

RICERCA BIBLIOGRAFICA COVID 19

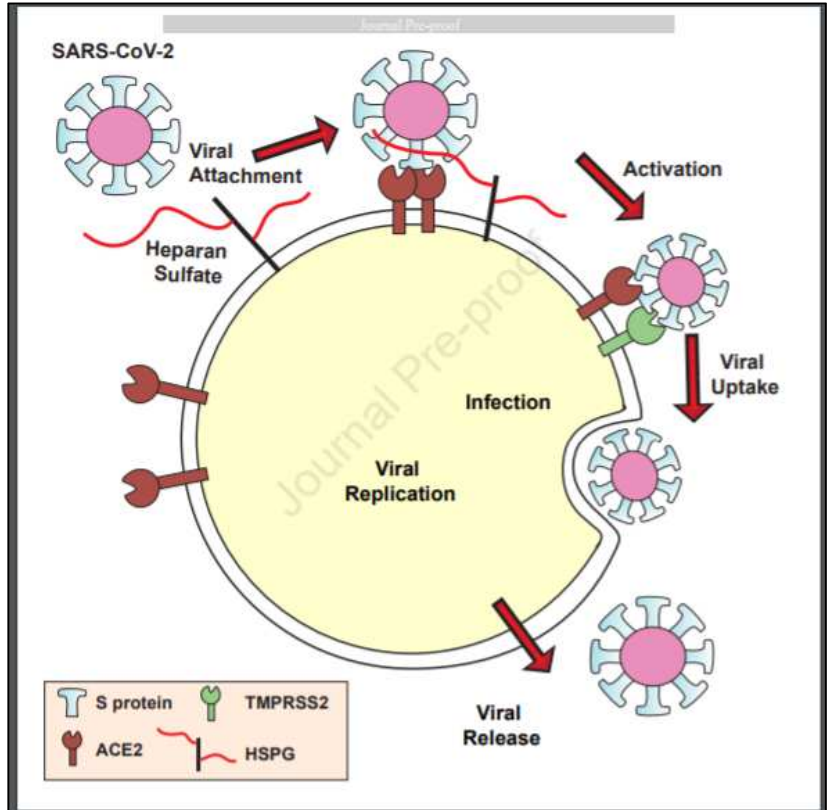
SETTIMANA 14-20.09.2020

FONDAZIONE POLICLINICO UNIVERSITARIO A. GEMELLI IRCCS, UOC MALATTIE INFETTIVE

DOTT.SSA ELEONORA TADDEI

AUTORE/RIVISTA	TITOLO	OUTCOME PRINCIPALE	ABSTRACT
Mandel Clausen T et al Cell https://www.sciencedirect.com/science/article/abs/pii/S0092867420312307	SARS-CoV-2 Infection Depends on Cellular Heparan Sulfate and ACE2	Il legame della proteina spike di superficie (S) di SARS-CoV-2 alla membrana cellulare dipende in pari misura dal recettore ACE2 e da eparansolfato. L'eparina compete con quest'ultimo legame, il che sarebbe alla base di parte della sua attività nella terapia contro SARS-CoV-2.	We show that SARS-CoV-2 spike protein interacts with both cellular heparan sulfate and angiotensin converting enzyme 2 (ACE2) through its Receptor Binding Domain (RBD). Docking studies suggest a heparin/heparan sulfate-binding site adjacent to the ACE2 binding site. Both ACE2 and heparin can bind independently to spike protein in vitro and a ternary complex can be generated using heparin as a scaffold. Electron micrographs of spike protein suggests that heparin enhances the open conformation of the RBD that binds ACE2. On cells, spike protein binding depends on both heparan sulfate and ACE2. Unfractionated heparin, non-anticoagulant heparin, heparin lyases, and lung heparan sulfate potentially block spike protein binding and/or infection by pseudotyped virus and authentic SARS-CoV-2 virus. We suggest a model in which viral attachment and infection involves heparan sulfate-dependent enhancement of binding to ACE2. Manipulation of heparan sulfate

or inhibition of viral adhesion by exogenous heparin presents new therapeutic opportunities.



Fuling Z et al

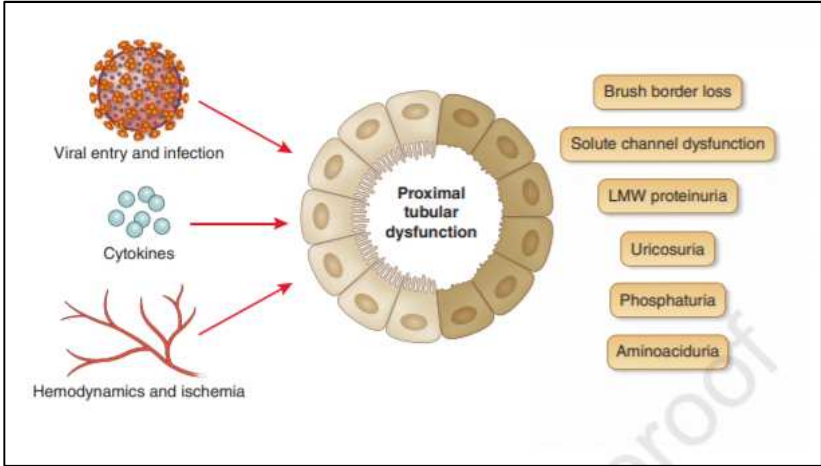
Eclinical Medicine - The Lancet

Tracing asymptomatic SARS-CoV-2 carriers among 3674

Studio cross-sectional per indagare la sieroprevalenza per SARS-CoV-2 su 3764 membri asintomatici di

Background Asymptomatic carriers were positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) without developing symptoms, which might be a potential source of infection outbreak. Here, we aim to clarify the epidemiologic and

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(20)30254-6/fulltext	<p>hospital staff: a cross-sectional survey</p>	<p>personale ospedaliero in Cina. Riscontro di 28 casi di infezione asintomatica sulla base di sierologia, tampone nasofaringeo e TAC torace (!).</p>	<p>influencing factors of asymptomatic carriers in the general population.</p> <p>Methods In our hospital, all hospital staff have received throat swab RT-PCR test, plasma COVID-19 IgM/IgG antibodies test and chest CT examination. We analyzed the correlation between infection rates and gender, age, job position, work place and COVID-19 knowledge training of the staff. After that, all asymptomatic staff were re-examined weekly for 3 weeks.</p> <p>Findings A total of 3764 hospital staff were included in this single-center cross-sectional study. Among them, 126 hospital staff had abnormal findings, and the proportion of asymptomatic infection accounted for 0.76% (28/3674). There were 26 staff with IgM+, 73 with IgG+, and 40 with ground glass shadow of chest CT. Of all staff with abnormal findings, the older they are, the more likely they are to be the staff with abnormal results, regardless of their gender. Of 3674 hospital staff, the positive rate of labor staff is obviously higher than that of health care workers (HCWs) and administrative staff ($P < 0.05$). In the course of participating in the treatment of COVID-19, there was no statistically significant difference in positive rates between high-risk departments and low-risk departments ($P > 0.05$). The positive rate of HCWs who participated in the COVID-19 knowledge training was lower than those did not participate in early training ($P < 0.01$). Importantly, it was found that there was no statistical difference between the titers of IgM antibody of asymptomatic infections and confirmed patients with COVID-19 in recovery period ($P > 0.05$). During 3 weeks follow-up, all asymptomatic patients did not present the development of clinical</p>
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			<p>symptoms or radiographic abnormalities after active intervention in isolation point.</p> <p>Interpretation To ensure the safety of resumption of work, institutions should conduct COVID-19 prevention training for staff and screening for asymptomatic patients, and take quarantine measures as soon as possible in areas with high density of population.</p>
<p>Braun F et al</p> <p>Kidney International</p> <p>https://www.kidney-international.org/article/S0085-2538(20)31070-X/fulltext</p>	<p>Proximal tubular dysfunction in patients with COVID-19: what have we learnt so far?</p>	<p>Disamina dei possibili meccanismi fisiopatologici (danno cellulare diretto, effetto citochinico o ischemia) alla base della disfunzione del tubulo rénale prossimale osservata in corso di infezione da SARS-CoV-2.</p>	<p>Recent studies have reported a variety of urine abnormalities in patients hospitalized due to SARS-CoV-2 infection. In a single center study from Belgium, Werion et al., now present a concise investigation of tubular dysfunction in COVID-19 patients identifying potential risk factors for increased disease severity. These data complement current evidence regarding SARS-CoV-2 presence and potential infection in the kidney.</p> 

<p>Shoar S et al</p> <p>The American Journal of Cardiology</p> <p>https://www.ajconline.org/article/S0002-9149(20)30902-4/fulltext</p>	<p>Meta-analysis of Cardiovascular Events and Related Biomarkers Comparing Survivors vs. Non-survivors in Patients with COVID-19.</p>	<p>Metanalisi sui dati di 1845 pazienti ricoverati per COVID-19 in cui si confrontano eventi cardiovascolari e relativi biomarcatori tra sopravvissuti e deceduti.</p>	<p>Since the emergence of the coronavirus disease 19 (COVID-19), a number of studies have reported the presence of cardiovascular diseases in affected patients and linked them with a higher risk of mortality. We conducted an online search in Medline/PubMed to identify original cohorts comparing data between survivors and non-survivors from COVID-19. The presence of cardiovascular events and related biomarkers were compared between the two groups. Data on 1,845 hospitalized patients with COVID-19 were pooled from 12 comparative studies. The overall mortality rate in relation to COVID-19 was 17.6%. Men aged > 50 years old were more likely to die from COVID-19. Significant co-morbidities contributing to mortality were hypertension, diabetes mellitus, smoking, a previous history of cardiovascular disease including chronic heart failure, and cerebrovascular accidents. A significant relationship was observed between mortality and patient presentation with dyspnea, fatigue, tachycardia, and hypoxemia. Cardiovascular disease-related laboratory biomarkers related to mortality were elevated serum level of lactate dehydrogenase, creatine kinase, and cardiac troponin I. Adverse cardiovascular disease-related clinical events preceding death were shock, arrhythmias, and acute myocardial injury. In conclusion, elevated biomarkers in COVID-19 patients with established risk factors can predict mortality from cardiovascular causes.</p>
<p>Zangrillo A et al</p> <p>Critical Care and Resuscitation Journal</p> <p>https://pubmed.ncbi.nlm.nih.gov/32900326/</p>	<p>Characteristics, treatment, outcomes and cause of death of invasively ventilated patients with COVID-19 ARDS in Milan, Italy.</p>	<p>Predittori di mortalità precoce (follow up mediano 19 giorni) in una serie di 73 pazienti ricoverati in rianimazione per ARDS da</p>	<p>Objective: Describe characteristics, daily care and outcomes of patients with coronavirus disease 2019 (COVID-19) acute respiratory distress syndrome (ARDS). Design: Case series of 73 patients. Setting: Large tertiary hospital in Milan.</p>

