Eleven things you need to know NOW about COVID-19 (As of November 2021)

Number of cases and virulence of COVID-19

- 1. How many people have been diagnosed with COVID-19 in Japan?
- 2. How many people will become very sick or die after being diagnosed with COVID-19?
- 3. Who is at higher risk for developing severe COVID-19 illness ?
- 4. Is the number of individuals diagnosed with COVID-19 higher in Japan than in other countries?

Infectivity of COVID-19

- 5. How long does a person with COVID-19 remain infectious?
- 6. Does everyone with COVID-19 infect others?
- 7. What precautions should we take to prevent the spread of COVID-19?

Testing and Treatment for COVID-19

- 8. What tests are being used to diagnose COVID-19?
- 9. What are the treatment options for COVID-19?
- 10. Which COVID-19 vaccine is used in Japan?

Variants of COVID-19

11. What is known about the COVID-19 variants?

1. How many people have been diagnosed with COVID-19 in Japan?

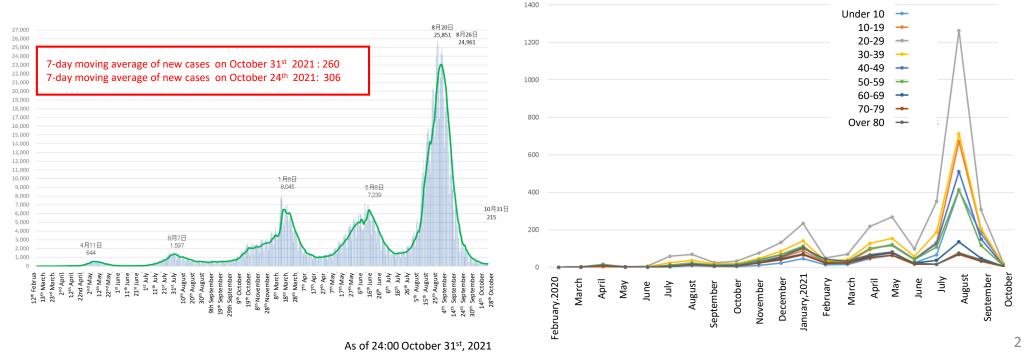
As of 0:00 November 1st 2021, **1,718,417 people have been diagnosed with COVID-19 in Japan. This accounts for 1.4%** of the total population.

For latest updates, please refer to the following link: <u>https://www.mhlw.go.jp/stf/covid-19/kokunainohasseijoukyou.html</u>

*The number of cases include only those who tested positive. Therefore it may miss those people who were actually infected but without symptoms and therefore did not seek medical care.

Number of newly confirmed cases per 100,000 population

Number of newly confirmed cases per 100,000 population by age group



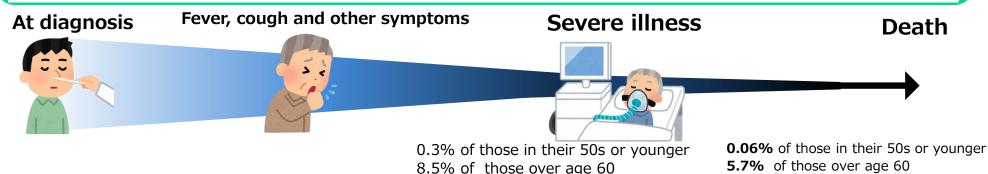
2. Among those diagnosed with COVID-19, how many people will get very sick or die?

Among those diagnosed with COVID-19, proportion of individuals getting severely ill or die significantly differs by age; overall severity and case fatality rates seem to have been in declining trends compared to those at the beginning of the pandemic.

Among those diagnosed with COVID-19 after June 2020,

• Severity rate is approximately 1.6% (0.3% in those in age 50 or younger, 8.5% in those over 60s)

• Case fatality rate is approximately 1.0% (0.06% in those in age 50 or younger, 5.7% in those over 60s) * "Severe illnesses" include either one or more of followings: admission to the Intensive Care Units, use of respirators, or deaths.



