

Supplementary materials

Appendix 1. Data source description

The Columbia University Irving Medical Center (CUIMC) database comprises electronic health records on more than 6 million patients, with data collection starting in 1985. CUIMC is a Northeast US quaternary care center with primary care practices in northern Manhattan and surrounding areas, and the database includes inpatient and outpatient care. The database currently holds information about the person (demographics), visits (inpatient and outpatient), conditions (billing diagnoses and problem lists), drugs (outpatient prescriptions and inpatient orders and administrations), devices, measurements (laboratory tests and vital signs), and other observations (symptoms). The data sources include current and previous electronic health record systems (homegrown Clinical Information System, homegrown WebCIS, Allscripts Sunrise Clinical Manager, Allscripts TouchWorks, Epic Systems), administrative systems (IBM PCS-ADS, Eagle Registration, IDX Systems, Epic Systems), and ancillary systems (homegrown LIS, Sunquest, Cerner Laboratory). Additionally, it contains the information on vaccination from New York City and State immunization registries.

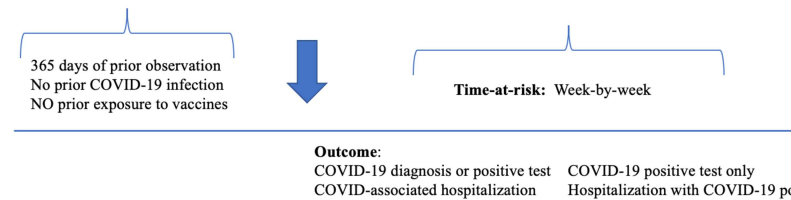
Appendix 2. Retrospective cohort COVID-19 vaccine effectiveness study design overview.

Main analysis

Target: patients with at least one dose (Ad26.COV2.S BNT162b2 and mRNA-1273) located in NYC
Comparator: unvaccinated patients matched on the date of vaccination located in NYC

Index event

Target: first dose
 Comparator: date matched to the date of vaccination in the target group



Sensitivity analyses

- Alternative comparator: Patients matched on the visit
- Alternative target: fully vaccinated patients
- Alternative target and comparator: patients with or without prior COVID-19
- Alternative TAR: 1 day– 365 days

Cox proportional hazard model with 1:1 large scale propensity score matching (covariates include demographics, index year, month, # of visits; condition and drug groups; procedure, device, observation, measurement; long and short-term excluding day 0)

Appendix 3. Cohort definitions and codes for the long-term COVID-19 vaccine effectiveness study

3.1 Cohort definitions for vaccinated, unvaccinated and outcome cohorts for studying effectiveness of COVID-19 vaccines.

	Definition and link to the public repository
Vaccinated cohorts	<p>Vaccinated patients were defined as patients with at least one dose of the corresponding vaccine (Pfizer BioNTech, Moderna, Janssen)</p> <p>Index event: first exposure to the corresponding vaccine</p> <p>Inclusion and exclusion criteria:</p> <ul style="list-style-type: none"> - 365 days of prior observation - no other COVID-19 vaccine exposure in 120 days prior and 120 days after the index date - no prior COVID-19 infection (diagnosis code of COVID-19 or positive test) - residence in New York City determined by the zip code recorded <p>For the analysis on fully vaccinated patients, we applied the same criteria and required patients to have a) the second dose of Pfizer or Moderna vaccine (if applicable) within 14 to 56 days after the first dose b) at least 14 days of observation after the second dose (one dose of Janssen).</p> <p>Links:</p> <p>https://atlas.ohdsi.org/#/cohortdefinition/498</p> <p>https://atlas.ohdsi.org/#/cohortdefinition/494</p> <p>https://atlas.ohdsi.org/#/cohortdefinition/497</p> <p>https://atlas.ohdsi.org/#/cohortdefinition/418</p> <p>https://atlas.ohdsi.org/#/cohortdefinition/417</p> <p>https://atlas.ohdsi.org/#/cohortdefinition/420</p>
Unvaccinated cohorts	<p>Unvaccinated cohorts were created separately for each vaccinated cohort by selecting patients with no COVID-19 vaccination in their record (any vaccine), 365 days of prior observation and New York City residence. The patients were matched on the index date of one of the vaccinated group participants for the unvaccinated patients anchored on a date and on the date of a healthcare encounter within 3-day corridor for the unvaccinated patients anchored on a visit.</p>

