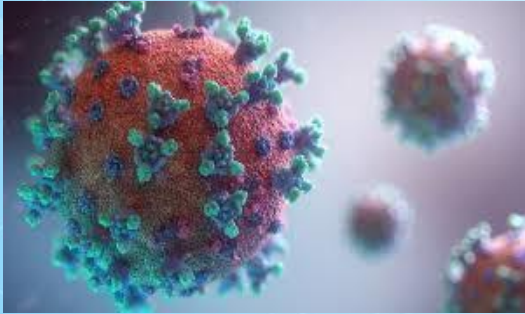


Impact of COVID-19 in stewardship and rapid diagnosis



Assistance Publique Hôpitaux de Paris, APHP

29.11.2021

Impact of COVID-19 in stewardship and rapid diagnosis

- Global COVID-19 Epidemic

Where are we standing now?

Total Cases	Total Deaths	Total Vaccine Doses Administered
259661587	5178928	7518754099
28-Day Cases	28-Day Deaths	28-Day Vaccine Doses Administered
13969099	201084	811512482

Germany

28-Day: 1050009 | 4634
Totals: 5580876 | 100139

US

28-Day: 2318700 | 32476
Totals: 48092485 | 775397

France

28-Day: 343966 | 1156
Totals: 7586187 | 119686

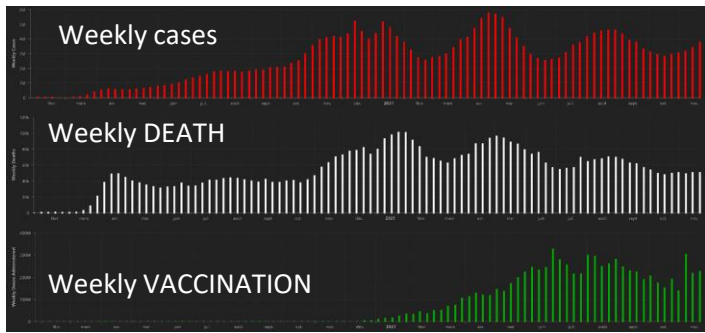
Italy

28-Day: 202217 | 1461
Totals: 4954585 | 133415

Spain

28-Day: 105167 | 615
Totals: 5111842 | 87904





World

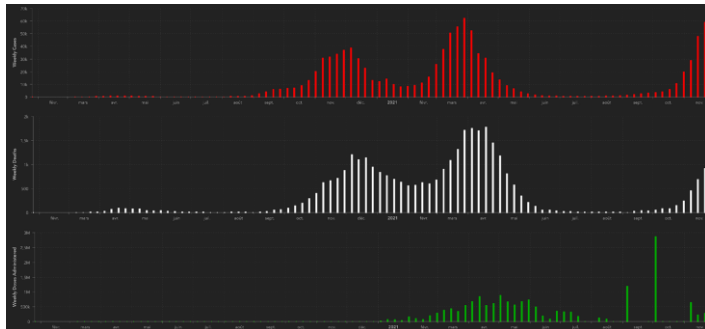
- End 2020: Diagnostic testing is an essential tool against COVID-19, as there is not yet a vaccine or specific treatment.
- 2021: Vaccination is essential
- 2022: Vaccination and anti-Covid-drugs

NEW B.1.1.529
FROM SOUTH AFRICA

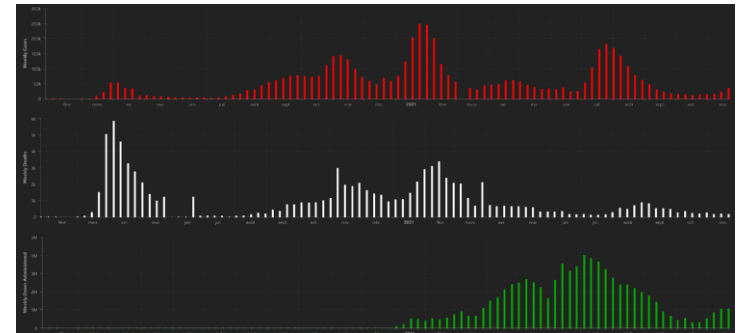


France

Spain

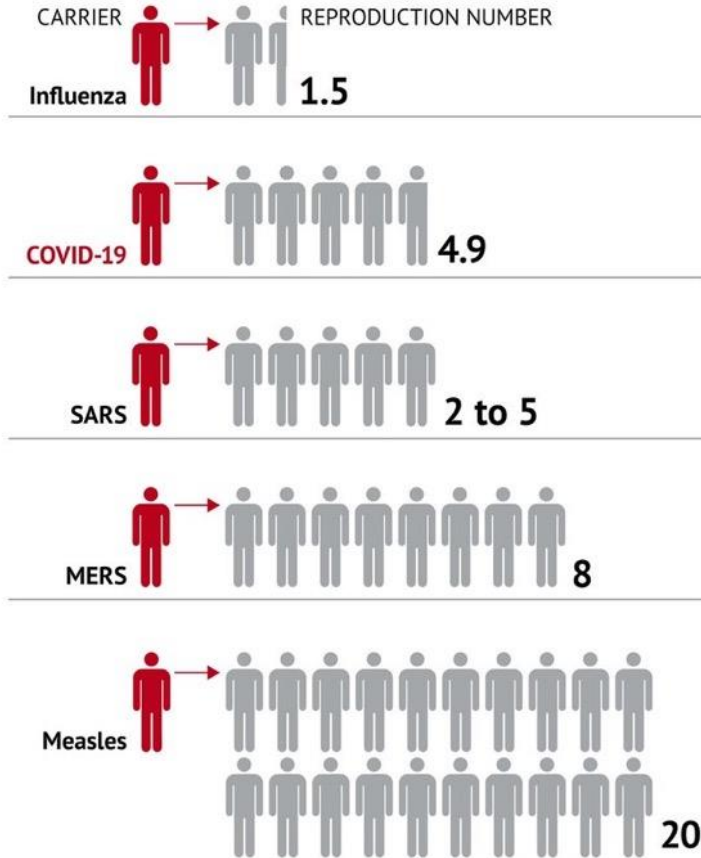


Hungary



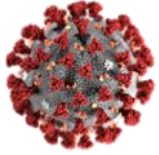
How contagious is the new coronavirus?

Scientists measure how contagious a virus is using 'reproduction numbers' - the likely number of people every sick person will infect assuming the whole population is susceptible.



Source: Professor James McGow and WHO

Contagiousity



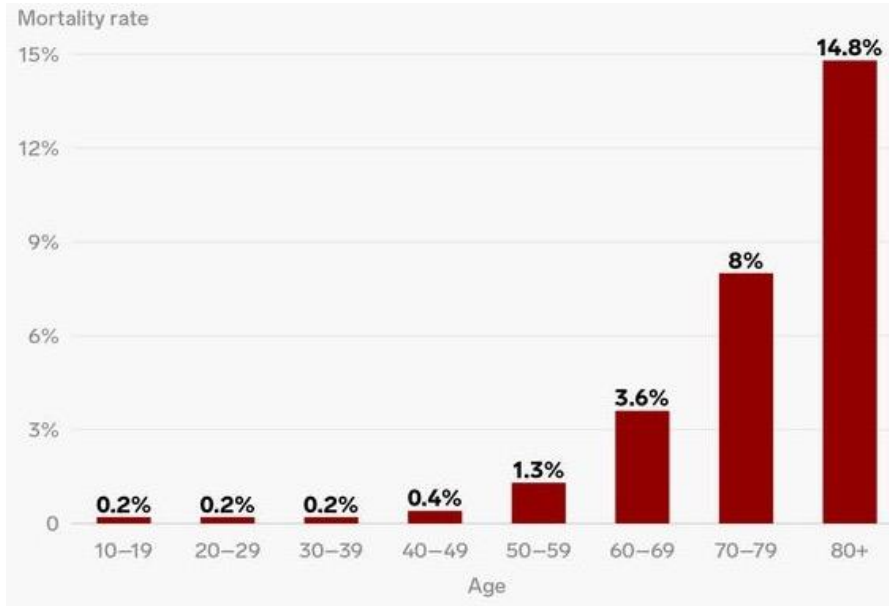
- Typically cited as 2-3 but may be as high as 4.9; varies by population density and exposure patterns
- Probably about twice as transmissible as influenza

