Supplementary Data

Supplementary Table 1. Variables and Models Used for IPTW weighting

Analysis	PSM Used	Variables Included in Model
Overall cohort	GBM	Age, gender, time period, renal disease, multiple high-risk conditions, moderate-risk conditions, vaccination status, days since vaccination, ethnicity
Patients aged <65 years	Log regression	Age, gender, time period, renal disease, multiple high-risk conditions, moderate-risk conditions, vaccination status, days since vaccination, ethnicity
Patients aged ≥65 years	Log regression	Age, gender, time period, renal disease, multiple high-risk conditions, moderate-risk conditions, vaccination status, days since vaccination, ethnicity
Patients without renal disease	Log regression	Age, gender, time period, multiple high-risk conditions, moderate-risk conditions, vaccination status, days since vaccination, ethnicity
Patients with renal disease	Log regression	Age, gender, time period, multiple high-risk conditions, moderate-risk conditions, vaccination status, days since vaccination, ethnicity
Shielded population	GBM	Age, gender, time period, multiple high-risk conditions, moderate-risk conditions, vaccination status, days since vaccination, ethnicity

Period 1	Log regression	Age, gender, renal disease, multiple high-risk conditions, moderate-risk conditions, vaccination status, days since vaccination, ethnicity
Period 2	Log regression	Age, gender, renal disease, multiple high-risk conditions, moderate-risk conditions, vaccination status, days since vaccination, ethnicity
Period 3	Log regression	Age, gender, renal disease, multiple high-risk conditions, moderate-risk conditions, vaccination status, days since vaccination, ethnicity

Abbreviations: GBM, gradient boosting machine; IPTW, inverse probability of treatment weighting; PSM, propensity score matching.

1 **Supplementary Table 2. IPTW Metrics (standardised differences)**

Variable	Overall Cohort	Patients Aged <65 Years	Patients Aged ≥65 Years	Patients without Renal Disease	Patients with Renal Disease	Shielded Population	Period 1	Period 2	Period 3
Age	0.08	0.08	0.03	0.03	–0.00	–0.01	0.11	0.07	–0.01
Gender									
Female	0.06	0.05	–0.02	0.05	0.04	–0.01	0.05	0.09	–0.06
Male	–0.06	–0.05	0.02	–0.05	–0.04	0.01	–0.05	–0.09	0.06
Ethnicity									
Asian/Asian British	0.01	0.07	0.03	0.07	0.04	–0.05	0.04	–0.02	0.03
Black/Black British	–0.08	–0.03	0.03	–0.07	0.03	–0.07	–0.16	–0.02	0.05
Mixed	–0.06	0.03	–0.01	0.09	–0.00	–0.05	0.02	–0.01	0.04
White	0.09	–0.02	–0.08	–0.00	–0.08	0.11	0.12	–0.02	–0.06
Other	–0.03	–0.05	0.06	–0.08	0.03	0.01	–0.10	0.08	–0.01
Null	0.00	–0.01	0.05	0.00	–0.00	–0.03	0.03	0.03	–0.01

Time period of COVID-19 diagnosis									
Period 1	–0.12	–0.07	–0.07	–0.01	0.05	–0.12	…	…	…
Period 2	0.10	0.02	0.04	–0.01	–0.02	0.11	…	…	…
Period 3	0.03	0.08	0.03	0.03	–0.04	0.03	…	…	…
Renal disease									
Yes	0.07	0.07	0.07	…	…	0.05	0.03	–0.02	–0.04
No	–0.07	–0.07	–0.07	…	…	–0.05	–0.03	0.02	0.04
Multiple high-risk conditions									
Yes	–0.06	–0.11	0.01	–0.11	–0.00	0.05	–0.16	–0.08	–0.03
No	0.06	0.11	–0.01	0.11	0.00	–0.05	0.16	0.08	0.03
Moderate-risk conditions									
Yes	0.06	0.02	0.01	0.01	0.03	–0.02	–0.06	0.02	–0.04
No	–0.06	–0.02	–0.01	–0.01	–0.03	0.02	0.06	–0.02	0.04
Solid-organ transplant recipient									
Yes	0.01	–0.02	0.00	–0.01	–0.00	0.05	–0.04	–0.01	–0.00
No	–0.01	0.02	–0.00	0.01	0.00	–0.05	0.04	0.01	0.00
Vaccination status									
Yes	0.03	–0.09	–0.06	–0.10	–0.07	0.00	–0.04	–0.03	–0.07
No	–0.03	0.09	0.06	0.10	0.07	–0.00	0.04	0.03	0.07

Days since last vaccination	–0.06	0.09	0.03	0.07	0.08	–0.09	–0.02	0.02	0.10

Abbreviations: IPTW, inverse probability of treatment weighting.

