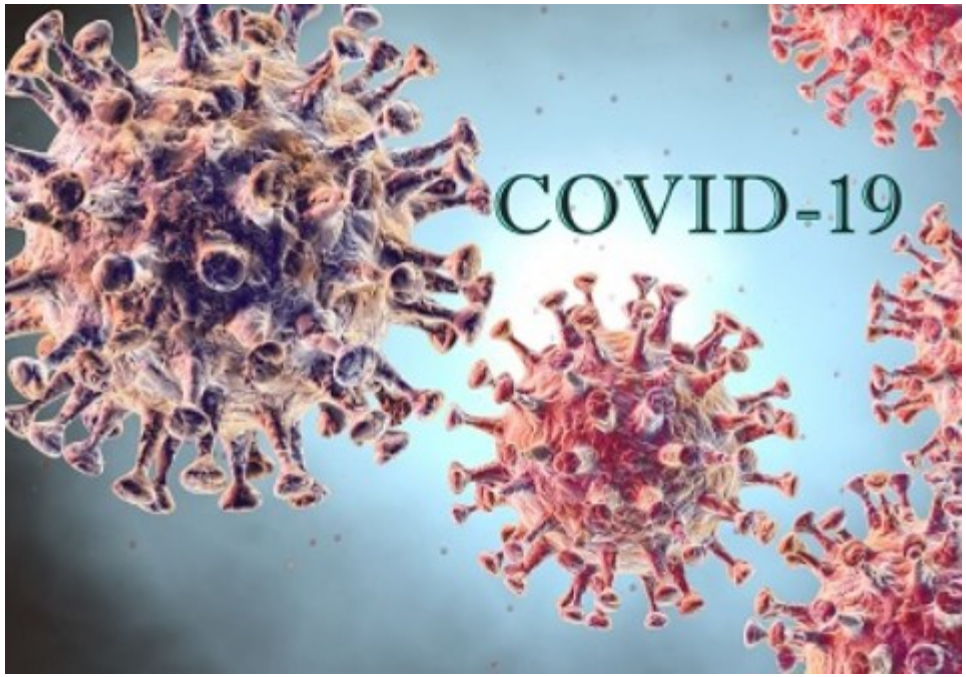
# Implicazioni dei vaccini per la salute pubblica




# Covid 19 2021

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# *Coronavirus*

- I Coronavirus di interesse medico sono stati scoperti negli anni ‘60, rinvenuti nelle cavità nasali di pazienti affetti da raffreddore comune.

- Questi «vecchi» Coronavirus sono attualmente conosciuti sia come residenti abituali di molte specie animali, sia come responsabili di patologie nei mammiferi e negli uccelli:

    - Gastroenteriti con diarrea nei bovini, nei suini, nei felini con possibilità di evoluzione fino a quadri di sepsi letale

    - Malattie respiratorie delle vie superiori nel pollame.

- Nell'uomo solitamente provocano infezioni delle alte vie respiratorie. Quando interessano le basse vie determinano polmoniti interstiziali generalmente autolimitanti, molto raramente gravi.

# *Coronavirus* LA STORIA

Fino al 2002 sono stati ai margini dell'interesse scientifico, in quanto causa di episodi infettivi per lo più banali a carico delle vie aeree superiori (rinite).

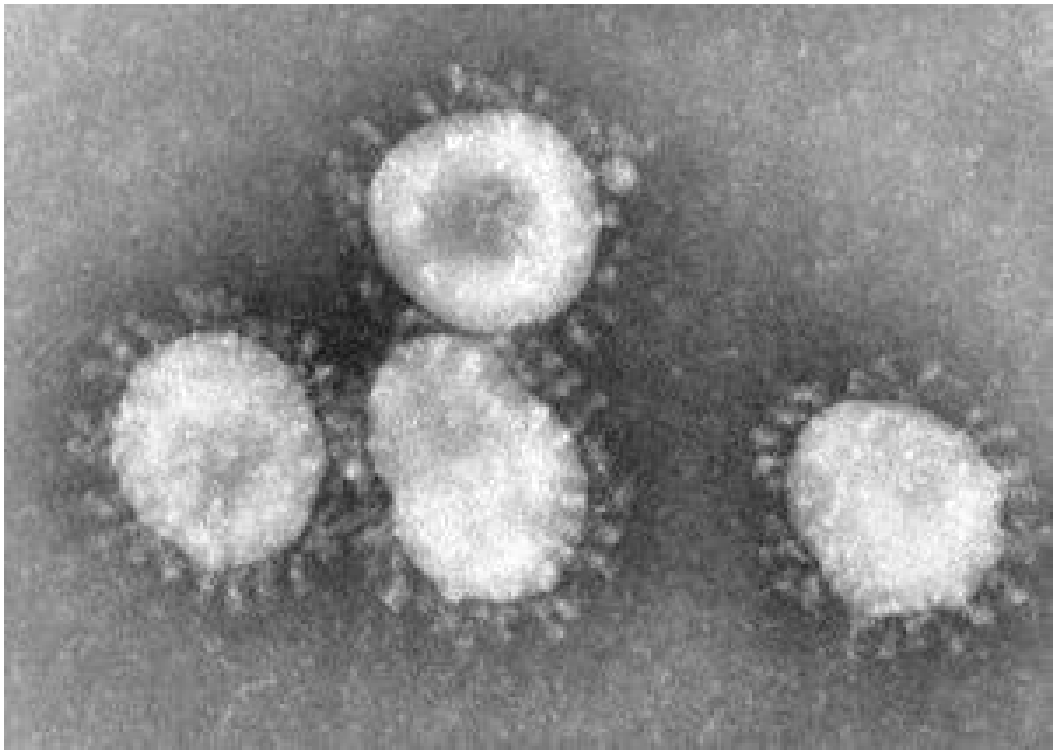
Ciò nonostante, per ragioni di ordine classificativo, ne erano stati caratterizzati 4 tipi su base molecolare:

