Norwegian
Medicines Agency

Reported suspected adverse reactions to coronavirus vaccines

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About the report

- A summary is presented below of all assessed reports concerning suspected adverse reactions following coronavirus vaccination from 27 December 2020, the date on which the first vaccine became available.

- The figures are taken from the Norwegian ADR Registry and include reports from healthcare professionals, the general population and Market Authorisation Holders in Norway.

- Only reports which have undergone quality assurance and been assessed in the Norwegian ADR Registry are included in the report. At any one time, there will be reports which are currently being assessed – these reports are not considered further in this summary.

- Reports of serious events are assessed first. The report therefore does not give a true picture of the distribution between serious and non-serious events.

- Symptoms or illnesses that occur after vaccination are reported if there is any *suspicion* of a possible link. As a result, it cannot be assumed that there is a causal relationship between the suspected adverse reaction and the vaccine.

- This report contains all suspected adverse reactions regardless of any possible causal link.

- Additional information from the reporter or new knowledge concerning the vaccine may become available at any time which alters the assessment of the reports.

- The Norwegian Medicines Agency, the European Medicines Agency (EMA), the World Health Organization (WHO) and pharmaceutical companies review the reports of adverse reactions and perform statistical calculations in order to identify unknown adverse reactions (i.e. signal detection). When a signal is identified, a more thorough analysis is carried out to assess whether it could be a new adverse reaction to the drug, or whether any other factors more likely explain the signal. Based on these analyses, it may be appropriate to update the product information with new adverse reactions or introduce measures aimed at minimising the risks.

- Weekly reports are published which summarise the adverse reactions reported following vaccination with the coronavirus vaccines.

Summary

This report is based on reports that are assessed until 15 June 2021. The assessed adverse reaction reports for this week do not provide a basis for revising the current recommendations regarding the use of the vaccines.

Common to all the vaccine types is that most adverse reaction reports following vaccination against COVID-19 concern transient adverse reactions such as headache, fatigue, malaise, fever, nausea and body pain. These usually appear on the first or second day after vaccination and last around 2-3 days. Most people tolerate these transient adverse reactions well, while others experience significant discomfort during the first few days after vaccination. The suspected adverse reactions which have been observed following vaccination are otherwise generally in line with what is described in the product information.

Amongst the reports that have been assessed, there were reported 185 deaths following vaccination. Nine deaths concern persons under the age of 60, but most relate to elderly nursing home residents in need of nursing care. The average age of those concerned is over 83 years. Several of the reporters state that no causal link to vaccination is suspected. The fact that a person dies soon after being vaccinated does not mean that there is a causal relationship. In order to analyse whether there could be a causal relationship, other data sources and advanced analyses are normally required.

In the case of some patients, there is always a possibility that relatively mild adverse reactions following the vaccination of frail elderly people contributed to a deterioration in their underlying illness.

Coronavirus vaccines approved in Norway

Four coronavirus vaccines are approved for use in Norway:

- Comirnaty (BioNTech/Pfizer), mRNA vaccine
- COVID-19 Vaccine Moderna (Moderna), mRNA vaccine
- Vaxzevria (COVID-19 Vaccine AstraZeneca), viral vector vaccine
- COVID-19 Vaccine Janssen (Janssen Cilag International NV), viral vector vaccine

The Norwegian Government is following the recommendation of the Norwegian Institute of Public Health and the Vorland committee and is removing the AstraZeneca vaccine from the Norwegian vaccination programme. The Janssen vaccine is offered outside the Norwegian vaccination programme.

The mRNA vaccines and Vaxzevria (COVID-19 vaccine AstraZeneca) vaccine are given as two doses a few weeks apart, while the Janssen COVID-19 vaccine is given as a single dose.

Statistics concerning reports of suspected adverse reactions as of 15 June 2021

So far, a total of 15,514 reports of suspected adverse reactions following COVID-19 vaccination; of these, 10,787 (70 %) have been assessed.

By 15 June 2021, over 2,006,000 people had received their first dose of COVID-19 vaccine, and over 1,365,000 people had received the second dose.