Outcome cohorts	<p>For the main analysis COVID-19 infection was defined as a COVID-19 test with the result 'Positive' or 'Detected'. COVID-19 associated hospitalization was defined as an inpatient, emergency department or intensive care unit admission with a positive COVID-19 test recorded within 30 days prior or during hospitalization. For a secondary analysis we applied the abovementioned criteria with adding COVID-19 diagnosis as an alternative for positive COVID-19 test.</p> <p>Links:</p> <p>https://atlas.ohdsi.org/#/cohortdefinition/425 https://atlas.ohdsi.org/#/cohortdefinition/422</p>
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3.2 Codes used in the study.

1. Pfizer vaccine:

RxNorm 2468235 SARS-CoV-2 (COVID-19) vaccine, mRNA-BNT162b2 0.1 MG/ML
Injectable Suspension

2. Moderna vaccine:

RxNorm 2470234 SARS-CoV-2 (COVID-19) vaccine, mRNA-1273 0.2 MG/ML Injectable
Suspension

3. Janssen vaccine:

CVX 212 SARS-COV-2 (COVID-19) vaccine, vector non-replicating, recombinant spike
protein-Ad26, preservative free, 0.5 mL

4. COVID-19 diagnosis:

ICD10-CM U07.1 Emergency use of U07.1 | COVID-19

5. COVID-19 test:

LOINC 94500-6 SARS-CoV-2 (COVID-19) RNA [Presence] in Respiratory specimen by NAA
with probe detection

LOINC 94558-4 SARS-CoV-2 (COVID-19) Ag [Presence] in Respiratory specimen by Rapid
immunoassay

Appendix 4. Negative controls

SNOMED concept id	SNOMED concept name
438945	Accidental poisoning by benzodiazepine-based tranquilizer
434455	Acquired claw toes
316211	Acquired spondylolisthesis
201612	Alcoholic liver damage
438730	Alkalosis
441258	Anemia in neoplastic disease
432513	Animal bite wound
4171556	Ankle ulcer
4098292	Antiphospholipid syndrome
77650	Aseptic necrosis of bone
4239873	Benign neoplasm of ciliary body
23731	Benign neoplasm of larynx
199764	Benign neoplasm of ovary
195500	Benign neoplasm of uterus
4145627	Biliary calculus
4108471	Burn of digit of hand
75121	Burn of lower leg
4284982	Calculus of bile duct without obstruction
434327	Cannabis abuse
78497	Cellulitis and abscess of toe
4001454	Cervical spine ankylosis
4068241	Chronic instability of knee
195596	Chronic pancreatitis
4206338	Chronic salpingitis
4058397	Claustrophobia
74816	Contusion of toe
73302	Curvature of spine
4151134	Cyst of pancreas
77638	Displacement of intervertebral disc without myelopathy
195864	Diverticulum of bladder
201346	Edema of penis
200461	Endometriosis of uterus
377877	Esotropia
193530	Follicular cyst of ovary
4094822	Foreign body in respiratory tract
443421	Gallbladder and bile duct calculi

4299408	Gouty tophus
135215	Hashimoto thyroiditis
442190	Hemorrhage of colon
43020475	High risk heterosexual behavior
194149	Hirschsprung's disease
443204	Human ehrlichiosis
4226238	Hyperosmolar coma due to diabetes mellitus
4032787	Hyperosmolarity
197032	Hyperplasia of prostate
140362	Hypoparathyroidism
435371	Hypothermia
138690	Infestation by Pediculus
4152376	Intentional self poisoning
192953	Intestinal adhesions with obstruction
196347	Intestinal parasitism
137977	Jaundice
317510	Leukemia
765053	Lump in right breast
378165	Nystagmus
434085	Obstruction of duodenum
4147016	Open wound of buttock
4129404	Open wound of upper arm
438120	Opioid dependence
75924	Osteodystrophy
432594	Osteomalacia
30365	Panhypopituitarism
4108371	Peripheral gangrene
440367	Plasmacytosis
439233	Poisoning by antidiabetic agent
442149	Poisoning by bee sting
4314086	Poisoning due to sting of ant
4147660	Postural kyphosis
434319	Premature ejaculation
199754	Primary malignant neoplasm of pancreas
4311499	Primary malignant neoplasm of respiratory tract
436635	Primary malignant neoplasm of sigmoid colon
196044	Primary malignant neoplasm of stomach
433716	Primary malignant neoplasm of testis
133424	Primary malignant neoplasm of thyroid gland

