HARDING CENTER FOR RISK LITERACY

ROBERT KOCH INSTITUT

Fact boxes on the mRNA vaccine against COVID-19

Introduction

These fact boxes are supposed to help you weigh the benefits and harms of a vaccination against COVID-19. The information and numbers in this fact box represent no final evaluation. They are based on the best scientific evidence currently available.

The fact boxes were created in a collaboration between the Robert Koch Institute (RKI, Berlin) and the Harding Center for Risk Literacy (University of Potsdam).

What is COVID-19?

The novel coronavirus (SARS-CoV-2) can cause the disease COVID-19, which is mild in most cases. However, in some people it can lead to pneumonia, neurological and cardiovascular short-term and long-term damages, respiratory distress to the point of requiring ventilation, and even death [1].

The coronavirus is transmitted by virus-containing droplets that are produced, for example, during talking, sneezing or coughing. Moreover, viruses can enter the respiratory tract through small particles that can float in the air for extended periods of time (aerosol particles). Although rare, infection is also possible through contact with surfaces (e.g., door handles or when shaking hands) contaminated with virus-containing secretions (saliva, sputum) [1].

In Germany, more than 3.3 million people were registered as having been infected with the coronavirus or having got sick with COVID-19. More than 82,000 of them died in connection with COVID-19 (as of 28/04/2021) [2]. Not everyone with a SARS-CoV-2 infection develops symptoms. Since many people with asymptomatic infections or mild diseases are not tested, it is assumed that cases are underreported [2, 3].

How does vaccination against COVID-19 with an mRNA vaccine work?

In general, the aim of all vaccinations is to teach the human body to fight a specific pathogen (e.g., bacteria or viruses). This helps prevent infections or at least the outbreak of the diseases or helps mitigate their course [4].

In contrast to already existing vaccines that contain inactive or weakened pathogens or components thereof, which are intended to prepare the immune system so that a subsequent infection can be fought off more quickly [4], mRNA vaccines contain a blueprint. This blueprint in the form of genetic information of the coronavirus (spike protein) is called messenger RNA or messenger RNA (mRNA). With its help, the spike proteins are produced in body cells after vaccination, which in turn stimulate the immune system to form specific antibodies and cellular defenses against the coronavirus. The immune system is then prepared for coronavirus infections.

The immunization usually takes effect 10–14 days after the administration (injection) of the first vaccine dose. Based on previous approvals and available efficacy data, the STIKO recommends an interval of 6 weeks between two vaccine doses for the mRNA vaccines [6].

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The mRNA itself is decomposed by the cells after a short time. After its decomposition, virus components are no longer produced. The mRNA does not enter the cell nucleus and thus does not become part of the human genetic makeup. Vaccines that are mRNA-based have the advantage that large quantities of vaccine doses can be produced relatively quickly [5].

Who may consider vaccination against COVID-19?

In general, all people for whom the vaccine is approved will be offered the COVID-19 vaccination. At first, however, only limited quantities of vaccine doses are available. Therefore, initial prioritization is necessary [5]. Currently, there is no vaccine approved for children and adolescents under 16 years of age in Germany [6]. The vaccination recommendations by the STIKO (Standing Committee on Vaccination) can be found here (German only).

What other measures help prevent infections?

The risk of infecting yourself and others can be reduced by following simple hygiene practices [1]:

- Keep a distance of at least 1.5 meters to others.
- Wear a mask to limit the spread of the virus and thus protect others from infection.
- Wash your hands thoroughly and regularly for at least 20 seconds with ordinary soap.
- Ventilate rooms often and regularly.
- Avoid closed rooms, groups and crowds, and conversations in close contact.
- Do not touch your face.
- Practice good respiratory hygiene:
    - Cover nose and mouth with a tissue when coughing and sneezing, or cough or sneeze into the crook of your arm.
    - After coughing, sneezing or blowing your nose, wash your hands thoroughly.
    - Use tissues only once and promptly dispose used tissues in closed trash cans.

How well can I protect others through my vaccination?

Although there could be vaccinated people who are infected and can spread the virus, current studies suggest that the transmission of the coronavirus is significantly reduced due to vaccination [6].

People who cannot be vaccinated are then protected by not being exposed to an infectious disease in the first place because enough other people have been vaccinated or have been immunized by overcoming the disease [7]. This is referred to as community protection ("herd immunity"). How many immune people are actually needed for this to work depends on how well the vaccine works and how long the vaccine protection lasts.

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Fact box: How safe and effective are COVID-19 mRNA vaccines for adults under the age of 60?