		<p>COVID19 e sottoposti a ventilazione meccanica.</p>	<p>Participants: Mechanically ventilated patients with confirmed COVID-19 admitted to the intensive care unit (ICU) between 20 February and 2 April 2020.</p> <p>Main outcome measures: Demographic and daily clinical data were collected to identify predictors of early mortality.</p> <p>Results: Of the 73 patients included in the study, most were male (83.6%), the median age was 61 years (interquartile range [IQR], 54-69 years), and hypertension affected 52.9% of patients.</p> <p>Lymphocytopenia (median, 0.77×10^3 per mm³; IQR, 0.58-1.00×10^3 per mm³), hyperinflammation with C-reactive protein (median, 184.5 mg/dL; IQR, 108.2-269.1 mg/dL) and pro-coagulant status with D-dimer (median, 10.1 µg/m; IQR, 5.0-23.8 µg/m) were present. Median tidal volume was 6.7 mL/kg (IQR, 6.0-7.5 mL/kg), and median positive end-expiratory pressure was 12 cmH₂O (IQR, 10-14 cmH₂O). In the first 3 days, prone positioning (12-16 h) was used in 63.8% of patients and extracorporeal membrane oxygenation in five patients (6.8%). After a median follow-up of 19.0 days (IQR, 15.0-27.0 days), 17 patients (23.3%) had died, 23 (31.5%) had been discharged from the ICU, and 33 (45.2%) were receiving invasive mechanical ventilation in the ICU. Older age (odds ratio [OR], 1.12; 95% CI, 1.04-1.22; P = 0.004) and hypertension (OR, 6.15; 95% CI, 1.75-29.11; P = 0.009) were associated with mortality, while early improvement in arterial partial pressure of oxygen (PaO₂) to fraction of inspired oxygen (FiO₂) ratio was associated with being discharged alive from the ICU (P = 0.002 for interaction).</p> <p>Conclusions: Despite multiple advanced critical care interventions, COVID-19 ARDS was associated with prolonged ventilation and high short term mortality. Older age and pre-admission hypertension were key mortality risk factors.</p>
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Luo K et al

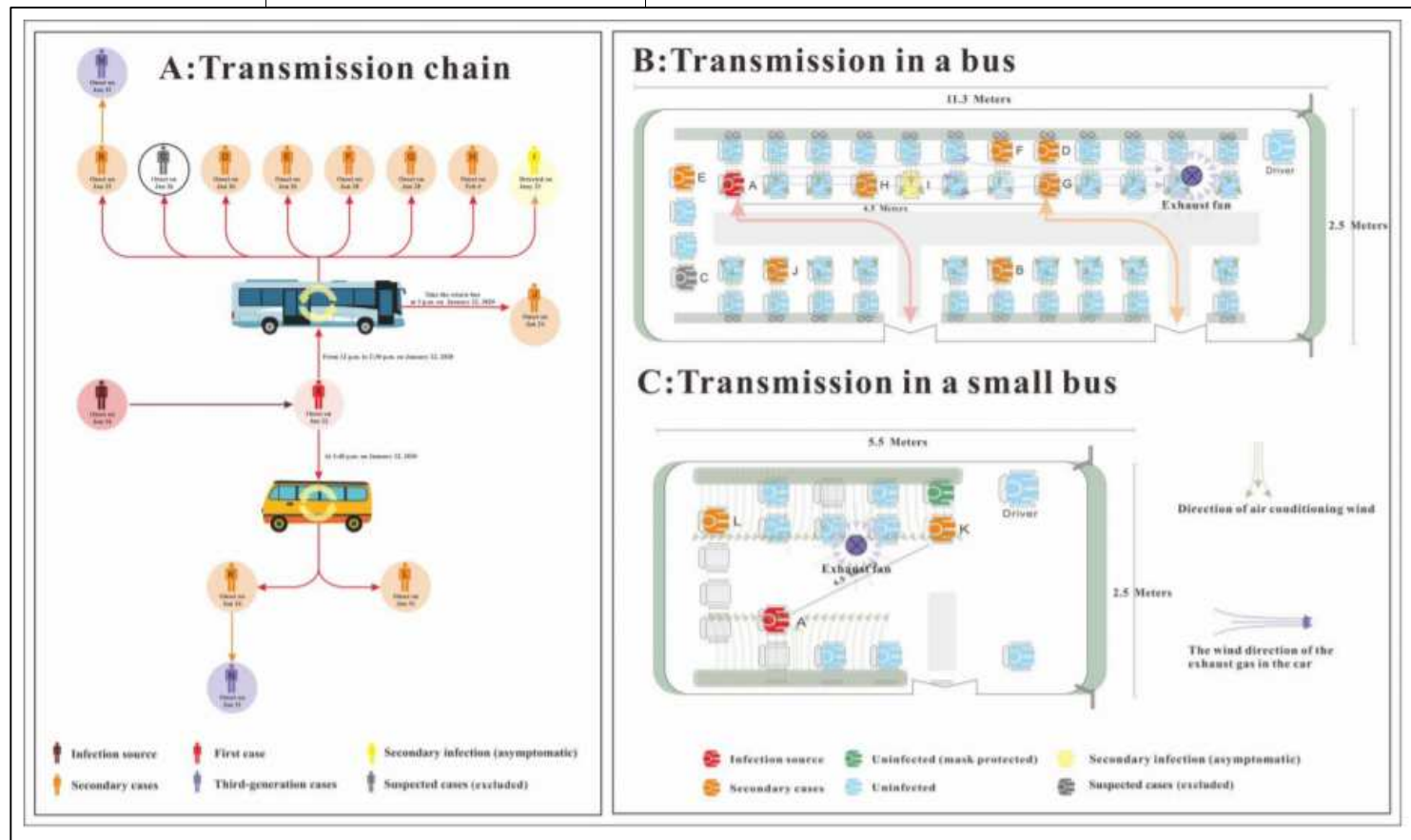
Open Forum Infectious Diseases

<https://academic.oup.com/ofid/advance-article/doi/10.1093/ofid/ofaa430/5905033>

Transmission of SARS-CoV-2 in Public Transportation Vehicles: A Case Study in Hunan Province, China.

Studio dei 243 contatti di un caso indice di infezione da SARS-CoV-2 che, all'esordio dei sintomi, aveva utilizzato due volte il trasporto pubblico per lunghe distanze in Cina.

Here we report a case study of a SARS-CoV-2 outbreak event during bus trips of an index patient in Hunan Province, China. This retrospective investigation suggests potential airborne transmission of SARS-CoV-2 and the possibility of superspreading events in certain close contact and closed space settings, which should be taken in to account when control strategies are planned.



<p>Poon KS et al</p> <p>Clinical Infectious Diseases</p> <p>https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1399/5905681</p>	<p>Caveats of Reporting Cycles Threshold from SARS-CoV-2 Qualitative PCR Assays: A Molecular Diagnostic Laboratory Perspective</p>	<p>Limiti dell'utilizzo del ciclo-soglia di positivizzazione della PCR per SARS-CoV-2 quale indicatore di carica virale.</p>	<p>We read the two recent commentaries published in Clinical Infectious Diseases by Binnicker 2020, and Tom & Mina 2020, respectively with great interest . Binnicker pointed out the potential pitfalls when interpreting real-time polymerase chain reaction (PCR) cycle threshold (Ct) values in his response to the study by Bullard et al. 2020. Tom & Mina in their response to the study by Xiao et al. 2020 suggested the implementation of reporting actual Ct values along with reference ranges or viral load equivalents from Ct conversion, or tiered Ct categories as high, medium or low. These discussions on Ct values raised concerns on the caveats of reporting Ct values generated by qualitative PCR assays in the clinical setting.</p>
<p>Muscatello DJ et al</p> <p>International Journal of Epidemiology</p> <p>https://academic.oup.com/ije/advance-article/doi/10.1093/ije/dyaa186/5905673</p>	<p>Comparing mortalities of the first wave of coronavirus disease 2019 (COVID-19) and of the 1918–19 winter pandemic influenza wave in the USA.</p>	<p>La mortalità per influenza nell'inverno 1918-1919 a New York fu 6.7 volte maggiore di quella registrata per COVID-19 fino al 2 giugno 2020. A propria volta la mortalità per COVID19 nello stesso periodo è stata circa 10 volte maggiore di quella di una stagione influenzale grave.</p>	<p>It has been argued that coronavirus disease 2019 (COVID19) mortality rates exceed those from the influenza pandemic in 1918–19, but comparisons can be misleading unless marked differences in age-specific mortality and changes in population age structure in the past century are taken into account. The need for application of fundamental epidemiological approaches in understanding COVID-19 has also been recognized.</p>

			<table><tr><th colspan="7">Table 2 Standardized mortality ratios (SMR) of comparator pandemics and epidemics in the USA relative to the first 2020 wave of COVID-19 infection in New York City^a</th></tr><tr><th>Period</th><th>Outcome</th><th>Age group (years)</th><th>Observed deaths</th><th>Expected deaths</th><th>Crude mortality ratio</th><th>SMR</th></tr><tr><td rowspan="3">1918–19²</td><td rowspan="3">Estimated influenza pandemic excess pneumonia and influenza deaths</td><td>All ages</td><td>546 000</td><td>102 194</td><td>2.1</td><td>5.3</td></tr><tr><td><65</td><td>538 000</td><td>48 914</td><td>7.0</td><td>11</td></tr><tr><td>≥65</td><td>8000</td><td>53 280</td><td>0.13</td><td>0.15</td></tr><tr><td rowspan="3">April 2009–April 2010⁷</td><td rowspan="3">Estimated pandemic influenza A(H1N1)pdm09 deaths</td><td>All ages</td><td>12 469</td><td>730 956</td><td>0.016</td><td>0.017</td></tr><tr><td>≤17</td><td>1282</td><td>597</td><td>2.1</td><td>2.1</td></tr><tr><td>18–64</td><td>9565</td><td>212 473</td><td>0.048</td><td>0.045</td></tr><tr><td rowspan="3"></td><td rowspan="3"></td><td>≥65</td><td>1621</td><td>517 886</td><td>0.0032</td><td>0.0031</td></tr><tr><td rowspan="3">2017–18 influenza season⁸</td><td rowspan="3">Estimated (preliminary) seasonal influenza deaths</td><td>All ages</td><td>61 099</td><td>857 505</td><td>0.073</td><td>0.071</td></tr><tr><td>≤17</td><td>643</td><td>592</td><td>1.1</td><td>1.1</td></tr><tr><td>18–64</td><td>9554</td><td>222 400</td><td>0.046</td><td>0.043</td></tr><tr><td></td><td></td><td>≥65</td><td>50 903</td><td>634 513</td><td>0.079</td><td>0.080</td></tr></table> <p>^a2020 COVID-19 confirmed and probable death rates by age (as at 2 June 2020).⁵ Of 21 649 deaths, 1 (0.0046%) death with unknown age and 198 (0.91%) with incomplete age information were excluded.</p>	Table 2 Standardized mortality ratios (SMR) of comparator pandemics and epidemics in the USA relative to the first 2020 wave of COVID-19 infection in New York City ^a							Period	Outcome	Age group (years)	Observed deaths	Expected deaths	Crude mortality ratio	SMR	1918–19 ²	Estimated influenza pandemic excess pneumonia and influenza deaths	All ages	546 000	102 194	2.1	5.3	<65	538 000	48 914	7.0	11	≥65	8000	53 280	0.13	0.15	April 2009–April 2010 ⁷	Estimated pandemic influenza A(H1N1)pdm09 deaths	All ages	12 469	730 956	0.016	0.017	≤17	1282	597	2.1	2.1	18–64	9565	212 473	0.048	0.045			≥65	1621	517 886	0.0032	0.0031	2017–18 influenza season ⁸	Estimated (preliminary) seasonal influenza deaths	All ages	61 099	857 505	0.073	0.071	≤17	643	592	1.1	1.1	18–64	9554	222 400	0.046	0.043			≥65	50 903	634 513	0.079	0.080
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Florez-Perdomo WA et al Clinical Neurology and Neurosurgery https://www.sciencedirect.com/science/article/pii/S0303846720305266	Relationship between the history of cerebrovascular disease and mortality in COVID-19 patients: A systematic review and meta-analysis.	Una storia di patologie cerebrovascolari è associata a maggior rischio di morte in pazienti con COVID19 secondo questa revisione sistematica sui dati di 3244 casi.	BACKGROUND AND OBJECTIVES: Past history of stroke has been associated with an increased risk of a new ischemic stroke. Several studies have indicated increased prevalence of strokes among coronavirus patients. However, the role of past history of stroke in COVID19 patients is still unclear. The purpose of this systematic review is to evaluate and summarize the level of evidence on past history of stroke in COVID19 patients. METHODS: A systematic review was performed according to the PRISMA guidelines was performed in PubMed, Embase, EBSCO Host, Scopus, Science Direct, Medline, and LILACS. Eligibility criteria: We evaluated studies including patients with diagnosis of COVID 19 and a past history of stroke. Risk of bias: was evaluated with the Newcastle- Ottawa Scale (NOS) and experimental studies were evaluated using the ROBINS-I scale. RESULTS: Seven articles out of the total 213 articles were evaluated and included, involving 3244 patients with SARS VOC 2 Disease (COVID19) of which 198 had a history of cerebrovascular																																																																															

