

Table S1. Variables used to define cohort entry and exclusion criteria, as well as study exposures, outcomes, adjustment, and stratification.

Assessment	Timing	Disease, procedure or condition	CIHI-DAD, SDS or NACRS ICD-10-CA diagnosis or CCI procedure codes	OHIP ICD-9 diagnosis or fee codes; or other data source	Validation studies or documentation for some codes
<i>Inclusion criteria</i>	ABO-Rh specimen date January 2007 to December 2020	Individuals with an ABO blood group test result in Ontario, Canada	--	LOINC codes 882-1, 883-9, 10331-7 in the Ontario Laboratory Information System (OLIS) - includes most outpatient laboratory information in Ontario	--
<i>Exclusion criteria</i>	SARS-CoV-2 specimen date January 15, 2020 to January 14, 2021	Individuals with a SARS-CoV-2 RNA PCR positive laboratory result in Ontario, Canada prior to time zero	--	OLISC19 - includes Test Request (TR)/LOINC codes for SARS-CoV-2 and other respiratory virus testing: TR12936-1, TR12937-9, 94315-9, 94314-2, 94316-7, XON13512-9, XON13529-3, XON13528-5, XON13531-9, XON13527-7. These codes, plus keywords such as "COVID", "SARS-CoV-2", "Novel coronavirus" or "nCOV" or microorganism SNOMED codes (840533007 [SARS-CoV-2], 168209000 [No Virus Identified]), were used to define the data pull from OLIS.	For the ICES methodology and Python script for cleaning and parsing OLIS lab results for SARS-CoV-2 and other respiratory viruses, see https://github.com/icescentral/C-OVID19-Lab-Results
	January 15, 2021 (time zero)	Implausible or missing sex, birth date or death date	--	Registered Persons Database (RPDB) - contains demographic information and encrypted healthcare numbers for all individuals eligible for OHIP	--
	Same as above	Non-Ontario resident or not eligible for OHIP at time zero	--	RPDB	--
	Same as above	Aged less < 12 years at time zero	--	RPDB	--

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	Same as above	Death occurred before baseline, before the vaccination date, or > 1 day before the SARS-CoV-2 specimen date	Discharge disposition is not alive (DAD , NACRS)	RPDB, COVAXON, OLISC19	--
	December 15, 2020 to June 13, 2021	Duplicate vaccination record	--	COVAXON	--
<i>Study exposures</i>	December 15, 2020 to June 13, 2021	COVID-19 partially vaccinated status	--	COVAXON	--
	Same as above	COVID-19 1 st dose type (mRNA, viral vector, unknown, none)	--	COVAXON	--
	Same as above	COVID-19 fully-vaccinated status (fully-vaccinated, partially-vaccinated, unvaccinated)	--	COVAXON	--
<i>Stratification variable</i>	January 2007 to December 2020	ABO blood group (O, other)	--	LOINC codes 882-1, 883-9, 10331-7 in OLIS	--
<i>Main study outcome</i>	SARS-CoV-2 specimen date January 15, 2021 (time zero) to June 27, 2021, censored at loss OHIP eligibility or the day after death.	Earliest SARS-CoV-2 positive test.	--	OLISC19	--

Assessment	Timing	Disease, procedure or condition	CIHI-DAD, SDS or NACRS ICD-10-CA diagnosis or CCI procedure codes	OHIP ICD-9 diagnosis or fee codes; or other data source	Validation studies or documentation for some codes
<i>Secondary study outcome</i>	SARS-CoV-2 specimen date January 15, 2021 (time zero) to June 30, 2021, censored at loss OHIP eligibility or the day after death.	Earliest SARS-CoV-2 positive test <u>AND</u> a hospital admission within +/- 3 days or death within -1 to +3 days of the SARS-CoV-2 specimen date.	DAD (hospital admission, not alive at discharge), NACRS (hospital admission, not alive at discharge), SDS (not alive at discharge)	OLISC19 (SARS-CoV-2 test), RPDB (death)	--
<i>Covariates</i>	January 15, 2021 (time zero)	Age	--	RPDB	--
	Same as above	Sex	--	RPDB	--
	Same as above	Area income quintile	--	Statistics Canada Census	--
	Same as above	Rural residence	--	Statistics Canada Census	--
	Any time before January 15, 2021 (time zero)	Diabetes mellitus	The ICES-derived ODD database was used to identify patients with diagnosed diabetes before the index date, based on 2 OHIP diagnostic codes or 1 OHIP fee code or 1 DAD/SDS diagnostic code, within 2 years. ICD-10-CA: E10, E11, E13, E14	OHIP ICD-9: 250 OHIP fee codes: Q040, K029, K030, K045, K046	https://pubmed.ncbi.nlm.nih.gov/11874939/

