Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

Coronavirus Vaccine - summary of Yellow Card reporting

Data included: 9/12/2020 to 21/04/2021

This information is also available on the gov.uk website

Produced by [Medicines and Healthcare products Regulatory Agency]

Alternative format versions of this report are available on request from [author's contact details].

Contents

Summary

At the time of this report, over 127,000 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, Pfizer/BioNTech, Oxford University/AstraZeneca and Moderna vaccines, 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 is now 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.

The 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 Oxford University/AstraZeneca vaccine 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 Moderna vaccine 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's role is also to continually monitor 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 most vaccines are being given to the most elderly people and people who have underlying illness.

This safety update report is based on detailed analysis of data up to 21 April 2021. At this date, an estimated 11.2 million first doses of the Pfizer/BioNTech vaccine and 22.0 million first doses of the Oxford University/AstraZeneca vaccine had been administered, and around 6.8 million and 4.4 million second doses of the Pfizer/BioNTech vaccine and Oxford University/AstraZeneca vaccine respectively. An approximate 0.1 million first doses of the Moderna vaccine have also now been administered.

As of 21 April 2021, for the UK, 52,130 Yellow Cards have been reported for the Pfizer/BioNTech vaccine, 153,098 have been reported for the Oxford University/AstraZeneca vaccine, 228 for the Moderna vaccine and 541 have been reported where the brand of the vaccine was not specified.

For the Pfizer/BioNTech and Oxford University/AstraZeneca vaccines the overall reporting rate is around 3 to 6 Yellow Cards per 1,000 doses administered.

In the week since the previous summary for 14 April 2021 we have received a further 2,108 Yellow Cards for the Pfizer/BioNTech vaccine, 7,104 for the Oxford University/AstraZeneca vaccine, 184 for the Moderna vaccine and 25 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 vaccinations as many factors can influence ADR reporting.

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.

Severe allergy

On 9 December 2020, the MHRA issued preliminary guidance on severe allergic reactions after the Pfizer/BioNTech vaccine due to early reports of anaphylaxis. Following further detailed review, this advice was amended on 30 December to the current advice. This advice is that people with a previous history of severe allergic reactions to any ingredients of the vaccine should not receive it. People who receive the vaccine should be monitored for at least 15 minutes afterwards.

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

Blood clots with concurrent low platelets

The MHRA has undertaken a thorough review into UK reports 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 is also considering other blood clotting cases (thromboembolic events) alongside low platelet levels.

On the basis of this ongoing scientific review, it has concluded that the evidence of a link with COVID-19 Vaccine AstraZeneca is stronger, but more work is still needed. An announcement on 7 April 2021 gave information about cases received up to 31 March 2021. In this report (page 13) we

provide updated information on cases received up to 21 April 2021. Our advice remains unchanged.

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 their second dose. Anyone who did not have these side effects should come forward for their second dose when invited.

The MHRA recently confirmed that the evidence to date does not suggest that the COVID-19 Vaccine AstraZeneca causes venous thromboembolism without a low platelet count.

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

- a severe headache that is not relieved with simple painkillers or is getting 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.

Conclusion

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

- As with all vaccines and medicines, the safety of COVID-19 vaccines is being continuously monitored

- Cases of an extremely rare specific type of blood clot with low blood platelets continue to be investigated.

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

1. 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 has played 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 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 they both occurred around the same time. 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 mRNA Pfizer/BioNTech, COVID-19 AstraZeneca vaccine and COVID-19 Moderna vaccine is 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 coronavirus (COVID-19) vaccines (COVID-19 mRNA Pfizer/BioNTech, COVID-19 Oxford University/AstraZeneca vaccine and COVID-19 vaccine Moderna), and MHRA's analysis of the

data, **between 9 December 2020 and 21 April 2021 (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.

2. Yellow Card reports

Vaccine doses administered

Data from the UK Public Health agencies show that at least 33,257,651 people have received their first vaccination in the UK by 21 April 2021, with 11,192,601 second doses administered. The current priority groups of the immunisation campaign include people over the age of 45 years, the clinically vulnerable, care home residents and workers, and frontline health and social care workers.

