



Medicines & Healthcare products  
Regulatory Agency

# Coronavirus Vaccines

## Summary of Yellow Card reporting

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This information is also available on the [gov.uk](https://www.gov.uk) website



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## Summary

At the time of this report, over 176,321 people across the UK have died within 28 days of a positive test for coronavirus (COVID-19). Vaccination is the single most effective way to reduce deaths and severe illness from COVID-19. A national immunisation campaign has been underway since early December 2020.

Three COVID-19 vaccines - the COVID-19 Pfizer/BioNTech Vaccine, COVID-19 Vaccine AstraZeneca and COVID-19 Vaccine Moderna – are currently being used in the UK. All have been authorised for supply by the Medicines and Healthcare products Regulatory Agency (MHRA) following a thorough review of safety, quality and efficacy information from clinical trials. In [clinical trials](#), the vaccines showed very high levels of protection against symptomatic infections with COVID-19. [Data](#) are available on the impact of the vaccination campaign in reducing infections and illness in the UK.

The MHRA confirmed on 9 September 2021 that the COVID-19 vaccines made by Pfizer and AstraZeneca can be used as safe and effective booster doses. Following review of data for the COVID-19 Vaccine Moderna vaccine, the MHRA and Commission on Human Medicine (CHM) experts also concluded that this vaccine can be used as a safe and effective booster dose.

All vaccines and medicines have some side effects. These side effects need to be continuously balanced against the expected benefits in preventing illness.

The COVID-19 Pfizer/BioNTech Vaccine was evaluated in clinical trials involving more than 44,000 participants. The most [frequent adverse reactions](#) in these trials were pain at the injection site, fatigue, headache, myalgia (muscle pains), chills, arthralgia (joint pains), and fever; these were each reported in more than 1 in 10 people. These reactions were usually mild or moderate in intensity and resolved within a few days after vaccination. Adverse reactions were reported less frequently in older adults (over 55 years) than in younger people.

The COVID-19 Vaccine AstraZeneca was evaluated in clinical trials involving more than 23,000 participants. The most [frequently reported adverse reactions](#) in these trials were injection-site tenderness, injection-site pain, headache, fatigue, myalgia, malaise, pyrexia (fever), chills, and arthralgia, and nausea; these were each reported in more than 1 in 10 people. The majority of adverse reactions were mild to moderate in severity and usually resolved within a few days after vaccination. Adverse reactions were generally milder and reported less frequently in older adults (65 years and older) than in younger people.

The COVID-19 Vaccine Moderna was evaluated in clinical trials involving more than 30,000 participants. The most [frequent adverse reactions](#) in these trials were pain at the injection

site, fatigue, headache, myalgia (muscle pains), arthralgia (joint pains), chills, nausea/vomiting, axillary swelling/tenderness (swelling/tenderness of glands in the armpit), fever, injection site swelling and redness; these were each reported in more than 1 in 10 people. These reactions were usually mild or moderate in intensity and resolved within a few days after vaccination. Adverse reactions were reported less frequently in older adults (over 65 years) than in younger people.

The MHRA continually monitors safety during widespread use of a vaccine. We have in place a [proactive strategy to do this](#). We also work closely with our public health partners in reviewing the effectiveness and impact of the vaccines to ensure the benefits continue to outweigh any possible side effects.

Part of our **monitoring role includes reviewing** reports of suspected side effects. Any member of the public or health professional can submit suspected side effects through the [Yellow Card scheme](#). The nature of Yellow Card reporting means that reported events are not always proven side effects. Some events may have happened anyway, regardless of vaccination. This is particularly the case when millions of people are vaccinated, and especially when vaccines are being given to the most elderly people and people who have underlying illness.

As of 4 May 2022, for the UK, 170,337 Yellow Cards have been reported for the COVID-19 Pfizer/BioNTech Vaccine, 245,089 have been reported for the COVID-19 Vaccine AstraZeneca, 38,197 for the COVID-19 Vaccine Moderna and 1,672 have been reported where the brand of the vaccine was not specified.

For the COVID-19 Pfizer/BioNTech Vaccine, COVID-19 Vaccine AstraZeneca and COVID-19 Vaccine Moderna the overall reporting rate is around 2 to 5 Yellow Cards per 1,000 doses administered.

In the 14 days since the previous summary for 20 April 2022 we have received a further 677 Yellow Cards for the COVID-19 Pfizer/BioNTech Vaccine, 181 for the COVID-19 Vaccine AstraZeneca, 719 for the COVID-19 Vaccine Moderna and 38 where the brand was not specified.

It is important to note that Yellow Card data cannot be used to derive side-effect rates or compare the safety profile of COVID-19 vaccines as many factors can influence ADR reporting. Additionally, it is important to consider that a Yellow Card report can include reference to more than one vaccine associated with a suspected reaction where different vaccines have been used as third or booster doses.

For all COVID-19 vaccines, the overwhelming majority of reports relate to injection-site reactions (sore arm for example) and generalised symptoms such as 'flu-like' illness, headache, chills, fatigue (tiredness), nausea (feeling sick), fever, dizziness, weakness,

aching muscles, and rapid heartbeat. Generally, these happen shortly after the vaccination and are not associated with more serious or lasting illness.

These types of reactions reflect the normal immune response triggered by the body to the vaccines. They are typically seen with most types of vaccine and tend to resolve within a day or two. The nature of reported suspected side effects is broadly similar across age groups, although, as was seen in clinical trials and as is usually seen with other vaccines, they may be reported more frequently in younger adults.

A number of detailed assessments of safety topics have been undertaken and we have updated our advice on these topics accordingly. Overall, our advice remains that the benefits of the vaccines outweigh the risks in the majority of people. Further comments on use in specific populations and details on the specific safety topics can be found within Section titled Analysis of data.

## Conclusion

Vaccines are the best way to protect people from COVID-19 and have already saved tens of thousands of lives. Everyone should continue to get their vaccination when invited to do so unless specifically advised otherwise.

- As with all vaccines and medicines, the safety of COVID-19 vaccines is being continuously monitored.
- The expected benefits of the vaccines in preventing COVID-19 and serious complications associated with COVID-19 far outweigh any currently known side effects in the majority of patients.

Further information on the type of suspected adverse reactions (ADRs) reported for the COVID-19 Pfizer/BioNTech Vaccine, the COVID-19 Vaccine AstraZeneca and the COVID-19 Vaccine Moderna is provided in Annex 1. It is important to read the attached guidance notes to ensure appropriate interpretation of the data.

# Introduction

The Medicines and Healthcare products Regulatory Agency (MHRA) is the executive Agency of the Department of Health and Social Care that acts to protect and promote public health and patient safety, by ensuring that medicines and medical devices meet appropriate standards of safety, quality and efficacy.

The MHRA operates the [Yellow Card scheme](#) on behalf of the Commission on Human Medicines (CHM). The scheme collects and monitors information on suspected safety concerns or incidents involving vaccines, medicines, medical devices, and e-cigarettes. The scheme relies on voluntary reporting of suspected adverse incidents by healthcare professionals and members of the public (patients, users, or carers). The purpose of the scheme is to provide an early warning that the safety of a product may require further investigation. Further information about the Yellow Card scheme, including its contribution to identifying safety issues can be found on the [Yellow Card website](#).

The MHRA is playing an active role in responding to the coronavirus pandemic. In relation to COVID-19 vaccines, the MHRA has authorised their supply following a rigorous review of their safety, quality and efficacy. The clinical trials of COVID-19 vaccines have shown them to be effective and acceptably safe; however, as part of its statutory functions, the MHRA is responsible for monitoring these vaccines on an ongoing basis to ensure their benefits continue to outweigh any risks. This is a requirement for all authorised medicines and vaccines in the UK. This monitoring strategy is continuous, proactive and based on a wide range of information sources, with a dedicated team of scientists reviewing information daily to look for safety issues or unexpected rare events.

This report summarises information received via the Yellow Card scheme and will be published regularly to include other safety investigations carried out by the MHRA under the [COVID-19 Vaccine Surveillance Strategy](#).

## What is a Yellow Card?

The Yellow Card scheme is a mechanism by which anybody can voluntarily report any suspected adverse reactions or side effects to the vaccine. It is very important to note that a Yellow Card report does not necessarily mean the vaccine caused that reaction or event. We ask for any suspicions to be reported, even if the reporter isn't sure if it was caused by the vaccine. Reports to the scheme are known as suspected adverse drug reactions (ADRs).

Many suspected ADRs reported on a Yellow Card do not have any relation to the vaccine or medicine and it is often coincidental that symptoms occurred around the same time as vaccination. The reports are continually reviewed to detect possible new side effects that may require regulatory action, and to differentiate these from things that would have

happened regardless of the vaccine or medicine being administered, for instance due to underlying or undiagnosed illness.

It is therefore important that the suspected ADRs described in this report are not interpreted as being proven side effects of COVID-19 vaccines. A list of the possible side effects of [COVID-19 Pfizer/BioNTech Vaccine](#), [COVID-19 Vaccine AstraZeneca](#) and [COVID-19 Vaccine Moderna](#) are provided in the product information document for healthcare professionals and the UK recipient information. These can also be found on the [Coronavirus Yellow Card](#) reporting site.