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	Same as above	History of heart failure	The ICES-derived CHF database was used to identify patients with CHF, based on 1 ED, hospitalization or outpatient claim, and a second claim in 1 year. <i>The CHF database is limited to those 40 years of age or older.</i> ICD-10-CA (DAD, SDS): I500, I501, I509	OHIP ICD-9: 428	https://pubmed.ncbi.nlm.nih.gov/23735455/
	Within 5 years before January 15, 2021 (time zero)	History of malignant neoplasm	ICD-10-CA (DAD, SDS, NACRS): C00-C97	--	--
	Same as above	Chronic kidney disease (CKD)	<u>CKD diagnosis</u> ICD-10-CA (DAD, NACRS): E102, E112, E132, E142, I12, I13, N08, N18, N19	<u>CKD diagnosis</u> ICD-9 (OHIP): 403, 585	https://pubmed.ncbi.nlm.nih.gov/23560464/

Assessment	Timing	Disease, procedure or condition	CIHI-DAD, SDS or NACRS ICD-10-CA diagnosis or CCI procedure codes	OHIP ICD-9 diagnosis or fee codes; or other data source	Validation studies or documentation for some codes
			<u>Chronic dialysis</u> At least 2 of the following CCI (DAD, SDS) codes separated by 90 days, but < 150 days, in the year before the index date: 1PZ21	<u>Chronic dialysis</u> At least 2 of the following OHIP fee codes separated by 90 days, but < 150 days, in the year before the index date: R849, G082, G083, G085, G090-G096, G294, G295, G323, G325, G326, G330-G333, G860-G866, H540, H740 Treatment codes (CORR): 060, 111, 112, 113, 121, 122, 123, 131, 132, 133, 141, 151, 152, 211, 221, 231, 241, 242, 251, 252, 311, 312, 313, 321, 322, 323, 331, 332, 333, 413, 423, 433, 443, 453	https://pubmed.ncbi.nlm.nih.gov/20613656/
			<u>Exclude kidney transplant</u> CCI (DAD): 1PC85	<u>Exclude kidney transplant</u> OHIP fee codes: S435, S434 CORR treatment code: 171 plus ≥ 1 Transplanted Organ Code [1-3]: 10, 11, 12, 18, 19	https://pubmed.ncbi.nlm.nih.gov/26019887/

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	Same as above	History of cardiac ischemia	<p>At least 1 hospitalization (DAD) or ED (NACRS) visit with a diagnosis or procedure coded with 1 of the following codes:</p> <p><u>Angina:</u> ICD-10-CA: I20, I2382, I24</p> <p><u>Chronic Ischemic Heart Disease:</u> ICD-10-CA: I25</p> <p><u>Myocardial infarction:</u> ICD-10-CA: I21, I22</p> <p><u>Coronary Artery Bypass Grafting:</u> CCI: 1I176, 1I180</p> <p><u>Percutaneous Coronary Intervention:</u> CCI: 1I126, 1I150, 1I155, 1I157</p>	--	https://pubmed.ncbi.nlm.nih.gov/20847972/

Assessment	Timing	Disease, procedure or condition	CIHI-DAD, SDS or NACRS ICD-10-CA diagnosis or CCI procedure codes	OHIP ICD-9 diagnosis or fee codes; or other data source	Validation studies or documentation for some codes
	Same as above	History of cardiac arrhythmia	<p>At least 1 hospitalization (DAD) or ED (NACRS) visit with a diagnosis or procedure coded with 1 of the following codes:</p> <p><u>Atrial Fibrillation/Atrial Flutter:</u> ICD-10-CA: I48</p> <p><u>Ventricular Arrhythmia & Tachycardia:</u> ICD-10-CA: I470, I472, I490, I493</p> <p><u>Permanent Pacemaker:</u> CCI: 1HZ53GRNM, 1HZ53LANM, 1HZ53GRNK, 1HZ53LANK, 1HZ53GRNL, 1HZ53LANL</p> <p><u>Implantable Cardioverter-Defibrillator:</u> CCI: 1HZ53GRFS, 1HZ53LAFS, 1HZ53SYFS, 1HZ53HAFS</p>	--	<p>https://pubmed.ncbi.nlm.nih.gov/19433698/</p> <p>https://www.ices.on.ca/Publications/Atlases-and-Reports/2006/Canadian-Institute-for-Health-Information</p> <p>https://pubmed.ncbi.nlm.nih.gov/17599603/</p>

