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The role of COVID-19 vaccines in preventing post-COVID-19 thromboembolic and cardiovascular complications

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ABSTRACT

Objective To study the association between COVID-19 vaccination and the risk of post-COVID-19 cardiac and thromboembolic complications.

Methods We conducted a staggered cohort study based on national vaccination campaigns using electronic health records from the UK, Spain and Estonia. Vaccine rollout was grouped into four stages with predefined enrolment periods. Each stage included all individuals eligible for vaccination, with no previous SARS-CoV-2 infection or COVID-19 vaccine at the start date. Vaccination status was used as a time-varying exposure. Outcomes included heart failure (HF), venous thromboembolism (VTE) and arterial thrombosis/thromboembolism (ATE) recorded in four time windows after SARS-CoV-2 infection: 0–30, 31–90, 91–180 and 181–365 days. Propensity score overlap weighting and empirical calibration were used to minimise observed and unobserved confounding, respectively.

Fine-Gray models estimated subdistribution hazard ratios (sHR). Random effect meta-analyses were conducted across staggered cohorts and databases.

Results The study included 10.17 million vaccinated and 10.39 million unvaccinated people. Vaccination was associated with reduced risks of acute (30-day) and post-acute COVID-19 VTE, ATE and HF: for example, meta-analytic sHR of 0.22 (95% CI 0.17 to 0.29), 0.53 (0.44 to 0.63) and 0.45 (0.38 to 0.53), respectively, for 0–30 days after SARS-CoV-2 infection, while in the 91–180 days sHR were 0.53 (0.40 to 0.70), 0.72 (0.58 to 0.88) and 0.61 (0.51 to 0.73), respectively.

Conclusions COVID-19 vaccination reduced the risk of post-COVID-19 cardiac and thromboembolic outcomes. These effects were more pronounced for acute COVID-19 outcomes, consistent with known reductions in disease severity following breakthrough versus unvaccinated SARS-CoV-2 infection.

INTRODUCTION

COVID-19 vaccines were approved under emergency authorisation in December 2020 and showed high effectiveness against SARS-CoV-2 infection, COVID-19-related hospitalisation and death.^{1 2} However, concerns were raised after

WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ COVID-19 vaccines proved to be highly effective in reducing the severity of acute SARS-CoV-2 infection.
- ⇒ While COVID-19 vaccines were associated with increased risk for cardiac and thromboembolic events, such as myocarditis and thrombosis, the risk of complications was substantially higher due to SARS-CoV-2 infection.

WHAT THIS STUDY ADDS

- ⇒ COVID-19 vaccination reduced the risk of heart failure, venous thromboembolism and arterial thrombosis/thromboembolism in the acute (30 days) and post-acute (31 to 365 days) phase following SARS-CoV-2 infection. This effect was stronger in the acute phase.
- ⇒ The overall additive effect of vaccination on the risk of post-vaccine and/or post-COVID thromboembolic and cardiac events needs further research.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ COVID-19 vaccines proved to be highly effective in reducing the risk of post-COVID cardiovascular and thromboembolic complications.

spontaneous reports of unusual thromboembolic events following adenovirus-based COVID-19 vaccines, an association that was further assessed in observational studies.^{3 4} More recently, mRNA-based vaccines were found to be associated with a risk of rare myocarditis events.^{5 6}

On the other hand, SARS-CoV-2 infection can trigger cardiac and thromboembolic complications.^{7 8} Previous studies showed that, while slowly decreasing over time, the risk for serious complications remain high for up to a year after infection.^{9 10} Although acute and post-acute cardiac and thromboembolic complications following COVID-19 are rare, they present a substantial burden to the



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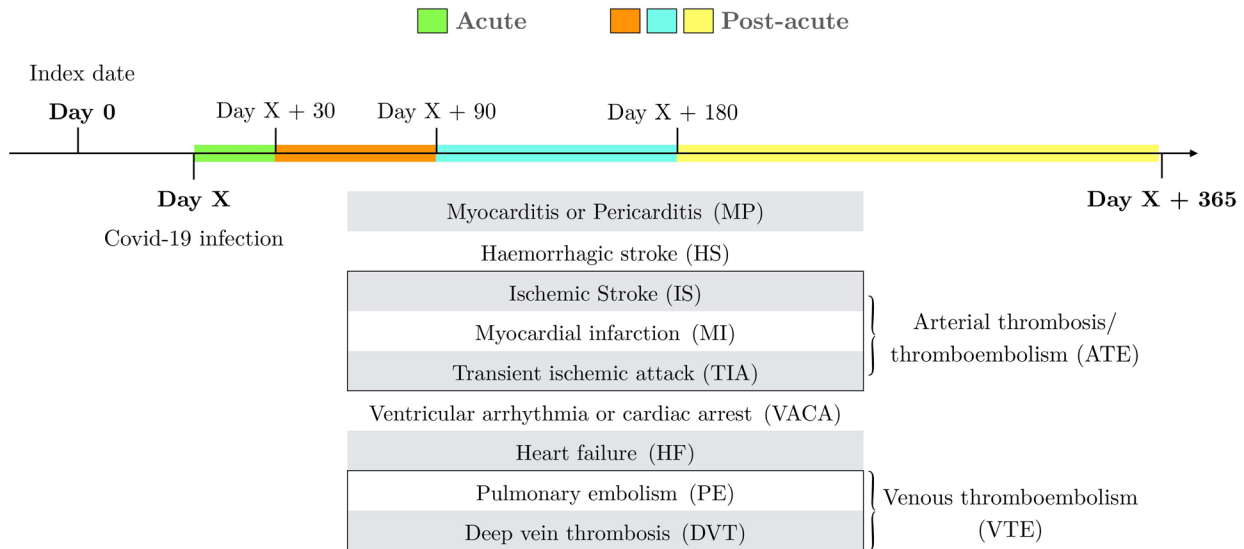


Figure 1 Study outcome design. Study outcomes of interest are defined as a COVID-19 infection followed by one of the complications in the figure, within a year after infection. Outcomes were ascertained in four different time windows after SARS-CoV-2 infection: 0–30 days (namely the acute phase), 31–90 days, 91–180 days and 181–365 days (these last three comprise the post-acute phase).

affected patients, and the absolute number of cases globally could become substantial.

Recent studies suggest that COVID-19 vaccination could protect against cardiac and thromboembolic complications attributable to COVID-19.^{11 12} However, most studies did not include long-term complications and were conducted among specific populations.

Evidence is still scarce as to whether the combined effects of COVID-19 vaccines protecting against SARS-CoV-2 infection and reducing post-COVID-19 cardiac and thromboembolic outcomes, outweigh any risks of these complications potentially associated with vaccination.

We therefore used large, representative data sources from three European countries to assess the overall effect of COVID-19 vaccines on the risk of acute and post-acute COVID-19 complications including venous thromboembolism (VTE), arterial thrombosis/thromboembolism (ATE) and other cardiac events. Additionally, we studied the comparative effects of ChAdOx1 versus BNT162b2 on the risk of these same outcomes.

METHODS

Data sources

We used four routinely collected population-based healthcare datasets from three European countries: the UK, Spain and Estonia.

For the UK, we used data from two primary care databases—namely, Clinical Practice Research Datalink, CPRD Aurum¹³ and CPRD Gold.¹⁴ CPRD Aurum currently covers 13 million people from predominantly English practices, while CPRD Gold comprises 3.1 million active participants mostly from GP practices in Wales and Scotland. Spanish data were provided by the Information System for the Development of Research in Primary Care (SIDIAP),¹⁵ which encompasses primary care records from 6 million active patients (around 75% of the population in the region of Catalonia) linked to hospital admissions data (Conjunt Mínim Bàsic de Dades d’Alta Hospitalària). Finally, the CORIVA dataset based on national health claims data from Estonia was used. It contains all COVID-19 cases from the

first year of the pandemic and ~440 000 randomly selected controls. CORIVA was linked to the death registry and all COVID-19 testing from the national health information system.

Databases included sociodemographic information, diagnoses, measurements, prescriptions and secondary care referrals and were linked to vaccine registries, including records of all administered vaccines from all healthcare settings. Data availability for CPRD Gold ended in December 2021, CPRD Aurum in January 2022, SIDIAP in June 2022 and CORIVA in December 2022.

All databases were mapped to the Observational Medical Outcomes Partnership Common Data Model (OMOP CDM)¹⁶ to facilitate federated analytics.

Multinational network staggered cohort study: study design and participants

The study design has been published in detail elsewhere.¹⁷ Briefly, we used a staggered cohort design considering vaccination as a time-varying exposure. Four staggered cohorts were designed with each cohort representing a country-specific vaccination rollout phase (eg, dates when people became eligible for vaccination, and eligibility criteria).

The source population comprised all adults registered in the respective database for at least 180 days at the start of the study (4 January 2021 for CPRD Gold and Aurum, 20 February 2021 for SIDIAP and 28 January 2021 for CORIVA). Subsequently, each staggered cohort corresponded to an enrolment period: all people eligible for vaccination during this time were included in the cohort and people with a history of SARS-CoV-2 infection or COVID-19 vaccination before the start of the enrolment period were excluded. Across countries, cohort 1 comprised older age groups, whereas cohort 2 comprised individuals at risk for severe COVID-19. Cohort 3 included people aged ≥40 and cohort 4 enrolled people aged ≥18.

In each cohort, people receiving a first vaccine dose during the enrolment period were allocated to the vaccinated group, with their index date being the date of vaccination. Individuals who did not receive a vaccine dose comprised the unvaccinated group and their index date was assigned within the enrolment period, based on the distribution of index dates in the vaccinated group. People with COVID-19 before the index date were excluded.

Table 1 Characteristics of weighted populations in CPRD Aurum database, stratified by staggered cohort and exposure status. Exposure is any COVID-19 vaccine

Characteristics	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
No (individuals)	154864	154245		420707	420931		463495	462463		818917	827124	
Age, median (Q25–Q75)	80 (76–84)	80 (76–84)	0.000	58 (44–67)	58 (44–67)	0.005	50 (41–58)	52 (40–58)	0.003	34 (26–42)	34 (26–42)	0.004
Sex: female, N (%)	88349 (57%)	87639 (57%)	0.005	248156 (59%)	249561 (59%)	0.006	245248 (53%)	245600 (53%)	0.004	351435 (43%)	358688 (43%)	0.009
Years of prior history*, median (Q25–Q75)	24 (10–35)	24 (10–36)	0.006	18 (8–29)	18 (8–29)	0.003	14 (6–24)	14 (7–24)	0.008	8 (4–17)	7 (3–18)	0.001
Number of GP visits, median (Q25–Q75)	10 (5–18)	10 (6–17)		8 (3–15)	8 (5–14)		4 (1–11)	6 (3–11)		2 (0–6)	2 (0–6)	
Number of PCR tests, median (Q25–Q75)	0 (0–0)	0 (0–0)		0 (0–0)	0 (0–0)		0 (0–0)	0 (0–0)		0 (0–0)	0 (0–0)	
Comorbidity†, N (%)												
Anxiety	23200 (15%)	22789 (15%)	0.006	94390 (22%)	91644 (22%)	0.016	92820 (20%)	90807 (20%)	0.010	123055 (15%)	125202 (15%)	0.003
Asthma	16978 (11%)	16663 (11%)	0.005	95770 (23%)	94550 (22%)	0.007	79642 (17%)	78266 (17%)	0.007	63687 (8%)	61472 (7%)	0.013
Chronic kidney disease	36149 (23%)	36046 (23%)	0.001	28181 (7%)	29756 (7%)	0.015	10283 (2%)	10577 (2%)	0.005	3840 (0%)	3572 (0%)	0.006
COPD	13385 (9%)	13181 (9%)	0.003	17447 (4%)	17999 (4%)	0.006	6062 (1%)	5754 (1%)	0.006	1901 (0%)	1918 (0%)	0.000
Dementia	9483 (6%)	8517 (6%)	0.026	4182 (1%)	3879 (1%)	0.007	1361 (0%)	1392 (0%)	0.001	276 (0%)	495 (0%)	0.012
Depressive disorder	18632 (12%)	18547 (12%)	0.000	85280 (20%)	81945 (19%)	0.020	81891 (18%)	79804 (17%)	0.011	94373 (12%)	97053 (12%)	0.007
Diabetes	29365 (19%)	28831 (19%)	0.007	49408 (12%)	48562 (12%)	0.006	26616 (6%)	28628 (6%)	0.019	12787 (2%)	12539 (2%)	0.004
GORD	8718 (6%)	8515 (6%)	0.005	19907 (5%)	18924 (4%)	0.011	15646 (3%)	14982 (3%)	0.008	13882 (2%)	13893 (2%)	0.001
Heart failure	9349 (6%)	8851 (6%)	0.013	7284 (2%)	6502 (2%)	0.015	2660 (1%)	2470 (1%)	0.005	930 (0%)	816 (0%)	0.005
Hypertension	81563 (53%)	80806 (52%)	0.006	97707 (23%)	98193 (23%)	0.002	54649 (12%)	55798 (12%)	0.008	22925 (3%)	24450 (3%)	0.009
Hypothyroidism	15125 (10%)	15098 (10%)	0.001	25579 (6%)	25962 (6%)	0.004	17162 (4%)	17580 (4%)	0.005	12427 (2%)	12641 (2%)	0.001
Malignant neoplastic disease	33467 (22%)	33024 (21%)	0.005	30194 (7%)	35085 (8%)	0.043	14815 (3%)	14140 (3%)	0.008	6447 (1%)	5766 (1%)	0.011
Myocardial infarction	824 (5%)	7731 (5%)	0.002	9964 (2%)	11319 (3%)	0.020	3787 (1%)	3664 (1%)	0.003	3115 (0%)	1069 (0%)	0.008
Osteoporosis	15275 (10%)	15373 (10%)	0.003	10626 (3%)	10718 (3%)	0.001	4113 (1%)	4131 (1%)	0.001	1376 (0%)	1472 (0%)	0.002
Pneumonia	8573 (6%)	7621 (5%)	0.027	11355 (3%)	10691 (3%)	0.010	6651 (1%)	6545 (1%)	0.002	5144 (1%)	5151 (1%)	0.001
Rheumatoid arthritis	3066 (2%)	3092 (2%)	0.002	6198 (1%)	6570 (2%)	0.007	2355 (1%)	3111 (1%)	0.021	1201 (0%)	859 (0%)	0.012
Stroke	7667 (5%)	7047 (5%)	0.018	8041 (2%)	8794 (2%)	0.013	3518 (1%)	3293 (1%)	0.006	1496 (0%)	1305 (0%)	0.006
Venous thromboembolism	9589 (6%)	9241 (6%)	0.008	11836 (3%)	12475 (3%)	0.009	6503 (1%)	8075 (2%)	0.028	4661 (1%)	2441 (0%)	0.042

The four cohorts represent vaccine rollout periods.

* Calculated as the days of previous observation in the database before index date.

† Assessed any time before index date.

ASMD, absolute standardised mean difference; COPD, chronic obstructive pulmonary disease; GORD, gastro-oesophageal reflux disease; GP, general practitioner; PCR, polymerase chain reaction.

Table 2 Number of records (and risk per 10000 individuals) for acute and post-acute COVID-19 cardiac and thromboembolic complications, across cohorts and databases for any COVID-19 vaccination

Cohort	Time window	Outcome	CPRD Aurum		CORIVA		CPRD Gold		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
Cohort 1			n=346674	n=552602	n=23982	n=26736	n=169100	n=118507	n=223962	n=89941
	0 to 30 days	VTE	93 (2.68)	117 (2.12)	77 (32.11)	45 (16.83)	8 (0.47)	8 (0.68)	74 (3.30)	96 (10.67)
		ATE	22 (0.63)	70 (1.27)	110 (45.87)	81 (30.30)	6 (0.35)	7 (0.59)	77 (3.44)	208 (23.13)
		HF	59 (1.70)	198 (3.58)	395 (164.71)	299 (111.83)	10 (0.59)	9 (0.76)	302 (13.48)	640 (71.16)
	31 to 90 days	VTE	19 (0.55)	40 (0.72)	37 (15.43)	30 (11.22)	< 5	< 5	16 (0.71)	46 (5.11)
		ATE	5 (0.14)	43 (0.78)	33 (13.76)	47 (17.58)	< 5	< 5	41 (1.83)	130 (14.45)
		HF	30 (0.87)	113 (2.04)	151 (62.96)	170 (63.58)	< 5	8 (0.68)	89 (3.97)	298 (33.13)
	91 to 180 days	VTE	10 (0.29)	21 (0.38)	21 (8.76)	35 (13.09)	< 5	< 5	20 (0.89)	40 (4.45)
		ATE	11 (0.32)	28 (0.51)	31 (12.93)	52 (19.45)	< 5	6 (0.51)	30 (1.34)	112 (12.45)
		HF	37 (1.07)	95 (1.72)	162 (67.55)	220 (82.29)	< 5	5 (0.42)	87 (3.88)	252 (28.02)
	181 to 365 days	VTE	10 (0.29)	11 (0.20)	45 (18.76)	35 (13.09)	< 5	< 5	10 (0.45)	13 (1.45)
		ATE	10 (0.29)	23 (0.42)	55 (22.93)	82 (30.67)	< 5	< 5	42 (1.88)	53 (5.89)
		HF	40 (1.15)	58 (1.05)	268 (111.75)	321 (120.06)	< 5	6 (0.51)	86 (3.84)	149 (16.57)
Cohort 2			n=1975726	n=1563569	n=34317	n=4572	n=583399	n=486619	n=433151	n=819590
	0 to 30 days	VTE	241 (1.22)	220 (1.41)	79 (23.02)	7 (15.31)	31 (0.53)	24 (0.49)	258 (5.96)	400 (4.88)
		ATE	41 (0.21)	104 (0.67)	110 (32.05)	5 (10.94)	< 5	6 (0.12)	173 (3.99)	669 (8.16)
		HF	45 (0.23)	146 (0.93)	364 (106.07)	23 (50.31)	5 (0.09)	13 (0.27)	378 (8.73)	1331 (16.24)
	31 to 90 days	VTE	43 (0.22)	76 (0.49)	31 (9.03)	5 (10.94)	< 5	9 (0.18)	59 (1.36)	195 (2.38)
		ATE	18 (0.09)	93 (0.59)	32 (9.32)	< 5	< 5	9 (0.18)	85 (1.96)	444 (5.42)
		HF	27 (0.14)	103 (0.66)	149 (43.42)	19 (41.56)	< 5	7 (0.14)	138 (3.19)	643 (7.85)
	91 to 180 days	VTE	28 (0.14)	40 (0.26)	26 (7.58)	6 (13.12)	6 (0.10)	< 5	58 (1.34)	125 (1.53)
		ATE	17 (0.09)	43 (0.28)	32 (9.32)	< 5	< 5	< 5	91 (2.10)	417 (5.09)
		HF	22 (0.11)	69 (0.44)	166 (48.37)	21 (45.93)	< 5	< 5	110 (2.54)	579 (7.06)
	181 to 365 days	VTE	9 (0.05)	13 (0.08)	44 (12.82)	8 (17.50)	< 5	< 5	16 (0.37)	64 (0.78)
		ATE	12 (0.06)	18 (0.12)	53 (15.44)	< 5	< 5	< 5	63 (1.45)	178 (2.17)
		HF	20 (0.10)	35 (0.22)	259 (75.47)	33 (72.18)	< 5	< 5	81 (1.87)	246 (3.00)
Cohort 3			n=1510401	n=1528031	n=96423	n=24050	n=417996	n=462832	n=869497	n=954232
	0 to 30 days	VTE	245 (1.62)	142 (0.93)	115 (11.93)	9 (3.74)	27 (0.65)	17 (0.37)	325 (3.74)	180 (1.89)
		ATE	29 (0.19)	49 (0.32)	119 (12.34)	12 (4.99)	< 5	12 (0.26)	213 (2.45)	275 (2.88)
		HF	31 (0.21)	38 (0.25)	380 (39.41)	23 (9.56)	< 5	< 5	364 (4.19)	256 (2.68)
	31 to 90 days	VTE	44 (0.29)	46 (0.30)	50 (5.19)	10 (4.16)	< 5	7 (0.15)	85 (0.98)	92 (0.96)
		ATE	11 (0.07)	33 (0.22)	48 (4.98)	9 (3.74)	< 5	8 (0.17)	109 (1.25)	210 (2.20)
		HF	15 (0.10)	26 (0.17)	180 (18.67)	25 (10.40)	< 5	< 5	137 (1.58)	157 (1.65)
	91 to 180 days	VTE	24 (0.16)	26 (0.17)	43 (4.46)	11 (4.57)	< 5	< 5	64 (0.74)	101 (1.06)
		ATE	< 5	28 (0.18)	44 (4.56)	10 (4.16)	< 5	< 5	113 (1.30)	206 (2.16)
		HF	11 (0.07)	14 (0.09)	216 (22.40)	30 (12.47)	< 5	< 5	120 (1.38)	138 (1.45)
	181 to 365 days	VTE	< 5	11 (0.07)	72 (7.47)	17 (7.07)	< 5	< 5	34 (0.39)	26 (0.27)
		ATE	< 5	< 5	80 (8.30)	8 (3.33)	< 5	< 5	51 (0.59)	67 (0.70)
		HF	5 (0.03)	< 5	324 (33.60)	37 (15.38)	< 5	< 5	62 (0.71)	44 (0.46)
Cohort 4			n=2027763	n=2085598	n=147545	n=22245	n=469876	n=550437	n=1061634	n=880950
	0 to 30 days	VTE	334 (1.65)	50 (0.24)	116 (7.86)	< 5	36 (0.77)	11 (0.20)	350 (3.30)	98 (1.11)
		ATE	26 (0.13)	8 (0.04)	116 (7.86)	10 (4.50)	< 5	< 5	231 (2.18)	95 (1.08)
		HF	28 (0.14)	< 5	364 (24.67)	17 (7.64)	< 5	< 5	362 (3.41)	75 (0.85)
	31 to 90 days	VTE	58 (0.29)	22 (0.11)	54 (3.66)	< 5	5 (0.11)	< 5	91 (0.86)	49 (0.56)
		ATE	12 (0.06)	9 (0.04)	46 (3.12)	5 (2.25)	< 5	< 5	118 (1.11)	76 (0.86)
		HF	14 (0.07)	9 (0.04)	176 (11.93)	13 (5.84)	< 5	< 5	142 (1.34)	47 (0.53)
	91 to 180 days	VTE	26 (0.13)	10 (0.05)	49 (3.32)	5 (2.25)	< 5	< 5	71 (0.67)	60 (0.68)
		ATE	< 5	6 (0.03)	41 (2.78)	7 (3.15)	< 5	< 5	128 (1.21)	90 (1.02)
		HF	10 (0.05)	< 5	208 (14.10)	18 (8.09)	< 5	< 5	139 (1.31)	55 (0.62)
	181 to 365 days	VTE	< 5	< 5	77 (5.22)	< 5	< 5	< 5	46 (0.43)	12 (0.14)
		ATE	< 5	< 5	73 (4.95)	9 (4.05)	< 5	< 5	54 (0.51)	28 (0.32)
		HF	< 5	< 5	301 (20.40)	16 (7.19)	< 5	< 5	57 (0.54)	15 (0.17)

The four cohorts represent vaccine rollout periods.

ATE, arterial thrombosis/thromboembolism (Ischaemic stroke+transient ischaemic attack+myocardial infarction); HF, heart failure; VTE, venous thromboembolism (deep vein thrombosis+pulmonary embolism).

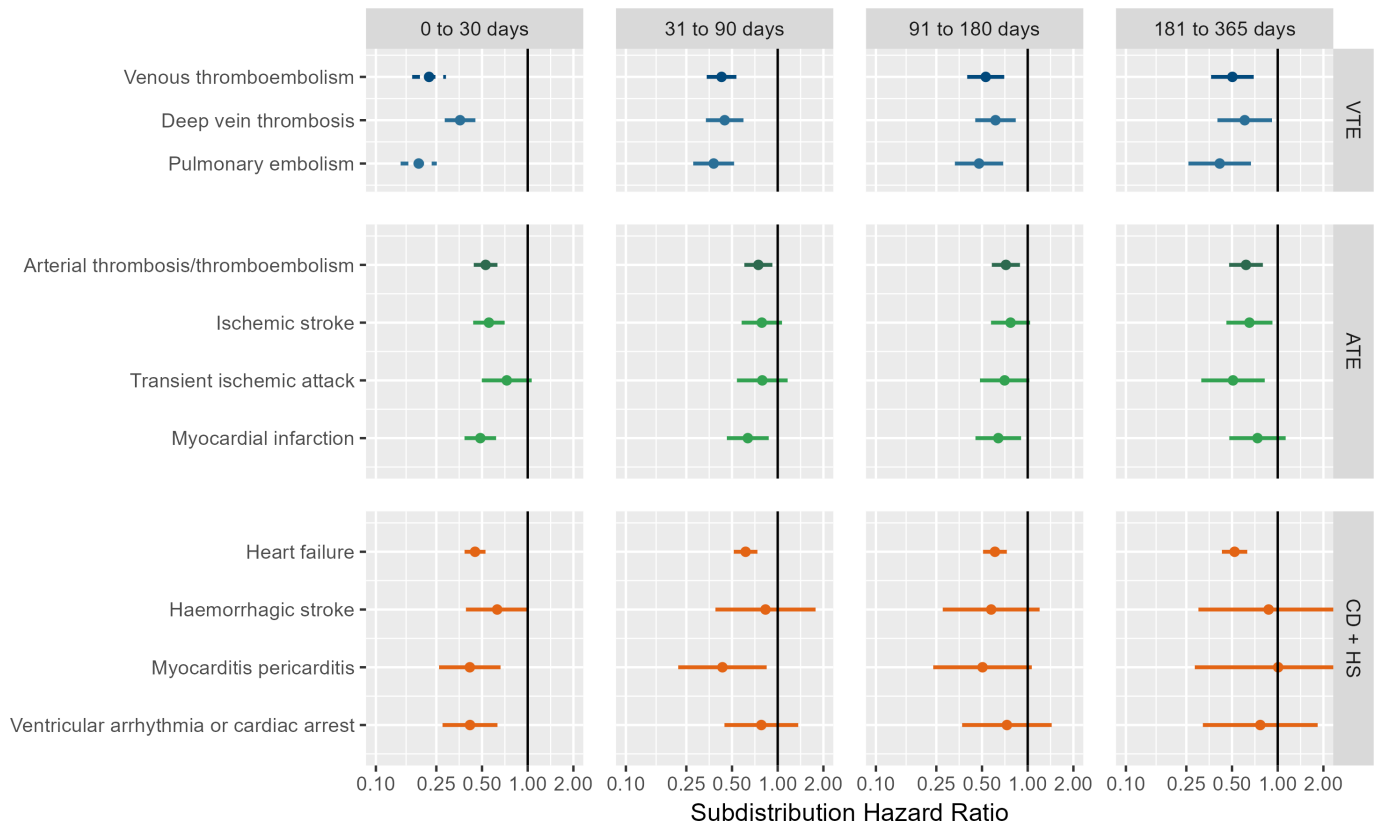


Figure 2 Forest plots for the effect of COVID-19 vaccines on post-COVID-19 cardiac and thromboembolic complications; meta-analysis across cohorts and databases. Dashed line represents a level of heterogeneity $I^2 > 0.4$. ATE, arterial thrombosis/thromboembolism; CD+HS, cardiac diseases and haemorrhagic stroke; VTE, venous thromboembolism.

Follow-up started from the index date until the earliest of end of available data, death, change in exposure status (first vaccine dose for those unvaccinated) or outcome of interest.

COVID-19 vaccination

All vaccines approved within the study period from January 2021 to July 2021—namely, ChAdOx1 (Oxford/AstraZeneca), BNT162b2 (BioNTech/Pfizer) Ad26.COV2.S (Janssen) and mRNA-1273 (Moderna), were included for this study.

Post-COVID-19 outcomes of interest

Outcomes of interest were defined as SARS-CoV-2 infection followed by a predefined thromboembolic or cardiac event of interest within a year after infection, and with no record of the same clinical event in the 6 months before COVID-19. Outcome date was set as the corresponding SARS-CoV-2 infection date.

COVID-19 was identified from either a positive SARS-CoV-2 test (polymerase chain reaction (PCR) or antigen), or a clinical COVID-19 diagnosis, with no record of COVID-19 in the previous 6 weeks. This wash-out period was imposed to exclude re-recordings of the same COVID-19 episode.

Post-COVID-19 outcome events were selected based on previous studies.^{11–13} Events comprised ischaemic stroke (IS), haemorrhagic stroke (HS), transient ischaemic attack (TIA), ventricular arrhythmia/cardiac arrest (VACA), myocarditis/pericarditis (MP), myocardial infarction (MI), heart failure (HF), pulmonary embolism (PE) and deep vein thrombosis (DVT). We used two composite outcomes: (1) VTE, as an aggregate of PE and DVT and (2) ATE, as a composite of IS, TIA and MI. To avoid re-recording of the same complication we imposed a wash-out

period of 90 days between records. Phenotypes for these complications were based on previously published studies.^{3 4 8 18}

All outcomes were ascertained in four different time periods following SARS-CoV-2 infection: the first period described the acute infection phase—that is, 0–30 days after COVID-19, whereas the later periods - which are 31–90 days, 91–180 days and 181–365 days, illustrate the post-acute phase (figure 1).

Negative control outcomes

Negative control outcomes (NCOs) were used to detect residual confounding. NCOs are outcomes which are not believed to be causally associated with the exposure, but share the same bias structure with the exposure and outcome of interest. Therefore, no significant association between exposure and NCO is to be expected. Our study used 43 different NCOs from previous work assessing vaccine effectiveness.¹⁹

Statistical analysis

Federated network analyses

A template for an analytical script was developed and subsequently tailored to include the country-specific aspects (eg, dates, priority groups) for the vaccination rollout. Analyses were conducted locally for each database. Only aggregated data were shared and person counts < 5 were clouded.

Propensity score weighting

Large-scale propensity scores (PS) were calculated to estimate the likelihood of a person receiving the vaccine based on their demographic and health-related characteristics (eg, conditions,

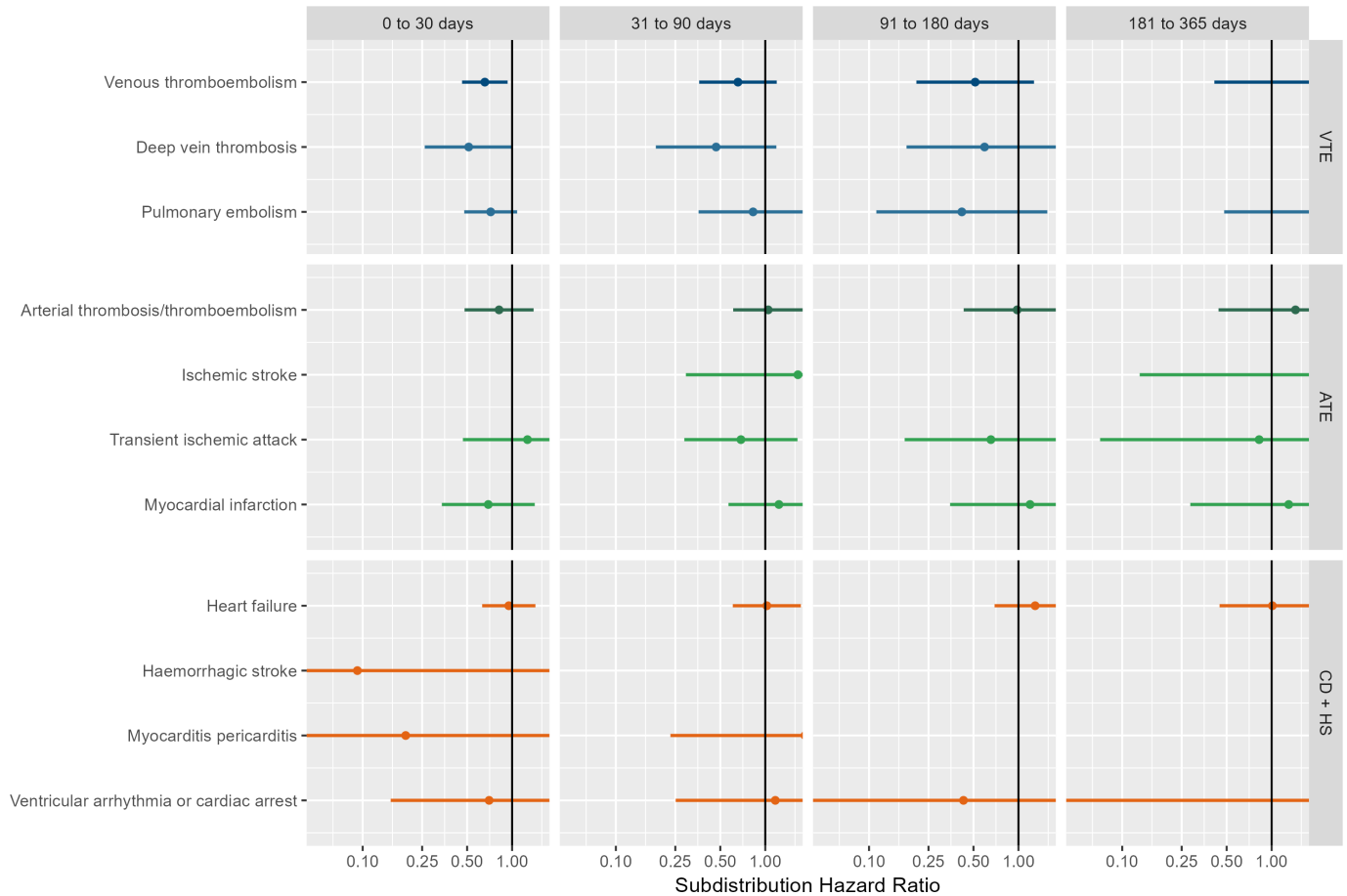


Figure 3 Forest plots for comparative vaccine effect (BNT162b2 vs ChAdOx1); meta-analysis across cohorts and databases. ATE, arterial thrombosis/thromboembolism; CD+HS, cardiac diseases and haemorrhagic stroke; VTE, venous thromboembolism.

medications) prior to the index date. PS were then used to minimise observed confounding by creating a weighted population (overlap weighting²⁰), in which individuals contributed with a different weight based on their PS and vaccination status.

Prespecified key variables included in the PS comprised age, sex, location, index date, prior observation time in the database, number of previous outpatient visits and previous SARS-CoV-2 PCR/antigen tests. Regional vaccination, testing and COVID-19 incidence rates were also forced into the PS equation for the UK databases²¹ and SIDIAP²². In addition, least absolute shrinkage and selection operator (LASSO) regression, a technique for variable selection, was used to identify additional variables from all recorded conditions and prescriptions within 0–30 days, 31–180 days and 181-any time (conditions only) before the index date that had a prevalence of >0.5% in the study population.

PS were then separately estimated for each staggered cohort and analysis. We considered covariate balance to be achieved if absolute standardised mean differences (ASMDs) were ≤0.1 after weighting. Baseline characteristics such as demographics and comorbidities were reported.

Effect estimation

To account for the competing risk of death associated with COVID-19, Fine-and-Grey models²³ were used to calculate subdistribution hazard ratios (sHRs). Subsequently, sHRs and confidence intervals were empirically calibrated from NCO estimates²⁴ to account for unmeasured confounding. To calibrate the estimates, the empirical null distribution was derived from NCO

estimates and was used to compute calibrated confidence intervals. For each outcome, sHRs from the four staggered cohorts were pooled using random-effect meta-analysis, both separately for each database and across all four databases.

Sensitivity analysis

Sensitivity analyses comprised 1) censoring follow-up for vaccinated people at the time when they received their second vaccine dose and 2) considering only the first post-COVID-19 outcome within the year after infection (online supplemental figure S1). In addition, comparative effectiveness analyses were conducted for BNT162b2 versus ChAdOx1.

Data and code availability

All analytic code for the study is available in GitHub (<https://github.com/oxford-pharmacoepi/vaccineEffectOnPostCovidCardiacThromboembolicEvents>), including code lists for vaccines, COVID-19 tests and diagnoses, cardiac and thromboembolic events, NCO and health conditions to prioritise patients for vaccination in each country. We used R version 4.2.3 and statistical packages survival (3.5–3), Empirical Calibration (3.1.1), glmnet (4.1–7), and Hmisc (5.0–1).

Patient and public involvement

Owing to the nature of the study and the limitations regarding data privacy, the study design, analysis, interpretation of data

and revision of the manuscript did not involve any patients or members of the public.

RESULTS

All aggregated results are available in a web application (<https://dpa-pde-oxford.shinyapps.io/PostCovidComplications/>).

We included over 10.17 million vaccinated individuals (1 618 395 from CPRD Gold; 5 729 800 from CPRD Aurum; 2 744 821 from SIDIAP and 77 603 from CORIVA) and 10.39 million unvaccinated individuals (1 640 371; 5 860 564; 2 588 518 and 302 267, respectively). Online supplemental figures S2-5 illustrate study inclusion for each database.

Adequate covariate balance was achieved after PS weighting in most studies: CORIVA (all cohorts) and SIDIAP (cohorts 1 and 4) did not contribute to ChAdOx1 subanalyses owing to sample size and covariate imbalance. ASMD results are accessible in the web application.

NCO analyses suggested residual bias after PS weighting, with a majority of NCOs associated positively with vaccination. Therefore, calibrated estimates are reported in this manuscript. Uncalibrated effect estimates and NCO analyses are available in the web interface.

Population characteristics

Table 1 presents baseline characteristics for the weighted populations in CPRD Aurum, for illustrative purposes. Online supplemental tables S1-25 summarise baseline characteristics for weighted and unweighted populations for each database and comparison. Across databases and cohorts, populations followed similar patterns: cohort 1 represented an older subpopulation (around 80 years old) with a high proportion of women (57%). Median age was lowest in cohort 4 ranging between 30 and 40 years.

COVID-19 vaccination and post-COVID-19 complications

Table 2 shows the incidence of post-COVID-19 VTE, ATE and HF, the three most common post-COVID-19 conditions among the studied outcomes. Outcome counts are presented separately for 0–30, 31–90, 91–180 and 181–365 days after SARS-CoV-2 infection. Online supplemental tables S26-36 include all studied complications, also for the sensitivity and subanalyses. Similar pattern for incidences were observed across all databases: higher outcome rates in the older populations (cohort 1) and decreasing frequency with increasing time after infection in all cohorts.

Results from calibrated estimates pooled in meta-analysis across cohorts and databases are shown in figure 2.

Reduced risk associated with vaccination is observed for acute and post-acute VTE, DVT, and PE: acute meta-analytic sHR are 0.22 (95% CI, 0.17–0.29); 0.36 (0.28–0.45); and 0.19 (0.15–0.25), respectively. For VTE in the post-acute phase, sHR estimates are 0.43 (0.34–0.53), 0.53 (0.40–0.70) and 0.50 (0.36–0.70) for 31–90, 91–180, and 181–365 days post COVID-19, respectively. Reduced risk of VTE outcomes was observed in vaccinated across databases and cohorts, see online supplemental figures S14–22.

Similarly, the risk of ATE, IS and MI in the acute phase after infection was reduced for the vaccinated group, sHR of 0.53 (0.44–0.63), 0.55 (0.43–0.70) and 0.49 (0.38–0.62), respectively. Reduced risk associated with vaccination persisted for post-acute ATE, with sHR of 0.74 (0.60–0.92), 0.72 (0.58–0.88) and 0.62 (0.48–0.80) for 31–90, 91–180 and 181–365 days post-COVID-19, respectively. Risk of post-acute MI remained lower for vaccinated in the 31–90 and 91–180 days after COVID-19,

with sHR of 0.64 (0.46–0.87) and 0.64 (0.45–0.90), respectively. Vaccination effect on post-COVID-19 TIA was seen only in the 181–365 days, with sHR of 0.51 (0.31–0.82). Online supplemental figures S23-31 show database-specific and cohort-specific estimates for ATE-related complications.

Risk of post-COVID-19 cardiac complications was reduced in vaccinated individuals. Meta-analytic estimates in the acute phase showed sHR of 0.45 (0.38–0.53) for HF, 0.41 (0.26–0.66) for MP and 0.41 (0.27–0.63) for VACA. Reduced risk persisted for post-acute COVID-19 HF: sHR 0.61 (0.51–0.73) for 31–90 days, 0.61 (0.51–0.73) for 91–180 days and 0.52 (0.43–0.63) for 181–365 days. For post-acute MP, risk was only lowered in the first post-acute window (31–90 days), with sHR of 0.43 (0.21–0.85). Vaccination showed no association with post-COVID-19 HS. Database-specific and cohort-specific results for these cardiac diseases are shown in online supplemental figures S32-40.

Stratified analyses by vaccine showed similar associations, except for ChAdOx1 which was not associated with reduced VTE and ATE risk in the last post-acute window. Sensitivity analyses were consistent with main results (online supplemental figures S6-13).

Figure 3 shows the results of comparative effects of BNT162b2 versus ChAdOx1, based on UK data. Meta-analytic estimates favoured BNT162b2 (sHR of 0.66 (0.46–0.93)) for VTE in the 0–30 days after infection, but no differences were seen for post-acute VTE or for any of the other outcomes. Results from sensitivity analyses, database-specific and cohort-specific estimates were in line with the main findings (online supplemental figures S41-51).

DISCUSSION

Key findings

Our analyses showed a substantial reduction of risk (45–81%) for thromboembolic and cardiac events in the acute phase of COVID-19 associated with vaccination. This finding was consistent across four databases and three different European countries. Risks for post-acute COVID-19 VTE, ATE and HF were reduced to a lesser extent (24–58%), whereas a reduced risk for post-COVID-19 MP and VACA in vaccinated people was seen only in the acute phase.

Results in context

The relationship between SARS-CoV-2 infection, COVID-19 vaccines and thromboembolic and/or cardiac complications is tangled. Some large studies report an increased risk of VTE and ATE following both ChAdOx1 and BNT162b2 vaccination,⁷ whereas other studies have not identified such a risk.²⁵ Elevated risk of VTE has also been reported among patients with COVID-19 and its occurrence can lead to poor prognosis and mortality.^{26,27} Similarly, several observational studies have found an association between COVID-19 mRNA vaccination and a short-term increased risk of myocarditis, particularly among younger male individuals.^{5,6} For instance, a self-controlled case series study conducted in England revealed about 30% increased risk of hospital admission due to myocarditis within 28 days following both ChAdOx1 and BNT162b2 vaccines. However, this same study also found a ninefold higher risk for myocarditis following a positive SARS-CoV-2 test, clearly offsetting the observed post-vaccine risk.

COVID-19 vaccines have demonstrated high efficacy and effectiveness in preventing infection and reducing the severity of acute-phase infection. However, with the emergence of

newer variants of the virus, such as omicron, and the waning protective effect of the vaccine over time, there is a growing interest in understanding whether the vaccine can also reduce the risk of complications after breakthrough infections. Recent studies suggested that COVID-19 vaccination could potentially protect against acute post-COVID-19 cardiac and thromboembolic events.^{11 12} A large prospective cohort study¹¹ reports risk of VTE after SARS-CoV-2 infection to be substantially reduced in fully vaccinated ambulatory patients. Likewise, Al-Aly *et al*¹² suggest a reduced risk for post-acute COVID-19 conditions in breakthrough infection versus SARS-CoV-2 infection without prior vaccination. However, the populations were limited to SARS-CoV-2 infected individuals and estimates did not include the effect of the vaccine to prevent COVID-19 in the first place. Other studies on post-acute COVID-19 conditions and symptoms have been conducted,^{28 29} but there has been limited reporting on the condition-specific risks associated with COVID-19, even though the prognosis for different complications can vary significantly.

In line with previous studies, our findings suggest a potential benefit of vaccination in reducing the risk of post-COVID-19 thromboembolic and cardiac complications. We included broader populations, estimated the risk in both acute and post-acute infection phases and replicated these using four large independent observational databases. By pooling results across different settings, we provided the most up-to-date and robust evidence on this topic.

Strengths and limitations

The study has several strengths. Our multinational study covering different healthcare systems and settings showed consistent results across all databases, which highlights the robustness and replicability of our findings. All databases had complete recordings of vaccination status (date and vaccine) and are representative of the respective general population. Algorithms to identify study outcomes were used in previous published network studies, including regulatory-funded research.^{3 4 8 18} Other strengths are the staggered cohort design which minimises confounding by indication and immortal time bias. PS overlap weighting and NCO empirical calibration have been shown to adequately minimise bias in vaccine effectiveness studies.¹⁹ Furthermore, our estimates include the vaccine effectiveness against COVID-19, which is crucial in the pathway to experience post-COVID-19 complications.

Our study has some limitations. The use of real-world data comes with inherent limitations including data quality concerns and risk of confounding. To deal with these limitations, we employed state-of-the-art methods, including large-scale propensity score weighting and calibration of effect estimates using NCO.^{19 24} A recent study³⁰ has demonstrated that methodologically sound observational studies based on routinely collected data can produce results similar to those of clinical trials. We acknowledge that results from NCO were positively associated with vaccination, and estimates might still be influenced by residual bias despite using calibration. Another limitation is potential under-reporting of post-COVID-19 complications: some asymptomatic and mild COVID-19 infections might have not been recorded. Additionally, post-COVID-19 outcomes of interest might be under-recorded in primary care databases (CPRD Aurum and Gold) without hospital linkage, which represent a large proportion of the data in the study. However, results in SIDIAP and CORIVA, which include secondary care data, were similar. Also, our study included a small number of

young men and male teenagers, who were the main population concerned with increased risks of myocarditis/pericarditis following vaccination.

CONCLUSIONS

Vaccination against SARS-CoV-2 substantially reduced the risk of acute post-COVID-19 thromboembolic and cardiac complications, probably through a reduction in the risk of SARS-CoV-2 infection and the severity of COVID-19 disease due to vaccine-induced immunity. Reduced risk in vaccinated people lasted for up to 1 year for post-COVID-19 VTE, ATE and HF, but not clearly for other complications. Findings from this study highlight yet another benefit of COVID-19 vaccination. However, further research is needed on the possible waning of the risk reduction over time and on the impact of booster vaccination.

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Data availability statement Data may be obtained from a third party and are not publicly available. CPRD: CPRD data were obtained under the CPRD multi-study license held by the University of Oxford after Research Data Governance (RDG) approval. Direct data sharing is not allowed. SIDIAP: In accordance with current European and national law, the data used in this study is only available for the researchers participating in this study. Thus, we are not allowed to distribute or make publicly available the data to other parties. However, researchers from public institutions can request data from SIDIAP if they comply with certain requirements. Further information is available online (<https://www.sidiap.org/index.php/menu-solicitudesen/application-procedure>) or by contacting SIDIAP (sidiap@idiapjgol.org). CORIVA: CORIVA data were obtained under the approval of Research Ethics Committee of the University of Tartu and the patient level data sharing is not allowed. All analyses in this study were conducted in a federated manner, where analytical code and aggregated (anonymised) results were shared, but no patient-level data was transferred across the collaborating institutions.

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SUPPLEMENT

The effectiveness of COVID-19 vaccines to prevent post COVID cardiac and thromboembolic complications.

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Figure S1: Follow-up in vaccinated and unvaccinated cohorts.

(A) Main analysis, (B) Follow-up ends at first vaccine dose after index date, (C) Post COVID sequelae refers just to the first outcome after infection.

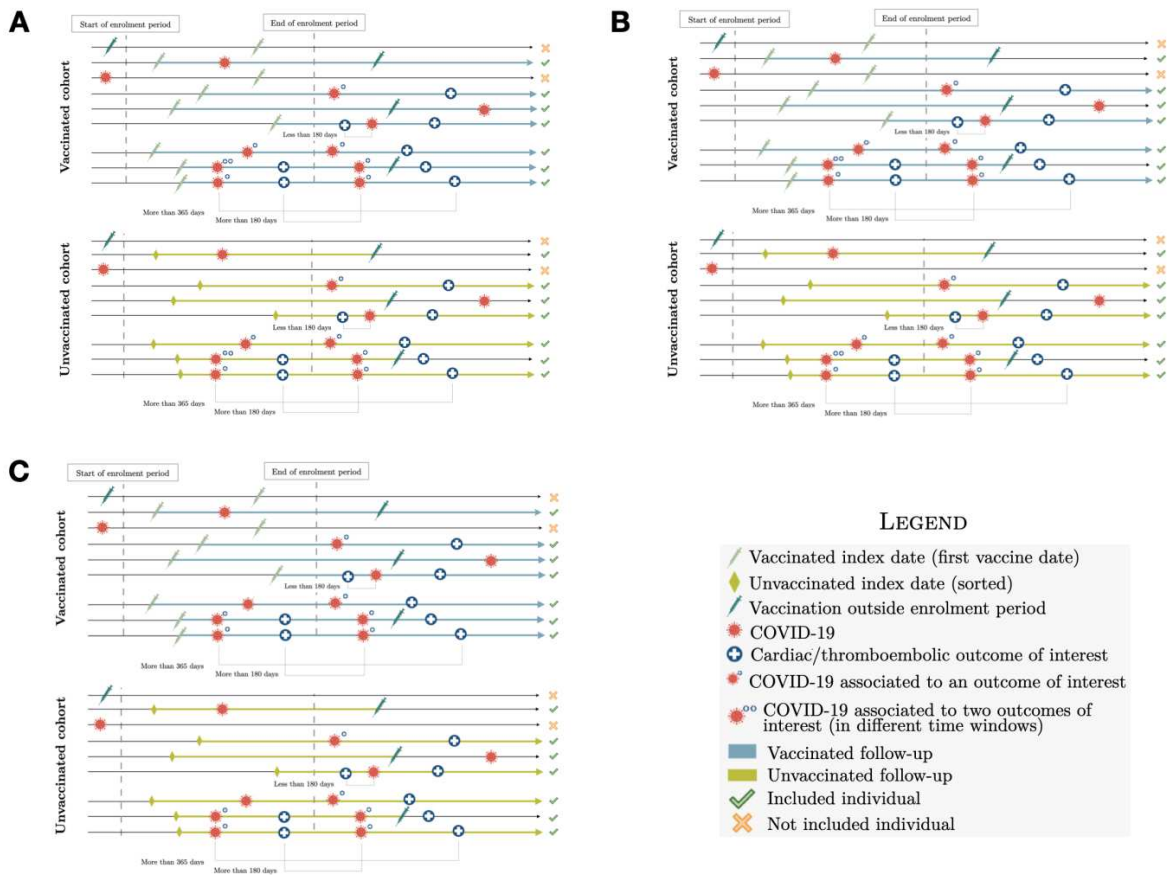


Figure S2: Study Inclusion Flowchart CPRD AURUM

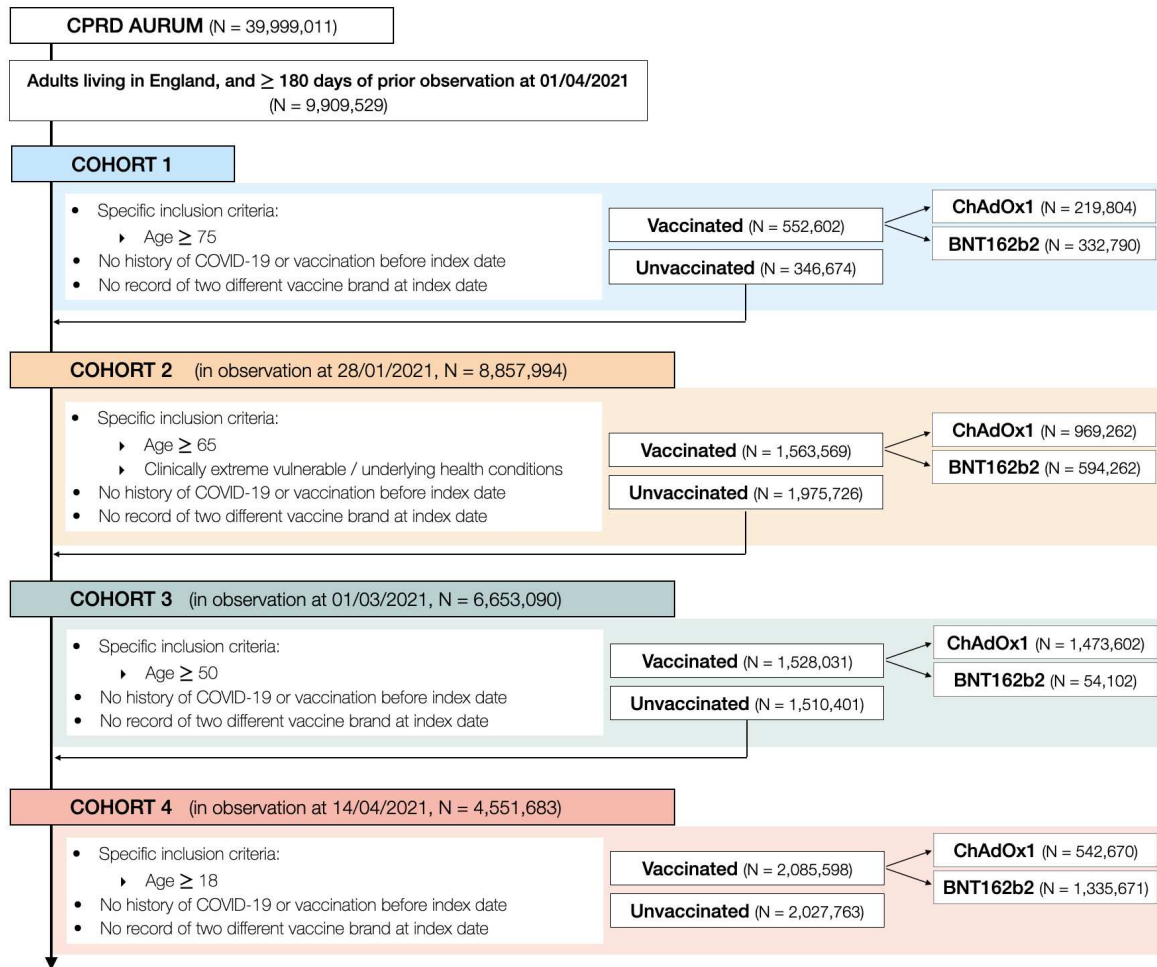


Figure S3: Study Inclusion Flowchart CPRD GOLD.

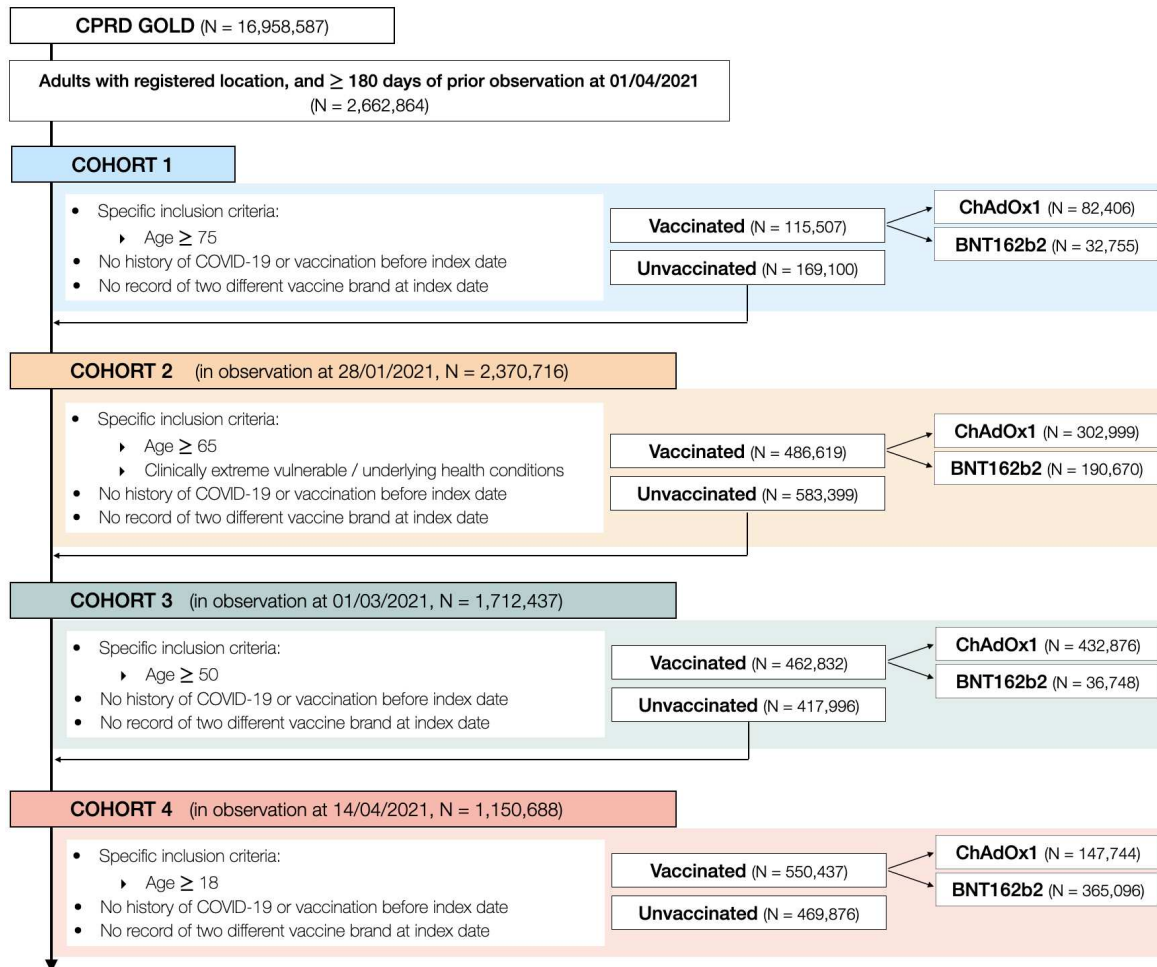


Figure S4: Study Inclusion Flowchart SIDIAP.

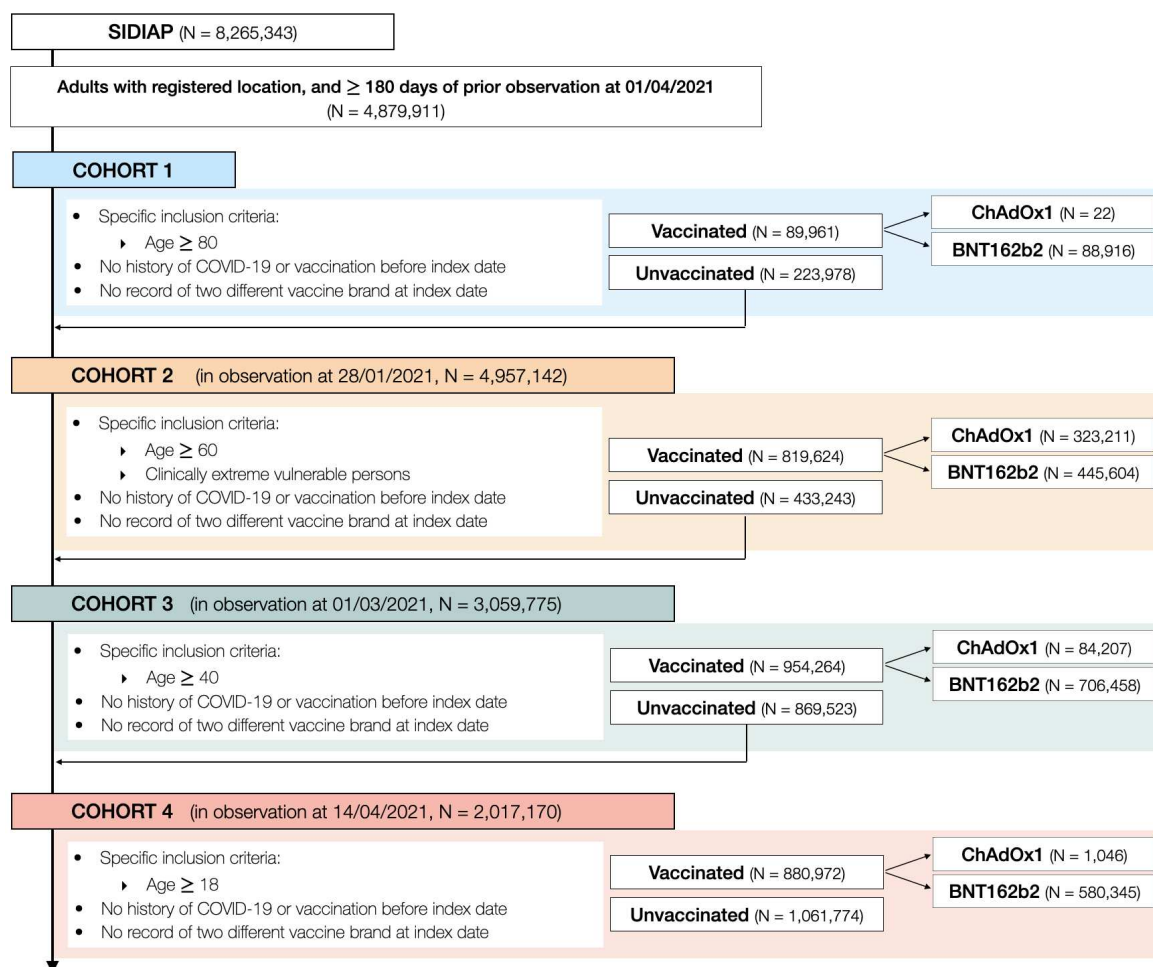


Figure S5: Study Inclusion Flowchart CORIVA.

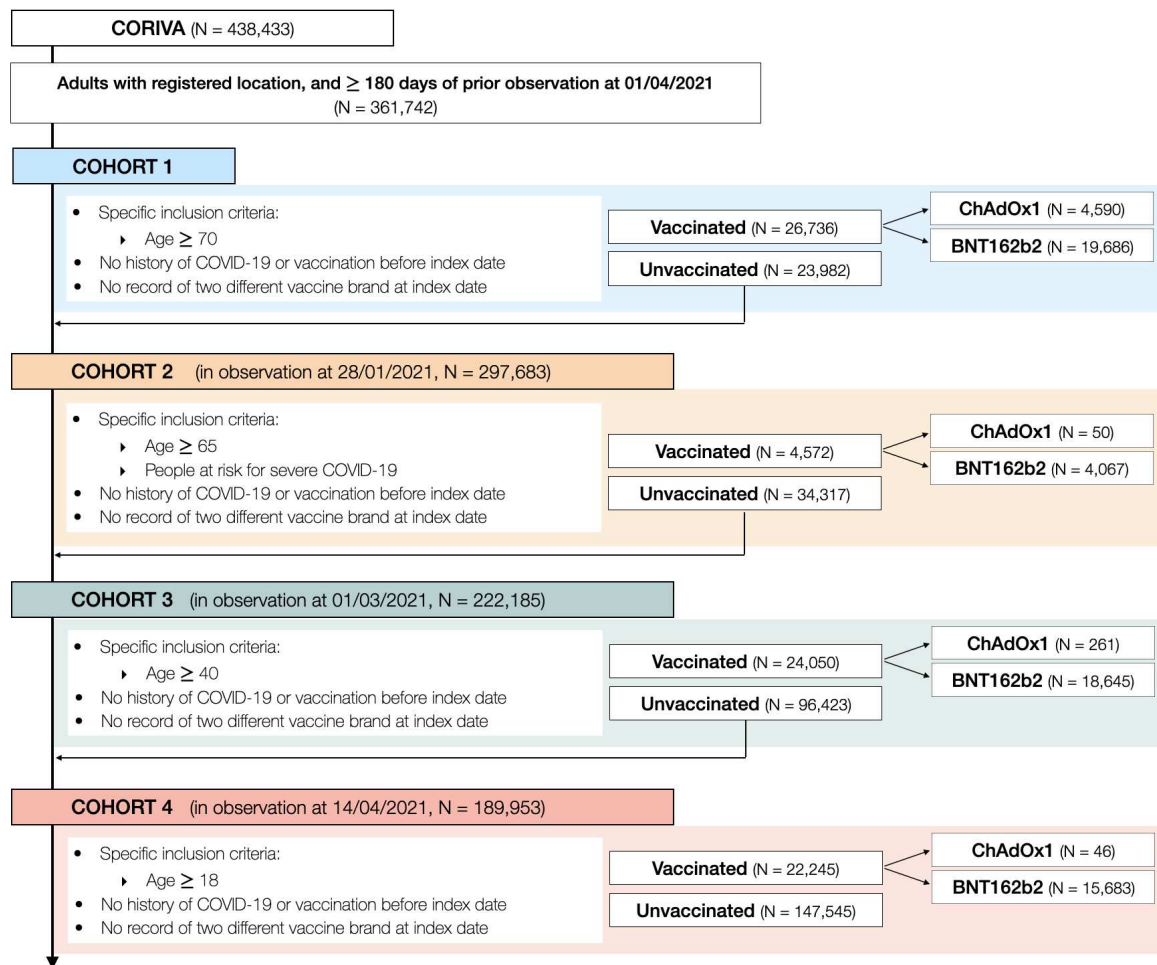


Table S1: Characteristics of unweighted populations in CPRD AURUM, database, stratified by staggered cohort and exposure status. Exposure is any COVID-19 vaccine.

