

Series COVID-19 & response strategy

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[This is the 27th document in a series of discussion notes addressing fundamental questions about COVID-19 and response strategies. These documents are based on the best scientific information available and may be updated as new information comes to light.]

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Photo: Isaac Planella/ Barcelona City Council. Guinardó Health Pavilion. Authors: Silvia de Sanjosé and Adelaida Sarukhan, on behalf of the Multidisciplinary Collaborative Group for the Scientific Monitoring of COVID-19 (GCMSC), a joint initiative of ISGlobal and the Barcelona Medical Council (COMB), in collaboration with the Catalan Association of Research Centres (ACER).*

A safe and effective vaccine against COV-ID-19 is the only way to achieve a level of herd immunity that will allow us to regain some degree of normality. Fortunately, technological advances and the experience acquired over the past few decades have made it possible to develop COVID-19 vaccines at unprecedented speed: a process that normally takes eight to ten years has been compressed into 12-18 months. Just three months after the SARS-CoV-2 virus (which causes COVID-19) was identified and sequenced, the first vaccine candidate, developed by the pharmaceutical company Moderna, was already being tested in humans. Ten months later, more than 130 vaccines are under development, 64 of which are being tested in humans. As of today, ten vaccines are in phase III clinical trials to test their efficacy in preventing disease or, better yet, infection.

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The Most Advanced Vaccine Candidates

With the exception of three vaccines based on inactivated whole virus, all of the candidates currently in phase III efficacy trials seek to **induce an immune response against the same viral antigen: the spike protein** (*see Table 1*). All of these vaccine candidates have been shown to be well tolerated and to induce a good immune response in humans—specifically, the production of neutralising antibodies. Some of them—at least the Moderna and AstraZeneca vaccines—also generate a T-cell response, even in people over 55 years of age. Moreover, all of the vaccines tested in non-human primates have been

*The members of the GCMSC are Silvia de Sanjosé (epidemiologist, NCI and PATH), Josep M. Miró (infectious disease specialist, Hospital Clinic and University of Barcelona), Quique Bassat (paediatrician, ICREA researcher at ISGlobal), Magda Campins (epidemiologist, Hospital Vall d'Hebron), Robert Guerri (internist, Hospital del Mar), Carles Brotons (family doctor, EAP Sardenya), Juana Díez (virologist, CEXS, Pompeu Fabra University), Julià Blanco (biochemist and immunologist, IrsiCaixa-IGHTP), Mireia Sans (family doctor, CAP Borrell), Olga Rubio (intensivist, Althaia and Catalan Bioethics Society) and Adelaida Sarukhan (immunologist and scientific writer at ISGlobal). This document is based on the GCMSC's <u>report on priority groups for vaccination against COVID-19</u>. found to **protect against the disease** (pulmonary pathology), although only two of them, the Janssen and Novavax vac-

cines, appear to **protect against upper respiratory tract infection**, as well.

Strategy	Company	Reported efficacy'	Storage	Doses negotiated with the European Union ²
Messenger RNA	Moderna	94%*	-20°C, 4°C (1 month)	80 million (up to 160 million)
	BioNTech/Pfizer	95%*	-70°C	200 million
Viral vector	AstraZeneca/Oxford [ChAd]	70%**	4°C	300 million
	Gamaleya Institute (Ad5, Ad26)	91.4%*	4°C	-
	CanSinoBio (Ad5)	Phase III underway	4°C	-
	Johnson & Johnson (Ad26)	Phase III underway	4°C	200 million
Protein	Novavax	Phase III underway	4°C?***	-
Inactivated virus	Sinopharm	Phase III underway	4°C	-
	Sinovac Biotech	Phase III underway	4°C	-
	Bharat Biotech	Phase III underway	4°C	-

Table 1. Vaccine Candidates Currently in Phase III Clinical Trials.

* Final phase III results.

** Preliminary phase III results.

*** The storage temperature is believed to be 4°C.

¹ Efficacy at preventing symptomatic cases in the vaccine group versus the placebo group.

