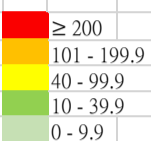


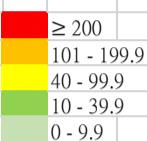
Supplementary Figure 1. Flowchart diagram of the study selection for systematic review on mRNA COVID-19 vaccine-associated myocarditis and pericarditis

a

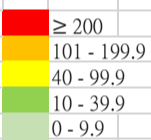
		Age									
		40	44-45	49-50	54-55	59-60	64-65	69-70	74-75	79	≥ 80
BNT 1st dose	Male										
Taiwan ¹		3.6					0.0				
US ²		0.6					0.4				
Japan ³		0.4	0.7	0.6	0.7	0.0	0.6	0.5	0.4	0.5	
BNT 2nd dose	Male										
Nordics ⁴		1.4									
Taiwan ¹		2.1					0.0				
US ²		3.5					0.7				
Japan ³		2.5	0.7	1.3	1.1	0.4	0.3	0.3	0.7	0.2	
BNT 1st dose	Female										
Nordics ⁴		1.6									
Taiwan ¹		1.6					0.0				
US ²		0.2					0.4				
Japan ³		0.4	0.0	0.6	0.0	0.3	0.6	0.7	0.3	0.6	
BNT 2nd dose	Female										
Taiwan ¹		0.0					0.0				
US ²		1.7					0.5				
Japan ³		0.4	0.6	0.0	0.3	1.0	0.0	0.7	0.3	0.1	



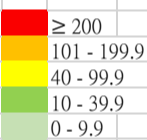
		Age									
		40	44-45	49-50	54-55	59-60	64-65	69-70	74-75	79	≥ 80
Moderna 1st dose	Male										
Taiwan ¹		0.0					0.0				
US ²		0.6					0.6				
Japan ³		1.0	0.0	0.0	0.0	2.0	0.0	0.0	0.0	0.0	
Moderna 2nd dose	Male										
Taiwan ¹		7.7					0.0				
US ²		4.3					0.9				
Japan ³		2.0	3.5	1.0	2.5	2.0	4.1	0.0	0.0	0.0	
Moderna 1st dose	Female										
Taiwan ¹		0.0					0.0				
US ²		0.2					0.7				
Japan ³		0.0	1.3	1.5	0.0	0.0	5.6	6.6	0.0	0.0	
Moderna 2nd dose	Female										
Taiwan ¹		0.0					0.0				
US ²		1.9					0.4				
Japan ³		0.0	0.0	2.9	0.0	0.0	5.6	0.0	0.0	0.0	

**b**

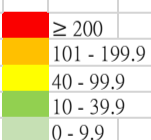
		Age									
		40	44-45	49-50	54-55	59-60	64-65	69-70	74-75	79	≥ 80
BNT 1st dose	Male										
Israel ⁵		6.5					1.0				
Nordics ^{4**}		5.5									
Taiwan ¹		3.6					0.0				
Japan ³		0.4	0.7	0.6	1.1	0.0	0.6	0.8	0.7	1.0	
BNT 2nd dose	Male										
Israel ⁵		11.5					2.1				
Nordics ^{4**}		6.5									
Taiwan ¹		2.1					0.0				
Japan ³		3.7	0.7	1.9	1.1	0.7	0.3	0.3	0.7	0.7	
BNT 1st dose	Female										
Israel ⁵		2.1					0.9				
Nordics ^{4**}		5.3									
Taiwan ¹		1.6					2.2				
Japan ³		0.7	0.3	0.8	0	0.3	0.6	1.1	0.3	0.8	
BNT 2nd dose	Female										
Israel ⁵		4.5					1.9				
Nordics ^{4**}		4.9									
Taiwan ¹		0.0					2.5				
Japan ³		0.4	0.6	0	0.6	1	0	0.7	0.3	0.8	



