COVID-19 u kontekstu eksposoma

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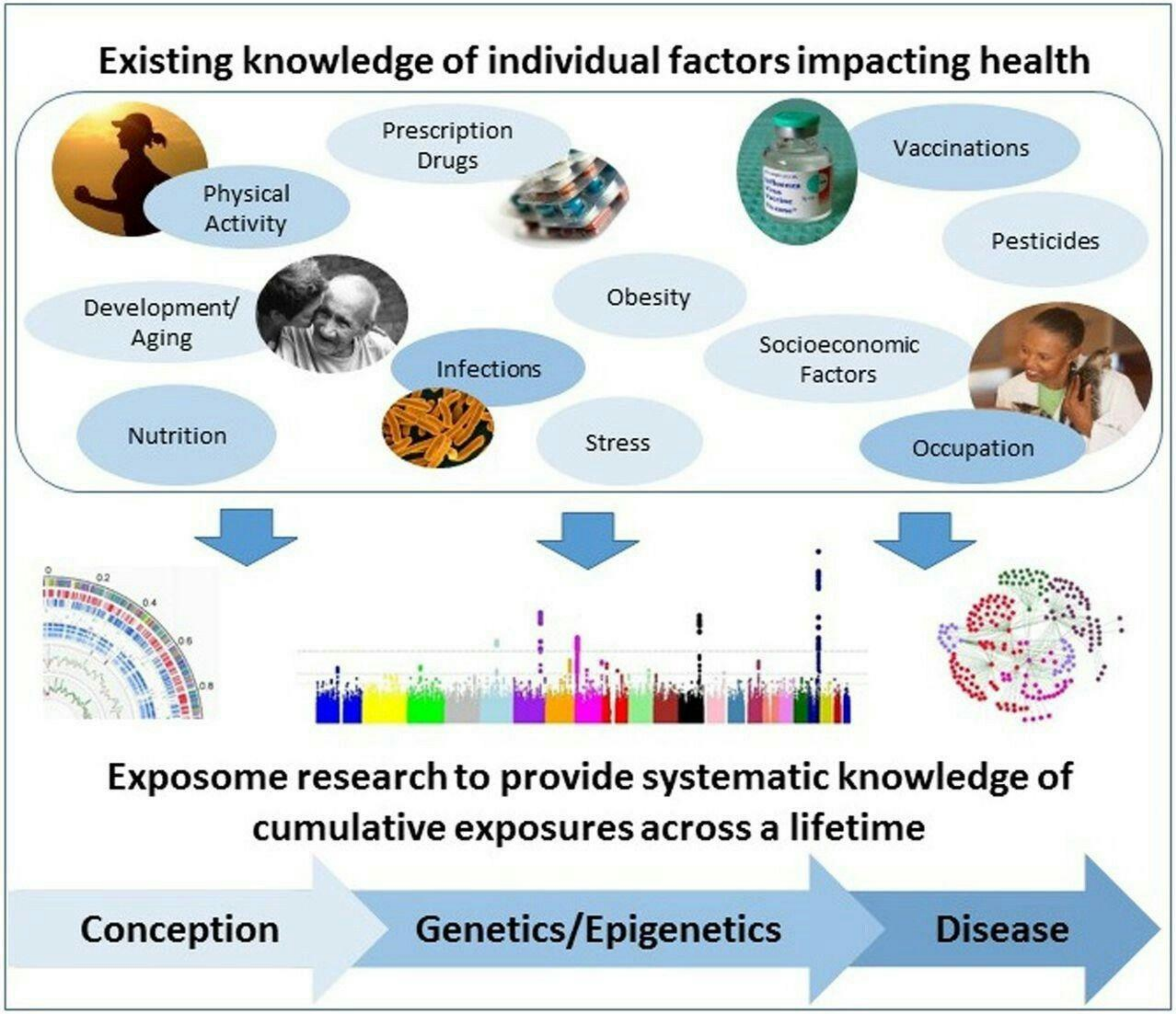
Eksposom



@inproceedings{DennisLETE, title={LE The Exposome : A New Frontier for Education}, author={Kristine K. Dennis} }