Case Fatality rate

- COVID-19: **0.7 to 3.4%** (>5% in Wuhan itself during peak)
 - Likely higher without access to healthcare, oxygen and ventilators
- Spanish Influenza 1918: **>2.5%**
Mostly younger people
- Seasonal Influenza: **0.1-0.2%**

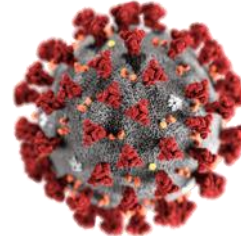
Mortality rate

COVID-19 mortality rate by age



COVID-19 mortality rate by Comorbidities

- 10.5% cardiovascular disease,
- 7% diabetes,
- 6% each for chronic respiratory disease, hypertension, and cancer.
- Case fatality for patients who developed respiratory failure, septic shock, or multiple organ dysfunction was 49%.



Impact of COVID-19 in stewardship and rapid diagnosis

- Place of RDTs in pandemic

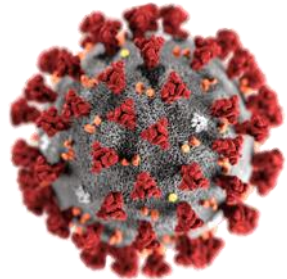
What can (and needs to be) done ?

COVID

- Rapid identification to isolate patients
- Vaccination
- Drugs for severely ill patients
- **5.2 million** official deaths in 23 months of pandemic

AMR

- Search and isolate
- Novel approaches (immunotherapies)
- Novel antibiotics
- **10 million** deaths by due to AMR if nothing is done by 2050



Diagnostics in the COVID-19 response

=> **Diagnostic testing is a critical component of the COVID-19 response, as it can be used to:**

- confirm infection in patients who fulfil COVID-19 clinical criteria
- rapidly screen suspected cases (especially in community settings)
- screen for infection in asymptomatic contacts of confirmed COVID-19 cases
- determine exposure (current and past) to the virus to understand the true extent of the outbreak, map the pandemic across countries and monitor trends.



=> **What is a rapid diagnostic test ?**

- Results in minutes to 1-2 hours
- Accurate, simple to use, low cost, easy to interpret, stable under extreme conditions, little or no processing, culturally acceptable
- Include “point of care” (for doctor) and “walk away” tests (home tests)

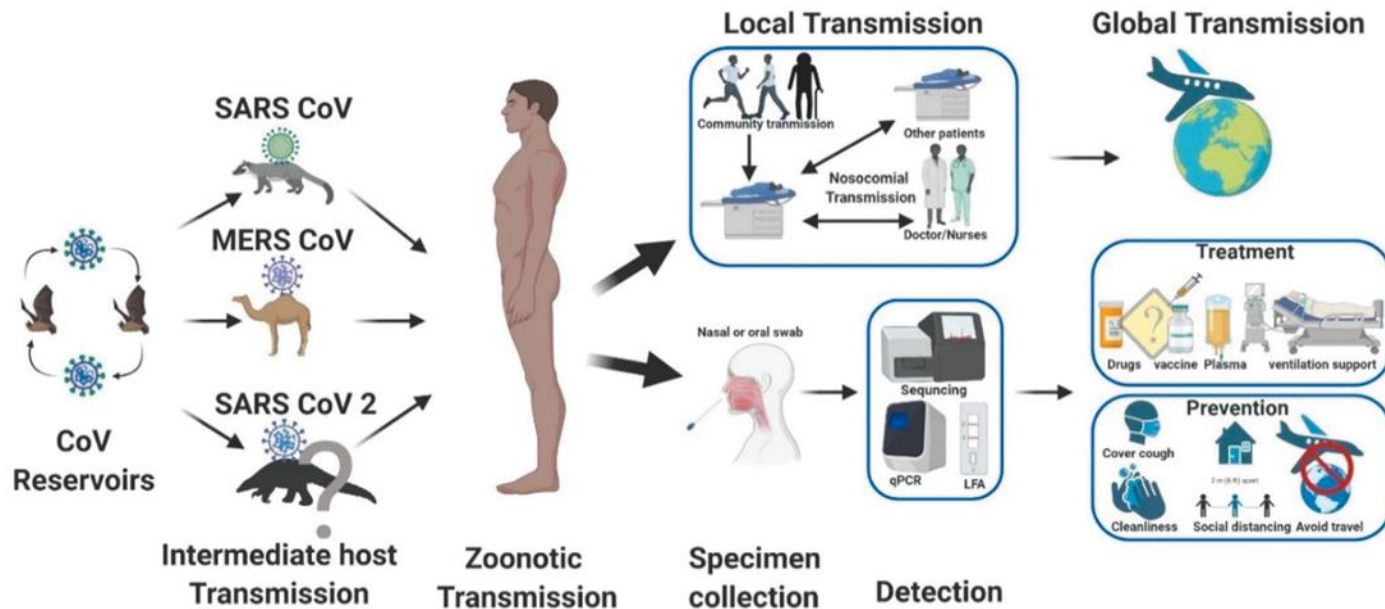
REVIEW



Diagnosis for COVID-19: current status and future prospects

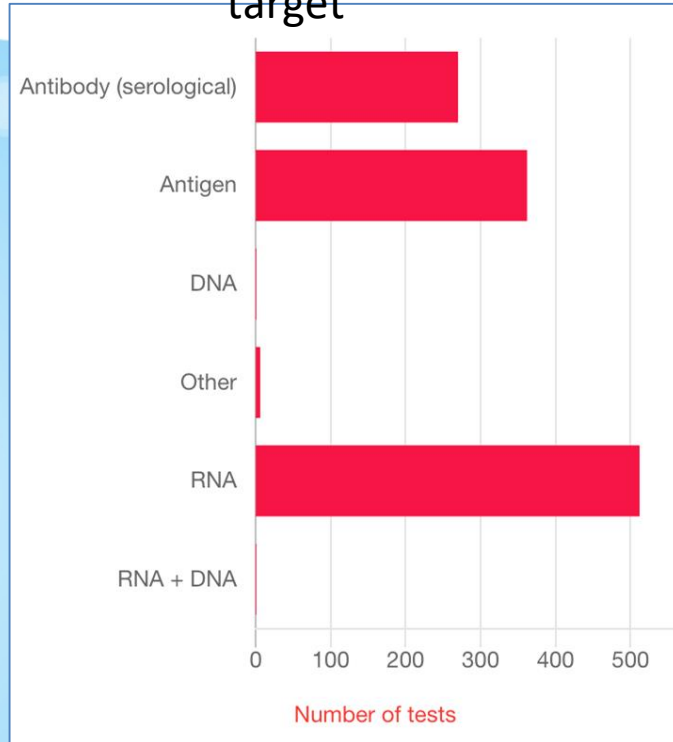
MD Alamgir Kabir^{a,b}, Rajib Ahmed^c, Sheikh Muhammad Asher Iqbal^{a,b}, Rasheduzzaman Chowdhury^d,
Ramasamy Paulmurugan^c, Utkan Demirci^c and Waseem Asghar^{a,b,e}

^aFlorida Atlantic University, Boca Raton, FL, USA; ^bCollege of Engineering and Computer Science, Boca Raton, FL, USA; ^cCanary Center at Stanford for Cancer Early Detection, Department of Radiology, Stanford School of Medicine, Palo Alto, CA, USA; ^dUniversity of California, San Francisco, CA, USA; ^eDepartment of Biological Sciences (Courtesy Appointment, Florida Atlantic University, Boca Raton, FL, USA

