Omicron: severity and VE

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Update to: https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/report-50-severity-omicron/

Statistical approach overview

- Conditional Poisson regression (v similar to case control design) – best approach to control for confounding (e.g. differences in distribution of Omicron and Delta by time, age, region etc)

- This implicitly adjusts for right-censoring of outcomes (due to limited follow-up)

- It also controls for "incidental" hospitalization – if hospitalisation was unrelated to COVID, variant would not be a significant predictor of hospitalisation risk given the analysis conditions on observed numbers of cases and hospitalisations within each stratum

- Stratify by day of test specimen × NHS region × sex × 10-year age band × ethnicity × IMD decile (and sometimes by vaccination category and past infection status)

- Variety of hospitalisation endpoints:

  ➢ Any hospital attendance (>=0 days) – any SUS or ECDS "hospital_in" date occurring on or up to 14 days after a positive specimen

  ➢ "Dashboard" definition: any attendance with known "hospital_in" and "hospital_out" dates, with positive specimen date from 14 days before "hospital_in" up to the day before discharge

  ➢ Any hospital attendance with known "hospital_in" and "hospital_out" dates and length of stay of 1 or more days, with positive specimen date between 0 and 14 days prior to the "hospital_in" date

  ➢ ECDS "admitted" or "transferred" - any SUS or ECDS "hospital_in" date occurring on or up to 14 days after a positive specimen and an ecds_discharge field of "Admitted" or "Transfer"

- Data up to 4/1/2022, using specimen dates up to and including 27/12/2021

Data

- Cases with specimen date between 1 and 27 December 2021

- Challenge – as endpoint severity increases, % of cases found in Pillar 2 declines

- % in Pillar 2 used to vary between Omicron and Delta for last two endpoints, but has now equalised

- Here combine cases from both Pillars in this analysis – though Pillar 2 still effectively acts as denominator

Endpoint	Variant	Pillar 1	Pillar 2	% Pillar 2
Cases	Unknown	99654	1158773	92.1%
	Omicron	14666	931070	98.4%
	Delta	9839	406805	97.6%
>=0 days	Unknown	10120	7401	42.2%
	Omicron	1257	3672	74.5%
	Delta	2689	5783	68.3%
Dashboard	Unknown	3947	6535	62.3%
	Omicron	582	3183	84.5%
	Delta	1711	5256	75.4%
>=1 days	Unknown	2917	1655	36.2%
	Omicron	375	680	64.5%
	Delta	1156	1591	57.9%
ECDS "admitted"	Unknown	4373	1252	22.3%
	Omicron	454	428	48.5%
	Delta	1531	1375	47.3%
Death	Unknown	914	161	15.0%
	Omicron	91	34	27.2%
	Delta	543	179	24.8%

Overall results (average over all cases)

- Overall reduction in risk of hospitalisation for Omicron relative to Delta of 35%-65%, depending on endpoint

- Preliminary estimate of 62% (95% CI: 28%-80%) reduction in risk of death within 28 days

- Past infection is highly protective against hospitalisation (>65%)

- ~11% of Omicron cases are known reinfections, but this is likely a ~3-fold underestimate

- Correcting for this under ascertainment increases the hazard ratio for hospitalisation for Omicron (for primary infections), decreases the hazard ratio for reinfections vs primaries

Endpoint	Reinfection in strata	Uncorrected		Corrected	
	Omicron:Delta	Omicron:Delta	Reinfection: primary infection	Omicron:Delta	Reinfection: primary infection
>=0 days	0.62 (0.58-0.67)	0.62 (0.58-0.67)	0.33 (0.29-0.38)	0.68 (0.63-0.73)	0.29 (0.25-0.32)
Dashboard	0.62 (0.58-0.68)	0.63 (0.58-0.68)	0.34 (0.29-0.39)	0.68 (0.63-0.73)	0.29 (0.25-0.34)
>= 1 day	0.55 (0.47-0.64)	0.54 (0.47-0.63)	0.2 (0.14-0.28)	0.6 (0.53-0.67)	0.17 (0.12-0.23)
ECDS "admitted"	0.35 (0.3-0.42)	0.36 (0.3-0.42)	0.25 (0.17-0.37)	0.39 (0.25-0.62)	0.22 (0.16-0.3)
Death	0.38 (0.2-0.72)	0.38 (0.2-0.72)	0	0.43 (0.08-2.36)	0.00

