Dr.Reza Hamzehloo DCLS, MPH
Head of Reference Health Lab of Tehran university of medical sciences

Disease

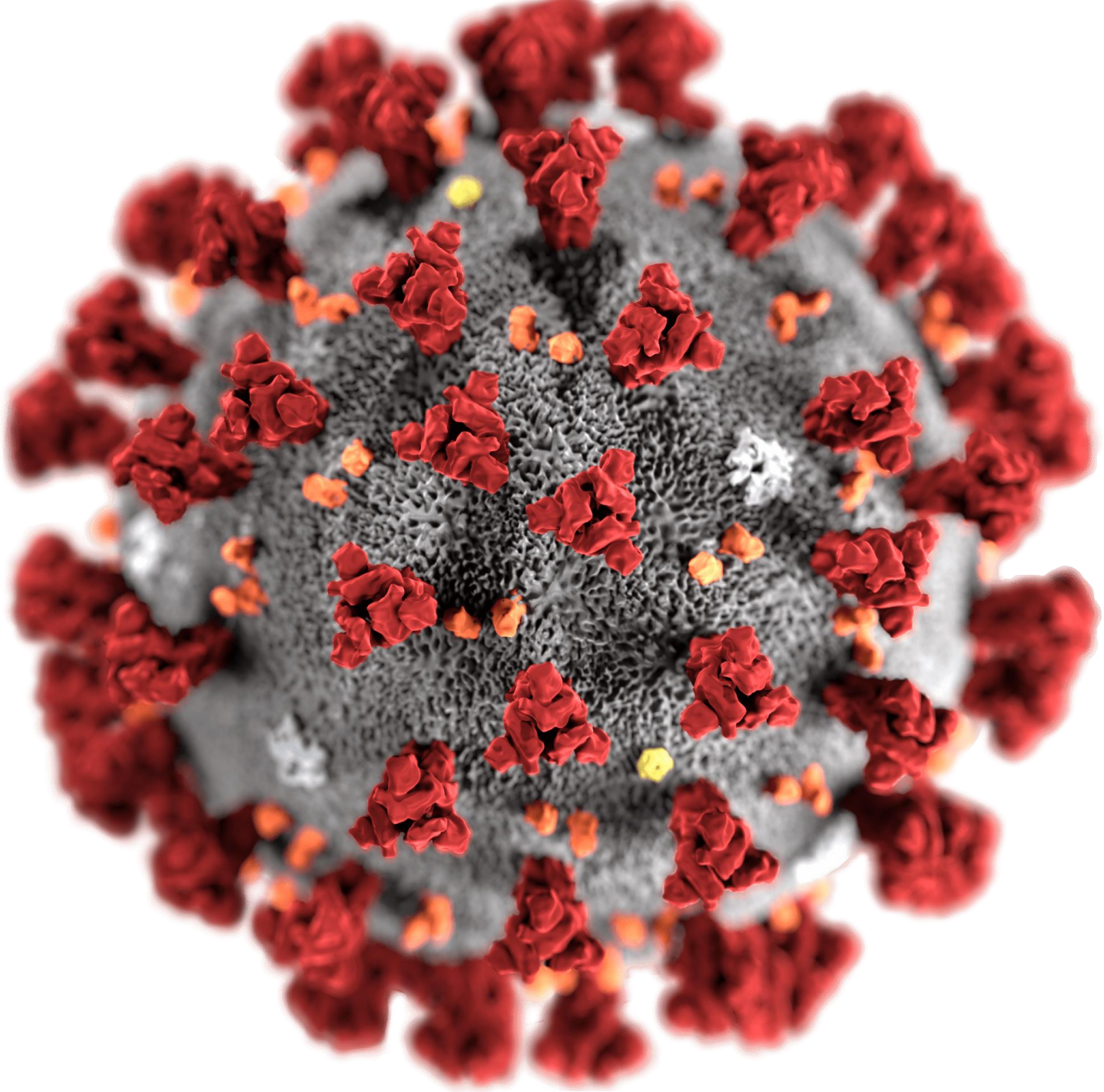
COVID-19

SARS-CoV-2

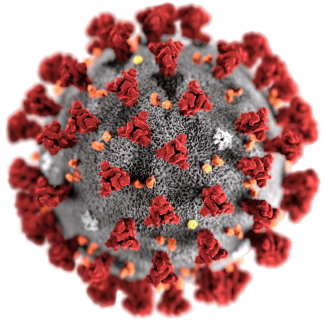
2019-nCov

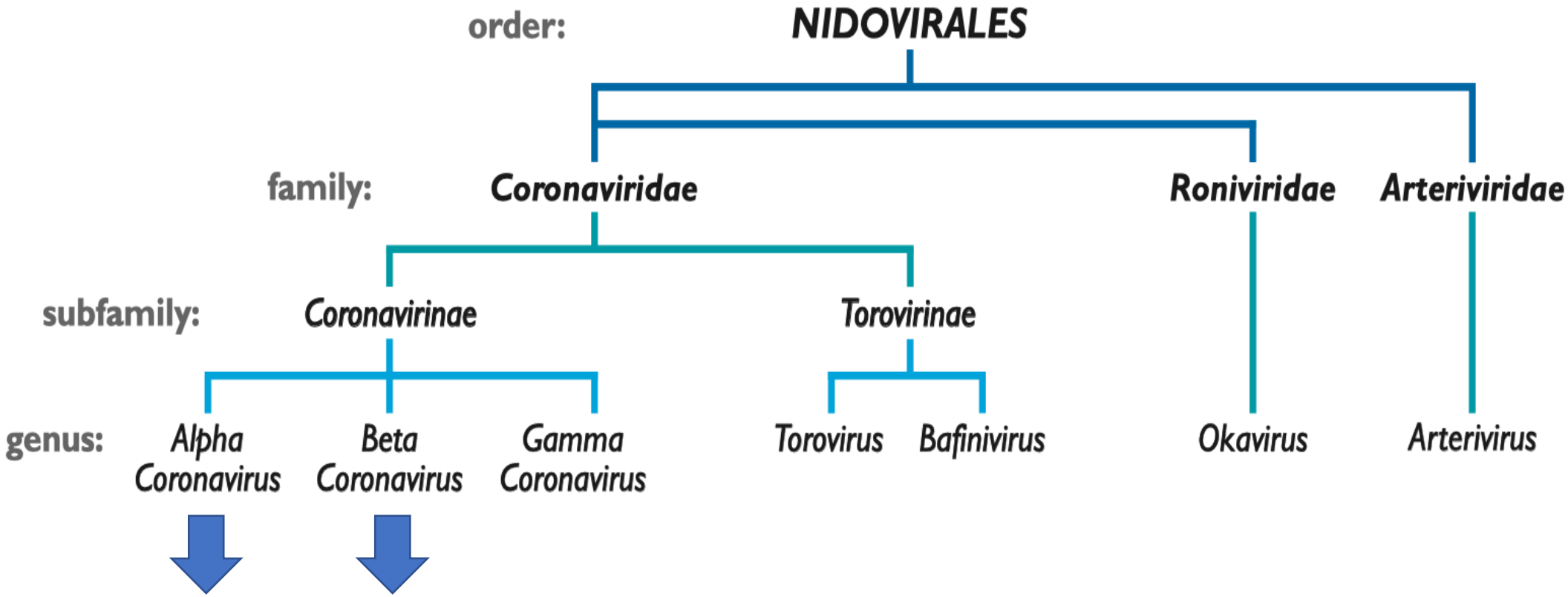
HCoV-19

Virus Name



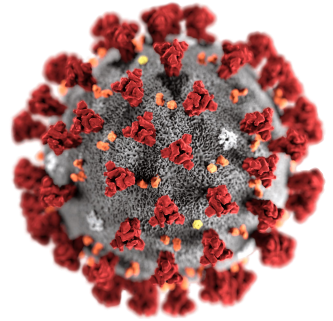
7 Human Coronaviruses: 4 normal; 3 “novel”

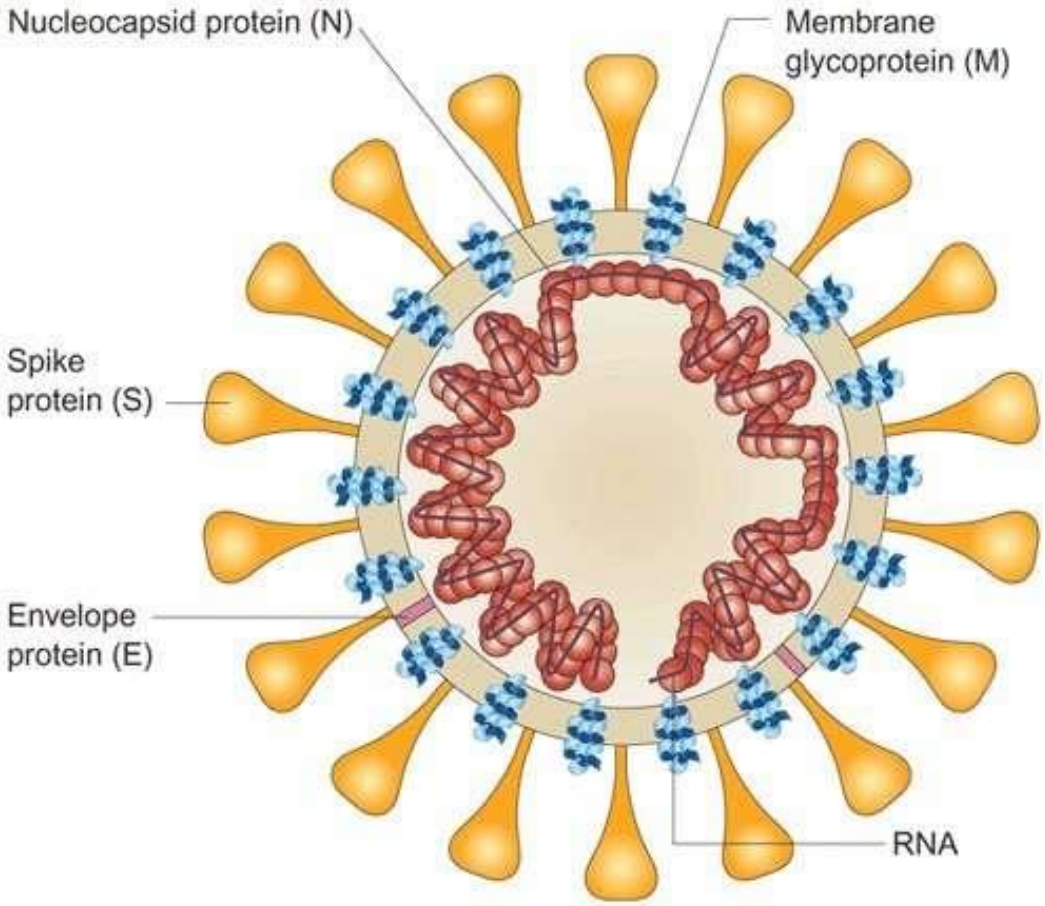




Alpha: **HCoV-229E**, **HCoV-NL63** Beta: **HCoV-HKU1**, **HCoV-OC43**, **MERS-CoV**, **SARS-CoV**, **SARS-CoV-2**

Coronavirus Structure



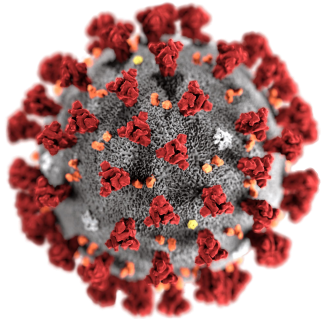


- Medium-sized virus size, but largest mRNA genome
- Enveloped +ve stranded RNA
- mRNA encased in nucleocapsid
- Lipid Bilayer – Soap works to disrupt this!

