Supplement:

Severity of SARS-CoV-2 alpha variant (B.1.1.7)

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1. Further information on OpenSAFELY

All data were linked, stored and analysed securely within the OpenSAFELY platform https://opensafely.org/. The dataset analysed within OpenSAFELY is based on 24 million people currently registered with GP surgeries using TPP SystmOne software. Data include pseudonymized data such as coded diagnoses, medications and physiological parameters. No free text data are included. All code is shared openly for review and re-use under MIT open license (https://github.com/opensafely/SGTF-CFR-research). Detailed pseudonymised patient data is potentially re-identifiable and therefore not shared. We rapidly delivered the OpenSAFELY data analysis platform without prior funding to deliver timely analyses on urgent research questions in the context of the global Covid-19 health emergency: now that the platform is established we are developing a formal process for external users to request access in collaboration with NHS England; details of this process will be published shortly on OpenSAFELY.org.

2. Information governance and ethics

NHS England is the data controller; TPP is the data processor; and the key researchers on OpenSAFELY are acting on behalf of NHS England. This implementation of OpenSAFELY is hosted within the TPP environment which is accredited to the ISO 27001 information security standard and is NHS IG Toolkit compliant;[1,2] patient data has been pseudonymised for analysis and linkage using industry standard cryptographic hashing techniques; all pseudonymised datasets transmitted for linkage onto OpenSAFELY are encrypted; access to the platform is via a virtual private network (VPN) connection, restricted to a small group of researchers; the researchers hold contracts with NHS England and only access the platform to initiate database queries and statistical models; all database activity is logged; only aggregate statistical outputs leave the platform environment following best practice for anonymisation of results such as statistical disclosure control for low cell counts.[3] The OpenSAFELY research platform adheres to the obligations of the UK General Data Protection Regulation (GDPR) and the Data Protection Act 2018. In March 2020, the Secretary of State for Health and Social Care used powers under the UK Health Service (Control of Patient Information) Regulations 2002 (COPI) to require organisations to process confidential patient information for the purposes of protecting public health, providing healthcare services to the public and monitoring and managing the COVID-19 outbreak and incidents of exposure; this sets aside the requirement for patient consent.[4] Taken together, these provide the legal bases to link patient datasets on the OpenSAFELY platform. GP practices, from which the primary care data are obtained, are required to share relevant health information to support the public health response to the pandemic, and have been informed of the OpenSAFELY analytics platform.

This study was approved by the Health Research Authority (REC reference 20/LO/0651) and by the LSHTM Ethics Board (reference 21863).

3. Details on data sources

We used several linked data sets in this analysis (Table S1).

Data	**Description**
SARS-CoV-2 tests	Positive and negative tests of people tested under the UK's Pillar 1 and Pillar 2 testing schemes are reported.[5] Pillar 2 generally is community tests and

	Pillar 1 is tests in hospital (patients and health care workers). Only some of the labs used for testing in England use the 3 channel PCR for which a "failure to detect the Spike-gene target" is indicative of the VOC, therefore not all positive tests have known SGTF status. The data come from Public Health England's (PHE) Second Generation Surveillance System.
General Practitioner (GP) data	GP data are drawn from patients who are registered at a practice that runs the TPP SystmOne (https://www.tpp-uk.com/products/systmone). This is approximately 40% of GPs in England. Each patient encounter with a GP is coded using CTV3 codes, which fully aligns with SNOMED-CT which describe the reason for the encounter, and these codes are used to define the health history of each individual.[6] Prescribed medications are also stored in the health record. Demographic data such as age and ethnicity are collected by GPs, as are some behavioural data like whether an individual smokes.
Hospital admission	Secondary Uses Statistics (SUS) data used to define hospital admission and ICU admission. Data are collected on hospital admissions with ICD-10 codes for conditions, and procedural codes for treatment. Whether the patient is admitted to intensive care during their hospital admission is also included. (https://digital.nhs.uk/services/secondary-uses-service-sus)
Mortality date	The date of death plus codes for the cause of death are from the Office for National Statistics. We only use date of death in this study.
Vaccination date	The date, dose number, vaccine manufacturer and batch are entered into their health record. We only use the date of administration of the first dose in this study.
Index of multiple deprivation (IMD)	We use the England IMD which is matched to individuals at the postcode level.
Urban/Rural classification	We use 5 categories of Urban/Rural classifications which are matched to individuals at the postcode level.