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 21 April 2021.

Country	Number of doses
England	27,891,208
Wales	1,727,455
Northern Ireland	883,813
Scotland	2,755,175

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 21 April 2021.

Country	Number of doses
England	9,346,865
Wales	635,655
Northern Ireland	311,850
Scotland	635,655

As of 21 April, an estimated 11.2 million first doses of the Pfizer/BioNTech vaccine, 22.0 million first doses of the Oxford University/AstraZeneca vaccine, and 0.1 million first doses of the Moderna vaccine had been administered, and around 6.8 million and 4.4 million second doses of the Pfizer/BioNTech vaccine and Oxford University/AstraZeneca vaccine respectively.

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

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. 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**. All reports are kept under continual review in order to identify possible new risks.

Up to and including 21 April 2021, the MHRA received and analysed 52,130 UK Yellow Cards from people who have received the COVID-19 mRNA Pfizer/BioNTech vaccine. These reports include a

total of 149,082 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 21 April 2021, the MHRA received and analysed a total of 153,098 UK reports of suspected ADRs to the COVID-19 Oxford University/AstraZeneca vaccine. These reports include a total of 573,650 suspected reactions (a single report may contain more than one symptom). The first report was received on 4 January 2021.

Up to and including 21 April 2021, the MHRA received and analysed a total of 228 UK reports of suspected ADRs to the COVID-19 Moderna vaccine. These include a total of 660 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 21 April 2021, the MHRA received 541 Yellow Card reports where the brand of vaccine was not specified by the reporter.

In the week since the previous summary for 14 April 2021 we have received a further 2,108 Yellow Cards for the Pfizer/BioNTech vaccine, 7,104 for the Oxford University/AstraZeneca vaccine, 184 for the Moderna vaccine and 25 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 vaccinations as many factors can influence ADR reporting.

Table 3: Number of suspected ADR reports received in the UK up to and including 21 April 2021.

	Number of reports			
Country	**Pfizer/ BioNtech**	**Oxford University/ AstraZeneca**	**Moderna**	**Brand unspecified**
England	41,168	130,431	144	283
Wales	3,013	6,696	38	31
Northern Ireland	1,131	1,557		4
Scotland	4,065	10,136	33	50

The figures in table 3 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 is in the order of 3 to 6 Yellow Cards per 1,000 doses administered for the Pfizer/BioNTech and Oxford University/AstraZeneca vaccines. It is known from the clinical trials that the more common side effects for both vaccines can occur at a rate of more than one in 10 doses (for example, local reactions or symptoms resembling transient flu-like symptoms).

3 Analysis of Data

One of MHRA's main roles is to continually monitor 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 vaccine 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 national epidemic, and because many of the millions of people offered the vaccine in the early phase of a vaccination campaign are elderly and/or have 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. 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, and this is discussed below.

We also take into account the international experience based on data from other countries using the same vaccines.

Overall safety

As with any vaccine, the COVID-19 vaccines will cause side effects in some people. The total number and the nature of Yellow Cards reported 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 both 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 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.

Comments on specific reports

The following reports reflect data up to 21 April 2021. The glossary provides an explanation of the clinical terms used.

Anaphylaxis (Severe allergic reactions)

The MHRA continues to monitor reports of serious allergic reactions with the Pfizer/BioNTech COVID-19 vaccine and has received 275 UK spontaneous adverse reactions associated with anaphylaxis or anaphylactoid reactions. The nature and frequency of these reports is in line with that reported in previous updates, and severe allergic reactions to the 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 Moderna COVID-19 vaccine and has received one report 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.

The MHRA also closely monitors reports of anaphylaxis or anaphylactoid reactions with the AstraZeneca vaccine, and has received 562 UK spontaneous adverse reactions associated with anaphylaxis or anaphylactoid reactions reported and is very rare. An update to the product information has been made to reflect the fact that cases of anaphylaxis have been reported for the AstraZeneca vaccine.

