

SUPPLEMENTAL MATERIAL

Effectiveness of BNT162b2 mRNA, mRNA-1273, and ChAdOx1 nCoV-19 vaccines against severe COVID-19 outcomes in a nationwide mass vaccination setting: a cohort study of 11 million vaccinated adults aged 50 years or older and their controls

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Table 1. Definition of covariables

Most covariables were defined based on ICD-10 codes and codes used for drugs.

- ICD-10 codes: any occurrence in 5 years prior to 2021 is used.
- ATC/CIP7/CIP13/UCD7/UCD13 codes (for drugs): having 3 dispensings or 2 when at least one concerned the dispensing of a large pack size) in the year 2020 is used.

Other codes were also detailed:

- o CCAM (*classification commune des actes médicaux*) for medical procedures
- o LPP (*liste des produits et prestations*) for medical devices or equipment
- o NABM (*nomenclature des actes de biologie médicale*) for medical biology laboratory
- o *Nature de prestations* for primary care delivery
- o LOINC (logical observation identifiers names and codes) for SARS-CoV-2 tests
- o GHM (groupe homogène de malade) for hospital stays, a French version of diagnosis-related groups

Further details are available in a published article (Rachas et al, medRxiv, 2020) and upon request.

Covariates	Codes
History of positive SARS-CoV-2	
<u>SARS-CoV-2 test results</u> LOINC	Reverse transcription PCR: 94309-2, 94500-6, 94845-5 Antigen: 94558-4 Antibody: 94507-1, 94508-9, 94563-4, 94564-2, 94762-2
<u>COVID-19-related hospitalization</u> ICD-10	U07.10 (COVID-19, respiratory form, virus identified), U07.11 (COVID-19, respiratory form, virus not identified), U07.14 (COVID-19, other clinical forms, virus identified), U07.15 (COVID-19, other clinical forms, virus not identified), U04.9 (severe acute respiratory syndrome) and exclusion of hospital stays with following GHM: iterative treatments (dialysis, chemotherapy, radiotherapy, immunotherapy), obstetrics, diseases of childhood and neonates.
Frailty* Primary care delivery LPP ICD-10	Having one of the following items: - ≥150 days with nursing care acts - oral or parenteral nutrition (LPP) - oxygen at home (LPP) - anti-decubitus equipment at home (LPP) - nursing home bed (LPP) - wheelchair (LPP) - ICD-10: E43, E44.0, R29.6, G81, G82, G83, R26.2, R26.30, Z74, R15, R32, L89, M80
Alcohol-related conditions ICD-10	E24.4, E51.2, F10, G31.2, G62.1, G72.1, I42.6, K29.2, K70, K86.0, R78.0, T51, X45, X65, Y15, Y90, Y91, Y57.3, Z50.2, Z71.4, or Z72.1
ATC	N07BB01, N07BB03, N07BB04, N07BB05 at least 2 dispensings in the 5 years preceding 2021. M03BX01 (baclofen) without following neurological disease (ICD-10): C70, C71, C79.3, C79.4, D32, D33, D42, D43, G04, G05, G06, G09, G12, G13, G24, G25, G26, G31, G32, G35, G36, G37, G46, G80, G81, G82, G83, G91, G93, G95
Laboratory test (NABM)	516, 517, 519 (gamma-GT)
Cardiovascular risk factors	
Smoking-related conditions	
ICD-10	Z716 F17 T652 Z720
ATC	N07BA
Primary care delivery	Tobacco consultation service (9566, 9526, 9527) in the 5 years preceding 2021 (at least once)
Hypertension	
ATC	C02AB02, C02AC01, C02AC02, C02AC05, C02AC06, C02CA01, C02CA06, C02DC01, C02LA01, C03AA01, C03AA03, C03BA04, C03BA10, C03BA11, C03BX03, C03CA01, C03CA02, C03CA03, C03DA01, C03DB01, C03EA, C03EA01, C03EA04, C07AA02, C07AA03, C07AA05, C07AA06, C07AA12, C07AA15, C07AA16, C07AA23, C07AB02, C07AB03, C07AB04, C07AB05, C07AB07, C07AB08, C07AB12, C07AG01, C07BA02, C07BB02, C07BB03,

Covariates	Codes
	C07BB07, C07BB12, C07CA03, C07DA06, C07FB02, C07FB03, C08CA01, C08CA02, C08CA03, C08CA04, C08CA05, C08CA08, C08CA09, C08CA11, C08CA13, C08CX01, C08DA01, C08DB01, C08GA02, C09AA01, C09AA02, C09AA03, C09AA04, C09AA05, C09AA06, C09AA07, C09AA08, C09AA09, C09AA10, C09AA13, C09AA15, C09AA16, C09BA01, C09BA02, C09BA03, C09BA04, C09BA05, C09BA06, C09BA07, C09BA09, C09BA15, C09BB02, C09BB04, C09BB10, C09BX02, C09CA01, C09CA02, C09CA03, C09CA04, C09CA06, C09CA07, C09CA08, C09DA01, C09DA02, C09DA03, C09DA04, C09DA06, C09DA07, C09DA08, C09DB01, C09DB02, C09DB04, C09XA02, C09XA52, C10BX03
Diabetes mellitus	
ICD-10	E10, E11, E12, E13, E14 G59.0, G63.2, G73.0, G99.0, H28.0, H36.0, I79.2, L97, M14.2, M14.6, N08.3
ATC	A10 excluding benfluorex (A10BX06)
Dyslipidemia	
ICD-10	E78
ATC	C10
Obesity-related conditions	
ICD-10	E66 excluding E66.03, E66.13, E66.83, E66.93 (since 2006)
CCAM	HFCA001, HFCC003, HFFA001, HFFA011, HFFC004, HFFC018, HFGC900, HFKA001, HFKA002, HFKC001, HFLC900, HFLE002, HFMA009, HFMA010, HFMA011, HFMC006, HFMC007, HFMC008, HGCA009, HGCC027 (bariatric surgery)
Cardiovascular diseases	
Acute or chronic coronary artery disease	
ICD-10	I20, I21, I22, I23, I24, I25
Heart failure	
ICD-10	I50, I11.0, I13.0, I13.2, I13.9, K76.1, J81 I50, I11, I13 only for those included in the list of long-term diseases
Cardiac rhythm disorder	
ICD-10	I44, I45, I47-I49
Valvular heart disease	
ICD-10	I05-I08, I34-I39
Occlusive peripheral arterial disease	
ICD-10	I70.2, I73.9, I74.0, I74.3, I74.4, I74.5 I70, I73, I74 only for those included in the list of long-term diseases
Stroke	
ICD-10	I60-I64, I67-I69
Pulmonary embolism	
ICD-10	I26
Chronic respiratory conditions	
ICD-10	J40, J41, J42, J43, J44, J45, J46, J47, J96 (excluding J96.0, J96.9), J98
ATC	R03 (drugs for obstructive airway diseases)
Dialysis	
ICD-10	N18 (long-term diseases), Z940
CCAM	JAEA003, HNEA002 JVJB001, JVJF004, JVJF008, JVRP004, JVRP007, JVRP008, YYYY007
GHM	27C06, 24M39Z, 11M17 11K02, 28Z01-28Z04
Billing code for dialysis session conducted at home, self-care dialysis, in a dialysis unit under medical supervision	D11-D16, D20-24
Kidney transplant	
ICD-10	Z940
CCAM	JAEA003, HNEA002
ATC	L04AA06, L04AA10, L04AA18, L04AD01, L04AD02, L04AX01
GHM	27C06Z, 27C061, 27C062, 27C063, 27C064, 24M39Z, 11M171, 11M172, 11M173, 11M174
Liver failure	
ICD-10	B18, I85, K70 to K76, Z94.4
ATC/CIP7/CIP13/UCD7/UCD13 NABM CCAM	Having one of the following items: - 3 reimbursements of a specific treatment for chronic hepatitis B: o ATC: J05AF08, J05AF10, J05AF11