Data stratified by age: both pillars

- Cases with specimen date between 1 and 27 December 2021

- Note that Omicron cases incidence was rising sharply in this time period, while Delta was flat/declining

- So, on average, substantially more follow-up time for Delta cases than Omicron

- Dividing hospitalisations by cases and comparing Omicron and Delta therefore not meaningful

- Analysis on next slide adjusts for this

- Comparing absolute numbers of hospitalisations between age groups within the same variant rather less biased

- Note that Pillar 2 testing much more common in younger people than older

Variant	Age group	All cases (both pillars)	Any hospital attendance	Dashboard	>=1 night stay	ECDS "admitted" or "transfer"
Delta	<1	1229	151	93	41	43
	1-4	10361	225	183	42	24
	5-9	52597	337	276	55	37
	10-14	52667	328	281	56	40
	15-24	46773	598	494	161	83
	25-34	62873	1361	1165	415	255
	35-49	110934	2264	1916	703	641
	50-69	58933	2103	1695	781	992
	70-79	4937	551	428	242	387
	80+	2558	531	425	246	401
Omicron	<1	987	103	53	19	26
	1-4	4506	87	56	9	9
	5-9	15306	77	51	14	5
	10-14	27509	102	79	24	11
	15-24	125777	806	627	160	108
	25-34	168801	1216	949	251	127
	35-49	164600	1086	861	216	131
	50-69	102525	745	587	160	179
	70-79	12522	198	155	63	90
	80+	4154	245	168	87	156

Age stratified results: both pillars

- Clear signal of a substantial increase in hospitalization risk in <5s

- Central estimates of 6.4-13.8 fold increase in <1 year-olds, 2.2-3.7 fold in 1-4 year-olds

- All other age groups show reduced risk from Omicron

- Differences in 10+ age groups may reflect varying historical exposure and vaccination coverage/timing

Variable	Any hospital attendance	Dashboard	>=1 night stay	ECDS "admitted" or "transfer"
% protection afforded by past infection (uncorrected for under ascertainment)	67 (62-71)	66 (61-71)	80 (72-86)	75 (63-83)
HR Omicron:Delta [%] - <1 years	828 (543-1262)	642 (386-1066)	792 (267-2351)	1376 (414-4570)
HR Omicron:Delta [%] - 1-4 years	273 (197-380)	223 (150-331)	335 (132-849)	365 (128-1045)
HR Omicron:Delta [%] - 5-9 years	56 (41-78)	53 (36-78)	92 (38-222)	56 (18-180)
HR Omicron:Delta [%] - 10-14 years	65 (48-87)	63 (45-88)	68 (35-132)	45 (19-105)
HR Omicron:Delta [%] - 15-24 years	81 (71-92)	80 (70-93)	70 (53-93)	81 (57-115)
HR Omicron:Delta [%] - 25-34 years	66 (59-73)	67 (60-75)	58 (47-73)	46 (34-62)
HR Omicron:Delta [%] - 35-49 years	53 (47-60)	54 (47-61)	47 (37-61)	25 (18-34)
HR Omicron:Delta [%] - 50-69 years	42 (36-51)	47 (39-57)	35 (25-49)	23 (16-32)
HR Omicron:Delta [%] - 70-79 years	36 (22-58)	46 (27-76)	45 (21-98)	22 (10-45)
HR Omicron:Delta [%] - 80+ years	36 (16-79)	34 (14-79)	40 (12-133)	35 (14-89)

Data stratified by age: Pillar 2 only

- Only a small proportion of hospitalisations in <1s have had a Pillar 2 test

- But proportion much higher in 1-4 year-olds

Variant	Age group	All cases (Pillar 2)	Any hospital attendance	Dashboard	>=1 night stay	ECDS "admitted" or "transfer"
Delta	<1	1106	71	56	12	9
	1-4	10211	196	167	33	19
	5-9	52020	298	257	42	22
	10-14	52191	296	261	47	24
	15-24	46014	477	431	118	50
	25-34	61505	1046	957	264	154
	35-49	108678	1755	1625	497	401
	50-69	56670	1256	1159	414	470
	70-79	4123	216	196	86	125
	80+	1596	150	136	73	99
Omicron	<1	914	56	36	5	6
	1-4	4459	73	51	6	3
	5-9	15200	66	43	6	1
	10-14	27268	88	72	20	5
	15-24	123700	607	547	106	59
	25-34	165562	958	842	179	72
	35-49	161838	860	766	151	75
	50-69	100461	521	475	99	87
	70-79	12106	110	103	33	39
	80+	3620	86	77	29	45

