

COVID-19 vaccination strategies

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Health Council of the Netherlands



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executive summary

Since the beginning of 2020, the world has been facing a COVID-19 pandemic caused by the novel coronavirus (SARS-CoV-2). The spread of the virus has since resulted in at least 40 million people becoming ill and approximately 1 million people being known to have died of the consequences of COVID-19.

Various vaccines are currently being developed in order to combat the pandemic. The Dutch Ministry of Health, Welfare and Sport asked the Health Council of the Netherlands to provide recommendations about vaccinations against COVID-19. No vaccines are yet available to assess. In anticipation of vaccines becoming available in the future, the Health Council's Permanent Committee on Vaccinations outlines which vaccination strategies could be used as soon as a vaccine becomes available, given that there will not immediately be sufficient vaccines

available to vaccinate everyone in the Netherlands.

High disease burden of COVID-19

COVID-19 is a respiratory tract infection caused by *severe acute respiratory syndrome coronavirus 2* (SARS-CoV-2). Although the disease only causes mild symptoms in some people, it can also lead to hospital admission and death. Evidence has shown that the elderly and people with serious underlying health conditions run a higher risk of becoming seriously ill or dying after an infection.

The Netherlands faces a high burden of disease. Until the beginning of October almost 145,000 confirmed cases and well over 6,400 deaths had been reported and more than 13,000 COVID-19 patients had been admitted to hospital. As not everyone who has or had symptoms is also

tested for the presence of SARS-CoV-2, the actual numbers are higher.

Current lack of effective treatment

Although the symptoms of COVID-19 can be mitigated using various (existing) pharmacotherapies and hospitalisation, there is no way yet to prevent people from becoming ill from the virus. Research into vaccines against COVID-19 is being conducted all over the world. The first vaccines are expected to become available in the spring of 2021. At the European level, the Netherlands has signed contracts for the purchase of six vaccines which are currently being developed.

In addition to vaccination, research is also being carried out into passive immunisation which involves the administration of antibodies.



Considerations for prioritisation

The amount and timing of vaccine availability in the Netherlands is not yet known. Initially, the number of available vaccines will be insufficient to vaccinate the entire adult population. As a result, the government will have to set priorities in terms of who will be offered vaccination first and why.

Prioritising groups for vaccination is a complex issue, because it cannot be based solely on medical and scientific data. In order to justify the choices made with regard to prioritisation, it is important to explain the ethical arguments on which they are based. General ethical principles which provide a guideline for prioritisation are utility and fairness.

- The *principle of utility* implies that the distribution of resources maximises (health) benefits for the population as a whole.
- The *principle of fairness* implies that equal weight is given to equal claims of people to resources.

Potential vaccination strategies

The ethical principles guide potential objectives for group prioritisation for vaccination. On the basis of those objectives the committee has devised the following potential vaccination strategies.

1) *Reducing severe morbidity and mortality as a consequence of COVID-19*

In the case of scarce resources during a pandemic, a common focus of utility is reducing severe morbidity and mortality. The fact that increased risks of severe morbidity and mortality fall on those who are already the most vulnerable, means that preventing deaths can also be defended by the principle of fairness. If this is applied to the distribution of a limited availability of vaccines against COVID-19, this would mean that priority should be given to groups that run the highest risk of becoming seriously ill or dying from COVID-19. These groups consist of people over the age of 60 and people with serious underlying health conditions affecting, for example, the heart or respiratory

system, or people with diabetes mellitus. If the medical risk groups cannot be vaccinated for medical reasons, indirect protection can be aimed for by vaccinating healthcare workers or informal carers who are in direct contact with people in medical risk groups. This would apply, for example, to employees in long-term care institutions, such as nursing homes.

A group that is also eligible for vaccination in this strategy are people who run a greater risk of becoming infected due to their profession or living conditions. This would apply, for example, to healthcare workers who are in direct contact with patients.

2) *Reducing transmission of SARS-CoV-2*

The spread of SARS-CoV-2 negatively affects everyone in society. Negative consequences include direct harm to individuals (varying from mild symptoms to serious illness and death) and indirect social harm in the form of downscaling regular healthcare, unemployment, educational disadvantages or loneliness. A vaccination strategy aimed at reducing transmission of the



virus implies that the ones being vaccinated first are the people who play a major role in spreading the virus in the population. This will provide indirect protection to vulnerable groups and reduce the level of indirect social harm. This strategy is underpinned by a broad interpretation of utility (not just health by itself). In this strategy, groups who contribute the most to spreading the virus are eligible for vaccination. However, more research is needed to determine the effect this strategy can achieve. Moreover, it is not yet clear whether candidate vaccines offer protection against transmission.

3) Preventing societal disruption

Another potential broad interpretation of the principle of utility involves retaining society's vital infrastructure. In this context, a distinction can be made between safeguarding continuity of healthcare and continuity of other vital processes, such as security, education and public administration. The focus on retaining society's vital infrastructure is not based solely on considerations of public health, but involves,

additionally, a broader societal choice. This vaccination strategy would involve prioritisation of people who work in healthcare and in other vital sectors. However, the decision to adopt this strategy in a situation of scarcity should be supported by a realistic threat of societal disruption. A key factor is the epidemiological situation (including absenteeism or mortality in certain sectors) at the moment the vaccine becomes available.

Advice

Which strategy can best be used depends on scientific data on the vaccines which, to this date, are still unavailable. It also depends on the pandemic situation at the time when the vaccines become available. Based on current scientific knowledge and the current number of infections and hospital admissions, the committee recommends opting to reduce severe morbidity and mortality (strategy 1). This strategy implies that, initially, the following groups are eligible for vaccination:

- medically vulnerable groups of people who run an increased risk of severe morbidity and mortality, namely people over the age of 60 and people with serious heart or respiratory conditions, diabetes mellitus, chronic renal insufficiency, immune disorders, or people being treated with immunosuppressants leading to reduced resistance to respiratory infections, people with mental disabilities who live in institutions and residents of nursing homes;
- if these medical risk groups cannot themselves be vaccinated for medical reasons, informal carers and healthcare workers who risk infecting them;
- healthcare workers who are in direct contact with patients.

Due to the limited quantities of vaccine that will be available, it is likely that within the proposed strategy further prioritisation will be necessary. The committee expects that the greatest health benefit can be achieved by starting with people aged over 60 who have serious health conditions,



followed by the oldest members of that group, or the informal carers and healthcare workers who risk infecting them if these groups cannot themselves be vaccinated for medical reasons.

The committee wishes to emphasise that these recommendations are provisional and that it may be necessary to review them once there is more certainty about the effectiveness of the various vaccines among different target groups. Also of importance is the epidemiological setting. In the event of a decrease in infections, greater collective health benefits may be achieved by using the limited number of vaccines to reduce community transmission (strategy 2). It is also possible to opt for a strategy in which the focus is primarily on preventing societal disruption (strategy 3), or on a combination of the different strategies. The committee could imagine that considerations such as continuity of healthcare are also factored in, meaning that societal choices will have to be made in addition to health-related choices.



01 introduction



1.1 Background

Since the beginning of 2020, the world has been facing a COVID-19 pandemic caused by SARS-CoV-2. Although a huge global effort is being made to develop a variety of COVID-19 vaccines, none is available at the moment. The first vaccines are expected to become available in the spring of 2021. Vaccines are essential in order to combat the pandemic effectively, in addition to various behavioural measures and testing policies. At the same time the use of neutralising antibodies (passive immunisation) can play a role in combatting the virus.

1.2 Request for advice

On 4 June 2020 the Minister of Health, Welfare and Sport [Volksgezondheid, Welzijn en Sport] (VWS) asked the Health Council of the Netherlands to advise on passive and active immunisation (vaccination) against SARS-CoV-2. The Minister asked for an indication to be given as soon as possible of what the various vaccination possibilities could be. The request for advice can be found at www.gezondheidsraad.nl.

This advisory report was drawn up by the Permanent Committee on Vaccinations of the Health Council of the Netherlands and assessed by its Standing Committee. The President of the Health Council of the Netherlands submitted the advisory report to the Minister of VWS on 19 November 2020. Information about the members of the committee can be found at the end of this advisory report.

1.3 Methodology

The committee primarily bases its advice on peer reviewed publications in scientific journals. In addition to this, the committee has access to an overview report that the National Institute for Public Health and the Environment [Rijksinstituut voor Volksgezondheid en Milieu] (RIVM) drew up for the committee which lists the most important scientific literature.¹ Up-to-date data about the epidemiology of COVID-19 in the Netherlands has also been obtained from RIVM.

The Health Council of the Netherlands uses a fixed assessment framework (Annex A) to advise on vaccinations. Because no vaccines are available yet, the committee is unable to make any comments on most of the criteria in the assessment framework. Instead it has outlined possible vaccination strategies on the basis of both the assessment framework and ethical principles.

The committee has assessed whether there is a reason to advise differently for the Caribbean Netherlands. Although the epidemiology and the social impact of COVID-19 appears to be different there compared to the situation in the European Netherlands, the content of this advisory report is also applicable to the Caribbean Netherlands.



1.4 Reading guide

In chapter 2 the committee describes the burden of disease as a consequence of COVID-19. A substantial burden of disease is the first criterion which has to be fulfilled before considering vaccination. Chapter 3 provides an overview of the vaccination mechanisms and a description of the vaccines which are being developed. Chapter 4 focuses on the normative considerations which may play a role in determining who is eligible for vaccination first. Chapter 5 outlines the potential strategies for COVID-19 vaccination and in chapter 6 the committee formulates its advice.



02 burden of disease



COVID-19 is a respiratory tract infection which can produce mild symptoms as well as very serious ones, leading to hospital admission and death. The disease is caused by an infection with a novel coronavirus that was first detected in people at the beginning of 2020. An outbreak of the virus in China led to a pandemic and a high burden of disease worldwide. The Netherlands is also experiencing a high disease burden with almost 145,000 confirmed cases and over 6,400 confirmed deaths up until the beginning of October 2020. As not everyone who has or had symptoms is also tested for the presence of SARS-CoV-2, the actual numbers are higher.

2.1 SARS-CoV-2 virus

China first reported a strikingly large number of people with unexplained pneumonia at the end of 2019.² At the beginning of January 2020 it became clear that the cause was a novel coronavirus which had not previously been detected in people.^{2,3} The *severe acute respiratory syndrome coronavirus 2* (SARS-CoV-2) derived from animals (probably bats). Genetically the virus is most closely related to SARS-CoV, another coronavirus which transferred from animals to humans at the beginning of this century and was responsible for *severe acute respiratory syndrome* (SARS).²

SARS-CoV-2 is primarily spread by droplets with a diameter of more than 5 micrometres (μm) which are expelled from the airways of infected people. Infected droplets are emitted by talking, coughing or sneezing and can

infect people standing close by.^{4,6} This is referred to as droplet infection. The virus can also spread via small droplets of less than 5 μm and via droplet nuclei in the air (aerogenic transmission).^{5,7} Infection is also possible if (sufficient) infected droplets from infected surfaces or objects reach a person's mucous membranes in their nose, mouth or eyes via their hands. At the moment it is unclear whether transmission is also possible via faeces and there is also uncertainty about how infectious the virus is. This is because it is not yet entirely clear when, to what extent and in which circumstances infected people can transmit the virus. However, we do know that people are infectious in both the symptomatic phase and the pre-symptomatic phase.^{6,7} In addition to this it is not yet exactly clear how long the virus can survive outside the body. Estimates of the basic reproduction number (R_0) vary between 2 and 4,⁸⁻¹⁰ which means that someone who is infected in a fully receptive population will infect, on average, between two and four other people.

2.2 Clinical presentation of COVID-19

An infection with SARS-CoV-2 can lead to the disease COVID-19.

