsequent to the primary infection (as opposed to subsequent to reinfection). The cumulative incidence of severe, critical or fatal COVID-19 after 3.14 years of follow-up was 0.45% (95% CI 0.43% to 0.47%), with two major jumps in incidence during the beta and omicron waves (figure 4A).

The incidence rate of severe, critical or fatal COVID-19 was 1.43 (95% CI 1.35 to 1.50) per 1000 person years throughout the pandemic (figure 5A). During the pre-omicron phase, the first omicron wave, and these two phases combined, it was 2.01 (95% CI 1.90 to 2.13), 3.70 (95% CI 3.25 to 4.22) and 2.18 (95% CI 2.07 to 2.30) per 1000 person years, respectively. In the post-first omicron phase, the incidence rate dropped drastically to 0.10 (95% CI 0.08 to 0.14) per 1000 person years, a 95.4% reduction compared with earlier phases.

The highest incidence rates were observed during the beta and first omicron waves, while the post-first omicron waves consistently had very low incidence rates (figure 3B).

The hazard rate for severe, critical or fatal COVID-19 exhibited fluctuations over time with the occurrence of waves (online supplemental figure S1A). Its peak was observed during the beta wave, but a rapid decline in the hazard rate followed, coinciding with the rapid scale-up of primary-series vaccination (refer to vaccination scale-up data in online supplemental figure S2). During the first omicron wave, the hazard rate swiftly declined, reaching a very low level by the end of this wave that was sustained for the remainder of the study despite several subsequent omicron subvariant waves.

### Incidence rate of fatal COVID-19

A total of 131 individuals developed fatal COVID-19 during follow-up, all of which occurred after the primary infection and none during reinfection. The cumulative incidence of fatal COVID-19 after 3.14 years of follow-up was 0.042% (95% CI 0.036% to 0.050%), with two major jumps in incidence during the beta and omicron waves (figure 4B).

The incidence rate of fatal COVID-19 was 0.13 (95% CI 0.11 to 0.16) per 1000 person years throughout the pandemic (figure 5B). During the pre-omicron phase,
Figure 3  Temporal patterns of infections and severe and fatal COVID-19 during the waves and phases of the pandemic. (A) Daily count of newly diagnosed SARS-CoV-2 infections. (B) Incidence rate of severe, critical or fatal COVID-19. (C) Incidence rate of fatal COVID-19.
the first omicron wave, and these two phases combined, it was 0.16 (95% CI 0.13 to 0.19), 0.60 (95% CI 0.44 to 0.83) and 0.20 (95% CI 0.17 to 0.24) per 1000 person years, respectively. In the post-first omicron phase, the incidence rate dropped drastically to 0.02 (95% CI 0.01 to 0.04) per 1000 person years, a 90.0% reduction compared with earlier phases.

The highest incidence rates were observed during the beta and first omicron waves, while the post-first omicron waves consistently had very low incidence rates (figure 3C).

The hazard rate for fatal COVID-19 exhibited fluctuations over time with the occurrence of waves, peaked during the beta wave, and very rapidly declined during

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**Figure 4** Cumulative incidence of (A) severe, critical or fatal COVID-19 and (B) fatal COVID-19 since the onset of the pandemic.

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the first omicron wave (online supplemental figure S1B). It reached a very low level by the end of the first omicron wave that was sustained for the remainder of the study despite several subsequent omicron subvariant waves.

**Associations with severe and fatal COVID-19**

The AHR for severe, critical or fatal COVID-19 was lower in females compared with males, increased exponentially with age and linearly with the number of coexisting conditions, and decreased extensively, in a dose—response relationship, with the number of vaccine doses (figure 6A–D). Similar associations were observed for fatal COVID-19 (figure 6E–H).

**DISCUSSION**

The end of the first omicron wave marked a turning point in the pandemic, with a 95% drop in the incidence rate of severe, critical or fatal cases of COVID-19 compared with earlier stages. Vaccinations and advancements in case management contributed to reducing severity and fatality gradually over time,8 20 27 and there was a rapid decline in severity during the mass scale-up of primary-series vaccination. However, the end of the first omicron wave served as the central turning point in severity. By the end of this wave, severity rates reached very low levels not seen since the onset of the pandemic, and these levels

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**Figure 5** Incidence rates of (A) severe, critical or fatal COVID-19 and (B) fatal COVID-19 during the pre-omicron phase, first omicron wave and post-first omicron phase.
Figure 6  Adjusted HRs for severe, critical or fatal COVID-19 and for only fatal COVID-19 across sex (A and E), age (B and F), number of coexisting conditions (C and G), and vaccination dose status (D and H), respectively.

*Upper bound of confidence interval truncated for better visibility due to wide interval.
have been sustained since then, despite the occurrence of several immune-evasive omicron subvariant waves. There has been no appreciable rebound in severity at any time since this first omicron wave, with nearly total decoupling between the incidence of infection and incidence of severe COVID-19.

This turning point is likely attributed to the rapid buildup of natural immunity during the first omicron wave, which had the highest infection incidence throughout the pandemic. This aligns with earlier studies in Qatar, demonstrating strong protection against severe reinfection among individuals with prior infection and limited waning in protection. Other factors, such as lower severity in omicron subvariants, the overall decreased infection incidence in the post-first omicron phase, and the forward displacement of deaths of individuals with relatively short life expectancy, have all also likely contributed to this shift in severity.

A defining aspect of this transition is the near-complete decoupling between infection and severity after the first omicron wave (figure 3), and between acute-care admissions and severe cases (figure 1A), as reported elsewhere. Meanwhile, there was some decoupling between ICU admissions and critical cases, although to a lesser extent (figure 1B), suggesting ICU admissions as an early warning indicator for changes in COVID-19 severity.

