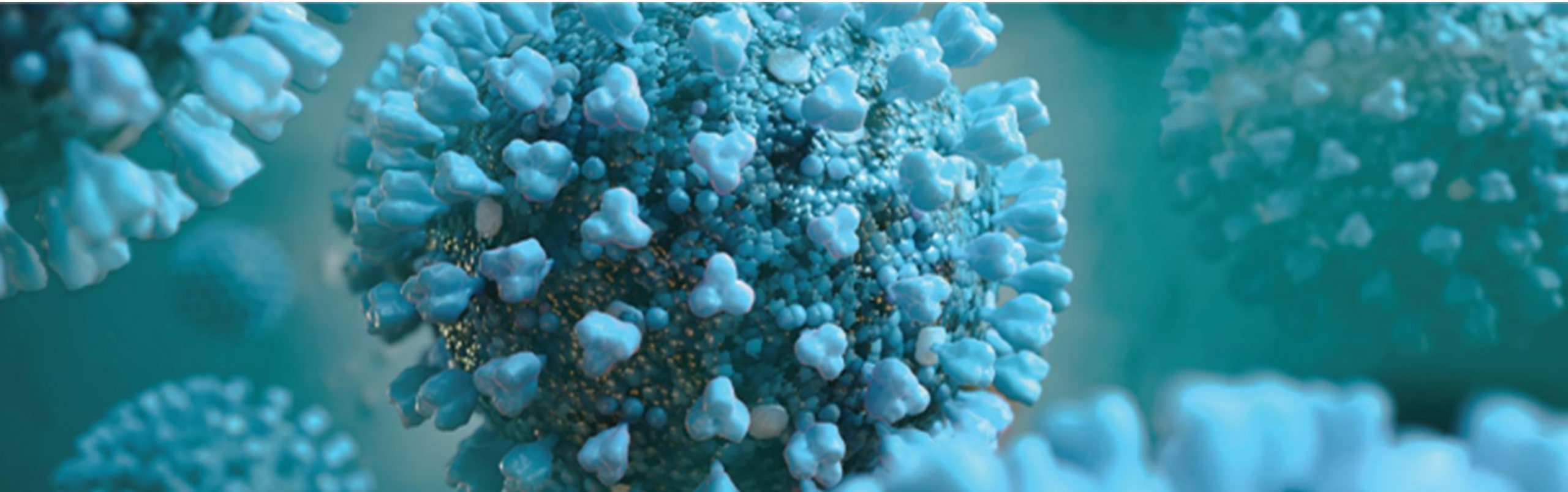
# Roche SARS-CoV-2 diagnostic testing

*ASLM ECHO session #18, July 10th 2020*

*Dr. Wim van der Helm, MD - Healthcare Development EMEA-LATAM – Global Access Program*



*All statements made in this document are based on the current state of scientific literature*

July 2020

# Value of Diagnostic Tests in the New World of COVID-19 Pandemic

## *The Problem*

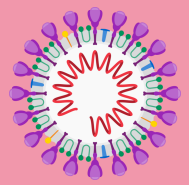
*In vitro diagnostic (IVD) tests are an essential service in the delivery of healthcare*

Patient pathway

**IVD tests**

**Prior to pandemic IVD test results influence 70% of clinical decisions**

**COVID-19**



Has opened a whole new window into the world of diagnostic testing.

- **Disrupted billions of lives**
- **Healthcare systems**
- **Global economy**

- **Effective treatments**
- **Preventative vaccines**

**Broad availability of fast, accurate and reliable testing**

https://pubs.rsna.org/doi/10.1148/radiol.2020201845, https://healthmanagement.org/c/imaging/news/value-of-diagnostic-tests-in-world-of-covid-19, https://www.medtecheurope.org/access-to-medical-technology/value-of-diagnostic-information-vodi/, https://www.medtecheurope.org/covid-19-information-hub/, https://www.roche.com/about/business/diagnostics/medical_value/testing-for-coronavirus.htm, https://www.roche.com/about/business/diagnostics/medical_value/testing-for-coronavirus.htm

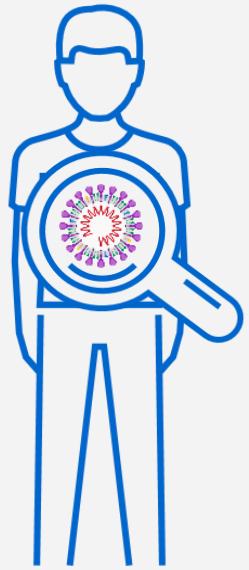
 

# Value of Diagnostic Tests in the New World of COVID-19 Pandemic

## *Roche solution*

*In vitro diagnostic (IVD) testing plays a vital role in testing who may have contracted COVID-19*

**IVD testing**



**Roche SARS-CoV-2 tests for present & past infection**

**Results**

Ensure healthcare professionals can **work safely**

**Quality care and treatment** available to those in need

Help flatten the curve **lowering the rate and spread of infection**

High quality **diagnostics** aid more accurate disease identification, leading to more appropriate patient care.

https://pubs.rsna.org/doi/10.1148/radiol.2020201845, https://healthmanagement.org/c/imaging/news/value-of-diagnostic-tests-in-world-of-covid-19, https://www.medtecheurope.org/access-to-medical-technology/value-of-diagnostic-information-vodi/, https://www.medtecheurope.org/covid-19-information-hub/, https://www.roche.com/about/business/diagnostics/medical_value/testing-for-coronavirus.htm, https://www.roche.com/about/business/diagnostics/medical_value/testing-for-coronavirus.htm

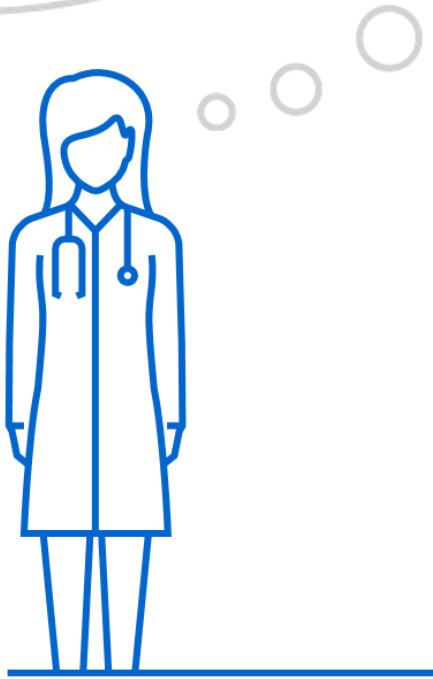
# What are we trying to find out?

*Testing Objectives*

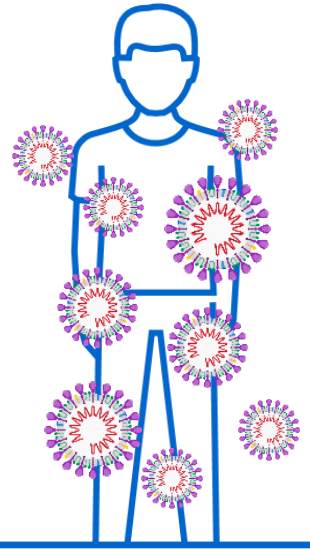
*"Should I advise isolation?"*

*"Could they still transmit the virus?"*

*"Have they previously been infected with the virus?"*

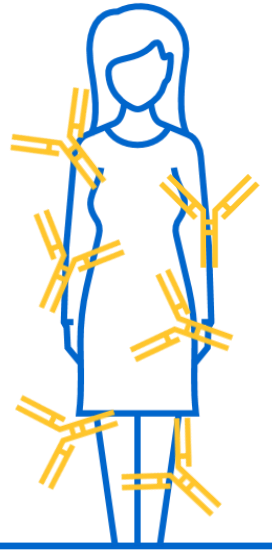


Is a person **currently infected** with SARS–CoV-2?



*or*

Has a person **previously been infected** with SARS–CoV-2?*

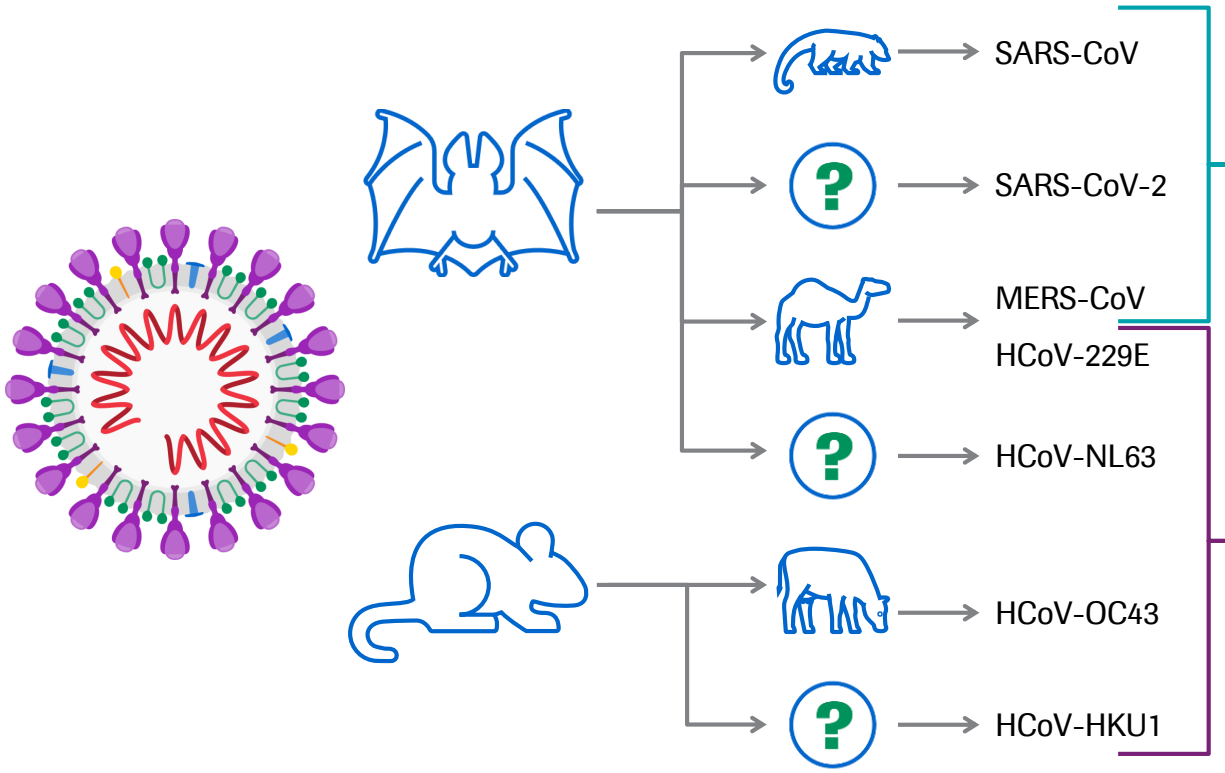


https://www.cdc.gov/coronavirus/2019-ncov/index.html, . World Health Organization. "Immunity passports" in the context of COVID-19
https://www.who.int/news-room/commentaries/detail/immunity-passports-in-the-context-of-covid-19

*It should be noted that currently there is no robust evidence that people who have recovered from COVID-19 and have antibodies are protected from a second infection

# Human coronaviruses are zoonotic

*Originate in animals and can infect humans*




**Widest variety seen in bats**

Severe respiratory syndrome viruses

**7 known human coronaviruses**

Common cold viruses

**Mammals may be intermediate hosts**

*Diagram Adapted from 1) and 3)*

*1. Zhu, N et al. (2020). N Engl J Med 2020;382:727-33; 2. Cui J, Li F, Shi ZL (2019). Nature Reviews. Microbiology. 17 (3): 181–92; 3. Su, S et al. (2016). Trends in Microbiology. 24 (6): 490–502; 4. Huynh J et al. (2012). Journal of Virology. 86 (23): 12816–25; 5. Masters PS (2006). Advances in Virus Research. Academic Press. 66: 193–292; 6. Vijgen, L. (2005). Journal of Virology. 79 (3): 1595–1604*