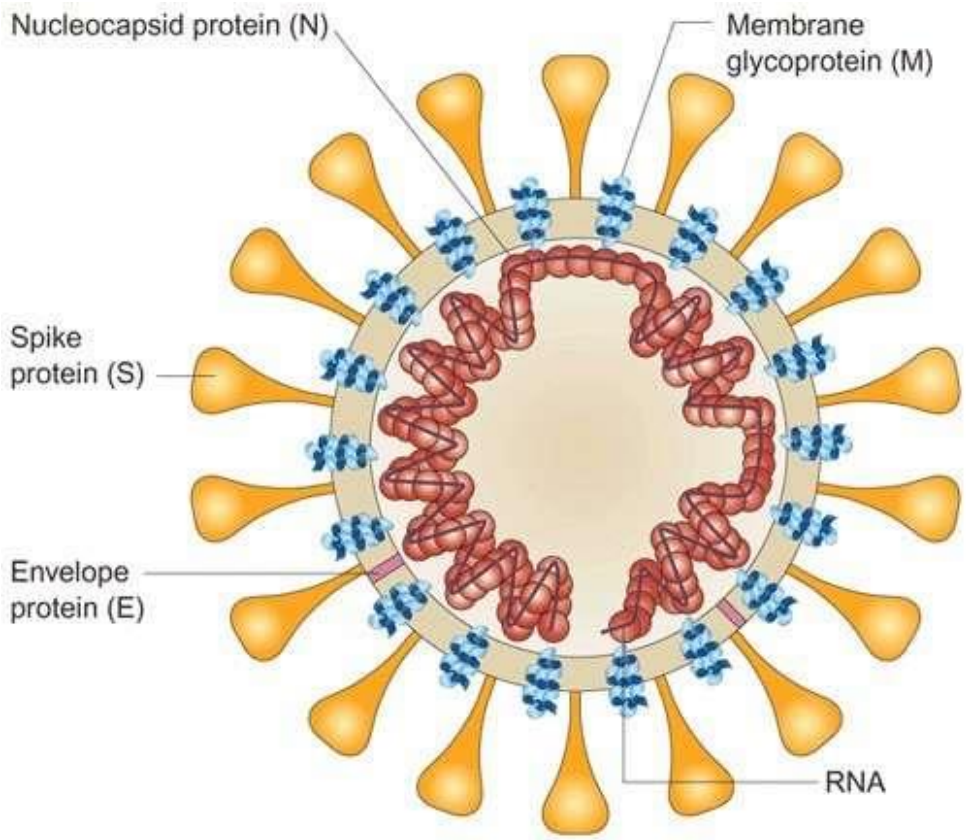
Corona = Crowns for Spikes

- Glycoprotein Spike (S) Peptomer
- Spikes allow it to attach to human cell receptors in upper or lower airway

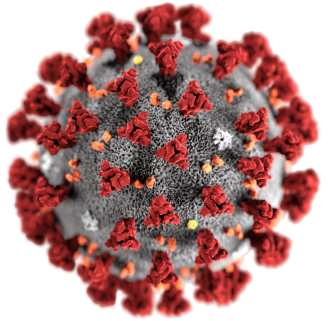
Coronavirus Genome



- Encodes four or five structural proteins:
  - **S** – spikes on the outside; **mediates receptor binding**
  - **M** – membrane protein; assists viral assembly
  - **N** – nucleocapsid protein; regulation of viral RNA synthesis, may interact with M protein during virus budding
  - **E** – small envelope protein; function necessary but not fully understood
  - **HE** – hemagglutinin-esterase glycoprotein in Beta coronavirus OC43 and HKU1 only; enhances uptake into mucosal cells

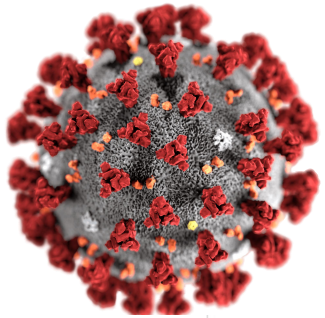


Key Definitions

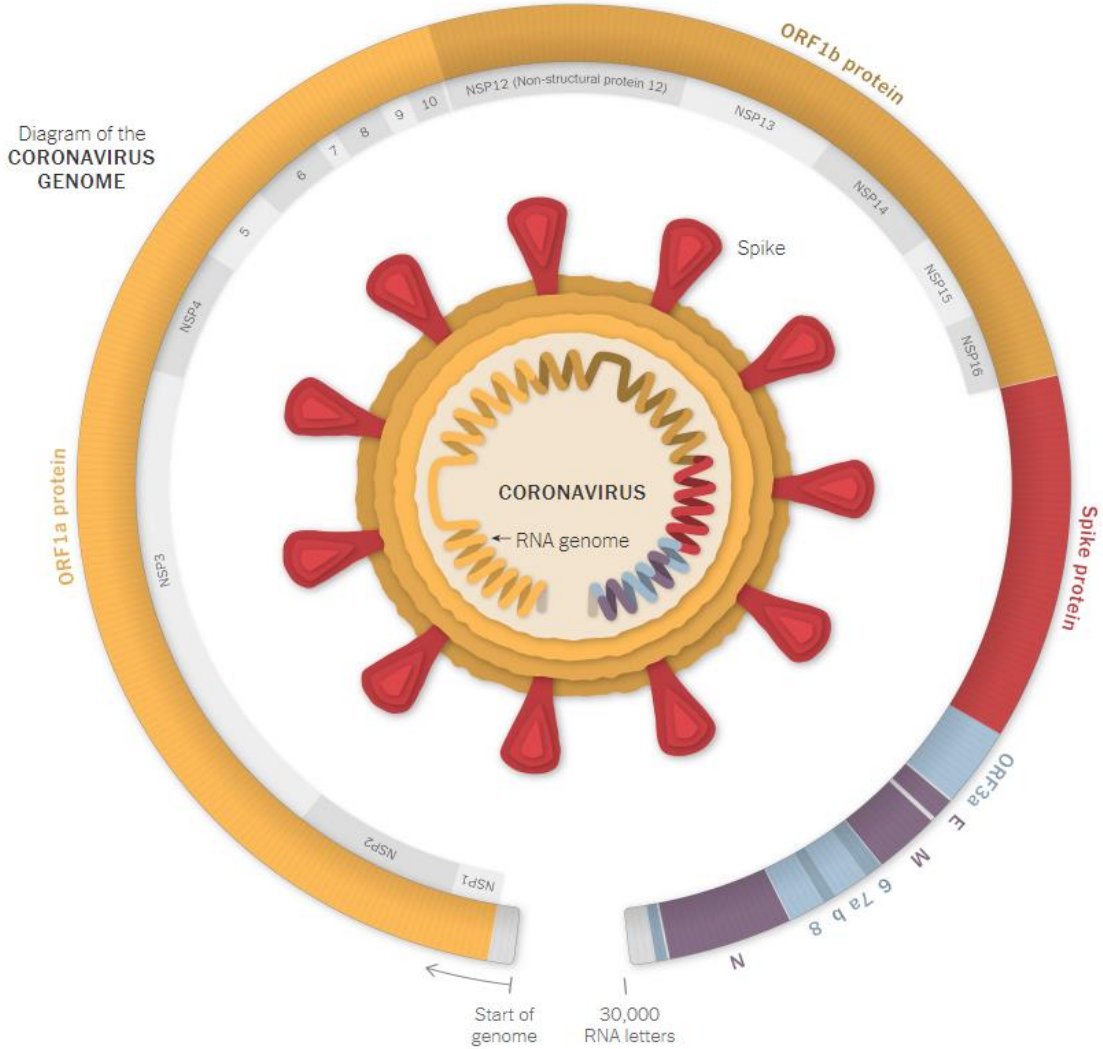


- **Mutation:** A mutation refers to a single change in a virus's genome (genetic code). Mutations happen frequently, but only sometimes change the characteristics of the virus.
- **جهش:** جهش به یک تغییر واحد در ژنوم ویروس (کد ژنتیکی) اشاره دارد. جهش اغلب اتفاق می افتد، اما فقط گاهی اوقات ویژگی های ویروس را تغییر می دهد.
- **Lineage:** A lineage is a group of closely related viruses with a common ancestor. SARS-CoV-2 has many lineages; all cause COVID-19.
- **دودمان:** دودمان گروهی از ویروس‌های نزدیک به هم با اجداد مشترک هستند. SARS-CoV-2 دودمان های زیادی دارد. همه باعث COVID-19 می شوند.
- **Variant:** A variant is a viral genome (genetic code) that may contain one or more mutations. In some cases, a group of variants with similar genetic changes, such as a lineage or group of lineages, may be designated by public health organizations as a Variant of Concern (VOC) or a Variant of Interest (VOI) due to shared attributes and characteristics that may require public health action.
- **نوع:** واریانت یک ژنوم ویروسی (کد ژنتیکی) است که ممکن است حاوی یک یا چند جهش باشد. در برخی موارد، گروهی از واریانت‌ها با تغییرات ژنتیکی مشابه، مانند دودمان یا گروهی از دودمان، ممکن است توسط سازمان‌های بهداشت عمومی به‌دلیل ویژگی‌های مشترک، به‌عنوان یک نوع نگرانی (VOC) یا یک نوع علاقه (VOI) تعیین شوند. ویژگی هایی که ممکن است به اقدامات بهداشت عمومی نیاز داشته باشد.

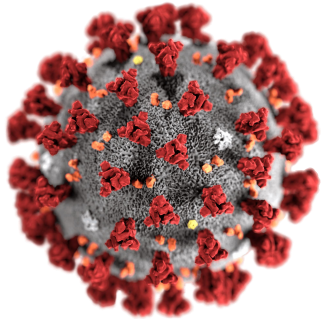
What Is a Variant?



- When an infected human cell assembles new coronaviruses, it occasionally makes tiny copying errors called **mutations**. Scientists can track mutations as they are passed down through a **lineage**, a branch of the coronavirus family tree. A group of coronaviruses that share the same inherited set of distinctive mutations is called a **variant**.



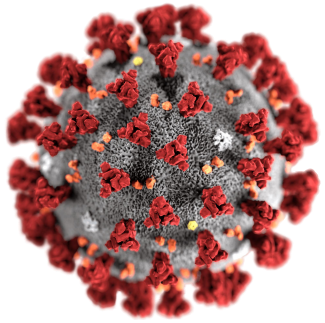
Characteristics of Selected SARS-CoV-2 Variants



- **WHO Label: Delta**
- **Pango Lineage: B.1.617.2 and AY lineages** (Pango lineageexternal icon)
- **Spike Protein Substitutions**: T19R, (V70F*), T95I, G142D, E156-, F157-, R158G, (A222V*), (W258L*), (K417N*), L452R, T478K, D614G, P681R, D950N
- **Nextstrain clade** (Nextstrainexternal icon): 21A/S:478K
- **First Identified**: India
- **Attributes**:
- Increased transmissibility
- Nearly all lineages designated as Delta are susceptible to Emergency Use Authorization (EUA) monoclonal antibody treatments. AY.1 and AY.2 lineages are not susceptible to some monoclonal antibody treatments.
- Reduction in neutralization by post-vaccination sera

Delta: The B.1.617.2 Lineage

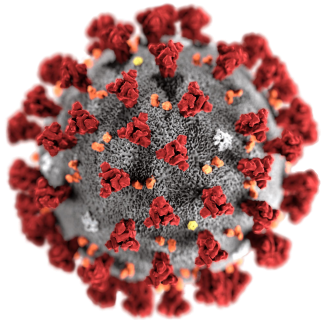
Coronaviruses that appear to be more infectious or cause more severe disease than other circulating coronaviruses.



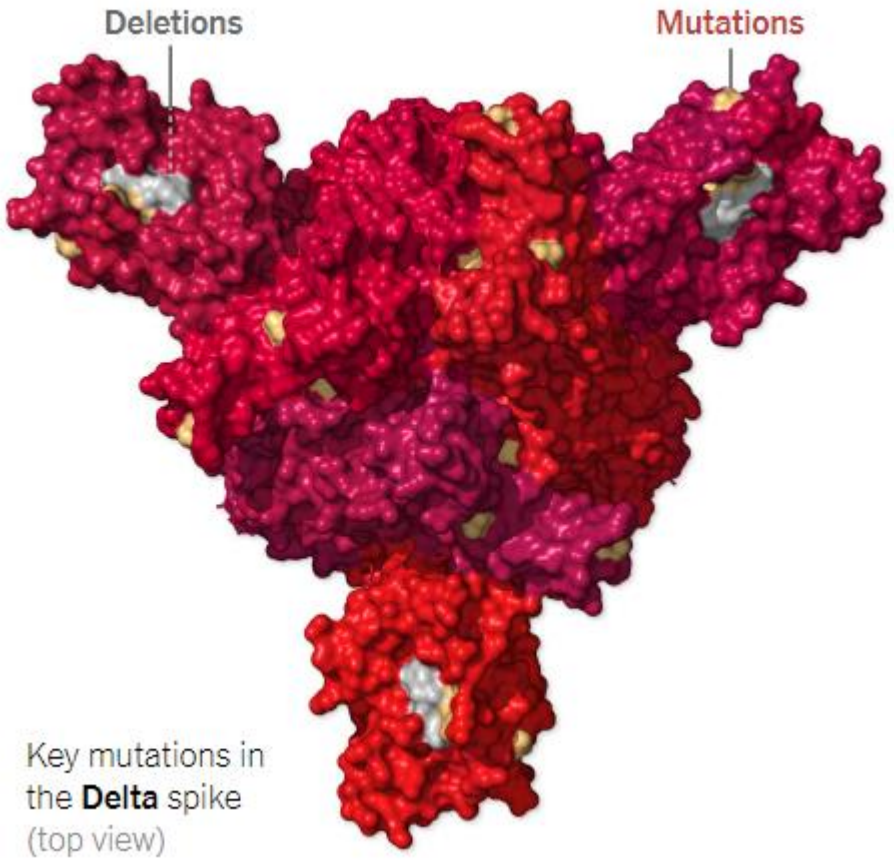
- **Delta**: The B.1.617.2 Lineage

- **Delta** is an aggressive variant that emerged in late 2020 and quickly became the most common variant in India. It continued spreading around the world and is currently the dominant variant.
- **KEY MUTATIONS**
- The variant emerged with more than a dozen mutations, but was initially called a “double mutant” because of two prominent mutations: **L452R** and **E484Q**, which lies at the same location as **E484K**, the “Eek” mutation.

Testing

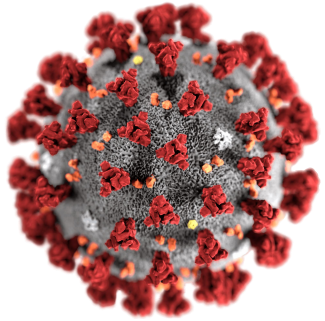


- As the **Delta** variant continues to spread around the world, some versions have developed additional spike mutations found in other variants of concern. These modified variants are sometimes referred to as **Delta Plus**.



