L'assistenza del malato oncologico nelle strutture ospedaliere La medicina di laboratorio nello screening e nella diagnostica della pandemia

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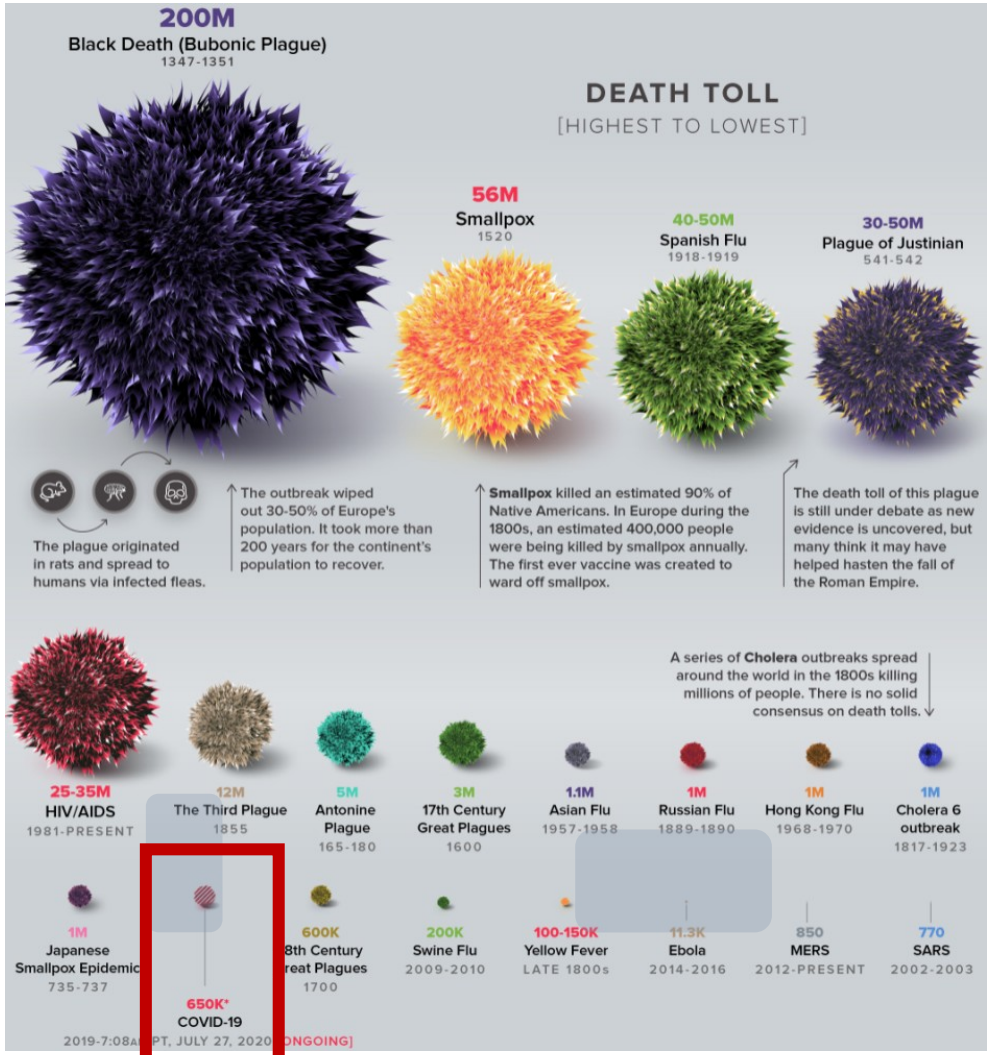
Coronavirus disease 2019 (COVID-19)

Coronavirus disease 2019 (COVID-19), Primo caso ufficialmente diagnosticato a Wuhan il 17 Novembre 2019. Agente eziologico nCoV-2019, rinominato poi **SARS-CoV-2**

- Terza epidemia di SARS negli ultimi 20 anni
- Sindrome respiratoria acuta severa (**SARS**) in 2002-2003
- Sindrome respiratori del Medio oriente (**MERS**) in 2012



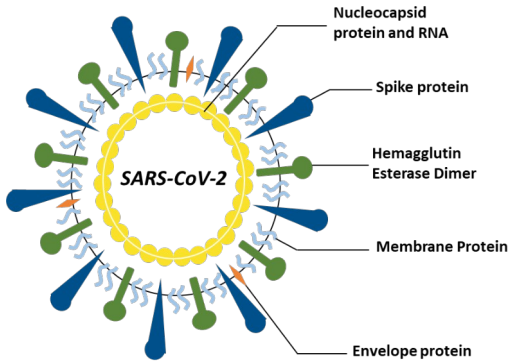
https://www.visualcapitalist.com/history-of-pandemics-deadliest/

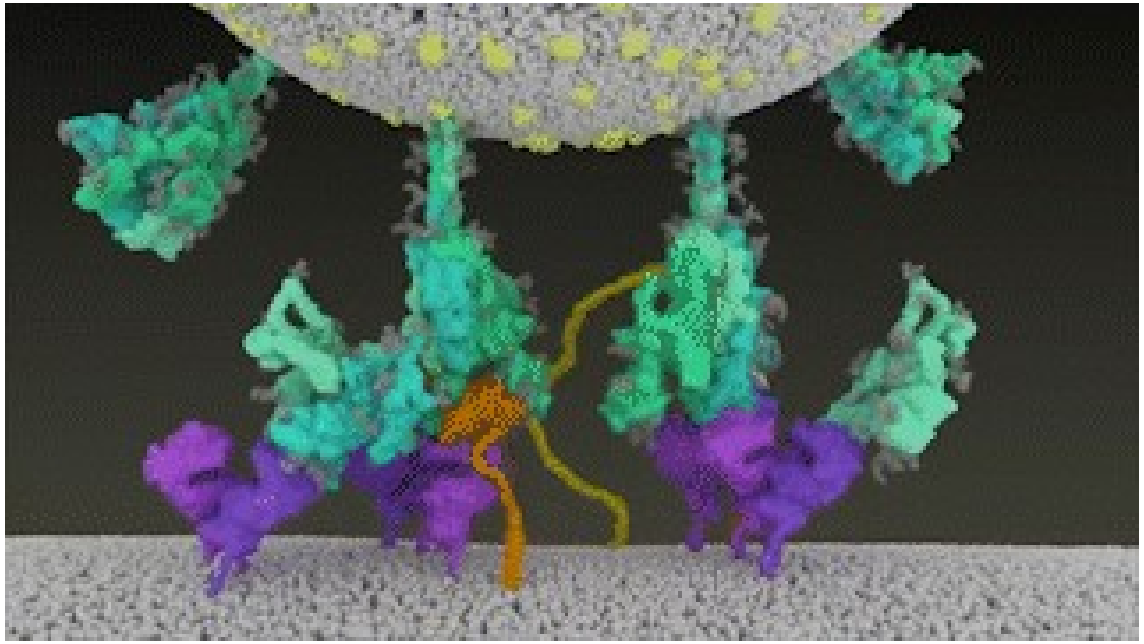
MEDICINA DI LABORATORIO e PANDEMIA

- ***La pandemia da Sars-Cov-2, molto più di numerose pubblicazioni scientifiche, ha fatto capire a tutti quale sia il valore dell'analisi di laboratorio.*** Il messaggio dell'importanza della diagnostica è arrivato forte e chiaro quando, nel corso della prima fase, alcuni lavori scientifici hanno dimostrato che anche gli asintomatici possono essere contagiosi. Il caso della nave da crociera Diamond Princess è stato, sotto quest'aspetto, quasi un modello di studio che si è avvalso della diagnostica molecolare per scovare i positivi.
- «La medicina di laboratorio – spiega Mario Plebani, docente di Biochimica clinica e Biologia molecolare e direttore del Dipartimento di Servizi di diagnostica integrata presso l'Azienda Ospedaliera Università di Padova – è fondamentale per poter avere una diagnosi, sia per confermare un'ipotesi clinica basata sull'osservazione dei sintomi, sia quando il paziente è asintomatico».

La Repubblica 17.11.2020

SARS-CoV-2: *Overview of Viral Characteristics*



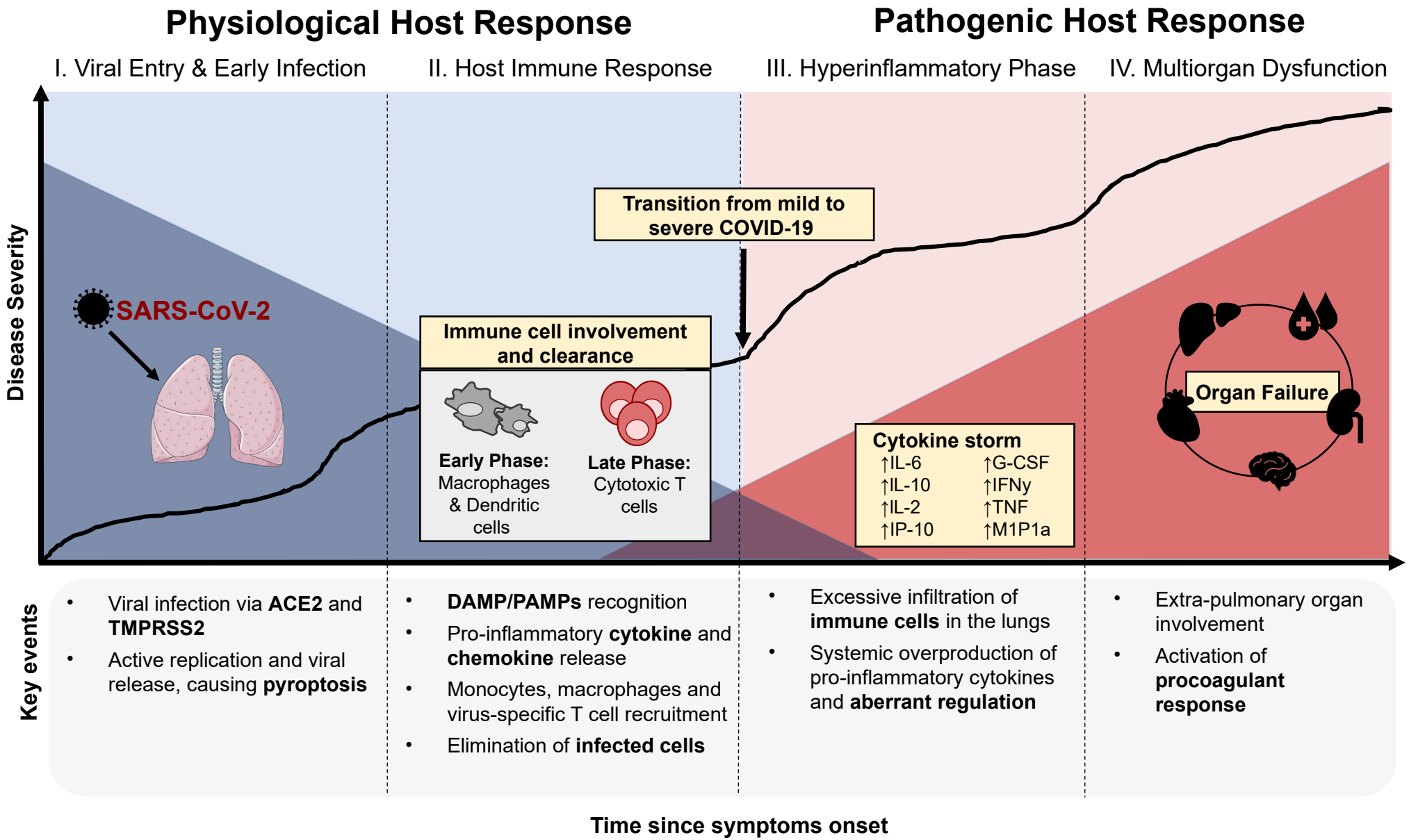


SARS-CoV-2 ha 4 glicoproteine principali:

