

COVID-19 hospitalisation risk for Omicron compared with Delta VOCs, by age group

MRC Biostatistics Unit, University of Cambridge and UKHSA COVID-19 Epidemiology Cell

Joint work with: UKHSA Joint Modelling Team; Statistics, Modelling and Economics Department; Genomics Cell; HO-COVID; Immunisation and Countermeasures Division

19th January 2022

Key findings

- **Adults**
 - **Lower** hospital admission risk for adult cases with Omicron compared with Delta variants
 - e.g. adjusted hazard ratio 0.25 (0.23-0.28) in 60-69 year olds
- **Children**
 - **No difference** in hospital admission risk between children under the age of 10 years with Omicron compared with Delta:
 - adjusted hazard ratio 1.00 (0.85-1.18)

Aim

To assess relative severity risks for COVID-19 cases with Omicron compared with Delta

Outcomes:

- **Hospital admission** within 14 days after positive test
- **Hospital admission or emergency care attendance** within 14 days after positive test

Admissions/attendances

- 1 day before to 14 days after specimen
- Excluding injury-related episodes

Admissions

- 1 day before to 14 days after specimen
- Excluding injury-related episodes
- Admitted or transferred according to emergency care records
- ≥ 1 night in hospital
- 0 nights in hospital, but with ICD code consistent with COVID-19
- 0 nights in hospital, and died in hospital same day

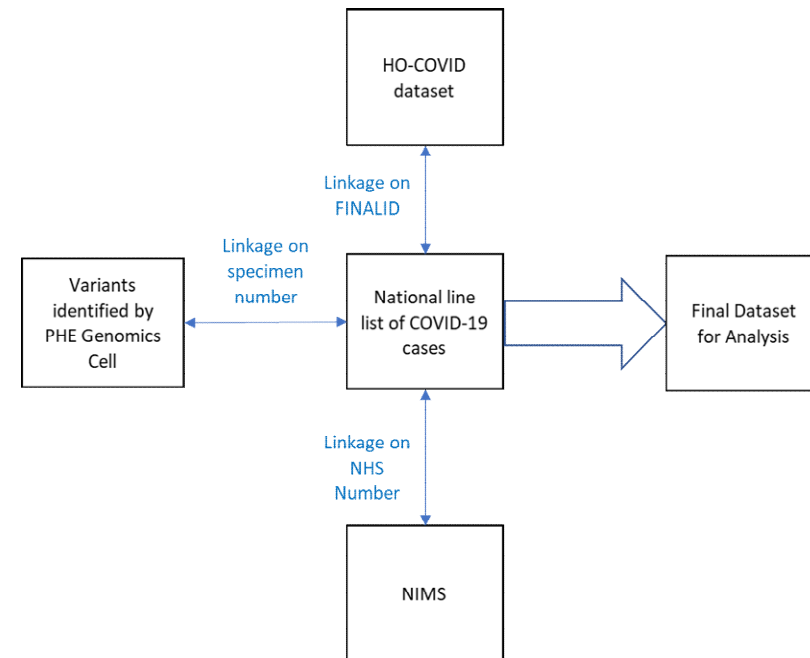
Data

Linkage of UKHSA data sources

- National line list of COVID-19 cases
- Whole genome sequencing or genotyping results with Omicron or Delta variants as defined by UKHSA Genomics Cell
- S gene target failure dataset
- NHS Immunisation Management Service
- Hospitalisation (HO-COVID) dataset
 - SUS hospitalisation dataset
 - ECDS emergency care dataset
- COVID-19 mortality dataset

Reinfections

- Positive test ≥ 90 days after earliest positive test
- Followed from the earliest of sequencing/genotyping or SGTF assessed reinfection positive test



Data

Inclusion: First or reinfection positive test 22nd November 2021 to 9th January 2022

- Sequencing-confirmed Omicron or Delta, if available
- *otherwise* Genotyping-confirmed Omicron or Delta, if available
- *otherwise* S gene negative and positive (if no known sequencing or genotyping-confirmed variant)

Retrospectively followed up until 17th January 2022

Inclusion summary

Reasons	n
Initially included in dataset	4215119
Variant unknown (no sequencing, genotyping or S gene data)	-1919208
Low QC	-509
Other variant than Omicron or Delta	-1549
Omicron or Delta cases	2293853
>14 days between positive test and sequenced PCR test	-3179
Death date before specimen date	-99
Missing NHS number	-122843
Duplicates	-308
Subtotal	2167424
Missing data on at least one adjustment variable	-2915
Total	2164509