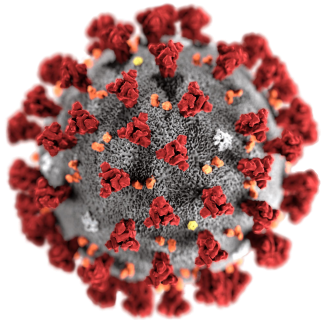
Key mutations in the **Delta** spike (top view)

Characteristics of Selected SARS-CoV-2 Variants



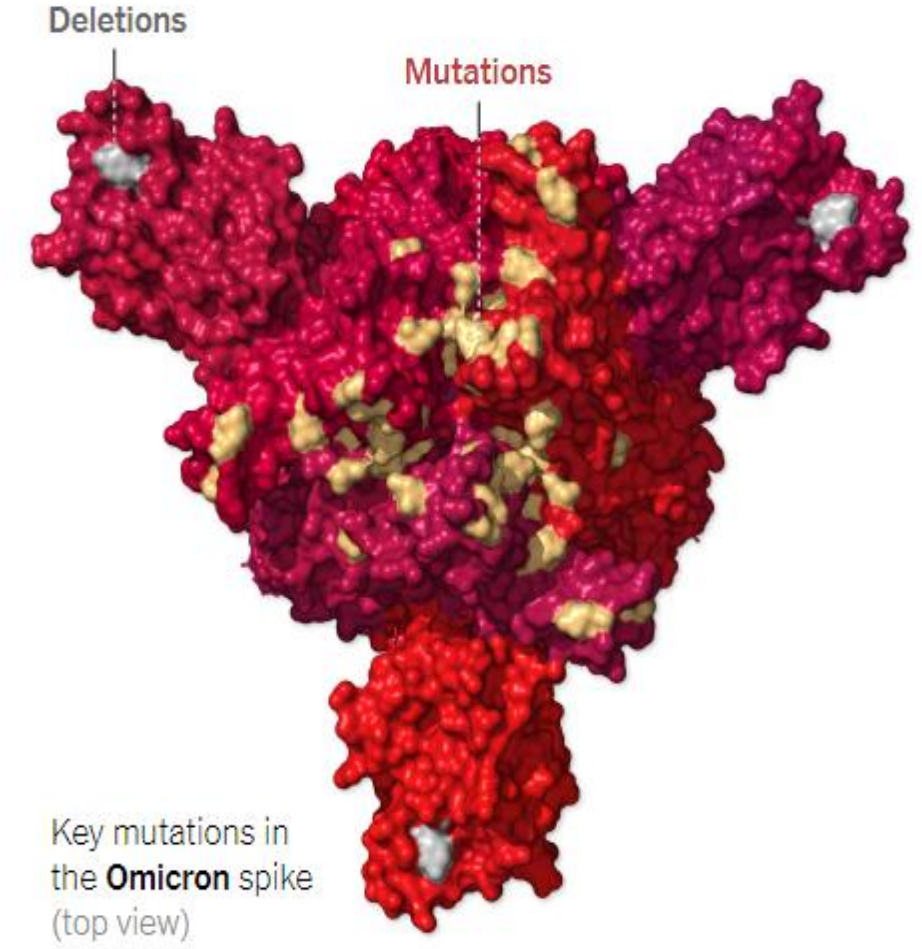
- **WHO Label: Omicron**
- **Pango Lineage: B.1.1.529 and BA lineages** (Pango lineageexternal icon)
- **Spike Protein Substitutions**: A67V, del69-70, T95I, del142-144, Y145D, del211, L212I, ins214EPE, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F
- **Nextstrain clade** (Nextstrainexternal icon): 21K
- **First Identified**: South Africa
- **Attributes**:
- Potential increased transmissibility
- Potential reduction in neutralization by some EUA monoclonal antibody treatments
- Potential reduction in neutralization by post-vaccination sera

OMICRON'S SPIKE MUTATIONS



- **Omicron** carries about 50 mutations not seen in combination before, including more than 30 mutations in the gene for the spike protein that the coronavirus uses to attach to human cells.

- **Omicron**'s spike protein has several mutations that are found in other variants of concern and that are thought to make the virus more infectious,including **D614G**, **N501Y** and **K417N**.



LAST UPDATE: 10 DECEMBER 2021

CORONAVIRUS
UPDATE
70

Update on
SARS-CoV-2 variant of concern Omicron

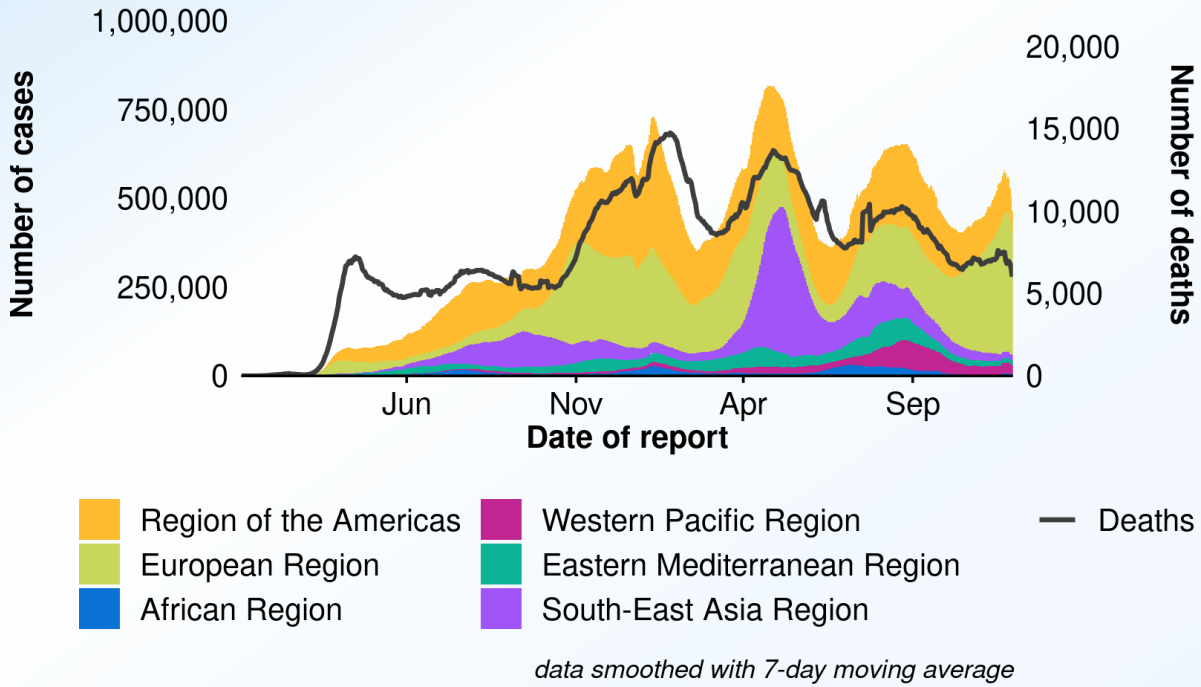
THE LATEST ON THE COVID-19 GLOBAL SITUATION
& SARS-CoV-2 variant of concern Omicron

World Health Organization | EPI•WiN | infodemic MANAGEMENT

Current global situation

CASES REPORTED TO WHO AS OF 10 DECEMBER 2021

- **Cases: > 262 million**
- **Deaths: > 5.2 million**



CHECK OUT THE LATEST GLOBAL SITUATION

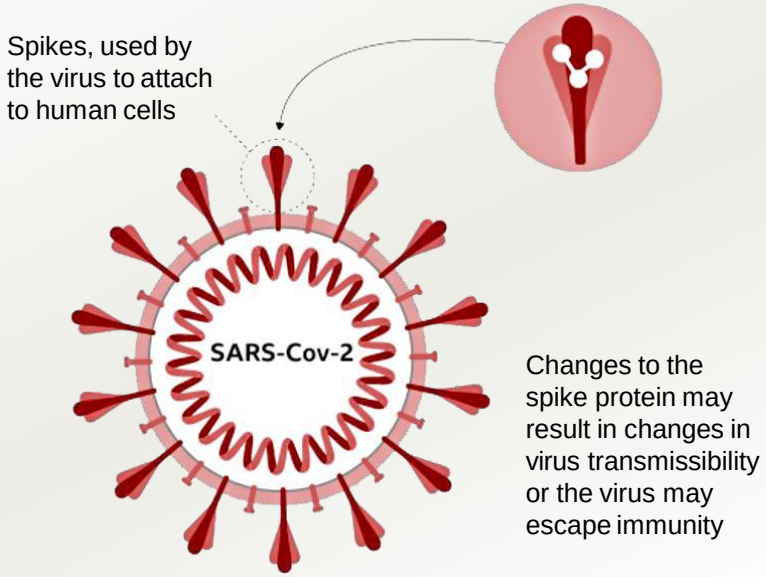
WHO Coronavirus Disease (COVID-19) Dashboard

** Data are incomplete for the current week. Cases depicted by bars; deaths depicted byline*

World Health Organization | EPI•WIN | infodemic MANAGEMENT

All viruses evolve over time

- The more the virus circulates, the more the virus will evolve
- Most changes have little to no impact on the virus's properties or behaviour
- However, some changes to SARS-CoV-2 lead to the emergence of variants that may affect:
  - virus transmissibility
  - disease severity and presentation
  - effectiveness of vaccines, therapeutics, diagnostic tools or public health and social measures
- Several SARS-CoV-2 variants have been identified and some have been characterized by WHO as variants of interest (VOI) or variants of concern (VOC)



https://www.who.int/news/item/26-11-2021-classification-of-omicron-(b.1.1.529)-sars-cov-2-variant-of-concern

SARS-CoV-2 variants of interest and variants ofconcern

SARS-CoV-2 variant of interest (VOI)

- **A variant with genetic changes that are predicted or known to affect virus characteristics** such as transmissibility, disease severity, immune escape, diagnostic or therapeutic escape; AND
- **Causes community transmission or multiple COVID-19 cases/clusters** in multiple countries with increasing relative prevalence or other epidemiological impacts to suggest an emerging risk to global public health

SARS-CoV-2 variant of concern (VOC)

- **Meets the definition of a VOI** and, through a comparative assessment, has been associated with one or more of the following changes at a degree of global public health significance:

➢ **increase in transmissibility** or detrimental change in COVID-19 epidemiology; OR
➢ **increase in virulence** or change in clinical disease presentation; OR
➢ **decrease in effectiveness of public health and social measures** or available diagnostics, vaccines, therapeutics

https://www.who.int/news/item/26-11-2021-classification-of-omicron-(b.1.1.529)-sars-cov-2-variant-of-concern

Omicron designated a variant of concern (VOC) by WHO

- On 26 November WHO designated B.1.1.529 a variant of concern (VOC) because of preliminary evidence of a detrimental change in COVID-19 epidemiology. As a VOC, it was named Omicron
- Omicron has a large number of mutations including more than 30 genetic mutations of the spike protein
- The spike protein of SARS-CoV-2 is targeted by some of the currently approved COVID-19 vaccines; mutations in the spike protein therefore need to be closely monitored
- Some mutations have previously been associated with increasing transmissibility and making it easier for the virus to bind and attach to cells

Fig: Delta compared to Omicron with mutations in the S1 domain of the spike protein

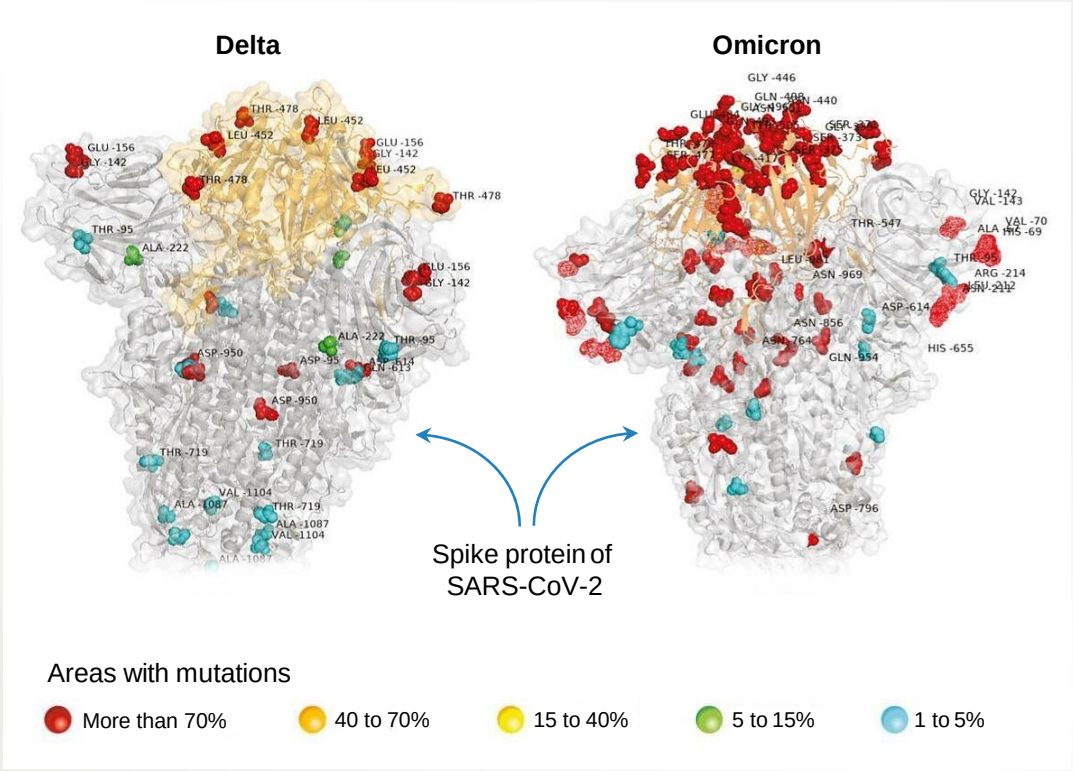
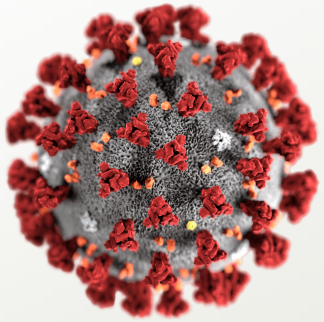


Image: AFP

https://www.who.int/news/item/26-11-2021-classification-of-omicron-(b.1.1.529)-sars-cov-2-variant-of-concern

Other variants of interest or concern around the world include:



Current variants of concern

Name	Lineage	Status
Omicron	B.1.1.529	Identified in southern Africa in Nov. 2021 and spread around the world. Within a month it was dominant in the U.S.
Delta	B.1.617.2	Emerged in India in late 2020 and spread around the world. Delta carries the L452R spike mutation, among others.
Gamma	P.1	Emerged in Brazil in late 2020.
Beta	B.1.351	Emerged in South Africa in late 2020.
Alpha	B.1.1.7	Emerged in Britain in late 2020.