Željko Cvetnić
Bolesti koje su mijenjale svijet
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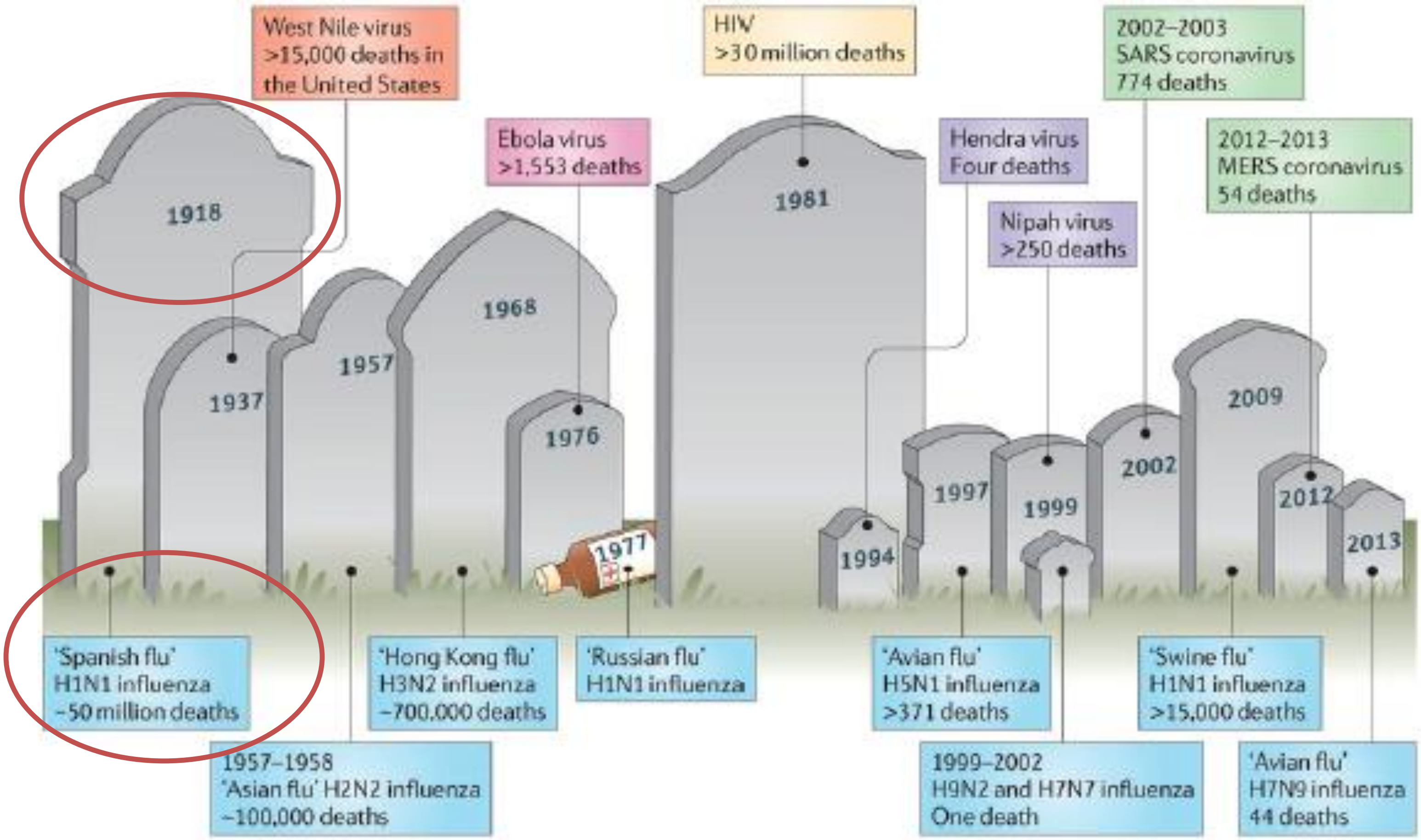
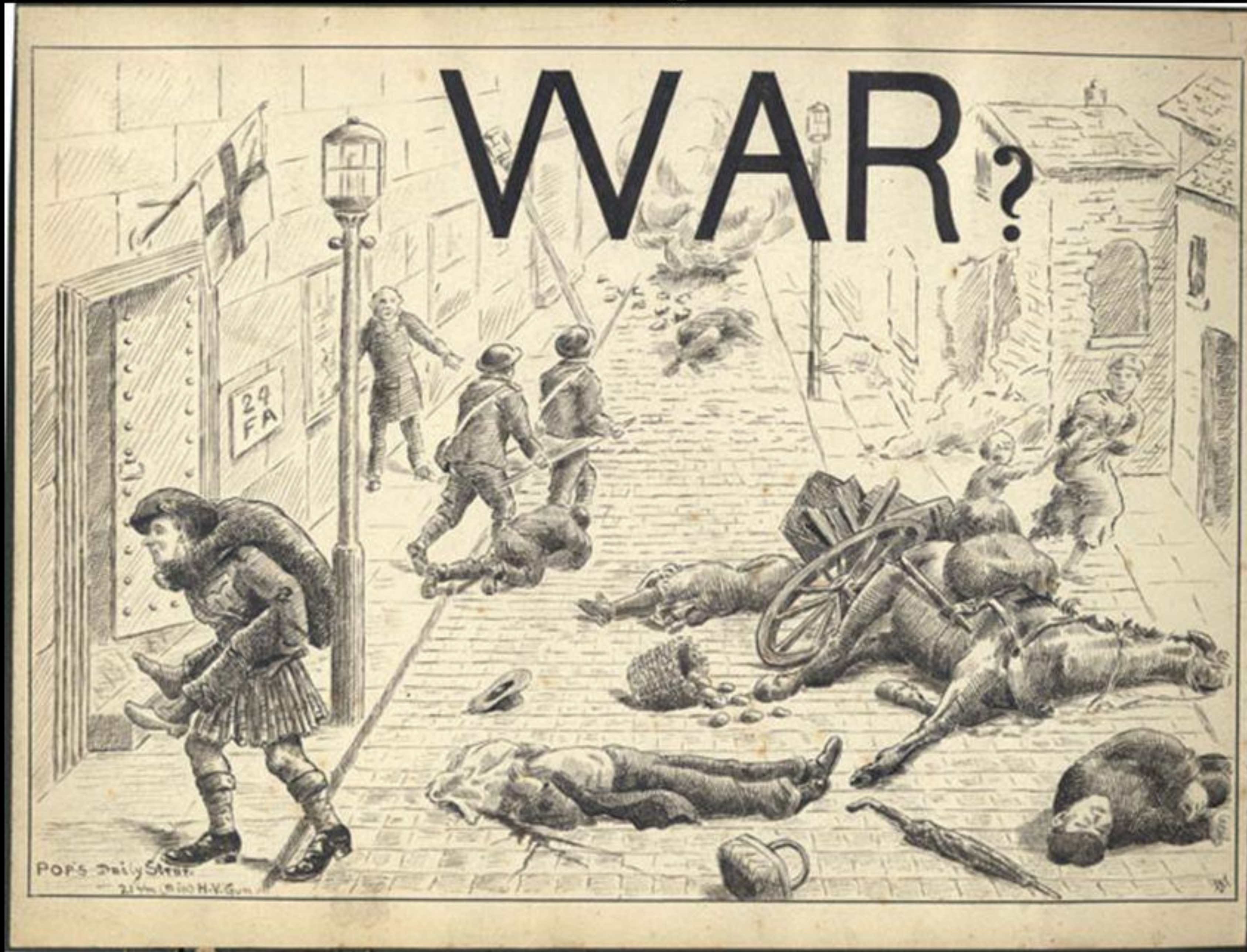
Emergentni patogeni – nevidljivi ubojice



WWI killed 10 million in battle

2 million died of hunger related to war



Power of viruses

Symposium "New Coronavirus from China: Biosecurity Threat and Challenge for Healthcare Professionals"

Authors:
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Ljiljana Žmak
Rok Čivljak
Ivan Christian Kurolt
Vida Demarin

The symposium "New Coronavirus from China: Biosecurity Threat and Challenge for Health Care Professionals" was held at the Croatian Academy of Sciences and Arts, on February 14, 2020. In late 2019, a severe respiratory infection caused by SARS-CoV-2 started to spread rapidly, resulting in high morbidity and mortality rates in Wuhan, China, and continued to spread even faster worldwide, causing immeasurable health and economic challenges.

