

# Myocarditis risk significantly higher after COVID-19 infection vs. after a COVID-19 vaccine

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A medical assistant prepares a dose of a COVID-19 vaccine to be administered to a patient. Credit: Public domain image courtesy of Lisa Ferdinando, U.S. Department of Defense

In a detailed analysis of nearly 43 million people, ages 13 and older, who received at least one dose of a COVID-19 vaccine in England, the risk of

myocarditis in unvaccinated individuals after COVID-19 infection was at least 11 times higher compared to people who developed myocarditis after receiving a COVID-19 vaccine or booster dose between December 1, 2020 and December 15, 2021, according to new research published today in the American Heart Association's flagship, peer-reviewed journal *Circulation*.

Several previous studies and reports from public health agencies around the world including the U.S. Centers for Disease Control and Prevention have highlighted a possible connection and potentially increased risk of myocarditis after receiving an mRNA COVID-19 [vaccine](#), generating considerable scientific, policy and public interest .

Typically triggered by a viral infection, myocarditis is the inflammation of the middle layer of the wall of the heart muscle, the myocardium. This condition is uncommon and may temporarily or permanently weaken the heart muscle and the heart's electrical system, which keeps the heart pumping normally. An episode of myocarditis may resolve on its own or with treatment, and may result in lasting damage to the heart. In the general population not during a global pandemic, it is estimated that approximately 10 to 20 people per 100,000 are diagnosed with myocarditis each year, according to the American Heart Association's 2021 [scientific statement](#) on myocarditis.

"We found that across this large dataset, the entire COVID-19-vaccinated population of England during an important 12-month period of the pandemic when the COVID-19 vaccines first became available, the risk of myocarditis following COVID-19 vaccination was quite small compared to the risk of myocarditis after COVID-19 infection," says first author of the study Martina Patone, Ph.D., a statistician at the Nuffield Department of Primary Health Care Sciences at the University of Oxford in Oxford, England. "This analysis provides important information that may help guide public health

vaccine campaigns, particularly since COVID-19 vaccination has expanded in many parts of the world to include children as young as 6 months old."

In this study, Patone and colleagues evaluated England's National Immunization database of COVID-19 vaccinations for all people ages 13 or older who had received at least one dose of the ChAdOx1 (a two-dose adenovirus-vector COVID-19 vaccine developed by the University of Oxford and AstraZeneca, most similar to the one-dose Johnson & Johnson/Janssen COVID-19 vaccine available in the U.S.), the Pfizer-BioNTech or the Moderna COVID-19 vaccine (the same mRNA vaccines available in the U.S.) between December 1, 2020 and December 15, 2021. This dataset totaled nearly 43 million people, which included more than 21 million who had received a booster dose of any of the COVID-19 vaccines (meaning they had received a total of 3 doses of a COVID-19 vaccine). The database detailed the type of COVID-19 vaccines received, dates received and dose sequencing, along with individual demographic information including age and sex for each individual. Nearly 6 million people tested positive for COVID-19 infection either before or after COVID-19 vaccination during the study period.

England's National Immunization database records were then cross-referenced and matched to the national offices with data on COVID-19 infection, hospital admission and death certificates for the same time period, December 1, 2020 through December 15, 2021. Individuals were classified based on age and sex to reveal which groups had the highest risk of myocarditis after a COVID-19 vaccine or after COVID-19 infection and hospitalization. The authors used the self-controlled case series (SCCS) method, which was developed to estimate the relative incidence of an acute event in a pre-defined post-vaccination risk period (1-28 days), compared to other times (pre-vaccination or long after vaccination). Being a within-person comparison, the analyses were

controlled to adjust for any fixed characteristics, including sex, race or ethnicity, or chronic health conditions.

In the overall dataset of nearly 43 million people, the analyses found:

- Fewer than 3,000 (n=2,861), or 0.007%, people were hospitalized or died with myocarditis during the one-year study period. 617 of these cases of myocarditis occurred during days 1-28 after receiving a COVID-19 vaccination, of which 514 were hospitalized.
- People who were infected with COVID-19 before receiving any doses of the COVID-19 vaccines were 11 times more at risk for developing myocarditis during days 1-28 after a COVID-19 positive test.
- The risk of COVID-19 infection-related myocarditis risk was cut in half among people infected after vaccination (received at least one dose of a COVID-19 vaccine).
- The risk of myocarditis increased after a first dose of the ChAdOx1 COVID-19 vaccine (an adenovirus-vector vaccine most similar to the Johnson & Johnson/Janssen COVID-19 vaccine available in the U.S.) and after a first, second and booster dose of any of the mRNA COVID-19 vaccines. However, the risk of vaccine-associated myocarditis was lower compared to the risk of COVID-19 infection-associated myocarditis, except for after a second dose of the Moderna vaccine.
- Myocarditis risk was found to be higher during days 1-28 after a second dose of the Moderna COVID-19 vaccine for people of all genders and ages, and the risk also persisted after a booster dose of the Moderna vaccine. However, people receiving a booster dose of Moderna were, on average, younger in comparison to those who received a booster dose of the ChAdOx1 or Pfizer-BioNTech vaccine, therefore, results may not be generalizable to

all adults.

