Risk of covid-19 related deaths for SARS-CoV-2 omicron (B.1.1.529) compared with delta (B.1.617.2): retrospective cohort study

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Additional material is published online only. To view please visit the journal online.

Cite this as: *BMJ* 2022;378:e070695 http://dx.doi.org/10.1136/bmj-2022-070695

Accepted: 23 June 2022

ABSTRACT

OBJECTIVE

To assess the risk of covid-19 death after infection with omicron BA.1 compared with delta (B.1.617.2).

DESIGN

Retrospective cohort study.

SETTING

England, United Kingdom, from 1 December 2021 to 30 December 2021.

PARTICIPANTS

1 035 149 people aged 18-100 years who tested positive for SARS-CoV-2 under the national surveillance programme and had an infection identified as omicron BA.1 or delta compatible.

MAIN OUTCOME MEASURES

The main outcome measure was covid-19 death as identified from death certification records. The exposure of interest was the SARS-CoV-2 variant identified from NHS Test and Trace PCR positive tests taken in the community (pillar 2) and analysed by Lighthouse laboratories. Cause specific Cox proportional hazard regression models (censoring non-covid-19 deaths) were adjusted for sex, age, vaccination status, previous infection, calendar time, ethnicity, index of multiple deprivation rank, household deprivation, university degree, keyworker status, country of birth, main language, region, disability, and comorbidities. Interactions between variant and sex, age, vaccination status, and comorbidities were also investigated.

RESULTS

The risk of covid-19 death was 66% lower (95% confidence interval 54% to 75%) for omicron BA.1 compared with delta after adjusting for a wide range of potential confounders. The reduction in the risk of covid-19 death for omicron compared with delta was more pronounced in people aged 18-59 years (number of deaths: delta=46, omicron=11; hazard ratio 0.14, 95% confidence interval 0.07 to 0.27) than in those aged ≥70 years (number of deaths: delta=113, omicron=135; hazard ratio 0.44, 95% confidence interval 0.32 to 0.61, P<0.0001). No evidence of a difference in risk was found between variant and number of comorbidities.

CONCLUSIONS

The results support earlier studies showing a reduction in severity of infection with omicron BA.1 compared with delta in terms of hospital admission. This study extends the research to also show a reduction in the risk of covid-19 death for the omicron variant compared with the delta variant.

WHAT IS ALREADY KNOWN ON THIS TOPIC

The omicron variant, which refers to the whole lineage (BA.1, BA.2, BA.3, BA.4, and BA.5), has been shown to be more transmissible than the delta variant

Evidence suggests that the risk of hospital admission and death within 28 days of a SARS-CoV-2 positive test is lower for the omicron variant than the delta variant

Research is lacking comparing the risk of covid-19 death identified from death certification records for the omicron and delta variants

WHAT THIS STUDY ADDS

Data from a large cohort of people with covid-19 infections that occurred in December 2021were used to compare the risk of covid-19 death (identified from death certification records) for the delta and omicron BA.1 variants

The risk of covid-19 death was reduced by 66% after infection with the omicron BA.1 variant compared with the delta variant after adjusting for a wide range of potential confounders, including vaccination status and comorbidities

Introduction

On 27 November 2021, the UK Health Security Agency identified the first people in the UK with covid-19 variant B.1.1.529 or BA.1, a variant of concern named omicron, together with its subvariants BA.2 and BA.3.[1] Because the omicron variant (which refers to the whole lineage, including BA.1, BA.2, BA.3) had been shown to be more transmissible, it was important to identify whether the severity of disease, risk of hospital admission, death, and long term complications were increased compared with the delta variant to enable pandemic policy planning.