**HCoV 229E**

**HCoV OC43**

**HCoV NL63**

**HCoV HKU1**



# COVID-19 - L’inizio

- Iniziata UFFICIALMENTE intorno alla fine di dicembre 2019 nella città di Wuhan, capoluogo della provincia cinese dell'Hubei, e successivamente diffusasi in quasi tutte le nazioni del mondo (PANDEMIA).

- I primi casi hanno coinvolto principalmente lavoratori del mercato del pesce di Wuhan, nel quale sono in vendita anche di animali vivi, tra cui mammiferi, alcuni dei quali vengono sacrificati in presenza del compratore.

- Nelle prime settimane di gennaio 2020 gli scienziati hanno isolato in questi soggetti un nuovo Coronavirus, dapprima designato come 2019-nCoV (Nuovo Coronavirus 2019) e, successivamente, SARS-CoV-2 (sequenza genica simile almeno all'85-90% a  quella del SARS-CoV).

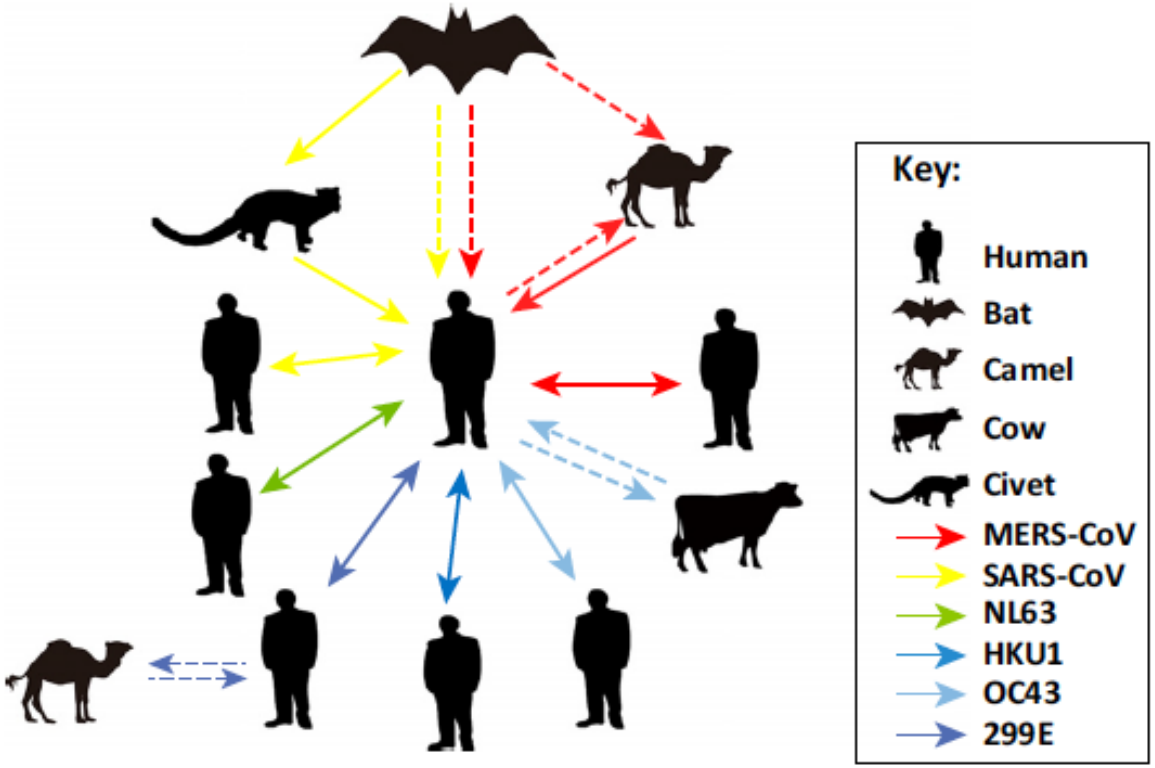
- La malattia associata è stata denominata COVID-19.