Severity rates among newly diagnosed cases (%)

Case fatality rates among newly diagnosed cases(%)

Age Month	<10	10 -19	20 -29	30 -39	40 -49	50 -59	60 -69	70 -79	80 -89	90-	Total	Age Month	<10	10 -19	20 -29	30 -39	40 -49	50 -59	60 -69	70 -79	80 -89	90-	Total
JunAug.	0.09	0.00	0.03	0.09	0.54	1.47	3.85	8.40	14.50	16.64	1.62	JunAug.	0.00	0.00	0.01	0.01	0.10	0.29	1.24	4.65	12.00	16.09	0.96
Jan.−Apr.	0.69	0.90	0.80	1.52	3.43	6.40	15.25	26.20	34.72	36.24	9.80	JanApr.	0.00	0.00	0.00	0.36	0.61	1.18	5.49	17.05	30.72	34.50	5.62

Source: Tables created from data presented at the 11th Advisory Board (Presented by Professor Nishiura, Kyoto University) on October 22nd, 2020

3. Among those diagnosed with COVID-19, who is at increased risk for severe illness and death ?

Among those diagnosed with COVID-19, **the elderly, those with underlying medical conditions, and some pregnant women in their third trimesters are more likely than others to develop severe illness or die.**

Comorbidities known to cause more severe illness include:

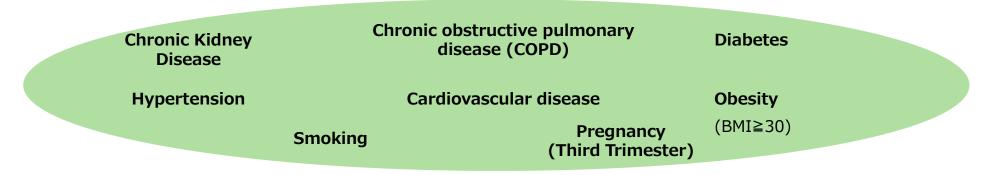
Chronic Obstructive Pulmonary Diseases (COPD), Chronic Kidney Diseases, Diabetes, Hypertension, Cardiovascular diseases, Obesity, and Smoking.

Full vaccination (two doses) is effective in preventing severe illness.

Proportion of individuals becoming severely ill by age group (shown as a relative risk when the risk of those in their 30s is considered as a reference (1.00))

Age	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	90+
Severity rates	0.5	0.2	0.3	1	4	10	25	47	71	78

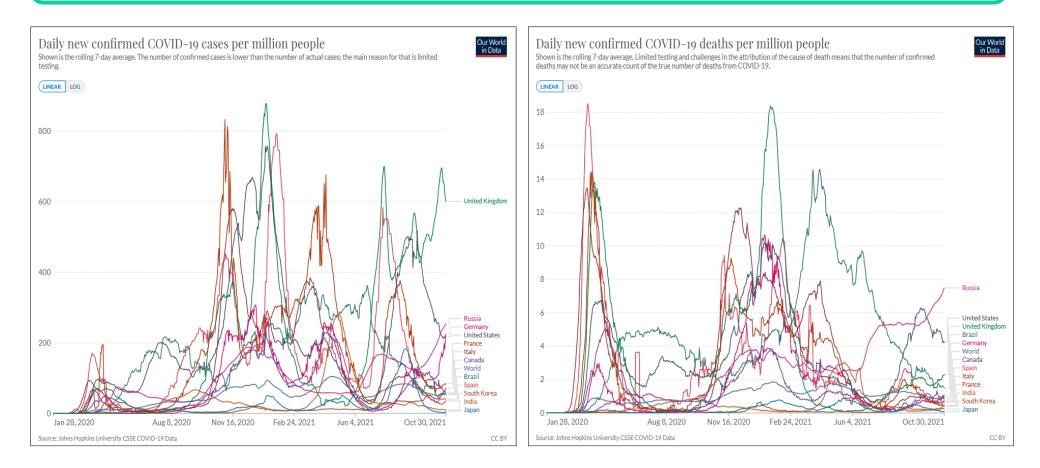
Comorbidities known to cause more severe illness:



*Table created from data presented by Professor Nishiura, Kyoto University, 4 and from the "Clinical Management of Patients with COVID-19" Version 6.0

4. Is the number of individuals diagnosed with COVID-19 higher in Japan than in other countries ?

The number of confirmed cases and deaths per 1 million population in Japan have remained low compared to other countries.