Distribution of reports by gender

Gender	Female	Male	Unknown gender
Number	8944	1836	7

Table 1: Gender breakdown amongst patients in the reports

Distribution of reports by age

	Age group									
	0-29	**30-39**	**40-49**	**50-59**	**60-69**	**70-79**	**80-89**	**90+**	**Unknown age**	**Total**
Serious reports	169	172	190	194	189	211	196	108	43	1472
Non serious reports	2237	2434	1972	1417	474	222	256	123	180	9315
Total	2406	2606	2162	1610	663	433	452	231	224	10787

Table 2: Age distribution of patients in the reports

Reports classified as serious

Reports of adverse reactions are generally classified as serious when the event:

1. results in or extended a stay in hospital
2. results in a prolonged reduction in function level
3. results in life-threatening illness or death
4. results in birth defects/congenital malformations
5. is on the EMA's list of important medical events (Important medical event (IME) list)

Reports concerning suspected deaths is mentioned below. In addition to the reports concerning suspected deaths, 1287 reports have so far been assessed which fulfil one of the other severity criteria listed above (table 3).

What types of events are classified as "serious" following COVID-19 vaccination?

Hospital admission is the most common reason why an event is classified as serious, and this applies to 49% of serious reports. In these cases, the descriptions provided by the person submitting the report cover everything from patients who are only kept under observation for a short period of time and go on to recover quickly, to patients with a life-threatening symptoms and illness which results in permanent injury.

Most of the serious suspected adverse reactions which have been reported concern medical conditions which are relatively common amongst the population and the timing following vaccination may therefore simply be coincidental.

The EMA has compiled a list of important medical events which are always to be classified as

serious (the IME list). The summary below lists the conditions on the IME list which are most frequently reported following COVID-19 vaccination.

The most frequently reported conditions on the IME list for all vaccines in descending order

- Blood clot in the lungs
- Fainting (syncope)
- Deep vein thrombosis
- Anaphylactic reaction
- Pericarditis
- Blood clots or bleeding in the brain
- Low blood platelet count (thrombocytopenia)
- Pneumonia
- Cerebral infarction
- Arrhythmia

The list shows that numerous serious suspected adverse effects have been reported following COVID-19 vaccination. The challenge is to respond if new combinations of symptoms following vaccination become apparent – or if common medical conditions occur more frequently following vaccination than we would expect. We have a three-pronged approach to identifying these links:

1. **Both health professionals and the government authorities assess individual cases of medical conditions and reports in order to look for unknown combinations of symptoms or to determine whether there are any factors associated with the progression of the conditions which would indicate a link with vaccination.**

   It was a combination of observant doctors at Oslo University Hospital, a robust and fast electronic monitoring system and analyses by the University Hospital of Northern Norway and the Preparedness Register which enabled Norway to help reveal that, in rare cases, Vaxzevria can give rise to a serious combination of symptoms involving blood clotting and low blood platelet counts.

2. **We carry out statistical analyses where we investigate whether the number of reports of a combination of symptoms is higher than expected.**

   Such statistical analyses of reported adverse reactions have shown that serious allergic reactions occur more frequently following COVID-19 vaccination than with vaccination with influenza vaccines. It also forms the basis for the EMA's current investigations aimed at determining whether indications of an increase in the prevalence of immune thrombocytopenia (ITP) are linked to the vaccine.

3. **Health registers are used to assess and investigate further, and to confirm or disprove possible links between vaccination and reported symptoms or diagnoses. This is done in partnership with the Norwegian Institute of Public Health.**

   Further investigation of possible links concerning symptoms reported via the

spontaneous reporting system can be carried out by linking the Norwegian Immunisation Register (SYSVAK) to other health registers, such as the Norwegian Patient Registry (NPR) or the Municipal Patient and User Registry (KPR), to see whether any diagnoses occur more frequently following vaccination than is otherwise the case.

The Norwegian Institute of Public Health and research institutions in many countries are also conducting registry studies to see whether there is any increase in the prevalence of diseases amongst vaccinated people that are not necessarily identified through the adverse reaction reports.