Covariates	Codes
	<ul style="list-style-type: none"> ○ UCD7: 9212525, 9212531 ○ CIP7: 3519671, 3519694 - 1 reimbursement on the same date of (L03AB05, L03AB09, L03AB10, L03AB11) and J05AB04 - 1 reimbursement of a direct-acting antiviral against hepatitis C virus (HCV) (J05AE11, J05AE12, J05AE14, J05AP08, J05AP51, J05AP55, J05AP56, J05AX14, J05AX15, J05AX16, J05AX65, J05AX67, J05AX68, J05AX (CIP13: 3400930108765, UCD13: 3400894287391)) - 1 reimbursement of HCV genotyping (4125) - 3 reimbursements of quantitative HCV RNA PCR (4124) - 2 reimbursements of an assessment of liver fibrosis <ul style="list-style-type: none"> ○ NABM: 1000, 1001, 1002 ○ CCAM: HLQM002, HLHB001, HLHH001, HLHH005, HLHJ003
Active cancer (in 2019 and 2020)	
ICD-10	C00-D09 Z08, Z51.0, Z51.1
Depression	
ICD-10	F30-F34, F38-F45, F48
ATC/CIP13	N06A (excluding CIP13 3400933338022), N05AN01, N03AG02 CIP13: 3400934876233, 3400934876691, 340093544427
Psychosis	
ICD-10	F20 to F25, F28, F29
ATC/CIP13	N05A (excluding N05AN01, N05AL06, 3400932896332 (CIP13))
Dementia	
ICD-10	F00, F01, F02, F03, F05.1, G30
ATC	N06DA04, N06DX01
Epilepsy	
ICD-10	G40, G41
Parkinson's disease	
ICD-10	G20, F02.3
ATC/CIP13	34009333284398 (CIP13), N04BA02, N04BA03, N04BC01, N04BC02, N04BC04, N04BC07, N04BD01, N04BD02, N04BX01, N04BX02 (excluding the following CIP7: 3644494, 3644502, 3644525, 3644548, 3914841, 3918394, 3918402, 3918425, 3918448, 3927163, 3927217, 3927269, 39227 298, 3933442, 3933502, 3933583, 3933637, 3935079, 3935263, 3935346 , 3005943)
Inflammatory bowel disease	
ICD-10	K50, K51, M07.4, M07.5
Rheumatoid arthritis	
ICD-10	M06, M06, M08 (excluding M08.1), M09
Ankylosing spondylitis	
ICD-10	M07 (excluding M07.4, M07.5), M08.1, M45, M46

*Frailty variable was created using the SNDS following published recommendations (Faurot KR et al, Pharmacoepidemiol Drug Saf, 2015; Kim et al, Pharmacoepidemiol Drug Saf, 2014) and was firstly applied in a study on the association between vitamin K agonists and myelodysplastic syndrome (Neumann et al, Blood, 2021).

Table 2. Demographic and clinical characteristics of vaccinated individuals by BNT162b2 mRNA vaccine and unvaccinated controls at baseline