Individuals with COVID-19 become infectious from **2 days prior to until approximately 7 to 10 days** after the onset of symptoms.*

Viral shedding is believed to be particularly high around the time of symptom onset.

Therefore, individuals diagnosed with COVID-19 should **refrain from going out for non-urgent reasons, regardless of symptoms, to stop the spread of infection**.

* From "Clinical Management of Patients with COVID-19." Version 6.0

6. What proportion of individuals with COVID-19 ends up infecting others?

Less than 20% of individuals diagnosed with COVID-19 infect others, while others do not.

Therefore, unless a super-spreading event where an individual with COVID-19 infect many others in an environment like 3Cs without proper precautions happens, spread of SARS-CoV-2 (which causes COVID-19) could be controlled.

You are strongly encouraged to take precautions such as not going out for nonurgent purposes when you are sick, and wearing a mask when meeting with others.

*Wearing masks reduce the amount of virus inhaled by individuals in close proximity to those with COVID-19. (By 60-80% when worn by individuals with COVID-19, and by 20-40% when worn by someone contacting with individuals with COVID-19).

Ueki, H., Furusawa, Y., Iwatsuki-Horimoto, K., Imai, M., Kabata, H., Nishimura, H., & Kawaoka, Y. (2020). Effectiveness of Face Masks in Preventing Airborne Transmission of SARS-CoV-2. mSphere, 5(5), e00637-20.

7. What precautions should we take to prevent the spread of COVID-19?

SARS-CoV-2 (a virus known to cause COVID-19) is generally thought to be transmitted by droplets or by close contact with an infected individual. This is why the risk of infection increases in a 3Cs (Closed spaces, Crowded places, Close-contact settings) environment.

Situations such as social gatherings, long feasts in large groups, having conversation without masks, living together in small limited spaces, and switching locations also increase the risk of infection and should be avoided.

"5 situations" that increase the risk of infection

Situation ① Social gatherings with drinking alcohol

Drinking alcohol improves mood and at the same time decreases attention. In addition, hearing is dulled and it leads to speaking in a louder voice. The risk of infection increases when large numbers of people are in a small space for a long time. In addition, sharing glasses and chopsticks increases the risk of infection.



Long feasts in large groups

Long-term meals, dinner receptions, drinking alcohol at night increase the risk of infection compared to a short meal.

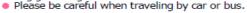
The risk of infection is increased by eating and drinking in a large group of people, for example, 5 or more people, because in groups you have to talk louder and droplets of saliva spread more often.



Conversation without a mask

Talking at close range without a mask increases the risk of airborne or micro-droplet infection. Cases of infection without masks were observed during gatherings in karaoke machines.

Situation ③



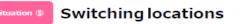


Living together in a small limited space

Living together in a small limited space increases the risk of infection because the enclosed space is shared by several people for a long time.

There have been reports of suspected infections in common areas such as dormitory bedrooms and bathrooms.





When you move to another location, such as when you take a break in a workplace, the risk of infection may increase due to the feeling of relaxation and changes of the environment.

Suspicious cases of infection were identified in breaking rooms, smoking areas and changing rooms.



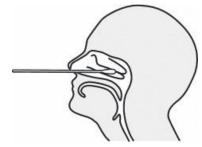
Tests for diagnosing COVID-19 include Nucleic acid detection tests (including PCR test), qualitative antigen test, and quantitative antigen test. These tests are all designed to detect SARS-CoV-2 virus (which causes COVID-19) in one's body and therefore can be used to see if someone is currently infected with the virus. Recent development of new method has enabled use of saliva and nasal cavity swab samples in selected situations and selected patient groups.

Antibody tests are only used to see if a person has previously been infected with SARS-CoV-2 (virus that causes COVID-19). Antibody tests are not for use to diagnose acute infection.