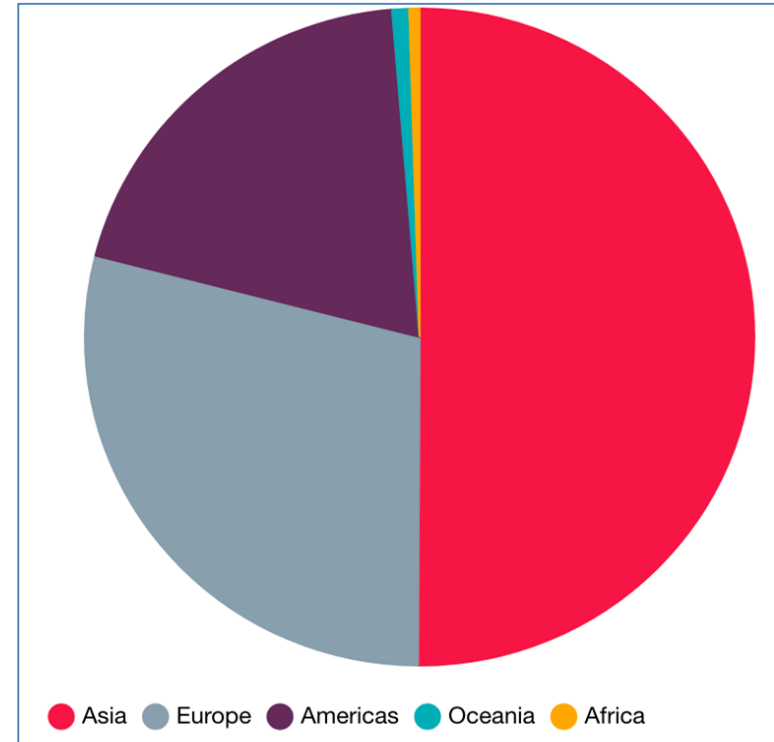


FIND, the global alliance for diagnostics, seeks to ensure equitable access to reliable diagnosis around the world.

**Assay
target**



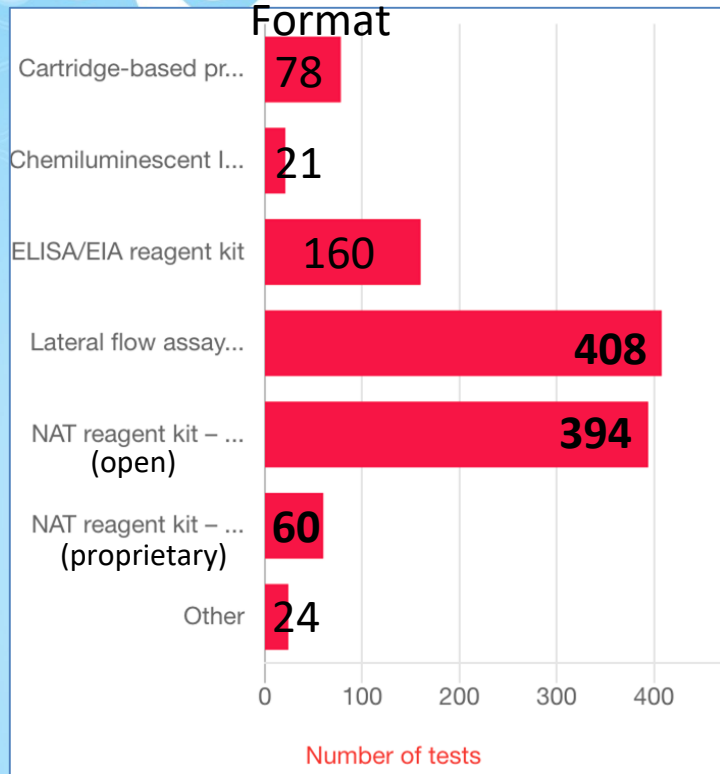
Manufacturer region



FIND, the global alliance for diagnostics, seeks to ensure equitable access to reliable diagnosis around the world.

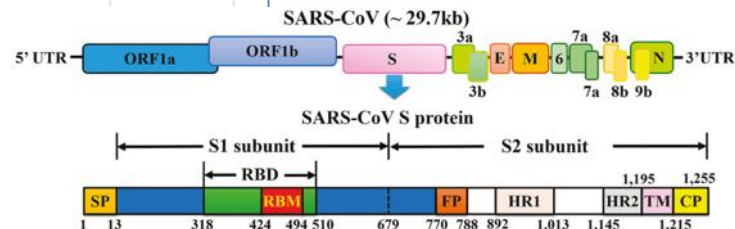
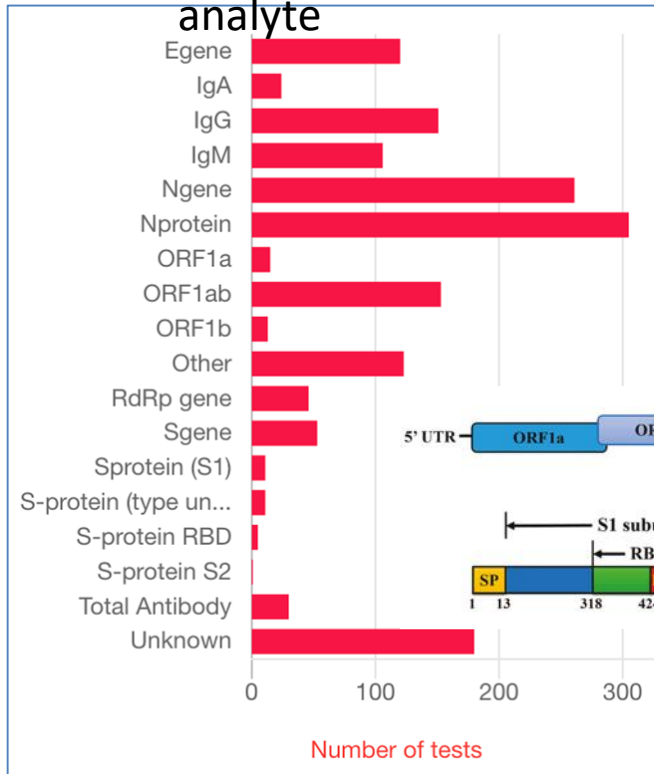
Test

Format



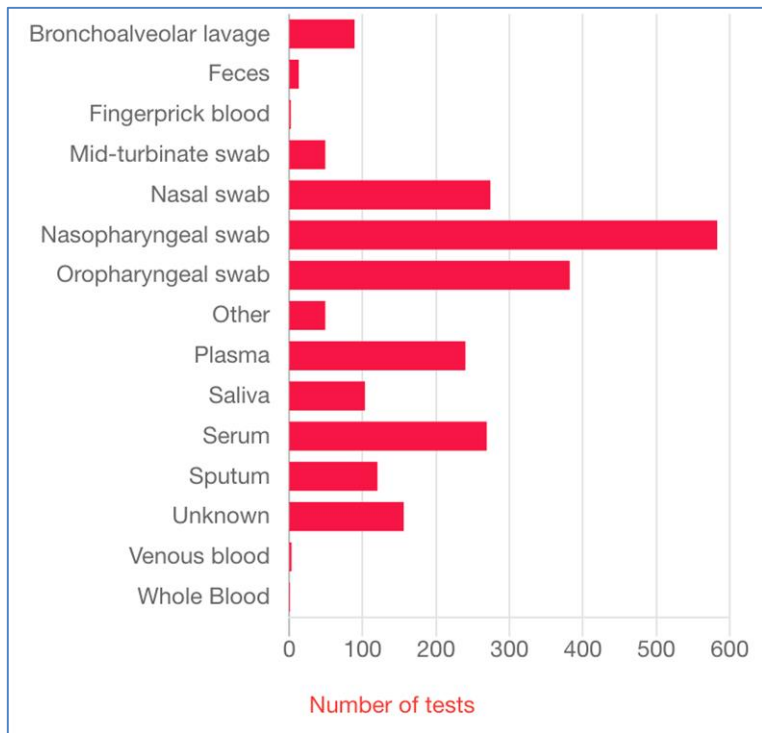
Target

analyte

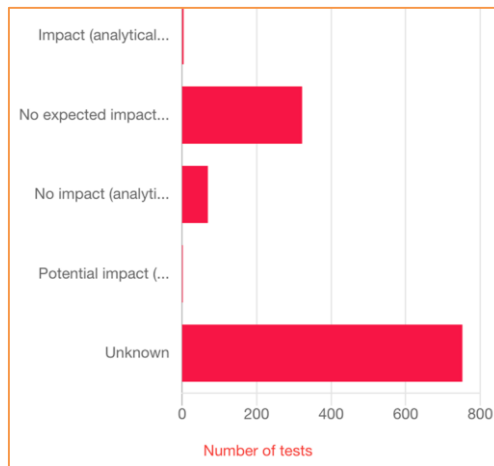


FIND, the global alliance for diagnostics, seeks to ensure equitable access to reliable diagnosis around the world.