This public summary provides an overview of all UK suspected ADRs associated with the new COVID-19 vaccines (the COVID-19 Pfizer/BioNTech Vaccine, COVID-19 Vaccine AstraZeneca and COVID-19 Vaccine Moderna), and the MHRA's analysis of the data, **between 9 December 2020 and 4 May 2022 (inclusive)**. A glossary of key terms is provided in Annex 2.

If identified, information on new and emerging safety concerns will be provided in future editions of this report together with details of any resulting regulatory action or changes to advice on use of the vaccines.

# Yellow Card reports

## Vaccine doses administered

Data from the UK [Public Health agencies](#) show that at least 53,264,512 people have received their first vaccination in the UK by 4 May 2022, with 49,780,389 second doses administered. Individuals are also being invited for their booster vaccination if it has been 3 months since their second dose and they are either aged 18 and over or are aged 16 and over with a health condition that puts them at high risk from COVID-19. All children aged 12 to 15 are now eligible to receive a first dose and second dose of vaccine. Some children aged 5 to 11 have been eligible for a first and second dose of the COVID-19 vaccine if either they have a condition that means they are at high risk of serious illness from COVID-19 or they live with someone who has a weakened immune system. All children aged 5 to 11 will be eligible for vaccination in the coming weeks.

**Table 1: Number of people who have received the first dose of a vaccination for COVID-19 in the UK between 8 December 2020 and end of 4 May 2022.**

Country	Number of doses
England	44,778,223
Wales	2,551,472
Northern Ireland	1,427,628
Scotland	4,507,189

**Table 2: Number of people who have received the second dose of a vaccination for COVID-19 in the UK between 8 December 2020 and end of 4 May 2022.**

Country	Number of doses
England	41,828,788
Wales	2,414,547
Northern Ireland	1,339,801
Scotland	4,197,253

As of 4 May 2022, an estimated 26.7 million first doses of the COVID-19 Pfizer/BioNTech Vaccine and 24.9 million first doses of the COVID-19 Vaccine AstraZeneca had been administered, and around 24.1 million second doses each of the COVID-19 Pfizer/BioNTech Vaccine and COVID-19 Vaccine AstraZeneca. An approximate 1.7 million first doses and approximately 1.5 million second doses of the COVID-19 Vaccine Moderna have also now been administered. An estimated 30 million third or booster doses of COVID-19 Pfizer/BioNTech, 56,315 third or booster doses of COVID-19 Vaccine AstraZeneca and 9.3 million doses of COVID-19 Vaccine Moderna have been given. These figures are based on numbers of exposures reported individually by the individual nations which are extrapolated to produce an estimate of the total number of doses. Data are not always reported weekly and can be updated for historical dates when vaccinations are recorded on the relevant system. Therefore, data for this may be incomplete and the resulting estimates are approximate.

The estimated number of doses administered differs from the estimated number of people vaccinated due to the different data sources used.

As of 4 May 2022, an estimated 39,345,313 people had received their booster or additional vaccination in the UK. The priority groups being offered a booster dose of coronavirus (COVID-19) vaccine for this part of the vaccination campaign include people aged 16 years and over, health and social care workers and the clinically vulnerable.

**Table 3: Number of people who have received the third or booster dose of a vaccination for COVID-19 in the UK between 8 December 2020 and end of 4 May 2022.**

Country	Number of doses
England	32,736,499
Wales	2,027,294
Northern Ireland	1,059,919
Scotland	3,521,601

## Yellow Card reporting trends

A report of a suspected ADR to the Yellow Card scheme does not necessarily mean that it was caused by the vaccine, only that the reporter has a suspicion it may have been. Underlying or previously undiagnosed illness unrelated to vaccination can also be factors in such reports. **The relative number and nature of reports should therefore not be used**

**to compare the safety of the different vaccines.** The MHRA may also refer to ‘cases’ as opposed to ‘reports’ within the analysis of the Yellow Card data; these typically refer to ADR reports that have undergone medical assessment and are considered to meet certain criteria for diagnosis of the reported event and have at least a plausible association with the vaccine. All cases and reports are kept under continual review in order to identify possible new risks.

Up to and including 4 May 2022, the MHRA received and analysed 170,337 UK Yellow Cards from people who have received the COVID-19 Pfizer/BioNTech Vaccine. These reports include a total of 490,234 suspected reactions (i.e. a single report may contain more than one symptom). The first report was received on 9 December 2020.

Up to and including 4 May 2022, the MHRA received and analysed a total of 245,089 UK reports of suspected ADRs to the COVID-19 Vaccine AstraZeneca. These reports include a total of 868,095 suspected reactions (a single report may contain more than one symptom). The first report was received on 4 January 2021.

Up to and including 4 May 2022, the MHRA received and analysed a total of 38,197 UK reports of suspected ADRs to the COVID-19 Vaccine Moderna. These include a total 126,834 suspected reactions (a single report may contain more than one symptom). The first report was received on 7 April 2021.

Additionally, up to and including 4 May 2022, the MHRA received 1,672 Yellow Card reports where the brand of vaccine was not specified by the reporter.

In the 14 days since the previous summary for 20 April 2022 we have received a further 677 Yellow Cards for the COVID-19 Pfizer/BioNTech Vaccine, 181 for the COVID-19 Vaccine AstraZeneca, 719 for the COVID-19 Vaccine Moderna and 38 where the brand was not specified. Please note that a Yellow Card report can include more than one vaccine suspected to have caused a reaction where different vaccines have been used as third or booster doses.

It is important to note that Yellow Card data cannot be used to derive side effect rates or compare the safety profile of COVID-19 vaccines as many factors can influence ADR reporting.

**Table 4: Number of suspected ADR reports received in the UK up to and including 4 May 2022.**

Country	Number of reports			
	COVID-19 Pfizer/ BioNTech Vaccine	COVID-19 Vaccine AstraZeneca	COVID-19 Vaccine Moderna	Brand unspecified
England	132,890	201,891	30,558	1,003
Wales	8,211	10,843	2,271	93
Northern Ireland	3,007	2,989	147	20
Scotland	12,804	17,477	3,298	172

The figures in Table 4 are based upon the postcode provided by the reporter. The sums of the reports in the table will not equal the total reports received for each vaccine as postcode may not have always been provided or may have been entered incorrectly. It is important to note that the number of reports received for each country does not directly equate to the number of people who may have experienced adverse reactions and therefore cannot be used to determine the incidence of reactions. ADR reporting rates are influenced by many aspects, including the extent of use.

We are working with public health bodies and encouraging all healthcare professionals and patients alike to report any suspected ADRs to the Yellow Card scheme. As expected, reports gradually increase in line with an increase in doses administered.

The overall reporting rate for first, second and third or booster doses is in the order of 2 to 5 Yellow Cards per 1,000 doses administered for the COVID-19 Pfizer/BioNTech Vaccine, COVID-19 Vaccine AstraZeneca and COVID-19 Vaccine Moderna. It is known from the clinical trials that the more common side effects for all vaccines can occur at a rate of more than one in 10 doses (for example, local reactions or symptoms resembling transient flu-like symptoms).

# Analysis of Data

One of the MHRA's main roles is to continually monitor the safety of medicines and vaccines during widespread use, and we have in place a [proactive strategy to do this for COVID-19 vaccines](#). We also work closely with our public health partners in reviewing the effectiveness and impact that the vaccines are having to ensure benefits continue to outweigh any possible side effects. In addition, we work with our international counterparts to gather information on the safety of vaccines in other countries.

Given the huge scale of the COVID-19 immunisation programme, with many millions of doses of vaccines administered over a relatively short time period, vigilance needs to be continuous, proactive and as near real-time as is possible. The importance of this is two-fold. First, we need to rapidly detect, confirm, and quantify any new risks and weigh these against the expected benefits. We can then take any necessary action to minimise risks to individuals.

Secondly, we need to very quickly establish if any serious medical events which are temporally related to vaccination are merely a coincidental association. These associations are likely while we are still in the midst of a major national vaccination programme, and because many of the millions of people offered the vaccine in the early phase of a vaccination campaign were elderly and/or had underlying medical conditions, which increases the likelihood of unrelated illnesses occurring soon after vaccination. As mentioned above, the nature of Yellow Card reporting means that reported events are not always proven adverse reactions, and some may have happened regardless of vaccination.

Yellow Card reports of suspected ADRs are evaluated, together with additional sources of evidence, by a team of safety experts to identify any new safety issues or side effects. We apply statistical techniques that can tell us if we are seeing more events than we would expect to see, based on what is known about background rates of illness in the absence of vaccination. This aims to account for factors such as coincidental illness. We also look at the clinical characteristics to see if new patterns of illness are emerging that could indicate a new safety concern.

We supplement this form of safety monitoring with other epidemiology studies including analysis of data on national vaccine usage, anonymised GP-based electronic healthcare records and other healthcare data to proactively monitor safety. We also take into account the international experience based on data from other countries using the same vaccines. These combined safety data enables the MHRA to detect side effects or safety issues associated with COVID-19 vaccines. As well as confirming new risks, an equally important objective of monitoring will be to quickly rule out risks – in other words to confirm that the vaccine is not responsible for a suspected side effect and to provide reassurance on its safety.

## Overall safety

As with any vaccine, COVID-19 vaccines will cause side effects in some people. The total number and the nature of the majority of Yellow Cards reports received so far is not unusual for a new vaccine for which members of the public and healthcare professionals are encouraged to report any suspected adverse reaction.