		BNT162b2 vaccine		Standardized difference
		No (n = 7,161,658)	Yes (n = 7,161,658)	
Matching variables				
Age (years)	Mean (SD)	72.70 (11.00)	72.70 (11.00)	0.00000
Age categories	50-54	377,325 (5.3)	377,325 (5.3)	
	55-59	537,178 (7.5)	537,178 (7.5)	
	60-64	846,820 (11.8)	846,820 (11.8)	
	65-69	1,049,776 (14.7)	1,049,776 (14.7)	
	70-74	1,347,207 (18.8)	1,347,207 (18.8)	
	75-79	978,840 (13.7)	978,840 (13.7)	
	80-84	856,384 (12.0)	856,384 (12.0)	
	85-89	669,000 (9.3)	669,000 (9.3)	
	90 or more	499,128 (7.0)	499,128 (7.0)	
Sex	Men	3,046,267 (42.5)	3,046,267 (42.5)	0.00000
	Women	4,115,391 (57.5)	4,115,391 (57.5)	
Residence area	Auvergne-Rhône-Alpes	841,801 (11.8)	841,801 (11.8)	0.00000
	Bourgogne-Franche-Comté	281,988 (3.9)	281,988 (3.9)	
	Bretagne	391,114 (5.5)	391,114 (5.5)	
	Centre-Val de Loire	296,583 (4.1)	296,583 (4.1)	
	Corse	54,351 (0.8)	54,351 (0.8)	
	Grand Est	589,212 (8.2)	589,212 (8.2)	
	Hauts-de-France	577,660 (8.1)	577,660 (8.1)	
	Ile-de-France	1,082,060 (15.1)	1,082,060 (15.1)	
	Normandie	367,197 (5.1)	367,197 (5.1)	
	Nouvelle-Aquitaine	738,685 (10.3)	738,685 (10.3)	
	Occitanie	745,627 (10.4)	745,627 (10.4)	
	Overseas departments	107,312 (1.5)	107,312 (1.5)	
	Pays de la Loire	418,607 (5.8)	418,607 (5.8)	
	Provence-Alpes-Côte d'Azur	669,461 (9.3)	669,461 (9.3)	
Nursing home	No	6,973,945 (97.4)	6,973,945 (97.4)	0.00000
	Yes, w/ inpatient pharmacy	30,819 (0.4)	30,819 (0.4)	
	Yes, w/o inpatient pharmacy	156,894 (2.2)	156,894 (2.2)	
Social deprivation index (quintiles)	1 (least deprived)	1,257,486 (17.6)	1,489,831 (20.8)	0.12028
	2	1,321,002 (18.4)	1,375,859 (19.2)	
	3	1,449,205 (20.2)	1,428,226 (19.9)	
	4	1,500,897 (21.0)	1,409,661 (19.7)	
	5 (most deprived)	1,460,106 (20.4)	1,281,541 (17.9)	
	Unknown	172,962 (2.4)	176,540 (2.4)	

		BNT162b2 vaccine		Standardized difference
		No (n = 7,161,658)	Yes (n = 7,161,658)	
History of COVID-19 status (hospitalisation, screening tests)	No	6,794,490 (94.9)	6,967,402 (97.3)	-0.12466
	Yes	367,168 (5.1)	194,256 (2.7)	
Influenza vaccines in 2018 or 2019	No	5,049,840 (70.5)	4,109,101 (57.4)	0.27617
	Yes	2,111,818 (29.5)	3,052,557 (42.6)	
Frailty	No	6,489,092 (90.6)	6,584,152 (91.9)	-0.04704
	Yes	672,566 (9.4)	577,506 (8.1)	
Alcohol-related conditions	No	7,070,172 (98.7)	7,093,321 (99.0)	-0.03078
	Yes	91,486 (1.3)	68,337 (1.0)	
Cardiovascular risk factors				
Smoking-related conditions	No	6,885,184 (96.1)	6,873,641 (96.0)	0.00828
	Yes	276,474 (3.9)	288,017 (4.0)	
Hypertension	No	3,752,796 (52.4)	3,489,021 (48.7)	0.07372
	Yes	3,408,862 (47.6)	3,672,637 (51.3)	
Diabetes mellitus	No	6,126,084 (85.5)	6,144,454 (85.8)	-0.00732
	Yes	1,035,574 (14.5)	1,017,204 (14.2)	
Dyslipidemia	No	5,260,844 (73.5)	4,947,355 (69.1)	0.09685
	Yes	1,900,814 (26.5)	2,214,303 (30.9)	
Obesity-related conditions	No	7,072,347 (98.8)	7,053,734 (98.5)	0.02230
	Yes	89,311 (1.2)	107,924 (1.5)	
Cardiovascular diseases				
Coronary heart disease	No	6,587,791 (92.0)	6,495,636 (90.7)	0.04577
	Yes	573,867 (8.0)	666,022 (9.3)	
Heart failure	No	6,907,936 (96.5)	6,934,751 (96.8)	-0.02079
	Yes	253,722 (3.5)	226,907 (3.2)	
Cardiac rhythm disorder	No	6,625,907 (92.5)	6,589,096 (92.0)	0.01924
	Yes	535,751 (7.5)	572,562 (8.0)	
Valvular heart disease	No	6,953,191 (97.1)	6,932,388 (96.8)	0.01688
	Yes	208,467 (2.9)	229,270 (3.2)	
Occlusive peripheral arterial disease	No	6,963,110 (97.2)	6,964,812 (97.3)	-0.00145
	Yes	198,548 (2.8)	196,846 (2.7)	

		BNT162b2 vaccine		Standardized difference
		No (n = 7,161,658)	Yes (n = 7,161,658)	
Stroke	No	6,896,241 (96.3)	6,902,632 (96.4)	-0.00475
	Yes	265,417 (3.7)	259,026 (3.6)	
Pulmonary embolism	No	7,120,381 (99.4)	7,115,603 (99.4)	0.00857
	Yes	41,277 (0.6)	46,055 (0.6)	
Other comorbidities				
Chronic respiratory conditions	No	6,545,415 (91.4)	6,491,622 (90.6)	0.02627
	Yes	616,243 (8.6)	670,036 (9.4)	
Dialysis	No	7,154,269 (99.9)	7,141,004 (99.7)	0.04191
	Yes	7,389 (0.1)	20,654 (0.3)	
Kidney transplant	No	7,157,321 (99.9)	7,147,617 (99.8)	0.03786
	Yes	4,337 (0.1)	14,041 (0.2)	
Liver failure	No	7,089,901 (99.0)	7,085,471 (98.9)	0.00612
	Yes	71,757 (1.0)	76,187 (1.1)	
Active cancer	No	6,844,908 (95.6)	6,737,753 (94.1)	0.06761
	Yes	316,750 (4.4)	423,905 (5.9)	
Depression	No	6,299,613 (88.0)	6,235,680 (87.1)	0.02701
	Yes	862,045 (12.0)	925,978 (12.9)	
Psychosis	No	7,035,499 (98.2)	7,052,876 (98.5)	-0.01910
	Yes	126,159 (1.8)	108,782 (1.5)	
Dementia	No	6,919,652 (96.6)	6,945,372 (97.0)	-0.02041
	Yes	242,006 (3.4)	216,286 (3.0)	
Epilepsy	No	7,116,180 (99.4)	7,118,810 (99.4)	-0.00469
	Yes	45,478 (0.6)	42,848 (0.6)	
Parkinson's disease	No	7,073,499 (98.8)	7,071,416 (98.7)	0.00262
	Yes	88,159 (1.2)	90,242 (1.3)	
Inflammatory bowel disease	No	7,131,749 (99.6)	7,119,801 (99.4)	0.02363
	Yes	29,909 (0.4)	41,857 (0.6)	
Rheumatoid arthritis	No	7,091,302 (99.0)	7,075,693 (98.8)	0.02098
	Yes	70,356 (1.0)	85,965 (1.2)	
Ankylosing spondylitis	No	7,131,515 (99.6)	7,118,103 (99.4)	0.02618
	Yes	30,143 (0.4)	43,555 (0.6)	