Omicron lineage BA.1 has a large number of mutations, 37 of which are in the spike (S) protein[2] which leads to S gene target failure (SGTF) in some molecular diagnostic assays.[3] This SGTF can be identified from non-detectable S gene and a cycle threshold (Ct) value of 30 or lower for the N and ORF1ab targets in positive PCR tests using national testing data for England (based on the NHS Test and Trace programme), supplemented with data from the National Pathology Exchange. Several studies have used a similar approach to compare the severity of alpha (B.1.1.7) and delta (B.1.617.2) with other variants.[4-6]

Emerging data also indicate that the risk of hospital admission is lower after omicron than after delta infection,[7 8] as is the risk of death within 28 days after

a SARS-CoV-2 test.[8] Nyberg and colleagues report that the risk of severe outcomes after positive SARS-CoV-2 tests was substantially lower for omicron than for delta. However, this analysis used death within 28 days of a positive test as a measure of covid-19 death, rather than covid-19 death identified using information from the death certificate, which includes deaths at any time period and a cause of death classified by the doctor who attended the patient during their final illness. Additionally, with a highly transmissible infection and increased levels of population testing, definition of death within 28 days is more likely to be susceptible to misclassification bias owing to asymptomatic coincidental infection than when infection rates are lower, resulting in severity estimates between variants being susceptible to bias.

In this study, we compared the risk of covid-19 death using death registration data in a large population based cohort study of people infected in England in December 2021, when delta and omicron BA.1 variants were circulating, but omicron BA.2 remained rare. We also adjusted for a range of potential confounders, including pre-existing health conditions.

Methods

Study data

We used data from the Office for National Statistics (ONS) Public Health Data Asset, a linked dataset combining the 2011 census, mortality records, the General Practice Extraction Service data for pandemic planning and research, Hospital Episode Statistics, NHS Test and Trace data (pillar 2—swab testing for the virus in the wider population), and national vaccination data from the National Immunisation Management Service (NIMS). The NIMS records all vaccinations administered to all people living in England since the vaccination programme started on 8 December 2020.

To obtain NHS numbers, the 2011 census was linked to the 2011-13 NHS Participant Registers. Of the 53 483 502 census records, 50 019 451 were linked deterministically; 555 291 additional matches were obtained using probabilistic matching (overall linkage rate 94.6%). All subsequent linkages were conducted using the NHS number. The ONS Public Health Data Asset includes data on 35 million adults, an estimated 79% of the population of England in 2020.

Study population

The study population consisted of all people aged 18-100 years who had a positive PCR test for covid-19 between 1 December 2021 and 30 December 2021, reported as part of pillar 2 of NHS Test and Trace and analysed by Lighthouse laboratories, who were enumerated in the 2011 census, were living in England, and were registered with a general practitioner on 1 November 2019. We specifically selected people who tested positive in December 2021 for our study population because delta and omicron BA.1 variants were circulating during this period, but omicron BA.2 remained rare. In January 2022, nearly all people who tested positive for covid-19 had the omicron BA.1 or BA.2 variants, limiting the possibility to compare outcomes with delta over the same period.

Our sample consisted of 1 035 149 people who tested positive for an omicron BA.1 or delta compatible infection between 1 and 31 December 2021 and could be linked to the ONS Public Health Data Asset (supplementary table S1); this covers approximately 44% of all positive tests in adults in England in December 2021. The denominator used was the number of people who tested positive each day in England for all age groups except those aged 18-19 years; for this age group, the proportion used was 40% of daily infections in the 20-24 age group owing to unavailability of the relevant data.[9] People entered the cohort on the index date, which is the date of the first positive PCR test recorded between 1 and 30 December 2021. People left the cohort at the end of the study (28 February 2022; censored), after death from covid-19 (event), or death from another cause (censored), whichever came first.

Outcome

The primary outcome was the time from a positive PCR test to covid-19 related death, which was defined as confirmed covid-19 death identified by international classification of diseases 10th revision code U07.1 mentioned anywhere on the death certificate. Use of the U07.1 code is when covid-19 has been confirmed by laboratory testing irrespective of severity of clinical signs or symptoms, but should only be stated on a death certificate when it is the primary or a contributory cause of death.