The goal of this symposium, organized by the Croatian Society for Biosafety and Biosecurity in cooperation with the Croatian Academy of Sciences and Arts and the University Hospital for Infectious Diseases "Dr. Fran Mihaljević", Zagreb, was to gather a large number of experts in the field of biosafety, infectious diseases, microbiology, epidemiology, molecular biology, as well as other health experts to discuss current possibilities in the treatment, diagnosis and prevention of the Coronavirus disease 2019 (COVID-19).

Due to the exceptional interest in the symposium, it was organised simultaneously in the large hall of the Croatian Academy of Sciences and Arts and the Library of the Croatian Academy of Sciences and Arts, which were linked by a video link. However, the interest in the symposium exceeded the capacity of these two conference rooms, thus the entire symposium was broadcasted live on YouTube. The symposium was also recorded, which enabled future watching both on YouTube and on the websites of the Croatian Society for Biosafety and Biosecurity, the Croatian Academy of Sciences and Arts and the University Hospital for Infectious Diseases "Dr. Fran Mihaljević".

Speeches at the symposium were held by leading exprets in the field. First, the director of the University Hospital for Infectious Diseases "Dr. Fran Mihaljević ", professor Alemka Markotić reminded the participants of the causes and consequences of previous dangerous infectious diseases epidemics and pandemics, from plague in the Middle Ages to Ebola in the 21th century. Academician Josip Madić spoke about coronaviruses in veterinary medicine, while professor Antoinette Kaić Rak, Head of the World Health Organization Office in the Republic of Croatia, spoke about the new coronavirus as a global threat.

The Minister of Health, Vili Beroš, was also a speaker at the symposium, reporting on the results of the meeting of the Ministers of Health of the European Union countries held on February 13 in Brussels. Professor Beroš convened the meeting as minister of health, as Croatia is currently holding the presidency of the Council of the European Union. The main goal of the meeting was to ensure better coordination of measures to combat the threat of coronavirus spread. The meeting pointed out possible issues in the procurement of medicines and medical equipment from China. Minister Beroš expressed satisfaction that such a meeting was organized in a short time, emphasizing that it is a success of Croatian diplomacy.

Bernard Kaić, MD, PhD, Head of the Infectious Diseases Epidemiology Service at the Croatian Institute of Public Health presented the epidemiological features of the recent coronaviruses causing-severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS) and the new coronavirus, SARS-CoV-2. The clinical features of the COVID-19 were described by assistant professor Rok Čivljak, Deputy Director of the University Hospital for Infectious Diseases "Dr. Fran Mihaljević". Assistant professor Marko Kutleša, Head of the Department of Intensive Care Medicine and Neuroinfectology, at the University Hospital for Infectious Diseases "Dr. Fran Mihaljević" covered the treatment of patients with severe respiratory infections admitted in the intensive care unit. Ivan Christian Kurolt, PhD from the University Hospital for Infectious Diseases "Dr. Fran Mihaljević", who established positive reverse transcriptase quantitative polymerase chain reaction (RT-qPCR) nucleic acid test for SARS CoV-2 in late January, and head of the Biosafety Level-3 (BSL-3) laboratory gave a speech about the molecular diagnosis of the new coronaviruseDr. Kurolt.

The first case of COVID-19 in Croatia was confirmed on February 25. Over the next two weeks, sporadic COVID-19 cases were reported, after which the number of new cases recorded per day gradually increased. Measures taken to limit and prevent the spread of SARS-CoV-2, prompt diagnosis and treatment of COVID-19 patients, have ranked Croatia among the world's top countries that have so far successfully fought this dangerous pandemic.

Etiologija

即时 准与消费支出挂钩比例 ▪消费提示：直播购物成为新型投诉热点 ▪浙江成立人才小贷公 客户端 搜索 频道 下一篇 春运大幕明将开启 回家路上新...

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专家称系新型冠状病毒 武汉不明原因的病毒性肺炎疫情病原学鉴定取得初步进展

2020-01-09 09:45:59 来源：新华网

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新华社北京1月9日电（记者屈婷）日前，就武汉不明原因的病毒性肺炎疫情病原学鉴定进展问题，记者采访了病原检测结果初步评估专家组组长、中国工程院院士徐建国。他表示，专家组认为，本次不明原因的病毒性肺炎病例的病原体初步判定为新型冠状病毒。

问题一：目前，武汉不明原因的病毒性肺炎疫情病原学鉴定有什么进展？

徐建国：截至2020年1月7日21时，实验室检出一种新型冠状病毒，获得该病毒的全基因组序列，经核酸检测方法共检出新型冠状病毒阳性结果15例，从1例阳性病人样本中分离出该病毒，电镜下呈现典型的冠状病毒形态。

On 31 December 2019, the Wuhan Municipal Health Commission in Wuhan City, Hubei province, China, reported a cluster of pneumonia cases (including seven severe cases) of unknown aetiology, with a common reported link to Wuhan's Huanan Seafood Wholesale Market, a wholesale fish and live animal market.