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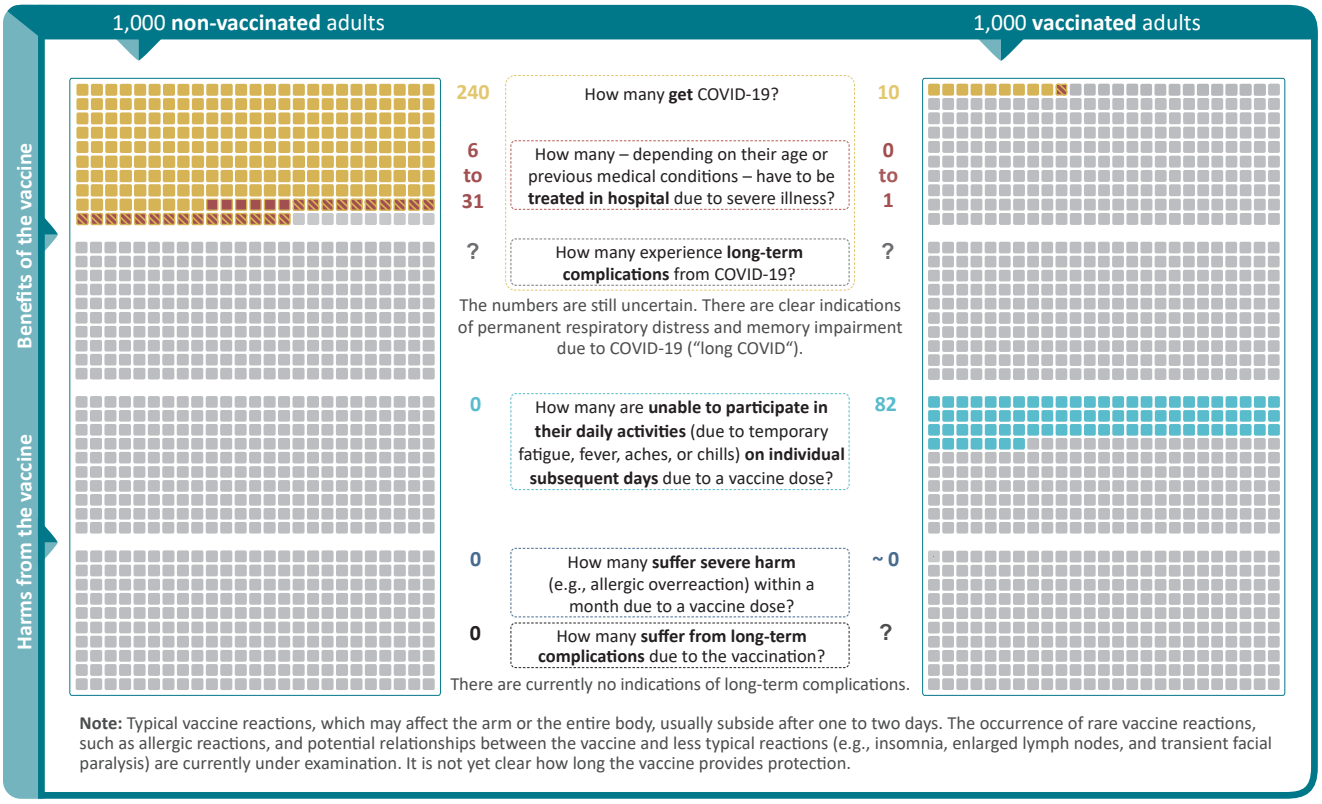
This fact box compares adults under the age of 60 years who have not been vaccinated against COVID-19 (left side) with vaccinated adults (right side).
It is assumed that 240 out of 1,000 unvaccinated people will get sick. This is comparable to your risk of getting sick if you have close contact with someone who is infected.



Note: Typical vaccine reactions, which may affect the arm or the entire body, usually subside after one to two days. The occurrence of rare vaccine reactions, such as allergic reactions, and potential relationships between the vaccine and less typical reactions (e.g., insomnia, enlarged lymph nodes, and transient facial paralysis) are currently under examination. It is not yet clear how long the vaccine provides protection.

Last update: *14 April 2021 | To view the studies, uncertainties, and the latest version please visit www.hardingcenter.de/en/fact-boxes*
Harding Centre for Risk Literacy (Faculty of Health Sciences Brandenburg, University of Potsdam)

Sources *for the vaccines Comirnaty (manufacturer BioNTech/Pfizer) and Moderna (manufacturer Moderna): Baden 2020. NEJM; BioNTech & Pfizer 2020. www.comirnatyeducation.de; CDC 2021. MMWR; EMA 2020. www.ema.europa.eu; FDA 2020. FDA Briefing Document; Polack 2020. NEJM; RKI 2020. reporting data; STIKO 2021. Epidemiological Bulletin.*

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Fact box: How safe and effective are COVID-19 mRNA vaccines for adults aged 60 years or older?