Current variants of interest

Name	Lineage	Status
Mu	B.1.621	Emerged in Colombia in early 2021.
Lambda	C.37	Emerged in Peru in late 2020.

Current knowledge about Omicron

Transmissibility:

It is not yet clear whether Omicron is more transmissible, causes more or less severe disease compared to other variants, or impacts the effectiveness of current COVID-19 vaccines

Reinfection:

Preliminary evidence suggests there may be an increased risk of reinfection with Omicron, however information is limited*

Detection:

Diagnostic tests, including PCR and antigen detection tests, continue to detect infection with Omicron

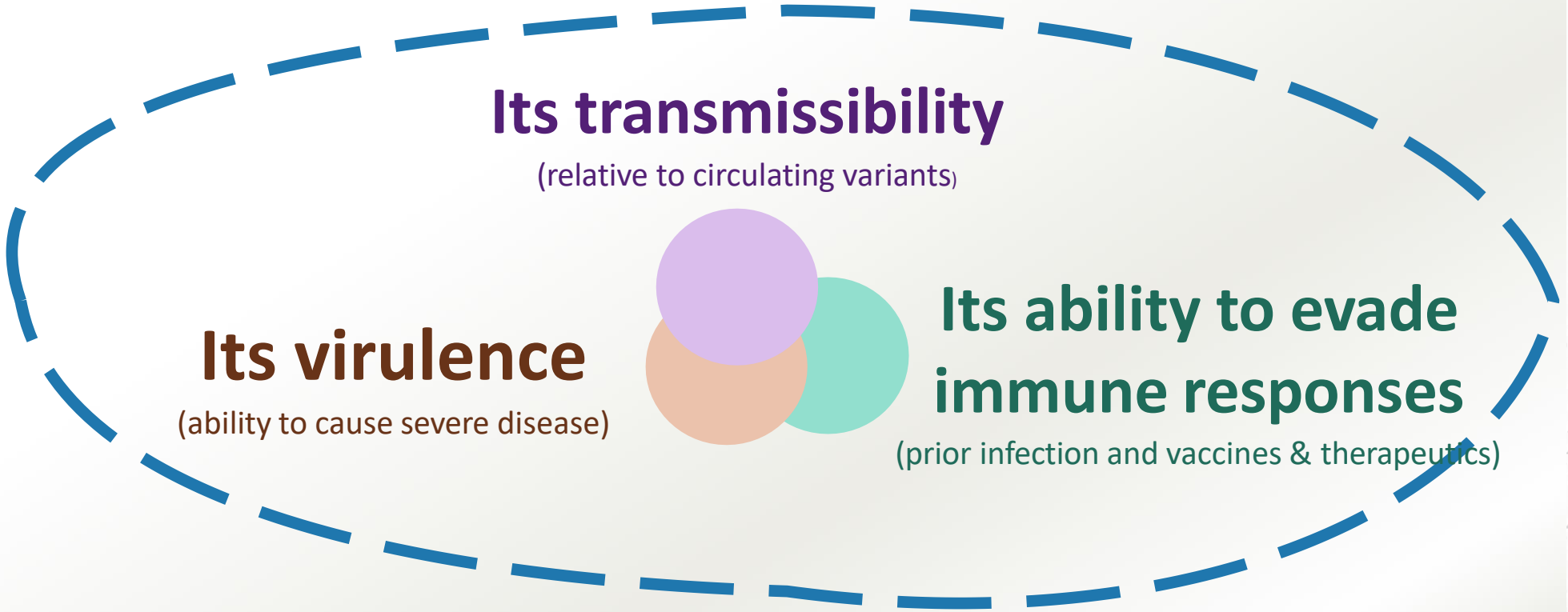
Clinical management:

Corticosteroids and IL-6 receptor blockers do not target the spike protein and are still effective for managing patients with severe COVID-19

While characteristics of Omicron are being studied, evidence shows that COVID-19 vaccines are still effective to protect against severe disease due to current circulating SARS-CoV-2 variants, including Delta

*https://www.who.int/news/item/28-11-2021-update-on-omicron

Three key properties of a variant are likely to influence the overall threat from it



https://www.who.int/groups/technical-advisory-group-on-covid-19-vaccine-composition-(tag-co-vac)

Types of tests used in the COVID-19 response (1)

Type	Target	Use	Method	Location
Molecular tests	Viral genetic material	Detect current SARS-CoV-2 infection	Amplification of small amounts of the viral genome (RNA) until reaching detectable levels	Laboratory or near patient
Antigen tests	Viral proteins	Detect current SARS-CoV-2 infection	Capture of antigens on a test strip causing color change (e.g., RDT for malaria)	Point of care
Antibody tests	Antibodies that patients develop in response to infection	Assess past infections	Capture of antibodies on a test strip[1] or in a test well causing color change, read manually or using an instrument	Laboratory or Point of care[1]

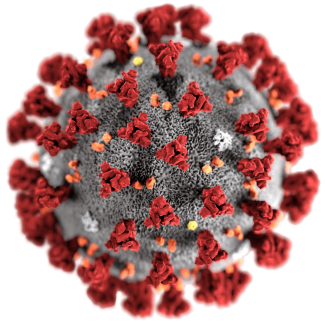
[1] Based on current evidence, WHO recommends the use of these new point-of-care immunodiagnostic tests only in research settings. They should not be used in any other setting, including for clinical decision-making, until evidence supporting use for specific indications is available.
World Health Organization. Advice on the use of point-of-care immunodiagnostic tests for COVID-19. Available from: https://www.who.int/publications/i/item/advice-on-the-use-of-point-of-care-immunodiagnostic-tests-for-covid-19-scientific-brief

Types of tests used in the COVID-19 response (3)

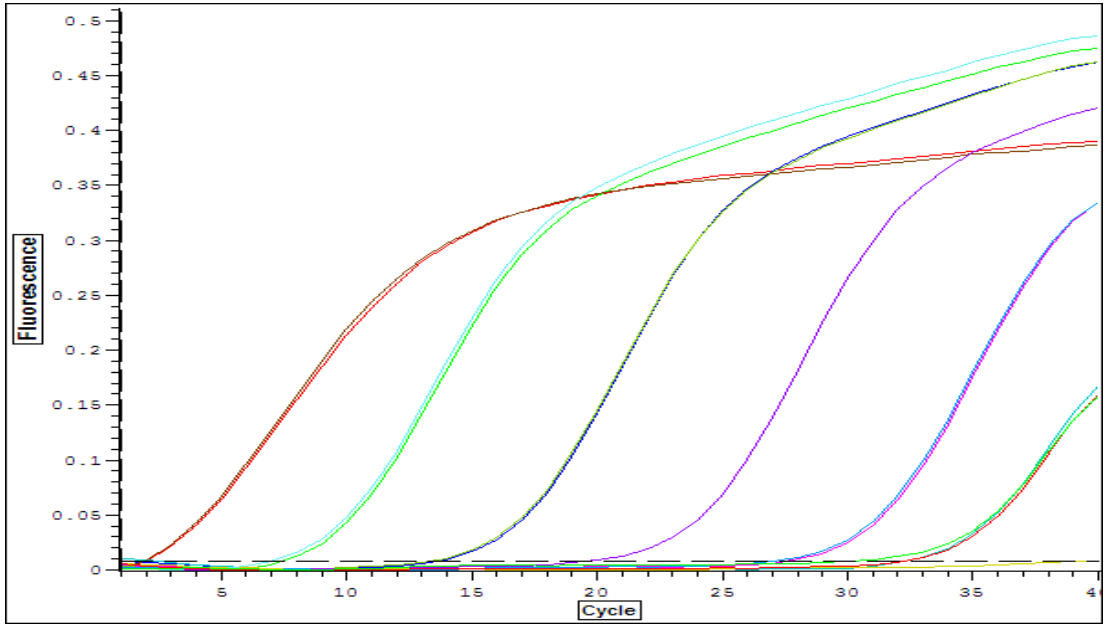
- Other test types:

Type	Target	Use	Method	Location
Sequencing	Viral genetic material	Identify variants: detect mutations of the virus in SARS-CoV-2 positive samples	Amplification and sequencing of part or all of the viral genome (RNA) to determine its composition (RNA sequence)	Specialized laboratory
Culture	Virus	Assess effect of drugs or antibodies on the virus growth	Grow the virus to perform specialized tests (reaction against antibodies for example)	Specialized laboratory

Testing



- RT-PCR:
  - Real-time Polymerase Chain Reaction of RNA
    - Nasal AND Orophangeal Swabs (Collect 2 swabs)
    - Sputum better (but more dangerous to collect?)
    - Stool – not generally used for testing
    - Blood or urine – virus not detected; blood could be tested for IgM, IgG later. DO get (bacterial) blood cultures for any sick patient.
- PCR ~ **60-80% sensitive**
  - A single negative RT-PCR *doesn't* exclude COVID-19 (*especially* if obtained from a nasopharyngeal source or relatively early in the disease course).
  - If RT-PCR is negative but suspicion remains, consider ongoing isolation and re-sampling several days later.
  - Sensitivity from private labs may vary; no data yet. Also dependent on collection technique and timing – early test on asymptomatic may not be accurate



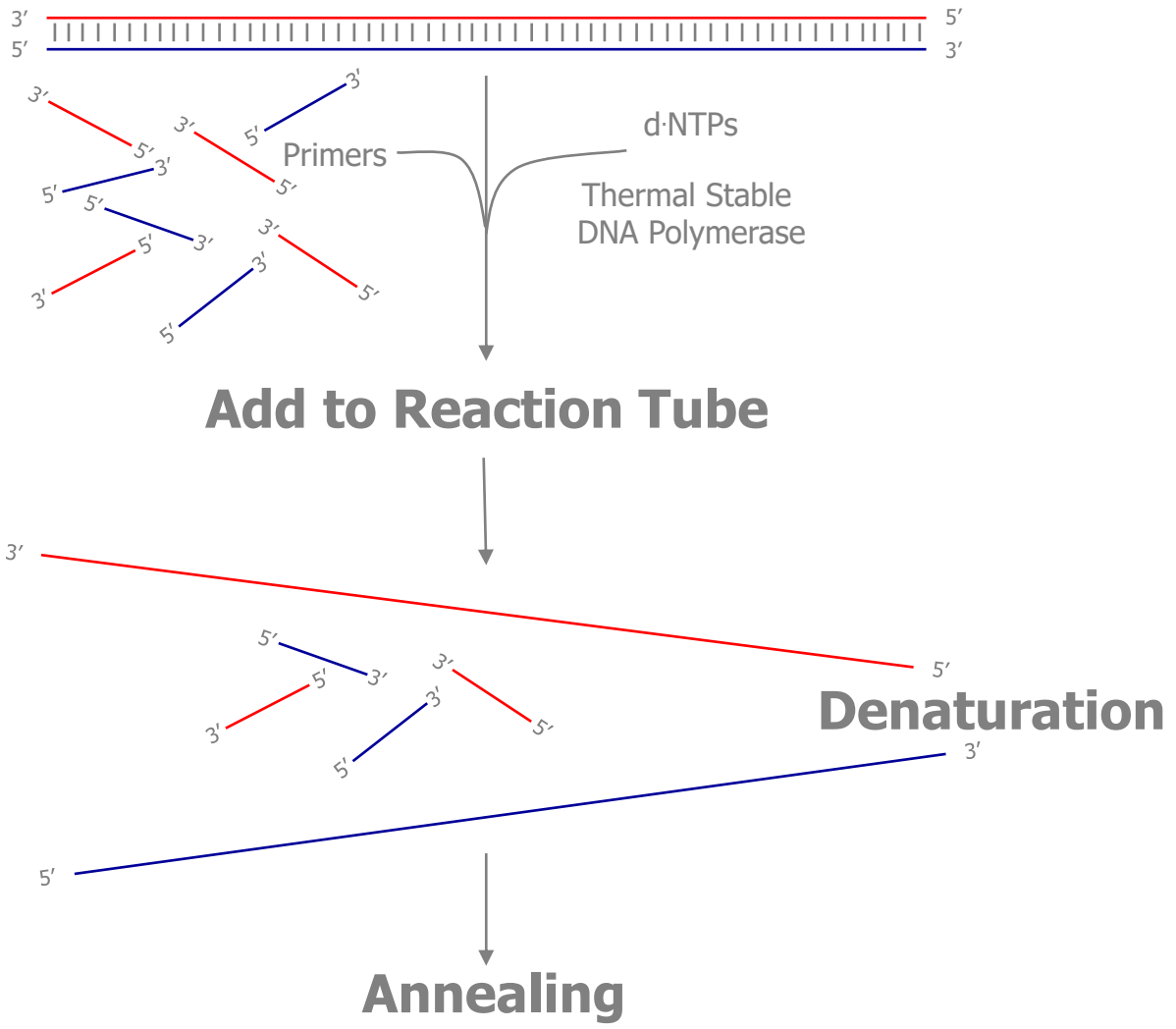
How does Real-Time PCR work?