			<p>disease. Meta-analysis of the data was performed, observing an increase in mortality in patients with a history of cerebrovascular disease compared to those with different comorbidities or those without underlying pathology (OR 2.78 95 % CI [1.42-5.46] p=0.007; I(2)=49 %) showing adequate heterogeneity. The presence of publication bias was evaluated using the Egger test in a funnel plot, showing adequate asymmetry, indicating that there is no publication bias; however, due to the low number of included studies, we could not rule out or confirm the presence of bias. CONCLUSIONS: The history of cerebrovascular disease was associated with a 2.78-fold increased risk of mortality compared to patients with other comorbidities or without underlying pathologies.</p>
<p>Meiler S et al</p> <p>European Journal of Radiology</p> <p>https://www.ejradiology.com/article/S0720-048X(20)30445-9/fulltext</p>	<p>Can CT performed in the early disease phase predict outcome of patients with COVID 19 pneumonia?</p> <p>Analysis of a cohort of 64 patients from Germany.</p>	<p>In una coorte tedesca di 64 pazienti vengono individuate le caratteristiche della TAC torace - eseguita entro 10 giorni dall'esordio - associate ad outcome avverso (ventilazione meccanica, ricovero in terapia intensiva, ossigenazione con membrana extracorporea - ECMO- e morte).</p>	<p>PURPOSE: The aim of this study was to investigate if CT performed in the early disease phase can predict the course of COVID-19 pneumonia in a German cohort. METHOD: All patients with RT-PCR proven COVID-19 pneumonia and chest CT performed within 10 days of symptom onset between March 1st and April 15th 2020 were retrospectively identified from two tertiary care hospitals. 12 CT features, their distribution in the lung and the global extent of opacifications were evaluated. For analysis of prognosis two compound outcomes were defined: positive outcome was defined as either discharge or regular ward care; negative outcome was defined as need for mechanical ventilation, treatment on intensive care unit, extracorporeal membrane oxygenation or death. Follow-up was performed until June 19th. For statistical analysis uni- and multivariable logistic regression models were calculated. RESULTS: 64 patients were included in the study. By univariable analysis the following parameters predicted a negative outcome: consolidation (p=0.034), crazy paving (p=0.004), geographic shape of opacification</p>

(p=0.022), dilatation of bronchi (p=0.002), air bronchogram (p=0.013), vessel enlargement (p=0.014), pleural effusion (p=0.05), bilateral disease (p=0.004), involvement of the upper lobes (p=0.004, p=0.015) or the right middle lobe (p<0.001) and severe extent of opacifications (p=0.002). Multivariable analysis revealed crazy paving and severe extent of parenchymal involvement to be independently predictive for a poor outcome. CONCLUSIONS: Easy to assess CT features in the early phase of disease independently predicted an adverse outcome of patients with COVID-19 pneumonia.

Table 5b

Multivariable logistic regression to analyze the predictive value of significant characteristics of parenchymal involvement on the endpoint (positive vs. negative outcome).

parameter	odds ratio*	p-value*
involvement right middle lobe	19.1 (95 %-CI: 0.89, 410)	0.060
extent of disease		
mild	reference	
moderate	1.33 (95 %-CI: 0.38, 4.68)	0.311
severe	6.04 (95 %-CI: 1.12, 32.6)	0.034

* Odds ratios and p-values were estimated by the penalized likelihood method by Firth.

Mbow M et al

Science

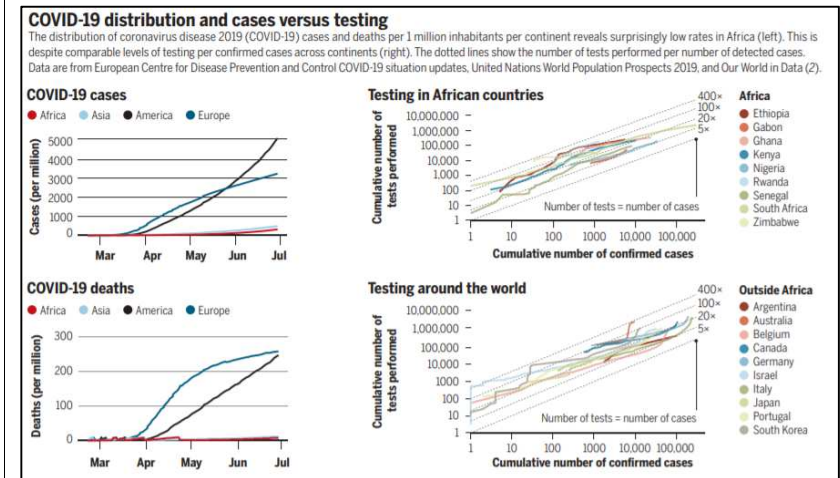
<https://science.sciencemag.org/content/369/6504/624.full>

COVID-19 in Africa:
Dampening the storm?

Possibili spiegazioni del decorso apparentemente diverso dell'epidemia di COVID19 in Africa rispetto ad altre zone del mondo.

Coronavirus disease 2019 (COVID-19) has spread rapidly and extensively to most countries in the world, resulting in considerable mortality in Europe and the United States, as well as in numerous upper-middle-income countries in South America and Asia. Experts predicted millions of COVID-19 deaths in Africa because many countries in the continent rank poorly on the United Nations Development Programme's Human Development Index. However, more than 4 months after the first cases in Africa were detected, prevalence and mortality are still low. It remains unclear if Africa is

really spared from substantial cases and deaths. However, differences between Africa and the most affected countries in reliable reporting and death registration, lockdown stringency, demography, sociocultural aspects, environmental exposures, genetics, and the immune system could help to explain the experience of COVID-19 in Africa.

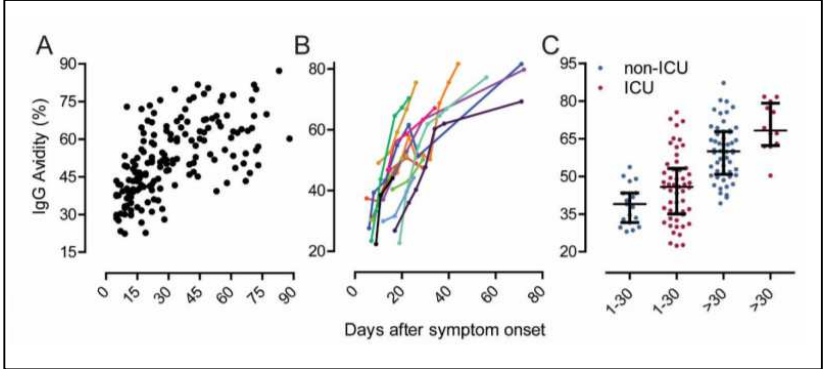


Dookie N et al
Clinical Infectious Diseases
<https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1400/5905579>

Tuberculosis Elimination in the Era of COVID-19: A Moving Target

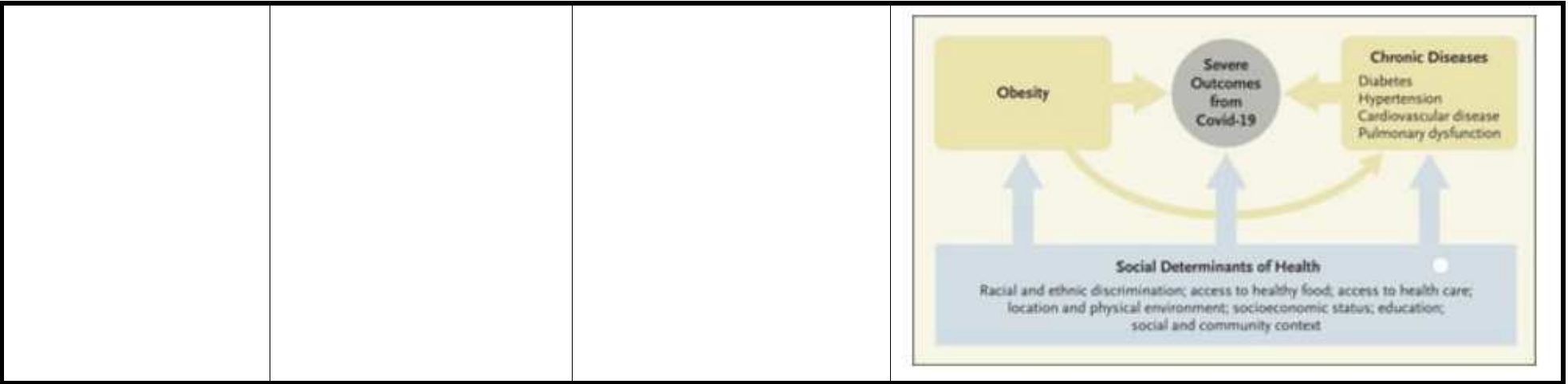
Prevedibili conseguenze negative della pandemia da COVID-19 sullo sforzo per l'eradicazione della tubercolosi.

The COVID-19 pandemic is likely to be the defining global health crisis of the 21st century with over 25 million cases and 800 000 deaths recorded since the emergence of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus. In addition to the direct health impact of the COVID-19 pandemic, there has been detrimental disruption in the provision of healthcare services for other diseases such as human immunodeficiency virus (HIV) and tuberculosis (TB). The TB epidemic in particular could suffer devastating consequences from COVID-19 related disruption, with

			modelling studies predicting an additional 6.3 million cases of TB and 1.4 million deaths over the next five years. This translates to a five to eight-year setback in TB control, receding even further away from the 2030 target of TB elimination.
<p>Luo YR et al</p> <p>Clinical Infectious Diseases</p> <p>https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1389/5905578</p>	<p>Kinetics of SARS-CoV-2 Antibody Avidity Maturation and Association with Disease Severity.</p>	<p>Maturazione dell'avidità delle IgG anti-SARS-CoV-2.</p>	<p>The kinetics of IgG avidity maturation during SARS-CoV-2 infection was studied. The IgG avidity assay used a novel label-free immunoassay technology. It was found that there was a strong correlation between IgG avidity and days since symptom onset, and peak readings were significantly higher in severe than mild disease cases.</p> 
<p>Milani GP et al</p> <p>JAMA Paediatrics</p> <p>https://jamanetwork.com/journals/jamapediatrics/fullarticle/2770117</p>	<p>Frequency of Children vs Adults Carrying Severe Acute Respiratory Syndrome Coronavirus 2 Asymptomatically.</p>	<p>Lavoro che contraddice l'ipotesi di un ruolo cruciale dei bambini asintomatici nella diffusione di SARS-CoV-2 : solo 1% dei bambini contro 9% degli adulti entrati in pronto soccorso nel periodo di studio senza sintomi di infezione sono</p>	<p>Children have been suggested as the facilitators of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission and amplification,¹ because many affected children might be asymptomatic.^{2,3} Accordingly, social and public health policies, such as school closure, have been implemented in many countries. However, the role of children in asymptotically carrying SARS-CoV-2 needs to be further explored. In this study, we investigated the frequency of individuals carrying SARS-CoV-2 among children admitted for noninfectious conditions and without any SARS-CoV-2–</p>