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
N (individuals)	346,674	552,602		1,975,726	1,563,569		1,510,401	1,528,031		2,027,763	2,085,598	
Age, median [Q25-Q75]	78 [76-82]	81 [78-86]	0.319	42 [32-55]	68 [60-73]	0.995	41 [31-53]	55 [51-60]	0.610	35 [27-45]	35 [27-43]	0.134
Sex: Female, N(%)	192,771 (56%)	314,141 (57%)	0.025	1,244,636 (63%)	852,976 (55%)	0.172	880,404 (58%)	771,929 (51%)	0.157	862,676 (43%)	958,124 (46%)	0.068
Years of prior history*, median [Q25-Q75]	24 [10-35]	25 [11-37]	0.056	15 [7-25]	21 [9-32]	0.278	13 [6-22]	17 [8-27]	0.207	8 [4-16]	8 [3-18]	0.032
Number of GP visits, median [Q25-Q75]	10 [5-17]	11 [6-19]	0.105	6 [2-11]	10 [6-17]	0.367	4 [1-10]	7 [3-12]	0.180	2 [0-5]	3 [1-7]	0.108
Number of PCR tests, median [Q25-Q75]	0[0-0]	0[0-0]	0.103	0[0-0]	0[0-0]	0.065	0[0-0]	0[0-0]	0.007	0[0-0]	0[0-0]	0.078
Comorbidities**, N(%)												
Anxiety	51,067 (15%)	82,765 (15%)	0.007	435,770 (22%)	309,567 (20%)	0.056	289,563 (19%)	292,336 (19%)	0.001	265,627 (13%)	338,058 (16%)	0.088
Asthma	36,474 (11%)	61,899 (11%)	0.022	501,209 (25%)	275,768 (18%)	0.189	294,123 (19%)	209,708 (14%)	0.155	138,317 (7%)	173,056 (8%)	0.056
Chronic kidney disease	71,083 (21%)	137,953 (25%)	0.107	55,104 (3%)	154,263 (10%)	0.294	24,340 (2%)	30,896 (2%)	0.031	18,625 (1%)	5,796 (0%)	0.083
COPD	28,665 (8%)	47,422 (9%)	0.011	29,729 (2%)	107,297 (7%)	0.270	13,433 (1%)	15,685 (1%)	0.014	10,543 (1%)	2,535 (0%)	0.071
Dementia	16,610 (5%)	32,934 (6%)	0.052	6,692 (0%)	15,828 (1%)	0.082	3,425 (0%)	3,219 (0%)	0.003	2,691 (0%)	575 (0%)	0.037
Depressive disorder	42,145 (12%)	64,840 (12%)	0.013	367,463 (19%)	283,390 (18%)	0.012	236,584 (16%)	265,876 (17%)	0.047	210,644 (10%)	253,317 (12%)	0.056
Diabetes	63,154 (18%)	101,682 (18%)	0.005	107,425 (5%)	253,026 (16%)	0.351	60,932 (4%)	84,224 (6%)	0.069	49,154 (2%)	22,968 (1%)	0.101
GERD	18,336 (5%)	32,360 (6%)	0.025	68,070 (3%)	84,985 (5%)	0.097	39,594 (3%)	58,961 (4%)	0.070	31,119 (2%)	38,612 (2%)	0.025
Heart failure	17,882 (5%)	33,578 (6%)	0.040	12,275 (1%)	37,396 (2%)	0.146	5,641 (0%)	7,204 (0%)	0.015	4,611 (0%)	1,163 (0%)	0.046
Hypertension	172,799 (50%)	301,294 (55%)	0.094	206,105 (10%)	545,782 (35%)	0.611	110,912 (7%)	240,120 (16%)	0.264	86,435 (4%)	54,357 (3%)	0.091
Hypothyroidism	31,444 (9%)	56,367 (10%)	0.038	78,934 (4%)	118,453 (8%)	0.154	43,892 (3%)	67,686 (4%)	0.081	30,993 (2%)	35,364 (2%)	0.013
Malignant neoplastic	68,984 (20%)	131,635	0.095	60,318 (3%)	207,240	0.379	29,689 (2%)	61,923 (4%)	0.122	22,701 (1%)	13,590 (1%)	0.050

disease	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
		(24%)			(13%)							
Myocardial infarction	16,027 (5%)	29,525 (5%)	0.033	20,259 (1%)	56,161 (4%)	0.172	7,396 (0%)	12,703 (1%)	0.042	5,764 (0%)	1,621 (0%)	0.049
Osteoporosis	29,909 (9%)	59,521 (11%)	0.072	18,263 (1%)	64,108 (4%)	0.204	8,846 (1%)	15,089 (1%)	0.045	6,922 (0%)	2,535 (0%)	0.046
Pneumonia	16,992 (5%)	28,398 (5%)	0.011	31,746 (2%)	50,739 (3%)	0.107	17,785 (1%)	22,064 (1%)	0.023	13,305 (1%)	13,282 (1%)	0.002
Rheumatoid arthritis	6,596 (2%)	11,237 (2%)	0.009	14,811 (1%)	33,173 (2%)	0.116	5,548 (0%)	9,130 (1%)	0.033	3,710 (0%)	1,816 (0%)	0.026
Stroke	15,249 (4%)	26,478 (5%)	0.019	16,942 (1%)	39,907 (3%)	0.131	7,422 (0%)	10,828 (1%)	0.028	6,030 (0%)	2,291 (0%)	0.042
Venous thromboembolism	19,607 (6%)	35,332 (6%)	0.031	28,876 (1%)	63,048 (4%)	0.158	13,608 (1%)	26,299 (2%)	0.072	12,945 (1%)	4,787 (0%)	0.062

The 4 cohorts represent vaccine rollout periods. *Calculated as the days of previous observation in the database before index date. **Assessed anytime before index date. ASMD = Absolute standardized mean difference, GP = General practice, PCR = Polymerase chain reaction, COPD = Chronic obstructive pulmonary disease, GERD = Gastro-Esophageal reflux disease

Table S2: Characteristics of weighted populations in CPRD AURUM, database, stratified by staggered cohort and exposure status. Exposure is ChAdOx1 vaccine.

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
N (individuals)	100,517	99,985		308,608	304,995		448,766	445,397		242,955	243,847	
Age, median [Q25-Q75]	78 [76-84]	78 [76-84]	0.001	62 [47-69]	62 [47-69]	0.007	50 [41-57]	52 [41-57]	0.001	44 [41-48]	44 [41-48]	0.003
Sex: Female, N(%)	57,756 (57%)	57,174 (57%)	0.006	179,574 (58%)	176,871 (58%)	0.004	236,260 (53%)	234,320 (53%)	0.001	101,805 (42%)	100,846 (41%)	0.011
Years of prior history*, median [Q25-Q75]	24 [10-36]	24 [10-36]	0.004	18 [8-29]	18 [8-29]	0.002	14 [6-24]	14 [6-24]	0.002	10 [5-18]	9 [5-18]	0.004
Number of GP visits, median [Q25-Q75]	10 [5-18]	10 [6-18]	0.003	8 [3-15]	8 [5-15]	0.003	4 [1-11]	6 [2-10]	0.007	2 [0-7]	2 [1-7]	0.016
Number of PCR tests, median [Q25-Q75]	0[0-0]	0[0-0]	0.011	0[0-0]	0[0-0]	0.003	0[0-0]	0[0-0]	0.003	0[0-0]	0[0-0]	0.005
Comorbidities**, N(%)												
Anxiety	15,457 (15%)	15,069 (15%)	0.009	67,125 (22%)	64,408 (21%)	0.015	90,806 (20%)	87,243 (20%)	0.016	37,475 (15%)	38,040 (16%)	0.005
Asthma	10,993 (11%)	10,863 (11%)	0.002	65,274 (21%)	62,424 (20%)	0.017	76,417 (17%)	75,841 (17%)	0.000	17,944 (7%)	17,468 (7%)	0.009
Chronic kidney disease	23,223 (23%)	22,872 (23%)	0.005	23,022 (7%)	24,288 (8%)	0.019	8,460 (2%)	8,356 (2%)	0.001	2,419 (1%)	2,043 (1%)	0.017
COPD	8,669 (9%)	8,770 (9%)	0.005	14,411 (5%)	15,226 (5%)	0.015	5,747 (1%)	4,794 (1%)	0.019	1,263 (1%)	1,250 (1%)	0.001
Dementia	6,529 (6%)	6,431 (6%)	0.003	3,880 (1%)	3,541 (1%)	0.009	898 (0%)	1,004 (0%)	0.006	203 (0%)	399 (0%)	0.023
Depressive disorder	12,559 (12%)	12,267 (12%)	0.007	60,745 (20%)	57,903 (19%)	0.018	80,264 (18%)	77,017 (17%)	0.016	32,304 (13%)	33,302 (14%)	0.011
Diabetes	18,750 (19%)	18,602 (19%)	0.001	39,262 (13%)	38,979 (13%)	0.002	25,334 (6%)	26,121 (6%)	0.009	6,679 (3%)	6,315 (3%)	0.010
GERD	5,590 (6%)	5,471 (5%)	0.004	14,645 (5%)	14,339 (5%)	0.002	14,758 (3%)	14,823 (3%)	0.002	5,727 (2%)	6,021 (2%)	0.007
Heart failure	6,181 (6%)	5,763 (6%)	0.016	6,098 (2%)	5,685 (2%)	0.008	2,241 (0%)	1,983 (0%)	0.008	610 (0%)	545 (0%)	0.006
Hypertension	52,737 (52%)	51,796 (52%)	0.013	78,623 (25%)	79,827 (26%)	0.016	51,054 (11%)	51,059 (11%)	0.003	15,350 (6%)	15,670 (6%)	0.004
Hypothyroidism	9,956 (10%)	9,690 (10%)	0.007	19,720 (6%)	19,562 (6%)	0.001	16,480 (4%)	16,361 (4%)	0.000	5,735 (2%)	5,984 (2%)	0.006
Malignant neoplastic	21,691 (22%)	21,468	0.003	25,191 (8%)	27,892 (9%)	0.035	13,140 (3%)	12,870 (3%)	0.002	4,003 (2%)	3,621 (1%)	0.013

disease	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
		(21%)										
Myocardial infarction	5,182 (5%)	4,988 (5%)	0.008	7,777 (3%)	8,594 (3%)	0.018	3,415 (1%)	3,228 (1%)	0.004	933 (0%)	636 (0%)	0.022
Osteoporosis	9,975 (10%)	10,018 (10%)	0.003	9,052 (3%)	9,423 (3%)	0.009	3,285 (1%)	3,499 (1%)	0.006	840 (0%)	934 (0%)	0.006
Pneumonia	5,770 (6%)	5,268 (5%)	0.021	9,096 (3%)	8,541 (3%)	0.009	6,196 (1%)	6,077 (1%)	0.001	1,923 (1%)	2,040 (1%)	0.005
Rheumatoid arthritis	2,002 (2%)	2,063 (2%)	0.005	4,856 (2%)	4,971 (2%)	0.004	2,266 (1%)	2,795 (1%)	0.016	665 (0%)	478 (0%)	0.016
Stroke	5,085 (5%)	4,791 (5%)	0.012	6,650 (2%)	6,616 (2%)	0.001	3,150 (1%)	2,942 (1%)	0.005	908 (0%)	773 (0%)	0.010
Venous thromboembolism	6,342 (6%)	6,069 (6%)	0.010	9,208 (3%)	9,850 (3%)	0.014	6,193 (1%)	7,393 (2%)	0.023	2,532 (1%)	1,239 (1%)	0.061

The 4 cohorts represent vaccine rollout periods. *Calculated as the days of previous observation in the database before index date. **Assessed anytime before index date. ASMD = Absolute standardized mean difference, GP = General practice, PCR = Polymerase chain reaction, COPD = Chronic obstructive pulmonary disease, GERD = Gastro-Esophageal reflux disease

Table S3: Characteristics of unweighted populations in CPRD AURUM, database, stratified by staggered cohort and exposure status. Exposure is ChAdOx1 vaccine.

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
N (individuals)	344,687	219,804		1,975,770	969,262		1,510,493	1,473,602		2,066,318	542,670	
Age, median [Q25-Q75]	78 [76-82]	80 [77-85]	0.240	42 [32-55]	69 [63-73]	1.059	41 [31-53]	55 [51-60]	0.605	34 [27-45]	45 [42-48]	0.507
Sex: Female, N(%)	191,649 (56%)	127,656 (58%)	0.050	1,244,532 (63%)	528,692 (55%)	0.172	880,468 (58%)	739,444 (50%)	0.163	880,225 (43%)	242,758 (45%)	0.043
Years of prior history*, median [Q25-Q75]	24 [10-35]	24 [9-36]	0.018	15 [7-25]	21 [9-33]	0.288	13 [6-22]	17 [8-27]	0.203	7 [4-16]	10 [5-18]	0.143
Number of GP visits, median [Q25-Q75]	10 [5-17]	12 [6-19]	0.121	6 [2-11]	10 [6-17]	0.359	4 [1-10]	7 [3-12]	0.169	2 [0-5]	3 [1-8]	0.146
Number of PCR tests, median [Q25-Q75]	0[0-0]	0[0-0]	0.194	0[0-0]	0[0-0]	0.070	0[0-0]	0[0-0]	0.005	0[0-0]	0[0-0]	0.066
Comorbidities**, N(%)												
Anxiety	50,786 (15%)	33,355 (15%)	0.012	435,737 (22%)	187,469 (19%)	0.067	289,618 (19%)	281,846 (19%)	0.001	268,451 (13%)	86,805 (16%)	0.085
Asthma	36,259 (11%)	24,009 (11%)	0.013	501,234 (25%)	159,162 (16%)	0.221	294,156 (19%)	200,995 (14%)	0.157	140,178 (7%)	41,393 (8%)	0.033
Chronic kidney disease	70,604 (20%)	51,053 (23%)	0.066	55,103 (3%)	97,339 (10%)	0.299	24,361 (2%)	24,198 (2%)	0.002	18,798 (1%)	2,879 (1%)	0.045
COPD	28,448 (8%)	19,105 (9%)	0.016	29,730 (2%)	67,700 (7%)	0.274	13,436 (1%)	13,621 (1%)	0.004	10,647 (1%)	1,510 (0%)	0.038
Dementia	16,327 (5%)	16,795 (8%)	0.121	6,689 (0%)	12,106 (1%)	0.103	3,424 (0%)	1,896 (0%)	0.023	2,729 (0%)	447 (0%)	0.015
Depressive disorder	41,905 (12%)	27,009 (12%)	0.004	367,500 (19%)	170,626 (18%)	0.026	236,628 (16%)	256,789 (17%)	0.047	212,626 (10%)	74,210 (14%)	0.104
Diabetes	62,733 (18%)	39,751 (18%)	0.003	107,449 (5%)	154,348 (16%)	0.344	60,968 (4%)	78,394 (5%)	0.061	49,223 (2%)	9,729 (2%)	0.041
GERD	18,253 (5%)	12,156 (6%)	0.010	68,089 (3%)	52,694 (5%)	0.097	39,619 (3%)	56,444 (4%)	0.068	31,367 (2%)	13,807 (3%)	0.073
Heart failure	17,716 (5%)	13,147 (6%)	0.037	12,277 (1%)	24,276 (3%)	0.152	5,638 (0%)	5,673 (0%)	0.002	4,625 (0%)	681 (0%)	0.024
Hypertension	171,846 (50%)	114,922 (52%)	0.049	206,105 (10%)	345,014 (36%)	0.626	110,975 (7%)	224,543 (15%)	0.251	87,010 (4%)	31,330 (6%)	0.072
Hypothyroidism	31,256 (9%)	21,855 (10%)	0.030	78,921 (4%)	73,992 (8%)	0.156	43,887 (3%)	64,026 (4%)	0.077	31,315 (2%)	13,920 (3%)	0.074
Malignant neoplastic disease	68,598 (20%)	49,023 (22%)	0.059	60,355 (3%)	131,135 (14%)	0.387	29,693 (2%)	55,601 (4%)	0.108	22,873 (1%)	7,505 (1%)	0.025

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
Myocardial infarction	15,938 (5%)	11,236 (5%)	0.023	20,262 (1%)	33,142 (3%)	0.163	7,401 (0%)	11,237 (1%)	0.035	5,781 (0%)	861 (0%)	0.026
Osteoporosis	29,704 (9%)	22,986 (10%)	0.063	18,255 (1%)	42,319 (4%)	0.216	8,856 (1%)	12,455 (1%)	0.031	6,980 (0%)	1,380 (0%)	0.015
Pneumonia	16,837 (5%)	12,101 (6%)	0.028	31,706 (2%)	33,170 (3%)	0.116	17,787 (1%)	20,399 (1%)	0.018	13,425 (1%)	4,297 (1%)	0.017
Rheumatoid arthritis	6,549 (2%)	4,544 (2%)	0.012	14,813 (1%)	20,294 (2%)	0.114	5,536 (0%)	8,463 (1%)	0.030	3,723 (0%)	821 (0%)	0.007
Stroke	15,118 (4%)	10,876 (5%)	0.027	16,944 (1%)	24,851 (3%)	0.132	7,424 (0%)	9,547 (1%)	0.021	6,059 (0%)	1,153 (0%)	0.016
Venous thromboembolism	19,455 (6%)	13,782 (6%)	0.026	28,887 (1%)	39,415 (4%)	0.159	13,609 (1%)	24,312 (2%)	0.067	13,021 (1%)	1,936 (0%)	0.039

The 4 cohorts represent vaccine rollout periods. *Calculated as the days of previous observation in the database before index date. **Assessed anytime before index date. ASMD = Absolute standardized mean difference, GP = General practice, PCR = Polymerase chain reaction, COPD = Chronic obstructive pulmonary disease, GERD = Gastro-Esophageal reflux disease

Table S4: Characteristics of weighted populations in CPRD AURUM, database, stratified by staggered cohort and exposure status. Exposure is BNT162b2 vaccine.

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
N (individuals)	105,853	106,684		255,400	253,164		37,236	37,227		630,449	633,628	
Age, median [Q25-Q75]	80 [77-85]	80 [77-85]	0.003	58 [46-67]	58 [46-68]	0.006	54 [45-64]	54 [45-64]	0.016	32 [25-37]	32 [25-37]	0.001
Sex: Female, N(%)	60,612 (57%)	60,891 (57%)	0.004	147,020 (58%)	146,572 (58%)	0.007	22,049 (59%)	22,144 (59%)	0.005	278,649 (44%)	282,744 (45%)	0.009
Years of prior history*, median [Q25-Q75]	24 [11-36]	24 [11-35]	0.005	18 [8-29]	18 [8-29]	0.007	16 [7-27]	17 [7-27]	0.007	7 [4-16]	7 [3-18]	0.006
Number of GP visits, median [Q25-Q75]	10 [5-18]	10 [6-17]	0.002	8 [3-15]	10 [5-15]	0.013	6 [2-15]	8 [4-14]	0.003	2 [0-6]	2 [0-6]	0.011
Number of PCR tests, median [Q25-Q75]	0[0-0]	0[0-0]	0.001	0[0-0]	0[0-0]	0.003	0[0-0]	0[0-0]	0.000	0[0-0]	0[0-0]	0.010
Comorbidities**, N(%)												
Anxiety	15,706 (15%)	15,578 (15%)	0.007	57,951 (23%)	55,594 (22%)	0.018	7,672 (21%)	7,363 (20%)	0.021	96,918 (15%)	96,528 (15%)	0.004
Asthma	11,563 (11%)	11,733 (11%)	0.002	60,265 (24%)	58,010 (23%)	0.016	6,397 (17%)	6,215 (17%)	0.013	50,849 (8%)	48,590 (8%)	0.015
Chronic kidney disease	25,741 (24%)	26,243 (25%)	0.007	17,219 (7%)	18,864 (7%)	0.028	2,790 (7%)	2,621 (7%)	0.017	2,035 (0%)	1,846 (0%)	0.006
COPD	9,240 (9%)	8,999 (8%)	0.011	11,625 (5%)	12,410 (5%)	0.017	1,224 (3%)	886 (2%)	0.055	859 (0%)	807 (0%)	0.002
Dementia	6,683 (6%)	5,727 (5%)	0.040	2,225 (1%)	1,309 (1%)	0.043	618 (2%)	529 (1%)	0.019	112 (0%)	107 (0%)	0.001
Depressive disorder	12,529 (12%)	12,450 (12%)	0.005	52,883 (21%)	50,765 (20%)	0.016	6,588 (18%)	6,431 (17%)	0.011	71,832 (11%)	71,139 (11%)	0.005
Diabetes	20,227 (19%)	20,182 (19%)	0.005	32,557 (13%)	32,989 (13%)	0.008	3,153 (8%)	3,212 (9%)	0.006	8,183 (1%)	7,675 (1%)	0.008
GERD	6,148 (6%)	5,937 (6%)	0.011	12,436 (5%)	12,160 (5%)	0.003	1,552 (4%)	1,509 (4%)	0.006	9,586 (2%)	10,173 (2%)	0.007
Heart failure	6,643 (6%)	6,329 (6%)	0.014	4,618 (2%)	3,987 (2%)	0.018	767 (2%)	552 (1%)	0.044	474 (0%)	344 (0%)	0.008
Hypertension	56,732 (54%)	57,023 (53%)	0.003	62,628 (25%)	63,500 (25%)	0.013	7,802 (21%)	7,697 (21%)	0.007	11,603 (2%)	12,098 (2%)	0.005
Hypothyroidism	10,528 (10%)	10,633 (10%)	0.001	16,084 (6%)	16,368 (6%)	0.007	2,046 (5%)	2,032 (5%)	0.002	8,722 (1%)	8,355 (1%)	0.006
Malignant neoplastic disease	23,367 (22%)	23,618 (22%)	0.002	19,432 (8%)	22,945 (9%)	0.053	2,799 (8%)	2,742 (7%)	0.006	3,432 (1%)	2,913 (0%)	0.012

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
Myocardial infarction	5,451 (5%)	5,473 (5%)	0.001	6,811 (3%)	7,856 (3%)	0.026	704 (2%)	637 (2%)	0.013	607 (0%)	569 (0%)	0.002
Osteoporosis	10,923 (10%)	10,997 (10%)	0.000	6,664 (3%)	6,208 (2%)	0.010	1,166 (3%)	1,014 (3%)	0.024	653 (0%)	702 (0%)	0.002
Pneumonia	5,814 (5%)	5,303 (5%)	0.023	7,059 (3%)	6,337 (3%)	0.016	991 (3%)	831 (2%)	0.028	3,698 (1%)	3,579 (1%)	0.003
Rheumatoid arthritis	2,115 (2%)	2,076 (2%)	0.004	4,061 (2%)	4,486 (2%)	0.014	330 (1%)	382 (1%)	0.014	723 (0%)	523 (0%)	0.010
Stroke	5,304 (5%)	4,911 (5%)	0.019	5,139 (2%)	5,592 (2%)	0.014	657 (2%)	560 (2%)	0.021	828 (0%)	669 (0%)	0.007
Venous thromboembolism	6,564 (6%)	6,603 (6%)	0.000	7,760 (3%)	7,984 (3%)	0.007	980 (3%)	965 (3%)	0.003	2,860 (0%)	1,602 (0%)	0.034

The 4 cohorts represent vaccine rollout periods. *Calculated as the days of previous observation in the database before index date. **Assessed anytime before index date. ASMD = Absolute standardized mean difference, GP = General practice, PCR = Polymerase chain reaction, COPD = Chronic obstructive pulmonary disease, GERD = Gastro-Esophageal reflux disease

Table S5: Characteristics of unweighted populations in CPRD AURUM, database, stratified by staggered cohort and exposure status. Exposure is BNT162b2 vaccine.

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
N (individuals)	348,052	332,790		1,976,163	594,262		1,510,323	54,102		2,014,161	1,335,671	
Age, median [Q25-Q75]	78 [76-82]	82 [79-86]	0.375	42 [32-55]	67 [56-73]	0.899	41 [31-53]	58 [50-82]	0.777	35 [27-45]	31 [25-37]	0.377
Sex: Female, N(%)	193,520 (56%)	186,481 (56%)	0.009	1,244,798 (63%)	324,259 (55%)	0.172	880,418 (58%)	32,310 (60%)	0.029	856,596 (43%)	625,195 (47%)	0.086
Years of prior history*, median [Q25-Q75]	23 [10-35]	26 [13-38]	0.081	15 [7-25]	21 [9-32]	0.261	13 [6-22]	19 [8-30]	0.308	8 [4-16]	7 [3-19]	0.012
Number of GP visits, median [Q25-Q75]	10 [5-17]	11 [6-18]	0.094	6 [2-11]	11 [6-17]	0.381	4 [1-10]	10 [5-17]	0.436	2 [0-5]	3 [1-7]	0.103
Number of PCR tests, median [Q25-Q75]	0[0-0]	0[0-0]	0.013	0[0-0]	0[0-0]	0.056	0[0-0]	0[0-0]	0.165	0[0-0]	0[0-0]	0.082
Comorbidities**, N(%)												
Anxiety	51,245 (15%)	49,410 (15%)	0.003	435,705 (22%)	122,087 (21%)	0.037	289,623 (19%)	10,441 (19%)	0.003	264,577 (13%)	218,144 (16%)	0.090
Asthma	36,625 (11%)	37,889 (11%)	0.028	501,289 (25%)	116,596 (20%)	0.138	294,101 (19%)	8,668 (16%)	0.090	137,548 (7%)	114,378 (9%)	0.065
Chronic kidney disease	71,413 (21%)	86,899 (26%)	0.133	55,136 (3%)	56,923 (10%)	0.285	24,372 (2%)	6,692 (12%)	0.431	18,579 (1%)	2,664 (0%)	0.097
COPD	28,829 (8%)	28,317 (9%)	0.008	29,793 (2%)	39,595 (7%)	0.263	13,430 (1%)	2,063 (4%)	0.194	10,501 (1%)	942 (0%)	0.083
Dementia	16,828 (5%)	16,138 (5%)	0.001	6,731 (0%)	3,720 (1%)	0.041	3,424 (0%)	1,323 (2%)	0.194	2,673 (0%)	119 (0%)	0.047
Depressive disorder	42,297 (12%)	37,831 (11%)	0.024	367,534 (19%)	112,753 (19%)	0.010	236,577 (16%)	9,046 (17%)	0.029	209,905 (10%)	155,037 (12%)	0.038
Diabetes	63,483 (18%)	61,929 (19%)	0.010	107,471 (5%)	98,676 (17%)	0.362	60,945 (4%)	5,817 (11%)	0.259	49,143 (2%)	12,040 (1%)	0.120
GERD	18,404 (5%)	20,204 (6%)	0.034	68,110 (3%)	32,288 (5%)	0.097	39,607 (3%)	2,506 (5%)	0.108	31,062 (2%)	21,599 (2%)	0.006
Heart failure	17,980 (5%)	20,430 (6%)	0.042	12,311 (1%)	13,120 (2%)	0.134	5,627 (0%)	1,529 (3%)	0.197	4,614 (0%)	448 (0%)	0.054
Hypertension	173,422 (50%)	186,367 (56%)	0.124	206,136 (10%)	200,762 (34%)	0.586	110,969 (7%)	15,536 (29%)	0.579	86,231 (4%)	19,649 (1%)	0.169
Hypothyroidism	31,595 (9%)	34,512 (10%)	0.044	78,935 (4%)	44,456 (7%)	0.150	43,876 (3%)	3,642 (7%)	0.179	30,913 (2%)	18,516 (1%)	0.012
Malignant neoplastic disease	69,247 (20%)	82,610 (25%)	0.118	60,370 (3%)	76,103 (13%)	0.367	29,693 (2%)	6,311 (12%)	0.392	22,630 (1%)	5,104 (0%)	0.086

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
Myocardial infarction	16,111 (5%)	18,289 (5%)	0.040	20,304 (1%)	23,019 (4%)	0.185	7,409 (0%)	1,464 (3%)	0.177	5,738 (0%)	715 (0%)	0.056
Osteoporosis	30,053 (9%)	36,535 (11%)	0.079	18,282 (1%)	21,789 (4%)	0.184	8,852 (1%)	2,632 (5%)	0.265	6,904 (0%)	1,028 (0%)	0.058
Pneumonia	17,134 (5%)	16,297 (5%)	0.001	31,724 (2%)	17,567 (3%)	0.091	17,791 (1%)	1,658 (3%)	0.131	13,263 (1%)	7,793 (1%)	0.010
Rheumatoid arthritis	6,613 (2%)	6,693 (2%)	0.008	14,823 (1%)	12,878 (2%)	0.118	5,533 (0%)	667 (1%)	0.097	3,692 (0%)	891 (0%)	0.033
Stroke	15,325 (4%)	15,601 (5%)	0.014	16,962 (1%)	15,056 (3%)	0.130	7,431 (0%)	1,281 (2%)	0.158	6,019 (0%)	1,022 (0%)	0.051
Venous thromboembolism	19,679 (6%)	21,549 (6%)	0.034	28,882 (1%)	23,632 (4%)	0.155	13,639 (1%)	1,980 (4%)	0.185	12,941 (1%)	2,541 (0%)	0.070

The 4 cohorts represent vaccine rollout periods. *Calculated as the days of previous observation in the database before index date. **Assessed anytime before index date. ASMD = Absolute standardized mean difference, GP = General practice, PCR = Polymerase chain reaction, COPD = Chronic obstructive pulmonary disease, GERD = Gastro-Esophageal reflux disease

Table S6: Characteristics of weighted populations in CPRD GOLD, database, stratified by staggered cohort and exposure status. Exposure is any COVID-19 vaccine.

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
N (individuals)	40,084	40,014		111,674	111,393		124,883	124,955		196,235	195,302	
Age, median [Q25-Q75]	82 [78-86]	82 [78-86]	0.004	62 [50-69]	62 [50-69]	0.005	50 [41-58]	52 [41-58]	0.000	34 [26-42]	34 [26-43]	0.004
Sex: Female, N(%)	23,206 (58%)	23,175 (58%)	0.000	63,290 (57%)	63,079 (57%)	0.001	63,572 (51%)	63,955 (51%)	0.006	84,762 (43%)	85,083 (44%)	0.007
Years of prior history*, median [Q25-Q75]	17 [13-20]	18 [13-20]	0.001	17 [11-19]	17 [11-19]	0.005	17 [9-19]	17 [9-19]	0.000	13 [6-18]	14 [5-18]	0.006
Number of GP visits, median [Q25-Q75]	12 [7-20]	12 [8-20]	0.000	8 [3-15]	10 [5-15]	0.000	4 [0-10]	4 [1-10]	0.009	0 [0-5]	2 [0-5]	0.004
Number of PCR tests, median [Q25-Q75]	0[0-0]	0[0-0]	0.002	0[0-0]	0[0-0]	0.009	0[0-0]	0[0-0]	0.003	0[0-0]	0[0-0]	0.000
Comorbidities**, N(%)												
Anxiety	4,933 (12%)	4,920 (12%)	0.000	22,884 (20%)	22,299 (20%)	0.012	24,993 (20%)	24,695 (20%)	0.006	31,360 (16%)	30,689 (16%)	0.007
Asthma	3,911 (10%)	3,931 (10%)	0.002	18,514 (17%)	18,209 (16%)	0.006	17,431 (14%)	17,388 (14%)	0.001	14,817 (8%)	14,596 (7%)	0.003
Chronic kidney disease	8,998 (22%)	8,953 (22%)	0.002	6,848 (6%)	7,431 (7%)	0.022	2,120 (2%)	2,287 (2%)	0.010	922 (0%)	807 (0%)	0.009
COPD	3,439 (9%)	3,341 (8%)	0.008	5,972 (5%)	6,496 (6%)	0.021	2,089 (2%)	1,938 (2%)	0.010	734 (0%)	688 (0%)	0.004
Dementia	2,634 (7%)	2,332 (6%)	0.031	1,383 (1%)	865 (1%)	0.046	283 (0%)	313 (0%)	0.005	78 (0%)	134 (0%)	0.013
Depressive disorder	3,783 (9%)	3,705 (9%)	0.006	20,874 (19%)	20,246 (18%)	0.013	22,015 (18%)	21,682 (17%)	0.007	23,010 (12%)	22,630 (12%)	0.004
Diabetes	5,928 (15%)	5,802 (14%)	0.008	11,000 (10%)	11,657 (10%)	0.020	5,345 (4%)	5,651 (5%)	0.012	2,586 (1%)	2,366 (1%)	0.009
GERD	1,930 (5%)	1,970 (5%)	0.005	4,521 (4%)	4,479 (4%)	0.001	3,343 (3%)	3,346 (3%)	0.000	2,657 (1%)	2,614 (1%)	0.001
Heart failure	2,417 (6%)	2,205 (6%)	0.022	2,002 (2%)	2,029 (2%)	0.002	639 (1%)	614 (0%)	0.003	250 (0%)	207 (0%)	0.006
Hypertension	14,288 (36%)	14,282 (36%)	0.001	22,488 (20%)	22,695 (20%)	0.006	11,108 (9%)	11,313 (9%)	0.006	4,318 (2%)	4,619 (2%)	0.011
Hypothyroidism	3,151 (8%)	3,155 (8%)	0.001	6,321 (6%)	6,361 (6%)	0.002	4,134 (3%)	4,055 (3%)	0.004	2,475 (1%)	2,621 (1%)	0.007
Malignant neoplastic disease	8,302 (21%)	8,283 (21%)	0.000	8,661 (8%)	10,177 (9%)	0.050	3,813 (3%)	3,777 (3%)	0.002	1,614 (1%)	1,676 (1%)	0.004

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
Myocardial infarction	2,119 (5%)	1,984 (5%)	0.015	3,308 (3%)	3,740 (3%)	0.023	1,193 (1%)	1,267 (1%)	0.006	430 (0%)	343 (0%)	0.010
Osteoporosis	3,702 (9%)	3,670 (9%)	0.002	3,154 (3%)	3,179 (3%)	0.002	1,038 (1%)	1,030 (1%)	0.001	363 (0%)	375 (0%)	0.002
Pneumonia	1,654 (4%)	1,452 (4%)	0.026	2,424 (2%)	2,211 (2%)	0.013	1,401 (1%)	1,314 (1%)	0.007	1,035 (1%)	1,055 (1%)	0.002
Rheumatoid arthritis	637 (2%)	624 (2%)	0.002	1,618 (1%)	1,818 (2%)	0.015	551 (0%)	760 (1%)	0.023	280 (0%)	157 (0%)	0.019
Stroke	2,103 (5%)	1,866 (5%)	0.027	2,468 (2%)	2,512 (2%)	0.003	916 (1%)	981 (1%)	0.006	385 (0%)	356 (0%)	0.003
Venous thromboembolism	1,732 (4%)	1,648 (4%)	0.010	2,639 (2%)	2,596 (2%)	0.002	1,466 (1%)	1,638 (1%)	0.012	959 (0%)	518 (0%)	0.036

The 4 cohorts represent vaccine rollout periods. *Calculated as the days of previous observation in the database before index date. **Assessed anytime before index date. ASMD = Absolute standardized mean difference, GP = General practice, PCR = Polymerase chain reaction, COPD = Chronic obstructive pulmonary disease, GERD = Gastro-Esophageal reflux disease

Table S7: Characteristics of unweighted populations in CPRD GOLD, database, stratified by staggered cohort and exposure status. Exposure is any COVID-19 vaccine.

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
N (individuals)	169,100	118,507		583,399	486,619		417,996	462,832		469,876	550,437	
Age, median [Q25-Q75]	78 [76-82]	84 [81-87]	0.550	45 [33-58]	71 [66-75]	1.117	42 [31-55]	56 [52-61]	0.546	37 [28-49]	35 [27-43]	0.250
Sex: Female, N(%)	93,719 (55%)	68,258 (58%)	0.044	344,747 (59%)	262,113 (54%)	0.106	230,567 (55%)	230,957 (50%)	0.105	208,184 (44%)	249,603 (45%)	0.021
Years of prior history*, median [Q25-Q75]	17 [13-20]	18 [14-20]	0.023	17 [10-19]	17 [13-20]	0.085	17 [9-19]	17 [10-19]	0.055	13 [6-18]	14 [6-18]	0.020
Number of GP visits, median [Q25-Q75]	11 [6-18]	14 [9-21]	0.180	5 [1-11]	11 [6-17]	0.414	3 [0-8]	6 [2-12]	0.239	0 [0-4]	2 [0-6]	0.115
Number of PCR tests, median [Q25-Q75]	0[0-0]	0[0-0]	0.052	0[0-0]	0[0-0]	0.069	0[0-0]	0[0-0]	0.016	0[0-0]	0[0-0]	0.044
Comorbidities**, N(%)												
Anxiety	20,097 (12%)	14,878 (13%)	0.020	132,282 (23%)	78,442 (16%)	0.166	83,022 (20%)	83,629 (18%)	0.046	65,306 (14%)	88,512 (16%)	0.061
Asthma	15,573 (9%)	12,090 (10%)	0.034	119,520 (20%)	61,821 (13%)	0.210	68,746 (16%)	52,312 (11%)	0.149	30,811 (7%)	46,774 (8%)	0.074
Chronic kidney disease	29,343 (17%)	29,934 (25%)	0.194	15,484 (3%)	49,550 (10%)	0.311	6,676 (2%)	8,145 (2%)	0.013	4,746 (1%)	1,376 (0%)	0.096
COPD	14,248 (8%)	9,602 (8%)	0.012	12,247 (2%)	39,371 (8%)	0.275	5,114 (1%)	6,699 (1%)	0.020	3,716 (1%)	953 (0%)	0.089
Dementia	6,678 (4%)	6,860 (6%)	0.086	1,986 (0%)	6,557 (1%)	0.110	1,188 (0%)	636 (0%)	0.032	774 (0%)	159 (0%)	0.044
Depressive disorder	16,339 (10%)	10,720 (9%)	0.021	111,568 (19%)	72,063 (15%)	0.115	66,705 (16%)	77,560 (17%)	0.022	50,341 (11%)	64,215 (12%)	0.030
Diabetes	23,579 (14%)	17,895 (15%)	0.033	29,125 (5%)	66,688 (14%)	0.303	12,407 (3%)	25,465 (6%)	0.126	9,225 (2%)	5,012 (1%)	0.089
GERD	7,610 (5%)	6,174 (5%)	0.033	18,053 (3%)	22,884 (5%)	0.083	8,864 (2%)	15,586 (3%)	0.076	5,920 (1%)	8,482 (2%)	0.024
Heart failure	7,475 (4%)	7,118 (6%)	0.071	4,013 (1%)	12,939 (3%)	0.154	1,732 (0%)	2,410 (1%)	0.016	1,274 (0%)	293 (0%)	0.054
Hypertension	56,298 (33%)	44,709 (38%)	0.093	58,662 (10%)	139,644 (29%)	0.485	24,457 (6%)	64,451 (14%)	0.273	16,440 (3%)	11,991 (2%)	0.080
Hypothyroidism	12,126 (7%)	9,825 (8%)	0.042	22,026 (4%)	31,923 (7%)	0.126	10,616 (3%)	19,001 (4%)	0.087	6,676 (1%)	7,790 (1%)	0.000
Malignant neoplastic disease	30,687 (18%)	26,725 (23%)	0.110	19,781 (3%)	65,779 (14%)	0.370	8,870 (2%)	19,474 (4%)	0.119	5,916 (1%)	4,164 (1%)	0.050

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
Myocardial infarction	7,707 (5%)	6,298 (5%)	0.035	8,409 (1%)	20,200 (4%)	0.165	2,665 (1%)	5,556 (1%)	0.059	2,003 (0%)	501 (0%)	0.066
Osteoporosis	12,736 (8%)	11,677 (10%)	0.082	5,836 (1%)	23,843 (5%)	0.232	2,580 (1%)	4,797 (1%)	0.046	1,855 (0%)	637 (0%)	0.055
Pneumonia	5,401 (3%)	4,381 (4%)	0.028	7,250 (1%)	12,120 (2%)	0.092	3,822 (1%)	4,889 (1%)	0.014	2,522 (1%)	2,797 (1%)	0.004
Rheumatoid arthritis	2,565 (2%)	1,833 (2%)	0.002	4,013 (1%)	9,000 (2%)	0.104	1,294 (0%)	2,566 (1%)	0.037	877 (0%)	316 (0%)	0.037
Stroke	7,214 (4%)	5,843 (5%)	0.032	5,886 (1%)	14,921 (3%)	0.146	2,170 (1%)	3,998 (1%)	0.042	1,591 (0%)	620 (0%)	0.048
Venous thromboembolism	6,188 (4%)	5,096 (4%)	0.033	7,342 (1%)	14,077 (3%)	0.115	3,067 (1%)	6,732 (1%)	0.069	2,611 (1%)	1,018 (0%)	0.061

The 4 cohorts represent vaccine rollout periods. *Calculated as the days of previous observation in the database before index date. **Assessed anytime before index date. ASMD = Absolute standardized mean difference, GP = General practice, PCR = Polymerase chain reaction, COPD = Chronic obstructive pulmonary disease, GERD = Gastro-Esophageal reflux disease

Table S8: Characteristics of weighted populations in CPRD GOLD, database, stratified by staggered cohort and exposure status. Exposure is ChAdOx1 vaccine.

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
N (individuals)	29,163	29,082		82,091	82,226		116,090	115,912		70,312	70,823	
Age, median [Q25-Q75]	82 [79-87]	82 [80-87]	0.002	64 [53-71]	64 [53-70]	0.001	52 [42-58]	52 [42-58]	0.003	42 [39-48]	42 [38-48]	0.000
Sex: Female, N(%)	17,126 (59%)	17,076 (59%)	0.000	45,269 (55%)	45,487 (55%)	0.003	58,599 (50%)	58,799 (51%)	0.005	29,480 (42%)	29,458 (42%)	0.007
Years of prior history*, median [Q25-Q75]	17 [13-20]	17 [14-20]	0.001	17 [11-19]	17 [11-19]	0.002	17 [9-19]	17 [8-19]	0.001	14 [7-18]	14 [6-18]	0.001
Number of GP visits, median [Q25-Q75]	12 [7-21]	12 [8-20]	0.005	8 [3-16]	10 [5-16]	0.002	4 [0-10]	4 [1-10]	0.014	0 [0-6]	2 [0-6]	0.003
Number of PCR tests, median [Q25-Q75]	0[0-0]	0[0-0]	0.005	0[0-0]	0[0-0]	0.005	0[0-0]	0[0-0]	0.004	0[0-0]	0[0-0]	0.000
Comorbidities**, N(%)												
Anxiety	3,481 (12%)	3,496 (12%)	0.003	16,202 (20%)	15,970 (19%)	0.008	23,083 (20%)	22,695 (20%)	0.008	12,154 (17%)	11,947 (17%)	0.011
Asthma	2,863 (10%)	2,870 (10%)	0.002	13,358 (16%)	13,192 (16%)	0.006	16,057 (14%)	16,029 (14%)	0.000	4,767 (7%)	4,744 (7%)	0.003
Chronic kidney disease	6,959 (24%)	6,928 (24%)	0.001	5,850 (7%)	6,384 (8%)	0.024	2,031 (2%)	2,104 (2%)	0.005	616 (1%)	517 (1%)	0.016
COPD	2,556 (9%)	2,485 (9%)	0.008	5,069 (6%)	5,523 (7%)	0.022	1,969 (2%)	1,874 (2%)	0.006	539 (1%)	478 (1%)	0.011
Dementia	2,042 (7%)	1,794 (6%)	0.034	1,319 (2%)	826 (1%)	0.053	263 (0%)	265 (0%)	0.000	59 (0%)	111 (0%)	0.021
Depressive disorder	2,641 (9%)	2,608 (9%)	0.003	14,875 (18%)	14,558 (18%)	0.011	20,497 (18%)	20,298 (18%)	0.004	10,492 (15%)	10,218 (14%)	0.014
Diabetes	4,346 (15%)	4,273 (15%)	0.006	8,933 (11%)	9,524 (12%)	0.022	5,139 (4%)	5,350 (5%)	0.009	1,459 (2%)	1,421 (2%)	0.005
GERD	1,366 (5%)	1,380 (5%)	0.003	3,514 (4%)	3,414 (4%)	0.006	3,153 (3%)	3,136 (3%)	0.001	1,258 (2%)	1,297 (2%)	0.003
Heart failure	1,844 (6%)	1,699 (6%)	0.020	1,793 (2%)	1,720 (2%)	0.006	613 (1%)	601 (1%)	0.001	177 (0%)	151 (0%)	0.008
Hypertension	10,466 (36%)	10,581 (36%)	0.010	17,843 (22%)	18,115 (22%)	0.007	10,489 (9%)	10,714 (9%)	0.007	3,119 (4%)	3,233 (5%)	0.006
Hypothyroidism	2,338 (8%)	2,360 (8%)	0.004	4,857 (6%)	4,837 (6%)	0.001	3,897 (3%)	3,742 (3%)	0.007	1,432 (2%)	1,412 (2%)	0.003
Malignant neoplastic disease	6,210 (21%)	6,164 (21%)	0.002	7,090 (9%)	8,270 (10%)	0.049	3,588 (3%)	3,590 (3%)	0.000	1,059 (2%)	1,117 (2%)	0.006
Myocardial infarction	1,569 (5%)	1,500 (5%)	0.010	2,720 (3%)	3,083 (4%)	0.024	1,155 (1%)	1,202 (1%)	0.004	319 (0%)	242 (0%)	0.018

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
Osteoporosis	2,838 (10%)	2,846 (10%)	0.002	2,715 (3%)	2,668 (3%)	0.004	944 (1%)	986 (1%)	0.004	252 (0%)	281 (0%)	0.006
Pneumonia	1,287 (4%)	1,147 (4%)	0.024	1,997 (2%)	1,883 (2%)	0.009	1,307 (1%)	1,245 (1%)	0.005	487 (1%)	473 (1%)	0.003
Rheumatoid arthritis	464 (2%)	445 (2%)	0.005	1,280 (2%)	1,491 (2%)	0.020	514 (0%)	743 (1%)	0.027	184 (0%)	120 (0%)	0.020
Stroke	1,600 (5%)	1,421 (5%)	0.027	2,073 (3%)	2,122 (3%)	0.003	873 (1%)	963 (1%)	0.009	263 (0%)	257 (0%)	0.002
Venous thromboembolism	1,339 (5%)	1,191 (4%)	0.024	2,112 (3%)	2,219 (3%)	0.008	1,407 (1%)	1,572 (1%)	0.013	590 (1%)	297 (0%)	0.053

The 4 cohorts represent vaccine rollout periods. *Calculated as the days of previous observation in the database before index date. **Assessed anytime before index date. ASMD = Absolute standardized mean difference, GP = General practice, PCR = Polymerase chain reaction, COPD = Chronic obstructive pulmonary disease, GERD = Gastro-Esophageal reflux disease

Table S9: Characteristics of unweighted populations in CPRD GOLD, database, stratified by staggered cohort and exposure status. Exposure is ChAdOx1 vaccine.

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
N (individuals)	168,972	82,406		582,791	302,999		418,184	423,876		485,154	147,744	
Age, median [Q25-Q75]	78 [76-82]	84 [82-88]	0.657	45 [33-58]	71 [66-76]	1.153	42 [31-55]	56 [52-61]	0.560	37 [28-49]	44 [41-48]	0.262
Sex: Female, N(%)	93,648 (55%)	47,915 (58%)	0.055	344,408 (59%)	162,753 (54%)	0.109	230,680 (55%)	210,283 (50%)	0.111	215,080 (44%)	64,999 (44%)	0.007
Years of prior history*, median [Q25-Q75]	17 [13-20]	17 [14-20]	0.016	17 [10-19]	17 [13-19]	0.090	17 [9-19]	17 [10-19]	0.047	13 [6-18]	14 [7-18]	0.054
Number of GP visits, median [Q25-Q75]	11 [6-18]	14 [9-21]	0.177	5 [1-11]	11 [7-18]	0.451	3 [0-8]	6 [2-12]	0.245	0 [0-4]	3 [0-7]	0.174
Number of PCR tests, median [Q25-Q75]	0[0-0]	0[0-0]	0.053	0[0-0]	0[0-0]	0.074	0[0-0]	0[0-0]	0.018	0[0-0]	0[0-0]	0.029
Comorbidities**, N(%)												
Anxiety	20,087 (12%)	9,923 (12%)	0.005	132,145 (23%)	49,010 (16%)	0.165	83,054 (20%)	75,258 (18%)	0.054	66,918 (14%)	24,601 (17%)	0.080
Asthma	15,567 (9%)	8,491 (10%)	0.037	119,442 (20%)	39,988 (13%)	0.196	68,792 (16%)	48,034 (11%)	0.148	31,538 (7%)	10,517 (7%)	0.025
Chronic kidney disease	29,280 (17%)	21,564 (26%)	0.216	15,435 (3%)	34,168 (11%)	0.344	6,675 (2%)	7,553 (2%)	0.014	4,947 (1%)	739 (1%)	0.060
COPD	14,234 (8%)	6,837 (8%)	0.005	12,242 (2%)	27,472 (9%)	0.307	5,122 (1%)	6,334 (1%)	0.023	3,834 (1%)	640 (0%)	0.046
Dementia	6,664 (4%)	4,773 (6%)	0.086	1,998 (0%)	5,124 (2%)	0.135	1,201 (0%)	548 (0%)	0.035	831 (0%)	126 (0%)	0.024
Depressive disorder	16,333 (10%)	6,998 (8%)	0.041	111,526 (19%)	45,154 (15%)	0.113	66,763 (16%)	70,703 (17%)	0.019	51,687 (11%)	21,711 (15%)	0.122
Diabetes	23,547 (14%)	12,387 (15%)	0.031	29,089 (5%)	43,647 (14%)	0.322	12,392 (3%)	24,219 (6%)	0.135	9,455 (2%)	2,254 (2%)	0.032
GERD	7,613 (5%)	4,054 (5%)	0.020	18,044 (3%)	14,294 (5%)	0.084	8,869 (2%)	14,447 (3%)	0.079	6,051 (1%)	2,883 (2%)	0.056
Heart failure	7,468 (4%)	5,058 (6%)	0.077	4,016 (1%)	9,180 (3%)	0.174	1,738 (0%)	2,308 (1%)	0.019	1,316 (0%)	191 (0%)	0.032
Hypertension	56,262 (33%)	31,217 (38%)	0.096	58,578 (10%)	88,833 (29%)	0.499	24,450 (6%)	59,554 (14%)	0.277	16,971 (3%)	6,761 (5%)	0.055
Hypothyroidism	12,132 (7%)	7,042 (9%)	0.051	21,999 (4%)	20,521 (7%)	0.134	10,622 (3%)	17,382 (4%)	0.087	6,848 (1%)	3,245 (2%)	0.059
Malignant neoplastic disease	30,670 (18%)	18,950 (23%)	0.120	19,707 (3%)	42,687 (14%)	0.386	8,893 (2%)	17,903 (4%)	0.120	6,143 (1%)	2,192 (1%)	0.019

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
Myocardial infarction	7,704 (5%)	4,500 (5%)	0.041	8,413 (1%)	13,456 (4%)	0.178	2,660 (1%)	5,280 (1%)	0.063	2,057 (0%)	330 (0%)	0.035
Osteoporosis	12,732 (8%)	8,564 (10%)	0.100	5,847 (1%)	16,117 (5%)	0.249	2,576 (1%)	4,330 (1%)	0.045	1,923 (0%)	408 (0%)	0.021
Pneumonia	5,401 (3%)	3,231 (4%)	0.039	7,241 (1%)	8,604 (3%)	0.113	3,814 (1%)	4,527 (1%)	0.016	2,615 (1%)	921 (1%)	0.011
Rheumatoid arthritis	2,559 (2%)	1,257 (2%)	0.001	4,017 (1%)	5,999 (2%)	0.113	1,286 (0%)	2,405 (1%)	0.039	918 (0%)	191 (0%)	0.015
Stroke	7,200 (4%)	4,193 (5%)	0.039	5,885 (1%)	10,213 (3%)	0.162	2,167 (1%)	3,789 (1%)	0.045	1,625 (0%)	369 (0%)	0.016
Venous thromboembolism	6,185 (4%)	3,550 (4%)	0.033	7,335 (1%)	9,466 (3%)	0.128	3,072 (1%)	6,339 (1%)	0.073	2,712 (1%)	460 (0%)	0.038

The 4 cohorts represent vaccine rollout periods. *Calculated as the days of previous observation in the database before index date. **Assessed anytime before index date. ASMD = Absolute standardized mean difference, GP = General practice, PCR = Polymerase chain reaction, COPD = Chronic obstructive pulmonary disease, GERD = Gastro-Esophageal reflux disease

Table S10: Characteristics of weighted populations in CPRD GOLD, database, stratified by staggered cohort and exposure status. Exposure is BNT162b2 vaccine.

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
N (individuals)	15,295	15,304		60,813	61,113		24,008	24,157		151,713	152,100	
Age, median [Q25-Q75]	80 [77-85]	80 [77-85]	0.000	64 [53-70]	66 [52-70]	0.008	52 [44-58]	52 [44-58]	0.004	32 [24-38]	32 [24-38]	0.003
Sex: Female, N(%)	8,644 (57%)	8,657 (57%)	0.001	34,612 (57%)	34,776 (57%)	0.000	12,846 (54%)	12,993 (54%)	0.006	66,947 (44%)	67,555 (44%)	0.006
Years of prior history*, median [Q25-Q75]	17 [12-20]	18 [12-21]	0.001	17 [12-19]	17 [11-19]	0.003	17 [11-19]	17 [11-19]	0.004	13 [6-18]	14 [5-18]	0.001
Number of GP visits, median [Q25-Q75]	12 [7-20]	12 [8-20]	0.001	8 [3-15]	8 [4-15]	0.009	4 [0-10]	4 [1-10]	0.006	0 [0-5]	2 [0-5]	0.007
Number of PCR tests, median [Q25-Q75]	0[0-0]	0[0-0]	0.006	0[0-0]	0[0-0]	0.004	0[0-0]	0[0-0]	0.001	0[0-0]	0[0-0]	0.013
Comorbidities**, N(%)												
Anxiety	1,969 (13%)	1,940 (13%)	0.006	11,790 (19%)	11,914 (19%)	0.003	5,342 (22%)	5,235 (22%)	0.014	24,455 (16%)	23,928 (16%)	0.011
Asthma	1,498 (10%)	1,488 (10%)	0.002	9,126 (15%)	9,093 (15%)	0.004	2,926 (12%)	2,985 (12%)	0.005	12,195 (8%)	11,929 (8%)	0.007
Chronic kidney disease	3,112 (20%)	3,057 (20%)	0.009	3,563 (6%)	3,764 (6%)	0.013	398 (2%)	407 (2%)	0.002	468 (0%)	346 (0%)	0.016
COPD	1,190 (8%)	1,151 (8%)	0.010	3,222 (5%)	3,237 (5%)	0.000	293 (1%)	274 (1%)	0.008	315 (0%)	250 (0%)	0.010
Dementia	1,087 (7%)	864 (6%)	0.060	646 (1%)	355 (1%)	0.053	55 (0%)	80 (0%)	0.019	21 (0%)	28 (0%)	0.004
Depressive disorder	1,527 (10%)	1,496 (10%)	0.007	10,709 (18%)	10,912 (18%)	0.006	4,382 (18%)	4,343 (18%)	0.007	17,112 (11%)	16,594 (11%)	0.012
Diabetes	2,193 (14%)	2,173 (14%)	0.004	6,057 (10%)	6,199 (10%)	0.006	883 (4%)	858 (4%)	0.007	1,609 (1%)	1,271 (1%)	0.023
GERD	880 (6%)	872 (6%)	0.003	2,440 (4%)	2,505 (4%)	0.004	659 (3%)	706 (3%)	0.011	1,935 (1%)	1,961 (1%)	0.001
Heart failure	857 (6%)	748 (5%)	0.032	1,097 (2%)	933 (2%)	0.022	119 (0%)	77 (0%)	0.027	107 (0%)	77 (0%)	0.008
Hypertension	5,338 (35%)	5,312 (35%)	0.004	12,828 (21%)	12,901 (21%)	0.000	2,597 (11%)	2,645 (11%)	0.004	2,260 (1%)	2,369 (2%)	0.006
Hypothyroidism	1,129 (7%)	1,067 (7%)	0.016	3,476 (6%)	3,416 (6%)	0.005	935 (4%)	954 (4%)	0.003	1,772 (1%)	1,653 (1%)	0.008
Malignant neoplastic disease	3,126 (20%)	3,097 (20%)	0.005	5,084 (8%)	5,529 (9%)	0.024	864 (4%)	922 (4%)	0.011	877 (1%)	902 (1%)	0.002
Myocardial infarction	764 (5%)	681 (4%)	0.026	1,797 (3%)	1,853 (3%)	0.005	230 (1%)	186 (1%)	0.020	189 (0%)	128 (0%)	0.013

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
Osteoporosis	1,312 (9%)	1,225 (8%)	0.021	1,775 (3%)	1,805 (3%)	0.002	251 (1%)	282 (1%)	0.012	154 (0%)	135 (0%)	0.004
Pneumonia	573 (4%)	475 (3%)	0.035	1,232 (2%)	1,107 (2%)	0.016	256 (1%)	244 (1%)	0.005	744 (0%)	698 (0%)	0.005
Rheumatoid arthritis	248 (2%)	234 (2%)	0.008	854 (1%)	945 (2%)	0.012	113 (0%)	102 (0%)	0.007	165 (0%)	62 (0%)	0.025
Stroke	739 (5%)	650 (4%)	0.028	1,291 (2%)	1,297 (2%)	0.000	172 (1%)	129 (1%)	0.023	204 (0%)	138 (0%)	0.013
Venous thromboembolism	640 (4%)	622 (4%)	0.006	1,355 (2%)	1,347 (2%)	0.002	273 (1%)	256 (1%)	0.008	604 (0%)	288 (0%)	0.039

The 4 cohorts represent vaccine rollout periods. *Calculated as the days of previous observation in the database before index date. **Assessed anytime before index date. ASMD = Absolute standardized mean difference, GP = General practice, PCR = Polymerase chain reaction, COPD = Chronic obstructive pulmonary disease, GERD = Gastro-Esophageal reflux disease

Table S11: Characteristics of unweighted populations in CPRD GOLD, database, stratified by staggered cohort and exposure status. Exposure is BNT162b2 vaccine.

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
N (individuals)	169,459	32,755		584,309	180,670		416,549	36,748		465,326	365,096	
Age, median [Q25-Q75]	78 [76-82]	81 [79-86]	0.306	45 [33-58]	70 [66-74]	1.059	42 [31-55]	54 [50-60]	0.407	37 [28-49]	31 [24-37]	0.445
Sex: Female, N(%)	93,939 (55%)	18,415 (56%)	0.016	345,249 (59%)	97,747 (54%)	0.101	229,807 (55%)	19,649 (53%)	0.034	206,080 (44%)	167,510 (46%)	0.032
Years of prior history*, median [Q25-Q75]	17 [13-20]	18 [13-21]	0.017	17 [10-19]	17 [12-19]	0.076	17 [9-19]	18 [12-20]	0.153	13 [6-18]	15 [6-18]	0.018
Number of GP visits, median [Q25-Q75]	11 [6-18]	14 [9-21]	0.172	5 [1-11]	10 [6-16]	0.348	3 [0-8]	6 [2-11]	0.183	0 [0-4]	2 [0-6]	0.092
Number of PCR tests, median [Q25-Q75]	0[0-0]	0[0-0]	0.046	0[0-0]	0[0-0]	0.061	0[0-0]	0[0-0]	0.005	0[0-0]	0[0-0]	0.045
Comorbidities**, N(%)												
Anxiety	20,145 (12%)	4,336 (13%)	0.041	132,397 (23%)	28,697 (16%)	0.172	82,752 (20%)	8,004 (22%)	0.047	64,849 (14%)	59,094 (16%)	0.063
Asthma	15,611 (9%)	3,250 (10%)	0.024	119,679 (20%)	21,396 (12%)	0.236	68,556 (16%)	4,053 (11%)	0.158	30,579 (7%)	33,240 (9%)	0.094
Chronic kidney disease	29,378 (17%)	7,430 (23%)	0.134	15,504 (3%)	15,033 (8%)	0.251	6,636 (2%)	566 (2%)	0.004	4,692 (1%)	578 (0%)	0.112
COPD	14,265 (8%)	2,417 (7%)	0.039	12,276 (2%)	11,545 (6%)	0.214	5,085 (1%)	348 (1%)	0.026	3,657 (1%)	285 (0%)	0.108
Dementia	6,705 (4%)	1,895 (6%)	0.085	2,008 (0%)	1,375 (1%)	0.056	1,168 (0%)	87 (0%)	0.009	746 (0%)	29 (0%)	0.053
Depressive disorder	16,385 (10%)	3,310 (10%)	0.015	111,708 (19%)	26,294 (15%)	0.122	66,510 (16%)	6,569 (18%)	0.051	49,969 (11%)	39,181 (11%)	0.000
Diabetes	23,614 (14%)	4,882 (15%)	0.028	29,200 (5%)	22,552 (12%)	0.267	12,338 (3%)	1,191 (3%)	0.016	9,143 (2%)	2,507 (1%)	0.112
GERD	7,655 (5%)	2,012 (6%)	0.072	18,069 (3%)	8,525 (5%)	0.084	8,839 (2%)	1,093 (3%)	0.054	5,864 (1%)	5,213 (1%)	0.015
Heart failure	7,502 (4%)	1,782 (5%)	0.047	4,026 (1%)	3,669 (2%)	0.116	1,715 (0%)	100 (0%)	0.024	1,236 (0%)	98 (0%)	0.063
Hypertension	56,411 (33%)	11,995 (37%)	0.070	58,749 (10%)	49,763 (28%)	0.459	24,301 (6%)	4,679 (13%)	0.239	16,363 (4%)	4,776 (1%)	0.144
Hypothyroidism	12,163 (7%)	2,373 (7%)	0.003	22,061 (4%)	11,106 (6%)	0.109	10,565 (3%)	1,553 (4%)	0.094	6,617 (1%)	4,180 (1%)	0.025
Malignant neoplastic disease	30,728 (18%)	6,972 (21%)	0.079	19,832 (3%)	22,617 (13%)	0.342	8,827 (2%)	1,522 (4%)	0.116	5,804 (1%)	1,796 (0%)	0.081

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
Myocardial infarction	7,716 (5%)	1,603 (5%)	0.016	8,437 (1%)	6,621 (4%)	0.141	2,644 (1%)	271 (1%)	0.012	1,985 (0%)	154 (0%)	0.080
Osteoporosis	12,776 (8%)	2,770 (8%)	0.034	5,867 (1%)	7,531 (4%)	0.200	2,558 (1%)	458 (1%)	0.066	1,841 (0%)	205 (0%)	0.072
Pneumonia	5,415 (3%)	1,032 (3%)	0.003	7,266 (1%)	3,418 (2%)	0.052	3,790 (1%)	345 (1%)	0.003	2,512 (1%)	1,696 (0%)	0.011
Rheumatoid arthritis	2,566 (2%)	512 (2%)	0.004	4,018 (1%)	2,929 (2%)	0.087	1,276 (0%)	154 (0%)	0.019	881 (0%)	111 (0%)	0.048
Stroke	7,203 (4%)	1,490 (5%)	0.015	5,907 (1%)	4,632 (3%)	0.117	2,152 (1%)	199 (1%)	0.003	1,578 (0%)	225 (0%)	0.062
Venous thromboembolism	6,198 (4%)	1,389 (4%)	0.030	7,333 (1%)	4,490 (2%)	0.091	3,056 (1%)	370 (1%)	0.029	2,585 (1%)	496 (0%)	0.072

The 4 cohorts represent vaccine rollout periods. *Calculated as the days of previous observation in the database before index date. **Assessed anytime before index date. ASMD = Absolute standardized mean difference, GP = General practice, PCR = Polymerase chain reaction, COPD = Chronic obstructive pulmonary disease, GERD = Gastro-Esophageal reflux disease

Table S12: Characteristics of weighted populations in SIDIAP, database, stratified by staggered cohort and exposure status. Exposure is any COVID-19 vaccine.