As highlighted above, it is known from the clinical trials that the most common side effects for all vaccines can occur at a rate of more than one per 10 doses (such as local reactions, symptoms resembling transient flu-like symptoms). Overall, Yellow Card reporting is therefore lower than the reporting rate of possible side effects from the clinical trials, although we generally do not expect all suspected side effects to be reported on Yellow Cards. The primary purpose of Yellow Card reporting is to detect new safety concerns.

For all COVID-19 vaccines, detailed review of all reports has found that the overwhelming majority relate to injection-site reactions (sore arm for example) and generalised symptoms such as a 'flu-like' illness, headache, chills, fatigue (tiredness), nausea (feeling sick), fever, dizziness, weakness, aching muscles, and rapid heartbeat. Generally, these happen shortly after the vaccination and are not associated with more serious or lasting illness. These types of reaction reflect the acute immune response triggered by the body to the vaccines, are typically seen with most types of vaccine and tend to resolve within a day or two. The nature of reported suspected ADRs across all ages is broadly similar, although, as seen in the clinical trials and as is usually seen with other vaccines, they may be reported more frequently in younger adults.

As we receive more reports of these types of reactions with more exposure to the COVID-19 vaccines, we are building a picture of how individuals are experiencing them and the different ways that side effects may present in people. Some people have reported a sudden feeling of cold with shivering/shaking accompanied by a rise in temperature, often with sweating, headache (including migraine-like headaches), nausea, muscle aches and feeling unwell, starting within a day of having the vaccine. Similar to the flu like illness reported in clinical trials, these effects may last a day or two.

It is important to note that it is possible to have caught COVID-19 and not realise until after vaccination. If other COVID symptoms are experienced or fever is high and lasts longer than two or three days, vaccine recipients should stay at home and arrange to have a test.

A number of detailed assessments of safety topics have been undertaken and we have updated our advice on these topics accordingly. Overall, our advice remains that the benefits of the vaccines outweigh the risks in the majority of people. Further comments on use in specific populations and details on the following safety topics can be found below.

## Comments on safety in specific populations

### Safety of COVID-19 vaccines in pregnancy

The MHRA closely monitors the safety of COVID-19 vaccine exposures in pregnancy, including published information as well as Yellow Card reports for COVID-19 vaccines used in pregnancy. These reports have been reviewed by the independent experts of the CHM's COVID-19 Vaccines Benefit Risk Expert Working Group and by the Medicines for Women's Health Expert Advisory Group (MWHEAG).

Pregnant women have the same risk of getting COVID-19 as non-pregnant women but they may be at an increased risk of becoming severely ill, particularly if they get infected in the third trimester or if they also have underlying medical problems, compared to non-pregnant women. The current advice of the Joint Committee on Vaccination and Immunisation (JCVI) is that the COVID-19 vaccines, including booster doses, should be offered to those who are pregnant as a clinical risk group in the COVID-19 vaccination programme. The COVID-19 Pfizer/BioNTech Vaccine and COVID-19 Vaccine Moderna vaccines are currently the preferred vaccines for use during pregnancy and can be given at any stage in pregnancy.

The numbers of Yellow Card reports for pregnant women are low in relation to the number of pregnant women who have received COVID-19 vaccines to date (more than 90,000 women in England and Wales have given birth up to end of December 2021<sup>1</sup> after receiving at least 1 dose of COVID-19 vaccine during or shortly before pregnancy and more than 28,000 women in Scotland have received at least 1 dose whilst pregnant up to end January 2022). Pregnant women have reported similar suspected reactions to the vaccines as people who are not pregnant. Reports of miscarriage and stillbirth are also low in comparison to how commonly these events occurred in the UK outside of the pandemic. A few reports of commonly occurring congenital anomalies and obstetric events have also been received. There is no pattern from the reports to suggest that any of the COVID-19 vaccines used in the UK, or any reactions to these vaccines, increase the risk of miscarriage, stillbirths, congenital anomalies or birth complications.

Sadly, miscarriage is estimated to occur in about 20 to 25 in 100 pregnancies in the UK and most occur in the first 12 to 13 weeks of pregnancy (the first trimester). Published studies from the USA<sup>2</sup> and Norway<sup>3</sup> have compared miscarriage rates for vaccinated and unvaccinated women who were pregnant over the same time periods. The studies included

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<sup>1</sup> Number of vaccinations during pregnancy are updated when data is made available by the UK Public Health bodies

<sup>2</sup> Kharbanda EO, et al. Spontaneous abortion following COVID-19 vaccination during pregnancy. JAMA. doi:10.1001/jama.2021.15494

<sup>3</sup> Magnus, MC et al. Covid-19 Vaccination during Pregnancy and First-Trimester Miscarriage N Engl J Med 2021; 385:2008-2010 DOI: 10.1056/NEJMc2114466

data from a large number of women (more than 15,000) who received the COVID-19 Pfizer/BioNTech Vaccine or COVID-19 Vaccine Moderna. Both studies found that the occurrence of miscarriage was equally likely amongst unvaccinated women as amongst women at the same stage of pregnancy who were vaccinated in the previous 3 to 5 weeks. These studies provide strong evidence for no increased risk of miscarriage in association with the mRNA vaccines in current use. Data on the COVID-19 Vaccine AstraZeneca is less extensive but is consistent with these findings.

Evidence for pregnancy outcomes other than miscarriage is accumulating as more pregnancies reach full term. Currently available evidence does not suggest any increased risks of pregnancy complications, stillbirths, preterm births or adverse neonatal outcomes following vaccination in later pregnancy.

Stillbirths are sadly estimated to occur in about 1 in 200 pregnancies in the UK. Information from surveillance by UKHSA (formerly Public Health England) has found similar rates of stillbirth amongst (more than 55,000) women who were vaccinated during pregnancy and those who gave birth over the same period and were unvaccinated. Likewise, surveillance by Public Health Scotland and the COPS study<sup>4</sup> has found similar rates of perinatal mortality (including stillbirths) amongst (more than 5,700) women who were vaccinated during pregnancy and those who gave birth over the same period and who were unvaccinated and not infected with COVID-19.

Although, like most vaccines and medicines, clinical trials of COVID-19 vaccines in pregnant women were not carried out prior to use of the vaccines in the general population, there is now growing evidence from clinical use which provides reassurance on the safety of the vaccines in pregnancy. This adds to the evidence from non-clinical studies of the COVID-19 vaccines which have not raised any concerns about safety in pregnancy. The COVID-19 vaccines do not contain organisms that can multiply in the body, so they cannot infect an unborn baby in the womb.

The product information for COVID-19 Pfizer/BioNTech Vaccine and COVID-19 Vaccine Moderna has been updated to reflect that the available data are reassuring on safety and that the vaccines can be used during pregnancy.

The MHRA will continue to closely monitor safety data for use of the COVID-19 vaccines in pregnancy, including through evaluation of electronic healthcare record data.

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<sup>4</sup> Stock SJ, et al SARS-CoV-2 infection and COVID-19 vaccination rates in pregnant women in Scotland Nature Medicine 2022 <https://www.nature.com/articles/s41591-021-01666-2> .

## **Safety of COVID-19 vaccines in those breastfeeding**

The MHRA closely monitors the safety of COVID-19 vaccines during breastfeeding, including evaluation of Yellow Card reports for COVID-19 vaccines from breastfeeding women. These reports have been reviewed by the independent experts of the CHM's COVID-19 Vaccines Benefit Risk Expert Working Group, by paediatric and breastfeeding experts.

There is no current evidence that COVID-19 vaccination while breastfeeding causes any harm to breastfed children or affects the ability to breastfeed.

COVID-19 vaccines do not contain live components and there is no known risk associated with being given a non-live vaccine whilst breastfeeding. The current advice of the Joint Committee on Vaccination and Immunisation (JCVI) is that breastfeeding parents may be offered any suitable COVID-19 vaccine depending on their age.

We have received about 4,000 Yellow Card reports from women breastfeeding at the time of vaccination. Most of these women reported only suspected reactions in themselves which were similar to reports for the general population, with no effects reported on their milk supply or in their breastfed children.

A small number of women have reported decreases in their milk supply, most of which were transient, or possible reactions in their breastfed child. A number of factors can affect milk supply and infant behaviour, including general maternal health, amount of sleep, and anxiety. The symptoms reported for the children (high temperature, rash, diarrhoea, vomiting and general irritability) are common conditions in children of this age, so some of the effects reported may have occurred by coincidence.

The product information for COVID-19 Pfizer/BioNTech Vaccine and COVID-19 Vaccine Moderna has been updated to reflect that the available data are reassuring on safety and that the vaccines can be used during breastfeeding.

A small number of women may experience a reduction in their breast milk production and it may be helpful for breastfeeding women to know how to maintain their breast milk supply, particularly if they are feeling unwell. The NHS website has a good resource for this: <https://www.nhs.uk/start4life/baby/breastfeeding/>.

## **Suspected side effects reported in individuals under 18 years old**

The MHRA closely monitors the safety of COVID-19 vaccine exposures in individuals under 18 years old, including Yellow Card reports for COVID-19 vaccines used in this age group.

Up to the 4 May 2022 there have been an estimated 3.8 million first doses, 2.2 million second doses, and 0.2 million additional or booster doses of the COVID-19 Pfizer/BioNTech Vaccine given to under 18s; approximately 11,600 first doses and 8,700 second doses of the COVID-19 Vaccine AstraZeneca given to this population; and 2,000 first doses and 1,600 second doses, and 3,000 additional or booster doses of the COVID-19 Vaccine Moderna given to individuals under 18. There has been extremely limited use of COVID-19 Vaccine AstraZeneca as boosters in those under 18 years.