Exposure

The exposure of interest was the covid-19 variant shown on PCR positive tests taken in the community (pillar 2) and analysed by Lighthouse laboratories; specifically, defined by SGTF as omicron BA.1 compatible if S negative, N positive, ORF1ab positive (with mean Ct<30 for N and ORF1ab); or delta compatible if S positive, N positive, ORF1ab positive, or S positive, N positive or ORF1ab positive, and with a mean Ct<30. Of all omicron BA.1 and delta compatible infections, a small proportion (2.9%) of total positive tests had mean Ct values >30, which indicates a low viral load; these were excluded because delta cases with high Ct values could be mistakenly classified as S negative (supplementary table S1).

Covariates

Our main objective was to compare the risk of covid-19 death in people infected with delta and omicron BA.1 variants. We adjusted for a wide range of potential confounders of the relation between variant type and the risk of covid-19 death once infected. These confounders related to vulnerability or testing behaviours and accounted for any bias in our study population of people who tested positive as part of the national surveillance programme.

doi: 10.1136/bmj-2022-070695 | *BMJ* 2022;378:e070695 | the bmj

Table 1 | Baseline characteristics of patients infected with omicron or delta variants

Variable and group	Delta, % (n=221 146)	Omicron, % (n=814 003)	Total
Country of birth			
Non-UK	11.3	11.4	117 764
UK	88.7	88.6	917 385
Degree			
No	71.5	77.5	788 964
Yes	28.5	22.5	246 185
Disability			
None or day-to-day activities not limited or limited a little	98.0	98.2	1 015 941
Day-to-day activities limited a lot	2.0	1.8	19 208
Ethnicity			
Black	2.1	4.3	39 305
Other	4.7	6.6	63 944
South Asian	4.2	4.5	46 034
White	89.0	84.6	885 866
Household deprivation			
1	59.1	58.6	607 754
2	26.6	27.2	280 530
3	10.2	9.9	103 552
4	3.0	2.7	28 721
5	0.3	0.2	2558
Missing	0.8	1.3	12 034
Key worker*			
No	27.2	23.7	253 009
Yes	72.8	76.3	782 140
Main language			
English	6.9	6.4	66 908
Other	93.1	93.6	968 241
Previous covid-19 infection			
No	99.0	93.4	979 297
Yes	1.0	6.6	55 852
Region			
North East	4.0	4.6	46 624
North West	16.6	19.1	192 220
Yorkshire and the Humber	12.7	11.4	120 800
East Midlands	9.2	7.7	83 248
West Midlands	11.5	8.1	91 289
East of England	13.3	10.9	118 094
London	12.0	19.9	188 942
South East	15.3	14.9	155 299
South West	5.3	3.3	38 633
Sex			
Male	45.9	46.3	478 268
Female	54.1	53.7	556 881
Count of comorbidities†			
0	88.5	87.6	908 641
1-2	11.1	12.0	122 585
3	0.4	0.4	3923
Vaccination status			
Booster	9.3	26.1	233 172
One dose	3.8	3.0	32 574
Two doses AstraZeneca>180 days	7.7	6.6	70 295
Two doses AstraZeneca ≤180 days	5.1	2.3	30 178
Two doses mRNA >180 days	25.2	16.2	187 980
Two doses mRNA ≤180 days	33.6	36.1	368 390
Unvaccinated	15.4	9.7	112 560

*Information on 2011 census variables that were used to define key worker status.
†Number of comorbidities grouped for disclosure control reasons, added as linear continuous predictor to fully adjusted model (model 4, adjusted for age, sex, vaccination status, previous infection, calendar time, socioeconomic factors, and comorbidities).