An infection does not lead directly to symptoms because the average incubation time is approximately six days, but varies between two and fourteen days.^{4,11} At the end of this period, various symptoms can occur, such as cold-like symptoms, coughing, fever, fatigue, dizziness, shortness of breath, nausea, stomach ache, aching muscles, headache and loss of sense of smell and/or taste.^{4,12} These symptoms, the extent to which they



occur and their severity differ per population studied. In the majority of cases there is a mild infection and the patient recovers after a couple of days or weeks, although long-term symptoms such as fatigue also occur. However, an infected person may also be asymptomatic, or may indeed become very seriously ill, necessitating hospital admission. The latter is the case when the virus reaches the lower respiratory tract and affects the alveoli, which then leads to (double) pneumonia. However, the clinical presentation can also suddenly deteriorate due to reproduction of the virus and hyperreactivity of the person's immune system, leading to further lung damage. This can result in acute respiratory distress syndrome, as a result of which patients experience even lower levels of oxygen and have to be provided invasive ventilation in an intensive care unit (ICU). In addition to respiratory symptoms, the infection can also lead to (serious) cardiac problems, such as inflammation of the heart, and neurological issues including encephalitis. The clinical presentation may also worsen due to coagulation-related problems, such as a pulmonary embolism, myocardial or cerebral infarction, septic shock and multi-organ failure, which can all be fatal.^{13,14} Once recovered from COVID-19 patients may still experience pulmonary, cardiac or neurological problems. These can also occur in patients who have experienced mild infection. A great deal is still unknown about the severity and duration of these symptoms in the long term. ICU patients may experience post-intensive care syndrome – a range of physical, psychological and cognitive impairments which can persist for years.¹⁵

2.3 Morbidity and mortality due to COVID-19

SARS-CoV-2 was first detected in inhabitants of the Chinese city of Wuhan at the beginning of 2020. After that the virus quickly spread across the globe, leading to a huge increase in the number of infections. On 11 March 2020 the World Health Organization (WHO) declared the outbreak of SARS-CoV-2 a pandemic.¹⁶

2.3.1 Netherlands

The first COVID-19 patient in the Netherlands was reported on 27 February 2020. It now appears that the virus must have been introduced to the Netherlands earlier than that. Patients who were diagnosed later as having COVID-19 reported that they had been experiencing COVID-related symptoms since the end of January or the beginning of February.¹⁷ Since then the virus has quickly spread, initially and primarily among residents in the south of the Netherlands. The transmission was probably accelerated by people celebrating Carnival (22-25 February) and the spring holiday (22 February – 1 March) when many people went on skiing holidays in areas where the virus was prevalent and consequently introduced the virus to the Netherlands. At the beginning of March the number of confirmed cases increased rapidly. On 10 March there were more than 500 confirmed cases and three days later there were more than 1,100. A peak in the number of confirmed cases was reached in the period between 24 March and 23 April. Every day there were, on average, approximately 1,000 new confirmed patients and, on average,



140 confirmed patients died (see figure 1). The incidence of confirmed cases during those weeks (24 March – 23 April) exceeded 40 per 100,000 people per week. After that the numbers declined, probably as a consequence of the measures taken by the government to minimise further transmission of the virus (see Coronavirus measures box). The incidence declined in the subsequent months to fewer than 10 confirmed cases per 100,000 people per week. However, since the end of July there has been a clear increase to almost 150 cases per 100,000 in the first week of October. In total there had been 144,999 confirmed cases and 6,482 confirmed deaths in the Netherlands by 10.00 a.m. on 6 October 2020. Because not everyone with symptoms was also tested for the disease (see Actual numbers box), the actual numbers are higher. Up until the beginning of October it is estimated that 1.1 million people had been infected (based on serological research) and according to calculations by Statistics Netherlands [Centraal Bureau voor de Statistiek] (CBS) it is possible that more than 10,000 people died from COVID-19 in the period from March to June 2020 (based on cause of death certificates).¹⁸

All the numbers referred to in this paragraph concern notifications to the Municipal Health Services [Gemeentelijke gezondheidsdienst] (GGD) and represent the state of affairs at 10.00 a.m. on 6 October 2020, unless stated otherwise.



Up to and including 6 October 2020, there had been approximately 145,000 confirmed cases of COVID-19 in the Netherlands, with a strong increase since the beginning of September

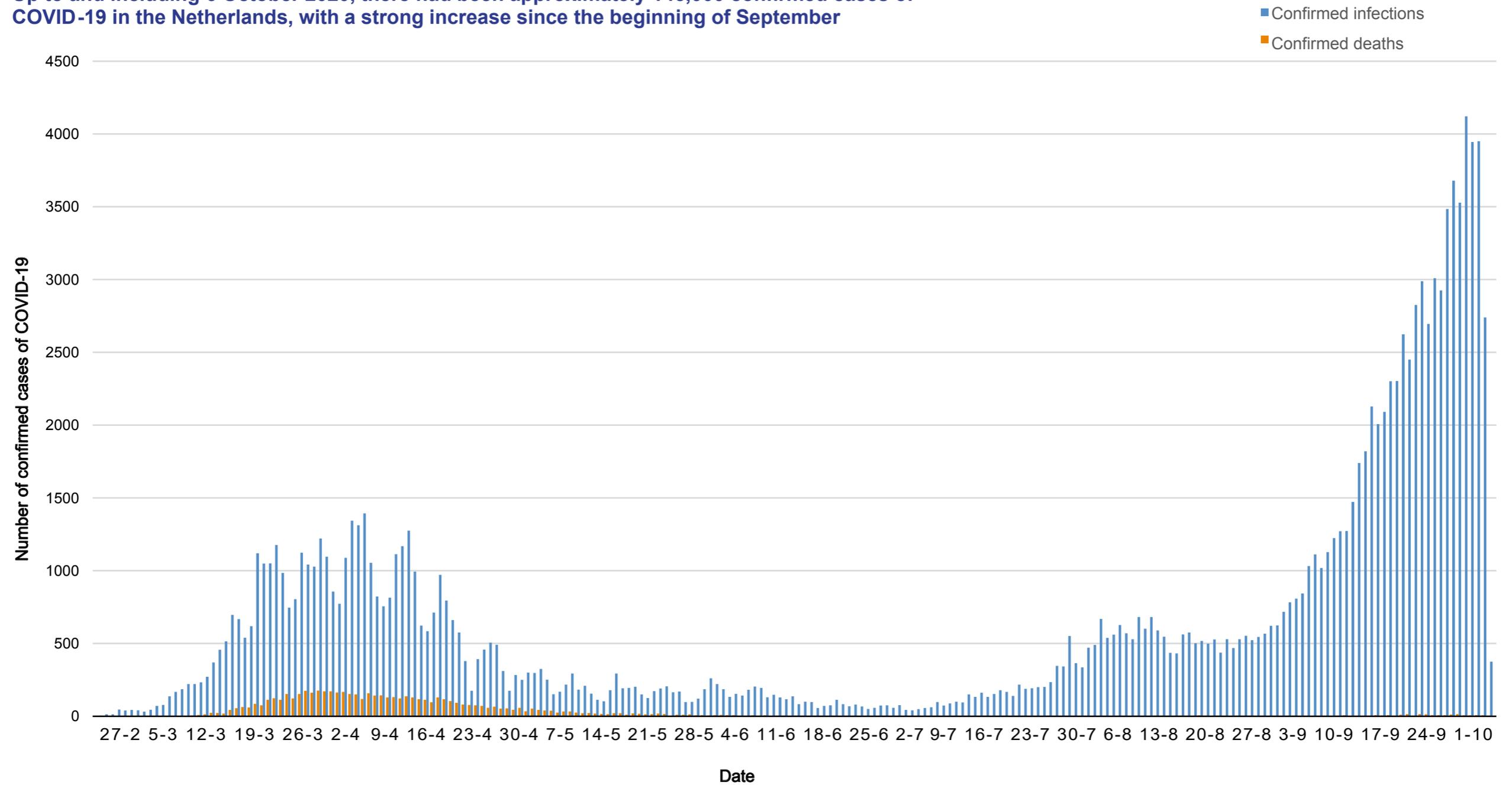


Figure 1: Number of confirmed cases and deaths on date



The numbers shown are an underestimation of the actual numbers, see Actual numbers box. The testing policy was amended as from 1 June 2020 and since then everyone with symptoms may be tested. The numbers regarding notifications to the GGD up until 10.00 a.m. on 6 October 2020.

COVID-19 occurs in all age categories. In the months from February up to and including May 2020 half of all confirmed cases were in people aged 59 or over. Since June the average age of confirmed cases has decreased to 35 years old and this can partially be explained by increased testing (see Actual numbers box). In the period before 1 June the incidence of confirmed cases was highest in the 85-89, 90-94 and 95+ age groups, with incidence figures of 1,532, 2,321 and 2,924 per 100,000 people respectively. In the period between June and the beginning of October the majority of confirmed cases were in the 20-29 age group (27,110), with an incidence of 1,214 per 100,000 people. In the period before 1 June the majority of confirmed cases were in the provinces of Noord-Brabant, Zuid-Holland and Noord-Holland. A total of 9,136 and 9,999 and 6,683 diagnoses were made and the incidence was 357, 270 and 232 per 100,000 people respectively. From June until the beginning of October the majority of confirmed cases came from the provinces of Noord-Holland and Zuid-Holland with 23,127 and 34,000 cases respectively and an incidence of 917 per 100,000 people in Zuid-Holland and 803 per 100,000 people in Noord-Holland. A large number of infections were in nursing homes. A total of well over 12,000 confirmed cases were reported in more

than 1,300 nursing homes (data up to and including 26 October 2020). The actual figures are higher because far from all residents were tested for SARS-CoV-2.

Up until 6 October 2020 a total of well over 13,000 COVID-19 patients had been admitted to hospital. In general patients were admitted to hospital between five and eight days after the first symptoms and were treated on nursing wards for seven to eight days. More than a quarter of these patients (n=3,594) were 70-79 years old. Half of all patients admitted to hospital were aged 68 or over. More than 3,400 patients were admitted to the IC.¹⁹ Of these more than 70% were men, more than 75% were overweight and approximately 35% had one or more existing conditions, such as a type of cancer.

A total of 6,482 people are known to have died from COVID-19. Of all confirmed deaths, approximately 60% were 80 or older, approximately 25% were 70-80 years old, approximately 10% were 60-70 years old and approximately 5% were under the age of 60. Patients who were younger than 70 and who were confirmed as having died from COVID-19 had, in many cases (approximately 70%) a previously diagnosed condition. In most cases these were cardiovascular conditions, chronic lung conditions, or diabetes mellitus. More than 3,400 confirmed deaths were residents of nursing homes (data up to and including 26 October 2020). Because not everyone who died was tested for SARS-CoV-2, the data on mortality



represent an underreporting (see Actual numbers box). In the period between the beginning of March and mid-May (the first nine weeks of the epidemic in the Netherlands) the CBS reported 32% excess mortality.²⁰ In that period of the year almost 9,000 more people died than would be expected and probably most of those deaths are attributable to COVID-19. At the beginning of October the CBS reported that, from March up to and including June, 7,797 people who died had been diagnosed as having

COVID-19 by the attending physician or pathologist.¹⁸ In 2,270 people who died the attending physician or the pathologist indicated that the cause of death was presumed to be COVID-19, which brings the total mortality rate in those four months to 10,067. Initial calculations show that the mortality rate of COVID-19 (*the infection fatality rate*) is approximately 1% (L. of Asten, personal notification).

Actual numbers

The number of COVID-19 cases and deaths is actually higher than reported. This is because not everyone who had COVID-19, or who died as a result of having it, was diagnosed as having the disease. This is due to the fact that not everyone with an infection is tested, for example because there are no, or almost no symptoms. There is also the possibility of false negative test results, or testing not being carried out properly. In addition, testing policy has a significant impact on the reported numbers. In the Netherlands the testing policy initially focused on people arriving in the country from areas where SARS-CoV-2 was prevalent and patients and healthcare workers with apparent COVID-19 symptoms in hospitals. Step-by-step the testing policy was expanded to include patients and healthcare workers outside hospitals and to other groups of professionals. Since 1 June it has been possible for anyone who has symptoms to be tested. Because tests are carried out in hospitals (repeatedly) in order to verify the diagnosis, the data regarding the number of hospital admissions and admissions to intensive care as a consequence of COVID-19 do paint an accurate picture.

It is possible to estimate the actual number of cases on the basis of data on hospital admissions, the number of positive test results and the seroprevalence (the presence of antibodies in the blood). Consequently, the total number of actual infections in the Netherlands up until the first week of September is estimated at approximately 1.1 million (95% confidence interval: 0.9 million - 1.38 million). The cause of death certificates which Statistics Netherlands collects and processes are used to determine what the established and presumed COVID-19 mortality has been. The (presumed) cause of death is determined by the attending physician or pathologist. The CBS reported that, in the period from March up to and including June, a total of 7,797 people died from COVID-19.¹⁸ A further 2,270 deaths are presumed to have been attributable to COVID-19. This brings the total number of deaths due to COVID-19 in these four months to 10,067.