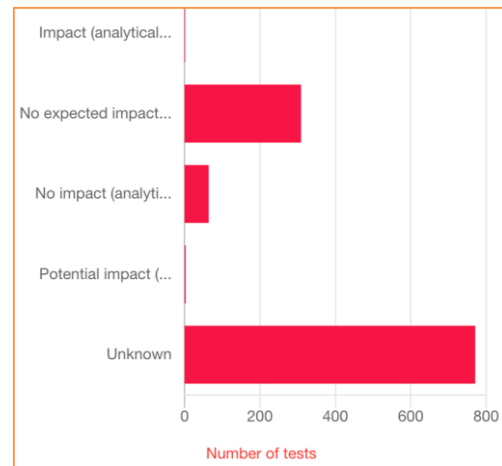
Validated sample types



Alpha variant



Beta variant



The gamma, delta, ... and now the Omicron..
A never ending story

HIDE FILTERS ✕

FILTER THE TEST LIST

Search by Test Name 🔍



APPLY FILTERS

MANUFACTURER

☒ NG Biotech (3)

REGION ①

☐ Europe (3)

COUNTRY ①

☐ France (3)

TYPE OF TECHNOLOGY

☐ Immunoassay (3)

SELF-TESTING/SELF-COLLECTION

☐ Intended for professional use only (2)☐ Intended for self-testing (version available) (1)

RESULTS (3)

EXPORT IN XLS

NG-Test SARS-CoV-2 Ag
NG Biotech >Ninonasal
NG Biotech >

Ninonasal Autotest >

 NG BIOTECH

MANUFACTURER PERFORMANCE DATA

SENSITIVITY

98%

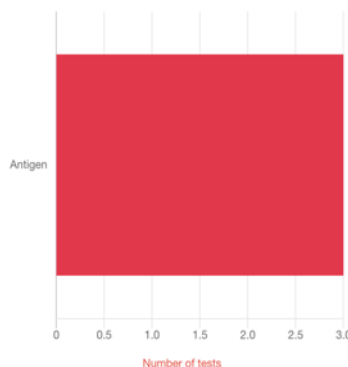
SPECIFICITY

99%

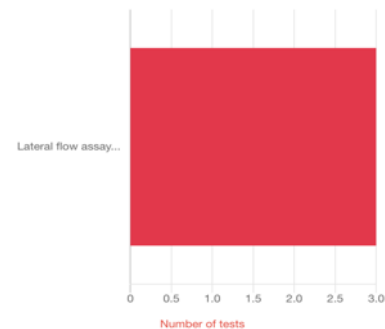
LEARN MORE ABOUT THIS TEST

COVID-diagnostics: another NG Biotech success story

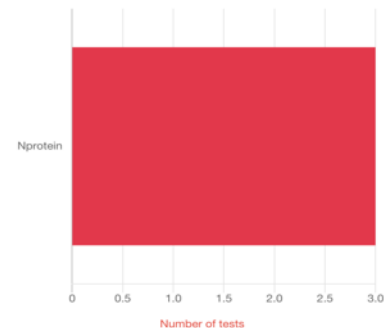
Assay target



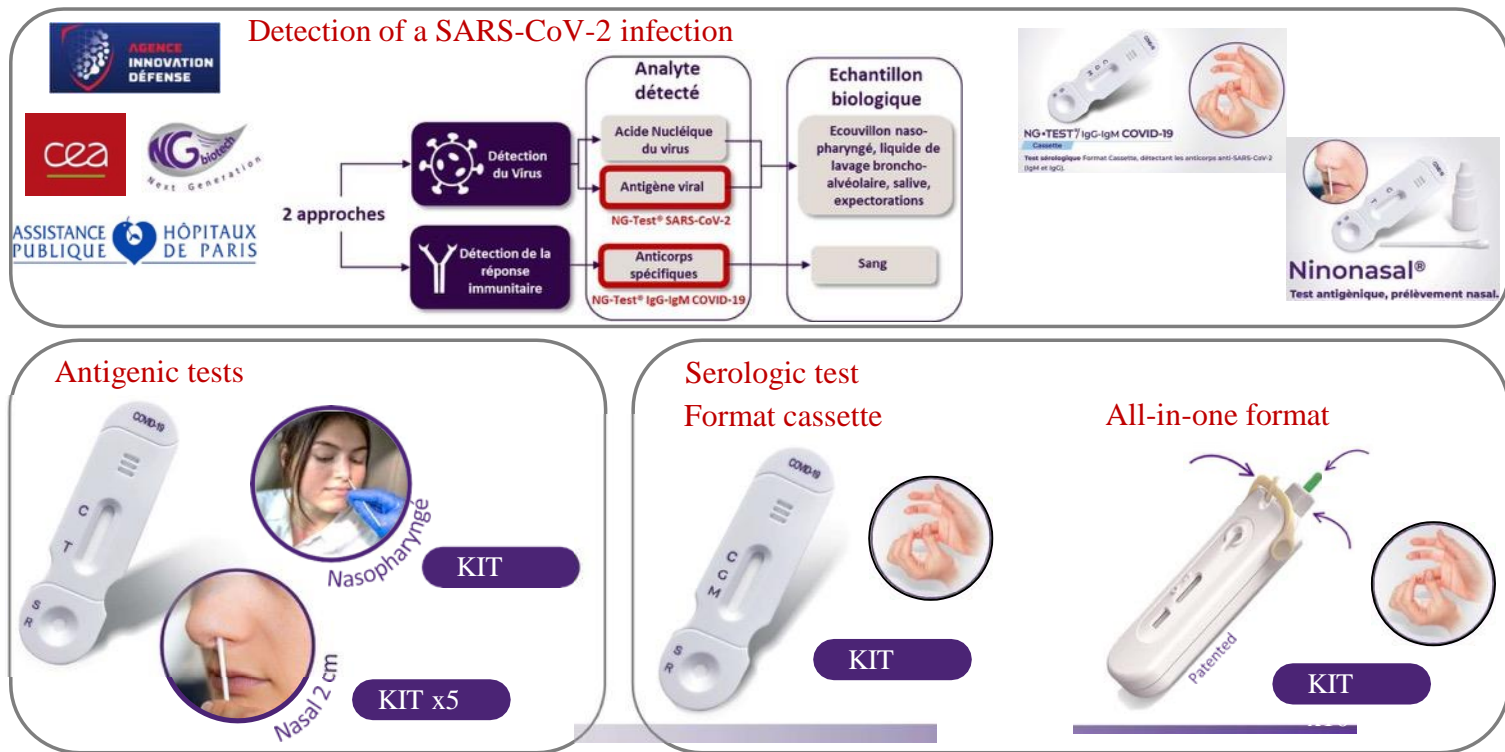
Test format



Target analyte



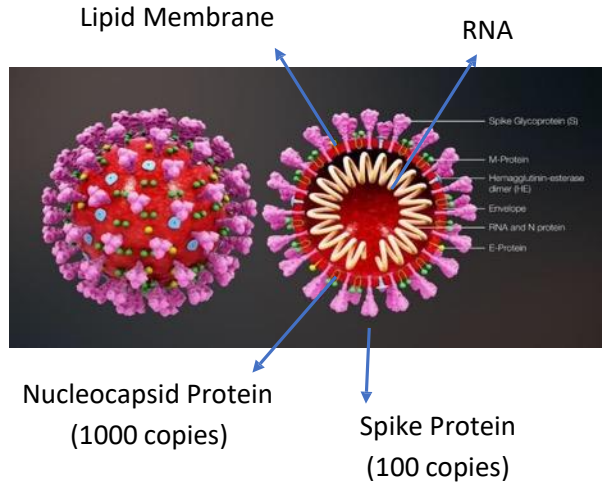
COVID-diagnostics: another NG Biotech success story