Age stratified results: Pillar 2 only

- Results similar to analysis of both pillars, but less power

- Also similar restricting only to symptomatic cases, but even less power (no power to look at 2 most severe outcomes yet)

Variable	All Pillar 2				Symptomatic Pillar 2 only	
	Any hospital attendance	Dashboard	>=1 night stay	ECDS "admitted" or "transfer"	Any hospital attendance	Dashboard
% protection afforded by past infection (uncorrected for under ascertainment)	57 (51-63)	62 (55-67)	70 (57-80)	55 (32-70)	59 (49-67)	66 (57-74)
HR Omicron:Delta [%] - <1 years	971 (612-1541)	737 (428-1270)	1470 (333-6494)	1200 (256-5611)	1037 (496-2168)	575 (236-1396)
HR Omicron:Delta [%] - 1-4 years	256 (179-366)	220 (145-334)	304 (98-949)	103 (18-575)	249 (152-406)	198 (111-353)
HR Omicron:Delta [%] - 5-9 years	54 (38-77)	48 (31-72)	33 (7-158)	20 (2-174)	54 (33-86)	46 (26-81)
HR Omicron:Delta [%] - 10-14 years	67 (48-92)	62 (43-88)	70 (33-149)	45 (15-134)	67 (43-106)	58 (35-96)
HR Omicron:Delta [%] - 15-24 years	76 (65-88)	77 (66-90)	62 (44-86)	66 (42-103)	66 (54-80)	65 (53-81)
HR Omicron:Delta [%] - 25-34 years	66 (59-74)	66 (59-75)	56 (43-73)	38 (26-55)	65 (55-76)	65 (55-77)
HR Omicron:Delta [%] - 35-49 years	52 (46-60)	52 (46-60)	41 (30-55)	18 (12-28)	54 (46-65)	54 (45-65)
HR Omicron:Delta [%] - 50-69 years	46 (37-57)	47 (38-58)	33 (22-51)	24 (16-37)	48 (35-65)	49 (35-68)
HR Omicron:Delta [%] - 70-79 years	44 (25-81)	48 (26-88)	52 (19-140)	20 (8-54)	32 (11-97)	39 (13-121)
HR Omicron:Delta [%] - 80+ years	27 (8-87)	27 (8-87)	41 (7-228)	13 (2-110)	39 (3-444)	39 (3-444)

Mean specimen date to hospitalisation date delays

- Key delay for these analyses – major differences between Omicron and Delta would undermine hazard ratio estimates
- Both pillars, same inclusion criteria as main analysis, excluding reinfections
- Specimen dates between 15/12/2021- 21/12/2021, to allow sufficient follow-up time and to compare cases in a similar time interval

➢ No evidence of major differences in delays between Omicron and Delta which could severely bias hazard ratio estimates