The MHRA has received 3,683 UK reports of suspected ADRs for the COVID-19 Pfizer/BioNTech Vaccine in which the individual was reported to be under 18 years old, 263 reports for the COVID-19 Vaccine AstraZeneca, 28 for the COVID-19 Vaccine Moderna and 27 where the brand of vaccine was unspecified.

For the COVID-19 Pfizer/BioNTech Vaccine, which is currently the preferred COVID-19 vaccine for the under 18s age group in the UK vaccination programme, the reporting rate in the under 18 years age group for all doses is less than 1 report per 1,000 doses. This is approximately half the reporting rate for the COVID-19 Pfizer/BioNTech Vaccine for those 18 years and over, which is around 2 per 1,000 doses.

As COVID-19 Vaccine AstraZeneca and COVID-19 Vaccine Moderna are not the preferred vaccines in under 18s there is insufficient experience in this age group to be able to make similar estimates.

The experience reported in under 18s, including in the different age subgroups (5-11, 12-15 and 16-17 year olds), is similar to that identified in the general population and a review of these reports does not raise any additional safety topics specific to this age group.

There has been a small number of reports for myocarditis and pericarditis (inflammation of the heart) in individuals under 18 years both in the UK and internationally. This is a recognised potential risk with the COVID-19 Pfizer/BioNTech Vaccine and COVID-19 Vaccine Moderna and the MHRA is closely monitoring these events. Further information surrounding these very rare reports of myocarditis and pericarditis within this population can be found within the specific section on this safety topic later in the summary. We will continue to closely monitor the safety of the COVID-19 vaccines in those under 18 years old.

## **Suspected side effects reported in individuals receiving a booster vaccination**

Safety monitoring plans have been agreed to ensure action can be taken on any emerging safety concerns from supplementary or booster doses.

As of 4 May 2022, an estimated 39.3 million COVID-19 third doses and booster doses have been administered in the UK. The COVID-19 Pfizer/BioNTech Vaccine and COVID-19

Vaccine Moderna are the preferred vaccines in the UK booster programme and make up the vast majority of doses administered.

Up to the 4 May 2022 the MHRA has received 31,198 UK reports of suspected ADRs where the COVID-19 Pfizer/BioNTech Vaccine was reported to be the booster dose, 548 reports where the COVID-19 Vaccine AstraZeneca was reported to be the booster dose, 17,303 reports where the COVID-19 Vaccine Moderna was reported to be the booster dose and 183 reports where the brand of vaccine booster was unspecified.

For the COVID-19 Pfizer/BioNTech Vaccine this represents a reporting rate of 1 report per 1,000 third or booster doses and for the COVID-19 Vaccine Moderna there is an estimated 2 reports per 1,000 third or booster doses. Both of these are lower than the reporting rate for COVID-19 vaccines for all vaccine doses combined, which is between 2-5 reports per 1,000 doses. For the COVID-19 Vaccine AstraZeneca there has been very limited number of booster doses in the UK and a very small number of reports. There is insufficient experience with COVID-19 Vaccine AstraZeneca as a booster vaccine to be able to make similar estimates of reporting rates.

The nature of events reported with third and booster doses is similar to that reported for the first two doses of the COVID-19 vaccines, and the vast majority of reports relate to expected reactogenicity events. Review of third and booster dose reports does not raise any new safety concerns. As part of the MHRA's booster safety monitoring strategy, reports of suspected adverse events following COVID-19 boosters given at the same time as seasonal flu vaccines have been closely monitored, and no new safety concerns have been identified in this data either.

There have been a small number of reports of suspected myocarditis and pericarditis (inflammation of the heart) following booster doses with Pfizer/BioNTech and Moderna COVID-19 vaccines. This is a recognised potential risk with the COVID-19 Pfizer/BioNTech Vaccine and COVID-19 Vaccine Moderna and the MHRA is closely monitoring these events. The reports after booster doses are extremely rare and there is no indication that these events are more serious after boosters. Further information surrounding these very rare reports of suspected myocarditis and pericarditis can be found within the specific section on this safety topic later in the summary.

We will continue to closely monitor the safety of booster and third doses of the COVID-19 vaccines.

## Comments on specific safety topics

The following reports reflect data up to 4 May 2022. The glossary provides an explanation of the clinical terms used.

## Anaphylaxis (severe allergic reactions)

On 9 December 2020, the MHRA issued preliminary guidance on severe allergic reactions after administration of the COVID-19 Pfizer/BioNTech Vaccine due to early reports of anaphylaxis. Following further detailed review, this advice was amended on 30 December 2020 to the current advice. The advice is that people with a previous history of severe allergic reactions to any ingredients of the vaccine should not receive it. On 14 December 2021 it was announced that following a CHM review of the Yellow Card data on anaphylaxis after the primary course and boosters there would be a [temporary suspension](#) of the post vaccination 15-minute monitoring time for the majority of individuals. This helped to accelerate the public health response to the Omicron variant. On 5 May the 15-minute observation period after vaccination with the COVID-19 Pfizer/BioNTech or Moderna vaccines was removed for individuals aged 12 years and over and who have no history of a severe allergic reaction (as outlined in the [Green Book](#)<sup>5</sup> advice). This followed careful review of the safety data by MHRA and advice from the CHM. A temporary suspension of the 15-minute observation period for children aged 5-11 years remains in place and this will be reviewed on a regular basis. The 15-minute observation period will remain in place for the small number of people who may have previously suffered anaphylaxis or other allergic reactions to a food, insect sting and most medicines or vaccines. The temporary suspension of the 15-minute observation time for children aged 5-11 years is under regular review by the CHM and the COVID-19 Vaccines Benefit Risk Expert Working Group.

Widespread use of the vaccine suggests that severe allergic reactions to the COVID-19 Pfizer/BioNTech Vaccine and COVID-19 Vaccine Moderna are very rare. Anaphylaxis can also be a very rare side effect associated with most other vaccines.

The MHRA continues to monitor reports of severe allergic reactions with the COVID-19 Pfizer/BioNTech Vaccine and has received 662 UK spontaneous adverse reactions associated with anaphylaxis or anaphylactoid reactions. Severe allergic reactions to the COVID-19 Pfizer/BioNTech Vaccine remain very rare. The MHRA's guidance remains that those with a previous history of allergic reactions to the ingredients of the vaccine should not receive it.

The MHRA is closely monitoring reports of anaphylaxis with the COVID-19 Vaccine Moderna and has received 93 reports of anaphylaxis in association with the vaccine. Anaphylaxis is a potential side effect of the vaccine, and it is recommended that those with known hypersensitivity to the ingredients of the vaccine should not receive it.

COVID-19 Pfizer/BioNTech Vaccine and COVID-19 Vaccine Moderna are the preferred vaccines in the UK booster programme. Reports of anaphylaxis or anaphylactoid reactions

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<sup>5</sup> The Green Book has the latest information on vaccines and vaccination procedures, for vaccine preventable infectious diseases in the UK.

remain very rare after booster doses. Analysis of the data shows that these events are about 5 times lower after booster doses compared to the first dose.

The MHRA also closely monitors reports of anaphylaxis or anaphylactoid reactions with the COVID-19 Vaccine AstraZeneca and has received 884 UK spontaneous adverse reactions associated with anaphylaxis or anaphylactoid reactions reported and such reports are very rare. The product information reflects the fact that reports of anaphylaxis have been received for the COVID-19 Vaccine AstraZeneca.

## **Bell's palsy**

Bell's palsy (BP) is temporary weakness or paralysis affecting one side of the face that develops gradually; most people recover from this condition within a few months. BP is known to be associated with a number of infectious diseases, including the SARS-CoV-2 virus. Reports of suspected BP following COVID-19 vaccination have been continuously reviewed by the MHRA. Whilst reporting of BP following COVID-19 vaccination is rare, evidence based on the latest available data shows that there may be an increased risk of BP following COVID-19 vaccination. To raise awareness of this potential adverse event amongst healthcare professionals and patients, facial paralysis has been included in the product information for COVID-19 Vaccine AstraZeneca, COVID-19 Vaccine Pfizer/BioNTech and COVID-19 Vaccine Moderna. We will continue to monitor these events following COVID-19 vaccination.

## **Transverse myelitis**

Transverse myelitis (TM) is a rare acute neurological disorder where parts of the spinal cord are inflamed. TM is known to be associated with a number of viruses, such as the herpes and influenza virus. The MHRA has continually monitored reports of suspected transverse myelitis following COVID-19 vaccination since the start of the vaccination programme. As of 4 May 2022, we have received 122 reports of suspected TM following administration of COVID-19 AstraZeneca, 38 reports following administration of COVID-19 Pfizer/BioNTech Vaccine and 4 reports following administration of COVID-19 vaccine Moderna. There were no reports of fatal events following suspected TM. Whilst the incidence rate of this adverse event with any of the COVID-19 vaccines used in the UK remains extremely rare (less than 1 report per 100,000 doses of each vaccine), the available evidence reviewed by the MHRA suggests an association between TM and COVID-19 AstraZeneca vaccine is possible. Due to the serious nature of this adverse event and as a precaution, the product information has been updated to raise healthcare professionals' and patients' awareness of the signs and symptoms associated with TM which may include muscle weakness, localised or radiating back pain, bladder and bowel symptoms and changes in sensation. It is recommended that patients who had an episode of transverse myelitis following the first dose of COVID-19 vaccine AstraZeneca should not receive a second dose of this vaccine.