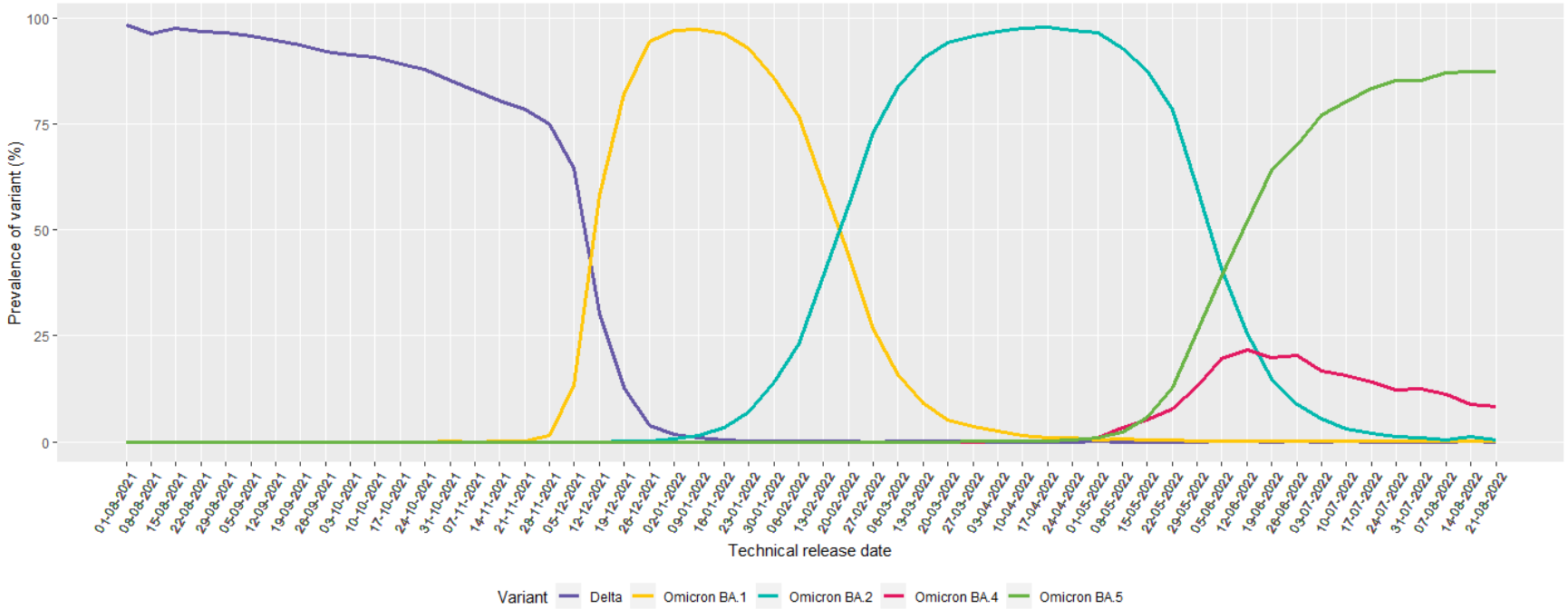
Supplementary Table 3. Power Calculations for IPTW Cox Models

						Power calculated when covariates are included	Power calculated when only treatment without covariates is considered	
Characteristic	**Subgroup**	**Outcome**	**n**	**Events**	**Power of the model**	**Sample size to detect the effect, power=0.8, alpha=0.05**	**N in experimental group**	**N in control group**
All	All	COVID hospitalisation or death	5790	117	0.612428795	9012		
		COVID hospitalisation	5790	97	0.708479937	7220		
		Death	5790	24	0.074230386	171,363		
Age	<65 years	COVID hospitalisation or death	4277	56	0.072947205	131,229		
		COVID hospitalisation	4277	53	0.115057787	58,135		
		Death	4277	<5	0.058320818	219,652		
	≥65 years	COVID hospitalisation or death	1513	61	0.618501287		324	1999
		COVID hospitalisation	1513	44	0.641503645		308	1895
		Death	1513	20	0.1158032945		2840	17,521
Time period	Period 1	COVID hospitalisation or death	2946	65	0.747771624	3350		
	Period 2	COVID hospitalisation or death	1978	31	0.163229749		2336	13,874