Included

N= 2,164,509 cases

- **n= 1,559,796 Omicron (of which n= 143,285 reinfections)**
- **n= 604,713 Delta (of which n= 6,666 reinfections)**

Statistical analysis: stratified Cox regression

Hazard ratios estimated through Cox regression

Stratified for:

- Date of specimen
- Area of residence: Lower tier local authority

Regression adjustment for other potential confounders:

- Age (10-year age bands + age-group-specific linear age terms to adjust for residual age confounding within age bands)
- Sex
- Ethnicity: White, Asian, Black, mixed/other/unknown
- Index of multiple deprivation rank (quintile groups + group-specific linear terms)
- International travel within 14 days before positive test
- Vaccination status at positive test:
 - Unvaccinated
 - <28 days after 1st dose
 - ≥28 days after 1st dose
 - ≥14 days after 2nd dose
 - ≥175 days after 2nd dose
 - ≥7 days after 3rd dose
 - ≥14 days after 3rd dose
- Reinfection status

Subgroup analyses by age group (10 year bands)

Reduced risk of hospital outcomes in adults. Suggestion of increased risk in children disappears once adjust for ***within-age-group differences***, leaving ***no difference in risk*** for children aged <10 yrs.

Without adjustment for within-age-group differences in baseline risk by age

Age group	Adjusted HR (95% CI), Omicron vs Delta	
	Hospital admission within 14 days	Hospital admission or emergency care attendance within 14 days
0-9	1.74 (1.49-2.05)	1.35 (1.24-1.47)
10-19	1.14 (0.95-1.37)	1.13 (1.03-1.23)
20-29	0.46 (0.41-0.52)	0.61 (0.58-0.65)
30-39	0.36 (0.33-0.40)	0.53 (0.50-0.56)
40-49	0.31 (0.27-0.34)	0.51 (0.48-0.54)
50-59	0.26 (0.24-0.29)	0.41 (0.39-0.44)
60-69	0.25 (0.23-0.28)	0.31 (0.28-0.33)
70-79	0.24 (0.22-0.27)	0.25 (0.23-0.27)
80+	0.37 (0.33-0.41)	0.36 (0.33-0.39)

With adjustment for within-age-group differences in baseline risk by age

Age group	Adjusted HR (95% CI), Omicron vs Delta	
	Hospital admission within 14 days	Hospital admission or emergency care attendance within 14 days
0-9	1.00 (0.85-1.18)	0.94 (0.87-1.02)
10-19	0.78 (0.65-0.94)	0.84 (0.77-0.92)
20-29	0.47 (0.42-0.53)	0.63 (0.59-0.67)
30-39	0.37 (0.33-0.41)	0.54 (0.51-0.57)
40-49	0.32 (0.28-0.35)	0.52 (0.49-0.55)
50-59	0.27 (0.24-0.30)	0.42 (0.39-0.45)
60-69	0.25 (0.23-0.28)	0.31 (0.28-0.33)
70-79	0.24 (0.22-0.27)	0.25 (0.23-0.27)
80+	0.38 (0.34-0.42)	0.37 (0.34-0.40)

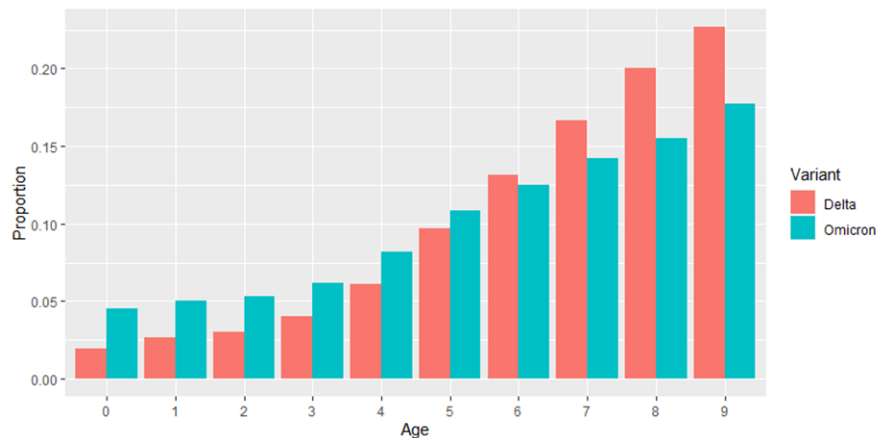
Context and explanation of results by age: Observed age distribution and proportions with outcomes in children aged <10 years