²As of 30 November 2020.

To be approved, vaccines must show a good safety profile and at least 50% efficacy after being administered to tens of thousands of volunteers from different age groups and ethnicities. Early phase III results for the Pfizer-BioNTech and Moderna vaccine candidates indicate efficacy greater than 90%—well above the established threshold. Although the final results of these trials have yet to be fully analysed, there is **reason for optimism**: the virus is "vaccinatable" and all other candidates using the same viral antigen have a high likelihood of success.

Therefore, one or more vaccines will very likely be approved by the regulatory authorities by the end of the year. However, even though the pharmaceutical companies have started mass-producing their vaccine candidates before we even know whether or not they work, the **number** of doses available in the first few months will be limited. (Pfizer, for example, <u>announced</u> that it will be able to supply 50 million doses by the end of the year—enough to vaccinate only 25 million people—although it plans to produce a billion doses over the course of 2021.)

Governments must now **develop vaccination plans** to achieve the greatest possible impact with an initially limited number of doses.

For now, a number of **questions sur**rounding the vaccine candidates remain unanswered. As the answers to these questions become clear, vaccination strategies should be revised accordingly (*see Box 1*). A number of **issues related to** vaccine distribution must also be taken into account (*see Box 2*).

Box 1. Unanswered Questions About the Effectiveness of Vaccine Candidates.



1. Protection in older

adults. It is still too early to know whether or not the vaccines effectively protect older adults (a particularly vulnerable group that often responds less optimally to vaccines).



2. Prevention of disease versus transmission.

Vaccination plans must take into account whether the approved vaccines protect only against disease or if they also prevent people from becoming infected and infecting others (i.e. interrupting transmission of the virus). Intranasal vaccines could be a good solution, as they induce a mucosal immune response and are therefore more effective at blocking the initial infection. Only two such vaccines are currently in clinical trials and neither is in phase III.



3. Duration of immunity.

It is still too early to know how long the protection conferred by the approved vaccines will last. Only through long-term follow-up of vaccinated individuals (phase IV trials) can we determine whether or not booster doses will be necessary.



Box 2. What About Vaccines that Require Ultra-low-temperature Storage?

If the first vaccines to be approved require **ultra-low-temperature storage** (-80°C), this may affect the selection of priority groups.

Vaccines are shipped by aircraft to a **central warehouse**, where they are then taken by **deep-freezer lorry to decentralised warehouses** in different regions. From there, the vaccines must then be taken to **vaccination centres**. In Spain, however, ultra-low-temperature freezers are only available at **hospitals and universities**.

To keep the vaccines at the required temperature, Pfizer provides special **boxes containing 200 vials** (five doses per vial). Once the box has been opened, the **1,000 doses have to be administered within five hours**.

This vaccine will therefore be **more difficult to administer** in the primary care system and, of course, very difficult to administer via home care visits to adults over 80 years of age who do not live in residential care facilities.

Identification of Priority Populations

"Several studies in Spain and other countries have shown that frontline health care workers are at higher risk of contracting the virus." Although there is still much that we do not know about the virus, as well as its transmission dynamics and the clinical course of COVID-19, our current knowledge allows us to set **preliminary priorities** by identifying the groups of people who are most exposed to the virus as well as those who are most vulnerable to the disease (*see Figure 1*).

1. The Most Exposed

1.a Health Care Workers in Contact With Patients

Several studies in Spain and other countries have shown that frontline health care workers are at higher risk of contracting the virus. As of 2018, there were 513,777 registered health workers in Spain. Within this group, it is possible to further prioritise workers by <u>degree of exposure</u>: nurses and care staff are at the greatest risk because of the long hours they spend in close contact with potentially infected people every day.

1.b Essential Workers

Essential workers make up a large percentage of the workforce and may be at greater risk of infection because they are frequently in contact with the public and do not always have adequate personal protective equipment. Care staff at residential elder-care facilities are a high-priority population, since they are not only more exposed but also at greater risk of spreading the virus. First responders-fire fighters, emergency personnel, police officers-are considered to be a particularly exposed population. Other essential workers include people working in public transport, education, food service, delivery, etc. In Spain, between two and seven million people could be considered essential workers, including first responders.