Age group	Dashboard		>= 1 day	
	Delta	Omicron	Delta	Omicron
<1	2.68 (0.83-4.53) [n=19]	1.22 (0.66-1.78) [n=23]	1.3 (0.00-3.57) [n=10]	0.5 (0.00-1.14) [n=10]
1-4	3.52 (2.06-4.98) [n=29]	4.33 (2.79-5.87) [n=27]	0.667 (0.00-1.57) [n=6]	4 (0.00-12.43) [n=3]
5-9	5.74 (4.62-6.86) [n=54]	3.85 (2.28-5.42) [n=27]	1.9 (0.35-3.45) [n=10]	0 (0.00-0.00) [n=7]
10-14	5.67 (4.45-6.89) [n=43]	5.41 (3.89-6.93) [n=34]	3.56 (0.91-6.21) [n=9]	2.89 (0.00-6.50) [n=9]
15-24	4.59 (3.82-5.36) [n=87]	6.1 (5.60-6.60) [n=279]	2.19 (1.32-3.06) [n=27]	3.99 (2.98-5.00) [n=73]
25-34	5.85 (5.32-6.38) [n=205]	5.74 (5.34-6.14) [n=444]	4.49 (3.37-5.61) [n=57]	3.4 (2.68-4.12) [n=128]
35-49	5.83 (5.43-6.23) [n=353]	5.61 (5.19-6.03) [n=380]	4.03 (3.22-4.84) [n=92]	2.98 (2.16-3.80) [n=89]
50-69	5.07 (4.56-5.58) [n=288]	5.32 (4.65-5.99) [n=269]	2.96 (2.28-3.64) [n=113]	3.56 (2.64-4.48) [n=71]
70-79	3.88 (2.79-4.97) [n=67]	3.29 (1.17-5.41) [n=68]	2.44 (1.29-3.59) [n=32]	3.55 (1.88-5.22) [n=29]
80+	1.89 (0.68-3.10) [n=64]	2.31 (0.91-3.71) [n=78]	1.25 (0.39-2.11) [n=40]	2.15 (1.10-3.20) [n=46]

Mean onset date to specimen date delays

- Symptomatic pillar 2 only, onset and specimen dates from 7/12/2021-27/12/2021, onset to specimen date delays >=0 day and <=14 days, reinfections excluded. Two endpoints examined.

- Strong caveat around reliability of reported Pillar 2 symptom onset dates

- Only limited differences between Omicron and Delta in non-hospitalized cases

- No statistically significant differences between hospitalised and non-hospitalised cases, within each stratum, except for <1 and 5-9 age groups

- But no statistically significant differences between Omicron and Delta for <1 year-olds

➢ No evidence that more severe cases are tested sooner, except for <1s and 5-9 year-olds

Age group	Dashboard				>= 1 day			
	Delta		*Omicron*		*Delta*		*Omicron*	
	Not hospitalised	Hospitalised	Not hospitalised	Hospitalised	Not hospitalised	Hospitalised	Not hospitalised	Hospitalised
<1	2.51 (2.30-2.72) [n=378]	1.25 (0.74-1.76) [n=16]	2.43 (2.27-2.59) [n=539]	1.43 (0.76-2.10) [n=21]	2.47 (2.26-2.68) [n=391]	0.667 (0.00-1.47) [n=3]	2.4 (2.24-2.56) [n=558]	1.5 (0.00-5.66) [n=2]
1-4	2.08 (2.02-2.14) [n=3031]	1.86 (1.38-2.34) [n=49]	2.31 (2.23-2.39) [n=2249]	2.67 (1.92-3.42) [n=30]	2.08 (2.02-2.14) [n=3072]	1.75 (0.89-2.61) [n=8]	2.32 (2.24-2.40) [n=2276]	2 (0.61-3.39) [n=3]
5-9	1.74 (1.72-1.76) [n=15422]	1.38 (1.05-1.71) [n=79]	1.95 (1.91-1.99) [n=7366]	1.32 (0.88-1.76) [n=25]	1.74 (1.72-1.76) [n=15490]	0.909 (0.32-1.49) [n=11]	1.95 (1.91-1.99) [n=7387]	1.25 (0.17-2.33) [n=4]
10-14	1.85 (1.82-1.88) [n=14644]	1.78 (1.47-2.09) [n=72]	1.99 (1.96-2.02) [n=13247]	2 (1.47-2.53) [n=39]	1.85 (1.82-1.88) [n=14702]	2.29 (1.71-2.87) [n=14]	1.99 (1.96-2.02) [n=13276]	1.8 (0.33-3.27) [n=10]
15-24	2.21 (2.18-2.24) [n=12547]	2.32 (1.99-2.65) [n=122]	2.27 (2.26-2.28) [n=58629]	2.35 (2.11-2.59) [n=274]	2.21 (2.18-2.24) [n=12640]	2.86 (2.04-3.68) [n=29]	2.27 (2.26-2.28) [n=58848]	2.02 (1.46-2.58) [n=55]
25-34	2.24 (2.21-2.27) [n=19349]	2.19 (2.00-2.38) [n=320]	2.24 (2.23-2.25) [n=83095]	2.17 (2.02-2.32) [n=477]	2.24 (2.21-2.27) [n=19600]	2.28 (1.92-2.64) [n=69]	2.24 (2.23-2.25) [n=83467]	2.14 (1.83-2.45) [n=105]
35-49	2.14 (2.12-2.16) [n=33696]	2.31 (2.14-2.48) [n=483]	2.13 (2.12-2.14) [n=83914]	2.09 (1.95-2.23) [n=450]	2.14 (2.12-2.16) [n=34048]	2.56 (2.21-2.91) [n=131]	2.13 (2.12-2.14) [n=84272]	2.05 (1.76-2.34) [n=92]
50-69	2.25 (2.22-2.28) [n=15299]	2.64 (2.41-2.87) [n=297]	2.08 (2.07-2.09) [n=50057]	2.29 (2.05-2.53) [n=241]	2.25 (2.22-2.28) [n=15501]	2.74 (2.34-3.14) [n=95]	2.08 (2.07-2.09) [n=50252]	2.8 (2.12-3.48) [n=46]
70-79	2.5 (2.38-2.62) [n=982]	2.75 (2.21-3.29) [n=55]	2.15 (2.10-2.20) [n=5277]	2.08 (1.68-2.48) [n=37]	2.51 (2.39-2.63) [n=1020]	2.53 (1.90-3.16) [n=17]	2.15 (2.10-2.20) [n=5300]	2.07 (1.49-2.65) [n=14]
80+	2.9 (2.67-3.13) [n=325]	2.88 (2.17-3.59) [n=24]	2.42 (2.32-2.52) [n=1379]	2.08 (1.54-2.62) [n=25]	2.91 (2.69-3.13) [n=334]	2.53 (1.54-3.52) [n=15]	2.42 (2.32-2.52) [n=1393]	2.18 (1.31-3.05) [n=11]