Coronavirus measures

Throughout the outbreak of SARS-CoV-2 the government has taken various measures to minimise further transmission of the virus. On 9 March 2020 the government advised people to no longer shake hands, to sneeze and cough into their elbows and to use paper tissues. People in the province of Noord-Brabant were advised to stay at home as much as possible. As from 10 March all events attended by more than 1,000 people were prohibited. Two days later people were asked to stay at home as much as possible, to work from home and by no means leave home if they were experiencing symptoms such as nasal congestion, coughing and fever. Gatherings of more than 100 people were prohibited, which resulted in the closing of public locations such as sports clubs, museums and theatres. Three days later, on 15 March, a decision was taken to close all hospitality venues (including bars and restaurants), childcare centres, primary schools and secondary schools. On 23 March the government announced more stringent measures and the 'one and a half metre society' was introduced.

Close contact services (for example hairdressers) were closed, and it was not allowed to be in a public space in groups of more than two people. People were submitted to physical distancing measures, meaning they could be fined if they did not maintain 1.5 metres distance from each other in public spaces. Households were allowed to receive a maximum of three visitors a day, provided they observed the 1.5 metres distance rule. When the number of hospital admissions declined a number of weeks later, the government decided to relax the measures. Schools, restaurants, gyms and cultural institutions were opened again and travel was also possible. Because the number of confirmed infections increased significantly after the summer, the government decided on 13 October 2020 to close all hospitality venues for a period of at least four weeks, as well as to ban any late-night shopping and team sports for adults. The wearing of face masks was made mandatory in public transport and people were strongly advised to wear face masks in public indoor spaces and secondary schools.

2.3.2 International

Following the outbreak in China at the end of 2019 the virus was detected in mid-January in Thailand, Japan and South Korea and even before 1 February 2020 in Europe, Australia, the United States (US) and Canada. In the meantime the number of confirmed cases worldwide had increased to more than 37 million and the number of confirmed deaths to approximately 1 million (data up until 11 October 2020).²¹ The actual figures will be much higher because only a limited proportion of people worldwide has been tested for SARS-CoV-2, and many death have not been confirmed as COVID-19-related. The worst affected country is the

US with more than 7.5 million confirmed cases and approximately 212,000 confirmed deaths.²¹ The cumulative incidence of the number of confirmed cases there exceeds 22,000 per million residents (see figure 2, data from 6 October 2020).²² Spain, Belgium and France have the highest incidence figures in Europe. The mortality rate is highest in Belgium, with more than 800 deaths per million residents (see figure 3, data from 6 October 2020).²² Once again the actual figures are higher than reported. What is more, the various differences in testing policies and reporting methods between countries need to be taken into account when interpreting the data.



The US has the highest number of confirmed cases of COVID-19 per million residents

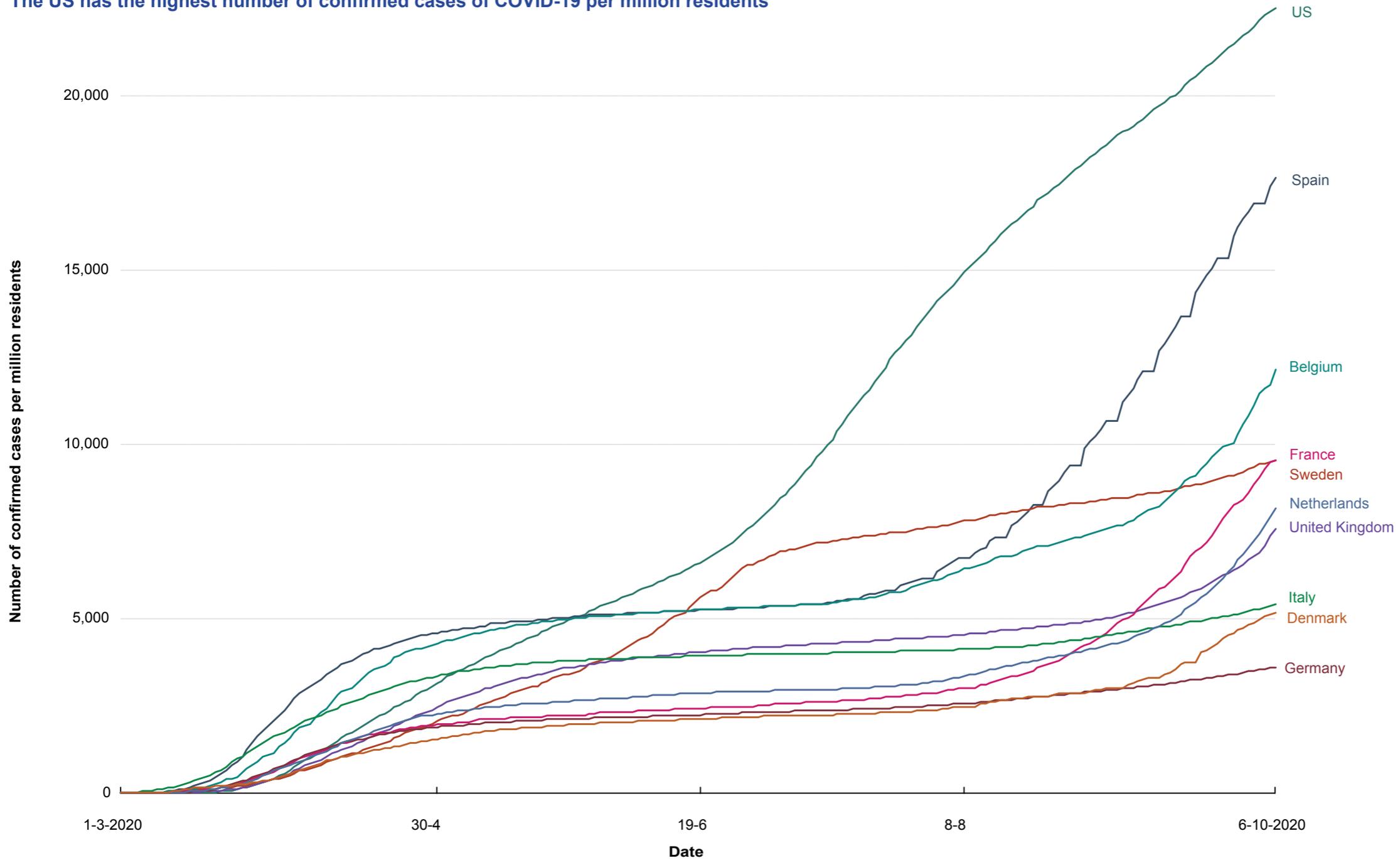


Figure 2. Confirmed cases per million residents in the Netherlands, Germany, France, Belgium, the United Kingdom, Spain, Italy, Sweden, Denmark, the US; cumulative figures from 6 October 2020. (Data taken from *Our World In Data*.²²)



Belgium has the highest number of confirmed deaths per million residents

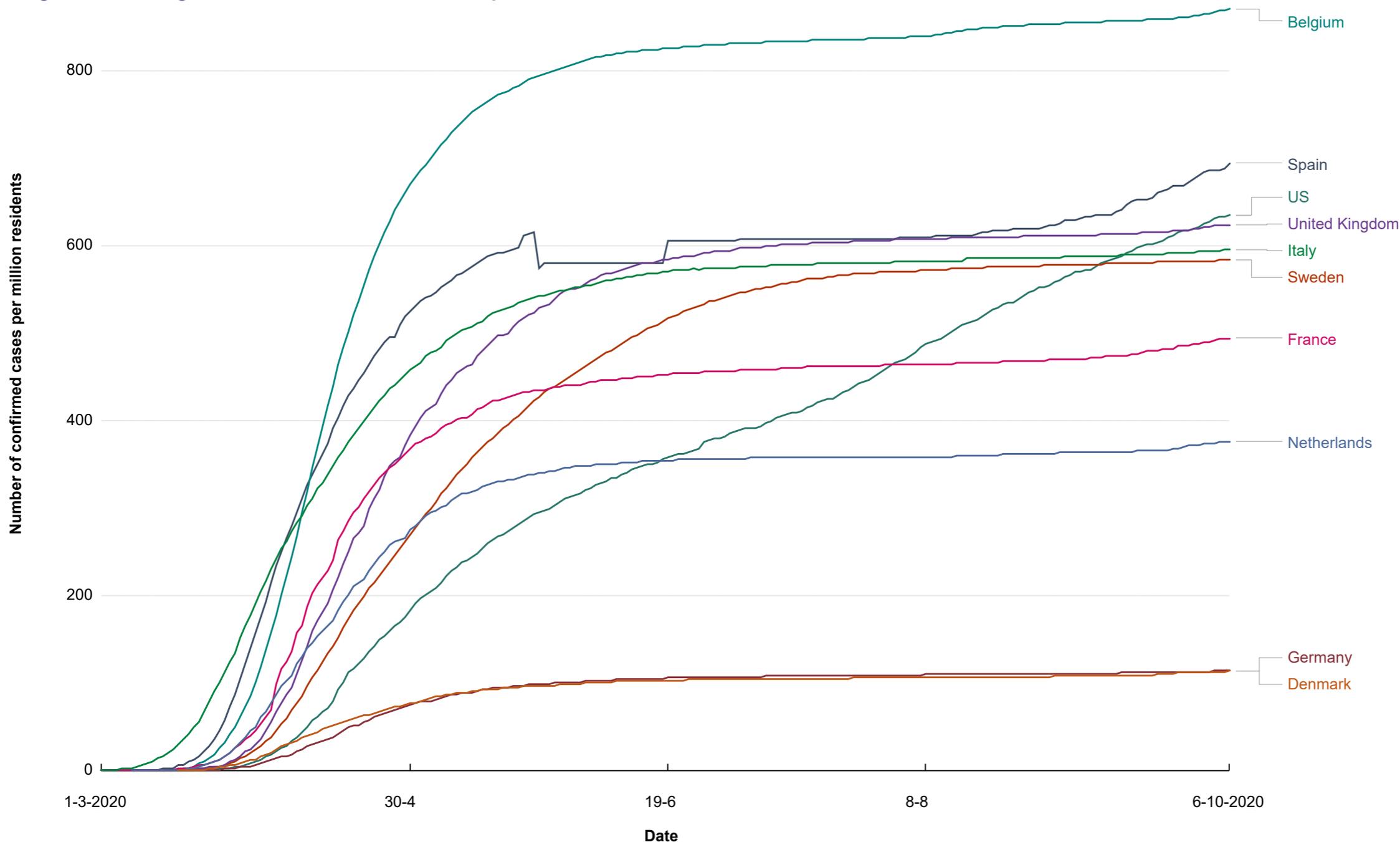


Figure 3. Confirmed cases per million residents in the Netherlands, Germany, France, Belgium, the United Kingdom, Spain, Italy, Sweden, Denmark, the US; cumulative figures from 6 October 2020. (Data taken from *Our World In Data*.²²)



03 immunisation and vaccination against COVID-19



At the European level, the Netherlands has signed contracts for the purchase of six vaccines which are currently being developed. It is not yet known when and in which quantities the contractually agreed doses will become available. Neither is there any clarity about the vaccines' efficacy and safety as this is still under investigation. The expectation is that all six vaccines will provide sufficient protection against developing COVID-19. According to the committee, passive immunisation whereby, in contrast to vaccination, a person's immune system is not activated, is not suitable for use in the general public. However, there might be a potential role in specific groups or in specific circumstances.

3.1 Passive immunisation

Vaccination involves active immunisation, meaning that the immune system is activated. This is not the case with passive immunisation. Passive immunisation consists of the administration of antibodies aimed against, in this case, SARS-CoV-2. Because the administered antibodies disintegrate in time, passive immunisation only has a temporary effect. If permanent protection is required, passive immunisation has to be regularly repeated.

Passive immunisation can be used to treat COVID-19 patients, as well as people without symptoms as prophylaxis to provide temporary protection against SARS-CoV-2. The necessary antibodies can be obtained in two ways, from the blood plasma of recovered COVID-19-patients (the

so-called convalescent plasma), or by production in a laboratory (monoclonal antibodies).

Research is currently being conducted into the use of convalescent plasma to treat COVID-19 patients and into the use of monoclonal antibodies as prophylaxis and as treatment.