# Human coronaviruses are zoonotic

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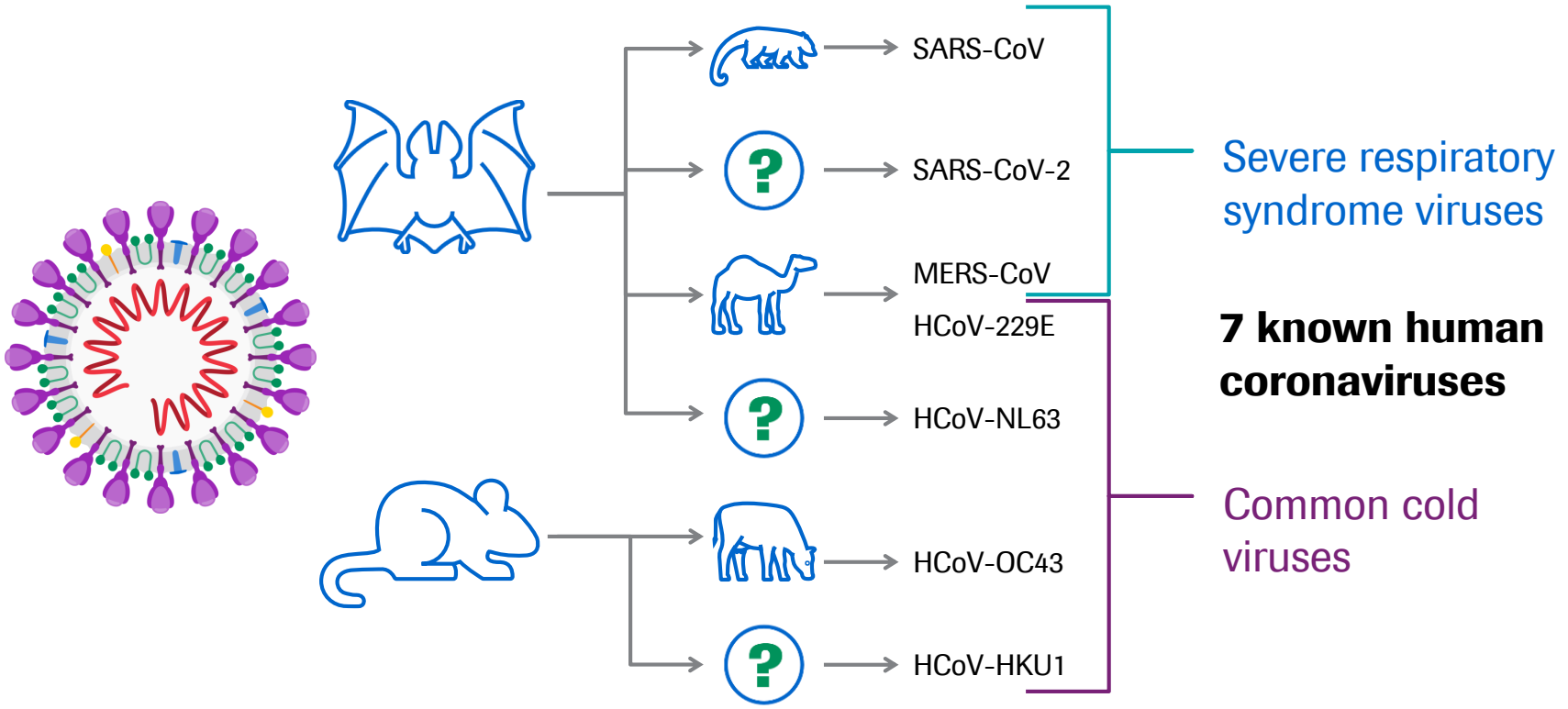


*Diagram Adapted from 1) and 3)*

**Two previous outbreaks:**

- Severe acute respiratory syndrome – SARS-CoV (2002; China)
- Middle East respiratory syndrome – MERS-CoV (2012; Saudi Arabia)


*1. Zhu, N et al. (2020). N Engl J Med 2020;382:727-33; 2. Cui J, Li F, Shi ZL (2019). Nature Reviews. Microbiology. 17 (3): 181–92; 3. Su, S et al. (2016). Trends in Microbiology. 24 (6): 490–502; 4. Huynh J et al. (2012). Journal of Virology. 86 (23): 12816–25; 5. Masters PS (2006). Advances in Virus Research. Academic Press. 66: 193–292; 6. Vijgen, L. (2005). Journal of Virology. 79 (3): 1595–1604*


 

# SARS-CoV-2 infection causes COVID-19

*Signs and Symptoms – an Overview*[1-7]


### Transmission

Person-to-person via respiratory secretions; indirectly through contaminated surfaces

### Incubation

Range of 2–14 days (median – 5 days)

### Main Symptoms

Fever, respiratory symptoms, Anosmia, diarrhea, vomiting, headache, myalgia

### Clinical presentation

Asymptomatic infection, mild illness, pneumonia, or fatal disease

### Clinical progression

Can cause severe respiratory disease, especially in 65+ and multi-morbid patients

### Case fatality rate*

Reported mortality rates vary from 0.8–15.5% (average 6.5%)

* CFR is unreliable during an outbreak

(1) Chen N et al. (2020). Lancet. 2020;395:507-13; (2) Holshue ML et al. (2020). N Engl J Med. 382:929-36; (3) Huang C et al. (2020). Lancet 395:497-506;
(4) Wang D et al. (2020).. JAMA 323:1061-1069; (5) CDC. https://www.cdc.gov/coronavirus/2019-nCoV/hcp/clinical-criteria.html
(6) Wu JT et al (2020). Lancet 395:689-97; (7) https://informationisbeautiful.net/visualizations/covid-19-coronavirus-infographic-datapack/

 

# COVID-19: risk factors for severe disease and death

*Accumulating evidence*[1]

**Evidence is rapidly accumulating about risk factors for COVID-19 progression, with data suggesting that the following factors may be associated with increased risk of severe disease and/or mortality**

**Older age**

**Male sex**

**Comorbidities**

(hypertension, diabetes, cardiovascular disease, chronic respiratory disease, cancer)

**Obesity**

**People who smoke**

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The **relative importance of different underlying health conditions is unclear**, owing to:

Inadequate adjustment for important confounding factors, insufficient follow-up, and likely under-reporting of pre-existing conditions

Studies are mainly among those patients at the highest risk admitted to hospital with full testing and **might not apply to the general population**

1 . Jordan RE, et al. BMJ (2020);368:m1198,doi: 10.1136/bmj.m1198.

# Coronaviruses

*Virion morphology and structural proteins*

## Large enveloped RNA viruses (80–120 nm)

### Lipid bilayer

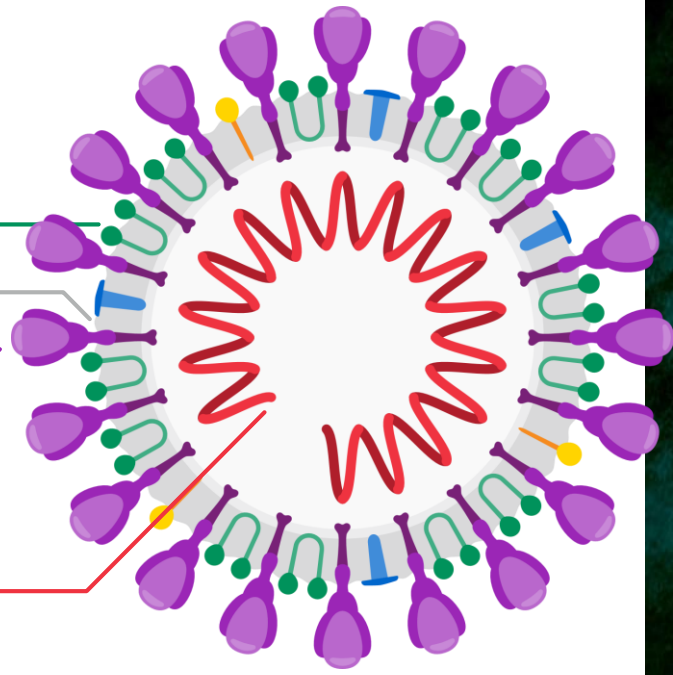
Membrane protein **(M)**

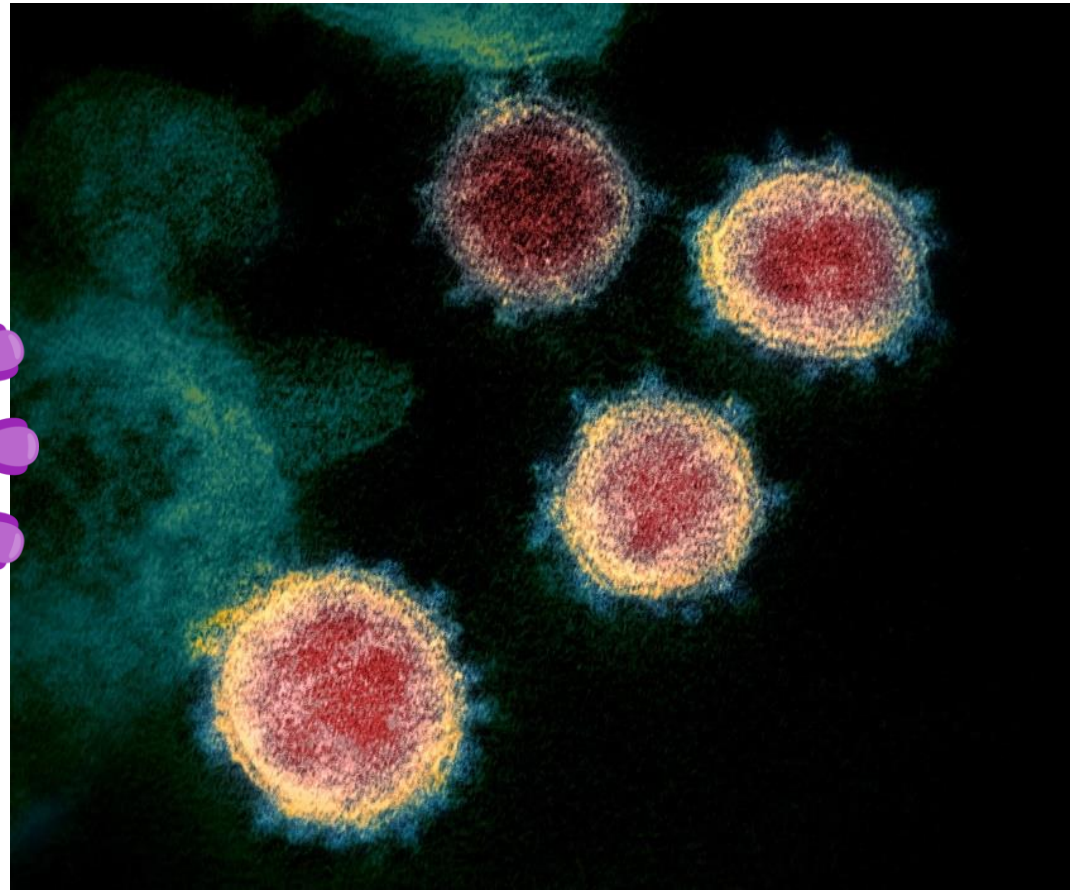
Envelope protein **(E)**

Spike protein **(S)**

### Nucleocapsid

Multiple copies of the **nucleocapsid (N protein)** bound to the RNA genome



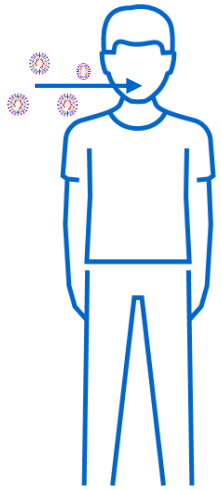


Masters PS (2006). Advances in Virus Research. Academic Press. 66: 193–292
Su, S et al. (2016). Trends in Microbiology. 24 (6): 490–502.
Paules CI et al. (2020). JAMA. 2020;323(8):707–708

# Following the infection path…

*Viral transmission*



Virus enters
the body via droplets

## Incubation

Range of 2–14 days
(median – 5 days)

## Transmission

Person-to-person via respiratory secretions; indirectly through contaminated surfaces

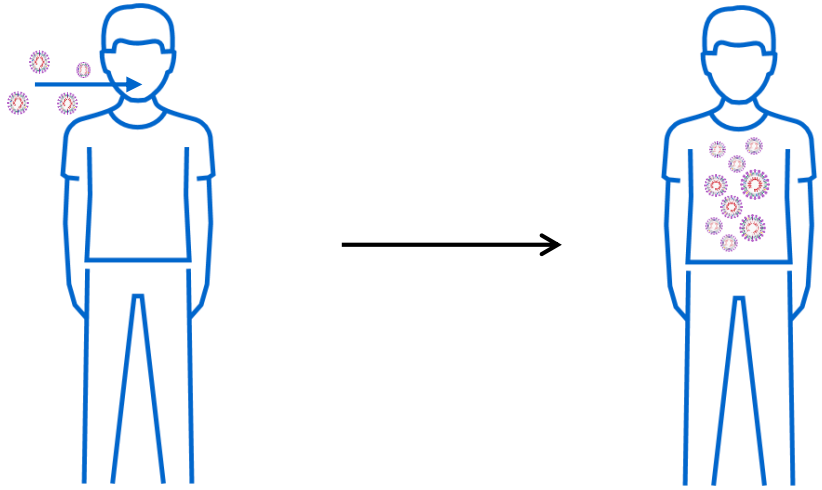
1. Li Q, et al. N Engl J Med (2020);doi.10.1056/NEJMoa2001316. 2. Backer JA, et al. Euro Surveill (2020);252000062.; 3. The World Health Organization https://www.who.int/news-room/q-a-detail/q-a-coronaviruses. Accessed 28 April 2020. 4. Zhou F, et al. Lancet (2020);395:1054–62. 5. Wu Y, et al. Lancet (2020);S2468–1253:30083. 1. Chen N, et al. Lancet (2020);395:507–513. PMID: 32007143; 2. Holshue ML, et al. N Engl J Med (2020);382:929–936. PMID: 32004427; 3. Huang C, et al. Lancet (2020);395:497–506. PMID: 31986264; 4. Wang D, et al. JAMA. (2020);323:1061–1069. PMID: 32031570; 5. Centers for Disease Control and Prevention. https://www.cdc.gov/coronavirus/2019-nCoV/hcp/clinical-criteria.html. Accessed March 4, 2020; 6. Wu JT, et al. Lancet (2020);395:689–697

# Following the infection path…

*Viral reproduction in host cells of lung*

## Broad range of symptoms and clinical presentation



Virus enters
the body via droplets

Virus reproduces

### Symptoms

Fever, respiratory symptoms, abdominal pain, diarrhea, vomiting, headache, myalgia