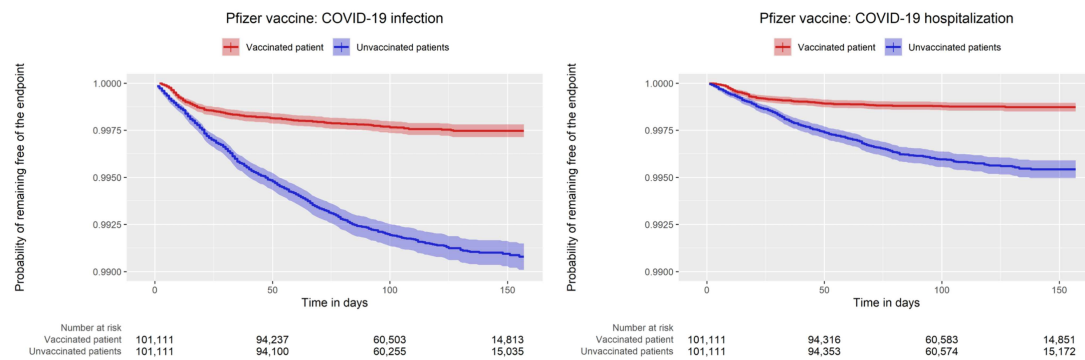
194997	Prostatitis
80286	Prosthetic joint loosening
443274	Psychostimulant dependence
314962	Raynaud's disease
37018294	Residual osteitis
4288241	Salmonella enterica subspecies arizonae infection
45757269	Sclerosing mesenteritis
74722	Secondary localized osteoarthritis of pelvic region
200348	Secondary malignant neoplasm of large intestine
43020446	Sedative withdrawal
74194	Sprain of spinal ligament
4194207	Tailor's bunion
193521	Tropical sprue
40482801	Type II diabetes mellitus uncontrolled
74719	Ulcer of foot
196625	Viral hepatitis A without hepatic coma
197494	Viral hepatitis C
4284533	Vitamin D-dependent rickets

Link to the original list of negative controls used in EUMAEUS study: https://ohdsi-studies.github.io/Eumaeus/Protocol.html#8_Research_Methods

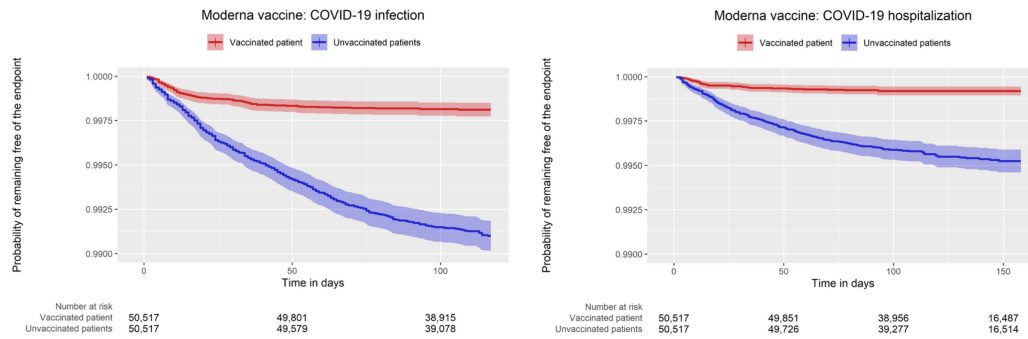
Appendix 5. Summary of manual chart review of COVID-19 infection cases during week 1 after the index date, patients vaccinated with mRNA vaccines and unvaccinated patients.