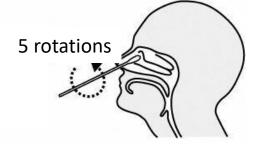
			acid detec uding PCR	tion tests (test)		Antigen te Quantitati		Antigen test (Qualitative)			
Intended to use for…		Nasopharynx	Nasal cavity	Saliva	Nasopharynx	Nasal cavity	Saliva	Nasopharynx	Nasal cavity	Saliva	
Symptomatic	Within 9 days of symptom onset	\bigcirc	\bigcirc	0	\bigcirc	\bigcirc	0	○ *1	○ *1	×	
Individuals	10 days or more from symptom onset	0	0	×	0	\bigcirc	×	[∆] ∗2	△ *2	×	
Asymptomatic individuals		0	×	\bigcirc	0	×	\bigcirc	× *3	× *3	×	

* 1 Additional Nucleic acid detection tests (e.g. nasopharyngeal PCR tests) is advised when tested negative. *3 Not advised to use for confirmatory tests. Can be used as screening tests in limited settings such as hospitals or nursing homes in disease spreading areas on condition that preventive measures should still be continued for individuals tested negative.

Example of Specimen Collection for Qualitative Antigen Test



Insert a swab through the nose and rub th nasopharynx several times (Performed by a healthcare provider, only)



Insert a swab about 2 cm from the nose, rotate it 5 times, and let it stand for about 5 seconds. (Self specimen collection is possible)

Nasopharyngeal specimen collection

Nasal cavity Specimen collection

9. What are the treatment options for COVID-19?

Most patients with mild COVID-19 recover without any specific treatment. So only supportive therapy such as antipyretics would be provided when necessary. In case of respiratory failure, oxygen therapy along with antivirals, steroids(to control inflammation), immunomodulators, and neutralizing antibodies^{**1} will be given. And if not responding well enough, intensive care with mechanical ventilation might be an option. Establishment of treatment options described above seems to have resulted in low case fatality rates for the hospitalized COVID-19 patients. Be sure to consult your GP or nearby clinic in case you have fever, cough or symptoms suggestive of COVID-19.

*1 As of November 1st 2021, drugs approved for the treatment of COVID-19 in Japan include Remdesivir (Veklury®), Dexamethasone, Baricitinib (olumiant®), Casirivimab/Imdevimab (Ronapreve®), and Sotrovimab (XEVUDY®, newly approved as fast-track approval on September 27th, 2021).

* 2 The percentage of COVID-19 cases who require intensive care or die is about 1.6% (0.3% for those in their 50s or younger, 8.5% for those in their 60s or older).

Treatment trends and case-fatality rates for hospitalized patients with COVID-19 (Results from the COVID-19 Registry Japan* 4)

Results showed that cases admitted after June 2020, compared to those before June 2020,

- were more likely to be treated using Remdesivir (approved for the treatment of COVID-19) and steroids.
- had lower case-fatality rates in all severity groups (mild, moderate, and severe) in all age groups.

Mild / moderate cases at admission

Severe cases at admission ^{** 5}

		Admitted before June 1st, 2020	Admitted from Jun. 1 st to Dec. 31st, 2020			Admitted before June 1st, 2020	Admitted from Jun.1 to Dec. 31, 2020
Medication	Remdesivir ^{% 6}	0.4%	13.9%	Madiantian	Remdesivir	1.3%	39.2%
Administered	Steroids (Expect for Ciclesonide)	6.9%	40.3%	Medication Administered	Steroids (Expect for Ciclesonide)	26.0%	74.1%
Case fatality	0-29	0.0%	0.0%		0-29	1.9%	0.0%
Case-fatality rates after	30-49	0.2%	0.1%	Case-fatality rates after	30-49	1.3%	0.6%
admission (by	50-69	1.3%	0.3%	admission	50-69	9.1%	3.7%
age group)	70-	9.7%	5.7%	(by age group)	70-	30.0%	17.3%
	All ages	2.4%	1.3%		All ages	17.1%	9.8%

*4. Based on data registered by February 15th, 2021 to the "COVID-19 Registry Japan (Principal Investigator: Dr. Norio OHMAGARI)" (Funded by the Health and Labour Sciences Research Grants)

*5. "Severe cases at admission" refers to either one or more of the followings: On supplemental oxygen therapy, On ventilators, SpO2(Oxygen Saturation) of 94% or less on room air, or respiratory rates \geq 24 breaths per minute.