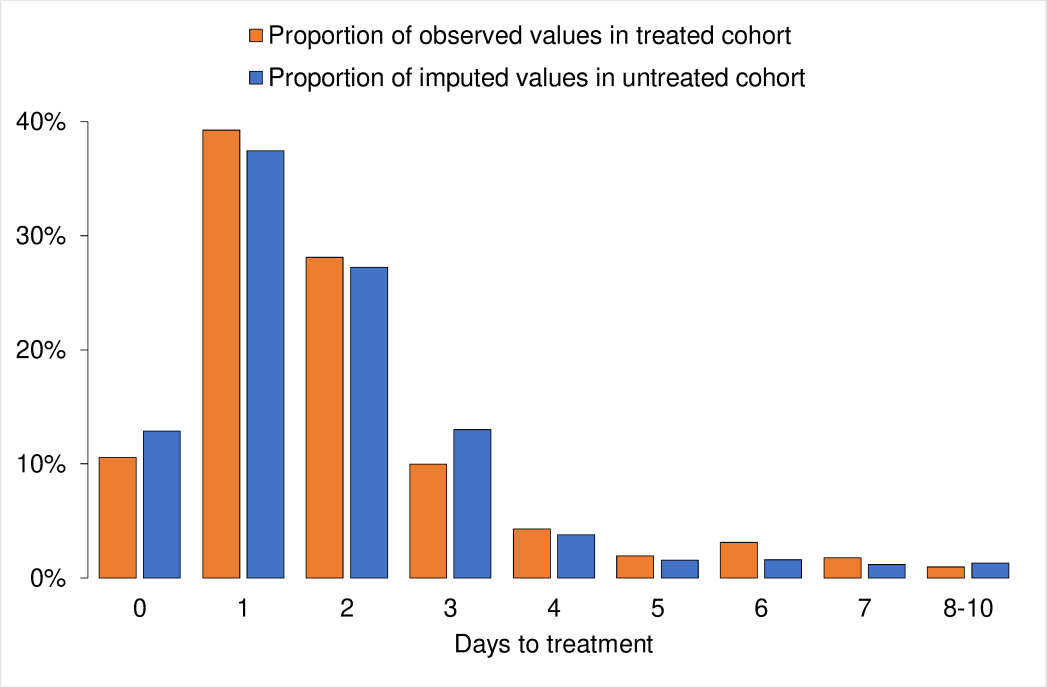
		COVID hospitalisation	1978	22	0.137672189		2962	17,592
		Death	1978	9	0.065472602		11,068	65,744
	Period 3	COVID hospitalisation or death	866	21	0.062033866	38,161		
		COVID hospitalisation	866	17	0.120772999	10,924		
		Death	866	6	0.027298667	4,732,766		
Renal disease	No	COVID hospitalisation or death	4442	66	0.248825474	21,221		
		COVID hospitalisation	4442	57	0.228764482	23,539		
		Death	4442	10	0.074942	128,927		
	Yes	COVID hospitalisation or death	1348	51	0.635931523		375	1613
		COVID hospitalisation	1348	40	0.65156293		362	1556
		Death	1348	14	0.1233399174		3102	13,357
Shielding flag	Yes	COVID hospitalisation or death	21320	261	0.06	1,285,303		
		COVID hospitalisation	21320	194	0.15	196,438		
		Death	21320	84	0.8	21,475		

5

Supplementary Figure 1. Omicron Subvariant Prevalence in England [1]



Supplementary Figure 2. Observed Time to Treatment, and Imputed Time to Treatment in Untreated Cohort



Exploratory analysis

In our previous descriptive analysis, we observed that a high proportion of those prescribed sotrovimab (39.2%) did not have a code [2]. Therefore, we performed an exploratory analysis whereby a SNOMED code (1300561000000107; high-risk category for developing complication from coronavirus disease 19 caused by severe acute respiratory syndrome coronavirus 2 infection) was used to identify patients who were identified as appropriate for "shielding" during the early phase of the pandemic. Only patients with the "shielding" SNOMED code were included in the exploratory analysis, which included patients with and without NHS highest-risk criteria. The same methods as described for the primary analysis were utilized for the exploratory analysis.

A total of 21 320 patients were identified as appropriate for "shielding". Of these, 17 921 (84.1%) had a shielding code but no specific highest risk-related diagnosis and 3399 (15.9%) had both. Of patients identified as appropriate for "shielding", 692 (3.2%) received sotrovimab and 20 628 (96.8%) were untreated. COVID-19-related hospitalizations were experienced by 1.4% (n=10/692) of sotrovimab-treated patients and 0.9% (n=184/20 628) of untreated patients. Death within 1 month of index was reported for fewer than 5 sotrovimab-treated patients and 0.4% of untreated patients (n=82/20 628). The IPTW HR for composite COVID-19 hospitalization or death was 1.14 (95% CI=0.48–2.66; *P*=.77) for sotrovimab versus no treatment; for COVID-19 hospitalization alone the IPTW HR was 1.46 (95% CI=0.59–3.57; *P*=.41). Sotrovimab treatment was associated with an 82% lower risk of death alone compared with the untreated group (HR=0.18; 95% CI=0.04–0.73; *P*=.02).

Supplementary References

1. UK Health Security Agency. SARS-CoV-2 variants of concern and variants under investigation in England: technical briefing 43. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1103533/Technical-Briefing-43-24June2022.pdf. Accessed 5 July 2023.

2. Patel V, Yarwood MJ, Levick B, et al. Characteristics and outcomes of patients with COVID-19 at high-risk of disease progression receiving sotrovimab, oral antivirals or no treatment in England. medRxiv [Preprint]. November 29, 2022 [cited 2023 Jul 5]. Available from: https://doi.org/10.1101/2022.11.28.22282808.