Sociodemographic characteristics included age at time of infection (as a natural spline with boundary knots at the 10th and 90th percentile and three interior knots), sex, ethnicity (white, black, South Asian, other), region (North East, North West, Yorkshire and the Humber, East Midlands, West Midlands, East of England, London, South East, South West), disability, key worker status, index of multiple deprivation rank (as a natural spline with boundary knots at the 5th and 95th percentile and three interior knots), country of birth (UK or non-UK), university degree, household deprivation, and English language ability. We also adjusted for baseline vaccination status (unvaccinated, one dose, two doses of AstraZeneca ≤180 days previously, two doses of mRNA vaccine (Pfizer or Moderna) ≤180 days previously, two doses of AstraZeneca >180 days previously, two doses of mRNA vaccine >180 days previously, any booster or third dose, which we refer to as boosters), previous infection (defined by a positive test at least 90 days before the date of the current positive test), calendar date of infection (as a natural spline with boundary knots at the 10th and 90th percentile and three interior knots), and clinical risk factors by counting the number of conditions identified as being associated with an increased risk of covid-19 death in the QCovid 3 risk model (0-8). QCovid risk factors were identified by using five years of General Practice Extraction Service data for Pandemic Planning and Research primary care data up to 31 March 2022; when a code for a condition was absent during this period, it was assumed the person did not have the condition. Supplementary table S2 presents further details of the comorbidities. For any other missing data, a missing category was included in the models, as shown in table 1. Characteristics of the study population were summarised overall, and stratified by variant type, using means for continuous variables and proportions for categorical variables.

We used a cause specific Cox proportional hazard regression model to estimate the hazard ratio of covid-19 related death for people infected with omicron BA.1 versus delta variants. Follow-up time was calculated as the period from a positive PCR test to covid-19 death or end of study. For non-covid-19 deaths, people were censored at the date of death if this occurred before the end of the study date. We estimated four models, sequentially adjusted for age, sex, vaccination status, and previous infection (model 1); plus, calendar time (model 2); plus socioeconomic factors (model 3); and finally, plus pre-existing health conditions (model 4).

To test whether the relative risk of death from omicron BA.1 varied by age and sex, we included interactions between variant type and age, and variant type and sex. To test whether the relative risk of death from omicron BA.1 varied by vaccination status (unvaccinated, one dose, two doses, and booster) and the number of comorbidities (0, 1-2, ≥3), we compared a model adjusted for interactions between variant type and age, and age and vaccination status (or comorbidities) with a model that included a three way interaction between variant type, age, and vaccination status (or comorbidities). The rationale for this approach was that vaccination status and the number of comorbidities are closely related to age, and in the absence of an interaction between variant type

Table 2 | Number of infections and number of deaths related to covid-19 and not related to covid-19

Infections and deaths	Total	Delta	Omicron
No of covid-19 infections	1 035 149	221 146	814 003
No of covid-19 deaths	364	204	160
Age 18-59	57	46	11
Age 60-69	59	45	14
Age ≥70	248	113	135
No of deaths not related to covid-19	272	76	196

and age, the interaction between vaccination status (or comorbidities) could capture the interaction between variant type and age.

We assessed the proportional hazard assumption by testing for the independence between the scaled Schoenfeld residuals and time at risk. We used Schoenfeld residuals from the fitted Cox models, smoothed using generalised additive models, to assess whether relative differences in the hazard of covid-19 death between variants was constant over time after a positive test.

Patient and public involvement

We did not directly involve patients and the public in the design and conception of the study, primarily because of the pace at which this study was conducted to inform the UK government's response to the covid-19 pandemic. However, the paper was read by several members of the public.

Results

Characteristics of study population

Our study population consisted of 1 035 149 people. Of these, 814 003 (78.6%) had omicron compatible infections and 221 146 (21.4%) had delta compatible infections, with the number of omicron infections increasing each day across the study period (supplementary fig S1); this covers approximately 44% of all positive tests in adults in England in December 2021.[9] In our study population, 54% of infections were in women (table 1). The mean age at infection was two years younger in those infected with omicron BA.1 (39.9 years, standard deviation 15.2) than in those with delta (42.2, 13.1 years). There were 160 covid-19 deaths and 196 non-covid-19 deaths in those infected with omicron BA.1, and 204 and 76, respectively, in those infected with delta (table 2). The mean time from a positive result to covid-19 death was 18 days (standard deviation 12.0) for omicron BA.1 and 18 days (12.2) for delta.