Table S1. Data sources used in this analysis.

4. Definition of comorbidities

A patient is identified as having a comorbidity if their health record includes codes indicative of each of the conditions (Table S2).

Condition	**Codelist defining presence of comorbidity**
Aplastic anaemia	https://codelists.opensafely.org/codelist/opensafely/aplastic-anaemia/
Asplenia	https://codelists.opensafely.org/codelist/opensafely/asplenia/
Asthma	https://codelists.opensafely.org/codelist/opensafely/asthma-diagnosis/ https://codelists.opensafely.org/codelist/opensafely/asthma-inhaler-salbutamol-medication/2020-04-15/ https://codelists.opensafely.org/codelist/opensafely/asthma-inhaler-steroid-medication/2020-04-15/ https://codelists.opensafely.org/codelist/opensafely/asthma-oral-prednisolone-medication/2020-04-27/
Bone marrow transplant	

Cancer	https://codelists.opensafely.org/codelist/opensafely/bone-marrow-transplant/2020-04-15/ https://codelists.opensafely.org/codelist/opensafely/cancer-excluding-lung-and-haematological/2020-04-15/ https://codelists.opensafely.org/codelist/opensafely/chemotherapy-or-radiotherapy-updated/2020-04-15/ https://codelists.opensafely.org/codelist/opensafely/haematological-cancer/2020-04-15/ https://codelists.opensafely.org/codelist/opensafely/lung-cancer/2020-04-15/
Chronic cardiac disease	https://codelists.opensafely.org/codelist/opensafely/chronic-cardiac-disease/2020-04-08/
Chronic respiratory disease	https://codelists.opensafely.org/codelist/opensafely/chronic-respiratory-disease/2020-04-10/
Chronic liver disease	https://codelists.opensafely.org/codelist/opensafely/chronic-liver-disease/2020-06-02/
Dementia	https://codelists.opensafely.org/codelist/opensafely/dementia/2020-04-22/
Diabetes	https://codelists.opensafely.org/codelist/opensafely/diabetes/2020-04-15/
Chronic kidney disease	https://codelists.opensafely.org/codelist/opensafely/chronic-kidney-disease/2020-04-14/
GI bleed	https://codelists.opensafely.org/codelist/opensafely/gi-bleed-or-ulcer/2020-04-08/
HIV	https://codelists.opensafely.org/codelist/opensafely/hiv/2020-07-13/
Permanent immunosuppression	https://codelists.opensafely.org/codelist/opensafely/permanent-immunosuppression/2020-06-02/
Temporary immunosuppression	https://codelists.opensafely.org/codelist/opensafely/temporary-immunosuppression/2020-04-24/
Hypertension	https://codelists.opensafely.org/codelist/opensafely/hypertension/2020-04-28/
Stroke	https://codelists.opensafely.org/codelist/opensafely/stroke-updated/2020-06-02/
Inflammatory bowel disease	https://codelists.opensafely.org/codelist/opensafely/inflammatory-bowel-disease/2020-04-07/
Neurological conditions	https://codelists.opensafely.org/codelist/opensafely/other-neurological-conditions/2020-06-02/
Psoriasis	https://codelists.opensafely.org/codelist/opensafely/ra-sle-psoriasis/2020-04-14/
Sickle cell disease	https://codelists.opensafely.org/codelist/opensafely/sickle-cell-disease/2020-04-14/
Smoking	https://codelists.opensafely.org/codelist/opensafely/smoking-clear/2020-04-29/
Organ transplant	https://codelists.opensafely.org/codelist/opensafely/smoking-unclear/2020-04-29/ https://codelists.opensafely.org/codelist/opensafely/solid-organ-transplantation/2020-04-10/

Table S2. Comorbidities and the codelists that determine if a patient is classified as having that comorbidity. All codelists are reviewed by clinicians.