On 9 January 2020, China's CDC reported that a novel coronavirus (later named SARS-CoV-2, the virus causing COVID-19) had been detected as the causative agent for 15 of the 59 cases of pneumonia

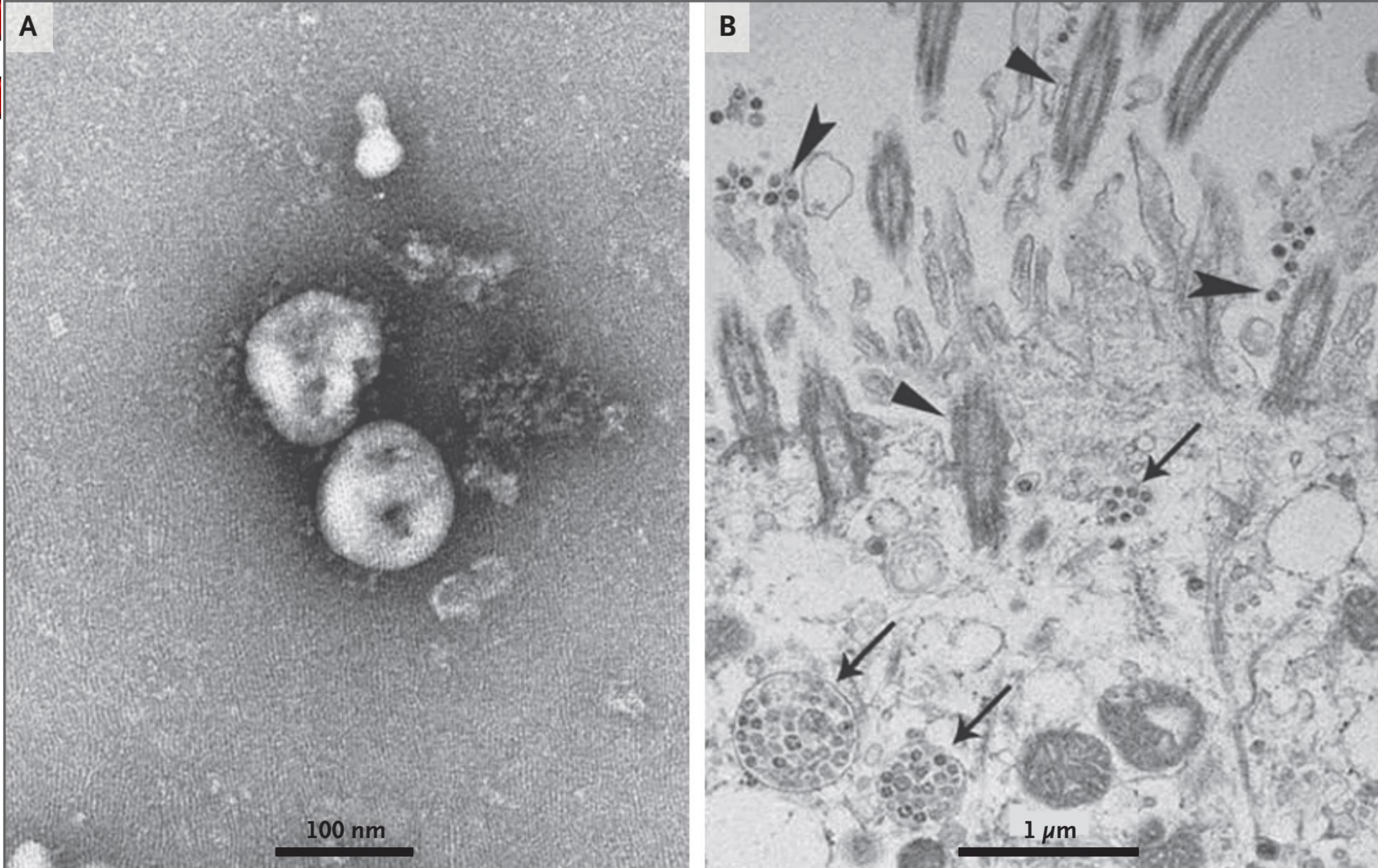


Figure 3. Visualization of 2019-nCoV with Transmission Electron Microscopy.

Negative-stained 2019-nCoV particles are shown in Panel A, and 2019-nCoV particles in the human airway epithelial cell ultrathin sections are shown in Panel B. Arrowheads indicate extracellular virus particles, arrows indicate inclusion bodies formed by virus components, and triangles indicate cilia.