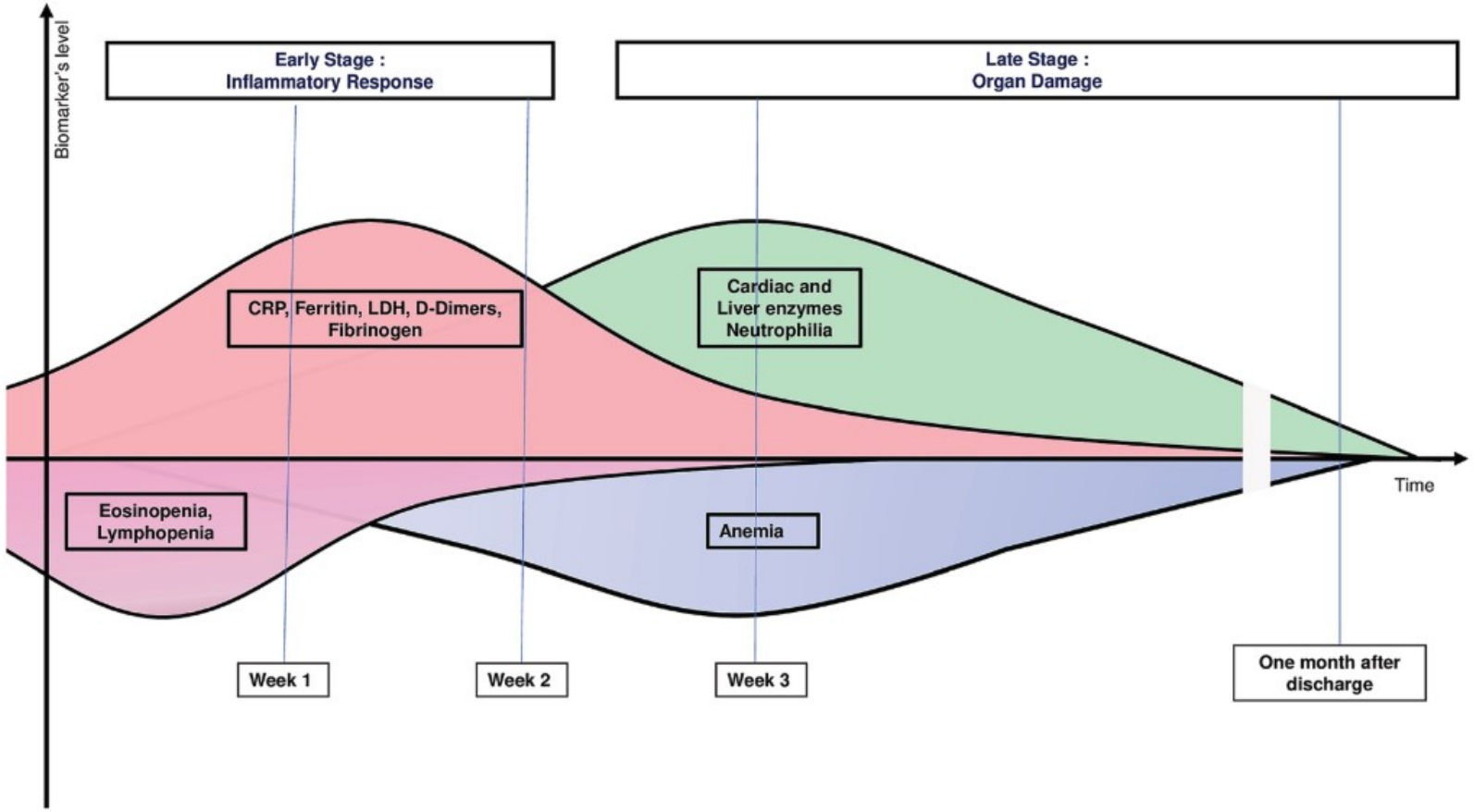
- ***spike (S),***
- ***membrana (M)***
- ***envelope (E)***
- ***nucleocapside (N)***

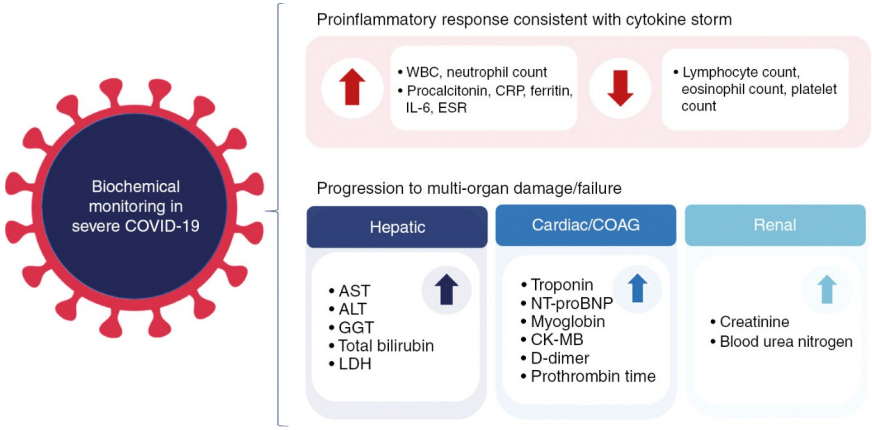
M, E, e N sono importanti per l'assemblaggio delle particelle virali
S (spike) è la proteina che permette l'ingress del virus nella cellula.

Il test molecolare usa un saggio chimato RT-PCR per amplificare il materiale genetico del virus, che è l'RNA

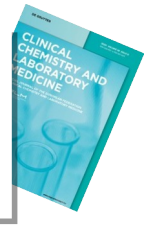

Physiological Host Response
Pathogenic Host Response
I. Viral Entry & Early Infection
II. Host Immune Response
III. Hyperinflammatory Phase
IV. Multiorgan Dysfunction
Disease Severity
SARS-CoV-2
Transition from mild to severe COVID-19
Immune cell involvement and clearance
Early Phase: Macrophages & Dendritic cells
Late Phase: Cytotoxic T cells
Cytokine storm
↑IL-6
↑IL-10
↑IL-2
↑IP-10
↑G-CSF
↑IFNy
↑TNF
↑M1P1a
Organ Failure
Key events
• Viral infection via ACE2 and TMPRSS2
• Active replication and viral release, causing pyroptosis
• DAMP/PAMPs recognition
• Pro-inflammatory cytokine and chemokine release
• Monocytes, macrophages and virus-specific T cell recruitment
• Elimination of infected cells
• Excessive infiltration of immune cells in the lungs
• Systemic overproduction of pro-inflammatory cytokines and aberrant regulation
• Extra-pulmonary organ involvement
• Activation of procoagulant response
Time since symptoms onset

Timeline of biochemical and hematological abnormalities in COVID-19 patients

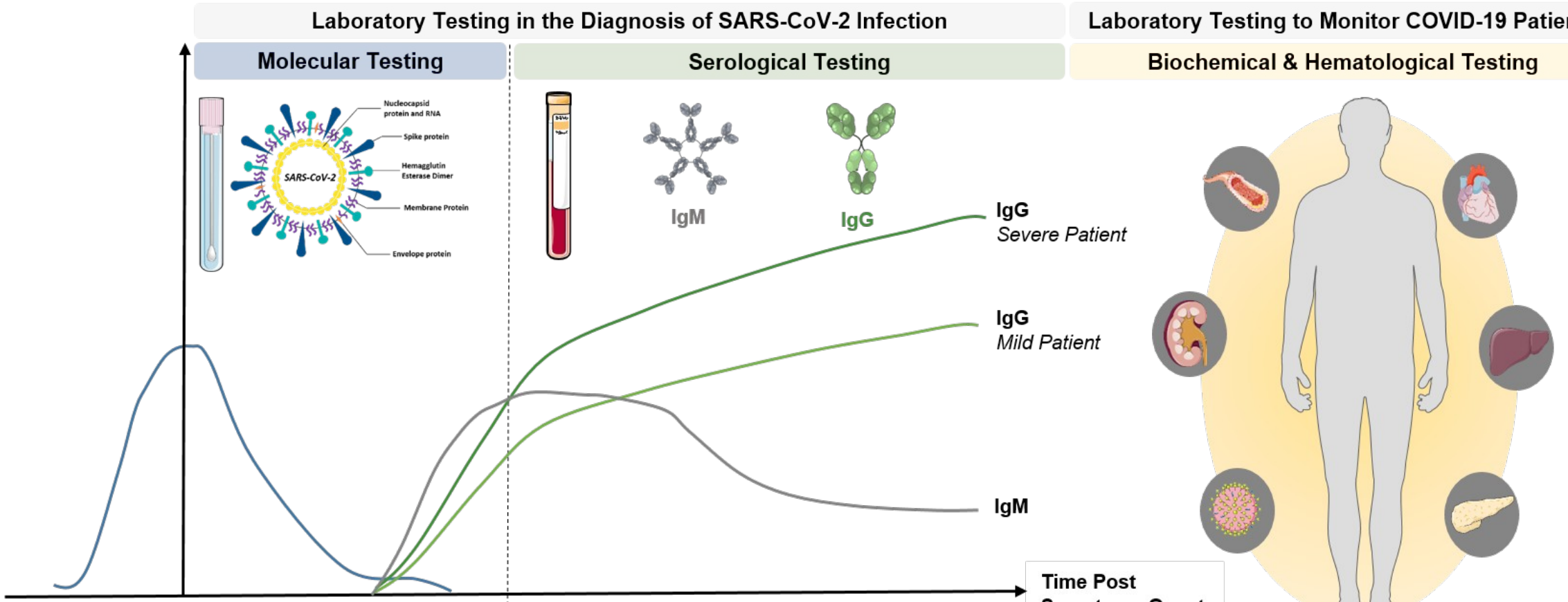




Khourssaji M, Chapelle V, Evenepoel A, Belkhir L, Yombi JC, Van Dievoet MA, et al. A biological profile for diagnosis and outcome of COVID-19 patients. *Clin Chem Lab Med*. 2020;58(12):2141–50.



Ruolo dei Laboratori clinici nella pandemia da COVID-19



Specimen Type:	Nasopharyngeal	Blood (serum, plasma, whole blood, finger prick)
Assay Principle:	NAAT	LFA, CLIA, or ELISA
General Use:	Identification of current SARS-CoV-2 infection	Identification of past SARS-CoV-2 infection

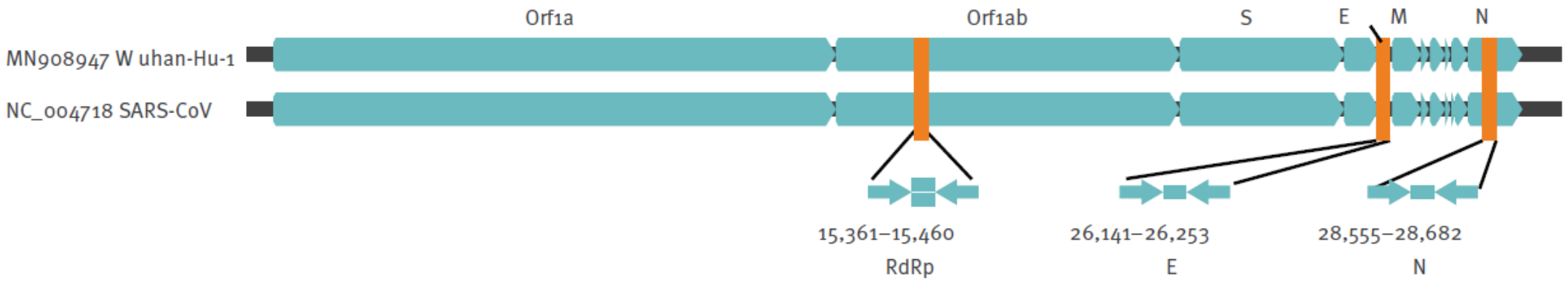
Lippi et al., CCLM (accepted)

Corman VM, et al.

Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR.

FIGURE 1

Relative positions of amplicon targets on the SARS coronavirus and the 2019 novel coronavirus genome



E: envelope protein gene; M: membrane protein gene; N: nucleocapsid protein gene; ORF: open reading frame; RdRp: RNA-dependent RNA polymerase gene; S: spike protein gene.

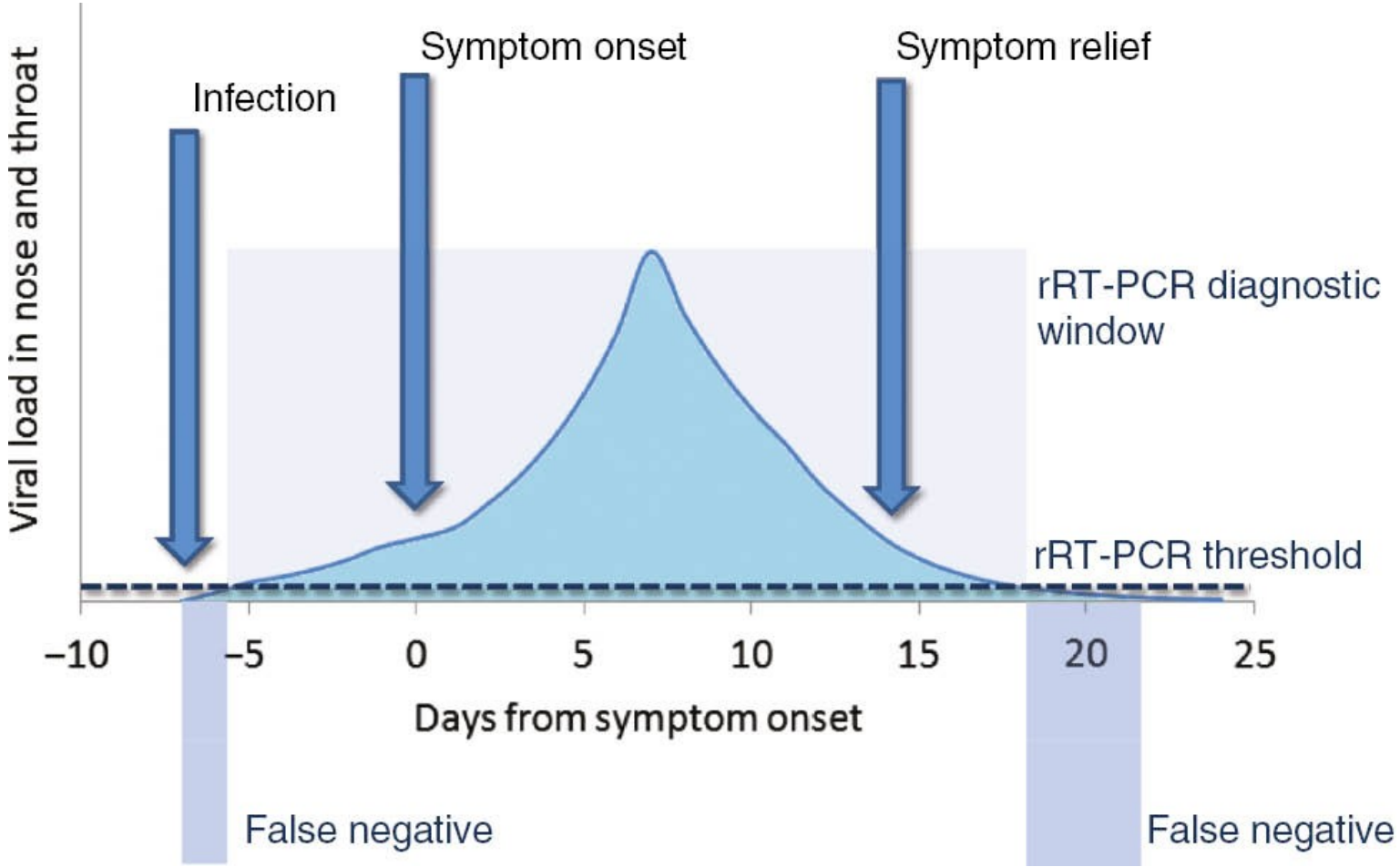


Figure 1: Corrispondenza tra la carica virale, il decorso clinico e la positività alla RT-PCR.