5. Table S3 Complete demographic and clinical characteristics

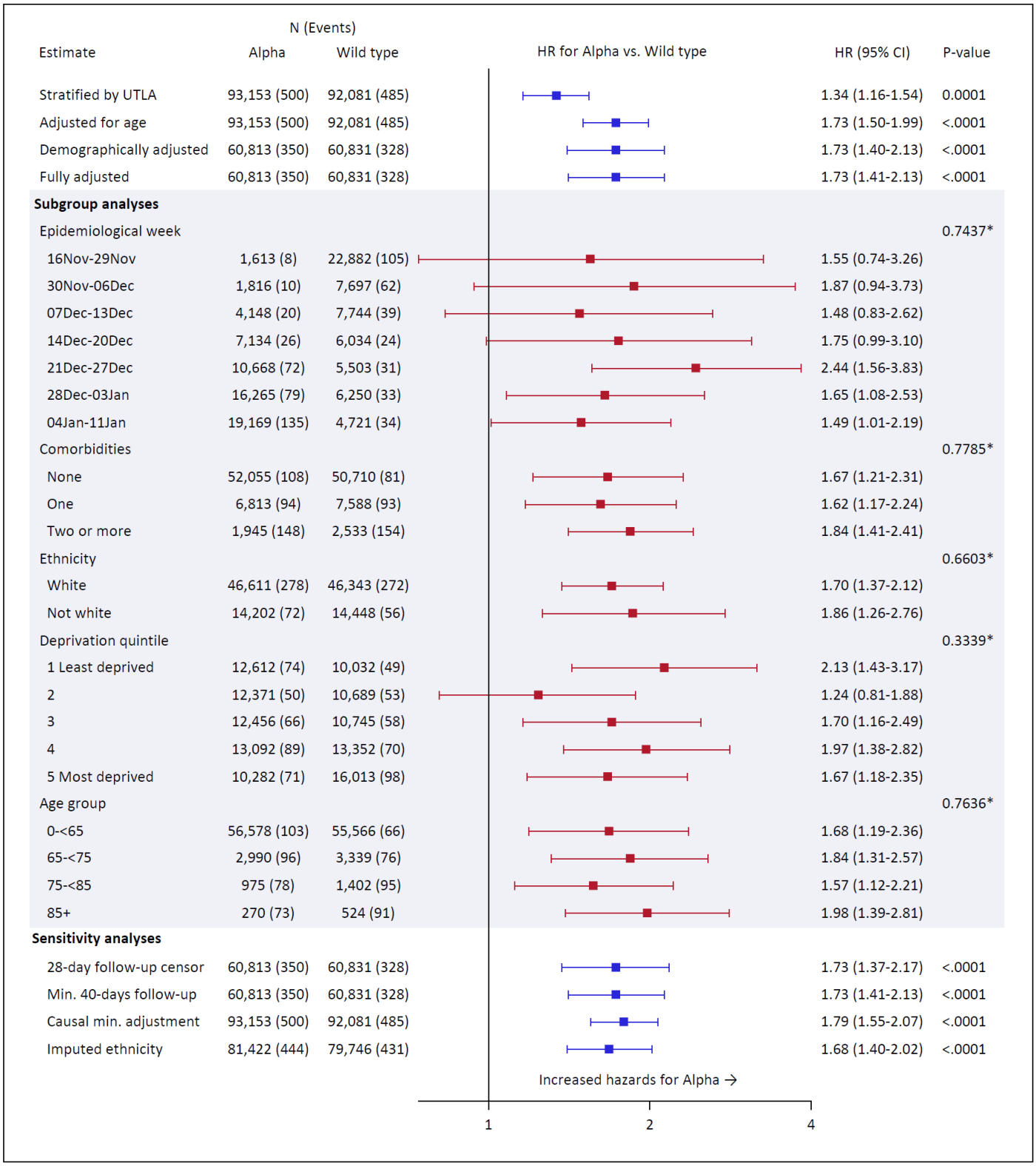
	Total	Wild type	Alpha
N	185,234	92,081	93,153
Died	985 (0.5)	485 (0.5)	500 (0.5)
Admitted to hospital	4,910 (2.7)	2,189 (2.4)	2,721 (2.9)
Admitted to intensive care unit	616 (0.3)	271 (0.3)	345 (0.4)
Died following hospital admission	669 (0.4)	300 (0.3)	369 (0.4)
Days spent in ICU			
Mean (SD)	12.0 (10.9)	12.9 (12.3)	11.3 (9.7)
Median (IQR)	8.0 (5.0-15.0)	9.0 (5.0-16.0)	8.0 (5.0-14.0)
Time to death			
Mean (SD)	20.0 (17.0)	20.1 (18.8)	19.8 (15.1)
Median (IQR)	15.0 (9.0-25.0)	13.0 (8.0-26.0)	16.0 (10.0-25.0)
Follow-up time			
Mean (SD)	95.4 (37.4)	102.2 (39.6)	88.8 (33.8)
Median (IQR)	105.0 (66.0-123.0)	109.0 (71.0-136.0)	102.0 (62.0-113.0)
Epidemiological week of study			
16Nov-22Nov	22,062 (11.9)	20,926 (22.7)	1,136 (1.2)
23Nov-29Nov	14,788 (8.0)	13,459 (14.6)	1,329 (1.4)
30Nov-06Dec	14,326 (7.7)	11,607 (12.6)	2,719 (2.9)
07Dec-13Dec	18,194 (9.8)	11,742 (12.8)	6,452 (6.9)