Mean onset date to hospitalisation date delays

- Symptomatic pillar 2 only, onset and specimen dates from 7/12/2021-27/12/2021, onset to specimen date delays >=0 day and <=14 days, onset to hospitalization >= 0 days, reinfections excluded

- Trend towards shorter delays for Omicron vs Delta for 25-69 year-olds, perhaps reflecting shorter follow-up times

- Delays shorter for more severe (>=1 day stay) endpoint

- Delays generally shorter for <15s than >15s

> No evidence of differences in delays between Omicron and Delta which could severely bias hazard ratio estimates

Age group	Dashboard		>= 1 day	
	Delta	Omicron	Delta	Omicron
<1	4.5 (2.72-6.28) [n=16]	3.62 (2.65-4.59) [n=21]	1.33 (0.00-3.45) [n=3]	3.5 (2.11-4.89) [n=2]
1-4	5.78 (4.59-6.97) [n=49]	5.57 (4.42-6.72) [n=30]	3.75 (1.82-5.68) [n=8]	2.33 (0.73-3.93) [n=3]
5-9	6.49 (5.55-7.43) [n=79]	5.64 (3.85-7.43) [n=25]	4.91 (2.13-7.69) [n=11]	3.5 (0.00-7.48) [n=4]
10-14	7.31 (6.30-8.32) [n=72]	7.38 (5.79-8.97) [n=39]	4.71 (3.05-6.37) [n=14]	4.5 (0.93-8.07) [n=10]
15-24	8.05 (7.34-8.76) [n=122]	7.99 (7.46-8.52) [n=274]	6.97 (5.75-8.19) [n=29]	6.95 (5.68-8.22) [n=55]
25-34	8.49 (8.05-8.93) [n=320]	7.39 (7.01-7.77) [n=477]	8.06 (7.09-9.03) [n=69]	6.27 (5.39-7.15) [n=105]
35-49	8.35 (8.02-8.68) [n=483]	7.37 (7.00-7.74) [n=450]	7.72 (7.11-8.33) [n=131]	5.79 (5.01-6.57) [n=92]
50-69	8.59 (8.16-9.02) [n=297]	7.56 (7.07-8.05) [n=241]	8.4 (7.63-9.17) [n=95]	6.96 (5.77-8.15) [n=46]
70-79	8.11 (7.30-8.92) [n=55]	7.35 (6.08-8.62) [n=37]	6.76 (5.64-7.88) [n=17]	7.36 (5.24-9.48) [n=14]
80+	7.25 (5.78-8.72) [n=24]	6.44 (4.85-8.03) [n=25]	5.53 (4.13-6.93) [n=15]	6.45 (4.16-8.74) [n=11]