### Clinical presentation

Asymptomatic infection, mild illness, pneumonia, or fatal disease

### Clinical progression

Can cause severe respiratory disease, especially in 65+ and multi-morbid patients

1. Li Q, et al. N Engl J Med (2020);doi.10.1056/NEJMoa2001316. 2. Backer JA, et al. Euro Surveill (2020);252000062.; 3. The World Health Organization https://www.who.int/news-room/q-a-detail/q-a-coronaviruses. Accessed 28 April 2020. 4. Zhou F, et al. Lancet (2020);395:1054–62. 5. Wu Y, et al. Lancet (2020);S2468–1253:30083. 1. Chen N, et al. Lancet (2020);395:507-513. PMID: 32007143; 2. Holshue ML, et al. N Engl J Med (2020);382:929–936. PMID: 32004427; 3. Huang C, et al. Lancet (2020);395:497–506. PMID: 31986264; 4. Wang D, et al. JAMA. (2020);323:1061–1069. PMID: 32031570; 5. Centers for Disease Control and Prevention. https://www.cdc.gov/coronavirus/2019-nCoV/hcp/clinical-criteria.html. Accessed March 4, 2020; 6. Wu JT, et al. Lancet (2020);395:689–697

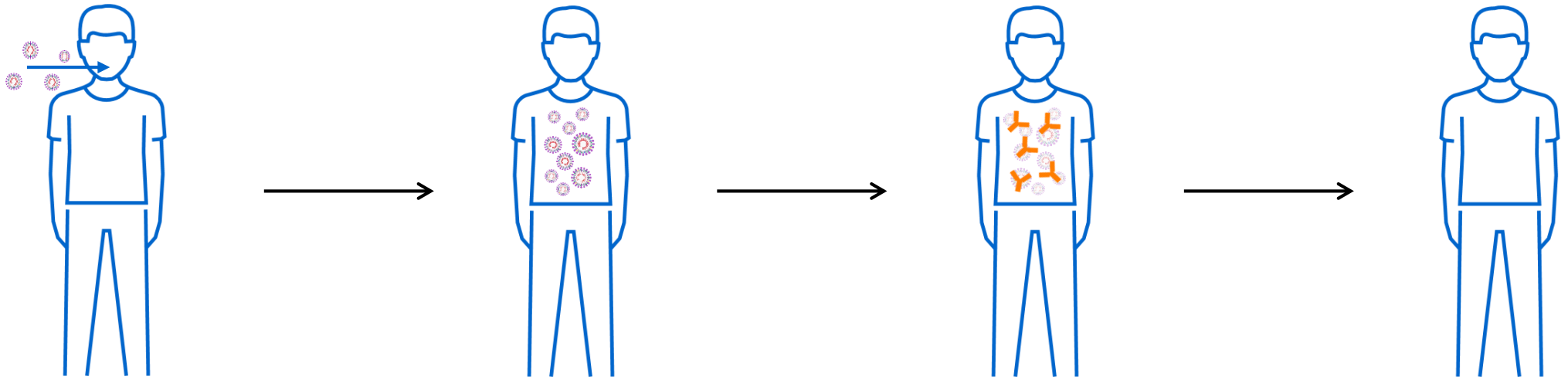
 

# Following the infection path…

*Stages of transient viral infections*

**Period a person is typically infectious**

**If small amounts of virus are present, individuals may still be infectious**



Virus enters the body via droplets

Virus reproduces

An immune response is triggered in the infected body

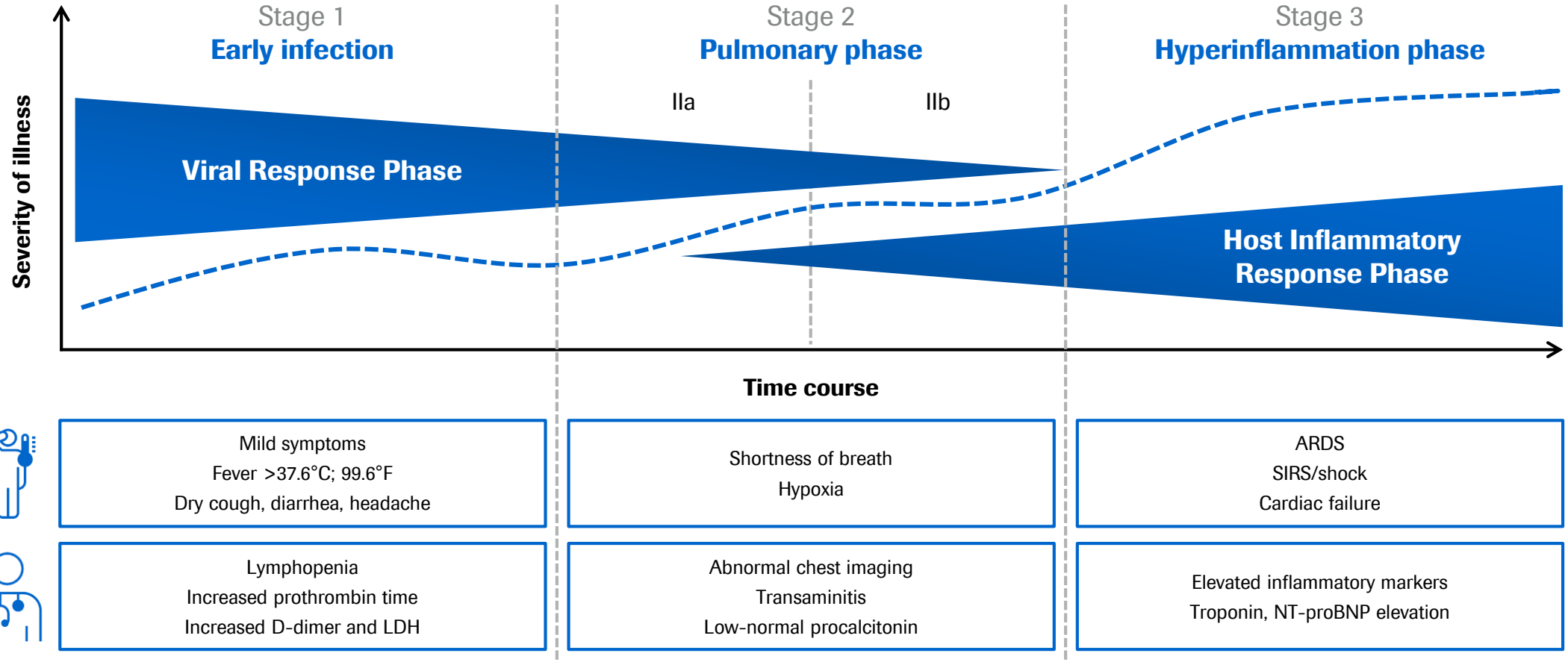
Virus is eliminated
The individual recovers

1. Li Q, et al. N Engl J Med (2020);doi.10.1056/NEJMoa2001316. 2. Backer JA, et al. Euro Surveill (2020);252000062.; 3. The World Health Organization https://www.who.int/news-room/q-a-detail/q-a-coronaviruses. Accessed 28 April 2020.
4. Zhou F, et al. Lancet (2020);395:1054–62. 5. Wu Y, et al. Lancet (2020);S2468–1253:30083.

# Clinical stages of COVID-19

*Potential therapeutic approaches*




1.Siddiqi H & Mehra M. J Heart Lung Transp (2020). In press. doi: https://doi.org/10.1016/j.healun.2020.03.012.
2.https://www.jhltonline.org/article/S1053-2498(20)31473-X/fulltext

# COVID-19 testing recommendations

**Criteria to guide evaluation and laboratory testing for COVID-19**

https://www.cdc.gov/coronavirus/2019-nCoV/hcp/clinical-criteria.html

**Laboratory support for COVID-19 in the EU/EEA**

https://www.ecdc.europa.eu/en/novel-coronavirus/laboratory-support

**Laboratory testing strategy recommendations for COVID-19**

https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/laboratory-guidance

**In summary:**

Nucleic Acid Amplification Test (NAAT) for diagnosis

Testing is needed to inform clinical decision making and public health policy

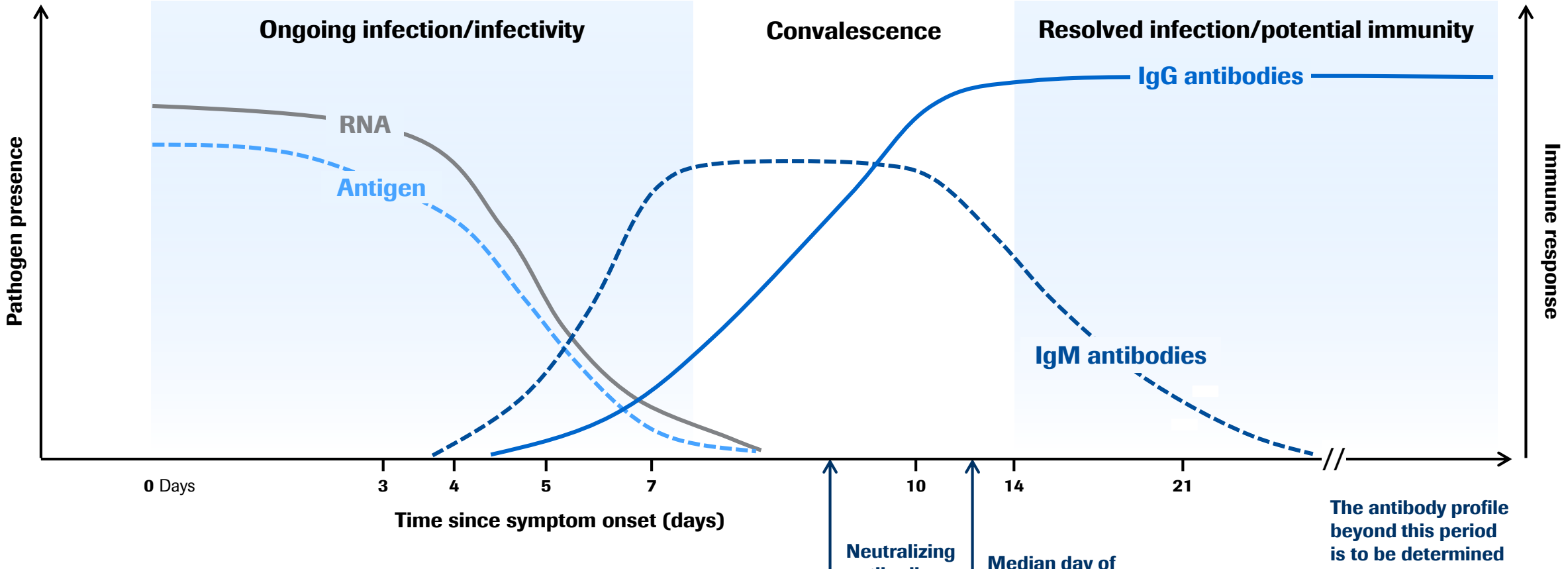
Prioritization of testing is needed when the availability of testing is limited

Criteria to Guide Evaluation and Laboratory Testing for COVID-19 . Available at: https://www.cdc.gov/coronavirus/2019-nCoV/hcp/clinical-criteria.html. Accessed April 2020.
https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines.html

# Course of molecular and serological biomarkers*

*SARS-CoV-2 infection*




*Illustrative only as sero conversion time not known as yet. Larger studies are required

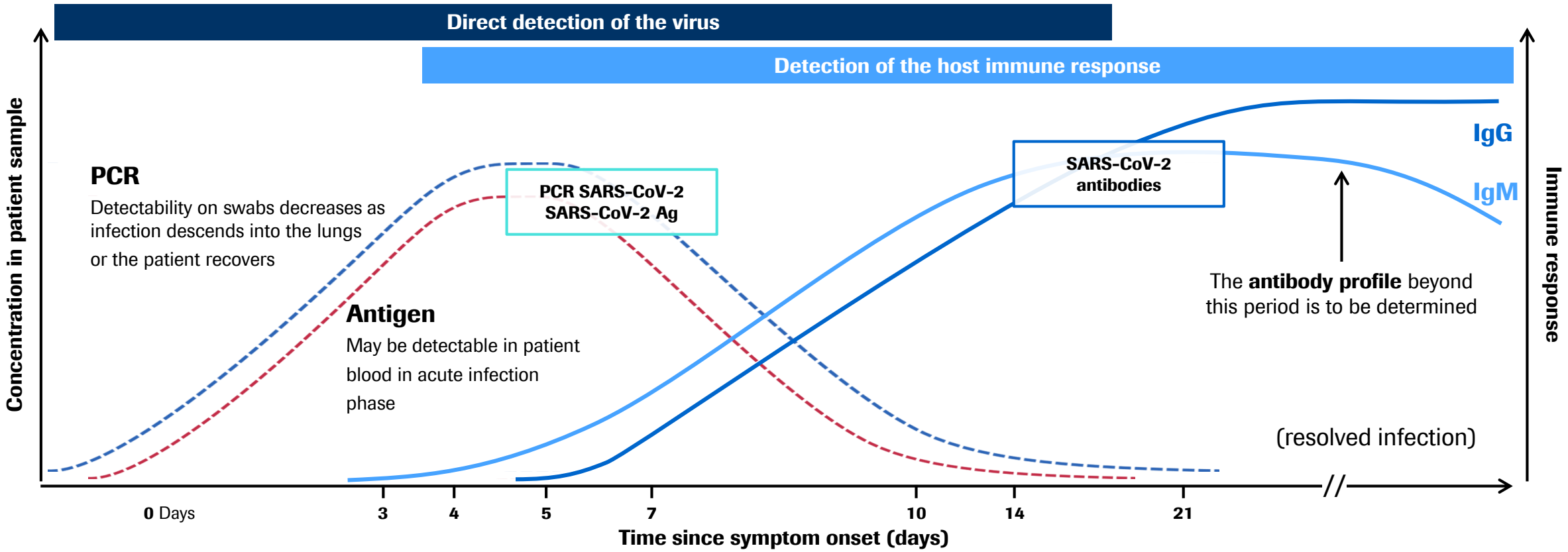
Xiang F, et al. Clin Infect Dis (2020);ciaa461. doi: 10.1093/cid/ciaa461; 2. Zhao J, et al. Clin Infect Dis (2020);pii:ciaa344. doi:10.1093/cid/ciaa344; 3. Wölfel R, et al. Nature (2020);[epub ahead of print]. doi.10.1038/s41586-020-291-x. 4. Jin Y, et al. Int J Infect Dis (2020). 5. Liu W, et al. J Clin Microbiol (2020);pii:JCM.00461-20.doi.10.1128/JCM.00461-20. 6. Guo L, et al. Clin Infect Dis (2020); doi.10.1093/cid/ciaa310. 7. Zhang W, et al. Emerg Microb Infect;9:386–389.