## **Thrombo-embolic (blood clotting) events with concurrent low platelets**

The MHRA has undertaken a thorough review into UK cases of an extremely rare and unlikely to occur specific type of blood clot in the brain, known as cerebral venous sinus thrombosis (CVST) occurring together with low levels of platelets (thrombocytopenia) following vaccination with the COVID-19 Vaccine AstraZeneca. It has also considered other blood clotting reports (thromboembolic events) alongside low platelet levels.

This scientific review concluded that the evidence of a link with COVID-19 Vaccine AstraZeneca is likely and [an announcement](#) was made on 7 April 2021 with a further statement on 7 May 2021. We have continued to publish the latest breakdown of all cases of these extremely rare side effects on a weekly basis.

Anyone who experienced cerebral or other major blood clots occurring with low levels of platelets after their first vaccine dose of COVID-19 Vaccine AstraZeneca should not have further doses. Anyone who did not have these side effects should come forward for their second dose when invited.

Anyone who experiences any of the following from around 4 days after vaccination should seek medical advice urgently:

- a severe headache that is not relieved with simple painkillers or gets worse or feels worse when you lie down or bend over
- an unusual headache that may be accompanied by blurred vision, confusion, difficulty with speech, weakness, drowsiness or seizures (fits)
- rash that looks like small bruises or bleeding under the skin beyond the injection site
- shortness of breath, chest pain, leg swelling or persistent abdominal (tummy) pain.

Up to 4 May 2022, the MHRA had received Yellow Card reports of 443 cases of major thromboembolic events (blood clots) with concurrent thrombocytopenia (low platelet counts) in the UK following vaccination with COVID-19 Vaccine AstraZeneca. Fifty-one of the 443 reports have been reported after a second dose. Of the 443 reports, 221 occurred in females, and 217 occurred in males aged from 18 to 93 years. The overall case fatality rate was 18% with 81 deaths, six of which occurred after the second dose.

Cerebral venous sinus thrombosis was reported in 160 cases (average age 46 years) and 283 had other major thromboembolic events (average age 54 years) with concurrent thrombocytopenia. The estimated number of first doses of COVID-19 Vaccine AstraZeneca administered in the UK by 4 May was 24.9 million and the estimated number of second doses was 24.1 million.

The overall incidence after first or unknown doses was 15.7 per million doses. Considering the different numbers of patients vaccinated with COVID-19 Vaccine AstraZeneca in different age groups, the data indicates that there is a higher reported incidence rate in the younger adult age groups following the first dose compared to the older groups (21.3 per million doses in those aged 18-49 years compared to 11.2 per million doses in those aged 50 years and over). The number of first doses given to those in the 18-49 years age group is estimated to be 8.5 million while an estimated 16.4 million first doses have been given to patients aged 50+ years. The MHRA advises that this evidence should be taken into account when considering the use of the vaccine. There is some evidence that the reported incidence rate is higher in females compared to men although this is not seen across all age groups and the difference remains small.

The overall incidence of thromboembolic events with concurrent low platelets after second doses was 2.2 cases per million doses. Taking into account the different numbers of patients vaccinated with COVID-19 Vaccine AstraZeneca in different age groups, the data indicates that there is a lower reported incidence rate in younger adult age groups following the second dose compared to the older groups (1.1 per million doses in those aged 18-49 years compared to 2.1 per million doses in those aged 50 years and over). The number of second doses given to those in the 18-49 years age group is estimated to be 8.1 million while an estimated 16.1 million second doses have been given to patients aged 50+ years. These rates after second doses should not be directly compared to the incidence rates reported after the first dose as the time for follow-up and identification of cases after second doses is more limited and differs across age groups. However, the data are reassuring, particularly regarding younger recipients where there is a significantly lower incidence after the second dose compared to the first, and there is overall no indication of an increased risk of these events after the second dose in any age group. Anyone who did not have these side effects should come forward for their second dose when invited.

These cases have also been analysed by the independent advisory body, the CHM's COVID-19 Vaccines Benefit Risk Expert Working Group, which includes lay representatives and advice from leading haematologists.

On the basis of this ongoing review, the advice remains that the benefits of the vaccine outweigh the risks in the majority of people.

**Table 5: Number of suspected thrombo-embolic events with concurrent thrombocytopenia ADR cases received for the COVID-19 Vaccine AstraZeneca in the UK up to and including 4 May 2022.**

Country	Number of cases
England	342
Wales	14
Northern Ireland	12
Scotland	36
Unknown	39

**Table 6: Number of UK suspected thrombo-embolic events with concurrent thrombocytopenia ADR cases received for the COVID-19 Vaccine AstraZeneca by patient age up to and including 4 May 2022.**

Age range (years)	Number of cases	Number of fatal cases
18-29	31	7
30-39	49	10
40-49	111	15
50-59	108	22
60-69	62	11
70-79	40	7
80-89	6	3
90-99	2	1
Unknown	34	5
<b>Total</b>	<b>443</b>	<b>81</b>

**Table 7: Number of UK suspected thrombo-embolic events with concurrent thrombocytopenia ADR cases received for the COVID-19 Vaccine AstraZeneca by patient sex up to and including 4 May 2022.**

<b>Sex</b>	<b>Number of cases</b>	<b>Number of fatal cases</b>
Male	217	35
Female	221	45
Unknown	5	1
<b>Total</b>	<b>443</b>	<b>81</b>

Up to 4 May 2022, the MHRA had received Yellow Card reports of 32 cases of major thromboembolic events (blood clots) with concurrent thrombocytopenia (low platelet counts) in the UK following use of the COVID-19 Pfizer/BioNTech Vaccine. These events occurred in 13 females, and 18 males aged from 18 to 91 years, and the overall case fatality rate was 13% with four deaths reported.

Up to 4 May 2022, the MHRA had received Yellow Card reports of 6 cases of major thromboembolic events (blood clots) with concurrent thrombocytopenia (low platelet counts) in the UK following the use of COVID-19 vaccine Moderna. These events occurred in 5 adult males and 1 adult female under the age of 85. There have been no fatal cases reported.

To note, direct comparison of the summary provided here, and the analysis prints is not possible. This review includes reports of CVST or other thrombo-embolic events with concurrent thrombocytopenia. Blood clotting events without lowered platelets are described below.

Yellow Card reports may contain more than one reported reaction and the analysis prints are listed by individual reactions rather than whole reports. Therefore, summing the reactions listed in the prints will not equate to the total cases included within this summary.

### **Thrombo-embolic (blood clotting) events without concurrent low platelets**

The MHRA has conducted a thorough review of events of cerebral venous sinus thrombosis (CVST) without concurrent low platelet levels following vaccination with the COVID-19 Vaccine AstraZeneca and sought advice from the CHM's Vaccine Benefit Risk Expert

Working Group. Blood clotting events with lowered platelets are described in a separate section (above). The scientific review concluded that there is a possible link between CVST without low platelets and COVID-19 Vaccine AstraZeneca. The product information for COVID-19 Vaccine AstraZeneca has been updated to include information that CVST events not associated with low levels of blood platelets occurred extremely rarely. The majority of the CVST events occurred within the first four weeks following vaccination. A potential cause has not been identified.

The MHRA has also confirmed that the evidence to date does not suggest that the COVID-19 Vaccine AstraZeneca increases the risk of venous thromboembolism (i.e. deep vein thrombosis/pulmonary embolism) in the absence of a low platelet count. The MHRA will continue to closely monitor reports of venous thromboembolism following COVID-19 vaccination.

## **Immune thrombocytopenia**

Immune thrombocytopenia (ITP) is a condition where the immune system does not function correctly and becomes involved in destroying platelets, which can lead to bleeding; these events are usually short-lived and of minor severity. Reports of ITP following COVID-19 vaccination have been closely monitored by the MHRA. A recent thorough review of all the available evidence confirmed that this type of event is reported extremely rarely for COVID-19 vaccine AstraZeneca in the UK, at approximately 4 reports per million doses. In approximately 10-20% of the reports, patients had a history of ITP or an underlying condition known to be associated with ITP. Following the most recent review, the available data suggested a possible link between COVID-19 vaccine AstraZeneca and ITP, and the product information for this vaccine has been updated to include information on the occurrence of ITP.

## **Capillary Leak Syndrome**

The MHRA has received 17 reports of suspected capillary leak syndrome (a condition where fluid leaks from the small blood vessels into the body) in the context of more than 49.1 million doses of COVID-19 Vaccine AstraZeneca given. Of these reports, 3 people had a history of capillary leak syndrome. This is an extremely rare relapsing-remitting condition and triggers for relapses are not well understood. As a precautionary measure, the MHRA is advising that COVID-19 Vaccine AstraZeneca is not used in people who have previously experienced episodes of capillary leak syndrome. The product information has been updated to reflect this advice.