Reports concerning thrombosis with thrombocytopenia syndrome (TTS)

In mid-March, cases were reported of a very rare but serious clinical picture involving a combination of blood clots, low blood platelet count and bleeding, now referred to as thrombosis with thrombocytopenia syndrome (TTS) or vaccine-induced immune thrombotic thrombocytopenia (VITT). These symptoms mainly occurred three to twenty-one days after vaccination with Vaxzevria (COVID-19 Vaccine AstraZeneca). As of 15 June 2021, Norway has reported seven confirmed cases of TTS/VITT after the Vaxzevria vaccine, four of which were fatal. In addition, one further suspected case of TTS has been reported but not confirmed, along with one case which does not meet the diagnostic criteria for TTS according to the Brighton Collaboration. TTS is now listed as a rare adverse reaction in the product information for Vaxzevria and the Janssen COVID-19 vaccine, but more research is needed to clarify what causes this reaction. Vaxzevria and the COVID-19 Vaccine Janssen is not used in the Norwegian vaccination programme, but the COVID-19 Vaccine Janssen is offered outside the Norwegian vaccination programme.

Five reports have also been received concerning both thrombosis and thrombocytopenia after vaccination with an mRNA vaccine. One of these is a patient report which will be assessed further. The remaining four reports have been reviewed and assessed according to the above-mentioned criteria for TTS from the Brighton Collaboration. The clinical picture for these cases differs from that seen after Vaxzevria vaccination; the patients are all close to 70 or older and have one or more underlying conditions and/or take medication that may increase the risk of thrombocytopenia (such as treatment for cancer) or thrombosis.

Vaccination figures per vaccine as of 13 June 2021 – Source: Weekly report NIPH

Vaccine	Comirnaty (Pfizer/BioNTech)		COVID-19 Vaccine Moderna		Vaxzevria (AstraZeneca)	Total
Number of doses administered	1.dose	2. dose	1.dose	2. dose	1.dose	
	1 581 983	1 094 350	239 010	128 254	137 064	
Total number of reports	**3518**		**570**		**6699**	**10 787**
Number of reports involving death	172		7		6	185
Serious reports other than death	735		124		428	1287
Non-serious reports	2611		439		6265	9315

Tablel 3: Distribution of reports of suspected adverse reactions according to severity.
** The fact that a person dies soon after being vaccinated does not necessarily mean that there is a causal relationship. Read more on page 3.*

The data concerning the various coronavirus vaccines are not directly comparable. The vaccines have been administered to a different number of people with different disease profile and ages.

NIPH's weekly report shows the number of people who have been vaccinated with the various vaccines both nationally and per county.

Reports on deaths

So far, 185 reports of deaths after vaccination have been assessed. Most deaths have occurred amongst elderly nursing home residents in need of nursing care, but the Norwegian Medicines Agency has also received nine reports of deaths concerning persons under the age of 60.

Reports concerning deaths in elderly persons

Many of the elderly nursing home residents who have been vaccinated are very frail or terminally ill patients. It is therefore to be expected that deaths will occur with a temporal link to vaccination, without there necessarily being any causal link to the vaccine. The reports on many of these deaths in the elderly state that no link with vaccination is suspected, and that the death is being reported for the sake of completeness.

An expert group of geriatric specialists have looked into the first 100 deaths that were reported after Comirnaty and assessed the causal relationship with vaccination after reported deaths in this patient group.

Reports of deaths of persons under the age of 60

As of 15 June 2021, four deaths have been reported of persons under the age of 60 after vaccination with Vaxzevria due to the very rare but serious adverse reaction, thrombosis with thrombocytopenia syndrome (TTS). TTS is described above.

Five deaths have also been reported of persons under the age of 60 after vaccination, which

are not related to this rare syndrome. The causal relationship with vaccination in these five cases is uncertain.