# L’ORIGINE del SARS-CoV-2

- Gli studi condotti fin ora suggeriscono che SARS-CoV-2 sia stato trasmesso dai pipistrelli
- In effetti la sequenza genetica di SARS-CoV-2 indica una chiara parentela con virus isolati da un pipistrello del genere Rhinolophus, più noto come ‘Ferro di cavallo’.
- Inizialmente si pensava che il pangolino fosse l’animale che aveva consentito il salto di specie, ma gli studi successivi lo hanno ‘scagionato’. Il pangolino è un animale in via d’estinzione che viene commercializzato per le squame di cheratina e la cui carne viene mangiata in Cina e in Vietnam.

# Images of the Wuhan Market from the Web

**Intra- and Inter-Species Transmission of Human Corona-viruses.** Red, yellow, green, blue, brown, and purple arrows represent transmission of MERS-CoV, SARS-CoV, NL63, HKU1, OC43, and 229E, respectively, between bats, camels, cows, humans, and masked palm civets (shown in a legend on the side of the figure). Unbroken arrows represent confirmed transmission between the two species in question, and broken arrows represent suspected transmission.



Epidemiology, Genetic Recombination, and Pathogenesis of Coronaviruses

Shuo Su,[1,*] Gary Wong,[2,3,4] Weifeng Shi,[5] Jun Liu,[4,6] Alexander C.K. Lai,[7] Jiyong Zhou,[1] Wenjun Liu,[3,4] Yuhai Bi,[2,3,4,*] and George F. Gao[2,3,4,6,8,9,*]

Trends in Microbiology, June 2016, Vol. 24, No. 6

## Concluding Remarks

…….it is likely not a matter of **if**, but **when**, the next recombinant CoV will emerge and cause another outbreak in the human population……

# COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU)

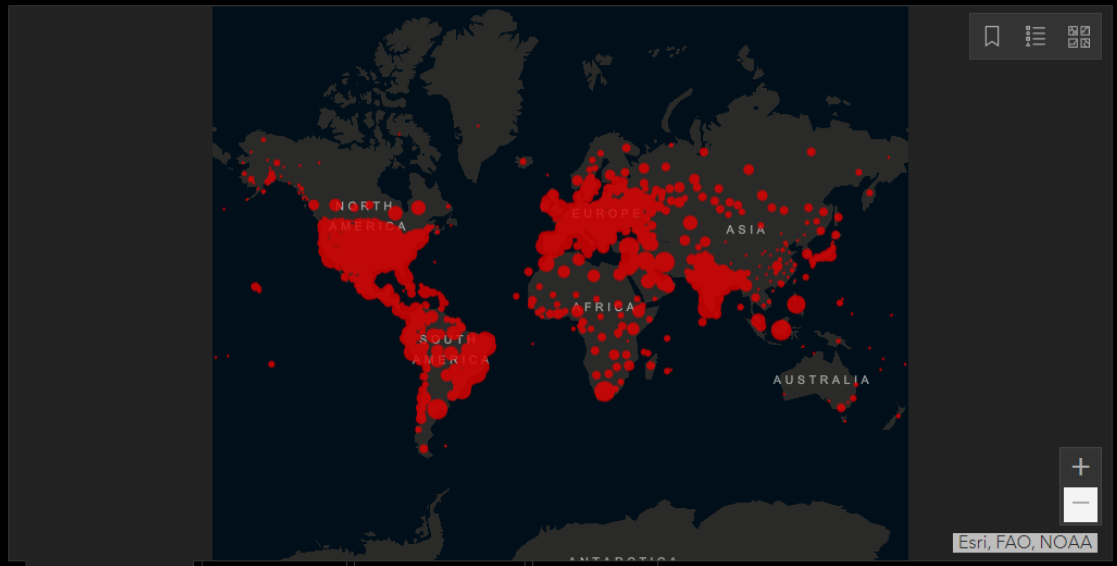
Global Cases
120.390.929

Cases by Country/Region/Sovereignty

29.502.485 US
11.519.609 Brazil
11.409.831 India
4.360.033 Russia
4.276.847 United Kingdom
4.132.151 France
3.238.394 Italy
3.195.062 Spain
2.894.893 Turkey