Diagnostics of covid-19



SARS-CoV-2 virus



Diagnostics strategies

1

DETECTION OF THE VIRUS RNA
GENETIC MATERIAL (**Nucleic acid test**)

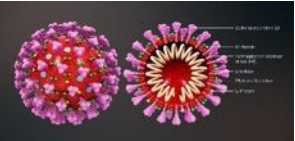
2

DETECTION OF THE INTACT VIRUS
(**Antigen detection test**)

3

DETECTION OF ANTIBODIES
(**Serological test**)



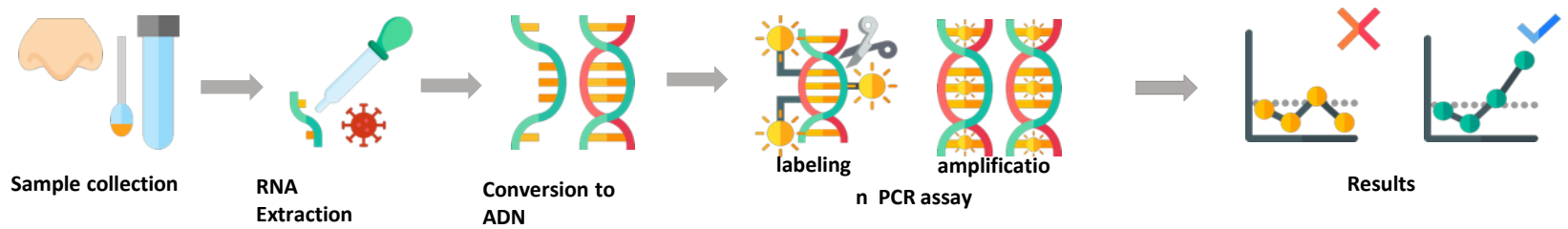


1

DETECTION OF THE VIRUS RNA GENETIC MATERIAL

Strategy based on the “Polymerase Chain Reaction” technique (PCR), LAMP, WGS

From **a few DNA copies**, and thanks to iterative cycles of, **high yield of genetic material** can be obtained, detected using fluorescent labels

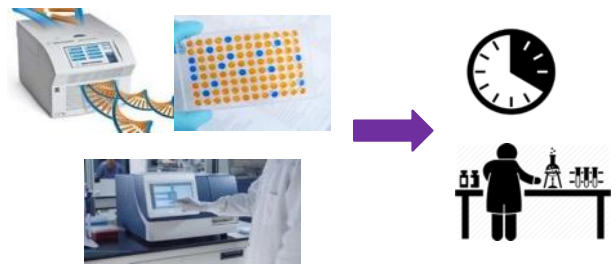


Nucleic Acid Amplification Tests (RT-

PCR)

Advantages: well-established commercial technique, high sensitivity, specificity, high scalability to thousands of detection kits.

Limitations: time consuming (2-5 h), reproducibility, trained personnel, limited to specialized laboratories, complex instrumentation, price.

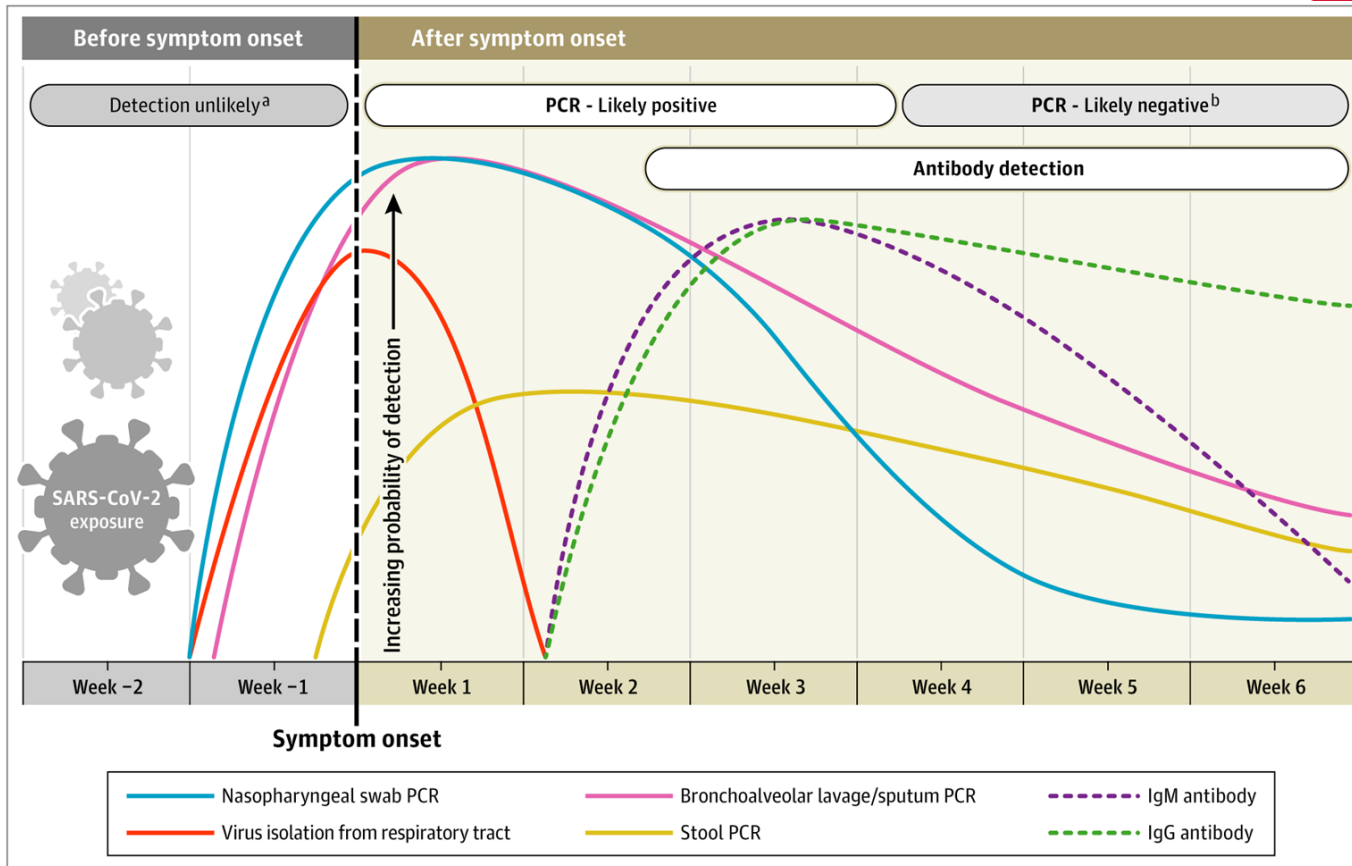


Time to Result and Lab requirements:
Main handicaps for massive population testing

DETECTION OF THE VIRAL RNA: WHEN ?