Relative risk of covid-19 death by variant

The risk of covid-19 death was 66% lower (hazard ratio 0.34, 95% confidence interval 0.25 to 0.46; supplementary table S4 for omicron BA.1 infection compared with delta infection in our fully adjusted model (model 4), accounting for sex, age, vaccination status, previous infection, calendar time, ethnicity, index of multiple deprivation rank, household deprivation, university degree, keyworker status, country of birth, main language, region, disability, and health risk factors defined in the QCovid 3 model (fig 1). In our minimally adjusted model (model 1) accounting only for sex, vaccination status, age and previous infection, the risk of death was 78% lower (0.22, 0.18 to 0.28) for omicron BA.1 versus delta. Adjusting for the date of infection (model 2) reduced the difference (0.32, 0.24 to 0.43). Further adjusting for sociodemographic characteristics (model 3) and pre-existing health conditions (model 4) had little impact on the relative difference in risk of covid-19 death for omicron BA.1 and delta variants (0.33 and 0.34, respectively). Sensitivity analyses using all cause death as the outcome, and several different covid-19 death definitions, also showed substantial risk reductions. As expected, given dilution bias from misclassification, for all cause death the reduction in risk for omicron BA.1 versus delta was slightly smaller, at 52% lower (0.48, 0.39 to 0.61; supplementary table S5).

Relative risk of covid-19 death by variant and age, sex, vaccination status, and comorbidities

Figure 2 presents estimates of the difference in the relative risk of covid-19 death between omicron BA.1 and delta variants by sex and age from a fully adjusted model. The difference in mortality risk varied strongly by age, with a greater reduction in covid-19 death with omicron BA.1 compared with delta for people aged 18-59 (hazard ratio 0.14, 95% confidence interval 0.07 to 0.27) compared with those aged 70 years and older (P<0.0001; 0.44, 0.32 to 0.61). The risk for omicron relative to delta was also reduced in people aged 60-69 years (0.21, 0.11 to 0.38), however this did not differ significantly compared with the 18-59 age group (P=0.33). For the interaction between sex and variant, the reduction in risk of covid-19 death was more pronounced in men (0.29, 0.2 to 0.41) than in women (0.42, 0.29 to 0.61), however this difference did not reach the threshold for significance (P=0.07).

We found a significant interaction between variant and vaccination status (χ^2 likelihood ratio test statistic (degrees of freedom): $\chi^2(25)=48.19$, P=0.004) compared with a model that only included interaction terms for variant and age, and age and vaccination status. Because of low counts of events in the one dose group, the hazard ratio for this group is not reported, but the level is included in the model. We found the relative risk was reduced for two doses and for a booster dose for omicron compared with delta (two doses: hazard ratio 0.61, 95% confidence interval 0.43 to 0.90; booster: 0.29, 0.21 to 0.40) and for unvaccinated people (0.28, 0.23 to 0.35; fig 2). We found a significant difference between people who had received two doses compared with those who were unvaccinated (P<0.001). There was no difference between people who had received a booster dose compared with the unvaccinated group (P=0.84). We found no significant interaction between number of comorbidities and variant ($\chi^2(5)=2.57$, P=0.77) compared with a model that only included interaction terms for variant and age, and age and number of comorbidities.