How does real-time PCR work?

To best understand what real-time PCR is, let’s review how regular PCR works...

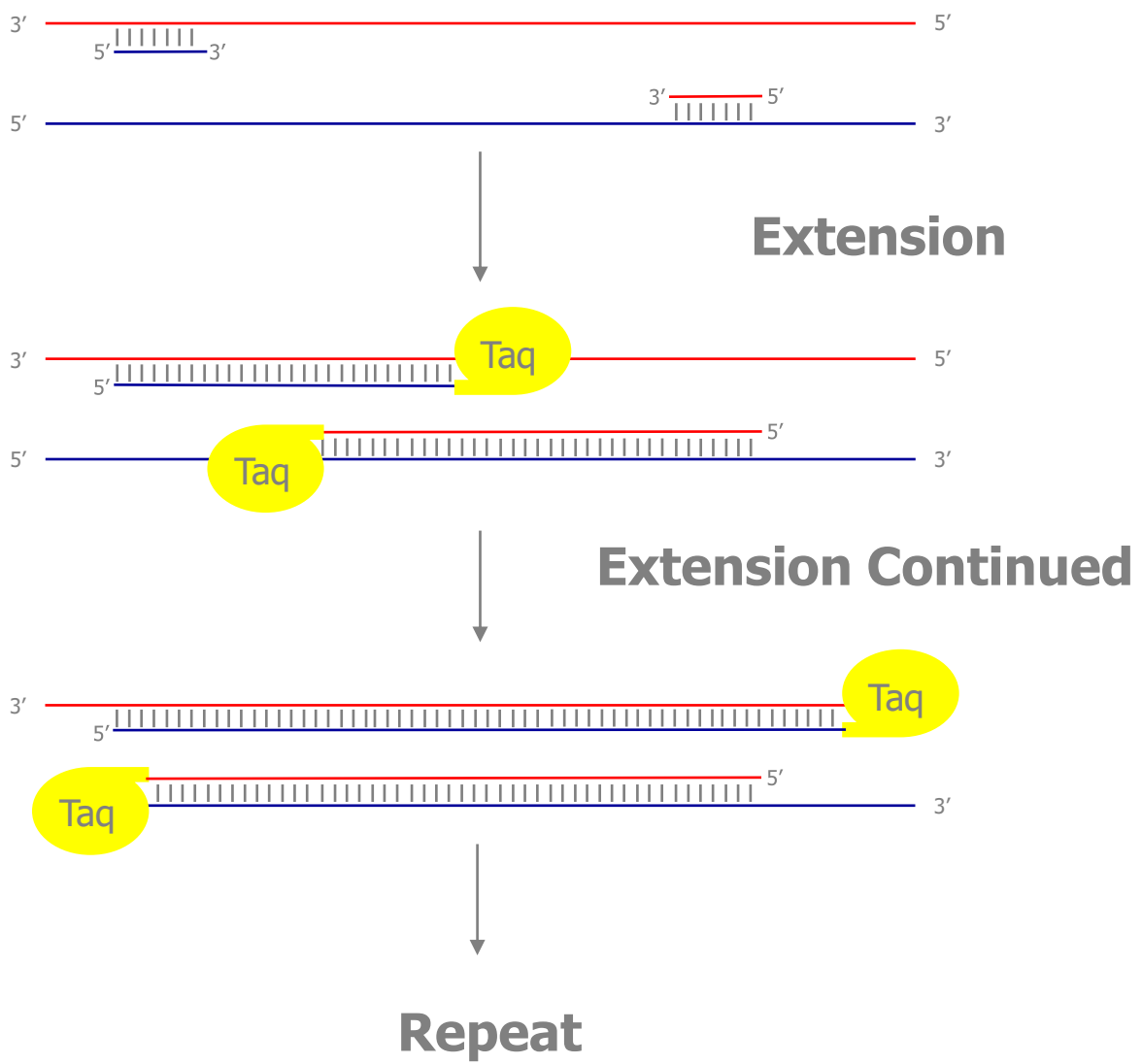
The Polymerase Chain Reaction

How does PCR work??



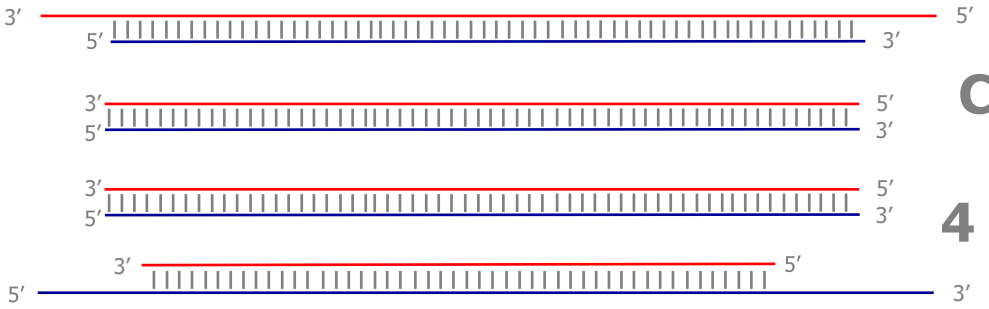
The Polymerase Chain Reaction

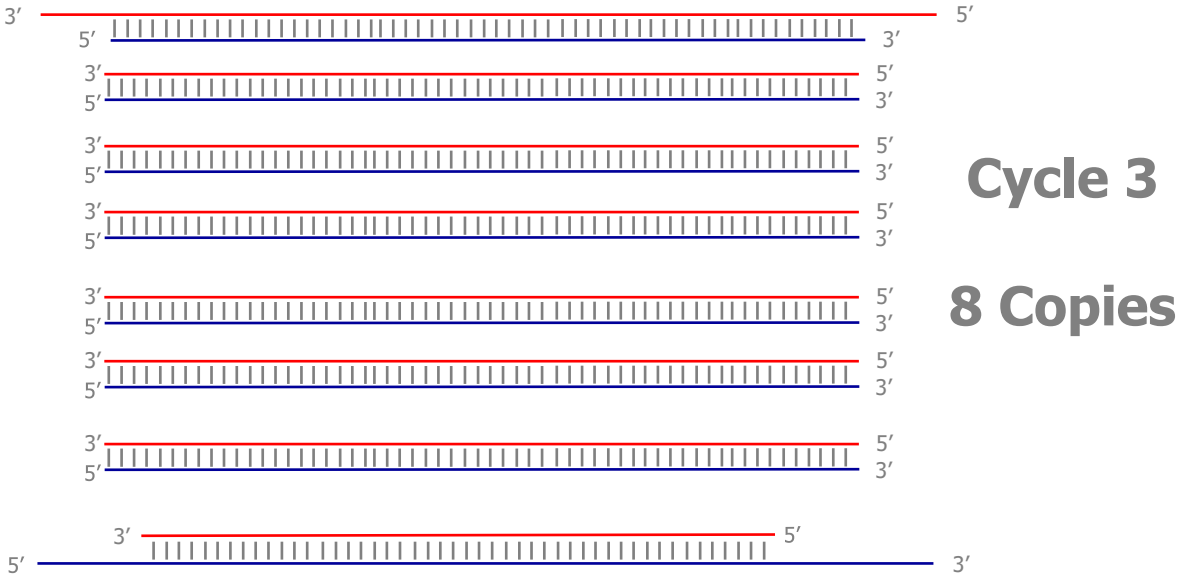
How does PCR work??



The Polymerase Chain Reaction

How does PCR work??