From: **Interpreting Diagnostic Tests for SARS-CoV-2**

JAMA. Published online May 06, 2020. doi:10.1001/jama.2020.8259

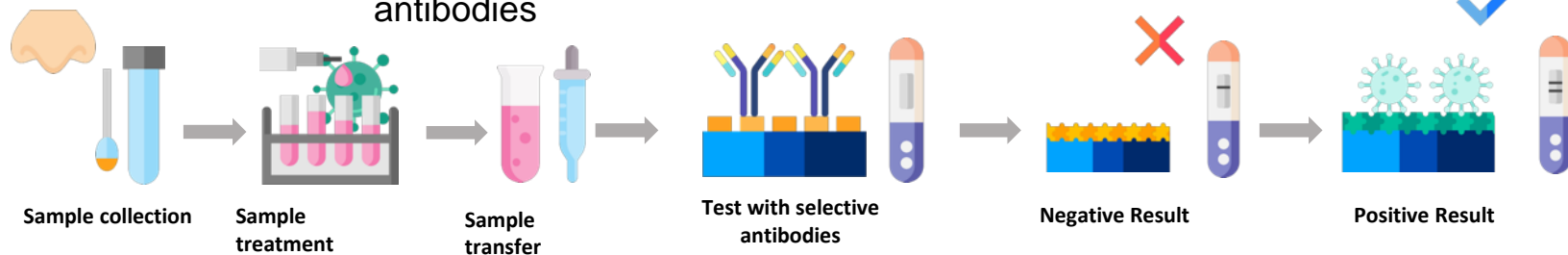
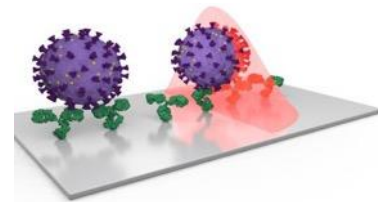




2

DETECTION OF THE INTACT VIRUS (Antigen detection test)

Detection of the intact virus through the outer virus proteins (viral antigens) by using specific antibodies



Advantages: Rapid test (5-15 min), well-established technique for other diseases (lateral flow immunoassay), low cost, massive production, at the point-of-need.

Limitations: limited sensitivity (false negative for low viral load), reproducibility issues between batches, qualitative results (YES/NO) but not the viral load.

**IDEAL TEST FOR A MASSIVE COVID-19
DETECTION**

BUT.....

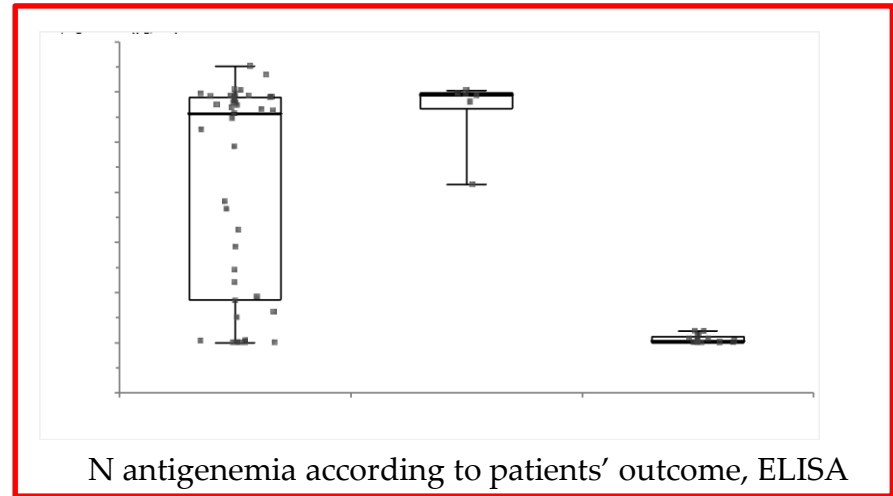
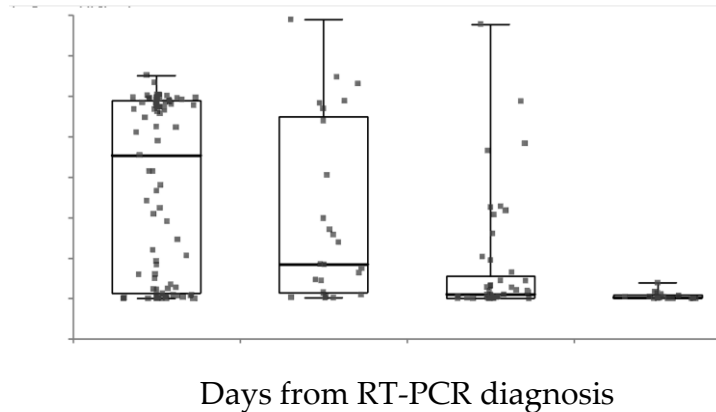
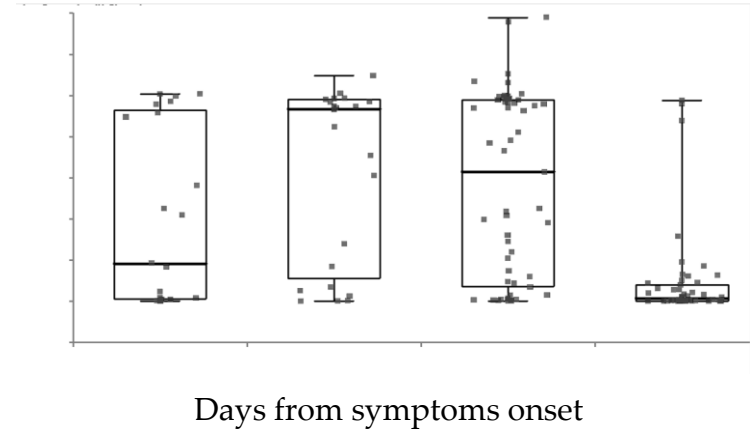
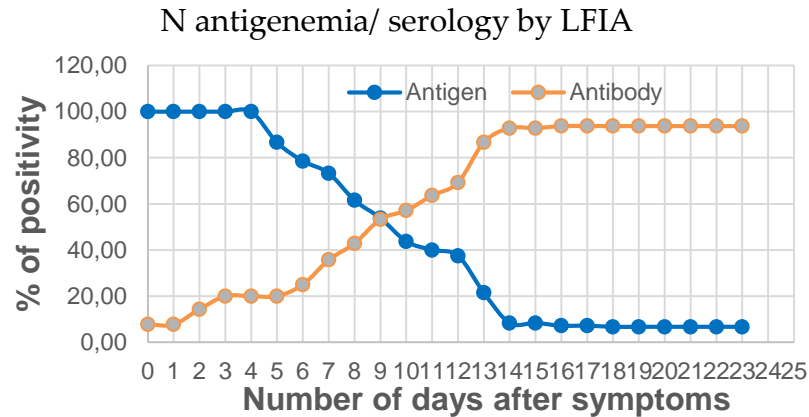
Evaluations, not always done properly
Lack of sensitivity, specificity
NP sampling difficult, nasal, saliva, SERUM?