		risultati positivi asintomatici per SARS-CoV-2 al tampone nasofaringeo.	<p>associated symptoms or signs and compare it with the frequency of individuals carrying SARS-CoV-2 among a similar adult population.</p> <table><caption>Table. Characteristics of the Included Children and Adults (N = 214)</caption><thead><tr><th rowspan="2">Characteristic</th><th colspan="2">Patients, No. (%)</th></tr><tr><th>Children</th><th>Adults</th></tr></thead><tbody><tr><td>No.</td><td>83</td><td>131</td></tr><tr><td>Female</td><td>34 (41)</td><td>51 (39)</td></tr><tr><td>Age, median (interquartile range), y</td><td>5.3 (1.1-11.0)</td><td>77 (57-84)</td></tr><tr><td>Positive for SARS-CoV-2</td><td>1 (1.2)</td><td>12 (9.2)</td></tr><tr><td colspan="3">Reason for hospital admission</td></tr><tr><td>Surgical intervention</td><td>22 (27)</td><td>28 (21)</td></tr><tr><td>Neurologic disease</td><td>18 (22)</td><td>32 (24)</td></tr><tr><td>Trauma</td><td>10 (12)</td><td>11 (8)</td></tr><tr><td>Cardiac disease</td><td>1 (1)</td><td>13 (10)</td></tr><tr><td>Psychiatric disorder</td><td>3 (4)</td><td>8 (6)</td></tr><tr><td>Intoxication</td><td>3 (4)</td><td>1 (1)</td></tr><tr><td>Other conditions</td><td>26 (31)</td><td>38 (29)</td></tr></tbody></table> <p>Abbreviation: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.</p>	Characteristic	Patients, No. (%)		Children	Adults	No.	83	131	Female	34 (41)	51 (39)	Age, median (interquartile range), y	5.3 (1.1-11.0)	77 (57-84)	Positive for SARS-CoV-2	1 (1.2)	12 (9.2)	Reason for hospital admission			Surgical intervention	22 (27)	28 (21)	Neurologic disease	18 (22)	32 (24)	Trauma	10 (12)	11 (8)	Cardiac disease	1 (1)	13 (10)	Psychiatric disorder	3 (4)	8 (6)	Intoxication	3 (4)	1 (1)	Other conditions	26 (31)	38 (29)
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McCaw Z et al Contemporary Clinical Trials https://reader.elsevier.com/reader/sd/pii/S1551714420302238?token=9312A50F0C2562DA138FD4D4F280B3E5A174811252DCE3106B2AC6C00AD79308	Selecting appropriate endpoints for assessing treatment effects in comparative clinical studies for COVID-19.	Un articolo di metodo che discute gli endpoint più appropriati per la valutazione dei trattamenti per COVID-19.	<p>To evaluate the efficacy and safety of a new treatment for COVID-19 vs. standard care, certain key endpoints are related to the duration of a specific event, such as hospitalization, ICU stay, or receipt of supplemental oxygen. However, since patients may die in the hospital during study follow-up, using, for example, the duration of hospitalization to assess treatment efficacy can be misleading. If the treatment tends to prolong patients' survival compared with standard care, patients in the new treatment group may spend more time in hospital. This can lead to a "survival bias" issue, where a treatment that is effective for preventing death appears to</p>																																									

8BFB57BA4955FF8524C2AB1762BCADE0			<p>prolong an undesirable outcome. On the other hand, by using hospital-free survival time as the endpoint, we can circumvent the survival bias issue. In this article, we use reconstructed data from a recent, large clinical trial for COVID-19 to illustrate the advantages of this approach. For the analysis of ICU stay or oxygen usage, where the initiating event is potentially an outcome of treatment, standard survival analysis techniques may not be appropriate. We also discuss issues with analyzing the durations of such events.</p>
<p>Belanger MJ et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMp2021264?query=featured_home</p>	<p>Covid-19 and Disparities in Nutrition and Obesity</p>	<p>Disuguaglianze all'epoca del COVID-19 : i determinanti sociali della salute sono alla base del peggiore outcome nelle minoranze svantaggiate.</p>	<p>Black, Latin and Native Americans are experiencing disproportionate burdens of infections, hospitalizations, and deaths from SARS-CoV-2 (Covid-19).¹ Similar disparities are observed in other countries where minority groups face hurdles in accessing health, education, and social services as well as affordable, healthy food. These stark manifestations of health inequities have emerged in the wake of a body of evidence linking obesity and obesity-related chronic diseases, such as hypertension, diabetes, and cardiovascular disease — conditions that disproportionately affect disadvantaged populations — with severe outcomes from Covid-19. Though the factors underlying racial and ethnic disparities in Covid-19 in the United States are multifaceted and complex, long-standing disparities in nutrition and obesity play a crucial role in the health inequities unfolding during the pandemic.</p>



Joung J et al

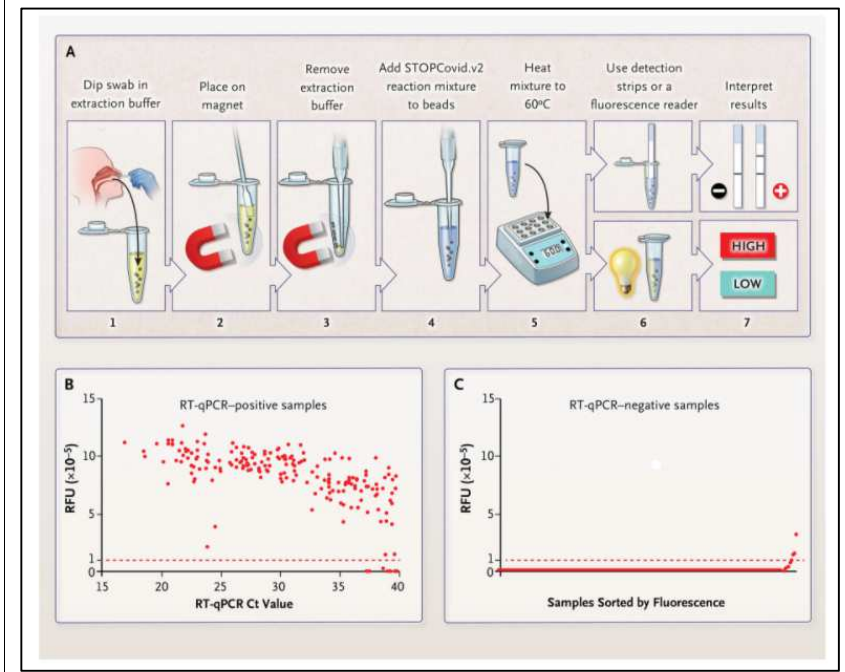
NEJM

https://www.nejm.org/doi/full/10.1056/NEJMc2026172?query=featured_home

Detection of SARS-CoV-2 with SHERLOCK One-Pot Testing

Metodo di ricerca di RNA virale di SARS-CoV-2 basato su estrazione semplificata, amplificazione isoterma e rilevamento tramite metodica CRISPR (clustered regularly interspaced short palindromic repeats).

CRISPR (clustered regularly interspaced short palindromic repeats)-based diagnostic tests collectively provide a nascent platform for the detection of viral and bacterial pathogens. Methods such as SHERLOCK (specific high-sensitivity enzymatic reporter unlocking), which typically use a two-step process (target amplification followed by CRISPR-mediated nucleic acid detection), have been used to detect SARS-CoV-2. These approaches, however, are more complex than those used in point-of-care testing because they depend on an RNA extraction step and multiple liquid-handling steps that increase the risk of cross-contamination of samples.



<p>Ben-Shmuel a et al</p> <p>Clinical Microbiology and Infection</p> <p>https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(20)30532-2/fulltext</p>	<p>Detection and infectivity potential of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) environmental contamination in isolation units and quarantine facilities.</p>	<p>Ricerca di RNA di SARS-CoV-2 su superfici entrate in contatto con pazienti infetti. Il materiale isolato non dà luogo a replicazione su coltura cellulare.</p>	<p>OBJECTIVES: Environmental surfaces have been suggested as likely contributors to the transmission of COVID-19. This study assessed the infectivity of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) contamination on surfaces and objects in hospital isolation units and a quarantine hotel. METHODS: SARS-CoV-2 virus stability and infectivity on non-porous surfaces was tested under controlled laboratory conditions. Surfaces and air sampling was conducted at two COVID-19 isolation units and in a quarantine hotel. Viral RNA detected by RT-PCR and infectivity was assessed by VERO E6 CPE test. RESULTS: In laboratory-controlled conditions, SARS-CoV-2 gradually lost its infectivity completely at day 4 at ambient temperature and the decay rate of viral viability on surfaces directly correlated with increase in temperature. Viral RNA detected in 29/55 (52.7%) and 16/42 (38%) surface samples from the surrounding of symptomatic COVID-19 patients in isolation units of two hospitals and in a quarantine hotel for asymptomatic and very mild COVID-19 patients. None of the surface and air samples from all three sites (0/97) were found to contain infectious titers SARS-Cov-2 in tissue culture assay. CONCLUSIONS: Despite prolonged viability of SARS-CoV-2 in laboratory-controlled conditions, uncultivable viral contamination on inanimate surfaces might suggest low feasibility for indirect fomite transmission.</p>
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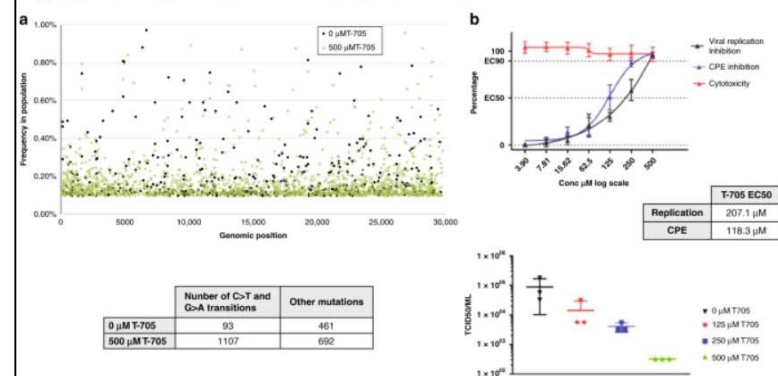
			<p>A</p> <p>Y-axis: Viable viral titer (log)</p> <p>X-axis: Incubation time (days)</p> <p>Legend: Plastic (green line), Metal (blue line)</p> <p>B</p> <p>Y-axis: Viable viral titer (log)</p> <p>X-axis: Incubation time (min)</p> <p>Legend: 40°C (orange line), 50°C (green line), 60°C (red line), 70°C (dark red line)</p> <p>Figure 1</p>
<p>Kanburoglu, MK et al</p> <p>The Pediatric Infectious Disease Journal</p> <p>https://journals.lww.com/pidj/Fulltext/2020/10000/A_Multicentered_Study_on_Epidemiologic_and_2.aspx</p>	<p>A Multicentered Study on Epidemiologic and Clinical Characteristics of 37 Neonates With Community-acquired COVID-19.</p>	<p>Studio di coorte prospettico condotto in Turchia che descrive le caratteristiche e l'esito dell'infezione di 37 neonati sintomatici con diagnosi di COVID-19.</p>	<p>BACKGROUND: Coronavirus disease 2019 (COVID-19) primarily affects adults and spares children, whereas very little is known about neonates. We tried to define the clinical characteristics, risk factors, laboratory, and imaging results of neonates with community-acquired COVID-19. METHODS: This prospective multicentered cohort study included 24 neonatal intensive care units around Turkey, wherein outpatient neonates with COVID-19 were registered in an online national database. Full-term and premature neonates diagnosed with COVID-19 were included in the study, whether hospitalized or followed up as ambulatory patients. Neonates without severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) via reverse transcriptase-polymerase chain reaction testing or whose mothers had been diagnosed with COVID-19 during pregnancy were excluded. RESULTS: Thirty-seven symptomatic neonates were included. The most frequent findings were fever, hypoxemia, and cough (49%, 41%, 27%, respectively). Oxygen administration (41%) and noninvasive ventilation (16%) were frequently required; however, mechanical ventilation (3%) was rarely needed. Median hospitalization was 11 days (1-35 days). One patient with Down syndrome and congenital cardiovascular</p>