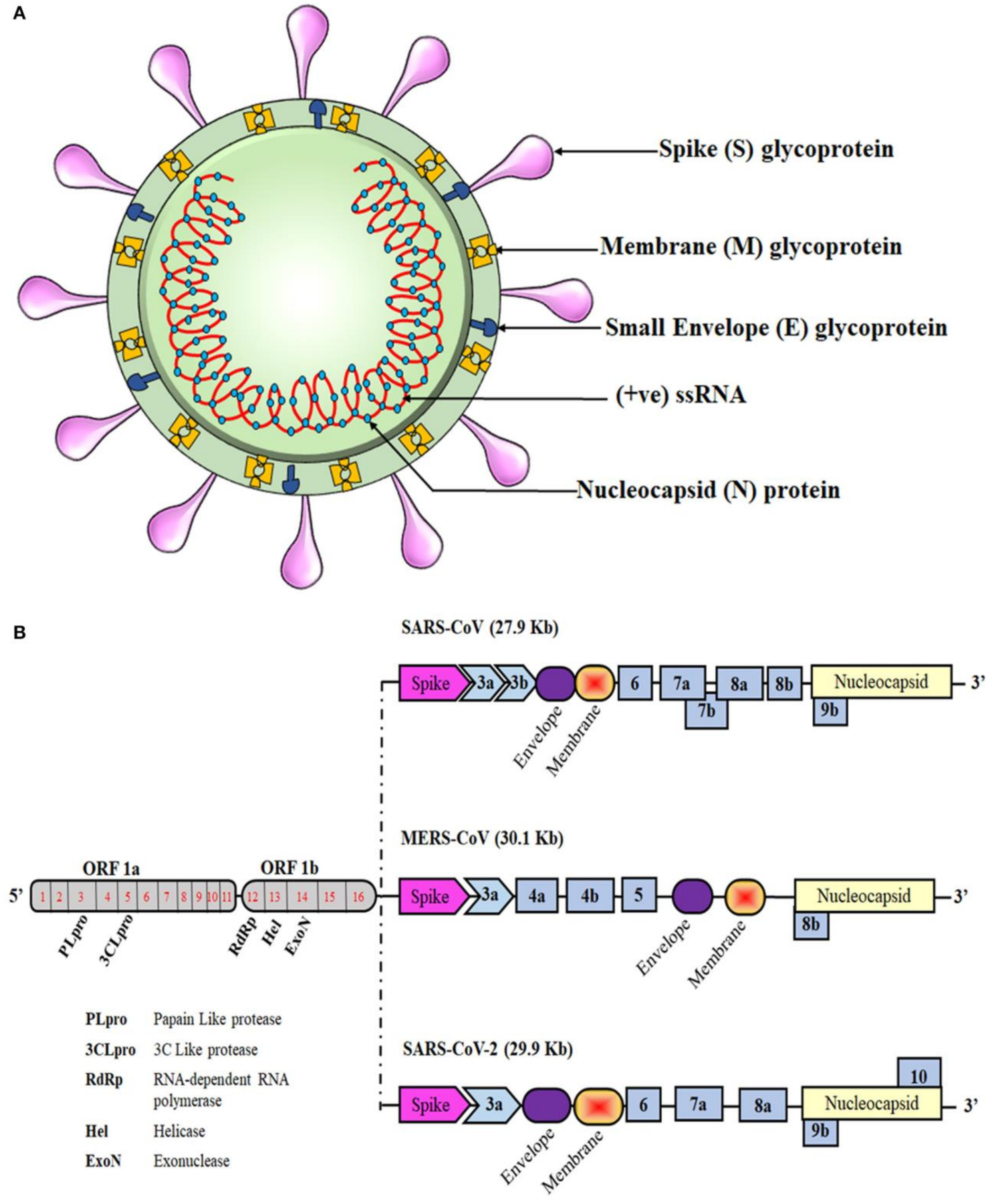


FIGURE 1 | Schematic representation of the coronavirus structure and genomic comparison of coronaviruses. **(A)** Representation of coronavirus showing different components of the particle, which is 100–160 nm in diameter. The single-stranded RNA (ssRNA) genome, covered with the envelope and membrane proteins, gains access into the host cell and hijacks the replication machinery. **(B)** The ssRNA of SARS-CoV-2 is about 30 kb and has similarities with the genomes of SARS-CoV and MERS-CoV. Translation of this ssRNA results in the formation of two polyproteins, namely pp1a and pp1ab, that are further sliced to generate numerous non-structural proteins (NSPs). The remaining ORFs encode for various structural and accessory proteins that help in assembly of the viral particle and evading immune response.

Citation:

Shah VK, Firmal P, Alam A, Ganguly D and Chattopadhyay S (2020) Overview of Immune Response During SARS-CoV-2 Infection: Lessons From the Past. Front. Immunol. 11:1949. doi: 10.3389/fimmu.2020.01949

Epidemiologija

On 9 January 2020, ECDC published a Threat Assessment Brief on the cluster of pneumonia possibly associated with a novel coronavirus in Wuhan, China.
On 17 January 2020, ECDC published its first risk assessment on the novel coronavirus.
By 20 January 2020, there were reports of **confirmed cases from three countries outside China: Thailand, Japan and South Korea** [4]. These cases had all been exported from China.
On 23 January 2020, Wuhan City was **locked down** – with all travel in and out of Wuhan prohibited – and movement inside the city was restricted [5].
On 24 January 2020, the first European case was reported in France. This case had a travel history to China [6].

REPUBLIKA HRVATSKA
Ministarstvo
zdravstva

Naslovnica > Vijesti > Prvi oboljeli od koronavirusa u Hrvatskoj je stabilno, ima blage simptome i nalazi se pod nadzorom >

Objavljeno: 25.02.2020.

Prvi oboljeli od koronavirusa u Hrvatskoj je stabilno, ima blage simptome i nalazi se pod nadzorom

U banskim dvorima održan je danas sastanak Nacionalnog stožera za civilnu zaštitu. Nakon sastanka, predsjednik Vlade Andrej Plenković je na konferenciji za medije izvijestio da je u Hrvatskoj potvrđen prvi slučaj pacijenta oboljelog od koronavirusa.

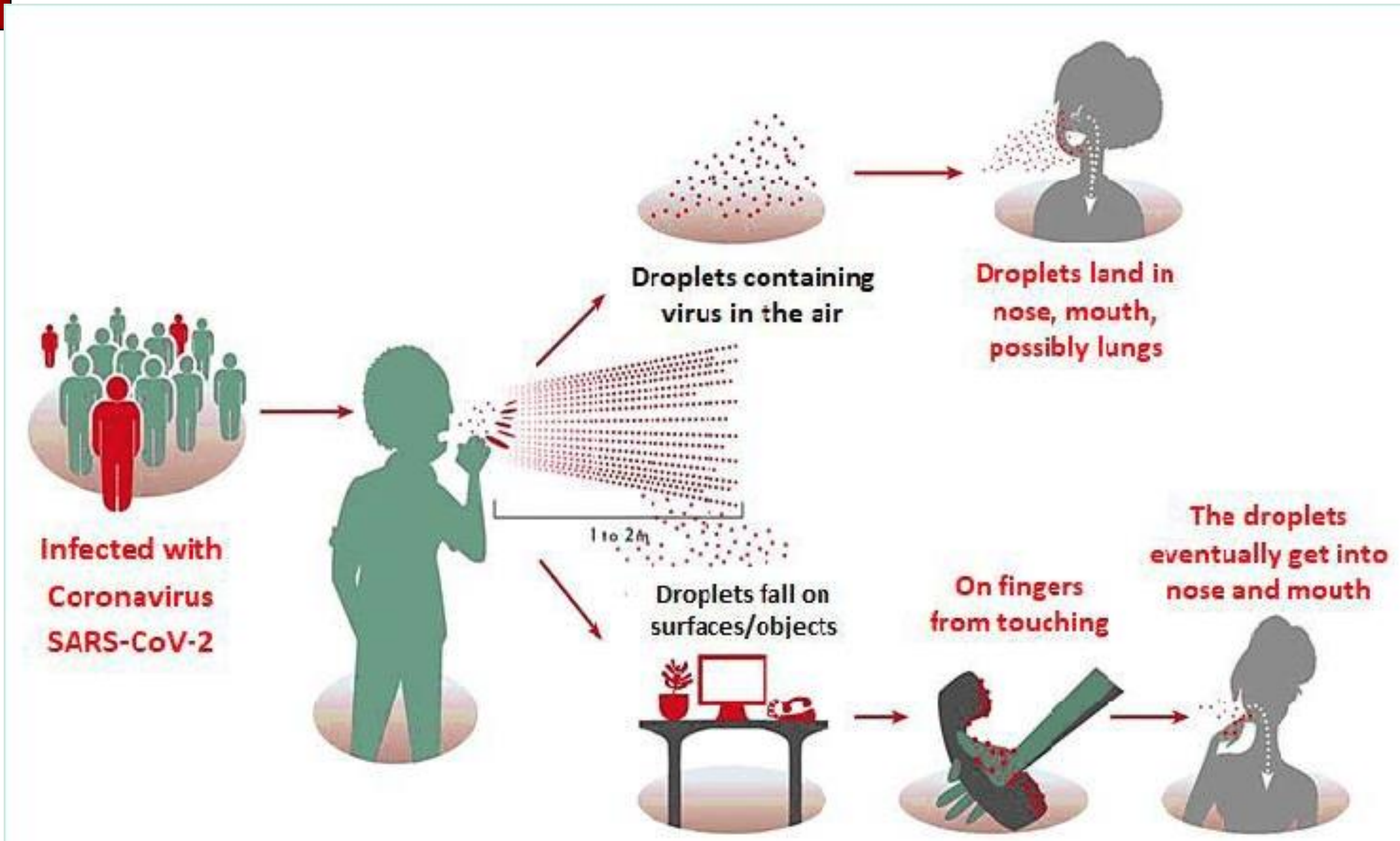
„Novost koju smo dobili tijekom sastanka stožera je da imamo prvog pacijenta kojem je potvrđen koronavirus. Pacijent se nalazi u Zagrebu u Klinici za infektivne bolesti „Dr. Fran Mihaljević“. Riječ je o mlađem čovjeku, ima blaži oblik bolesti, izoliran je i njegovo stanje je zasad dobro“, kazao je predsjednik Vlade.