Potential preanalytical and analytical vulnerabilities in the laboratory diagnosis of coronavirus disease 2019 (COVID-19)

Lippi G, Simundic AM, Plebani M. Clin Chem Lab Med. 2020 Mar 16. [Epub ahead of print] PMID: 32172228.

Il GOLD STANDARD per la diagnostica (RT-PCR)

Il gold standard attuale per la diagnosi eziologica dell'infezione di SARS-CoV-2 è la (real-time) reverse transcription polymerase chain reaction (**rRT-PCR**) su campioni prelevati dal tratto respiratorio.

L'accuratezza diagnostica è eccellente, ma come per tutti i test di Laboratorio ci sono dei prerequisiti ***pre-analitici e analitici***.

Table 1: Potential preanalytical and analytical vulnerabilities in the laboratory diagnosis of coronavirus disease 2019 (COVID-19) using (real time) reverse transcription polymerase chain reaction (rRT-PCR).

Preanalytical
General
– Lack of identification/misidentification
– Inadequate procedures for specimen (e.g. swab) collection, handling, transport and storage
– Collection of inappropriate or inadequate material for quality or volume
– Presence of interfering substances
– Manual (pipetting) errors
Specific
– Sample contamination
– Testing in patients receiving antiretroviral therapy
Analytical
– Testing carried out outside of the diagnostic window
– Active viral recombination
– Use of non-adequately validated assays
– Lack of harmonization of primers and probes
– Instrument malfunctioning
– Insufficient or inadequate material
– Non-specific PCR annealing
– Misinterpretation of expression profiles

The critical role of laboratory medicine during coronavirus disease 2019 (COVID-19) and other viral outbreaks

Lippi G, Plebani M. Clin Chem Lab Med. 2020 Mar 19. doi: 10.1515/cclm-2020-0240. [Epub ahead of print] PMID: 32191623.

Table 3: Practical indications to minimize the risk of diagnostic errors in identifying severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.

Combine results of SARS-CoV-2 RT-PCR infection with – Clinical and epidemiologic evidence (probability of exposure, signs, symptoms, negative diagnostic tests especially for other respiratory illnesses) – Chest computed tomography (CT; most frequently appear with ground-glass opacities, consolidation with or without vascular enlargement, air bronchogram signs, interlobular septal thickening)
Recollect and test upper respiratory specimens in patients with negative RT-PCR test results and high suspicion or probability of SARS-CoV-2 infection
Provide clear instructions on how nasopharyngeal and oropharyngeal swabs shall be correctly collected, managed and stored
Thorough compliance with assay procedures, including quality assurance
Validate extensively RT-PCR assay before clinical usage
Further refinement of molecular target(s)

rRT-PCR, (real time) reverse transcription polymerase chain reaction.

Potential preanalytical and analytical vulnerabilities in the laboratory diagnosis of coronavirus disease 2019 (COVID-19)

Lippi G, Simundic AM, Plebani M. Clin Chem Lab Med. 2020 Mar 16. [Epub ahead of print] PMID: 32172228.

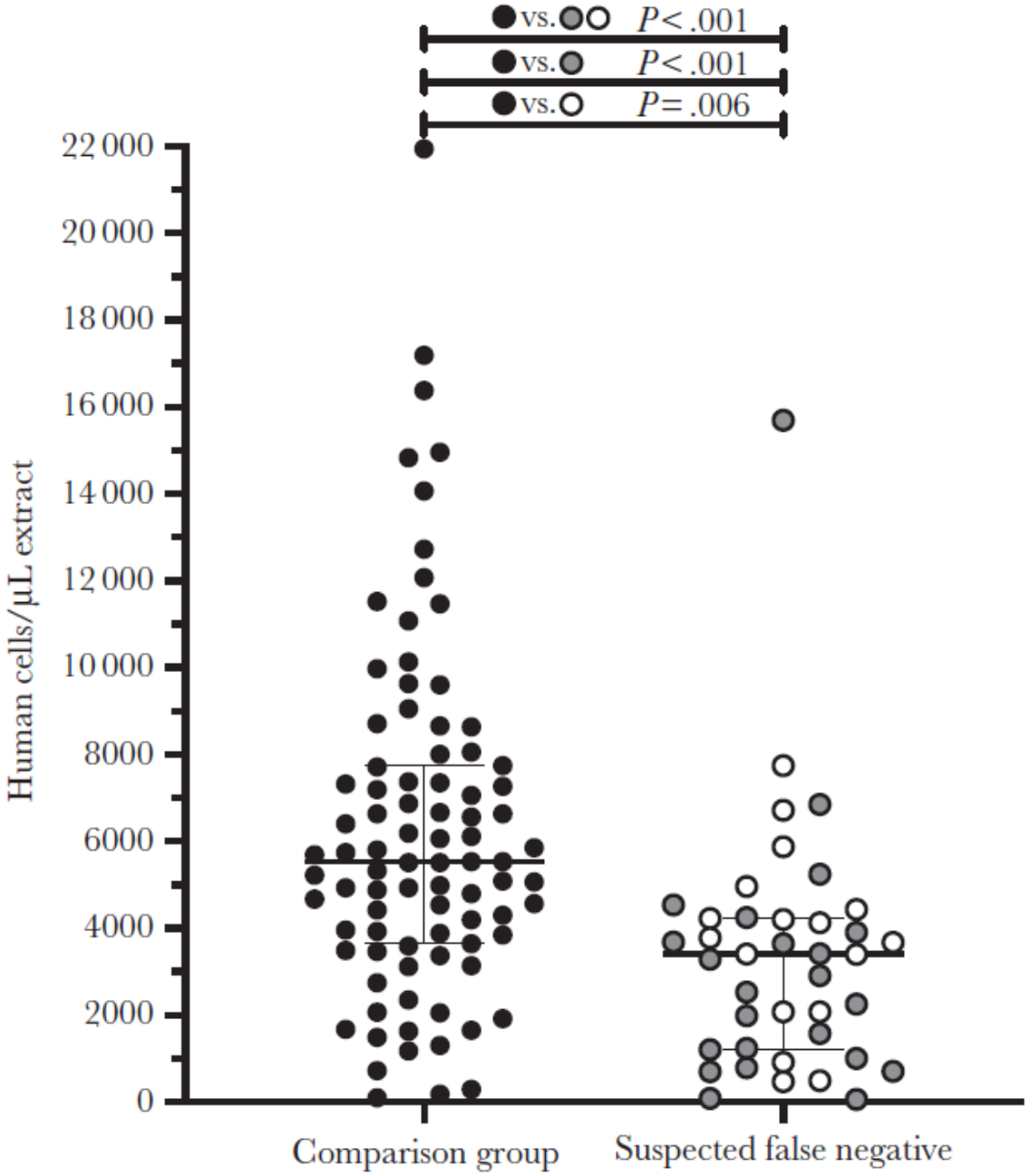
La raccolta eseguita scorrettamente causa risultati erroneamente negativi

The Journal of Infectious Diseases

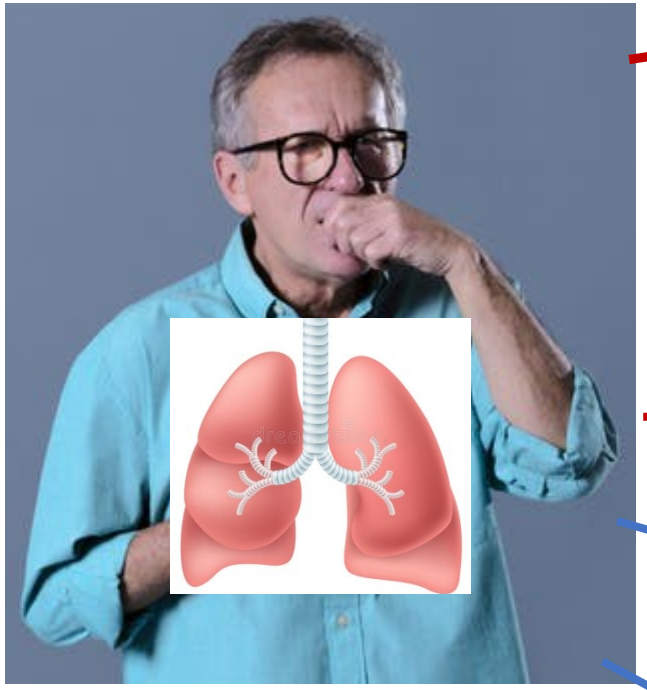
BRIEF REPORT

Suboptimal Biological Sampling as a Probable Cause of False-Negative COVID-19 Diagnostic Test Results

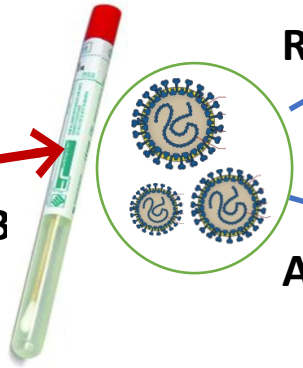
Natalie N. Kinloch,[1,2] Gordon Ritchie,[3,4] Chanson J. Brumme,[2,5] Winnie Dong,[2] Weiyan Dong,[2] Tanya Lawson,[3] R. Brad Jones,[6] Julio S. G. Montaner,[2,5] Victor Leung,[3,4] Marc G. Romney,[3,4] Aleksandra Stefanovic,[3,4] Nancy Matic,[3,4] Christopher F. Lowe,[3,4,a] and Zabrina L. Brumme[1,2,a]



Ruolo della Medicina di laboratorio nella diagnostica per SARS-CoV-2



SWAB



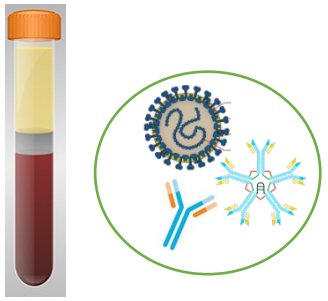
RNA
- RT-qPCR
- RT-LAMP
- dd PCR
- CRISPR

ANTIGEN
- Lateral Flow (ICT)
- Chemiluminescence (CLIA)
- Fluorescent (FIA)

SALIVA
- RT-PCR
- CLIA

EXHALED BREATH
- RT-PCR
- Gas-chromatography-ion mobility spec
- Multiplexed nano material-based sensor

BLOOD



- Lateral Flow (??)
- ELISA
- Chemiluminescence immunoassays

Medicina di laboratorio

Esistono test alternativi per SARS-CoV-2

- **Test molecolari innovatiti e rapidi**
- CRISPR-based diagnostics
- ***Antigen tests (rapid and laboratory-based)***
- ***Mass spectrometry***
- Breath tests
- Serological tests (for SARS-CoV-2 Antibodies)

Cochrane Library

Cochrane Database of Systematic Reviews

Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection (Review)

- **We did not find any studies at low risk of bias for all quality domains and had concerns about applicability of results across all studies. We judged patient selection to be at high risk of bias in 50% of the studies because of deliberate over-sampling of samples with confirmed COVID-19 infection and unclear in seven out of 18 studies because of poor reporting. Sixteen (89%) studies used only a single, negative RTPCR to confirm the absence of COVID-19 infection, risking missing infection. There was a lack of information on blinding of index test (n =11), and around participant exclusions from analyses (n = 10). We did not observe differences in methodological quality between antigen and molecular test evaluations.**
- **Antigen tests**
- **Sensitivity varied considerably across studies (from 0% to 94%): the average sensitivity was 56.2% (95% CI 29.5 to 79.8%) and average specificity was 99.5% (95% CI 98.1% to 99.9%; based on 8 evaluations in 5 studies on 943 samples). Data for individual antigen tests were limited with no more than two studies for any test.**

Rapid molecular tests				
Evaluations (studies)	**Samples**	**Confirmed SARS-CoV-2 samples**	**Average sensitivity (95% CI) [Range]**	**Average specificity (95% CI) [Range]**
13 (11)	2255	1179	95.2 (86.7 to 98.3) [68% to 100%]	98.9 (97.3 to 99.5) [92% to 100%]