14Dec-20Dec	20,010 (10.8)	9,078 (9.9)	10,932 (11.7)
21Dec-27Dec	24,444 (13.2)	8,279 (9.0)	16,165 (17.4)
28Dec-03Jan	34,589 (18.7)	9,518 (10.3)	25,071 (26.9)
04Jan-11Jan	36,821 (19.9)	7,472 (8.1)	29,349 (31.5)
Female	98,308 (53.1)	49,629 (53.9)	48,679 (52.3)
Age (years)			
Mean (SD)	38.2 (18.1)	38.6 (18.5)	37.9 (17.7)
Median (IQR)	38.0 (24.0-52.0)	38.0 (24.0-52.0)	37.0 (24.0-51.0)
Grouped age			
0-<18	27,276 (14.7)	14,334 (15.6)	12,942 (13.9)
18-<30	37,059 (20.0)	17,353 (18.8)	19,706 (21.2)
30-<40	34,337 (18.5)	16,821 (18.3)	17,516 (18.8)
40-<50	32,854 (17.7)	15,951 (17.3)	16,903 (18.1)
50-<60	30,601 (16.5)	15,344 (16.7)	15,257 (16.4)
60-<70	14,869 (8.0)	7,618 (8.3)	7,251 (7.8)
70-<80	5,882 (3.2)	3,139 (3.4)	2,743 (2.9)
80+	2,356 (1.3)	1,521 (1.7)	835 (0.9)
Ethnicity			
White	106,257 (57.4)	53,145 (57.7)	53,112 (57.0)
South Asian	21,692 (11.7)	11,950 (13.0)	9,742 (10.5)
Black	4,556 (2.5)	1,760 (1.9)	2,796 (3.0)
Mixed	2,654 (1.4)	1,192 (1.3)	1,462 (1.6)
Other	3,003 (1.6)	1,362 (1.5)	1,641 (1.8)