*6. Only include administration of drugs for the treatment of COVID-19. For steroids, pre-admission use for purposes other than COVID-19 is excluded.

COVID-19 vaccine

As of November 1st 2021, three COVID-19 vaccines developed by Pfizer Inc., Takeda/Moderna Inc. and AstraZeneca plc are being rolled out in Japan.

The Pfizer and Modena vaccines, which are messenger RNA vaccines, are given to people over 12 years of age.

The AstraZeneca vaccine, which is a viral vector vaccine, is generally given to people over 40 years of age (\times 1).

% Individuals over 18 years old may also be eligible for this vaccine in some cases.

OEfficacy

All these vaccines are effective in preventing COVID-19. Vaccinated individuals were reported to be less likely to develop COVID-19 symptoms (such as fever or coughs) compared to unvaccinated individuals (Vaccine Effectiveness is reported to be around 70%-95%*) In addition, research results suggesting the infection-preventive effects of COVID-19 are accumulating.

○Safety

*Source: Package inserts of COMIRNATY, COVID-19 Vaccine Moderna and VAXZEVRIA

Localized pain in the injected sites, fatigue, and headache have been reported to occur in more than 50%, and muscle and joint pain, chills, diarrhea, and fever in more than 10% of vaccinated individuals. Most of these symptoms subside within a few days. Cases of anaphylaxis (an acute allergic reaction) have also been reported. Vaccination sites, clinics or hospitals providing vaccination are equipped with medicine and other supplies to respond immediately in case of anaphylaxis.

Vaccination Rate	12~19	20's	30's	40's	50's	60~64	65~69	70's	80's	90's	Over 100
First dose	66.89%	69.17%	72.25%	78.52%	86.05%	88.13%	88.56%	93.20%	95.00%	93.65%	88.29%
Fully vaccinated	47.78%	57.06%	60.82%	70.04%	80.45%	85.12%	87.41%	92.25%	93.90%	92.15%	86.09%

Vaccination status in Japan	(As of October 25 th ,2021)
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Number of Vaccinations	12~19	20's	30's	40's	50's	60~64	65~69	70's	80's	90's	Over 100
Population	9,010,292	12,819,569	14,372,705	18,424,463	16,810,584	7,412,109	8,098,283	16,227,232	9,058,480	2,303,363	80,636
First dose	6,026,586	8,866,820	10,384,760	14,466,393	14,465,320	6,532,162	7,171,815	15,124,209	8,605,183	2,157,181	71,192
Fully vaccinated	4,305,468	7,315,157	8,740,955	12,903,589	13,523,276	6,309,324	7,079,091	14,969,554	8,506,066	2,122,435	69,417

Source: Webpage of Prime Minister's Office of Japan

11. What is known about the SARS-CoV-2 (virus that causes COVID-19) variants?

Viruses usually mutate and change gradually over time as they grow or spread. This leads to the emergence of new variants. SARS-CoV-2(virus that causes COVID-19) is believed to show approximately one base mutation in two weeks. Currently such newly emerging variants of SARS-CoV-2 have continuously been reported from all around the world and **we have to be more vigilant on such new variants than before.**

In Japan, B.1.617.2 lineage (Delta variant) becoming more and more prevalent, and the infection rate of Delta variant in variant PCR tests nationwide is about 90% (estimate). Recently, the percentage of delta variant is estimated to be close to 100% in many areas, suggesting that they have replaced B.1.1.7 lineage (Alpha variant).

In response to this, the Ministry of Health, Labour and Welfare (MHLW) has been conducting a nationwide genomic sequencing of the SARS-CoV-2 to monitor for the variants. The MHLW communicates closely with the World Health Organization (WHO) and experts to analyze and characterize variants, and is strengthening the national surveillance system. The MHLW also strengthens its testing capacity and epidemiological investigation (tracing) when cases of such variants are reported to prevent further spread.

Preventive measures such as avoiding the "three Cs" (and "Five situations" that increase the risk of infection), wearing masks, and washing hands remain as effective against the variants. Therefore individuals are strongly encouraged to continue taking these precautions.

*1. B.1.617 lineage (Delta variants) was first detected in India in October, 2020.