3.1.1 Convalescent plasma

In two studies involving 5 and 10 seriously ill patients with COVID-19 respectively, clinical status improved after they had received convalescent plasma with neutralising SARS-CoV-2 antibodies.^{23,24} Due to the limited number of patients and the research design, no causal link could be demonstrated. It is also still unclear what the optimal dosage, timing and duration of this passive immunisation treatment ought to be and whether the severity of COVID-19 in the 'donor patient' influences the treatment effect in the recipient.²⁵ A randomised controlled trial (RCT) involving 103 patients with severe or life-threatening COVID-19 did not reveal any difference in mortality or time to clinical improvement between patients who received convalescent plasma and patients who received standard treatment.²⁶ One problem with this study was that, due to a reduction in the number of cases, it was terminated before the originally intended number of 200 patients had been reached. This may be the reason why the study had insufficient power to detect clinically relevant results.^{26,27}



In the Netherlands an RCT was carried out into the treatment effect of convalescent plasma on COVID-19 patients who had been admitted to hospital.²⁸ The trial was terminated prematurely because 79% (44/56) of the tested patients had started producing neutralising antibodies with an average titre that was comparable to those of the 115 plasma donors. The administration of plasma had no effect on mortality and duration of hospital admission. These results, among others, are now being used as a basis for a study (the CoV-Early study) to establish whether the administration of convalescent plasma to COVID-19 patients may be of use at an earlier stage in the disease process. In this RCT convalescent plasma is administered to early stage COVID-19 patients who have not yet been admitted to hospital and who have an increased chance of severe disease.²⁹

The research into the effect of treating COVID-19 patients with convalescent plasma is being carried out in various ways and with variable patient populations. In order to draw conclusions from this diverse data at the earliest opportunity, Cochrane has started a so-called *living systematic review*. The first publication on the subject included 20 studies.³⁰ Based on their analysis, the authors conclude that it is very uncertain whether convalescent plasma has a favourable effect in patients who are admitted to hospital because of COVID-19. In addition, according to the authors, the evidence for the treatment's safety only provides a low level of certainty. Incidentally, an analysis from the US, which was based on the

data of treatment with convalescent plasma involving 20,000 COVID-19 patients who had been admitted to hospital, revealed no indications of detrimental effects.³¹

3.1.2 Monoclonal antibodies

In contrast to convalescent plasma that contains a mixture of antibodies with different specificity, monoclonal antibodies are aimed at specific pathogens, in this case SARS-CoV-2.

Compared to the research into the effects of convalescent plasma, the number of trials with monoclonal antibodies is much smaller. Several trials focus on the use of monoclonal antibodies as prophylaxis or post-exposure prophylaxis - a special type of prophylaxis whereby antibodies are administered after (potential) exposure but before the (possible) symptoms develop. LY-CoV555 is a monoclonal antibody developed by the companies Lilly and AbCellera. A scheduled interim analysis of a phase II trial involving patients with mild to moderate COVID-19 revealed that administration of LY-CoV555 in a dosage of 2,800 mg to some of the patients resulted in a faster reduction of the viral RNA than in patients who received a placebo.³² This effect was not visible in patients who received a lower (700 mg) or higher (7,000 mg) dosage of LY-CoV555. A phase III trial involving 2,400 residents and staff of nursing homes where COVID-19 had recently been detected studied the effect of administering a single



dosage of LY-CoV555 on the occurrence of infection by SARS-CoV-2 after four weeks and on COVID-19 complications after eight weeks.³³

REGN-COV2 is a combination of two monoclonal antibodies developed by the company Regeneron. In a press release which was published at the end of October 2020 the manufacturer states that the administration of REGN-COV2 to early stage COVID-19 patients who had not yet been admitted to hospital resulted, in a combined phase II/III trial, in a faster reduction in the viral RNA than in the case of patients who received a placebo and in a 57% decrease in medical care related to COVID-19 compared to the placebo. In the case of the patients with medical risk factors this decrease was even greater (72%).³⁴ The preventive effect of administering REGN-COV2 is being studied in non-infected people who are, or have been, in close contact with a COVID-19 patient (for example housemates).³⁵ The aim is to determine the effect of administering REGN-COV2 on the occurrence of infection by SARS-CoV-2.

VIR-7831, developed by the companies Vir Biotechnology and GlaxoSmithKline, is being tested in a phase III trial involving 1,300 COVID-19 patients who have a high risk of being admitted to hospital as a consequence of COVID-19. The aim is to establish whether treatment with VIR-7831 has an effect on hospital admission or mortality within 29 days after randomisation. VIR-7831 was adapted using laboratory techniques in

such a way that it extended the half-life (a criterion for the duration of the disintegration of antibodies).³⁶

3.1.3 Possible use of passive immunisation

Even if future results are favourable, the committee generally believes that the disadvantage of passive immunisation, compared to active immunisation, is that it has to be repeated at fairly short intervals in order to have a lasting effect (VIR-7831 may be an exception). This makes passive immunisation unsuitable for use in the general population. However, the committee can imagine a situation in which passive immunisation is used for specific groups of people, or in specific circumstances. One example would be passive immunisation as prophylaxis for patients with a compromised immune system, or for patients in nursing homes where COVID-19 has been detected.

3.2 Vaccination

Vaccination, also referred to as active immunisation, involves activating the immune system. This can provide protection against:

- becoming infected with the virus;
- becoming ill as a consequence of infection;
- excretion of the virus during and after infection (and therefore against further transmission of the virus).



For individual protection it is important that vaccination results in a reduced risk of infection or, if infection occurs after all, in a reduction in the severity of disease. For indirect protection, it is important that vaccination results in a reduced risk of infection, and in a reduction of the excretion of the virus.

3.2.1 Vaccines against SARS-CoV-2

Various types of vaccines are being developed, namely vaccines based on SARS-CoV-2 proteins, such as inactivated vaccines and subunit vaccines, and vaccines based on genetic material from the virus - such as vector-based vaccines and DNA/RNA vaccines.

Due to the limited experience with COVID-19 vaccines to this date, only general statements can be made about how the general characteristics of vaccination play out in the different types of vaccines against SARS-CoV-2. This advisory report only discusses the way in which vaccines may or may not be able to produce and activate various types of cells of the immune system which are specifically targeted against SARS-CoV-2, namely B-cells, CD4+ T-cells and CD8+ T-cells. Other aspects of vaccines which strengthen the immune response, for example adjuvants, are not considered here. Something of a different order, but still important, is that it has, up to now, appeared to be challenging to induce immunological memory against coronaviruses following a natural infection.^{37,38}

Neutralising antibodies against the so-called spike protein of SARS-CoV-2 are important for protection against infection in that they prevent the virus from becoming attached to the receptor. This implies that vaccination should not only lead to the production of specific B-cells, but also – in connection with the role during the maturation of those B-cells – to the production of specific CD4+ T-cells. In principle the various candidate vaccines which are now available ought to meet this condition. A study into infectiousness of patients with COVID-19 established that it was more difficult to grow the virus if a situation of increasing levels of neutralising antibodies in the blood.³⁹ This suggests that vaccines which are aimed at the development of neutralising antibodies may also have an effect on infectiousness.

In addition to neutralising antibodies, vaccines can differ in terms of other immunological effects, such as the induction of specific CD8+ T-cells. In order to obtain those cells it is necessary for the vaccine to contain genetic information for virus proteins. That genetic information is absorbed into the cell and translated into the protein in question which is then presented as an endogenous peptide. The production of CD8+ T-cells is possible after vaccination with vector-based vaccines and DNA/RNA vaccines. Vaccines based on proteins of SARS-CoV-2, such as inactivated vaccines and subunit vaccines, do not lead to the production of CD8+ T-cells. It is unclear what effect the various components of the



immune response have on reducing virus excretion. Data from trials and additional studies might provide insight in this topic.

3.3 State of affairs with regard to the development of vaccines against SARS-CoV-2

According to the WHO, 212 vaccines are currently being developed, of which 164 are in the preclinical phase, while clinical trials are being carried out with 48 vaccines (data from 12 November 2020).⁴⁰ Up to now the Netherlands has made verbal agreements at the European level regarding six candidate vaccines (see Table 1). Contracts have been concluded with four manufacturers, namely AstraZeneca, Janssen Pharmaceutica, Sanofi Pasteur/GSK and BioNTech/Pfizer. Negotiations on a contract for a seventh candidate vaccine (Novavax) are ongoing.

3.3.1 University of Oxford/AstraZeneca

The vaccine being developed by the University of Oxford/AstraZeneca is a recombinant vector vaccine, which means that it uses a carrier virus to which genetic material from SARS-CoV-2 is added. The carrier virus is an adenovirus that occurs in chimpanzees but not people.^{41,42} The genetic material contains the code for the spike protein of SARS-CoV-2.⁴¹ Vaccination consists of two doses which have to be administered at least four weeks apart.⁴³

The vaccine was demonstrated as having a protective effect in an animal study. After vaccination the animals became less sick than unvaccinated animals and less virus was found in their airways.⁴¹ In a phase I-II trial it was demonstrated, in approximately 1,000 people with an average age of 35, that the vaccine led to the production of antibodies and T-cell responses.⁴² Vaccination resulted in mild side-effects, with more than 60% of the participants experiencing fatigue, headache, malaise and pain and sensitivity at the site of the injection. In the United Kingdom, Brazil and South Africa phase II-III trials have started enrolling at least 10,000 people, including older people (aged over 55). In the US a phase III trial is currently taking place in which approximately 30,000 adults are enrolled, of which 25% are older than 65.⁴³ The first interim results regarding efficacy and safety are expected at the end of 2020.

The European Union has entered into a contract for 300 million doses, with an option for a further 100 million doses. The Netherlands is entitled to purchase approximately 3.9% of this total (approximately 11.7 and 3.9 million doses respectively). The vaccine may become available in the spring of 2021. It is not yet certain how many doses will be available for the Netherlands, nor exactly when.



3.3.2 Janssen Pharmaceutica

Just like the vaccine being developed by the University of Oxford/AstraZeneca, the Janssen Pharmaceutica vaccine is a recombinant vector vaccine. In this case the carrier virus is an adenovirus that causes colds in people.⁴⁴ The genetic material contains the code for the spike protein of SARS-CoV-2.⁴⁴ The vaccine has to be administered once or twice.

Two animal studies showed that the vaccine has a protective effect.^{44,45} Vaccination led to the production of antibodies and the animals showed less symptoms after exposure to SARS-CoV-2. No virus was found in their lungs after vaccination. Interim analyses of a phase I-II trial in people aged between 18 and 55 and people aged over 65 revealed that vaccination led to the development of antibodies and T-cell responses.⁴⁶ In the majority of participants the vaccine caused mild side-effects, with pain at the site of the injection, fatigue, headache and muscle ache being those most commonly referred to. Phase II trials are still going on in the Netherlands, Germany and Spain involving approximately 550 healthy adults.⁴⁷ In the US a phase III trial has now started which plans to enroll approximately 60,000 people aged 18 and older, some of whom have underlying health conditions (approximately 30% are aged 60 and older with approximately 20% aged between 18 and 40).⁴⁸ The first interim results regarding efficacy and safety are expected at the end of 2020, or at the beginning of 2021.

The European Union has entered into a contract for 200 million doses, with an option for a further 200 million doses. The Netherlands is entitled to purchase approximately 3.9% of this total (approximately 7.8 million doses at a time). The vaccine may become available in the spring of 2021. It is not yet certain how many doses will be available for the Netherlands, nor exactly when.

3.3.3 Sanofi Pasteur/GSK

The Sanofi Pasteur/GSK vaccine is a subunit vaccine. This means that the vaccine contains virus proteins of, in this case, the spike protein of SARS-CoV-2. Subunit vaccines lead to the production of antibodies and the induction of CD4+ T-cells, but not to the production of CD8+ T-cells. Adjuvants are added to this vaccine. Adjuvants are often added to subunit vaccines in order to strengthen the immune response. Vaccination consists of 2 doses.⁴⁰

The results of preclinical studies and clinical trials in phases I-II have not yet been published. A phase III trial is expected to start at the end of 2020.

The European Union has entered into a contract for 300 million doses. The Netherlands is entitled to purchase approximately 3.9% of this total (approximately 11.7 million doses). The vaccine may become available in the summer of 2021. It is not yet certain how many doses will be available for the Netherlands, nor exactly when.



3.3.4 Moderna

The Moderna vaccine is an mRNA vaccine, which means that it contains genetic material (*messenger RNA*) of SARS-CoV-2. The genetic material contains the code for the viral spike protein.⁴⁹ The vaccination consists of 2 doses.⁵⁰

Animal studies showed that the vaccine had a protective effect.^{49,51}

Vaccination leads to the production of antibodies and CD4+ T-cell responses, but not to CD8+ T-cell responses. After vaccination the animals demonstrated less symptoms and no virus was detected in their noses. A phase I trial involving 45 people with an average age of 33 and 40 people with an average age of 69 showed that vaccination led to the production of antibodies and CD4+ T-cell responses, while there was almost no CD8+ T-cell response.^{50,52} Vaccination produced mainly mild local and systemic side-effects. In both groups more than 60% of the participants reported pain at the site of the injection, headache, muscle ache and fatigue. Phase II trials and phase III trials have now started in the US. Approximately 30,000 people are planned to be recruited into the phase III trial, of which 25 to 40% will be older than 65, or younger than 65 but with an increased risk of COVID-19 complications.⁵³ A company press release of 16 November 2020 stated that the vaccine demonstrated 94.5% efficacy.⁵⁴ At this moment no primary data is available.