Average sensitivity and specificity applied to a hypothetical cohort of 1000 patients

Prevalence of COVID-19	**TP**	**FP**	**FN**	**TN**	**PPV [b] (95% CI)**	**NPV [c] (95% CI)**
5%	48	10	2	940	83% (71% to 91%)	100% (99% to 100%)
10%	95	10	5	890	90% (83% to 95%)	99% (99% to 100%)
20%	190	9	10	791	95% (92% to 98%)	99% (98% to 99%)

ALTERNATIVE TESTING FOR SARS-CoV- 2

- Innovative and «rapid» molecular tests
- CRISPR-based diagnostics
- ***Test antigenici (rapidi o di laboratorio)***
- ***Mass spectrometry***
- Breath tests
- Serological tests (for SARS-CoV-2 Antibodies)

Cochrane Library

Cochrane Database of Systematic Reviews

Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection (Review)

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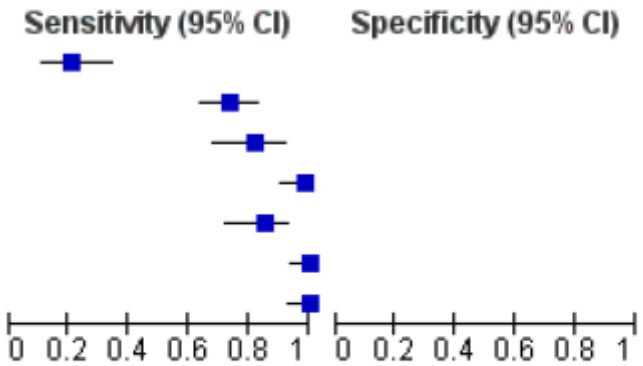
Antigen tests						
Evaluations (studies)	**Samples**		**Confirmed SARS-CoV-2 samples**		**Average sensitivity (95% CI) [Range]**	**Average specificity (95% CI) [Range]**
8 (5)	943		596		56.2 (29.5 to 79.8) [0% to 94%][a]	99.5 (98.1 to 99.9) [90% to 100%]
Average sensitivity and specificity applied to a hypothetical cohort of 1000 patients [a]						
Prevalence of COVID-19	**TP**	**FP**	**FN**	**TN**	**PPV** [b]	**NPV** [c]
5%	28[a]	5	22[a]	945	85% (68% to 95%)[a]	98% (97% to 99%)
10%	56[a]	5	44[a]	896	92% (82% to 97%)[a]	95% (94% to 97%)[a]
20%	112[a]	4	88[a]	796	97% (91% to 99%)[a]	90% (88% to 92%)[a]

Figure 5. Forest plot of studies evaluating antigen tests according to viral load: high (≤ 25 Ct) versus low viral load (> 30 Ct in Diao 2020). Studies grouped by test

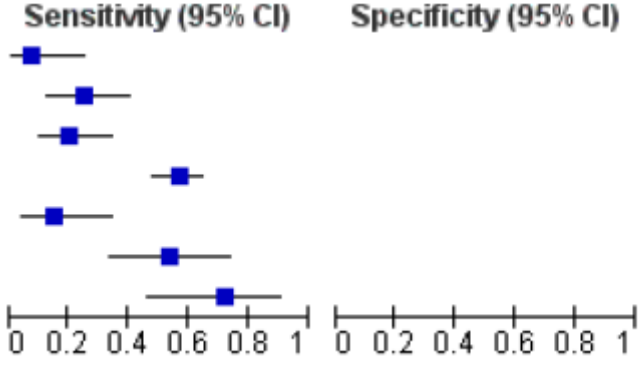
Antigen tests - high viral load

Study	TP	FP	FN	TN	Test	Sensitivity (95% CI)	Specificity (95% CI)
Weitzel 2020 [C]	11	0	41	0	Beijing Savant - FIA	0.21 [0.11, 0.35]	Not estimable
Mertens 2020	65	0	23	0	Coris BioConcept - CGIA	0.74 [0.63, 0.83]	Not estimable
Lambert-Niclot 2020	37	0	8	0	Coris BioConcept - CGIA	0.82 [0.68, 0.92]	Not estimable
Diao 2020	55	0	1	0	In-house - FIA	0.98 [0.90, 1.00]	Not estimable
Weitzel 2020 [A]	45	0	8	0	RapiGEN Inc - CGIA	0.85 [0.72, 0.93]	Not estimable
Weitzel 2020 [D]	54	0	0	0	Shenzhen Bioeasy - FIA	1.00 [0.93, 1.00]	Not estimable
Porte 2020	52	0	0	0	Shenzhen Bioeasy - FIA	1.00 [0.93, 1.00]	Not estimable



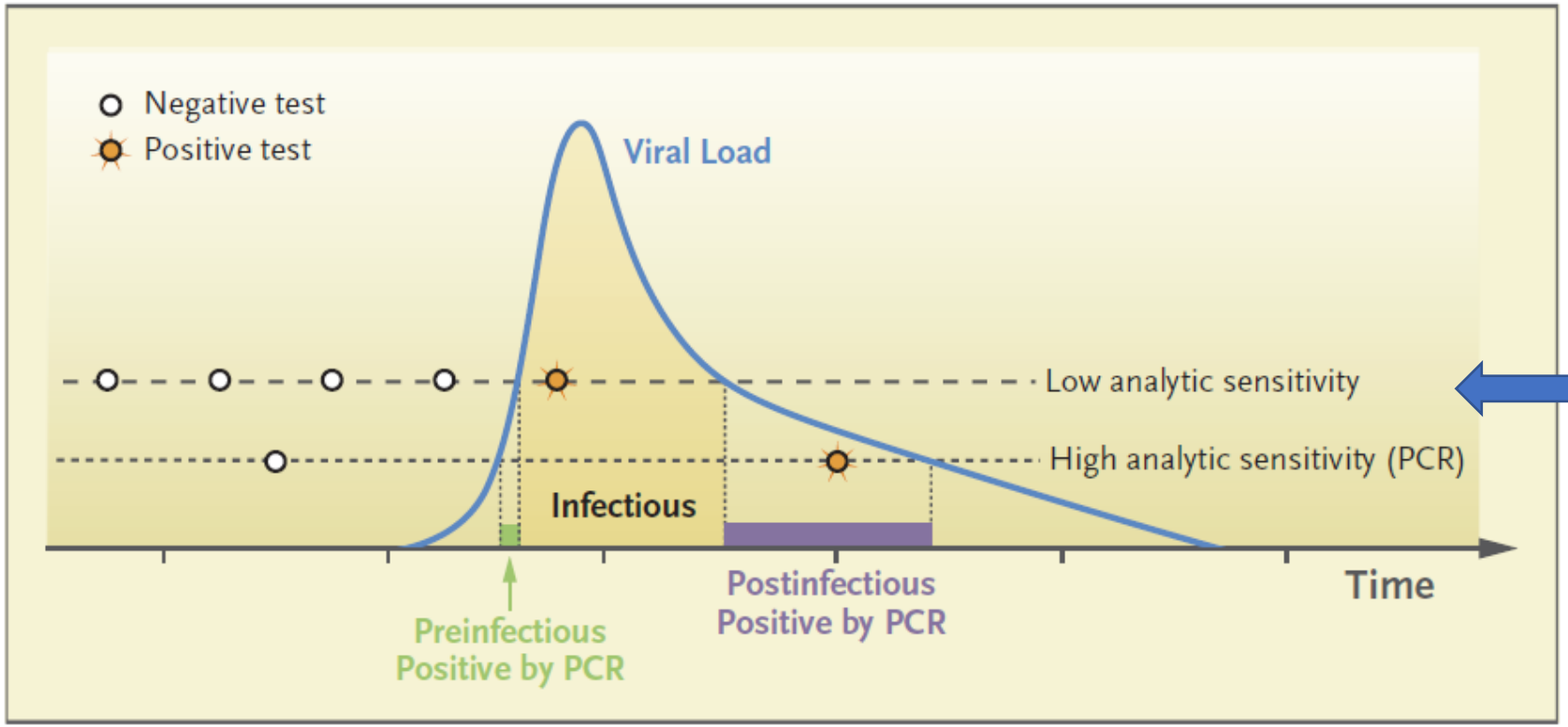
Antigen tests - low viral load

Study	TP	FP	FN	TN	Test	Sensitivity (95% CI)	Specificity (95% CI)
Weitzel 2020 [C]	2	0	24	0	Beijing Savant - FIA	0.08 [0.01, 0.25]	Not estimable
Mertens 2020	11	0	33	0	Coris BioConcept - CGIA	0.25 [0.13, 0.40]	Not estimable
Lambert-Niclot 2020	10	0	39	0	Coris BioConcept - CGIA	0.20 [0.10, 0.34]	Not estimable
Diao 2020	86	0	66	0	In-house - FIA	0.57 [0.48, 0.65]	Not estimable
Weitzel 2020 [A]	4	0	22	0	RapiGEN Inc - CGIA	0.15 [0.04, 0.35]	Not estimable
Weitzel 2020 [D]	14	0	12	0	Shenzhen Bioeasy - FIA	0.54 [0.33, 0.73]	Not estimable
Porte 2020	13	0	5	0	Shenzhen Bioeasy - FIA	0.72 [0.47, 0.90]	Not estimable



Rethinking Covid-19 Test Sensitivity — A Strategy for Containment

Michael J. Mina, M.D., Ph.D., Roy Parker, Ph.D., and Daniel B. Larremore, Ph.D.



High-Frequency Testing with Low Analytic Sensitivity versus Low-Frequency Testing with High Analytic Sensitivity.

N Engl J Med 2020

Rapid Antigen

COVID-19 rapid tests are inexpensive and fast but sometimes give incorrect results*

1 in 5 patients with symptoms and confirmed COVID-19 received a negative rapid antigen test result

* 1,098 paired nasal swabs collected at 2 universities in Wisconsin, September 28–October 9, were tested using Sofia SARS Antigen FIA and compared to rRT-PCR/viral culture results.

People with **symptoms** and a **negative rapid test** should

Get a confirmation (RT-PCR) test

Wear a mask

Stay home in a separate room

CDC.GOV bit.ly/MMWR123120 MMWR

Table 1 | Advantages and limitations of lateral flow tests compared with PCR tests*

Advantages	Limitations
Rapid time to results (10-30 minutes)	Some infectious individuals will have negative results
Does not need laboratory analysis and so can facilitate frequent decentralised testing at scale	End-to-end single test performance falls when used by untrained staff or public—less so when repeated
Good detector of the most infectious cases and less likely to detect post-infectious people with residual shedding	Infectious window is early and short lived, narrowing the window to find cases before they transmit infection
Effective contact tracing depends on speed, and modelling suggests testing frequency and speed of reporting more important than sensitivity alone for surveillance and controlling transmission	Current lateral flow test does not quantify the level of virus material detected to reflect a level of infectiousness

* See appendix for performance results.

TO BE REMEMBERED:
TESTS ALONE ARE NOT ENOUGH AND ARE NOT THE ANSWER

Lateral flow tests cannot rule out SARS-CoV-2 infection

People testing negative must stick to infection control recommendations

Jonathan J Deeks, [1] Angela E Raffle[2]

Cite this as: *BMJ* 2020;371:m4787

mainly those with symptoms. Detection rates (sensitivity) were 73% (95% confidence interval 64% to 85%) when tested by skilled NIHR research nurses and 79% (73% to 85%) when tested by Porton Down laboratory scientists.[8 9] But testing by Boots test centre employees (following written instructions) achieved sensitivity of just 58% (52% to 63%). This is important, because it is closest to the circumstances for staff, student, visitor, and community testing.

MA NESSUNO AVEVA MESSO IN EVIDENZA CHE L 'ACCURATEZZA DIPENDE ANCHE DALLA COMPETENZA DELL'ESECUTORE ?