	Pfizer-BioNTech	Moderna	Pfizer-BioNTech and Moderna	Unvaccinated patients
Total	36	25	61	28
Average age	65.0	67.8	65.8	58.0
COVID-19 symptoms				
Severe	14 (39%)	7 (28 %)	21 (34%)	6 (21%)
Mild	18 (50%)	11 (44%)	29 (48%)	11 (39%)
Asymptomatic	4 (11%)	7 (28%)	11 (18%)	11 (39%)
Reason for coming for initial healthcare encounter				
COVID-19 symptoms	18 (50%)	12 (48%)	30 (49%)	18 (64%)
Exposure to COVID-19	3 (8%)	4 (16%)	7 (12%)	6 (21%)
For other reason (co-morbidities, procedures etc.)	15 (42%)	9 (36%)	24 (39%)	4 (14%)
Type of initial healthcare encounter				
Telehealth/phone	5 (14%)	6 (24%)	11 (18%)	3 (11%)
Test only	3 (8%)	2 (8%)	5 (8%)	6 (21%)
Outpatient visit	4 (11%)	3 (12%)	7 (12%)	1 (4%)
Emergency room or inpatient visit	24 (67%)	14 (56%)	38 (62%)	18 (64%)

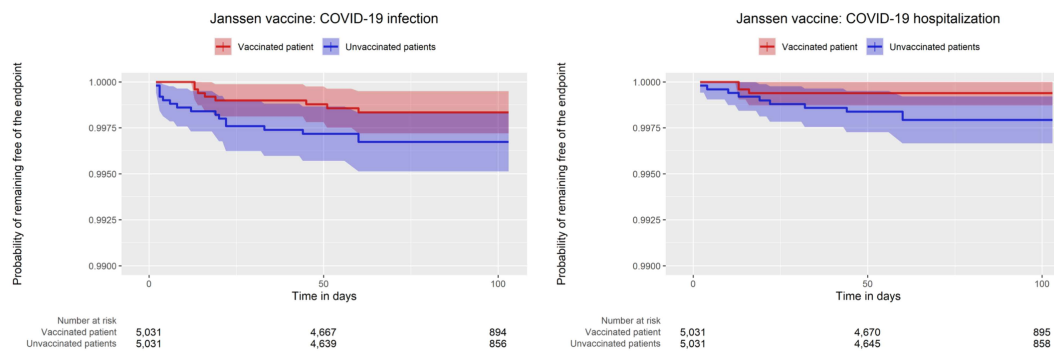
Appendix 6. Kaplan-Meier curves for effectiveness of COVID-19 Pfizer-BioNTech vaccine for time-at-risk of 1 day – 365 days after the first dose compared to the unvaccinated patients residing in New York City.



Appendix 7. Kaplan-Meier curves for effectiveness of COVID-19 Moderna vaccine for time-at-risk of 1 day – 365 days after the first dose compared to the unvaccinated patients residing in New York City.



Appendix 8. Kaplan-Meier curves for effectiveness of COVID-19 Janssen vaccine for time-at-risk of 1 day – 365 days after the first dose compared to the unvaccinated patients residing in New York City.