Admin0

Last Updated at (M/D/YYYY)
3/16/2021, 5:26 PM




Cumulative Cases | Incidence Rate | Case-Fatality Ratio | Testing Rate

192
countries/regions

*Lancet Inf Dis* Article: Here. Mobile Version: Here. Data sources: Full list. Downloadable database: GitHub, Feature Layer.
Lead by JHU CSSE. Technical Support: Esri Living Atlas team and JHU APL. Financial Support:

Global Deaths
2.663.741

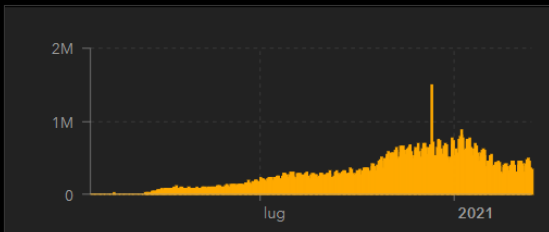
535.994 deaths
US
279.286 deaths
Brazil
194.944 deaths
Mexico
158.856 deaths
India
125.817 deaths

Global Deaths

Total Test Results in US
374.442.857

51.263.837 tests
California US
41.323.595 tests
New York US
22.930.335 tests
Florida US
20.406.104 tests
Texas US
19.170.243 tests