Missing	47,072 (25.4)	22,672 (24.6)	24,400 (26.2)
Evidence of obesity (missing set to none)[a]			
No record of obesity	144,599 (78.1)	70,816 (76.9)	73,783 (79.2)
Obese I (30-34.9)	24,597 (13.3)	12,709 (13.8)	11,888 (12.8)
Obese II (35-39.9)	10,416 (5.6)	5,470 (5.9)	4,946 (5.3)
Obese III (40+)	5,622 (3.0)	3,086 (3.4)	2,536 (2.7)
Smoking status (missing set to never)[b]			
Never	115,730 (62.5)	57,917 (62.9)	57,813 (62.1)
Former	50,135 (27.1)	25,014 (27.2)	25,121 (27.0)
Current	19,369 (10.5)	9,150 (9.9)	10,219 (11.0)
Number of comorbidities			
No comorbidity	158,613 (85.6)	77,886 (84.6)	80,727 (86.7)
1 comorbidity	20,410 (11.0)	10,679 (11.6)	9,731 (10.4)
2+ comorbidities	6,211 (3.4)	3,516 (3.8)	2,695 (2.9)
Index of Multiple Deprivation (IMD)			
1 least deprived	36,621 (19.8)	16,013 (17.4)	20,608 (22.1)
2	35,461 (19.1)	16,329 (17.7)	19,132 (20.5)
3	34,698 (18.7)	16,006 (17.4)	18,692 (20.1)
4	38,685 (20.9)	19,536 (21.2)	19,149 (20.6)
5 most deprived	39,769 (21.5)	24,197 (26.3)	15,572 (16.7)
Categorical household size			
1-2	47,658 (25.7)	24,096 (26.2)	23,562 (25.3)
3-5	92,886 (50.1)	45,170 (49.1)	47,716 (51.2)
6-10	18,728 (10.1)	9,503 (10.3)	9,225 (9.9)
11+	1,943 (1.0)	1,008 (1.1)	935 (1.0)
Missing	24,019 (13.0)	12,304 (13.4)	11,715 (12.6)
Care home status[c]			
Private home	184,756 (99.7)	91,726 (99.6)	93,030 (99.9)
Care home	478 (0.3)	355 (0.4)	123 (0.1)
NHS England region			
East	44,658 (24.1)	9,712 (10.5)	34,946 (37.5)
East Midlands	26,579 (14.3)	18,736 (20.3)	7,843 (8.4)
London	15,986 (8.6)	4,501 (4.9)	11,485 (12.3)
North East	7,091 (3.8)	5,850 (6.4)	1,241 (1.3)
North West	25,018 (13.5)	14,725 (16.0)	10,293 (11.0)
South East	9,565 (5.2)	2,656 (2.9)	6,909 (7.4)
South West	9,072 (4.9)	4,897 (5.3)	4,175 (4.5)
West Midlands	15,280 (8.2)	7,668 (8.3)	7,612 (8.2)
Yorkshire and the Humber	31,923 (17.2)	23,290 (25.3)	8,633 (9.3)
Rural Urban in five categories			
Urban major conurbation	57,827 (31.2)	28,089 (30.5)	29,738 (31.9)
Urban minor conurbation	8,920 (4.8)	6,827 (7.4)	2,093 (2.2)
Urban city and town	91,201 (49.2)	43,483 (47.2)	47,718 (51.2)
Rural town and fringe	16,417 (8.9)	8,540 (9.3)	7,877 (8.5)
Rural village and dispersed	9,213 (5.0)	4,172 (4.5)	5,041 (5.4)