## **Menstrual disorders (period problems) and unexpected vaginal bleeding**

The MHRA is reviewing reports of suspected side effects of menstrual disorders (period problems) and unexpected vaginal bleeding following vaccination against COVID-19 in the UK. These reports are also being reviewed by the independent experts of the CHM's COVID-19 Vaccines Benefit Risk Expert Working Group and the Medicines for Women's Health Expert Advisory Group. The rigorous evaluation completed to date does not support a link between changes to menstrual periods and related symptoms and COVID-19 vaccines.

Up to 4 May 2022 a total of 51,129 suspected reactions relating to a variety of menstrual disorders have been reported after all three of the COVID-19 vaccines including heavier than usual periods, delayed periods and unexpected vaginal bleeding. These suspected reactions have been reported in 39,839 individual Yellow Card reports (as each report may contain more than one suspected reaction). This is following approximately 73.9 million COVID-19 vaccine doses administered to women up to 4 May 2022. The number of reports of menstrual disorders and vaginal bleeding is low in relation to both the number of people who have received COVID-19 vaccines to date and how common menstrual disorders are generally.

The menstrual changes reported are mostly transient in nature. There is no evidence to suggest that COVID-19 vaccines will affect fertility and your ability to have children.

Whilst uncomfortable or distressing, period problems are extremely common and stressful life events can disrupt menstrual periods. Changes to the menstrual cycle have also been reported following infection with COVID-19 and in people affected by long-COVID. General advice about period problems and/or unexpected vaginal bleeding is available from the [NHS website](#). It is important that anyone experiencing changes to their periods that are unusual for them, persist over time, or has any new vaginal bleeding after the menopause, following COVID-19 vaccination, should contact their doctor. Anyone presenting with menstrual disorders and/or unexpected vaginal bleeding following COVID-19 vaccination should be treated according to clinical guidelines for these conditions, as usual.

The MHRA continues to closely review reports of suspected side effects of menstrual disorders and unexpected vaginal bleeding.

## **Myocarditis and pericarditis (Inflammation of the heart)**

The MHRA has undertaken a thorough review of both UK and international reports of suspected myocarditis and pericarditis following vaccination against COVID-19. There has been a consistent pattern of higher reporting of these suspected events with the COVID-19 Pfizer/BioNTech and COVID-19 Vaccine Moderna, and of these occurring more frequently in

males. These reports have also been analysed by the government's independent advisory body, the CHM and its COVID-19 Vaccines Benefit Risk Expert Working Group. Following their advice, the product information for the COVID-19 Vaccine Moderna and COVID-19 Pfizer/BioNTech Vaccines was updated to inform of these reports and advise healthcare professionals and patients to be aware of important symptoms for myocarditis and pericarditis.

These reports are very rare, and the events reported are typically mild with individuals usually recovering within a short time with standard treatment and rest.

People should come forward for their second and booster vaccination when invited to do so, unless advised otherwise.

It is important that anyone who experiences new onset of symptoms such as chest pain, shortness of breath or feelings of having a fast-beating, fluttering, or pounding heart seeks medical attention.

Up to and including 4 May 2022, we have received 786 reports of myocarditis and 532 reports of pericarditis following use of the COVID-19 Pfizer/BioNTech Vaccine, as well as ten reports of carditis, four reports for viral myocarditis, three reports each for viral pericarditis and infective pericarditis, two reports each for myocarditis mycotic and endocarditis, and one report each of constrictive pericarditis, pleuropericarditis, lupus pericarditis, non-infective endocarditis, infectious myocarditis, eosinophilic myocarditis, hypersensitivity myocarditis, myocarditis post infection, bacterial myocarditis, septic myocarditis and streptococcal endocarditis.

For COVID-19 Vaccine AstraZeneca there have been 226 reports of myocarditis and 220 reports of pericarditis following vaccination up to and including 4 May 2022 as well as eight reports for endocarditis, five reports for viral pericarditis, three reports for viral myocarditis, two reports each for bacterial endocarditis, carditis, and acute endocarditis, and one report each for infectious myocarditis, myocarditis post infection and autoimmune myocarditis.

There have been 221 reports of myocarditis, 127 reports of pericarditis, three reports of carditis and one report each of hypersensitivity myocarditis, pleuropericarditis, viral myocarditis and endocarditis following use of COVID-19 Vaccine Moderna up to the same date.

Five fatal suspected myocarditis or pericarditis events have been reported associated with the COVID-19 Pfizer/BioNTech Vaccine and four fatal events associated with the COVID-19 Vaccine AstraZeneca. There have been no fatal myocarditis or pericarditis events reported with the COVID-19 Vaccine Moderna to date. Fatal events are being monitored closely and are carefully followed up to gather relevant information. The majority of fatal reports describe

underlying illnesses in these patients that could provide alternative explanations for the events reported.

Based on reports of suspected ADRs in the UK, the overall reporting rate across all age groups for suspected myocarditis (including viral myocarditis), after first, second and booster or third doses, is 10 reports per million doses of COVID-19 Pfizer/BioNTech Vaccine and for suspected pericarditis (including viral pericarditis and infective pericarditis) the overall reporting rate is 7 reports per million doses. For COVID-19 Vaccine Moderna, the overall reporting rate for suspected myocarditis (including hypersensitivity myocarditis and viral myocarditis) is 18 per million doses and for suspected pericarditis (including pleuropericarditis) is 10 per million doses. For COVID-19 Vaccine AstraZeneca the overall reporting rate for suspected myocarditis (including viral myocarditis and infectious myocarditis) is 5 per million doses and for suspected pericarditis (including viral pericarditis) is 5 per million doses. It should be noted that an individual report can contain more than one event and therefore the total number of reports will not be equal to the number of events.

When the reporting rate is calculated by age group (see Table 8) the reporting rate for suspected myocarditis and pericarditis is highest in the 18-29-year age group for the Pfizer/BioNTech and Moderna COVID-19 vaccines. A more even spread in reporting rates across the age groups is seen for AstraZeneca COVID-19 vaccine. For all vaccines there is a trend for decreased reporting in the older age groups.

Pfizer/BioNTech is currently the preferred COVID-19 vaccine for the under 18s age group in the UK vaccination programme, and for this vaccine there is no indication in the current data that there is an increased reporting rate of suspected myocarditis and pericarditis in this age group overall compared to young adults. Furthermore, the reporting rates for the 12-15 year and 16-17 year age group are lower than that in the young adult 18-29 age group after the first and second doses. Due to very limited experience in the 5–11 year age group it is not possible to reliably make the same estimations for this population. There have been no reports of suspected myo/pericarditis following booster doses in the under 18-year age group.

There are largely similar reporting rates between the first and second doses of the Pfizer/BioNTech and AstraZeneca COVID-19 vaccines. There is greater variability between first and second dose reporting rates with Moderna however the reporting rate estimates for Moderna may lack precision due to the more limited experience with Moderna in the UK and small numbers of suspected reports. This introduces more uncertainty into the data.

COVID-19 Pfizer/BioNTech Vaccine and COVID-19 Vaccine Moderna are the preferred vaccines in the UK booster programme, and the reporting rates for suspected myocarditis and pericarditis following booster or third doses of these vaccines are lower than those estimated for the first and second doses; these events are very rare after booster doses.

There is no indication that these events are more severe after booster doses compared to first and second doses; most reports describe mild events with a rapid recovery and are similar to those experienced after the first and second doses. There is extremely limited usage of COVID-19 Vaccine AstraZeneca as a booster. Due to this limited usage and very small numbers of reports of suspected myocarditis and pericarditis after booster doses, it is not possible to calculate a reliable reporting rate for the COVID-19 Vaccine AstraZeneca when used as a booster; no association has been established between myocarditis or pericarditis and the COVID-19 Vaccine AstraZeneca.

It is important to note that Yellow Card data cannot be used to compare the safety profile of COVID-19 vaccines as many factors can influence ADR reporting.

These reporting rates may also be subject to change as more experience is gathered in the UK.

**Table 8: Reporting rates per million doses for UK ADR reports of suspected myocarditis and pericarditis associated with COVID-19 Vaccines, by patient age and dose, up to and including 4 May 2022.**

Age range (years)	COVID-19 Pfizer/BioNTech 1st or unknown dose	COVID-19 Pfizer/BioNTech 2nd dose	COVID-19 Pfizer/BioNTech 3rd or booster dose	COVID-19 Vaccine Moderna 1st or unknown dose	COVID-19 Vaccine Moderna 2nd dose	COVID-19 Vaccine Moderna 3rd or booster dose	COVID-19 Vaccine AstraZeneca 1st or unknown dose	COVID-19 Vaccine AstraZeneca 2nd dose
Under 18	14	11	Not calculated*	Not applicable*	Not applicable**	Not applicable**	Not applicable**	Not applicable**
18-29	26	28	16	63	67	19	10	16
30-39	23	24	15	58	54	20	14	12
40-49	19	19	13	49	31	15	12	9
50-59	9	17	8	Not calculated*	Not calculated*	8	8	7
60-69	7	14	6	Not calculated*	Not applicable**	7	7	6

70+	4	5	4	Not calculated*	Not applicable**	2	4	4
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\*There is currently insufficient data to calculate a reliable estimate of the reporting rate in the UK due to the relatively limited exposure and small numbers of suspected reports in these individuals.

\*\*There have been no reports of suspected heart inflammation events received for individuals in these age groups.