Table 3. Demographic and clinical characteristics of vaccinated individuals by mRNA-1273 vaccine and unvaccinated controls at baseline

		mRNA-1273 vaccine		Standardized difference
		No (n = 856,599)	Yes (n = 856,599)	
Matching variables				
Age (years)	Mean (SD)	71.35 (10.78)	71.35 (10.78)	0.00000
Age categories	50-54	55,167 (6.4)	55,167 (6.4)	
	55-59	75,542 (8.8)	75,542 (8.8)	
	60-64	107,143 (12.5)	107,143 (12.5)	
	65-69	132,543 (15.5)	132,543 (15.5)	
	70-74	183,281 (21.4)	183,281 (21.4)	
	75-79	99,719 (11.6)	99,719 (11.6)	
	80-84	88,274 (10.3)	88,274 (10.3)	
	85-89	69,720 (8.1)	69,720 (8.1)	
	90 or more	45,210 (5.3)	45,210 (5.3)	
Sex	Men	370,469 (43.2)	370,469 (43.2)	0.00000
	Women	486,130 (56.8)	486,130 (56.8)	
Residence area	Auvergne-Rhône-Alpes	107,028 (12.5)	107,028 (12.5)	0.00000
	Bourgogne-Franche-Comté	67,089 (7.8)	67,089 (7.8)	
	Bretagne	34,373 (4.0)	34,373 (4.0)	
	Centre-Val de Loire	34,651 (4.0)	34,651 (4.0)	
	Corse	5,480 (0.6)	5,480 (0.6)	
	Grand Est	85,690 (10.0)	85,690 (10.0)	
	Hauts-de-France	53,838 (6.3)	53,838 (6.3)	
	Ile-de-France	149,954 (17.5)	149,954 (17.5)	
	Normandie	45,665 (5.3)	45,665 (5.3)	
	Nouvelle-Aquitaine	92,921 (10.8)	92,921 (10.8)	
	Occitanie	64,099 (7.5)	64,099 (7.5)	
	Overseas departments	152 (0.0)	152 (0.0)	
	Pays de la Loire	31,969 (3.7)	31,969 (3.7)	
Provence-Alpes-Côte d'Azur	83,690 (9.8)	83,690 (9.8)		
Nursing home	No	856,426 (100)	856,426 (100)	0.00000
	Yes, w/ inpatient pharmacy	29 (0.0)	29 (0.0)	
	Yes, w/o inpatient pharmacy	144 (0.0)	144 (0.0)	
Social deprivation index (quintiles)	1 (least deprived)	160,171 (18.7)	189,927 (22.2)	0.13181
	2	159,929 (18.7)	176,113 (20.6)	
	3	173,172 (20.2)	175,924 (20.5)	
	4	177,979 (20.8)	164,960 (19.3)	
	5 (most deprived)	178,409 (20.8)	142,471 (16.6)	
	Unknown	6,939 (0.8)	7,204 (0.8)	

		mRNA-1273 vaccine		Standardized difference
		No (n = 856,599)	Yes (n = 856,599)	
History of COVID-19 status (hospitalisation, screening tests)	No	814,740 (95.1)	834,137 (97.4)	-0.11933
	Yes	41,859 (4.9)	22,462 (2.6)	
Influenza vaccines in 2018 or 2019	No	624,005 (72.8)	509,056 (59.4)	0.28645
	Yes	232,594 (27.2)	347,543 (40.6)	
Frailty	No	786,064 (91.8)	792,411 (92.5)	-0.02753
	Yes	70,535 (8.2)	64,188 (7.5)	
Alcohol-related conditions	No	845,470 (98.7)	847,900 (99.0)	-0.02653
	Yes	11,129 (1.3)	8,699 (1.0)	
Cardiovascular risk factors				
Smoking-related conditions	No	821,403 (95.9)	819,372 (95.7)	0.01178
	Yes	35,196 (4.1)	37,227 (4.3)	
Hypertension	No	463,865 (54.2)	426,444 (49.8)	0.08752
	Yes	392,734 (45.8)	430,155 (50.2)	
Diabetes mellitus	No	736,501 (86.0)	736,214 (85.9)	0.00096
	Yes	120,098 (14.0)	120,385 (14.1)	
Dyslipidemia	No	633,584 (74.0)	593,300 (69.3)	0.10445
	Yes	223,015 (26.0)	263,299 (30.7)	
Obesity-related conditions	No	845,490 (98.7)	842,650 (98.4)	0.02762
	Yes	11,109 (1.3)	13,949 (1.6)	
Cardiovascular diseases				
Coronary heart disease	No	791,566 (92.4)	779,875 (91.0)	0.04956
	Yes	65,033 (7.6)	76,724 (9.0)	
Heart failure	No	830,419 (96.9)	832,957 (97.2)	-0.01763
	Yes	26,180 (3.1)	23,642 (2.8)	
Cardiac rhythm disorder	No	799,495 (93.3)	794,712 (92.8)	0.02196
	Yes	57,104 (6.7)	61,887 (7.2)	
Valvular heart disease	No	834,614 (97.4)	832,135 (97.1)	0.01782
	Yes	21,985 (2.6)	24,464 (2.9)	
Occlusive peripheral arterial disease	No	834,530 (97.4)	834,086 (97.4)	0.00326
	Yes	22,069 (2.6)	22,513 (2.6)	
Stroke	No	829,053 (96.8)	829,548 (96.8)	-0.00329
	Yes	27,546 (3.2)	27,051 (3.2)	

