

# COVID-19, Myocarditis and Pericarditis

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## Supplementary Data

### Tables

Supplementary Table 1. Animal models of myocarditis<sup>1-4</sup>

	<b>Virus-only models</b> (e.g., CVB3*, EMCV, Rheovirus)	<b>Autoimmune virus models</b> (e.g., EAM, CVB3, MCMV)	<b>Autoimmune models</b> (e.g., EAM)
<b>Survival</b>	20-30% by day 7	100% survival	100% survival
<b>Necrosis</b>	High levels	Low, appears day 35	Low, appears day 45
<b>Viral replication</b>	10 <sup>7</sup> -10 <sup>9</sup> PFU/g heart	10 <sup>3</sup> -10 <sup>5</sup> PFU/g heart	No virus in model
<b>Acute myocarditis</b>	Peak at day 7	Peak at day 10	Peak at day 21
<b>Key cell mediators</b>	CVB3: $\gamma\delta$ T cells & CD8 T cells	CVB3: CD11b+ macrophages & MCs, T & B cells	CD11b+ macrophages & MCs, T & B cells
<b>Chronic myocarditis</b>	Most do not survive	Starts day 35	Starts day 45
<b>Progression to DCM</b>	Yes, in survivors	Yes (BALB/c, A/J)	Yes (BALB/c, A/J)
<b>Sex differences</b>	Males worse	Males worse	Males worse

\* **Abbreviations:** CVB3, coxsackievirus B3; DCM, dilated cardiomyopathy; EAM, experimental autoimmune myocarditis; EMCV, encephalomyocarditis virus; MCMV, murine cytomegalovirus; MCs, mast cells; PFU, plaque forming units.

Supplementary Table 2. Several large epidemiological studies of SARS-CoV-2 myocarditis and pericarditis

<b>Location</b>	<b>n</b>	<b>Incidence or increased risk of myocarditis/ pericarditis after COVID-19*</b>	<b>Reference</b>
<b>US</b>	1,452,773	16x greater risk with COVID; 9/100,000 no COVID vs. 150/100,000 with COVID; myocarditis occurred 42.3% more in 2020 than 2019; risk higher in males than females	5
<b>US</b>	718,365	5% increase myocarditis & 1.5% pericarditis	6
<b>US</b>	691,455	1-12 months after COVID infection, myocarditis HR=4.41, 95% CI 2.89-6.72; pericarditis HR=1.62, 95% CI 1.45-1.81, more cases in younger age under 40 and in males	7
<b>Israel</b>	233,392	Myocarditis RR=18.28, 95% CI 3.95-25.12; incidence myocarditis 11/100,000 and 11/100,000 pericarditis after COVID	8

<b>Israel</b>	196,992	No association of myocarditis or pericarditis with “long-COVID” (i.e., developing after acute infection resolves)	9
<b>US</b>	193,113	14% increased risk of sequelae including myocarditis/cardiomyopathy	10
<b>US</b>	107,699	COVID-19 group, 79 (0.12%) patients had new-onset myocarditis compared to 29 (0.04%) in the non-COVID-19 control	11
<b>Spain</b>	74,814	Myopericarditis OR=4.43, 95% CI 3.98-4.94	12
<b>US</b>	70,288	Myocarditis (OR 8.17, 95% CI 3.58–18.62, absolute risk 0.1%)	13
<b>Europe and US</b>	56,963	Myocarditis (definite/ probable) 240/100,000, (possible) 410/100,000 patients hospitalized for COVID-19	14
<b>Hong Kong</b>	11,441	Compared to the background rate, the rate of myopericarditis among vaccinated subjects in Hong Kong was similar 0.55/100,000 (5.5/million)	15

\*Abbreviations: aRR, adjusted relative risk; CI, confidence intervals; IRR, incidence rate ratio; OR, odds ratio; RI, relative incidence; RR, relative risk or risk ratio

Supplemental Table 3. Large epidemiological studies of COVID-19 vaccine-associated myocarditis/pericarditis

<b>Location</b>	<b>Vaccine</b>	<b>Incidence of myocarditis/pericarditis after 2<sup>nd</sup> dose (95% CI)*</b>	<b><i>n</i></b>	<b>Reference</b>
<b>Worldwide</b>	Moderna	Overall 9.23/100,000, males 18-24 years 53.76/100,000, males <40 years RR=3.10, (2.68-3.58)	252,000,000	16
<b>US</b>	Pfizer Moderna	US VAERS 82% of cases were male, 69% of cases were White; reporting rates highest after second dose: males 12-15 years 7.1/100,000, males 16-17 10.6/100,000, males 18-24 5.2/100,000 (Pfizer) and 5.6/100,000 (Moderna)	192,405,448	17
<b>UK</b>	Pfizer Moderna AstraZeneca	1/100,000 (Pfizer), 1.4/100,000 (Moderna), 0.5/100,000 (AstraZeneca) reporting rates overall for all doses, highest in 18-29 years group and males for mRNA vaccines, especially after second dose	53,000,000	18
<b>Canada</b>	Pfizer Moderna AstraZeneca Noravax Janssen Medicago	97.8% associated with mRNA vaccines, 62% of those associated with second dose: 65% male, median age 25 years (Pfizer); 76% male, median age 28 (Moderna)	32,438,982	19