# *Assessing the response to infection*

# Opportunities for detection of SARS-CoV-2 infection & recovery phases*

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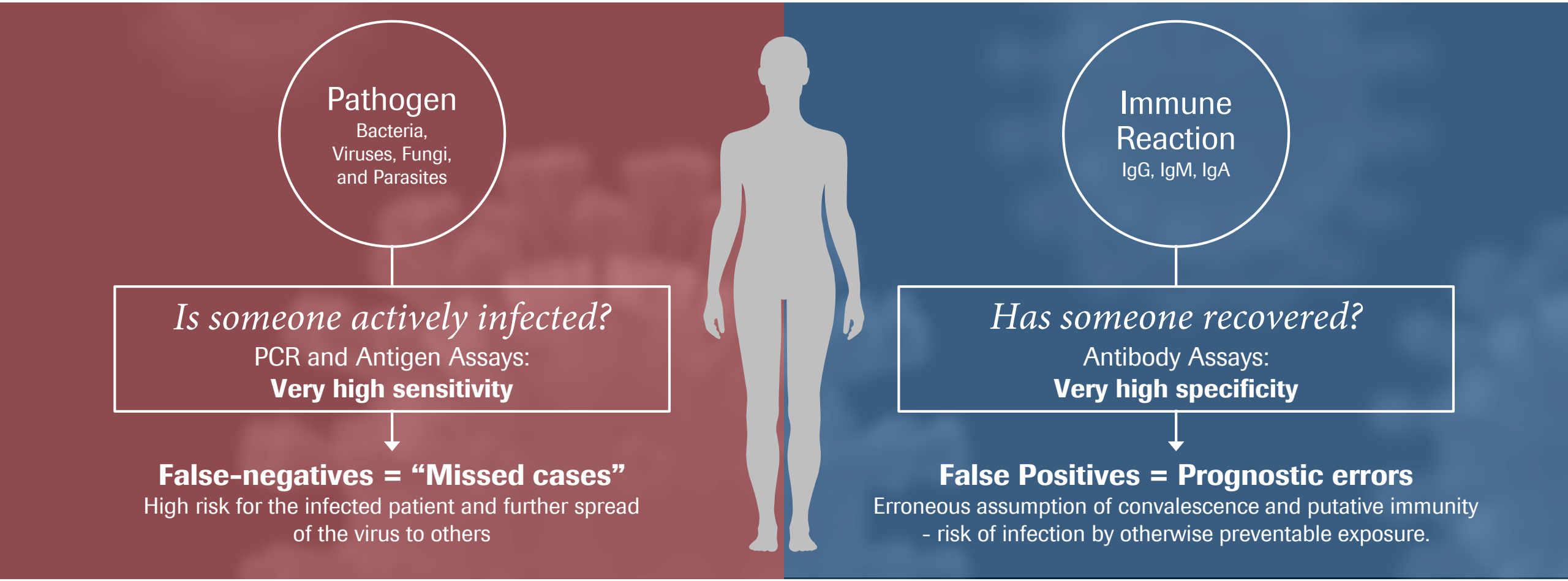
# SARS-CoV-2 infection

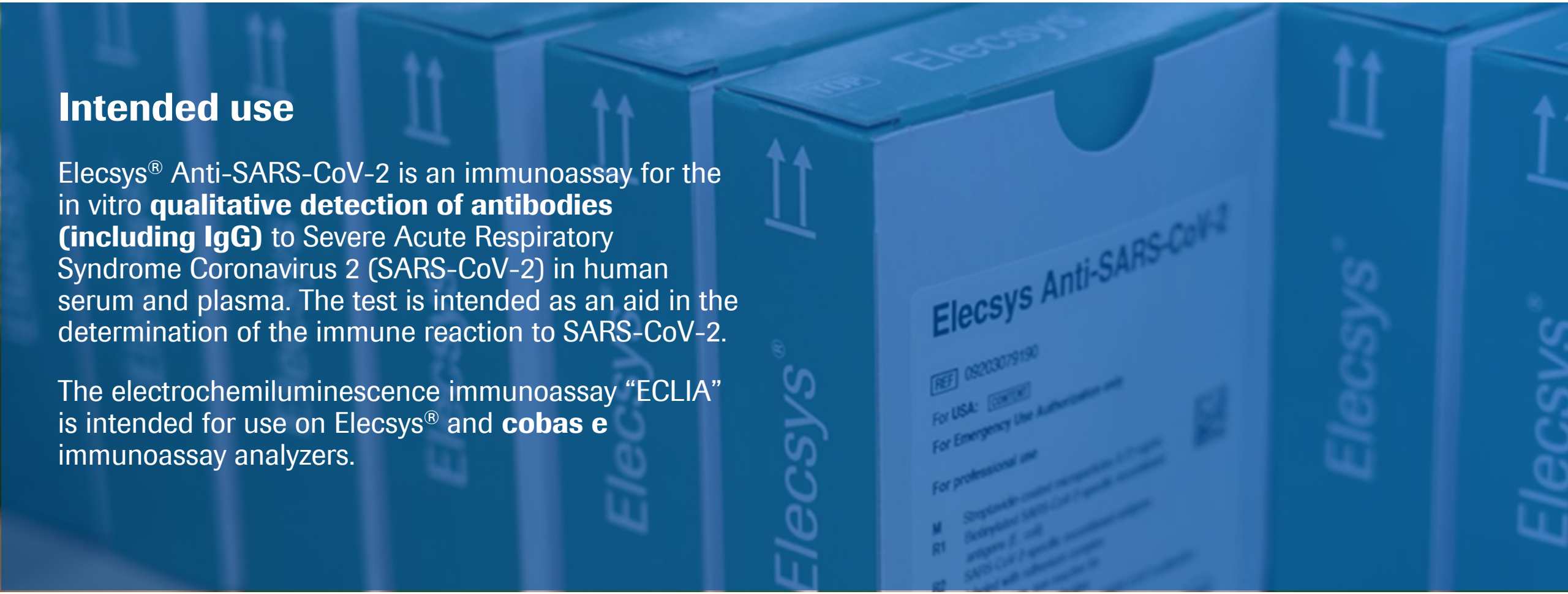
*Molecular and serology tests serve different use cases*




*Patel R et al. (2020). mBio Mar 2020, 11 (2) e00722-20; DOI: 10.1128/mBio.00722-20*

# Elecsys® Anti-SARS-CoV-2




## Intended use

Elecsys® Anti-SARS-CoV-2 is an immunoassay for the in vitro **qualitative detection of antibodies (including IgG)** to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in human serum and plasma. The test is intended as an aid in the determination of the immune reaction to SARS-CoV-2.

The electrochemiluminescence immunoassay "ECLIA" is intended for use on Elecsys® and **cobas e** immunoassay analyzers.

# Links to educational & technical material

*Our commitment to help put a stop to the COVID-19 pandemic*

## Real-time RT-PCR test

Detecting SARS-CoV-2 in currently infected patients with high sensitivity

The **cobas**® SARS-CoV-2 Test is a real-time RT-PCR test intended for the qualitative detection of SARS-CoV-2 in nasopharyngeal and oropharyngeal swab samples from patients.

This test can run on Roche's fully automated **cobas**® 6800 and **cobas**® 8800 Systems under Emergency Use Authorization. The test is also available for countries accepting the CE-mark.

**cobas**® SARS-CoV-2 Test ›

**cobas**® 6800 System ›

**cobas**® 8800 System ›

## Antibody test

Detecting a patient's immune response to SARS CoV-2 with high specificity

The Elecsys® Anti-SARS-CoV-2 is an immunoassay for the in vitro qualitative detection of antibodies (including IgG) to SARS-CoV-2 in human serum and plasma. The test is intended as an aid in the determination of the immune reaction to SARS-CoV-2.

The electrochemiluminescence immunoassay "ECLIA" is intended for use on **cobas e** immunoassay analyzers.

Elecsys® Anti-SARS-CoV-2 ›

**cobas e** 411 analyzer ›

**cobas e** 601 module ›

**cobas e** 602 module ›

**cobas e** 801 module ›

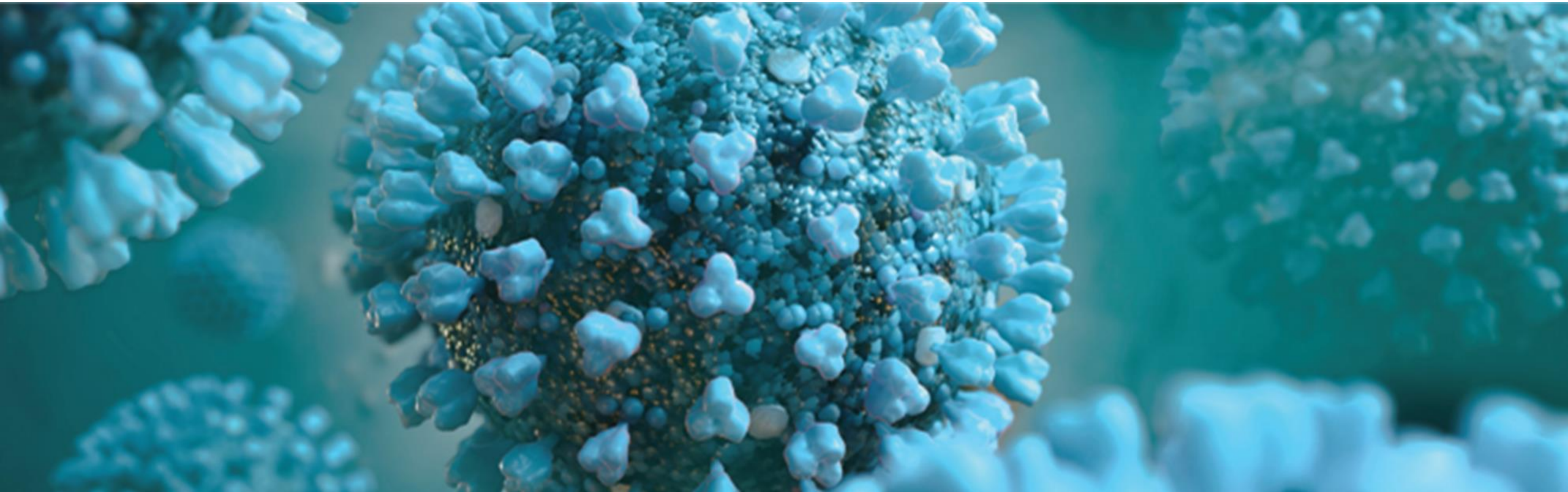
https://diagnostics.roche.com/global/en/c/covid-19-pandemic.html

https://dialog.roche.com/global/en_us/covid/run2.html

# Roche SARS-CoV-2 diagnostic testing

*ASLM echo session, July 10th 2020*

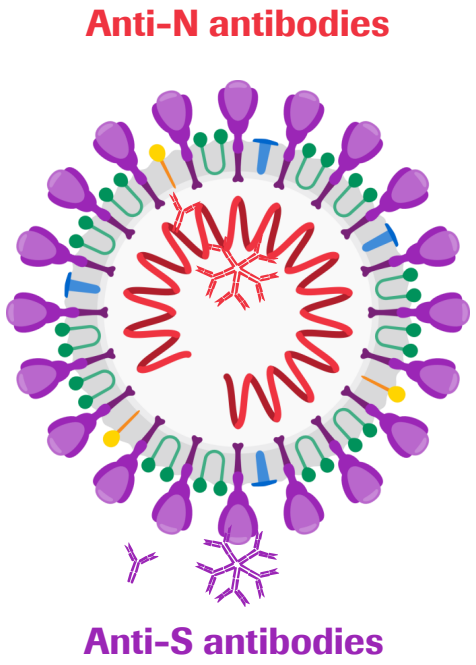
*Dr. Matthias Strobl, Senior Clinical Science Leader - Infectious Diseases*