US Test Results



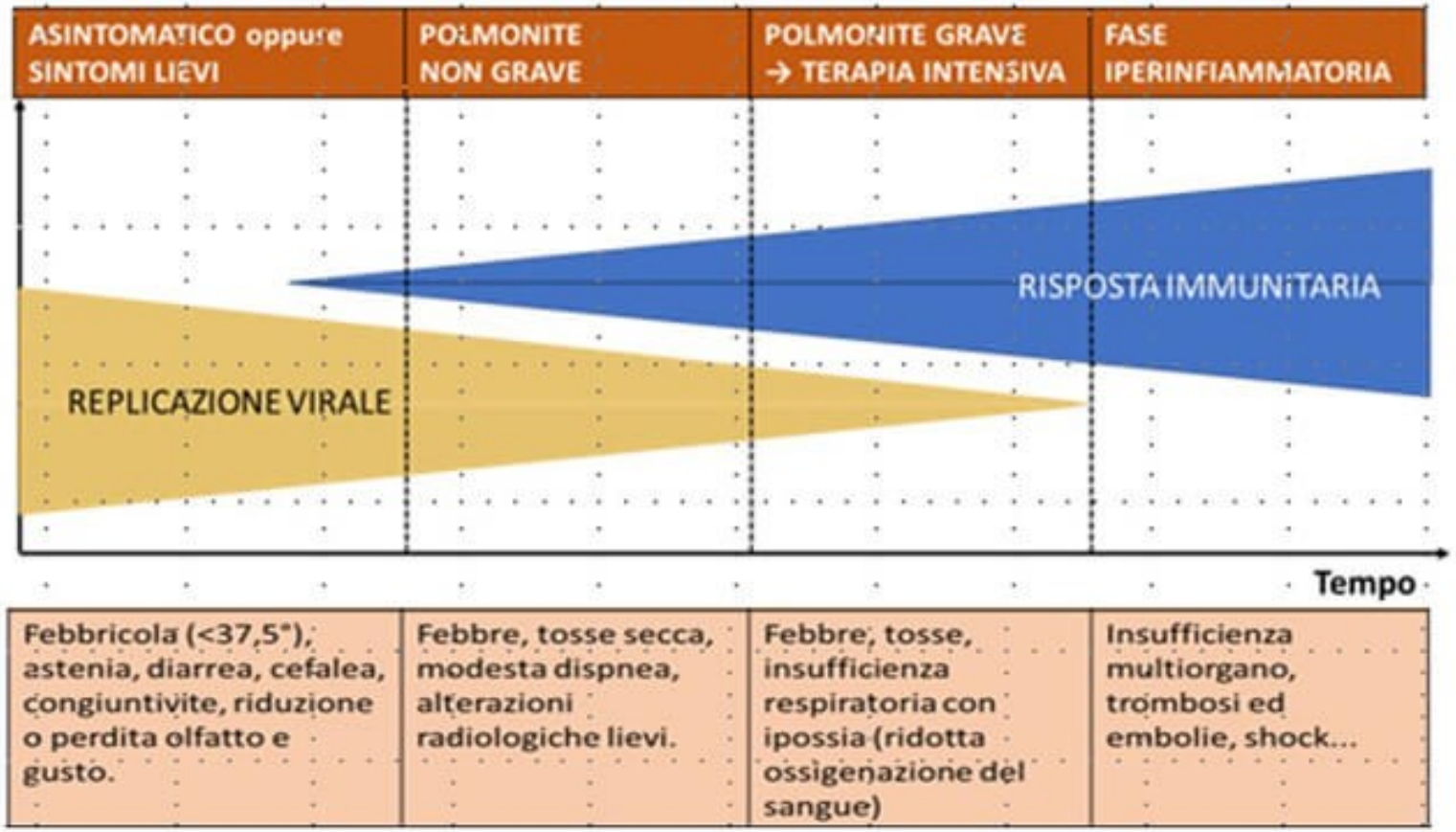

Daily Cases

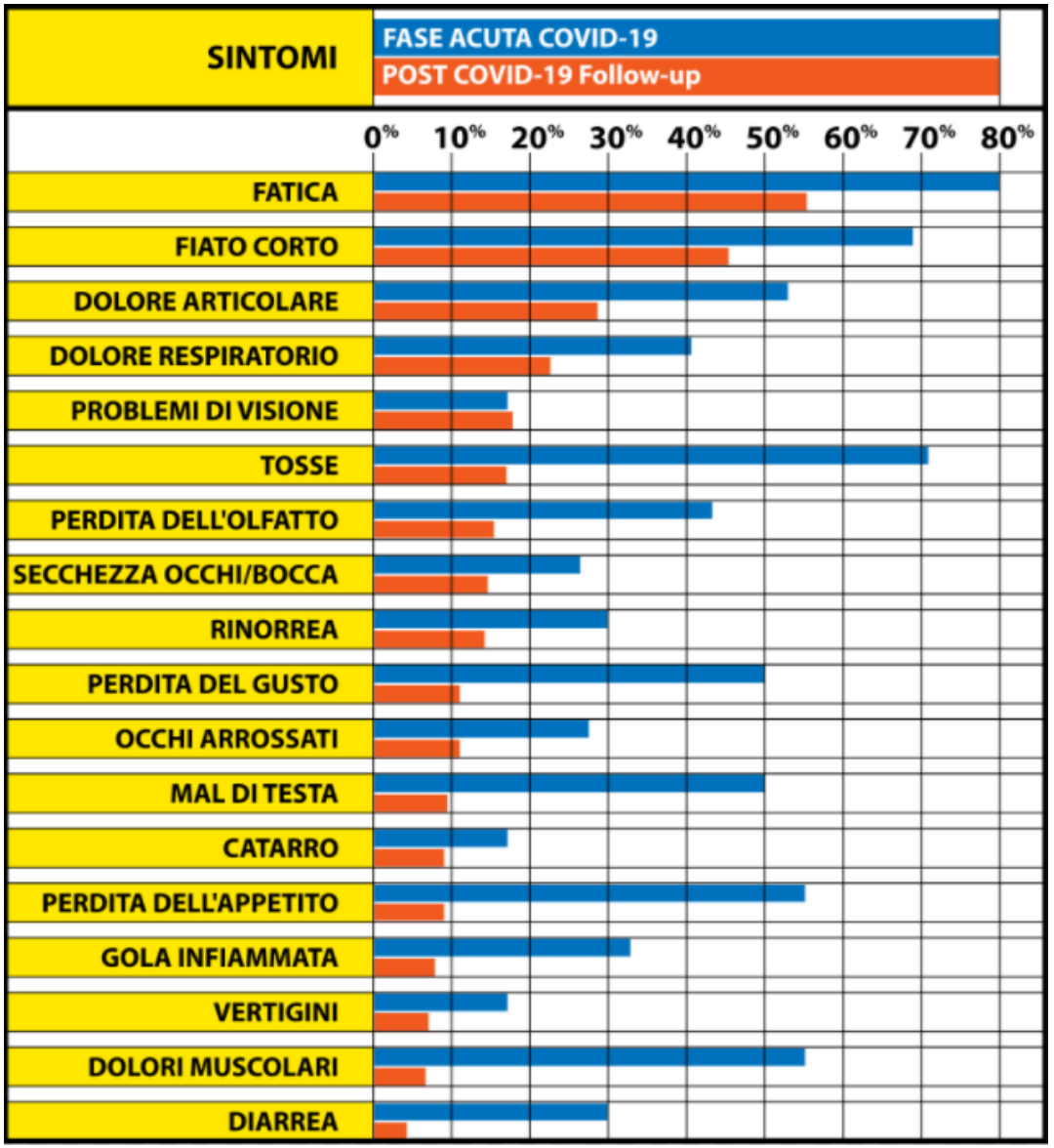
due cenni di

# CLINICA

**Il periodo di incubazione** varia dai 2 ai 14 giorni con un periodo medio di 5-6 giorni.

# COVID-19: le fasi della malattia




SINTOMI
FASE ACUTA COVID-19
POST COVID-19 Follow-up
0%
10%
20%
30%
40%
50%
60%
70%
80%
FATICA
FIATO CORTO
DOLORE ARTICOLARE
DOLORE RESPIRATORIO
PROBLEMI DI VISIONE
TOSSE
PERDITA DELL'OLFATTO
SECCHEZZA OCCHI/BOCCA
RINORREA
PERDITA DEL GUSTO
OCCHI ARROSSATI
MAL DI TESTA
CATARRO
PERDITA DELL'APPETITO
GOLA INFIAMMATA
VERTIGINI
DOLORI MUSCOLARI
DIARREA

Benchè siano numerose le sofferenze d'organo descritte in corso di COVID-19, è a carico dei **polmoni** che si realizzano i quadri clinici di maggior gravità;

La compromissione di numerose aree polmonari riduce la capacità ventilatoria dei pazienti e comporta la necessità di **ASSISTENZA VENTILATORIA;**

Questa può realizzarsi con il semplice uso degli **occhialini/cannule nasali** (arricchimento in ossigeno dell'aria inspirata), con l'uso di **maschere respiratorie** (e.g. maschera di Venturi), con il ricorso alla **CPAP** (continuous positive air pressure) con uso di caschi respiratori;

I casi più gravi richiedono l'intubazione.

## Casi

Totale | Italia

| Casi | Guarigioni | Decessi |
| --- | --- | --- |
| 3,24 Mln | 2,61 Mln | 102.000 |
| +15.252 | +15.807 | +354 |

| Luogo | Casi ↓ | Guarigioni | Decessi |
| --- | --- | --- | --- |
| **Marche** | **78.590** | **65.726** | **2.422** |
| | +415 | +872 | +11 |

# Il problema delle VARIANTI virali

## SARS-CoV-2 è mutato?

- Ad oggi, i ricercatori hanno identificato numerose varianti principali di SARS-CoV-2 e numerosissime varianti minori

# Perché SARS-CoV-2 sta mutando?

- I Coronavirus, come tutte le specie viventi, cercano di moltiplicarsi