The European Union has entered into a contract for 80 million doses, with an option for a further 80 million doses. The Netherlands is entitled to purchase approximately 3.9% of this total (approximately 3.1 million doses at a time). The vaccine may become available in the spring of 2021. It is not yet certain how many doses will be available for the Netherlands, nor exactly when.

3.3.5 CureVac

Just like the Moderna vaccine, the CureVac vaccine is an mRNA vaccine with genetic material containing the code for the spike protein. The vaccination consists of 2 doses.⁴⁰

The results of preclinical studies and phase I trials have not yet been published. Currently a phase II trial is being carried out with approximately 700 healthy adults.⁵⁵ A phase III trial is expected to start at the end of 2020. The European Union has entered into a contract for an initial 225 million doses, with an option for a further 180 million doses. The Netherlands is entitled to purchase approximately 3.9% of this total (approximately 8.7 million and 7 million doses respectively). The vaccine may become available in the summer of 2021. It is not yet certain how many doses will be available for the Netherlands, nor exactly when.



3.3.6 BioNTech/Pfizer

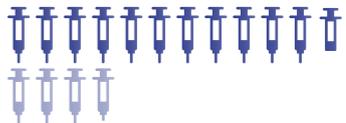
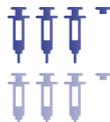
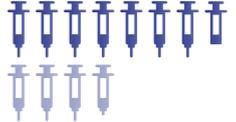
Just like the Moderna vaccine CureVac, the BioNTech/Pfizer vaccine is an mRNA vaccine with genetic material containing the code for the spike protein. The vaccination consists of 2 doses.⁵⁶

An animal study showed that the vaccine has a protective effect.⁵⁷

Vaccination produced antibodies and T-cell responses and no virus was detected in the animals' lungs. A phase I-II trial with people aged between 18 and 55 and between 65 and 85 showed that vaccination led to the production of antibodies and possibly also to T-cell responses. After vaccination both groups experienced local and systemic side-effects. The most frequent side-effects were pain at the site of the injection and fatigue.⁵⁶ In various countries phase II-III trials are being carried out enrolling a total of approximately 44,000 people aged over 16, of whom approximately 40% will be over the age of 55.⁵⁸ At the beginning of November 2020 the company stated in a press release that an initial interim analysis had shown that the vaccine offered around 90% protection.⁵⁹ At this moment no primary data is available.

The European Union has entered into a contract for an initial 200 million doses, with an option for a further 100 million doses. The Netherlands is entitled to purchase approximately 3.9% of this total (approximately 7.8 million and 3.9 million doses respectively). The vaccine may become available in the spring of 2021. It is not yet certain how many doses will be available for the Netherlands, nor exactly when.

Table 1: Overview of candidate vaccines

Vaccines	Type	Expected	Number of doses
University of Oxford/ AstraZeneca	Vector vaccine 	Spring of 2021 	± 11.7 million (possibly additional ± 3.9) 
Janssen Pharmaceutical Companies	Vector vaccine 	Spring of 2021 	± 7.8 million (possibly twice) 
Sanofi Pasteur/GSK	Subunit vaccine 	Summer of 2021 	± 11.7 million 
Moderna	RNA-vaccine 	Spring of 2021 	± 3.1 million (possibly twice) 
CureVac	RNA-vaccine 	Summer of 2021 	± 8.7 million (possibly additional ± 7) 
BioNTech/Pfizer	RNA-vaccine 	Spring of 2021 	± 7.8 million (possibly additional ± 3.9) 



04 ethical considerations



Once the first COVID-19 vaccines receive market approval, the availability of vaccines will not be enough to vaccinate everyone in the Netherlands. Consequently, decisions have to be taken about which groups will be offered vaccination first. Based on general ethical principles, the committee has formulated objectives for vaccine prioritisation which can be used to arrive at ethically sound decisions.

4.1 Need for prioritisation

To anyone in the Netherlands there is a non-negligible risk of infection with SARS-CoV-2. In addition, anyone who is infected with the virus, even those who do not show symptoms, can in turn infect others. As long as a substantial portion of the population has not acquired immunity against SARS-CoV-2, it will remain necessary to take preventive measures. Assuming that, over time, a vaccine which has been proven to be effective and safe becomes sufficiently available, all adults in the Netherlands will have the opportunity, in this phase of the pandemic, to get vaccinated against SARS-CoV-2.

However, the expectation is that when the first vaccine has received market approval, the availability of vaccines will initially not be enough to vaccinate everyone in the Netherlands. This means that choices will have to be made regarding who will be offered vaccination first. Prioritising groups for vaccination during a pandemic is a controversial, ethical issue⁶⁰ because it cannot be based purely on medical and scientific grounds.

In the literature, groups that are often prioritised for vaccination during a pandemic are children, clinically vulnerable populations, healthcare workers and key workers (for example people who work in public security and those involved in the provision of food and other key goods).⁶¹

The question is on which grounds could certain groups be prioritised over others? In order to justify allocation choices, it is important to clarify the ethical considerations on which those choices would be based.

4.2 Ethical principles

The prioritisation of groups for vaccination during a pandemic can be based on wide-ranging and often conflicting ethical considerations.⁶¹ Nevertheless there exists significant overlap in a number of areas. Two general ethical principles which are often applied in matters of prioritisation are utility and fairness.⁶⁰

Principle of utility

An important principle when distributing scarce resources during a pandemic is the maximisation of (health) benefits for the population as a whole. This is also referred to as the principle of utility. This principle is an element of a *consequentialist* theory which asserts that the rightness of our actions is determined by their consequences. In the context of the distribution of scarce resources during a pandemic, a common interpretation of the principle of utility is the prevention of severe morbidity and mortality.^{60,61} There are wide-ranging ideas about what this exactly



means. Does it mean saving as many lives as possible in general, gaining as many life years as possible, or saving the lives of the people who contribute most to combatting the pandemic, or maintaining a stable society?⁶⁰ The interpretation of the principle of utility as ‘saving as many lives as possible’ is generally the most widely accepted interpretation.⁶⁰ It is also clear and unequivocal in terms of its usage. What is more, this interpretation is also compatible with non-consequentialist theories: if all have an equal right to life, it follows that saving lives per se should be the objective during scarcity.⁶⁰ Prioritising groups to indirectly save lives could be considered to fall under the objective of saving lives, such as prioritising healthcare workers for vaccination in order to save other lives. Prioritisation exercises undertaken for this advice report did not directly take account of severe morbidity, as the risk of this will be closely correlated with the risk of death. Similarly, long-term sequelae from SARS-CoV-2 infection have not been taken into account as evidence on chronic morbidity is still emerging. Based on the principle of utility, a small number of ethical publications formulate reducing virus transmission in the population as the leading objective for prioritisation. One example of this would be to vaccinate adolescents, not for their personal health benefit, but to reduce transmission. Others recommend vaccinating healthcare workers in order to prevent downscaling of regular healthcare services.⁶¹⁻⁶³ In some instances, other societal benefits are considered which are not related to (public) health. This could imply, for example, prioritising groups with the goal of gaining societal or economic benefits.^{60,61}

Fairness

The principle of fairness implies that equal weight is given to equal claims of people to a particular resource. In doing so, the appropriateness of our actions is then not measured against the consequences of those actions, but on the grounds of pre-specified standards. The question is then who holds a legitimate claim towards a scarce resource and why? The argument often made on the basis of considerations of fairness is that priority has to be given to the ‘worst off’, in other words those who run the greatest risk, are the most vulnerable, or are most deprived (assuming that vaccination also has an actual effect on correcting such inequalities).⁶⁰ Various interpretations exist about who are the worst off. Also terms such as ‘vulnerable’ and ‘high-risk’ are often insufficiently defined.⁶¹ That is why in this advisory report the use of such terms will be specified as much as possible. Another fairness-based criterion is that prioritisation reduces social inequalities and does not discriminate.^{60,64} A specific and more controversial interpretation of the principle of fairness is the ‘fair innings’ argument.^{60,61} This implies that young people have a greater claim to life-saving treatment in the event of scarcity than older people, based on the fact that the latter group has already had more opportunity to achieve a ‘normal’ lifespan.⁶⁵ Reciprocity is also a principle which can be grouped under the term ‘fairness’. On the grounds of reciprocity healthcare workers could be prioritised for vaccination as they run a professional risk which can be compensated by offering protection.^{60,61,63}



Procedural justice

The principles of utility and fairness may lead to conflicting outcomes.⁶⁰ They may also be interpreted differently in discussions about vaccine prioritisation. Whenever choices have to be made on the basis of conflicting values, the principle of procedural justice could provide a way out.^{60,61} Procedural justice states that a just decision-making process is necessary in order to establish just protocols.⁶⁶ In 2009 a subcommittee of the *Centers for Disease Control and Prevention* (United States) established an ethical guideline for pandemic planning.⁶⁷ The guideline describes the conditions that an ideal process has to fulfil in order to achieve fair outcomes. The conditions referred to are well-founded decisions based on accurate information, consistent use of standards, impartial decision-makers and stakeholders' approval of the procedures.⁶⁷ Transparency is also an essential element. This can be achieved by publishing the arguments, including the relevant values and principles, underlying the various choices.⁶⁶

4.3 Possible objectives of prioritisation

The principles of utility and fairness can be used to formulate legitimate objectives of vaccine prioritisation. In other words, what ought to be the primary goal(s) of vaccine prioritisation? The committee has outlined three potential objectives (see also Table 2). These objectives point towards the groups that ought to be vaccinated first in order to fulfil the chosen objective as much as possible.

Reduce severe morbidity and mortality as a consequence of COVID-19

The primary aim of vaccination is to directly protect people against a particular infectious disease. In this case, vaccination aims to protect against COVID-19. Not everyone runs the same risks when they become infected with SARS-CoV-2. Some people in society run proportionally larger risks of serious health problems as a consequence of COVID-19. Prioritising groups with the aim of reducing (severe) morbidity and mortality is consistent with the principle of utility. This entails prioritising groups who are 'clinically vulnerable', as this would save most lives. On the grounds of the principle of fairness it can also be argued that this group should be vaccinated first, based on prioritising the 'worst off'. There are also groups with an increased risk of infection without individual group members running an increased risk of severe morbidity and mortality. Consequently groups with an increased risk of virus infection could contribute more to the disease burden in society than groups without an increased risk. The extent to which groups contribute to the burden of disease is the product of the group size, the risk of infection and the extent of the potential harm as a consequence of the disease.

Reducing transmission of SARS-CoV-2

In addition to individual protection, vaccination can also offer group protection. This means that vaccines would be prioritised to reduce transmission in an attempt to prevent collective harms (to people's health). The spread of SARS-CoV-2 negatively affects everyone in society.



The higher the prevalence of SARS-CoV-2 in society, the greater the collective harms. Those collective harms may relate to public health, for example if regular healthcare has to be scaled down due to increasing rates of infection. However the disadvantages can also be socio-economic in nature (unemployment or educational disadvantage) or socio-emotional in nature (loneliness).⁶³ Prioritisation with the aim of reducing the transmission of SARS-CoV-2 is therefore consistent with a broad interpretation of the principle of utility, and focuses on groups that play the greatest role in spreading the virus. Prioritising these groups could also be argued for on the basis of the idea that establishing indirect protection also benefits the people who are most vulnerable.

Preventing societal disruption

In the context of the COVID-19 pandemic, a third objective for vaccine prioritisation may exist, namely the preservation of society's vital infrastructure. Lockdowns and restrictive measures (such as closing schools, hospitality venues and the arts and culture sector) disrupt society. The negative (socio-economic) effects are substantial and only increase the longer the pandemic lasts. Absenteeism due to illness (or worse, mortality) among key workers is threatening society's vital infrastructure. The healthcare sector has had to downscale their services and maintaining essential healthcare services has required huge efforts. Vaccination could help prevent societal disruption if it is aimed at groups that are important to maintaining healthcare and preserving society's vital

infrastructure (security services, public administration, provision of food and other key goods). This too is in line with a broad interpretation of the principle of utility. In some instances prioritisation of key workers could also be defended on the grounds of reciprocity arguments (fairness), insofar as these groups run an actual increased risk. The argument goes that these people expose themselves to risks in order to maintain society's stability and vaccination is a way to compensate those risks.