2. The Most Vulnerable

Several factors, including age and underlying conditions, are clearly associated with an increased risk of serious disease or death from COVID-19.

2.a Age

The risk of dying from COVID-19 increases dramatically with age: people over 80 years of age are 20 times more likely to die of the virus than people 50-59 years of age (see Figure 2). For people under 55 years of age, the risk is much lower. In some European countries, more than half of the deaths from COVID-19 have occurred at residential elder-care facilities. During the period in which the supply of vaccine doses is very limited, the greatest benefit (in terms of mortality) can be obtained by vaccinating people over 80 years of age, followed by people over 65 years of age as more doses become available. In Spain, there are nearly 3 million people over 80 years of age and 9 million people over 65 (see Table 2).



Figure 1. Age-specific Hospitalisation and Case-fatality Rates Due to COVID-19 in the European Union.

Source: Adapted from the COVID-19 Surveillance Report.

Table 2. Estimated Number of People in Potential Vaccination Priority Groups in Spain.

Potential priority groups in phases 1-2	Number of people in Spain	Source	
Health care workers (in contact with patients)	513,777	<u>Spanish Ministry of Health</u> <u>Cadena SER</u>	
Doctors, nurses and other health professionals	149,342 186,000 331,000	Spanish Ministry of Health	
Emergency health personnel	19,000	Spanish Ministry of Health	
First responders and essential workers	1.7/7.5 million	List of essential activities	
80+ years old	2,851,868	Spanish National Statistics Institute	
64+ years old (19%)	9 million	Spanish National Statistics Institute	
64+ years old with diabetes (21%)	2.12 million*	Fundación para la Diabetes Novo Nordisk	
People with type 2 diabetes	5.3 million*	<u>Fundación para la Diabetes Novo Nordisk</u> Ruiz/García et al. 2020.	
People with obesity	10.8 million*	Fundación para la Diabetes Novo Nordisk	
Incarcerated population	59,589	Spanish Ministry of the Interior	
TOTAL POPULATION OF SPAIN	47.3 million		

*Estimated figures, since high-quality population statistics are unavailable.

2.b Sex

Men are at higher risk than women of dying from COVID-19. However, sex is not considered a factor for prioritisation.

2.c People With Underlying Health Conditions

Clinical data indicate that certain underlying health conditions increase the risk of serious disease or death from COV-ID-19. Such comorbidities include **type 2 diabetes, cardiovascular disease, chronic respiratory disease, immunocompromised status, cancer** and **obesity** (*see Table 3*). In Spain, for example, there are about 5 million people with diabetes and 10 million people with obesity (*see Table 2*).

Condition	Severe	%	Fatal	%
Cardiovascular disease (except hypertension)	3,241	23.9	7,481	28.3
Diabetes	2,662	19.7	4,643	17.6
Cancer	987	7.3	2,771	10.5
Hypertension	768	5.7	2,450	9.3
Chronic respiratory disease (except asthma)	965	7.1	1,720	6.5
None	3,204	23.7	3,598	13.6
TOTAL	13,540	100	26,452	100

Table 3. Cases of Severe and Fatal COVID-19 by Underlying Condition in Europe.

Source: European Centre for Disease Prevention and Control (ECDC).

2.d Certain Ethnic Groups and Disadvantaged Populations

There is clear evidence showing that certain ethnic groups are at greater risk of infection and serious illness. In the United Kingdom, for example, black men are 3.3 times more likely than white men to die of COVID-19. Similarly, African-American and Hispanic populations in the United States have been disproportionately affected by the virus. One reason for these discrepancies has to do with socioeconomic conditions, including the inability to telecommute or isolate in the event of illness. We do not yet have enough information on the impact of the virus on ethnic groups or disadvantaged populations in Spain. However, institutionalised people, whose ability to isolate is limited (because they live, for example, in prisons or immigrant detention facilities), and people at risk of social exclusion (migrants, homeless people, etc.) should be considered vulnerable to infection.