Assessment	Timing	Disease, procedure or condition	CIHI-DAD, SDS or NACRS ICD-10-CA diagnosis or CCI procedure codes	OHIP ICD-9 diagnosis or fee codes; or other data source	Validation studies or documentation for some codes
	Same as above	History of pulmonary embolism, deep vein thrombosis, or other venous thromboembolism	<p>ICD-10-CA (DAD, SDS, NACRS): I260, I269, O88201, O88202, O88203, O88204, O88209, I636, I822, I828, I829, I801, I802, I803, I808, I809, O22301, O22303, O22309, O22501, O22503, O22509, O87102, O87104, O87109, O87304, O87309, I676, I81, I820, I823, O228, O229, O878, O879</p> <p><u>AND</u></p> <p>one of the following CCI codes for diagnostic imaging during the same admission: 3KX30DA, 3KX30DB, 3KX30DC, 3KX30DD, 3KR10VC, 3KR10VN, 3KR12VA, 3KX10VA, 3KX10VC, 3KX10VN, 3KX10VX, 3KX12VA, 3IM10VC, 3IM10VX, 3IM10VY, 3IM12VA, 3GT70CA, 3GT70CC, 3GT70CE, 3GT70KC, 3GT70KD, 3GT70KE, 3JY10VA, 3JY10VC, 3JY10VN, 3JY10VX, 3JY12VA, 3JY20WC</p>	<p>OHIP ICD-9: 677, 415, 671, 451, 452</p> <p><u>AND</u></p> <p>one of the following OHIP radiological professional fee codes for a VTE diagnostic test billed within 3 days: J198, J498, J193, J493, J202, J502, J206, J506, J182, J482, X406, X407, X125, X188, X401, X405, X408, X126, X410, X231, X232, X233, X127, X413, X421, X425, J659, J660, J859, J860</p>	--

Assessment	Timing	Disease, procedure or condition	CIHI-DAD, SDS or NACRS ICD-10-CA diagnosis or CCI procedure codes	OHIP ICD-9 diagnosis or fee codes; or other data source	Validation studies or documentation for some codes
<i>Other baseline variables</i>	Any time before January 15, 2021 (time zero)	Asthma	The ICES-derived ASTHMA database was used to identify patients with diagnosed asthma before the index date, based on 2 OHIP diagnostic codes or 1 DAD diagnostic code. ICD-10-CA: J45, J46	OHIP ICD-9: 493	https://pubmed.ncbi.nlm.nih.gov/20011725/
	Same as above	Chronic obstructive pulmonary disease (COPD)	The ICES-derived COPD database was used to identify patients with diagnosed COPD before the index date, based on 1 OHIP diagnostic code or 1 DAD diagnostic code. ICD-10-CA: J41-J44	OHIP ICD-9: 491, 492, 496	https://pubmed.ncbi.nlm.nih.gov/19863368/ <i>The COPD algorithm was validated in those aged ≥ 35 years.</i>
	Same as above	Chronic hypertension	The ICES-derived HYPER database was used to identify patients with: a) 1 hospital admission with a hypertension diagnosis, or b) an OHIP claim with a hypertension diagnosis followed within 2 years by either an OHIP claim or a hospital admission with a hypertension diagnosis. ICD-10-CA (DAD, SDS): I10-I13, I15	OHIP ICD-9: 401-405	https://pubmed.ncbi.nlm.nih.gov/20101286/

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	Same as above	Immunocompromised (HIV or organ transplant)	--	The ICES-derived HIV database was used to identify patients with pre-existing HIV, based on 3 physician claims in 3 years. OHIP ICD-9: 042-044 CORRLINK links CORR and DAD data and includes patients who received an organ transplant, and does not include dialysis patients.	https://pubmed.ncbi.nlm.nih.gov/21738786/
	Same as above	Dementia	The ICES-derived DEMENTIA database was used to identify individuals with 1 hospitalization for dementia and/or 3 outpatient visits for dementia, each separated by 30 days, within 2 years, or 1 prescription from ODB. ICD-10-CA (DAD, SDS): F00-F03, G30	OHIP ICD-9: 290, 331 ODB 1 prescription for a cholinesterase inhibitor	https://pubmed.ncbi.nlm.nih.gov/27567819/