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
N (individuals)	58,342	58,535		235,543	235,780		344,520	342,678		413,428	412,893	
Age, median [Q25-Q75]	86 [83-89]	86 [82-89]	0.002	68 [63-73]	68 [63-74]	0.003	52 [46-58]	52 [46-59]	0.000	36 [28-44]	36 [28-44]	0.002
Sex: Female, N(%)	36,115 (62%)	36,214 (62%)	0.001	128,806 (55%)	129,053 (55%)	0.001	164,316 (48%)	163,188 (48%)	0.001	188,426 (46%)	188,471 (46%)	0.001
Years of prior history*, median [Q25-Q75]	15 [15-15]	15 [15-15]	0.001	15 [15-15]	15 [15-15]	0.000	15 [15-15]	15 [15-15]	0.003	15 [13-16]	15 [13-16]	0.004
Number of GP visits, median [Q25-Q75]	8 [3-15]	8 [4-15]	0.007	4 [0-9]	4 [1-9]	0.014	0 [0-6]	2 [0-6]	0.001	0 [0-4]	0 [0-5]	0.014
Number of PCR tests, median [Q25-Q75]	0[0-0]	0[0-0]	0.006	0[0-0]	0[0-0]	0.002	0[0-0]	0[0-0]	0.004	0[0-0]	0[0-0]	0.009
Comorbidities**, N(%)												
Anxiety	11,384 (20%)	11,467 (20%)	0.002	52,314 (22%)	52,262 (22%)	0.001	81,514 (24%)	80,775 (24%)	0.002	84,856 (21%)	83,145 (20%)	0.010
Asthma	3,708 (6%)	3,627 (6%)	0.007	10,973 (5%)	10,703 (5%)	0.006	14,915 (4%)	14,492 (4%)	0.005	19,969 (5%)	19,628 (5%)	0.004
Chronic kidney disease	18,755 (32%)	18,803 (32%)	0.001	21,147 (9%)	21,249 (9%)	0.001	7,411 (2%)	7,335 (2%)	0.001	3,293 (1%)	2,846 (1%)	0.012
COPD	7,008 (12%)	6,983 (12%)	0.002	17,160 (7%)	16,784 (7%)	0.006	8,852 (3%)	8,622 (3%)	0.003	3,210 (1%)	3,215 (1%)	0.000
Dementia	5,686 (10%)	5,812 (10%)	0.006	4,628 (2%)	4,425 (2%)	0.006	1,247 (0%)	1,229 (0%)	0.001	673 (0%)	689 (0%)	0.001
Depressive disorder	10,960 (19%)	11,020 (19%)	0.001	34,232 (15%)	34,571 (15%)	0.004	34,243 (10%)	32,427 (9%)	0.016	23,679 (6%)	23,024 (6%)	0.007
Diabetes	14,529 (25%)	14,269 (24%)	0.012	39,335 (17%)	39,133 (17%)	0.003	25,964 (8%)	26,135 (8%)	0.003	14,136 (3%)	14,091 (3%)	0.000
GERD	6,898 (12%)	6,871 (12%)	0.003	21,088 (9%)	21,212 (9%)	0.002	16,959 (5%)	17,024 (5%)	0.002	10,569 (3%)	10,903 (3%)	0.005
Heart failure	9,320 (16%)	9,141 (16%)	0.010	10,251 (4%)	10,196 (4%)	0.001	4,001 (1%)	3,743 (1%)	0.007	1,606 (0%)	1,565 (0%)	0.002
Hypertension	38,140 (65%)	37,917 (65%)	0.013	96,384 (41%)	96,118 (41%)	0.003	58,596 (17%)	57,241 (17%)	0.008	22,160 (5%)	22,739 (6%)	0.006
Hypothyroidism	7,350 (13%)	7,236 (12%)	0.007	24,054 (10%)	24,260 (10%)	0.003	21,956 (6%)	21,573 (6%)	0.003	17,452 (4%)	17,758 (4%)	0.004
Malignant neoplastic disease	15,402 (26%)	15,230 (26%)	0.009	37,052 (16%)	38,490 (16%)	0.016	19,765 (6%)	19,599 (6%)	0.001	9,413 (2%)	8,865 (2%)	0.009

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
Myocardial infarction	2,258 (4%)	2,235 (4%)	0.003	5,972 (3%)	5,812 (2%)	0.005	3,615 (1%)	3,448 (1%)	0.004	1,362 (0%)	1,364 (0%)	0.000
Osteoporosis	9,270 (16%)	9,151 (16%)	0.007	18,870 (8%)	19,036 (8%)	0.002	7,126 (2%)	7,039 (2%)	0.001	2,254 (1%)	2,040 (0%)	0.007
Pneumonia	6,643 (11%)	6,563 (11%)	0.005	15,630 (7%)	15,557 (7%)	0.002	14,821 (4%)	14,580 (4%)	0.002	14,171 (3%)	14,083 (3%)	0.001
Rheumatoid arthritis	765 (1%)	727 (1%)	0.006	2,274 (1%)	2,286 (1%)	0.000	1,544 (0%)	1,592 (0%)	0.002	754 (0%)	646 (0%)	0.006
Stroke	5,119 (9%)	5,043 (9%)	0.006	8,750 (4%)	7,706 (3%)	0.024	4,343 (1%)	4,147 (1%)	0.005	1,828 (0%)	1,840 (0%)	0.001
Venous thromboembolism	2,469 (4%)	2,418 (4%)	0.005	4,745 (2%)	4,419 (2%)	0.010	3,365 (1%)	2,982 (1%)	0.011	1,931 (0%)	1,777 (0%)	0.005

The 4 cohorts represent vaccine rollout periods. *Calculated as the days of previous observation in the database before index date. **Assessed anytime before index date. ASMD = Absolute standardized mean difference, GP = General practice, PCR = Polymerase chain reaction, COPD = Chronic obstructive pulmonary disease, GERD = Gastro-Esophageal reflux disease

Table S13: Characteristics of unweighted populations in SIDIAP, database, stratified by staggered cohort and exposure status. Exposure is any COVID-19 vaccine.

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
N (individuals)	223,962	89,941		433,151	819,590		869,497	954,232		1,061,634	880,950	
Age, median [Q25-Q75]	85 [82-88]	87 [83-90]	0.253	67 [62-72]	72 [65-78]	0.391	48 [43-57]	54 [49-58]	0.192	38 [28-51]	37 [29-43]	0.246
Sex: Female, N(%)	136,888 (61%)	56,235 (63%)	0.029	237,494 (55%)	443,019 (54%)	0.016	409,207 (47%)	462,599 (48%)	0.028	488,499 (46%)	408,555 (46%)	0.007
Years of prior history*, median [Q25-Q75]	15 [15-15]	15 [15-15]	0.051	15 [15-15]	15 [15-15]	0.185	15 [15-15]	15 [15-15]	0.246	15 [10-16]	15 [15-16]	0.195
Number of GP visits, median [Q25-Q75]	7 [2-13]	10 [5-18]	0.251	3 [0-8]	6 [2-11]	0.168	1 [0-5]	2 [0-7]	0.105	0 [0-4]	2 [0-6]	0.060
Number of PCR tests, median [Q25-Q75]	0[0-0]	0[0-1]	0.070	0[0-0]	0[0-1]	0.042	0[0-0]	0[0-1]	0.073	0[0-0]	0[0-1]	0.123
Comorbidities**, N(%)												
Anxiety	41,908 (19%)	18,117 (20%)	0.036	97,857 (23%)	181,286 (22%)	0.011	197,922 (23%)	233,123 (24%)	0.039	203,019 (19%)	186,562 (21%)	0.051
Asthma	13,371 (6%)	5,841 (6%)	0.022	19,809 (5%)	41,966 (5%)	0.025	36,811 (4%)	42,221 (4%)	0.009	45,374 (4%)	46,776 (5%)	0.049
Chronic kidney disease	63,041 (28%)	31,132 (35%)	0.140	32,450 (7%)	101,792 (12%)	0.165	22,454 (3%)	20,303 (2%)	0.030	20,368 (2%)	5,314 (1%)	0.118
COPD	24,459 (11%)	11,292 (13%)	0.051	28,780 (7%)	67,795 (8%)	0.062	19,020 (2%)	27,451 (3%)	0.044	15,415 (1%)	5,836 (1%)	0.077
Dementia	16,743 (7%)	10,455 (12%)	0.142	7,404 (2%)	19,153 (2%)	0.045	6,009 (1%)	2,787 (0%)	0.057	5,866 (1%)	1,310 (0%)	0.068
Depressive disorder	38,148 (17%)	18,040 (20%)	0.078	61,308 (14%)	124,929 (15%)	0.031	77,039 (9%)	98,723 (10%)	0.050	66,864 (6%)	49,608 (6%)	0.028
Diabetes	51,964 (23%)	22,968 (26%)	0.054	65,572 (15%)	155,362 (19%)	0.102	60,254 (7%)	78,356 (8%)	0.048	49,331 (5%)	29,768 (3%)	0.065
GERD	25,376 (11%)	10,728 (12%)	0.019	34,715 (8%)	87,626 (11%)	0.092	37,828 (4%)	53,565 (6%)	0.058	31,600 (3%)	23,657 (3%)	0.018
Heart failure	28,538 (13%)	16,202 (18%)	0.147	16,697 (4%)	42,924 (5%)	0.066	11,909 (1%)	10,469 (1%)	0.025	10,738 (1%)	2,776 (0%)	0.086
Hypertension	138,631 (62%)	60,128 (67%)	0.104	157,290 (36%)	390,610 (48%)	0.231	125,239 (14%)	188,390 (20%)	0.142	97,835 (9%)	43,351 (5%)	0.168

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
Hypothyroidism	26,875 (12%)	11,473 (13%)	0.023	42,245 (10%)	89,496 (11%)	0.038	50,396 (6%)	64,873 (7%)	0.041	49,279 (5%)	38,477 (4%)	0.013
Malignant neoplastic disease	54,714 (24%)	24,173 (27%)	0.056	81,394 (19%)	151,745 (19%)	0.007	48,971 (6%)	59,566 (6%)	0.026	37,755 (4%)	18,021 (2%)	0.092
Myocardial infarction	7,886 (4%)	3,642 (4%)	0.028	9,894 (2%)	22,773 (3%)	0.031	7,570 (1%)	11,483 (1%)	0.033	6,171 (1%)	2,459 (0%)	0.046
Osteoporosis	32,239 (14%)	14,846 (17%)	0.058	29,512 (7%)	81,707 (10%)	0.114	16,393 (2%)	21,679 (2%)	0.027	14,373 (1%)	3,343 (0%)	0.105
Pneumonia	22,254 (10%)	10,959 (12%)	0.072	27,837 (6%)	61,325 (7%)	0.042	34,513 (4%)	44,236 (5%)	0.033	36,413 (3%)	32,657 (4%)	0.015
Rheumatoid arthritis	2,666 (1%)	1,204 (1%)	0.013	3,771 (1%)	8,890 (1%)	0.022	3,239 (0%)	4,770 (0%)	0.019	2,706 (0%)	1,281 (0%)	0.024
Stroke	16,690 (7%)	8,542 (9%)	0.073	14,256 (3%)	32,612 (4%)	0.037	10,877 (1%)	12,068 (1%)	0.001	9,400 (1%)	3,384 (0%)	0.063
Venous thromboembolism	8,014 (4%)	4,126 (5%)	0.051	8,172 (2%)	17,846 (2%)	0.021	7,747 (1%)	8,920 (1%)	0.005	6,632 (1%)	3,768 (0%)	0.027

The 4 cohorts represent vaccine rollout periods. *Calculated as the days of previous observation in the database before index date. **Assessed anytime before index date. ASMD = Absolute standardized mean difference, GP = General practice, PCR = Polymerase chain reaction, COPD = Chronic obstructive pulmonary disease, GERD = Gastro-Esophageal reflux disease

Table S14: Characteristics of weighted populations in SIDIAP, database, stratified by staggered cohort and exposure status. Exposure is BNT162b2 vaccine.

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
N (individuals)	57,981	57,843		99,838	99,488		276,241	273,593		312,492	313,346	
Age, median [Q25-Q75]	86 [83-89]	86 [82-89]	0.000	74 [71-81]	74 [72-81]	0.006	50 [45-56]	50 [45-56]	0.003	36 [29-43]	36 [29-43]	0.004
Sex: Female, N(%)	35,828 (62%)	35,895 (62%)	0.005	58,343 (58%)	57,844 (58%)	0.006	130,375 (47%)	129,701 (47%)	0.004	145,270 (46%)	144,384 (46%)	0.008
Years of prior history*, median [Q25-Q75]	15 [15-15]	15 [15-15]	0.002	15 [15-15]	15 [15-15]	0.005	15 [15-15]	15 [15-15]	0.001	15 [13-16]	15 [14-16]	0.004
Number of GP visits, median [Q25-Q75]	8 [3-15]	8 [4-15]	0.008	4 [0-10]	6 [2-10]	0.013	0 [0-5]	2 [0-6]	0.000	0 [0-4]	0 [0-5]	0.012
Number of PCR tests, median [Q25-Q75]	0[0-0]	0[0-0]	0.006	0[0-0]	0[0-0]	0.009	0[0-0]	0[0-0]	0.005	0[0-0]	0[0-0]	0.010
Comorbidities**, N(%)												
Anxiety	11,327 (20%)	11,359 (20%)	0.003	20,281 (20%)	20,181 (20%)	0.001	67,000 (24%)	63,263 (23%)	0.027	65,060 (21%)	64,616 (21%)	0.005
Asthma	3,734 (6%)	3,583 (6%)	0.010	5,213 (5%)	5,179 (5%)	0.001	12,220 (4%)	11,760 (4%)	0.006	15,491 (5%)	15,211 (5%)	0.005
Chronic kidney disease	18,610 (32%)	18,576 (32%)	0.000	15,548 (16%)	15,607 (16%)	0.003	5,583 (2%)	5,399 (2%)	0.003	1,999 (1%)	2,008 (1%)	0.000
COPD	6,980 (12%)	6,907 (12%)	0.003	9,163 (9%)	9,045 (9%)	0.003	6,020 (2%)	6,047 (2%)	0.002	1,998 (1%)	2,000 (1%)	0.000
Dementia	5,678 (10%)	5,771 (10%)	0.006	4,152 (4%)	3,716 (4%)	0.022	1,037 (0%)	980 (0%)	0.003	502 (0%)	506 (0%)	0.000
Depressive disorder	10,920 (19%)	10,923 (19%)	0.001	15,653 (16%)	15,532 (16%)	0.002	26,419 (10%)	24,357 (9%)	0.023	17,262 (6%)	17,507 (6%)	0.003
Diabetes	14,416 (25%)	14,096 (24%)	0.011	20,461 (20%)	20,645 (21%)	0.006	19,302 (7%)	18,543 (7%)	0.008	10,119 (3%)	10,440 (3%)	0.005
GERD	6,784 (12%)	6,826 (12%)	0.003	10,187 (10%)	10,088 (10%)	0.002	12,811 (5%)	12,805 (5%)	0.002	7,750 (2%)	8,224 (3%)	0.009
Heart failure	9,390 (16%)	8,983 (16%)	0.018	7,563 (8%)	7,296 (7%)	0.009	3,044 (1%)	2,699 (1%)	0.011	1,069 (0%)	1,049 (0%)	0.001
Hypertension	37,879 (65%)	37,465 (65%)	0.012	51,262 (51%)	50,608 (51%)	0.010	42,266 (15%)	41,291 (15%)	0.006	15,063 (5%)	15,323 (5%)	0.003
Hypothyroidism	7,310 (13%)	7,166 (12%)	0.007	11,611 (12%)	11,249 (11%)	0.010	16,597 (6%)	16,509 (6%)	0.001	13,155 (4%)	13,617 (4%)	0.007
Malignant neoplastic disease	15,302 (26%)	14,971 (26%)	0.012	19,393 (19%)	18,719 (19%)	0.015	14,311 (5%)	13,981 (5%)	0.003	6,555 (2%)	6,398 (2%)	0.004
Myocardial infarction	2,286 (4%)	2,182 (4%)	0.009	3,130 (3%)	2,924 (3%)	0.011	2,569 (1%)	2,451 (1%)	0.004	875 (0%)	880 (0%)	0.000

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
Osteoporosis	9,170 (16%)	9,085 (16%)	0.003	11,182 (11%)	11,201 (11%)	0.002	4,764 (2%)	4,639 (2%)	0.002	1,344 (0%)	1,306 (0%)	0.002
Pneumonia	6,588 (11%)	6,476 (11%)	0.005	7,945 (8%)	7,918 (8%)	0.000	11,759 (4%)	11,273 (4%)	0.007	10,730 (3%)	10,798 (3%)	0.001
Rheumatoid arthritis	755 (1%)	718 (1%)	0.006	1,064 (1%)	1,111 (1%)	0.005	1,113 (0%)	1,026 (0%)	0.004	536 (0%)	461 (0%)	0.006
Stroke	5,070 (9%)	5,006 (9%)	0.003	5,363 (5%)	5,086 (5%)	0.012	3,121 (1%)	3,043 (1%)	0.002	1,199 (0%)	1,253 (0%)	0.003
Venous thromboembolism	2,452 (4%)	2,378 (4%)	0.006	2,660 (3%)	2,526 (3%)	0.008	2,527 (1%)	2,211 (1%)	0.012	1,394 (0%)	1,327 (0%)	0.003

The 4 cohorts represent vaccine rollout periods. *Calculated as the days of previous observation in the database before index date. **Assessed anytime before index date. ASMD = Absolute standardized mean difference, GP = General practice, PCR = Polymerase chain reaction, COPD = Chronic obstructive pulmonary disease, GERD = Gastro-Esophageal reflux disease

Table S15: Characteristics of unweighted populations in SIDIAP, database, stratified by staggered cohort and exposure status. Exposure is BNT162b2 vaccine.

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
N (individuals)	223,960	88,896		433,111	445,581		869,109	706,435		1,068,043	580,329	
Age, median [Q25-Q75]	85 [82-88]	87 [84-90]	0.258	67 [62-72]	78 [74-83]	0.943	48 [43-57]	53 [48-57]	0.127	38 [28-51]	38 [31-43]	0.231
Sex: Female, N(%)	136,891 (61%)	55,704 (63%)	0.032	237,440 (55%)	254,378 (57%)	0.046	409,076 (47%)	341,289 (48%)	0.025	491,528 (46%)	274,150 (47%)	0.024
Years of prior history*, median [Q25-Q75]	15 [15-15]	15 [15-15]	0.051	15 [15-15]	15 [15-15]	0.206	15 [15-15]	15 [15-15]	0.244	15 [10-16]	15 [15-16]	0.211
Number of GP visits, median [Q25-Q75]	7 [2-13]	10 [5-18]	0.253	3 [0-8]	7 [3-12]	0.247	1 [0-5]	2 [0-7]	0.093	0 [0-4]	2 [0-6]	0.059
Number of PCR tests, median [Q25-Q75]	0[0-0]	0[0-1]	0.067	0[0-0]	0[0-1]	0.019	0[0-0]	0[0-1]	0.074	0[0-0]	0[0-1]	0.121
Comorbidities**, N(%)												
Anxiety	41,914 (19%)	17,962 (20%)	0.038	97,901 (23%)	91,620 (21%)	0.050	197,933 (23%)	172,434 (24%)	0.039	204,108 (19%)	125,466 (22%)	0.062
Asthma	13,370 (6%)	5,796 (7%)	0.023	19,824 (5%)	25,291 (6%)	0.050	36,788 (4%)	31,586 (4%)	0.012	45,747 (4%)	30,865 (5%)	0.048
Chronic kidney disease	63,046 (28%)	30,745 (35%)	0.139	32,447 (7%)	83,968 (19%)	0.341	22,494 (3%)	13,920 (2%)	0.041	20,416 (2%)	3,171 (1%)	0.124
COPD	24,471 (11%)	11,169 (13%)	0.051	28,773 (7%)	44,207 (10%)	0.119	19,028 (2%)	17,815 (3%)	0.022	15,424 (1%)	3,218 (1%)	0.090
Dementia	16,748 (7%)	10,393 (12%)	0.143	7,389 (2%)	17,606 (4%)	0.136	6,003 (1%)	2,033 (0%)	0.058	5,878 (1%)	856 (0%)	0.068
Depressive disorder	38,161 (17%)	17,894 (20%)	0.079	61,309 (14%)	72,447 (16%)	0.059	77,050 (9%)	69,517 (10%)	0.033	67,070 (6%)	32,476 (6%)	0.029
Diabetes	51,948 (23%)	22,682 (26%)	0.054	65,583 (15%)	99,692 (22%)	0.186	60,242 (7%)	53,330 (8%)	0.024	49,433 (5%)	19,502 (3%)	0.065
GERD	25,370 (11%)	10,611 (12%)	0.019	34,704 (8%)	53,110 (12%)	0.131	37,842 (4%)	37,707 (5%)	0.046	31,662 (3%)	15,544 (3%)	0.017
Heart failure	28,525 (13%)	16,041 (18%)	0.147	16,686 (4%)	34,932 (8%)	0.171	11,920 (1%)	7,057 (1%)	0.034	10,734 (1%)	1,642 (0%)	0.090
Hypertension	138,655 (62%)	59,414 (67%)	0.103	157,291 (36%)	252,365 (57%)	0.416	125,235 (14%)	128,859 (18%)	0.104	97,944 (9%)	26,383 (5%)	0.184

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
Hypothyroidism	26,868 (12%)	11,363 (13%)	0.024	42,216 (10%)	53,488 (12%)	0.073	50,384 (6%)	46,214 (7%)	0.031	49,424 (5%)	25,961 (4%)	0.007
Malignant neoplastic disease	54,729 (24%)	23,784 (27%)	0.053	81,399 (19%)	96,204 (22%)	0.070	48,967 (6%)	40,510 (6%)	0.004	37,874 (4%)	11,535 (2%)	0.095
Myocardial infarction	7,890 (4%)	3,590 (4%)	0.027	9,892 (2%)	14,140 (3%)	0.055	7,573 (1%)	7,753 (1%)	0.023	6,182 (1%)	1,405 (0%)	0.053
Osteoporosis	32,250 (14%)	14,701 (17%)	0.059	29,528 (7%)	56,885 (13%)	0.201	16,385 (2%)	14,126 (2%)	0.008	14,380 (1%)	1,876 (0%)	0.113
Pneumonia	22,249 (10%)	10,811 (12%)	0.071	27,831 (6%)	38,127 (9%)	0.081	34,511 (4%)	31,972 (5%)	0.028	36,645 (3%)	21,355 (4%)	0.013
Rheumatoid arthritis	2,666 (1%)	1,189 (1%)	0.013	3,769 (1%)	5,143 (1%)	0.028	3,242 (0%)	2,843 (0%)	0.005	2,700 (0%)	812 (0%)	0.026
Stroke	16,693 (7%)	8,475 (10%)	0.075	14,244 (3%)	24,307 (5%)	0.106	10,868 (1%)	8,114 (1%)	0.009	9,394 (1%)	2,033 (0%)	0.068
Venous thromboembolism	8,023 (4%)	4,072 (5%)	0.050	8,162 (2%)	12,564 (3%)	0.062	7,738 (1%)	6,066 (1%)	0.003	6,658 (1%)	2,434 (0%)	0.028

The 4 cohorts represent vaccine rollout periods. *Calculated as the days of previous observation in the database before index date. **Assessed anytime before index date. ASMD = Absolute standardized mean difference, GP = General practice, PCR = Polymerase chain reaction, COPD = Chronic obstructive pulmonary disease, GERD = Gastro-Esophageal reflux disease

Table S16: Characteristics of weighted populations in SIDIAP, database, stratified by staggered cohort and exposure status. Exposure is ChAdOx1 vaccine.

	Cohort 2			Cohort 3		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
N (individuals)	120,307	120,802		44,033	43,901	
Age, median [Q25-Q75]	64 [61-66]	64 [61-66]	0.000	64 [61-66]	64 [61-67]	0.002
Sex: Female, N(%)	62,434 (52%)	62,425 (52%)	0.004	23,009 (52%)	22,980 (52%)	0.002
Years of prior history*, median [Q25-Q75]	15 [15-15]	15 [15-15]	0.003	15 [15-15]	15 [15-15]	0.005
Number of GP visits, median [Q25-Q75]	2 [0-7]	4 [1-8]	0.017	2 [0-7]	2 [0-7]	0.003
Number of PCR tests, median [Q25-Q75]	0[0-0]	0[0-0]	0.013	0[0-0]	0[0-0]	0.005
Comorbidities**, N(%)						
Anxiety	28,213 (23%)	27,989 (23%)	0.007	10,333 (23%)	9,717 (22%)	0.032
Asthma	4,909 (4%)	4,785 (4%)	0.006	1,664 (4%)	1,639 (4%)	0.002
Chronic kidney disease	4,390 (4%)	4,526 (4%)	0.005	1,556 (4%)	1,597 (4%)	0.006
COPD	6,702 (6%)	6,846 (6%)	0.004	2,405 (5%)	2,350 (5%)	0.005
Dementia	470 (0%)	397 (0%)	0.010	170 (0%)	171 (0%)	0.000
Depressive disorder	16,483 (14%)	16,258 (13%)	0.007	5,940 (13%)	5,813 (13%)	0.007
Diabetes	16,127 (13%)	16,418 (14%)	0.005	5,698 (13%)	5,705 (13%)	0.002
GERD	9,580 (8%)	9,569 (8%)	0.002	3,206 (7%)	3,216 (7%)	0.002
Heart failure	2,268 (2%)	2,236 (2%)	0.003	844 (2%)	847 (2%)	0.001
Hypertension	39,422 (33%)	39,551 (33%)	0.001	13,589 (31%)	13,737 (31%)	0.009
Hypothyroidism	10,965 (9%)	11,173 (9%)	0.005	4,002 (9%)	3,830 (9%)	0.013
Malignant neoplastic disease	12,621 (10%)	12,418 (10%)	0.007	4,304 (10%)	3,910 (9%)	0.030
Myocardial infarction	2,553 (2%)	2,500 (2%)	0.004	888 (2%)	868 (2%)	0.003
Osteoporosis	6,687 (6%)	6,679 (6%)	0.001	2,155 (5%)	2,200 (5%)	0.005
Pneumonia	6,452 (5%)	6,392 (5%)	0.003	2,243 (5%)	2,167 (5%)	0.007
Rheumatoid arthritis	1,009 (1%)	931 (1%)	0.008	337 (1%)	259 (1%)	0.021
Stroke	2,693 (2%)	2,582 (2%)	0.007	965 (2%)	1,000 (2%)	0.006
Venous thromboembolism	1,686 (1%)	1,469 (1%)	0.016	659 (1%)	541 (1%)	0.023

The 4 cohorts represent vaccine rollout periods. *Calculated as the days of previous observation in the database before index date. **Assessed anytime before index date. ASMD = Absolute standardized mean difference, GP = General practice, PCR = Polymerase chain reaction, COPD = Chronic obstructive pulmonary disease, GERD = Gastro-Esophageal reflux disease

Table S17: Characteristics of unweighted populations in SIDIAP, database, stratified by staggered cohort and exposure status. Exposure is ChAdOx1 vaccine.

	Cohort 2			Cohort 3		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
N (individuals)	433,636	323,204		873,400	84,204	
Age, median [Q25-Q75]	67 [62-72]	64 [62-67]	0.241	48 [43-57]	64 [61-67]	0.986
Sex: Female, N(%)	237,722 (55%)	162,269 (50%)	0.093	411,107 (47%)	44,374 (53%)	0.113
Years of prior history*, median [Q25-Q75]	15 [15-15]	15 [15-15]	0.158	15 [15-15]	15 [15-15]	0.281
Number of GP visits, median [Q25-Q75]	3 [0-8]	4 [1-9]	0.037	1 [0-5]	4 [1-8]	0.182
Number of PCR tests, median [Q25-Q75]	0[0-0]	0[0-1]	0.047	0[0-0]	0[0-0]	0.029
Comorbidities**, N(%)						
Anxiety	97,950 (23%)	77,793 (24%)	0.035	198,282 (23%)	19,626 (23%)	0.014
Asthma	19,861 (5%)	13,894 (4%)	0.014	36,915 (4%)	3,283 (4%)	0.017
Chronic kidney disease	32,497 (7%)	12,206 (4%)	0.162	22,570 (3%)	3,199 (4%)	0.069
COPD	28,826 (7%)	18,658 (6%)	0.036	19,103 (2%)	4,996 (6%)	0.191
Dementia	7,407 (2%)	1,009 (0%)	0.140	6,041 (1%)	345 (0%)	0.038
Depressive disorder	61,377 (14%)	44,463 (14%)	0.011	77,249 (9%)	11,874 (14%)	0.166
Diabetes	65,666 (15%)	45,453 (14%)	0.031	60,383 (7%)	12,142 (14%)	0.245
GERD	34,755 (8%)	28,610 (9%)	0.030	37,840 (4%)	6,754 (8%)	0.154
Heart failure	16,741 (4%)	5,636 (2%)	0.129	11,981 (1%)	1,703 (2%)	0.050
Hypertension	157,484 (36%)	114,179 (35%)	0.021	125,527 (14%)	28,314 (34%)	0.463
Hypothyroidism	42,257 (10%)	30,350 (9%)	0.012	50,476 (6%)	7,763 (9%)	0.131
Malignant neoplastic disease	81,510 (19%)	36,352 (11%)	0.212	49,066 (6%)	7,842 (9%)	0.141
Myocardial infarction	9,910 (2%)	7,242 (2%)	0.003	7,561 (1%)	1,784 (2%)	0.103
Osteoporosis	29,546 (7%)	19,864 (6%)	0.027	16,434 (2%)	4,382 (5%)	0.180
Pneumonia	27,865 (6%)	18,329 (6%)	0.032	34,617 (4%)	4,445 (5%)	0.063
Rheumatoid arthritis	3,762 (1%)	2,557 (1%)	0.008	3,246 (0%)	535 (1%)	0.037
Stroke	14,284 (3%)	6,369 (2%)	0.083	10,884 (1%)	1,915 (2%)	0.078
Venous thromboembolism	8,163 (2%)	3,613 (1%)	0.063	7,746 (1%)	1,110 (1%)	0.041

The 4 cohorts represent vaccine rollout periods. *Calculated as the days of previous observation in the database before index date. **Assessed anytime before index date. ASMD = Absolute standardized mean difference, GP = General practice, PCR = Polymerase chain reaction, COPD = Chronic obstructive pulmonary disease, GERD = Gastro-Esophageal reflux disease

Table S18: Characteristics of weighted populations in CORIVA, database, stratified by staggered cohort and exposure status. Exposure is any COVID-19 vaccine.

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
N (individuals)	10,630	10,630		3,863	3,863		17,929	17,929		18,740	18,740	
Age, median [Q25-Q75]	78 [72-83]	78 [72-83]	0.000	70 [65-75]	70 [65-75]	0.000	52 [45-59]	50 [45-59]	0.000	40 [30-51]	40 [30-51]	0.000
Sex: Female, N(%)	7,165 (67%)	7,165 (67%)	0.000	2,439 (63%)	2,439 (63%)	0.000	9,054 (50%)	9,054 (50%)	0.000	8,493 (45%)	8,493 (45%)	0.000
Years of prior history*, median [Q25-Q75]	4 [4-4]	4 [4-4]	0.000	4 [4-4]	4 [4-4]	0.000	4 [4-4]	4 [4-4]	0.000	5 [4-5]	5 [4-5]	0.000
Number of GP visits, median [Q25-Q75]	14 [4-24]	14 [6-23]	0.004	12 [3-23]	12 [5-22]	0.000	2 [0-11]	4 [1-10]	0.002	2 [0-8]	2 [0-8]	0.005
Number of PCR tests, median [Q25-Q75]	0[0-0]	0[0-0]	0.003	0[0-0]	0[0-0]	0.002	0[0-0]	0[0-0]	0.000	0[0-0]	0[0-0]	0.002
Comorbidities**, N(%)												
Anxiety	1,060 (10%)	1,076 (10%)	0.005	405 (10%)	415 (11%)	0.008	1,545 (9%)	1,500 (8%)	0.009	1,552 (8%)	1,495 (8%)	0.011
Asthma	996 (9%)	917 (9%)	0.026	372 (10%)	365 (9%)	0.006	936 (5%)	894 (5%)	0.011	845 (5%)	782 (4%)	0.016
Chronic kidney disease	1,015 (10%)	999 (9%)	0.005	336 (9%)	309 (8%)	0.025	347 (2%)	339 (2%)	0.003	212 (1%)	194 (1%)	0.009
COPD	757 (7%)	723 (7%)	0.012	264 (7%)	258 (7%)	0.006	442 (2%)	417 (2%)	0.009	318 (2%)	249 (1%)	0.030
Dementia	438 (4%)	412 (4%)	0.013	106 (3%)	90 (2%)	0.027	120 (1%)	131 (1%)	0.008	71 (0%)	70 (0%)	0.001
Depressive disorder	1,076 (10%)	1,083 (10%)	0.002	462 (12%)	433 (11%)	0.023	1,787 (10%)	1,764 (10%)	0.004	1,679 (9%)	1,739 (9%)	0.011
Diabetes	1,861 (18%)	1,833 (17%)	0.007	640 (17%)	588 (15%)	0.037	1,012 (6%)	963 (5%)	0.012	814 (4%)	764 (4%)	0.014
GERD	1,416 (13%)	1,458 (14%)	0.011	523 (14%)	531 (14%)	0.006	1,562 (9%)	1,600 (9%)	0.007	1,166 (6%)	1,172 (6%)	0.001
Heart failure	3,898 (37%)	3,839 (36%)	0.011	1,003 (26%)	970 (25%)	0.020	1,348 (8%)	1,324 (7%)	0.005	781 (4%)	737 (4%)	0.012
Hypertension	8,016 (75%)	8,221 (77%)	0.045	2,569 (67%)	2,641 (68%)	0.040	5,521 (31%)	5,643 (31%)	0.015	3,359 (18%)	3,538 (19%)	0.025
Hypothyroidism	1,218 (11%)	1,160 (11%)	0.017	419 (11%)	428 (11%)	0.007	981 (5%)	948 (5%)	0.008	654 (3%)	675 (4%)	0.006
Malignant neoplastic disease	1,655 (16%)	1,732 (16%)	0.020	640 (17%)	659 (17%)	0.013	771 (4%)	782 (4%)	0.003	455 (2%)	453 (2%)	0.001
Myocardial infarction	269 (3%)	264 (2%)	0.003	86 (2%)	71 (2%)	0.026	127 (1%)	116 (1%)	0.008	81 (0%)	75 (0%)	0.005
Osteoporosis	675 (6%)	685 (6%)	0.004	187 (5%)	176 (5%)	0.013	233 (1%)	230 (1%)	0.001	131 (1%)	146 (1%)	0.009
Pneumonia	771 (7%)	768 (7%)	0.001	249 (6%)	244 (6%)	0.005	657 (4%)	670 (4%)	0.004	567 (3%)	562 (3%)	0.002
Rheumatoid arthritis	268 (3%)	273 (3%)	0.003	139 (4%)	122 (3%)	0.024	209 (1%)	187 (1%)	0.012	130 (1%)	116 (1%)	0.009

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
Stroke	460 (4%)	461 (4%)	0.001	147 (4%)	144 (4%)	0.004	179 (1%)	189 (1%)	0.006	112 (1%)	116 (1%)	0.003
Venous thromboembolism	469 (4%)	472 (4%)	0.001	171 (4%)	123 (3%)	0.064	306 (2%)	301 (2%)	0.002	219 (1%)	201 (1%)	0.009

The 4 cohorts represent vaccine rollout periods. *Calculated as the days of previous observation in the database before index date. **Assessed anytime before index date. ASMD = Absolute standardized mean difference, GP = General practice, PCR = Polymerase chain reaction, COPD = Chronic obstructive pulmonary disease, GERD = Gastro-Esophageal reflux disease

Table S19: Characteristics of unweighted populations in CORIVA, database, stratified by staggered cohort and exposure status. Exposure is any COVID-19 vaccine.

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
N (individuals)	23,982	26,736		34,317	4,572		96,423	24,050		147,545	22,245	
Age, median [Q25-Q75]	79 [73-85]	77 [73-82]	0.127	72 [67-81]	70 [66-75]	0.177	54 [46-66]	51 [45-59]	0.227	42 [32-58]	40 [30-51]	0.186
Sex: Female, N(%)	16,532 (69%)	17,342 (65%)	0.087	21,862 (64%)	2,891 (63%)	0.010	48,984 (51%)	12,233 (51%)	0.001	72,057 (49%)	10,026 (45%)	0.076
Years of prior history*, median [Q25-Q75]	4 [4-4]	4 [4-4]	0.019	4 [4-4]	4 [4-4]	0.002	4 [4-4]	4 [4-4]	0.002	5 [4-5]	5 [4-5]	0.003
Number of GP visits, median [Q25-Q75]	11 [1-22]	16 [8-26]	0.216	9 [1-20]	13 [6-23]	0.147	2 [0-10]	5 [1-11]	0.088	1 [0-6]	3 [1-8]	0.106
Number of PCR tests, median [Q25-Q75]	0[0-0]	0[0-0]	0.029	0[0-0]	0[0-0]	0.027	0[0-0]	0[0-0]	0.008	0[0-0]	0[0-0]	0.035
Comorbidities**, N(%)												
Anxiety	1,966 (8%)	3,238 (12%)	0.130	2,817 (8%)	513 (11%)	0.102	6,406 (7%)	2,162 (9%)	0.087	9,287 (6%)	1,847 (8%)	0.077
Asthma	1,986 (8%)	2,668 (10%)	0.059	2,653 (8%)	447 (10%)	0.072	4,385 (5%)	1,250 (5%)	0.030	5,405 (4%)	968 (4%)	0.035
Chronic kidney disease	2,270 (9%)	2,507 (9%)	0.003	2,939 (9%)	367 (8%)	0.019	2,523 (3%)	415 (2%)	0.061	2,335 (2%)	221 (1%)	0.052
COPD	1,569 (7%)	1,976 (7%)	0.033	2,015 (6%)	312 (7%)	0.039	2,743 (3%)	529 (2%)	0.041	2,558 (2%)	294 (1%)	0.034
Dementia	1,152 (5%)	819 (3%)	0.090	1,297 (4%)	100 (2%)	0.094	1,147 (1%)	151 (1%)	0.059	1,067 (1%)	76 (0%)	0.052
Depressive disorder	2,066 (9%)	3,233 (12%)	0.114	3,189 (9%)	535 (12%)	0.079	7,286 (8%)	2,561 (11%)	0.108	10,034 (7%)	2,152 (10%)	0.105
Diabetes	3,971 (17%)	4,734 (18%)	0.030	4,818 (14%)	712 (16%)	0.043	6,065 (6%)	1,228 (5%)	0.051	6,594 (4%)	901 (4%)	0.021
GERD	2,533 (11%)	4,585 (17%)	0.192	3,364 (10%)	667 (15%)	0.147	6,287 (7%)	2,322 (10%)	0.115	7,455 (5%)	1,427 (6%)	0.059
Heart failure	8,724 (36%)	9,642 (36%)	0.007	9,570 (28%)	1,139 (25%)	0.068	9,982 (10%)	1,607 (7%)	0.132	9,182 (6%)	828 (4%)	0.115
Hypertension	16,651 (69%)	21,677 (81%)	0.272	20,654 (60%)	3,167 (69%)	0.191	29,974 (31%)	7,555 (31%)	0.007	27,992 (19%)	4,172 (19%)	0.006
Hypothyroidism	2,496 (10%)	3,094 (12%)	0.037	3,198 (9%)	515 (11%)	0.064	4,725 (5%)	1,309 (5%)	0.025	5,180 (4%)	799 (4%)	0.004
Malignant neoplastic disease	3,194 (13%)	5,044 (19%)	0.151	5,061 (15%)	782 (17%)	0.064	4,587 (5%)	1,011 (4%)	0.027	4,134 (3%)	523 (2%)	0.028
Myocardial infarction	548 (2%)	743 (3%)	0.031	696 (2%)	86 (2%)	0.011	840 (1%)	146 (1%)	0.031	777 (1%)	87 (0%)	0.020
Osteoporosis	1,273 (5%)	2,015 (8%)	0.091	1,446 (4%)	212 (5%)	0.021	1,545 (2%)	289 (1%)	0.034	1,408 (1%)	164 (1%)	0.024
Pneumonia	1,611 (7%)	2,046 (8%)	0.036	2,081 (6%)	291 (6%)	0.012	3,342 (3%)	898 (4%)	0.014	3,919 (3%)	683 (3%)	0.025

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
Rheumatoid arthritis	493 (2%)	817 (3%)	0.063	891 (3%)	153 (3%)	0.044	1,022 (1%)	250 (1%)	0.002	987 (1%)	137 (1%)	0.007
Stroke	1,137 (5%)	1,011 (4%)	0.048	1,450 (4%)	169 (4%)	0.027	1,359 (1%)	232 (1%)	0.041	1,256 (1%)	133 (1%)	0.030
Venous thromboembolism	1,058 (4%)	1,207 (5%)	0.005	1,349 (4%)	149 (3%)	0.036	1,808 (2%)	387 (2%)	0.020	1,788 (1%)	235 (1%)	0.015

The 4 cohorts represent vaccine rollout periods. *Calculated as the days of previous observation in the database before index date. **Assessed anytime before index date. ASMD = Absolute standardized mean difference, GP = General practice, PCR = Polymerase chain reaction, COPD = Chronic obstructive pulmonary disease, GERD = Gastro-Esophageal reflux disease

Table S20: Characteristics of weighted populations in CORIVA, database, stratified by staggered cohort and exposure status. Exposure is BNT162b2 vaccine.

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
N (individuals)	9,118	9,118		3,465	3,465		14,414	14,414		13,759	13,759	
Age, median [Q25-Q75]	78 [73-83]	78 [73-83]	0.000	70 [65-75]	70 [65-75]	0.000	50 [45-59]	50 [45-59]	0.000	38 [30-50]	38 [30-50]	0.000
Sex: Female, N(%)	6,206 (68%)	6,206 (68%)	0.000	2,197 (63%)	2,197 (63%)	0.000	7,324 (51%)	7,324 (51%)	0.000	6,552 (48%)	6,552 (48%)	0.000
Years of prior history*, median [Q25-Q75]	4 [4-4]	4 [4-4]	0.000	4 [4-4]	4 [4-4]	0.000	4 [4-4]	4 [4-4]	0.000	5 [4-5]	5 [4-5]	0.000
Number of GP visits, median [Q25-Q75]	14 [4-25]	14 [7-24]	0.004	12 [3-23]	12 [5-22]	0.000	2 [0-10]	4 [1-10]	0.002	2 [0-8]	2 [0-8]	0.004
Number of PCR tests, median [Q25-Q75]	0[0-0]	0[0-0]	0.002	0[0-0]	0[0-0]	0.003	0[0-0]	0[0-0]	0.000	0[0-0]	0[0-0]	0.001
Comorbidities**, N(%)												
Anxiety	935 (10%)	956 (10%)	0.007	367 (11%)	373 (11%)	0.006	1,284 (9%)	1,278 (9%)	0.001	1,206 (9%)	1,170 (9%)	0.009
Asthma	891 (10%)	822 (9%)	0.026	340 (10%)	333 (10%)	0.007	747 (5%)	718 (5%)	0.009	644 (5%)	615 (4%)	0.010
Chronic kidney disease	939 (10%)	905 (10%)	0.012	302 (9%)	278 (8%)	0.025	225 (2%)	220 (2%)	0.003	144 (1%)	132 (1%)	0.008
COPD	666 (7%)	639 (7%)	0.011	238 (7%)	227 (7%)	0.013	333 (2%)	316 (2%)	0.008	223 (2%)	171 (1%)	0.032
Dementia	403 (4%)	377 (4%)	0.014	91 (3%)	81 (2%)	0.018	75 (1%)	72 (0%)	0.002	46 (0%)	38 (0%)	0.012
Depressive disorder	960 (11%)	966 (11%)	0.002	420 (12%)	411 (12%)	0.008	1,472 (10%)	1,485 (10%)	0.003	1,311 (10%)	1,367 (10%)	0.014
Diabetes	1,647 (18%)	1,624 (18%)	0.007	576 (17%)	531 (15%)	0.036	747 (5%)	731 (5%)	0.005	596 (4%)	565 (4%)	0.011
GERD	1,240 (14%)	1,268 (14%)	0.009	476 (14%)	473 (14%)	0.003	1,283 (9%)	1,322 (9%)	0.009	892 (6%)	900 (7%)	0.002
Heart failure	3,527 (39%)	3,470 (38%)	0.013	911 (26%)	877 (25%)	0.022	920 (6%)	899 (6%)	0.006	519 (4%)	484 (4%)	0.014
Hypertension	7,040 (77%)	7,234 (79%)	0.051	2,327 (67%)	2,384 (69%)	0.036	4,296 (30%)	4,340 (30%)	0.007	2,391 (17%)	2,479 (18%)	0.017
Hypothyroidism	1,080 (12%)	1,035 (11%)	0.015	376 (11%)	388 (11%)	0.011	770 (5%)	743 (5%)	0.009	500 (4%)	503 (4%)	0.001
Malignant neoplastic disease	1,485 (16%)	1,565 (17%)	0.023	579 (17%)	594 (17%)	0.012	582 (4%)	606 (4%)	0.008	324 (2%)	317 (2%)	0.003
Myocardial infarction	248 (3%)	234 (3%)	0.010	78 (2%)	68 (2%)	0.020	97 (1%)	88 (1%)	0.008	52 (0%)	52 (0%)	0.000
Osteoporosis	615 (7%)	632 (7%)	0.007	170 (5%)	167 (5%)	0.003	167 (1%)	161 (1%)	0.004	97 (1%)	107 (1%)	0.008
Pneumonia	698 (8%)	696 (8%)	0.001	222 (6%)	222 (6%)	0.001	543 (4%)	505 (4%)	0.014	418 (3%)	429 (3%)	0.005
Rheumatoid arthritis	240 (3%)	239 (3%)	0.001	128 (4%)	110 (3%)	0.028	167 (1%)	148 (1%)	0.013	97 (1%)	88 (1%)	0.008
Stroke	419 (5%)	417 (5%)	0.001	134 (4%)	131 (4%)	0.004	121 (1%)	130 (1%)	0.007	74 (1%)	82 (1%)	0.008

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
Venous thromboembolism	438 (5%)	416 (5%)	0.011	153 (4%)	117 (3%)	0.053	220 (2%)	214 (1%)	0.003	159 (1%)	138 (1%)	0.015

The 4 cohorts represent vaccine rollout periods. *Calculated as the days of previous observation in the database before index date. **Assessed anytime before index date. ASMD = Absolute standardized mean difference, GP = General practice, PCR = Polymerase chain reaction, COPD = Chronic obstructive pulmonary disease, GERD = Gastro-Esophageal reflux disease

Table S21: Characteristics of unweighted populations in CORIVA, database, stratified by staggered cohort and exposure status. Exposure is BNT162b2 vaccine.

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
N (individuals)	24,073	19,686		34,320	4,067		96,471	18,645		147,553	15,683	
Age, median [Q25-Q75]	79 [73-85]	79 [74-83]	0.040	72 [67-81]	70 [66-75]	0.174	54 [46-66]	51 [45-59]	0.257	42 [32-58]	38 [30-50]	0.216
Sex: Female, N(%)	16,582 (69%)	13,022 (66%)	0.058	21,867 (64%)	2,582 (63%)	0.005	49,023 (51%)	9,570 (51%)	0.010	72,056 (49%)	7,500 (48%)	0.020
Years of prior history*, median [Q25-Q75]	4 [4-4]	4 [4-4]	0.026	4 [4-4]	4 [4-4]	0.000	4 [4-4]	4 [4-4]	0.000	5 [4-5]	5 [4-5]	0.003
Number of GP visits, median [Q25-Q75]	11 [1-22]	17 [9-27]	0.252	9 [1-20]	13 [6-23]	0.150	2 [0-10]	5 [1-11]	0.077	1 [0-6]	4 [1-9]	0.116
Number of PCR tests, median [Q25-Q75]	0[0-0]	0[0-0]	0.021	0[0-0]	0[0-0]	0.038	0[0-0]	0[0-0]	0.020	0[0-0]	0[0-0]	0.037
Comorbidities**, N(%)												
Anxiety	1,966 (8%)	2,429 (12%)	0.138	2,816 (8%)	458 (11%)	0.103	6,416 (7%)	1,780 (10%)	0.106	9,291 (6%)	1,384 (9%)	0.096
Asthma	2,004 (8%)	2,029 (10%)	0.068	2,653 (8%)	404 (10%)	0.078	4,393 (5%)	969 (5%)	0.030	5,403 (4%)	730 (5%)	0.050
Chronic kidney disease	2,284 (9%)	2,041 (10%)	0.029	2,943 (9%)	326 (8%)	0.020	2,537 (3%)	263 (1%)	0.087	2,339 (2%)	146 (1%)	0.059
COPD	1,587 (7%)	1,501 (8%)	0.040	2,013 (6%)	274 (7%)	0.036	2,746 (3%)	388 (2%)	0.049	2,560 (2%)	193 (1%)	0.042
Dementia	1,162 (5%)	688 (3%)	0.067	1,301 (4%)	90 (2%)	0.093	1,136 (1%)	81 (0%)	0.083	1,062 (1%)	40 (0%)	0.067
Depressive disorder	2,070 (9%)	2,449 (12%)	0.125	3,188 (9%)	502 (12%)	0.098	7,303 (8%)	2,075 (11%)	0.122	10,051 (7%)	1,623 (10%)	0.127
Diabetes	3,964 (16%)	3,599 (18%)	0.048	4,814 (14%)	638 (16%)	0.047	6,071 (6%)	900 (5%)	0.064	6,594 (4%)	644 (4%)	0.018
GERD	2,532 (11%)	3,307 (17%)	0.184	3,364 (10%)	587 (14%)	0.142	6,296 (7%)	1,858 (10%)	0.125	7,446 (5%)	1,050 (7%)	0.070
Heart failure	8,750 (36%)	7,743 (39%)	0.062	9,570 (28%)	1,026 (25%)	0.060	10,000 (10%)	1,057 (6%)	0.174	9,185 (6%)	525 (3%)	0.135
Hypertension	16,718 (69%)	16,325 (83%)	0.321	20,659 (60%)	2,838 (70%)	0.202	29,995 (31%)	5,624 (30%)	0.020	27,979 (19%)	2,798 (18%)	0.029
Hypothyroidism	2,526 (10%)	2,352 (12%)	0.046	3,197 (9%)	464 (11%)	0.069	4,732 (5%)	988 (5%)	0.018	5,173 (4%)	576 (4%)	0.009
Malignant neoplastic disease	3,216 (13%)	3,873 (20%)	0.171	5,060 (15%)	700 (17%)	0.067	4,587 (5%)	764 (4%)	0.032	4,139 (3%)	352 (2%)	0.036
Myocardial infarction	539 (2%)	591 (3%)	0.048	696 (2%)	82 (2%)	0.001	850 (1%)	108 (1%)	0.035	779 (1%)	58 (0%)	0.024
Osteoporosis	1,283 (5%)	1,628 (8%)	0.117	1,447 (4%)	200 (5%)	0.034	1,550 (2%)	197 (1%)	0.048	1,403 (1%)	117 (1%)	0.022
Pneumonia	1,621 (7%)	1,624 (8%)	0.058	2,080 (6%)	264 (6%)	0.018	3,353 (3%)	672 (4%)	0.007	3,920 (3%)	499 (3%)	0.031

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD	Unvaccinated	Vaccinated	ASMD
Rheumatoid arthritis	491 (2%)	603 (3%)	0.065	892 (3%)	137 (3%)	0.045	1,025 (1%)	190 (1%)	0.004	990 (1%)	99 (1%)	0.005
Stroke	1,129 (5%)	834 (4%)	0.022	1,447 (4%)	152 (4%)	0.025	1,370 (1%)	155 (1%)	0.056	1,254 (1%)	90 (1%)	0.033
Venous thromboembolism	1,067 (4%)	972 (5%)	0.024	1,353 (4%)	140 (3%)	0.027	1,808 (2%)	266 (1%)	0.035	1,785 (1%)	156 (1%)	0.021

The 4 cohorts represent vaccine rollout periods. *Calculated as the days of previous observation in the database before index date. **Assessed anytime before index date. ASMD = Absolute standardized mean difference, GP = General practice, PCR = Polymerase chain reaction, COPD = Chronic obstructive pulmonary disease, GERD = Gastro-Esophageal reflux disease

Table S22: Characteristics of weighted populations in CPRD AURUM database, stratified by staggered cohort and vaccine.

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	ChAdOx1	BNT162b2	ASMD	ChAdOx1	BNT162b2	ASMD	ChAdOx1	BNT162b2	ASMD	ChAdOx1	BNT162b2	ASMD
N (individuals)	48,138	48,432		306,114	307,972		35,517	35,840		117,220	116,722	
Age, median [Q25-Q75]	80 [77-85]	80 [77-85]	0.003	66 [57-72]	66 [57-72]	0.003	54 [46-60]	54 [46-60]	0.000	42 [39-46]	42 [39-46]	0.004
Sex: Female, N(%)	27,920 (58%)	27,962 (58%)	0.005	167,623 (55%)	168,473 (55%)	0.001	21,299 (60%)	21,484 (60%)	0.000	54,350 (46%)	54,304 (47%)	0.003
Years of prior history*, median [Q25-Q75]	24 [9-36]	25 [11-36]	0.011	21 [9-32]	21 [9-32]	0.000	17 [8-27]	17 [7-27]	0.007	9 [4-17]	9 [4-17]	0.001
Number of GP visits, median [Q25-Q75]	12 [6-19]	12 [6-19]	0.003	10 [5-16]	10 [6-16]	0.001	8 [4-14]	8 [4-14]	0.012	4 [1-8]	4 [1-8]	0.008
Number of PCR tests, median [Q25-Q75]	0[0-0]	0[0-0]	0.006	0[0-0]	0[0-0]	0.003	0[0-0]	0[0-0]	0.013	0[0-0]	0[0-0]	0.003
Comorbidities**, N(%)												
Anxiety	7,101 (15%)	7,442 (15%)	0.017	62,230 (20%)	61,892 (20%)	0.006	7,419 (21%)	7,362 (21%)	0.009	19,086 (16%)	19,543 (17%)	0.012
Asthma	5,241 (11%)	5,396 (11%)	0.008	57,043 (19%)	56,551 (18%)	0.007	6,365 (18%)	6,097 (17%)	0.024	9,186 (8%)	9,059 (8%)	0.003
Chronic kidney disease	11,403 (24%)	11,809 (24%)	0.016	28,219 (9%)	29,790 (10%)	0.016	1,565 (4%)	1,700 (5%)	0.016	793 (1%)	897 (1%)	0.011
COPD	4,080 (8%)	4,014 (8%)	0.007	20,765 (7%)	20,456 (7%)	0.006	661 (2%)	669 (2%)	0.000	424 (0%)	471 (0%)	0.007
Dementia	3,667 (8%)	3,510 (7%)	0.014	2,733 (1%)	2,137 (1%)	0.022	419 (1%)	288 (1%)	0.038	109 (0%)	60 (0%)	0.016
Depressive disorder	5,666 (12%)	5,885 (12%)	0.012	56,642 (19%)	57,377 (19%)	0.003	6,508 (18%)	6,556 (18%)	0.001	16,027 (14%)	16,191 (14%)	0.006
Diabetes	8,849 (18%)	9,020 (19%)	0.006	50,019 (16%)	50,218 (16%)	0.001	2,560 (7%)	2,850 (8%)	0.028	3,231 (3%)	3,106 (3%)	0.006
GERD	2,637 (5%)	2,694 (6%)	0.004	16,666 (5%)	16,658 (5%)	0.002	1,479 (4%)	1,443 (4%)	0.007	3,087 (3%)	3,046 (3%)	0.001
Heart failure	2,843 (6%)	2,904 (6%)	0.004	6,822 (2%)	6,936 (2%)	0.002	443 (1%)	361 (1%)	0.023	204 (0%)	202 (0%)	0.000
Hypertension	25,422 (53%)	26,106 (54%)	0.022	103,545 (34%)	105,521 (34%)	0.009	6,295 (18%)	6,514 (18%)	0.012	6,692 (6%)	6,522 (6%)	0.005
Hypothyroidism	4,806 (10%)	4,978 (10%)	0.010	22,667 (7%)	23,290 (8%)	0.006	1,845 (5%)	1,886 (5%)	0.003	2,985 (3%)	3,025 (3%)	0.003
Malignant neoplastic disease	10,958 (23%)	11,284 (23%)	0.013	38,507 (13%)	40,499 (13%)	0.017	2,019 (6%)	2,152 (6%)	0.014	1,504 (1%)	1,576 (1%)	0.006
Myocardial infarction	2,481 (5%)	2,516 (5%)	0.002	11,083 (4%)	11,197 (4%)	0.001	425 (1%)	521 (1%)	0.022	256 (0%)	349 (0%)	0.016
Osteoporosis	5,117 (11%)	5,335 (11%)	0.012	11,759 (4%)	11,858 (4%)	0.000	719 (2%)	667 (2%)	0.012	344 (0%)	372 (0%)	0.004

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	ChAdOx1	BNT162b2	ASMD	ChAdOx1	BNT162b2	ASMD	ChAdOx1	BNT162b2	ASMD	ChAdOx1	BNT162b2	ASMD
Pneumonia	2,576 (5%)	2,527 (5%)	0.006	9,543 (3%)	9,423 (3%)	0.003	808 (2%)	692 (2%)	0.024	979 (1%)	904 (1%)	0.007
Rheumatoid arthritis	935 (2%)	1,005 (2%)	0.010	6,476 (2%)	6,640 (2%)	0.003	284 (1%)	344 (1%)	0.017	216 (0%)	258 (0%)	0.008
Stroke	2,314 (5%)	2,418 (5%)	0.009	7,284 (2%)	7,949 (3%)	0.013	446 (1%)	414 (1%)	0.009	294 (0%)	336 (0%)	0.007
Venous thromboembolism	3,001 (6%)	3,101 (6%)	0.007	11,833 (4%)	12,315 (4%)	0.007	812 (2%)	853 (2%)	0.006	601 (1%)	765 (1%)	0.019

The 4 cohorts represent vaccine rollout periods. *Calculated as the days of previous observation in the database before index date. **Assessed anytime before index date. ASMD = Absolute standardized mean difference, GP = General practice, PCR = Polymerase chain reaction, COPD = Chronic obstructive pulmonary disease, GERD = Gastro-Esophageal reflux disease

Table S23: Characteristics of unweighted populations in CPRD AURUM database, stratified by staggered cohort and vaccine.

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	ChAdOx1	BNT162b2	ASMD	ChAdOx1	BNT162b2	ASMD	ChAdOx1	BNT162b2	ASMD	ChAdOx1	BNT162b2	ASMD
N (individuals)	219,804	332,790		969,262	594,262		1,473,602	54,102		542,670	1,335,671	
Age, median [Q25-Q75]	80 [77-85]	82 [79-86]	0.129	69 [63-73]	67 [56-73]	0.148	55 [51-60]	58 [50-82]	0.381	45 [42-48]	31 [25-37]	1.319
Sex: Female, N(%)	127,656 (58%)	186,481 (56%)	0.041	528,692 (55%)	324,259 (55%)	0.000	739,444 (50%)	32,310 (60%)	0.193	242,758 (45%)	625,195 (47%)	0.042
Years of prior history*, median [Q25-Q75]	24 [9-36]	26 [13-38]	0.059	21 [9-33]	21 [9-32]	0.028	17 [8-27]	19 [8-30]	0.116	10 [5-18]	7 [3-19]	0.146
Number of GP visits, median [Q25-Q75]	12 [6-19]	11 [6-18]	0.038	10 [6-17]	11 [6-17]	0.015	7 [3-12]	10 [5-17]	0.294	3 [1-8]	3 [1-7]	0.045
Number of PCR tests, median [Q25-Q75]	0[0-0]	0[0-0]	0.183	0[0-0]	0[0-0]	0.014	0[0-0]	0[0-0]	0.171	0[0-0]	0[0-0]	0.008
Comorbidities**, N(%)												
Anxiety	33,355 (15%)	49,410 (15%)	0.009	187,469 (19%)	122,087 (21%)	0.030	281,846 (19%)	10,441 (19%)	0.004	86,805 (16%)	218,144 (16%)	0.009
Asthma	24,009 (11%)	37,889 (11%)	0.015	159,162 (16%)	116,596 (20%)	0.083	200,995 (14%)	8,668 (16%)	0.067	41,393 (8%)	114,378 (9%)	0.034
Chronic kidney disease	51,053 (23%)	86,899 (26%)	0.067	97,339 (10%)	56,923 (10%)	0.016	24,198 (2%)	6,692 (12%)	0.430	2,879 (1%)	2,664 (0%)	0.055
COPD	19,105 (9%)	28,317 (9%)	0.007	67,700 (7%)	39,595 (7%)	0.013	13,621 (1%)	2,063 (4%)	0.191	1,510 (0%)	942 (0%)	0.050
Dementia	16,795 (8%)	16,138 (5%)	0.116	12,106 (1%)	3,720 (1%)	0.065	1,896 (0%)	1,323 (2%)	0.207	447 (0%)	119 (0%)	0.034
Depressive disorder	27,009 (12%)	37,831 (11%)	0.028	170,626 (18%)	112,753 (19%)	0.035	256,789 (17%)	9,046 (17%)	0.019	74,210 (14%)	155,037 (12%)	0.062
Diabetes	39,751 (18%)	61,929 (19%)	0.014	154,348 (16%)	98,676 (17%)	0.018	78,394 (5%)	5,817 (11%)	0.201	9,729 (2%)	12,040 (1%)	0.077
GERD	12,156 (6%)	20,204 (6%)	0.023	52,694 (5%)	32,288 (5%)	0.000	56,444 (4%)	2,506 (5%)	0.040	13,807 (3%)	21,599 (2%)	0.065
Heart failure	13,147 (6%)	20,430 (6%)	0.007	24,276 (3%)	13,120 (2%)	0.020	5,673 (0%)	1,529 (3%)	0.195	681 (0%)	448 (0%)	0.033
Hypertension	114,922 (52%)	186,367 (56%)	0.075	345,014 (36%)	200,762 (34%)	0.038	224,543 (15%)	15,536 (29%)	0.330	31,330 (6%)	19,649 (1%)	0.232
Hypothyroidism	21,855 (10%)	34,512 (10%)	0.014	73,992 (8%)	44,456 (7%)	0.006	64,026 (4%)	3,642 (7%)	0.104	13,920 (3%)	18,516 (1%)	0.085
Malignant neoplastic disease	49,023 (22%)	82,610 (25%)	0.059	131,135 (14%)	76,103 (13%)	0.021	55,601 (4%)	6,311 (12%)	0.299	7,505 (1%)	5,104 (0%)	0.107
Myocardial infarction	11,236 (5%)	18,289 (5%)	0.017	33,142 (3%)	23,019 (4%)	0.024	11,237 (1%)	1,464 (3%)	0.149	861 (0%)	715 (0%)	0.032

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	ChAdOx1	BNT162b2	ASMD	ChAdOx1	BNT162b2	ASMD	ChAdOx1	BNT162b2	ASMD	ChAdOx1	BNT162b2	ASMD
Osteoporosis	22,986 (10%)	36,535 (11%)	0.017	42,319 (4%)	21,789 (4%)	0.036	12,455 (1%)	2,632 (5%)	0.243	1,380 (0%)	1,028 (0%)	0.044
Pneumonia	12,101 (6%)	16,297 (5%)	0.027	33,170 (3%)	17,567 (3%)	0.027	20,399 (1%)	1,658 (3%)	0.114	4,297 (1%)	7,793 (1%)	0.025
Rheumatoid arthritis	4,544 (2%)	6,693 (2%)	0.004	20,294 (2%)	12,878 (2%)	0.005	8,463 (1%)	667 (1%)	0.070	821 (0%)	891 (0%)	0.026
Stroke	10,876 (5%)	15,601 (5%)	0.012	24,851 (3%)	15,056 (3%)	0.002	9,547 (1%)	1,281 (2%)	0.141	1,153 (0%)	1,022 (0%)	0.036
Venous thromboembolism	13,782 (6%)	21,549 (6%)	0.008	39,415 (4%)	23,632 (4%)	0.005	24,312 (2%)	1,980 (4%)	0.125	1,936 (0%)	2,541 (0%)	0.032

The 4 cohorts represent vaccine rollout periods. *Calculated as the days of previous observation in the database before index date. **Assessed anytime before index date. ASMD = Absolute standardized mean difference, GP = General practice, PCR = Polymerase chain reaction, COPD = Chronic obstructive pulmonary disease, GERD = Gastro-Esophageal reflux disease

Table S24: Characteristics of weighted populations in CPRD GOLD database, stratified by staggered cohort and vaccine.