Reactions which health professionals should be aware of

Other serious events have also been observed following vaccination where no causal relationship has been established. The Norwegian Medicines Agency wishes healthcare professionals to be aware of the following conditions in persons who are vaccinated:

- chest pain and breathing difficulties suspected as being due to blood clots
- numbness
- absence or reduced sensation and paralysis
- persistent headache
- inflammation of the pericardium (pericarditis)

Some of these symptoms were also observed in studies which formed the basis for the temporary authorisation of the vaccines, but insufficient data is currently available to establish any link to the vaccine. A number of the reactions have been included in the list of possible adverse reactions of particular interest which the pharmaceutical authorities in Europe are closely monitoring.

Common adverse reactions to vaccines can aggravate existing medical conditions

In exactly the same way as with infections, common transient reactions to vaccines, such as fever, vomiting and diarrhoea, can trigger symptoms or aggravate existing medical conditions. An overview is presented here of some conditions which patients should pay particular attention to during the first few days after being vaccinated:

Table 4: Overview of conditions that can be aggravated by common reactions to vaccines

Condition	What could happen?	Action
Diabetes (Patients taking insulin)	Elevated blood sugar levels, need for higher insulin dose, ketoacidosis	More frequent monitoring of blood sugar level, insulin dose adjustment. Contact your doctor in the case of persistently high blood sugar levels.
Epilepsy	Greater risk of epileptic seizures in persons with a tendency to suffer fever-triggered seizures	Take fever-reducing medication (paracetamol) upon vaccination.
Addison's disease	Greater need for steroids, triggering of Addisonian crisis	Follow the guidelines for enhanced treatment in the case of fever and illness (higher cortisol dose, drink more fluids, increase salt intake). Tell your doctor if these steps do not have the desired effect, e.g. in the case of lethargy, vomiting and general malaise
Blood-thinning medication (applies to warfarin, (Marevan))	Altered effect of blood-thinning medication, with increased blood thinning (higher INR level).	Additional INR checks for signs of increased blood thinning – bleeding from the gums, nose bleeds and skin bleeds. Temporary dose adjustment may be necessary. Contact your doctor for advice.

Heart failure	Aggravated heart failure symptoms	Paracetamol in the case of fever, monitor fluid balance in the case of vomiting and diarrhoea. Look out for swelling of the legs. See your doctor if your heart failure symptoms worsen.
Arthritis, Bekhterev's disease, etc.	Worsening symptoms of joint pain and joint stiffness	Reduce pain and fever using paracetamol or anti-inflammatory medication. Ask your doctor for advice if the symptoms become severe.
High blood pressure	Increase in blood pressure following vaccination	Patients who monitor their blood pressure themselves can take additional readings. Other patients should be aware of symptoms which could indicate severely elevated blood pressure – headache, wheezing, coughing, blurred vision. In such cases, you should see your doctor to have your blood pressure checked. Some pharmacies also measure blood pressure.

Number of suspected adverse reactions according to category

A single adverse reaction report can include a number of suspected adverse reactions or symptoms. Suspected adverse reactions are presented below, grouped according to the category to which they belong for each vaccine type and the types of suspected adverse reactions which have been reported most frequently. The categories are the highest level in a hierarchical, standardised medical terminology which is used internationally (MedDRA). Using this terminology makes it possible compare reports internationally.

Suspected adverse reactions to mRNA vaccines

- Comirnaty (Pfizer/BioNTech)
- COVID-19 Vaccine Moderna (Moderna)

The most frequently reported symptoms following vaccination with the mRNA vaccines primarily consist of known adverse reactions within the general symptoms category, and include reactions at the vaccine injection site, decreased general condition, fever and general malaise. Headache, dizziness and drowsiness after vaccination are also frequently reported, as well as gastrointestinal symptoms such as diarrhoea, nausea and vomiting. The symptoms have arisen within 1-2 days after vaccination and have generally disappeared within a few days. Some reports have been received where the patient has developed infections such as pneumonia and influenza. As the mRNA vaccines are not live, they cannot cause conditions which are being vaccinated against or other infections.