- Per **moltiplicarsi più rapidamente** cercano di diventare più diffusivi, ossia più contagiosi (in pratica ottengono questo migliorando le capacità di adesione alle cellule dell'ospite, l'efficienza dei meccanismi di moltiplicazione endocellulare, ecc..)
- Inoltre cercano di mutare, ossia cambiare, per non essere più riconosciuti dai **meccanismi di difesa dell'ospite**
- Peraltro, le mutazioni possono aiutare i virus a sfuggire all'azione dei **farmaci** (il virus modifica il bersaglio dei farmaci)
- Infine, non va dimenticata la pressione selettiva esercitata dai **vaccini**: vengono in pratica selezionati (avvantaggiati) i virus che meno risentono dell'azione degli anticorpi

# Nella pratica clinica:
# Le mutazioni virali possono ridurre l'efficacia dei farmaci?

- **NO** per quelli che agiscono sui meccanismi fisiopatologici umani (cortisteroidi, antipiretici, antidolorifici, antinfiammatori, integratori, ecc.)

- **SI'** per quelli che agiscono direttamente sul virus se la mutazione riguarda il bersaglio del farmaco

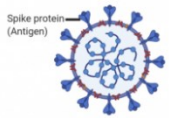
# TYPES OF VACCINES

## Live Attenuated Vaccine

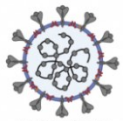
These vaccines contain **live virus** particles that have been **weakened** to keep them from causing disease.

They create a strong immune response

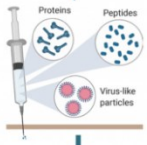
Some attenuated vaccines might not be suitable for people with compromised immune systems

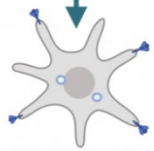



Disease-causing virus



Weakened virus



Antigen is presented to the immune cells on **Antigen Presenting Cells**

**Immune Response and Memory**

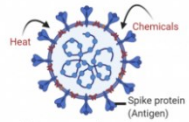
**Currently used in:**
MMR (Measles/mumps/rubella)
Chickenpox
**COVID vaccines in the pipeline:**
Codagenix; Indian Immunologicals Ltd

## Inactivated Vaccine

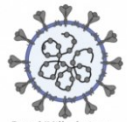
These vaccines contain **whole virus particles**, that have been **killed or inactivated** to keep them from causing disease.