doi: 10.1136/bmj-2022-070695 | BMJ 2022;378:e070695 | the bmj

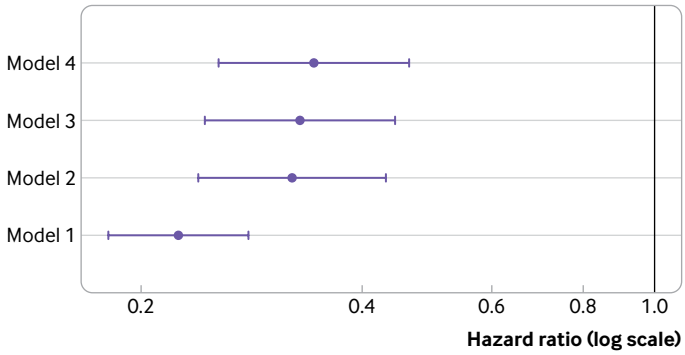

Fig 1 | Hazard ratio for covid-19 death for omicron BA.1 infection compared with delta infection using fully adjusted (model 4) and alternative models. Black line shows the null (omicron BA.1 no different to delta). Model 1 adjusted for sex, age (natural spline), vaccination status and previous infection; model 2 also adjusted for calendar time (natural spline); model 3 also adjusted for ethnicity, index of multiple deprivation rank (natural spline), household deprivation, university degree, keyworker status, country of birth, main language, region and disability; model 4 also adjusted for comorbidities

We tested the proportional hazard assumption by assessing the independence between the scaled Schoenfeld residuals and time at risk (P=0.03). The test failed to reject the independence for the key exposure (variant, P=0.43), suggesting that the proportional hazard assumption was unlikely to be violated.

Discussion

Main findings

We used data from a large cohort of people with covid-19 infection that occurred in December 2021 to examine the relative difference in covid-19 mortality between the delta and omicron BA.1 variants. Our study shows that the risk of covid-19 death was reduced by 66% after infection with the omicron BA.1 variant compared with the delta variant after adjusting for a wide range of potential confounders, including vaccination status and comorbidities. Importantly, we found that the relative risk of covid-19 death after omicron infection versus delta infection varied by age, with lower relative risk in younger people. The risk also varied by vaccination status, with the difference in covid-19 death between the delta and omicron BA.1 variants being lower for all vaccination statuses but less pronounced for people who had received two vaccinations.

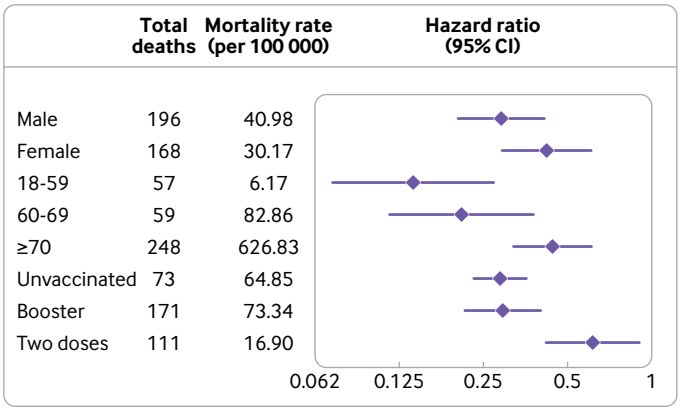

Fig 2 | Hazard ratio for covid-19 death for omicron BA.1 infection versus delta infection by sex, age, and vaccination status. To investigate the interaction between variant type and sex, the model was fully adjusted (model 4, adjusted for age, sex, vaccination status, previous infection, calendar time, socioeconomic factors, and comorbidities) with an interaction term for variant and sex. For the interaction between variant and age, the fully adjusted model also included a variable for age group (18-59, 60-69, or ≥70). For the interaction between variant and vaccination status, additional interaction terms were included between variant and vaccination categories and adjusted for an interaction between variant and age

