

Supplementary Information

Supplementary Table 1 | Sample flow

Filters	Number of individuals
Present in 2011 Census (not imputed), present in PDS and has a valid NHS number	55,081,056
Usual resident of UK and resident in England	51,801,515
Alive on 21 March 2021	51,797,278
Age 16+ on 21 March 2021	41,950,323
Non erroneous/ambiguous vaccination data	41,855,563
Sample of data	583,840

Supplementary Table 2: | Variables used in the analyses

Variable	Coding	Source
Outcomes		
Death involving COVID-19	Confirmed or suspected COVID-19 (ICD -10 codes U07.1 and U07.2) as underlying or contributory cause of death on the death certificate	2020 - 2022 ONS Death registrations
COVID-19 hospitalisation	An inpatient episode where either of the ICD10 codes, U07.1 (COVID-19, virus identified) or U07.2 (COVID-19, virus not identified) is the primary diagnosis. Where an individual has more than one COVID-19 hospitalisation, the earliest is used.	Hospital Episode Statistics
Exposure		
Vaccination status	Time-updated covariate. Categories are: <ul style="list-style-type: none"> Unvaccinated (no vaccination to <21 days post first dose) First dose (≥ 21 days post second dose to earliest of < 91 days post first dose or < 21 days post second dose) First dose 3+ months (≥ 91 days post first dose to <21 days post second dose) Second dose (≥ 21 days post second dose to earliest of < 91 days post second dose or < 21 days post third dose) Second dose 3-6 months (≥ 91 days post second dose to earliest of < 182 days post second dose or < 21 days post third dose) Second dose 6+ months (≥ 182 days post second dose to < 21 days post third dose) Third dose (≥ 21 days post third dose to <91 days post third dose) Third dose 3+ months (≥ 91 days post third dose) 	National Immunisation Management Service (NIMS)
Confounding factors		
Age on 21 March 2021	Natural spline, boundary knots at 10% and 90%, internal knots at 25%, 50% and 75% quantiles of the full dataset or the age specific datasets used for the age stratified results.	2021 Census

Sex	Female, Male	2021 Census
Self-reported ethnic group	Black, Mixed, White, Asian, Other	2021 Census
Religious affiliation	Christian, Buddhist, Hindu, Jewish, Muslim, Sikh, Other Religion, No religion, Religion Not Stated, No code required	2021 Census
Region of residence in 2019	Government Office region (E12000001-9)	Derived from 2021 Census OA
Index of Multiple Deprivation (IMD)	Binary variables representing deciles of deprivation	Derived from 2021 Census LSOA
Level of highest qualification	No qualification, Level 1 (1-4 GCSEs any grade or equivalent), Level 2 (5+ GCSEs grade A*-C or equivalent), Apprenticeship, Level 3 (2+ A Levels or equivalent), Level 4+ (Degree), Other, No code required	2021 Census
English language proficiency	Can speak English very well, Can speak English well, Cannot speak English well, Cannot speak English, No code required	2021 Census
National Statistics Socio-economic classification (NS-SEC)	The SOC 2020 classifications were grouped into the NS-SEC 8 analytic classes [26]: Higher managerial (cat 1), Lower managerial, administrative and professional occupations (cat 2), Administrative and professional occupations, Intermediate occupations (cat 3), Small employers and own account workers (cat 4), Lower supervisory and technical occupations (cat 5), Semi-routine occupations (cat 6), Routine occupations (cat 7), Never worked and long-term unemployed (cat 8), Full-time students and not classified (cat 9)	2021 Census
Key worker status	Based on SOC 2020 classification. Taxi and cab drivers and chauffeurs, Support staff, Bus and coach drivers, Sanitary workers, Social care, Van drivers, Health associate professionals, Food retail & distribution, Other transport workers, Health professionals, Food production, Education, Police & Protective Services, Non-essential workers	2021 Census
Care home residency	Binary variable for residency in a care home. 1 if the person is a resident in communal accommodation that is a local authority care home with nursing, a local authority care home without nursing, a care home with nursing or a care home without nursing.	2021 Census
Long term health problem or disability	Day-to-day activities limited a lot, Day-to-day activities limited a little, Day-to-day activities not limited	2021 Census
Self-reported general health	Very good health, Good health, Fair health, Bad health, Very bad health	2021 Census
Body Mass Index (kg/m ²)	Underweight (< 18.5), Ideal (18.5 – 25), Overweight (25 to 30), Obese (>= 30), Unclassified, Under 20 nulls	GDPPR V3