Test antigenici di laboratorio per COVID-19

- Metodi chemiluminescenti per una sensibilità analitica più alta
- Migliori caratteristiche diagnostiche
- Soddisfacente correlazione con la carica virale e RT-PCR
- Sufficientemente Rapidi (TAT 35 min)
- Sufficientemente in grado di essere eseguiti su tante persone in tempi ridotti (60-120 test per ora)

ScienceAdvances

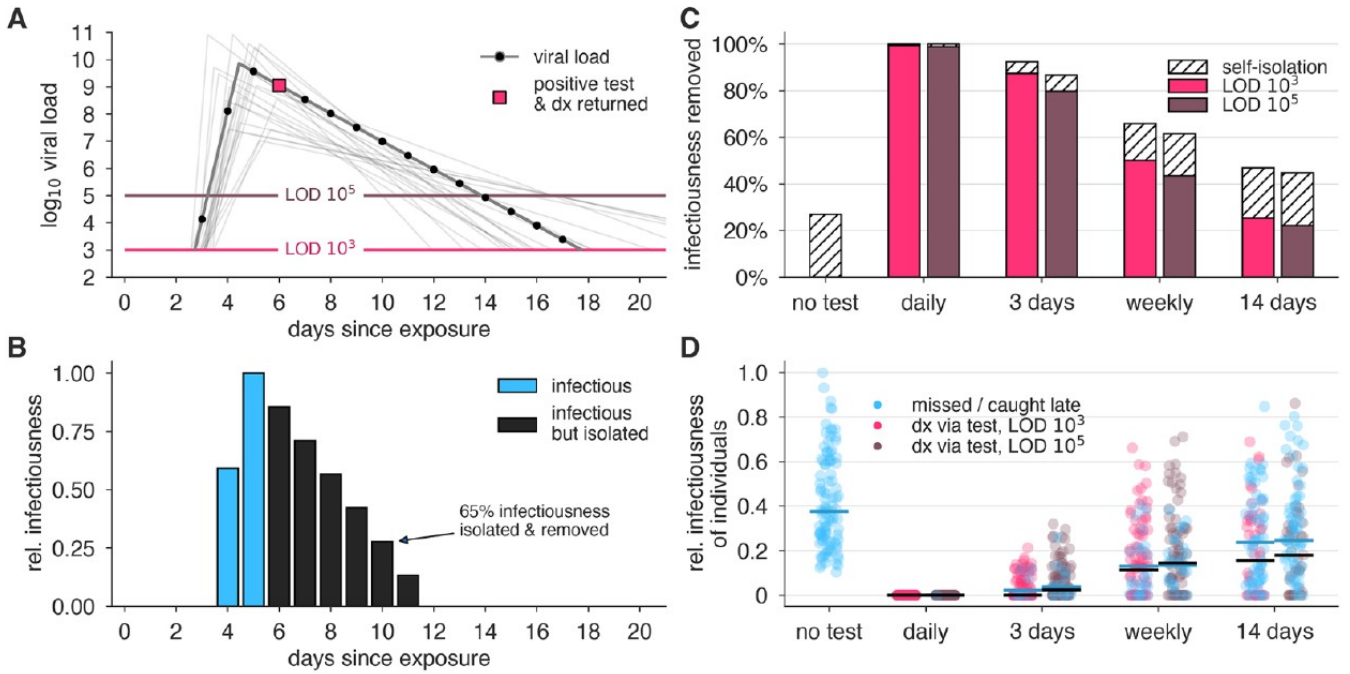
RESEARCH ARTICLES

Screening:

Cite as: D. B. Larremore *et al.*, *Sci. Adv.* 10.1126/sciadv.abd5393 (2020).

Test sensitivity is secondary to frequency and turnaround time for COVID-19 screening

Daniel B. Larremore,[1,2*] Bryan Wilder,[3] Evan Lester,[6,5] Soraya Shehata,[4,5] James M. Burke,[6] James A. Hay,[7,8] Milind Tambe,[3] Michael J. Mina[7,8,9*†] and Roy Parker[4,6,10,2*†]



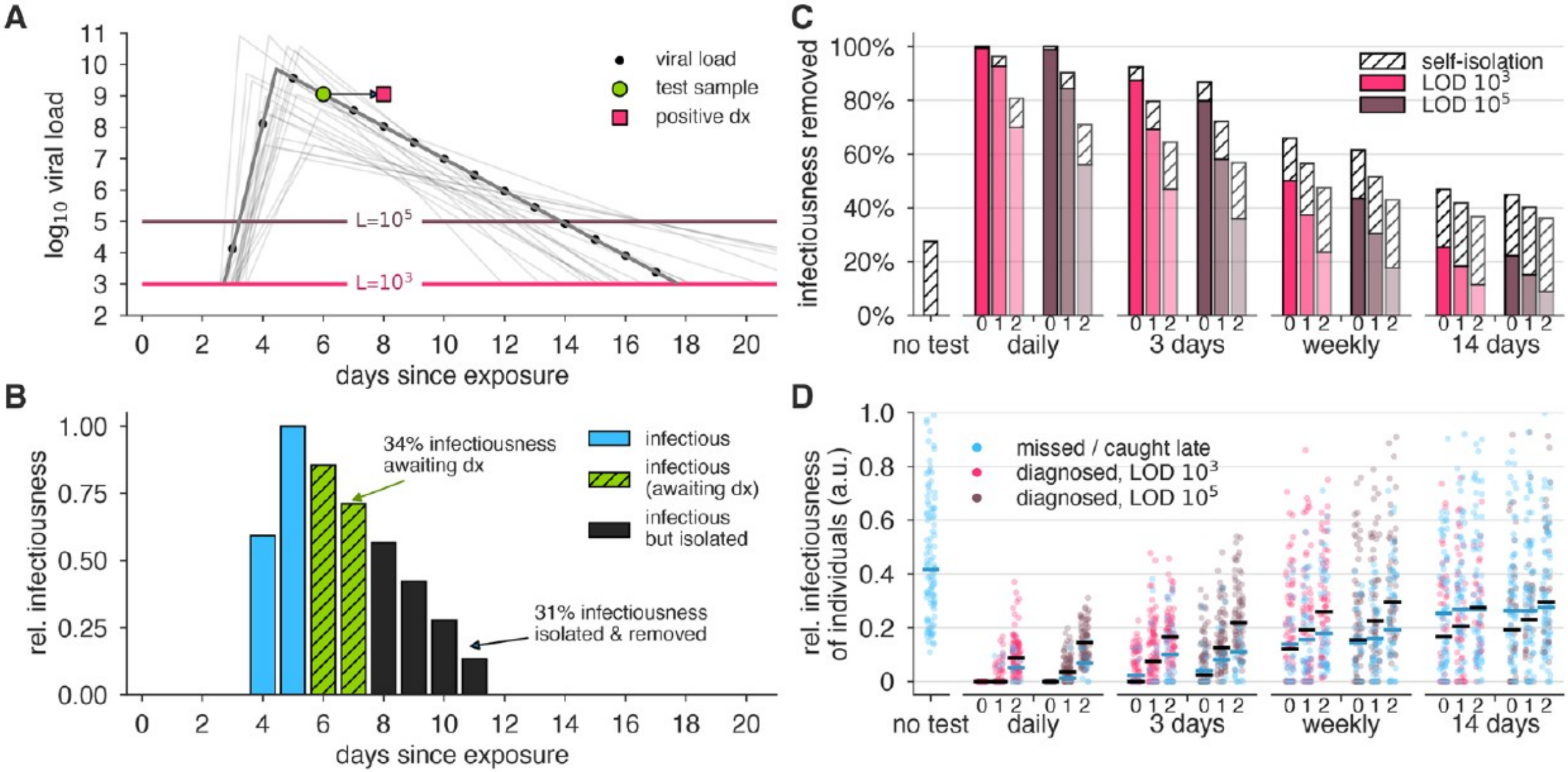
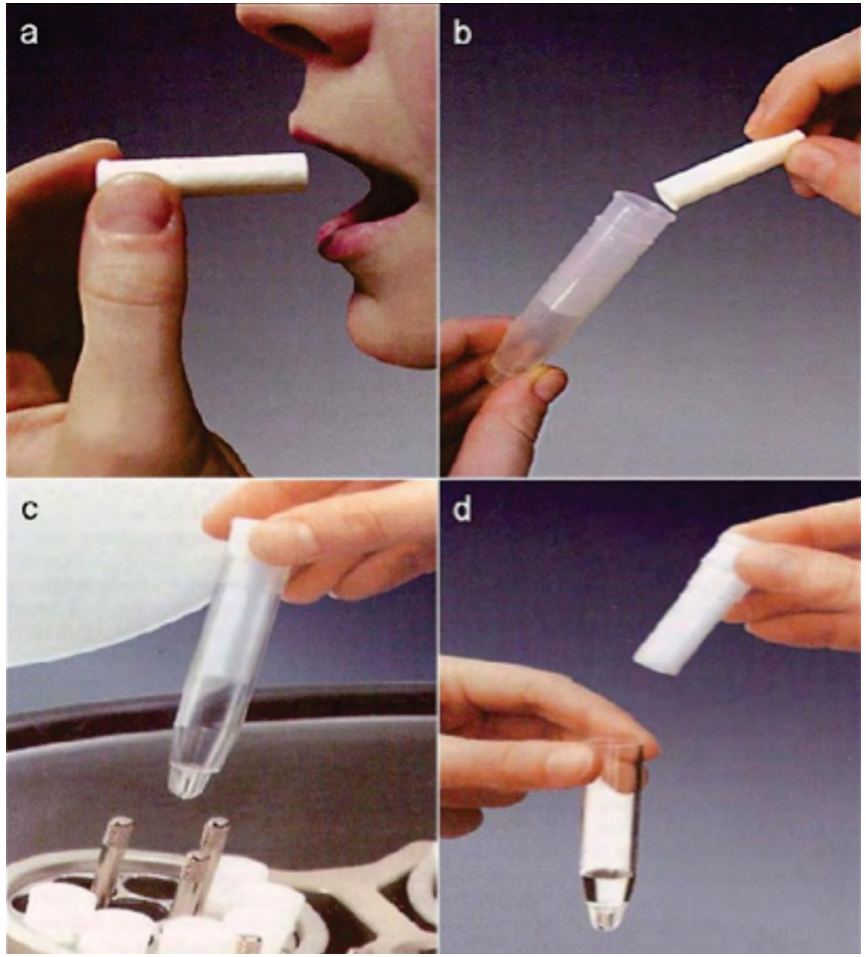


Fig. 4. Effectiveness of screening is compromised by delays in reporting. (A) An example viral load

Strategie per il testing

Crozier A et al. BMJ 2021

SALIVA come campione alternativo



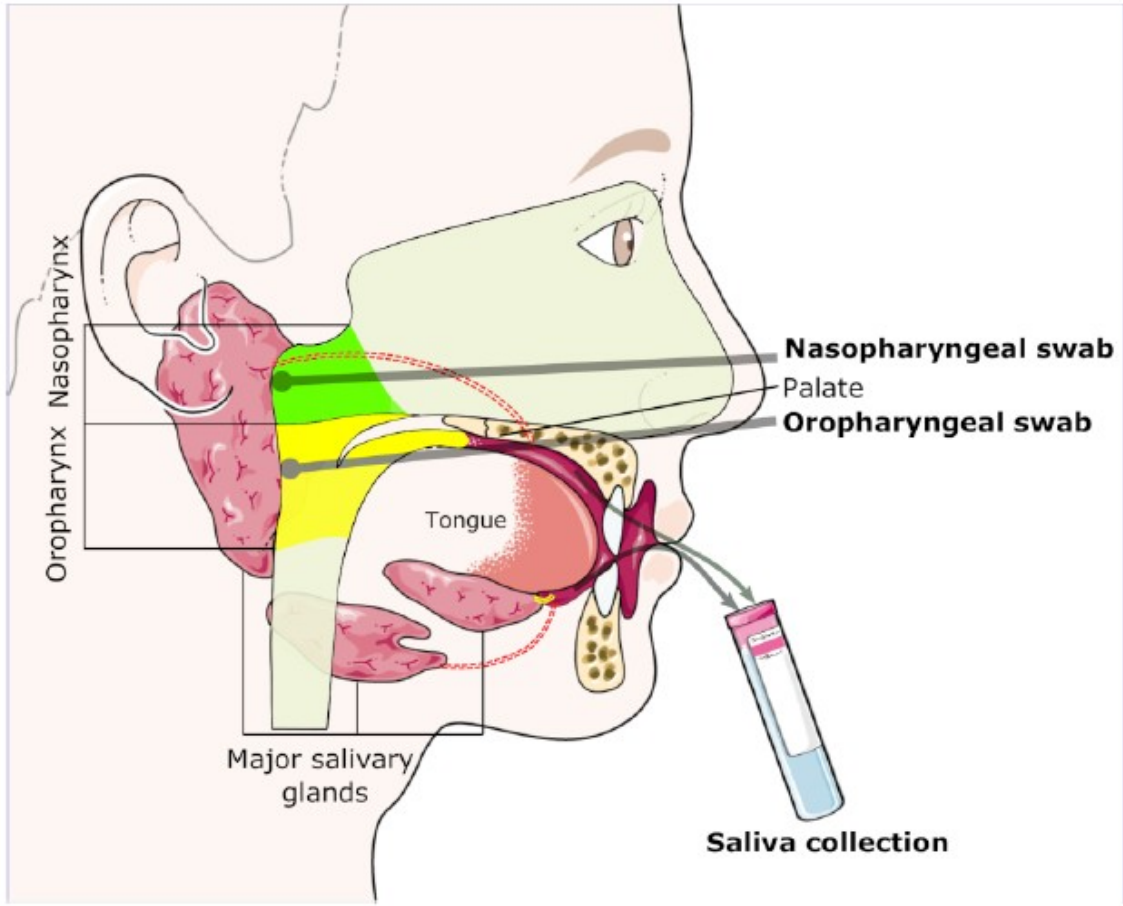


Figure 2 Schematic illustration demonstrating major salivary glands (parotid, submandibular and sublingual) and their respective ducts, oropharynx and nasopharynx, and approximate anatomic locations for collection of oropharyngeal and nasopharyngeal swabs.

Sapkota D et al. J Clin Pathol 2020

Table 1 Advantages and disadvantages of saliva sampling

Advantages	Disadvantages
Non-invasive approach for disease diagnosis and monitoring of general health.	Not always reliable for measurement of certain markers.
Painless (no patient discomfort and anxiety for sampling).	Contents of saliva can be influenced by the method of collection, degree of stimulation of salivary flow, interindividual variation and oral hygiene status.
Easy collection and applicable in remote areas.	Serum markers can reach whole saliva in an unpredictable way.
Relatively cheap technology.	Medications may affect salivary gland function and consequently the quantity and composition of saliva.
Cost-effective applicability for screening large populations.	Possibility for degradation of salivary proteins due to presence of proteolytic enzymes.
Suitable for children, anxious/disabled/elderly patients.	
Possible multisampling.	
Safer collection for health professionals than other biological samples such as nasopharyngeal swabs and blood.	
Cheap to store and ship.	
Easy to handle.	
No need for expensive equipment/instruments (swabs, suction tubes or special collection devices) for collection. Only needs a sterile container.	