Missing	1,656 (0.9)	970 (1.1)	686 (0.7)

[a]59,230 Missing values set to no evidence of obesity; [b]28,068 missing values set to never smoking status;
[c]Based on address linkage with CQC data as of 1st Feb 2020: 1,656 missing values set to private home.

6. Figure S1 Case fatality subgroup and sensitivity analyses

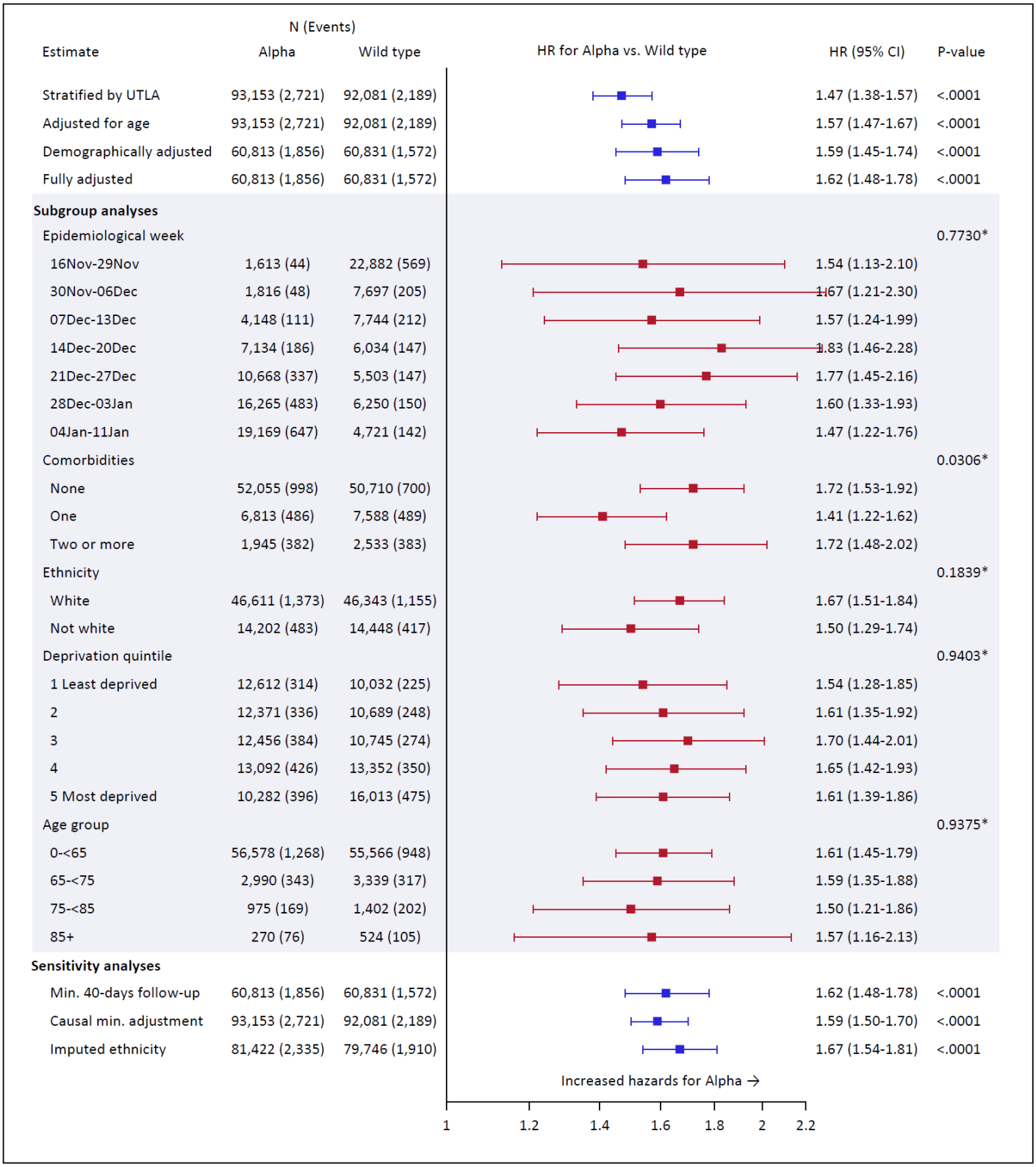


7. Table S4 Complete demographic and clinical characteristics of people admitted to hospital

	Total	Wild type	Alpha
N	4,910	2,189	2,721
Died	669 (13.6)	300 (13.7)	369 (13.6)
Discharged from hospital	4,320 (88.0)	1,924 (87.9)	2,396 (88.1)
Time to death			
Median (IQR)	18.0 (11.0-27.0)	17.0 (11.0-28.5)	18.0 (12.0-26.0)
Follow-up time			
Median (IQR)	60.0 (37.0-94.0)	66.0 (41.0-98.0)	56.0 (35.0-90.0)
Epidemiological week of study			
16Nov-22Nov	497 (10.1)	476 (21.7)	21 (0.8)
23Nov-29Nov	375 (7.6)	333 (15.2)	42 (1.5)
30Nov-06Dec	353 (7.2)	284 (13.0)	69 (2.5)
07Dec-13Dec	448 (9.1)	285 (13.0)	163 (6.0)
14Dec-20Dec	455 (9.3)	195 (8.9)	260 (9.6)
21Dec-27Dec	668 (13.6)	198 (9.0)	470 (17.3)
28Dec-03Jan	947 (19.3)	216 (9.9)	731 (26.9)
04Jan-11Jan	1,167 (23.8)	202 (9.2)	965 (35.5)
Female	2,158 (44.0)	985 (45.0)	1,173 (43.1)
Age (years), median (IQR)	58.0 (47.0-70.0)	59.0 (48.0-72.0)	57.0 (47.0-68.0)
Grouped age			
0-<18	45 (0.9)	24 (1.1)	21 (0.8)
18-<30	196 (4.0)	95 (4.3)	101 (3.7)
30-<40	458 (9.3)	191 (8.7)	267 (9.8)
40-<50	750 (15.3)	312 (14.3)	438 (16.1)
50-<60	1,171 (23.8)	480 (21.9)	691 (25.4)
60-<70	1,037 (21.1)	427 (19.5)	610 (22.4)
70-<80	775 (15.8)	376 (17.2)	399 (14.7)
80+	478 (9.7)	284 (13.0)	194 (7.1)
Ethnicity			
White	2,896 (59.0)	1,304 (59.6)	1,592 (58.5)
South Asian	739 (15.1)	356 (16.3)	383 (14.1)
Black	128 (2.6)	47 (2.1)	81 (3.0)
Mixed	56 (1.1)	23 (1.1)	33 (1.2)
Other	98 (2.0)	42 (1.9)	56 (2.1)
Missing	993 (20.2)	417 (19.0)	576 (21.2)
Evidence of obesity (missing set to none)			
No record of obesity	2,677 (54.5)	1,194 (54.5)	1,483 (54.5)
Obese I (30-34.9)	1,188 (24.2)	531 (24.3)	657 (24.1)
Obese II (35-39.9)	613 (12.5)	267 (12.2)	346 (12.7)
Obese III (40+)	432 (8.8)	197 (9.0)	235 (8.6)
Smoking status (missing set to never)			
Never	2,258 (46.0)	969 (44.3)	1,289 (47.4)