Comparison with other studies

Early work exploring the clinical severity of the covid-19 omicron variant in a South African cohort found considerably reduced odds of hospital admission after SGTF versus non-SGTF infection across the same period.[7] A subsequent study in California on positive PCR tests between 30 November 2021 and 1 January 2022 also showed risk reductions for hospital admission, ICU admission, and mortality after omicron infection compared with delta infection.[10] In Canada, in a matched sample, the risk of hospital admission or death was found to be 65% lower among those with the omicron variant than in people with the delta variant.[11] Emerging evidence has found that omicron replicates more readily in the upper airways than the lungs, potentially indicating a biological mechanism for the reduction in risk of covid-19 death after infection with omicron compared with delta.[12]

Our results extend these initial analyses quantifying the risk of omicron severity in terms of hospital admission to covid-19 mortality. Nyberg and colleagues[8] report a reduction in death after omicron infection (hazard ratio 0.31) compared with delta, which is similar to our findings. Importantly, our results account for more sociodemographic factors and comorbidities, and highlight that the reduction in risk remains consistent even after adjusting for these additional variables. Furthermore, our study specifically quantifies the risk of cause specific covid-19 mortality, using death registration data, unlike previous work which has defined covid-19 death as death within 28 days of a positive SARS-CoV-2 test.

Because the emergence of the omicron variant resulted in an increased rate of transmission, the number of people infected with the omicron variant in our sample increased considerably across the study period. To account for the difference in infection rate across the period, a cubic spline for calendar time was included in models 2-4. While the BA.2 subvariant of omicron does not have the spike gene deletion that causes SGTF, the UK only recorded an increase in the number of people with subvariant BA.2 in the week commencing 3 January 2022.[13] Our data include omicron compatible and delta compatible infections identified between 1 and 30 December 2021, which was a period when BA.1 was prominent and omicron could be identified from SGTF. These results provide clear evidence that in the UK the risk of covid-19

mortality after infection with omicron is considerably less than for delta.

Strengths and limitations of this study

We used a large sample of positive cases from the national testing programme, allowing us to estimate the relative risk of covid-19 death after infection with omicron BA.1 and delta. By linking these infection data to information on vaccination status, comprehensive sociodemographic characteristics from the census and information on pre-existing conditions based on primary care and hospital data, we were able to estimate the relative difference in mortality between the omicron BA.1 and delta variants, adjusting for a wide range of potential confounders, including vaccination status with manufacturer type and key worker status. We also tested whether the relative mortality risk for omicron BA.1 versus delta depended on vaccination status and the number of comorbidities by including interactions between variant type and vaccination status (or comorbidities). This is an important result because we show that regardless of vaccination status omicron was milder than delta. However, no difference was found by number of comorbidities. To control for the prioritisation of the vaccination rollout, we adjusted for the interaction between vaccination status and age.

We used death certificate data to confirm covid-19 mortality, which prevented people who died from other causes after a positive covid-19 test being included in our sample. Additionally, it is important to note that the number of covid-19 deaths was low in people younger than 70 years of age, with 68.1% of events occurring in those aged ≥70. However, we had sufficient power to show important risk reductions in younger age groups, adjusting for a wide range of potential confounders. We also compared the outcomes during the same time periods to minimise bias from management of patients with covid-19 in healthcare settings during the pandemic.

One study limitation is an ascertainment bias because the data do not cover all SARS-CoV-2 infections, but only a subset of people who tested positive as part of the national testing programme in the community and analysed by Lighthouse laboratories. Tests conducted in the community but processed by other laboratories and tests conducted in hospitals could not be used because they do not use the S gene molecular diagnostic assay, which we used to identify the variant type. A limitation of our work is not having access to data to determine covid-19 variants from tests in hospital (NHS pillar 1), which explains why our total sample is smaller than those used in other research.[8] Differences in testing behaviours between groups could bias the estimates of risk of covid-19 death among people who tested positive. If some people only get tested if they experience severe symptoms, the estimated risk of death would be higher in this group than in people who get tested more routinely, even if the population has the same underlying risk. To mitigate this issue, we also adjusted the models for factors that might affect the propensity to get tested and might also be related to the severity of a SARS-CoV-2 infection, including ethnicity, region, calendar date of infection, and key worker status. However, adjusting for these factors in models 3 and 4 had little effect on our overall estimates, suggesting that any selection effects according to these characteristics had smaller impacts than might be hypothesised. One explanation for this could be the restriction of our analysis to a short time period when both variants were circulating. Sociodemographic information was obtained from the 2011 census, which was the most up to date at the time of the study, however future validation work should be conducted when 2021 census data have been released and potentially using more breakdowns of variables, such as region.