4.4 Additional considerations

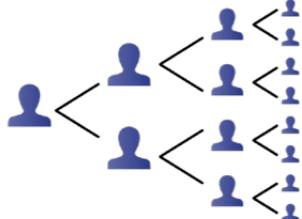
The principles of utility and fairness provide the ethical underpinnings for prioritising certain target groups. Additional considerations may come into play once it becomes necessary to prioritise even further within target groups. For further prioritisation between and within these target groups, new scientific insights will have to be taken into account. That means substantiating claims that vaccine prioritisation of specific groups actually contributes to the chosen objective. Groups which contribute more to a given objective ought to be prioritised over groups which contribute less. This contribution depends on, among other things, the quantified risk per group of contracting and transmitting SARS-CoV-2 and the risk of (severe) morbidity, the risk-benefit ratio of specific vaccines (proportionality) and whether reasonable alternatives are available for certain groups (subsidiarity). The vaccination strategy cannot exist in isolation, but should be considered in conjunction with other measures such as at-source measures (quarantine, isolation at home), collective measures (physical



distancing, testing policy, track and trace), personal hygiene, PPE and medical interventions (antivirals, passive immunisation).⁶¹ If two groups are deemed to quantitatively contribute equally to a particular objective, the principles of subsidiarity and proportionality could be applied, as well as additional considerations of utility and fairness. For example, in the event of an equal probability of severe morbidity or mortality, the number of life years gained (utility) could be taken into account. Another way of looking at it is to focus on the extent to which a professional group is exposed to a risk of infection in order to help others (fairness and reciprocity).



Table 2. Objectives and corresponding target groups for the allocation of vaccines against SARS-CoV-2 in the event of scarcity. The target groups are not arranged hierarchically.

Objective	Target group		
Reduce (severe) morbidity and mortality as a consequence of COVID-19		Groups which, on the basis of personal characteristics, run an increased risk of severe morbidity and mortality after virus infection (clinically vulnerable groups).	
		Groups that run an increased risk of transmitting the virus to people belonging to medical risk groups, despite preventive measures, or because preventive measures are unavailable or impossible.	
Reduce transmission of SARS-CoV-2		Groups that run an increased risk of becoming infected due to their work or living environment.	
Reduce transmission of SARS-CoV-2			Groups that run an increased risk of transmitting the virus to others.
Prevent societal disruption			Groups that are critical to preserving healthcare services and society's vital infrastructure.

4.5 Proposals for prioritisation abroad

Individual countries

A number of countries have already published their provisional recommendations for a national vaccination policy. These include the United Kingdom, France, Belgium, the United States and Germany.⁶⁸⁻⁷² All countries assign high priority to people with the greatest risk of severe morbidity and mortality as a consequence of COVID-19. The majority of countries specify this group as being the elderly and medical risk groups. Healthcare workers are also considered to be a high priority, although this group is often left unspecified. The reports refer to three justificatory reasons for prioritising healthcare workers. They are said to have an increased risk of becoming infected, an increased risk of transmitting the virus to clinically vulnerable patients and they are important in terms of maintaining healthcare services. The reports do not stipulate whether healthcare workers should take precedence over clinically vulnerable groups.

The United States and Germany also regard key workers as a high priority.^{70,72} Although France and Belgium mention these groups, the medical and scientific advisory bodies in these countries have left the decision to prioritise key workers who are not healthcare workers explicitly to other authorities.^{69,71} The US and German recommendations also focus on groups which are vulnerable from a socio-economic perspective.^{70,72} The US *National Academies of Sciences, Engineering, and Medicine*

explicitly states that the allocation of vaccines must also be used to reduce social inequalities in the United States.⁷³

The advice is for the prioritisation to take account of an index based on socio-economic status, race, ethnicity, residential situation and transportation options.

The medical and scientific advisory bodies in the above-mentioned countries stress that key data on the specific vaccines is still unavailable, including data on efficacy and safety, and on the epidemiology and risk factors for COVID-19. Prioritisation policies are said to be established on the available information and on the assumption that the vaccine is equally effective and safe in all groups and can reduce both the burden of disease and transmission. That is why prioritisation policies are considered (highly) provisional. Some countries make more emphatic recommendations than others. France, for example, presents various vaccination strategies but states that it is currently impossible to make a definitive choice.⁶⁹ All reports mention that the vaccination policy will be worked out in more detail or amended as soon as more data becomes available.

European Commission

On 15 October 2020 the European Commission published its policy recommendations on vaccination against SARS-CoV-2 in member states of the European Union (EU). The guiding principle of group prioritisation is to save as many lives as possible.⁷⁴ According to the European



Commission the focus should therefore be on protecting the most vulnerable groups and individuals, and on reducing transmission of the virus. The European Commission has published a list of examples of groups that EU countries should consider for vaccine prioritisation (without placing them in order of importance).⁷⁴ The report states that additional prioritisation and specific recommendations are only possible after the characteristics of specific vaccines are known, including efficacy and safety when administering the vaccines to specific groups. The list of groups to be considered includes healthcare workers and employees in long-term care institutions, people over the age of 60, groups who are medically vulnerable due to chronic disease or comorbidity, employees in vital sectors other than healthcare, groups that are vulnerable from a socio-economic perspective and groups that are unable to keep physical distance (due to their living or work conditions).⁷⁴

World Health Organization (WHO)

In its *WHO SAGE Roadmap* the World Health Organisation (WHO) outlines three epidemiological scenarios which may help countries with the national prioritisation of vaccines, related to varying vaccine availability.⁷⁵ In the first scenario the prevalence of the virus in the population is high, in the second scenario there are sporadic cases or local outbreaks and in the third scenario there are no longer any known cases in the country. In the first scenario (lots of cases) the vaccination strategy has two aims, namely to reduce severe morbidity and mortality

and maintain the country's vital infrastructure. If the vaccine is only available on a very limited scale (enough for 1-10% of the population), the WHO advises starting with healthcare workers with a high to very high risk of contracting and transmitting the virus. The reasoning behind this is that there is evidence that healthcare workers run a high risk of virus infection and potentially also of severe morbidity and mortality.^{76,77}

Prioritisation of healthcare workers will then help to protect vulnerable patients and maintain COVID-19-related care and regular healthcare services. According to the WHO this decision is also based on the principle of reciprocity: healthcare workers are under a great deal of pressure and are exposed to risks while helping others. Lastly, a practical argument is also mentioned, namely that healthcare workers can, as a group, be vaccinated quickly, meaning that more time is available for the roll-out to other prioritised groups. In this scenario healthcare workers with a high risk of infection are followed by elderly people in order of age-related risk of severe morbidity and mortality. When the availability of vaccines increases (11-20% of the population) the priority shifts to elderly people, medical risk groups, socio-demographic groups with a significantly increased risk of severe morbidity and mortality (for example asylum seekers) and high-priority teaching staff. When the vaccine becomes available to 50% of the population, other teaching staff will be added, as well as key workers other than those in healthcare and education, pregnant women, care workers with a low to average risk of virus infection and groups with an increased risk of virus infection on the grounds of their



profession or living environment. In the second scenario (local outbreaks) the vaccination policy aims are the same, but a new aim is to reduce transmission in the population. When the first vaccines (1-10%) become available the advice in this scenario is to start with healthcare workers with a high to very high risk of contracting and transmitting the virus and those who work in environments where prevalence is high. In addition, elderly people must be vaccinated *simultaneously* in order of age-related risk of severe morbidity and mortality, as well as people who work in environments where virus prevalence is high. In the third scenario (no cases) the advice is to use the first vaccines to prevent any import of the virus from abroad. High priority will be given to groups who go on essential trips abroad and groups involved in border control. On the grounds of reciprocity arguments the advice is also to offer the vaccine, in the first stage (1-10% availability), to healthcare workers with a high risk of virus infection and transmission.

Scientific-ethical literature

To this date, very little scientific-ethical literature has been published on the prioritisation of groups for vaccination against SARS-CoV-2. Most of the publications are written by authors from US institutes. Two US articles argue specifically in favour of prioritising healthcare workers and first responders (including fire fighters and the police), followed by groups with the highest risk of severe morbidity and mortality.^{62,63} According to the authors, the group with the highest risk consists of people over the age of 60 and people with comorbidities. In the case of limited vaccine

availability, the authors propose a lottery system to allocate vaccines among these groups. Young people would, in any event, not be considered a priority because of their low risk of becoming seriously ill as a result of infection. On the other hand, if evidence shows that young people play an important role in virus transmission, this would actually be a reason to prioritise young people.⁶² Schmidt et al. highlight the US recommendation to take account of social inequalities when allocating vaccines.⁶⁴ According to the authors, vaccines should be offered to deprived groups in proportion to their situation and the extent to which they are affected by the pandemic. A special index (*Social Vulnerability Index*, SVI) is proposed to help identify vulnerable groups.⁶⁴ Giubilini et al. favour prioritising children due to their alleged prominent role in transmission, with the argument being that vaccinating children would be the most efficient way of protecting clinically vulnerable groups.⁷⁸



05 vaccination strategies



The committee outlines four potential strategies for COVID-19 vaccination, in a situation of limited availability of vaccines. The objectives of the first three strategies are respectively to reduce severe morbidity and mortality, to reduce transmission of SARS-CoV-2 and to prevent societal disruption. A fourth strategy consists of a combination of these objectives.

5.1 Strategy 1: reduce severe morbidity and mortality as a consequence of COVID-19

The objective of this vaccination strategy is to minimise severe morbidity and mortality as a consequence of COVID-19. To do so, it is necessary to identify groups that contribute most to the burden of disease and mortality. This includes, in any event, people who run an increased risk of severe morbidity and mortality as a consequence of COVID-19 and people with an increased risk of infection due to their profession or living environment. Prioritising these groups will help save as many lives as possible, including life years (utility), and offers equal opportunities to people who are vulnerable due to an increased risk of serious health consequences, or an increased risk of virus infection due to their profession or living environment (fairness).

5.1.1 Possible target groups

Clinically vulnerable groups

Data from Dutch hospitals and the available literature show that elderly people and people with a chronic condition have an increased risk of severe morbidity and mortality as a consequence of COVID-19.⁷⁹⁻⁸⁵

In the Netherlands people aged 50 and over are regarded as having an increased risk of serious disease and this risk increases with age. The risk of mortality increases substantially from the age of approximately 60 and continues to increase with age. Calculations have revealed that the risk of mortality in ICUs is approximately 5 times higher for people aged between 60 and 65 (*odds ratio* (OR) 4.97 (95% confidence interval: 3.33-7.41)) and 18 times higher for people aged between 80 and 85 (OR 18.14 (9.90-33.25)) compared to people under the age of 50.¹⁹ People with chronic conditions, such as cardiovascular disease, lung disease and diabetes mellitus, also have an increased risk of severe morbidity and mortality compared to healthy people. Their mortality risk is approximately twice as high compared to people without chronic conditions (data not adjusted for age).¹⁹ Table 3 provides a description of these medical risk groups. This description is partly based on medical risk groups identified by the Health Council of the Netherlands at the time of the influenza A/H1N1 pandemic in 2009.⁸⁶



Table 3: Medical risk groups for COVID-19

- Patients with anomalies and functional impairments of the airways and lungs and patients with chronic heart conditions
- Patients with diabetes mellitus
- Patients with chronic renal insufficiency (dialysis and kidney transplant patients)
- Patients with an immune disorder or who are being treated with immunosuppressants leading to reduced resistance to respiratory tract infections
- People with a cognitive disabilities who live in institutions and care home residents

Groups that run an increased risk of infecting people in medical risk groups

If the medical risk groups cannot themselves be vaccinated, for example because a vaccine is contraindicated, or if it transpires that vaccinating these groups is ineffective, indirect protection can be aimed for by vaccinating healthcare workers or informal carers who are in direct contact with people in medical risk groups. This would apply, for example, to employees in long-term care institutions, such as nursing homes.

Groups that run an increased risk of virus infection due to their work or living environment

Various people may run an increased risk of becoming infected due to their profession, for example because it is impossible for them to work from home, or because they provide close contact services.

Approximately 10% of the cases of which the infection setting is known occurred in the workplace.⁸⁷ The committee has identified a number of

examples of sectors with increased risk of infection. The first group consists of healthcare workers (including people working in home care, geriatric care and long-term care) because, during their daily work, they are in close contact with people who have health issues, including COVID-19 patients. This group of healthcare workers can be subdivided into groups of people with varying risks of infection, depending on the extent to which they have contact with confirmed or suspected COVID-19 patients and the availability and use of PPE. People in other professions whereby direct contact with patients or clients is necessary, such as dentists, physiotherapists, hairdressers, police and law enforcement officers, may also run a greater risk of infection. In addition, employees (particularly labour migrants) in the agricultural and food industries (the meat processing industry and businesses that process fresh products such as vegetables, meat and fish) may have an increased infection risk due to them working in cold rooms with high levels of humidity. Other factors probably also play a role, such as living and housing conditions, which are sometimes below average in the case of labour migrants. It is possible that there is an increased risk of infection in certain living conditions, such as prisons and asylum seeker centres, where observing physical distance is almost impossible.