		mRNA-1273 vaccine		Standardized difference
		No (n = 856,599)	Yes (n = 856,599)	
Pulmonary embolism	No	852,066 (99.5)	851,504 (99.4)	0.00878
	Yes	4,533 (0.5)	5,095 (0.6)	
Other comorbidities				
Chronic respiratory conditions	No	785,035 (91.6)	777,945 (90.8)	0.02927
	Yes	71,564 (8.4)	78,654 (9.2)	
Dialysis	No	855,875 (99.9)	853,520 (99.6)	0.05844
	Yes	724 (0.1)	3,079 (0.4)	
Kidney transplant	No	856,091 (99.9)	854,574 (99.8)	0.04610
	Yes	508 (0.1)	2,025 (0.2)	
Liver failure	No	848,032 (99.0)	847,291 (98.9)	0.00851
	Yes	8,567 (1.0)	9,308 (1.1)	
Active cancer	No	820,682 (95.8)	806,380 (94.1)	0.07646
	Yes	35,917 (4.2)	50,219 (5.9)	
Depression	No	760,797 (88.8)	752,088 (87.8)	0.03164
	Yes	95,802 (11.2)	104,511 (12.2)	
Psychosis	No	844,183 (98.6)	846,039 (98.8)	-0.01884
	Yes	12,416 (1.4)	10,560 (1.2)	
Dementia	No	838,912 (97.9)	843,824 (98.5)	-0.04340
	Yes	17,687 (2.1)	12,775 (1.5)	
Epilepsy	No	851,649 (99.4)	851,720 (99.4)	-0.00110
	Yes	4,950 (0.6)	4,879 (0.6)	
Parkinson's disease	No	847,775 (99.0)	847,400 (98.9)	0.00429
	Yes	8,824 (1.0)	9,199 (1.1)	
Inflammatory bowel disease	No	852,833 (99.6)	851,417 (99.4)	0.02293
	Yes	3,766 (0.4)	5,182 (0.6)	
Rheumatoid arthritis	No	848,485 (99.1)	846,632 (98.8)	0.02117
	Yes	8,114 (0.9)	9,967 (1.2)	
Ankylosing spondylitis	No	852,848 (99.6)	851,370 (99.4)	0.02390
	Yes	3,751 (0.4)	5,229 (0.6)	

Table 4. Demographic and clinical characteristics of vaccinated individuals by ChAdOx1 nCoV-19 vaccine and unvaccinated controls at baseline

		ChAdOx1 nCoV-19 vaccine		Standardized difference
		No (n = 3,238,575)	Yes (n = 3,238,575)	
Matching variables				
Age (years)	Mean (SD)	65.12 (7.55)	65.12 (7.55)	0.00000
Age categories	50-54	171,769 (5.3)	171,769 (5.3)	
	55-59	643,022 (19.9)	643,022 (19.9)	
	60-64	769,338 (23.8)	769,338 (23.8)	
	65-69	774,172 (23.9)	774,172 (23.9)	
	70-74	684,629 (21.1)	684,629 (21.1)	
	75-79	74,189 (2.3)	74,189 (2.3)	
	80-84	47,256 (1.5)	47,256 (1.5)	
	85-89	40,975 (1.3)	40,975 (1.3)	
	90 or more	33,225 (1.0)	33,225 (1.0)	
Sex	Men	1,659,165 (51.2)	1,659,165 (51.2)	0.00000
	Women	1,579,410 (48.8)	1,579,410 (48.8)	
Residence area	Auvergne-Rhône-Alpes	384,565 (11.9)	384,565 (11.9)	0.00000
	Bourgogne-Franche-Comté	139,519 (4.3)	139,519 (4.3)	
	Bretagne	203,205 (6.3)	203,205 (6.3)	
	Centre-Val de Loire	133,607 (4.1)	133,607 (4.1)	
	Corse	7,438 (0.2)	7,438 (0.2)	
	Grand Est	286,427 (8.8)	286,427 (8.8)	
	Hauts-de-France	353,666 (10.9)	353,666 (10.9)	
	Ile-de-France	483,113 (14.9)	483,113 (14.9)	
	Normandie	184,751 (5.7)	184,751 (5.7)	
	Nouvelle-Aquitaine	346,196 (10.7)	346,196 (10.7)	
	Occitanie	296,694 (9.2)	296,694 (9.2)	
	Overseas departments	3,943 (0.1)	3,943 (0.1)	
	Pays de la Loire	205,586 (6.3)	205,586 (6.3)	
	Provence-Alpes-Côte d'Azur	209,865 (6.5)	209,865 (6.5)	
Nursing home	No	3,238,572 (100)	3,238,572 (100)	0.00000
	Yes, w/o inpatient pharmacy	3 (0.0)	3 (0.0)	
Social deprivation index (quintiles)	1 (least deprived)	572,837 (17.7)	686,070 (21.2)	0.10128
	2	618,182 (19.1)	663,072 (20.5)	
	3	651,040 (20.1)	654,273 (20.2)	
	4	693,554 (21.4)	641,172 (19.8)	
	5 (most deprived)	685,683 (21.2)	576,992 (17.8)	
	Unknown	17,279 (0.5)	16,996 (0.5)	