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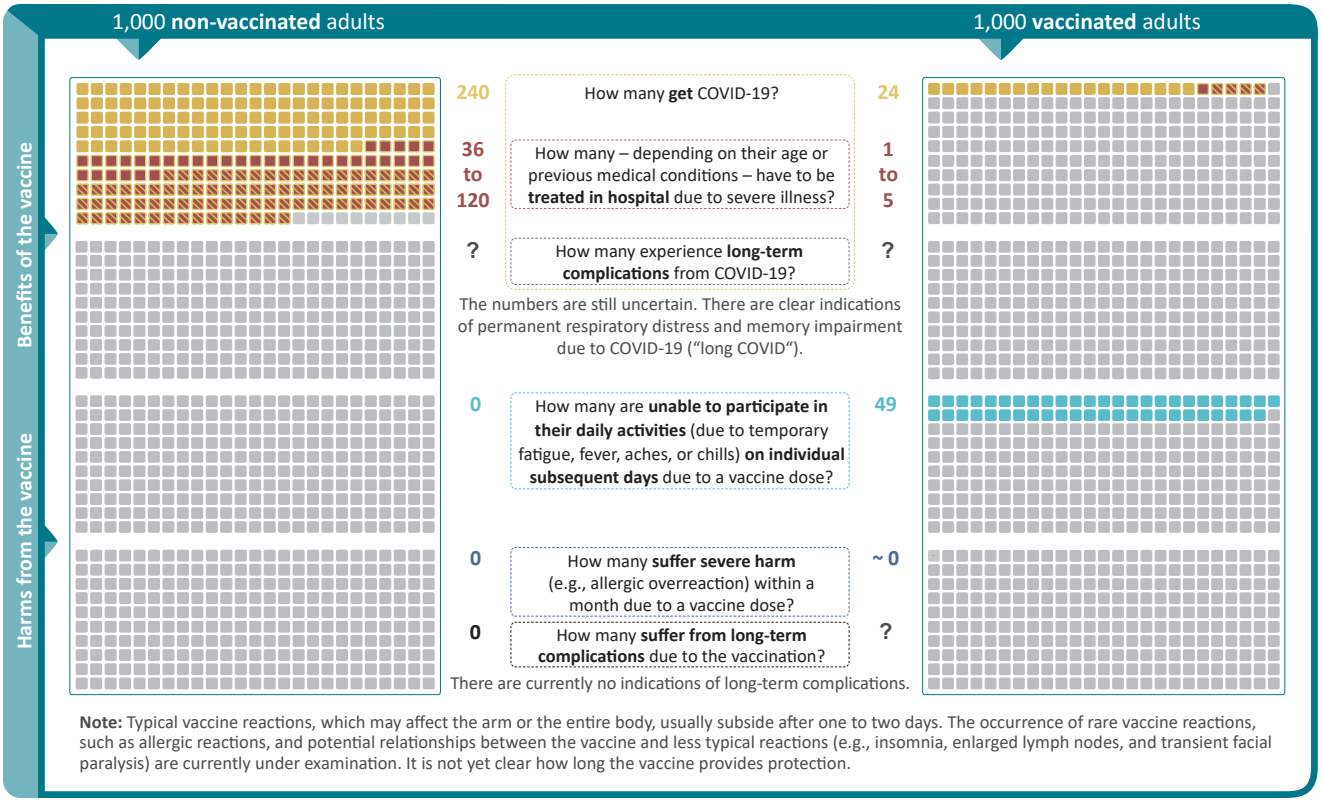
This fact box compares adults aged about 60 years and older who have not been vaccinated against COVID-19 (left side) with vaccinated adults (right side).
It is assumed that 240 out of 1,000 unvaccinated people will get sick. This is comparable to your risk of getting sick if you have close contact with someone who is infected.



Note: Typical vaccine reactions, which may affect the arm or the entire body, usually subside after one to two days. The occurrence of rare vaccine reactions, such as allergic reactions, and potential relationships between the vaccine and less typical reactions (e.g., insomnia, enlarged lymph nodes, and transient facial paralysis) are currently under examination. It is not yet clear how long the vaccine provides protection.

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What do the fact boxes show?