Number of QCovid comorbidities	<p>The QCOVID comorbidities included are:</p> <p>Motor neurone disease, multiple sclerosis, myasthenia or Huntington's Chorea; leukolaba; liver cirrhosis; asthma; prior fracture of hip, wrist, spine or humerous; Severe combined immunodeficiency; severe mental illness; epilepsy; cystic fibrosis or bronchiectasis alveolitis; heart failure; lung or oral cancer; pulmonary hypertension or fibrosis; Inflammatory bowel disease; prescription for prednisolone; HIV; dementia; diabetes type 1; diabetes type 2; chronic kidney disease; atrial fibrillation; schizophrenia; cancer of blood or bone marrow; Chronic obstructive pulmonary disease; rheumatoid arthritis or Systemic lupus erythematosus; cerebral palsy; Parkinson's disease; learning disability or Down's syndrome; thrombosis or pulmonary embolism; stroke or Transient ischaemic attack; immunosuppressants; congenital heart problem; coronary heart disease.</p> <p>Grouping: 0, 1, 2-4, 5+.</p>	GDPPR V3
Frailty flag	Flag is 1 if individual experienced at least 1 hospital episode ending in the 5 years prior to 21 March 2021 where a primary or secondary diagnosis corresponding to frailty has been recorded. The ICD10 codes for frailty are as defined in the Hospital Frailty Risk Score [27].	HES
Hospitalisation status	Binary, time-updated covariate. Status is 1 if currently hospitalised or if had a hospital spell that started less than 21 days prior to date. Hospitalisations with a primary diagnosis code of COVID-19 (U07.1 or U07.2), that are related to birth or pregnancy or that last less than 1 day are not included.	HES
Variant period	Time-varying covariate defined as 'pre-omicron' from start of study 21 March to 19 December 2021 and 'omicron' from 20 December 2021 to end of study 31 March 2022.	Created variable
Vaccine vector	Time-varying covariate for the vaccine vector type used for a particular vaccination status which changes at the same intervals as the time-varying covariate for vaccination status. Variable is a combination of the vaccination status variable and either 'none' (if vaccination status is unvaccinated), 'mRNA' (vaccine is BNT162b2 (Pfizer-BioNTech) or Moderna) or 'not mRNA or unknown' (vaccine is ChAdOx1-S (Oxford/AstraZeneca), any other vaccine, or an unknown vaccine).	NIMS

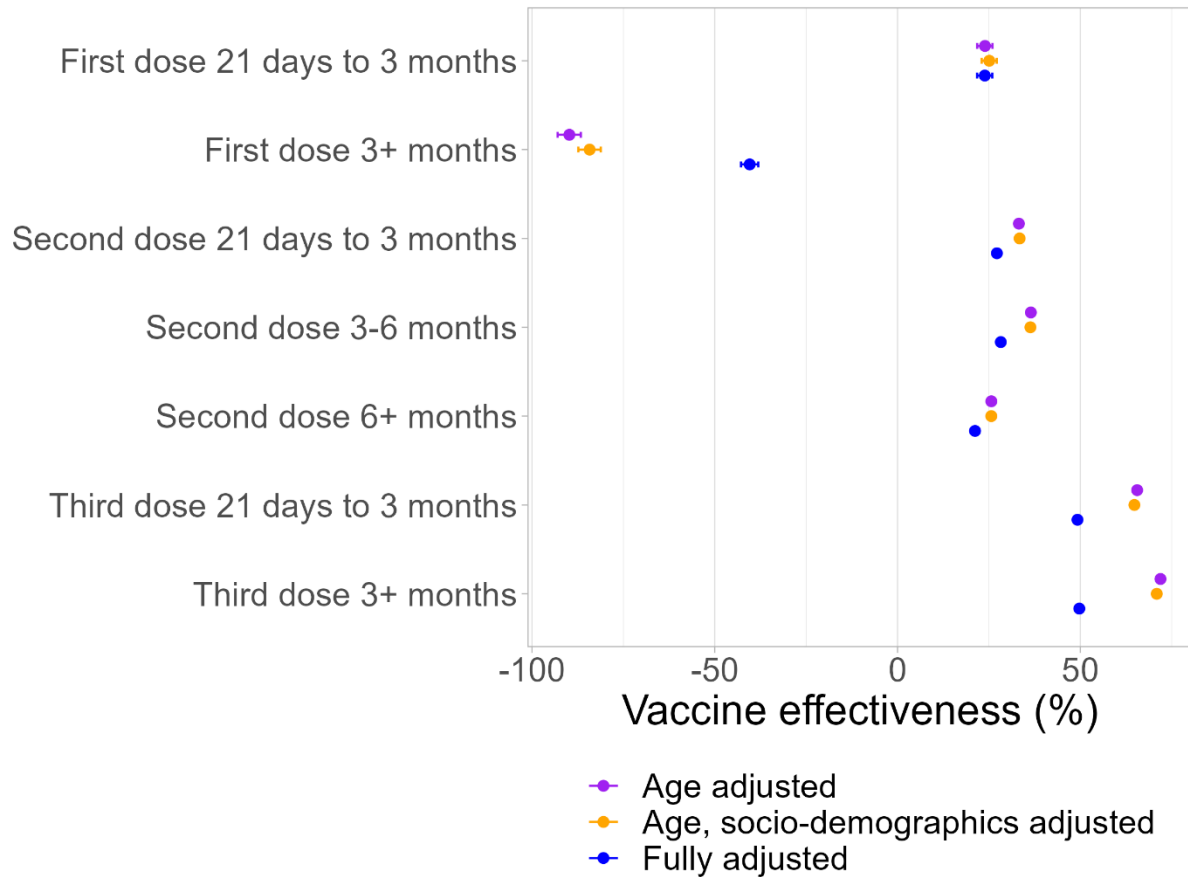
Supplementary Table 3 | Key worker status SOC 2020 groupings