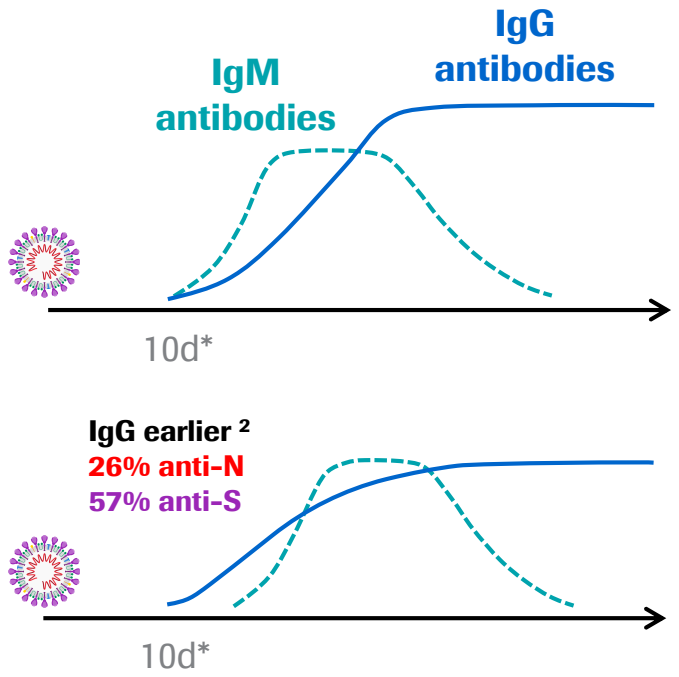
# Serum antibody responses during infection by SARS-CoV-2

*Anti-SARS-CoV-2 IgM is not a specific indicator of early infection*

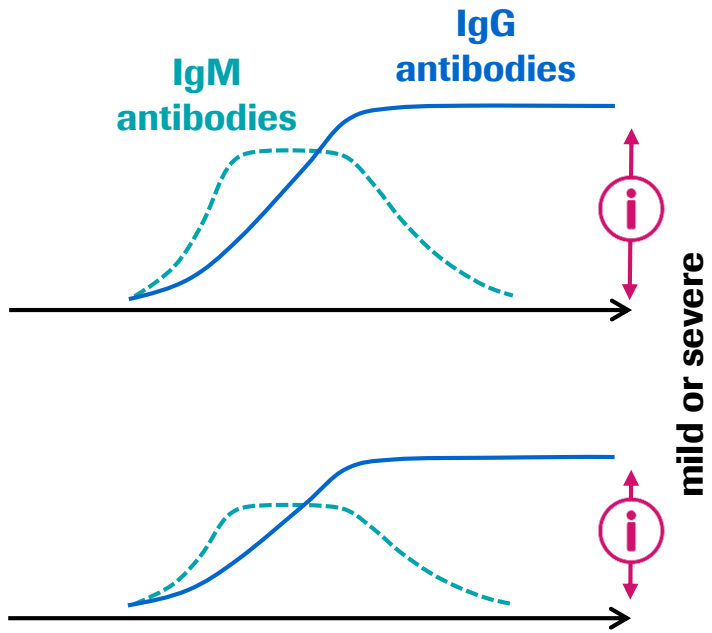
**Antibodies are generated against the spike (S) and the nucleocapsid (N) protein [1,2]**




**IgM and IgG appear mostly at the same time, but IgG can rise earlier than IgM! [2,3]**




**Antibody levels are not directly correlated with clinical severity [2-4]**





*(1) Okba NMA, Müller MA, Li W, Wang C, et al. medRxiv 2020.03.18.20038059; (2) To KKW et al. (2020). Lancet Infect Dis 2020; DOI:10.1016/ S1473-3099(20)30196-1*
*(3) Wu F et al. medRxiv 2020.03.30.20047365; doi: https://doi.org/10.1101/2020.03.30.20047365; (4) Long et al. (2020). Nat Med. https://doi.org/10.1038/s41591-020-0897-1*


**after symptom onset*

# Nucleocapsid selected as target antigen

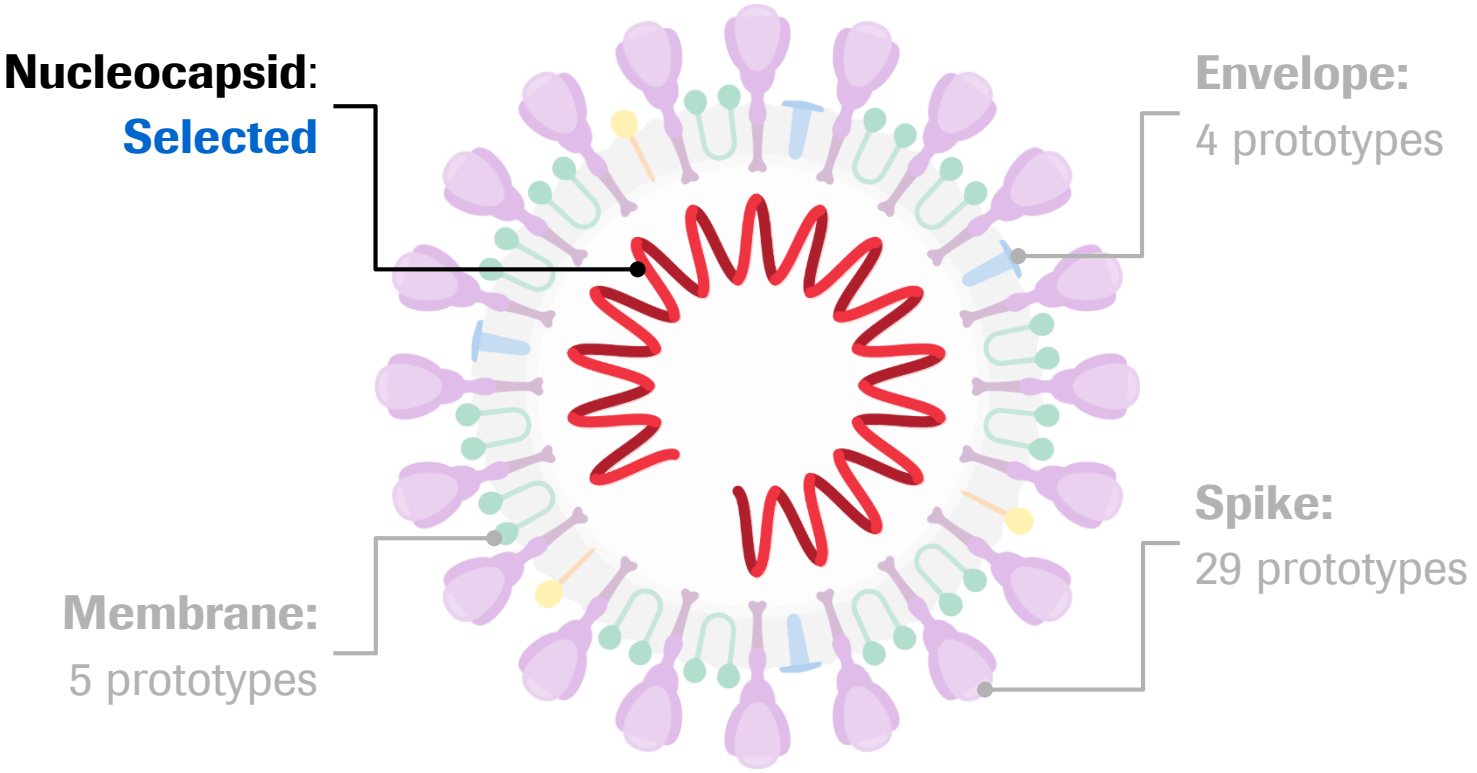
*Elecsys® Anti-SARS-CoV-2*

**N selected based on experimental data and manufacturability:**

- Performed better than all other targets in several hundred clinical samples
- Can be synthesized in soluble form
- Large-scale production in a fast and reliable manner

**Main performance requirement for selection:**

- High specificity



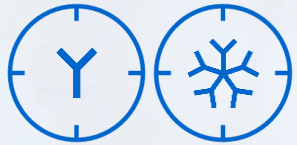

 

# Considerations when testing for SARS-CoV-2 antibodies

*Epidemiological screening*

For SARS-CoV-2 epidemiological screening, the aim is to **correctly identify** all patients who have been **exposed to the SARS-CoV-2** to better understand the prevalence, epidemiology and dynamics of the virus and COVID-19[1,2]

For this purpose, a **high positive predictive value** is highly desirable[2]



Given that **levels** and **chronological** order of IgM and IgG antibody appearance are **variable,** targeting both antibodies simultaneously following a total antibody approach may be beneficial for increasing the **sensitivity** of a test[3,4]

1. Patel R, *et al.* mBio (2020);11: pii: e00722-20. doi: 10.1128/mBio.00722-20 ; 10. Wu LP, *et al*. Emerg Infect Dis. 2007.*13*:1562–4; 2. Trevethan R. Front Public Health 2017 5(307); doi: 10.3389/fpubh.2017.00307 3. To K *et al.* Lancet *Infect Dis* 2020. doi:10.1016/S1473-3099(20)30196-1; 4. Zhao J, *et al*. lin *Infect Dis* 2020; doi: 10.1093/cid/ciaa344.

# Considerations when testing for SARS-CoV-2 antibodies[1,2]

*Antibody maturity*

| Ab Main Types → | Early/Immature | Mature | Neutralizing |
|---|---|---|---|
| **Description** | • Appear in early infection phase<br>• **Do not effectively recognize the virus** | • Appear in convalescent phase<br>• **Effectively recognize the virus** | • Appear in convalescent/ immunity phase<br>• **Effectively neutralize the virus** |
| **Examples** | IgM, early/immature IgA, IgG | Late/mature Igs | Neutralizing antibodies (*sub-set of mature Igs*) |
| **Relevance/ Purpose** | Initial host response to start understanding the virus | Host memory of the virus for future recognition | Render the virus ineffective against the host |

**Note:** All neutralizing antibodies are mature antibodies BUT not all mature antibodies are neutralizing antibodies[1,2]

*Targeting mature antibodies may be beneficial in increasing testing specificity*

1. George A.J.T. (2000) The Antibody Molecule. In: George A.J.T., Urch C.E. (eds) Diagnostic and Therapeutic Antibodies. Methods in Molecular Medicine, vol 40. Humana Press;; https://www.britannica.com/science/antibody (accessed April 2020); 2 Roche internal data

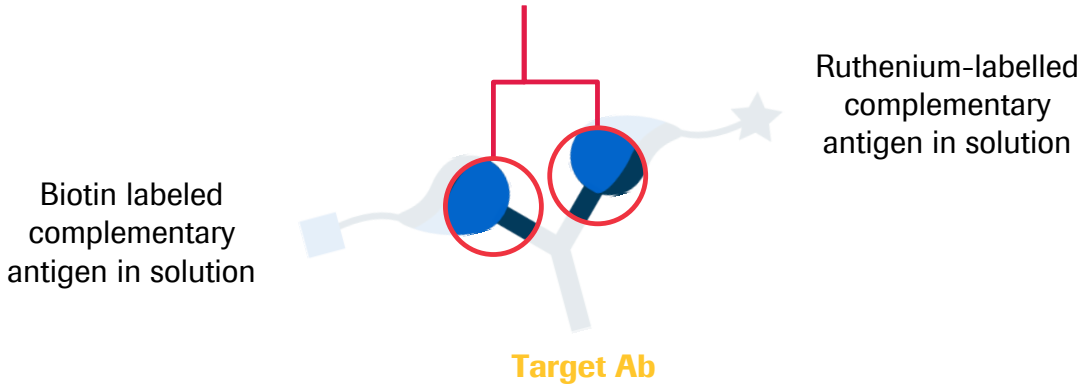
 

# Fit for Purpose Antibody Assay Formats

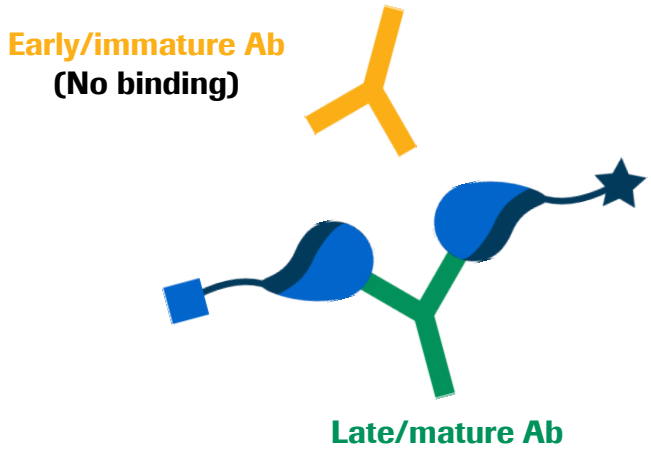
## Mature High Affinity Total Antibody Assay

### In-solution Double Antigen Sandwich[2]

**Single arm (high affinity) binding is necessary to give positive result**




Complementary antigens (Ag) are in solution




Assay requirement of 2 independent binding antibodies to complementary Ags enables specific, preferential detection of late/mature Abs

[1] Roche internal data; [2] Faatz, E., Finke, A et al. (2019).. In *Analytical Electrogenerated Chemiluminescence* (pp. 443-470)