#### Risk of COVID-19 vaccine-associated myocarditis among women:

- Of the nearly 21 million women, 7.2 million (34%) were younger than age 40, and a slightly increased risk of myocarditis was found among this younger age group after receiving a second dose of the Moderna COVID-19 vaccine: 7 estimated extra cases of myocarditis for every one million women vaccinated.
- Among women older than age 40, a slight increased risk of myocarditis was associated with receiving a first or third dose of the Pfizer-BioNTech COVID-19 vaccine, respectively 3 and 2 estimated additional cases of myocarditis for every one million women vaccinated.

#### Risk of COVID-19 infection-associated myocarditis among women:

- Among women younger than age 40, the risk of infection-associated myocarditis was higher compared to the risk of vaccine-associated myocarditis: 8 extra cases associated with having COVID-19 infection before vaccination.
- Among women older than age 40, the risk of infection-associated myocarditis was higher compared to the risk of vaccine-associated myocarditis: 51 extra cases associated with having COVID-19 infection before vaccination.

#### Risk of COVID-19 vaccine-associated myocarditis among men:

- Among the 18 million men in the dataset, all of whom received at least one COVID-19 vaccine, more than 6 million men (34%) were younger than age 40.
- An increased risk of vaccine-associated myocarditis was found in men ages 40 and younger after a first dose of either of the

mRNA COVID-19 vaccines (4 and 14 estimated extra cases for every one million men vaccinated with respectively Pfizer or Moderna vaccine), or a second dose of any of the three COVID-19 vaccines available in England during the study period: 14, 11 and 97 estimated additional cases of myocarditis for every one million men vaccinated, respectively for the ChAdOx1, the Pfizer-BioNTech or the Moderna vaccine.

- The increased risk of developing myocarditis among males younger than age 40 was also higher after receiving two doses of the Moderna vaccine when compared to the risk of myocarditis after COVID-19 infection. The researchers noted, however, the average age of people who received the Moderna vaccine was 32 years, compared to the majority of those who received the other vaccines were older than age 40.
- In men ages 40 and older, a slightly increased risk of myocarditis was found after a booster dose of either of the two mRNA vaccines (Pfizer-BioNTech or Moderna): 3 estimated extra cases of myocarditis for every one million men vaccinated with either mRNA vaccine.

#### Risk of COVID-19 infection-associated myocarditis among men:

- Among men younger than age 40, the risk of infection-associated myocarditis was higher compared to the risk of vaccine-associated myocarditis: 16 extra cases associated with having infection before vaccination, with the only exception of a second dose of Moderna vaccine.
- Among men older than age 40, the risk of infection-associated myocarditis was higher compared to the risk of vaccine-associated myocarditis: 85 extra cases associated with having infection before vaccination.

"It is important for the public to understand that myocarditis is rare, and



the risk of developing myocarditis after a COVID-19 vaccine is also rare. This risk should be balanced against the benefits of the COVID-19 vaccines in preventing severe COVID-19 infection. It is also crucial to understand who is at a higher risk for myocarditis and which vaccine type is associated with increased myocarditis risk, " said Professor Nicholas Mills, Ph.D., the Butler British Heart Foundation Chair of Cardiology at the University of Edinburgh and a co-author of the paper.

"These findings are valuable to help inform recommendations on the type of COVID-19 vaccines available for younger people and may also help shape public health policy and strategy for COVID-19 vaccine boosters. The SARS-CoV-2 virus continues to shift, and more contagious variants arise; our hope is that this data may enable a more well-informed discussion on the risk of vaccine-associated myocarditis when considered in contrast to the net benefits of COVID-19 vaccination," said another co-author Julia Hippisley-Cox, F.R.C.P., professor of clinical epidemiology and general practice at the University of Oxford.

Authors noted there are two unanswered questions that likely require further investigation. The first is about myocarditis risk among children ages 13-17 because there were too few cases of myocarditis to quantify the risk specific to this age group. Secondly, researchers were not able to directly compare the death rate after COVID-19 infection vs. death after COVID-19 vaccination since the database only included people who had received at least one COVID-19 vaccine. More expansive data and a different analysis are still needed to address these questions and numerous other COVID-19 topics.

The study has two notable limitations. The number of cases of myocarditis among individuals who received a [booster dose](#) of the ChAdOx1 or Moderna vaccines was too small to calculate the risk of myocarditis. Additionally, researchers cannot exclude the possibility of

over- or under-estimated risk due to misclassification of any health information in the database, though the U.K.'s National Health Service is known to provide timely and accurate data.

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**More information:** Martina Patone et al, Risk of Myocarditis After Sequential Doses of COVID-19 Vaccine and SARS-CoV-2 Infection by Age and Sex, *Circulation* (2022). DOI: 10.1161/CIRCULATIONAHA.122.059970 , [www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.122.059970](https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.122.059970)

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