3. Those Most Likely to Spread the Virus?

From a population perspective, blocking transmission could have a greater impact than reducing disease-induced mortality. Models estimate that people aged 30-50 years are responsible for a majority of transmission, so they could also be a priority population for vaccination. However, as noted above, we do not yet know whether or not the first vaccines approved will be able to prevent infection and, therefore, block the spread of the virus. Therefore, in the early stages of vaccination, the main objective will be to reduce mortality and morbidity from COVID-19 by protecting those who are most exposed and vulnerable •



"Priorities should be based on achieving the maximum health benefit from a limited number of vaccines, providing protection first to the most vulnerable and those most at risk (essential workers)." There are two ways to set vaccination priorities: either by using models based on infection dynamics, with the aim of achieving **maximum impact**, or by using risk/ benefit criteria based on **ethical considerations**. The latter approach has been endorsed by various institutions, including the World Health Organisation (WHO).

The strategies published by the <u>Royal Society</u> in the United Kingdom, the <u>Nation-</u> <u>al Academy of Medicine</u> and the <u>Advisory</u> <u>Committee on Immunisation Practices</u> in the United States, the <u>WHO</u> and the <u>European Centre for Disease Prevention and</u> <u>Control (ECDC)</u> all identify the **same priority groups**, although the **order** of prioritisation varies slightly from one proposal to the next. The key groups identified include health workers and care staff, older adults, people with underlying conditions, essential workers, socioeconomically vulnerable groups (including homeless people) and institutionalised people.

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Figure 2. Priority Groups for COVID-19 Vaccination.

Health workers In contact with patients including nursing homes and first responders

People aged 80 or more and institutionalized elderly

Adults aged 65 to 79 years

People with comorbidities Type 2 diabetes, coronary heart disease, COPD, chronic kidney disease, obesity, chemotherapy, immunosuppression

Institutionalised people and at risk of social exclusion Prisons, refugee centers, migrants...

Essential workers Transportation, education, food

Over 55 years old

Vaccines for all



People with evidence of previous SARS-CoV-2 infection (PCR, antigen testing, or serology) should not be considered a priority when accessing vaccines.

Source: ISGlobal, based on the conclusions of the Multidisciplinary Collaborative Group for the Scientific Monitoring of COVID-19.

Proposal of the Multidisciplinary Collaborative Group for the Scientific Monitoring of COVID-19

Following a review of the scientific literature and the reports cited above, the Multidisciplinary Collaborative Group for the Scientific Monitoring of COVID-19 (GCMSC) agreed that vaccination priorities will need to be established, and that these priorities should be based on achieving the **maximum health benefit from a limited number of vaccines**, providing protection first to the most vulnerable and those most at risk (essential workers).

As vaccine doses become available, we propose that groups be prioritised as follows (see Figure 1):

1. Health workers in contact with patients, including workers at residential elder-care facilities and first responders (fire fighters, police officers and other emergency personnel).

2. People aged 80+ years and institutionalised elderly people.

3. Adults aged 65-79 years.

4. People with underlying conditions: a. Type 2 diabetes mellitus.

b. Chronic heart disease, including ischemic heart disease.

c. Chronic obstructive pulmonary disease.

d. Kidney disease.

e. Class 3 obesity (BMI >40 kg/m²).

f. Cancer patients under chemotherapy (if the type of vaccine allows it).

g. Immunocompromised condition (if the type of vaccine allows it). **h. Any underlying condition** that could affect response to SARS-CoV-2.

5. Institutionalised people with limited ability to isolate (prisons, immigrant detention facilities, etc.).

6. Essential workers (public transport, education, food service, etc.)

7. Adults aged 55+ years.

8. Everyone else.

It should be noted, however, that **people with evidence of previous SARS-CoV-2 infection** (PCR, antigen test or serology) should not be prioritised for access to vaccination in the early stages.