For many professional groups it is not yet known precisely what the actual risk is of them becoming infected (at work) and, by extension, their contribution to the number of hospital admissions and mortality as



a consequence of COVID-19. In general these groups consist of individuals who do not have an intrinsic increased risk of severe morbidity or mortality. Another aspect to be considered is the extent to which this risk can be reduced using PPE and preventive measures. Although there is evidence in other countries that healthcare workers run a high risk of virus infection and possibly also of severe morbidity and mortality^{76,77}, there is little data on this for the Netherlands. The percentage of healthcare workers that have tested positive since 1 June 2020 was around 6 percent and this is comparable to the percentages in education and among informal carers and is slightly lower than in law enforcement and close contact professions.⁸⁷ Only a small number of care workers have been admitted to hospital (~2% of the cases have been care workers) or have died (<0.1% of cases have been care workers).⁸⁷ Nevertheless it is important to continue recording which healthcare workers have the greatest risk of infection, and how great the infection risks actually are.

5.1.2 Vaccine characteristics

For the objective of this strategy, a vaccine has to be sufficiently effective to prevent severe morbidity and mortality in the listed target groups and it must be safe. In terms of vaccinating elderly people, account must be taken of the fact that, as people get older, their immune system will gradually start to deteriorate (*immunosenescence*) and therefore vaccines will generally be less effective. It is also likely that information will not be

available in the beginning on potential contraindications, specifically for certain medical risk groups.

5.1.3 Required doses of the vaccine

In order to vaccinate all elderly people and medical risk groups with an increased risk of mortality, it is estimated that at least 5 million people would have to be vaccinated. In order to vaccinate healthcare workers in nursing homes, home care and long-term care, as well as informal carers who are in direct contact with medical risk groups, it is estimated that approximately 1.5 million people would have to be vaccinated.

5.2 Strategy 2: reduce transmission of SARS-CoV-2

The objective of this vaccination strategy is to reduce transmission of SARS-CoV-2 in the population. Translated into epidemiological terms, the aim of the strategy is to achieve a reproduction number (R) of below 1. The idea behind this strategy is to protect the elderly and medical risk groups *indirectly* and, by doing so, to reduce the negative societal consequences of the pandemic. In this strategy priority is given to people who run the highest risk of becoming infected and of further transmitting the virus among the population after infection.



5.2.1 Possible target groups

The group of people who run the greatest risk of further transmitting the virus among the population can change over time. In order to properly define this group at a certain point in time, an assessment has to be made of the current epidemiological situation. At the moment, in the autumn of 2020, young people in the 20-30 age group are contributing most to the transmission of SARS-CoV-2. In this strategy, these groups would need to be prioritised for vaccination. Because people in this group benefit less from vaccination due to their already low risk of developing disease, the benefit-risk ratio of vaccination may be less favourable for them. However, modelling research is necessary to determine which effect can be achieved by vaccinating this or other groups that play a role in transmission.

5.2.2 Vaccine characteristics

This strategy requires a vaccine that is not only sufficiently safe and effective, but must also prevent transmission of the virus. The effect of vaccination on transmission is being investigated in a number of the phase III clinical trials currently being carried out. At this moment the committee cannot tell whether these trials will generate sufficient data to make any assertions about the use of vaccines for this purpose.

5.2.3 Required doses of the vaccine

The quantity of required vaccine doses depends very much on the choices made. The 20-30 age group comprises approximately 2 million people.

5.3 Strategy 3: prevent societal disruption

The objective of this vaccination strategy is to prevent societal disruption. In this strategy groups are prioritised based on their importance to preserve society's vital infrastructure. The aim is to prevent the pandemic's most detrimental consequences for society (utility). In the more public health-oriented interpretation of this objective, the focus is primarily on preserving the healthcare sector in order to minimise the impact of the pandemic on public and individual health. In this strategy healthcare workers are therefore prioritised for other reasons than in strategy 1. Prioritisation is aimed at maintaining a critical functioning of healthcare services, not at directly reducing severe morbidity and mortality. The committee wishes to emphasise that this strategy is not solely based on public health and scientific medical considerations, but also on socio-political considerations.

5.3.1 Possible target groups

Those eligible for vaccination are key workers, such as people working in healthcare, security, education and public administration. In order to minimise the impact of the pandemic on public health as a whole, healthcare workers would need to be prioritised above other professional groups. However, opting for this strategy, especially in the case of limited availability of vaccines, will need to be supported by an actual threat of societal disruption. The epidemiological situation at the time (absenteeism due to morbidity or mortality in certain sectors) is important in this respect.



5.3.2 Vaccine characteristics

Before it can be used in this strategy, a vaccine has to be sufficiently effective to prevent serious morbidity and mortality and it must be safe.

5.3.3 Required doses of the vaccine

In order to vaccinate all healthcare workers (including nursing homes and home care) and informal carers, it is estimated that at least 2 million people will have to be vaccinated.

5.4 Strategy 4: combination strategy

This strategy is a combination of two or three of the first strategies. An example of a combination strategy is one in which the goal is to prevent severe morbidity and mortality (strategy 1) but also to maintain healthcare services (strategy 3). If strategy 3 (preventing societal disruption) is included in such a combination strategy, this means that socio-political considerations will play a role in addition to public health considerations. The fourth strategy also requires decisions about how many vaccines are to be used to which end. How vaccines are allocated over the different groups would require an allocation key that includes socio-political considerations. Within each of the elements a different prioritisation must be chosen in the event of limited vaccine availability.

The various elements relevant to strategy implementation as discussed for the first three strategies (eligible groups, characteristics and required doses of the vaccine, follow-up) are also important in the fourth strategy.

5.5 Additional factors which are relevant to the choice of strategy

In addition to factors such as the efficacy and availability of one or more vaccines, other factors also play a role when choosing a vaccination strategy. One key factor is the epidemiological situation. It is conceivable that, in the event of widespread virus circulation and a large number of cases, a different strategy will be chosen than in the event of small-scale circulation and only local outbreaks. Another criterion is the general measures which apply at the time of vaccination. Measures such as physical distancing and working from home and the extent to which people observe these measures can have a significant effect on transmission of the virus and, with that, the choice of strategy. The same applies to the testing policy (for example the possibility of rapid testing of large groups) and the capacity of source and contact tracing. Another relevant factor is the expected degree of participation in any vaccination programme, particularly when a certain strategy requires a specific level of vaccination coverage. Lastly it is important that the implementation of a strategy is practically feasible. For example, one of the aspects that need to be taken into account is whether the target group can be selected and reached in practice, as well as the setting in which vaccines have to be administered.



06 advice



The committee has outlined four potential strategies for COVID-19 vaccination, for the situation in which the availability of vaccines is limited. Which strategy can best be used depends on – currently unavailable – scientific data on the vaccines, the pandemic situation at the moment that the vaccines become available, and on normative considerations. Based on the current epidemiological situation, and given the uncertainties regarding the characteristics and available quantities of the vaccines, the committee advises to prioritise people with the highest risk of severe morbidity and mortality as a consequence of COVID-19. This group consists of elderly people over the age of 60 and medical risk groups. The committee could imagine a situation in which vaccines are also made available for healthcare workers in order to ensure the continuity of healthcare services.

6.1 Reduce severe morbidity and mortality as a consequence of COVID-19

The committee has established that the burden of disease caused by COVID-19 is high enough to recommend vaccinating the Dutch population. In time, sufficient vaccine will be available to vaccinate all adults in the Netherlands, including the Caribbean Netherlands. For the time being insufficient vaccine will be available and that is why prioritisation is necessarily. Based on current scientific knowledge and the current epidemiological situation, the committee recommends vaccination strategy 1, based on health or medical considerations. The objective to prevent

(severe) morbidity and mortality as a consequence of COVID-19 finds its ethical justification in both the principle of utility and fairness. According to the committee strategy 1 means that the following three target groups should be prioritised for vaccination: clinically vulnerable groups that run an increased risk of severe morbidity and mortality, groups that run an increased risk of infecting people from medical risk groups and groups that run an increased risk of virus infection due to their work or living environment.

6.1.1 Prioritising within strategy 1

The committee has established that elderly people aged 60 and over and medical risk groups currently run the highest risk of severe morbidity and mortality as a consequence of COVID-19. On this basis the committee recommends that these groups are vaccinated as a priority, whereby the highest priority should be given to people aged over 60 who also belong to medical risk groups, which includes people with serious heart or respiratory conditions, diabetes mellitus, chronic renal insufficiency, immune disorders, or people being treated with immunosuppressants leading to reduced resistance to respiratory infections, people with a cognitive disabilities who live in institutions and residents of nursing homes. Within this group of elderly people with medical risks, the eldest age group should be vaccinated first because they face the greatest risk of severe morbidity and mortality. Hereafter vaccination should be offered to people aged 60 and over, once again starting with the oldest people first,



followed by people under the age of 60 who belong to medical risk groups. People from these groups who have already been infected should not be excluded from vaccination because reinfection is possible. Given the current knowledge and the state of the pandemic, this approach could achieve the greatest health benefit and provide protection to the most vulnerable groups. In terms of a more detailed specification of the medical risk groups, the committee recommends involving the Dutch Association of Medical Specialists [Federatie van medisch specialisten].

If medical risk groups cannot themselves be vaccinated, for example because a vaccine is contraindicated, or if it turns out that the vaccines in these groups are ineffective, the committee advises aiming for indirect protection by offering vaccination to healthcare workers or informal carers who run an increased risk of infecting people in medical risk groups. By this the committee means employees in long-term care institutions, such as nursing homes.

In addition to the above-mentioned groups, the committee recommends vaccinating healthcare workers who are in direct contact with patients. Although it is not yet known exactly what the professional risk is of various healthcare workers, vaccinating them may help to maintain healthcare services and prevent healthcare workers from infecting patients (see 6.2).

The committee wishes to emphasise that this advisory report is a provisional report and is based on current – limited - scientific knowledge. The eventual vaccination strategy will depend on many factors, such as the characteristics of the vaccine, the quantity of available doses, the epidemiological situation in the Netherlands, the measures that apply at the time, socio-political choices made with regard to vaccination and practical feasibility. For example it is still unclear whether the first available vaccine is effective and safe for the groups that are currently first in line for vaccination. What is more, in the event of small-scale virus circulation and only local outbreaks, the greatest collective health benefit may be achieved by using vaccines to prevent transmission (strategy 2).

The committee also wishes to emphasise that the vaccination strategy must be incorporated into the general policy to combat COVID-19. Vaccination will have to be considered in relation to other measures, such as physical distancing, the (partial) closure of sectors such as culture and hospitality and the shutting down of international borders.

6.2 Healthcare workers

The COVID-19 pandemic is placing the Dutch healthcare system under huge pressure and is demanding a great deal of healthcare workers. For various reasons, healthcare workers could be given priority when it comes to vaccination, for example to reduce the direct burden of disease (strategy 1), to prevent transmission (strategy 2) or to maintain healthcare services (strategy 3). The committee has established that strategy 3



focuses not only on health or medical considerations, but also on socio-political choices, and considerations of reciprocity may then also play a role. While the committee opts for strategy 1 based on predominantly medical and scientific considerations, the committee could imagine a situation in which the government decides to reserve vaccines for healthcare workers on the basis of societal considerations – in line with the objective of strategy 3. In the case of a combination strategy like this (strategies 1 and 3) a decision also has to be made regarding the distribution of the vaccines across the various groups (elderly people, medical risk groups and healthcare workers).

6.3 Passive immunisation

The committee can imagine a situation in which passive immunisation is used temporarily in specific groups of people, or in specific circumstances, for example in the event of outbreaks in long-term care institutions. However, the committee regards passive immunisation as less suitable for use in the general population. That is not only because of the current lack of scientific knowledge, but also because, compared to active immunisation, passive immunisation most likely needs to be repeated more frequently.

6.4 Follow-up

6.4.1 Research into COVID-19 vaccines

The committee expects that publications on the COVID-19 vaccine trials will generate significant insights. Therefore, the committee will monitor

new research findings and issue new advice when sufficient scientific data becomes available. In addition to this the committee expects that modelling research will generate insights into, among other things, the possibilities of reducing transmission of SARS-CoV-2 by vaccination. The committee therefore recommends to initiate such modelling research.