Former	2,416 (49.2)	1,119 (51.1)	1,297 (47.7)
Current	236 (4.8)	101 (4.6)	135 (5.0)
Number of comorbidities			
No comorbidity	2,487 (50.7)	989 (45.2)	1,498 (55.1)
1 comorbidity	1,346 (27.4)	649 (29.6)	697 (25.6)
2+ comorbidities	1,077 (21.9)	551 (25.2)	526 (19.3)
Index of Multiple Deprivation (IMD)			
1 least deprived	849 (17.3)	342 (15.6)	507 (18.6)
2	863 (17.6)	347 (15.9)	516 (19.0)
3	931 (19.0)	375 (17.1)	556 (20.4)
4	1,060 (21.6)	478 (21.8)	582 (21.4)
5 most deprived	1,207 (24.6)	647 (29.6)	560 (20.6)
Categorical household size			
1-2	1,984 (40.4)	935 (42.7)	1,049 (38.6)
3-5	1,774 (36.1)	738 (33.7)	1,036 (38.1)
6-10	427 (8.7)	201 (9.2)	226 (8.3)
11+	62 (1.3)	37 (1.7)	25 (0.9)
Missing	663 (13.5)	278 (12.7)	385 (14.1)
Care home status			
Private home	4,844 (98.7)	2,146 (98.0)	2,698 (99.2)
Care home	66 (1.3)	43 (2.0)	23 (0.8)
NHS England region			
East	901 (18.4)	166 (7.6)	735 (27.0)
East Midlands	736 (15.0)	446 (20.4)	290 (10.7)
London	419 (8.5)	94 (4.3)	325 (11.9)
North East	170 (3.5)	125 (5.7)	45 (1.7)
North West	841 (17.1)	405 (18.5)	436 (16.0)
South East	260 (5.3)	51 (2.3)	209 (7.7)
South West	363 (7.4)	179 (8.2)	184 (6.8)
West Midlands	396 (8.1)	166 (7.6)	230 (8.5)
Yorkshire and the Humber	822 (16.7)	556 (25.4)	266 (9.8)
Rural Urban in five categories			
Urban major conurbation	1,480 (30.1)	624 (28.5)	856 (31.5)
Urban minor conurbation	221 (4.5)	149 (6.8)	72 (2.6)
Urban city and town	2,466 (50.2)	1,072 (49.0)	1,394 (51.2)
Rural town and fringe	438 (8.9)	209 (9.5)	229 (8.4)
Rural village and dispersed	242 (4.9)	102 (4.7)	140 (5.1)
Missing	63 (1.3)	33 (1.5)	30 (1.1)

8. Figure S2 Hospital admission subgroup and sensitivity analyses



9. References

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