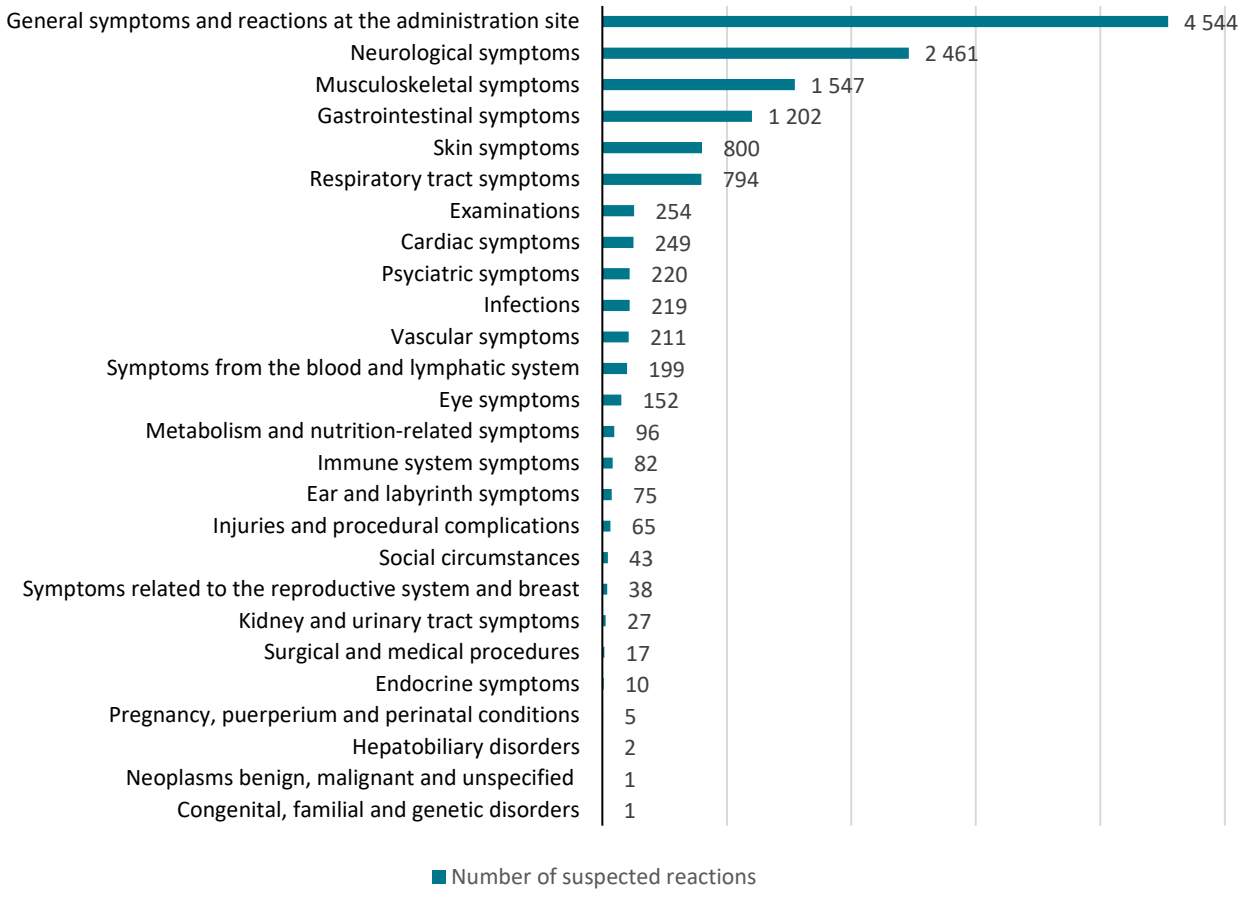

Figure 1: Reported suspected adverse reactions by category for mRNA vaccines (Comirnaty and COVID-19 Vaccine Moderna)