			<p>disorders died in the study period. C-reactive protein (CRP) and prothrombin time (PT) levels were found to be higher in patients who needed supplemental oxygen (0.9 [0.1-8.6] vs. 5.8 [0.3-69.2] p = 0.002, 11.9 [10.1-17.2] vs. 15.2 [11.7-18.0] p = 0.01, respectively) or who were severe/critical (1.0 [0.01-8.6] vs. 4.5 [0.1-69.2] p = 0.01, 11.7 [10.1-13.9] vs. 15.0 [11.7-18.0] p = 0.001, respectively). CONCLUSIONS: Symptomatic neonates with COVID-19 had high rates of respiratory support requirements. High CRP levels or a greater PT should alert the physician to more severe disease.</p>
<p>Grasso S et al</p> <p>Critical Care Medicine</p> <p>https://journals.lww.com/ccmjournal/Abstract/9000/Effects_of_Positive_End_Expiratory_Pressure_in_95511.aspx</p>	<p>Effects of Positive End-Expiratory Pressure in "High Compliance" Severe Acute Respiratory Syndrome Coronavirus 2 Acute Respiratory Distress Syndrome.</p>	<p>Studio su 8 pazienti ventilati con infezione da SARS-CoV-2 ed elevata compliance polmonare statica. Si osserva che utilizzare una elevata PEEP (pressione positiva di fine espirazione) nella ventilazione incrementa l'ossigenazione e l'aerazione polmonare ma può indurre iperinflazione alveolare.</p>	<p>OBJECTIVES: Clinical observation suggests that early acute respiratory distress syndrome induced by the severe acute respiratory syndrome coronavirus 2 may be "atypical" due to a discrepancy between a relatively unaffected static respiratory system compliance and a significant hypoxemia. This would imply an "atypical" response to the positive end-expiratory pressure. DESIGN: Single-center, unblinded, crossover study. SETTING: ICU of Bari Policlinico Academic Hospital (Italy), dedicated to care patients with confirmed diagnosis of novel coronavirus disease 2019. PATIENTS: Eight patients with early severe acute respiratory syndrome coronavirus 2 acute respiratory distress syndrome and static respiratory compliance higher than or equal to 50 mL/cm H₂O. INTERVENTIONS: We compared a "lower" and a "higher" positive end-expiratory pressure approach, respectively, according to the intervention arms of the acute respiratory distress syndrome network and the positive end-expiratory pressure setting in adults with acute respiratory distress syndrome studies. MEASUREMENTS AND MAIN RESULTS: Patients were ventilated with the acute respiratory distress syndrome network and, subsequently, with the ExPress protocol. After 1 hour of ventilation, for each protocol, we recorded arterial blood gas, respiratory mechanics, alveolar</p>

			<p>recruitment, and hemodynamic variables. Comparisons were performed with analysis of variance for repeated measures or Friedman test as appropriate. Positive end-expiratory pressure was increased from 9 +/- 3.5 to 17.7 +/- 1.7 cm H2O (p < 0.01). Alveolar recruitment was 450 +/- 111 mL. Static respiratory system compliance decreased from 58.3 +/- 7.6 mL/cm H2O to 47.4 +/- 14.5 mL/cm H2O (p = 0.018) and the "stress index" increased from 0.97 +/- 0.03 to 1.22 +/- 0.07 (p < 0.001). The PaO2/FiO2 ratio increased from 131 +/- 22 to 207 +/- 41 (p < 0.001), and the PaCO2 increased from 45.9 +/- 12.7 to 49.8 +/- 13.2 mm Hg (p < 0.001). The cardiac index went from 3.6 +/- 0.4 to 2.9 +/- 0.6 L/min/m (p = 0.01).</p> <p>CONCLUSIONS: Our data suggest that the "higher" positive end-expiratory pressure approach in patients with severe acute respiratory syndrome coronavirus 2 acute respiratory distress syndrome and high compliance improves oxygenation and lung aeration but may result in alveolar hyperinflation and hemodynamic alterations.</p>
<p>Ashleigh S et al</p> <p>Nature communications</p> <p>https://www.nature.com/articles/s41467-020-18463-z</p>	<p>Rapid incorporation of Favipiravir by the fast and permissive viral RNA polymerase complex results in SARS-CoV-2 lethal mutagenesis</p>	<p>Effetto mutageno dell'incorporazione dell'antivirale favipiravir (analogo nucleosidico, T-705) nel complesso della RNA polimerasi RNA-dipendente di SARS-CoV-2.</p>	<p>The ongoing Corona Virus Disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has emphasized the urgent need for antiviral therapeutics. The viral RNA-dependent-RNA-polymerase (RdRp) is a promising target with polymerase inhibitors successfully used for the treatment of several viral diseases. We demonstrate here that Favipiravir predominantly exerts an antiviral effect through lethal mutagenesis. The SARS-CoV RdRp complex is at least 10-fold more active than any other viral RdRp known. It possesses both unusually high nucleotide incorporation rates and high-error rates allowing facile insertion of Favipiravir into viral RNA, provoking C-to-U and G-to-A transitions in the already low cytosine content SARS-CoV-2 genome. The coronavirus RdRp complex represents an Achilles heel</p>

for SARS-CoV, supporting nucleoside analogues as promising candidates for the treatment of COVID-19.

Fig. 1: Antiviral effects of T-705 on SARS-CoV-2.



a In vitro effects of T-705 on SARS-CoV-2. Distribution of the mutations along the SARS-CoV-2 genome and number of mutations observed in presence or absence of T-705. A 3-fold increase in the presence of the drug is observed ($P < 0.001$, Pearson's χ^2 test with Yates' continuity correction). **b** Quantification of the antiviral effect of T-705 by genome copy number, virus-mediated CPE and number of infectious particles. Mean \pm standard deviation (SD) shown ($n = 3$). Source data are provided as a Source Data file.

Larremore DB et al

Preprint medRxiv

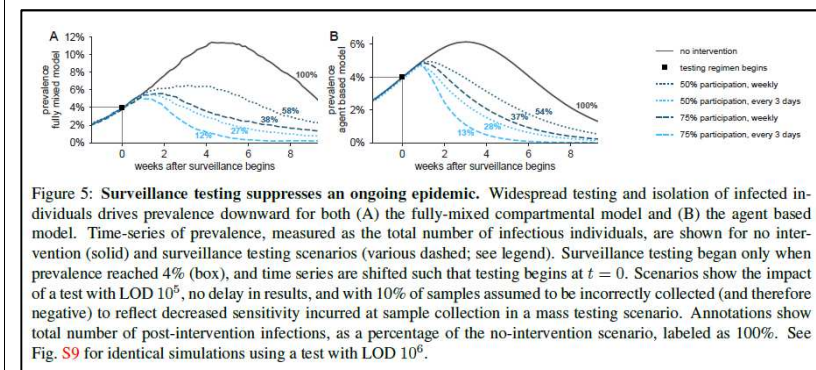
<https://pubmed.ncbi.nlm.nih.gov/32607516/>

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

Modelli predittivi di efficacia della sorveglianza dell'infezione da SARS-CoV-2 : ruolo cruciale di frequenza dei test e rapidità di notifica.

The COVID-19 pandemic has created a public health crisis. Because SARS-CoV-2 can spread from individuals with pre-symptomatic, symptomatic, and asymptomatic infections, the re-opening of societies and the control of virus spread will be facilitated by robust surveillance, for which virus testing will often be central. After infection, individuals undergo a period of incubation during which viral titers are usually too low to detect, followed by an exponential viral growth, leading to a peak viral load and infectiousness, and ending with declining viral levels and clearance. Given the pattern of viral load kinetics, we model surveillance effectiveness considering test sensitivities, frequency, and sample-to-answer reporting time. These results demonstrate that effective surveillance depends

largely on frequency of testing and the speed of reporting, and is only marginally improved by high test sensitivity. We therefore conclude that surveillance should prioritize accessibility, frequency, and sample-to-answer time; analytical limits of detection should be secondary.



Rydyznski Moderbacher
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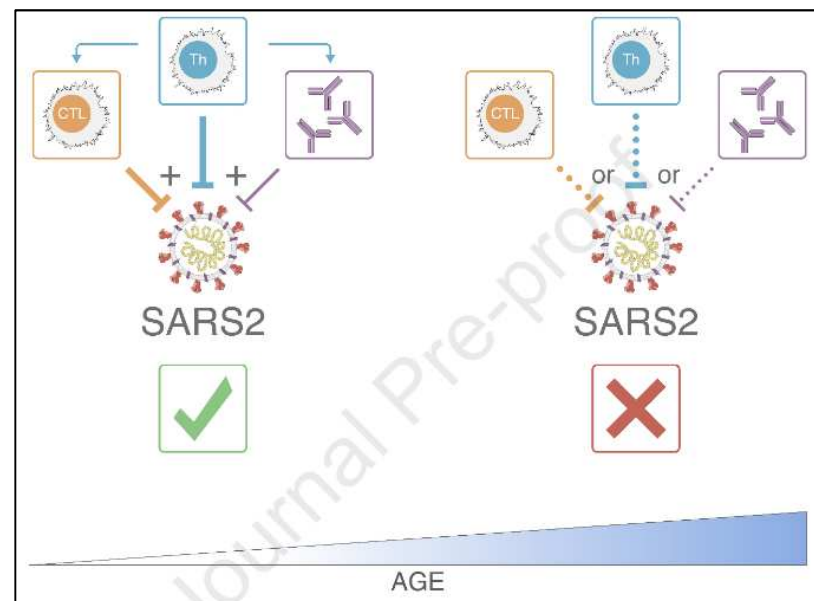
<https://www.sciencedirect.com/science/article/pii/S0092867420312356>

Antigen-specific adaptive immunity to SARS-CoV-2 in acute COVID-19 and associations with age and disease severity

Studio dei tre bracci dell'immunità adattiva (anticorpi, linfociti CD4+ e CD8+) e dell'associazione dei loro livelli con l'outcome di 54 pazienti con infezione da SARS-CoV-2.

Limited knowledge is available on the relationship between antigen-specific immune responses and COVID-19 disease severity. We completed a combined examination of all three branches of adaptive immunity at the level of SARS-CoV-2-specific CD4+ and CD8+ T cell and neutralizing antibody responses in acute and convalescent subjects. SARS-CoV-2-specific CD4+ and CD8+ T cells were each associated with milder disease. Coordinated SARS-CoV-2-specific adaptive immune responses were associated with milder disease, suggesting roles for both CD4+ and CD8+ T cells in protective immunity in COVID-19. Notably, coordination of SARS-CoV-2 antigen-specific responses was disrupted in individuals > 65 years old. Scarcity of naive T cells was also associated with ageing and poor disease outcomes. A parsimonious explanation

is that coordinated CD4+ T cell, CD8+ T cell, and antibody responses are protective, but uncoordinated responses frequently fail to control disease, with a connection between ageing and impaired adaptive immune responses to SARS-CoV-2.



The Lancet COVID-19 Commissioners, Task Force Chairs, and Commission Secretariat

The Lancet

<https://www.thelancet.com/action/showPdf?pii=S0140-6736%2820%2931927-9>

Lancet COVID-19 Commission Statement on the occasion of the 75th session of the UN General Assembly

Dichiarazione della Commissione COVID-19 della rivista *Lancet* alle Nazioni Unite. Dettaglio delle 10 azioni fondamentali di lotta alla pandemia.

The Lancet COVID-19 Commission was launched on July 9, 2020, to assist governments, civil society, and UN institutions in responding effectively to the COVID-19 pandemic. The Commission aims to offer practical solutions to the four main global challenges posed by the pandemic: suppressing the pandemic by means of pharmaceutical and non-pharmaceutical interventions; overcoming humanitarian emergencies, including poverty, hunger, and mental distress, caused by the pandemic; restructuring public and private finances in the wake of the pandemic; and rebuilding the world economy in an inclusive, resilient, and sustainable way that is

aligned with the Sustainable Development Goals (SDGs) and the Paris Climate Agreement. Many creative solutions are already being implemented, and a key aim of the Commission is to accelerate their adoption worldwide.