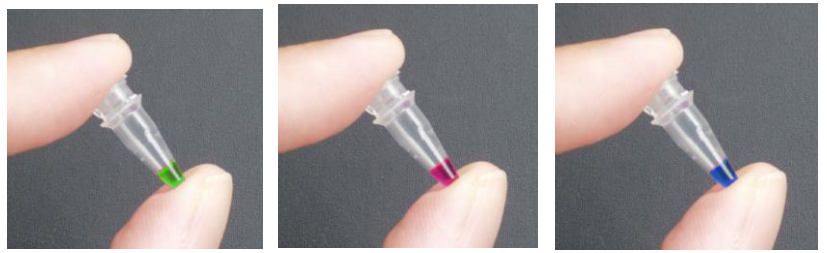




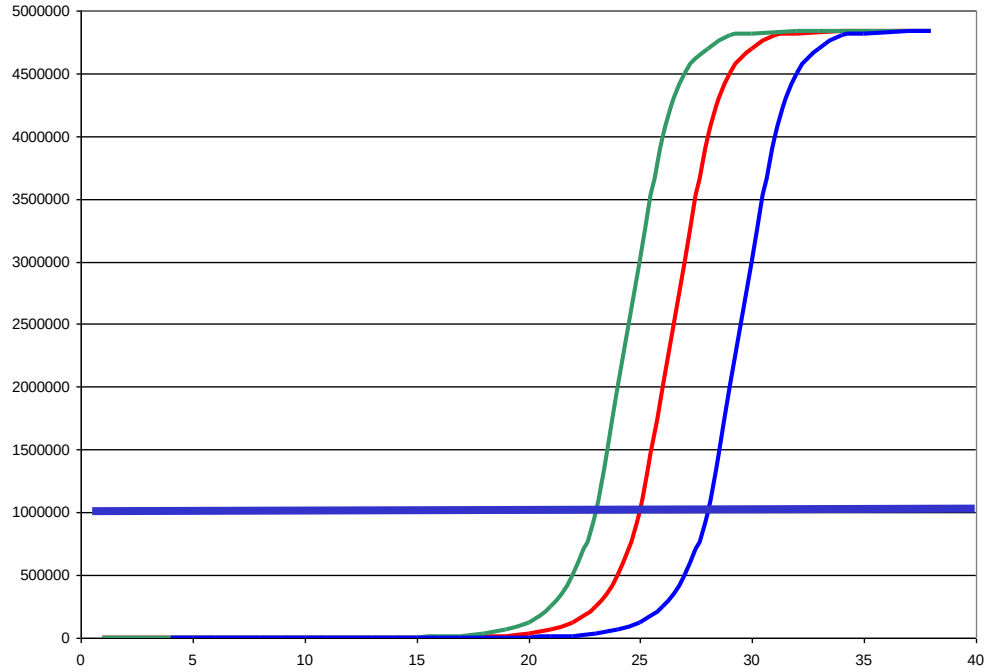
Imagining Real-Time PCR

Measuring Quantities

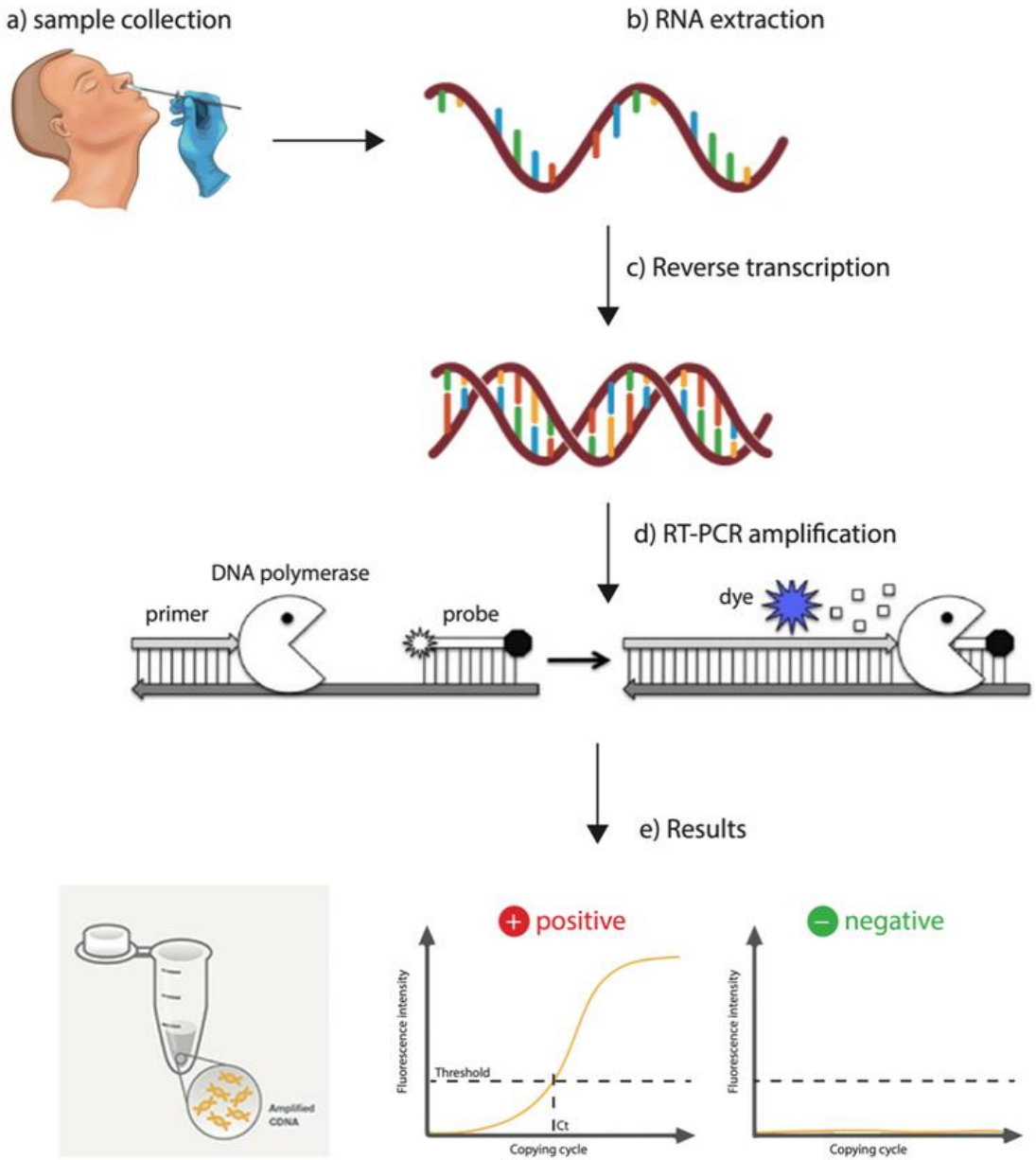
Let's recap…



4 units Ct=23 | **1 unit Ct=25** | **1/8 unit Ct=28**



RT-PCR


a) sample collection
b) RNA extraction
c) Reverse transcription
d) RT-PCR amplification
DNA polymerase
primer
probe
dye
e) Results
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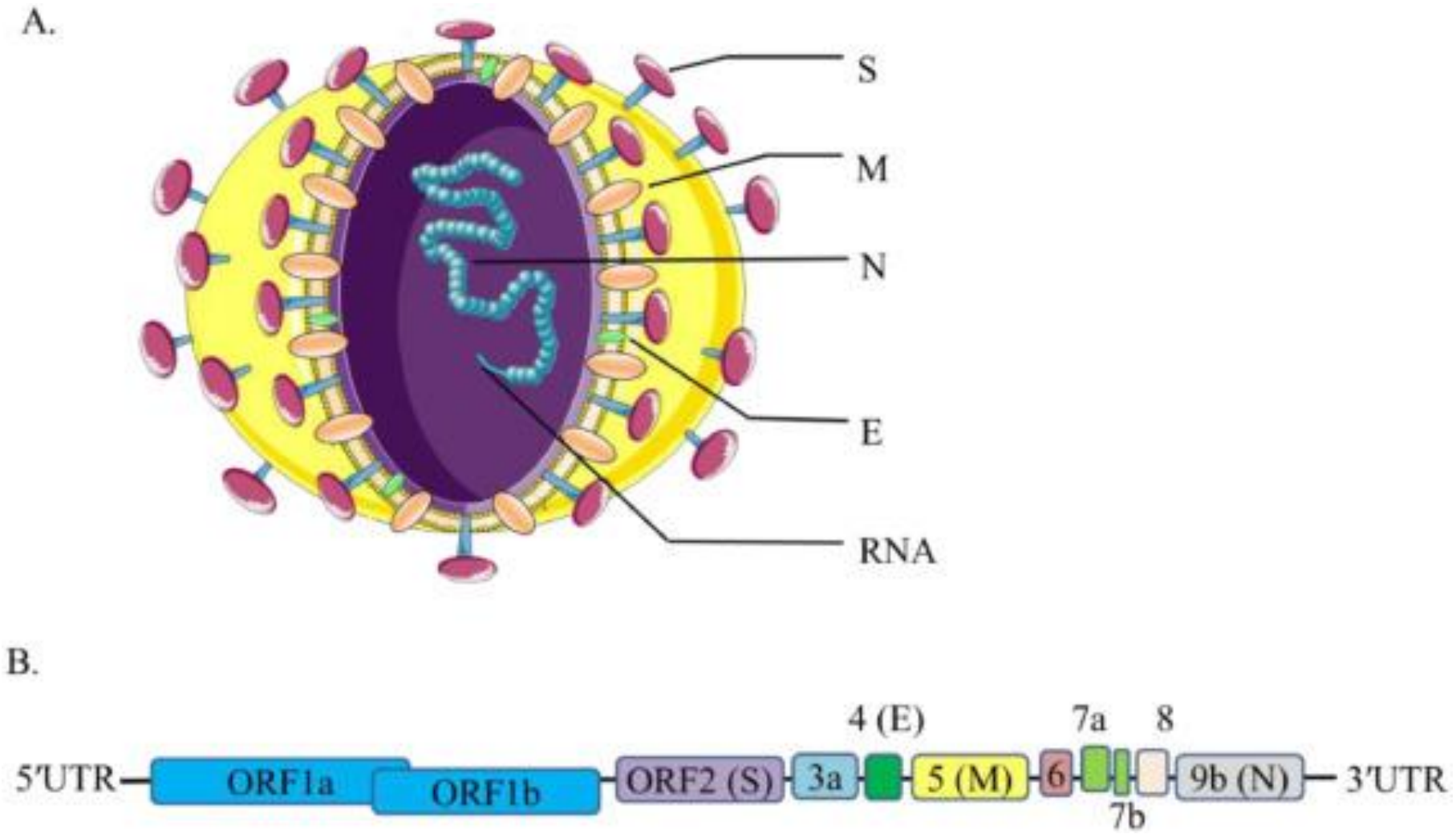
Structure and genome of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)



Li H, 2020

RT-PCR

Omicron

اساس تست

مخلوط پرایمر و پروب این کیت به صورت Triple target gene بوده که نواحی هدف از ژنهای N و S و ORF1a ویروس SARS-CoV-2 را شناسایی کرده که در صورت شناسایی توسط مخلوط واکنش موجود در کیت این نواحی تکثیرشده و آزاد سازی سیگنال فلورسنس ایجاد شده توسط دستگاه Real Time PCR سنجش می‌شود.

کنترل داخلی در این کیت شامل یک طراحی پرایمر و پروب اختصاصی برای RNA ژن RNase P بصورت اندوژن می باشد که علاوه بر بررسی مراحل نمونه برداری و استخراج الگو، کیفیت قابل قبول RNA استخراج شده را مشخص کرده تا مانع از نتایج منفی کاذب شود.

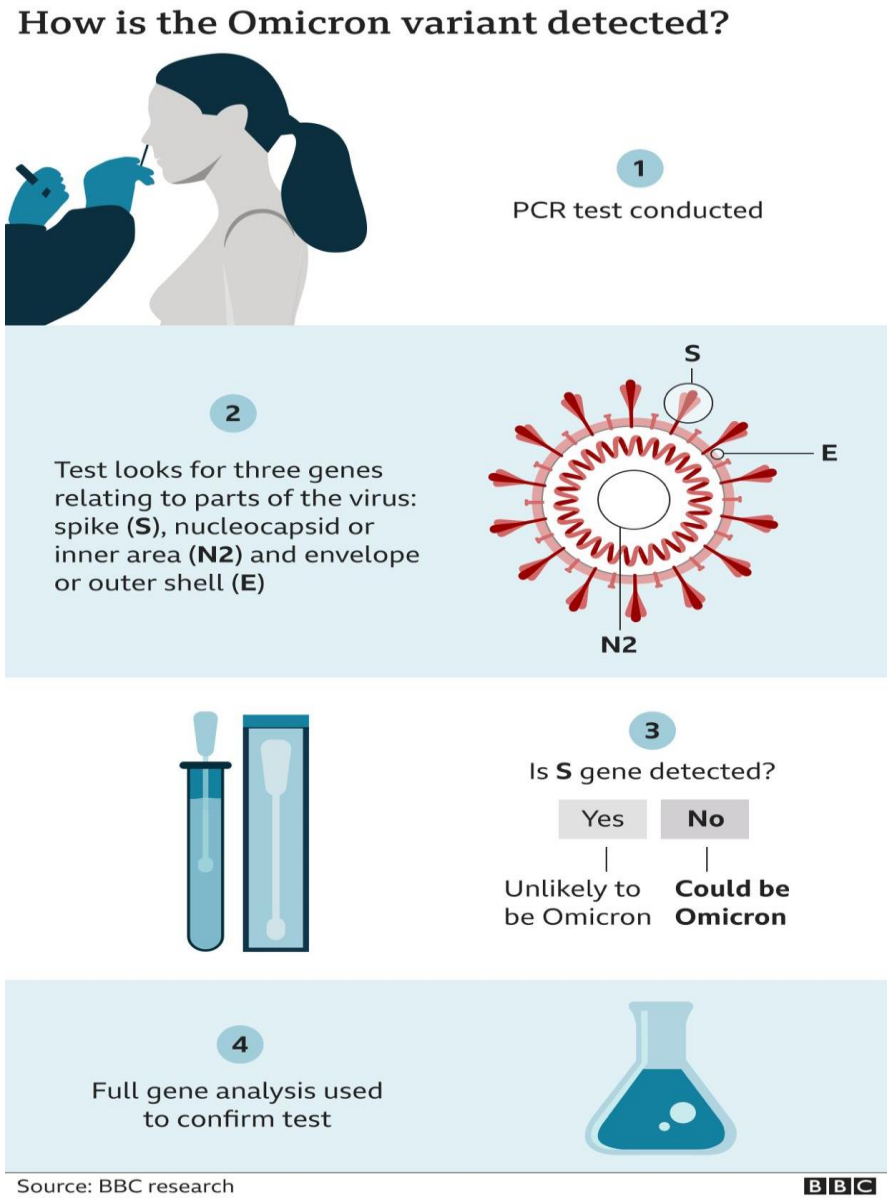
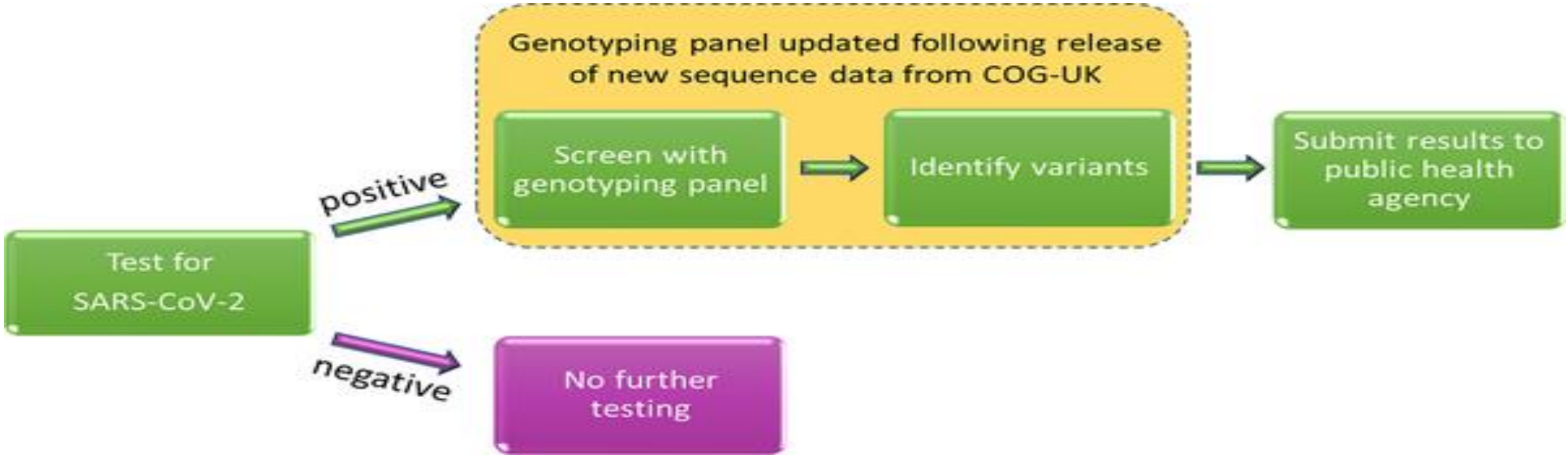
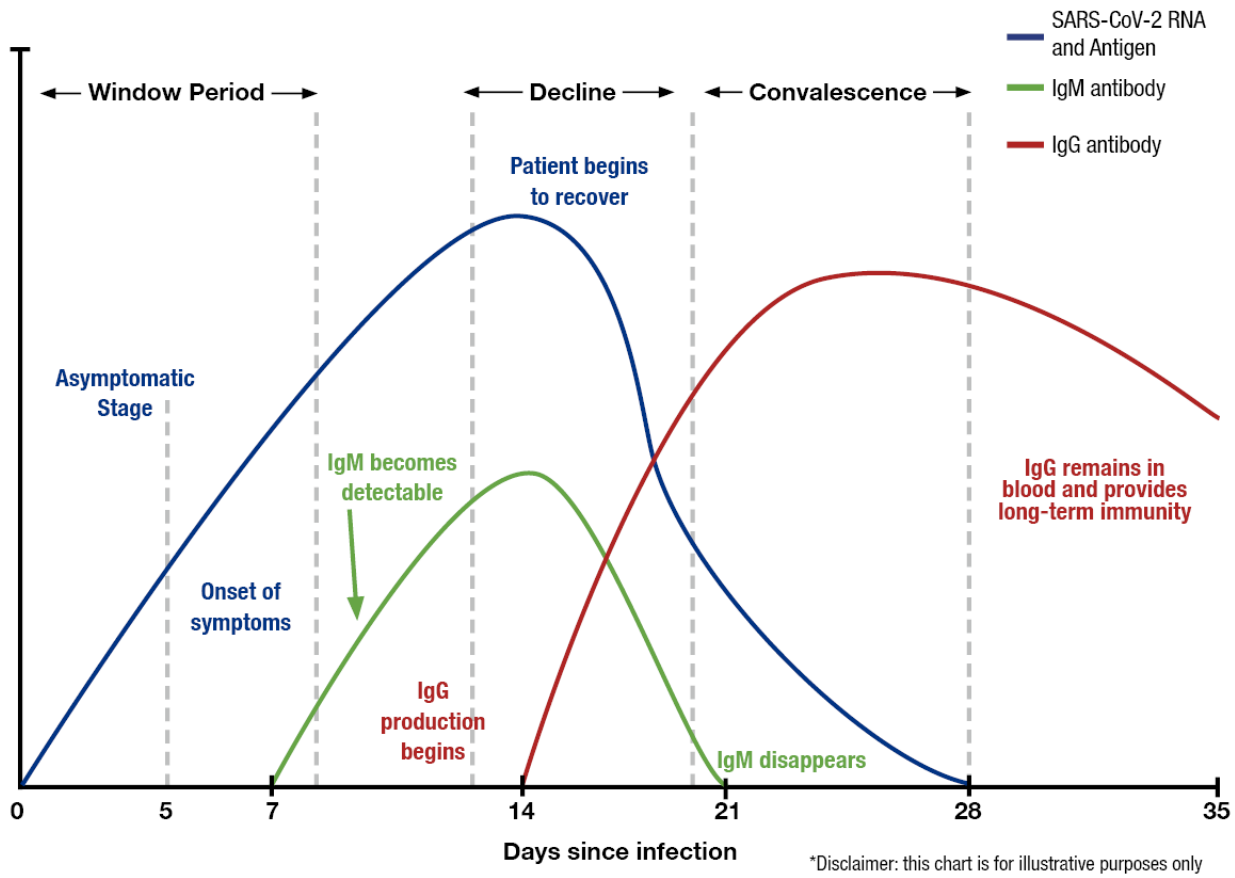