Plenković je rekao da će se Nacionalni stožer za civilnu zaštitu – kojeg će voditi potpredsjednik Vlade i ministar unutarnjih poslova Davor Božinović – sastajati koliko bude potrebno kako bi koordinirao sve aktivnosti.

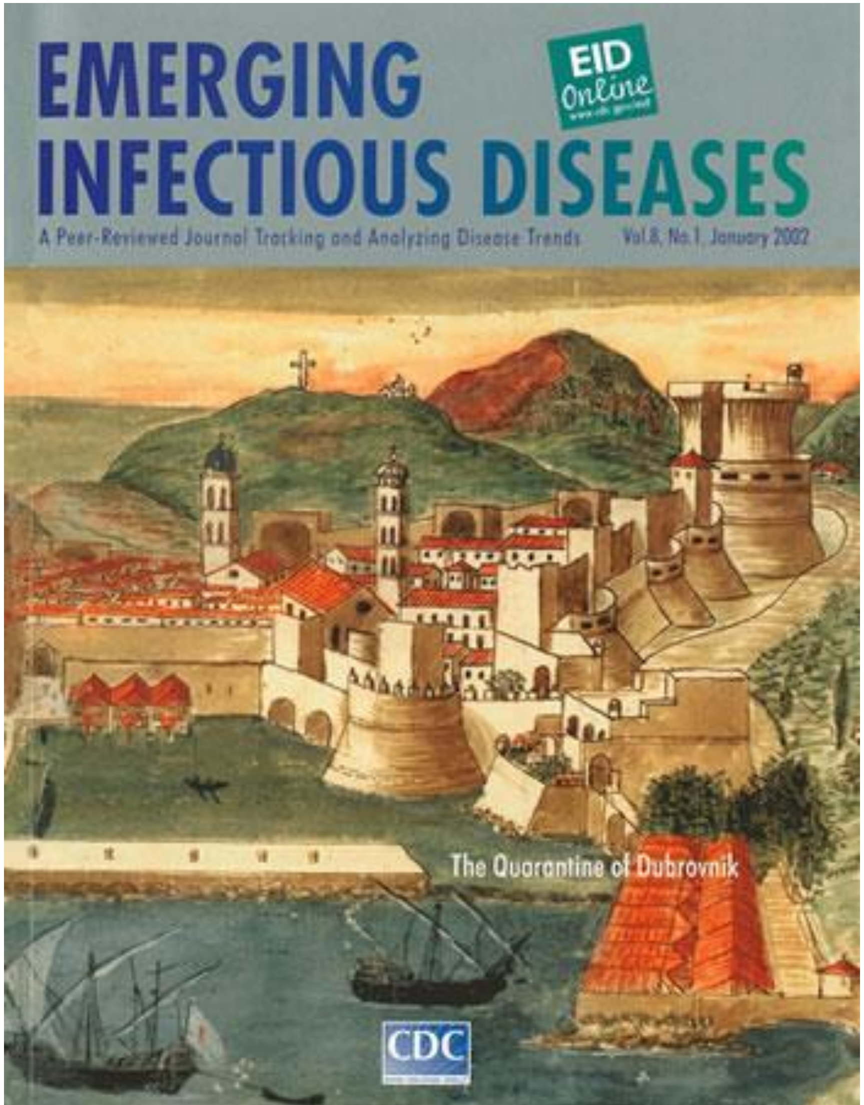
Najavio je da će potpredsjednik Vlade Božinović u srijedu sazvati načelnike županijskih stožera civilne zaštite, kako bi se i oni uključili u sve aktivnosti vezane za prevenciju širenja koronavirusa.

„S obzirom na događanja u Italiji, osigurat ćemo da sve nadležne službe – od Ministarstva zdravstva, Ministarstva unutarnjih poslova, Državnog inspektorata, svih nadležnih tijela, osobito epidemioloških – budu u punoj pripravnosti i budu aktivni u sprječavanju širenja koronavirusa“, kazao je.

Sve nadležne službe maksimalno angažirane



https://www.researchgate.net/figure/COVID-19-Transmission-and-infection_fig2_340384913



XIV.