**Table 9\*: Number of UK ADR reports associated with suspected myocarditis, pericarditis and other related terms received for the COVID-19 Vaccine AstraZeneca, COVID-19 Pfizer/BioNTech Vaccine and COVID-19 Vaccine Moderna by patient age up to and including 4 May 2022.**

Age range (years)	Number of reports		
	COVID-19 Pfizer/BioNTech Vaccine	COVID-19 Vaccine Moderna	COVID-19 Vaccine AstraZeneca
Under 18	77	0	0
18-29	382	119	31
30-39	308	95	48
40-49	140	52	115
50-59	97	22	103
60+	151	17	104
Unknown	150	34	46
<b>Total</b>	<b>1305</b>	<b>339</b>	<b>447</b>

\* Due to the dynamic nature of the Yellow Card data these figures may change both as new cases are received, and as duplicate cases are identified and managed.

**Table 10\*: Number of UK ADR reports associated with suspected myocarditis, pericarditis and other related terms received for the COVID-19 Vaccine AstraZeneca, COVID-19 Pfizer/BioNTech Vaccine and COVID-19 Vaccine Moderna by patient sex up to and including 4 May 2022.**

Sex	Number of reports		
	COVID-19 Pfizer/BioNTech Vaccine	COVID-19 Vaccine Moderna	COVID-19 Vaccine AstraZeneca
Female	506	110	202
Male	758	219	235
Unknown	41	10	10
<b>Total</b>	<b>1305</b>	<b>339</b>	<b>447</b>

\* Due to the dynamic nature of the Yellow Card data these figures may change both as new cases are received, and as duplicate cases are identified and managed.

Two large European epidemiological studies have estimated the excess risk of myocarditis following vaccination with COVID-19 Pfizer/BioNTech Vaccine and COVID-19 Vaccine Moderna. One study showed that in a period of 7 days after the second dose of COVID-19 Pfizer/BioNTech Vaccine there were about 27 (95% CI 26 - 28) extra cases of myocarditis in 12-29 year old males per million compared to unvaccinated individuals, and for COVID-19 vaccine Moderna there were about 132 (95% CI 130 – 133) extra cases of myocarditis in 12-29 year old males per million. In another study, in a period of 28 days after the second dose of the COVID-19 Pfizer/BioNTech Vaccine there were 57 [95% CI 39 – 75] extra cases of myocarditis in 16-24 year old males per million compared to unvaccinated persons, and for COVID-19 vaccine Moderna there were 188 (95% CI 96 – 280) extra cases of myocarditis in 16-24 year old males per million individuals compared to unvaccinated individuals. These studies have shown that these events are very rare post vaccination with the mRNA vaccines, and that these events are more frequent in younger males. The findings of these studies are consistent with the trends seen in the Yellow Card data.

International data has shown that these suspected events have been observed to occur most frequently approximately 3 days after the first vaccine and 2 days after the second vaccine, and both UK and international data have identified that the large majority of suspected events occur within 7 days of vaccination. In the UK the body of evidence shows that for COVID-19 Pfizer/BioNTech in particular, there is similar frequency of reporting after the first and second dose.

Longer term follow up in both the UK and US to at least 90 days following identification of cases of suspected myocarditis after COVID-19 Pfizer/BioNTech and COVID-19 Vaccine Moderna found that the majority of individuals were fully recovered and back to normal activities.

Myocarditis and pericarditis happen very rarely in the general population, and it is estimated that in the UK there are about 60 new cases of myocarditis diagnosed per million patients per year and about 100 new cases of pericarditis diagnosed per million patients per year. Myocarditis is also known to be associated with COVID-19 infection, with an estimated 1,500 cases of myocarditis per million patients with COVID-19.

The MHRA will continue to closely monitor reports of suspected myocarditis and pericarditis with all currently authorised COVID-19 vaccines.

## **Delayed hypersensitivity reactions**

The MHRA has been reviewing reports of skin reactions occurring around the vaccination site that appear a little while after vaccination. These reactions are suggestive of a delayed hypersensitivity reaction that occurs 4-11 days after vaccination. The reactions are characterized by a rash, swelling and tenderness that can cover the whole upper arm and may be itchy and/or painful and warm to the touch. The majority of the reports received have been with the COVID-19 Vaccine Moderna and the product information for this vaccine has been updated to highlight the possibility of delayed injection site reactions.

The reactions are usually self-limiting and resolve within a day or two, although in some patients it can take slightly longer to disappear. Individuals who experience this reaction after their first dose may experience a similar reaction in shorter timeframe following the second dose, however, none of the reports received have been serious and people should still take their second dose when invited. Those who experience delayed skin reactions after their COVID-19 vaccination which do not resolve within a few days should seek medical advice.

## **Guillain-Barré Syndrome**

Guillain-Barré Syndrome is a very rare condition which causes inflammation of the nerves and can lead to numbness, weakness and pain, usually in the feet, hands and limbs and can spread to the chest and face. Guillain-Barré Syndrome tends to affect both sides of the body at once. This condition is known to be associated with certain infectious diseases.

Up to and including the 4 May 2022, the MHRA has received 495 reports of suspected Guillain-Barré Syndrome with the COVID-19 Vaccine AstraZeneca and 29 reports of a related disease called Miller Fisher syndrome. Up to the same date, the MHRA has received 102 reports of Guillain-Barré Syndrome following use of the COVID-19 Pfizer/BioNTech Vaccine and 5 reports of Miller Fisher syndrome and for the COVID-19 Vaccine Moderna there have been 17 reports of Guillain-Barré Syndrome.

The MHRA has been closely monitoring and assessing reports of suspected Guillain-Barré Syndrome (GBS) received following administration of the COVID-19 vaccine. Following the most recent review of the available data the evidence of a possible association has

strengthened. Therefore, following advice from the government's independent advisory body, the CHM and its COVID-19 Vaccines Benefit Risk Expert Working Group, the product information for the COVID-19 Vaccine AstraZeneca was further updated to include GBS in the tabulated list of adverse reactions associated with the COVID-19 Vaccine AstraZeneca and to encourage healthcare professionals and the public to look out for signs of GBS.

The MHRA will continue to review reports of Guillain-Barré Syndrome received following vaccination with COVID-19 vaccines to further assess a possible association, with independent advice from its Vaccine Benefit-Risk Working Group.

## **Swelling of the vaccinated limb**

There have been rare reports of extensive swelling of the vaccinated limb after receiving the COVID-19 Pfizer/BioNTech Vaccine. The product information has been updated to include "extensive swelling of the vaccinated limb" as a side effect of the vaccine. This type of swelling is also recognised to occur with other (non-COVID-19) vaccines.

## **Facial swelling in those with a history of facial dermal fillers**

Rare reports of facial swelling occurring 1-2 days after vaccination in vaccine recipients with a history of injection of facial dermal fillers were observed in the clinical trials for the COVID-19 Vaccine Moderna. Information about this possible side effect has been included in the product information for the COVID-19 Vaccine Moderna since it was first authorised for use.

The MHRA has also received Yellow Card reports of facial swelling in those with a history of injection of facial dermal fillers for the COVID-19 Pfizer/BioNTech Vaccine. A review of the world-wide ADR data for the COVID-19 Pfizer/BioNTech Vaccine found that, in most instances, the facial swelling was mild, transient and was localised to the site of the dermal filler. The product information for the COVID-19 Pfizer/BioNTech Vaccine has been updated to include facial swelling in those with a history of injection of facial dermatological fillers as a side effect of the vaccine.

## **Events with a fatal outcome**

Vaccination and surveillance of large populations means that, by chance, some people will experience and report a new illness or events in the days and weeks after vaccination. A high proportion of people vaccinated early in the vaccination campaign were very elderly, and/or had pre-existing medical conditions. Older age and chronic underlying illnesses make it more likely that coincidental adverse events will occur, especially given the millions of people vaccinated. It is therefore important that we carefully review these reports to distinguish possible side effects from illness that would have occurred irrespective of vaccination.

Part of our continuous analysis includes an evaluation of natural death rates over time, to determine if any specific trends or patterns are occurring that might indicate a vaccine safety concern. Based on age-stratified all-cause mortality in England and Wales taken from the [Office for National Statistics death registrations](#), several thousand deaths are expected to have occurred, naturally, within 7 days of the many millions of doses of vaccines administered so far, mostly in the elderly.

A [recent study](#) published by the Office for National Statistics (ONS) and the Office for Health Improvement and Disparities (OHID) analysed data on COVID 19 vaccination and mortality in young people during the coronavirus pandemic. The study found no indication of an increased risk of death from cardiac-related or other causes in those aged 12-29 years, following COVID-19 vaccination in the six weeks following vaccination. This is consistent with our own findings from our rigorous safety monitoring activities. The study also suggested that the excess in death registrations in young people in 2021 was due to delays in the registration process and early indications of increased numbers of deaths due to non-vaccine related external causes. The study data were reviewed by the independent experts of the CHM's COVID-19 Vaccines Benefit Risk Expert Working Group who agreed with the conclusion of the report that COVID-19 vaccines were not associated with an increased risk of death in young people.

The MHRA has received 763 UK reports of suspected ADRs to the COVID-19 Pfizer/BioNTech Vaccine in which the patient died shortly after vaccination, 1,272 reports for the COVID-19 Vaccine AstraZeneca, 53 for the COVID-19 Vaccine Moderna and 44 where the brand of vaccine was unspecified. The majority of these reports were in elderly people or people with underlying illness. Usage of the vaccines has increased over the course of the campaigns and as such, so has reporting of fatal events with a temporal association with vaccination. However, this does not mean that there is a link between vaccination and the fatalities reported. Review of specific fatal reports is provided in the summaries above. The pattern of reporting for all other fatal reports does not suggest the vaccines played a role in these deaths.