COVID-19 severity varied throughout the pandemic based on the circulating variant and infection incidence, as well as population immunity due to vaccination and previous infections. The beta wave exhibited the highest severity due to the severity of that variant and concentrated incidence (figure 3). The first omicron wave followed with high severity, despite the lower severity of the omicron variant compared with earlier variants. This was primarily due to a high concentration of infections within a short duration, and perhaps a stretched healthcare system dealing with a large number of severe cases. The introduction of the delta variant, occurring throughout the pandemic. This aligns with earlier studies in Qatar, demonstrating strong protection against severe reinfection among individuals with prior infection and limited waning in protection. Other factors, such as lower severity in omicron subvariants, the overall decreased infection incidence in the post-first omicron phase, and the forward displacement of deaths of individuals with relatively short life expectancy, have all also likely contributed to this shift in severity.

In summary, while vaccinations and advancements in case management have contributed to a gradual reduction in severity and fatality over time in Qatar, the end of the first omicron wave marked a significant turning point in the trajectory of severity during this pandemic. The post-first omicron phase exhibited a remarkable 95% reduction in the incidence rate of severe, critical, or fatal cases compared with earlier stages, accompanied by a 90% decrease in the incidence rate of fatal COVID-19. Severity reached sustained very low levels with no rebound despite subsequent occurrence of several immune-evasive omicron subvariant waves. This shift in severity is believed to be driven by the rapid accumulation of natural immunity during the initial omicron wave. Given the limited observed waning in the protection provided by natural immunity against severe reinfection, it is plausible that the phase of low severity could be sustained as long as the virus does not undergo extensive evolution beyond what has been observed since the introduction of omicron, and the population does not have high rates of comorbidity, which could dangerously exacerbate a repeat infection.
Supplemental material

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REFERENCES


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. 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.

Starting from November 1, 2022, SARS-CoV-2 testing was substantially reduced, but still about 1% of the population are tested every week. 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{1,2,5-10}
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\(^1\) of random positive clinical samples,\(^2\)\(^{12-16}\) complemented by deep sequencing of wastewater samples.\(^14\)\(^{17}\)\(^{18}\) 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.\(^1\)\(^2\)\(^4\)\(^8\)\(^{12-16}\)\(^{19-23}\)
Section S3. COVID-19 severity, criticality, and fatality classification

Classification of Coronavirus Disease 2019 (COVID-19) case severity (acute-care hospitalizations),\textsuperscript{24} criticality (intensive-care-unit hospitalizations),\textsuperscript{24} and fatality\textsuperscript{25} 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)”.\textsuperscript{24} Detailed WHO criteria for classifying Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection severity can be found in the WHO technical report.\textsuperscript{24}

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”\textsuperscript{24}. Detailed WHO criteria for classifying SARS-CoV-2 infection criticality can be found in the WHO technical report.\textsuperscript{24}

**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”\textsuperscript{25}. Detailed WHO criteria for classifying COVID-19 death can be found in the WHO technical report.\textsuperscript{25}
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><strong>Title and abstract</strong></td>
<td></td>
<td></td>
</tr>
<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><strong>Introduction</strong></td>
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<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><strong>Methods</strong></td>
<td></td>
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<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>
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<tr>
<td><strong>Bias</strong></td>
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<tr>
<td>9</td>
<td>Describe any efforts to address potential sources of bias</td>
<td>Methods (‘Statistical analysis’)</td>
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<tr>
<td><strong>Study size</strong></td>
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<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>
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<tr>
<td><strong>Quantitative variables</strong></td>
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<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><strong>Statistical methods</strong></td>
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<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’), 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>
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<tr>
<td><strong>Results</strong></td>
<td></td>
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<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>Supplemental material</th>
<th>BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)</th>
</tr>
</thead>
</table>

**Outcome data**

15. Report numbers of outcome events or summary measures over time

Results (‘Incidence rate of severe, critical, or fatal COVID-19’, paragraphs 1-2, & ‘Incidence rate of fatal COVID-19’, paragraph 1) & Figures 3-4

**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 (‘Incidence rate of severe, critical, or fatal COVID-19’, paragraphs 3-5, ‘Incidence rate of fatal COVID-19’, paragraphs 2-4, & ‘Associations with severe and fatal COVID-19’), Figures 3-6, & Figure S1 in Supplementary Material

(b) Report category boundaries when continuous variables were categorized

Table 1

(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 (‘Incidence rate of severe, critical, or fatal COVID-19’, paragraphs 3-5, ‘Incidence rate of fatal COVID-19’, paragraphs 2-4, & ‘Associations with severe and fatal COVID-19’) & Figures 3-6

**Discussion**

18. Summarise key results with reference to study objectives

Discussion, paragraphs 1-4

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 5-8

20. Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence

Discussion, paragraph 9

21. Discuss the generalisability (external validity) of the study results

Discussion, paragraphs 7-8

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
Figure S1. The hazard rate for A) severe, critical, or fatal COVID-19 and B) fatal COVID-19 since the onset of the pandemic.

A

Time in which primary-series vaccination was being scaled up

B

Smoothing hazard rate for fatal COVID-19

Smoothing hazard rate for severe, critical, or fatal COVID-19

Months since onset of 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


29. Altarawneh HN, Chemaitelly H, Ayoub HH, et al. Effects of previous infection, vaccination, and hybrid immunity against symptomatic Alpha, Beta, and Delta SARS-CoV-2 infections: an observational...