PESTE

LIBRO VERDE

Cap. IL.

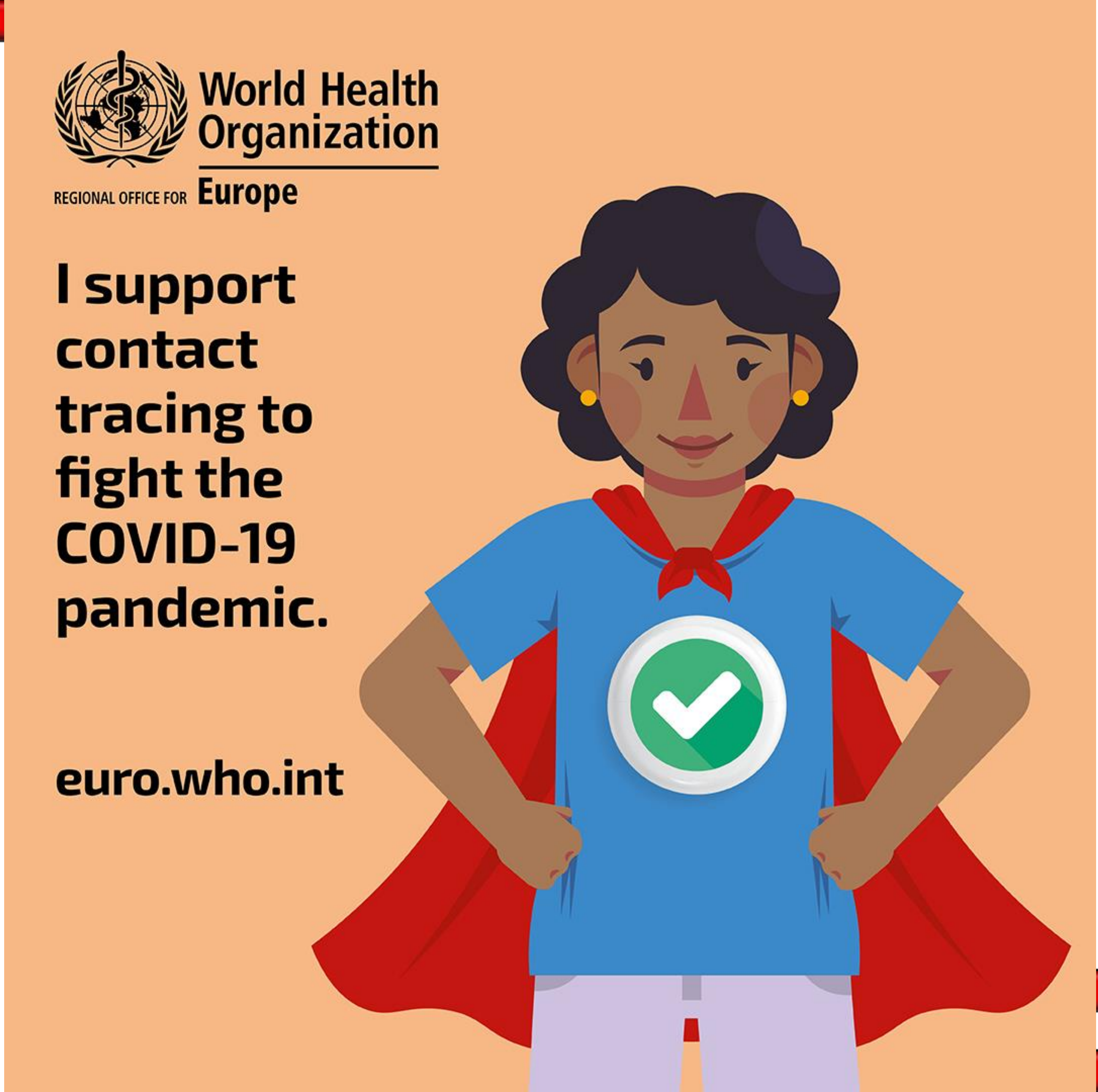
Veniens de locis pestiferis non intret Racusium vel districtum.

1. A. D. 1377 die 27 Julii in Consilio Maiori . . . . ecc. Consil. 67. captum p. 34 quod tam nostrates quam advenae venientes de locis pestiferis non recipiantur in Racusium, nec ad eius districtum, nisi steterint prius ad purgandum se in *Mercana* seu in *Civitate veteri* per unum mensem.
2. Item per consiliarios 44 eiusdem consilii captum fuit: quod nulla persona de Ragusio, vel suo districtu, audeat vel praesumat ire ad illos qui venient de locis pestiferis et **stabunt in Mercana,** vel civitate veteri
3. sub poena standi ibidem per unum mensem;
4. et qui portabunt illis de victualibus, seu de alis necessariis, non possint ire ad illos sine licentia officialium ad hoc ordinandorum cum ordine ab ipsis officialibus eis dando
5. sub dicta poena standi ibidem per unum mensem.
6. Item per consiliarios 29 . . . . captum fuit et firmatum, quod quicumque non observaverit praedicta . . . . solvere debeat de poena ipp. 50, et nihilominus praedicta teneatur observare.

MJERE!