The fact boxes compare 1,000 people with and without vaccination. Since the incidence of infection is constantly changing, an assumption must now be made about the number of unvaccinated people affected: 240 out of every 1,000 elderly people (24%) contract COVID-19 in this scenario. These 24% are comparable to one's own risk of contracting COVID-19 if one comes into close contact with an infected person, for example, at home. Now imagine 1,000 people of the same age who have been vaccinated. Among these, 24 people would be expected to contract COVID-19, given an efficacy of 90%. Thus, 216 cases (240-24) would be prevented by vaccination. The ranges of numbers for severe courses account for people of different ages, with and without preexisting conditions.

What scientific evidence are the fact boxes based on?

The fact boxes are based on phase III trials of the Comirnaty vaccine by BioNTech/Pfizer (about 44,000 participants) [8, 9] and the Moderna vaccine (about 30,000 study participants) [10, 11]. A summary of these studies can be found in the scientific explanation for the STIKO vaccination recommendation. For a description of efficacy, see table 5; for a description of safety, see table 6 (German only).

What other aspects should be considered?

New evidence is continually being gathered, and more vaccines are being developed and approved, so that we will continue to update the fact boxes. Thus, the Standing Committee on Vaccination is also constantly adapting its recommendations (Living Guideline by STIKO).

The outcomes in the fact boxes were selected according to the following principles: efficacy and safety, age group, observation time points, patient relevance, vaccination-specific information needs of citizens according to a quasi-representative internet survey (COMPASS by Infratest dimap) are included, primary before secondary outcomes, expert discussion.

Do the results provide proof (evidence) for the benefits and harms of vaccination?

STIKO considers the quality of scientific evidence on the prevention of COVID-19 to be *moderate* regarding the Comirnaty and Moderna vaccines, and *low* regarding people over 75 years of age [6]. This assessment includes a risk of bias with "some concerns," including lack of data on several thousand study participants (Comirnaty). The quality of evidence on the prevention of hospitalizations (estimated based on the effect on severe COVID-19 cases) is now also considered to be moderate based on prior controlled trials.

Moderate quality of evidence means that we are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low quality of evidence means that our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect for people over 75 years of age.

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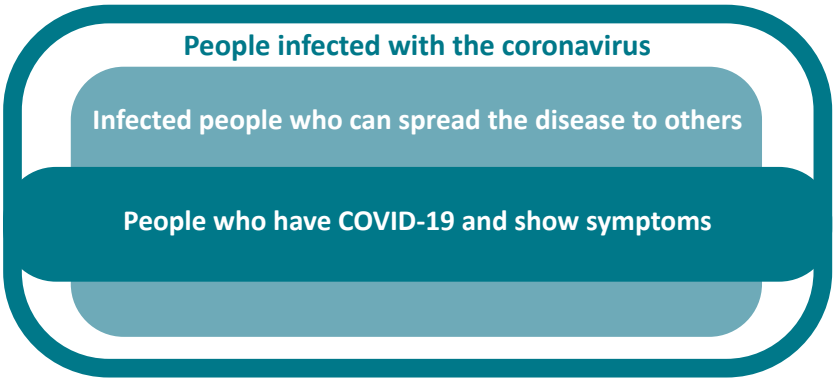
Appendix: Uncertainty regarding the new coronavirus vaccines

Infecting spreading, having COVID-19 – what is the difference?



Becoming **infected** with the coronavirus means that the virus not only enters your body, but also resides in it. However, this does not automatically mean that you can also spread the virus to others. That only happens when the virus has been able to multiply in your body to such an extent that it can be **spreaded** (e.g., by coughing, speaking or singing). But this in turn does not mean that you are sick. Many patients are contagious and spread the virus to other people, yet do not show symptoms at that time (presymptomatic) or do not develop symptoms at all (asymptomatic). When you start to feel or show symptoms that can be attributed to the coronavirus, then you **have COVID-19**.

Does vaccination protect against spreading the coronavirus to other people?

To prevent infections, vaccination must be effective not only against symptomatic infections but also against those without symptoms. In summary, studies from England and Israel show that mRNA vaccination leads to a significant reduction of any infections. Furthermore, fewer viruses are detected in vaccinated people who become infected, and these viruses are detected over a shorter period of time. Although there may be vaccinated individuals who can spread the virus due to an infection, the data suggest significantly reduced transmission due to vaccination [6].

Does vaccination work equally well in everyone?

Vaccination prevents COVID-19 with symptoms in healthy people aged 16 years and older as well as in people with certain underlying diseases. There is currently no vaccine approved for children under 16 years of age because efficacy and safety in children and adolescents have not been adequately studied yet. Additional data on specific groups are needed to reduce uncertainty.