Panel 1: Ten priority actions

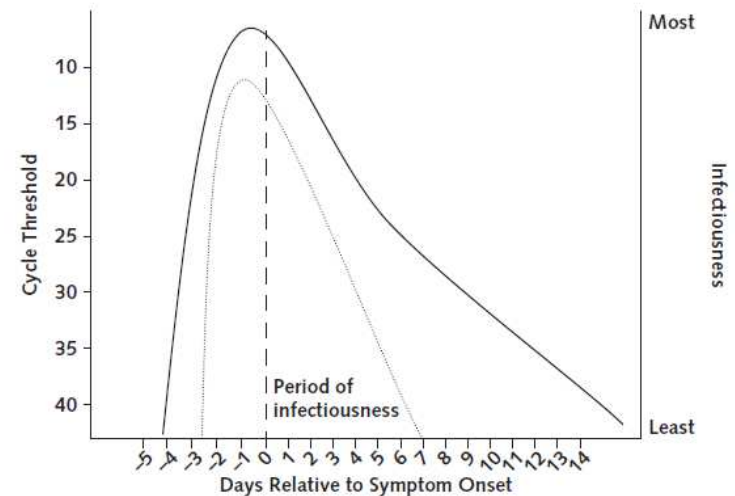
- 1 Origins: track down the origins of the virus in an open, scientific, and unbiased way not influenced by geopolitical agendas
- 2 Non-pharmaceutical interventions: suppress the epidemic through the proven package of non-pharmaceutical interventions, as accomplished by several countries including several in the Asia-Pacific region
- 3 Science-based policy making: base policy making on objective scientific evidence and stop politicians and others in positions of power from subverting clinical trials and other scientific protocols
- 4 Timely and consistent data: collect and publish timely and internationally consistent data on the state of the pandemic, including humanitarian and economic consequences
- 5 Justice in access to tools to fight COVID-19: ensure universal access to the tools to fight COVID-19, including test kits, therapeutics, and prospective vaccines
- 6 Emergency financing: secure access of developing countries to financing from international sources, especially from the International Monetary Fund and World Bank
- 7 Protect vulnerable groups: direct urgent protection towards vulnerable groups, including older people, people in poverty and hunger, women who are vulnerable, children, people with chronic diseases and disabilities, the homeless, migrants, refugees, Indigenous Peoples, and ethnic and racial minorities
- 8 Long-term financial reform: prepare for a deep restructuring of global finances, including debt relief, new forms of international financing, and reform of monetary arrangements
- 9 Green and resilient recovery: economic recovery will be based on public-investment-led growth in green, digital, and inclusive technologies, based on the Sustainable Development Goals
- 10 Global peace and cooperation: support UN institutions and the UN Charter, resisting any attempts at a new cold war

<p>Zeng W et al</p> <p>JAMA</p> <p>https://jamanetwork.com/journals/jamaophthalmology/fullarticle/2770872</p>	<p>Association of Daily Wear of Eyeglasses With Susceptibility to Coronavirus Disease 2019 Infection.</p>	<p>In una coorte di 276 pazienti ricoverati per infezione da SARS-CoV-2, la percentuale di persone che indossava gli occhiali da vista per almeno 8 ore al giorno è inferiore a quella della popolazione generale, il che suggerisce un possibile effetto protettivo rispetto al contagio.</p>	<p>Importance The proportion of daily wearers of eyeglasses among patients with coronavirus disease 2019 (COVID-19) is small, and the association between daily wear of eyeglasses and COVID-19 susceptibility has not been reported.</p> <p>Objective To study the association between the daily wearing of eyeglasses and the susceptibility to COVID-19.</p> <p>Design, Setting, and Participants This cohort study enrolled all inpatients with COVID-19 in Suizhou Zengdu Hospital, Suizhou, China, a designated hospital for COVID-19 treatment in the area, from January 27 to March 13, 2020. COVID-19 was diagnosed according to the fifth edition of Chinese COVID-19 diagnostic guidelines. The proportion of persons with myopia who wore eyeglasses in Hubei province was based on data from a previous study.</p> <p>Exposures Daily wearing of eyeglasses for more than 8 hours.</p> <p>Main Outcomes and Measures The main outcomes were the proportions of daily wearers of eyeglasses among patients admitted to the hospital with COVID-19 and among the local population. Data on exposure history, clinical symptoms, underlying diseases, duration of wearing glasses, and myopia status and the proportion of people with myopia who wore eyeglasses in Hubei province were collected. People who wore glasses for more than 8 hours a day were defined as long-term wearers.</p> <p>Results A total of 276 patients with COVID-19 were enrolled. Of these, 155 (56.2%) were male, and the median age was 51 (interquartile range, 41-58) years. All those who wore glasses for more than 8 hours a day had myopia and included 16 of 276 patients (5.8%; 95% CI, 3.04%-8.55%). The proportion of people with myopia in Hubei province, based on a previous study, was</p>
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			<p>31.5%, which was much higher than the proportion of patients with COVID-19 who had myopia in this sample.</p> <p>Conclusions and Relevance In this cohort study of patients hospitalized with COVID-19 in Suizhou, China, the proportion of inpatients with COVID-19 who wore glasses for extended daily periods (>8 h/d) was smaller than that in the general population, suggesting that daily wearers of eyeglasses may be less susceptible to COVID-19.</p>
<p>Evans ML et al</p> <p>NEJM</p> <p>https://www.nejm.org/doi/full/10.1056/NEJMp2024046?query=featured_home</p>	<p>A Pandemic within a Pandemic — Intimate Partner Violence during Covid-19</p>	<p>Una riflessione sul rischio di esacerbazione degli episodi di violenza domestica durante l'epidemia da SARS-CoV-2 e proposte di soluzione.</p>	<p>As Covid-19 cases surged in the United States in March 2020, stay-at-home orders were put in place. Schools closed, and many workers were furloughed, laid off, or told to work from home. With personal movement limited and people confined to their homes, advocates expressed concern about a potential increase in intimate partner violence (IPV). Stay-at-home orders, intended to protect the public and prevent widespread infection, left many IPV victims trapped with their abusers. Domestic-violence hotlines prepared for an increase in demand for services as states enforced these mandates, but many organizations experienced the opposite. In some regions, the number of calls dropped by more than 50%.¹ Experts in the field knew that rates of IPV had not decreased, but rather that victims were unable to safely connect with services. Though restrictions on movement have been lifted in most regions, the pandemic and its effects rage on, and there is widespread agreement that areas that have seen a drop in caseloads are likely to experience a second surge. This pandemic has reinforced important truths: inequities related to social determinants of health are magnified during a crisis, and sheltering in place does not inflict equivalent hardship on all people.</p>

<p>Meyerowitz EA et al</p> <p>Annals of Internal Medicine</p> <p>https://pubmed.ncbi.nlm.nih.gov/32941052/</p>	<p>Transmission of SARS-CoV-2: A Review of Viral, Host, and Environmental Factors</p>	<p>Revisione della letteratura per rispondere a domande chiave sulla trasmissione di SARS-CoV-2.</p>	<p>Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the etiologic agent of coronavirus disease 2019 (COVID-19), has spread globally in a few short months. Substantial evidence now supports preliminary conclusions about transmission that can inform rational, evidence-based policies and reduce misinformation on this critical topic. This article presents a comprehensive review of the evidence on transmission of this virus. Although several experimental studies have cultured live virus from aerosols and surfaces hours after inoculation, the real-world studies that detect viral RNA in the environment report very low levels, and few have isolated viable virus. Strong evidence from case and cluster reports indicates that respiratory transmission is dominant, with proximity and ventilation being key determinants of transmission risk. In the few cases where direct contact or fomite transmission is presumed, respiratory transmission has not been completely excluded. Infectiousness peaks around a day before symptom onset and declines within a week of symptom onset, and no late linked transmissions (after a patient has had symptoms for about a week) have been documented. The virus has heterogeneous transmission dynamics: Most persons do not transmit virus, whereas some cause many secondary cases in transmission clusters called "superspreading events." Evidence-based policies and practices should incorporate the accumulating knowledge about transmission of SARS-CoV-2 to help educate the public and slow the spread of this virus.</p>
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Figure 1. The period of infectiousness for immunocompetent, symptomatic adults (*dotted line*) and respiratory tract viral load with time (*solid line*).



The vertical dashed line represents symptom onset.

Khanh NC et al

Emerging Infectious Diseases

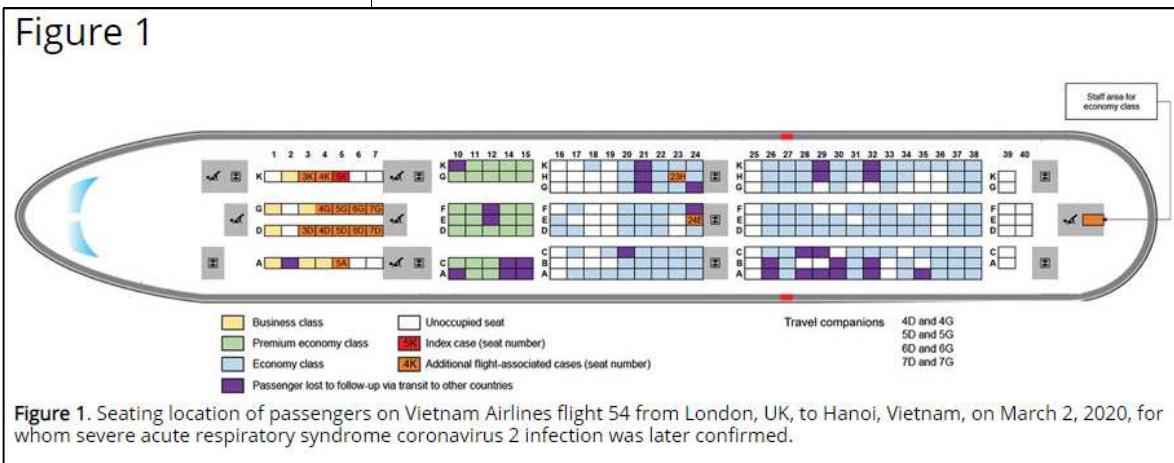
https://wwwnc.cdc.gov/eid/article/26/11/20-3299_article

Transmission of severe acute respiratory syndrome coronavirus 2 during long flight

Tracciamento di 217 persone entrate in contatto, a bordo di un volo intercontinentale diretto ad Hanoi, con un caso di infezione sintomatica da SARS-CoV-2.

To assess the role of in-flight transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), we investigated a cluster of cases among passengers on a 10-hour commercial flight. Affected persons were passengers, crew, and their close contacts. We traced 217 passengers and crew to their final destinations and interviewed, tested, and quarantined them. Among the 16 persons in whom SARS-CoV-2 infection was detected, 12 (75%) were passengers seated in business class along with the only symptomatic person (attack rate 62%). Seating proximity was strongly associated with increased infection risk (risk ratio 7.3, 95% CI 1.2–46.2). We found no strong evidence supporting alternative transmission scenarios. In-flight transmission that probably

originated from 1 symptomatic passenger caused a large cluster of cases during a long flight. Guidelines for preventing SARS-CoV-2 infection among air passengers should consider individual passengers' risk for infection, the number of passengers traveling, and flight duration.



Ko JY et al

Clinical Infectious Diseases

<https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1419/5908300?searchresult=1>

Risk Factors for COVID-19-associated hospitalization: COVID-19-Associated Hospitalization Surveillance Network and Behavioral Risk Factor Surveillance System

Studio cross-sectional su 5416 adulti residenti negli USA alla ricerca di fattori associati alla ospedalizzazione per COVID19, al fine di identificare i gruppi che necessitano di interventi mirati di prevenzione e terapia.