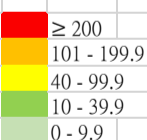
		Age									
		40	44-45	49-50	54-55	59-60	64-65	69-70	74-75	79	≥ 80
Moderna 1st dose	Male										
Nordics ^{4**}		9.6									
Taiwan ¹		5.9					3.9				
Japan ³		1.0	0.0	0.0	0.0	2.0	0.0	0.0	0.0	0.0	
Moderna 2nd dose	Male										
Nordics ^{4**}		19.5									
Taiwan ¹		7.7					0.0				
Japan ³		3.0	3.5	1.0	2.5	2.0	4.1	0.0	0.0	0.0	
Moderna 1st dose	Female										
Taiwan ¹		0.0					0.0				
Japan ³		0.0	2.6	1.5	0.0	0.0	5.6	6.6	0.0	0.0	
Moderna 2nd dose	Female										
Taiwan ¹		0.0					0.0				
Japan ³		0.0	2.7	2.9	0.0	0.0	5.6	0.0	0.0	0.0	

**c**

		Age									
		40	44-45	49-50	54-55	59-60	64-65	69-70	74-75	79	≥ 80
BNT 1st dose	Male										
Ontario, Canada ⁶		0.0									
Taiwan ¹		5.4					0.0				
Japan ³		0.4	1.0	1.0	1.1	0.0	1.6	0.8	1.8	1.5	
BNT 2nd dose	Male										
Ontario, Canada ⁶		0.0									
Australia ⁷		14					7				
Taiwan ¹		2.1					0.0				
Japan ³		4.2	1.3	1.9	1.1	0.7	0.9	0.3	1.4	2.9	
BNT 1st dose	Female										
Ontario, Canada ⁶		0.0									
Taiwan ¹		1.6					2.2				
Japan ³		1.4	0.6	1.4	0.3	0.6	1.4	1.3	0.6	1.3	
BNT 2nd dose	Female										
Ontario, Canada ⁶		0.0									
Australia ⁷		18					4				
Taiwan ¹		0.0					2.5				
Japan ³		0.4	0.6	0.3	0.6	1.6	0.0	0.9	0.3	2.3	



		Age									
		40	44-45	49-50	54-55	59-60	64-65	69-70	74-75	79	≥ 80
Moderna 1st dose	Male										
Ontario, Canada ⁶		18.3									
Taiwan ¹		5.9					3.9				
Japan ³		3.0	1.7	0.0	1.2	2.0	0.0	0.0	0.0	0.0	
Moderna 2nd dose	Male										
Ontario, Canada ⁶		0.0									
Australia ⁷		33					2				
Taiwan ¹		7.7					4.6				
Japan ³		4.0	4.4	1.9	3.7	2.0	4.1	0.0	0.0	0.0	
Moderna 1st dose	Female										
Ontario, Canada ⁶		0.0									
Taiwan ¹		0.0					2.5				
Japan ³		1.5	2.6	2.9	0.0	0.0	5.6	6.6	0.0	0.0	
Moderna 2nd dose	Female										
Ontario, Canada ⁶		0.0									
Australia ⁷		20					25				
Taiwan ¹		0.0					0.0				
Japan ³		1.5	4.0	2.9	0.0	3.2	5.6	0.0	0.0	0.0	



Supplementary Figure 2. Reported rates of myocarditis (per million persons) after the first and second doses of BNT162b2 (BNT) and mRNA-1273 (Moderna) vaccine according to sex and age group (> 40 years old)

a) Studies from Taiwan, the US, and Japan reported absolute risks of myocarditis (including myopericarditis but excluding pericarditis alone) in vaccinees over 40 years old at **0-7 days** after the first and second doses of BNT162b2 (BNT) and mRNA-1273 (Moderna) vaccine. Each risk stratum was marked with a corresponding color;

b) Studies from Israel, Taiwan, and Japan reported absolute risks of myocarditis (including myopericarditis but excluding pericarditis alone) in vaccinees over 40 years old at **0-21 days** after the first and second doses of BNT162b2 (BNT) and mRNA-1273 (Moderna) vaccine. Study from Nordics reported the risk at 0-28 days. Each risk stratum was marked with a corresponding color. ******The observation period after vaccination was 28 days;

c) Studies from Ontario Canada, Australia, Taiwan, and Japan reported absolute risks of myocarditis (including myopericarditis but excluding pericarditis alone) in vaccinees over 40 years old **without restriction on time** after the first and second doses of BNT162b2 (BNT) and mRNA-1273 (Moderna) vaccine. Each risk stratum was marked with a corresponding color.