A range of other isolated events or series of reports of non-fatal, serious suspected ADRs have been reported. These all remain under continual review, including thorough analysis of expected rates in the absence of vaccine. There are currently no indications of specific patterns or rates of reporting that would suggest the vaccine has played a role.

## Conclusion

At the time of this report, over 176,321 people across the UK have died within 28 days of a positive test for coronavirus.

Vaccination is the single most effective way to reduce deaths and severe illness from COVID-19. A national immunisation campaign has been underway since early December 2020.

In [clinical trials](#), the COVID-19 Pfizer/BioNTech Vaccine, COVID-19 Vaccine AstraZeneca and COVID-19 Vaccine Moderna have demonstrated very high levels of protection against symptomatic infection. [Data](#) are available on the impact of the vaccination campaign in reducing infections and illness in the UK.

All vaccines and medicines have some side effects. These side effects need to be continuously balanced against the expected benefits in preventing illness.

Following widespread use of these vaccines across the UK, the vast majority of suspected adverse reaction reports confirm the safety profile seen in clinical trials. Most reports relate to injection-site reactions (sore arm for example) and generalised symptoms such as a 'flu-like' illness, headache, chills, fatigue, nausea, fever, dizziness, weakness, aching muscles, and rapid heartbeat. Generally, these reactions are not associated with more serious illness and likely reflect an expected, normal immune response to the vaccines.

The expected benefits of the vaccines in preventing COVID-19 and serious complications associated with COVID-19 far outweigh any currently known side effects. As with all vaccines and medicines, the safety of COVID-19 vaccines is continuously monitored and benefits and possible risks remain under review.

We take every report of a suspected ADR seriously and encourage everyone to report through the Yellow Card scheme.

# Annex 1 Vaccine Analysis Print

The attached Vaccine Analysis Prints contain a complete listing of all suspected adverse reactions that have been reported to the MHRA via the Yellow Card scheme for the COVID-19 Pfizer/BioNTech Vaccine, the COVID-19 Vaccine AstraZeneca, the COVID-19 Vaccine Moderna and where the brand of the vaccine was not specified. This includes all reports received from healthcare professionals, members of the public, and pharmaceutical companies.

This information does not represent an overview of the potential side effects associated with the vaccines. A list of the recognised adverse effects of COVID-19 vaccines is provided in the information for healthcare professionals and the recipient information [here](#). These can also be found on the [Coronavirus Yellow Card](#) reporting site. Conclusions on the safety and risks of the vaccines cannot be made on the data shown in the Print alone.

When viewing the vaccine analysis print you should remember that:

- Reporters are asked to submit Yellow Card reports even if they only have a suspicion that the medicine or vaccine may have caused the adverse reaction. The existence of an adverse reaction report in the print does not necessarily mean that the vaccine has caused the suspected reaction.
- It may be difficult to tell the difference between something that has occurred naturally and a suspected adverse reaction. Sometimes these events can be part of the condition being treated rather than being caused by the vaccine.
- Many factors have to be considered when assessing whether the vaccine has caused a reported adverse reaction. When monitoring the safety of vaccines and medicines, MHRA staff carry out careful analysis of these factors.

For a medicine or vaccine to be considered safe, the expected benefits will be greater than the risk of having harmful reactions. It is important to note that most people take medicines and vaccines without having any serious side effects.

[Vaccine Analysis Print – COVID-19 Pfizer/BioNTech Vaccine](#)

[Vaccine Analysis Print - COVID-19 Vaccine AstraZeneca](#)

[Vaccine Analysis Print – COVID-19 Vaccine Moderna](#)

[Vaccine Analysis Print - Brand unspecified](#)

## Annex 2 Glossary

### **Anaphylaxis or anaphylactoid reactions**

Anaphylaxis is a severe and potentially life-threatening allergic reaction. These reactions can occur after an exposure to a trigger, such as a certain ingredient in foods or medicines or an insect sting. Anaphylaxis and anaphylactoid reactions can be treated with adrenaline.

### **Bell's palsy**

Bell's palsy is a condition that causes temporary weakness or paralysis (lack of movement) of the muscles in one side of the face. It is the most common cause of facial paralysis. For most people, the facial paralysis is temporary. Viral infections such as those with herpes viruses have been linked to Bell's palsy.

### **Booster dose/vaccination**

A COVID-19 booster vaccine dose helps improve the protection obtained from the first two doses of the vaccine. It helps give longer-term protection against getting seriously ill from COVID-19.

### **Capillary Leak Syndrome (CLS)**

Capillary Leak Syndrome (CLS) occurs when fluid leaks from the small blood vessels into the body.

### **Cerebral venous sinus thrombosis (CVST)**

Cerebral venous sinus thrombosis occurs when the brain's venous sinuses or the smaller veins draining into them are partially or completely blocked by a blood clot. This prevents blood from draining out of the brain. As a result, the oxygen supply to nerve cells may be impaired and blood cells can leak into the brain tissue causing damage to the brain (haemorrhagic infarction).

### **Clinical Practice Research Datalink (CPRD)**

[Clinical Practice Research Datalink \(CPRD\)](#) is a real-world research service to support public health and clinical studies. CPRD is jointly sponsored by the Medicines and Healthcare products Regulatory Agency and the National Institute for Health Research (NIHR), as part of the Department of Health and Social Care. CPRD collects anonymised patient data from a network of GP practices across the UK.

## **Commission on Human Medicines (CHM)**

The [Commission on Human Medicines \(CHM\)](#) advises ministers on the safety, efficacy and quality of medicinal products. For COVID-19 vaccines, the CHM has a COVID-19 Vaccines Safety Surveillance Methodologies Expert Working Group and a COVID-19 Vaccines Benefit Risk Expert Working Group.

## **Endocarditis**

Endocarditis is inflammation of the inner lining of the heart (endocardium).

## **Epidemiology studies**

Epidemiological studies include large numbers of people and are designed to compare the risk of a particular event in an exposed population, in this case those who have received a vaccine, to those who have not. They attempt to account for differences in the different groups to help us understand if any difference in risk is caused by the exposure.

Epidemiological studies measure the risk of illness or death in an exposed population compared to that risk in an identical, unexposed population.

## **Guillain-Barré Syndrome**

Guillain-Barré Syndrome is inflammation of the nerves and can lead to numbness, weakness and pain, usually in the feet, hands and limbs and can spread to the chest and face. This syndrome has been associated with viral infections such as the flu.

## **Immune thrombocytopenia Immune thrombocytopenia (ITP)**

ITP is an auto-immune condition characterised by low blood platelet count (thrombocytopenia) and is associated with an increase risk in bleeding which often presents as bruising or petechia/purpura.

## **Miller-Fisher Syndrome**

Miller-Fisher syndrome is a variation of Guillain-Barré Syndrome that affects the nervous system and can cause weakness in the face and a lack of balance and co-ordination. Similar to Guillain-Barré Syndrome, this syndrome has been associated with viral infections such as the flu.

## **Miscarriage**

The loss of a pregnancy during the first 23 weeks.

## **Myocarditis**

Myocarditis is the inflammation of the heart muscle (myocardium).

## **Non-clinical studies**

Non-clinical studies refer to studies that are not performed on the human body. These are largely done before clinical trials in humans and can include animal safety and efficacy studies, human tissue sample studies or toxicology.

## **Pericarditis**

Pericarditis is inflammation of the pericardium, the protective sac that surrounds your heart.

## **Regulation 174 authorisation**

Temporary authorisation for supply of a medicine or vaccine by the UK Department of Health and Social Care and the Medicines and Healthcare products Regulatory Agency. This temporary authorisation grants permission for a medicine (vaccine) to be used for active immunisation to prevent COVID-19 disease caused by SARS-CoV-2 virus. Authorisation is subject to a number of conditions. These are available for each vaccine on the MHRA website.

## **Suspected adverse reactions**

Also known as side effects. All medicines or vaccines can cause adverse reactions in some people. Adverse drug reactions reported to the MHRA are looked at and used to assess the balance of risks and benefits of medicines and vaccines.

## **Stillbirth**

A stillbirth is when a baby is born dead after 24 completed weeks of pregnancy. If the baby dies before 24 completed weeks, it's known as a miscarriage.

## **Temporal Association**

Events occurring following vaccination but may or may not be caused by the vaccine.

## **Third dose/vaccination**

A COVID-19 third vaccine is being offered to those who had a weakened immune system when they had the first two doses of the COVID-19 vaccination. The third dose may help to improve immune response and give better protection.

## **Thrombocytopenia**

Thrombocytopenia is where the blood contains a lower than normal number of platelets. Platelets are the smallest of the blood cells and are involved in the clotting process.

## **Transverse Myelitis**

Transverse myelitis is a rare acute neurological disorder causing inflammation of the spinal cord, the part of the central nervous system that sends impulses from the brain to nerves in the body.

## **Yellow Card scheme**

The MHRA's scheme for healthcare professionals and members of the public to report suspected adverse reactions for a medicine or vaccine, as well as medical devices and other products. The [dedicated Coronavirus Yellow Card reporting site](#) was launched in May 2020 specifically for medicines and medical devices used in COVID-19, as well as COVID-19 vaccines when authorised.