Background : Data on risk factors for COVID-19-associated hospitalization are needed to guide prevention efforts and clinical care. We sought to identify factors independently associated with COVID-19-associated hospitalizations

Methods : U.S. community-dwelling adults (≥ 18 years) hospitalized with laboratory-confirmed COVID-19 during March 1–June 23, 2020 were identified from the COVID-19-Associated Hospitalization Surveillance Network (COVID-NET), a multi-state surveillance system. To calculate hospitalization rates by age, sex, and race/ethnicity strata, COVID-NET data served as the numerator and Behavioral Risk Factor Surveillance System estimates served as the population denominator for characteristics of interest. Underlying medical conditions examined included hypertension, coronary

			<p>artery disease, history of stroke, diabetes, obesity [BMI ≥ 30 kg/m²], severe obesity [BMI ≥ 40 kg/m²], chronic kidney disease, asthma, and chronic obstructive pulmonary disease. Generalized Poisson regression models were used to calculate adjusted rate ratios (aRR) for hospitalization</p> <p>Results : Among 5,416 adults, hospitalization rates were higher among those with ≥ 3 underlying conditions (versus without)(aRR: 5.0; 95%CI: 3.9, 6.3), severe obesity (aRR:4.4; 95%CI: 3.4, 5.7), chronic kidney disease (aRR:4.0; 95%CI: 3.0, 5.2), diabetes (aRR:3.2; 95%CI: 2.5, 4.1), obesity (aRR:2.9; 95%CI: 2.3, 3.5), hypertension (aRR:2.8; 95%CI: 2.3, 3.4), and asthma (aRR:1.4; 95%CI: 1.1, 1.7), after adjusting for age, sex, and race/ethnicity. Adjusting for the presence of an individual underlying medical condition, higher hospitalization rates were observed for adults aged ≥ 65, 45-64 (versus 18-44 years), males (versus females), and non-Hispanic black and other race/ethnicities (versus non-Hispanic whites)</p> <p>Conclusion : Our findings elucidate groups with higher hospitalization risk that may benefit from targeted preventive and therapeutic interventions</p>
<p>Lee SW et al</p> <p>The Lancet</p> <p>https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(20)30421-1/fulltext</p>	<p>Association between mental illness and COVID-19 susceptibility and clinical outcomes in South Korea: a nationwide cohort study.</p>	<p>Studio di coorte condotto in Corea del Sud su pazienti adulti per verificare l'associazione fra malattia mentale (codificata secondo ICD-10) e infezione da SARS-CoV-2: nessuna associazione. Lievemente aumentato il rischio di avere un decorso grave per gli</p>	<p>Background : Evidence for the associations between mental illness and the likelihood of a positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) test result and the clinical outcomes of COVID-19 is scarce. We aimed to investigate these associations with data from a national register in South Korea.</p> <p>Methods : A nationwide cohort study with propensity score matching was done in South Korea using data collected from the Health Insurance Review and Assessment Service of Korea. We defined mental illness as present if one of the relevant ICD-10 codes was recorded at least twice within 1 year for an outpatient or inpatient. Severe mental illness was considered as non-affective or</p>

		infetti con storia di malattia mentale grave.	<p>affective disorders with psychotic features. We included all patients aged older than 20 years who were tested for SARS-CoV-2 through services facilitated by the Korea Centers for Disease Control and Prevention, the Health Insurance Review and Assessment Service of Korea, and the Ministry of Health and Welfare, South Korea. We investigated the primary outcome (SARS-CoV-2 test positivity) in the entire cohort and the secondary outcomes (severe clinical outcomes of COVID-19: death, admission to the intensive care unit, or invasive ventilation) among those who tested positive.</p> <p>Findings : Between Jan 1 and May 15, 2020, 216 418 people were tested for SARS-CoV-2, of whom 7160 (3·3%) tested positive. In the entire cohort with propensity score matching, 1391 (3·0%) of 47 058 patients without a mental illness tested positive for SARS-CoV-2, compared with 1383 (2·9%) of 48 058 with a mental illness (adjusted odds ratio [OR] 1·00, 95% CI 0·93–1·08). Among the patients who tested positive for SARS-CoV-2, after propensity score matching, 109 (8·3%) of 1320 patients without a mental illness had severe clinical outcomes of COVID-19 compared with 128 (9·7%) of 1320 with a mental illness (adjusted OR 1·27, 95% CI 1·01–1·66).</p> <p>Interpretation : Diagnosis of a mental illness was not associated with increased likelihood of testing positive for SARS-CoV-2. Patients with a severe mental illness had a slightly higher risk for severe clinical outcomes of COVID-19 than patients without a history of mental illness. Clinicians treating patients with COVID-19 should be aware of the risk associated with pre-existing mental illness.</p>
Agren D Lancet	Understanding Mexican health worker COVID-19 deaths.	Commento sulle possibili ragioni della elevata mortalità per COVID-19 degli operatori sanitari in Messico, fra carenza di	An Amnesty International report says that more health workers have died in Mexico than anywhere else. David Agren explores why. Less than 3 weeks after Mexico recorded its first COVID-19 case, staff from a Mexican Social Security Institute (IMSS) hospital

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31955-3/fulltext		dispositivi di protezione e precarietà lavorativa.	blocked a Mexico City road, demanding medical supplies and personal protective equipment (PPE). At least 70 protests have followed, according to a report by six former health secretaries, with medical staff decrying shortages of supplies and tests, along with a lack of hospital infrastructure and even proper training.
<p>Elsoukkary SS et al</p> <p>Pathobiology</p> <p>https://www.karger.com/Article/FullText/511325</p>	Autopsy Findings in 32 Patients with COVID-19: A Single-Institution Experience	Esito degli esami autoptici eseguiti su 32 pazienti deceduti per COVID-19 : frequente riscontro di danno alveolare diffuso (94%) e tromboembolia disseminata (88%).	<p>BACKGROUND: A novel coronavirus, SARS-CoV-2, was identified in Wuhan, China in late 2019. This virus rapidly spread around the world causing disease ranging from minimal symptoms to severe pneumonia, which was termed coronavirus disease (i.e., COVID). Postmortem examination is a valuable tool for studying the pathobiology of this new infection. METHODS: We report the clinicopathologic findings from 32 autopsy studies conducted on patients who died of COVID-19 including routine gross and microscopic examination with applicable special and immunohistochemical staining techniques. RESULTS: SARS-CoV-2 infection was confirmed by nasopharyngeal RT-PCR in 31 cases (97%) and by immunohistochemical staining for SARS-CoV-2 spike-protein in the lung in the remaining 1 case (3%). The ethnically diverse cohort consisted of 22 males and 10 females with a mean age of 68 years (range: 30-100). Patients most commonly presented with cough (17 [55%]), shortness of breath (26 [81%]), and a low-grade fever (17 [55%]). Thirty-one (97%) of the patients had at least 1 comorbidity (mean = 4). Twenty-eight patients (88%) had widespread thromboembolic disease, as well as diffuse alveolar damage (30 [94%]), diabetic nephropathy (17 [57%]) and acute tubular injury. Patterns of liver injury were heterogeneous, featuring 10 (36%) with frequent large basophilic structures in sinusoidal endothelium, and increased immunoblast-like cells in lymph nodes. CONCLUSION: This series of autopsies from patients with COVID-19 confirms the observation that the majority of</p>

severely affected patients have significant pulmonary pathology. However, many patients also have widespread microscopic thromboses, as well as characteristic findings in the liver and lymph nodes.

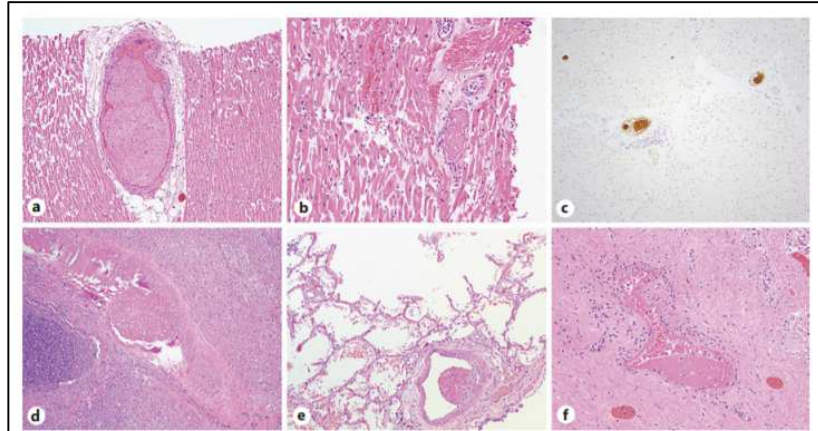


Fig. 1. Multisystem microscopic thromboses were common including in the intracardiac arteries and arterioles (**a, b**; $\times 20$ and $\times 40$), highlighted by CD61 immunohistochemistry (**c**; $\times 20$), in the lung with (**d**; $\times 20$) or without (**e**; $\times 20$) associated infarction and in other organs including the prostate (**f**; $\times 40$).

Benton DJ et al

Nature

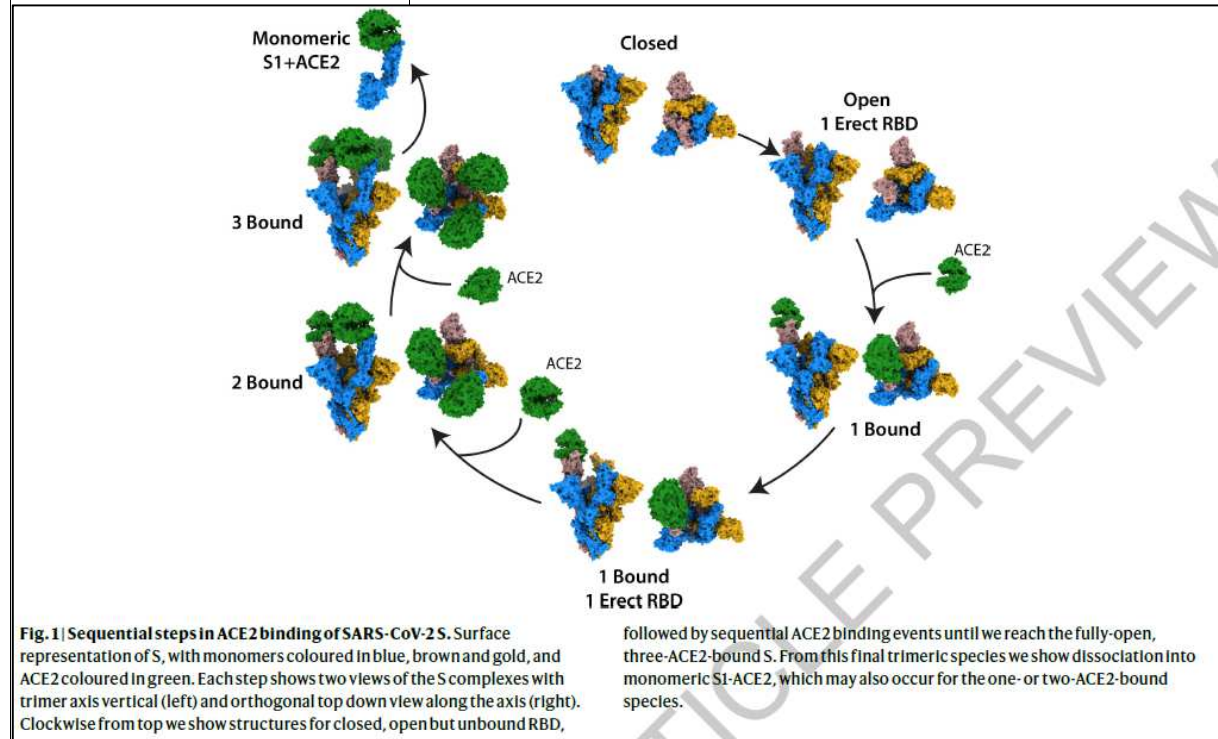
<https://www.nature.com/articles/s41586-020-2772-0>

Receptor binding and priming of the spike protein of SARS-CoV-2 for membrane fusion.