It is important to note that **these pri**oritisation criteria can change as we learn more about the degree and duration of the protection provided by the different vaccines in specific risk groups. For example, if approved, a vaccine that reduces the spread of the virus but is less effective at protecting against the disease could be used preferentially to immunise the younger population.

We believe the following are needed:

• **Practical criteria for identifying members of priority groups**, particularly those with underlying conditions.

• A communication plan to counter vaccine hesitancy or refusal. The speed of development and the new technologies used in COVID-19 vaccines may raise concerns among the public. It is therefore crucial to clearly communicate the risks and benefits of the different vaccines being rolled out as well as the prioritisation criteria.

• Ongoing promotion of additional preventive measures (masks, ventilation, physical distancing) until transmission has been sufficiently reduced.

• A follow-up plan (including a national registry) to monitor the coverage, effectiveness (degree and duration of protection) and safety of the vaccines, as well as pharmacovigilance mechanisms to guarantee a rapid response in the event of serious side effects. This includes preparing a government-sponsored compensation programme.

Our Proposal vs Spanish Government Plan

The Spanish government outlined its <u>COVID-19 Vaccination Strategy</u> on 24 November, indicating the objectives and governance of the strategy, the main vaccine candidates that could soon reach the country (those for which the European Union has approved contracts) and the priority groups for the first stage of vaccination (during which the supply of doses will be very limited).

These first groups are as follows:

• Residents and health and social care workers at residential facilities for the elderly or disabled.

• Frontline health care workers.

• Other health and social care workers.

• People with disabilities who require intensive support measures (severely dependent population).

With the exception of **people with disabilities**, these first groups correspond to groups 1 and 2 on our priority list. **Essential workers and first responders** (who are prioritised, for example, for flu vaccination) are not included in the government's first priority block. **People with evidence of previous SARS-CoV-2 infection**, who therefore enjoy some degree of natural immunity, also deserve special mention; it appears that they will be vaccinated later, along with the general population and specific age groups.

The government briefly mentioned the remaining priority groups that will be vaccinated once more doses become available (i.e. second and third stages), noting that **prioritisation criteria** will be established according to risk of serious morbidity and mortality, exposure, socioeconomic impact and transmission. As both proposals note, prioritisation in subsequent phases will also depend on the characteristics of the vaccines that become available.

The other vaccination priority groups are as follows:

• General population over 64 years of age

• People at risk due to underlying conditions (differentiating between low-risk and high-risk)

• People who work in "closed communities or environments"

• People who are vulnerable because of their socioeconomic situation

- Essential workers
- Teachers
- Children

• Adolescents and young people (16+ years of age)

• Adult population (without specifying age range)

• People in areas with high incidence rates or specific outbreaks

• Pregnant women and breastfeeding mothers

• People with some natural immunity (seropositive for SARS-CoV-2 antibodies)

In any case, it will be important to establish a **single order of prioritisation** based on the **criteria** agreed upon by the Inter-Regional Health Council and adopted by all of Spain's autonomous communities and cities, as set out in the Governance section of the COVID-19 Vaccination Strategy.

Finally, as recommended in our proposal, the government's vaccination strategy includes a **distribution plan**, a **monitoring plan** (via a vaccination register) and a **communication plan** to build public trust in the vaccines. Our proposal, which is in line with the government's public health messaging, also explicitly **emphasises the need for additional preventive measures** (masks, social distancing) until a sufficiently large percentage of the population has been vaccinated and epidemiological indicators show a decrease in transmission of the virus •

TO LEARN MORE

• Krammer F. SARS-CoV-2 vaccines in development. Nature. October 2020.

• <u>Ethics and COVID-19: resource allocation and priority-setting</u>. World Health Organisation. 2020.

• The plight of essential workers during the COVID-19 pandemic. *The Lancet*. May 2020.

• <u>Key aspects regarding the introduction and prioritisation of COVID-19 vaccination in the EU/EEA and the UK</u>. European Centre for Disease Prevention and Control (<u>ECDC</u>) Technical Report. October 2020.