Category	Number of suspected adverse reactions
General symptoms and reactions at the vaccine administration site E.g.: Pain and reactions at the injection site, discomfort, fever, fatigue, decreased general condition	4544
Neurological symptoms E.g.: Headache, dizziness, drowsiness, syncope	2461
Musculoskeletal symptoms E.g.: Muscle pain, joint pain, muscle stiffness, pain in the extremities	1547
Gastrointestinal symptoms E.g.: Stomach pain, nausea, vomiting, diarrhoea	1202
Skin symptoms E.g.: Rash, itching, redness, cold sweats	800
Respiratory tract symptoms E.g.: Difficulty breathing, shortness of breath, cough, irritation of the respiratory	794
Examinations E.g.: Abnormal and raised heart rate, decreased blood pressure, decrease in oxygen saturation	254
Cardiac symptoms E.g.: Bradycardia, tachycardia, pericarditis	249
Psychiatric symptoms E.g.: Sleep abnormalities, restlessness, lethargy, hallucination	220
Infections E.g.: Pneumonia, cold symptoms	219
Vascular symptoms E.g.: Flushes, pallor, low blood pressure	211
Symptoms from the blood and lymphatic system E.g.: Swollen lymph nodes	199
Eye symptoms E.g.: Blurred vision, twitch	152
Metabolic and nutrition-related symptoms E.g.: Reduced appetite	96
Immune system symptoms E.g.: Allergic reaction	82
Ear and labyrinth symptoms E.g.: Discomfort in the ear	75
Injuries and procedural complications E.g.: Fall	65
Social circumstances E.g.: Bedridden	43
Symptoms relating to the reproductive organs and breast E.g.: Breast pain	38
Kidney and urinary tract symptoms E.g.: Urinary tract infection	27
Surgical and medical procedures E.g.: Oxygen therapy, revaccination with other Covid-19 vaccine	17
Endocrine symptoms E.g.: Hypothyroidism	10

Pregnancy, puerperium and perinatal conditions	5
Hepatobiliary disorders	2
Neoplasms benign, malignant and unspecified	1
Congenital, familial and genetic disorders	1

Table 4: Reported suspected adverse reactions by category for mRNA vaccines (Comirnaty and COVID-19 Vaccine Moderna). A report can cover several adverse reactions and there will therefore be many more adverse reactions than reports.

Suspected adverse reactions to viral vector vaccines

- Vaxzevria (COVID-19 Vaccine AstraZeneca)(AstraZeneca)

Viral-vector vaccines are not part of the Norwegian vaccination programme. See separate paragraph on reports concerning thrombosis with thrombocytopenia syndrome (TTS).

Many people have reported significant reactions after the first dose of Vaxzevria, and most reports concern known adverse reactions, such as reactions around the injection site, headache, fever, fatigue and deterioration in general condition.