How long does vaccination protect against COVID-19?

This is currently uncertain. Currently, there are no long-term data that allow for a statement about the duration of the protection. In order to reduce uncertainty over a longer period of time, independent observations are being conducted.

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Do people suffer from severe or long-term complications due to vaccination?	During the first two to three months, no long-term complications attributable to vaccination were observed. In rare cases (10 in 1 million vaccinations), there was a severe allergic reaction (anaphylaxis) to the vaccine. Most occurred within 15 minutes of vaccination. 8 out of 10 affected individuals had experienced allergic reactions of varying severity before [12]. Temporary phenomena such as lymph node enlargement and paralysis in one side of the face (facial nerve paralysis) occurred in some cases. Whether there is a causal relationship between the paralysis and vaccination is questionable and requires further research. Currently, there are no long-term data that can be used to make a statement about mid-term and long-term safety. Independent long-term observations are being conducted to reduce uncertainty over a longer period of time. Experience with vaccines over many years has shown that most side effects occur shortly after vaccination.
Do people who get vaccinated become severely ill or die?	Some people will die shortly after being vaccinated, even though the vaccination has nothing to do with their deaths (e.g., through a fatal car accident, cancer or a heart attack). The key point is that disease and death can strike both vaccinated and non-vaccinated people at any time. Provided both groups are affected about equally, a connection to the vaccine can be ruled out. This is ensured by long-term observations of both groups.
Does the faster process of vaccine development and approval (within 10 months instead of up to 10 years) have disadvantages?	All necessary pivotal studies were conducted, but in some cases simultaneously to save time. These studies are of the same quality as pivotal studies for other vaccines. An advantage is that the number of participants included is larger than in comparable studies. On the one hand, this makes it easier to provide conclusive proof of efficacy. On the other hand, this means that rare vaccine side effects may be observed. The fast procedure is furthermore enabled by the wide spread of the coronavirus. For example, if infections were less frequent, the efficacy of the vaccine could only be observed at a very late stage. Data regarding efficacy and safety over a time frame of more than three months still need to be determined in future studies.
Can the vaccine amplify an infection with the coronavirus?	There has been no evidence of an amplification of infection, neither in any animal trial nor in any infected individual from the COVID-19 vaccine studies to date. There is evidence from other diseases (e.g., MERS-CoV, SARS-CoV) of single cases of infection-amplifying antibodies that may be formed after having these diseases or after vaccination. These antibodies would make it easier for viruses to penetrate cells and multiply in the body. A research paper on this subject, which should further reduce uncertainty, is currently in progress at the Paul Ehrlich Institute [13].

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Can messenger RNA, which induces the production of viral components, alter the human genetic makeup?	Messenger RNA cannot be incorporated into human genetic material because it does not enter the cell nucleus. Messenger RNA is always distributed in numerous variants throughout the body, which is why cell nuclei are inherently protected from it. Moreover, RNA cannot be integrated into the genetic material because of its different chemical structure [13].
Which is the best vaccine for whom?	Generally, the available mRNA vaccines are to be regarded as equivalent. This means that they are comparably effective and safe according to the study results. The vaccines have not yet been tested against each other.
Can I get vaccinated if I have pre-existing conditions?	studies show no evidence of relevant differences in vaccine efficacy and safety between people with and without pre-existing conditions. For example, more than 7,700 participants with pre-existing conditions, such as respiratory, nervous, and cardiovascular impairments, as well as diabetes mellitus, were included in the phase II/III trials of Comirnaty (BioNTech/Pfizer). Regarding potential benefits, it should also be considered that pre-existing conditions such as atrial fibrillation, heart failure, coronary artery disease, diabetes mellitus, obesity, chronic kidney and liver disease, cancer, COPD, and central nervous system and autoimmune diseases also increase the risk of dying from COVID-19 [6]. Explicitly excluded from the studies were people with known drug allergies or immune deficiencies. For these people, the data available to date is insufficient, which means that no specific statement can be made regarding efficacy and safety.
Am I immune to the coronavirus (SARS-CoV-2) after an infection?	This is uncertain. One study examined COVID-19 patients with asymptomatic to severe courses over up to eight months. Different parts of the immune system showed varying degrees of stability over the period since disease onset [14]. It is still uncertain how strong the immune response based on this would be after eight months or longer periods. Based on experience with other coronaviruses, there is evidence that the quality and extent of infection affects the response of the immune system and also its "memory" with respect to future disease.

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