Bell's Palsy

MHRA continues to review cases reporting Bell's Palsy and to analyse case reports against the number expected to occur by chance in the absence of vaccination (the 'natural rate'). The number of reports of facial paralysis received so far is similar to the expected natural rate and does not currently suggest an increased risk following the vaccines. We will continue to monitor these events, including through evaluation of electronic healthcare record data.

Thrombo-embolic events with concurrent low platelets

Up to 21 April 2021, the MHRA had received Yellow Card reports of 209 cases of major thromboembolic events (blood clots) with concurrent thrombocytopenia (low platelet counts) in the UK following vaccination with COVID-19 Vaccine AstraZeneca. These events occurred in 120 women and 89 men aged from 18 to 93 years and the overall case fatality rate was 19% with 41 deaths. Four cases have been reported after a second dose. Cerebral venous sinus thrombosis was reported in 84 cases (average age 47 years) and 123 had other major thromboembolic events (average age 55 years) with concurrent thrombocytopenia. Diagnosis was unclear in the remaining two cases. The estimated number of first doses of COVID-19 Vaccine AstraZeneca administered in the UK by 21 April was 22 million giving an overall case incidence of 9.3 per million doses. The data suggest there is a higher incidence reported in the younger adult age groups and the MHRA advises that this evolving evidence should be taken into account when considering the use of the vaccine. These reports have also been analysed by the Government's independent advisory body, the 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 4: Number of suspected thrombo-embolic events with concurrent thrombocytopenia ADR reports received for the Oxford University/AstraZeneca vaccine in the UK up to and including 21 April 2021.

Country	Number of reports
England	169
Wales	7
Northern Ireland	5
Scotland	16
Unknown	12

Age range (years)	Number of reports	Number of fatal reports
18 -29	24	6
30-39	28	8
40-49	30	4
50-59	59	12
60-69	31	6
70-79	20	3
80-89	5	2
90-99	1	0
Unknown	11	0

Sex	Number of reports	Number of fatal reports
Male	89	17
Female	120	24

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. 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.

Capillary Leak Syndrome

The MHRA has received 4 reports of capillary leak syndrome (a condition where blood leaks from the small blood vessels into the body) in the context of more than 20 million doses of COVID-19 Vaccine AstraZeneca given. The current evidence does not suggest that capillary leak syndrome is caused by COVID-19 Vaccine AstraZeneca. The MHRA will continue to monitor this issue closely.

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. Fatal cases associated with extremely rare blood clots with lowered platelets are described above.

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.

The MHRA has received 347 UK reports of suspected ADRs to the Pfizer/BioNTech vaccine in which the patient died shortly after vaccination, 685 reports for the Oxford University/AstraZeneca vaccine, 2 for the Moderna vaccine and 13 where the brand of vaccine was unspecified. The majority of these reports were in elderly people or people with underlying illness. Usage of the Oxford University/AstraZeneca vaccine has increased rapidly and as such, so has reporting of fatal events with a temporal association with vaccination however, this does not indicate a link between vaccination and the fatalities reported. Review of individual reports and patterns of reporting does not suggest the vaccine played a role in the death.

A range of other isolated or series of reports of non-fatal, serious suspected ADRs have been reported. These all remain under continual review, including through 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.

4 Conclusion

At the time of this report, over 127,000 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 Pfizer/BioNTech, Oxford University/AstraZeneca and Moderna COVID-19 vaccines have demonstrated very high levels of protection against symptomatic infection. Data is now 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 so far 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.

Cases of an extremely rare specific type of blood clot with low blood platelets is being investigated and updated advice has been provided.

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 Profiles 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 mRNA Pfizer/BioNTech vaccine, COVID-19 Oxford University/AstraZeneca vaccine, COVID-19 Moderna vaccine 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 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 Profile – Pfizer BioNTech

Vaccine Analysis Profile - Oxford University/AstraZeneca

Vaccine Analysis Profile - Moderna

Vaccine Analysis Profile - 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.

Capillary Leak Syndrome (CLS)

Capillary Leak Syndrome (CLS) occurs when blood 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.

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.

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.

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

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.

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.