Supplementary Material 1. Brighton Collaboration myocarditis case definition and levels of diagnostic certainty⁸

Level of certainty 1 (definitive case)	
	Histopathologic examination of myocardial tissue (autopsy or endomyocardial biopsy) showed myocardial inflammation
OR	
	Elevated myocardial biomarkers (at least one of the findings below)
	Troponin T Troponin I
AND	
	Abnormal imaging study
	Abnormal cardiac magnetic resonance study (at least one of the findings below)
	Edema on T2-weighted study, typically patchy in nature Late gadolinium enhancement on T1-weighted study with an increased enhancement ratio between myocardial and skeletal muscle typically involving at least one non-ischemic regional distribution with recovery (myocyte injury).
OR	
	Abnormal echocardiogram (at least one of the findings below)
	New focal or diffuse left or right ventricular function abnormalities (e.g., decreased ejection fraction) Segmental wall motion abnormalities Global systolic or diastolic function depression or abnormality Ventricular dilation Wall thickness change

Level of certainty 2 (probable case)**Clinical symptoms****Cardiac symptoms (at least one finding below)**

Acute chest pain or pressure
Palpitations
Dyspnea after exercise, at rest, or lying down
Diaphoresis
Sudden death

OR**Non-specific symptoms (at least two findings below)**

Fatigue
Abdominal pain
Dizziness or syncope
Edema
Cough

OR**Infants and young children (at least two findings below)**

Irritability
Vomiting
Poor feeding
Tachypnea
Lethargy

AND**Testing supporting diagnosis (biomarkers, echocardiogram, and electrocardiogram)****Abnormal cardiac magnetic resonance study (see level 1 case definition)****OR****Elevated myocardial biomarkers (at least one of the findings below)**

Troponin T
Troponin I
Creatine kinase-myocardial band

OR**Abnormal echocardiogram (See level 1 case definition)****OR****Electrocardiogram abnormalities that are new and/or normalize on recovery (at least 1 of the findings below)**

Paroxysmal or sustained atrial or ventricular arrhythmias (premature atrial or ventricular beats, and/or supraventricular or ventricular tachycardia, interventricular conduction delay, abnormal Q waves, low voltages)
AV nodal conduction delays or intraventricular conduction defects (atrioventricular block (grade I-III), new bundle branch block)
Continuous ambulatory electrocardiographic monitoring that detects frequent atrial or ventricular ectopy

AND**No alternative diagnosis for symptoms**

Level of certainty 3 (possible case)

Clinical symptoms (see level 2 case definition)

AND

Testing supporting diagnosis (biomarkers and electrocardiogram)

Elevated biomarkers supporting evidence of inflammation (at least 1 of the findings below)

Elevated c-reactive protein or high-sensitivity c-reactive protein

Elevated erythrocyte sedimentation rate

Elevated D-dimer

OR

Electrocardiogram abnormalities that are new and/or normalize on recovery (at least 1 of the findings below)

ST-segment or T-wave abnormalities (elevation or inversion)

Newly reduced r-wave height, low voltage, or abnormal q waves

PACs and PVCs

AND

No alternative diagnosis for symptoms

Supplementary Material 2. Brighton Collaboration pericarditis case definition and levels of diagnostic certainty⁸

Level of certainty 1 (definitive case)	
	Histopathologic examination of myocardial tissue (autopsy or pericardial biopsy) showed pericardial inflammation
OR	
	Abnormal testing (at least two of the following three findings below): Evidence of abnormal fluid collection or pericardial inflammation by imaging (echocardiogram, magnetic resonance, cardiac magnetic resonance, computed tomography)
OR	
	Electrocardiogram abnormalities that are new or normalize on recovery (must have all findings below)
	Diffuse concave-upward ST-segment elevation ST-segment depression in augmented vector right PR-depression throughout the leads without reciprocal ST-segment changes
OR	
	Physical examination finding (at least one finding below)
	Pericardial friction rub Distant heart sounds (infants and children) Pulsus paradoxus

Level of certainty 2 (probable case)

Clinical symptoms

Cardiac symptoms (at least one finding below)

Acute chest pain or pressure
Palpitations
Dyspnea after exercise, at rest, or lying down
Diaphoresis
Sudden death

OR

Infants and young children (at least two findings below)

Irritability
Vomiting
Poor feeding
Tachypnea
Lethargy

AND

Physical examination findings: (at least one finding below)

Pericardial friction rub
Pulsus paradoxus

OR

Evidence of abnormal fluid collection or pericardial inflammation by imaging (echocardiogram, magnetic resonance, cardiac magnetic resonance, computed tomography)

OR

Electrocardiogram abnormalities that are new and/or normalize on recovery (at least 1 finding below)

Diffuse concave-upward ST-segment elevation
ST-segment depression in augmented vector right
PR-depression throughout the leads without reciprocal ST-segment changes

AND

No alternative diagnosis for symptoms (myocardial infarction, pulmonary embolus, mediastinitis etc.)