Key worker status	SOC 2020 unit groups	
Health professionals	2211	Generalist medical practitioners
	2212	Specialist medical practitioners
	2225	Clinical psychologists
	2226	Other psychologists
	2251	Pharmacists
Health associate professionals	2231	Midwifery nurses
	2232	Registered community nurses
	2233	Registered specialist nurses
	2234	Registered nurse practitioners
	2235	Registered mental health nurses
	2236	Registered children's nurses
	2237	Other registered nursing professionals
	-	-
	2254	Medical radiographers
	2255	Paramedics
	2256	Podiatrists
	3219	Health associate professionals n.e.c.
	3212	Pharmaceutical technicians
	3213	Medical and dental technicians
	1171	Health services and public health managers and directors
	1231	Health care practice managers
	2221	Physiotherapists
	2259	Other health professionals n.e.c.
	2222	Occupational therapists
	2223	Speech and language therapists
	2229	Therapy professionals n.e.c.
	2252	Optometrists
	2253	Dental practitioners
	6133	Dental nurses
	3240	Veterinary nurses
	2240	Veterinarians
	3211	Dispensing opticians
	3214	Complementary health associate professionals
	2224	Psychotherapists and cognitive behaviour therapists
	2225	Clinical psychologists
	2226	Other psychologists
	7114	Pharmacy and optical dispensing assistants
Support staff	4211	Medical secretaries
	6131	Nursing auxiliaries and assistants
	6132	Ambulance staff (excluding paramedics)
	7114	Pharmacy and optical dispensing assistants
	9262	Hospital porters
Social care	1172	Social services managers and directors
	1232	Residential, day and domiciliary care managers and proprietors