They are safer as the virus is already dead

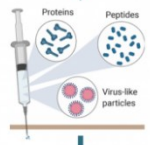
Inactivated vaccines require booster doses as the immunity conferred by these vaccines is weaker than live vaccines

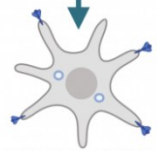



Disease-causing virus



Dead/Killed virus



Antigen is presented to the immune cells on **Antigen Presenting Cells**

**Immune Response and Memory**

**Currently used in:**
Polio
**COVID vaccines in the pipeline:**
Sinovac; Sinopharma; Bharat Biotech

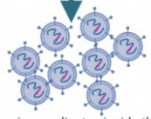
## Replicating Viral Vector Vaccine

These vaccines use **low-pathogenic viruses**, which are largely harmless, and alter them into **viral vectors** that will produce some of the same proteins as the disease-causing virus.

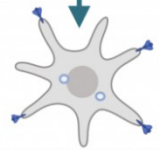
This creates a **strong immune response**, but may not work for people who are already immune to the low pathogenic virus.

Disease-causing virus  Low - pathogenic virus

Viral vector encoding target antigen



The virus replicates inside the body



Antigen is presented to the immune cells on **Antigen Presenting Cells**

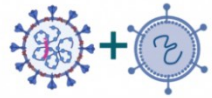
**Immune Response and Memory**

**Currently used in:**
Used in veterinary medicine
**COVID vaccines in the pipeline:**
Themis Bioscience; University of Pisttsburg

## Non-Replicating Viral Vector Vaccine

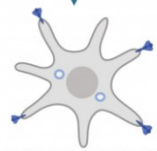
These vaccines are **similar** to **replicating viral vector** vaccines except that they **cannot replicate** inside the body as the key viral replication genes is deleted from the low pathogenic vector virus.

Improved **efficacy and safety,** but require high doses to confer immunity.



Disease-causing virus  Low - pathogenic virus

Viral vector encoding target antigen



Antigen is presented to the immune cells on **Antigen Presenting Cells**

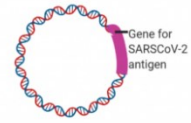
**Immune Response and Memory**

**Currently used in:**
Ebola
**COVID vaccines in the pipeline:**
University of Oxford and & AstraZeneca

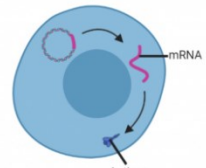
## DNA Vaccine

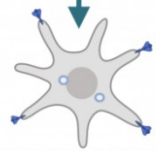
These vaccines use **DNA plasmids** containing a **gene for SARSCoV-2** along with additional genetic elements that will produce some of the same **antigenic proteins** as the disease-causing virus.

They are easy to develop and produce. There is no risk of infection but there is a possibility that the immune system does not fight against the antigen (tolerance to the antigen).




DNA Plasmid



Antigen is presented to the immune cells on **Antigen Presenting Cells**

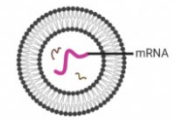
**Immune Response and Memory**

**Currently used in:**
No currently available human DNA vaccines
**COVID vaccines in the pipeline:**
Inovio;Genexine;Zydus cadila

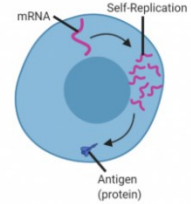
## RNA Vaccine

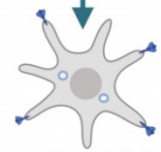
These vaccines use a piece of **messenger RNA (mRNA)** that will produce some of the same **antigenic proteins** as the disease-causing virus.

Risk of being integrated to the host genome is averted but, sometimes the RNA molecules may trigger an unintended immune response in the body




Lipid Delivery Vehicle



Antigen is presented to the immune cells on **Antigen Presenting Cells**

**Immune Response and Memory**

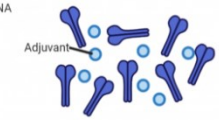
**Currently used in:**
No currently available human RNA vaccines
**COVID vaccines in the pipeline:**
Moderna;CureVac;Pfizer, BioNTech, Fosun Pharma

## Subunit Vaccine

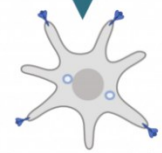
These vaccines use **antigenic protein** from the disease causing virus **without** any **genetic material**.