Fig 1. How the SARS-CoV-2 genotyping panel can be used to identify circulating SARS-CoV-2 variants.



Harper H, Burridge A, Winfield M, Finn A, Davidson A, et al. (2021) Detecting SARS-CoV-2 variants with SNP genotyping. PLOS ONE 16(2): e0243185. https://doi.org/10.1371/journal.pone.0243185
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0243185

Variation of the Levels of SARS-CoV-2 RNA and Antigen, IgM and IgG after infection



Basic terms

Antigen

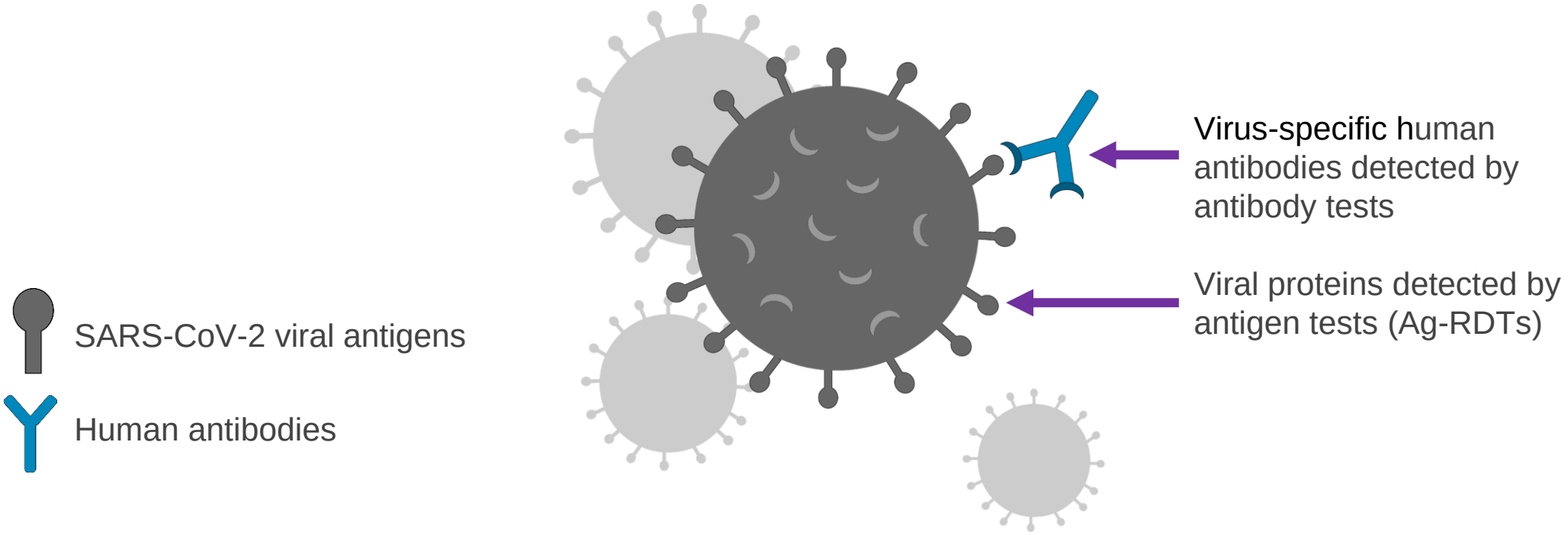
Antigens are foreign molecular structures that can trigger an immune response.

Antibody

An antibody is a protein (also called immunoglobulin) made by the body's immune system that can recognize and target an antigen for destruction.

Types of tests used in the COVID-19 response (2)

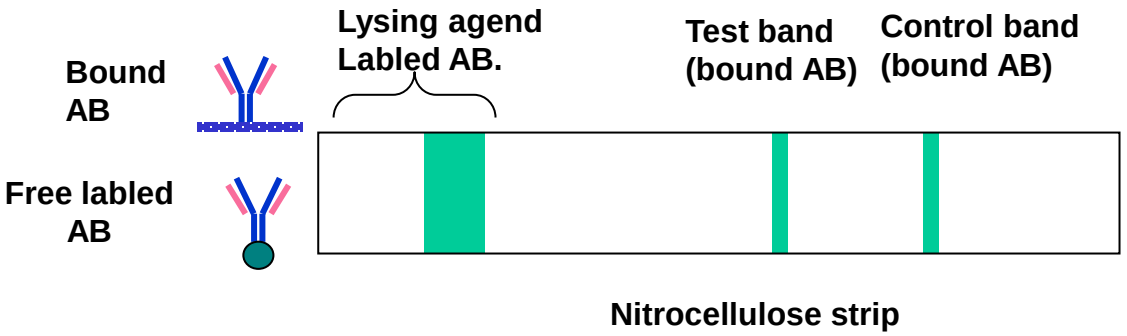
Simplified schematic representation of SARS-CoV-2 proteins detected by Ag-RDTs and of human antibodies



Structure of Ag-RDTs

Ag-RDTs detect antigens from clinical specimens using a simple-to-use immunochromatographic (lateral flow) test format, as commonly used for HIV and malaria rapid testing *(8)*.
RDTs are typically a nitrocellulose strip enclosed in a plastic cassette with a sample well. When the infected patient's sample is combined with the test buffer and added to the sample well of the test strip, target antigens in the mixture bind to labelled antibodies and migrate together; they are subsequently captured by an antibody bound to the test line, triggering a detectable colour change.
Depending on the test (and the antibody labels used), the colour change can be read by the operator with or without the aid of a reader instrument *(8)*. RDTs for COVID-19 can produce results in around 10-30 minutes versus the many hours required for most NAATs *(8)*.

Immunochromatography



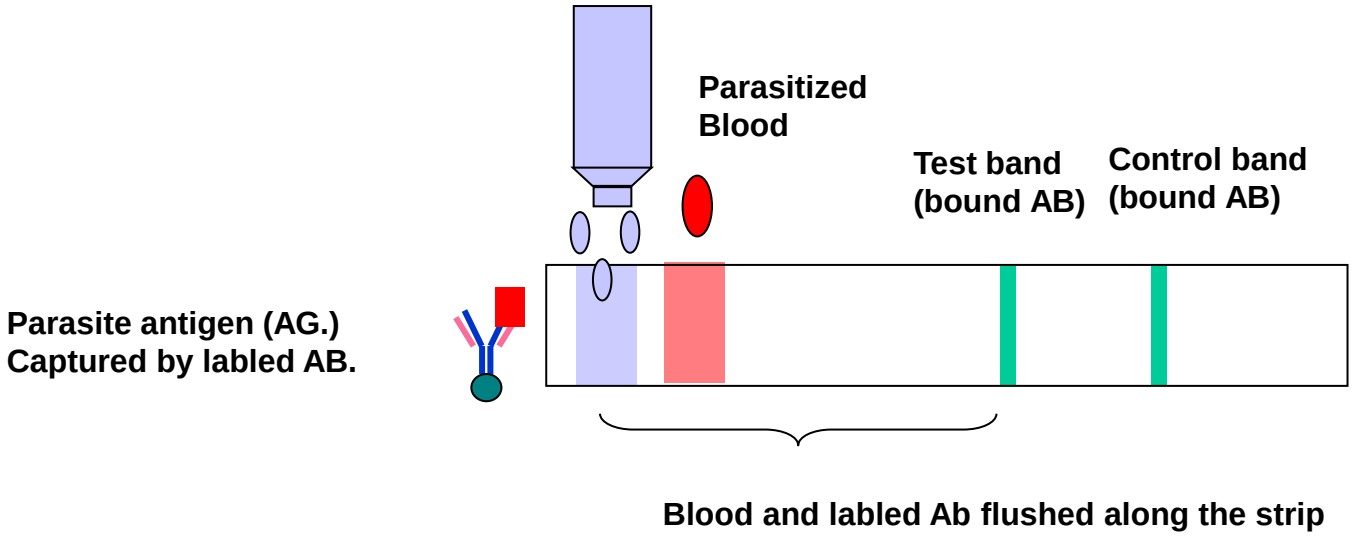
http://www.rapid-diagnostics.org/

Dye-labelled antibody, specific for target antigen, is present on the lower end of nitrocellulose strip or in a plastic well provided with the strip

Antibody, also specific for the target antigen, is bound to the strip in a thin (test) line, and either antibody specific for the labelled antibody, or antigen, is bound at the control line

Source: http://www.wpro.who.int/rdt

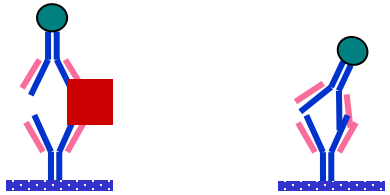
Immunochromatography



Blood and buffer, which have been placed on strip or in the well, are mixed with labelled antibody and are drawn up strip across the lines of bound antibody

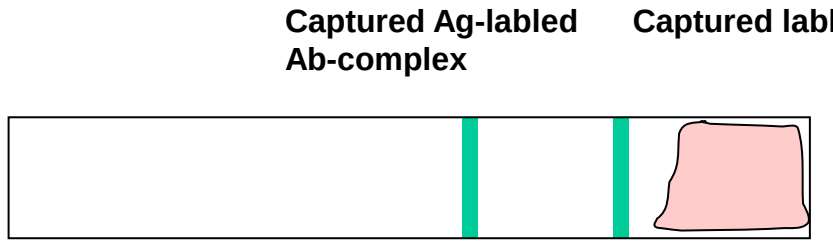
Source: http://www.wpro.who.int/rdt

Immunochromatography



Labled AB-AG-complex Captured by bound AB of test band

Labled AB-AG-complex Captured by bound AB of control band



If antigen is present, some labelled antibody will be trapped on the test line. Excess-labelled antibody is trapped on the control line