Sapkota D et al. J Clin Pathol 2020

A novel strategy for SARS-CoV-2 mass screening with quantitative antigen testing of saliva: a diagnostic accuracy study

Isao Yokota, Peter Y Shane*, Kazufumi Okada, Yoko Unoki, Yichi Yang, Sumio Iwasaki, Shinichi Fujisawa, Mutsumi Nishida, Takanori Teshima*

Lancet Microbe 2021

Interpretation CLEIA testing of self-collected saliva is simple and provides results quickly, and is thus suitable for mass testing. To improve accuracy, we propose a two-step screening strategy with an initial CLEIA test followed by confirmatory RT-qPCR for intermediate concentrations, varying positive and negative thresholds depending on local prevalence. Implementation of this strategy has expedited sample processing at Japanese airports since July, 2020, and might apply to other large-scale mass screening initiatives.

Clinica Chimica Acta 517 (2021) 54–59

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Clinica Chimica Acta

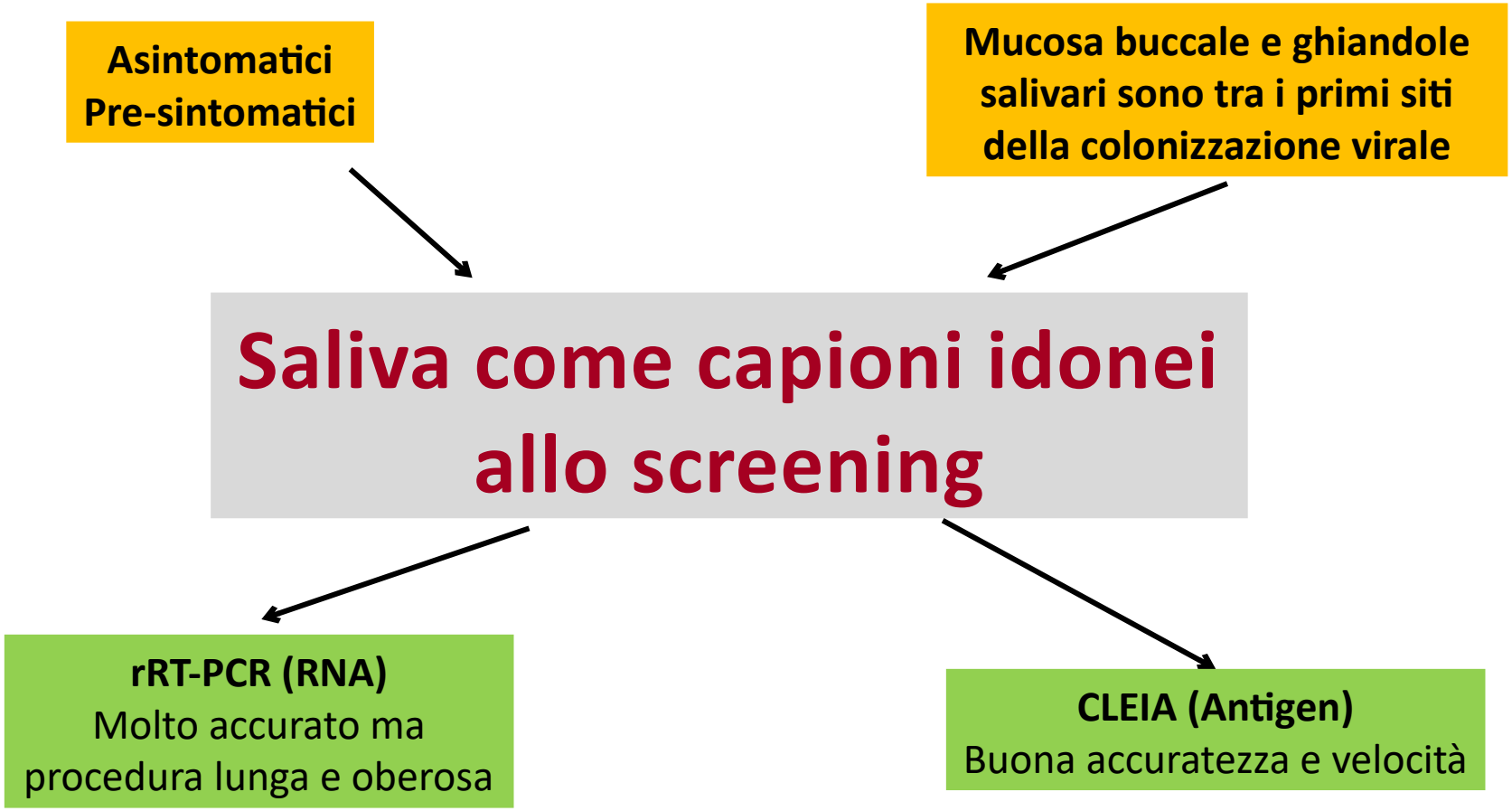
journal homepage: www.elsevier.com/locate/cca

Salivary SARS-CoV-2 antigen rapid detection: A prospective cohort study

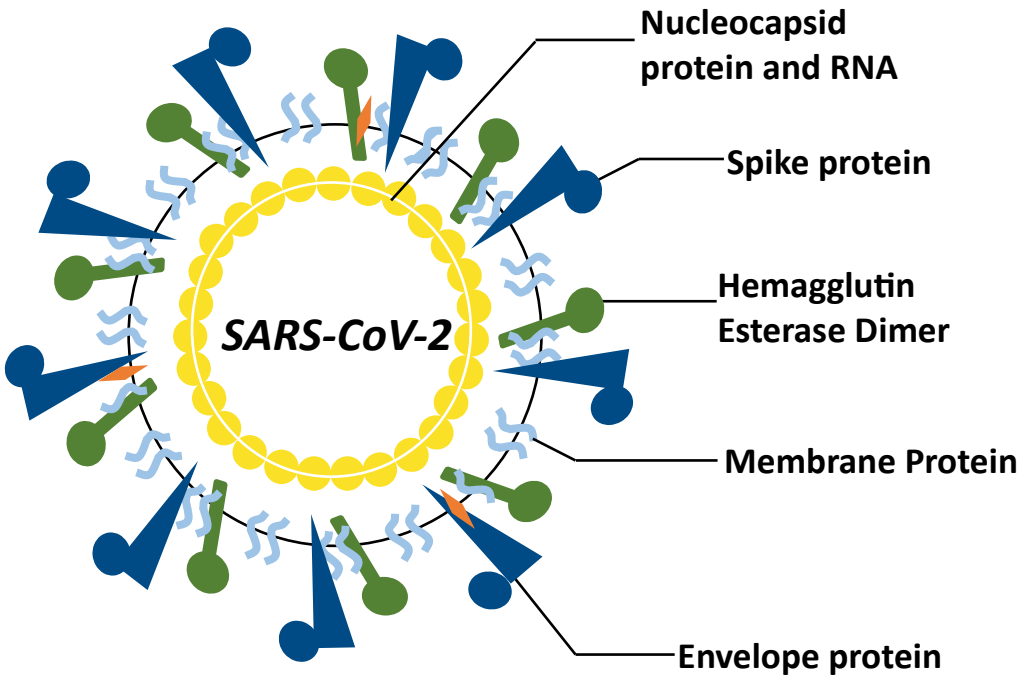
Daniela Basso [a,1,*], Ada Aita [a,1], Andrea Padoan [a], Chiara Cosma [a], Filippo Navaglia [a], Stefania Moz [a], Nicole Contran [a], Carlo-Federico Zambon [a], Anna Maria Cattelan [b], Mario Plebani [a]

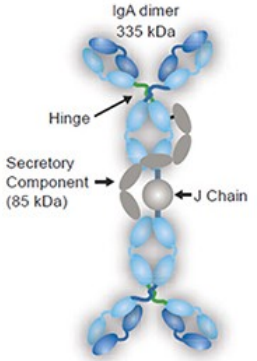
Results: The overall agreement between NPS and saliva rRT-PCR was 78.7%, reaching 91.7% at the first week from symptoms. SARS-CoV-2 CLEIA antigen was highly accurate in distinguishing positive and negative NPS (ROC-AUC = 0.939, 95%CI:0.903–0.977), with 81.6% sensitivity and 93.8% specificity. This assay on saliva reached the optimal value within 7 days from symptoms onset (Sensitivity: 72%; Specificity: 97%). Saliva POC antigen was limited in sensitivity (13%), performing better in NPS (Sensitivity: 48% and 66%; Specificity: 100% and 99% for Espline and Abbott respectively), depending on viral loads.

Conclusions: Self-collected saliva is a valid alternative to NPS for SARS-CoV-2 detection by molecular, but also by CLEIA antigen testing, which is therefore potentially useful for large scale screening.

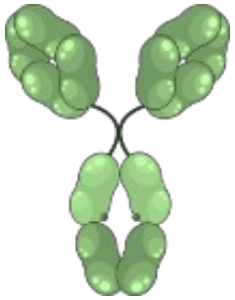

Asintomatici
Pre-sintomatici
Mucosa buccale e ghiandole salivari sono tra i primi siti della colonizzazione virale
Saliva come capioni idonei allo screening
rRT-PCR (RNA)
Molto accurato ma procedura lunga e oberosa
CLEIA (Antigen)
Buona accuratezza e velocità

Serological Testing: *SARS-CoV-2 Antibodies*

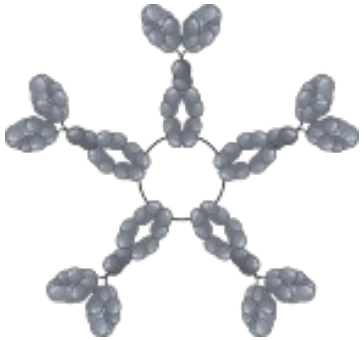




IgA



IgG



IgM

- Gli ultimi test Ab sono verso la porzione RBD di spike

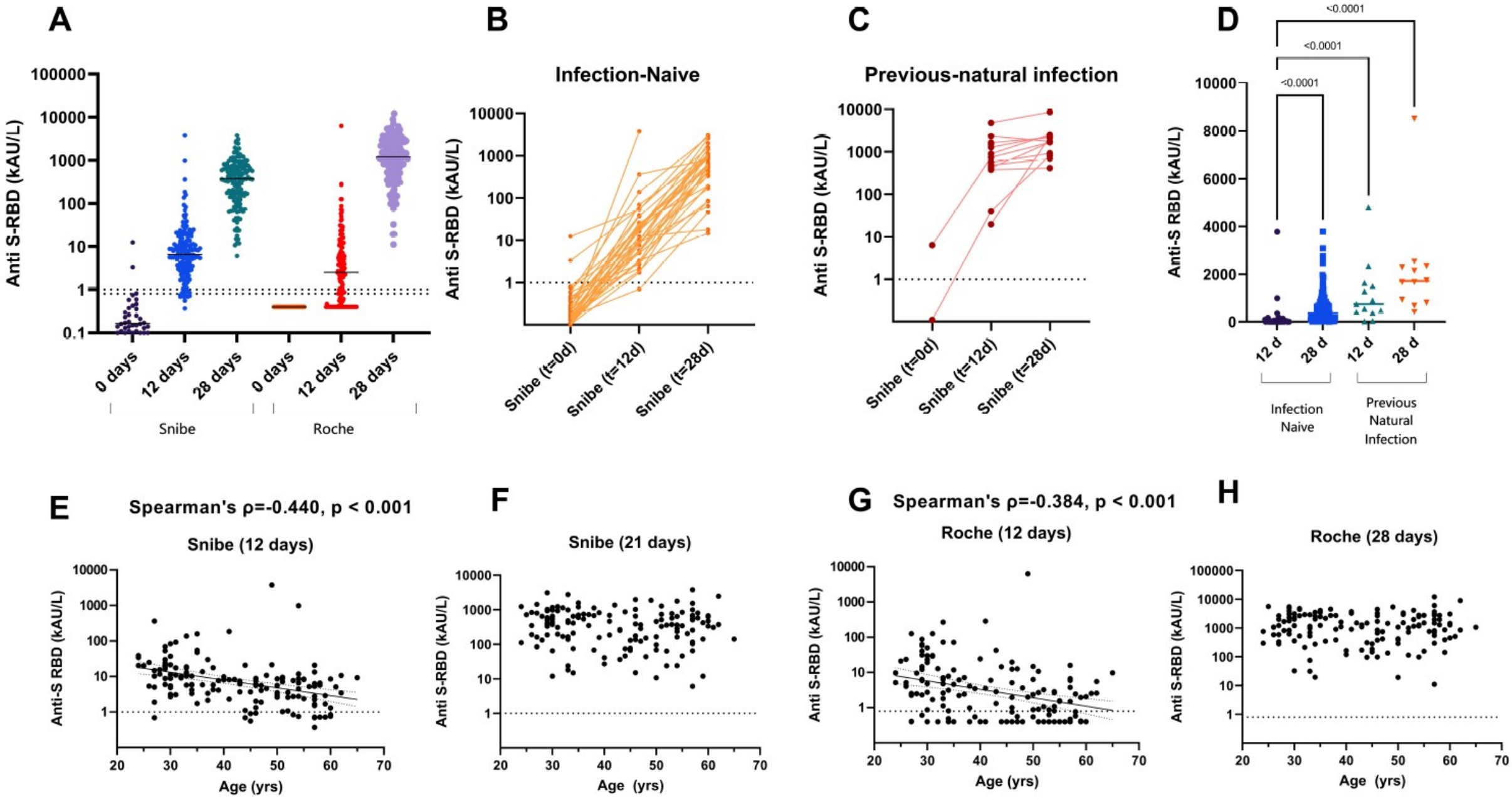
POTENTIAL UTILITY OF SARS-COV-2 ANTIBODY TESTING

Reali applicazioni supportate dale evidenze

- *Studi di siero-prevalenza*
- *Identificazione di contatti precedenti*
- *Donazioni per plasma iperimmune*
- *Valutazione della risposta anticorpale al vaccino (manca consenso sui livelli)*