		ChAdOx1 nCoV-19 vaccine		Standardized difference
		No (n = 3,238,575)	Yes (n = 3,238,575)	
History of COVID-19 status (hospitalisation, screening tests)	No	3,084,341 (95.2)	3,171,637 (97.9)	-0.14884
	Yes	154,234 (4.8)	66,938 (2.1)	
Influenza vaccines in 2018 or 2019	No	2,736,891 (84.5)	2,333,067 (72.0)	0.30589
	Yes	501,684 (15.5)	905,508 (28.0)	
Frailty	No	3,104,595 (95.9)	3,109,300 (96.0)	-0.00736
	Yes	133,980 (4.1)	129,275 (4.0)	
Alcohol-related conditions	No	3,179,282 (98.2)	3,169,378 (97.9)	0.02193
	Yes	59,293 (1.8)	69,197 (2.1)	
Cardiovascular risk factors				
Smoking-related conditions	No	3,059,369 (94.5)	3,005,702 (92.8)	0.06793
	Yes	179,206 (5.5)	232,873 (7.2)	
Hypertension	No	2,069,858 (63.9)	1,710,110 (52.8)	0.22678
	Yes	1,168,717 (36.1)	1,528,465 (47.2)	
Diabetes mellitus	No	2,867,919 (88.6)	2,660,795 (82.2)	0.18165
	Yes	370,656 (11.4)	577,780 (17.8)	
Dyslipidemia	No	2,537,120 (78.3)	2,221,268 (68.6)	0.22225
	Yes	701,455 (21.7)	1,017,307 (31.4)	
Obesity-related conditions	No	3,189,786 (98.5)	3,158,190 (97.5)	0.06983
	Yes	48,789 (1.5)	80,385 (2.5)	
Cardiovascular diseases				
Coronary heart disease	No	3,058,810 (94.4)	2,974,074 (91.8)	0.10366
	Yes	179,765 (5.6)	264,501 (8.2)	
Heart failure	No	3,194,259 (98.6)	3,188,551 (98.5)	0.01471
	Yes	44,316 (1.4)	50,024 (1.5)	
Cardiac rhythm disorder	No	3,129,934 (96.6)	3,098,837 (95.7)	0.05002
	Yes	108,641 (3.4)	139,738 (4.3)	
Valvular heart disease	No	3,196,485 (98.7)	3,183,536 (98.3)	0.03290
	Yes	42,090 (1.3)	55,039 (1.7)	
Occlusive peripheral arterial disease	No	3,176,702 (98.1)	3,160,054 (97.6)	0.03531
	Yes	61,873 (1.9)	78,521 (2.4)	
Stroke	No	3,172,257 (98.0)	3,158,044 (97.5)	0.02949
	Yes	66,318 (2.0)	80,531 (2.5)	

		ChAdOx1 nCoV-19 vaccine		Standardized difference
		No (n = 3,238,575)	Yes (n = 3,238,575)	
Pulmonary embolism	No	3,227,404 (99.7)	3,227,202 (99.6)	0.00106
	Yes	11,171 (0.3)	11,373 (0.4)	
Other comorbidities				
Chronic respiratory conditions	No	3,007,814 (92.9)	2,924,087 (90.3)	0.09321
	Yes	230,761 (7.1)	314,488 (9.7)	
Dialysis	No	3,236,927 (99.9)	3,238,270 (100)	-0.02389
	Yes	1,648 (0.1)	305 (0.0)	
Kidney transplant	No	3,236,326 (99.9)	3,237,414 (100)	-0.01465
	Yes	2,249 (0.1)	1,161 (0.0)	
Liver failure	No	3,204,043 (98.9)	3,197,626 (98.7)	0.01846
	Yes	34,532 (1.1)	40,949 (1.3)	
Active cancer	No	3,134,610 (96.8)	3,113,654 (96.1)	0.03505
	Yes	103,965 (3.2)	124,921 (3.9)	
Depression	No	2,922,626 (90.2)	2,829,158 (87.4)	0.09162
	Yes	315,949 (9.8)	409,417 (12.6)	
Psychosis	No	3,192,075 (98.6)	3,183,030 (98.3)	0.02243
	Yes	46,500 (1.4)	55,545 (1.7)	
Dementia	No	3,219,223 (99.4)	3,222,392 (99.5)	-0.01325
	Yes	19,352 (0.6)	16,183 (0.5)	
Epilepsy	No	3,221,221 (99.5)	3,218,186 (99.4)	0.01231
	Yes	17,354 (0.5)	20,389 (0.6)	
Parkinson's disease	No	3,220,652 (99.4)	3,215,420 (99.3)	0.02035
	Yes	17,923 (0.6)	23,155 (0.7)	
Inflammatory bowel disease	No	3,222,669 (99.5)	3,218,228 (99.4)	0.01838
	Yes	15,906 (0.5)	20,347 (0.6)	
Rheumatoid arthritis	No	3,214,589 (99.3)	3,209,931 (99.1)	0.01602
	Yes	23,986 (0.7)	28,644 (0.9)	
Ankylosing spondylitis	No	3,222,878 (99.5)	3,217,156 (99.3)	0.02341
	Yes	15,697 (0.5)	21,419 (0.7)	

Table 5. Description of vaccine products for the first and second doses

	Vaccine product: first dose (n, %)			Total
	BNT162b2	mRNA-1273	ChAdOx1 nCoV-19	
Vaccine product: second dose (n, %)				
BNT162b2	6,894,688	2,766	252,570	7,150,024
	96.27	0.32	7.80	
mRNA-1273	2,169	820,322	66,917	889,408
	0.03	95.77	2.07	
ChAdOx1 nCoV-19	0	0	2,802,944	2,802,944
	0	0	86.55	
Ad26.COV2.S	212	34	808	1,054
	0	0	0.02	
<i>Receiving only one dose</i>	264,589	33,477	115,336	413,402
	3.69	3.91	3.56	
Total	7,161,658	856,599	3,238,575	11,256,832

Table 6. Two-dose vaccine effectiveness against COVID-19-related hospitalisation after excluding individuals who received different vaccine products between the first and second doses and their matched controls

Vaccine product	Vaccination status	n(hosp)/N(group) (%)	Median follow-up [IQR]	Model 1* HR (95% CI)	Model 2† Adjusted HR (95% CI)	Vaccine effectiveness (%) (95% CI)
BNT162b2	No	8250/3701379 (0.22%)	62 [25 - 98]	1	1	-
	Yes	810/3701379 (0.02%)	62 [25 - 98]	0.10 (0.09 - 0.10)	0.09 (0.08 - 0.09)	91% (91 to 92)
mRNA-1273	No	831/425555 (0.2%)	63 [25 - 98]	1	1	-
	Yes	48/425555 (0.01%)	64 [25 - 98]	0.06 (0.04 - 0.08)	0.05 (0.04 - 0.07)	95% (93 to 96)
ChAdOx1 nCoV-19	No	542/878639 (0.06%)	43 [27 - 61]	1	1	-
	Yes	60/878639 (0.01%)	43 [27 - 61]	0.11 (0.08 - 0.14)	0.09 (0.07 - 0.12)	91% (88 to 93)

IQR: interquartile range; HR: hazard ratio; CI: confidence interval.