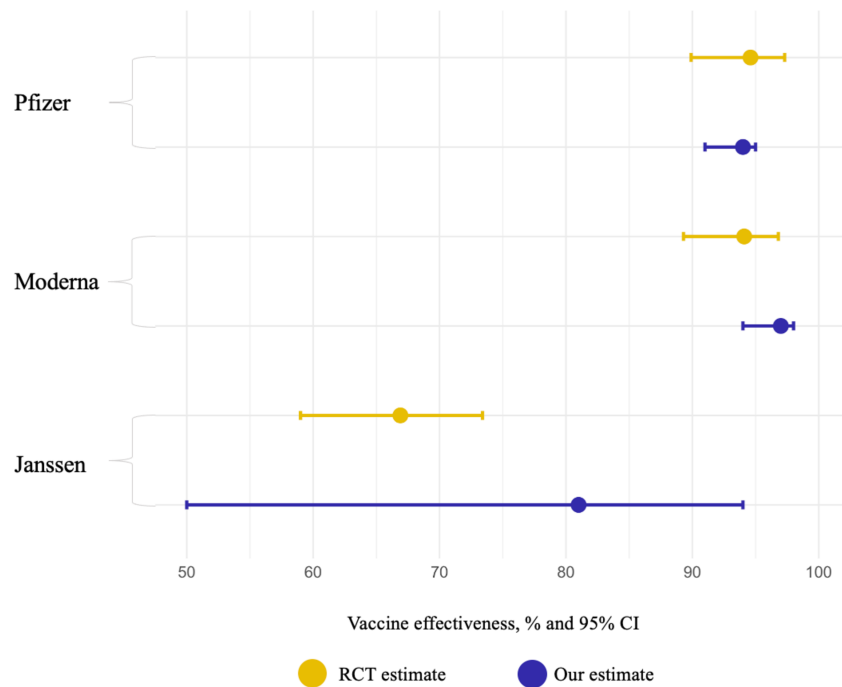
Appendix 9. Estimates for long-term effectiveness of COVID-19 vaccines for time-at-risk of 1 day – 365 days after the first dose in the vaccinated patients without prior COVID-19 infection compared to unvaccinated patients residing in NYC.

	COVID-19 infection		COVID-19 hospitalization		COVID-19 positive test only		COVID-19 positive test only hospitalization	
	VE (95% CI), %	P-value	VE (95% CI), %	P-value	VE (95% CI), %	P-value	VE (95% CI), %	P-value
Pfizer-BioNTech	42 (37 – 47)	<0.01	63 (56–70)	<0.01	71 (66 – 75)	<0.01	69 (62 – 75)	<0.01
Moderna	54 (48 – 60)	<0.01	76 (69 – 82)	<0.01	78 (73 – 83)	<0.01	81 (74 – 87)	<0.01
Janssen	24 (0-55)	0.31	64 (0.1 – 1.06)	0.09	53 (0 – 82)	0.1	70 (2 – 93)	0.08

Appendix 10. Estimates for effectiveness of COVID-19 vaccines for time-at-risk of 1 day – 365 days after full vaccination in fully vaccinated patients without prior COVID-19 infection compared to unvaccinated patients residing in NYC.

	COVID-19 positive test only		COVID-19 positive test only hospitalization		COVID-19 infection		COVID-19 hospitalization	
	VE (95% CI), %	P-value	VE (95% CI), %	P-value	VE (95% CI), %	P-value	VE (95% CI), %	P-value
Pfizer-BioNTech	94 (91-95)	<0.01	95 (92-97)	<0.01	70 (66-74)	<0.01	88 (84-92)	<0.01
Moderna	97 (94-98)	<0.01	96 (92-99)	<0.01	72 (66 – 77)	<0.01	92 (87-95)	<0.01
Janssen	81 (50-94)	<0.01	92 (58-100)	0.03	55 (23 – 75)	0.01	87 (56-98)	0.01

Appendix 11. Comparison of the effectiveness estimates in fully vaccinated patients obtained in our study and those from the randomized clinical trials of the corresponding vaccines.



Appendix 12. Estimates for effectiveness of COVID-19 vaccines for time-at-risk of 1 day – 365 days after the first dose in the vaccinated patients with or without prior COVID-19 infection compared to unvaccinated patients residing in NYC.

	COVID-19 infection		COVID-19 hospitalization		COVID-19 positive test only		COVID-19 positive test only hospitalization	
	VE (95% CI), %	P-value	VE (95% CI), %	P-value	VE (95% CI), %	P-value	VE (95% CI), %	P-value
Pfizer-BioNTech	43 (38-48)	<0.01	64 (57-70)	<0.01	71 (66-75)	<0.01	71(64-76)	<0.01
Moderna	51 (45-57)	<0.01	71 (63-78)	<0.01	76 (71-81)	<0.01	81 (73-86)	<0.01
Janssen	15 (0-49)	0.52	60 (2-86)	0.06	45 (0-75)	0.12	63 (0-90)	0.09