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	ChAdOx1	BNT162b2	ASMD	ChAdOx1	BNT162b2	ASMD	ChAdOx1	BNT162b2	ASMD	ChAdOx1	BNT162b2	ASMD
N (individuals)	7,490	7,490		77,012	76,978		24,590	24,597		49,538	49,577	
Age, median [Q25-Q75]	82 [78-86]	80 [78-86]	0.000	70 [65-74]	70 [65-74]	0.004	54 [49-59]	54 [49-59]	0.009	42 [37-46]	42 [37-47]	0.003
Sex: Female, N(%)	4,266 (57%)	4,266 (57%)	0.000	41,394 (54%)	41,607 (54%)	0.006	13,052 (53%)	13,078 (53%)	0.002	22,308 (45%)	22,520 (45%)	0.008
Years of prior history*, median [Q25-Q75]	18 [12-21]	18 [11-21]	0.000	17 [12-20]	17 [12-20]	0.005	17 [12-20]	17 [12-20]	0.004	14 [6-18]	14 [6-18]	0.005
Number of GP visits, median [Q25-Q75]	14 [9-21]	14 [9-21]	0.007	10 [6-16]	10 [6-17]	0.012	6 [2-11]	6 [2-11]	0.009	2 [0-6]	2 [0-7]	0.008
Number of PCR tests, median [Q25-Q75]	0[0-0]	0[0-0]	0.004	0[0-0]	0[0-0]	0.002	0[0-0]	0[0-0]	0.011	0[0-0]	0[0-0]	0.002
Comorbidities**, N(%)												
Anxiety	1,008 (13%)	1,015 (14%)	0.002	12,765 (17%)	12,897 (17%)	0.005	5,218 (21%)	5,293 (22%)	0.007	8,501 (17%)	8,578 (17%)	0.004
Asthma	783 (10%)	774 (10%)	0.004	9,867 (13%)	10,028 (13%)	0.006	2,993 (12%)	2,826 (11%)	0.021	3,700 (7%)	3,568 (7%)	0.010
Chronic kidney disease	1,711 (23%)	1,694 (23%)	0.005	7,209 (9%)	7,045 (9%)	0.007	530 (2%)	411 (2%)	0.035	193 (0%)	202 (0%)	0.003
COPD	568 (8%)	583 (8%)	0.008	5,739 (7%)	5,725 (7%)	0.001	321 (1%)	274 (1%)	0.017	170 (0%)	165 (0%)	0.002
Dementia	543 (7%)	495 (7%)	0.025	726 (1%)	737 (1%)	0.001	55 (0%)	74 (0%)	0.015	28 (0%)	21 (0%)	0.006
Depressive disorder	733 (10%)	729 (10%)	0.002	11,461 (15%)	11,746 (15%)	0.011	4,478 (18%)	4,427 (18%)	0.005	7,038 (14%)	7,119 (14%)	0.004
Diabetes	1,114 (15%)	1,107 (15%)	0.003	10,260 (13%)	10,130 (13%)	0.005	1,051 (4%)	963 (4%)	0.018	768 (2%)	654 (1%)	0.019
GERD	451 (6%)	447 (6%)	0.002	3,691 (5%)	3,753 (5%)	0.004	763 (3%)	770 (3%)	0.001	975 (2%)	978 (2%)	0.000
Heart failure	395 (5%)	411 (5%)	0.009	1,763 (2%)	1,819 (2%)	0.005	125 (1%)	81 (0%)	0.028	50 (0%)	54 (0%)	0.002
Hypertension	2,761 (37%)	2,754 (37%)	0.002	21,627 (28%)	21,686 (28%)	0.002	3,184 (13%)	3,261 (13%)	0.009	1,842 (4%)	1,975 (4%)	0.014
Hypothyroidism	579 (8%)	566 (8%)	0.007	4,932 (6%)	4,869 (6%)	0.003	1,064 (4%)	1,065 (4%)	0.000	979 (2%)	1,028 (2%)	0.007
Malignant neoplastic disease	1,632 (22%)	1,744 (23%)	0.036	10,682 (14%)	9,986 (13%)	0.026	1,007 (4%)	1,089 (4%)	0.017	598 (1%)	660 (1%)	0.011
Myocardial infarction	330 (4%)	325 (4%)	0.004	2,919 (4%)	2,943 (4%)	0.002	239 (1%)	217 (1%)	0.010	90 (0%)	85 (0%)	0.002

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	ChAdOx1	BNT162b2	ASMD	ChAdOx1	BNT162b2	ASMD	ChAdOx1	BNT162b2	ASMD	ChAdOx1	BNT162b2	ASMD
Osteoporosis	665 (9%)	638 (9%)	0.013	3,388 (4%)	3,496 (5%)	0.007	323 (1%)	314 (1%)	0.003	103 (0%)	92 (0%)	0.005
Pneumonia	286 (4%)	258 (3%)	0.020	1,807 (2%)	1,724 (2%)	0.007	263 (1%)	252 (1%)	0.005	271 (1%)	265 (1%)	0.002
Rheumatoid arthritis	111 (1%)	111 (1%)	0.001	1,437 (2%)	1,460 (2%)	0.002	123 (1%)	115 (0%)	0.005	58 (0%)	40 (0%)	0.011
Stroke	325 (4%)	321 (4%)	0.003	2,134 (3%)	2,072 (3%)	0.005	207 (1%)	148 (1%)	0.028	96 (0%)	91 (0%)	0.002
Venous thromboembolism	306 (4%)	341 (5%)	0.023	2,125 (3%)	2,153 (3%)	0.002	288 (1%)	285 (1%)	0.001	146 (0%)	198 (0%)	0.018

The 4 cohorts represent vaccine rollout periods. *Calculated as the days of previous observation in the database before index date. **Assessed anytime before index date. ASMD = Absolute standardized mean difference, GP = General practice, PCR = Polymerase chain reaction, COPD = Chronic obstructive pulmonary disease, GERD = Gastro-Esophageal reflux disease

Table S25: Characteristics of unweighted populations in CPRD GOLD database, stratified by staggered cohort and vaccine.

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	ChAdOx1	BNT162b2	ASMD	ChAdOx1	BNT162b2	ASMD	ChAdOx1	BNT162b2	ASMD	ChAdOx1	BNT162b2	ASMD
N (individuals)	82,406	32,755		302,999	180,670		423,876	36,748		147,744	365,096	
Age, median [Q25-Q75]	84 [82-88]	81 [79-86]	0.351	71 [66-76]	70 [66-74]	0.132	56 [52-61]	54 [50-60]	0.171	44 [41-48]	31 [24-37]	1.090
Sex: Female, N(%)	47,915 (58%)	18,415 (56%)	0.039	162,753 (54%)	97,747 (54%)	0.008	210,283 (50%)	19,649 (53%)	0.077	64,999 (44%)	167,510 (46%)	0.038
Years of prior history*, median [Q25-Q75]	17 [14-20]	18 [13-21]	0.001	17 [13-19]	17 [12-19]	0.014	17 [10-19]	18 [12-20]	0.107	14 [7-18]	15 [6-18]	0.017
Number of GP visits, median [Q25-Q75]	14 [9-21]	14 [9-21]	0.005	11 [7-18]	10 [6-16]	0.122	6 [2-12]	6 [2-11]	0.069	3 [0-7]	2 [0-6]	0.098
Number of PCR tests, median [Q25-Q75]	0[0-0]	0[0-0]	0.006	0[0-0]	0[0-0]	0.009	0[0-0]	0[0-0]	0.021	0[0-0]	0[0-0]	0.011
Comorbidities**, N(%)												
Anxiety	9,923 (12%)	4,336 (13%)	0.036	49,010 (16%)	28,697 (16%)	0.008	75,258 (18%)	8,004 (22%)	0.101	24,601 (17%)	59,094 (16%)	0.013
Asthma	8,491 (10%)	3,250 (10%)	0.013	39,988 (13%)	21,396 (12%)	0.041	48,034 (11%)	4,053 (11%)	0.010	10,517 (7%)	33,240 (9%)	0.073
Chronic kidney disease	21,564 (26%)	7,430 (23%)	0.081	34,168 (11%)	15,033 (8%)	0.100	7,553 (2%)	566 (2%)	0.019	739 (1%)	578 (0%)	0.060
COPD	6,837 (8%)	2,417 (7%)	0.034	27,472 (9%)	11,545 (6%)	0.100	6,334 (1%)	348 (1%)	0.050	640 (0%)	285 (0%)	0.070
Dementia	4,773 (6%)	1,895 (6%)	0.000	5,124 (2%)	1,375 (1%)	0.085	548 (0%)	87 (0%)	0.025	126 (0%)	29 (0%)	0.036
Depressive disorder	6,998 (8%)	3,310 (10%)	0.056	45,154 (15%)	26,294 (15%)	0.010	70,703 (17%)	6,569 (18%)	0.032	21,711 (15%)	39,181 (11%)	0.119
Diabetes	12,387 (15%)	4,882 (15%)	0.004	43,647 (14%)	22,552 (12%)	0.056	24,219 (6%)	1,191 (3%)	0.120	2,254 (2%)	2,507 (1%)	0.080
GERD	4,054 (5%)	2,012 (6%)	0.054	14,294 (5%)	8,525 (5%)	0.000	14,447 (3%)	1,093 (3%)	0.025	2,883 (2%)	5,213 (1%)	0.041
Heart failure	5,058 (6%)	1,782 (5%)	0.030	9,180 (3%)	3,669 (2%)	0.064	2,308 (1%)	100 (0%)	0.043	191 (0%)	98 (0%)	0.037
Hypertension	31,217 (38%)	11,995 (37%)	0.026	88,833 (29%)	49,763 (28%)	0.039	59,554 (14%)	4,679 (13%)	0.039	6,761 (5%)	4,776 (1%)	0.194
Hypothyroidism	7,042 (9%)	2,373 (7%)	0.048	20,521 (7%)	11,106 (6%)	0.025	17,382 (4%)	1,553 (4%)	0.006	3,245 (2%)	4,180 (1%)	0.082
Malignant neoplastic disease	18,950 (23%)	6,972 (21%)	0.041	42,687 (14%)	22,617 (13%)	0.046	17,903 (4%)	1,522 (4%)	0.004	2,192 (1%)	1,796 (0%)	0.100
Myocardial infarction	4,500 (5%)	1,603 (5%)	0.026	13,456 (4%)	6,621 (4%)	0.039	5,280 (1%)	271 (1%)	0.051	330 (0%)	154 (0%)	0.050

	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
	ChAdOx1	BNT162b2	ASMD	ChAdOx1	BNT162b2	ASMD	ChAdOx1	BNT162b2	ASMD	ChAdOx1	BNT162b2	ASMD
Osteoporosis	8,564 (10%)	2,770 (8%)	0.066	16,117 (5%)	7,531 (4%)	0.054	4,330 (1%)	458 (1%)	0.021	408 (0%)	205 (0%)	0.054
Pneumonia	3,231 (4%)	1,032 (3%)	0.042	8,604 (3%)	3,418 (2%)	0.062	4,527 (1%)	345 (1%)	0.013	921 (1%)	1,696 (0%)	0.022
Rheumatoid arthritis	1,257 (2%)	512 (2%)	0.003	5,999 (2%)	2,929 (2%)	0.027	2,405 (1%)	154 (0%)	0.021	191 (0%)	111 (0%)	0.035
Stroke	4,193 (5%)	1,490 (5%)	0.025	10,213 (3%)	4,632 (3%)	0.048	3,789 (1%)	199 (1%)	0.042	369 (0%)	225 (0%)	0.048
Venous thromboembolism	3,550 (4%)	1,389 (4%)	0.003	9,466 (3%)	4,490 (2%)	0.039	6,339 (1%)	370 (1%)	0.044	460 (0%)	496 (0%)	0.037

The 4 cohorts represent vaccine rollout periods. *Calculated as the days of previous observation in the database before index date. **Assessed anytime before index date. ASMD = Absolute standardized mean difference, GP = General practice, PCR = Polymerase chain reaction, COPD = Chronic obstructive pulmonary disease, GERD = Gastro-Esophageal reflux disease

Table S26: Number of records (and risk per 10,000 individuals) for post COVID-19 cardiac and thromboembolic complications, across cohorts and databases, stratified by exposure status (any COVID-19 vaccine). Follow-up ends at first vaccine dose after index date.

Cohort	Time window	Outcome	AURUM		CORIVA		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
Cohort 1			N = 346,674	N = 552,602	N = 23,982	N = 26,736	N = 169,100	N = 118,507	N = 223,962	N = 89,941
0 to 30 days	VTE	VTE	93 (2.68)	45 (0.81)	77 (32.11)	6 (2.24)	8 (0.47)	< 5	74 (3.30)	< 5
		DVT	22 (0.63)	10 (0.18)	12 (5.00)	< 5	< 5	< 5	19 (0.85)	< 5
		PE	75 (2.16)	37 (0.67)	67 (27.94)	5 (1.87)	7 (0.41)	< 5	59 (2.63)	< 5
		ATE	22 (0.63)	28 (0.51)	110 (45.87)	6 (2.24)	6 (0.35)	< 5	77 (3.44)	6 (0.67)
		IS	8 (0.23)	< 5	64 (26.69)	< 5	< 5	< 5	45 (2.01)	< 5
		TIA	< 5	6 (0.11)	20 (8.34)	< 5	< 5	< 5	7 (0.31)	< 5
		MI	11 (0.32)	20 (0.36)	35 (14.59)	5 (1.87)	< 5	< 5	27 (1.21)	< 5
		HF	59 (1.70)	73 (1.32)	395 (164.71)	27 (10.10)	10 (0.59)	< 5	302 (13.48)	23 (2.56)
		HS	< 5	< 5	< 5	< 5	< 5	< 5	7 (0.31)	< 5
		MP	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5
31 to 90 days	VTE	VTE	19 (0.55)	20 (0.36)	37 (15.43)	< 5	< 5	< 5	16 (0.71)	< 5
		DVT	10 (0.29)	7 (0.13)	20 (8.34)	< 5	< 5	< 5	10 (0.45)	< 5
		PE	9 (0.26)	13 (0.24)	21 (8.76)	< 5	< 5	< 5	6 (0.27)	< 5
		ATE	5 (0.14)	16 (0.29)	33 (13.76)	< 5	< 5	< 5	41 (1.83)	5 (0.56)
		IS	< 5	< 5	19 (7.92)	< 5	< 5	< 5	20 (0.89)	< 5
		TIA	< 5	6 (0.11)	8 (3.34)	< 5	< 5	< 5	13 (0.58)	< 5
		MI	< 5	7 (0.13)	12 (5.00)	< 5	< 5	< 5	11 (0.49)	< 5
		HF	30 (0.87)	56 (1.01)	151 (62.96)	14 (5.24)	< 5	< 5	89 (3.97)	8 (0.89)
		HS	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5
91 to 180 days	VTE	VTE	10 (0.29)	9 (0.16)	21 (8.76)	5 (1.87)	< 5	< 5	20 (0.89)	< 5
		DVT	5 (0.14)	< 5	14 (5.84)	< 5	< 5	< 5	9 (0.40)	< 5
		PE	5 (0.14)	5 (0.09)	9 (3.75)	< 5	< 5	< 5	11 (0.49)	< 5
		ATE	11 (0.32)	14 (0.25)	31 (12.93)	< 5	< 5	< 5	30 (1.34)	< 5
		IS	< 5	< 5	16 (6.67)	< 5	< 5	< 5	16 (0.71)	< 5
		TIA	5 (0.14)	6 (0.11)	8 (3.34)	< 5	< 5	< 5	8 (0.36)	< 5
		MI	5 (0.14)	< 5	10 (4.17)	< 5	< 5	< 5	7 (0.31)	< 5
		HF	37 (1.07)	51 (0.92)	162 (67.55)	21 (7.85)	< 5	< 5	87 (3.88)	7 (0.78)
		HS	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5

Cohort	Time window	Outcome	AURUM		CORIVA		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
	181 to 365 days	VTE	10 (0.29)	8 (0.14)	45 (18.76)	7 (2.62)	< 5	< 5	10 (0.45)	< 5
		DVT	5 (0.14)	< 5	16 (6.67)	< 5	< 5	< 5	6 (0.27)	< 5
		PE	5 (0.14)	< 5	34 (14.18)	< 5	< 5	< 5	< 5	< 5
		ATE	10 (0.29)	19 (0.34)	55 (22.93)	11 (4.11)	< 5	< 5	42 (1.88)	8 (0.89)
		IS	< 5	6 (0.11)	32 (13.34)	10 (3.74)	< 5	< 5	21 (0.94)	5 (0.56)
		TIA	6 (0.17)	< 5	16 (6.67)	< 5	< 5	< 5	10 (0.45)	< 5
		MI	< 5	10 (0.18)	14 (5.84)	< 5	< 5	< 5	11 (0.49)	< 5
		HF	40 (1.15)	53 (0.96)	268 (111.75)	48 (17.95)	< 5	6 (0.51)	86 (3.84)	20 (2.22)
		HS	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5
Cohort 2			N = 1,975,726	N = 1,563,569	N = 34,317	N = 4,572	N = 583,399	N = 486,619	N = 433,151	N = 819,590
	0 to 30 days	VTE	241 (1.22)	54 (0.35)	79 (23.02)	< 5	31 (0.53)	7 (0.14)	258 (5.96)	27 (0.33)
		DVT	41 (0.21)	19 (0.12)	12 (3.50)	< 5	8 (0.14)	< 5	63 (1.45)	9 (0.11)
		PE	204 (1.03)	38 (0.24)	69 (20.11)	< 5	24 (0.41)	6 (0.12)	213 (4.92)	20 (0.24)
		ATE	41 (0.21)	25 (0.16)	110 (32.05)	< 5	< 5	< 5	173 (3.99)	29 (0.35)
		IS	7 (0.04)	5 (0.03)	68 (19.82)	< 5	< 5	< 5	96 (2.22)	12 (0.15)
		TIA	8 (0.04)	< 5	18 (5.25)	< 5	< 5	< 5	17 (0.39)	6 (0.07)
		MI	26 (0.13)	17 (0.11)	35 (10.20)	< 5	< 5	< 5	64 (1.48)	11 (0.13)
		HF	45 (0.23)	47 (0.30)	364 (106.07)	< 5	5 (0.09)	< 5	378 (8.73)	76 (0.93)
		HS	6 (0.03)	< 5	< 5	< 5	< 5	< 5	18 (0.42)	< 5
		MP	12 (0.06)	< 5	< 5	< 5	< 5	< 5	14 (0.32)	< 5
	31 to 90 days	VTE	43 (0.22)	13 (0.08)	31 (9.03)	< 5	< 5	< 5	59 (1.36)	9 (0.11)
		DVT	24 (0.12)	6 (0.04)	16 (4.66)	< 5	< 5	< 5	32 (0.74)	5 (0.06)
		PE	23 (0.12)	8 (0.05)	18 (5.25)	< 5	< 5	< 5	33 (0.76)	< 5
		ATE	18 (0.09)	18 (0.12)	32 (9.32)	< 5	< 5	< 5	85 (1.96)	14 (0.17)
		IS	< 5	< 5	20 (5.83)	< 5	< 5	< 5	43 (0.99)	6 (0.07)
		TIA	< 5	7 (0.04)	< 5	< 5	< 5	< 5	23 (0.53)	5 (0.06)
		MI	13 (0.07)	10 (0.06)	13 (3.79)	< 5	< 5	< 5	26 (0.60)	< 5
		HF	27 (0.14)	30 (0.19)	149 (43.42)	< 5	< 5	< 5	138 (3.19)	29 (0.35)
		HS	< 5	< 5	< 5	< 5	< 5	< 5	7 (0.16)	< 5
		MP	6 (0.03)	< 5	< 5	< 5	< 5	< 5	< 5	< 5
	91 to 180 days	VTE	28 (0.14)	15 (0.10)	26 (7.58)	< 5	6 (0.10)	< 5	58 (1.34)	6 (0.07)
		DVT	13 (0.07)	9 (0.06)	15 (4.37)	< 5	< 5	< 5	31 (0.72)	6 (0.07)
		PE	15 (0.08)	6 (0.04)	12 (3.50)	< 5	< 5	< 5	30 (0.69)	< 5

Cohort	Time window	Outcome	AURUM		CORIVA		GOLD		SIDIAP			
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated		
		ATE	17 (0.09)	15 (0.10)	32 (9.32)	< 5	< 5	< 5	91 (2.10)	19 (0.23)		
		IS	< 5	< 5	15 (4.37)	< 5	< 5	< 5	49 (1.13)	9 (0.11)		
		TIA	9 (0.05)	5 (0.03)	11 (3.21)	< 5	< 5	< 5	20 (0.46)	5 (0.06)		
		MI	9 (0.05)	10 (0.06)	8 (2.33)	< 5	< 5	< 5	25 (0.58)	6 (0.07)		
		HF	22 (0.11)	27 (0.17)	166 (48.37)	< 5	< 5	< 5	110 (2.54)	41 (0.50)		
		HS	< 5	< 5	< 5	< 5	< 5	< 5	7 (0.16)	< 5		
		MP	< 5	< 5	< 5	< 5	< 5	< 5	7 (0.16)	< 5		
	181 to 365 days	VTE	9 (0.05)	12 (0.08)	44 (12.82)	< 5	< 5	< 5	16 (0.37)	23 (0.28)		
		DVT	< 5	5 (0.03)	20 (5.83)	< 5	< 5	< 5	9 (0.21)	14 (0.17)		
		PE	5 (0.03)	7 (0.04)	27 (7.87)	< 5	< 5	< 5	8 (0.18)	10 (0.12)		
		ATE	12 (0.06)	16 (0.10)	53 (15.44)	< 5	< 5	< 5	63 (1.45)	33 (0.40)		
		IS	< 5	< 5	31 (9.03)	< 5	< 5	< 5	35 (0.81)	11 (0.13)		
		TIA	< 5	< 5	12 (3.50)	< 5	< 5	< 5	16 (0.37)	13 (0.16)		
		MI	8 (0.04)	10 (0.06)	15 (4.37)	< 5	< 5	< 5	14 (0.32)	10 (0.12)		
		HF	20 (0.10)	31 (0.20)	259 (75.47)	5 (10.94)	< 5	< 5	81 (1.87)	41 (0.50)		
		HS	< 5	< 5	< 5	< 5	< 5	< 5	< 5	5 (0.06)		
		MP	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5		
		Cohort 3			N = 1,510,401	N = 1,528,031	N = 96,423	N = 24,050	N = 417,996	N = 462,832	N = 869,497	N = 954,232
		0 to 30 days	VTE	245 (1.62)	25 (0.16)	115 (11.93)	< 5	27 (0.65)	< 5	325 (3.74)	27 (0.28)	
DVT	45 (0.30)		< 5	22 (2.28)	< 5	6 (0.14)	< 5	90 (1.04)	7 (0.07)			
PE	209 (1.38)		22 (0.14)	96 (9.96)	< 5	22 (0.53)	< 5	262 (3.01)	22 (0.23)			
ATE	29 (0.19)		10 (0.07)	119 (12.34)	< 5	< 5	< 5	213 (2.45)	14 (0.15)			
IS	< 5		< 5	70 (7.26)	< 5	< 5	< 5	102 (1.17)	5 (0.05)			
TIA	5 (0.03)		< 5	19 (1.97)	< 5	< 5	< 5	20 (0.23)	< 5			
MI	20 (0.13)		8 (0.05)	40 (4.15)	< 5	< 5	< 5	97 (1.12)	7 (0.07)			
HF	31 (0.21)		18 (0.12)	380 (39.41)	< 5	< 5	< 5	364 (4.19)	23 (0.24)			
HS	< 5		< 5	< 5	< 5	< 5	< 5	20 (0.23)	< 5			
MP	9 (0.06)		< 5	6 (0.62)	< 5	< 5	< 5	19 (0.22)	< 5			
31 to 90 days	VTE		44 (0.29)	< 5	50 (5.19)	< 5	< 5	< 5	85 (0.98)	9 (0.09)		
	DVT		20 (0.13)	< 5	28 (2.90)	< 5	< 5	< 5	57 (0.66)	5 (0.05)		
	PE	27 (0.18)	< 5	26 (2.70)	< 5	< 5	< 5	38 (0.44)	< 5			
	ATE	11 (0.07)	7 (0.05)	48 (4.98)	< 5	< 5	< 5	109 (1.25)	10 (0.10)			
	IS	< 5	< 5	24 (2.49)	< 5	< 5	< 5	54 (0.62)	6 (0.06)			
	TIA	< 5	< 5	7 (0.73)	< 5	< 5	< 5	27 (0.31)	< 5			

Cohort	Time window	Outcome	AURUM		CORIVA		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
	91 to 180 days	MI	9 (0.06)	< 5	20 (2.07)	< 5	< 5	< 5	36 (0.41)	< 5
		HF	15 (0.10)	8 (0.05)	180 (18.67)	< 5	< 5	< 5	137 (1.58)	13 (0.14)
		HS	< 5	< 5	< 5	< 5	< 5	< 5	7 (0.08)	< 5
		MP	8 (0.05)	< 5	5 (0.52)	< 5	< 5	< 5	8 (0.09)	< 5
		VTE	24 (0.16)	8 (0.05)	43 (4.46)	< 5	< 5	< 5	64 (0.74)	8 (0.08)
		DVT	11 (0.07)	6 (0.04)	26 (2.70)	< 5	< 5	< 5	36 (0.41)	7 (0.07)
		PE	14 (0.09)	< 5	18 (1.87)	< 5	< 5	< 5	32 (0.37)	< 5
		ATE	< 5	7 (0.05)	44 (4.56)	< 5	< 5	< 5	113 (1.30)	20 (0.21)
		IS	< 5	< 5	21 (2.18)	< 5	< 5	< 5	57 (0.66)	12 (0.13)
		TIA	< 5	< 5	13 (1.35)	< 5	< 5	< 5	22 (0.25)	< 5
		MI	< 5	< 5	15 (1.56)	< 5	< 5	< 5	37 (0.43)	6 (0.06)
		HF	11 (0.07)	6 (0.04)	216 (22.40)	< 5	< 5	< 5	120 (1.38)	15 (0.16)
		HS	< 5	< 5	< 5	< 5	< 5	< 5	9 (0.10)	< 5
		MP	< 5	< 5	< 5	< 5	< 5	< 5	8 (0.09)	< 5
	181 to 365 days	VTE	< 5	9 (0.06)	72 (7.47)	< 5	< 5	< 5	34 (0.39)	5 (0.05)
	DVT	< 5	< 5	39 (4.04)	< 5	< 5	< 5	20 (0.23)	< 5	
	PE	< 5	6 (0.04)	37 (3.84)	< 5	< 5	< 5	16 (0.18)	< 5	
	ATE	< 5	< 5	80 (8.30)	< 5	< 5	< 5	51 (0.59)	18 (0.19)	
	IS	< 5	< 5	36 (3.73)	< 5	< 5	< 5	24 (0.28)	9 (0.09)	
	TIA	< 5	< 5	19 (1.97)	< 5	< 5	< 5	11 (0.13)	< 5	
	MI	< 5	< 5	32 (3.32)	< 5	< 5	< 5	17 (0.20)	7 (0.07)	
	HF	5 (0.03)	< 5	324 (33.60)	< 5	< 5	< 5	62 (0.71)	13 (0.14)	
	HS	< 5	< 5	7 (0.73)	< 5	< 5	< 5	< 5	< 5	
	MP	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5	
Cohort 4			N = 2,027,763	N = 2,085,598	N = 147,545	N = 22,245	N = 469,876	N = 550,437	N = 1,061,634	N = 880,950
0 to 30 days	VTE	334 (1.65)	19 (0.09)	116 (7.86)	< 5	36 (0.77)	7 (0.13)	350 (3.30)	38 (0.43)	
	DVT	55 (0.27)	6 (0.03)	22 (1.49)	< 5	6 (0.13)	< 5	106 (1.00)	14 (0.16)	
	PE	291 (1.44)	13 (0.06)	97 (6.57)	< 5	31 (0.66)	7 (0.13)	272 (2.56)	25 (0.28)	
	ATE	26 (0.13)	5 (0.02)	116 (7.86)	< 5	< 5	< 5	231 (2.18)	35 (0.40)	
	IS	< 5	< 5	69 (4.68)	< 5	< 5	< 5	115 (1.08)	17 (0.19)	
	TIA	6 (0.03)	< 5	18 (1.22)	< 5	< 5	< 5	26 (0.24)	< 5	
	MI	16 (0.08)	< 5	38 (2.58)	< 5	< 5	< 5	96 (0.90)	15 (0.17)	
	HF	28 (0.14)	< 5	364 (24.67)	< 5	< 5	< 5	362 (3.41)	28 (0.32)	
	HS	< 5	< 5	5 (0.34)	< 5	< 5	< 5	23 (0.22)	< 5	

Cohort	Time window	Outcome	AURUM		CORIVA		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
31 to 90 days	MP	12 (0.06)	< 5	7 (0.47)	< 5	< 5	< 5	26 (0.24)	9 (0.10)	
	VTE	58 (0.29)	11 (0.05)	54 (3.66)	< 5	5 (0.11)	< 5	91 (0.86)	12 (0.14)	
	DVT	21 (0.10)	< 5	32 (2.17)	< 5	< 5	< 5	61 (0.57)	7 (0.08)	
	PE	40 (0.20)	7 (0.03)	26 (1.76)	< 5	< 5	< 5	40 (0.38)	6 (0.07)	
	ATE	12 (0.06)	< 5	46 (3.12)	< 5	< 5	< 5	118 (1.11)	18 (0.20)	
	IS	< 5	< 5	24 (1.63)	< 5	< 5	< 5	52 (0.49)	7 (0.08)	
	TIA	< 5	< 5	6 (0.41)	< 5	< 5	< 5	33 (0.31)	7 (0.08)	
	MI	9 (0.04)	< 5	19 (1.29)	< 5	< 5	< 5	41 (0.39)	< 5	
	HF	14 (0.07)	8 (0.04)	176 (11.93)	< 5	< 5	< 5	142 (1.34)	17 (0.19)	
	HS	< 5	< 5	< 5	< 5	< 5	< 5	8 (0.08)	< 5	
	MP	7 (0.03)	< 5	5 (0.34)	< 5	< 5	< 5	10 (0.09)	< 5	
91 to 180 days	VTE	26 (0.13)	9 (0.04)	49 (3.32)	< 5	< 5	< 5	71 (0.67)	11 (0.12)	
	DVT	10 (0.05)	7 (0.03)	31 (2.10)	< 5	< 5	< 5	42 (0.40)	6 (0.07)	
	PE	17 (0.08)	< 5	19 (1.29)	< 5	< 5	< 5	32 (0.30)	6 (0.07)	
	ATE	< 5	5 (0.02)	41 (2.78)	< 5	< 5	< 5	128 (1.21)	21 (0.24)	
	IS	< 5	< 5	19 (1.29)	< 5	< 5	< 5	65 (0.61)	11 (0.12)	
	TIA	< 5	< 5	12 (0.81)	< 5	< 5	< 5	29 (0.27)	< 5	
	MI	< 5	< 5	14 (0.95)	< 5	< 5	< 5	37 (0.35)	7 (0.08)	
	HF	10 (0.05)	< 5	208 (14.10)	< 5	< 5	< 5	139 (1.31)	19 (0.22)	
	HS	< 5	< 5	< 5	< 5	< 5	< 5	14 (0.13)	< 5	
	MP	< 5	< 5	5 (0.34)	< 5	< 5	< 5	11 (0.10)	< 5	
	181 to 365 days	VTE	< 5	< 5	77 (5.22)	< 5	< 5	< 5	46 (0.43)	9 (0.10)
DVT		< 5	< 5	46 (3.12)	< 5	< 5	< 5	33 (0.31)	5 (0.06)	
PE		< 5	< 5	35 (2.37)	< 5	< 5	< 5	14 (0.13)	< 5	
ATE		< 5	< 5	73 (4.95)	< 5	< 5	< 5	54 (0.51)	22 (0.25)	
IS		< 5	< 5	33 (2.24)	< 5	< 5	< 5	27 (0.25)	15 (0.17)	
TIA		< 5	< 5	19 (1.29)	< 5	< 5	< 5	12 (0.11)	< 5	
MI		< 5	< 5	27 (1.83)	< 5	< 5	< 5	16 (0.15)	7 (0.08)	
HF		< 5	< 5	301 (20.40)	< 5	< 5	< 5	57 (0.54)	11 (0.12)	
HS		< 5	< 5	8 (0.54)	< 5	< 5	< 5	< 5	< 5	
MP		< 5	< 5	5 (0.34)	< 5	< 5	< 5	7 (0.07)	< 5	

VTE = Venous thromboembolism (DVT + PE), DVT = Deep vein thrombosis, PE = Pulmonary embolism, ATE = Arterial thrombosis/thromboembolism (IS + TIA + MI), IS = Ischemic stroke, TIA = Transient ischemic attack, MI = Myocardial infarction, HF = Heart failure, HS = Hemorrhagic stroke, MP = Myocarditis or Pericarditis

Table S27: Number of records (and risk per 10,000 individuals) for post COVID-19 cardiac and thromboembolic complications, across cohorts and databases, stratified by exposure status (any COVID-19 vaccine). Only first outcome after COVID-19 captured.

Cohort	Time window	Outcome	AURUM		CORIVA		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
Cohort 1			N = 346,674	N = 552,602	N = 23,982	N = 26,736	N = 169,100	N = 118,507	N = 223,962	N = 89,941
0 to 30 days	VTE	93 (2.68)	117 (2.12)	77 (32.11)	45 (16.83)	8 (0.47)	8 (0.68)	74 (3.30)	96 (10.67)	
	DVT	22 (0.63)	27 (0.49)	12 (5.00)	14 (5.24)	< 5	< 5	19 (0.85)	29 (3.22)	
	PE	75 (2.16)	95 (1.72)	67 (27.94)	33 (12.34)	7 (0.41)	7 (0.59)	59 (2.63)	77 (8.56)	
	ATE	22 (0.63)	70 (1.27)	110 (45.87)	81 (30.30)	6 (0.35)	7 (0.59)	77 (3.44)	208 (23.13)	
	IS	8 (0.23)	5 (0.09)	64 (26.69)	37 (13.84)	< 5	< 5	45 (2.01)	116 (12.90)	
	TIA	< 5	18 (0.33)	20 (8.34)	18 (6.73)	< 5	< 5	7 (0.31)	41 (4.56)	
	MI	11 (0.32)	46 (0.83)	35 (14.59)	35 (13.09)	< 5	5 (0.42)	27 (1.21)	63 (7.00)	
	HF	59 (1.70)	198 (3.58)	395 (164.71)	299 (111.83)	10 (0.59)	9 (0.76)	302 (13.48)	640 (71.16)	
	HS	< 5	7 (0.13)	< 5	< 5	< 5	< 5	7 (0.31)	14 (1.56)	
	MP	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5	
31 to 90 days	VTE	19 (0.55)	39 (0.71)	35 (14.59)	29 (10.85)	< 5	< 5	15 (0.67)	45 (5.00)	
	DVT	10 (0.29)	15 (0.27)	19 (7.92)	15 (5.61)	< 5	< 5	9 (0.40)	29 (3.22)	
	PE	9 (0.26)	25 (0.45)	20 (8.34)	14 (5.24)	< 5	< 5	6 (0.27)	20 (2.22)	
	ATE	5 (0.14)	43 (0.78)	29 (12.09)	44 (16.46)	< 5	< 5	39 (1.74)	127 (14.12)	
	IS	< 5	< 5	16 (6.67)	19 (7.11)	< 5	< 5	20 (0.89)	70 (7.78)	
	TIA	< 5	19 (0.34)	8 (3.34)	17 (6.36)	< 5	< 5	13 (0.58)	32 (3.56)	
	MI	< 5	20 (0.36)	10 (4.17)	11 (4.11)	< 5	< 5	9 (0.40)	29 (3.22)	
	HF	30 (0.87)	109 (1.97)	134 (55.88)	162 (60.59)	< 5	8 (0.68)	85 (3.80)	290 (32.24)	
	HS	< 5	< 5	< 5	< 5	< 5	< 5	< 5	12 (1.33)	
	MP	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5	
91 to 180 days	VTE	10 (0.29)	18 (0.33)	16 (6.67)	29 (10.85)	< 5	< 5	18 (0.80)	35 (3.89)	
	DVT	5 (0.14)	8 (0.14)	9 (3.75)	16 (5.98)	< 5	< 5	7 (0.31)	19 (2.11)	
	PE	5 (0.14)	10 (0.18)	9 (3.75)	15 (5.61)	< 5	< 5	11 (0.49)	18 (2.00)	
	ATE	11 (0.32)	28 (0.51)	28 (11.68)	45 (16.83)	< 5	6 (0.51)	25 (1.12)	104 (11.56)	
	IS	< 5	8 (0.14)	13 (5.42)	19 (7.11)	< 5	< 5	13 (0.58)	57 (6.34)	
	TIA	5 (0.14)	12 (0.22)	8 (3.34)	15 (5.61)	< 5	< 5	7 (0.31)	34 (3.78)	
	MI	5 (0.14)	8 (0.14)	9 (3.75)	16 (5.98)	< 5	5 (0.42)	6 (0.27)	23 (2.56)	
	HF	35 (1.01)	89 (1.61)	143 (59.63)	203 (75.93)	< 5	5 (0.42)	81 (3.62)	228 (25.35)	
	HS	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5	
	MP	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5	

Cohort	Time window	Outcome	AURUM		CORIVA		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
	181 to 365 days	VTE	9 (0.26)	11 (0.20)	29 (12.09)	27 (10.10)	< 5	< 5	5 (0.22)	11 (1.22)
		DVT	< 5	6 (0.11)	10 (4.17)	17 (6.36)	< 5	< 5	< 5	7 (0.78)
		PE	5 (0.14)	5 (0.09)	24 (10.01)	11 (4.11)	< 5	< 5	< 5	< 5
		ATE	10 (0.29)	23 (0.42)	45 (18.76)	74 (27.68)	< 5	< 5	35 (1.56)	39 (4.34)
		IS	< 5	6 (0.11)	26 (10.84)	34 (12.72)	< 5	< 5	18 (0.80)	24 (2.67)
		TIA	6 (0.17)	7 (0.13)	15 (6.25)	29 (10.85)	< 5	< 5	9 (0.40)	9 (1.00)
		MI	< 5	11 (0.20)	10 (4.17)	17 (6.36)	< 5	< 5	8 (0.36)	7 (0.78)
		HF	36 (1.04)	53 (0.96)	213 (88.82)	292 (109.22)	< 5	6 (0.51)	75 (3.35)	117 (13.01)
		HS	< 5	< 5	< 5	< 5	< 5	< 5	< 5	7 (0.78)
		MP	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5
Cohort 2			N = 1,975,726	N = 1,563,569	N = 34,317	N = 4,572	N = 583,399	N = 486,619	N = 433,151	N = 819,590
	0 to 30 days	VTE	241 (1.22)	220 (1.41)	79 (23.02)	7 (15.31)	31 (0.53)	24 (0.49)	258 (5.96)	400 (4.88)
		DVT	41 (0.21)	65 (0.42)	12 (3.50)	< 5	8 (0.14)	5 (0.10)	63 (1.45)	165 (2.01)
		PE	204 (1.03)	165 (1.06)	69 (20.11)	5 (10.94)	24 (0.41)	19 (0.39)	213 (4.92)	269 (3.28)
		ATE	41 (0.21)	104 (0.67)	110 (32.05)	5 (10.94)	< 5	6 (0.12)	173 (3.99)	669 (8.16)
		IS	7 (0.04)	14 (0.09)	68 (19.82)	< 5	< 5	< 5	96 (2.22)	346 (4.22)
		TIA	8 (0.04)	24 (0.15)	18 (5.25)	< 5	< 5	< 5	17 (0.39)	122 (1.49)
		MI	26 (0.13)	68 (0.43)	35 (10.20)	< 5	< 5	6 (0.12)	64 (1.48)	239 (2.92)
		HF	45 (0.23)	146 (0.93)	364 (106.07)	23 (50.31)	5 (0.09)	13 (0.27)	378 (8.73)	1,331 (16.24)
		HS	6 (0.03)	5 (0.03)	< 5	< 5	< 5	< 5	18 (0.42)	77 (0.94)
		MP	12 (0.06)	7 (0.04)	< 5	< 5	< 5	< 5	14 (0.32)	37 (0.45)
	31 to 90 days	VTE	41 (0.21)	75 (0.48)	28 (8.16)	5 (10.94)	< 5	9 (0.18)	56 (1.29)	187 (2.28)
		DVT	23 (0.12)	32 (0.20)	15 (4.37)	5 (10.94)	< 5	5 (0.10)	30 (0.69)	119 (1.45)
		PE	22 (0.11)	45 (0.29)	16 (4.66)	< 5	< 5	< 5	31 (0.72)	87 (1.06)
		ATE	18 (0.09)	92 (0.59)	29 (8.45)	< 5	< 5	9 (0.18)	84 (1.94)	437 (5.33)
		IS	< 5	11 (0.07)	18 (5.25)	< 5	< 5	< 5	43 (0.99)	231 (2.82)
		TIA	< 5	33 (0.21)	< 5	< 5	< 5	6 (0.12)	23 (0.53)	115 (1.40)
		MI	13 (0.07)	50 (0.32)	11 (3.21)	< 5	< 5	< 5	25 (0.58)	113 (1.38)
		HF	27 (0.14)	99 (0.63)	137 (39.92)	19 (41.56)	< 5	7 (0.14)	132 (3.05)	622 (7.59)
		HS	< 5	< 5	< 5	< 5	< 5	< 5	7 (0.16)	27 (0.33)
		MP	6 (0.03)	< 5	< 5	< 5	< 5	< 5	< 5	8 (0.10)
	91 to 180 days	VTE	25 (0.13)	37 (0.24)	21 (6.12)	6 (13.12)	6 (0.10)	< 5	53 (1.22)	109 (1.33)
		DVT	12 (0.06)	21 (0.13)	10 (2.91)	< 5	< 5	< 5	29 (0.67)	71 (0.87)
		PE	13 (0.07)	19 (0.12)	12 (3.50)	< 5	< 5	< 5	27 (0.62)	46 (0.56)

Cohort	Time window	Outcome	AURUM		CORIVA		GOLD		SIDIAP			
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated		
		ATE	15 (0.08)	43 (0.28)	31 (9.03)	< 5	< 5	< 5	81 (1.87)	394 (4.81)		
		IS	< 5	< 5	14 (4.08)	< 5	< 5	< 5	43 (0.99)	202 (2.46)		
		TIA	8 (0.04)	18 (0.12)	11 (3.21)	< 5	< 5	< 5	19 (0.44)	109 (1.33)		
		MI	8 (0.04)	25 (0.16)	8 (2.33)	< 5	< 5	< 5	22 (0.51)	104 (1.27)		
		HF	22 (0.11)	65 (0.42)	149 (43.42)	20 (43.74)	< 5	< 5	100 (2.31)	534 (6.52)		
		HS	< 5	< 5	< 5	< 5	< 5	< 5	7 (0.16)	35 (0.43)		
		MP	< 5	< 5	< 5	< 5	< 5	< 5	7 (0.16)	9 (0.11)		
	181 to 365 days	VTE	8 (0.04)	12 (0.08)	30 (8.74)	5 (10.94)	< 5	< 5	14 (0.32)	52 (0.63)		
		DVT	< 5	5 (0.03)	15 (4.37)	< 5	< 5	< 5	8 (0.18)	36 (0.44)		
		PE	< 5	8 (0.05)	18 (5.25)	< 5	< 5	< 5	7 (0.16)	19 (0.23)		
		ATE	10 (0.05)	17 (0.11)	44 (12.82)	< 5	< 5	< 5	53 (1.22)	151 (1.84)		
		IS	< 5	< 5	25 (7.29)	< 5	< 5	< 5	30 (0.69)	71 (0.87)		
		TIA	< 5	5 (0.03)	12 (3.50)	< 5	< 5	< 5	14 (0.32)	46 (0.56)		
		MI	6 (0.03)	10 (0.06)	11 (3.21)	< 5	< 5	< 5	11 (0.25)	45 (0.55)		
		HF	19 (0.10)	34 (0.22)	210 (61.19)	29 (63.43)	< 5	< 5	72 (1.66)	209 (2.55)		
		HS	< 5	< 5	< 5	< 5	< 5	< 5	< 5	10 (0.12)		
		MP	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5		
		Cohort 3			N = 1,510,401	N = 1,528,031	N = 96,423	N = 24,050	N = 417,996	N = 462,832	N = 869,497	N = 954,232
		0 to 30 days	VTE	245 (1.62)	142 (0.93)	115 (11.93)	9 (3.74)	27 (0.65)	17 (0.37)	325 (3.74)	180 (1.89)	
DVT	45 (0.30)		41 (0.27)	22 (2.28)	7 (2.91)	6 (0.14)	< 5	90 (1.04)	78 (0.82)			
PE	209 (1.38)		105 (0.69)	96 (9.96)	< 5	22 (0.53)	13 (0.28)	262 (3.01)	118 (1.24)			
ATE	29 (0.19)		49 (0.32)	119 (12.34)	12 (4.99)	< 5	12 (0.26)	213 (2.45)	275 (2.88)			
IS	< 5		5 (0.03)	70 (7.26)	9 (3.74)	< 5	< 5	102 (1.17)	130 (1.36)			
TIA	5 (0.03)		17 (0.11)	19 (1.97)	< 5	< 5	< 5	20 (0.23)	53 (0.56)			
MI	20 (0.13)		27 (0.18)	40 (4.15)	< 5	< 5	9 (0.19)	97 (1.12)	113 (1.18)			
HF	31 (0.21)		38 (0.25)	380 (39.41)	23 (9.56)	< 5	< 5	364 (4.19)	256 (2.68)			
HS	< 5		< 5	< 5	< 5	< 5	< 5	20 (0.23)	35 (0.37)			
MP	9 (0.06)		6 (0.04)	6 (0.62)	< 5	< 5	< 5	19 (0.22)	20 (0.21)			
31 to 90 days	VTE	41 (0.27)	46 (0.30)	45 (4.67)	10 (4.16)	< 5	6 (0.13)	81 (0.93)	90 (0.94)			
	DVT	19 (0.13)	27 (0.18)	25 (2.59)	7 (2.91)	< 5	< 5	54 (0.62)	60 (0.63)			
	PE	25 (0.17)	19 (0.12)	23 (2.39)	< 5	< 5	< 5	36 (0.41)	37 (0.39)			
	ATE	11 (0.07)	33 (0.22)	45 (4.67)	8 (3.33)	< 5	8 (0.17)	108 (1.24)	207 (2.17)			
	IS	< 5	< 5	22 (2.28)	< 5	< 5	< 5	54 (0.62)	87 (0.91)			
		TIA	< 5	14 (0.09)	7 (0.73)	< 5	< 5	< 5	27 (0.31)	35 (0.37)		

Cohort	Time window	Outcome	AURUM		CORIVA		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
	91 to 180 days	MI	9 (0.06)	16 (0.10)	18 (1.87)	< 5	< 5	5 (0.11)	35 (0.40)	93 (0.97)
		HF	15 (0.10)	26 (0.17)	166 (17.22)	25 (10.40)	< 5	< 5	130 (1.50)	154 (1.61)
		HS	< 5	< 5	< 5	< 5	< 5	< 5	7 (0.08)	19 (0.20)
		MP	8 (0.05)	8 (0.05)	< 5	< 5	< 5	< 5	8 (0.09)	11 (0.12)
		VTE	23 (0.15)	25 (0.16)	34 (3.53)	11 (4.57)	< 5	< 5	57 (0.66)	92 (0.96)
		DVT	10 (0.07)	15 (0.10)	20 (2.07)	7 (2.91)	< 5	< 5	33 (0.38)	61 (0.64)
		PE	14 (0.09)	13 (0.09)	15 (1.56)	< 5	< 5	< 5	28 (0.32)	34 (0.36)
		ATE	< 5	28 (0.18)	40 (4.15)	8 (3.33)	< 5	< 5	102 (1.17)	199 (2.09)
		IS	< 5	< 5	20 (2.07)	< 5	< 5	< 5	49 (0.56)	92 (0.96)
		TIA	< 5	9 (0.06)	13 (1.35)	< 5	< 5	< 5	20 (0.23)	47 (0.49)
		MI	< 5	18 (0.12)	13 (1.35)	< 5	< 5	< 5	35 (0.40)	69 (0.72)
		HF	11 (0.07)	12 (0.08)	194 (20.12)	27 (11.23)	< 5	< 5	110 (1.27)	133 (1.39)
		HS	< 5	< 5	< 5	< 5	< 5	< 5	9 (0.10)	13 (0.14)
		MP	< 5	< 5	< 5	< 5	< 5	< 5	8 (0.09)	14 (0.15)
	181 to 365 days	VTE	< 5	9 (0.06)	50 (5.19)	16 (6.65)	< 5	< 5	31 (0.36)	19 (0.20)
	DVT	< 5	< 5	29 (3.01)	13 (5.41)	< 5	< 5	18 (0.21)	14 (0.15)	
	PE	< 5	6 (0.04)	24 (2.49)	< 5	< 5	< 5	15 (0.17)	6 (0.06)	
	ATE	< 5	< 5	66 (6.84)	7 (2.91)	< 5	< 5	42 (0.48)	58 (0.61)	
	IS	< 5	< 5	30 (3.11)	< 5	< 5	< 5	19 (0.22)	22 (0.23)	
	TIA	< 5	< 5	17 (1.76)	< 5	< 5	< 5	10 (0.12)	7 (0.07)	
	MI	< 5	< 5	24 (2.49)	< 5	< 5	< 5	14 (0.16)	32 (0.34)	
	HF	5 (0.03)	< 5	262 (27.17)	31 (12.89)	< 5	< 5	54 (0.62)	36 (0.38)	
	HS	< 5	< 5	7 (0.73)	< 5	< 5	< 5	< 5	< 5	
MP	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5		
Cohort 4			N = 2,027,763	N = 2,085,598	N = 147,545	N = 22,245	N = 469,876	N = 550,437	N = 1,061,634	N = 880,950
0 to 30 days	VTE	334 (1.65)	50 (0.24)	116 (7.86)	< 5	36 (0.77)	11 (0.20)	350 (3.30)	98 (1.11)	
	DVT	55 (0.27)	17 (0.08)	22 (1.49)	< 5	6 (0.13)	< 5	106 (1.00)	48 (0.54)	
	PE	291 (1.44)	34 (0.16)	97 (6.57)	< 5	31 (0.66)	8 (0.15)	272 (2.56)	55 (0.62)	
	ATE	26 (0.13)	8 (0.04)	116 (7.86)	10 (4.50)	< 5	< 5	231 (2.18)	95 (1.08)	
	IS	< 5	< 5	69 (4.68)	< 5	< 5	< 5	115 (1.08)	47 (0.53)	
	TIA	6 (0.03)	< 5	18 (1.22)	< 5	< 5	< 5	26 (0.24)	12 (0.14)	
	MI	16 (0.08)	< 5	38 (2.58)	< 5	< 5	< 5	96 (0.90)	39 (0.44)	
	HF	28 (0.14)	< 5	364 (24.67)	17 (7.64)	< 5	< 5	362 (3.41)	75 (0.85)	
	HS	< 5	< 5	5 (0.34)	< 5	< 5	< 5	23 (0.22)	13 (0.15)	

Cohort	Time window	Outcome	AURUM		CORIVA		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
31 to 90 days	MP	12 (0.06)	8 (0.04)	7 (0.47)	< 5	< 5	< 5	26 (0.24)	17 (0.19)	
	VTE	55 (0.27)	22 (0.11)	49 (3.32)	< 5	5 (0.11)	< 5	86 (0.81)	48 (0.54)	
	DVT	20 (0.10)	12 (0.06)	29 (1.97)	< 5	< 5	< 5	57 (0.54)	32 (0.36)	
	PE	38 (0.19)	10 (0.05)	23 (1.56)	< 5	< 5	< 5	38 (0.36)	17 (0.19)	
	ATE	12 (0.06)	9 (0.04)	43 (2.91)	5 (2.25)	< 5	< 5	117 (1.10)	75 (0.85)	
	IS	< 5	< 5	22 (1.49)	< 5	< 5	< 5	52 (0.49)	30 (0.34)	
	TIA	< 5	< 5	6 (0.41)	< 5	< 5	< 5	33 (0.31)	23 (0.26)	
	MI	9 (0.04)	7 (0.03)	17 (1.15)	< 5	< 5	< 5	40 (0.38)	25 (0.28)	
	HF	14 (0.07)	9 (0.04)	162 (10.98)	13 (5.84)	< 5	< 5	135 (1.27)	47 (0.53)	
	HS	< 5	< 5	< 5	< 5	< 5	< 5	8 (0.08)	5 (0.06)	
91 to 180 days	MP	7 (0.03)	< 5	< 5	< 5	< 5	< 5	10 (0.09)	11 (0.12)	
	VTE	25 (0.12)	9 (0.04)	40 (2.71)	< 5	< 5	< 5	65 (0.61)	52 (0.59)	
	DVT	9 (0.04)	7 (0.03)	25 (1.69)	< 5	< 5	< 5	39 (0.37)	33 (0.37)	
	PE	17 (0.08)	< 5	16 (1.08)	< 5	< 5	< 5	29 (0.27)	22 (0.25)	
	ATE	< 5	6 (0.03)	38 (2.58)	6 (2.70)	< 5	< 5	116 (1.09)	86 (0.98)	
	IS	< 5	< 5	18 (1.22)	< 5	< 5	< 5	57 (0.54)	42 (0.48)	
	TIA	< 5	< 5	12 (0.81)	< 5	< 5	< 5	26 (0.24)	17 (0.19)	
	MI	< 5	< 5	12 (0.81)	< 5	< 5	< 5	35 (0.33)	27 (0.31)	
	HF	10 (0.05)	< 5	187 (12.67)	18 (8.09)	< 5	< 5	127 (1.20)	54 (0.61)	
	HS	< 5	< 5	< 5	< 5	< 5	< 5	13 (0.12)	6 (0.07)	
181 to 365 days	MP	< 5	< 5	< 5	< 5	< 5	< 5	11 (0.10)	6 (0.07)	
	VTE	< 5	< 5	53 (3.59)	< 5	< 5	< 5	42 (0.40)	8 (0.09)	
	DVT	< 5	< 5	33 (2.24)	< 5	< 5	< 5	30 (0.28)	6 (0.07)	
	PE	< 5	< 5	23 (1.56)	< 5	< 5	< 5	13 (0.12)	< 5	
	ATE	< 5	< 5	64 (4.34)	9 (4.05)	< 5	< 5	42 (0.40)	16 (0.18)	
	IS	< 5	< 5	29 (1.97)	5 (2.25)	< 5	< 5	20 (0.19)	11 (0.12)	
	TIA	< 5	< 5	19 (1.29)	< 5	< 5	< 5	10 (0.09)	< 5	
	MI	< 5	< 5	21 (1.42)	< 5	< 5	< 5	13 (0.12)	5 (0.06)	
	HF	< 5	< 5	243 (16.47)	12 (5.39)	< 5	< 5	47 (0.44)	11 (0.12)	
	HS	< 5	< 5	8 (0.54)	< 5	< 5	< 5	< 5	< 5	
MP	< 5	< 5	< 5	< 5	< 5	< 5	7 (0.07)	< 5		

VTE = Venous thromboembolism (DVT + PE), DVT = Deep vein thrombosis, PE = Pulmonary embolism, ATE = Arterial thrombosis/thromboembolism (IS + TIA + MI), IS = Ischemic stroke, TIA = Transient ischemic attack, MI = Myocardial infarction, HF = Heart failure, HS = Hemorrhagic stroke, MP = Myocarditis or Pericarditis

Table S28: Number of records (and risk per 10,000 individuals) for post COVID-19 cardiac and thromboembolic complications, across cohorts and databases, stratified by exposure status (ChAdOx1 vaccine).

Cohort	Time window	Outcome	AURUM		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
Cohort 1			N = 344,687	N = 219,804	N = 168,972	N = 82,406		
	0 to 30 days	VTE	77 (2.23)	41 (1.87)	7 (0.41)	< 5		
		DVT	16 (0.46)	12 (0.55)	< 5	< 5		
		PE	64 (1.86)	31 (1.41)	6 (0.36)	< 5		
		ATE	18 (0.52)	25 (1.14)	7 (0.41)	6 (0.73)		
		IS	6 (0.17)	< 5	< 5	< 5		
		TIA	< 5	7 (0.32)	< 5	< 5		
		MI	9 (0.26)	17 (0.77)	5 (0.30)	< 5		
		HF	42 (1.22)	72 (3.28)	9 (0.53)	5 (0.61)		
		HS	< 5	< 5	< 5	< 5		
		MP	< 5	< 5	< 5	< 5		
	31 to 90 days	VTE	12 (0.35)	14 (0.64)	< 5	< 5		
		DVT	5 (0.15)	8 (0.36)	< 5	< 5		
		PE	7 (0.20)	7 (0.32)	< 5	< 5		
		ATE	6 (0.17)	20 (0.91)	< 5	< 5		
		IS	< 5	< 5	< 5	< 5		
		TIA	< 5	9 (0.41)	< 5	< 5		
		MI	5 (0.15)	9 (0.41)	< 5	< 5		
		HF	26 (0.75)	42 (1.91)	< 5	5 (0.61)		
		HS	< 5	< 5	< 5	< 5		
		MP	< 5	< 5	< 5	< 5		
	91 to 180 days	VTE	6 (0.17)	15 (0.68)	< 5	< 5		
		DVT	< 5	5 (0.23)	< 5	< 5		
		PE	< 5	10 (0.45)	< 5	< 5		
		ATE	10 (0.29)	10 (0.45)	< 5	6 (0.73)		
		IS	< 5	< 5	< 5	< 5		
		TIA	5 (0.15)	6 (0.27)	< 5	< 5		
		MI	< 5	< 5	< 5	5 (0.61)		
		HF	31 (0.90)	38 (1.73)	< 5	< 5		
		HS	< 5	< 5	< 5	< 5		
		MP	< 5	< 5	< 5	< 5		

Cohort	Time window	Outcome	AURUM		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
	181 to 365 days	VTE	5 (0.15)	< 5	< 5	< 5		
		DVT	< 5	< 5	< 5	< 5		
		PE	< 5	< 5	< 5	< 5		
		ATE	9 (0.26)	9 (0.41)	< 5	< 5		
		IS	< 5	< 5	< 5	< 5		
		TIA	< 5	< 5	< 5	< 5		
		MI	< 5	< 5	< 5	< 5		
		HF	35 (1.02)	20 (0.91)	< 5	5 (0.61)		
		HS	< 5	< 5	< 5	< 5		
		MP	< 5	< 5	< 5	< 5		
Cohort 2			N = 1,975,770	N = 969,262	N = 582,791	N = 302,999	N = 433,636	N = 323,204
	0 to 30 days	VTE	243 (1.23)	158 (1.63)	33 (0.57)	19 (0.63)	262 (6.04)	90 (2.78)
		DVT	42 (0.21)	47 (0.48)	8 (0.14)	< 5	65 (1.50)	45 (1.39)
		PE	206 (1.04)	120 (1.24)	26 (0.45)	15 (0.50)	218 (5.03)	55 (1.70)
		ATE	38 (0.19)	75 (0.77)	< 5	< 5	177 (4.08)	131 (4.05)
		IS	6 (0.03)	12 (0.12)	< 5	< 5	97 (2.24)	52 (1.61)
		TIA	7 (0.04)	13 (0.13)	< 5	< 5	17 (0.39)	23 (0.71)
		MI	25 (0.13)	52 (0.54)	< 5	< 5	67 (1.55)	62 (1.92)
		HF	46 (0.23)	103 (1.06)	5 (0.09)	11 (0.36)	379 (8.74)	123 (3.81)
		HS	5 (0.03)	< 5	< 5	< 5	21 (0.48)	7 (0.22)
		MP	11 (0.06)	6 (0.06)	< 5	< 5	15 (0.35)	10 (0.31)
	31 to 90 days	VTE	49 (0.25)	55 (0.57)	< 5	9 (0.30)	60 (1.38)	36 (1.11)
		DVT	25 (0.13)	25 (0.26)	< 5	5 (0.17)	32 (0.74)	25 (0.77)
		PE	27 (0.14)	32 (0.33)	< 5	< 5	34 (0.78)	18 (0.56)
		ATE	16 (0.08)	57 (0.59)	< 5	5 (0.17)	86 (1.98)	107 (3.31)
		IS	< 5	6 (0.06)	< 5	< 5	42 (0.97)	58 (1.79)
		TIA	< 5	25 (0.26)	< 5	< 5	23 (0.53)	24 (0.74)
		MI	11 (0.06)	28 (0.29)	< 5	< 5	28 (0.65)	27 (0.84)
		HF	24 (0.12)	68 (0.70)	< 5	7 (0.23)	140 (3.23)	62 (1.92)
		HS	< 5	< 5	< 5	< 5	7 (0.16)	7 (0.22)
		MP	6 (0.03)	< 5	< 5	< 5	< 5	< 5
	91 to 180 days	VTE	25 (0.13)	30 (0.31)	< 5	< 5	58 (1.34)	23 (0.71)
		DVT	11 (0.06)	16 (0.17)	< 5	< 5	31 (0.71)	16 (0.50)
		PE	14 (0.07)	16 (0.17)	< 5	< 5	29 (0.67)	8 (0.25)

Cohort	Time window	Outcome	AURUM		GOLD		SIDIAP		
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	
		ATE	12 (0.06)	28 (0.29)	< 5	< 5	94 (2.17)	106 (3.28)	
		IS	< 5	< 5	< 5	< 5	51 (1.18)	40 (1.24)	
		TIA	7 (0.04)	13 (0.13)	< 5	< 5	21 (0.48)	32 (0.99)	
		MI	6 (0.03)	15 (0.15)	< 5	< 5	25 (0.58)	37 (1.14)	
		HF	16 (0.08)	44 (0.45)	< 5	< 5	115 (2.65)	60 (1.86)	
		HS	< 5	< 5	< 5	< 5	8 (0.18)	< 5	
		MP	< 5	< 5	< 5	< 5	8 (0.18)	< 5	
	181 to 365 days	VTE	14 (0.07)	5 (0.05)	< 5	< 5	18 (0.42)	16 (0.50)	
		DVT	< 5	< 5	< 5	< 5	10 (0.23)	13 (0.40)	
		PE	10 (0.05)	< 5	< 5	< 5	9 (0.21)	< 5	
		ATE	11 (0.06)	11 (0.11)	< 5	< 5	71 (1.64)	46 (1.42)	
		IS	< 5	< 5	< 5	< 5	38 (0.88)	21 (0.65)	
		TIA	< 5	< 5	< 5	< 5	20 (0.46)	13 (0.40)	
		MI	8 (0.04)	7 (0.07)	< 5	< 5	15 (0.35)	16 (0.50)	
		HF	18 (0.09)	23 (0.24)	< 5	< 5	81 (1.87)	26 (0.80)	
		HS	< 5	< 5	< 5	< 5	5 (0.12)	< 5	
		MP	< 5	< 5	< 5	< 5	< 5	< 5	
		Cohort 3		N = 1,510,493	N = 1,473,602	N = 418,184	N = 423,876	N = 873,400	N = 84,204
		0 to 30 days	VTE	244 (1.62)	139 (0.94)	28 (0.67)	16 (0.38)	332 (3.80)	27 (3.21)
			DVT	44 (0.29)	41 (0.28)	6 (0.14)	< 5	95 (1.09)	9 (1.07)
PE	209 (1.38)		101 (0.69)	23 (0.55)	12 (0.28)	266 (3.05)	22 (2.61)		
ATE	28 (0.19)		47 (0.32)	< 5	12 (0.28)	216 (2.47)	32 (3.80)		
IS	< 5		5 (0.03)	< 5	< 5	103 (1.18)	13 (1.54)		
TIA	5 (0.03)		16 (0.11)	< 5	< 5	22 (0.25)	5 (0.59)		
MI	19 (0.13)		26 (0.18)	< 5	9 (0.21)	97 (1.11)	16 (1.90)		
HF	30 (0.20)		28 (0.19)	< 5	< 5	372 (4.26)	51 (6.06)		
HS	< 5		< 5	< 5	< 5	20 (0.23)	< 5		
MP	9 (0.06)		6 (0.04)	< 5	< 5	20 (0.23)	6 (0.71)		
31 to 90 days	VTE		46 (0.30)	44 (0.30)	< 5	7 (0.17)	85 (0.97)	9 (1.07)	
	DVT		21 (0.14)	26 (0.18)	< 5	< 5	57 (0.65)	< 5	
	PE		28 (0.19)	18 (0.12)	< 5	< 5	38 (0.44)	6 (0.71)	
	ATE	11 (0.07)	31 (0.21)	< 5	7 (0.17)	109 (1.25)	25 (2.97)		
	IS	< 5	< 5	< 5	< 5	52 (0.60)	11 (1.31)		
		TIA	< 5	13 (0.09)	< 5	< 5	27 (0.31)	< 5	

Cohort	Time window	Outcome	AURUM		GOLD		SIDIAP		
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	
Cohort 4	91 to 180 days	MI	9 (0.06)	16 (0.11)	< 5	< 5	38 (0.44)	10 (1.19)	
		HF	14 (0.09)	23 (0.16)	< 5	< 5	142 (1.63)	25 (2.97)	
		HS	< 5	< 5	< 5	< 5	7 (0.08)	< 5	
		MP	8 (0.05)	7 (0.05)	< 5	< 5	9 (0.10)	< 5	
		VTE	24 (0.16)	26 (0.18)	< 5	< 5	65 (0.74)	14 (1.66)	
		DVT	11 (0.07)	15 (0.10)	< 5	< 5	36 (0.41)	7 (0.83)	
		PE	14 (0.09)	14 (0.10)	< 5	< 5	33 (0.38)	8 (0.95)	
		ATE	< 5	26 (0.18)	< 5	< 5	115 (1.32)	30 (3.56)	
		IS	< 5	< 5	< 5	< 5	58 (0.66)	14 (1.66)	
		TIA	< 5	8 (0.05)	< 5	< 5	22 (0.25)	10 (1.19)	
		MI	< 5	17 (0.12)	< 5	< 5	38 (0.44)	8 (0.95)	
		HF	10 (0.07)	12 (0.08)	< 5	< 5	122 (1.40)	12 (1.43)	
		HS	< 5	< 5	< 5	< 5	9 (0.10)	< 5	
		MP	< 5	< 5	< 5	< 5	8 (0.09)	< 5	
	181 to 365 days	VTE	< 5	11 (0.07)	< 5	< 5	35 (0.40)	7 (0.83)	
	DVT	< 5	5 (0.03)	< 5	< 5	21 (0.24)	< 5		
	PE	< 5	7 (0.05)	< 5	< 5	16 (0.18)	5 (0.59)		
	ATE	< 5	< 5	< 5	< 5	57 (0.65)	15 (1.78)		
	IS	< 5	< 5	< 5	< 5	26 (0.30)	6 (0.71)		
	TIA	< 5	< 5	< 5	< 5	12 (0.14)	< 5		
	MI	< 5	< 5	< 5	< 5	20 (0.23)	8 (0.95)		
	HF	< 5	< 5	< 5	< 5	64 (0.73)	6 (0.71)		
	HS	< 5	< 5	< 5	< 5	< 5	< 5		
	MP	< 5	< 5	< 5	< 5	< 5	< 5		
	Cohort 4			N = 2,066,318	N = 542,670	N = 485,154	N = 147,744		
	Cohort 4	0 to 30 days	VTE	346 (1.67)	27 (0.50)	38 (0.78)	8 (0.54)		
DVT			56 (0.27)	7 (0.13)	6 (0.12)	< 5			
PE			302 (1.46)	21 (0.39)	33 (0.68)	6 (0.41)			
ATE			26 (0.13)	5 (0.09)	< 5	< 5			
IS			< 5	< 5	< 5	< 5			
TIA			5 (0.02)	< 5	< 5	< 5			
MI			17 (0.08)	< 5	< 5	< 5			
HF			28 (0.14)	< 5	< 5	< 5			
HS			< 5	< 5	< 5	< 5			

Cohort	Time window	Outcome	AURUM		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
		MP	14 (0.07)	< 5	< 5	< 5		
	31 to 90 days	VTE	60 (0.29)	14 (0.26)	< 5	< 5		
		DVT	23 (0.11)	8 (0.15)	< 5	< 5		
		PE	40 (0.19)	6 (0.11)	< 5	< 5		
		ATE	13 (0.06)	< 5	< 5	< 5		
		IS	< 5	< 5	< 5	< 5		
		TIA	< 5	< 5	< 5	< 5		
		MI	9 (0.04)	< 5	< 5	< 5		
		HF	14 (0.07)	< 5	< 5	< 5		
		HS	< 5	< 5	< 5	< 5		
		MP	7 (0.03)	< 5	< 5	< 5		
		91 to 180 days	VTE	29 (0.14)	< 5	< 5	< 5	
	DVT		10 (0.05)	< 5	< 5	< 5		
	PE		20 (0.10)	< 5	< 5	< 5		
	ATE		< 5	< 5	< 5	< 5		
	IS		< 5	< 5	< 5	< 5		
	TIA		< 5	< 5	< 5	< 5		
	MI		< 5	< 5	< 5	< 5		
	HF		10 (0.05)	< 5	< 5	< 5		
	HS		< 5	< 5	< 5	< 5		
	MP		< 5	< 5	< 5	< 5		
	181 to 365 days		VTE	< 5	< 5	< 5	< 5	
		DVT	< 5	< 5	< 5	< 5		
		PE	< 5	< 5	< 5	< 5		
		ATE	< 5	< 5	< 5	< 5		
		IS	< 5	< 5	< 5	< 5		
		TIA	< 5	< 5	< 5	< 5		
		MI	< 5	< 5	< 5	< 5		
		HF	< 5	< 5	< 5	< 5		
		HS	< 5	< 5	< 5	< 5		
	MP	< 5	< 5	< 5	< 5			

VTE = Venous thromboembolism (DVT + PE), DVT = Deep vein thrombosis, PE = Pulmonary embolism, ATE = Arterial thrombosis/thromboembolism (IS + TIA + MI), IS = Ischemic stroke, TIA = Transient ischemic attack, MI = Myocardial infarction, HF = Heart failure, HS = Hemorrhagic stroke, MP = Myocarditis or Pericarditis

Table S29: Number of records (and risk per 10,000 individuals) for post COVID-19 cardiac and thromboembolic complications, across cohorts and databases, stratified by exposure status (ChAdOx1 vaccine). Follow-up ends at first vaccine dose after index date.