# SARS-CoV-2 neutralizing antibodies

*Spike vs nucleocapsid as target antigen*

## How do antibodies inhibit viruses? [1-4]

Block access to receptors used by the virus to enter host cells

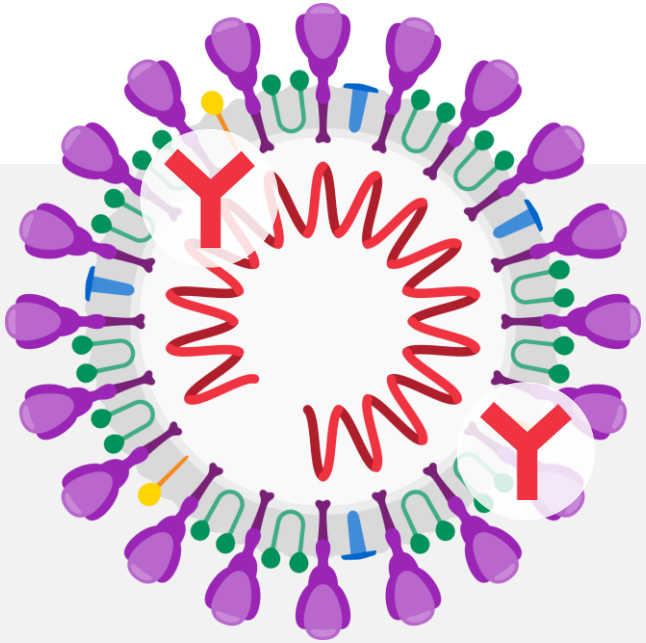
Interfere with viral life cycle via complex interactions* [5-8]

**Neutralizing Abs may confer protection**

Also considered critical for selection of convalescent plasma for therapeutic or prophylactic uses,and for vaccine assessment

Studies show **anti-nucleocapsid & anti-spike Ab** correlate with neutralization, i.e. putative clinical immunity [9-11]

**In the Elecsys® assay format, the nucleocapsid antigen confers high specificity**



** Examples of non-neutralizing complex interactions[2-4]: 1) Tagging cells for destruction by effector cells before viruses have a chance to exit (e.g. antibody-dependent cellular cytotoxicity (ADCC); 2) Induction of complement-mediated cytolysis, increased T cell responses associated with enhanced dendritic cell function, and reduced viral replication in culture; 3) Cooperatively elicit robust protective immunity when combined virus-specific CD8 T cells[4] NOTE: also cellular immunity plays a role[6,7]*

(1) Burton, D (2002). Nat Rev Immunol 2, 706–713; (2) Payne S (2017). Viruses: Chapter 6 - Immunity and Resistance to Viruses, Editor(s): Susan Payne, Academic Press; (3) Coughlin MM (2012). Rev Med Virol. 22(1):2–17.; (4) Zhou G et al. (2020). Int J Biol Sci;16(10):1718–1723; (5) Murin CD et al. (2019). Nat Microbiol 4, 734–747, (6) Damian M et al. (2008). J Immunol;181(6):4168-4176; (7) Laidlaw BJ et al. (2013). PLoS Pathog 9(3): e1003207; (8) Enayatkhani M et al. (2020). PLoS Pathog 9(3): e1003207; (9) To K et al. Lancet Infect Dis. 20(5), 565-74; (10) Wu F et al. (2020). JAMA. 323(13), 1239-1242; (11) Okba N et al. medRxiv. 2020. preprint doi: https://doi.org/10.1101/2020.03.18.20038059

# Correlation of Elecsys® Anti-SARS-CoV-2 with neutralization

*Positive correlation with neutralizing capacity*

- **A positive test result with Elecsys Anti-SARS-CoV-2 correlates well with neutralization capacity in the same sample.**
- **Number of negative samples is too low to determine specificity, but no false positive results were observed with Elecsys® Anti-SARS-CoV-2.**

**Roche internal study: 46 clinical samples from individual patients [1]**

| | | Pseudo-Neutralisation[2] | | |
|---|---|---|---|---|
| | | **Pos** | **Neg** | **Total** |
| **Elecsys® Anti-SARS-CoV-2** | **Pos** | 38 | 0 | 38 |
| | **Neg** | 6 | 2 | 8 |
| | **Total** | 44 | 2 | 46 |

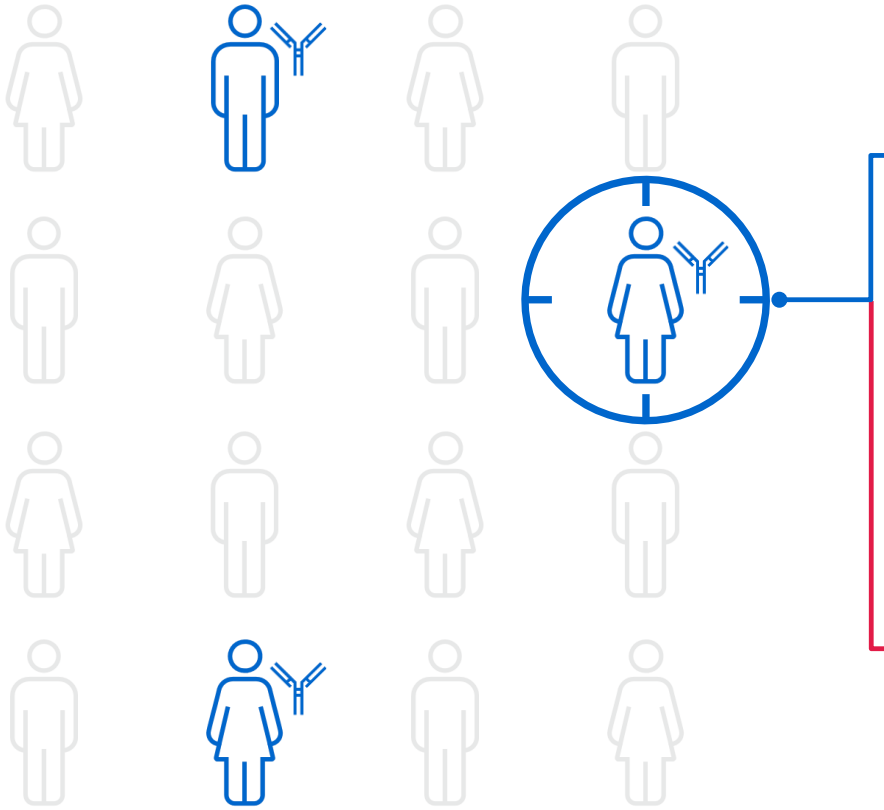
| | |
|---|---|
| **PPA** | **86.4 %** (73.3 % - 93.6 %)* |
| **PNA** | **100.0 %** (34.2 % - 100.0 %)* |
| **POA** | **87.0 %** (74.3 % - 93.9 %)* |

*PPA: percent positive agreement, PNA: percent negative agreement, POA: percent overall agreement; N: nucleocapsid, S: spike*
** 95% confidence interval; # antibody tests were performed 49 days after PCR.*

*1) Roche, data on internal file; 2) Meyer B, Torriani G, Yerly S, et al. Validation of a commercially available SARS-CoV-2 serological Immunoassay. medRxiv. 2020. https://doi.org/10.1101/2020.05.02.20080879*

# What are the objectives for testing for antibodies to SARS-CoV-2



## What can antibody detection tell us?

Serologic assays that accurately assess prior infection to SARS–CoV-2 will be essential for **epidemiologic studies**, ongoing **surveillance, and vaccine studies**[1]

## What can't antibody detection tell us?

Negative results cannot exclude SARS–CoV-2 infection, particularly among those with recent exposure to the virus[1]

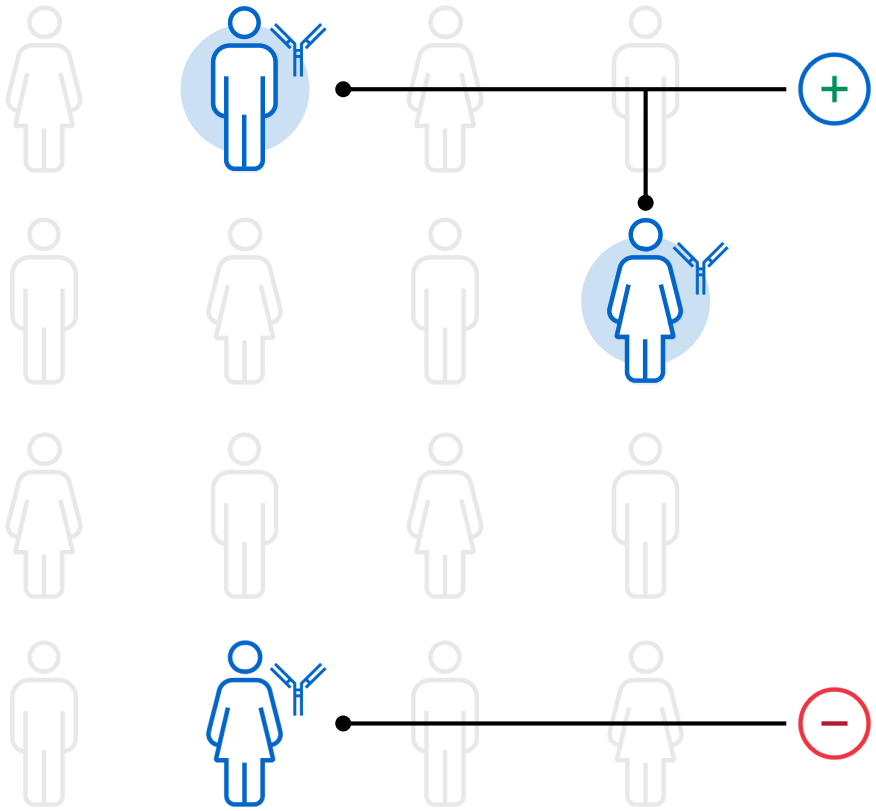
There is currently no conclusive evidence that people who have recovered from COVID-19 and have antibodies are protected from a second infection[2]

1. Cheng MP, *et al*. Ann Intern Med 2020: DOI: 10.7326/M20-1301; 2. World Health Organization. "Immunity passports" in the context of COVID-19. Available at: https://www.who.int/news-room/commentaries/detail/immunity-passports-in-the-context-of-covid-19 (accessed April 2020)

# When testing for antibodies……

*Importance of sensitivity*



**True positives**

**False negative**

**Sensitivity**

**Highly sensitive** antibody tests:

High likelihood of correctly **identifying someone who was infected, as having been infected**

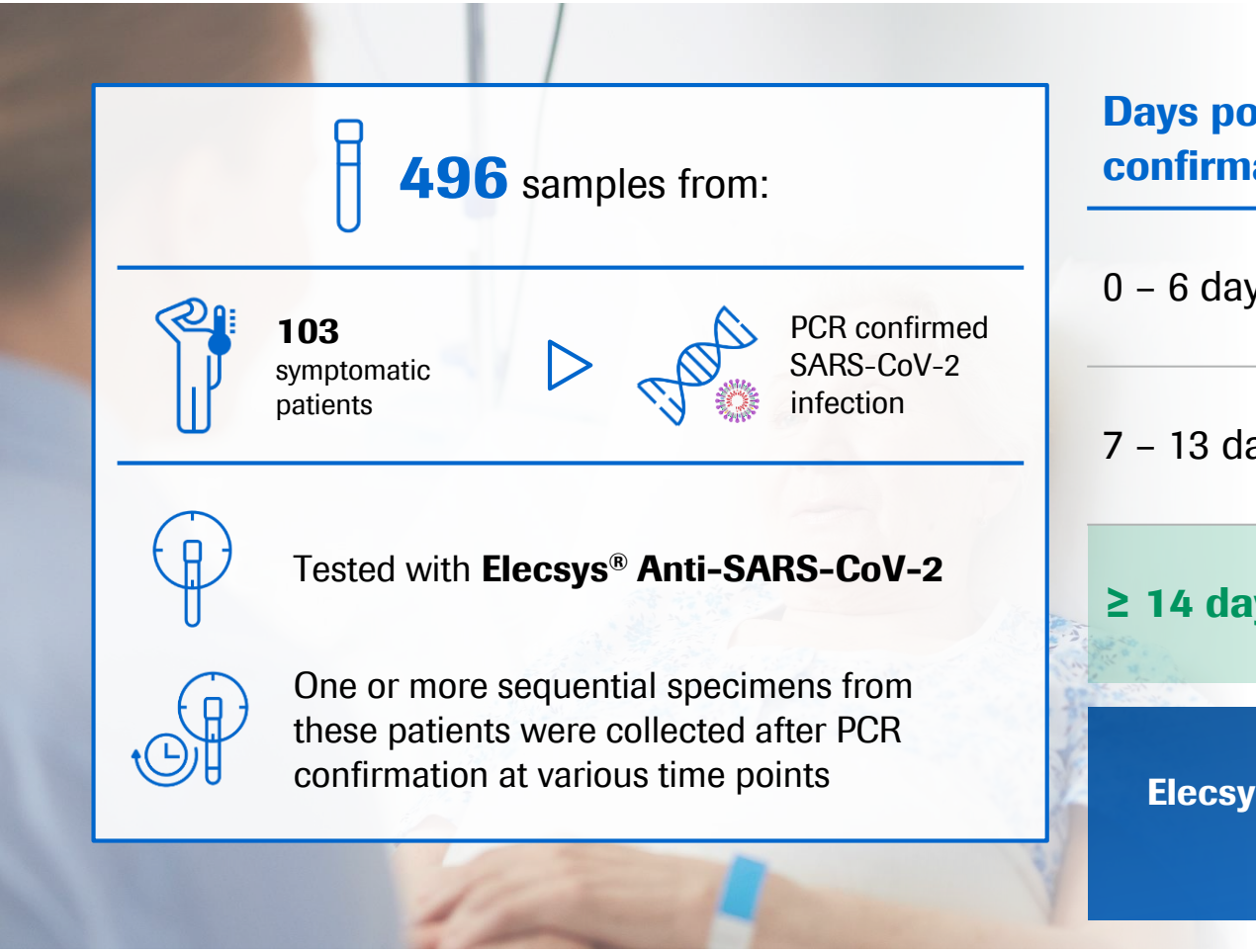
Avoid reporting someone who was infected, as having not been infected