Because of death registration delays, not all deaths that occurred in the period might have been registered at the time of the study. Deaths that occurred among people who tested positive in late December are less likely to have been registered than those that occurred in people who tested positive at the beginning of the month. As the proportion of omicron BA.1 infections increased during December, the delay in death registration, if unaccounted for, could lead to underestimation of the severity of the omicron BA.1 variant. However, we accounted for the effect of registration delay in December by adjusting for calendar time of infection in our models, reducing the difference between omicron BA.1 compared with delta as expected. To fully assess the impact of covid-19, additional outcome measures such as hospital admission need to be considered. Furthermore, if the data allow, symptom profiles could be used to predict outcomes to enable better management of healthcare requirements.

Conclusions

With the emergence of the more transmissible omicron BA.1 variant, there was an urgent healthcare need to estimate the risk of covid-19 death compared with other variants to support pandemic planning responses. Our results support earlier studies that show a reduction in severity of omicron BA.1 infection compared with delta when hospital admission rates were considered. Our study extended this research to investigate covid-19 deaths and assessed cause specific mortality using death certification to accurately capture covid-19 deaths. Our work highlights the importance of the vaccination booster campaign because the reduction in risk of covid-19 death was most pronounced in people who had received a booster or third vaccination. However, mortality is only one measure that should be considered when assessing the impact of covid-19. Further studies should investigate long term outcomes of infection, such as the prevalence of long covid after omicron BA.1 infection compared with delta.

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Contributors: ILW, ASW, and VN conceptualised and designed the study. ILW and CB prepared the study data. ILW performed the statistical analysis, which was quality checked by CB, DA, and VN. All authors contributed to interpretation of the findings. ILW and VN wrote the original draft. All authors contributed to review and editing of the manuscript and approved the final manuscript. VN is the guarantor. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Funding: This study received no specific funding. TY received funding from a grant from the UK Research and Innovation (UKRI; Medical Research Council, MRC)-Department of Health and Social Care (DHSC; National Institute for Health Research, NIHR) COVID-19 Rapid Response Rolling Call (MR/V020536/1) and is part of the Data and Connectivity National Core Study, led by Health Data Research UK in partnership with the Office for National Statistics and funded by UK Research and Innovation (HDRUK2020.138). ASW is an NIHR senior investigator and is supported by the Oxford Biomedical Research Centre. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR, UK Health Security Agency, or the DHSC. KBP is supported by the Huo Family Foundation.

Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/disclosure-of-interest/ and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; KK is chair of the ethnicity subgroup of the UK Scientific Advisory Group for Emergencies (SAGE) and is a member of SAGE. JH-C is chair of the NERVTAG risk stratification subgroup and is a member of SAGE.

Ethical approval: Ethical approval was obtained from the National Statistician's Data Ethics Advisory Committee (NSDEC(20)12).

Data sharing: In accordance with NHS Digital's Information Governance requirements, the study data cannot be shared.

The lead author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Dissemination to participants and related patient and public communities: The use of deidentified data precludes direct dissemination to participants. For the purpose of open access, the authors have applied a Creative Commons Attribution (CC BY) licence to any author accepted manuscript version arising. Results will also be disseminated by all coauthors through their home institutions.

Provenance and peer review: Not commissioned; externally peer reviewed.

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Web appendix: Supplementary tables and figure