Level of certainty 3 (possible case)

Clinical symptoms

Cardiac symptoms (at least one finding below)

Acute chest pain or pressure
Palpitations
Dyspnea after exercise, at rest, or lying down

AND

Non-specific symptoms (at least two findings below)

Cough
Weakness
Gastrointestinal – nausea, vomiting, diarrhea
Shoulder/upper back pain
Cyanosis
Low grade intermittent fever
Altered mental status
Edema
Fatigue

OR

Infants and young children (at least two findings below)

Irritability
Vomiting
Poor feeding
Tachypnea
Lethargy

AND

Abnormal testing supporting diagnosis

Abnormal chest radiograph showing enlarged heart

OR

Nonspecific electrocardiogram abnormalities other than those listed in LOC 1 and LOC 2 that are new or normalize on recovery

AND

No alternative diagnosis for symptoms (myocardial infarction, pulmonary embolus, mediastinitis etc.)

Supplementary Material 3. CDC case definitions for myocarditis and pericarditis⁹

Acute Myocarditis

Clinical myocarditis

Probable Case

1. Presence of ≥ 1 new or worsening of the following clinical symptoms:
 - chest pain/pressure/discomfort
 - dyspnea/shortness of breath/pain with breathing
 - palpitations
 - syncope

OR, infants and children <12 years of age may instead present with ≥ 2 of:

 - irritability
 - vomiting
 - poor feeding
 - tachypnea
 - lethargy
- AND**
2. ≥ 1 new finding of:
 - troponin level above upper limit of normal (any type of troponin)
 - abnormal electrocardiogram (ECG or EKG) or rhythm monitoring findings consistent with myocarditis*
 - abnormal cardiac function or wall motion abnormalities on echocardiogram
 - cMRI findings consistent with myocarditis[†]
- AND**
3. No other identifiable cause of the symptoms and findings

Confirmed Case

1. Presence of ≥ 1 new or worsening of the following clinical symptoms:
 - chest pain/pressure/discomfort
 - dyspnea/shortness of breath/pain with breathing
 - palpitations
 - syncope

OR, infants and children <12 years of age may instead present with ≥ 2 of:

 - irritability
 - vomiting
 - poor feeding
 - tachypnea
 - lethargy
- AND**
2. ≥ 1 new finding of
 - Histopathologic confirmation of myocarditis[§]
 - cMRI findings consistent with myocarditis[†] in the presence of troponin level above upper limit of normal (any type of troponin)
- AND**
3. No other identifiable cause of the symptoms and findings

*To meet the ECG or rhythm monitoring criterion, must include at least one of:

- ST-segment or T-wave abnormalities
- Paroxysmal or sustained atrial, supraventricular, or ventricular arrhythmias
- AV nodal conduction delays or intraventricular conduction defects

[†]Using either the original or the revised Lake Louise criteria (Ferreira et al. *J Am Coll Cardiol.* 2018;72:3158-76)

[§]Using the Dallas criteria (Aretz et al. *Am J Cardiovasc Pathol.* 1987;1:3-14)

Notes:

1. Autopsy cases may be classified as confirmed clinical myocarditis on the basis of meeting histopathologic criteria if no other identifiable cause
2. Cases with individuals who lack the listed symptoms but who meet other criteria may be classified as subclinical myocarditis (probable or confirmed)

Acute Pericarditis

Presence of ≥ 2 new or worsening of the following clinical features:

- acute chest pain*
- pericardial rub on exam,
- new ST-elevation or PR-depression on EKG, or
- new or worsening pericardial effusion on echocardiogram or MRI

*typically described as pain made worse by lying down, deep inspiration, or cough and relieved by sitting up or leaning forward, although other types of chest pain may occur.

Notes:

1. Autopsy cases may be classified as pericarditis on basis of meeting histopathologic criteria of the pericardium

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