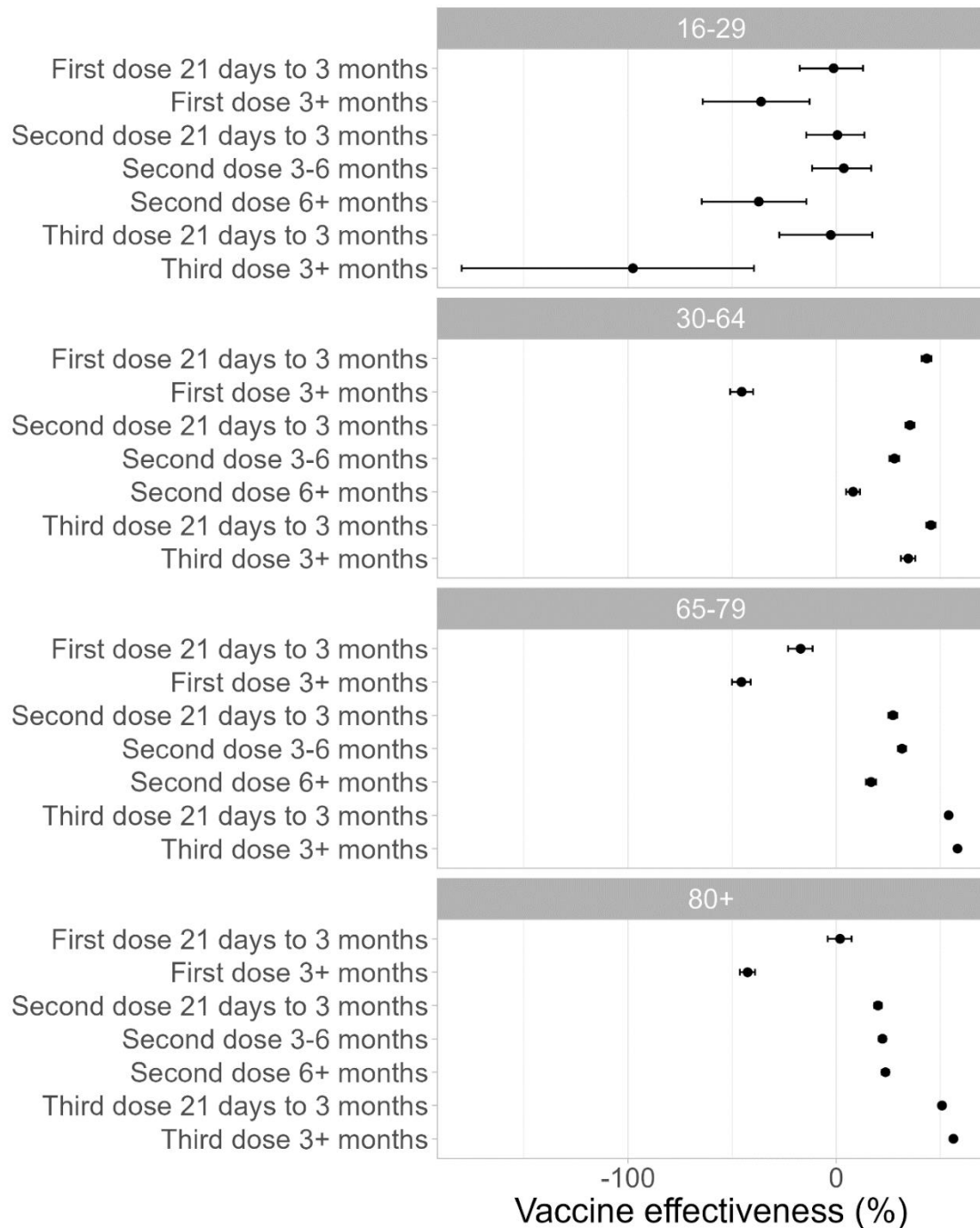
	2461	Social workers
	2463	Clergy
	3221	Youth and community workers
	2464	Youth work professionals
	3223	Housing officers
	2469	Welfare professionals n.e.c.
	3229	Welfare and housing associate professionals n.e.c.
	6134	Houseparents and residential wardens
	6135	Care workers and home carers
	6136	Senior care workers
	6137	Care escorts
	6232	Caretakers
	6138	Undertakers, mortuary and crematorium assistants
Education	2311	Higher education teaching professionals
	2312	Further education teaching professionals
	2313	Secondary education teaching professionals
	2314	Primary education teaching professionals
	2315	Nursery education teaching professionals
	2316	Special and additional needs education teaching professionals
	2317	Teachers of english as a foreign language
	2321	Head teachers and principals
	2322	Education managers
	2324	Early education and childcare services managers
	2329	Other educational professionals n.e.c
	1233	Early education and childcare services proprietors
	2323	Education advisers and school inspectors
	2319	Teaching professionals n.e.c.
	6111	Early education and childcare assistants
	3232	Early education and childcare practitioners
	6112	Teaching assistants
	3231	Higher level teaching assistants
	6113	Educational support assistants
Food and retail distribution	7131	Shopkeepers and owners - retail and wholesale
	5431	Butchers
	5432	Bakers and flour confectioners
	5433	Fishmongers and poultry dressers
	7111	Sales and retail assistants
	7112	Retail cashiers and check-out operators
	7132	Sales supervisors - retail and wholesale
	9241	Shelf fillers
	9249	Elementary sales occupations n.e.c.
	1242	Managers in storage and warehousing
	1150	Managers and directors in retail and wholesale
Food production	8111	Food, drink and tobacco process operatives
	1211	Managers and proprietors in agriculture and horticulture
	1212	Managers and proprietors in forestry, fishing and related services