Median age (IQR) in youngest age group

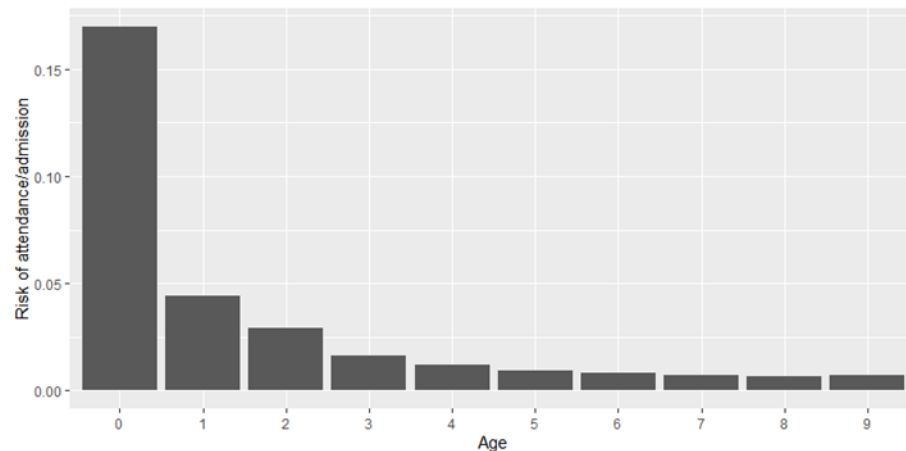
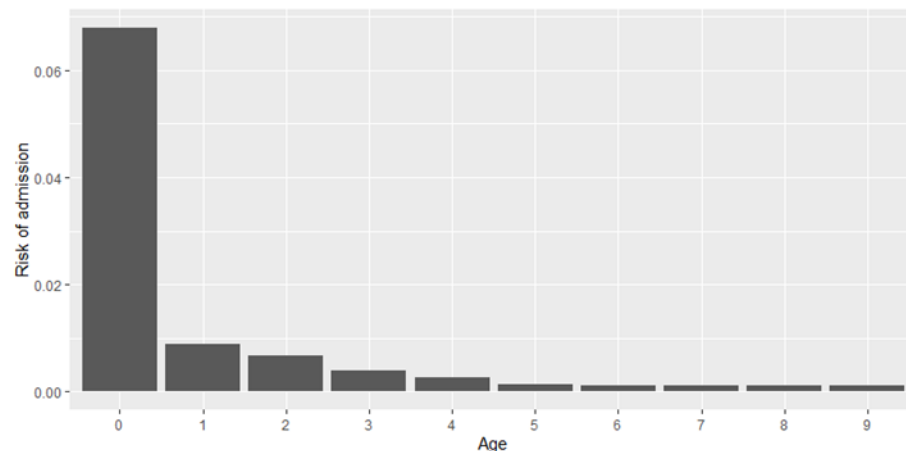
- Omicron: 6yr (4-8yr)
- Delta: 7yr (5-8yr)

Residual confounding due to age differences within age groups are important to avoid residual confounding

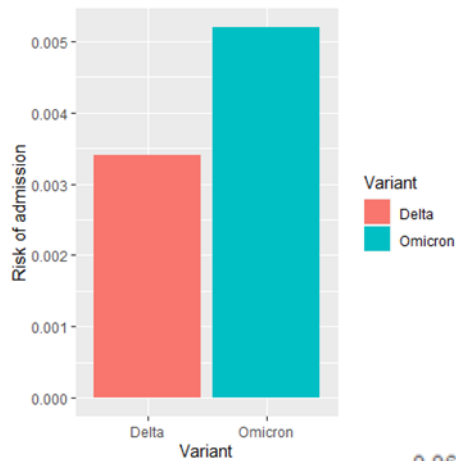
Observed proportion of cases in children aged <10 years by year of age and variant:



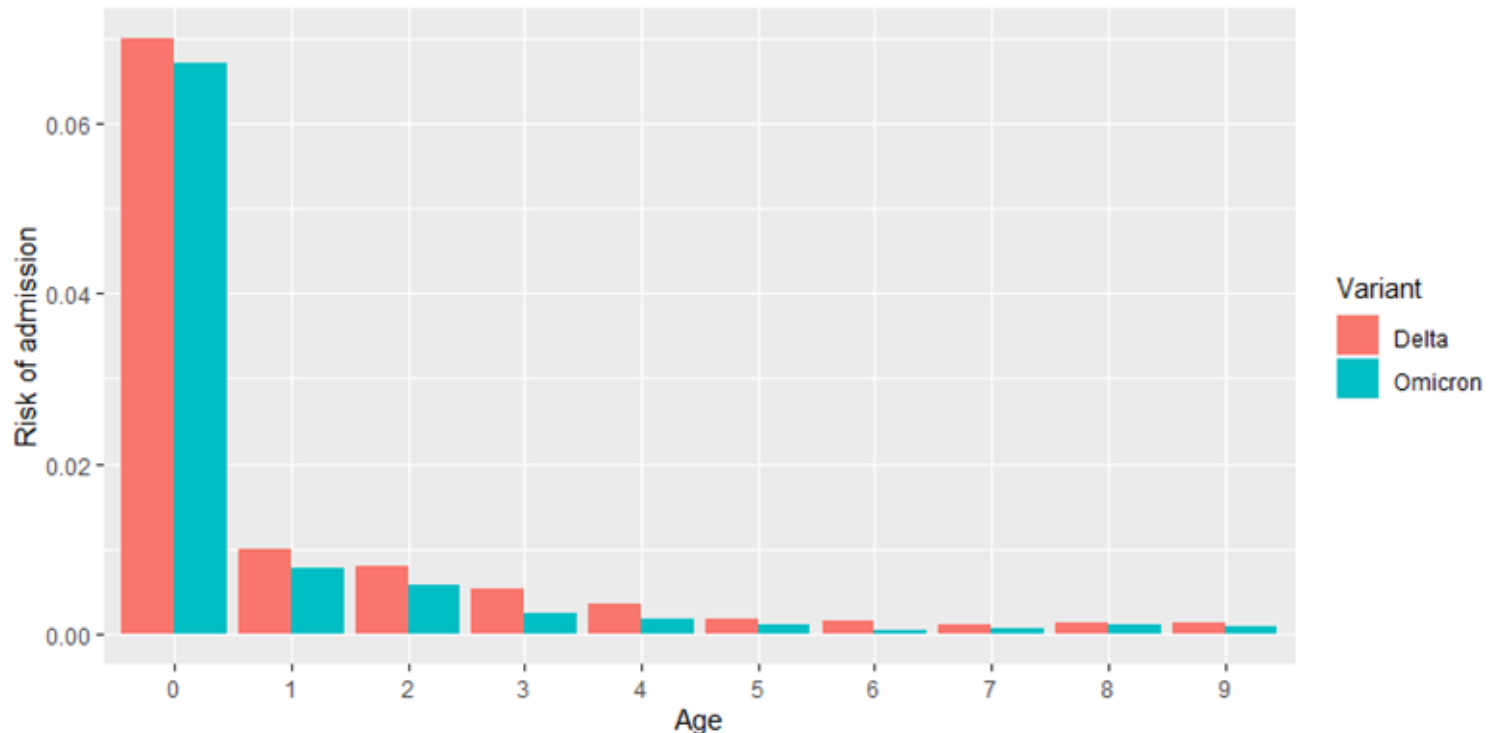
Observed proportion of cases with admission or attendance/admission outcomes, among children aged <10 years by year of age:



Observed proportion admitted in children aged <10 yrs, by variant and single year of age



Over all 0-9 year old cases, the observed proportion admitted to hospital is higher for Omicron than for Delta. **However**, when looking at the observed proportion admitted by single year of age, the proportions are similar for each variant. The overall proportions are skewed by the younger age distribution of Omicron cases than of Delta cases.



Results: adjusted HRs by finer age group (<5yr, 5-9yr)

Similarly, suggested increased risk disappears once adjust for within-age-group differences

Without adjustment for within-age-group differences in baseline risk by age

Age group	Adjusted HR (95% CI), Omicron vs Delta	
	Hospital admission within 14 days	Hospital admission or emergency care attendance within 14 days
0-4	1.35 (1.12-1.62)	1.12 (1.01-1.24)
5-9	0.86 (0.61-1.22)	0.92 (0.80-1.05)
10-19	1.15 (0.96-1.38)	1.14 (1.04-1.24)
20-29	0.46 (0.41-0.52)	0.62 (0.58-0.66)
30-39	0.36 (0.33-0.40)	0.53 (0.51-0.56)
40-49	0.31 (0.28-0.35)	0.51 (0.48-0.54)
50-59	0.27 (0.24-0.30)	0.41 (0.39-0.44)
60-69	0.26 (0.23-0.29)	0.31 (0.29-0.33)
70-79	0.24 (0.22-0.27)	0.25 (0.23-0.28)
80+	0.37 (0.33-0.41)	0.36 (0.33-0.39)