Applicazioni non supportate dalle evidenze

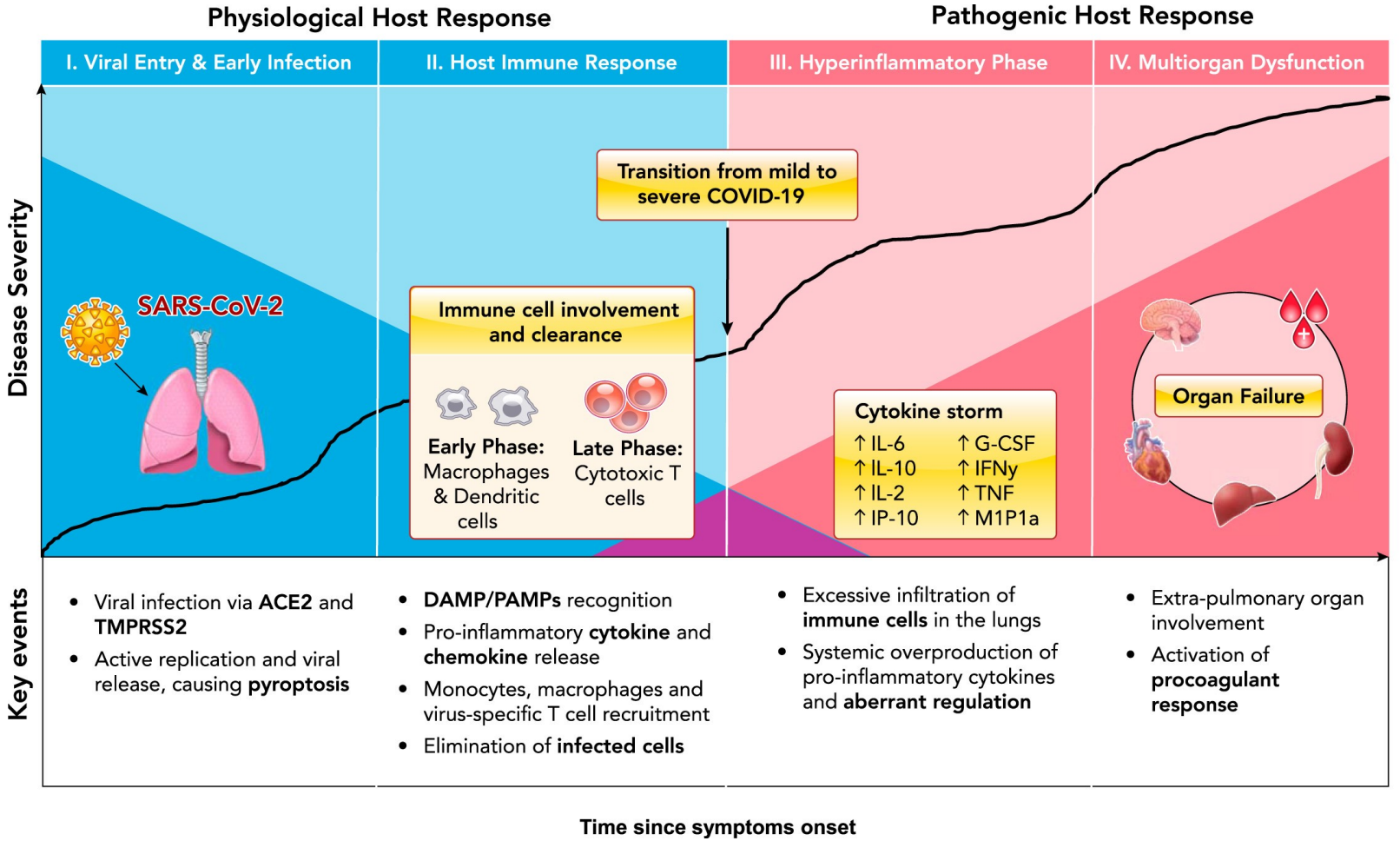
- *Diagnosi*
- *Prognosi*
- *Screening delle sacche di sangue per SARS-CoV-2*



Padoan A et al. Clin Chim Acta 2021

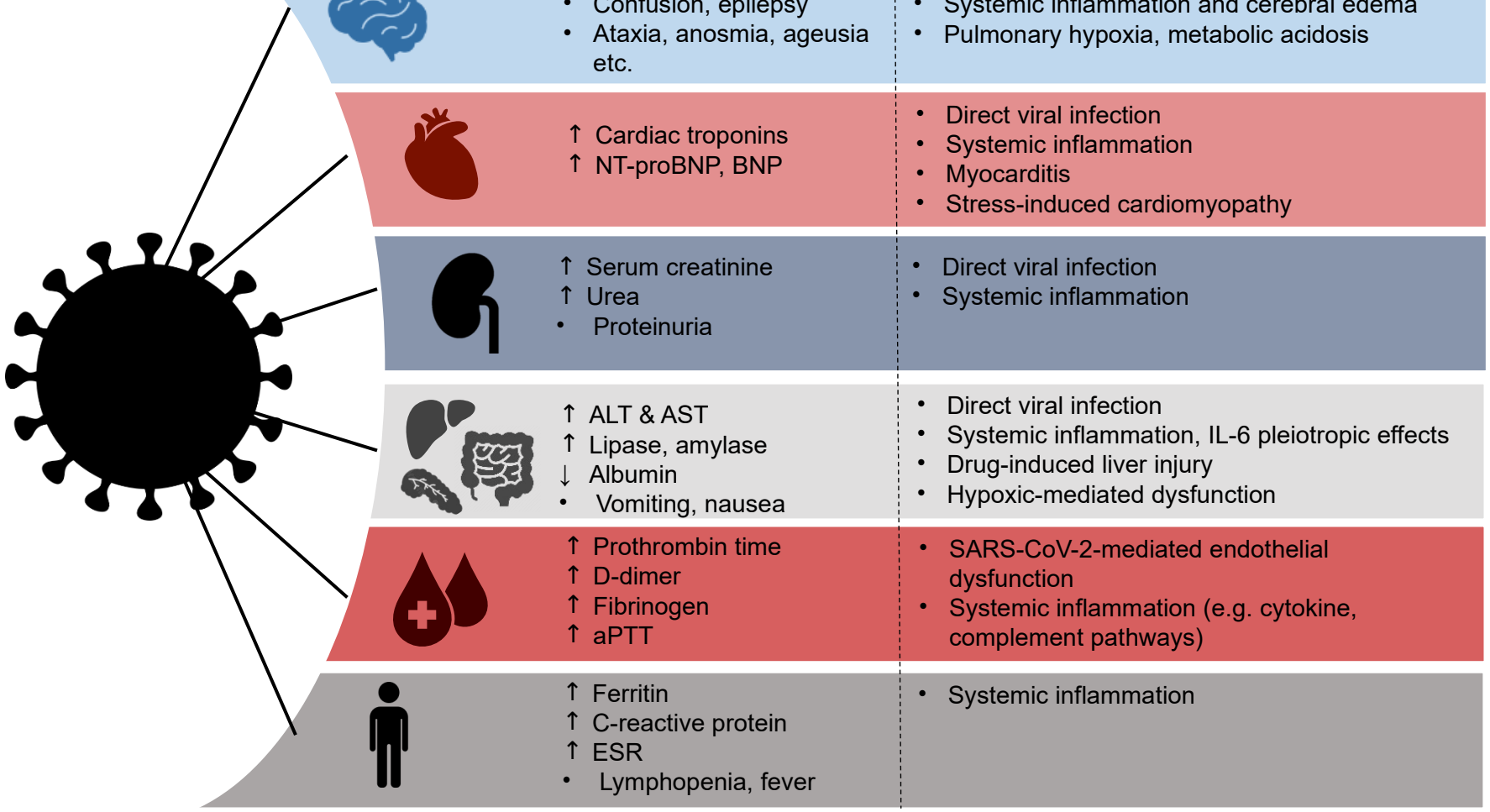
Biochemical and Hematological Monitoring of COVID-19 Patients

In addition to providing diagnostic information through molecular and serological testing, clinical laboratories have also supported the monitoring of patients with COVID-19 through routine & specialized biochemical and hematological testing



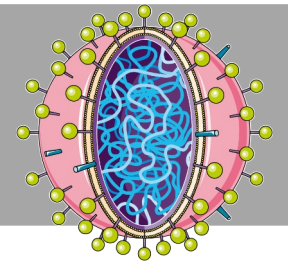
Bohn MK, et al. Physiology. 2020 Sep 1;35(5):288-301.

COVID-19 Clinical Presentation and Pathophysiological Mechanisms



Key potential mechanisms link back to inflammation!

COVID-19: *Monitoring Markers of Inflammation*



Clinical Manifestations/Complications:

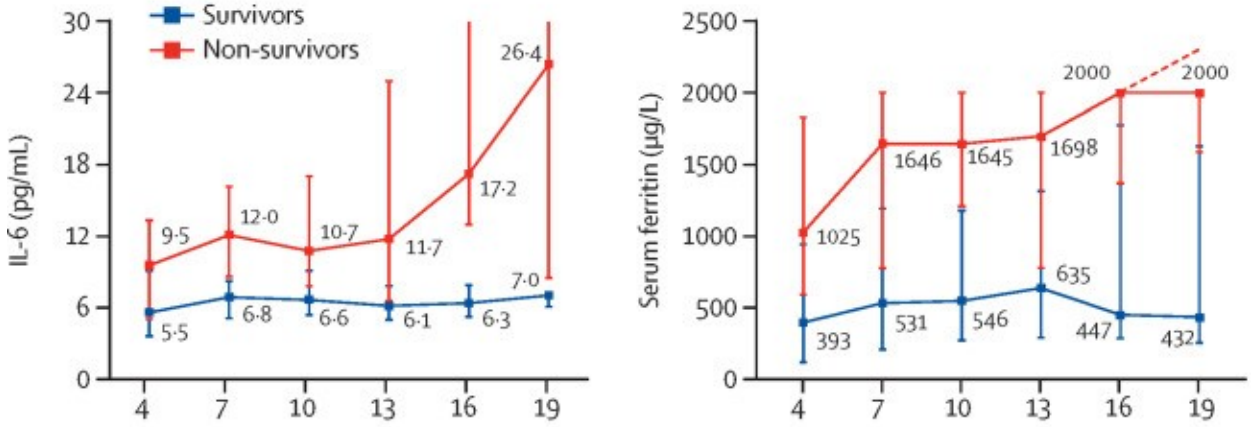
- Cytokine storm (hyperinflammatory reaction)
- Progression to multisystem organ failure and death

Key Prognostic Laboratory Indicators:

- ↑ CRP, ferritin, IL-6, ESR
- ↓ Lymphocyte count

Potential Pathophysiological Mechanisms:

- Maladaptive cytokine release as a result of a combined Th1 and Th2 cell response
- T-cell redistribution via pulmonary recruitment, exhaustion, as well as depletion through TNF-α-mediated apoptosis or even direct cytopathic injury
- Direct viral infection of immune cells such as monocytes and macrophages
- Antibody-dependent enhancement (ADE)



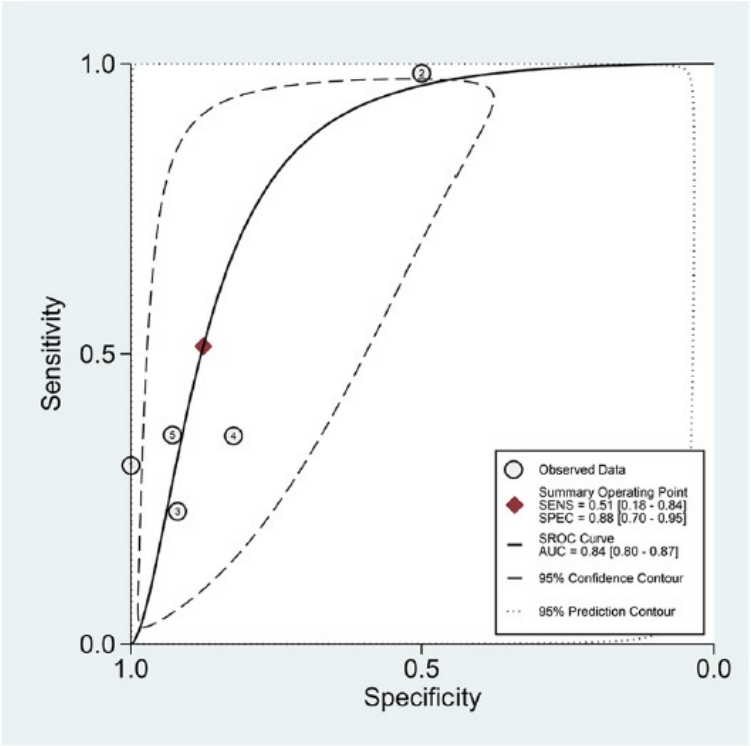
Temporal changes in IL-6 and ferritin from illness onset in patients hospitalized with COVID-19.