Cohort	Time window	Outcome	AURUM		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
Cohort 1			N = 344,687	N = 219,804	N = 168,972	N = 82,406		
	0 to 30 days	VTE	77 (2.23)	14 (0.64)	7 (0.41)	< 5		
		DVT	16 (0.46)	< 5	< 5	< 5		
		PE	64 (1.86)	13 (0.59)	6 (0.36)	< 5		
		ATE	18 (0.52)	10 (0.45)	7 (0.41)	< 5		
		IS	6 (0.17)	< 5	< 5	< 5		
		TIA	< 5	< 5	< 5	< 5		
		MI	9 (0.26)	6 (0.27)	5 (0.30)	< 5		
		HF	42 (1.22)	28 (1.27)	9 (0.53)	< 5		
		HS	< 5	< 5	< 5	< 5		
		MP	< 5	< 5	< 5	< 5		
		31 to 90 days	VTE	12 (0.35)	5 (0.23)	< 5	< 5	
	DVT		5 (0.15)	< 5	< 5	< 5		
	PE		7 (0.20)	< 5	< 5	< 5		
	ATE		6 (0.17)	8 (0.36)	< 5	< 5		
	IS		< 5	< 5	< 5	< 5		
	TIA		< 5	< 5	< 5	< 5		
	MI		5 (0.15)	< 5	< 5	< 5		
	HF		26 (0.75)	20 (0.91)	< 5	< 5		
	HS		< 5	< 5	< 5	< 5		
	MP		< 5	< 5	< 5	< 5		
	91 to 180 days		VTE	6 (0.17)	5 (0.23)	< 5	< 5	
		DVT	< 5	< 5	< 5	< 5		
		PE	< 5	< 5	< 5	< 5		
		ATE	10 (0.29)	< 5	< 5	< 5		
		IS	< 5	< 5	< 5	< 5		
		TIA	5 (0.15)	< 5	< 5	< 5		
		MI	< 5	< 5	< 5	< 5		
		HF	31 (0.90)	19 (0.86)	< 5	< 5		
		HS	< 5	< 5	< 5	< 5		
		MP	< 5	< 5	< 5	< 5		

Cohort	Time window	Outcome	AURUM		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
	181 to 365 days	VTE	5 (0.15)	< 5	< 5	< 5		
		DVT	< 5	< 5	< 5	< 5		
		PE	< 5	< 5	< 5	< 5		
		ATE	9 (0.26)	8 (0.36)	< 5	< 5		
		IS	< 5	< 5	< 5	< 5		
		TIA	< 5	< 5	< 5	< 5		
		MI	< 5	< 5	< 5	< 5		
		HF	35 (1.02)	18 (0.82)	< 5	5 (0.61)		
		HS	< 5	< 5	< 5	< 5		
		MP	< 5	< 5	< 5	< 5		
Cohort 2			N = 1,975,770	N = 969,262	N = 582,791	N = 302,999	N = 433,636	N = 323,204
	0 to 30 days	VTE	243 (1.23)	40 (0.41)	33 (0.57)	< 5	262 (6.04)	9 (0.28)
		DVT	42 (0.21)	13 (0.13)	8 (0.14)	< 5	65 (1.50)	5 (0.15)
		PE	206 (1.04)	30 (0.31)	26 (0.45)	< 5	218 (5.03)	6 (0.19)
		ATE	38 (0.19)	11 (0.11)	< 5	< 5	177 (4.08)	6 (0.19)
		IS	6 (0.03)	< 5	< 5	< 5	97 (2.24)	< 5
		TIA	7 (0.04)	< 5	< 5	< 5	17 (0.39)	< 5
		MI	25 (0.13)	9 (0.09)	< 5	< 5	67 (1.55)	< 5
		HF	46 (0.23)	32 (0.33)	5 (0.09)	< 5	379 (8.74)	12 (0.37)
		HS	5 (0.03)	< 5	< 5	< 5	21 (0.48)	< 5
		MP	11 (0.06)	< 5	< 5	< 5	15 (0.35)	< 5
	31 to 90 days	VTE	49 (0.25)	8 (0.08)	< 5	< 5	60 (1.38)	< 5
		DVT	25 (0.13)	5 (0.05)	< 5	< 5	32 (0.74)	< 5
		PE	27 (0.14)	< 5	< 5	< 5	34 (0.78)	< 5
		ATE	16 (0.08)	9 (0.09)	< 5	< 5	86 (1.98)	6 (0.19)
		IS	< 5	< 5	< 5	< 5	42 (0.97)	< 5
		TIA	< 5	< 5	< 5	< 5	23 (0.53)	< 5
		MI	11 (0.06)	6 (0.06)	< 5	< 5	28 (0.65)	< 5
		HF	24 (0.12)	13 (0.13)	< 5	< 5	140 (3.23)	7 (0.22)
		HS	< 5	< 5	< 5	< 5	7 (0.16)	< 5
		MP	6 (0.03)	< 5	< 5	< 5	< 5	< 5
	91 to 180 days	VTE	25 (0.13)	12 (0.12)	< 5	< 5	58 (1.34)	< 5
		DVT	11 (0.06)	7 (0.07)	< 5	< 5	31 (0.71)	< 5
		PE	14 (0.07)	5 (0.05)	< 5	< 5	29 (0.67)	< 5

Cohort	Time window	Outcome	AURUM		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
		ATE	12 (0.06)	10 (0.10)	< 5	< 5	94 (2.17)	6 (0.19)
		IS	< 5	< 5	< 5	< 5	51 (1.18)	< 5
		TIA	7 (0.04)	< 5	< 5	< 5	21 (0.48)	< 5
		MI	6 (0.03)	6 (0.06)	< 5	< 5	25 (0.58)	< 5
		HF	16 (0.08)	18 (0.19)	< 5	< 5	115 (2.65)	< 5
		HS	< 5	< 5	< 5	< 5	8 (0.18)	< 5
		MP	< 5	< 5	< 5	< 5	8 (0.18)	< 5
	181 to 365 days	VTE	14 (0.07)	5 (0.05)	< 5	< 5	18 (0.42)	9 (0.28)
		DVT	< 5	< 5	< 5	< 5	10 (0.23)	7 (0.22)
		PE	10 (0.05)	< 5	< 5	< 5	9 (0.21)	< 5
		ATE	11 (0.06)	10 (0.10)	< 5	< 5	71 (1.64)	10 (0.31)
		IS	< 5	< 5	< 5	< 5	38 (0.88)	< 5
		TIA	< 5	< 5	< 5	< 5	20 (0.46)	< 5
		MI	8 (0.04)	6 (0.06)	< 5	< 5	15 (0.35)	5 (0.15)
		HF	18 (0.09)	20 (0.21)	< 5	< 5	81 (1.87)	9 (0.28)
		HS	< 5	< 5	< 5	< 5	5 (0.12)	< 5
		MP	< 5	< 5	< 5	< 5	< 5	< 5
Cohort 3			N = 1,510,493	N = 1,473,602	N = 418,184	N = 423,876	N = 873,400	N = 84,204
	0 to 30 days	VTE	244 (1.62)	23 (0.16)	28 (0.67)	< 5	332 (3.80)	5 (0.59)
		DVT	44 (0.29)	< 5	6 (0.14)	< 5	95 (1.09)	< 5
		PE	209 (1.38)	19 (0.13)	23 (0.55)	< 5	266 (3.05)	< 5
		ATE	28 (0.19)	8 (0.05)	< 5	< 5	216 (2.47)	< 5
		IS	< 5	< 5	< 5	< 5	103 (1.18)	< 5
		TIA	5 (0.03)	< 5	< 5	< 5	22 (0.25)	< 5
		MI	19 (0.13)	7 (0.05)	< 5	< 5	97 (1.11)	< 5
		HF	30 (0.20)	11 (0.07)	< 5	< 5	372 (4.26)	5 (0.59)
		HS	< 5	< 5	< 5	< 5	20 (0.23)	< 5
		MP	9 (0.06)	< 5	< 5	< 5	20 (0.23)	< 5
	31 to 90 days	VTE	46 (0.30)	< 5	< 5	< 5	85 (0.97)	< 5
		DVT	21 (0.14)	< 5	< 5	< 5	57 (0.65)	< 5
		PE	28 (0.19)	< 5	< 5	< 5	38 (0.44)	< 5
		ATE	11 (0.07)	6 (0.04)	< 5	< 5	109 (1.25)	< 5
		IS	< 5	< 5	< 5	< 5	52 (0.60)	< 5
		TIA	< 5	< 5	< 5	27 (0.31)	< 5	

Cohort	Time window	Outcome	AURUM		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
	91 to 180 days	MI	9 (0.06)	< 5	< 5	< 5	38 (0.44)	< 5
		HF	14 (0.09)	5 (0.03)	< 5	< 5	142 (1.63)	< 5
		HS	< 5	< 5	< 5	< 5	7 (0.08)	< 5
		MP	8 (0.05)	< 5	< 5	< 5	9 (0.10)	< 5
		VTE	24 (0.16)	8 (0.05)	< 5	< 5	65 (0.74)	< 5
		DVT	11 (0.07)	6 (0.04)	< 5	< 5	36 (0.41)	< 5
		PE	14 (0.09)	< 5	< 5	< 5	33 (0.38)	< 5
		ATE	< 5	7 (0.05)	< 5	< 5	115 (1.32)	6 (0.71)
		IS	< 5	< 5	< 5	< 5	58 (0.66)	5 (0.59)
		TIA	< 5	< 5	< 5	< 5	22 (0.25)	< 5
		MI	< 5	< 5	< 5	< 5	38 (0.44)	< 5
		HF	10 (0.07)	< 5	< 5	< 5	122 (1.40)	< 5
	HS	< 5	< 5	< 5	< 5	9 (0.10)	< 5	
	MP	< 5	< 5	< 5	< 5	8 (0.09)	< 5	
	181 to 365 days	VTE	< 5	9 (0.06)	< 5	< 5	35 (0.40)	< 5
		DVT	< 5	< 5	< 5	< 5	21 (0.24)	< 5
		PE	< 5	6 (0.04)	< 5	< 5	16 (0.18)	< 5
		ATE	< 5	< 5	< 5	< 5	57 (0.65)	8 (0.95)
		IS	< 5	< 5	< 5	< 5	26 (0.30)	< 5
		TIA	< 5	< 5	< 5	< 5	12 (0.14)	< 5
		MI	< 5	< 5	< 5	< 5	20 (0.23)	< 5
		HF	< 5	< 5	< 5	< 5	64 (0.73)	5 (0.59)
		HS	< 5	< 5	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5	< 5	< 5
Cohort 4			N = 2,066,318	N = 542,670	N = 485,154	N = 147,744		
0 to 30 days		VTE	346 (1.67)	8 (0.15)	38 (0.78)	6 (0.41)		
	DVT	56 (0.27)	< 5	6 (0.12)	< 5			
	PE	302 (1.46)	7 (0.13)	33 (0.68)	6 (0.41)			
	ATE	26 (0.13)	< 5	< 5	< 5			
	IS	< 5	< 5	< 5	< 5			
	TIA	5 (0.02)	< 5	< 5	< 5			
	MI	17 (0.08)	< 5	< 5	< 5			
	HF	28 (0.14)	< 5	< 5	< 5			
	HS	< 5	< 5	< 5	< 5			

Cohort	Time window	Outcome	AURUM		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
		MP	14 (0.07)	< 5	< 5	< 5		
	31 to 90 days	VTE	60 (0.29)	8 (0.15)	< 5	< 5		
		DVT	23 (0.11)	< 5	< 5	< 5		
		PE	40 (0.19)	5 (0.09)	< 5	< 5		
		ATE	13 (0.06)	< 5	< 5	< 5		
		IS	< 5	< 5	< 5	< 5		
		TIA	< 5	< 5	< 5	< 5		
		MI	9 (0.04)	< 5	< 5	< 5		
		HF	14 (0.07)	< 5	< 5	< 5		
		HS	< 5	< 5	< 5	< 5		
		MP	7 (0.03)	< 5	< 5	< 5		
		91 to 180 days	VTE	29 (0.14)	< 5	< 5	< 5	
	DVT		10 (0.05)	< 5	< 5	< 5		
	PE		20 (0.10)	< 5	< 5	< 5		
	ATE		< 5	< 5	< 5	< 5		
	IS		< 5	< 5	< 5	< 5		
	TIA		< 5	< 5	< 5	< 5		
	MI		< 5	< 5	< 5	< 5		
	HF		10 (0.05)	< 5	< 5	< 5		
	HS		< 5	< 5	< 5	< 5		
	MP		< 5	< 5	< 5	< 5		
	181 to 365 days		VTE	< 5	< 5	< 5	< 5	
		DVT	< 5	< 5	< 5	< 5		
		PE	< 5	< 5	< 5	< 5		
		ATE	< 5	< 5	< 5	< 5		
		IS	< 5	< 5	< 5	< 5		
		TIA	< 5	< 5	< 5	< 5		
		MI	< 5	< 5	< 5	< 5		
		HF	< 5	< 5	< 5	< 5		
		HS	< 5	< 5	< 5	< 5		
	MP	< 5	< 5	< 5	< 5			

VTE = Venous thromboembolism (DVT + PE), DVT = Deep vein thrombosis, PE = Pulmonary embolism, ATE = Arterial thrombosis/thromboembolism (IS + TIA + MI), IS = Ischemic stroke, TIA = Transient ischemic attack, MI = Myocardial infarction, HF = Heart failure, HS = Hemorrhagic stroke, MP = Myocarditis or Pericarditis

Table S30: Number of records (and risk per 10,000 individuals) for post COVID-19 cardiac and thromboembolic complications, across cohorts and databases, stratified by exposure status (ChAdOx1 vaccine). Only first outcome after COVID-19 captured.

Cohort	Time window	Outcome	AURUM		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
Cohort 1			N = 344,687	N = 219,804	N = 168,972	N = 82,406		
	0 to 30 days	VTE	77 (2.23)	41 (1.87)	7 (0.41)	< 5		
		DVT	16 (0.46)	12 (0.55)	< 5	< 5		
		PE	64 (1.86)	31 (1.41)	6 (0.36)	< 5		
		ATE	18 (0.52)	25 (1.14)	7 (0.41)	6 (0.73)		
		IS	6 (0.17)	< 5	< 5	< 5		
		TIA	< 5	7 (0.32)	< 5	< 5		
		MI	9 (0.26)	17 (0.77)	5 (0.30)	< 5		
		HF	42 (1.22)	72 (3.28)	9 (0.53)	5 (0.61)		
		HS	< 5	< 5	< 5	< 5		
		MP	< 5	< 5	< 5	< 5		
	31 to 90 days	VTE	12 (0.35)	14 (0.64)	< 5	< 5		
		DVT	5 (0.15)	8 (0.36)	< 5	< 5		
		PE	7 (0.20)	7 (0.32)	< 5	< 5		
		ATE	6 (0.17)	20 (0.91)	< 5	< 5		
		IS	< 5	< 5	< 5	< 5		
		TIA	< 5	9 (0.41)	< 5	< 5		
		MI	5 (0.15)	9 (0.41)	< 5	< 5		
		HF	26 (0.75)	39 (1.77)	< 5	5 (0.61)		
		HS	< 5	< 5	< 5	< 5		
		MP	< 5	< 5	< 5	< 5		
	91 to 180 days	VTE	6 (0.17)	15 (0.68)	< 5	< 5		
		DVT	< 5	5 (0.23)	< 5	< 5		
		PE	< 5	10 (0.45)	< 5	< 5		
		ATE	10 (0.29)	10 (0.45)	< 5	6 (0.73)		
		IS	< 5	< 5	< 5	< 5		
		TIA	5 (0.15)	6 (0.27)	< 5	< 5		
		MI	< 5	< 5	< 5	5 (0.61)		
		HF	28 (0.81)	35 (1.59)	< 5	< 5		
		HS	< 5	< 5	< 5	< 5		
		MP	< 5	< 5	< 5	< 5		

Cohort	Time window	Outcome	AURUM		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
	181 to 365 days	VTE	< 5	< 5	< 5	< 5		
		DVT	< 5	< 5	< 5	< 5		
		PE	< 5	< 5	< 5	< 5		
		ATE	9 (0.26)	9 (0.41)	< 5	< 5		
		IS	< 5	< 5	< 5	< 5		
		TIA	< 5	< 5	< 5	< 5		
		MI	< 5	< 5	< 5	< 5		
		HF	32 (0.93)	18 (0.82)	< 5	5 (0.61)		
		HS	< 5	< 5	< 5	< 5		
		MP	< 5	< 5	< 5	< 5		
Cohort 2			N = 1,975,770	N = 969,262	N = 582,791	N = 302,999	N = 433,636	N = 323,204
	0 to 30 days	VTE	243 (1.23)	158 (1.63)	33 (0.57)	19 (0.63)	262 (6.04)	90 (2.78)
		DVT	42 (0.21)	47 (0.48)	8 (0.14)	< 5	65 (1.50)	45 (1.39)
		PE	206 (1.04)	120 (1.24)	26 (0.45)	15 (0.50)	218 (5.03)	55 (1.70)
		ATE	38 (0.19)	75 (0.77)	< 5	< 5	177 (4.08)	131 (4.05)
		IS	6 (0.03)	12 (0.12)	< 5	< 5	97 (2.24)	52 (1.61)
		TIA	7 (0.04)	13 (0.13)	< 5	< 5	17 (0.39)	23 (0.71)
		MI	25 (0.13)	52 (0.54)	< 5	< 5	67 (1.55)	62 (1.92)
		HF	46 (0.23)	103 (1.06)	5 (0.09)	11 (0.36)	379 (8.74)	123 (3.81)
		HS	5 (0.03)	< 5	< 5	< 5	21 (0.48)	7 (0.22)
		MP	11 (0.06)	6 (0.06)	< 5	< 5	15 (0.35)	10 (0.31)
	31 to 90 days	VTE	46 (0.23)	54 (0.56)	< 5	9 (0.30)	57 (1.31)	34 (1.05)
		DVT	24 (0.12)	25 (0.26)	< 5	5 (0.17)	30 (0.69)	23 (0.71)
		PE	25 (0.13)	31 (0.32)	< 5	< 5	32 (0.74)	16 (0.50)
		ATE	16 (0.08)	56 (0.58)	< 5	5 (0.17)	84 (1.94)	106 (3.28)
		IS	< 5	6 (0.06)	< 5	< 5	42 (0.97)	57 (1.76)
		TIA	< 5	24 (0.25)	< 5	< 5	23 (0.53)	24 (0.74)
		MI	11 (0.06)	28 (0.29)	< 5	< 5	26 (0.60)	27 (0.84)
		HF	24 (0.12)	65 (0.67)	< 5	7 (0.23)	134 (3.09)	61 (1.89)
		HS	< 5	< 5	< 5	< 5	7 (0.16)	7 (0.22)
		MP	6 (0.03)	< 5	< 5	< 5	< 5	< 5
	91 to 180 days	VTE	22 (0.11)	28 (0.29)	< 5	< 5	52 (1.20)	21 (0.65)
		DVT	10 (0.05)	15 (0.15)	< 5	< 5	28 (0.65)	16 (0.50)
		PE	12 (0.06)	15 (0.15)	< 5	< 5	26 (0.60)	6 (0.19)

Cohort	Time window	Outcome	AURUM		GOLD		SIDIAP			
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated		
		ATE	11 (0.06)	28 (0.29)	< 5	< 5	83 (1.91)	106 (3.28)		
		IS	< 5	< 5	< 5	< 5	45 (1.04)	40 (1.24)		
		TIA	7 (0.04)	13 (0.13)	< 5	< 5	20 (0.46)	32 (0.99)		
		MI	5 (0.03)	15 (0.15)	< 5	< 5	21 (0.48)	37 (1.14)		
		HF	16 (0.08)	41 (0.42)	< 5	< 5	105 (2.42)	54 (1.67)		
		HS	< 5	< 5	< 5	< 5	7 (0.16)	< 5		
		MP	< 5	< 5	< 5	< 5	7 (0.16)	< 5		
	181 to 365 days	VTE	14 (0.07)	< 5	< 5	< 5	17 (0.39)	14 (0.43)		
		DVT	< 5	< 5	< 5	< 5	9 (0.21)	12 (0.37)		
		PE	10 (0.05)	< 5	< 5	< 5	9 (0.21)	< 5		
		ATE	10 (0.05)	10 (0.10)	< 5	< 5	61 (1.41)	40 (1.24)		
		IS	< 5	< 5	< 5	< 5	33 (0.76)	19 (0.59)		
		TIA	< 5	< 5	< 5	< 5	18 (0.42)	12 (0.37)		
		MI	7 (0.04)	6 (0.06)	< 5	< 5	12 (0.28)	13 (0.40)		
		HF	17 (0.09)	22 (0.23)	< 5	< 5	70 (1.61)	25 (0.77)		
		HS	< 5	< 5	< 5	< 5	< 5	< 5		
		MP	< 5	< 5	< 5	< 5	< 5	< 5		
		Cohort 3			N = 1,510,493	N = 1,473,602	N = 418,184	N = 423,876	N = 873,400	N = 84,204
		0 to 30 days	VTE	244 (1.62)	139 (0.94)	28 (0.67)	16 (0.38)	332 (3.80)	27 (3.21)	
			DVT	44 (0.29)	41 (0.28)	6 (0.14)	< 5	95 (1.09)	9 (1.07)	
PE	209 (1.38)		101 (0.69)	23 (0.55)	12 (0.28)	266 (3.05)	22 (2.61)			
ATE	28 (0.19)		47 (0.32)	< 5	12 (0.28)	216 (2.47)	32 (3.80)			
IS	< 5		5 (0.03)	< 5	< 5	103 (1.18)	13 (1.54)			
TIA	5 (0.03)		16 (0.11)	< 5	< 5	22 (0.25)	5 (0.59)			
MI	19 (0.13)		26 (0.18)	< 5	9 (0.21)	97 (1.11)	16 (1.90)			
HF	30 (0.20)		28 (0.19)	< 5	< 5	372 (4.26)	51 (6.06)			
HS	< 5		< 5	< 5	< 5	20 (0.23)	< 5			
MP	9 (0.06)		6 (0.04)	< 5	< 5	20 (0.23)	6 (0.71)			
31 to 90 days	VTE	43 (0.28)	44 (0.30)	< 5	6 (0.14)	81 (0.93)	9 (1.07)			
	DVT	20 (0.13)	26 (0.18)	< 5	< 5	54 (0.62)	< 5			
	PE	26 (0.17)	18 (0.12)	< 5	< 5	36 (0.41)	6 (0.71)			
	ATE	11 (0.07)	31 (0.21)	< 5	7 (0.17)	108 (1.24)	25 (2.97)			
	IS	< 5	< 5	< 5	< 5	52 (0.60)	11 (1.31)			
		TIA	< 5	13 (0.09)	< 5	< 5	27 (0.31)	< 5		

Cohort	Time window	Outcome	AURUM		GOLD		SIDIAP		
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	
Cohort 3		MI	9 (0.06)	16 (0.11)	< 5	< 5	37 (0.42)	10 (1.19)	
		HF	14 (0.09)	23 (0.16)	< 5	< 5	135 (1.55)	25 (2.97)	
		HS	< 5	< 5	< 5	< 5	7 (0.08)	< 5	
		MP	8 (0.05)	7 (0.05)	< 5	< 5	9 (0.10)	< 5	
	91 to 180 days	VTE	23 (0.15)	25 (0.17)	< 5	< 5	58 (0.66)	13 (1.54)	
		DVT	10 (0.07)	15 (0.10)	< 5	< 5	33 (0.38)	7 (0.83)	
		PE	14 (0.09)	13 (0.09)	< 5	< 5	29 (0.33)	7 (0.83)	
		ATE	< 5	26 (0.18)	< 5	< 5	104 (1.19)	28 (3.33)	
		IS	< 5	< 5	< 5	< 5	50 (0.57)	12 (1.43)	
		TIA	< 5	8 (0.05)	< 5	< 5	20 (0.23)	10 (1.19)	
		MI	< 5	17 (0.12)	< 5	< 5	36 (0.41)	8 (0.95)	
		HF	10 (0.07)	10 (0.07)	< 5	< 5	111 (1.27)	12 (1.43)	
		HS	< 5	< 5	< 5	< 5	9 (0.10)	< 5	
		MP	< 5	< 5	< 5	< 5	8 (0.09)	< 5	
		181 to 365 days	VTE	< 5	9 (0.06)	< 5	< 5	31 (0.35)	< 5
			DVT	< 5	< 5	< 5	< 5	18 (0.21)	< 5
	PE		< 5	6 (0.04)	< 5	< 5	15 (0.17)	< 5	
	ATE		< 5	< 5	< 5	< 5	48 (0.55)	15 (1.78)	
	IS		< 5	< 5	< 5	< 5	21 (0.24)	6 (0.71)	
	TIA		< 5	< 5	< 5	< 5	11 (0.13)	< 5	
	MI		< 5	< 5	< 5	< 5	17 (0.19)	8 (0.95)	
	HF		< 5	< 5	< 5	< 5	55 (0.63)	6 (0.71)	
	HS		< 5	< 5	< 5	< 5	< 5	< 5	
	MP		< 5	< 5	< 5	< 5	< 5	< 5	
	Cohort 4		N = 2,066,318	N = 542,670	N = 485,154	N = 147,744			
	0 to 30 days	VTE	346 (1.67)	27 (0.50)	38 (0.78)	8 (0.54)			
DVT		56 (0.27)	7 (0.13)	6 (0.12)	< 5				
PE		302 (1.46)	21 (0.39)	33 (0.68)	6 (0.41)				
ATE		26 (0.13)	5 (0.09)	< 5	< 5				
IS		< 5	< 5	< 5	< 5				
TIA		5 (0.02)	< 5	< 5	< 5				
MI		17 (0.08)	< 5	< 5	< 5				
HF		28 (0.14)	< 5	< 5	< 5				
HS		< 5	< 5	< 5	< 5				

Cohort	Time window	Outcome	AURUM		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
		MP	14 (0.07)	< 5	< 5	< 5		
	31 to 90 days	VTE	57 (0.28)	14 (0.26)	< 5	< 5		
		DVT	22 (0.11)	8 (0.15)	< 5	< 5		
		PE	38 (0.18)	6 (0.11)	< 5	< 5		
		ATE	13 (0.06)	< 5	< 5	< 5		
		IS	< 5	< 5	< 5	< 5		
		TIA	< 5	< 5	< 5	< 5		
		MI	9 (0.04)	< 5	< 5	< 5		
		HF	14 (0.07)	< 5	< 5	< 5		
		HS	< 5	< 5	< 5	< 5		
		MP	7 (0.03)	< 5	< 5	< 5		
		91 to 180 days	VTE	28 (0.14)	< 5	< 5	< 5	
	DVT		9 (0.04)	< 5	< 5	< 5		
	PE		20 (0.10)	< 5	< 5	< 5		
	ATE		< 5	< 5	< 5	< 5		
	IS		< 5	< 5	< 5	< 5		
	TIA		< 5	< 5	< 5	< 5		
	MI		< 5	< 5	< 5	< 5		
	HF		10 (0.05)	< 5	< 5	< 5		
	HS		< 5	< 5	< 5	< 5		
	MP		< 5	< 5	< 5	< 5		
	181 to 365 days		VTE	< 5	< 5	< 5	< 5	
		DVT	< 5	< 5	< 5	< 5		
		PE	< 5	< 5	< 5	< 5		
		ATE	< 5	< 5	< 5	< 5		
		IS	< 5	< 5	< 5	< 5		
		TIA	< 5	< 5	< 5	< 5		
		MI	< 5	< 5	< 5	< 5		
		HF	< 5	< 5	< 5	< 5		
		HS	< 5	< 5	< 5	< 5		
		MP	< 5	< 5	< 5	< 5		

VTE = Venous thromboembolism (DVT + PE), DVT = Deep vein thrombosis, PE = Pulmonary embolism, ATE = Arterial thrombosis/thromboembolism (IS + TIA + MI), IS = Ischemic stroke, TIA = Transient ischemic attack, MI = Myocardial infarction, HF = Heart failure, HS = Hemorrhagic stroke, MP = Myocarditis or Pericarditis

Table S31: Number of records (and risk per 10,000 individuals) for post COVID-19 cardiac and thromboembolic complications, across cohorts and databases, stratified by exposure status (BNT162b2 vaccine).

Cohort	Time window	Outcome	AURUM		CORIVA		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
Cohort 1			N = 348,052	N = 332,790	N = 24,073	N = 19,686	N = 169,459	N = 32,755	N = 223,960	N = 88,896
0 to 30 days	VTE	106 (3.05)	76 (2.28)	76 (31.57)	40 (20.32)	8 (0.47)	< 5	75 (3.35)	94 (10.57)	
	DVT	21 (0.60)	15 (0.45)	14 (5.82)	13 (6.60)	< 5	< 5	20 (0.89)	29 (3.26)	
	PE	90 (2.59)	64 (1.92)	64 (26.59)	28 (14.22)	6 (0.35)	< 5	60 (2.68)	75 (8.44)	
	ATE	27 (0.78)	45 (1.35)	114 (47.36)	61 (30.99)	6 (0.35)	< 5	79 (3.53)	206 (23.17)	
	IS	9 (0.26)	5 (0.15)	68 (28.25)	26 (13.21)	< 5	< 5	46 (2.05)	116 (13.05)	
	TIA	5 (0.14)	11 (0.33)	22 (9.14)	15 (7.62)	< 5	< 5	7 (0.31)	41 (4.61)	
	MI	14 (0.40)	29 (0.87)	34 (14.12)	27 (13.72)	< 5	< 5	28 (1.25)	61 (6.86)	
	HF	59 (1.70)	126 (3.79)	393 (163.25)	231 (117.34)	9 (0.53)	< 5	299 (13.35)	634 (71.32)	
	HS	< 5	< 5	< 5	< 5	< 5	< 5	7 (0.31)	14 (1.57)	
	MP	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5	
31 to 90 days	VTE	18 (0.52)	26 (0.78)	40 (16.62)	24 (12.19)	< 5	< 5	16 (0.71)	44 (4.95)	
	DVT	9 (0.26)	7 (0.21)	19 (7.89)	14 (7.11)	< 5	< 5	10 (0.45)	29 (3.26)	
	PE	9 (0.26)	19 (0.57)	24 (9.97)	10 (5.08)	< 5	< 5	6 (0.27)	19 (2.14)	
	ATE	9 (0.26)	23 (0.69)	31 (12.88)	35 (17.78)	< 5	< 5	41 (1.83)	128 (14.40)	
	IS	< 5	< 5	18 (7.48)	14 (7.11)	< 5	< 5	20 (0.89)	71 (7.99)	
	TIA	5 (0.14)	10 (0.30)	7 (2.91)	14 (7.11)	< 5	< 5	13 (0.58)	32 (3.60)	
	MI	5 (0.14)	11 (0.33)	11 (4.57)	10 (5.08)	< 5	< 5	11 (0.49)	29 (3.26)	
	HF	32 (0.92)	71 (2.13)	151 (62.73)	141 (71.62)	< 5	< 5	87 (3.88)	296 (33.30)	
	HS	< 5	< 5	< 5	< 5	< 5	< 5	< 5	13 (1.46)	
	MP	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5	
91 to 180 days	VTE	10 (0.29)	6 (0.18)	19 (7.89)	27 (13.72)	< 5	< 5	21 (0.94)	40 (4.50)	
	DVT	< 5	< 5	11 (4.57)	14 (7.11)	< 5	< 5	9 (0.40)	23 (2.59)	
	PE	6 (0.17)	< 5	9 (3.74)	14 (7.11)	< 5	< 5	12 (0.54)	20 (2.25)	
	ATE	15 (0.43)	18 (0.54)	31 (12.88)	40 (20.32)	< 5	< 5	31 (1.38)	110 (12.37)	
	IS	< 5	6 (0.18)	16 (6.65)	17 (8.64)	< 5	< 5	17 (0.76)	59 (6.64)	
	TIA	8 (0.23)	6 (0.18)	8 (3.32)	11 (5.59)	< 5	< 5	8 (0.36)	34 (3.82)	
	MI	5 (0.14)	6 (0.18)	8 (3.32)	16 (8.13)	< 5	< 5	7 (0.31)	26 (2.92)	
	HF	43 (1.24)	57 (1.71)	166 (68.96)	169 (85.85)	< 5	< 5	87 (3.88)	249 (28.01)	
	HS	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5	
	MP	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5	

Cohort	Time window	Outcome	AURUM		CORIVA		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
	181 to 365 days	VTE	14 (0.40)	10 (0.30)	43 (17.86)	31 (15.75)	< 5	< 5	10 (0.45)	12 (1.35)
		DVT	< 5	6 (0.18)	16 (6.65)	18 (9.14)	< 5	< 5	5 (0.22)	8 (0.90)
		PE	11 (0.32)	< 5	31 (12.88)	14 (7.11)	< 5	< 5	5 (0.22)	< 5
		ATE	15 (0.43)	14 (0.42)	57 (23.68)	62 (31.49)	< 5	< 5	41 (1.83)	52 (5.85)
		IS	< 5	< 5	32 (13.29)	30 (15.24)	< 5	< 5	20 (0.89)	33 (3.71)
		TIA	10 (0.29)	< 5	16 (6.65)	24 (12.19)	< 5	< 5	11 (0.49)	13 (1.46)
		MI	< 5	7 (0.21)	14 (5.82)	16 (8.13)	< 5	< 5	10 (0.45)	8 (0.90)
		HF	52 (1.49)	38 (1.14)	278 (115.48)	244 (123.95)	< 5	< 5	82 (3.66)	149 (16.76)
		HS	< 5	< 5	< 5	< 5	< 5	< 5	< 5	9 (1.01)
		MP	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5
Cohort 2			N = 1,976,163	N = 594,262			N = 584,309	N = 180,670	N = 433,111	N = 445,581
	0 to 30 days	VTE	240 (1.21)	62 (1.04)			29 (0.50)	5 (0.28)	259 (5.98)	265 (5.95)
		DVT	39 (0.20)	18 (0.30)			7 (0.12)	< 5	63 (1.45)	96 (2.15)
		PE	205 (1.04)	45 (0.76)			23 (0.39)	< 5	215 (4.96)	189 (4.24)
		ATE	39 (0.20)	29 (0.49)			< 5	< 5	172 (3.97)	489 (10.97)
		IS	7 (0.04)	< 5			< 5	< 5	94 (2.17)	267 (5.99)
		TIA	6 (0.03)	11 (0.19)			< 5	< 5	17 (0.39)	90 (2.02)
		MI	26 (0.13)	16 (0.27)			< 5	< 5	65 (1.50)	163 (3.66)
		HF	50 (0.25)	43 (0.72)			6 (0.10)	< 5	380 (8.77)	1,137 (25.52)
		HS	6 (0.03)	< 5			< 5	< 5	18 (0.42)	61 (1.37)
		MP	11 (0.06)	< 5			< 5	< 5	14 (0.32)	22 (0.49)
	31 to 90 days	VTE	49 (0.25)	21 (0.35)			< 5	< 5	60 (1.39)	128 (2.87)
		DVT	26 (0.13)	7 (0.12)			< 5	< 5	33 (0.76)	81 (1.82)
		PE	26 (0.13)	14 (0.24)			< 5	< 5	34 (0.79)	56 (1.26)
		ATE	17 (0.09)	36 (0.61)			< 5	< 5	86 (1.99)	313 (7.02)
		IS	< 5	5 (0.08)			< 5	< 5	43 (0.99)	167 (3.75)
		TIA	< 5	9 (0.15)			< 5	< 5	24 (0.55)	86 (1.93)
		MI	11 (0.06)	22 (0.37)			< 5	< 5	26 (0.60)	80 (1.80)
		HF	27 (0.14)	35 (0.59)			< 5	< 5	137 (3.16)	554 (12.43)
		HS	< 5	< 5			< 5	< 5	7 (0.16)	19 (0.43)
		MP	6 (0.03)	< 5			< 5	< 5	< 5	< 5
	91 to 180 days	VTE	28 (0.14)	10 (0.17)			5 (0.09)	< 5	59 (1.36)	96 (2.15)
		DVT	12 (0.06)	6 (0.10)			< 5	< 5	32 (0.74)	59 (1.32)
		PE	16 (0.08)	5 (0.08)			< 5	< 5	30 (0.69)	45 (1.01)

Cohort	Time window	Outcome	AURUM		CORIVA		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
		ATE	14 (0.07)	15 (0.25)			< 5	< 5	90 (2.08)	287 (6.44)
		IS	< 5	< 5			< 5	< 5	49 (1.13)	168 (3.77)
		TIA	7 (0.04)	5 (0.08)			< 5	< 5	21 (0.48)	76 (1.71)
		MI	8 (0.04)	10 (0.17)			< 5	< 5	23 (0.53)	63 (1.41)
		HF	19 (0.10)	25 (0.42)			< 5	< 5	110 (2.54)	472 (10.59)
		HS	< 5	< 5			< 5	< 5	7 (0.16)	34 (0.76)
		MP	< 5	< 5			< 5	< 5	7 (0.16)	< 5
	181 to 365 days	VTE	10 (0.05)	8 (0.13)			< 5	< 5	16 (0.37)	40 (0.90)
		DVT	< 5	< 5			< 5	< 5	10 (0.23)	26 (0.58)
		PE	8 (0.04)	7 (0.12)			< 5	< 5	8 (0.18)	16 (0.36)
		ATE	12 (0.06)	7 (0.12)			< 5	< 5	59 (1.36)	123 (2.76)
		IS	< 5	< 5			< 5	< 5	29 (0.67)	58 (1.30)
		TIA	< 5	< 5			< 5	< 5	18 (0.42)	39 (0.88)
		MI	9 (0.05)	< 5			< 5	< 5	14 (0.32)	32 (0.72)
		HF	23 (0.12)	12 (0.20)			< 5	< 5	73 (1.69)	212 (4.76)
		HS	< 5	< 5			< 5	< 5	6 (0.14)	12 (0.27)
		MP	< 5	< 5			< 5	< 5	< 5	< 5
Cohort 3			N = 1,510,323	N = 54,102			N = 416,549	N = 36,748	N = 869,109	N = 706,435
	0 to 30 days	VTE	244 (1.62)	< 5			28 (0.67)	< 5	321 (3.69)	114 (1.61)
		DVT	44 (0.29)	< 5			6 (0.14)	< 5	89 (1.02)	51 (0.72)
		PE	209 (1.38)	< 5			23 (0.55)	< 5	259 (2.98)	71 (1.01)
		ATE	29 (0.19)	< 5			< 5	< 5	211 (2.43)	197 (2.79)
		IS	< 5	< 5			< 5	< 5	102 (1.17)	95 (1.34)
		TIA	5 (0.03)	< 5			< 5	< 5	20 (0.23)	42 (0.59)
		MI	20 (0.13)	< 5			< 5	< 5	95 (1.09)	78 (1.10)
		HF	30 (0.20)	10 (1.85)			< 5	< 5	366 (4.21)	163 (2.31)
		HS	< 5	< 5			< 5	< 5	20 (0.23)	26 (0.37)
		MP	9 (0.06)	< 5			< 5	< 5	19 (0.22)	13 (0.18)
	31 to 90 days	VTE	44 (0.29)	< 5			< 5	< 5	84 (0.97)	65 (0.92)
		DVT	20 (0.13)	< 5			< 5	< 5	56 (0.64)	47 (0.67)
		PE	27 (0.18)	< 5			< 5	< 5	38 (0.44)	23 (0.33)
		ATE	11 (0.07)	< 5			< 5	< 5	107 (1.23)	144 (2.04)
		IS	< 5	< 5			< 5	< 5	53 (0.61)	55 (0.78)
		TIA	< 5	< 5			< 5	< 5	27 (0.31)	28 (0.40)

Cohort	Time window	Outcome	AURUM		CORIVA		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
	91 to 180 days	MI	9 (0.06)	< 5			< 5	< 5	35 (0.40)	69 (0.98)
		HF	15 (0.10)	< 5			< 5	< 5	139 (1.60)	111 (1.57)
		HS	< 5	< 5			< 5	< 5	7 (0.08)	14 (0.20)
		MP	8 (0.05)	< 5			< 5	< 5	8 (0.09)	9 (0.13)
		VTE	24 (0.16)	< 5			< 5	< 5	63 (0.72)	71 (1.01)
		DVT	11 (0.07)	< 5			< 5	< 5	35 (0.40)	45 (0.64)
		PE	14 (0.09)	< 5			< 5	< 5	32 (0.37)	27 (0.38)
		ATE	< 5	< 5			< 5	< 5	112 (1.29)	141 (2.00)
		IS	< 5	< 5			< 5	< 5	57 (0.66)	65 (0.92)
		TIA	< 5	< 5			< 5	< 5	22 (0.25)	29 (0.41)
		MI	< 5	< 5			< 5	< 5	36 (0.41)	53 (0.75)
		HF	10 (0.07)	< 5			< 5	< 5	121 (1.39)	100 (1.42)
		HS	< 5	< 5			< 5	< 5	9 (0.10)	10 (0.14)
		MP	< 5	< 5			< 5	< 5	7 (0.08)	9 (0.13)
	181 to 365 days	VTE	< 5	< 5			< 5	< 5	36 (0.41)	17 (0.24)
	DVT	< 5	< 5			< 5	< 5	22 (0.25)	14 (0.20)	
	PE	< 5	< 5			< 5	< 5	16 (0.18)	< 5	
	ATE	< 5	< 5			< 5	< 5	48 (0.55)	45 (0.64)	
	IS	< 5	< 5			< 5	< 5	23 (0.26)	17 (0.24)	
	TIA	< 5	< 5			< 5	< 5	9 (0.10)	7 (0.10)	
	MI	< 5	< 5			< 5	< 5	17 (0.20)	24 (0.34)	
	HF	5 (0.03)	< 5			< 5	< 5	61 (0.70)	31 (0.44)	
	HS	< 5	< 5			< 5	< 5	< 5	< 5	
	MP	< 5	< 5			< 5	< 5	< 5	< 5	
Cohort 4			N = 2,014,161	N = 1,335,671	N = 147,553	N = 15,683	N = 465,326	N = 365,096	N = 1,068,043	N = 580,329
0 to 30 days	VTE	328 (1.63)	20 (0.15)	116 (7.86)	< 5	36 (0.77)	< 5	350 (3.28)	66 (1.14)	
	DVT	52 (0.26)	9 (0.07)	22 (1.49)	< 5	6 (0.13)	< 5	107 (1.00)	35 (0.60)	
	PE	287 (1.42)	11 (0.08)	97 (6.57)	< 5	31 (0.67)	< 5	271 (2.54)	35 (0.60)	
	ATE	25 (0.12)	< 5	116 (7.86)	< 5	< 5	< 5	233 (2.18)	55 (0.95)	
	IS	< 5	< 5	69 (4.68)	< 5	< 5	< 5	114 (1.07)	29 (0.50)	
	TIA	6 (0.03)	< 5	18 (1.22)	< 5	< 5	< 5	28 (0.26)	7 (0.12)	
	MI	15 (0.07)	< 5	38 (2.58)	< 5	< 5	< 5	97 (0.91)	20 (0.34)	
	HF	26 (0.13)	< 5	362 (24.53)	8 (5.10)	< 5	< 5	369 (3.45)	44 (0.76)	
	HS	< 5	< 5	5 (0.34)	< 5	< 5	< 5	24 (0.22)	7 (0.12)	

Cohort	Time window	Outcome	AURUM		CORIVA		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
31 to 90 days	MP	13 (0.06)	< 5	7 (0.47)	< 5	< 5	< 5	26 (0.24)	11 (0.19)	
	VTE	56 (0.28)	7 (0.05)	54 (3.66)	< 5	< 5	< 5	93 (0.87)	33 (0.57)	
	DVT	20 (0.10)	< 5	32 (2.17)	< 5	< 5	< 5	62 (0.58)	23 (0.40)	
	PE	39 (0.19)	< 5	26 (1.76)	< 5	< 5	< 5	41 (0.38)	11 (0.19)	
	ATE	13 (0.06)	< 5	46 (3.12)	< 5	< 5	< 5	115 (1.08)	51 (0.88)	
	IS	< 5	< 5	24 (1.63)	< 5	< 5	< 5	51 (0.48)	21 (0.36)	
	TIA	< 5	< 5	6 (0.41)	< 5	< 5	< 5	31 (0.29)	12 (0.21)	
	MI	9 (0.04)	< 5	19 (1.29)	< 5	< 5	< 5	41 (0.38)	21 (0.36)	
	HF	14 (0.07)	6 (0.04)	174 (11.79)	5 (3.19)	< 5	< 5	143 (1.34)	28 (0.48)	
	HS	< 5	< 5	< 5	< 5	< 5	< 5	10 (0.09)	5 (0.09)	
	MP	7 (0.03)	< 5	5 (0.34)	< 5	< 5	< 5	12 (0.11)	8 (0.14)	
91 to 180 days	VTE	24 (0.12)	9 (0.07)	49 (3.32)	< 5	< 5	< 5	77 (0.72)	45 (0.78)	
	DVT	11 (0.05)	7 (0.05)	31 (2.10)	< 5	< 5	< 5	42 (0.39)	28 (0.48)	
	PE	14 (0.07)	< 5	19 (1.29)	< 5	< 5	< 5	38 (0.36)	20 (0.34)	
	ATE	< 5	< 5	41 (2.78)	< 5	< 5	< 5	134 (1.25)	71 (1.22)	
	IS	< 5	< 5	19 (1.29)	< 5	< 5	< 5	66 (0.62)	37 (0.64)	
	TIA	< 5	< 5	12 (0.81)	< 5	< 5	< 5	31 (0.29)	14 (0.24)	
	MI	< 5	< 5	14 (0.95)	< 5	< 5	< 5	40 (0.37)	20 (0.34)	
	HF	9 (0.04)	< 5	208 (14.10)	< 5	< 5	< 5	145 (1.36)	35 (0.60)	
	HS	< 5	< 5	< 5	< 5	< 5	< 5	15 (0.14)	< 5	
	MP	< 5	< 5	5 (0.34)	< 5	< 5	< 5	13 (0.12)	< 5	
	181 to 365 days	VTE	< 5	< 5	77 (5.22)	5 (3.19)	< 5	< 5	52 (0.49)	10 (0.17)
DVT		< 5	< 5	46 (3.12)	< 5	< 5	< 5	36 (0.34)	8 (0.14)	
PE		< 5	< 5	35 (2.37)	< 5	< 5	< 5	18 (0.17)	< 5	
ATE		< 5	< 5	72 (4.88)	< 5	< 5	< 5	52 (0.49)	21 (0.36)	
IS		< 5	< 5	33 (2.24)	< 5	< 5	< 5	28 (0.26)	11 (0.19)	
TIA		< 5	< 5	18 (1.22)	< 5	< 5	< 5	10 (0.09)	< 5	
MI		< 5	< 5	27 (1.83)	< 5	< 5	< 5	15 (0.14)	9 (0.16)	
HF		< 5	< 5	298 (20.20)	5 (3.19)	< 5	< 5	58 (0.54)	8 (0.14)	
HS		< 5	< 5	8 (0.54)	< 5	< 5	< 5	5 (0.05)	< 5	
MP		< 5	< 5	5 (0.34)	< 5	< 5	< 5	6 (0.06)	< 5	

VTE = Venous thromboembolism (DVT + PE), DVT = Deep vein thrombosis, PE = Pulmonary embolism, ATE = Arterial thrombosis/thromboembolism (IS + TIA + MI), IS = Ischemic stroke, TIA = Transient ischemic attack, MI = Myocardial infarction, HF = Heart failure, HS = Hemorrhagic stroke, MP = Myocarditis or Pericarditis

Table S32: Number of records (and risk per 10,000 individuals) for post COVID-19 cardiac and thromboembolic complications, across cohorts and databases, stratified by exposure status (BNT162b2 vaccine). Follow-up ends at first vaccine dose after index date.

Cohort	Time window	Outcome	AURUM		CORIVA		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
Cohort 1			N = 348,052	N = 332,790	N = 24,073	N = 19,686	N = 169,459	N = 32,755	N = 223,960	N = 88,896
	0 to 30 days	VTE	106 (3.05)	31 (0.93)	76 (31.57)	< 5	8 (0.47)	< 5	75 (3.35)	< 5
		DVT	21 (0.60)	8 (0.24)	14 (5.82)	< 5	< 5	< 5	20 (0.89)	< 5
		PE	90 (2.59)	24 (0.72)	64 (26.59)	< 5	6 (0.35)	< 5	60 (2.68)	< 5
		ATE	27 (0.78)	18 (0.54)	114 (47.36)	< 5	6 (0.35)	< 5	79 (3.53)	5 (0.56)
		IS	9 (0.26)	< 5	68 (28.25)	< 5	< 5	< 5	46 (2.05)	< 5
		TIA	5 (0.14)	< 5	22 (9.14)	< 5	< 5	< 5	7 (0.31)	< 5
		MI	14 (0.40)	14 (0.42)	34 (14.12)	< 5	< 5	< 5	28 (1.25)	< 5
		HF	59 (1.70)	45 (1.35)	393 (163.25)	20 (10.16)	9 (0.53)	< 5	299 (13.35)	23 (2.59)
		HS	< 5	< 5	< 5	< 5	< 5	< 5	7 (0.31)	< 5
		MP	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5
	31 to 90 days	VTE	18 (0.52)	15 (0.45)	40 (16.62)	< 5	< 5	< 5	16 (0.71)	< 5
		DVT	9 (0.26)	< 5	19 (7.89)	< 5	< 5	< 5	10 (0.45)	< 5
		PE	9 (0.26)	11 (0.33)	24 (9.97)	< 5	< 5	< 5	6 (0.27)	< 5
		ATE	9 (0.26)	8 (0.24)	31 (12.88)	< 5	< 5	< 5	41 (1.83)	5 (0.56)
		IS	< 5	< 5	18 (7.48)	< 5	< 5	< 5	20 (0.89)	< 5
		TIA	5 (0.14)	< 5	7 (2.91)	< 5	< 5	< 5	13 (0.58)	< 5
		MI	5 (0.14)	< 5	11 (4.57)	< 5	< 5	< 5	11 (0.49)	< 5
		HF	32 (0.92)	36 (1.08)	151 (62.73)	11 (5.59)	< 5	< 5	87 (3.88)	8 (0.90)
		HS	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5
	91 to 180 days	VTE	10 (0.29)	< 5	19 (7.89)	< 5	< 5	< 5	21 (0.94)	< 5
		DVT	< 5	< 5	11 (4.57)	< 5	< 5	< 5	9 (0.40)	< 5
		PE	6 (0.17)	< 5	9 (3.74)	< 5	< 5	< 5	12 (0.54)	< 5
		ATE	15 (0.43)	10 (0.30)	31 (12.88)	< 5	< 5	< 5	31 (1.38)	< 5
		IS	< 5	< 5	16 (6.65)	< 5	< 5	< 5	17 (0.76)	< 5
		TIA	8 (0.23)	< 5	8 (3.32)	< 5	< 5	< 5	8 (0.36)	< 5
		MI	5 (0.14)	< 5	8 (3.32)	< 5	< 5	< 5	7 (0.31)	< 5
		HF	43 (1.24)	32 (0.96)	166 (68.96)	14 (7.11)	< 5	< 5	87 (3.88)	6 (0.67)
		HS	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5

Cohort	Time window	Outcome	AURUM		CORIVA		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
	181 to 365 days	VTE	14 (0.40)	7 (0.21)	43 (17.86)	6 (3.05)	< 5	< 5	10 (0.45)	< 5
		DVT	< 5	< 5	16 (6.65)	< 5	< 5	< 5	5 (0.22)	< 5
		PE	11 (0.32)	< 5	31 (12.88)	< 5	< 5	< 5	5 (0.22)	< 5
		ATE	15 (0.43)	11 (0.33)	57 (23.68)	10 (5.08)	< 5	< 5	41 (1.83)	8 (0.90)
		IS	< 5	< 5	32 (13.29)	9 (4.57)	< 5	< 5	20 (0.89)	5 (0.56)
		TIA	10 (0.29)	< 5	16 (6.65)	< 5	< 5	< 5	11 (0.49)	< 5
		MI	< 5	6 (0.18)	14 (5.82)	< 5	< 5	< 5	10 (0.45)	< 5
		HF	52 (1.49)	35 (1.05)	278 (115.48)	37 (18.80)	< 5	< 5	82 (3.66)	20 (2.25)
		HS	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5
Cohort 2			N = 1,976,163	N = 594,262			N = 584,309	N = 180,670	N = 433,111	N = 445,581
	0 to 30 days	VTE	240 (1.21)	14 (0.24)			29 (0.50)	< 5	259 (5.98)	14 (0.31)
		DVT	39 (0.20)	6 (0.10)			7 (0.12)	< 5	63 (1.45)	< 5
		PE	205 (1.04)	8 (0.13)			23 (0.39)	< 5	215 (4.96)	12 (0.27)
		ATE	39 (0.20)	14 (0.24)			< 5	< 5	172 (3.97)	16 (0.36)
		IS	7 (0.04)	< 5			< 5	< 5	94 (2.17)	8 (0.18)
		TIA	6 (0.03)	< 5			< 5	< 5	17 (0.39)	< 5
		MI	26 (0.13)	8 (0.13)			< 5	< 5	65 (1.50)	5 (0.11)
		HF	50 (0.25)	15 (0.25)			6 (0.10)	< 5	380 (8.77)	56 (1.26)
		HS	6 (0.03)	< 5			< 5	< 5	18 (0.42)	< 5
		MP	11 (0.06)	< 5			< 5	< 5	14 (0.32)	< 5
	31 to 90 days	VTE	49 (0.25)	5 (0.08)			< 5	< 5	60 (1.39)	6 (0.13)
		DVT	26 (0.13)	< 5			< 5	< 5	33 (0.76)	< 5
		PE	26 (0.13)	< 5			< 5	< 5	34 (0.79)	< 5
ATE		17 (0.09)	9 (0.15)			< 5	< 5	86 (1.99)	7 (0.16)	
91 to 180 days	VTE	28 (0.14)	< 5			5 (0.09)	< 5	59 (1.36)	< 5	
	DVT	12 (0.06)	< 5			< 5	< 5	32 (0.74)	< 5	
	PE	16 (0.08)	< 5			< 5	< 5	30 (0.69)	< 5	

Cohort	Time window	Outcome	AURUM		CORIVA		GOLD		SIDIAP			
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated		
		ATE	14 (0.07)	5 (0.08)			< 5	< 5	90 (2.08)	10 (0.22)		
		IS	< 5	< 5			< 5	< 5	49 (1.13)	5 (0.11)		
		TIA	7 (0.04)	< 5			< 5	< 5	21 (0.48)	< 5		
		MI	8 (0.04)	< 5			< 5	< 5	23 (0.53)	< 5		
		HF	19 (0.10)	9 (0.15)			< 5	< 5	110 (2.54)	25 (0.56)		
		HS	< 5	< 5			< 5	< 5	7 (0.16)	< 5		
		MP	< 5	< 5			< 5	< 5	7 (0.16)	< 5		
	181 to 365 days	VTE	10 (0.05)	7 (0.12)			< 5	< 5	16 (0.37)	10 (0.22)		
		DVT	< 5	< 5			< 5	< 5	10 (0.23)	6 (0.13)		
		PE	8 (0.04)	5 (0.08)			< 5	< 5	8 (0.18)	< 5		
		ATE	12 (0.06)	6 (0.10)			< 5	< 5	59 (1.36)	19 (0.43)		
		IS	< 5	< 5			< 5	< 5	29 (0.67)	9 (0.20)		
		TIA	< 5	< 5			< 5	< 5	18 (0.42)	5 (0.11)		
		MI	9 (0.05)	< 5			< 5	< 5	14 (0.32)	5 (0.11)		
		HF	23 (0.12)	11 (0.19)			< 5	< 5	73 (1.69)	27 (0.61)		
		HS	< 5	< 5			< 5	< 5	6 (0.14)	< 5		
		MP	< 5	< 5			< 5	< 5	< 5	< 5		
		Cohort 3			N = 1,510,323 N = 54,102				N = 416,549	N = 36,748	N = 869,109	N = 706,435
		0 to 30 days	VTE	244 (1.62)	< 5			28 (0.67)	< 5	321 (3.69)	< 5	
			DVT	44 (0.29)	< 5			6 (0.14)	< 5	89 (1.02)	< 5	
PE	209 (1.38)		< 5			23 (0.55)	< 5	259 (2.98)	< 5			
ATE	29 (0.19)		< 5			< 5	< 5	211 (2.43)	< 5			
IS	< 5		< 5			< 5	< 5	102 (1.17)	< 5			
TIA	5 (0.03)		< 5			< 5	< 5	20 (0.23)	< 5			
MI	20 (0.13)		< 5			< 5	< 5	95 (1.09)	< 5			
HF	30 (0.20)		7 (1.29)			< 5	< 5	366 (4.21)	5 (0.07)			
HS	< 5		< 5			< 5	< 5	20 (0.23)	< 5			
MP	9 (0.06)		< 5			< 5	< 5	19 (0.22)	< 5			
31 to 90 days	VTE		44 (0.29)	< 5			< 5	< 5	84 (0.97)	< 5		
	DVT		20 (0.13)	< 5			< 5	< 5	56 (0.64)	< 5		
	PE		27 (0.18)	< 5			< 5	< 5	38 (0.44)	< 5		
	ATE	11 (0.07)	< 5			< 5	< 5	107 (1.23)	< 5			
	IS	< 5	< 5			< 5	< 5	53 (0.61)	< 5			
	TIA	< 5	< 5			< 5	< 5	27 (0.31)	< 5			

Cohort	Time window	Outcome	AURUM		CORIVA		GOLD		SIDIAP		
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	
	91 to 180 days	MI	9 (0.06)	< 5			< 5	< 5	35 (0.40)	< 5	
		HF	15 (0.10)	< 5			< 5	< 5	139 (1.60)	< 5	
		HS	< 5	< 5			< 5	< 5	7 (0.08)	< 5	
		MP	8 (0.05)	< 5			< 5	< 5	8 (0.09)	< 5	
		VTE	24 (0.16)	< 5			< 5	< 5	63 (0.72)	< 5	
		DVT	11 (0.07)	< 5			< 5	< 5	35 (0.40)	< 5	
		PE	14 (0.09)	< 5			< 5	< 5	32 (0.37)	< 5	
		ATE	< 5	< 5			< 5	< 5	112 (1.29)	6 (0.08)	
		IS	< 5	< 5			< 5	< 5	57 (0.66)	< 5	
		TIA	< 5	< 5			< 5	< 5	22 (0.25)	< 5	
		MI	< 5	< 5			< 5	< 5	36 (0.41)	< 5	
		HF	10 (0.07)	< 5			< 5	< 5	121 (1.39)	< 5	
	HS	< 5	< 5			< 5	< 5	9 (0.10)	< 5		
	MP	< 5	< 5			< 5	< 5	7 (0.08)	< 5		
	181 to 365 days	VTE	< 5	< 5			< 5	< 5	36 (0.41)	< 5	
		DVT	< 5	< 5			< 5	< 5	22 (0.25)	< 5	
		PE	< 5	< 5			< 5	< 5	16 (0.18)	< 5	
		ATE	< 5	< 5			< 5	< 5	48 (0.55)	6 (0.08)	
		IS	< 5	< 5			< 5	< 5	23 (0.26)	< 5	
		TIA	< 5	< 5			< 5	< 5	9 (0.10)	< 5	
		MI	< 5	< 5			< 5	< 5	17 (0.20)	< 5	
		HF	5 (0.03)	< 5			< 5	< 5	61 (0.70)	< 5	
		HS	< 5	< 5			< 5	< 5	< 5	< 5	
		MP	< 5	< 5			< 5	< 5	< 5	< 5	
Cohort 4				N = 2,014,161	N = 1,335,671	N = 147,553	N = 15,683	N = 465,326	N = 365,096	N = 1,068,043	N = 580,329
0 to 30 days		VTE	328 (1.63)	9 (0.07)	116 (7.86)	< 5	36 (0.77)	< 5	350 (3.28)	18 (0.31)	
	DVT	52 (0.26)	5 (0.04)	22 (1.49)	< 5	6 (0.13)	< 5	107 (1.00)	8 (0.14)		
	PE	287 (1.42)	< 5	97 (6.57)	< 5	31 (0.67)	< 5	271 (2.54)	10 (0.17)		
	ATE	25 (0.12)	< 5	116 (7.86)	< 5	< 5	< 5	233 (2.18)	9 (0.16)		
	IS	< 5	< 5	69 (4.68)	< 5	< 5	< 5	114 (1.07)	6 (0.10)		
	TIA	6 (0.03)	< 5	18 (1.22)	< 5	< 5	< 5	28 (0.26)	< 5		
	MI	15 (0.07)	< 5	38 (2.58)	< 5	< 5	< 5	97 (0.91)	< 5		
	HF	26 (0.13)	< 5	362 (24.53)	6 (3.83)	< 5	< 5	369 (3.45)	7 (0.12)		
	HS	< 5	< 5	5 (0.34)	< 5	< 5	< 5	24 (0.22)	< 5		

Cohort	Time window	Outcome	AURUM		CORIVA		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
31 to 90 days	MP	13 (0.06)	< 5	7 (0.47)	< 5	< 5	< 5	26 (0.24)	< 5	
	VTE	56 (0.28)	< 5	54 (3.66)	< 5	< 5	< 5	93 (0.87)	6 (0.10)	
	DVT	20 (0.10)	< 5	32 (2.17)	< 5	< 5	< 5	62 (0.58)	< 5	
	PE	39 (0.19)	< 5	26 (1.76)	< 5	< 5	< 5	41 (0.38)	< 5	
	ATE	13 (0.06)	< 5	46 (3.12)	< 5	< 5	< 5	115 (1.08)	< 5	
	IS	< 5	< 5	24 (1.63)	< 5	< 5	< 5	51 (0.48)	< 5	
	TIA	< 5	< 5	6 (0.41)	< 5	< 5	< 5	31 (0.29)	< 5	
	MI	9 (0.04)	< 5	19 (1.29)	< 5	< 5	< 5	41 (0.38)	< 5	
	HF	14 (0.07)	6 (0.04)	174 (11.79)	< 5	< 5	< 5	143 (1.34)	< 5	
	HS	< 5	< 5	< 5	< 5	< 5	< 5	10 (0.09)	< 5	
	MP	7 (0.03)	< 5	5 (0.34)	< 5	< 5	< 5	12 (0.11)	< 5	
91 to 180 days	VTE	24 (0.12)	8 (0.06)	49 (3.32)	< 5	< 5	< 5	77 (0.72)	< 5	
	DVT	11 (0.05)	7 (0.05)	31 (2.10)	< 5	< 5	< 5	42 (0.39)	< 5	
	PE	14 (0.07)	< 5	19 (1.29)	< 5	< 5	< 5	38 (0.36)	< 5	
	ATE	< 5	< 5	41 (2.78)	< 5	< 5	< 5	134 (1.25)	9 (0.16)	
	IS	< 5	< 5	19 (1.29)	< 5	< 5	< 5	66 (0.62)	7 (0.12)	
	TIA	< 5	< 5	12 (0.81)	< 5	< 5	< 5	31 (0.29)	< 5	
	MI	< 5	< 5	14 (0.95)	< 5	< 5	< 5	40 (0.37)	< 5	
	HF	9 (0.04)	< 5	208 (14.10)	< 5	< 5	< 5	145 (1.36)	9 (0.16)	
	HS	< 5	< 5	< 5	< 5	< 5	< 5	15 (0.14)	< 5	
	MP	< 5	< 5	5 (0.34)	< 5	< 5	< 5	13 (0.12)	< 5	
	181 to 365 days	VTE	< 5	< 5	77 (5.22)	5 (3.19)	< 5	< 5	52 (0.49)	7 (0.12)
DVT		< 5	< 5	46 (3.12)	< 5	< 5	< 5	36 (0.34)	5 (0.09)	
PE		< 5	< 5	35 (2.37)	< 5	< 5	< 5	18 (0.17)	< 5	
ATE		< 5	< 5	72 (4.88)	< 5	< 5	< 5	52 (0.49)	15 (0.26)	
IS		< 5	< 5	33 (2.24)	< 5	< 5	< 5	28 (0.26)	10 (0.17)	
TIA		< 5	< 5	18 (1.22)	< 5	< 5	< 5	10 (0.09)	< 5	
MI		< 5	< 5	27 (1.83)	< 5	< 5	< 5	15 (0.14)	5 (0.09)	
HF		< 5	< 5	298 (20.20)	< 5	< 5	< 5	58 (0.54)	< 5	
HS		< 5	< 5	8 (0.54)	< 5	< 5	< 5	5 (0.05)	< 5	
MP		< 5	< 5	5 (0.34)	< 5	< 5	< 5	6 (0.06)	< 5	

VTE = Venous thromboembolism (DVT + PE), DVT = Deep vein thrombosis, PE = Pulmonary embolism, ATE = Arterial thrombosis/thromboembolism (IS + TIA + MI), IS = Ischemic stroke, TIA = Transient ischemic attack, MI = Myocardial infarction, HF = Heart failure, HS = Hemorrhagic stroke, MP = Myocarditis or Pericarditis

Table S33: Number of records (and risk per 10,000 individuals) for post COVID-19 cardiac and thromboembolic complications, across cohorts and databases, stratified by exposure status (BNT162b2 vaccine). Only first outcome after COVID-19 captured.