1.Trevethan R. Front Public Health 2017 5(307); doi: 10.3389/fpubh.2017.00307
2.https://www.roche.com/media/releases/med-cor-2020-05-03.htm

# Elecsys® Anti-SARS-CoV-2

*High clinical sensitivity in patients with proven past infection (extended data set*)*



**496** samples from:

**103** symptomatic patients ▷ PCR confirmed SARS-CoV-2 infection

Tested with **Elecsys® Anti-SARS-CoV-2**

One or more sequential specimens from these patients were collected after PCR confirmation at various time points

| Days post PCR confirmation | N | Non-reactive | Sensitivity (95 % CI*) |
|---|---|---|---|
| 0 – 6 days | 161 | 64 | 60.2 % (52.3 – 67.8%) |
| 7 – 13 days | 150 | 22 | 85.3% (78.6 – 90.6%) |
| **≥ 14 days** | **185** | **1#** | **99.5% (97.1 – 100%)** |

**Elecsys® Anti-SARS-CoV-2 has 99.5% sensitivity in detecting antibodies after the reported median day of seroconversion**

Roche Diagnostics GmbH, R&D department; Penzberg, Germany. R&D record ACOV2-113-118_sensi-speci
*confidence interval; #1 patient was non-reactive at day 14 (0.696 COI) but reactive at day 16 (4.48 COI)

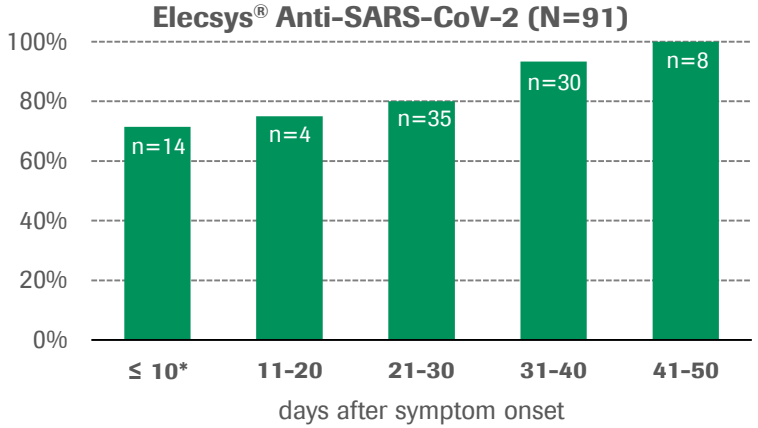
# Clinical sensitivity

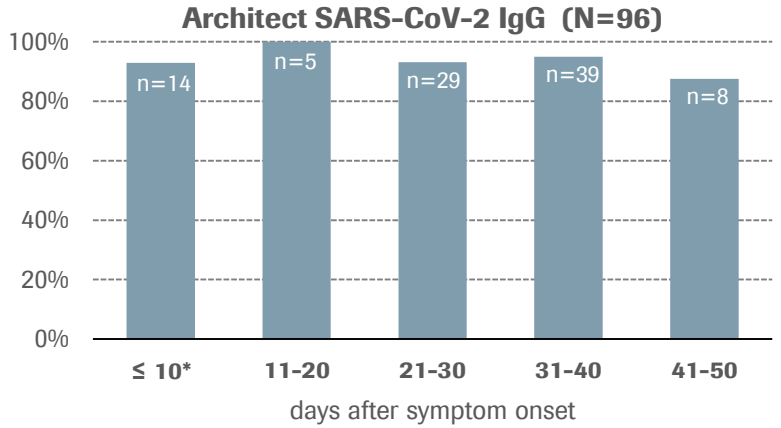
*Public Health England assay evaluations*

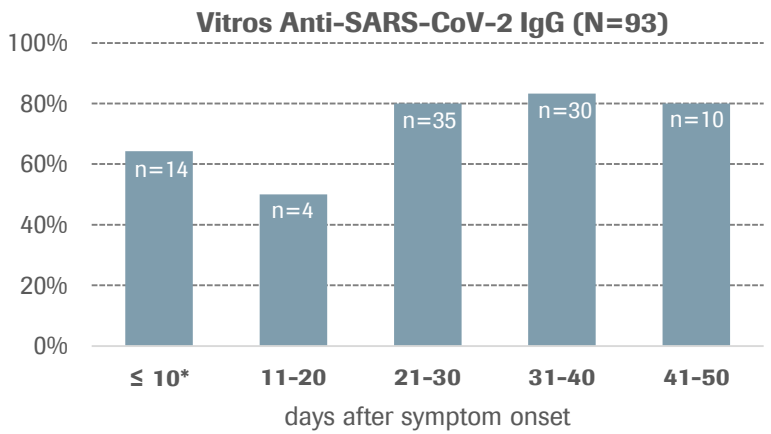
**Sensitivity of Elecsys® increases with time after symptom onset, indicating correlation with sero-conversion and/or increasing proportion of late, high-affinity antibodies.**

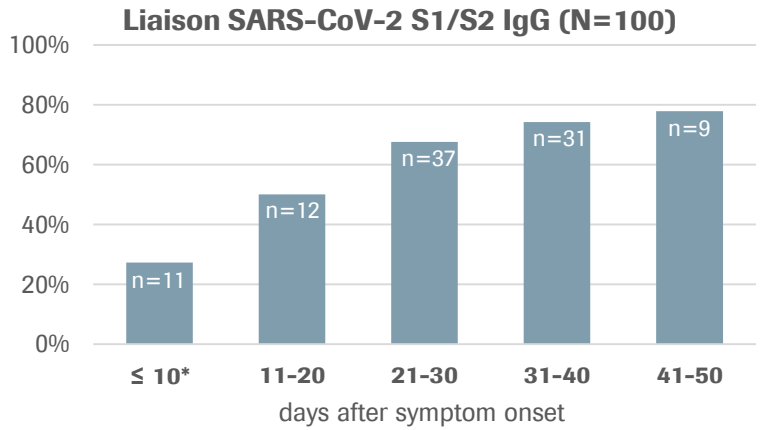
**Sensitivity of Architect at the same level across all time intervals indicating detection of low- and high-affinity antibodies.**

**Sensitivity of Vitros and Liaison is insufficient.**



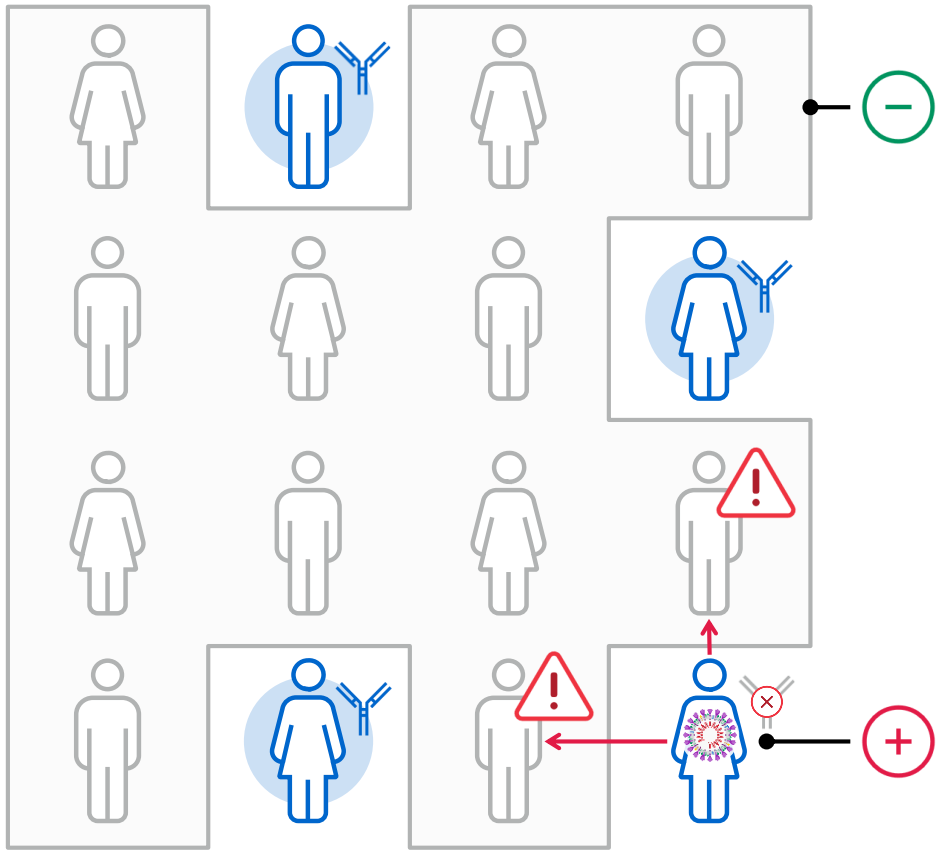

* unclear interval, as the date from admission into hospital was supplied rather than the date of symptom onset

*1) Duggan J et al. (2020). 2) Duggane t al. (2020)*

# When testing for antibodies……

*Importance of specificity*



**True negatives**

**False positive**

**Specificity**

**Highly specific** antibody test:

Avoid reporting someone who was infected, as having not been infected

Avoid reporting someone who was not infected, as having been infected

1. Trevethan R. Front Public Health 2017 5(307); doi: 10.3389/fpubh.2017.00307

# Elecsys® Anti-SARS-CoV-2

*Fit-for-purpose clinical specificity proven in a large sample cohort*

**10533** samples from:

- Diagnostic routine
- Blood donors
- A common cold panel
- A coronavirus panel* obtained before December 2019

Tested with **Elecsys® Anti-SARS-CoV-2**

| Cohort | N | Reactive | Specificity % (95 % CI) |
|---|---|---|---|
| Diagnostic routine | 6305 | 12 | 99.81 % (99.67 – 99.90 %) |
| Blood donors | 4148 | 9 | 99.78 % (99.59 – 99.90 %) |
| Common cold panel | 40 | 0 | 100% (91.19 – 100%) |
| Coronavirus panel* | 40 | 0 | 100% (91.19 – 100%) |
| **Overall** | **10453** | **21** | **99.80 % (99.69 - 99.88 %)** |

**Elecsys® Anti-SARS-CoV-2 has 99.80% overall specificity.**

**No cross-reactivity with the common cold coronaviruses was observed.**

*40 potentially cross-reactive samples from individuals with past infection with coronavirus HKU1, NL63, 229E, or OC43, confirmed by PCR.

Roche Diagnostics GmbH, R&D department; Penzberg, Germany. R&D record ACOV2-113-118_sensi-speci Elecsys® Anti-SARS-CoV-2 method sheet (v1, Apr 2020).

# Elecsys® Anti-SARS-CoV-2

*Fit-for-purpose clinical specificity proven in a large sample cohort*

**747** potentially cross-reactive samples including:

**40 samples** from individuals with common cold symptoms

**40 samples** from individuals confirmed to be infected with one of the four common cold CoVs*

Tested with **Elecsys® Anti-SARS-CoV-2**

| Cohort | N | Reactive | Specificity % (95 % CI) |
|---|---|---|---|
| Common cold panel | 40 | 0 | 100% (91.19 – 100%) |
| Coronavirus panel* | 40 | 0 | 100% (91.19 – 100%) |
| Other potentially cross-reacting samples§ | 667 | 4# | 99.4% (95.6 – 99.8%) |
| **Overall** | **747** | 4 | **99.47% (98.63 – 99.85%)** |

**No cross-reactivity with the endemic common cold coronaviruses was observed.**

*from individuals with past infection with coronavirus HKU1, NL63, 229E, or OC43, confirmed by PCR; § Pre-pandemic samples with reactivity for various other indications, which could have an elevated potential for unspecific interference, were tested for reactivity in the Elecsys anti-SARS-CoV-2 assay; # acute CMV infection (IgM+, IgG+): 1; acute EBV infection (IgM+, VCA IgG+): 2; systemic lupus erythematosus: 1. Roche Diagnostics GmbH, R&D department; Penzberg, Germany. R&D record ACOV2-113-118_sensi-speci

# Elecsys® Anti-SARS-CoV-2

*Only assay confirmed to not cross-react with endemic coronavirus samples*

| | Roche | Abbott | DiaSorin | Biomérieux | OCD | Siemens | Beckman | Snibe | Mindray |
|---|---|---|---|---|---|---|---|---|---|
| **Test name** | Elecsys Anti-SARS-CoV-2 | Architect SARS-CoV-2 IgG | Liaison SARS-CoV-2 S1/S2 IgG | Vidas SARS-COV-2 IgM | Vitros Anti-SARS-CoV-2 Total / IgG | Atellica SARS-CoV-2 Total | Access SARS-CoV-2 IgG | Maglumi 2019 n-CoV IgG | SARS-CoV-2 IgG |
| **HKU1, NL63, OC43 or 229E** | 40 samples | No data | Only 4 samples | No data | No data | No data | No data | No data | Only 5 samples |
| **Interference** | No interference | Potential interference | Missing NL63 229E | Missing NL63 229E | Potential interference | Potential interference | Potential interference | Potential interference | Missing NL63 HKU1 |