Rapid immunochromatographic point-of-care diagnostic devices for detection of SARS CoV-2 antigens in NP and serum samples,

Ag detection in	(Ct<20)	(20≤Ct<25)	(25≤Ct<30)	(30≤Ct)	All RT-PCR+ NP samples	Infectious samples ^a (Ct≤ 33)
NP	100% n =25 (83.4-100)	98% n=48 (87.5-99.9)	82% n=57 (69.6-90.8)	36% n=53 (23.5-50.3)	75 % n=183 (68-81)	86% n=160 (79-90.5)
Serum (LFIA)	89% n=9 (50.7-99.4)	67% n=9 (30.9-99.4)	94% n=16 (67.7-99.7)	27% n=22 (11.6-50.4)	59% n=56 (45-72)	76% n=38 (59.4-88)
Serum (ELISA)	89% n=9 (68-100)	78% n=9 (50-100)	88% n=16 (60.4-97.8)	32% n=22 (14.7-54.9)	63% n=56 (50-75)	84% n=38 (72-96)

(S. Oueslati, submitted)

Rapid immunochromatographic point-of-care diagnostic devices for detection of SARS CoV-2 antigens in NP and serum samples,



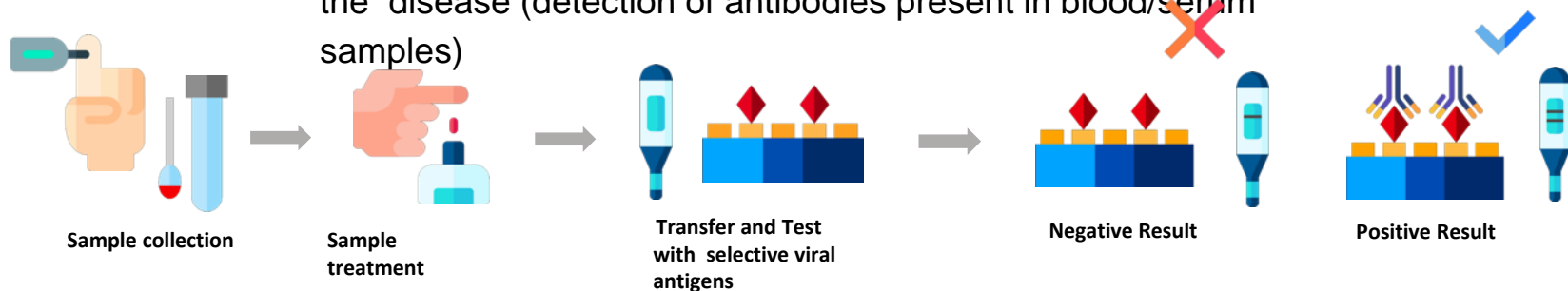


3

DETECTION OF ANTIBODIES (SEROLOGICAL TEST)

INDIRECT DETECTION

Detection of antibodies produced by the infected person during the disease (detection of antibodies present in blood/serum samples)



Advantages: Rapid test (5-15 min), well-established technique, easy sample extraction, non-infective sample, low cost, massive production, at the point-of-need, required selectivity.

Limitations: limited sensitivity (false negative and false positive), qualitative results (YES/NO) but not the antibody levels, variability of the immunoresponse in the population, not indicated for infection diagnosis.

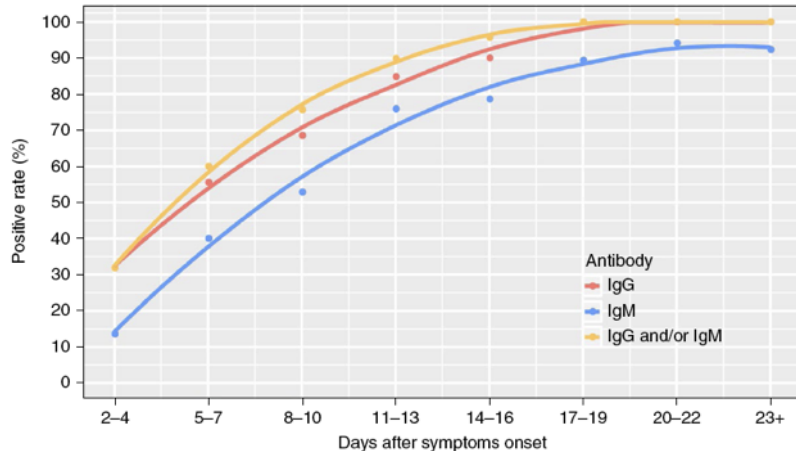
- Most of the Rapid test for serological analysis have NOT the required level of sensitivity (*false positive and false negative*)
- There is no information yet about the duration and the quality of the immunity
- Immunity Passport is NOT possible now

Positivity of anti-SARS-CoV-2 serologies



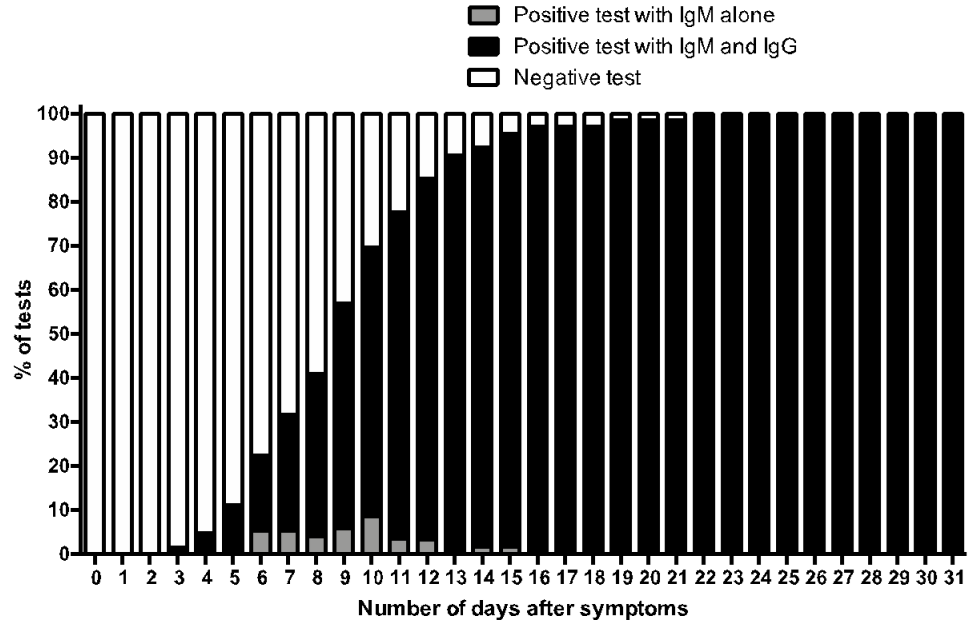
Antibody responses to SARS-CoV-2 in patients with COVID-19

Lang QX et al. Nature Med 2020



- 285 patients COVID +
- Technic **ELISA**
- **100%** with Ig anti-SARS-CoV-2 et **19 days post-symptômes**

Dortet L et al. Emerg Microbes Infect. 2020)



- 101 patients COVID +
- LFIA
- **> 95%** of patients with IgM and IgG anti-SARS-CoV-2 at **16 days post-symptoms** (100% at 23 days)

We have tested for you

Tests sérologiques		Nombre total de sérums testés	Tests non interprétables	Sensibilité selon la date de début des symptômes				Spécificité	Nombre de sérums testés pour évaluer la spécificité (sérums de patients COVID -)	
				Nombre total de sérums testés pour évaluer la sensibilité (sérums de patients COVID +)	J0-9	J10-14	J>14			
Tests rapides	NG-Biotech (IgM/IgG)	494	0	247	42,0% (42/100)	75,0% (63/84)	93,7% (59/63)	99,2% (96,8%-99,9%)	247	*
	Autobio (IgM/IgG)	496	0	247	52,0% (52/100)	87,1% (74/85)	90,3% (56/62)	94,4% (90,5%-96,8%)	249	
	Avioq (IgM/IgG)	482	1	243	46,5% (47/101)	76,5% (62/81)	91,8% (56/61)	94,5% (90,6%-97,0%)	238	
	^a Nadal (IgM/IgG)	449	0	226	56,8% (50/88)	89,9% (71/79)	91,5% (54/59)	99,1% (96,5% - 99,8%)	223	*
	Finecare (Ac Totaux)	498	0	249	55,4% (56/101)	92,9% (79/85)	95,2% (60/63)	98,4% (95,7% - 99,5%)	249	*
	Wondfo (Ac Totaux)	498	0	249	55,4% (56/101)	92,9% (79/85)	92,1% (58/63)	96,4% (93,0% - 99,7%)	249	
	^a Biosynex (IgM/IgG)	198	0	97	58,0% (18/31)	88,6% (31/35)	87,1% (27/31)	98,0% (92,3%-99,7%)	101	
	Innovita (IgM/IgG)	497	0	249	31,7% (32/101)	65,9% (56/85)	80,1% (51/63)	98,8% (96,2%-99,7%)	248	
	Biolidics (IgM/IgG)	237	0	157	35,7% (25/70)	78,8% (41/52)	93,3% (42/45)	92,5% (83,8%-96,9%)	80	
	Vedal Lab (IgM/IgG)	483	3	238	55,7% (54/97)	81,3% (65/80)	88,5% (54/61)	75,6% (69,6%-80,8%)	242	
ELISA	^a Abbott (Ac totaux)	279	0	230	41,0% (39/95)	73,1% (57/78)	84,2% (48/57)	100% (90,9%-100%)	49 ^b	
	IdVet (Ac totaux)	474	0	246	26,0% (26/100)	72,9% (62/85)	80,3% (49/61)	100% (97,9%-100%)	228	
	Orgentec (IgM/IgG)	493	0	247	48,5% (48/99)	77,4% (65/84)	88,9% (56/63)	98,8% (96,2%-99,7%)	246	