Cohort	Time window	Outcome	AURUM		CORIVA		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
Cohort 1			N = 348,052	N = 332,790	N = 24,073	N = 19,686	N = 169,459	N = 32,755	N = 223,960	N = 88,896
0 to 30 days	VTE	106 (3.05)	76 (2.28)	76 (31.57)	40 (20.32)	8 (0.47)	< 5	75 (3.35)	94 (10.57)	
	DVT	21 (0.60)	15 (0.45)	14 (5.82)	13 (6.60)	< 5	< 5	20 (0.89)	29 (3.26)	
	PE	90 (2.59)	64 (1.92)	64 (26.59)	28 (14.22)	6 (0.35)	< 5	60 (2.68)	75 (8.44)	
	ATE	27 (0.78)	45 (1.35)	114 (47.36)	61 (30.99)	6 (0.35)	< 5	79 (3.53)	206 (23.17)	
	IS	9 (0.26)	5 (0.15)	68 (28.25)	26 (13.21)	< 5	< 5	46 (2.05)	116 (13.05)	
	TIA	5 (0.14)	11 (0.33)	22 (9.14)	15 (7.62)	< 5	< 5	7 (0.31)	41 (4.61)	
	MI	14 (0.40)	29 (0.87)	34 (14.12)	27 (13.72)	< 5	< 5	28 (1.25)	61 (6.86)	
	HF	59 (1.70)	126 (3.79)	393 (163.25)	231 (117.34)	9 (0.53)	< 5	299 (13.35)	634 (71.32)	
	HS	< 5	< 5	< 5	< 5	< 5	< 5	7 (0.31)	14 (1.57)	
	MP	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5	
31 to 90 days	VTE	18 (0.52)	25 (0.75)	37 (15.37)	23 (11.68)	< 5	< 5	15 (0.67)	43 (4.84)	
	DVT	9 (0.26)	7 (0.21)	18 (7.48)	13 (6.60)	< 5	< 5	9 (0.40)	28 (3.15)	
	PE	9 (0.26)	18 (0.54)	22 (9.14)	10 (5.08)	< 5	< 5	6 (0.27)	19 (2.14)	
	ATE	9 (0.26)	23 (0.69)	27 (11.22)	33 (16.76)	< 5	< 5	39 (1.74)	125 (14.06)	
	IS	< 5	< 5	15 (6.23)	13 (6.60)	< 5	< 5	20 (0.89)	69 (7.76)	
	TIA	5 (0.14)	10 (0.30)	7 (2.91)	14 (7.11)	< 5	< 5	13 (0.58)	32 (3.60)	
	MI	5 (0.14)	11 (0.33)	9 (3.74)	8 (4.06)	< 5	< 5	9 (0.40)	28 (3.15)	
	HF	32 (0.92)	70 (2.10)	136 (56.49)	135 (68.58)	< 5	< 5	83 (3.71)	288 (32.40)	
	HS	< 5	< 5	< 5	< 5	< 5	< 5	< 5	12 (1.35)	
	MP	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5	
91 to 180 days	VTE	10 (0.29)	< 5	14 (5.82)	22 (11.18)	< 5	< 5	19 (0.85)	35 (3.94)	
	DVT	< 5	< 5	6 (2.49)	11 (5.59)	< 5	< 5	7 (0.31)	19 (2.14)	
	PE	6 (0.17)	< 5	9 (3.74)	12 (6.10)	< 5	< 5	12 (0.54)	18 (2.02)	
	ATE	15 (0.43)	18 (0.54)	29 (12.05)	35 (17.78)	< 5	< 5	26 (1.16)	102 (11.47)	
	IS	< 5	6 (0.18)	14 (5.82)	14 (7.11)	< 5	< 5	14 (0.63)	56 (6.30)	
	TIA	8 (0.23)	6 (0.18)	8 (3.32)	10 (5.08)	< 5	< 5	7 (0.31)	33 (3.71)	
	MI	5 (0.14)	6 (0.18)	8 (3.32)	15 (7.62)	< 5	< 5	6 (0.27)	22 (2.47)	
	HF	40 (1.15)	54 (1.62)	147 (61.06)	159 (80.77)	< 5	< 5	81 (3.62)	226 (25.42)	
	HS	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5	
	MP	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5	

Cohort	Time window	Outcome	AURUM		CORIVA		GOLD		SIDIAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
181 to 365 days	VTE	VTE	11 (0.32)	10 (0.30)	27 (11.22)	24 (12.19)	< 5	< 5	5 (0.22)	10 (1.12)
		DVT	< 5	6 (0.18)	10 (4.15)	14 (7.11)	< 5	< 5	< 5	7 (0.79)
		PE	9 (0.26)	< 5	21 (8.72)	11 (5.59)	< 5	< 5	< 5	< 5
		ATE	14 (0.40)	14 (0.42)	47 (19.52)	58 (29.46)	< 5	< 5	34 (1.52)	38 (4.27)
		IS	< 5	< 5	26 (10.80)	27 (13.72)	< 5	< 5	17 (0.76)	23 (2.59)
		TIA	9 (0.26)	< 5	15 (6.23)	24 (12.19)	< 5	< 5	10 (0.45)	9 (1.01)
		MI	< 5	7 (0.21)	10 (4.15)	12 (6.10)	< 5	< 5	7 (0.31)	7 (0.79)
		HF	47 (1.35)	35 (1.05)	226 (93.88)	223 (113.28)	< 5	< 5	70 (3.13)	117 (13.16)
		HS	< 5	< 5	< 5	< 5	< 5	< 5	< 5	7 (0.79)
		MP	< 5	< 5	< 5	< 5	< 5	< 5	< 5	< 5
Cohort 2			N = 1,976,163	N = 594,262			N = 584,309	N = 180,670	N = 433,111	N = 445,581
0 to 30 days	VTE	VTE	240 (1.21)	62 (1.04)			29 (0.50)	5 (0.28)	259 (5.98)	265 (5.95)
		DVT	39 (0.20)	18 (0.30)			7 (0.12)	< 5	63 (1.45)	96 (2.15)
		PE	205 (1.04)	45 (0.76)			23 (0.39)	< 5	215 (4.96)	189 (4.24)
		ATE	39 (0.20)	29 (0.49)			< 5	< 5	172 (3.97)	489 (10.97)
		IS	7 (0.04)	< 5			< 5	< 5	94 (2.17)	267 (5.99)
		TIA	6 (0.03)	11 (0.19)			< 5	< 5	17 (0.39)	90 (2.02)
		MI	26 (0.13)	16 (0.27)			< 5	< 5	65 (1.50)	163 (3.66)
		HF	50 (0.25)	43 (0.72)			6 (0.10)	< 5	380 (8.77)	1,137 (25.52)
		HS	6 (0.03)	< 5			< 5	< 5	18 (0.42)	61 (1.37)
		MP	11 (0.06)	< 5			< 5	< 5	14 (0.32)	22 (0.49)
31 to 90 days	VTE	VTE	46 (0.23)	21 (0.35)			< 5	< 5	57 (1.32)	123 (2.76)
		DVT	25 (0.13)	7 (0.12)			< 5	< 5	31 (0.72)	77 (1.73)
		PE	24 (0.12)	14 (0.24)			< 5	< 5	32 (0.74)	55 (1.23)
		ATE	17 (0.09)	36 (0.61)			< 5	< 5	84 (1.94)	307 (6.89)
		IS	< 5	5 (0.08)			< 5	< 5	43 (0.99)	162 (3.64)
		TIA	< 5	9 (0.15)			< 5	< 5	24 (0.55)	85 (1.91)
		MI	11 (0.06)	22 (0.37)			< 5	< 5	24 (0.55)	79 (1.77)
		HF	27 (0.14)	34 (0.57)			< 5	< 5	131 (3.02)	534 (11.98)
		HS	< 5	< 5			< 5	< 5	7 (0.16)	19 (0.43)
		MP	6 (0.03)	< 5			< 5	< 5	< 5	< 5
91 to 180 days	VTE	VTE	25 (0.13)	9 (0.15)			5 (0.09)	< 5	53 (1.22)	84 (1.89)
		DVT	11 (0.06)	6 (0.10)			< 5	< 5	29 (0.67)	52 (1.17)
		PE	14 (0.07)	< 5			< 5	< 5	27 (0.62)	39 (0.88)

Cohort	Time window	Outcome	AURUM		CORIVA		GOLD		SIDAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
		ATE	13 (0.07)	15 (0.25)			< 5	< 5	80 (1.85)	265 (5.95)
		IS	< 5	< 5			< 5	< 5	43 (0.99)	148 (3.32)
		TIA	7 (0.04)	5 (0.08)			< 5	< 5	19 (0.44)	72 (1.62)
		MI	7 (0.04)	10 (0.17)			< 5	< 5	21 (0.48)	62 (1.39)
		HF	19 (0.10)	24 (0.40)			< 5	< 5	101 (2.33)	438 (9.83)
		HS	< 5	< 5			< 5	< 5	7 (0.16)	33 (0.74)
		MP	< 5	< 5			< 5	< 5	7 (0.16)	< 5
	181 to 365 days	VTE	9 (0.05)	8 (0.13)			< 5	< 5	15 (0.35)	30 (0.67)
		DVT	< 5	< 5			< 5	< 5	9 (0.21)	20 (0.45)
		PE	7 (0.04)	7 (0.12)			< 5	< 5	8 (0.18)	12 (0.27)
		ATE	9 (0.05)	7 (0.12)			< 5	< 5	50 (1.15)	103 (2.31)
		IS	< 5	< 5			< 5	< 5	25 (0.58)	51 (1.14)
		TIA	< 5	< 5			< 5	< 5	16 (0.37)	29 (0.65)
		MI	7 (0.04)	< 5			< 5	< 5	11 (0.25)	29 (0.65)
		HF	22 (0.11)	12 (0.20)			< 5	< 5	63 (1.45)	178 (3.99)
		HS	< 5	< 5			< 5	< 5	5 (0.12)	9 (0.20)
		MP	< 5	< 5			< 5	< 5	< 5	< 5
Cohort 3			N = 1,510,323	N = 54,102			N = 416,549	N = 36,748	N = 869,109	N = 706,435
	0 to 30 days	VTE	244 (1.62)	< 5			28 (0.67)	< 5	321 (3.69)	114 (1.61)
		DVT	44 (0.29)	< 5			6 (0.14)	< 5	89 (1.02)	51 (0.72)
		PE	209 (1.38)	< 5			23 (0.55)	< 5	259 (2.98)	71 (1.01)
		ATE	29 (0.19)	< 5			< 5	< 5	211 (2.43)	197 (2.79)
		IS	< 5	< 5			< 5	< 5	102 (1.17)	95 (1.34)
		TIA	5 (0.03)	< 5			< 5	< 5	20 (0.23)	42 (0.59)
		MI	20 (0.13)	< 5			< 5	< 5	95 (1.09)	78 (1.10)
		HF	30 (0.20)	10 (1.85)			< 5	< 5	366 (4.21)	163 (2.31)
		HS	< 5	< 5			< 5	< 5	20 (0.23)	26 (0.37)
		MP	9 (0.06)	< 5			< 5	< 5	19 (0.22)	13 (0.18)
	31 to 90 days	VTE	41 (0.27)	< 5			< 5	< 5	80 (0.92)	63 (0.89)
		DVT	19 (0.13)	< 5			< 5	< 5	53 (0.61)	47 (0.67)
		PE	25 (0.17)	< 5			< 5	< 5	36 (0.41)	21 (0.30)
		ATE	11 (0.07)	< 5			< 5	< 5	106 (1.22)	142 (2.01)
		IS	< 5	< 5			< 5	< 5	53 (0.61)	54 (0.76)
		TIA	< 5	< 5			< 5	< 5	27 (0.31)	27 (0.38)

Cohort	Time window	Outcome	AURUM		CORIVA		GOLD		SIDAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
	91 to 180 days	MI	9 (0.06)	< 5			< 5	< 5	34 (0.39)	69 (0.98)
		HF	15 (0.10)	< 5			< 5	< 5	132 (1.52)	108 (1.53)
		HS	< 5	< 5			< 5	< 5	7 (0.08)	14 (0.20)
		MP	8 (0.05)	< 5			< 5	< 5	8 (0.09)	9 (0.13)
		VTE	23 (0.15)	< 5			< 5	< 5	56 (0.64)	67 (0.95)
		DVT	10 (0.07)	< 5			< 5	< 5	32 (0.37)	43 (0.61)
		PE	14 (0.09)	< 5			< 5	< 5	28 (0.32)	25 (0.35)
		ATE	< 5	< 5			< 5	< 5	101 (1.16)	137 (1.94)
		IS	< 5	< 5			< 5	< 5	49 (0.56)	62 (0.88)
		TIA	< 5	< 5			< 5	< 5	20 (0.23)	28 (0.40)
		MI	< 5	< 5			< 5	< 5	34 (0.39)	53 (0.75)
		HF	10 (0.07)	< 5			< 5	< 5	110 (1.27)	97 (1.37)
		HS	< 5	< 5			< 5	< 5	9 (0.10)	10 (0.14)
		MP	< 5	< 5			< 5	< 5	7 (0.08)	9 (0.13)
	181 to 365 days	VTE	< 5	< 5			< 5	< 5	33 (0.38)	13 (0.18)
	DVT	< 5	< 5			< 5	< 5	20 (0.23)	11 (0.16)	
	PE	< 5	< 5			< 5	< 5	15 (0.17)	< 5	
	ATE	< 5	< 5			< 5	< 5	39 (0.45)	36 (0.51)	
	IS	< 5	< 5			< 5	< 5	18 (0.21)	13 (0.18)	
	TIA	< 5	< 5			< 5	< 5	8 (0.09)	5 (0.07)	
	MI	< 5	< 5			< 5	< 5	14 (0.16)	21 (0.30)	
	HF	5 (0.03)	< 5			< 5	< 5	53 (0.61)	25 (0.35)	
	HS	< 5	< 5			< 5	< 5	< 5	< 5	
	MP	< 5	< 5			< 5	< 5	< 5	< 5	
Cohort 4			N = 2,014,161	N = 1,335,671	N = 147,553	N = 15,683	N = 465,326	N = 365,096	N = 1,068,043	N = 580,329
0 to 30 days	VTE	328 (1.63)	20 (0.15)	116 (7.86)	< 5	36 (0.77)	< 5	350 (3.28)	66 (1.14)	
	DVT	52 (0.26)	9 (0.07)	22 (1.49)	< 5	6 (0.13)	< 5	107 (1.00)	35 (0.60)	
	PE	287 (1.42)	11 (0.08)	97 (6.57)	< 5	31 (0.67)	< 5	271 (2.54)	35 (0.60)	
	ATE	25 (0.12)	< 5	116 (7.86)	< 5	< 5	< 5	233 (2.18)	55 (0.95)	
	IS	< 5	< 5	69 (4.68)	< 5	< 5	< 5	114 (1.07)	29 (0.50)	
	TIA	6 (0.03)	< 5	18 (1.22)	< 5	< 5	< 5	28 (0.26)	7 (0.12)	
	MI	15 (0.07)	< 5	38 (2.58)	< 5	< 5	< 5	97 (0.91)	20 (0.34)	
	HF	26 (0.13)	< 5	362 (24.53)	8 (5.10)	< 5	< 5	369 (3.45)	44 (0.76)	
	HS	< 5	< 5	5 (0.34)	< 5	< 5	< 5	24 (0.22)	7 (0.12)	

Cohort	Time window	Outcome	AURUM		CORIVA		GOLD		SIDAP	
			Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
31 to 90 days		MP	13 (0.06)	< 5	7 (0.47)	< 5	< 5	< 5	26 (0.24)	11 (0.19)
		VTE	53 (0.26)	7 (0.05)	49 (3.32)	< 5	< 5	< 5	88 (0.82)	32 (0.55)
		DVT	19 (0.09)	< 5	29 (1.97)	< 5	< 5	< 5	58 (0.54)	23 (0.40)
		PE	37 (0.18)	< 5	23 (1.56)	< 5	< 5	< 5	39 (0.37)	10 (0.17)
		ATE	13 (0.06)	< 5	43 (2.91)	< 5	< 5	< 5	114 (1.07)	51 (0.88)
		IS	< 5	< 5	22 (1.49)	< 5	< 5	< 5	51 (0.48)	21 (0.36)
		TIA	< 5	< 5	6 (0.41)	< 5	< 5	< 5	31 (0.29)	12 (0.21)
		MI	9 (0.04)	< 5	17 (1.15)	< 5	< 5	< 5	40 (0.37)	21 (0.36)
		HF	14 (0.07)	6 (0.04)	160 (10.84)	5 (3.19)	< 5	< 5	136 (1.27)	28 (0.48)
		HS	< 5	< 5	< 5	< 5	< 5	< 5	10 (0.09)	5 (0.09)
91 to 180 days		MP	7 (0.03)	< 5	< 5	< 5	< 5	< 5	12 (0.11)	8 (0.14)
		VTE	23 (0.11)	9 (0.07)	40 (2.71)	< 5	< 5	< 5	71 (0.66)	40 (0.69)
		DVT	10 (0.05)	7 (0.05)	25 (1.69)	< 5	< 5	< 5	40 (0.37)	25 (0.43)
		PE	14 (0.07)	< 5	16 (1.08)	< 5	< 5	< 5	34 (0.32)	18 (0.31)
		ATE	< 5	< 5	38 (2.58)	< 5	< 5	< 5	122 (1.14)	68 (1.17)
		IS	< 5	< 5	18 (1.22)	< 5	< 5	< 5	58 (0.54)	34 (0.59)
		TIA	< 5	< 5	12 (0.81)	< 5	< 5	< 5	28 (0.26)	14 (0.24)
		MI	< 5	< 5	12 (0.81)	< 5	< 5	< 5	38 (0.36)	20 (0.34)
		HF	9 (0.04)	< 5	187 (12.67)	< 5	< 5	< 5	132 (1.24)	35 (0.60)
		HS	< 5	< 5	< 5	< 5	< 5	< 5	14 (0.13)	< 5
181 to 365 days		MP	< 5	< 5	< 5	< 5	< 5	< 5	13 (0.12)	< 5
		VTE	< 5	< 5	53 (3.59)	< 5	< 5	< 5	44 (0.41)	7 (0.12)
		DVT	< 5	< 5	33 (2.24)	< 5	< 5	< 5	31 (0.29)	6 (0.10)
		PE	< 5	< 5	23 (1.56)	< 5	< 5	< 5	15 (0.14)	< 5
		ATE	< 5	< 5	63 (4.27)	< 5	< 5	< 5	41 (0.38)	9 (0.16)
		IS	< 5	< 5	29 (1.97)	< 5	< 5	< 5	20 (0.19)	6 (0.10)
		TIA	< 5	< 5	18 (1.22)	< 5	< 5	< 5	9 (0.08)	< 5
		MI	< 5	< 5	21 (1.42)	< 5	< 5	< 5	13 (0.12)	< 5
		HF	< 5	< 5	240 (16.27)	< 5	< 5	< 5	49 (0.46)	5 (0.09)
		HS	< 5	< 5	8 (0.54)	< 5	< 5	< 5	5 (0.05)	< 5
	MP	< 5	< 5	< 5	< 5	< 5	< 5	6 (0.06)	< 5	

VTE = Venous thromboembolism (DVT + PE), DVT = Deep vein thrombosis, PE = Pulmonary embolism, ATE = Arterial thrombosis/thromboembolism (IS + TIA + MI), IS = Ischemic stroke, TIA = Transient ischemic attack, MI = Myocardial infarction, HF = Heart failure, HS = Hemorrhagic stroke, MP = Myocarditis or Pericarditis

Table S34: Number of records (and risk per 10,000 individuals) for post COVID-19 cardiac and thromboembolic complications, across cohorts and databases, stratified by vaccine (BNT162b2 - ChAdOx1).

Cohort	Time window	Outcome	AURUM		GOLD	
			BNT162b2	ChAdOx1	BNT162b2	ChAdOx1
Cohort 1			N = 332,790	N = 219,804	N = 32,755	N = 82,406
	0 to 30 days	VTE	76 (2.28)	41 (1.87)	< 5	< 5
		DVT	15 (0.45)	12 (0.55)	< 5	< 5
		PE	64 (1.92)	31 (1.41)	< 5	< 5
		ATE	45 (1.35)	25 (1.14)	< 5	6 (0.73)
		IS	5 (0.15)	< 5	< 5	< 5
		TIA	11 (0.33)	7 (0.32)	< 5	< 5
		MI	29 (0.87)	17 (0.77)	< 5	< 5
		HF	126 (3.79)	72 (3.28)	< 5	5 (0.61)
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5
	31 to 90 days	VTE	26 (0.78)	14 (0.64)	< 5	< 5
		DVT	7 (0.21)	8 (0.36)	< 5	< 5
		PE	19 (0.57)	7 (0.32)	< 5	< 5
		ATE	23 (0.69)	20 (0.91)	< 5	< 5
		IS	< 5	< 5	< 5	< 5
		TIA	10 (0.30)	9 (0.41)	< 5	< 5
		MI	11 (0.33)	9 (0.41)	< 5	< 5
		HF	71 (2.13)	42 (1.91)	< 5	5 (0.61)
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5
	91 to 180 days	VTE	6 (0.18)	15 (0.68)	< 5	< 5
		DVT	< 5	5 (0.23)	< 5	< 5
		PE	< 5	10 (0.45)	< 5	< 5
		ATE	18 (0.54)	10 (0.45)	< 5	6 (0.73)
		IS	6 (0.18)	< 5	< 5	< 5
		TIA	6 (0.18)	6 (0.27)	< 5	< 5
		MI	6 (0.18)	< 5	< 5	5 (0.61)
		HF	57 (1.71)	38 (1.73)	< 5	< 5
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5

Cohort	Time window	Outcome	AURUM		GOLD	
			BNT162b2	ChAdOx1	BNT162b2	ChAdOx1
	181 to 365 days	VTE	10 (0.30)	< 5	< 5	< 5
		DVT	6 (0.18)	< 5	< 5	< 5
		PE	< 5	< 5	< 5	< 5
		ATE	14 (0.42)	9 (0.41)	< 5	< 5
		IS	< 5	< 5	< 5	< 5
		TIA	< 5	< 5	< 5	< 5
		MI	7 (0.21)	< 5	< 5	< 5
		HF	38 (1.14)	20 (0.91)	< 5	5 (0.61)
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5
Cohort 2			N = 594,262	N = 969,262	N = 180,670	N = 302,999
	0 to 30 days	VTE	62 (1.04)	158 (1.63)	5 (0.28)	19 (0.63)
		DVT	18 (0.30)	47 (0.48)	< 5	< 5
		PE	45 (0.76)	120 (1.24)	< 5	15 (0.50)
		ATE	29 (0.49)	75 (0.77)	< 5	< 5
		IS	< 5	12 (0.12)	< 5	< 5
		TIA	11 (0.19)	13 (0.13)	< 5	< 5
		MI	16 (0.27)	52 (0.54)	< 5	< 5
		HF	43 (0.72)	103 (1.06)	< 5	11 (0.36)
		HS	< 5	< 5	< 5	< 5
		MP	< 5	6 (0.06)	< 5	< 5
	31 to 90 days	VTE	21 (0.35)	55 (0.57)	< 5	9 (0.30)
		DVT	7 (0.12)	25 (0.26)	< 5	5 (0.17)
		PE	14 (0.24)	32 (0.33)	< 5	< 5
		ATE	36 (0.61)	57 (0.59)	< 5	5 (0.17)
		IS	5 (0.08)	6 (0.06)	< 5	< 5
		TIA	9 (0.15)	25 (0.26)	< 5	< 5
		MI	22 (0.37)	28 (0.29)	< 5	< 5
		HF	35 (0.59)	68 (0.70)	< 5	7 (0.23)
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5
	91 to 180 days	VTE	10 (0.17)	30 (0.31)	< 5	< 5
		DVT	6 (0.10)	16 (0.17)	< 5	< 5
		PE	5 (0.08)	16 (0.17)	< 5	< 5

Cohort	Time window	Outcome	AURUM		GOLD	
			BNT162b2	ChAdOx1	BNT162b2	ChAdOx1
		ATE	15 (0.25)	28 (0.29)	< 5	< 5
		IS	< 5	< 5	< 5	< 5
		TIA	5 (0.08)	13 (0.13)	< 5	< 5
		MI	10 (0.17)	15 (0.15)	< 5	< 5
		HF	25 (0.42)	44 (0.45)	< 5	< 5
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5
	181 to 365 days	VTE	8 (0.13)	5 (0.05)	< 5	< 5
		DVT	< 5	< 5	< 5	< 5
		PE	7 (0.12)	< 5	< 5	< 5
		ATE	7 (0.12)	11 (0.11)	< 5	< 5
		IS	< 5	< 5	< 5	< 5
		TIA	< 5	< 5	< 5	< 5
		MI	< 5	7 (0.07)	< 5	< 5
		HF	12 (0.20)	23 (0.24)	< 5	< 5
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5
Cohort 3			N = 54,102	N = 1,473,602	N = 36,748	N = 423,876
	0 to 30 days	VTE	< 5	139 (0.94)	< 5	16 (0.38)
		DVT	< 5	41 (0.28)	< 5	< 5
		PE	< 5	101 (0.69)	< 5	12 (0.28)
		ATE	< 5	47 (0.32)	< 5	12 (0.28)
		IS	< 5	5 (0.03)	< 5	< 5
		TIA	< 5	16 (0.11)	< 5	< 5
		MI	< 5	26 (0.18)	< 5	9 (0.21)
		HF	10 (1.85)	28 (0.19)	< 5	< 5
		HS	< 5	< 5	< 5	< 5
		MP	< 5	6 (0.04)	< 5	< 5
	31 to 90 days	VTE	< 5	44 (0.30)	< 5	7 (0.17)
		DVT	< 5	26 (0.18)	< 5	< 5
		PE	< 5	18 (0.12)	< 5	< 5
		ATE	< 5	31 (0.21)	< 5	7 (0.17)
		TIA	< 5	13 (0.09)	< 5	< 5

Cohort	Time window	Outcome	AURUM		GOLD		
			BNT162b2	ChAdOx1	BNT162b2	ChAdOx1	
	91 to 180 days	MI	< 5	16 (0.11)	< 5	< 5	
		HF	< 5	23 (0.16)	< 5	< 5	
		HS	< 5	< 5	< 5	< 5	
		MP	< 5	7 (0.05)	< 5	< 5	
		VTE	< 5	26 (0.18)	< 5	< 5	
		DVT	< 5	15 (0.10)	< 5	< 5	
		PE	< 5	14 (0.10)	< 5	< 5	
		ATE	< 5	26 (0.18)	< 5	< 5	
		IS	< 5	< 5	< 5	< 5	
		TIA	< 5	8 (0.05)	< 5	< 5	
		MI	< 5	17 (0.12)	< 5	< 5	
		HF	< 5	12 (0.08)	< 5	< 5	
		HS	< 5	< 5	< 5	< 5	
		MP	< 5	< 5	< 5	< 5	
	181 to 365 days	VTE	< 5	11 (0.07)	< 5	< 5	
	DVT	< 5	5 (0.03)	< 5	< 5		
	PE	< 5	7 (0.05)	< 5	< 5		
	ATE	< 5	< 5	< 5	< 5		
	IS	< 5	< 5	< 5	< 5		
	TIA	< 5	< 5	< 5	< 5		
	MI	< 5	< 5	< 5	< 5		
	HF	< 5	< 5	< 5	< 5		
	HS	< 5	< 5	< 5	< 5		
	MP	< 5	< 5	< 5	< 5		
	Cohort 4			N = 1,335,671	N = 542,670	N = 365,096	N = 147,744
	0 to 30 days	VTE	20 (0.15)	27 (0.50)	< 5	8 (0.54)	
DVT		9 (0.07)	7 (0.13)	< 5	< 5		
PE		11 (0.08)	21 (0.39)	< 5	6 (0.41)		
ATE		< 5	5 (0.09)	< 5	< 5		
IS		< 5	< 5	< 5	< 5		
TIA		< 5	< 5	< 5	< 5		
MI		< 5	< 5	< 5	< 5		
HF		< 5	< 5	< 5	< 5		
HS		< 5	< 5	< 5	< 5		

Cohort	Time window	Outcome	AURUM		GOLD	
			BNT162b2	ChAdOx1	BNT162b2	ChAdOx1
		MP	< 5	< 5	< 5	< 5
	31 to 90 days	VTE	7 (0.05)	14 (0.26)	< 5	< 5
		DVT	< 5	8 (0.15)	< 5	< 5
		PE	< 5	6 (0.11)	< 5	< 5
		ATE	< 5	< 5	< 5	< 5
		IS	< 5	< 5	< 5	< 5
		TIA	< 5	< 5	< 5	< 5
		MI	< 5	< 5	< 5	< 5
		HF	6 (0.04)	< 5	< 5	< 5
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5
		91 to 180 days	VTE	9 (0.07)	< 5	< 5
	DVT		7 (0.05)	< 5	< 5	< 5
	PE		< 5	< 5	< 5	< 5
	ATE		< 5	< 5	< 5	< 5
	IS		< 5	< 5	< 5	< 5
	TIA		< 5	< 5	< 5	< 5
	MI		< 5	< 5	< 5	< 5
	HF		< 5	< 5	< 5	< 5
	HS		< 5	< 5	< 5	< 5
	MP		< 5	< 5	< 5	< 5
	181 to 365 days		VTE	< 5	< 5	< 5
		DVT	< 5	< 5	< 5	< 5
		PE	< 5	< 5	< 5	< 5
		ATE	< 5	< 5	< 5	< 5
		IS	< 5	< 5	< 5	< 5
		TIA	< 5	< 5	< 5	< 5
		MI	< 5	< 5	< 5	< 5
		HF	< 5	< 5	< 5	< 5
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5

VTE = Venous thromboembolism (DVT + PE), DVT = Deep vein thrombosis, PE = Pulmonary embolism, ATE = Arterial thrombosis/thromboembolism (IS + TIA + MI), IS = Ischemic stroke, TIA = Transient ischemic attack, MI = Myocardial infarction, HF = Heart failure, HS = Hemorrhagic stroke, MP = Myocarditis or Pericarditis

Table S35: Number of records (and risk per 10,000 individuals) for post COVID-19 cardiac and thromboembolic complications, across cohorts and databases, stratified by vaccine (BNT162b2 - ChAdOx1). Follow-up ends at first vaccine dose after index date.

Cohort	Time window	Outcome	AURUM		GOLD	
			BNT162b2	ChAdOx1	BNT162b2	ChAdOx1
Cohort 1			N = 332,790	N = 219,804	N = 32,755	N = 82,406
	0 to 30 days	VTE	31 (0.93)	14 (0.64)	< 5	< 5
		DVT	8 (0.24)	< 5	< 5	< 5
		PE	24 (0.72)	13 (0.59)	< 5	< 5
		ATE	18 (0.54)	10 (0.45)	< 5	< 5
		IS	< 5	< 5	< 5	< 5
		TIA	< 5	< 5	< 5	< 5
		MI	14 (0.42)	6 (0.27)	< 5	< 5
		HF	45 (1.35)	28 (1.27)	< 5	< 5
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5
	31 to 90 days	VTE	15 (0.45)	5 (0.23)	< 5	< 5
		DVT	< 5	< 5	< 5	< 5
		PE	11 (0.33)	< 5	< 5	< 5
		ATE	8 (0.24)	8 (0.36)	< 5	< 5
		IS	< 5	< 5	< 5	< 5
		TIA	< 5	< 5	< 5	< 5
		MI	< 5	< 5	< 5	< 5
		HF	36 (1.08)	20 (0.91)	< 5	< 5
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5
	91 to 180 days	VTE	< 5	5 (0.23)	< 5	< 5
		DVT	< 5	< 5	< 5	< 5
		PE	< 5	< 5	< 5	< 5
		ATE	10 (0.30)	< 5	< 5	< 5
		IS	< 5	< 5	< 5	< 5
		TIA	< 5	< 5	< 5	< 5
		MI	< 5	< 5	< 5	< 5
		HF	32 (0.96)	19 (0.86)	< 5	< 5
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5

Cohort	Time window	Outcome	AURUM		GOLD	
			BNT162b2	ChAdOx1	BNT162b2	ChAdOx1
	181 to 365 days	VTE	7 (0.21)	< 5	< 5	< 5
		DVT	< 5	< 5	< 5	< 5
		PE	< 5	< 5	< 5	< 5
		ATE	11 (0.33)	8 (0.36)	< 5	< 5
		IS	< 5	< 5	< 5	< 5
		TIA	< 5	< 5	< 5	< 5
		MI	6 (0.18)	< 5	< 5	< 5
		HF	35 (1.05)	18 (0.82)	< 5	5 (0.61)
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5
Cohort 2			N = 594,262	N = 969,262	N = 180,670	N = 302,999
	0 to 30 days	VTE	14 (0.24)	40 (0.41)	< 5	< 5
		DVT	6 (0.10)	13 (0.13)	< 5	< 5
		PE	8 (0.13)	30 (0.31)	< 5	< 5
		ATE	14 (0.24)	11 (0.11)	< 5	< 5
		IS	< 5	< 5	< 5	< 5
		TIA	< 5	< 5	< 5	< 5
		MI	8 (0.13)	9 (0.09)	< 5	< 5
		HF	15 (0.25)	32 (0.33)	< 5	< 5
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5
	31 to 90 days	VTE	5 (0.08)	8 (0.08)	< 5	< 5
		DVT	< 5	5 (0.05)	< 5	< 5
		PE	< 5	< 5	< 5	< 5
		ATE	9 (0.15)	9 (0.09)	< 5	< 5
		IS	< 5	< 5	< 5	< 5
		TIA	< 5	< 5	< 5	< 5
		MI	< 5	6 (0.06)	< 5	< 5
		HF	17 (0.29)	13 (0.13)	< 5	< 5
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5
	91 to 180 days	VTE	< 5	12 (0.12)	< 5	< 5
		DVT	< 5	7 (0.07)	< 5	< 5
		PE	< 5	5 (0.05)	< 5	< 5

Cohort	Time window	Outcome	AURUM		GOLD	
			BNT162b2	ChAdOx1	BNT162b2	ChAdOx1
		ATE	5 (0.08)	10 (0.10)	< 5	< 5
		IS	< 5	< 5	< 5	< 5
		TIA	< 5	< 5	< 5	< 5
		MI	< 5	6 (0.06)	< 5	< 5
		HF	9 (0.15)	18 (0.19)	< 5	< 5
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5
	181 to 365 days	VTE	7 (0.12)	5 (0.05)	< 5	< 5
		DVT	< 5	< 5	< 5	< 5
		PE	5 (0.08)	< 5	< 5	< 5
		ATE	6 (0.10)	10 (0.10)	< 5	< 5
		IS	< 5	< 5	< 5	< 5
		TIA	< 5	< 5	< 5	< 5
		MI	< 5	6 (0.06)	< 5	< 5
		HF	11 (0.19)	20 (0.21)	< 5	< 5
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5
Cohort 3			N = 54,102	N = 1,473,602	N = 36,748	N = 423,876
	0 to 30 days	VTE	< 5	23 (0.16)	< 5	< 5
		DVT	< 5	< 5	< 5	< 5
		PE	< 5	19 (0.13)	< 5	< 5
		ATE	< 5	8 (0.05)	< 5	< 5
		IS	< 5	< 5	< 5	< 5
		TIA	< 5	< 5	< 5	< 5
		MI	< 5	7 (0.05)	< 5	< 5
		HF	7 (1.29)	11 (0.07)	< 5	< 5
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5
	31 to 90 days	VTE	< 5	< 5	< 5	< 5
		DVT	< 5	< 5	< 5	< 5
		PE	< 5	< 5	< 5	< 5
		ATE	< 5	6 (0.04)	< 5	< 5
		TIA	< 5	< 5	< 5	< 5

Cohort	Time window	Outcome	AURUM		GOLD	
			BNT162b2	ChAdOx1	BNT162b2	ChAdOx1
		MI	< 5	< 5	< 5	< 5
		HF	< 5	5 (0.03)	< 5	< 5
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5
	91 to 180 days	VTE	< 5	8 (0.05)	< 5	< 5
		DVT	< 5	6 (0.04)	< 5	< 5
		PE	< 5	< 5	< 5	< 5
		ATE	< 5	7 (0.05)	< 5	< 5
		IS	< 5	< 5	< 5	< 5
		TIA	< 5	< 5	< 5	< 5
		MI	< 5	< 5	< 5	< 5
		HF	< 5	< 5	< 5	< 5
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5
	181 to 365 days	VTE	< 5	9 (0.06)	< 5	< 5
		DVT	< 5	< 5	< 5	< 5
		PE	< 5	6 (0.04)	< 5	< 5
		ATE	< 5	< 5	< 5	< 5
		IS	< 5	< 5	< 5	< 5
		TIA	< 5	< 5	< 5	< 5
		MI	< 5	< 5	< 5	< 5
		HF	< 5	< 5	< 5	< 5
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5
Cohort 4		N = 1,335,671	N = 542,670	N = 365,096	N = 147,744	
0 to 30 days	VTE	9 (0.07)	8 (0.15)	< 5	6 (0.41)	
	DVT	5 (0.04)	< 5	< 5	< 5	
	PE	< 5	7 (0.13)	< 5	6 (0.41)	
	ATE	< 5	< 5	< 5	< 5	
	IS	< 5	< 5	< 5	< 5	
	TIA	< 5	< 5	< 5	< 5	
	MI	< 5	< 5	< 5	< 5	
	HF	< 5	< 5	< 5	< 5	
	HS	< 5	< 5	< 5	< 5	

Cohort	Time window	Outcome	AURUM		GOLD	
			BNT162b2	ChAdOx1	BNT162b2	ChAdOx1
		MP	< 5	< 5	< 5	< 5
	31 to 90 days	VTE	< 5	8 (0.15)	< 5	< 5
		DVT	< 5	< 5	< 5	< 5
		PE	< 5	5 (0.09)	< 5	< 5
		ATE	< 5	< 5	< 5	< 5
		IS	< 5	< 5	< 5	< 5
		TIA	< 5	< 5	< 5	< 5
		MI	< 5	< 5	< 5	< 5
		HF	6 (0.04)	< 5	< 5	< 5
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5
		91 to 180 days	VTE	8 (0.06)	< 5	< 5
	DVT		7 (0.05)	< 5	< 5	< 5
	PE		< 5	< 5	< 5	< 5
	ATE		< 5	< 5	< 5	< 5
	IS		< 5	< 5	< 5	< 5
	TIA		< 5	< 5	< 5	< 5
	MI		< 5	< 5	< 5	< 5
	HF		< 5	< 5	< 5	< 5
	HS		< 5	< 5	< 5	< 5
	MP		< 5	< 5	< 5	< 5
	181 to 365 days		VTE	< 5	< 5	< 5
		DVT	< 5	< 5	< 5	< 5
		PE	< 5	< 5	< 5	< 5
		ATE	< 5	< 5	< 5	< 5
		IS	< 5	< 5	< 5	< 5
		TIA	< 5	< 5	< 5	< 5
		MI	< 5	< 5	< 5	< 5
		HF	< 5	< 5	< 5	< 5
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5

VTE = Venous thromboembolism (DVT + PE), DVT = Deep vein thrombosis, PE = Pulmonary embolism, ATE = Arterial thrombosis/thromboembolism (IS + TIA + MI), IS = Ischemic stroke, TIA = Transient ischemic attack, MI = Myocardial infarction, HF = Heart failure, HS = Hemorrhagic stroke, MP = Myocarditis or Pericarditis

Table S36: Number of records (and risk per 10,000 individuals) for post COVID-19 cardiac and thromboembolic complications, across cohorts and databases, stratified by vaccine (BNT162b2 - ChAdOx1). Only first outcome after COVID-19 captured.

Cohort	Time window	Outcome	AURUM		GOLD	
			BNT162b2	ChAdOx1	BNT162b2	ChAdOx1
Cohort 1			N = 332,790	N = 219,804	N = 32,755	N = 82,406
	0 to 30 days	VTE	76 (2.28)	41 (1.87)	< 5	< 5
		DVT	15 (0.45)	12 (0.55)	< 5	< 5
		PE	64 (1.92)	31 (1.41)	< 5	< 5
		ATE	45 (1.35)	25 (1.14)	< 5	6 (0.73)
		IS	5 (0.15)	< 5	< 5	< 5
		TIA	11 (0.33)	7 (0.32)	< 5	< 5
		MI	29 (0.87)	17 (0.77)	< 5	< 5
		HF	126 (3.79)	72 (3.28)	< 5	5 (0.61)
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5
	31 to 90 days	VTE	25 (0.75)	14 (0.64)	< 5	< 5
		DVT	7 (0.21)	8 (0.36)	< 5	< 5
		PE	18 (0.54)	7 (0.32)	< 5	< 5
		ATE	23 (0.69)	20 (0.91)	< 5	< 5
		IS	< 5	< 5	< 5	< 5
		TIA	10 (0.30)	9 (0.41)	< 5	< 5
		MI	11 (0.33)	9 (0.41)	< 5	< 5
		HF	70 (2.10)	39 (1.77)	< 5	5 (0.61)
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5
	91 to 180 days	VTE	< 5	15 (0.68)	< 5	< 5
		DVT	< 5	5 (0.23)	< 5	< 5
		PE	< 5	10 (0.45)	< 5	< 5
		ATE	18 (0.54)	10 (0.45)	< 5	6 (0.73)
		IS	6 (0.18)	< 5	< 5	< 5
		TIA	6 (0.18)	6 (0.27)	< 5	< 5
		MI	6 (0.18)	< 5	< 5	5 (0.61)
		HF	54 (1.62)	35 (1.59)	< 5	< 5
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5

Cohort	Time window	Outcome	AURUM		GOLD	
			BNT162b2	ChAdOx1	BNT162b2	ChAdOx1
	181 to 365 days	VTE	10 (0.30)	< 5	< 5	< 5
		DVT	6 (0.18)	< 5	< 5	< 5
		PE	< 5	< 5	< 5	< 5
		ATE	14 (0.42)	9 (0.41)	< 5	< 5
		IS	< 5	< 5	< 5	< 5
		TIA	< 5	< 5	< 5	< 5
		MI	7 (0.21)	< 5	< 5	< 5
		HF	35 (1.05)	18 (0.82)	< 5	5 (0.61)
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5
Cohort 2			N = 594,262	N = 969,262	N = 180,670	N = 302,999
	0 to 30 days	VTE	62 (1.04)	158 (1.63)	5 (0.28)	19 (0.63)
		DVT	18 (0.30)	47 (0.48)	< 5	< 5
		PE	45 (0.76)	120 (1.24)	< 5	15 (0.50)
		ATE	29 (0.49)	75 (0.77)	< 5	< 5
		IS	< 5	12 (0.12)	< 5	< 5
		TIA	11 (0.19)	13 (0.13)	< 5	< 5
		MI	16 (0.27)	52 (0.54)	< 5	< 5
		HF	43 (0.72)	103 (1.06)	< 5	11 (0.36)
		HS	< 5	< 5	< 5	< 5
		MP	< 5	6 (0.06)	< 5	< 5
	31 to 90 days	VTE	21 (0.35)	54 (0.56)	< 5	9 (0.30)
		DVT	7 (0.12)	25 (0.26)	< 5	5 (0.17)
		PE	14 (0.24)	31 (0.32)	< 5	< 5
		ATE	36 (0.61)	56 (0.58)	< 5	5 (0.17)
		IS	5 (0.08)	6 (0.06)	< 5	< 5
		TIA	9 (0.15)	24 (0.25)	< 5	< 5
		MI	22 (0.37)	28 (0.29)	< 5	< 5
		HF	34 (0.57)	65 (0.67)	< 5	7 (0.23)
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5
	91 to 180 days	VTE	9 (0.15)	28 (0.29)	< 5	< 5
		DVT	6 (0.10)	15 (0.15)	< 5	< 5
		PE	< 5	15 (0.15)	< 5	< 5

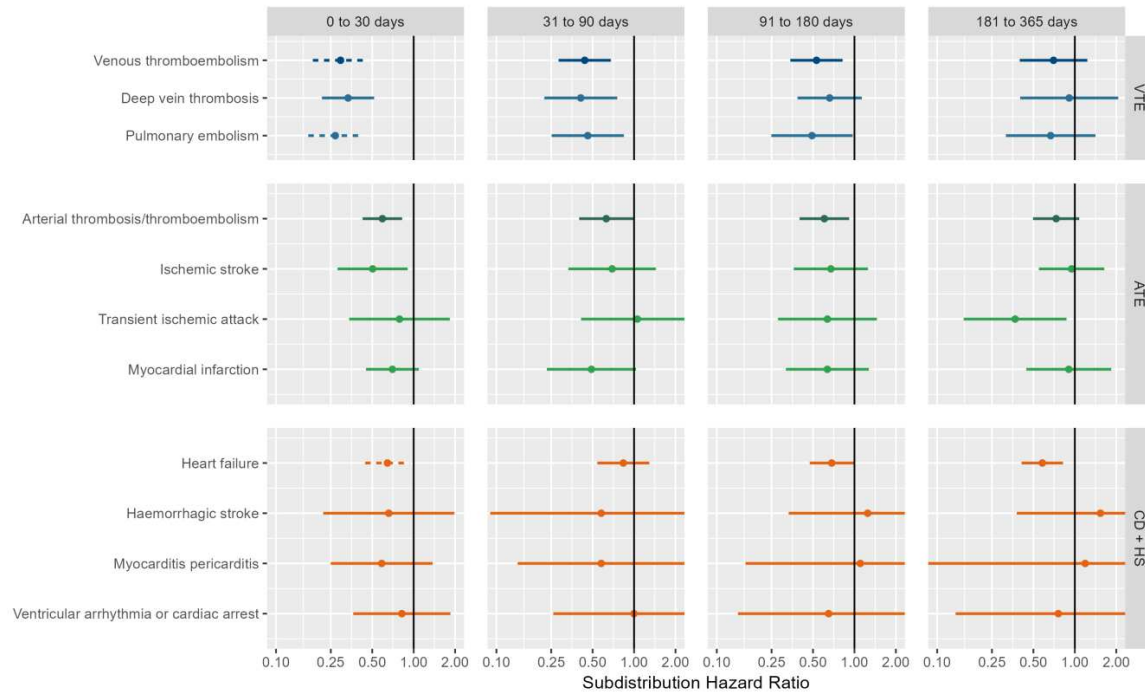
Cohort	Time window	Outcome	AURUM		GOLD	
			BNT162b2	ChAdOx1	BNT162b2	ChAdOx1
		ATE	15 (0.25)	28 (0.29)	< 5	< 5
		IS	< 5	< 5	< 5	< 5
		TIA	5 (0.08)	13 (0.13)	< 5	< 5
		MI	10 (0.17)	15 (0.15)	< 5	< 5
		HF	24 (0.40)	41 (0.42)	< 5	< 5
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5
	181 to 365 days	VTE	8 (0.13)	< 5	< 5	< 5
		DVT	< 5	< 5	< 5	< 5
		PE	7 (0.12)	< 5	< 5	< 5
		ATE	7 (0.12)	10 (0.10)	< 5	< 5
		IS	< 5	< 5	< 5	< 5
		TIA	< 5	< 5	< 5	< 5
		MI	< 5	6 (0.06)	< 5	< 5
		HF	12 (0.20)	22 (0.23)	< 5	< 5
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5
Cohort 3			N = 54,102	N = 1,473,602	N = 36,748	N = 423,876
	0 to 30 days	VTE	< 5	139 (0.94)	< 5	16 (0.38)
		DVT	< 5	41 (0.28)	< 5	< 5
		PE	< 5	101 (0.69)	< 5	12 (0.28)
		ATE	< 5	47 (0.32)	< 5	12 (0.28)
		IS	< 5	5 (0.03)	< 5	< 5
		TIA	< 5	16 (0.11)	< 5	< 5
		MI	< 5	26 (0.18)	< 5	9 (0.21)
		HF	10 (1.85)	28 (0.19)	< 5	< 5
		HS	< 5	< 5	< 5	< 5
		MP	< 5	6 (0.04)	< 5	< 5
	31 to 90 days	VTE	< 5	44 (0.30)	< 5	6 (0.14)
		DVT	< 5	26 (0.18)	< 5	< 5
		PE	< 5	18 (0.12)	< 5	< 5
		ATE	< 5	31 (0.21)	< 5	7 (0.17)
		TIA	< 5	13 (0.09)	< 5	< 5

Cohort	Time window	Outcome	AURUM		GOLD		
			BNT162b2	ChAdOx1	BNT162b2	ChAdOx1	
		MI	< 5	16 (0.11)	< 5	< 5	
		HF	< 5	23 (0.16)	< 5	< 5	
		HS	< 5	< 5	< 5	< 5	
		MP	< 5	7 (0.05)	< 5	< 5	
	91 to 180 days	VTE	< 5	25 (0.17)	< 5	< 5	
		DVT	< 5	15 (0.10)	< 5	< 5	
		PE	< 5	13 (0.09)	< 5	< 5	
		ATE	< 5	26 (0.18)	< 5	< 5	
		IS	< 5	< 5	< 5	< 5	
		TIA	< 5	8 (0.05)	< 5	< 5	
		MI	< 5	17 (0.12)	< 5	< 5	
		HF	< 5	10 (0.07)	< 5	< 5	
		HS	< 5	< 5	< 5	< 5	
		MP	< 5	< 5	< 5	< 5	
		181 to 365 days	VTE	< 5	9 (0.06)	< 5	< 5
			DVT	< 5	< 5	< 5	< 5
	PE		< 5	6 (0.04)	< 5	< 5	
	ATE		< 5	< 5	< 5	< 5	
	IS		< 5	< 5	< 5	< 5	
	TIA		< 5	< 5	< 5	< 5	
	MI		< 5	< 5	< 5	< 5	
	HF		< 5	< 5	< 5	< 5	
	HS		< 5	< 5	< 5	< 5	
	MP		< 5	< 5	< 5	< 5	
	Cohort 4		N = 1,335,671	N = 542,670	N = 365,096	N = 147,744	
	0 to 30 days	VTE	20 (0.15)	27 (0.50)	< 5	8 (0.54)	
DVT		9 (0.07)	7 (0.13)	< 5	< 5		
PE		11 (0.08)	21 (0.39)	< 5	6 (0.41)		
ATE		< 5	5 (0.09)	< 5	< 5		
IS		< 5	< 5	< 5	< 5		
TIA		< 5	< 5	< 5	< 5		
MI		< 5	< 5	< 5	< 5		
HF		< 5	< 5	< 5	< 5		
HS		< 5	< 5	< 5	< 5		

Cohort	Time window	Outcome	AURUM		GOLD	
			BNT162b2	ChAdOx1	BNT162b2	ChAdOx1
		MP	< 5	< 5	< 5	< 5
	31 to 90 days	VTE	7 (0.05)	14 (0.26)	< 5	< 5
		DVT	< 5	8 (0.15)	< 5	< 5
		PE	< 5	6 (0.11)	< 5	< 5
		ATE	< 5	< 5	< 5	< 5
		IS	< 5	< 5	< 5	< 5
		TIA	< 5	< 5	< 5	< 5
		MI	< 5	< 5	< 5	< 5
		HF	6 (0.04)	< 5	< 5	< 5
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5
		91 to 180 days	VTE	9 (0.07)	< 5	< 5
	DVT		7 (0.05)	< 5	< 5	< 5
	PE		< 5	< 5	< 5	< 5
	ATE		< 5	< 5	< 5	< 5
	IS		< 5	< 5	< 5	< 5
	TIA		< 5	< 5	< 5	< 5
	MI		< 5	< 5	< 5	< 5
	HF		< 5	< 5	< 5	< 5
	HS		< 5	< 5	< 5	< 5
	MP		< 5	< 5	< 5	< 5
	181 to 365 days		VTE	< 5	< 5	< 5
		DVT	< 5	< 5	< 5	< 5
		PE	< 5	< 5	< 5	< 5
		ATE	< 5	< 5	< 5	< 5
		IS	< 5	< 5	< 5	< 5
		TIA	< 5	< 5	< 5	< 5
		MI	< 5	< 5	< 5	< 5
		HF	< 5	< 5	< 5	< 5
		HS	< 5	< 5	< 5	< 5
		MP	< 5	< 5	< 5	< 5

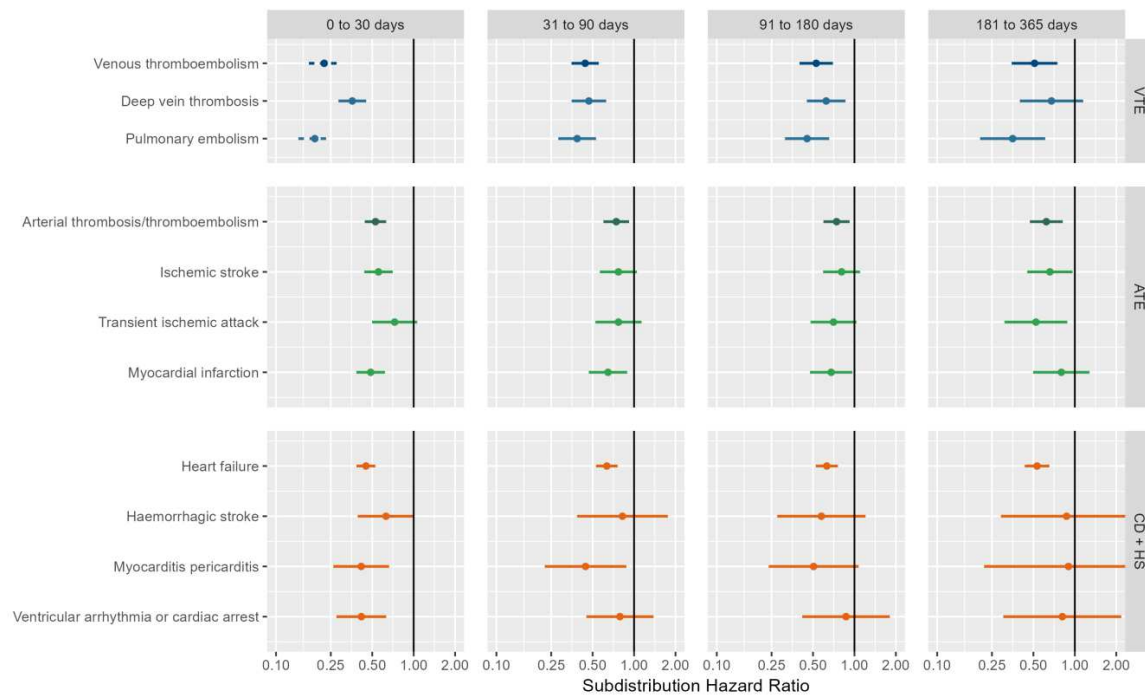
VTE = Venous thromboembolism (DVT + PE), DVT = Deep vein thrombosis, PE = Pulmonary embolism, ATE = Arterial thrombosis/thromboembolism (IS + TIA + MI), IS = Ischemic stroke, TIA = Transient ischemic attack, MI = Myocardial infarction, HF = Heart failure, HS = Hemorrhagic stroke, MP = Myocarditis or Pericarditis

Figure S6: Forest plots for vaccine effect (any COVID-19 vaccine), meta-analysis across cohorts and databases. Follow-up ends at first vaccine dose after index date. Dashed line represents a level of heterogeneity $I^2 > 0.4$.



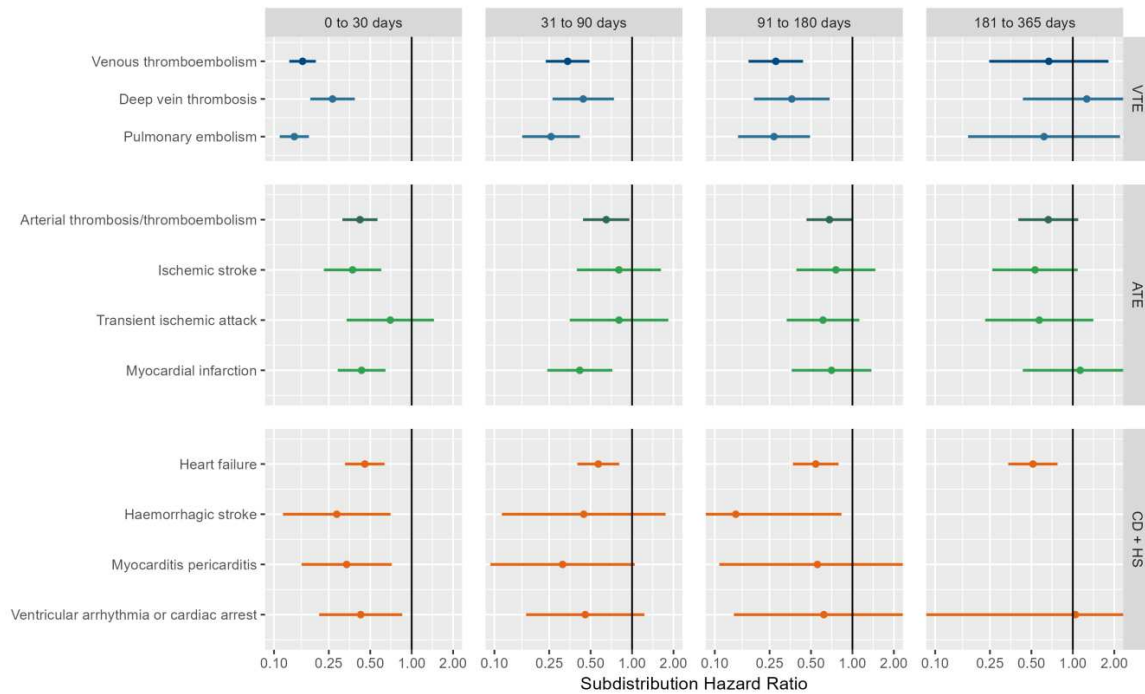
VTE = Venous thromboembolism, ATE = Arterial thrombosis/thromboembolism, CD + HS = Cardiac diseases and Hemorrhagic stroke

Figure S7: Forest plots for vaccine effect (any COVID-19 vaccine), meta-analysis across cohorts and databases. Only first outcome after COVID-19 captured. Dashed line represents a level of heterogeneity $I^2 > 0.4$.