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	Within 1 year before January 15, 2021 (time zero)	Frailty	Identified based on the following rules, using DAD and OHIP databases: 1. Long-term care residence (i.e., admitted from/discharged to, a nursing home after hospital stay, or location of physician billing claim was long-term care facility); 2. Receipt of palliative care; 3. Two or more domains derived from frailty scales (i.e., cognitive impairment, falls, general health status, incontinence, nutrition issues, functional performance) and health services utilization (i.e., ≥ 2 hospital stays or ED visits, geriatrician or home care visit).	--	https://pubmed.ncbi.nlm.nih.gov/28974280/
	Within 5 years before January 15, 2021 (time zero)	Anemia	ICD-10-CA (DAD, SDS, NACRS): D50-D53, D55, D56, D572-D574, D58-D61, D63, P55, P560, P570	OHIP ICD-9: 280-285, 773	--

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	Same as above	History of transient ischemic attack or acute ischemic stroke	<p><u>Transient Ischemic Attack:</u> At least 1 hospitalization or ED visit with 1 of the following diagnosis codes:</p> <p>ICD-10-CA (DAD, NACRS): G450-G453, G458, G459, H340</p> <p><u>Acute Ischemic Stroke:</u> 1 hospitalization with a main diagnosis coded with one of the following codes:</p> <p>ICD-10-CA (DAD): I63 (except I636), I64, H341</p>	--	http://canadiansrokenetwork.ca/en/wp-content/uploads/2014/08/Stroke_Core_ENG.pdf

ASTHMA: Ontario Asthma dataset; CCI: Canadian Classification of Interventions; CHF: Ontario Congestive Heart Failure dataset; CIHI: Canadian Institute for Health Information; CORR: Canadian Organ Replacement Registry; COVAXON: Ontario COVID-19 Vaccine Data; DAD: Discharge Abstract Database; DEMENTIA: Ontario Dementia dataset; ED: Emergency Department; HIV: Ontario HIV dataset; HYPER: Ontario Hypertension dataset; ICD-9: International Classification of Diseases, 9th Revision; ICD-10-CA: International Classification of Diseases, 10th Revision, Canada; ICU: Intensive Care Unit; LHIN: Local Health Integration Network; LOINC: Logical Observation Identifiers Names and Codes; NACRS: National Ambulatory Care Reporting System; ODB: Ontario Drug Benefit; ODD: Ontario Diabetes Dataset; OHIP: Ontario Health Insurance Plan; OLIS: Ontario Laboratories Information System; OLISC19: Ontario Laboratories Information System COVID-19 Laboratory Data; RPDB: Registered Persons Database; SDS: Same Day Surgery

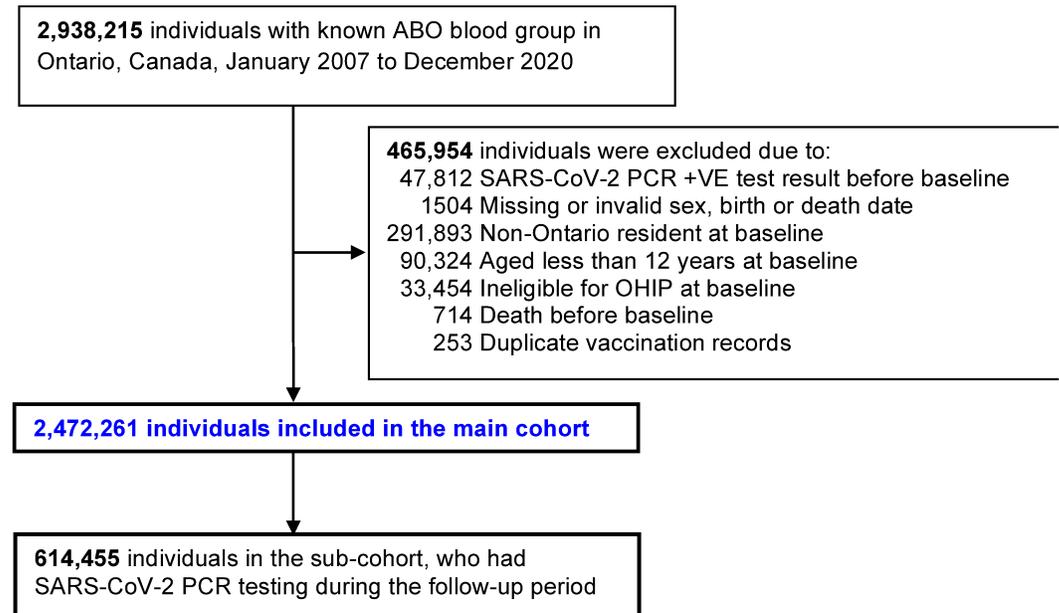
Figure S1. Study cohort creation.