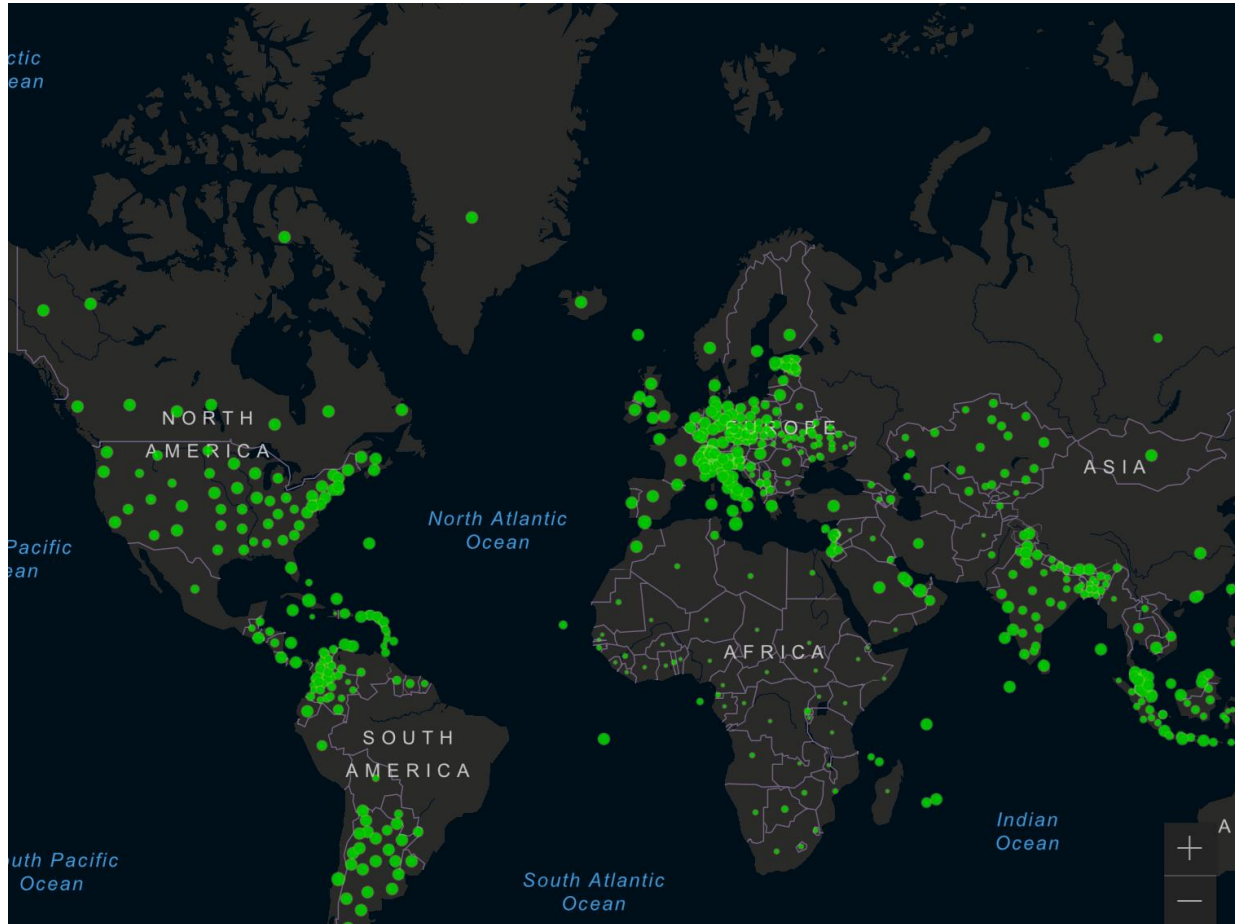
Evaluating 10 Commercially Available SARS-CoV-2 Rapid Serological Tests by Use of the STARD (Standards for Reporting of Diagnostic Accuracy Studies) Method

JCM, 2020

● Laurent Dortet,^{a,b} Jean-Baptiste Ronat,^{b,c} Christelle Vauloup-Fellous,^{d,e} Céline Langendorf,^f David-Alexis Mendels,^g Cécile Emeraud,^{a,b} Saoussen Oueslati,^b Delphine Girlich,^b Anthony Chauvin,^b Ali Afdjei,^h Sandrine Bernabeu,^{a,b} Samuel Le Pape,^d Rim Kallala,^d Alice Rochard,^b Celine Verstuyft,^j Nicolas Fortineau,^{a,b} Anne-Marie Roque-Afonso,^{d,e} ● Thierry Naas^{a,b}

Limites fixées par la HAS		
	Sensibilité	Spécificité
Acceptable	95%-100%	98%-100%
	90%-95%	
Non conforme	85%-90%	95%-98%
	80-85%	90%-95%
Désastreux	<80%	<90%

The solution: Global vaccination, but room to improve



Lessons from the COVID-19 pandemic: almost everything has changed, all around the world.

- ▶ Our lifes
- ▶ our economies
- ▶ Our inter human relationships
- ▶ Our habits
- ▶ Loss of common sens to many people, and of clinical sens to some doctors
- ▶ Revealed difficulties and weaknesses
 - ▶ Of our societies
 - ▶ Of our administrations
 - ▶ Of our health systems
 - ▶ At the hospital
 - ▶ In the community
 - ▶ At the level of training of our doctors

Lessons from the COVID-19 pandemic: almost everything has changed, all around the world.

► Positive points

- Knowledge on diseases has never evolved so fast
- All the publications on preprint servers and open access
- Unprecedented developement of Rapid diagnostics, and their use
- Health has no price anymore for COVID (« What ever it cost», E. Macron)

► Negative points

- The articles, are not read anymore: mostly title and conclusions
- Scientific results presented in TV, by self declared experts, who comment the data without knowledge
- The after crisis should benefit from the lessons learned ? (societies, living together, medical and diagnostics) ?

Will AMR benefit from the pandemic ?

- Will mask wearing and hydroalcoholic solutions have an impact on AMR spread?
- Restrictions in trips: reduction of 25% of CPEs (mostly imported cases, F-NRC)
- Increased usage of antibiotics for intubated COVID patients: consequence on AMR?
- Will RDT have the same boost as anti COVID-RDTs? Reimbursement accelerated?

- We have to keep in mind that AMR may lead to 10 million deaths if nothing is done:

⇒ It is time to act, and as for COVID, diagnostics is in the heart of any strategy against AMR
(search and isolate strategy and antibiotic stewardship)

And not to forget: social distancing, and hand hygiene

Hand washing technique with soap and water



Issued by **deb** www.debgroup.com



World Health Organization

Adapted from World Health Organization Guidelines on Hand Hygiene in Health Care 2009

UKL175X793214





THANK YOU
FOR YOUR ATTENTION!

Detection in 30 min



EIT Health is supported by the EIT,
a body of the European Union