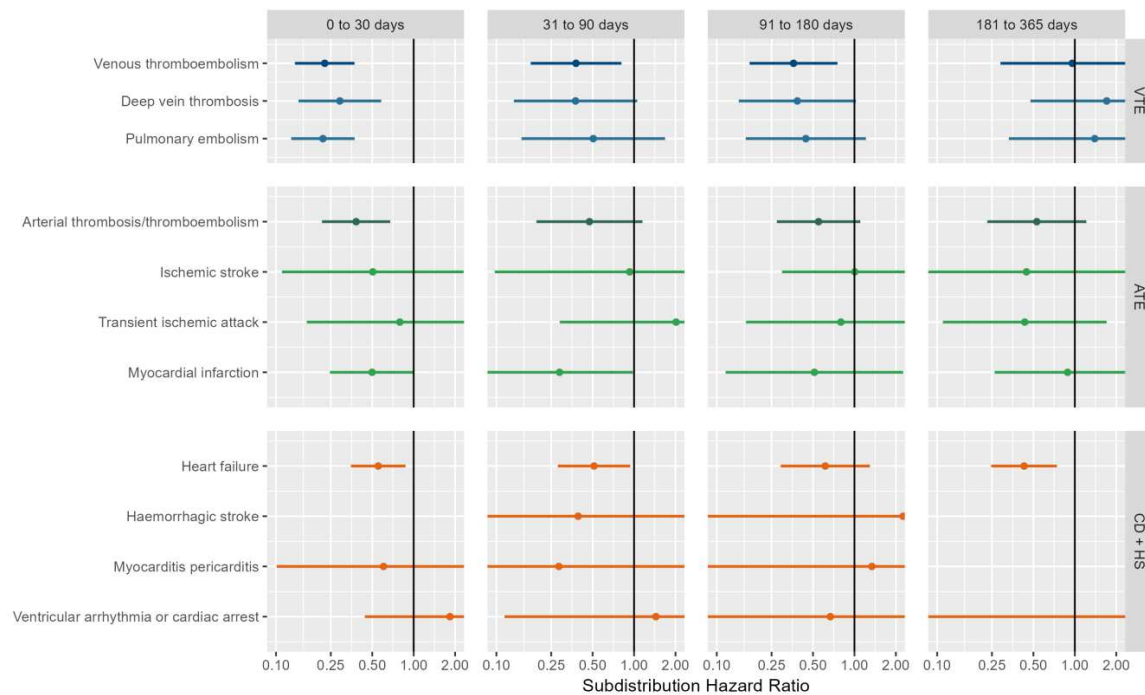
VTE = Venous thromboembolism, ATE = Arterial thrombosis/thromboembolism, CD + HS = Cardiac diseases and Hemorrhagic stroke

Figure S8: Forest plots for vaccine effect (ChAdOx1 vaccine), meta-analysis across cohorts and databases. Dashed line represents a level of heterogeneity $I^2 > 0.4$.



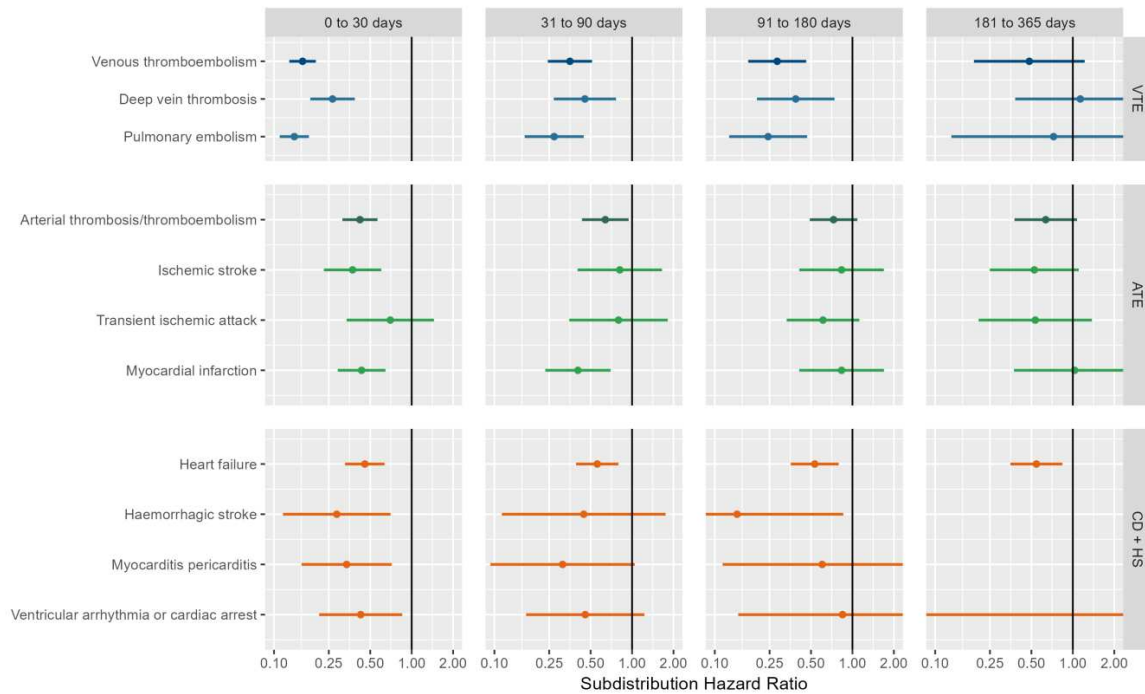
VTE = Venous thromboembolism, ATE = Arterial thrombosis/thromboembolism, CD + HS = Cardiac diseases and Hemorrhagic stroke

Figure S9: Forest plots for vaccine effect (ChAdOx1 vaccine), meta-analysis across cohorts and databases. Follow-up ends at first vaccine dose after index date. Dashed line represents a level of heterogeneity $I^2 > 0.4$.



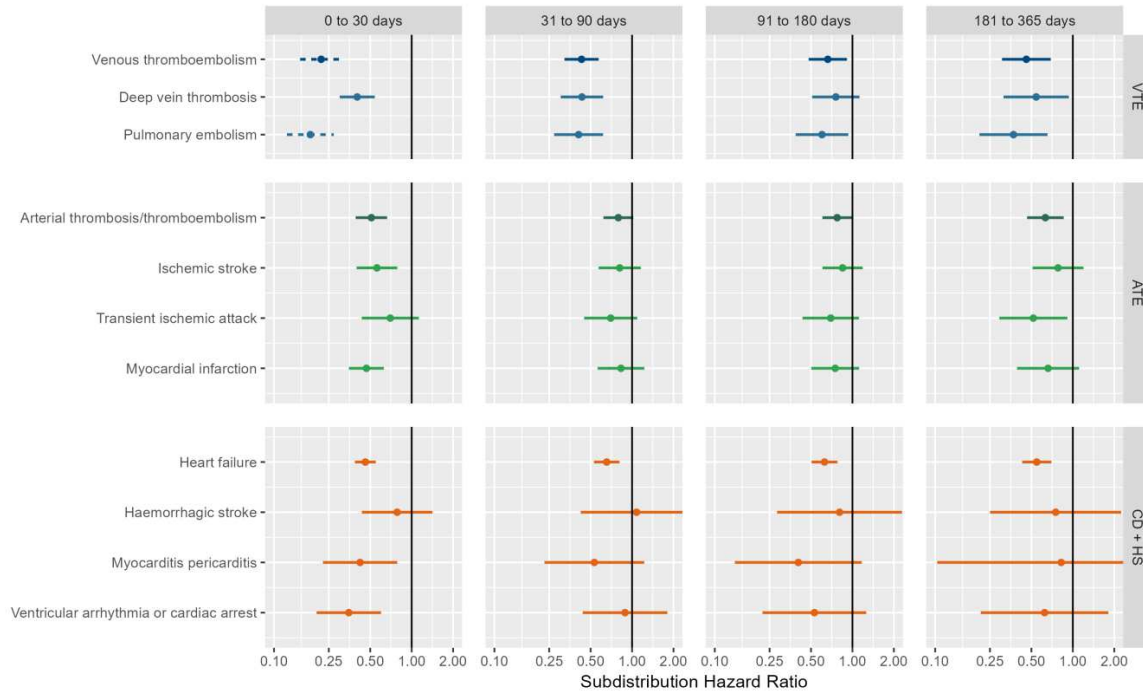
VTE = Venous thromboembolism, ATE = Arterial thrombosis/thromboembolism, CD + HS = Cardiac diseases and Hemorrhagic stroke

Figure S10: Forest plots for vaccine effect (ChAdOx1 vaccine), meta-analysis across cohorts and databases. Only first outcome after COVID-19 captured. Dashed line represents a level of heterogeneity $I^2 > 0.4$.



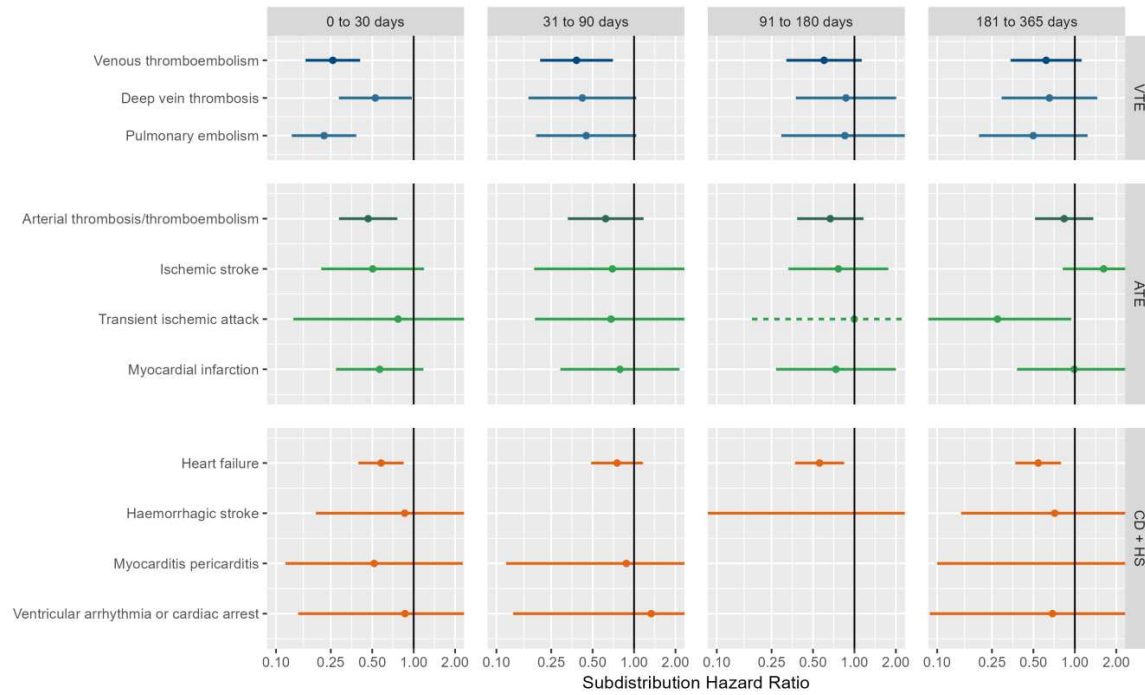
VTE = Venous thromboembolism, ATE = Arterial thrombosis/thromboembolism, CD + HS = Cardiac diseases and Hemorrhagic stroke

Figure S11: Forest plots for vaccine effect (BNT162b2 vaccine), meta-analysis across cohorts and databases. Dashed line represents a level of heterogeneity $I^2 > 0.4$.



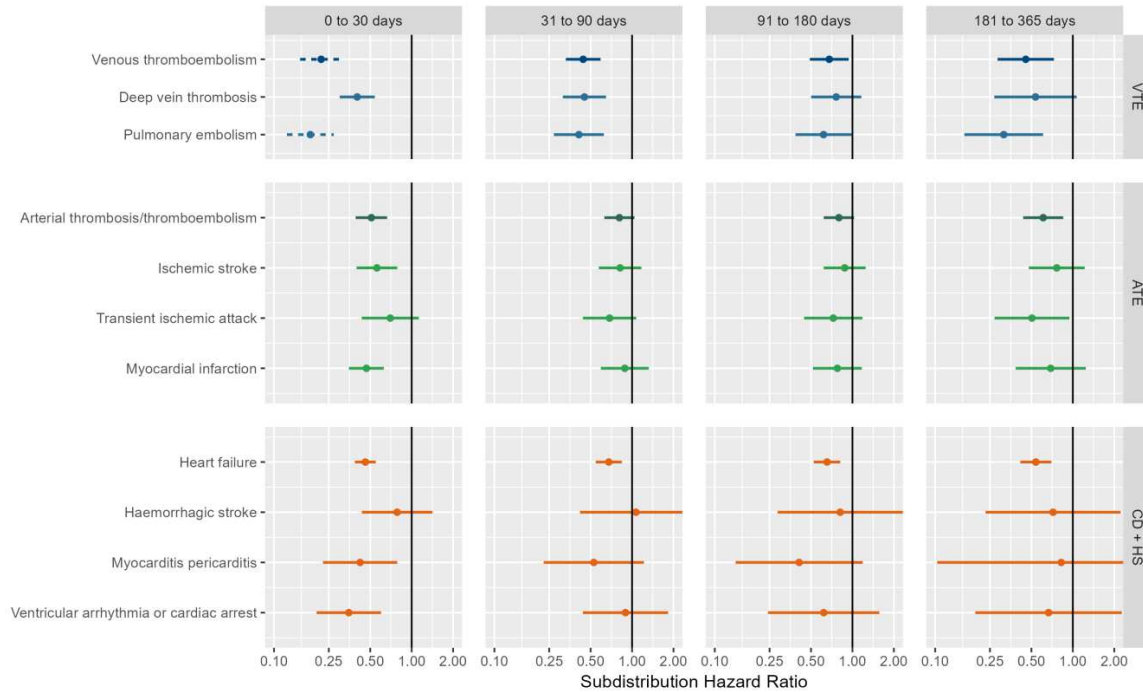
VTE = Venous thromboembolism, ATE = Arterial thrombosis/thromboembolism, CD + HS = Cardiac diseases and Hemorrhagic stroke

Figure S12: Forest plots for vaccine effect (BNT162b2 vaccine), meta-analysis across cohorts and databases. Follow-up ends at first vaccine dose after index date. Dashed line represents a level of heterogeneity $I^2 > 0.4$.



VTE = Venous thromboembolism, ATE = Arterial thrombosis/thromboembolism, CD + HS = Cardiac diseases and Hemorrhagic stroke

Figure S13: Forest plots for vaccine effect (BNT162b2 vaccine), meta-analysis across cohorts and databases. Only first outcome after COVID-19 captured. Dashed line represents a level of heterogeneity $I^2 > 0.4$.



VTE = Venous thromboembolism, ATE = Arterial thrombosis/thromboembolism, CD + HS = Cardiac diseases and Hemorrhagic stroke

Figure S14: Forest plots for vaccine effect (any COVID-19 vaccine) on preventing venous thromboembolism complications, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Dashed line represents a level of heterogeneity $I^2 > 0.4$.

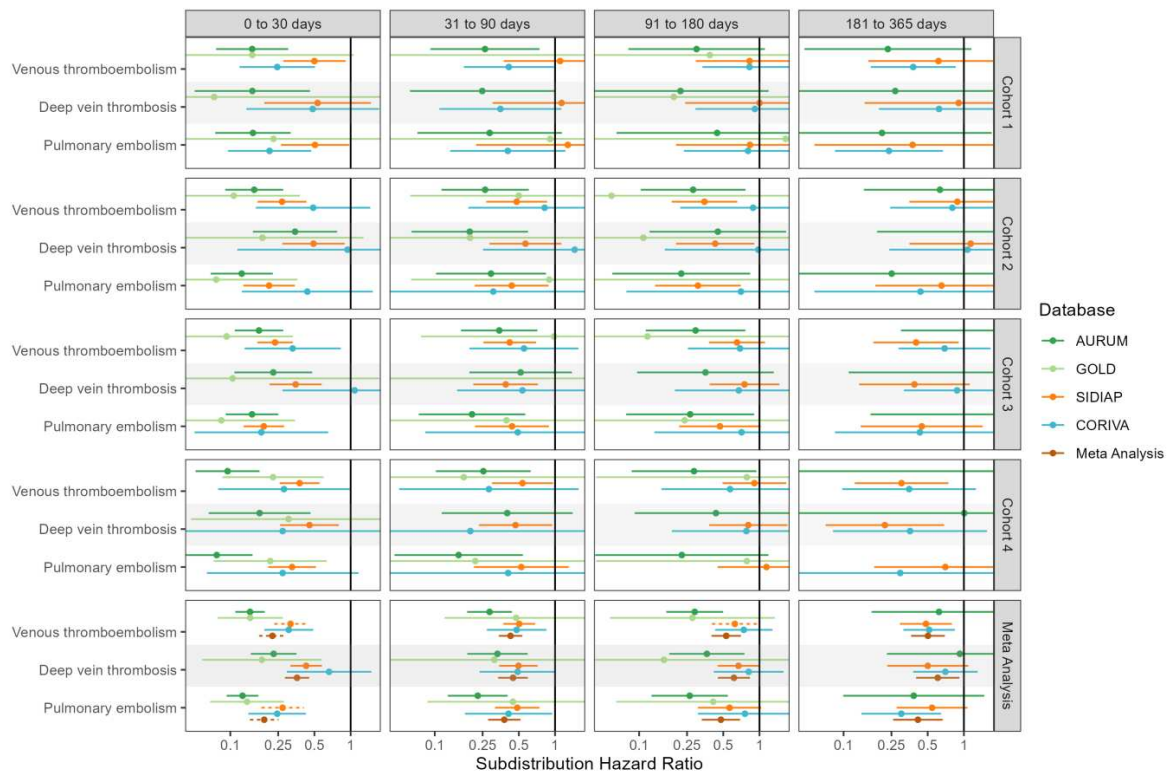


Figure S15: Forest plots for vaccine effect (any COVID-19 vaccine) on preventing venous thromboembolism complications, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Follow-up ends at first vaccine dose after index date. Dashed line represents a level of heterogeneity $I^2 > 0.4$.

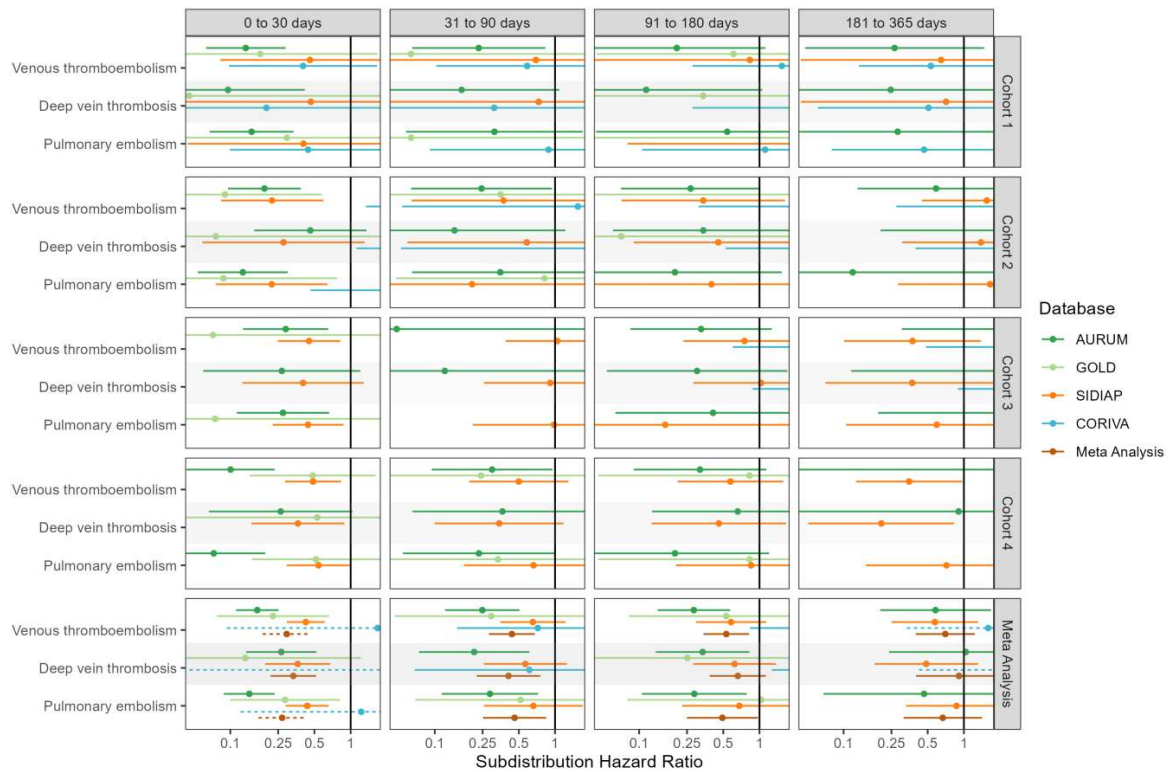


Figure S16: Forest plots for vaccine effect (any COVID-19 vaccine) on preventing venous thromboembolism complications, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Only first outcome after COVID-19 captured. Dashed line represents a level of heterogeneity $I^2 > 0.4$.

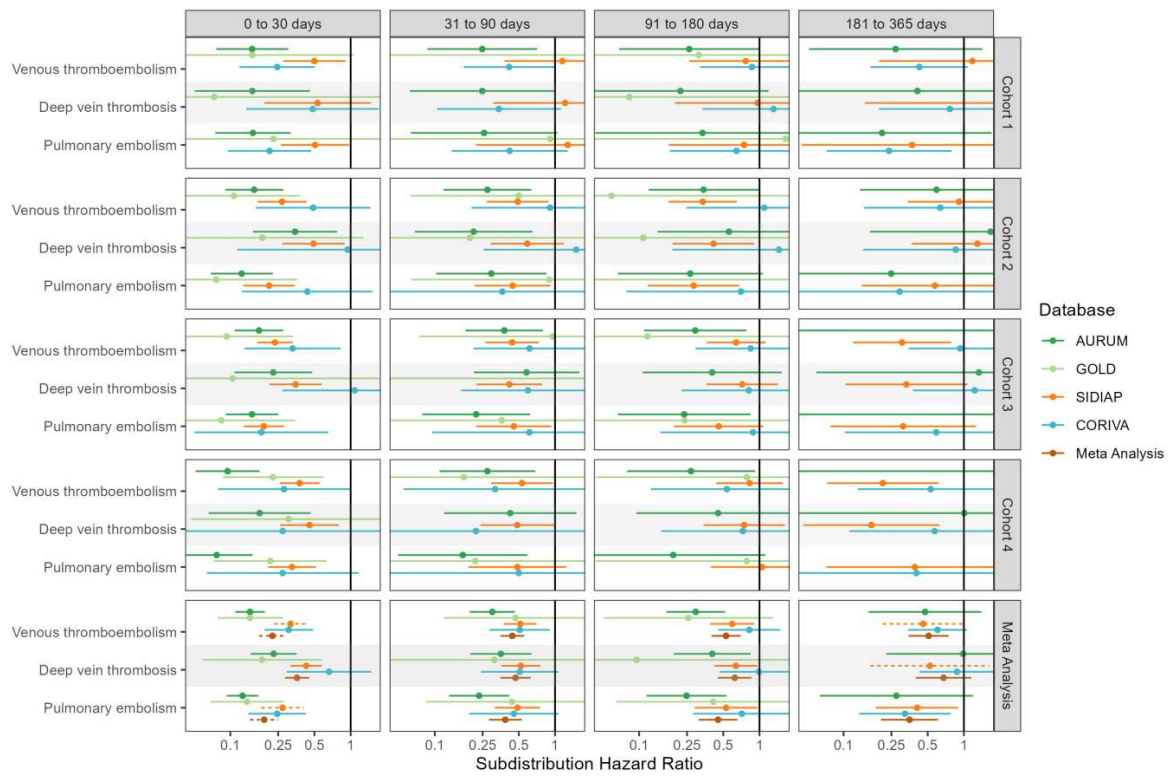


Figure S17: Forest plots for vaccine effect (ChAdOx1 vaccine) on preventing venous thromboembolism complications, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Dashed line represents a level of heterogeneity $I^2 > 0.4$.

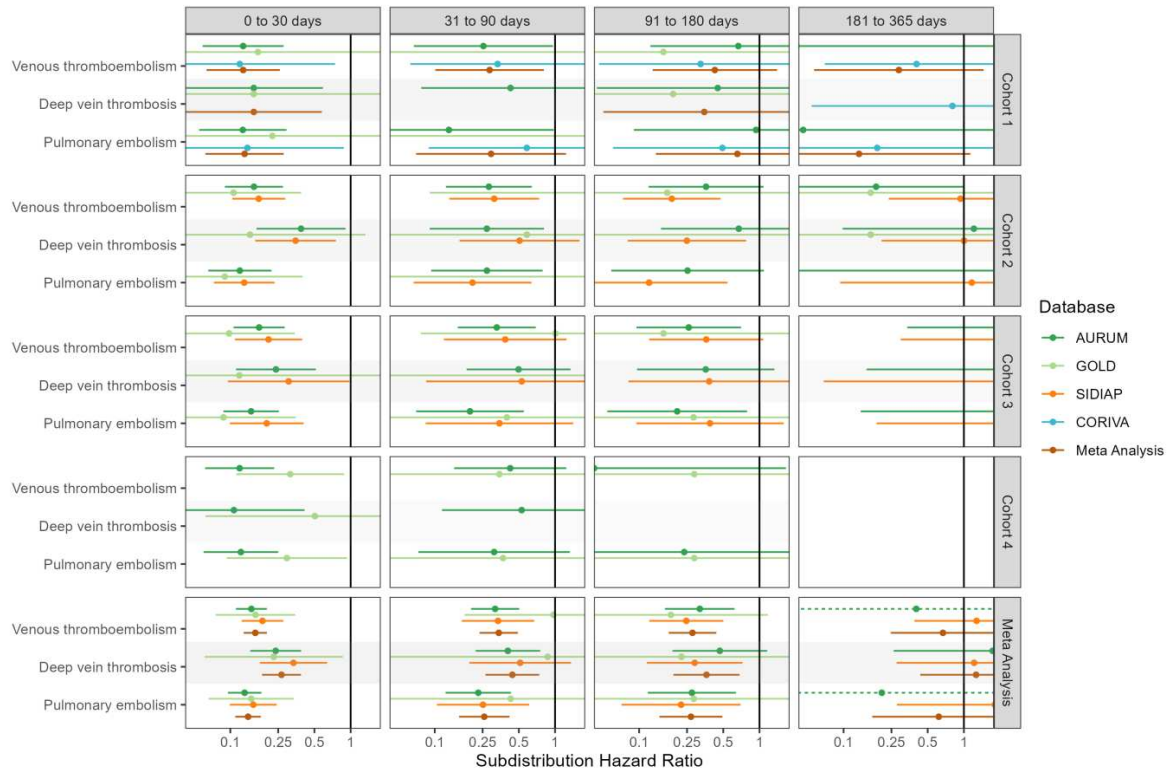


Figure S18: Forest plots for vaccine effect (ChAdOx1 vaccine) on preventing venous thromboembolism complications, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Follow-up ends at first vaccine dose after index date. Dashed line represents a level of heterogeneity $I^2 > 0.4$.

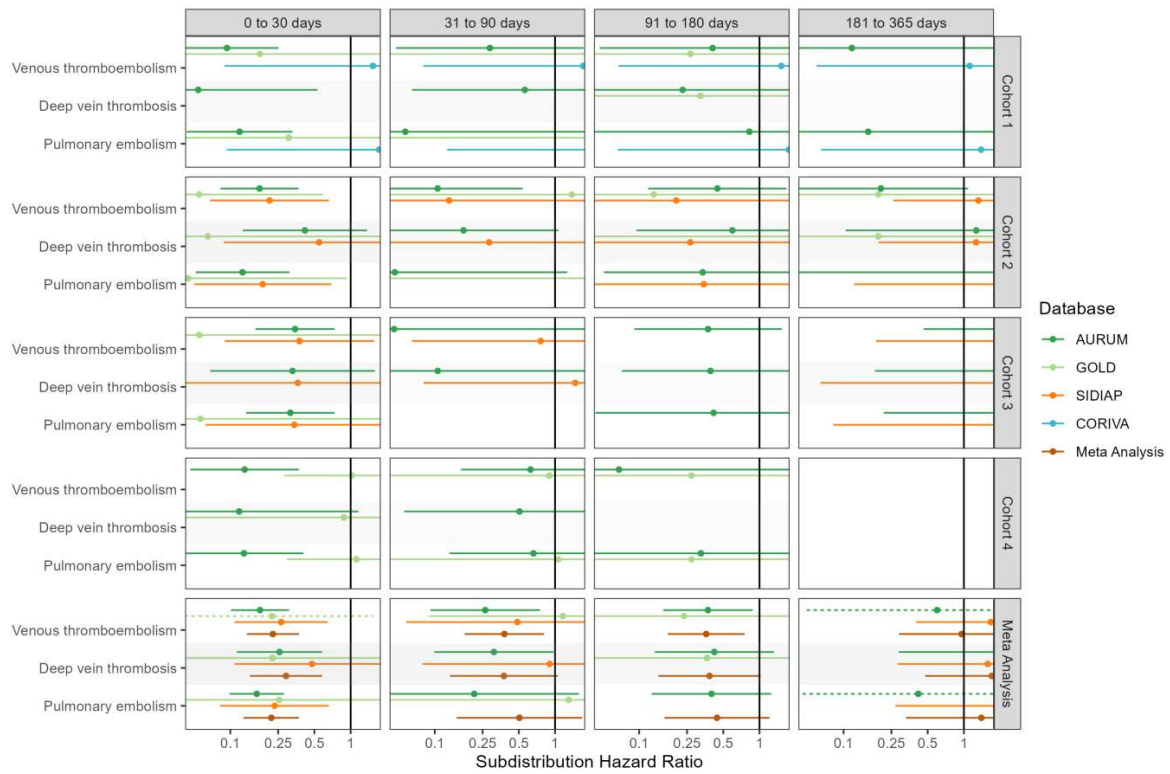


Figure S19: Forest plots for vaccine effect (ChAdOx1 vaccine) on preventing venous thromboembolism complications, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Only first outcome after COVID-19 captured. Dashed line represents a level of heterogeneity $I^2 > 0.4$.

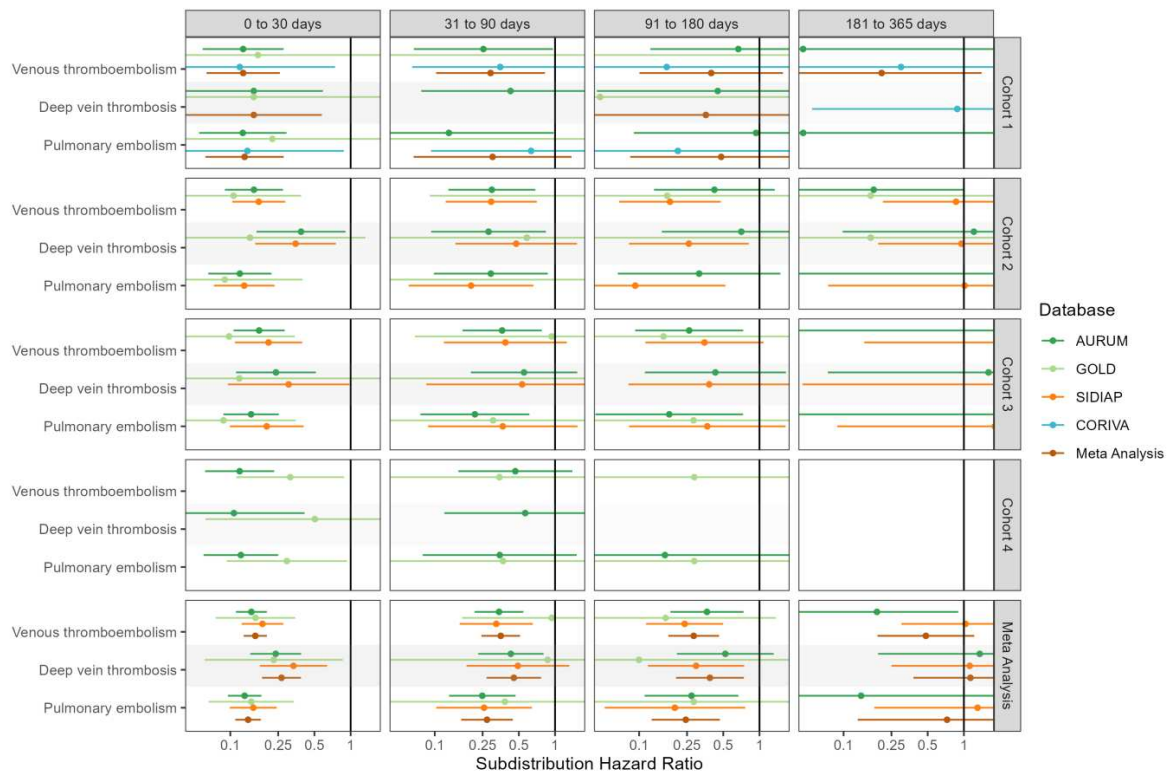


Figure S20: Forest plots for vaccine effect (BNT162b2 vaccine) on preventing venous thromboembolism complications, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Dashed line represents a level of heterogeneity $I^2 > 0.4$.

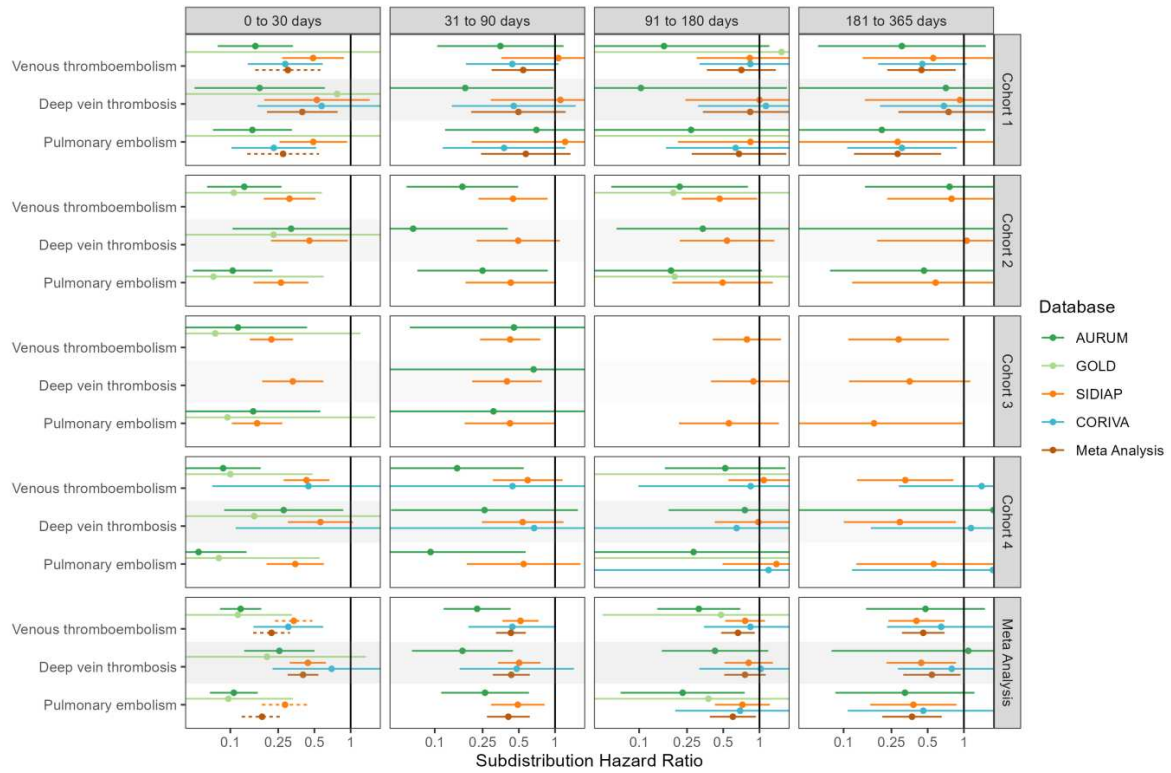


Figure S21: Forest plots for vaccine effect (BNT162b2 vaccine) on preventing venous thromboembolism complications, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Follow-up ends at first vaccine dose after index date. Dashed line represents a level of heterogeneity $I^2 > 0.4$.

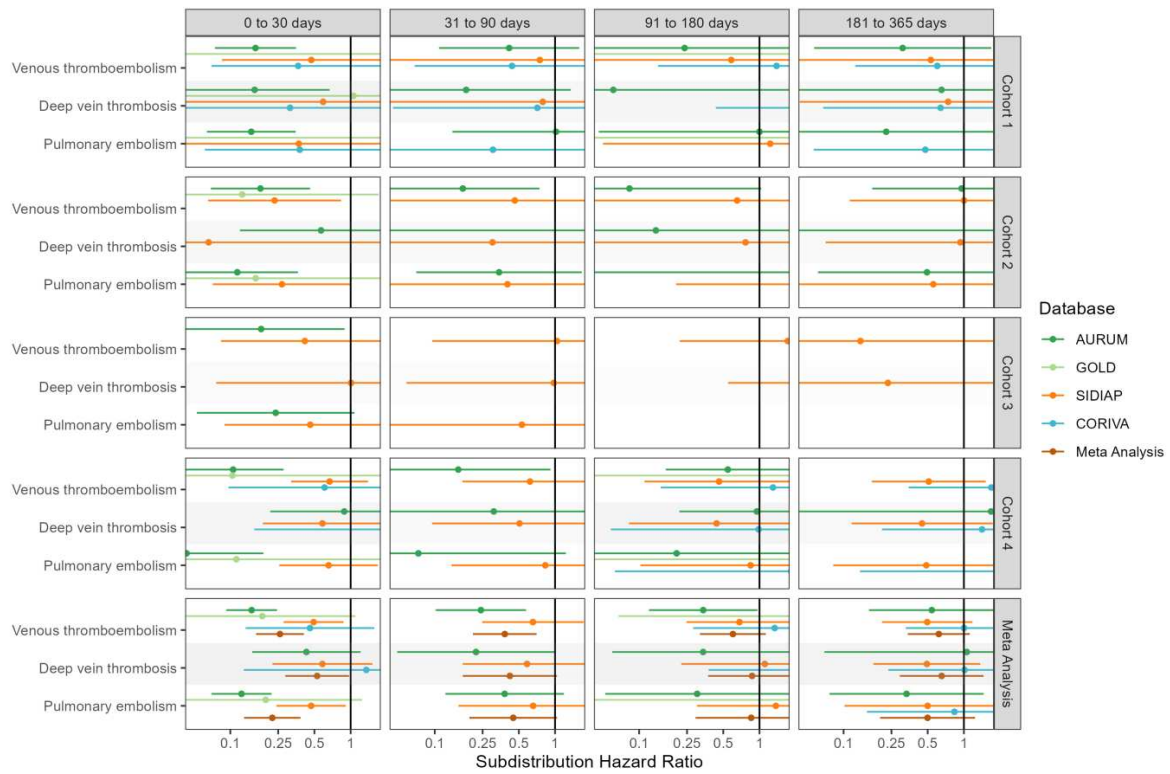


Figure S22: Forest plots for vaccine effect (BNT162b2 vaccine) on preventing venous thromboembolism complications, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Only first outcome after COVID-19 captured. Dashed line represents a level of heterogeneity $I^2 > 0.4$.

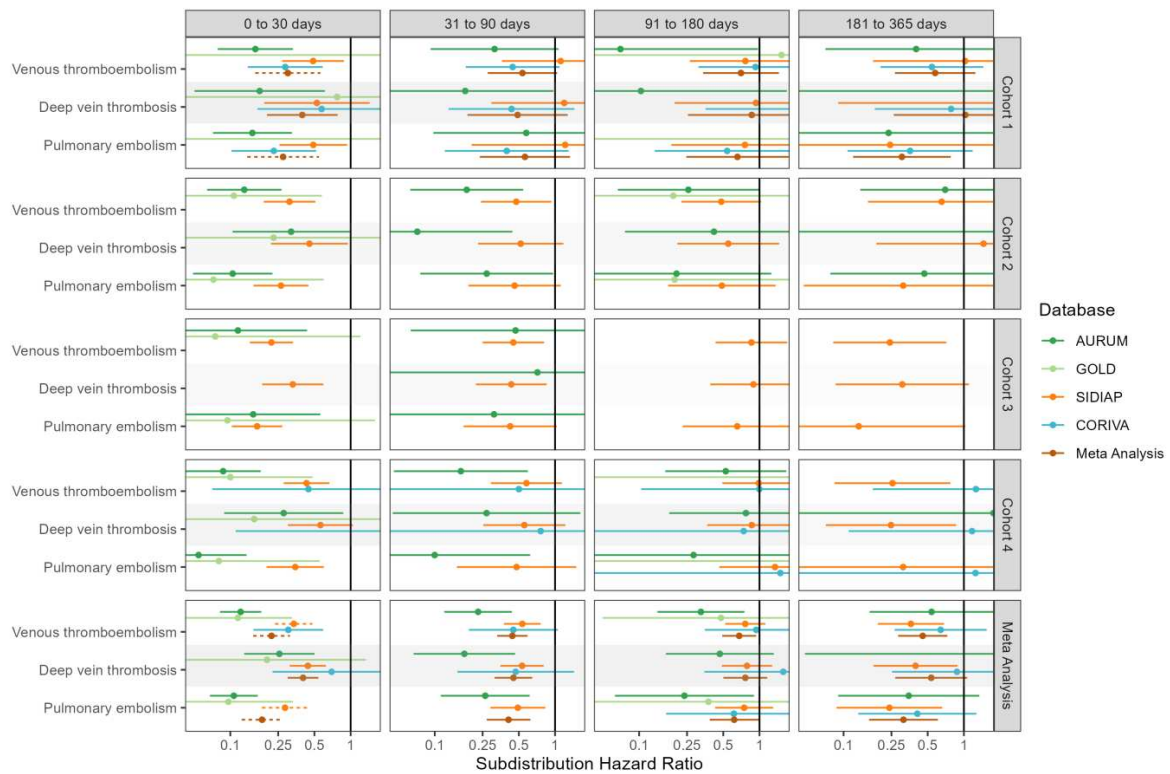


Figure S23: Forest plots for vaccine effect (any COVID-19 vaccine) on preventing arterial thrombosis/thromboembolism complications, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Dashed line represents a level of heterogeneity $I^2 > 0.4$.

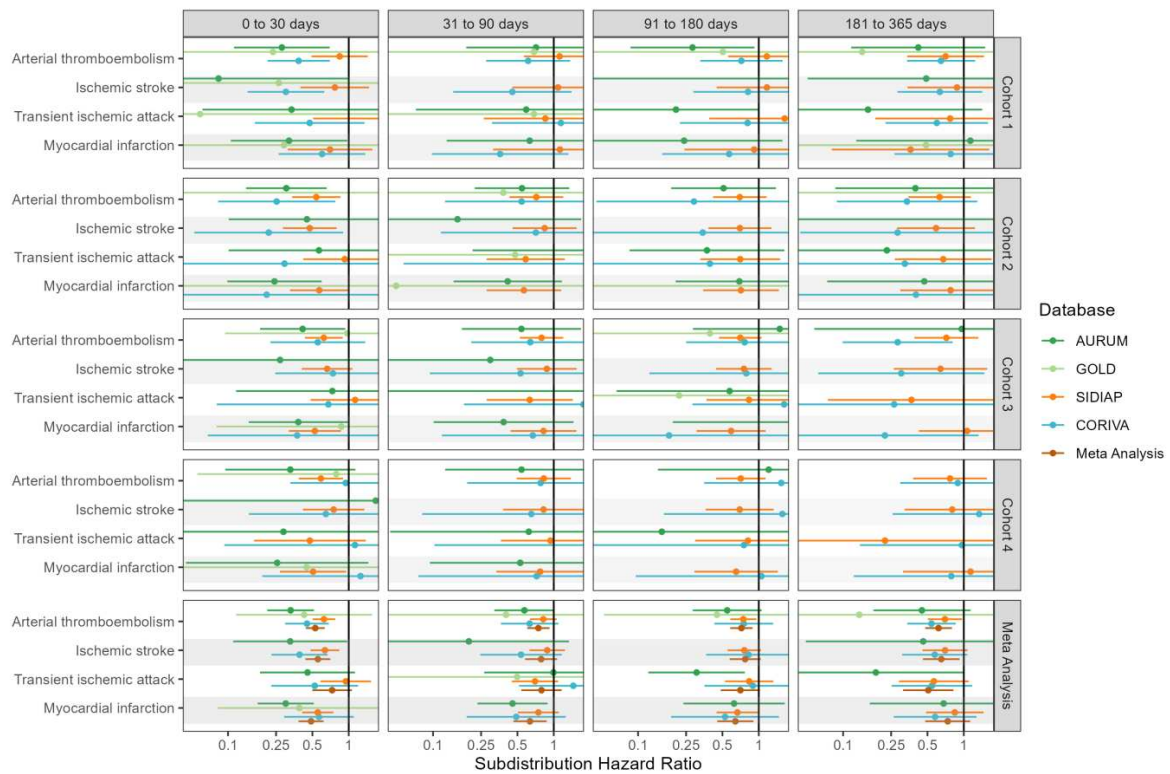


Figure S24: Forest plots for vaccine effect (any COVID-19 vaccine) on preventing arterial thrombosis/thromboembolism complications, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Follow-up ends at first vaccine dose after index date. Dashed line represents a level of heterogeneity $I^2 > 0.4$.

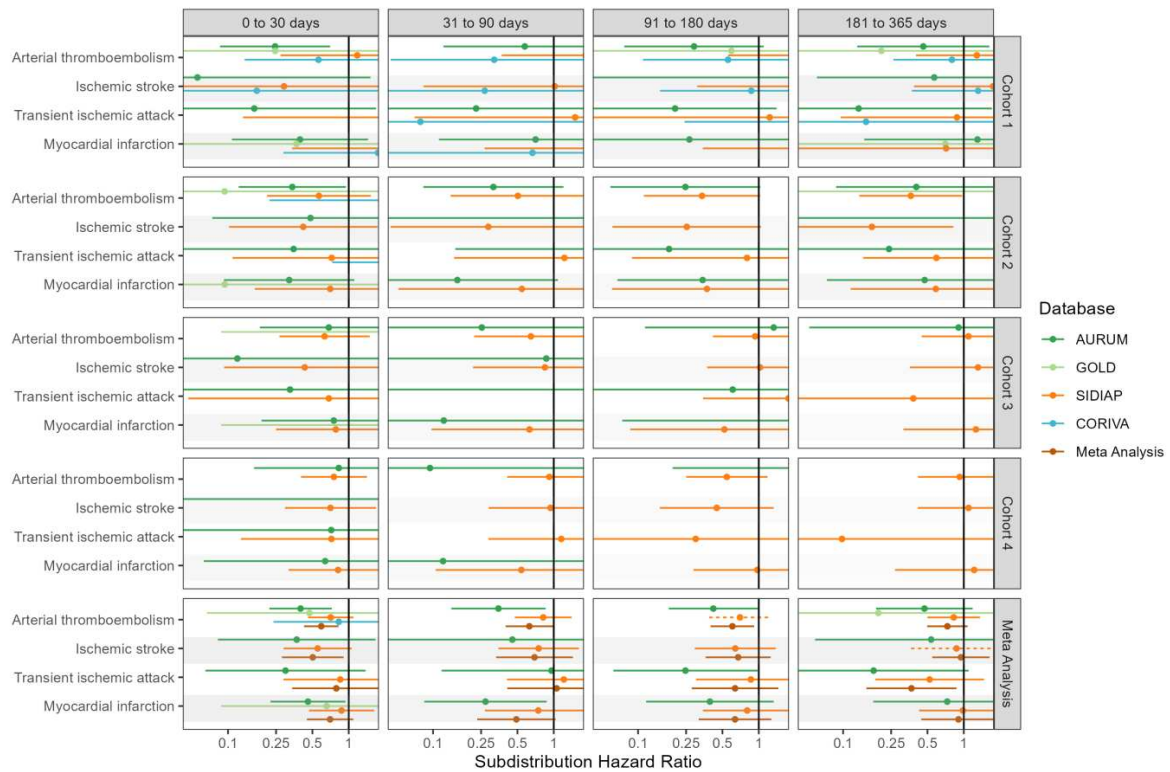


Figure S25: Forest plots for vaccine effect (any COVID-19 vaccine) on preventing arterial thrombosis/thromboembolism complications, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Only first outcome after COVID-19 captured. Dashed line represents a level of heterogeneity $I^2 > 0.4$.

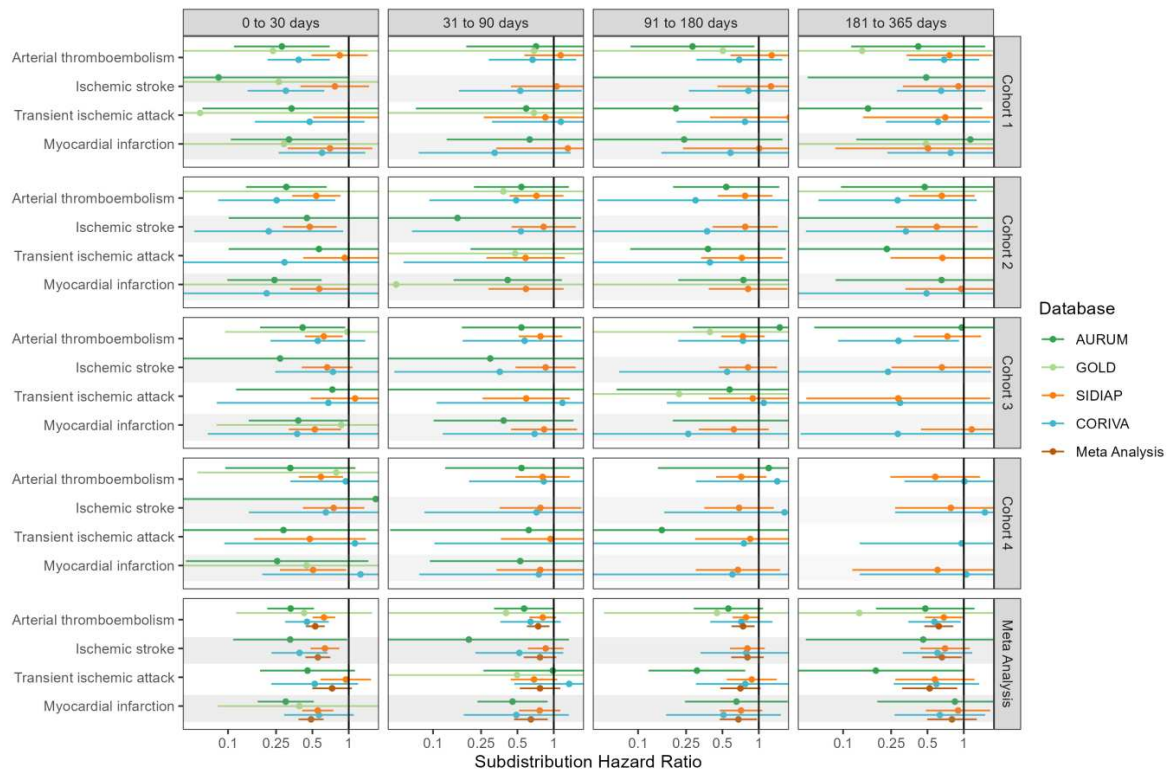


Figure S26: Forest plots for vaccine effect (ChAdOx1 vaccine) on preventing arterial thrombosis/thromboembolism complications, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Dashed line represents a level of heterogeneity $I^2 > 0.4$.

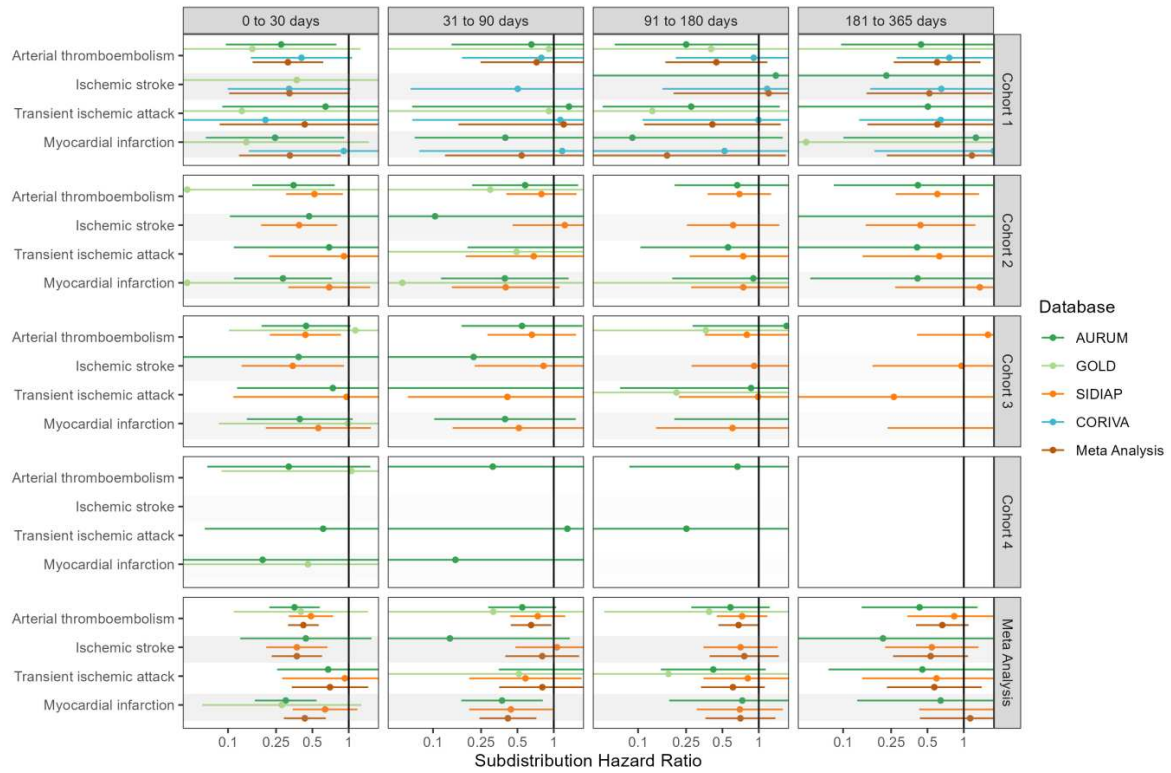


Figure S27: Forest plots for vaccine effect (ChAdOx1 vaccine) on preventing arterial thrombosis/thromboembolism complications, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Follow-up ends at first vaccine dose after index date. Dashed line represents a level of heterogeneity $I^2 > 0.4$.

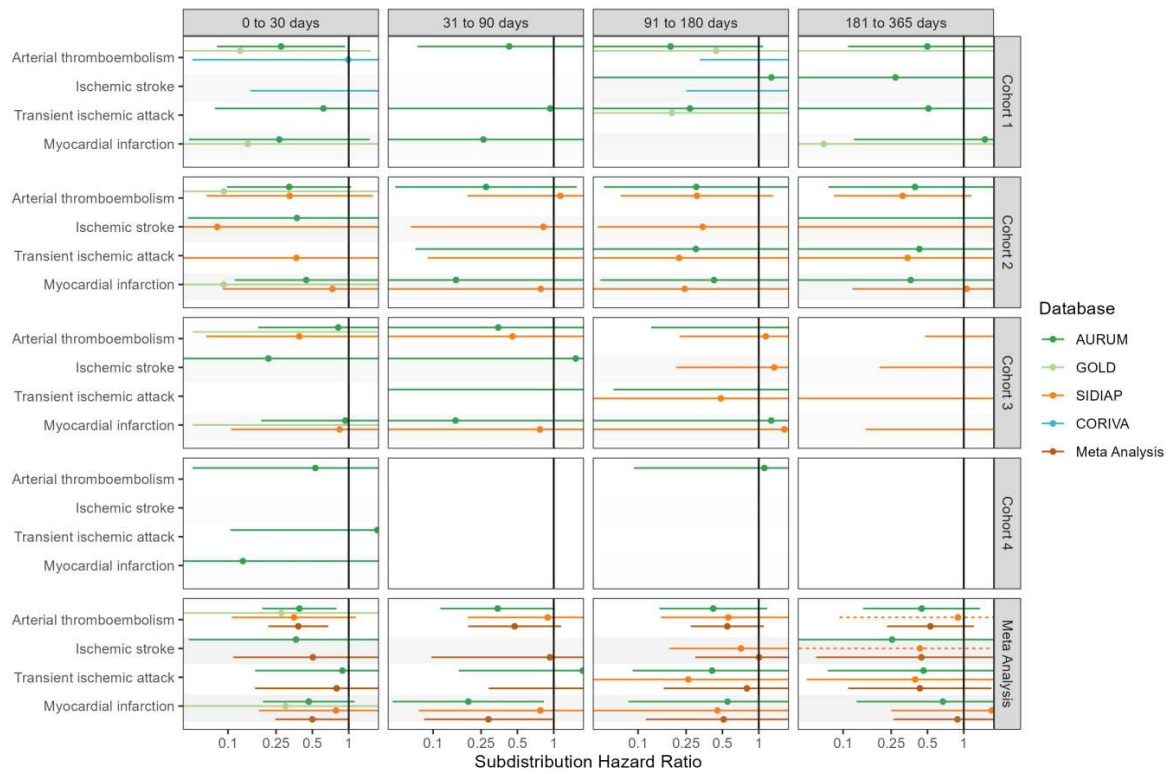


Figure S28: Forest plots for vaccine effect (ChAdOx1 vaccine) on preventing arterial thrombosis/thromboembolism complications, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Only first outcome after COVID-19 captured. Dashed line represents a level of heterogeneity $I^2 > 0.4$.

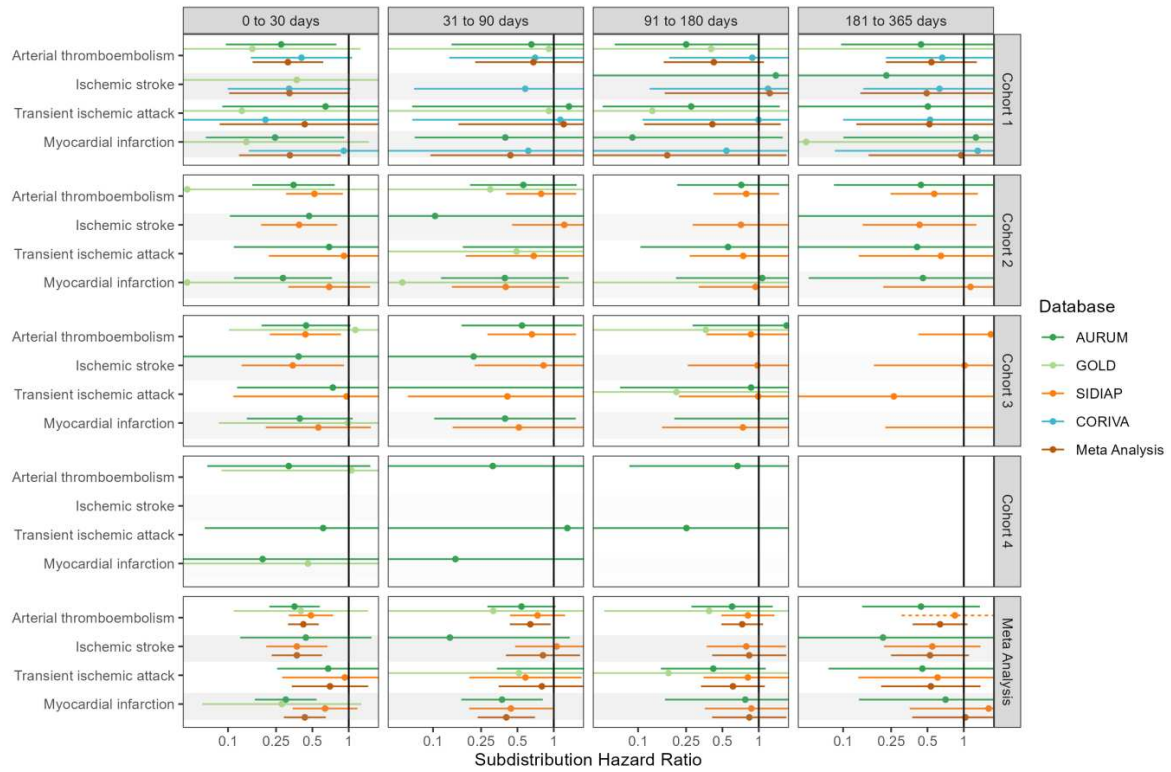


Figure S29: Forest plots for vaccine effect (BNT162b2 vaccine) on preventing arterial thrombosis/thromboembolism complications, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Dashed line represents a level of heterogeneity $I^2 > 0.4$.

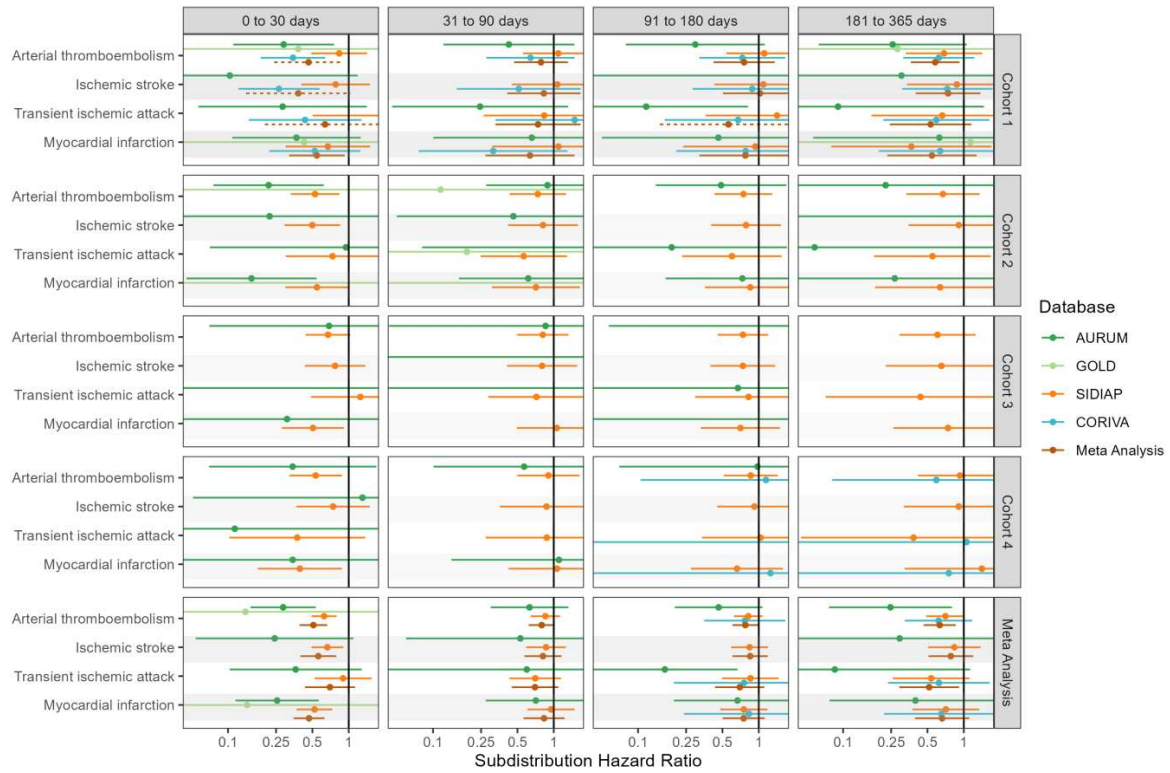


Figure S30: Forest plots for vaccine effect (BNT162b2 vaccine) on preventing arterial thrombosis/thromboembolism complications, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Follow-up ends at first vaccine dose after index date. Dashed line represents a level of heterogeneity $I^2 > 0.4$.