	5111	Farmers
	5112	Horticultural trades
	5119	Agricultural and fishing trades n.e.c.
	9111	Farm workers
	9119	Fishing and other elementary agriculture occupations n.e.c.
Taxi and cab drivers and chauffeurs	8213	Taxi and cab drivers and chauffeurs
Bus and coach drivers	8212	Bus and coach drivers
Van drivers	8214	Delivery drivers and couriers
Other transport workers	1241	Managers in transport and distribution
	8231	Train and tram drivers
	6214	Rail travel assistants
	8211	Large goods vehicle drivers
	8234	Rail transport operatives
	9211	Postal workers, mail sorters and messengers
	6214	Rail travel assistants
	8232	Marine and waterways transport operatives
	8233	Air transport operatives
	8239	Other drivers and transport operatives n.e.c.
	8219	Road transport drivers n.e.c.
Police and Protective Services	1162	Senior police officers
	1163	Senior officers in fire, ambulance, prison and related services
	3311	Non-commissioned officers and other ranks
	3312	Police officers (sergeant and below)
	3313	Fire service officers (watch manager and below)
	3314	Prison service officers (below principal officer)
	3319	Protective service associate professionals n.e.c.
	2462	Probation officers
Sanitary workers	6311	Police community support officers
	9221	Window cleaners
	9222	Street cleaners
	9223	Cleaners and domestics
	9225	Refuse and salvage occupations
	9229	Elementary cleaning occupations n.e.c.
Non-essential workers	9224	Launderers, dry cleaners and pressers
		All other codes

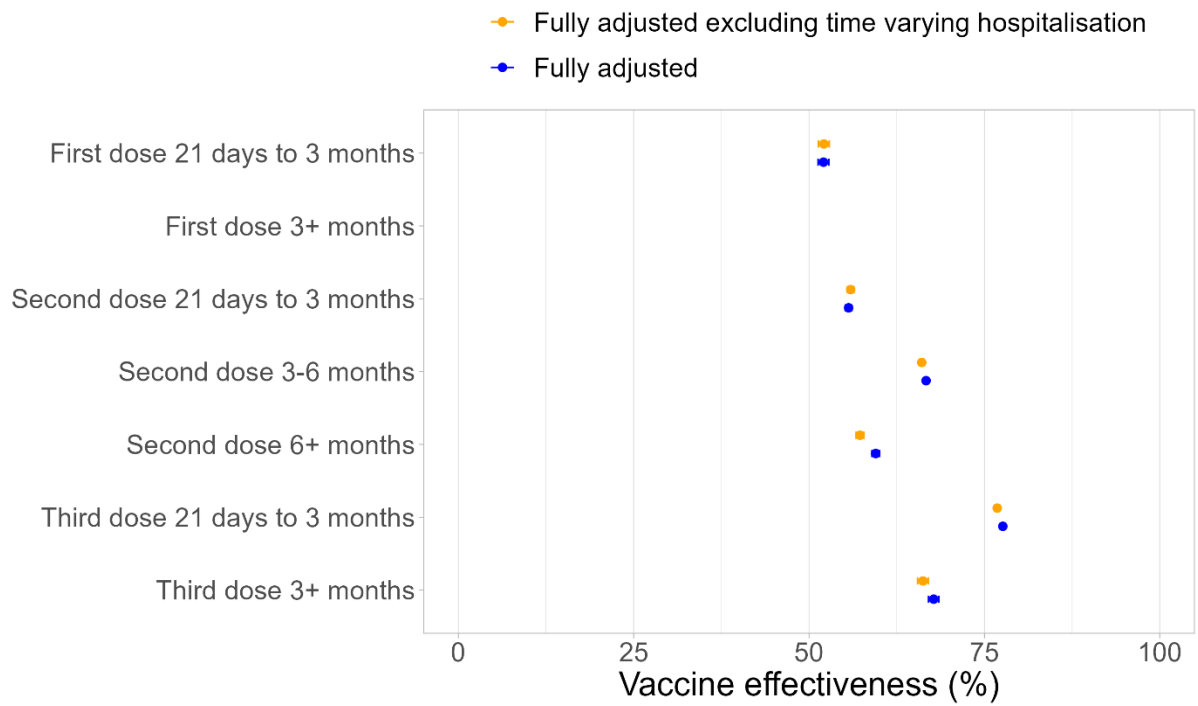
Supplementary Figure 1 | Non-COVID-19 VE against death for the study population. The model adjustments are age (as a natural spline), plus socio-demographic characteristics (sex, region, ethnicity, religion, IMD decile, NSSEC category, highest qualification, English language proficiency, key worker status), plus health-related characteristics (disability, self-reported health, care home residency, number of QCovid comorbidities (grouped), BMI category, frailty flag and hospitalisation within the last 21 days).