Source: http://www.wpro.who.int/rdt

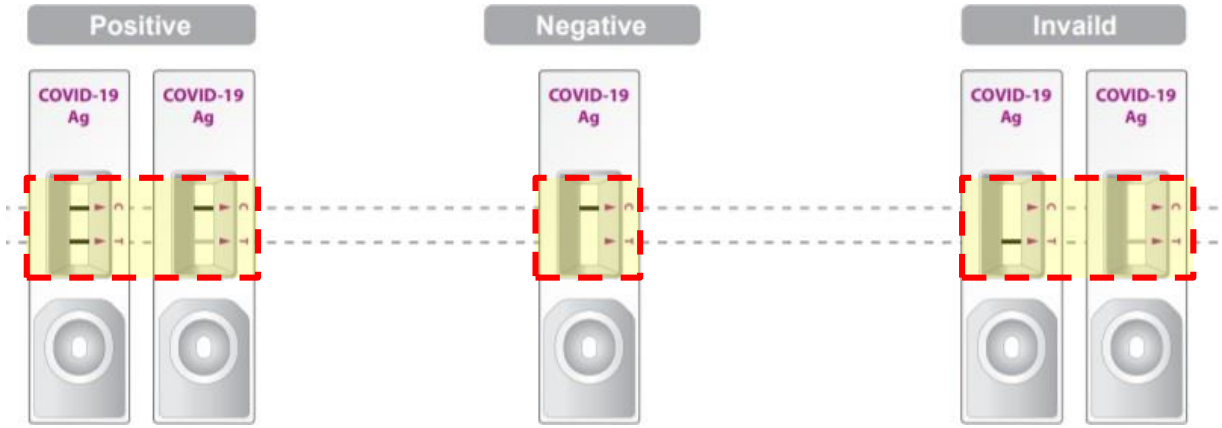
④ Test Procedure

7. Running of the assay

Read the test result in 15 - 30 minutes

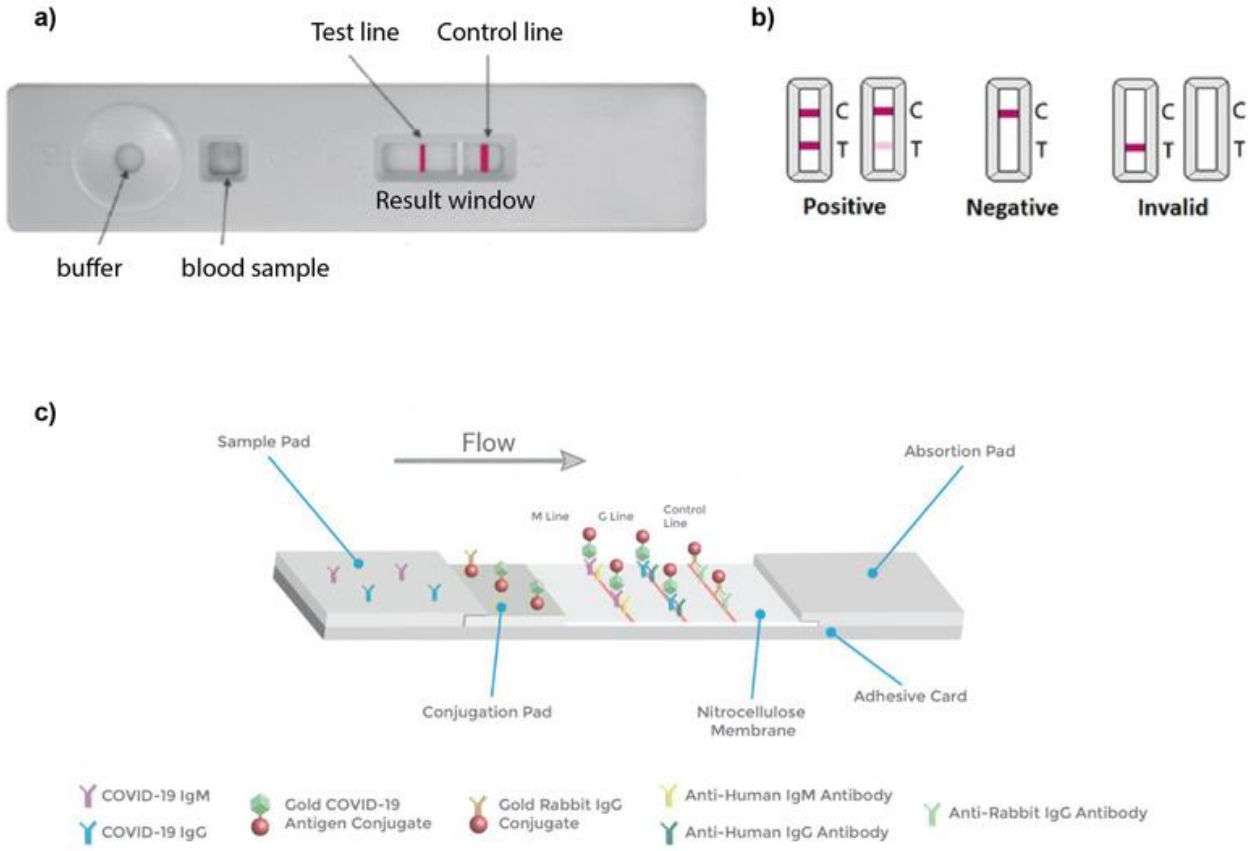
INTERPRETATION OF TEST RESULT

* "C“ Control Line "T Test line



Do not read test result after 30 minutes. It may show false result.
In case of invalid, we recommend re-test

Lateral flow assay for a serological test



Critical elements required for the safe and effective implementation of SARS-CoV-2 Ag-RDTs

Interpreting Ag-RDT performance

Ag-RDT performance is determined by the sensitivity and specificity of the test to detect a SARS-CoV-2 infection compared to a NAAT reference standard (generally rRT-PCR).

Sensitivity is the percentage of cases positive by a NAAT reference standard that are detected as positive by the Ag-RDT under evaluation.

$$\text{Sensitivity is calculated as: } \frac{\textit{(true positives)}}{\textit{(true positives + false negatives)}} \textit{ x 100}$$

Specificity is the percentage of cases negative by a NAAT reference standard that are detected as negative by the Ag-RDT under evaluation.

$$\text{Specificity is calculated as: } \frac{\textit{(true negatives)}}{\textit{(true negatives + false positives)}} \textit{ x 100}$$

Interpreting Ag-RDT performance

The prevalence of disease in the community being tested strongly affects the test's predictive value in terms of positive predictive value (PPV) and negative predictive value (NPV). PPV is the probability that a person with a positive test result truly has the disease. NPV is the probability that a person with a negative test result truly does not have the disease. The prevalence of disease should be estimated based on surveillance to determine the positive and negative predictive values for Ag-RDTs in order to enable optimal interpretation of the results. The following formulae show how PPV and NPV can be calculated.

PPV is calculated as: $\frac{\textit{(true positives)}}{\textit{(true positives + false positives)}} \textit{ x 100}$

NPV is calculated as: $\frac{\textit{(true negatives)}}{\textit{(true negatives + false negatives)}} \textit{ x 100}$

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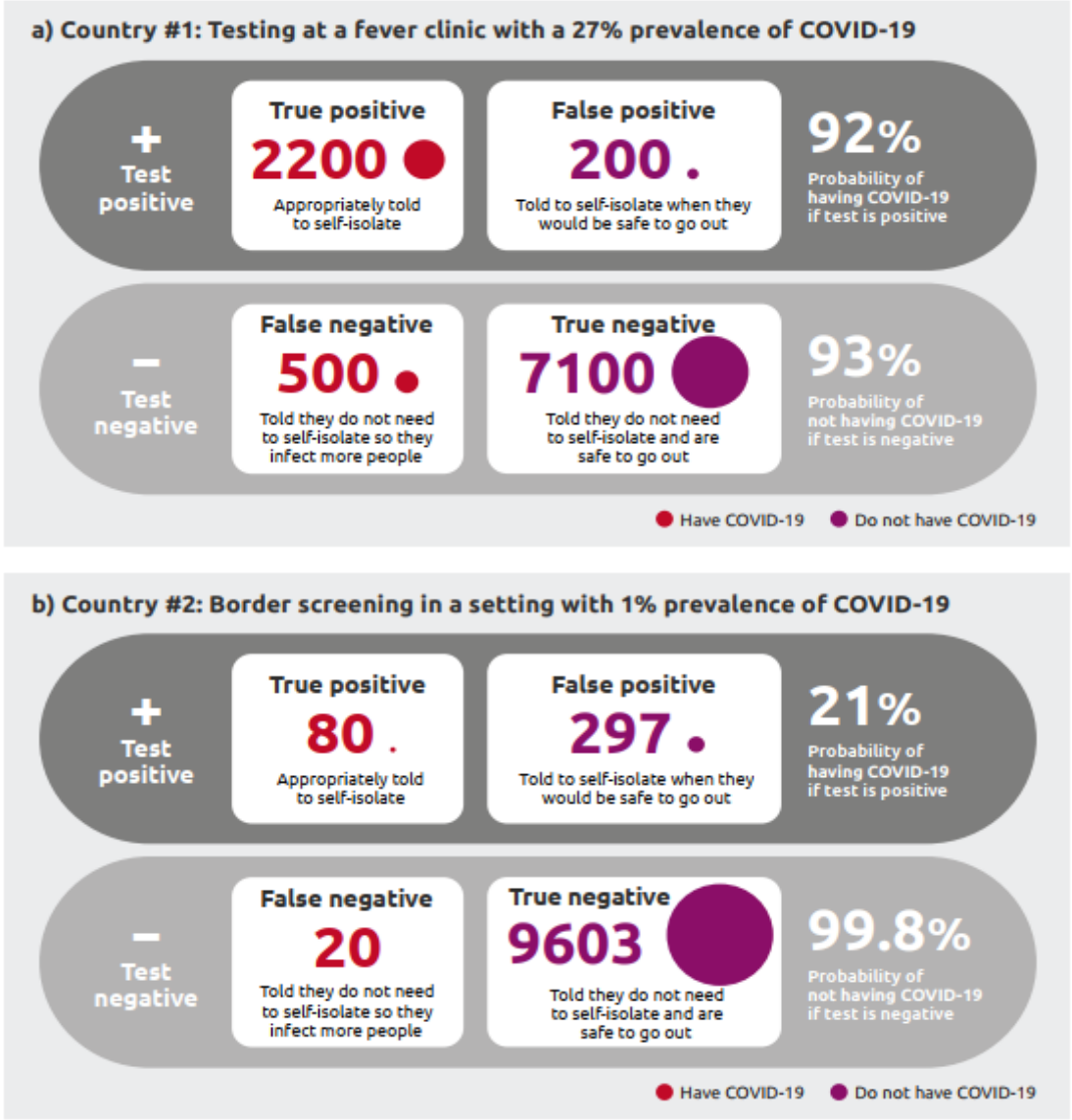
Fig. 2. Predictive value of Ag-RDT with 80% sensitivity and 97% specificity in a) a fever clinic with a 27% prevalence of COVID-19 and b) at border screening with a 1% prevalence of COVID-19, in a population of 10 000 people



The interim guidance also highlights three practical considerations for Ag RDT roll-out

1

Consider **initially deploying Ag RDTs in settings where NAAT is currently available** to confirm performance & allow staff to gain confidence

2

Where NAAT confirmation is not feasible, **triangulation with clinical symptoms or settings is needed** to confirm result validity

3

Use of Ag-RDTs **is not recommended in low prevalence settings** until specificity of tests is >99% because of high rate of false positives

#GlobalGoalUnite

Source: World Health Organization. Antigen-detection in the diagnosis of SARS-CoV-2 infection using rapid immunoassays. Interim guidance. 11 September 2020

The guidance also highlights 6 scenarios in which Ag RDT should not be used, based on expected initial test performance

Scenario	Explanation
In individuals without symptoms unless the person is a contact of a confirmed case	Pre-test probability is low.
Where there are zero or only sporadic cases	Ag-RDTs are not recommended for routine surveillance purposes or case management in this setting. Positive test results would likely be false positives. Molecular testing is preferred.
Appropriate biosafety and infection prevention and control measures (IPC) are lacking	To safeguard health workers, testing requires that operators wear gloves, gown, mask and face shield or goggles
Management of the patient does not change based on the result of the test	If test-positive and test-negative patients will be treated the same way because of unknown or low PPV and/or NPV, then there is no benefit to testing.
For airport or border screening at points of entry	Prevalence of COVID-19 will be highly variable among travellers, and it is therefore not possible to determine PPV and NPV of test results.
In screening prior to blood donation	A positive RDT result would not necessarily correlate with presence of viremia.

Source: World Health Organization. Antigen-detection in the diagnosis of SARS-CoV-2 infection using rapid immunoassays. Interim guidance. 11 September 2020

FIND
Because diagnosis matters

A s seen below, a test with sensitivity and 98% specificity), when applied to a **prevalence setting,** number of true positives and false positives (PPV: ~50%), will result in roughly the same **high performance** (95% **low**whereas when applied to a higher prevalence population would result in a much higher positive predictive value (PPV: 95%), with the majority of positive results associated with actual cases.
Alternatively the use of a **mid-or lower-performing test** might be considered for a **high prevalence population** (PPV: 68-78%), but would lead to such high numbers of false positives when testing a **low prevalence population that this would likely do more harm than good**.
Across a range of sensitivities and prevalence, the negative predictive value remains relatively high, but the consequence of missed cases for epidemic control and case management can be detrimental

Cohort	Pre-test probability (prevalence)	Sensitivity	Specificity	Cases	Non-cases	True positive (TP)	False negative (FN)	True negative (TN)	False positive (FP)	PPV	NPV
High performance											
1,000	2.0%	95%	98%	20	980	19	1	960	20	49.2%	100%
1,000	5.0%	95%	98%	50	950	48	2	931	19	71.4%	100%
1,000	10.0%	95%	98%	100	900	95	5	882	18	84.1%	99%
1,000	30.0%	95%	98%	300	700	285	15	686	14	95%	98%
Mid performance											
1,000	2.0%	85%	90%	20	980	17	3	882	98	14.8%	100%
1,000	5.0%	85%	90%	50	950	43	8	855	95	30.9%	99%
1,000	10.0%	85%	90%	100	900	85	15	810	90	48.6%	98%
1,000	30.0%	85%	90%	300	700	255	45	630	70	78%	93%
Low performance											
1,000	2.0%	75%	85%	20	980	15	5	833	147	9.3%	99%
1,000	5.0%	75%	85%	50	950	38	13	808	143	20.8%	98%
1,000	10.0%	75%	85%	100	900	75	25	765	135	35.7%	97%
1,000	30.0%	75%	85%	300	700	225	75	595	105	68%	89%

References

- https://emcrit.org/ibcc/COVID19/
- UpToDate on Coronaviruses, SARS, MERS, COVID-19
- CDC: https://www.cdc.gov/coronavirus/2019-ncov/index.html
- WHO: https://www.who.int/health-topics/coronavirus
  - Online courses at: https://openwho.org/
- https://www.worldometers.info/coronavirus/
- https://coronavirus.1point3acres.com/en?fbclid=IwAR3A3clE1Ztxi-fNBgTWtVOobWuUBGFJ1S3NBPFlAaYVruBcAtzeOcqpIjQ
- Dr James Lawler Presentation at American Hospital Association/ National Ebola Training and Education Center


Tanks