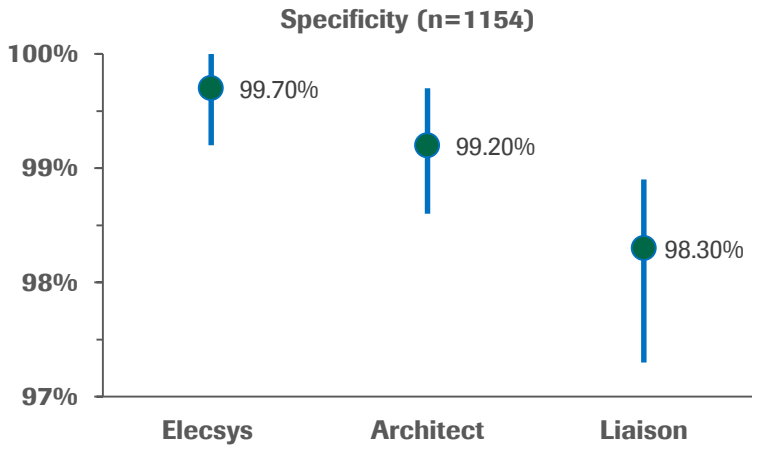
*Elecsys Anti-SARS-CoV-2 Method sheet (April 2020); Snibe Maglumi 2019-nCoV IgG & IgM Method sheet (March 2020); Abbott Architect SARS-CoV-2 IgG Method Sheet (April 2020) DiaSorin LIAISON® SARS-CoV-2 S1/S2 IgG Method Sheet (April 2020); Mindray SARS-CoV-2 IgG & IgM (CLIA) Method Sheet (March 2020); Ortho Clinical Diagnostics VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Reagent Pack Method Sheet (April 2020); Shenzhen Yhlo Biotech iFlash-SARS-CoV-2 IgG & IgM Flyer; Qian Ch, Zhou M, et al. 2020. Development and Multicenter Performance Evaluation of The First Fully Automated SARS-CoV-2 IgM and IgG Immunoassays. medRxiv preprint doi: https://doi.org/10.1101/2020.04.16.20067231.*

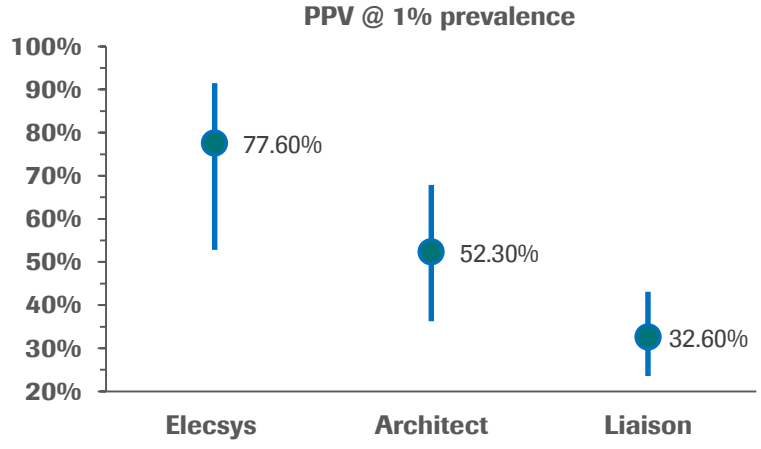
 

# Head-to-head comparison of three automated antibody assays

*Elecsys® with highest PPV at low prevalence*

- **While all three assays presented with high specificities, at low prevalence, the minor differences in specificity resulted in profound discrepancies of positive predictability.**
- **At 1% prevalence, the PPV values of Roche and DiaSorin differ so clearly that not even the 95% CI intervals overlap.**



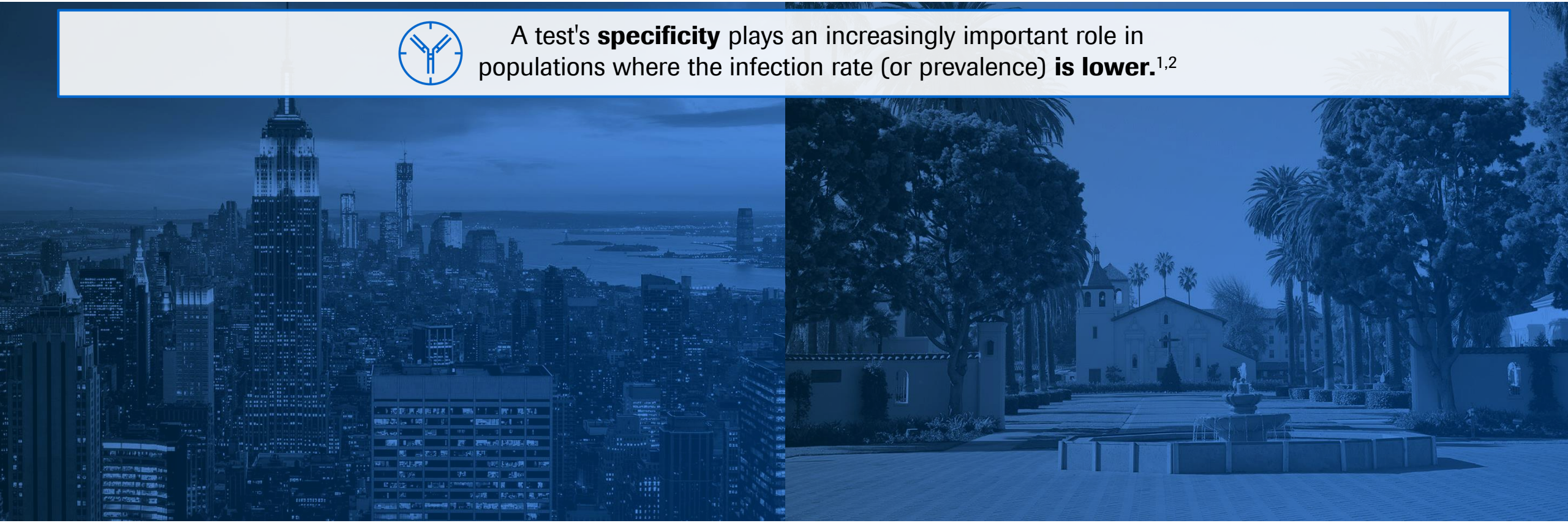




*Perkmann T et al. Side by side comparison of three fully automated SARS-CoV-2 antibody assays with a focus on specificity. medRxiv 2020.06.04.20117911; doi: https://doi.org/10.1101/2020.06.04.20117911*

# The importance of a high-specificity test

*A positive test result in New York is different from a positive test result in Santa Clara…*



A test's **specificity** plays an increasingly important role in populations where the infection rate (or prevalence) **is lower.**[1,2]

*The positive predictive value is the probability that persons with a positive test result truly have the disease.

1. Bonislawski, A. (2020, April 27). New York, California Serology Studies Give Early Estimates of COVID-19 Prevalence. Retreived from: https://www.360dx.com/infectious-disease/new-york-california-serology-studies-give-early-estimates-covid-19-prevalence?utm_source=Sailthru&utm_medium=email&utm_campaign=360DN%20Tues%202020-04-28&utm_term=360Dx%20Daily%20News#.Xqv_4qgzZaR
2. Saplakoglu, Y., Writer, S. (2020, April 23). 1 in 5 people tested in New York City had antibodies for the coronavirus. Retrieved from: https://www.livescience.com/covid-antibody-test-results-new-york-test.html
3. Bendavid, E. et al. (2020, April 11). COVID-19 Antibody Seroprevalence in Santa Clara County, California. medRxiv preprint doi: https://doi.org/10.1101/2020.04.14.20062463

# The importance of a high-specificity test

*A positive test result in New York is different from a positive test result in Santa Clara…*

A test's **specificity** plays an increasingly important role in populations where the infection rate (or prevalence) **is lower.**[1,2]

## New York

**100,000** people tested

**15,000** infected with SARS-CoV-2

**15%** prevalence[1,2]

Other on-market antibody test with **98.80% specificity**

**16,020** positive results

**6%** probability that the positive result is **incorrect**

**94%** probability that the positive result is **correct***

Elecsys® Anti-SARS-CoV-2 with **99.80% specificity**

**15,170** positive results

**1%** probability that the positive result is **incorrect**

**99%** probability that the positive result is **correct***

## Santa Clara

**100,000** people tested

**1,500** infected with SARS-CoV-2

**1.5%** prevalence[3]

Other on-market antibody test with **98.80% specificity**

**2,682** positive results

**44%** probability that the positive result is **incorrect**

**56%** probability that the positive result is **correct***

Elecsys® Anti-SARS-CoV-2 with **99.80% specificity**

**1,697** positive results

**12%** probability that the positive result is **incorrect**

**88%** probability that the positive result is **correct***

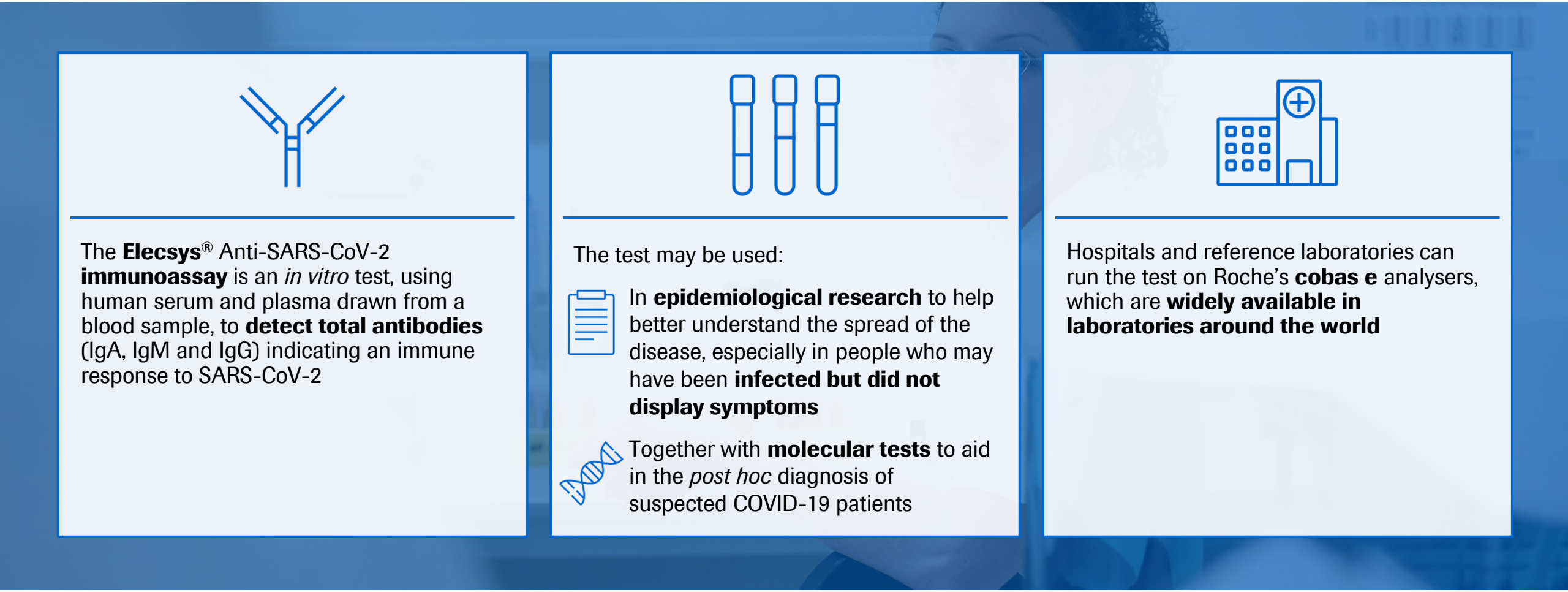
*The positive predictive value is the probability that persons with a positive test result truly have the disease.

1. Bonislawski, A. (2020, April 27). New York, California Serology Studies Give Early Estimates of COVID-19 Prevalence. Retreived from: https://www.360dx.com/infectious-disease/new-york-california-serology-studies-give-early-estimates-covid-19-prevalence?utm_source=Sailthru&utm_medium=email&utm_campaign=360DN%20Tues%202020-04-28&utm_term=360Dx%20Daily%20News#.Xqv_4qgzZaR
2. Saplakoglu, Y., Writer, S. (2020, April 23). 1 in 5 people tested in New York City had antibodies for the coronavirus. Retrieved from: https://www.livescience.com/covid-antibody-test-results-new-york-test.html
3. Bendavid, E. et al. (2020, April 11). COVID-19 Antibody Seroprevalence in Santa Clara County, California. medRxiv preprint doi: https://doi.org/10.1101/2020.04.14.20062463

# How does Elecsys® Anti-SARS-CoV-2 serology test provide value

*An antibody detection test*



The **Elecsys®** Anti-SARS-CoV-2 **immunoassay** is an *in vitro* test, using human serum and plasma drawn from a blood sample, to **detect total antibodies** (IgA, IgM and IgG) indicating an immune response to SARS-CoV-2

The test may be used:

In **epidemiological research** to help better understand the spread of the disease, especially in people who may have been **infected but did not display symptoms**

Together with **molecular tests** to aid in the *post hoc* diagnosis of suspected COVID-19 patients

Hospitals and reference laboratories can run the test on Roche's **cobas e** analysers, which are **widely available in laboratories around the world**

Roche. Press Release, April 17 2020. Available at: https://www.roche.com/media/releases/med-cor-2020-04-17.htm. Accessed April 2020.

# What are the unanswered questions for COVID-19 / SARS-CoV-2?

*Do antibodies confer reliable immunity?*

*How long do antibodies confer immunity?*

*How long is a patient infective?*

*From when on is a patient protected?*

*Doing now what patients need next*