Length of stay

- Hospitalised cases, looking at "any hospital attendance" (LoS >=0 day) and LoS >=1 day endpoints, where "hospital_out" date is known
- Both endpoints only include cases where hospitalisation occurs 0-14 days after a positive test
- Reinfections excluded
- Also restrict to cases with specimen date in the 7 days 15/12/2021-21/12/2021 and to cases with LoS <=7 days, to allow comparable and sufficient follow-up time for both Omicron and Delta cases

➢ No statistically significant difference in LoS for either endpoint between Omicron and Delta for each age group

Age group	>=0 day		>= 1 day	
	Delta	Omicron	Delta	Omicron
<1	0.53 (0.16-0.90) [n=32]	0.33 (0.10-0.55) [n=49]	1.70 (0.88-2.52) [n=10]	1.60 (0.90-2.30) [n=10]
1-4	0.22 (0.03-0.41) [n=41]	0.08 (0.00-0.18) [n=36]	1.50 (0.77-2.23) [n=6]	1.00 (1.00-1.00) [n=3]
5-9	0.18 (0.07-0.28) [n=62]	0.20 (0.05-0.34) [n=41]	1.10 (0.89-1.31) [n=10]	1.14 (0.84-1.44) [n=7]
10-14	0.17 (0.07-0.28) [n=52]	0.36 (0.09-0.62) [n=45]	1.00 (1.00-1.00) [n=9]	1.78 (0.94-2.61) [n=9]
15-24	0.28 (0.17-0.40) [n=113]	0.22 (0.17-0.27) [n=354]	1.19 (0.88-1.49) [n=27]	1.07 (0.96-1.18) [n=73]
25-34	0.28 (0.20-0.36) [n=251]	0.27 (0.23-0.32) [n=550]	1.23 (1.03-1.43) [n=57]	1.17 (1.07-1.27) [n=128]
35-49	0.30 (0.23-0.37) [n=418]	0.26 (0.20-0.32) [n=458]	1.36 (1.15-1.57) [n=92]	1.33 (1.12-1.53) [n=89]
50-69	0.36 (0.29-0.43) [n=392]	0.23 (0.18-0.28) [n=335]	1.25 (1.10-1.40) [n=112]	1.08 (1.00-1.17) [n=71]
70-79	0.35 (0.22-0.48) [n=102]	0.38 (0.23-0.53) [n=92]	1.16 (0.90-1.42) [n=31]	1.21 (0.92-1.49) [n=29]
80+	0.60 (0.39-0.81) [n=87]	0.46 (0.34-0.57) [n=112]	1.30 (0.96-1.64) [n=40]	1.11 (0.97-1.25) [n=46]

Sensitivity analysis: finer age stratification (both pillars)

- Split 0-10 age band into 0-4, 5-9 bands in the case-control stratification

- Hazard ratio for <1 reduced but still >2-fold

- Hazard ratio for both 1-4 and 4-9 no longer statistically significantly different from 1

- Similar central estimates (with even less power) including <1 in the stratification

Variable	Any hospital attendance	Dashboard	>=1 night stay	ECDS "admitted" or "transfer"
% protection afforded by past infection (uncorrected for under ascertainment)	67 (62-71)	66 (61-71)	80 (71-86)	75 (63-83)
HR Omicron:Delta [%] - <1 years	351 (207-597)	266 (142-501)	285 (81-1007)	282 (85-935)
HR Omicron:Delta [%] - 1-4 years	115 (74-177)	77 (45-131)	71 (21-242)	105 (29-381)
HR Omicron:Delta [%] - 5-9 years	93 (63-139)	83 (53-132)	128 (43-386)	122 (28-532)
HR Omicron:Delta [%] - 10-14 years	65 (48-87)	63 (45-88)	68 (35-132)	45 (19-105)
HR Omicron:Delta [%] - 15-24 years	81 (71-92)	80 (70-93)	70 (53-93)	81 (57-115)
HR Omicron:Delta [%] - 25-34 years	66 (59-73)	67 (60-75)	58 (47-73)	46 (34-62)
HR Omicron:Delta [%] - 35-49 years	53 (47-60)	54 (47-61)	47 (37-61)	25 (18-34)
HR Omicron:Delta [%] - 50-69 years	42 (36-51)	47 (39-57)	35 (25-49)	23 (16-32)
HR Omicron:Delta [%] - 70-79 years	36 (22-58)	46 (27-76)	45 (21-98)	22 (10-45)
HR Omicron:Delta [%] - 80+ years	43 (22-84)	43 (21-86)	53 (19-151)	41 (19-92)