With adjustment for within-age-group differences in baseline risk by age

Age group	Adjusted HR (95% CI), Omicron vs Delta	
	Hospital admission within 14 days	Hospital admission or emergency care attendance within 14 days
0-4	1.00 (0.83-1.20)	0.88 (0.80-0.98)
5-9	0.87 (0.61-1.23)	0.91 (0.80-1.05)
10-19	0.79 (0.65-0.96)	0.84 (0.77-0.92)
20-29	0.48 (0.42-0.54)	0.63 (0.59-0.67)
30-39	0.37 (0.33-0.41)	0.54 (0.51-0.57)
40-49	0.31 (0.28-0.35)	0.52 (0.49-0.55)
50-59	0.27 (0.24-0.30)	0.42 (0.39-0.45)
60-69	0.25 (0.23-0.28)	0.31 (0.28-0.33)
70-79	0.24 (0.22-0.27)	0.25 (0.23-0.27)
80+	0.38 (0.34-0.43)	0.37 (0.34-0.40)

Results: even finer age groups (<1yr, 1-4yrs, 5-9yrs)

Adjusting for within-age-group differences makes less difference once we look at <1 year-olds separately, as have already grouped finely enough to take account of the within-age-group heterogeneity.

Without adjustment for within-age-group differences in baseline risk by age

With adjustment for within-age-group differences in baseline risk by age

Age group	Adjusted HR (95% CI), Omicron vs Delta	
	Hospital admission within 14 days	Hospital admission or emergency care attendance within 14 days
<1	1.08 (0.86-1.36)	0.95 (0.82-1.09)
1-4	0.89 (0.65-1.21)	0.88 (0.76-1.02)
5-9	0.87 (0.61-1.23)	0.92 (0.80-1.05)
10-19	1.15 (0.96-1.38)	1.14 (1.04-1.24)
20-29	0.46 (0.41-0.52)	0.62 (0.58-0.66)
30-39	0.36 (0.33-0.40)	0.53 (0.51-0.56)
40-49	0.31 (0.28-0.35)	0.51 (0.48-0.54)
50-59	0.27 (0.24-0.30)	0.42 (0.39-0.44)
60-69	0.26 (0.23-0.29)	0.31 (0.29-0.33)
70-79	0.24 (0.22-0.27)	0.25 (0.23-0.28)
80+	0.37 (0.33-0.41)	0.36 (0.33-0.39)

Age group	Adjusted HR (95% CI), Omicron vs Delta	
	Hospital admission within 14 days	Hospital admission or emergency care attendance within 14 days
<1	1.09 (0.87-1.37)	0.95 (0.82-1.10)
1-4	0.81 (0.59-1.11)	0.80 (0.69-0.93)
5-9	0.87 (0.61-1.23)	0.91 (0.80-1.05)
10-19	0.79 (0.65-0.96)	0.84 (0.77-0.92)
20-29	0.48 (0.42-0.53)	0.63 (0.59-0.67)
30-39	0.37 (0.33-0.41)	0.54 (0.51-0.57)
40-49	0.31 (0.28-0.35)	0.52 (0.49-0.55)
50-59	0.27 (0.24-0.30)	0.42 (0.39-0.45)
60-69	0.25 (0.23-0.28)	0.31 (0.28-0.33)
70-79	0.24 (0.22-0.27)	0.25 (0.23-0.27)
80+	0.38 (0.34-0.43)	0.37 (0.34-0.40)

Conclusion

The results suggest

- **Adults: Lower hospital admission risk for Omicron compared with Delta**
- **Children aged <10 years: Similar hospital admission risk for Omicron compared with Delta**

Caveats

- **Lower risks do not necessarily imply lower hospital burden, if Omicron has higher vaccine escape and transmissibility than Delta**
 - **Omicron being less severe than Delta should be interpreted in the context that the Delta hospital admission risk was estimated to be greater than for Alpha; and the Alpha hospital admission risk was estimated to be greater than previous variants.**
- **Reporting delays for hospital events**
 - Less likely to be differential by lineage after stratification for calendar period and area
- **Selection bias**
 - Coverage ~50% of cases during study period
 - Sequencing, genotyping and SGTF assessment requires low Ct counts, may reflect more severe cases
 - (Epidemic phase bias: higher incidence variant may cause bias toward overestimation of risk – implies true HR more likely to be lower than higher compared to those estimated)
- **Lack of data on confounders**
 - Comorbidity