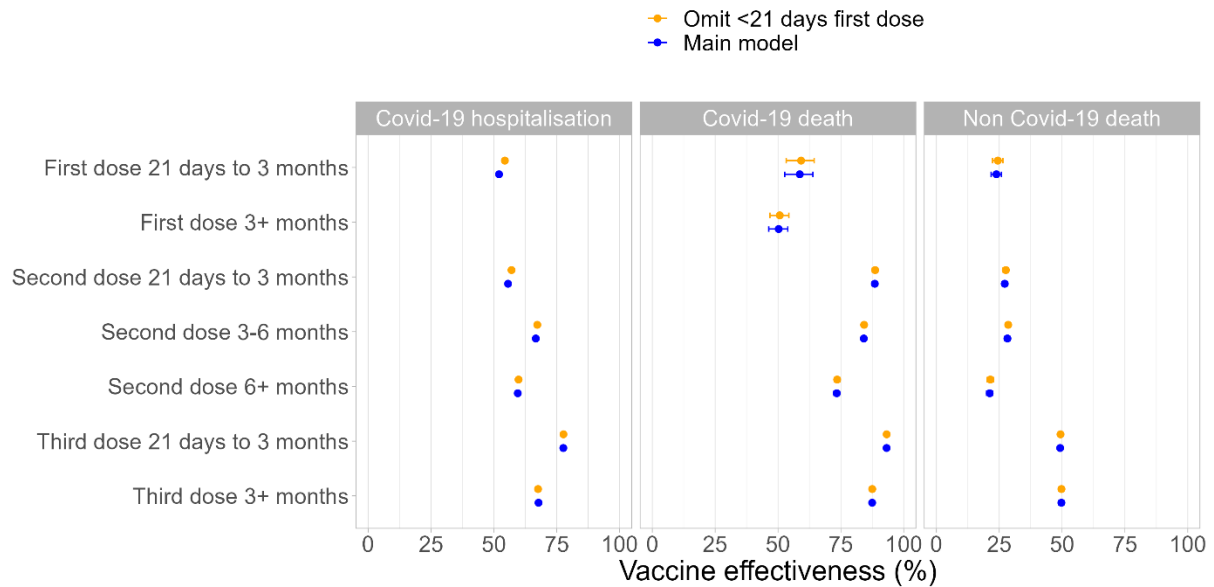
Supplementary Figure 2 | Vaccine effectiveness against non-COVID-19 mortality, stratified by age group. The model is fully adjusted. The covariates adjusted for are age (as a natural spline), sex, region, ethnicity, religion, IMD decile, NSSEC category, highest qualification, English language proficiency, key worker status, disability, self-reported health, care home residency, number of QCovid comorbidities (grouped), BMI category, frailty flag and hospitalisation within the last 21 days.



Supplementary Figure 3 | Vaccine effectiveness against COVID-19 hospitalisation, omitting the time-varying variable for current hospitalisation or hospitalisation in the preceding 21 days. All other covariates are adjusted for. These are age (as a natural spline), sex, region, ethnicity, religion, IMD decile, NSSEC category, highest qualification, English language proficiency, key worker status, disability, self-reported health, care home residency, number of QCovid comorbidities (grouped), BMI category and frailty flag.



Supplementary Figure 4 | Vaccine effectiveness against all outcomes, omitting the first 21 days after the first dose from the unvaccinated vaccination status. The model was adjusted for age (as a natural spline), plus socio-demographic characteristics (sex, region, ethnicity, religion, IMD decile, NSSEC category, highest qualification, English language proficiency, key worker status), plus health-related characteristics (disability, self-reported health, care home residency, number of QCovid comorbidities (grouped), BMI category, frailty flag and hospitalisation within the last 21 days.



Supplementary Figure 6 | Vaccine effectiveness against COVID-19 hospitalisation, by variant period, stratified by age group. The model is adjusted for age (as a natural spline), sex, region, ethnicity, religion, IMD decile, NSSEC category, highest qualification, English language proficiency, key worker status, disability, self-reported health, care home residency, number of QCovid comorbidities (grouped), BMI category, frailty flag and hospitalisation within the last 21 days. Vaccination status is interacted with variant period.