VE(hosp|inf)

- Protection from past infection assumed to apply to both variants and all vaccination categories

- Correction for under ascertainment of reinfection calculated from unvaccinated group (delta method for CI)

- No decay of immunity included – estimates are averages over everyone in each vaccination category

- VE increases as endpoint becomes more severe

	Dashboard		>=1 night stay		ECDS "admitted" or "transfer"	
Variable	Uncorrected	Corrected	Uncorrected	Corrected	Uncorrected	Corrected
Risk from Omicron relative to Delta (%)	44.5 (39.9-49.5)	52.6 (46.4-59.8)	32.7 (26.8-39.8)	40.0 (31.4-51.0)	25.5 (20.4-31.8)	30.8 (23.5-40.2)
Protection from past infection (%)	67.4 (62.5-71.7)	71.1 (67.1-74.7)	80.7 (73.3-86.0)	83.2 (77.6-87.4)	75.5 (65.8-82.4)	78.5 (70.9-84.1)
Vaccination category	Delta VE(hosp|inf)	Omicron VE(hosp|inf)	Delta VE(hosp|inf)	Omicron VE(hosp|inf)	Delta VE(hosp|inf)	Omicron VE(hosp|inf)
AZ:D1:<21	-	-	-	-	-	-
AZ:D1:21+	-	-	45.2 (18.7-63.0)	-	56.4 (36.3-70.1)	-
AZ:D2:<14	68.5 (7.1-89.3)	-	93.7 (38.9-99.3)	-	81.4 (18.0-95.8)	-
AZ:D2:14+	63.3 (60.1-66.3)	44.6 (36.9-12.1)	73.9 (70.1-77.2)	43.9 (28.8-21.2)	81.8 (79.1-84.1)	65.8 (54.9-24.1)
AZ:D3:<14	79.7 (76.4-82.6)	64.0 (57.0-69.8)	86.3 (82.3-89.3)	79.5 (69.7-86.1)	91.9 (89.5-93.7)	85.5 (78.3-90.3)
AZ:D3:14+	64.8 (58.0-70.6)	62.3 (55.5-68.1)	77.7 (70.1-83.3)	75.5 (66.3-82.2)	84.6 (80.1-88.0)	88.2 (83.5-91.5)
PF/MD:D1:<21	-	-	-	-	-	-
PF/MD:D1:21+	44.2 (34.8-52.3)	19.0 (0.8-33.8)	53.6 (38.6-65.0)	-	62.8 (47.5-73.6)	-
PF/MD:D2:<14	66.9 (37.8-82.4)	-	74.4 (17.7-92.0)	-	78.9 (21.6-94.3)	-
PF/MD:D2:14+	73.3 (70.4-75.9)	45.2 (38.7-51.1)	82.3 (78.7-85.3)	51.7 (39.8-61.2)	88.4 (85.6-90.6)	61.3 (49.5-70.4)
PF/MD:D3:<14	77.6 (70.3-83.1)	67.4 (59.9-73.5)	80.4 (69.2-87.5)	77.4 (64.4-85.6)	89.9 (83.6-93.7)	79.3 (66.2-87.2)
PF/MD:D3:14+	68.7 (63.0-73.6)	52.9 (44.7-59.9)	83.4 (78.1-87.5)	74.9 (65.3-81.8)	87.8 (84.4-90.5)	88.2 (83.4-91.6)

VE(hosp|inf) – with decay of immunity

- Estimate peak protection (21, 14 and 14 days after doses 1, 2, 3 respectively)