6.4.2 Notes on implementation

If results of clinical trials show that COVID-19 vaccines are sufficiently safe and effective to proceed with (large-scale) implementation, various aspects need to be taken into account according to the committee.

Registration and monitoring

Registration ('who has received which vaccine') is essential in order to gain insight into the effectiveness, impact and safety of the vaccines outside the current trials. After all, any serious side-effects of vaccination, which in themselves are very rare, will only come to light after large scale administration. Monitoring safety must therefore be part of the registration process. Registration and monitoring is even more important if several COVID-19 vaccines start to be used.

In the event of a scarcity of vaccines, registration is important in order to gain insight into (any) underutilisation of vaccines in (some of the) prioritised groups. Research into the vaccination acceptance may help to prevent this. The committee suggests that, if the data clearly reveals



underutilisation in one of the selected groups, consideration should be given to a redistribution of the available vaccine doses.

Public information

A number of specific information aspects need to be taken into account with regard to COVID-19 vaccination. In anticipation of vaccines becoming available, the committee highlights two more general points about public information requirements.

The intensity with which vaccines are being developed worldwide is unprecedented. Some people are concerned that the speed at which the work is being carried out will mean that the risks associated with vaccines will not be properly identified. Such concerns may cause a reduced level of participation. It is important to communicate to people that regulatory authorities follow the same procedures for assessing vaccine safety as for other medicines under review for approval.

Vaccine prioritisation inevitably leads to de-prioritising of certain groups, despite the fact that they will benefit from vaccination. Such choices make it all the more important to be transparent and to clearly communicate how those choices were made and why.



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A assessment framework

The expected or required government involvement increases as vaccination begins to serve a clearer public health or social interest. This government involvement in vaccination is based on two points of departure. Firstly it is the government's task to protect the population and society. Secondly it must try to ensure the fair distribution of healthcare services. Table C.1 shows the details of these points of departure for the entire spectrum of vaccination care.⁸⁸ The table layout in columns from left to right with individual, collective and public interest is clearly based on the level of government involvement, but is not subject to hard and fast limits. It is therefore essential to recognise that the spectrum represents a continuum.

Columns in the table inadvertently place a significant emphasis on vaccination funding. While government support is not entirely logical in terms of vaccination in the individual domain, on the other hand the National Vaccination Programme (RVP) is funded entirely by the government. In between other funding options (including the national budgets, (supplementary) healthcare insurance, or a personal contribution) can, in principle, be considered. The term collective funding in the middle column must not be interpreted as 'the healthcare insurance'. This may be the case if the Dutch National Health Care Institute [Zorginstituut] is able to interpret vaccination as 'specified prevention'.⁸⁹



Table C.1 The spectrum of vaccination care and related government tasks.

	Individual healthcare		Public healthcare
	Healthcare paid by an individual or a company	Essential care, financed collectively	Public programmes
Explanation of government involvement	The provision of vaccines to protect individuals	Promoting equal access to essential care	Protecting the population and society against serious infectious diseases
Government tasks in relevant aspects of vaccination care	<ul style="list-style-type: none"> • Market authorisation of vaccines • Public information • Legislation and regulations and healthcare supervision • Monitoring potential harm (registration of side effects) 	<ul style="list-style-type: none"> • Decision about implementation and financing: inclusion in group package, perhaps in a programmatic fashion, financing via Health Insurance Act [Zorgverzekeringswet] or national budget, personal contribution • Public information • Legislation and regulations and healthcare supervision • Monitoring whether the intended effect (equal access and effectiveness in selected cases) is achieved; monitoring undesirable effects at individual and population level 	<ul style="list-style-type: none"> • Decision about implementation and financing: programmatic content, practical organisation, financing via national budget • Public information • Legislation and regulations and healthcare supervision • Monitoring whether the intended effects (high vaccination coverage/herd immunity, effectiveness) are achieved; monitoring undesirable effects at individual and population level
Assessment framework	<ul style="list-style-type: none"> • Assessment of quality, efficacy and potential harm by medicines agencies • Guidelines for medical treatment 	<ul style="list-style-type: none"> • Criteria for collective financing • Considerations relating to programmatic implementation: urgency, effectiveness, efficiency, quality • Guidelines for medical treatment 	<ul style="list-style-type: none"> • Criteria for including a vaccination in a public programme • Standpoints of the WHO and other international public health organisations • International context • Guidelines for medical treatment
Examples	<ul style="list-style-type: none"> • Travel vaccinations • Vaccination in the context of occupational healthcare (insofar as this concerns employee protection) 	<ul style="list-style-type: none"> • Vaccinating people with an identified condition, meaning that they have a higher risk of infection complications, against hepatitis A, hepatitis B, pneumococcal disease and rabies • Programmatic vaccination for vulnerable groups, e.g.: <ul style="list-style-type: none"> • Elderly people and medical risk groups against seasonal flu • Certain groups of patients against Q fever 	<ul style="list-style-type: none"> • National Immunisation Programme • BCG vaccination of children or parents from risk countries • Vaccinating people from risk groups (homosexual men, intravenous drug users) against hepatitis B • Vaccination in the event of a health crisis, such as a flu pandemic • Vaccination within the framework of occupational healthcare (insofar as this concerns protecting third parties)



Criteria for including a vaccination in a public programme

Protecting the population and society is even more explicitly a government task in the event that a highly transmissible infection impedes and even disrupts society and in the event that individuals become less and less able to protect themselves. This applies especially in the context of infectious diseases and particularly if there is a risk of infection. An infectious disease can undermine the health of individuals who, in turn, can unintentionally damage the health of others. If a dangerous microorganism spreads quickly throughout the community, the burden of disease and fear of infection can paralyse society. The committee would describe such a situation as being one in which the public interest is at stake. The Health Council of the Netherlands uses seven criteria to assess whether there are good reasons to include a vaccination in a public programme (Table C.2).⁸⁸

Table C.2 Criteria for including a vaccination in a public programme.

Seriousness and extent of the burden of disease

1. The infectious disease is leading to a substantial burden of disease in the population:
 - the infectious disease is serious for individuals, and
 - the infectious disease is affecting/will potentially affect a substantial group.

Effectiveness and safety of the vaccination

2. The vaccination is leading to a substantial reduction in the burden of disease in the population:
 - the vaccine is effective in preventing disease or reducing symptoms;
 - the required vaccination coverage (if eradication of the disease or herd immunity is the aim) is achieved.
3. Any detrimental health effects of the vaccination (side effects) do not detract from the health benefit in the population.

Acceptability of the vaccination

4. The inconvenience an individual experiences *due to individual vaccination* is in reasonable proportion to the health benefit for the person himself and the population as a whole.
5. The inconvenience an individual experiences *due to the total vaccination programme* is in reasonable proportion to the health benefit for the person himself and the population as a whole.

Effectiveness of the vaccination

6. The relationship between costs and health benefit is favourable in comparison with that of other possibilities of reducing the burden of disease.

Prioritisation of the vaccination

7. Opting for the vaccination serves a (potentially) urgent public health interest.



In principle, the criteria in Table C.2 provide a hierarchical framework for a systematic discussion of arguments for or against inclusion in a public programme. Each question assumes that the previous question has already been answered in the affirmative. However, the situation is almost never that black and white and judgements are always qualified. The criteria require a thorough weighing-up of the scientific knowledge before a well-considered opinion can be expressed about the strengths and weaknesses of vaccination. The situation becomes even more complex if several vaccination options can be considered, each with their own strengths and weaknesses.

When does vaccination serve a collective interest?

When determining a collective interest, it has to be possible to characterise the vaccination as *essential* care. In that respect it is important that those groups are protected for whom protection is most urgent. The government's responsibility may then be to promote equal accessibility and a fair distribution of vaccination (often with a form of collective financing as well).

When assessing the question of whether a vaccination serves a collective interest, the Health Council of the Netherlands applies the criteria of Table C.3 (a slightly less detailed form of Table C.2). The Health Council of the Netherlands advisory report entitled 'The individual, collective and public interest of vaccination', which dates from 2013, discusses this less extensive assessment framework and the difference between a public and collective programme.

Table C.3 Criteria for being able to characterise a vaccination as essential care.^a

Seriousness and extent of the burden of disease

1. The infectious disease is leading to a substantial individual burden of disease.

Effectiveness and safety of the vaccination

2. The vaccination leads to a substantial reduction in the burden of disease, meaning that the vaccine is effective in preventing disease or reducing symptoms.
3. Any detrimental health effects of the vaccination (side effects) do not detract from the health benefit.

Effectiveness of the vaccination

4. The relationship between costs and health benefit is favourable in comparison with that of other possibilities of reducing the burden of disease.

^a The criteria numbering corresponds to the numbering used of the criteria for including a vaccination in a public programme (Table C.2).



The committee and the experts consulted

Members of the COVID-19 vaccination strategies committee

- Prof. G.A. Zielhuis, Emeritus Professor of Epidemiology, Radboudumc, Nijmegen, *chairperson*
- Prof. M.P.G. Koopmans, Professor of Virology, Head of the Viroscience Department, Erasmus MC, Rotterdam, *vice-chairperson*
- M.W.H. van Beek, Clinical Geriatrician, Catharina Ziekenhuis, Eindhoven
- Prof. J. Berkhof, Professor of Biostatistics and Health Economic Modelling, Amsterdam UMC
- Dr. N.G. Hartwig, Paediatrician-Infectiologist, Franciscus Gasthuis & Vlietland, Rotterdam
- Prof. C.J.P.A. Hoebe, Professor of Social Medicine, Maastricht UMC
- Dr. J.A.R. van den Hoek, Medical Expert in Travel Health and Infectious Disease Control, Amsterdam
- Dr. F.J. Meijman, Medical Doctor, Amsterdam
- Dr. R.H.M. Pierik, Associate Professor of Legal Philosophy, University of Amsterdam
- Prof. M.H.N. Schermer, Professor of Philosophy of Medicine and Human Enhancement, Erasmus MC, Rotterdam
- Dr. S. Schoenmakers, Gynaecologist, Erasmus MC, Rotterdam
- Prof. C. Schultsz, Medical Microbiologist, Professor of Global Health, Department of Global Health, Amsterdam UMC
- Dr. A. Simon, Internist-Infectious Disease Specialist, Department of General Internal Medicine, Radboudumc, Nijmegen
- E. Vlaanderen, Community Medicine Physician, GGD Zaanstreek&Waterland, Zaandam

Experts consulted on a structural basis^a

- Prof. S.E. Geerlings, Professor of Internal Medicine, Amsterdam UMC
- Dr. H.E. de Melker, Epidemiologist, Centre for Infectious Disease Control, RIVM, Bilthoven
- Dr. J.J. Maas, Occupational Physician-Epidemiologist, Amsterdam UMC

Observers^a

- D. van Bentem, MSc., Ministry of Health, Welfare and Sport (VWS), The Hague
- C. van den Born-Oudenaarden, MSc., Ministry of Health, Welfare and Sport (VWS), The Hague
- E. van Daalen, MSc., Ministry of Health, Welfare and Sport (VWS), The Hague
- E. van Meer, Ministry of Social Affairs and Employment (SZW), The Hague
- Dr. S. Knies, National Health Care Institute, Diemen
- Dr. T.G.J. van Rossum, Medicines Evaluation Board, Utrecht
- Prof. T. Smid, Amsterdam UMC
- J.A. van Vliet, Centre for Infectious Disease Control, RIVM, Bilthoven
- Dr. J.M. van der Waal, National Health Care Institute, Diemen

Secretaries

- Dr. J.D. van der Berg, Health Council of the Netherlands, The Hague
- Dr. K. Groeneveld, Health Council of the Netherlands, The Hague
- Dr. R. Hofman, Health Council of the Netherlands, The Hague
- Dr. S. Kalkman, Health Council of the Netherlands, The Hague

^a For this advisory report the committee consulted external experts. Structurally consulted experts and observers are entitled to speak during the meeting. They do not have any voting rights and do not bear any responsibility for the content of the committee's advisory report.



The Health Council of the Netherlands, established in 1902, is an independent scientific advisory body. Its remit is “to advise the government and Parliament on the current level of knowledge with respect to public health issues and health (services) research...” (Section 22, Health Act).

The Health Council receives most requests for advice from the Ministers of Health, Welfare and Sport, Infrastructure and Water Management, Social Affairs and Employment, and Agriculture, Nature and Food Quality. The Council can publish advisory reports on its own initiative. It usually does this in order to ask attention for developments or trends that are thought to be relevant to government policy.

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