They are relatively safer as there is no genetic material and they cannot replicate inside the body. They focus the immune response on the most important part of the virus for protection.

These vaccines require multiple doses for long term immunity. They require adjuvants which are ingredients that help create a stronger immune response.




SARSCoV-2 antigen and adjuvants



Antigen is presented to the immune cells on **Antigen Presenting Cells**

**Immune Response and Memory**

**Currently used in:**
HPV(Human Papilloma virus); Pertussis; Hepatitis B
**COVID vaccines in the pipeline:**
Novavax; AdaptVac

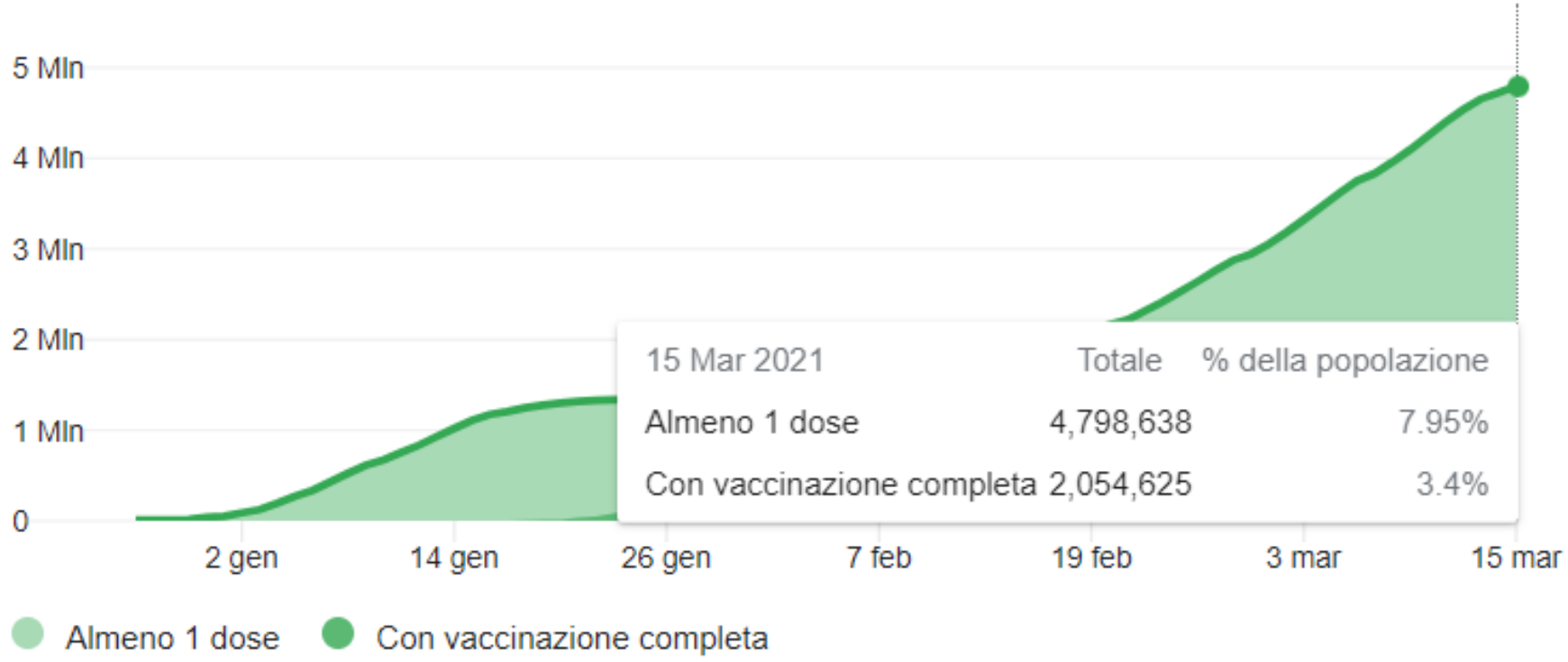
COVID RESPONSE CORPS @epiCOVIDcorps

Created by **Nikitha Ramesh** using BioRender.com
References avaialable at **https://sites.bu.edu/covid-corps**

# Vaccinazioni

Da OurWorldInData · Last Updated: 2 giorni fa

Totale | Italia | Dall'inizio



# Vaccine doses overview

From Our World in Data · Last Updated: 2 days ago

## Italy

| Doses given | Fully vaccinated | % of population fully vaccinated |
|---|---|---|
| 6.85M | 2.05M | 3.40% |

## Worldwide

| Doses given | Fully vaccinated | % of population fully vaccinated |
|---|---|---|
| 381M | 85.6M | 1.10% |
| +8.34M | +2.66M | +0.03% |