- And increase in hazard ratio of vaccinated classes vs unvaccinated with time after peak (assumed identical for both variants and all vaccine categories)

- Cases in people <21, <14, <14 days after doses 1, 2, 3 respectively are discarded

- Estimated rates of increase in hazard ratio translate into slow declines in VE

- PD3 VE(hosp|inf) v similar for Omicron and Delta, but PD2 is lower for Omicron, esp for PF/MD

	Dashboard		>=1 night stay		ECDS "admitted" or "transfer"	
Variable	**Uncorrected**	**Corrected**	**Uncorrected**	**Corrected**	**Uncorrected**	**Corrected**
Risk from Omicron relative to Delta (%)	45.1 (40.5-50.3)	53.7 (47.2-61.2)	32.6 (26.6-39.8)	40 (31.2-51.2)	26.7 (21.3-33.4)	32.7 (24.8-43.1)
Protection from past infection (%)	69.5 (64.6-73.8)	73.1 (69-76.6)	81.6 (74.1-86.9)	84.1 (78.4-88.2)	80.8 (71.9-86.9)	83.3 (76.5-88.1)
Fold increase in HR per 30 days after peak: VE(t)=1-HR(t)[1-VE(0)]	1.101 (1.076-1.126)		1.17 (1.122-1.22)		1.26 (1.201-1.322)	
Vaccination category	Delta VE(hosp|inf)	Omicron VE(hosp|inf)	Delta VE(hosp|inf)	Omicron VE(hosp|inf)	Delta VE(hosp|inf)	Omicron VE(hosp|inf)
AZ:D1 (peak)	61.7 (48.7-71.5)	42.3 (13-61.8)	83.2 (72.2-89.9)	-	92.1 (86.7-95.4)	87.7 (71-94.8)
AZ:D2 (peak)	78.6 (75-81.7)	69.2 (62.8-74.5)	89.3 (85.9-91.8)	78.4 (69.4-84.7)	95.2 (93.4-96.5)	91.7 (87.5-94.4)
AZ:D3 (peak)	66 (59.3-71.6)	65.5 (59.2-70.9)	78 (70.4-83.6)	77.3 (68.6-83.6)	85.1 (80.7-88.5)	89.5 (85.3-92.5)
PF/MD:D1 (peak)	60.2 (52.5-66.7)	42.3 (28.1-53.7)	75.1 (65.3-82.2)	61.1 (39.7-75)	86.3 (79.1-91)	72.5 (52.5-84.1)
PF/MD:D2 (peak)	82.8 (80-85.2)	64 (58.1-69.1)	91.7 (89-93.7)	76.4 (68.3-82.4)	96.7 (95.3-97.7)	87.5 (81.9-91.3)
PF/MD:D3 (peak)	70.9 (65.5-75.5)	59.2 (51.9-65.4)	84.5 (79.4-88.3)	78.7 (70.5-84.7)	89 (85.7-91.5)	90.4 (86.4-93.3)

Summary

- Overall 1/3 reduction in risk of any hospital attendance associated with Omicron compared with Delta

- ~2/3 reduction in risk of more severe endpoints (formal admission or death)

- Substantial increase in risk of hospitalisation in <1 year-olds

- Picture less clear in 1-10 year-olds, but may not be seeing severity reduction of older age groups

- No evidence of major differences in key delays (specimen date to hospitalisation date, onset date to specimen date, or onset date to hospitalisation date) between Omicron and Delta which might bias estimates

- Past infection offers 70-85% protection against hospitalisation, correcting for under ascertainment of reinfections

- VE against hospitalisation (conditional on infection) remains above 75% for PD3 vaccination categories and the more severe endpoints, but in the approx. range 40-60% for PD2 categories

- Unconditional VE estimates a work in progress – past infection status in unvaccinated now a real challenge

- Caveats:
  - Limited follow-up time
  - Assumes distribution of delay from test date to hospitalisation is the same for Delta and Omicron cases testing positive on the same day
  - Needed to combine pillars, since the majority of hospitalisations in older age groups only appear in Pillar 1
  - Can't prove causality – though use of a highly stratified analysis (similar to case-control study) makes confounding less likely