Studio, tramite microscopia crio-elettronica, dell'interazione fra proteina S di SARS-CoV-2 e recettore cellulare ACE2.

SARS-CoV-2 infection is initiated by virus binding to ACE2 cell surface receptors, followed by fusion of virus and cell membranes to release the virus genome into the cell. Both receptor binding and membrane fusion activities are mediated by the virus Spike glycoprotein, S. As with other class I membrane fusion proteins, S is post-translationally cleaved, in this case by furin, into S1 and S2 components that remain associated following cleavage. Fusion activation following receptor binding is proposed to involve the exposure of a second proteolytic site (S2'), cleavage of which is required for the fusion peptide release. We have investigated the binding of ACE2 to the furin-cleaved form of SARS-CoV-2 S by cryoEM. We classify ten different molecular species including the

unbound, closed spike trimer, the fully open ACE2-bound trimer, and dissociated monomeric S1 bound to ACE2. The ten structures describe ACE2 binding events which destabilise the spike trimer, progressively opening up, and out, the individual S1 components. The opening process reduces S1 contacts and un-shields the trimeric S2 core, priming fusion activation and dissociation of ACE2-bound S1 monomers. The structures also reveal refolding of an S1 subdomain following ACE2 binding, that disrupts interactions with S2, notably involving Asp614(13-15), leading to destabilisation of the structure of S2 proximal to the secondary (S2') cleavage site.



Lopez AS et al

Morbidity and Mortality
Weekly Report

https://www.cdc.gov/mmwr/volumes/69/wr/mm6937e3.htm?s_cid=mm6937e3_w

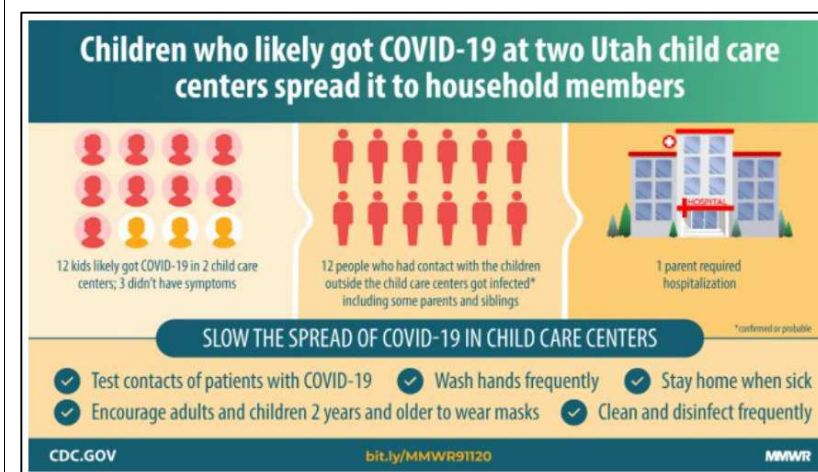
Transmission Dynamics of
COVID-19 Outbreaks
Associated with Child Care
Facilities - Salt Lake City,
Utah, April-July 2020.

Studio di tre focolai di
trasmissione di SARS-CoV-2
a partenza da centri diurni
per bambini nello Utah.
Trasmissione da 12 bambini,
di cui 2 asintomatici, ad
almeno 12 contatti esterni
al centro. Emerge
l'importanza delle misure di
protezione e della ricerca
attiva di casi anche tra
asintomatici in presenza di
un caso indice.

What is already known about this topic? Children aged ≥ 10 years have been shown to transmit SARS-CoV-2 in school settings.

What is added by this report? Twelve children acquired COVID-19 in child care facilities. Transmission was documented from these children to at least 12 (26%) of 46 nonfacility contacts (confirmed or probable cases). One parent was hospitalized. Transmission was observed from two of three children with confirmed, asymptomatic COVID-19.

What are the implications for public health practice? SARS-CoV-2 Infections among young children acquired in child care settings were transmitted to their household members. Testing of contacts of laboratory-confirmed COVID-19 cases in child care settings, including children who might not have symptoms, could improve control of transmission from child care attendees to family members.



* 3 focolai descritti nel testo, 2 menzionati in figura

Westblade et al

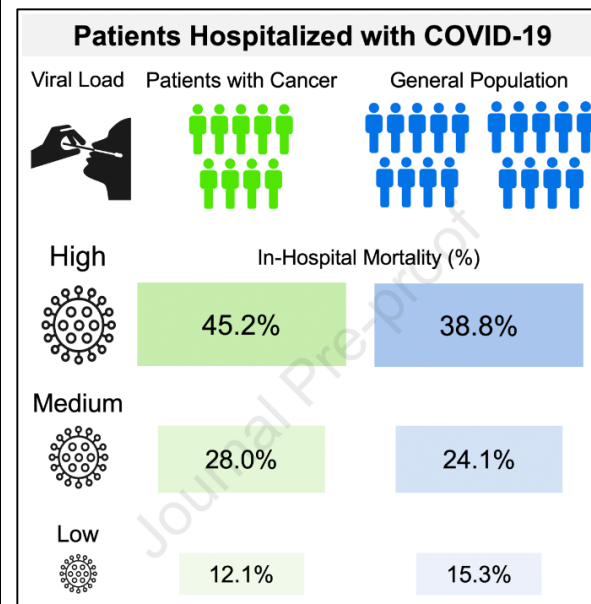
Cancer Cell

<https://www.sciencedirect.com/science/article/pii/S1535610820304815?via%3Dihub>

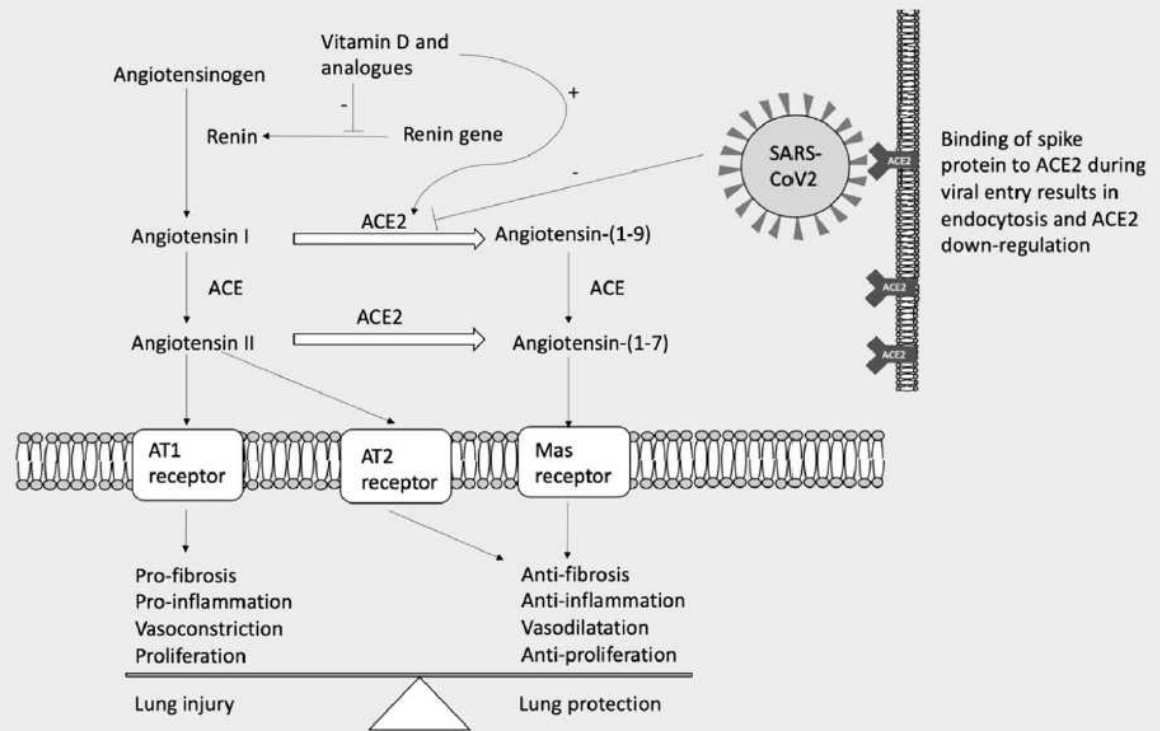
SARS-CoV-2 Viral Load Predicts Mortality in Patients with and Without Cancer Who Are Hospitalized with COVID-19

Confronto fra 100 pazienti affetti da neoplasia attiva e 2914 non affetti, tutti con infezione da SARS-CoV-2. Una elevata carica virale nel tampone nasofaringeo alla presentazione in pronto soccorso, definita come ciclo soglia di positivizzazione della PCR real time <27, è associato alla mortalità intraospedaliera in entrambi i gruppi. I pazienti con neoplasia ematologica e recente chemioterapia hanno carica più elevata all'ingresso rispetto agli altri.

Patients with cancer may be at increased risk of severe coronavirus disease 2019 (COVID-19), but the role of viral load on this risk is unknown. We measured SARS-CoV-2 viral load using cycle threshold (CT) values from reverse transcription-polymerase chain reaction assays applied to nasopharyngeal swab specimens in 100 patients with cancer and 2914 without cancer who were admitted to three New York City hospitals. Overall, the in-hospital mortality rate was 38.8% among patients with a high viral load, 24.1% among patients with a medium viral load, and 15.3% among patients with a low viral load ($P<0.001$). Similar findings were observed in patients with cancer (high, 45.2% mortality; medium, 28.0%; low, 12.1%; $P=0.008$). Patients with hematologic malignancies had higher median viral loads (CT=25.0) than patients without cancer (CT=29.2; $P=0.0039$). SARS-CoV-2 viral load results may offer vital prognostic information for patients with and without cancer who are hospitalized with COVID-19.



<p>White- Dzuro G et al</p> <p>Postgraduate Medicine</p> <p>https://pubmed.ncbi.nlm.nih.gov/32921198/</p>	<p>Multisystem effects of COVID-19: A concise review for practitioners</p>	<p>Disamina delle manifestazioni multisistemiche di COVID-19, sintetizzate in tre pannelli.</p>	<p>While COVID-19 has primarily been characterized by the respiratory impact of viral pneumonia, it affects every organ system and carries a high consequent risk of death in critically ill patients. Higher sequential organ failure assessment (SOFA) scores have been associated with increased mortality in patients critically ill patients with COVID-19. It is important that clinicians managing critically ill COVID-19 patients be aware of the multisystem impact of the disease so that care can be focused on the prevention of end-organ injuries to potentially improve clinical outcomes. We review the multisystem complications of COVID-19 and associated treatment strategies to improve the care of critically ill COVID-19 patients.</p>
<p>Hoong CWS et al</p> <p>Hormone and Metabolic Research</p> <p>https://www.thieme-connect.de/products/ejournals/abstract/10.1055/a-1243-5462</p>	<p>Are Adequate Vitamin D Levels Helpful in Fighting COVID-19? A Look at the Evidence.</p>	<p>Revisione delle evidenze a favore del potenziale ruolo della vitamina D fra i trattamenti a disposizione per COVID-19, in base a un possibile effetto immunomodulatore.</p>	<p>COVID-19 is a global pandemic with high mortality in vulnerable groups. Given the current lack of definitive treatment or vaccine that significantly reduces mortality rate, governments, researchers and healthcare providers are racing to find possible solutions to the crisis. Vitamin D and its analogues have been previously studied for their non-skeletal benefits. In particular, questions regarding their role in the modulation of immunity have re-surfaced, in view of possible epidemiological links observed between COVID-19 and vitamin D levels in selected populations. In this review, we highlight potential mechanisms and summarise the evidence for and against the potential role of vitamin D supplementation in our fight against COVID-19.</p>



► **Fig. 3** Mechanism of possible lung protective effect of vitamin D and its analogues in COVID-19 infection via upregulation of ACE2-Ang-(1-7)-Mas axis.