(Zhou , et al. Lancet. 2020 Mar 28;395(10229):1054-1062)

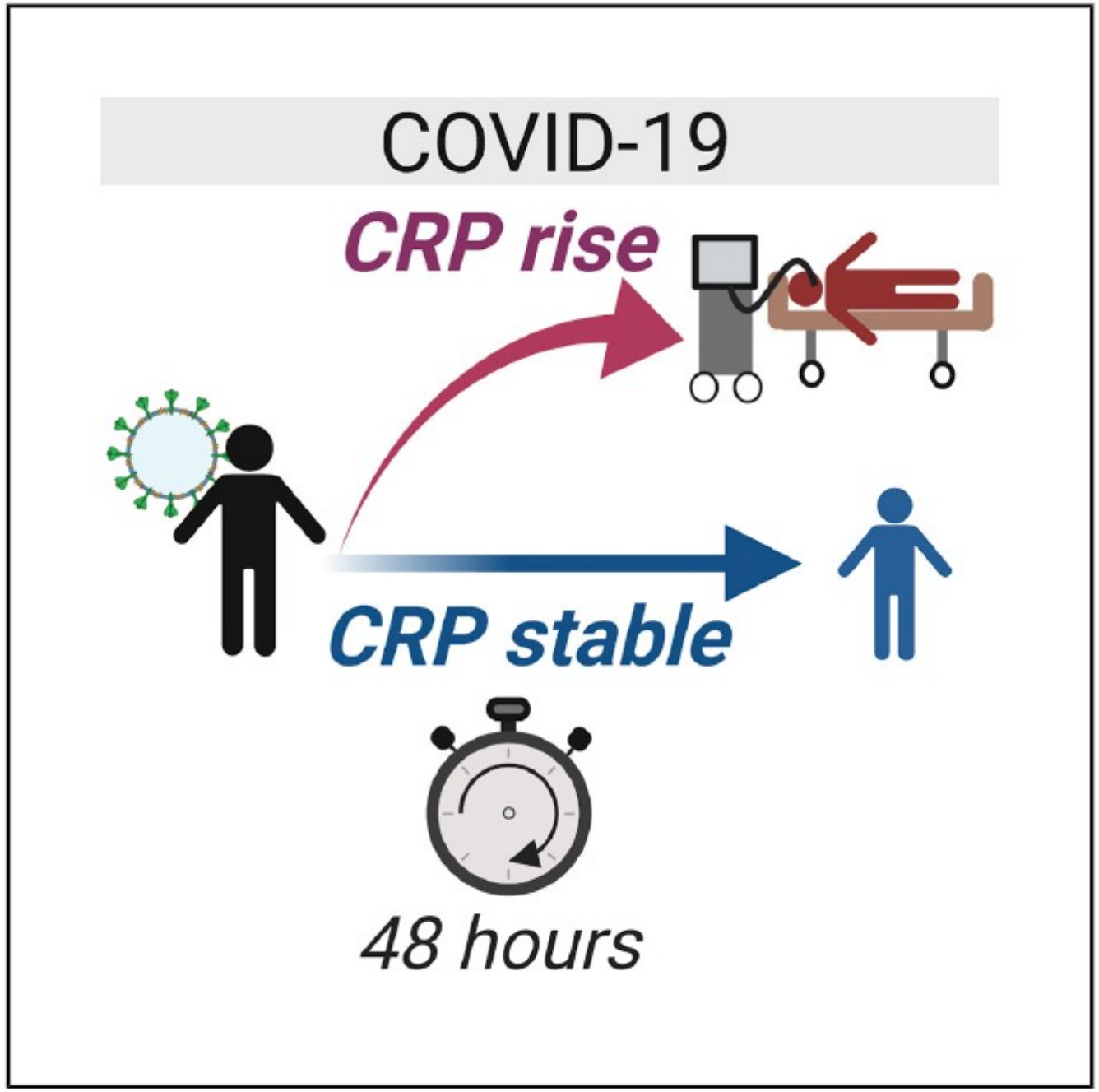
Tay MZ et al. Nature Reviews Immunology. 2020 Apr 28:1-2.

C-REACTIVE PROTEIN and COVID-19

A meta-analysis of 13 studies shows that an elevated serum CRP is associated with an increased poor outcome [RR 1.84, p<0.001], with a severe COVID-19 disease [RR 1.4 p<0,001] and need for ICU care [RR 1.96, p<0,001]



Huang I et al. Ther Adv Respir Dis 2020



Cell Reports Medicine

CellPress
OPEN ACCESS

Report

Inflammatory Biomarker Trends Predict Respiratory Decline in COVID-19 Patients

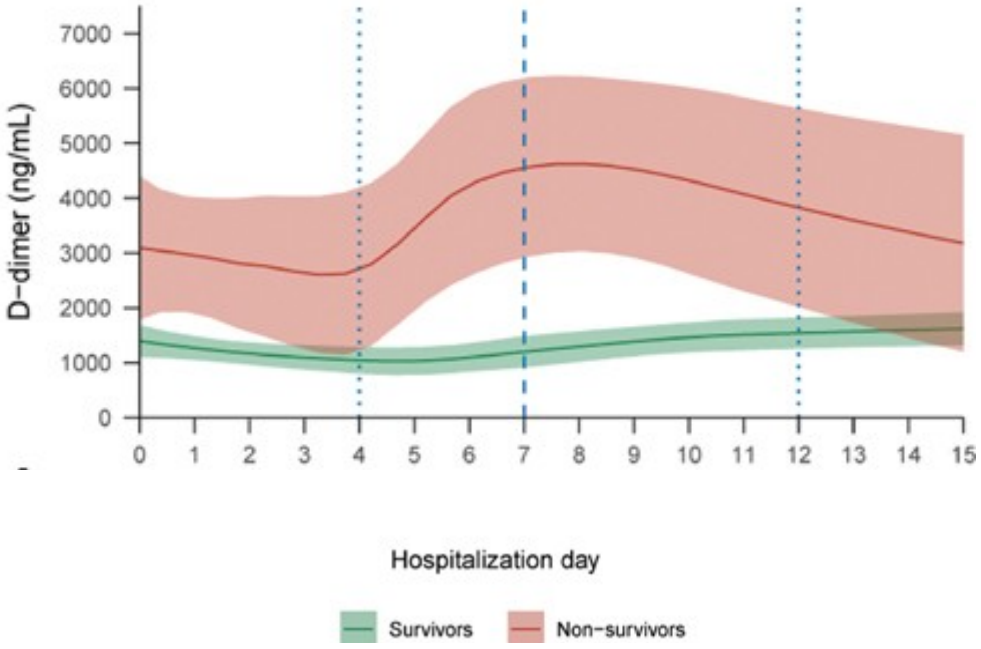
Alisa A. Mueller,[1,2,6] Tomoyoshi Tamura,[2,3,6] Conor P. Crowley,[3] Jeremy R. DeGrado,[4] Hibah Haider,[3] Julia L. Jezmir,[2,5] Gregory Keras,[1] Erin H. Penn,[1,2] Anthony F. Massaro,[2,3] and Edy Y. Kim[2,3,7,*]

COVID-19 Patient Monitoring: D-Dimer

- Studies have reported an increase (up to 3-4 fold) in D-dimer and fibrinogen concentrations in the early stages of COVID-19 disease
- Underlying diseases such as **diabetes, cancer, stroke, and pregnancy** may trigger an increased D-dimer
- Measuring the level of D-dimer and coagulation parameters from the early stage of the disease can also be useful in **controlling and managing of COVID-19 disease**

Potential mechanisms include: *pulmonary endothelial injury with inflammation-associated deposits, SARS-CoV-2 systemic endothelial injury and coagulopathy*

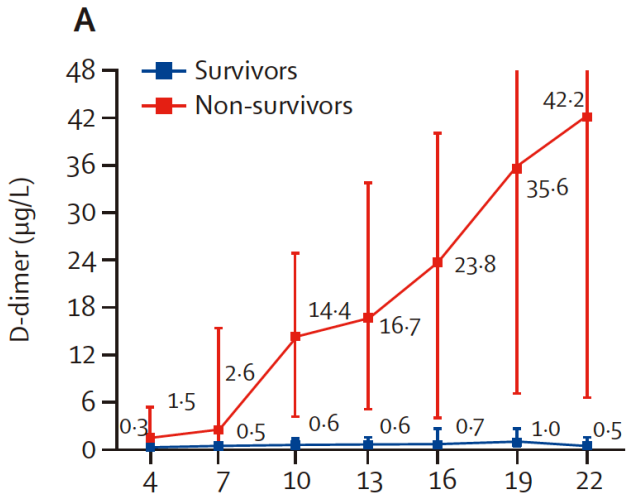
In-hospital trends of D-dimer levels in surviving and nonsurviving patients with COVID-19 by days since admission.



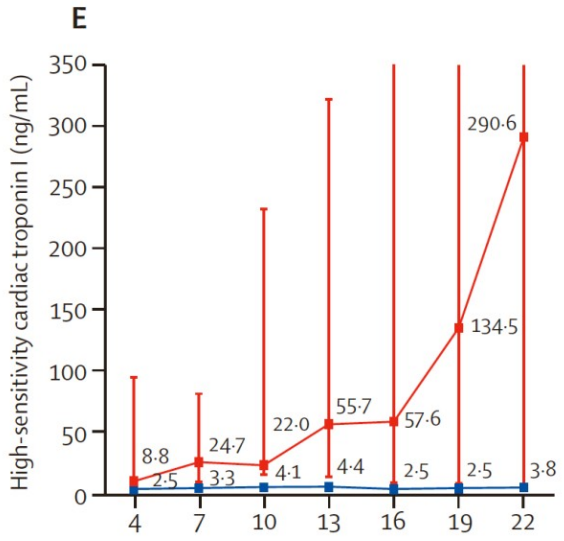
Thrombosis and Haemostasis. 2021 Jan;121(1):98.
Expert review of hematology. 2020 Nov 1;13(11):1265-75.

Crucial biomarkers to evaluate mortality risk of COVID-19

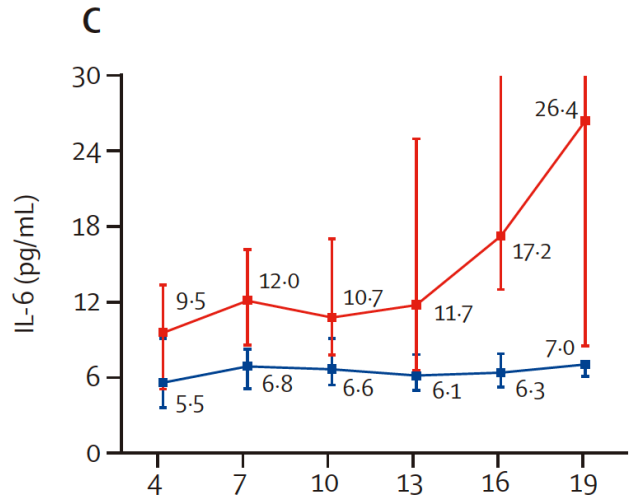
- **D-dimer**



- **hs-Troponin I**



- **IL-6**



- **Serum Ferritin**

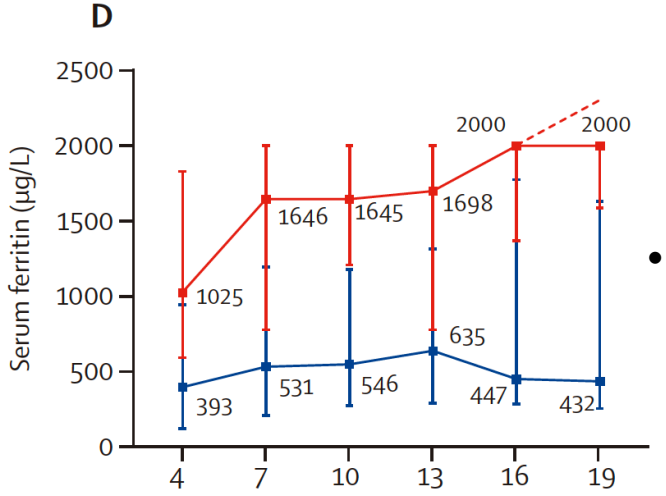


Fig.13 Temporal changes in laboratory markers from illness onset in patients hospitalized with COVID-19 [12]

LA SALUTE GLOBALE

Se i virus caratterizzano un mondo senza più confini, una pandemia richiede una migliore ***governance***. E, in un certo senso, la crisi in cui ci troviamo oggi è una crisi, in primis, di ***governance***, che riguarda il modo di affrontare i rischi che ci presenta il mondo oggi.

Jeffrey Sachs