*Model 1: adjusted for matching variables (age, sex, region of residence, nursing home status)

†Model 2: Model 1 with further adjustment for social deprivation index, history of positive COVID-19 status, history of influenza vaccination, frailty, alcohol-related conditions, smoking-related conditions, hypertension, diabetes mellitus, dyslipidemia, obesity-related conditions, coronary heart disease, heart failure, cardiac rhythm disorder, valvular heart disease, occlusive peripheral arterial disease, stroke, pulmonary embolism, chronic respiratory conditions, dialysis, kidney transplant, liver failure, active cancer, depression, psychosis, dementia, epilepsy, Parkinson's disease, inflammatory bowel disease, rheumatoid arthritis, ankylosing spondylitis.

Table 7. Two-dose vaccine effectiveness against COVID-19-related hospitalisation by age categories

Age categories (years)	Vaccine product	Vaccination status	n(hosp)/N(group) (%)	Median follow-up [IQR]	Model 1* HR (95% CI)	Model 2† Adjusted HR (95% CI)	Vaccine effectiveness (%) (95% CI)
50-64	BNT162b2	No	890/964839 (0.09%)	59 [30 - 81]	1	1	-
		Yes	91/964839 (0.01%)	59 [30 - 81]	0.10 (0.08 to 0.13)	0.07 (0.06 to 0.09)	93% (91 to 94)
	mRNA-1273	No	97/128756 (0.08%)	59 [26 - 83]	1	1	-
		Yes	15/128756 (0.01%)	59 [26 - 83]	0.15 (0.09 to 0.27)	0.11 (0.06 to 0.20)	89% (80 to 94)
	ChAdOx1 nCoV-19	No	321/554588 (0.06%)	42 [24 - 62]	1	1	-
		Yes	17/554588 (0%)	42 [24 - 62]	0.05 (0.03 to 0.09)	0.04 (0.02 to 0.07)	96% (93 to 98)
65-74	BNT162b2	No	1298/1085149 (0.12%)	63 [29 - 88]	1	1	-
		Yes	106/1085149 (0.01%)	64 [29 - 88]	0.08 (0.07 to 0.10)	0.06 (0.05 to 0.07)	94% (93 to 95)
	mRNA-1273	No	138/137694 (0.1%)	64 [27 - 92]	1	1	-
		Yes	6/137694 (0%)	64 [27 - 92]	0.04 (0.02 to 0.10)	0.03 (0.01 to 0.07)	97% (93 to 99)
	ChAdOx1 nCoV-19	No	240/382312 (0.06%)	44 [29 - 60]	1	1	-
		Yes	31/382312 (0.01%)	44 [29 - 60]	0.13 (0.09 to 0.19)	0.11 (0.08 to 0.17)	89% (83 to 92)
75-84	BNT162b2	No	3141/995104 (0.32%)	56 [19 - 114]	1	1	-
		Yes	221/995104 (0.02%)	57 [19 - 114]	0.07 (0.06 to 0.08)	0.05 (0.04 to 0.06)	95% (94 to 96)
	mRNA-1273	No	313/95893 (0.33%)	67 [20 - 114]	1	1	-
		Yes	8/95893 (0.01%)	69 [20 - 114]	0.02 (0.01 to 0.05)	0.02 (0.01 to 0.04)	98% (96 to 99)
	ChAdOx1 nCoV-19	No	31/35292 (0.09%)	55 [39 - 67]	1	1	-
		Yes	8/35292 (0.02%)	55 [39 - 67]	0.26 (0.12 to 0.56)	0.20 (0.09 to 0.48)	80% (52 to 91)
≥85	BNT162b2	No	2921/657006 (0.44%)	83 [27 - 118]	1	1	-
		Yes	392/657006 (0.06%)	86 [27 - 119]	0.13 (0.12 to 0.14)	0.10 (0.09 to 0.11)	90% (89 to 91)
	mRNA-1273	No	283/64274 (0.44%)	92 [28 - 115]	1	1	-

Age categories (years)	Vaccine product	Vaccination status	n(hosp)/N(group) (%)	Median follow-up [IQR]	Model 1* HR (95% CI)	Model 2† Adjusted HR (95% CI)	Vaccine effectiveness (%) (95% CI)
		Yes	19/64274 (0.03%)	94 [29 - 116]	0.06 (0.04 to 0.10)	0.05 (0.03 to 0.08)	95% (92 to 97)

IQR: interquartile range; HR: hazard ratio; CI: confidence interval.

*Model 1: adjusted for matching variables (age, sex, region of residence, nursing home status)

†Model 2: Model 1 with further adjustment for social deprivation index, history of positive COVID-19 status, history of influenza vaccination, frailty, alcohol-related conditions, smoking-related conditions, hypertension, diabetes mellitus, dyslipidemia, obesity-related conditions, coronary heart disease, heart failure, cardiac rhythm disorder, valvular heart disease, occlusive peripheral arterial disease, stroke, pulmonary embolism, chronic respiratory conditions, dialysis, kidney transplant, liver failure, active cancer, depression, psychosis, dementia, epilepsy, Parkinson's disease, inflammatory bowel disease, rheumatoid arthritis, ankylosing spondylitis.