Table S2 (Additional analysis 1). SARS-CoV-2 vaccination and associated risk of SARS-CoV-2 infection, or severe COVID-19 (hospitalization or death) – each assessed starting at least 14 days after the first vaccination. This analysis is limited to 614,455 individuals who had SARS-CoV-2 PCR testing during the follow-up period, from January 15, 2021 onward.

Study outcome	Exposure state ^a	No. person-days of follow-up ^a	No. with outcome (rate per 10,000 person-days)	Unadjusted hazard ratio (95% CI%)	Adjusted hazard ratio (95% CI%) ^b
SARS-CoV-2 infection	Unvaccinated (N = 609,129)	67,185,613	51,187 (7.62)	1.00 (referent)	1.00 (referent)
	Vaccinated (N = 439,058)	27,220,438	4995 (1.84)	0.25 (0.25 to 0.26)	0.28 (0.27 to 0.29)
Severe COVID-19	Unvaccinated (N = 609,129)	71,414,615	2890 (0.40)	1.00 (referent)	1.00 (referent)
	Vaccinated (N = 439,058)	27,470,663	491 (0.18)	0.50 (0.46 to 0.56)	0.22 (0.20 to 0.25)

^aExposure is time-varying, therefore, some individuals may have contributed time as unvaccinated, and then subsequently, as vaccinated.

^bAdjusted for age, sex, rural residence, area income quintile – each at baseline -- as well as prior diabetes mellitus, malignancy, heart failure, cardiac ischemia or arrhythmia, chronic kidney disease or venous thromboembolism.

Table S3. SARS-CoV-2 vaccination and associated risk of SARS-CoV-2 infection, or severe COVID-19 (hospitalization or death), stratified by O and non-O blood groups, among the entire cohort. Data are presented by time-varying exposure after first vaccination type vs. unvaccinated, with study outcomes assessed starting at least 14 days after the first vaccination.

Study outcome	Stratified by blood group	Exposure state ^a	No. person-days of follow-up ^a	No. with outcome (rate per 10,000 person-days)	Adjusted hazard ratio (95% CI) ^b
SARS-CoV-2 infection	Non-O	Unvaccinated (N = 1,401,213)	172,490,490	30,685 (1.78)	1.00 (referent)
		Adenovirus-vectored (N = 80,411)	4,637,314	260 (0.56)	0.49 (0.43 to 0.55)
		Modified RNA (N = 912,274)	48,108,108	2717 (0.56)	0.46 (0.44 to 0.48)
	O	Unvaccinated (N = 1,063,785)	130,718,702	20,502 (1.57)	1.00 (referent)
		Adenovirus-vectored (N = 62,947)	3,626,421	174 (0.48)	0.49 (0.42 to 0.57)
		Modified RNA (N = 688,250)	36,951,138	1844 (0.50)	0.46 (0.44 to 0.48)
Severe COVID-19	Non-O	Unvaccinated (N = 1,401,213)	175,034,046	1677 (0.10)	1.00 (referent)
		Adenovirus-vectored (N = 80,411)	4,649,419	15 (0.03)	0.27 (0.16 to 0.45)
		Modified RNA (N = 912,274)	48,242,495	296 (0.06)	0.31 (0.27 to 0.36)
	O	Unvaccinated (N = 1,063,785)	132,404,148	1213 (0.09)	1.00 (referent)
		Adenovirus-vectored (N = 62,947)	3,634,743	12 (0.03)	0.33 (0.18 to 0.58)
		Modified RNA (N = 688,250)	37,046,550	168 (0.05)	0.27 (0.22 to 0.32)

^aExposure is time-varying, therefore, some individuals may have contributed time as unvaccinated, and then subsequently, as vaccinated.

^bAdjusted for age, sex, rural residence, area income quintile – each at baseline -- as well as prior diabetes mellitus, malignancy, heart failure, cardiac ischemia or arrhythmia, chronic kidney disease or venous thromboembolism.