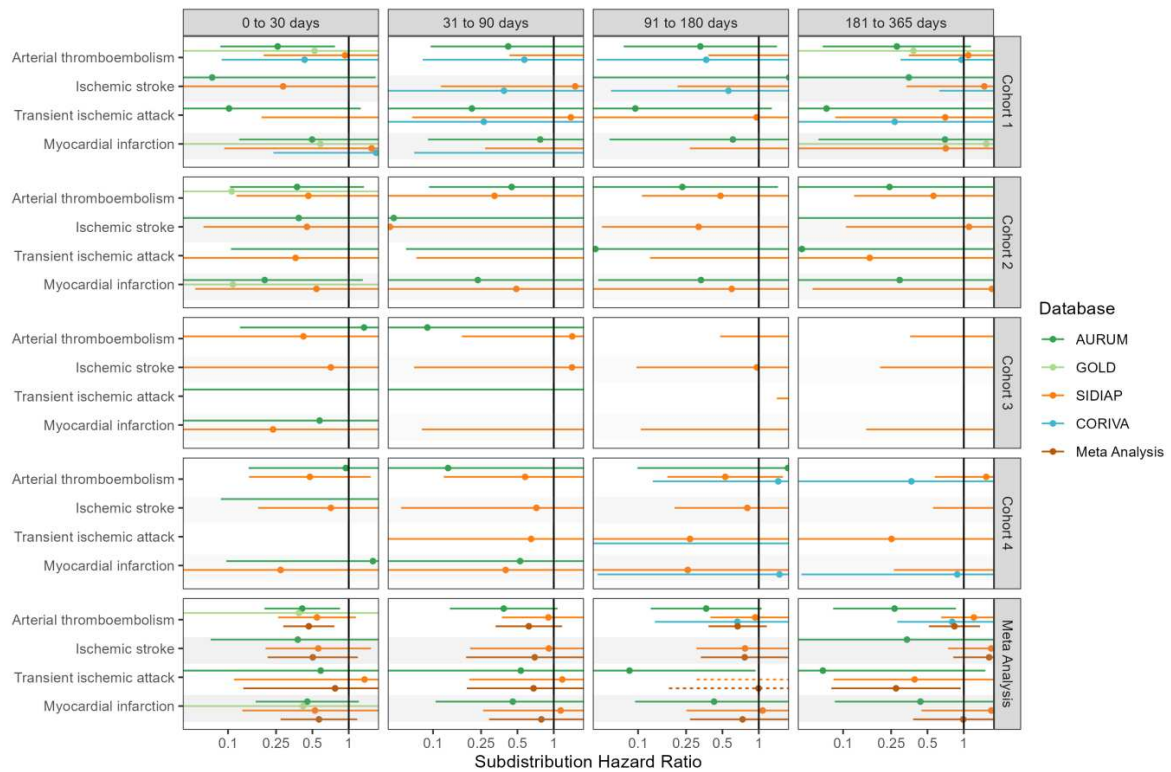


Figure S31: Forest plots for vaccine effect (BNT162b2 vaccine) on preventing arterial thrombosis/thromboembolism complications, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Only first outcome after COVID-19 captured. Dashed line represents a level of heterogeneity $I^2 > 0.4$.

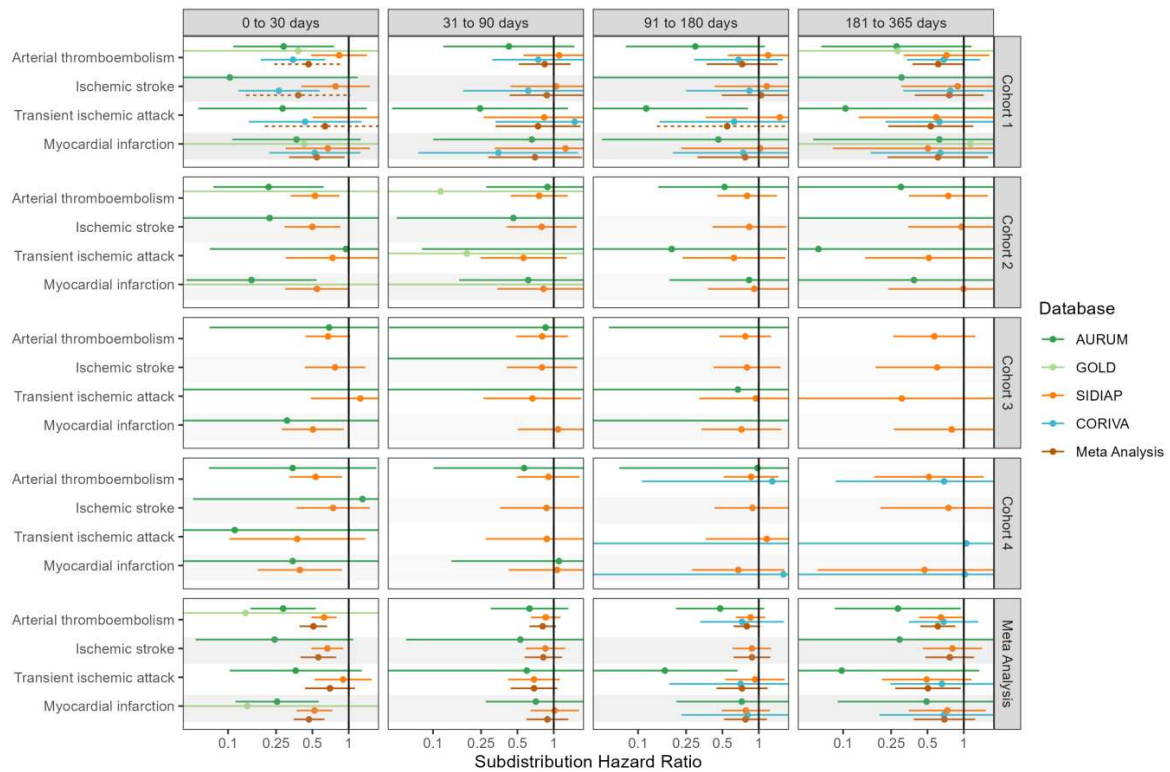


Figure S32: Forest plots for vaccine effect (any COVID-19 vaccine) on preventing cardiac diseases and hemorrhagic stroke, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Dashed line represents a level of heterogeneity $I^2 > 0.4$.

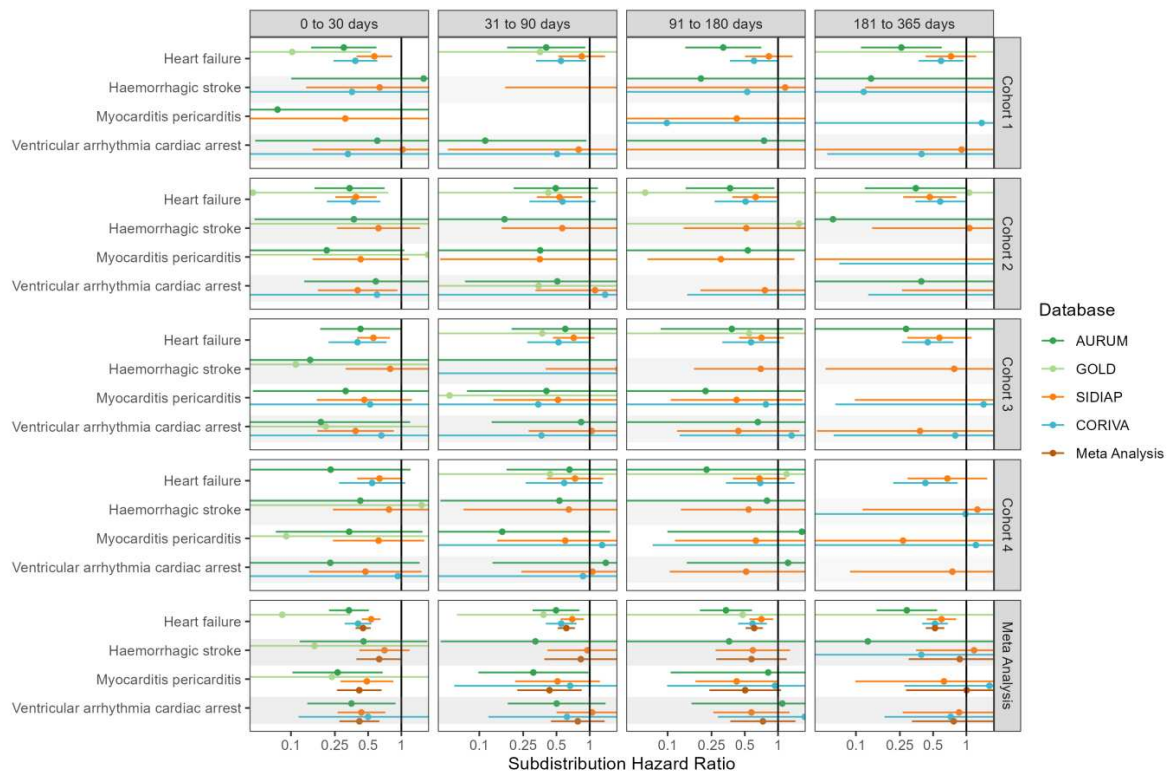


Figure S33: Forest plots for vaccine effect (any COVID-19 vaccine) on preventing cardiac diseases and hemorrhagic stroke, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Follow-up ends at first vaccine dose after index date. Dashed line represents a level of heterogeneity $I^2 > 0.4$.

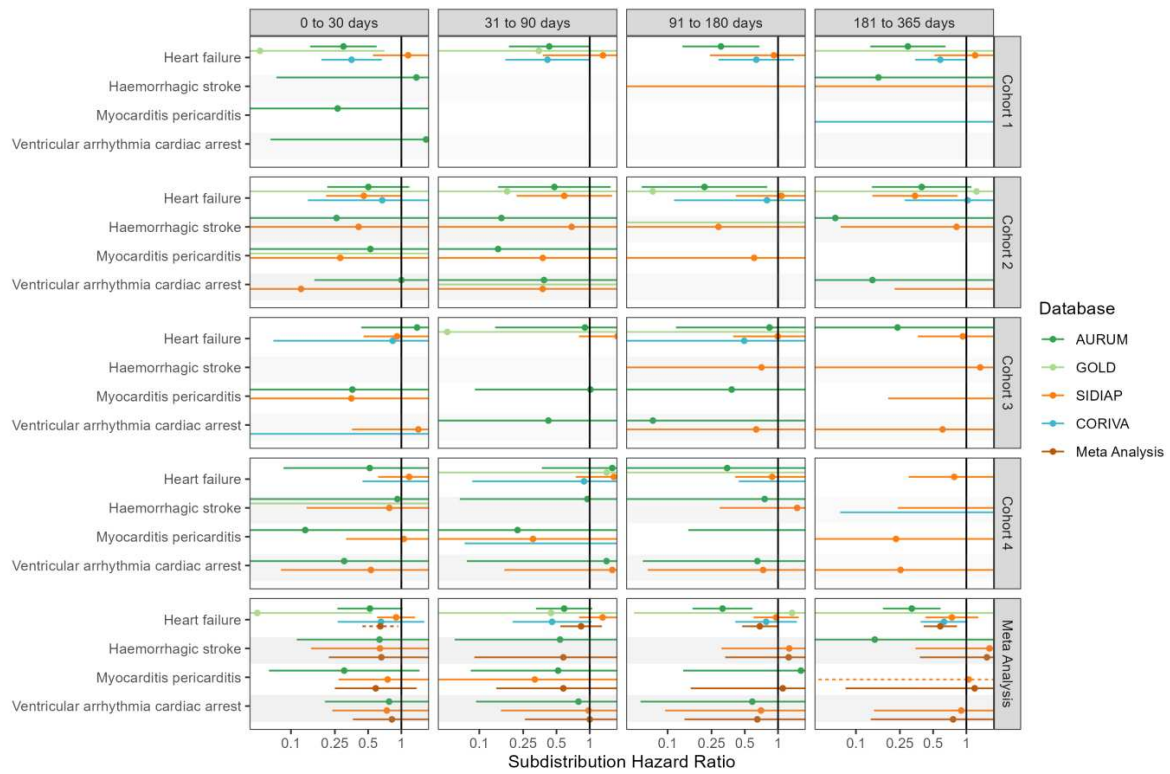


Figure S34: Forest plots for vaccine effect (any COVID-19 vaccine) on preventing cardiac diseases and hemorrhagic stroke, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Only first outcome after COVID-19 captured. Dashed line represents a level of heterogeneity $I^2 > 0.4$.

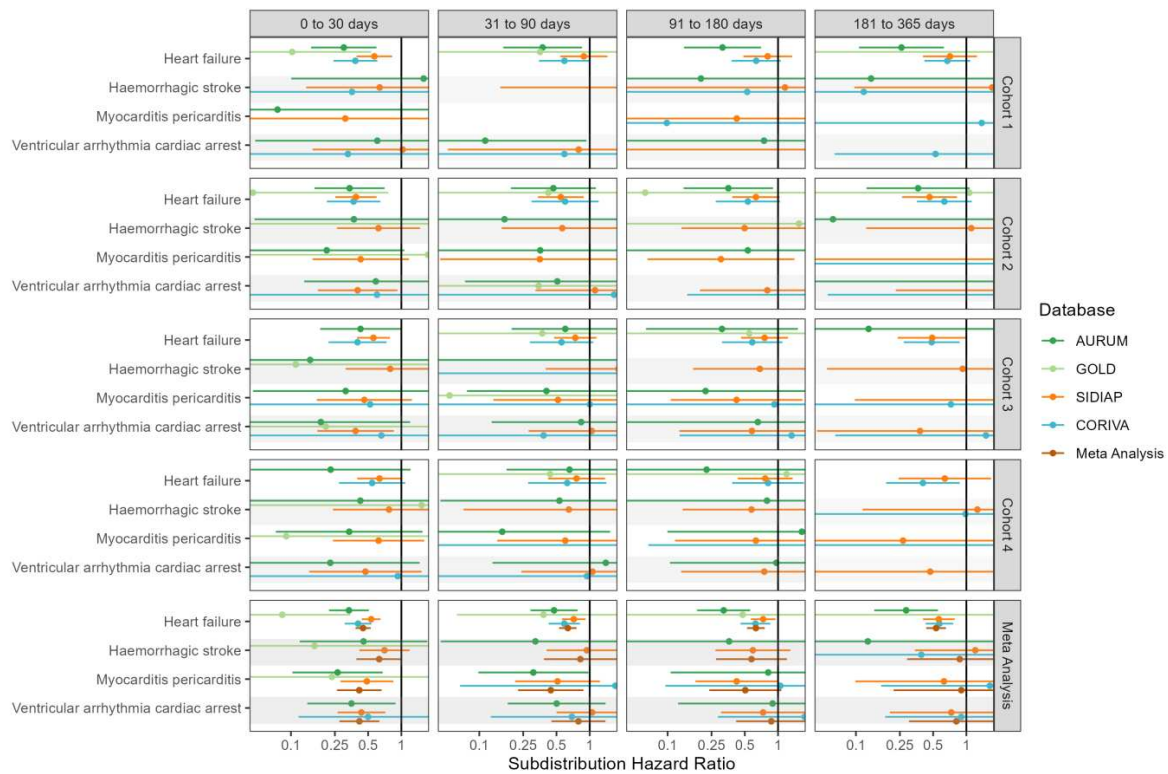


Figure S35: Forest plots for vaccine effect (ChAdOx1 vaccine) on preventing cardiac diseases and hemorrhagic stroke, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Dashed line represents a level of heterogeneity $I^2 > 0.4$.

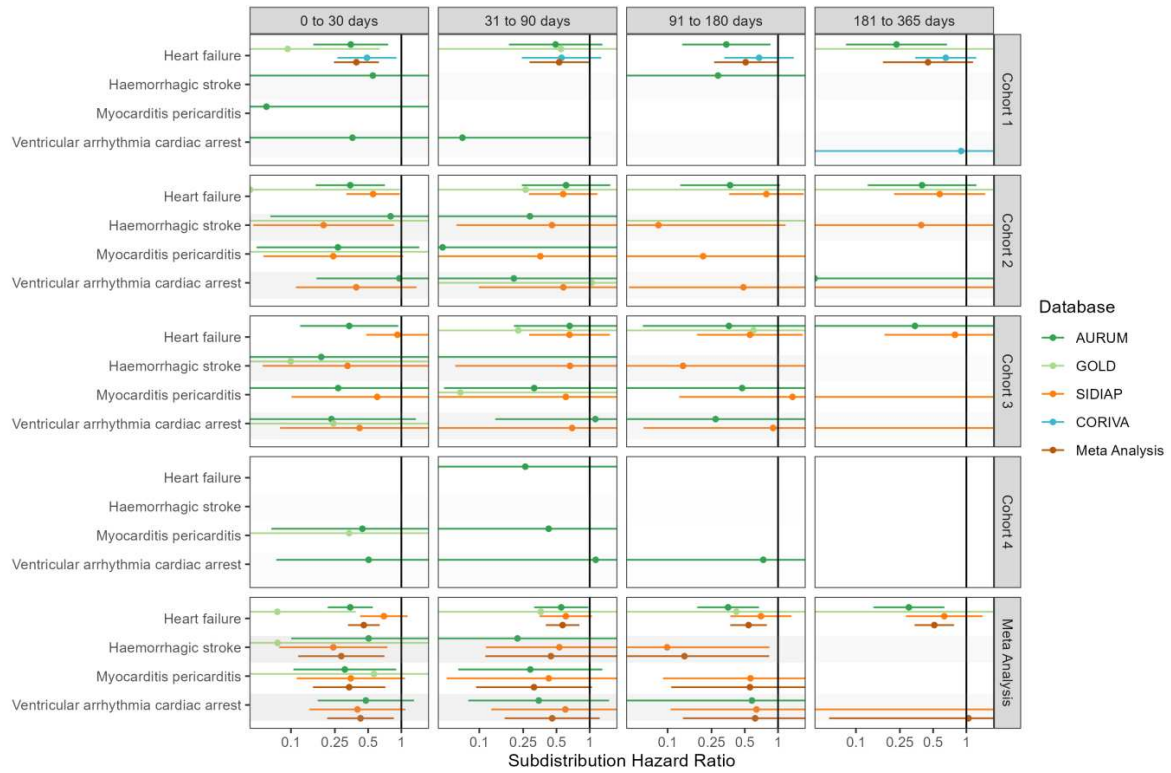


Figure S36: Forest plots for vaccine effect (ChAdOx1 vaccine) on preventing cardiac diseases and hemorrhagic stroke, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Follow-up ends at first vaccine dose after index date. Dashed line represents a level of heterogeneity $I^2 > 0.4$.

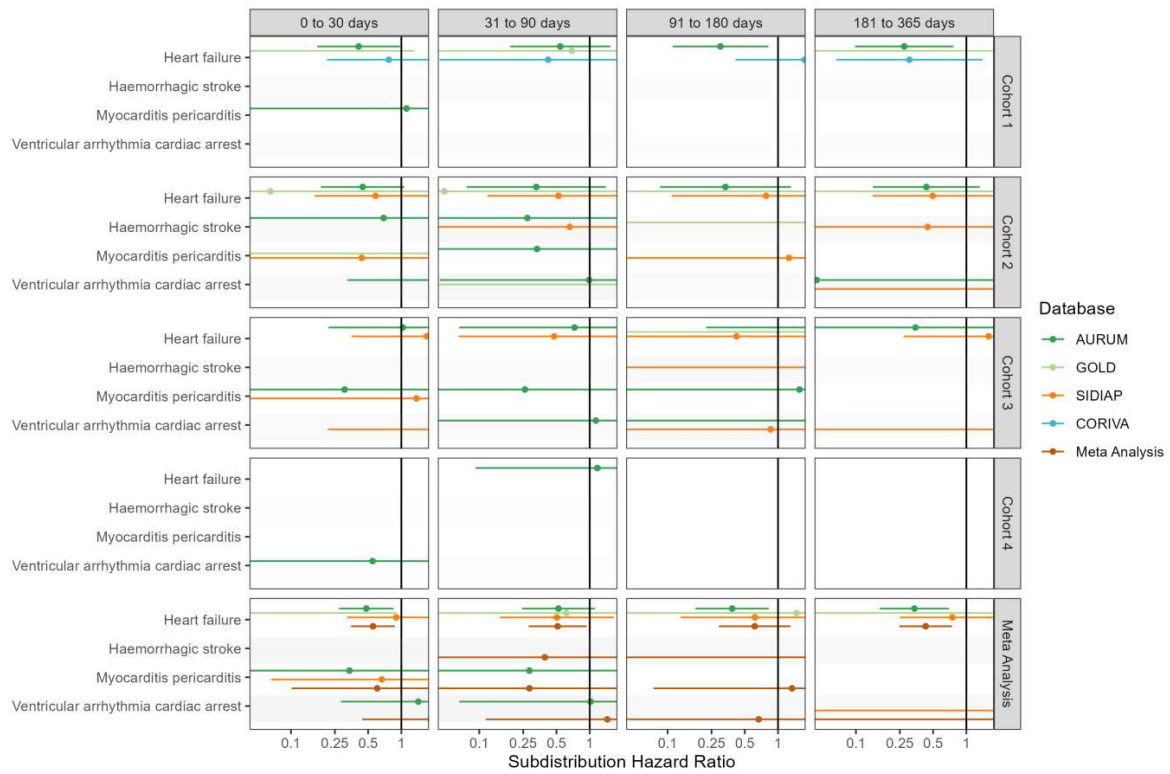


Figure S37: Forest plots for vaccine effect (ChAdOx1 vaccine) on preventing cardiac diseases and hemorrhagic stroke, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Only first outcome after COVID-19 captured. Dashed line represents a level of heterogeneity $I^2 > 0.4$.

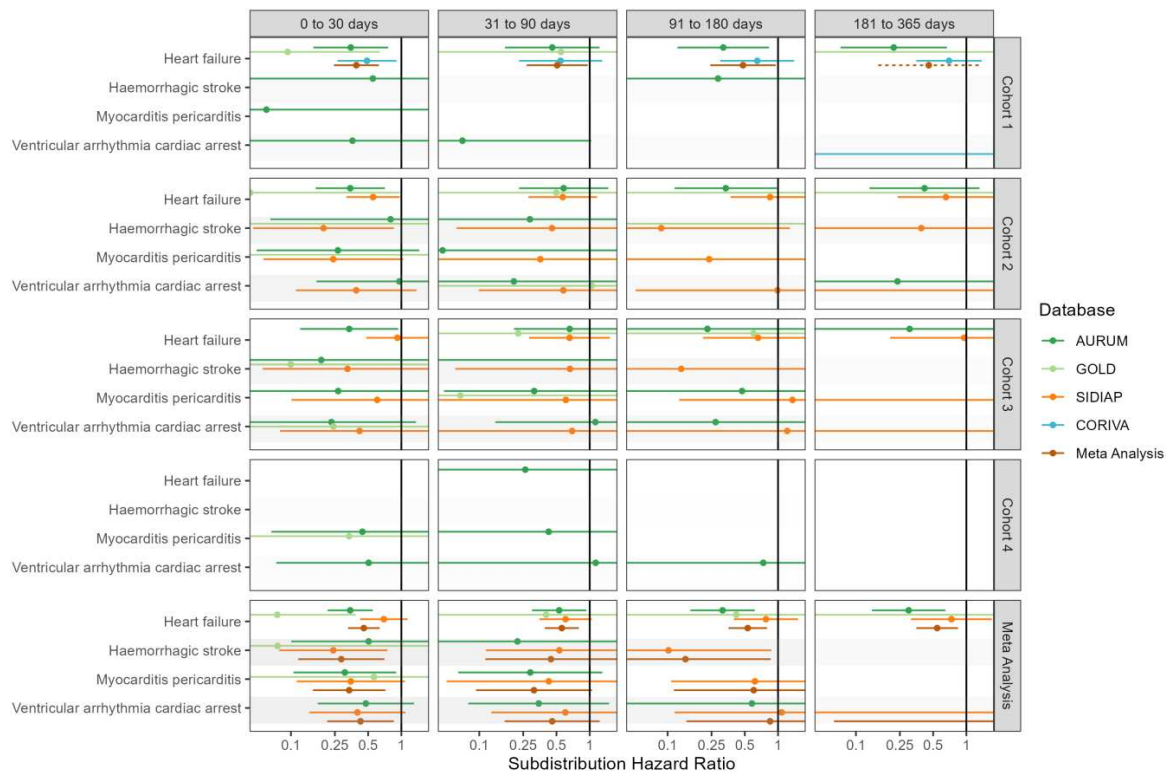


Figure S38: Forest plots for vaccine effect (BNT162b2 vaccine) on preventing cardiac diseases and hemorrhagic stroke, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Dashed line represents a level of heterogeneity $I^2 > 0.4$.

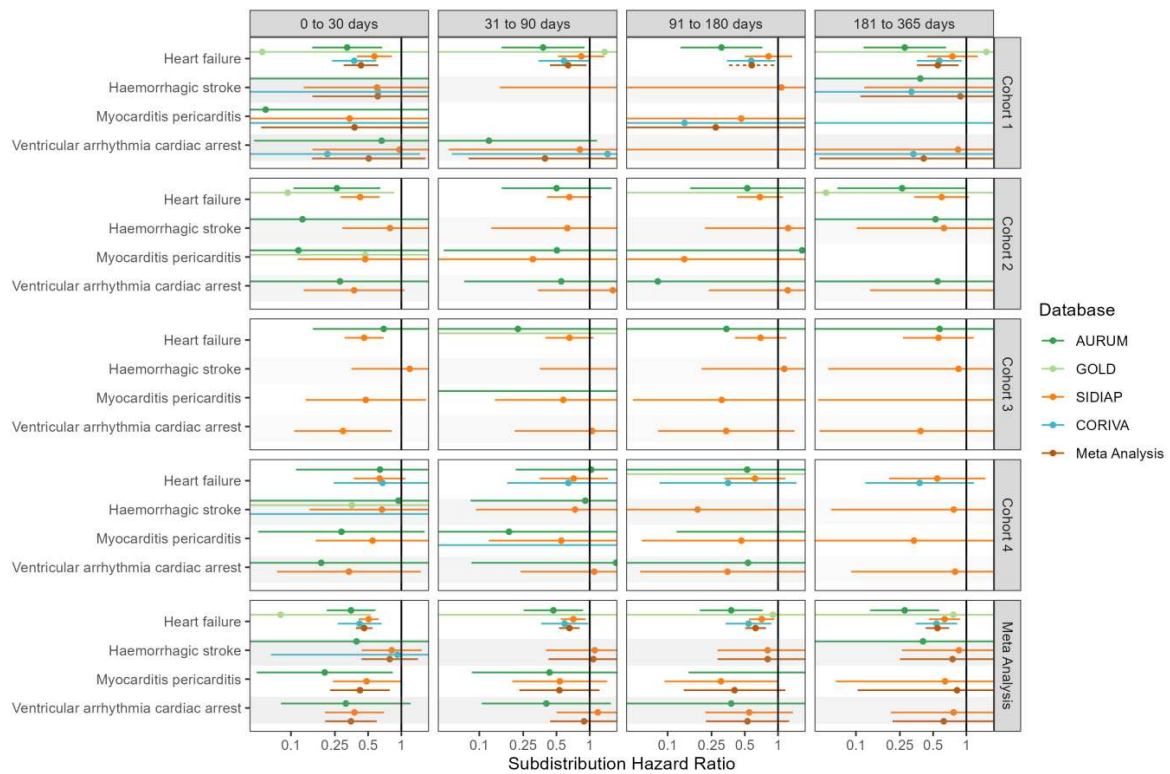


Figure S39: Forest plots for vaccine effect (BNT162b2 vaccine) on preventing cardiac diseases and hemorrhagic stroke, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Follow-up ends at first vaccine dose after index date. Dashed line represents a level of heterogeneity $I^2 > 0.4$.

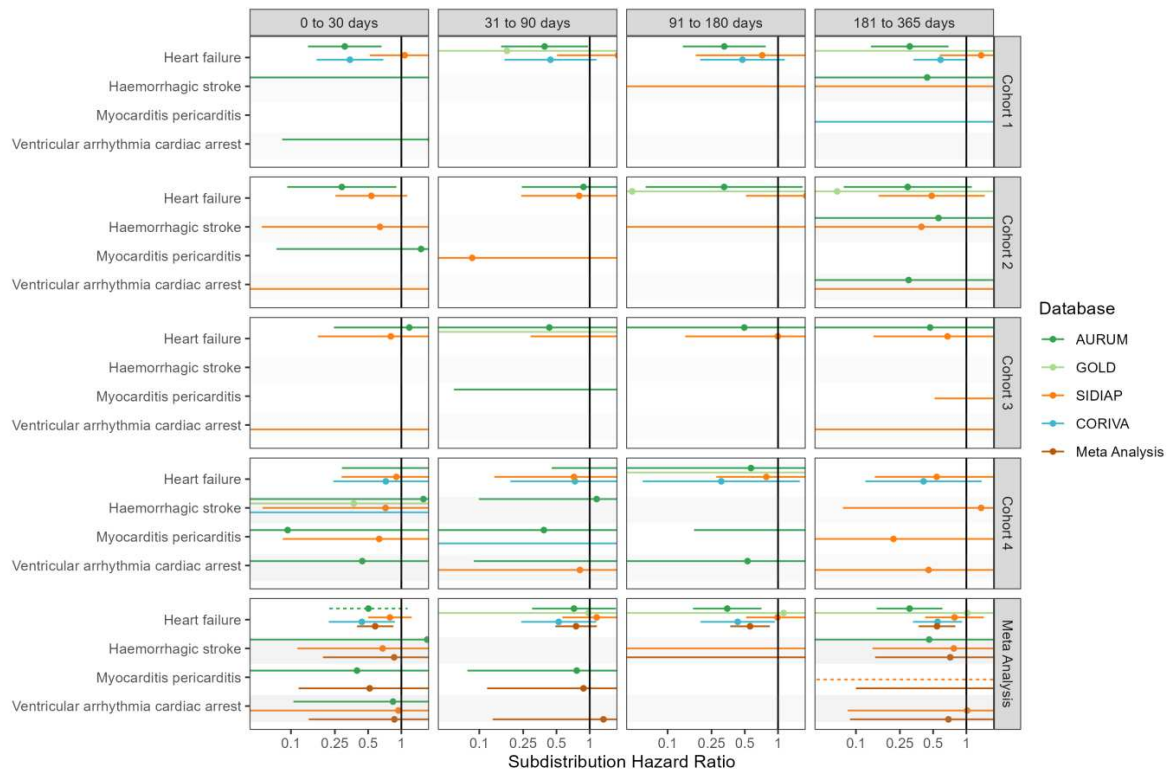


Figure S40: Forest plots for vaccine effect (BNT162b2 vaccine) on preventing cardiac diseases and hemorrhagic stroke, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Only first outcome after COVID-19 captured. Dashed line represents a level of heterogeneity $I^2 > 0.4$.

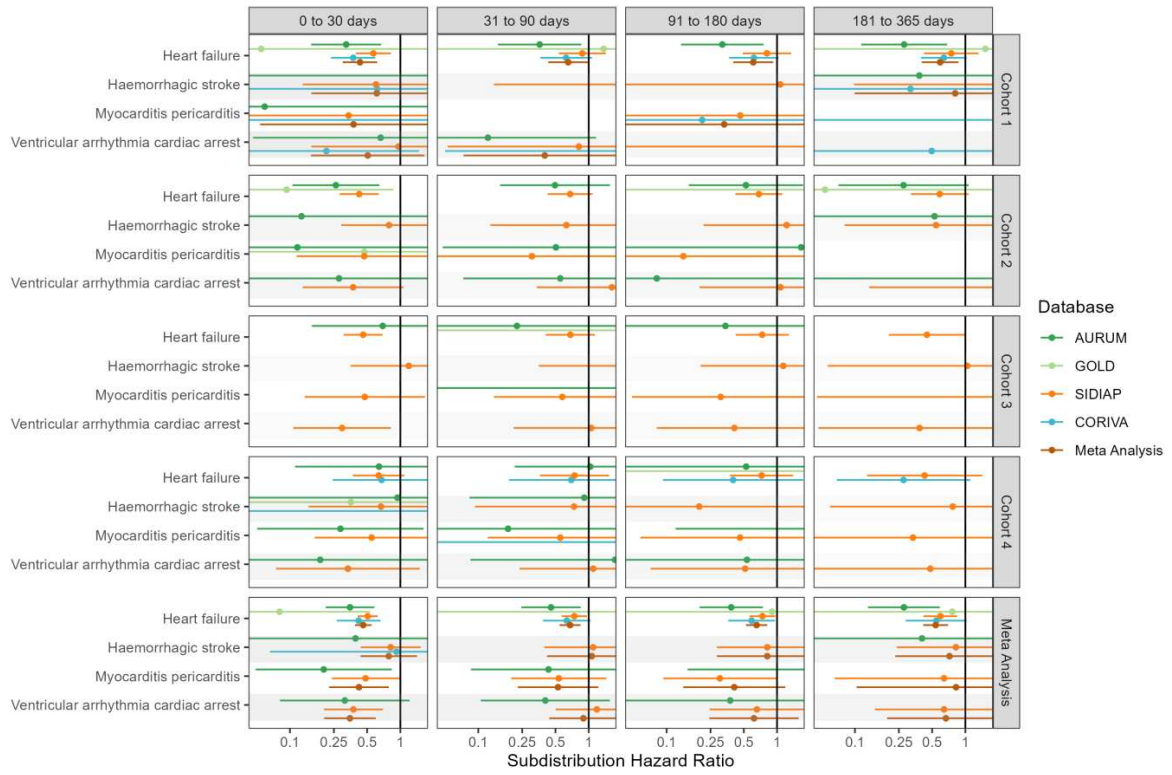
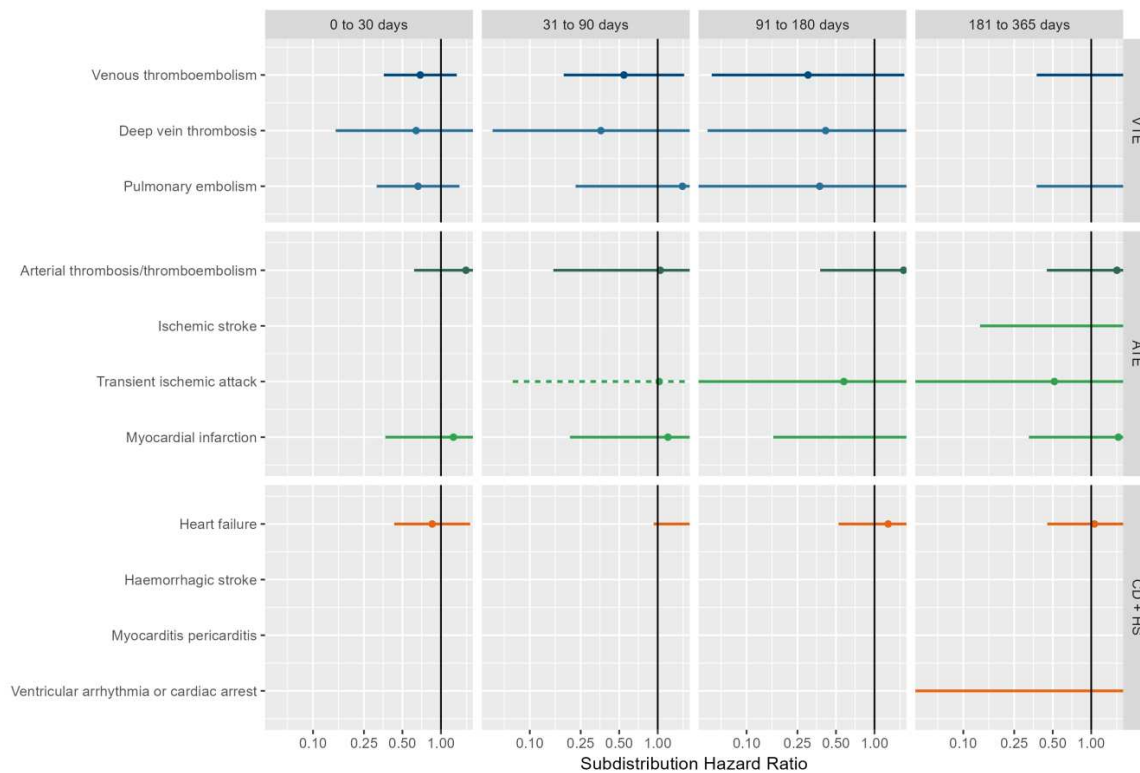
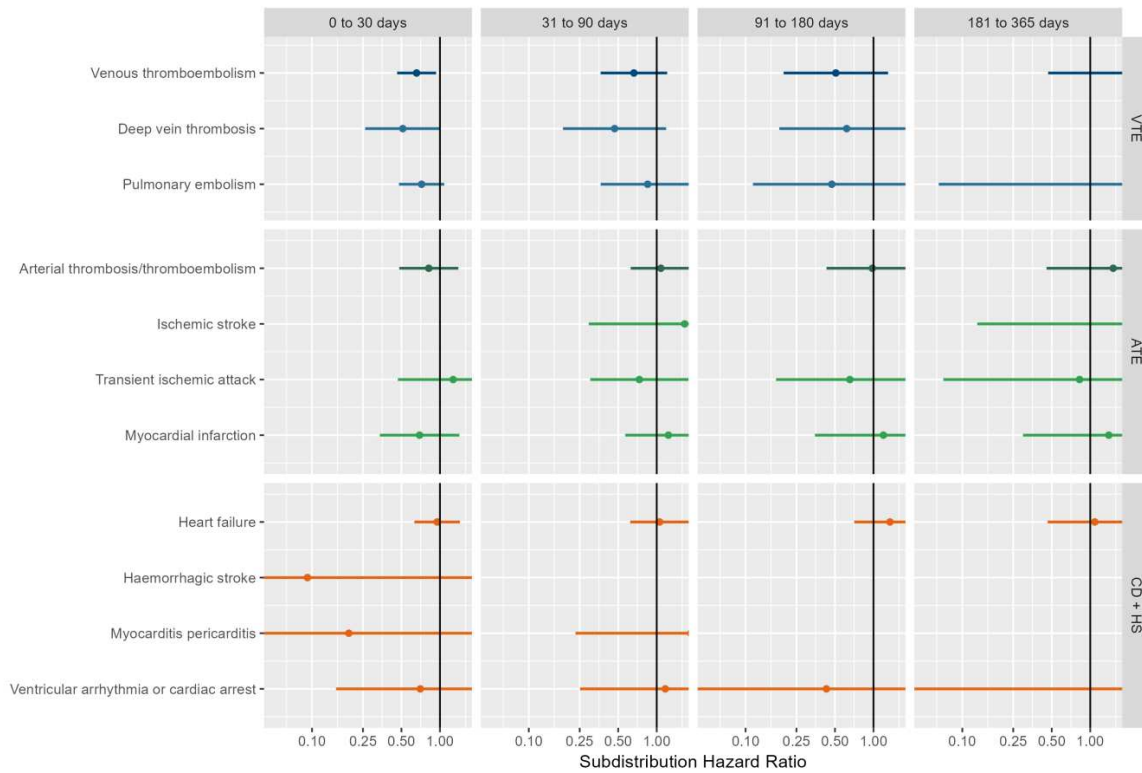


Figure S41: Forest plots for comparative effect, meta-analysis across cohorts and databases. Follow-up ends at first vaccine dose after index date. Dashed line represents a level of heterogeneity $I^2 > 0.4$.



VTE = Venous thromboembolism, ATE = Arterial thrombosis/thromboembolism, CD + HS = Cardiac diseases and Hemorrhagic stroke

Figure S42: Forest plots for comparative effect, meta-analysis across cohorts and databases. Only first outcome after COVID-19 captured. Dashed line represents a level of heterogeneity $I^2 > 0.4$.



VTE = Venous thromboembolism, ATE = Arterial thrombosis/thromboembolism, CD + HS = Cardiac diseases and Hemorrhagic stroke

Figure S43: Forest plots for comparative effect on preventing venous thromboembolism complications, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Dashed line represents a level of heterogeneity $I^2 > 0.4$.

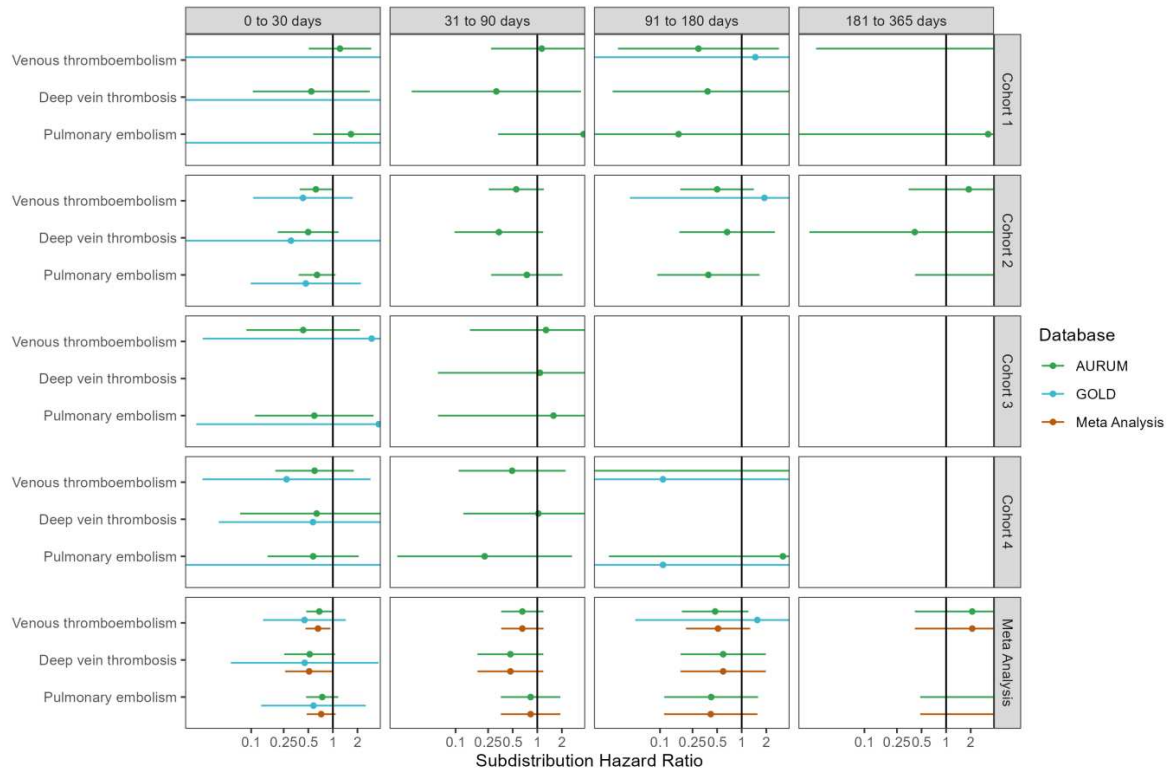


Figure S44: Forest plots for comparative effect on preventing venous thromboembolism complications, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Follow-up ends at first vaccine dose after index date. Dashed line represents a level of heterogeneity $I^2 > 0.4$.

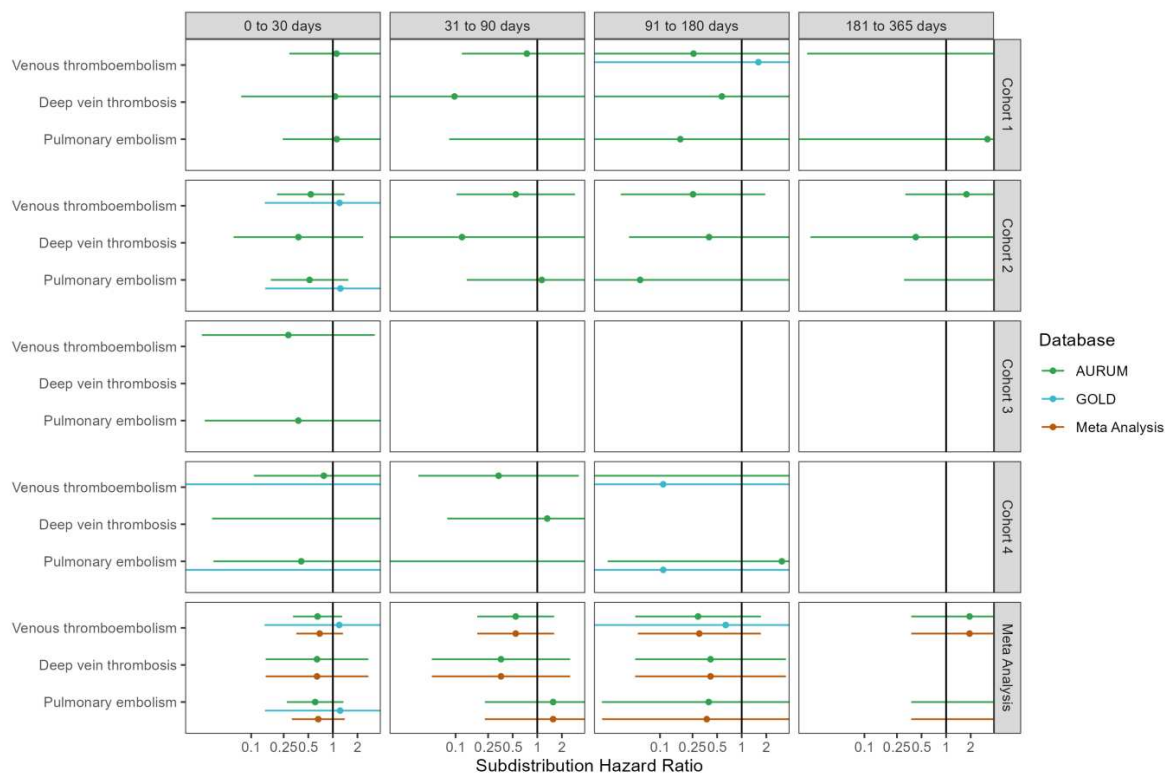


Figure S45: Forest plots for comparative effect on preventing venous thromboembolism complications, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Only first outcome after COVID-19 captured. Dashed line represents a level of heterogeneity $I^2 > 0.4$.

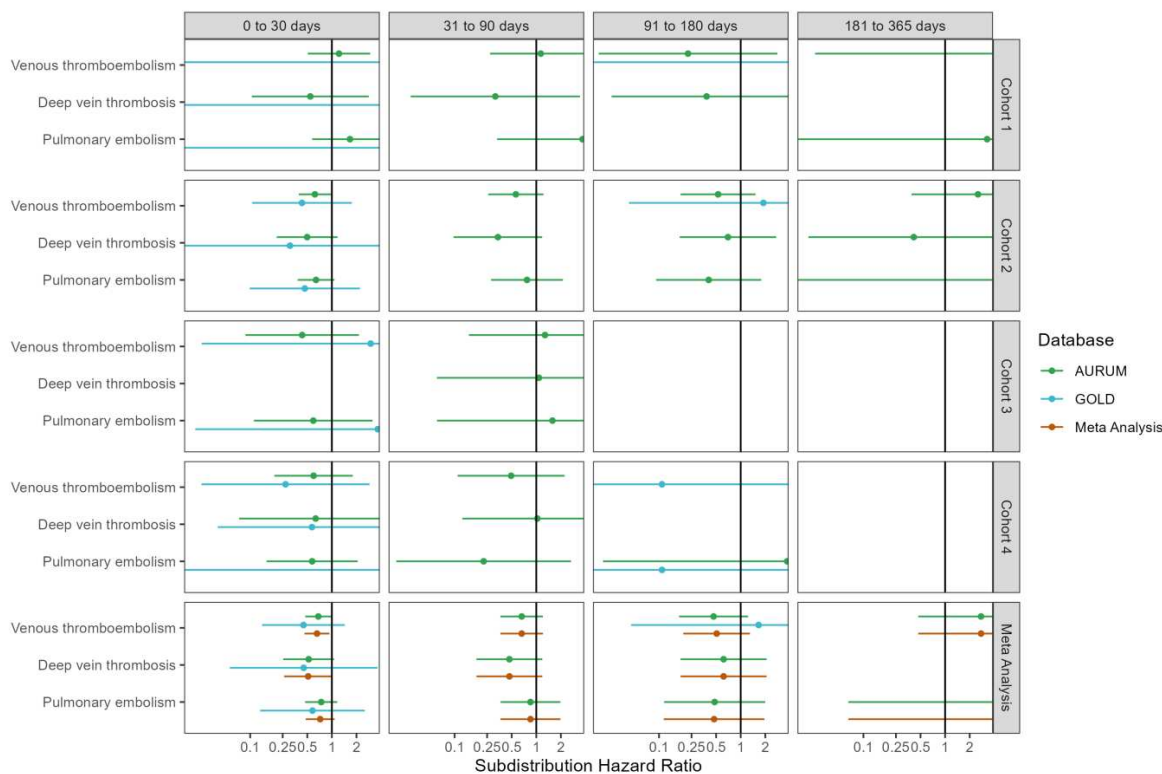


Figure S46: Forest plots for comparative effect on preventing arterial thrombosis/thromboembolism complications, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Dashed line represents a level of heterogeneity $I^2 > 0.4$.

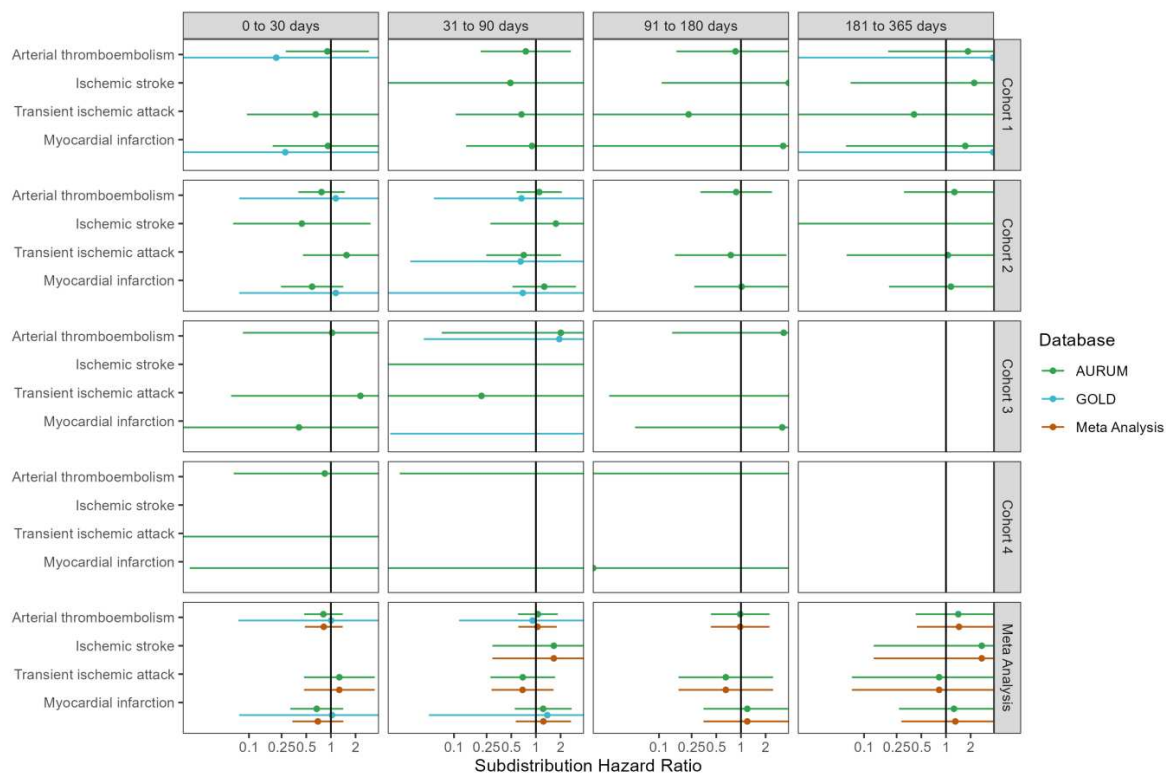


Figure S47: Forest plots for comparative effect on preventing arterial thrombosis/thromboembolism complications, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Follow-up ends at first vaccine dose after index date. Dashed line represents a level of heterogeneity $I^2 > 0.4$.

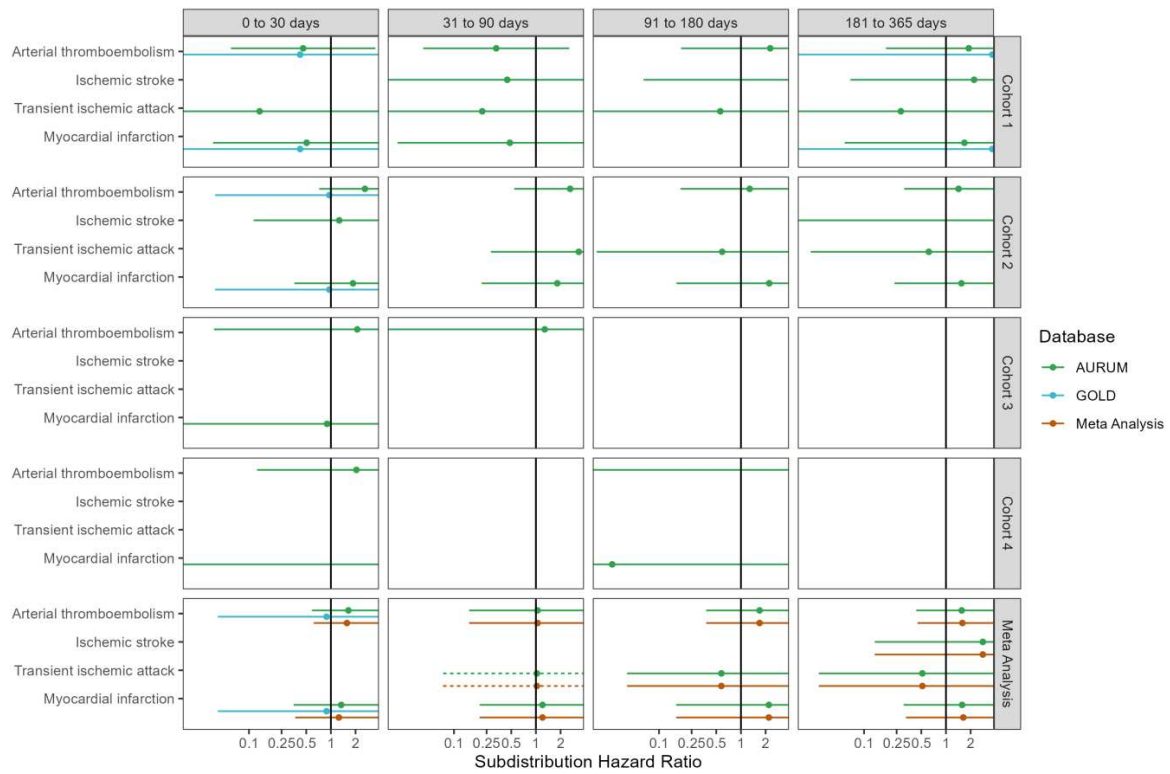


Figure S48: Forest plots for comparative effect on preventing arterial thrombosis/thromboembolism complications, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Only first outcome after COVID-19 captured. Dashed line represents a level of heterogeneity $I^2 > 0.4$.

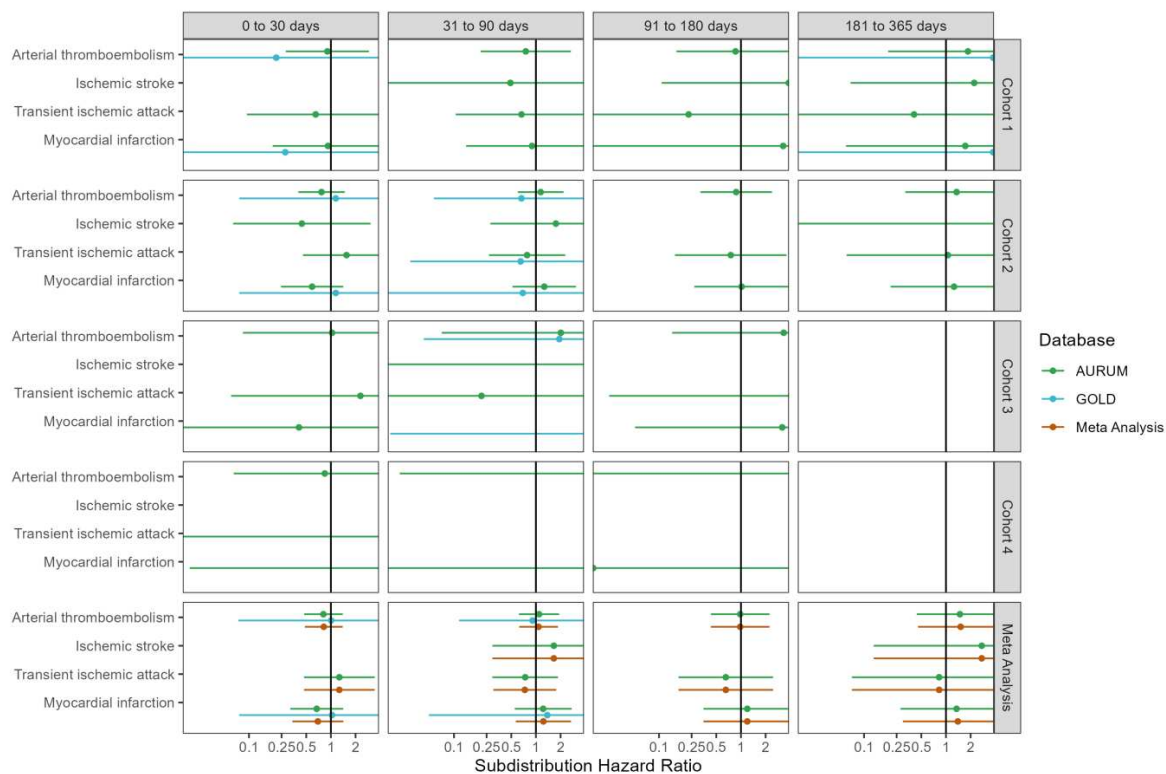


Figure S49: Forest plots for comparative effect on preventing cardiac diseases and hemorrhagic stroke, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Dashed line represents a level of heterogeneity $I^2 > 0.4$.

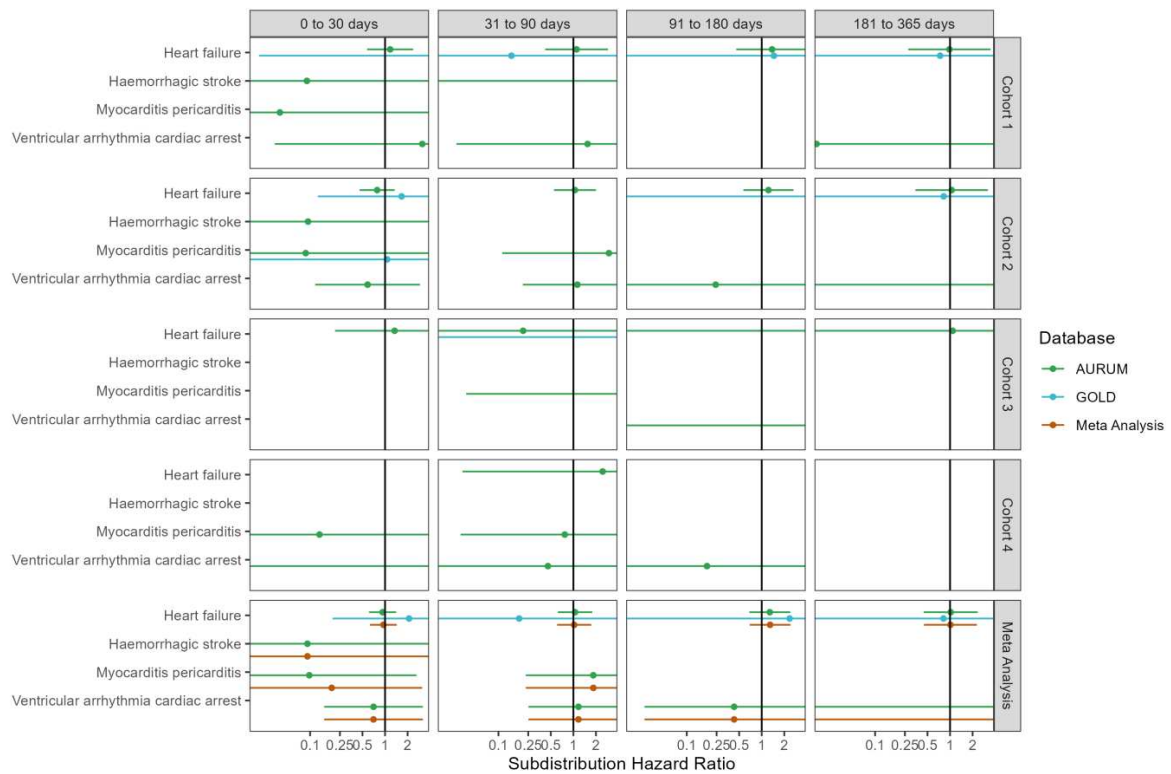


Figure S50: Forest plots for comparative effect on preventing cardiac diseases and hemorrhagic stroke, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Follow-up ends at first vaccine dose after index date. Dashed line represents a level of heterogeneity $I^2 > 0.4$.

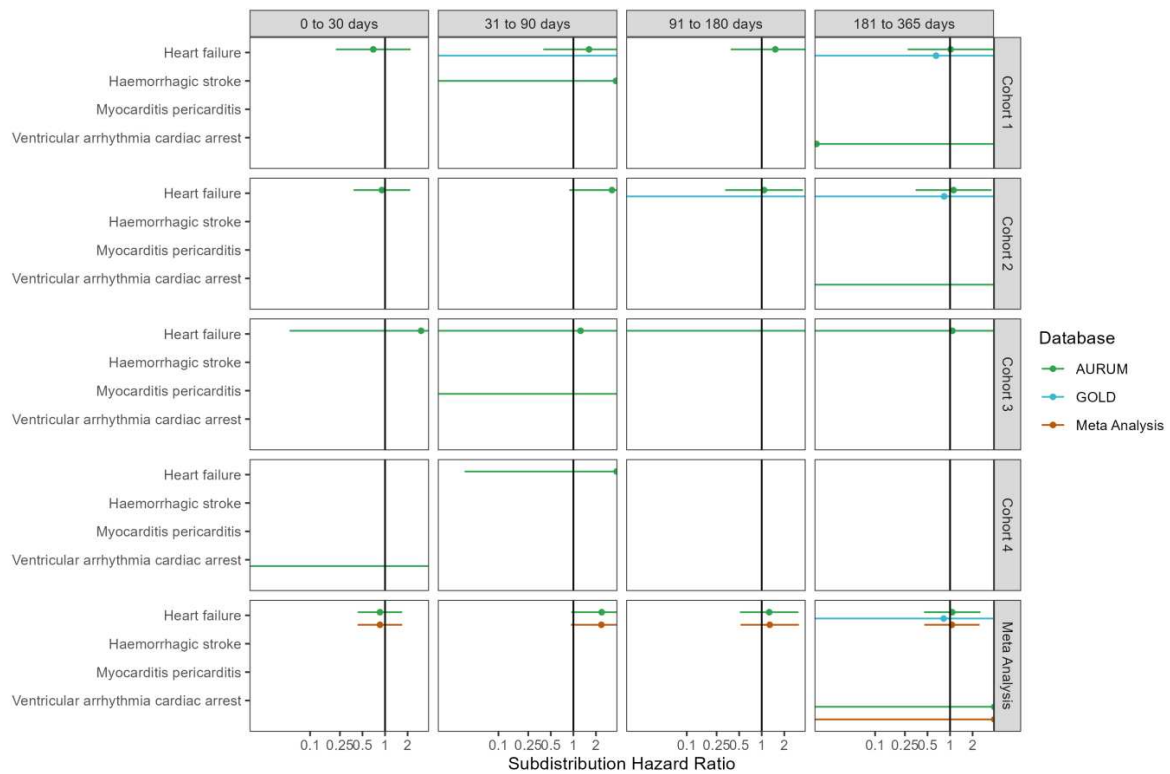


Figure S51: Forest plots for comparative effect on preventing cardiac diseases and hemorrhagic stroke, for each cohort and database (meta-analysis estimates across cohorts in the last panel). Only first outcome after COVID-19 captured. Dashed line represents a level of heterogeneity $I^2 > 0.4$.

