

# Risk factors of myocarditis and pericarditis following mRNA-1273 vaccination: a population-based case-cohort study in five VAC4EU European databases

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## BACKGROUND

- Myocarditis and pericarditis are uncommon inflammatory conditions that most frequently follow viral infections; they are typically self-limited in otherwise healthy individuals
- An increased risk of myocarditis and pericarditis has been observed following mRNA COVID-19 vaccination
- Events occur mostly among adolescent and young adult males and after the second vaccination dose in the primary series, although cases remain rare and generally have a favourable clinical course
- Other risk factors remain to be elucidated

**OBJECTIVE** To investigate potential risk factors associated with the occurrence of myocarditis and/or pericarditis after mRNA-1273 vaccination

## METHODS

**Data:** Secondary healthcare data from 5 VAC4EU network data expert and access partners (DEAPs) across 4 European countries:



### Inclusion criteria (base cohort):

- $\geq 1$  dose of mRNA-1273 during the study period (01/2021 – 08/2024)
- $\geq 1$  year enrollment in database before vaccination
- No myocarditis/pericarditis within the 6 months before vaccination

**Study design:** Case-cohort with base cohort consisting of individuals who received mRNA-1273 during study period

**Cases:** myocarditis or pericarditis diagnosis within 30 days following mRNA-1273 receipt; fulfill criteria for being a definitive, probable, or possible case according to Brighton Collaboration Case Definition

**Controls:** individuals from the base cohort without myocarditis or pericarditis diagnosis. 4 controls per case were sampled from base cohort based on month of mRNA-1273 receipt. Control sampling was performed 1,000 times and results pooled across samples.

### Analyses:

- Cases and controls were described in terms of baseline characteristics and previous health status
- Multivariable logistic regression was used with age, sex and previous SARS-CoV-2 infection always included in the model. Other variables, including prior comorbidities and healthcare use, were considered through a variable selection procedure
- Analyses were performed separately per data source. Regression results were pooled using fixed-effects meta-analysis.

## CONCLUSIONS

Males are at higher risk of developing post-mRNA-1273 myo-/pericarditis. Previous SARS-CoV-2 infection, younger age, prior comorbidities and healthcare utilisation may be associated with a higher risk. The findings do not indicate any subgroup for whom mRNA-1273 vaccination should be avoided or discouraged.

## RESULTS

- >11 million mRNA-1273 recipients across 5 databases (Table 1)
- 11-30 myocarditis cases and 12-39 pericarditis cases included per database

**Pooled incidences** before adjudication: 17.9 (myocarditis) and 29.2 (pericarditis) per 1 million mRNA-1273 recipients

### Descriptive results based on adjudicated cases:

- ♂ Myocarditis and pericarditis cases were more often male than controls
- 🎂 Median age of myocarditis and pericarditis cases was 2.5-10 years lower than median age of controls
- 🏠 Pericarditis cases had more prior comorbidities than controls; this was not observed for myocarditis

### Multivariable logistic regression analyses based on adjudicated cases (Table 2):

- ♀ Females had 74% lower odds of myocarditis and 63% lower odds of pericarditis
- 🦠 Previous SARS-CoV-2 infection was associated with 244% higher odds of pericarditis after mRNA-1273 receipt

Other variables of interest were not included in the models during variable selection procedure

**Sensitivity analyses** were performed including all identified cases based on diagnosis codes, regardless of adjudication level. Results found that younger age, prior comorbidities, and previous healthcare utilisation were associated with higher risks of post-mRNA-1273 myocarditis and pericarditis.

**Table 1. Number of mRNA-1273 recipients, cases, and controls per DEAP \***

	Danish registries	Norwegian registries	CPRD Aurum	SIDIAP	VID
mRNA-1273 recipients	691,486	1,560,965	3,778,915	2,731,597	2,150,033
<b>Number of cases &amp; controls included in analyses</b>					
<i>Myocarditis</i>					
Cases	0*	28	11	24	30
Controls	100*	112	44	96	128
<i>Pericarditis</i>					
Cases	0*	39	12	25	24
Controls	100*	156	48	100	100

\*Total case numbers for Danish registries were rounded to the nearest 100, such that the 0 indicates that the number was between 0 and 50;

**Table 2. Pooled odds ratios (ORs) and corresponding 95% confidence intervals of the logistic regression analyses**

	Pooled OR (95% CI)
<b>Myocarditis</b>	
Age	0.99 (0.96, 1.01)
Female sex	0.26 (0.16, 0.42)
Previous SARS-CoV-2 infection	1.10 (0.51, 2.36)
<b>Pericarditis</b>	
Age	1.00 (0.99, 1.02)
Female sex	0.37 (0.23, 0.58)
Previous SARS-CoV-2 infection	3.44 (1.41, 8.41)
<b>Myo- and/or pericarditis</b>	
Age	0.99 (0.99, 1.00)
Female sex	0.33 (0.23, 0.47)
Previous SARS-CoV-2 infection	1.16 (0.63, 2.11)

DEAP-specific results were pooled using fixed effects meta-analyses.