		other		
<b>France</b>	Pfizer Moderna	Pfizer/BNT162b2 myocarditis OR=6.9 (5.7–8.4), pericarditis OR=2.7 (2.2–3.5); Moderna/mRNA-1273 myocarditis OR=27 (19–39), pericarditis OR=5.3 (3.3–8.4)	32,000,000	20
<b>Europe</b>	Pfizer Moderna AstraZeneca	Increased risk after 1st & 2nd dose. Myocarditis Pfizer/BNT162b2 aRR=1.75 (1.43-2.14), Moderna/mRNA-1273 aRR=6.57 (4.64-9.28), Males 16-24 years BNT162b2 aRR=5.31 (3.68-7.68), mRNA-1273 aRR=13.83 (8.08-23.68)	23,122,522	21
<b>UK</b>	Pfizer Moderna AstraZeneca	Increased risk from 1 <sup>st</sup> and 2 <sup>nd</sup> dose but increased risk of myocarditis only in those under 40 years of age	20,615,911	22
<b>Singapore</b>	Pfizer Moderna	Overall 0.1-1/100,000, incidence highest in young males <30 years	5,241,294	23
<b>Israel</b>	Pfizer	Myocarditis RR=5.34 (4.48-6.40), males 16-19 years greatest risk: IRR=13.60 (9.30-19.20)	5,000,000	24
<b>Denmark</b>	Pfizer Moderna AstraZeneca Janssen	40% of cases in patients 12-39 years, 73% of cases were male; Pfizer/BNT162b2 overall 1.4/100,000; males 1.5/100,000; females 1.3 females; age 12-39 males & females 1.6/100,000; Moderna/mRNA-1273 overall 4.2/100,00; males 6.3/100,000; females 2.0/100,000; age 12-39 males & females 5.7/100,000	3,482,295 498,814	25
<b>Italy</b>	Pfizer Moderna	Increased risk with Pfizer after 2nd dose and with Moderna for 1st and 2nd dose; Myocarditis BNT162b2 RR=1.99 (1.30 to 3.05); mRNA-1273 RR=2.63 (1.21 to 5.71); highest risk males 12-39 years with mRNA-1273 RI=11.91 (3.88 to 36.53)	2,861,809	26
<b>US Military</b>	Pfizer Moderna	Incidence not reported	2,810,000	27
<b>Israel</b>	Pfizer	Myocarditis 1st dose: 2.13/100,000 (1.56-2.70); Males 16-29 years 10.69/100,000 (6.93 to 14.46)	2,500,000	28

<b>US</b>	Pfizer Moderna	Increased risk in 18-39 years, 2.2/100,000 (Pfizer), 3.1/100,000 (Moderna), 86% of cases were male	2,403,307	29
<b>US</b>	Pfizer Moderna	Myocarditis 2.7 (95% CI, 1.4-4.8)- all were males, study did not separate data by vaccine type, all under 40 years of age- most under 25 years; 64% White	2,392,924	30
<b>Hong Kong</b>	Pfizer Sinovac	Sex and age not reported for myocarditis risk, myocarditis and pericarditis combined 10/100,000 (Pfizer), 3/100,000 (CoronaVac)	2,333,379	31
<b>US</b>	Pfizer Moderna J&J	Myocarditis 1 case/100,000; pericarditis 1.9 cases/100,000; 75% males for both; myocarditis young under 40 years, pericarditis older over 50 years; myocarditis 95% White, pericarditis 84% White	2,000,287	32
<b>Israel</b>	Pfizer	Vaccinated & matched controls of same size 2.7/100,000 (1.0-4.6); RR=3.24 (1.55 to 12.44), no analysis by sex and age	884,828	8

\*Abbreviations: aRR, adjusted relative risk; CI, confidence intervals; IRR, incidence rate ratio; OR, odds ratio; RI, relative incidence; RR, relative risk or risk ratio; VAERS, vaccine adverse event reporting system

Supplementary Table 4. Most common COVID-19 vaccines<sup>33-35</sup>

<b>Developer</b>	<b>Common names</b>	<b>Vaccine type</b>	<b>Emergency Use Listing by WHO</b>	<b>Main usage</b>
<b>BioNTech/ Pfizer</b>	BNT162b2, Comirnaty, Tozinameran	nucleoside modified mRNA	31-Dec-20	approved in US, widely used
<b>AstraZeneca</b>	Oxford- AstraZeneca, CHADOX1 NCOV-19, Covishield, Vaxzevria, AZD1222, ChAdOx1_nCoV1, SII	recombinant ChAdOx1 adenoviral vector encoding spike protein antigen	16-Feb-21	widely used

<b>Johnson &amp; Johnson</b>	J&J, Janssen, Jcovden, Ad26.COV 2.S	recombinant, replication incompetent adenovirus type 26 vector vaccine encoding spike protein	12-Mar-21	approved in US, widely used
<b>Moderna</b>	Moderna, Elasmoran, SpikeVax, mRNA 1273	mRNA	30-Apr-21	approved in US, widely used
<b>China National Pharmaceutical Group</b>	Sinopharm BIBP	Inactivated virus, produced in Vero cells	7-May-21	Southeast Asia, Africa, South America
<b>Sinovac Biotech</b>	Coronavac	Inactivated virus, produced in Vero cells	1-Jun-21	Southeast Asia, Africa, South America
<b>Bharat Biotech</b>	COVAXIN, BBV152		3-Nov-21	South Asia, Africa, South America
<b>Novavax</b>	NVX-CoV2373, Covovax, Nuvaxovoid	protein subunit vaccine	20-Dec-21	approved in US, widely used
<b>Gamaleya Research Institute</b>	Sputnik V	human adenovirus vector-based	n/a	Russia

\*Abbreviations: n/a, not available; US, United States; WHO, World Health Organization.

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