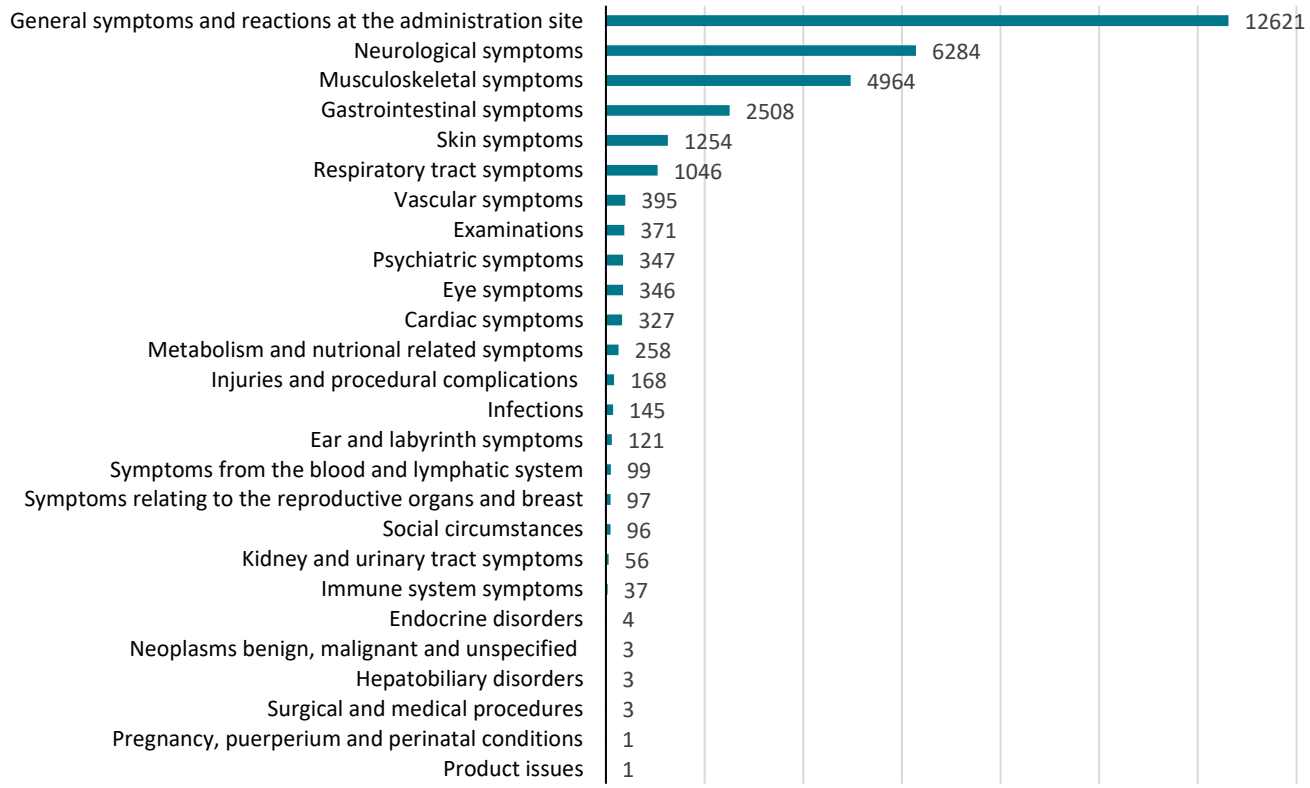

Figure 2: Number of reported suspected adverse reactions by category for viral vector vaccines (COVID-19 Vaccine AstraZeneca)

Category	Number of reported adverse reactions
General symptoms and reactions at the vaccine administration site E.g.: Pain and reactions at the injection site, discomfort, fever, fatigue, decreased general condition	12621
Neurological symptoms E.g.: Headache, dizziness, drowsiness, numbness	6284
Musculoskeletal symptoms E.g.: Muscle pain, joint pain, back pain	4964
Gastrointestinal symptoms E.g.: Stomach pain, nausea, vomiting, diarrhoea	2508
Skin symptoms E.g.: Rash, skin pain, cold sweats	1254
Respiratory tract symptoms E.g.: Difficulty breathing, hyperventilation, nasal congestion, pain and swelling of pharynx	1046
Vascular symptoms E.g. Flushing	395
Examinations E.g.: Abnormal and raised heart rate	371
Psychiatric symptoms E.g.: Sleep abnormalities, insomnia	347
Eye symptoms E.g.: Blurred vision, twitch, eye pain	46
Cardiac symptoms E.g.: Palpitations	327
Metabolic and nutrition-related symptoms E.g.: Reduced appetite	258
Injuries and procedural complications E.g. Contusion	168
Infections E.g. Sinus infection, cold symptoms	145
Ear and labyrinth symptoms E.g.: Discomfort in the ear, sound sensitivity	121
Symptoms from the blood and lymphatic system E.g.: Swollen lymph nodes	99
Symptoms relating to the reproductive organs and breast: E.g. Pain in reproductive organs and nipples	97
Social circumstances E.g.: Bedridden	96
Kidney and urinary tract symptoms E.g.: Frequent urination	56
Immune system symptoms	37

E.g.: anaphylactic reaction, allergic reaction	
Endocrine disorders	4
Neoplasms, benign, malignant and unspecified	3
Hepatobiliary disorders	3
Surgical and medical procedures	3
Pregnancy, puerperium and perinatal conditions	2
Product issues	1

Table 4: Reported suspected adverse reactions by category for viral vector vaccines (COVID-19 Vaccine AstraZeneca). A report can cover several adverse reactions and there will therefore be many more adverse reactions than reports.