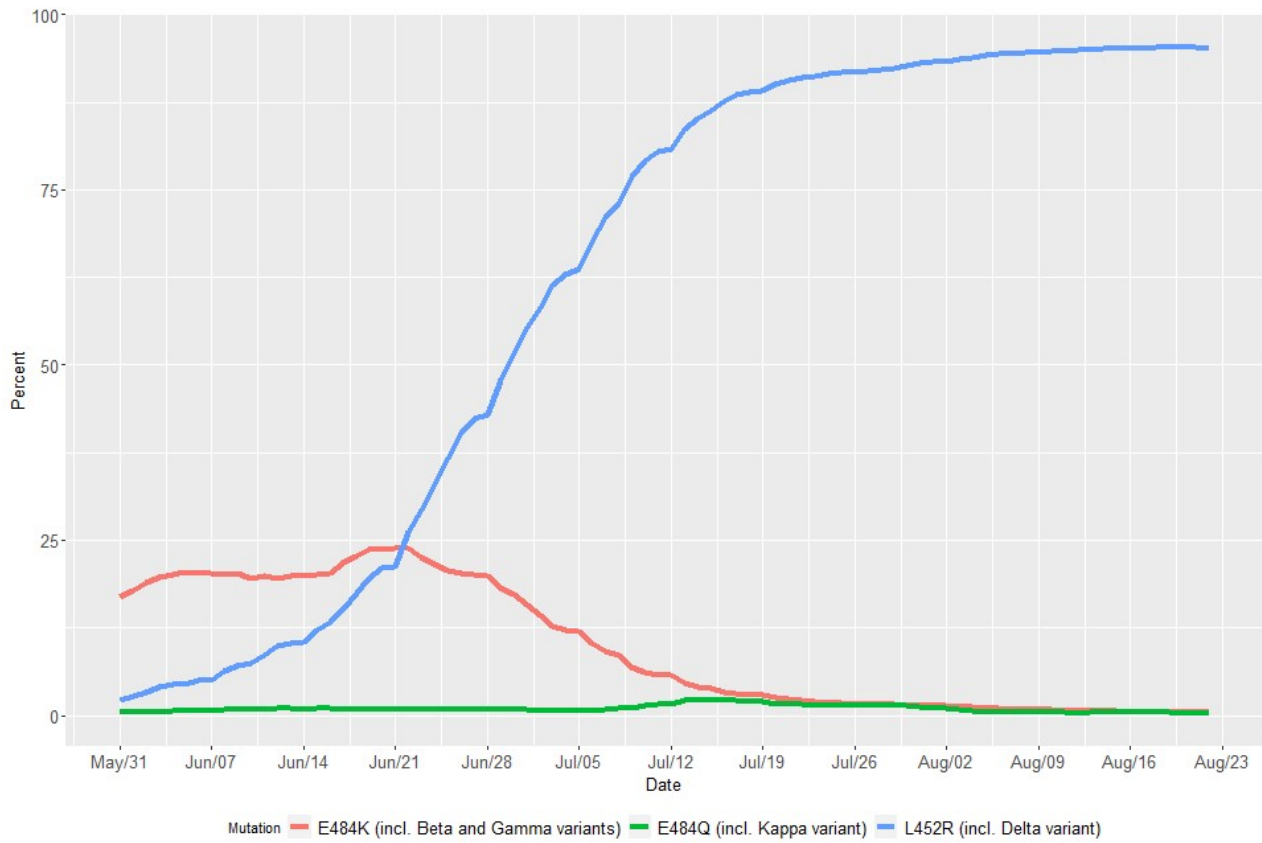
Table 8. Two-dose vaccine effectiveness against COVID-19-related hospitalisation by sex

Sex	Vaccine product	Vaccination status	n(hosp)/N(group) (%)	Median follow-up [IQR]	Model 1* HR (95% CI)	Model 2† Adjusted HR (95% CI)	Vaccine effectiveness (%) (95% CI)
Men	BNT162b2	No	3927/1575121 (0.25%)	60 [24 - 96]	1	1	-
		Yes	433/1575121 (0.03%)	61 [24 - 98]	0.11 (0.10 to 0.12)	0.09 (0.08 to 0.10)	91% (90 to 92)
	mRNA-1273	No	391/184286 (0.21%)	62 [24 - 98]	1	1	-
		Yes	27/184286 (0.01%)	63 [24 - 98]	0.07 (0.05 to 0.10)	0.06 (0.04 to 0.09)	94% (91 to 96)
	ChAdOx1 nCoV-19	No	364/514618 (0.07%)	43 [27 - 62]	1	1	-
		Yes	40/514618 (0.01%)	43 [27 - 62]	0.11 (0.08 to 0.15)	0.09 (0.07 to 0.13)	91% (87 to 93)
Women	BNT162b2	No	4323/2126977 (0.2%)	63 [26 - 98]	1	1	-
		Yes	377/2126977 (0.02%)	63 [26 - 99]	0.09 (0.08 to 0.10)	0.08 (0.07 to 0.09)	92% (91 to 93)
	mRNA-1273	No	440/242331 (0.18%)	64 [25 - 98]	1	1	-
		Yes	21/242331 (0.01%)	64 [25 - 99]	0.05 (0.03 to 0.07)	0.04 (0.03 to 0.07)	96% (93 to 97)
	ChAdOx1 nCoV-19	No	253/487158 (0.05%)	44 [27 - 62]	1	1	-
		Yes	22/487158 (0%)	44 [27 - 62]	0.09 (0.06 to 0.13)	0.08 (0.05 to 0.12)	92% (88 to 95)

IQR: interquartile range; HR: hazard ratio; CI: confidence interval.

*Model 1: adjusted for matching variables (age, sex, region of residence, nursing home status)

†Model 2: Model 1 with further adjustment for social deprivation index, history of positive COVID-19 status, history of influenza vaccination, frailty, alcohol-related conditions, smoking-related conditions, hypertension, diabetes mellitus, dyslipidemia, obesity-related conditions, coronary heart disease, heart failure, cardiac rhythm disorder, valvular heart disease, occlusive peripheral arterial disease, stroke, pulmonary embolism, chronic respiratory conditions, dialysis, kidney transplant, liver failure, active cancer, depression, psychosis, dementia, epilepsy, Parkinson's disease, inflammatory bowel disease, rheumatoid arthritis, ankylosing spondylitis.

Figure 1. Surveillance of SARS-CoV-2 variants in France

Information on variants of SARS-CoV-2 has been collected in the SI-DEP database. Aggregated data are made available by the National Public Health Agency (*Santé Publique France*) in the website www.data.gouv.fr/fr/datasets/donnees-de-laboratoires-pour-le-depistage-indicateurs-sur-les-mutations.