Dezinfekcija

Martinje


World Health Organization
REGIONAL OFFICE FOR Europe
I support contact tracing to fight the COVID-19 pandemic.
euro.who.int

Exposome-based public health interventions for infectious diseases in urban settings

Xanthi D. Andrianou [a,b], Anjoeka Pronk [c], Karen S. Galea [d], Rob Stierum [c], Miranda Loh [d], Flavia Riccardo [b], Patrizio Pezzotti [b], Konstantinos C. Makris [a,*]

[a] *Cyprus International Institute for Environmental and Public Health, Cyprus University of Technology, Limassol, Cyprus*
[b] *Department of Infectious Diseases, Italian National Institute of Health, Rome, Italy*
[c] *The Netherlands Organisation for Applied Scientific Research TNO, Utrecht, the Netherlands*
[d] *Institute of Occupational Medicine (IOM), Edinburgh, UK*

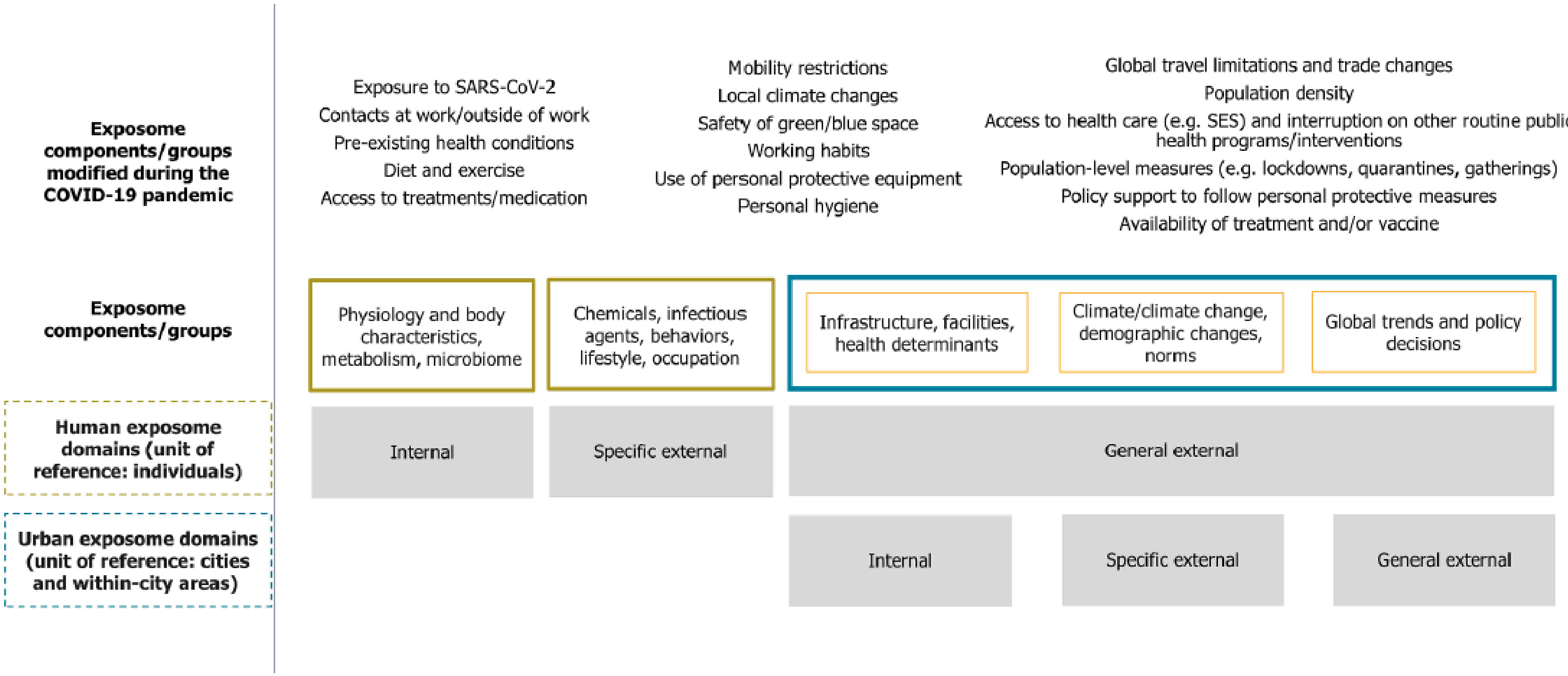


Fig. 1. Schematic of urban exposome and human exposome domains and examples of relevant exposome components and their groups that were modified due to COVID-19 pandemic.

Table 1
Examples of public health response measures and non – pharmacological interventions used to contain and mitigate COVID-19, using the exposome concept, its domains and related tools. Their field deployment could be part of health prevention and promotion efforts, as well. Their application could take place either at baseline, during, and/or after a pandemic crisis, or periodically.

		Enhanced contact tracing	Quarantine and isolation	Use of personal protective equipment and personal hygiene	Closure of facilities (e. g. schools, universities, green/ blue space)	Physical distancing and confinement (lockdowns)
Exposome domainsinvolved (i. e. internal, specific and general external)	Urban exposome	Internal: e.g. intra- and inter-city disease clusters	Internal and specific external: e.g. facilities for quarantine and isolation and services for those in quarantine or isolation	Internal and external: e.g. intra-urban variable availability of equipment, procurement and budget availability at national or global level	Internal: e.g. impact on learning opportunities, maintenance of closed facilities, city income due to decreased use of facilities	Internal, general and specific external domains: e. g. intra-urban impacts due to infrastructure/facilities/ services capacity, mobility and availability of goods
	Human exposome	Specific external: e.g. individuals affected depending on their habits/lifestyle/ contacts	Internal: e.g. lifestyle and habits modified, as well as routine exposures	Internal and specific external: e.g. use of equipment might lead to differential exposure to infectious diseases or chemicals, as well as change in behaviors/habits	Internal and specific external: e.g. limiting access to facilities leads to increased time indoors and decreased time outdoors	Internal, and general externalor specific external: e.g. adhering to physical distancing rules might add on mental health burden, if services become unavailable, personal and group plans to be adjusted
Intervention outcomes		Allow timely intervention in case of infection	Reduce risk of transmission	Reduce individual risk of infection and prevent transmission	Reduce risk of transmission and protect vulnerable groups (i.e. children) and those coming to contact with them	Reduce risk of transmission/ infection
Resolution ("unit") of analysis		Individuals	Individuals/groups	Individuals and groups based on occupation (e.g. essential workers)	Individual, small area (e. g. neighborhood), group (e.g. specific age groups)	Individual, small area, city
Study Designs		Surveys, network analysis		Surveys, trials, qualitative studies	Trials, cohorts/cross-sectional studies, surveys, qualitative studies	Trials, surveys, qualitative studies
Primary sample/data collection		Questionnaires, geocoded data travel/ contacts history		Questionnaires, interviews	Questionnaire, policy analysis	
Secondary data collection		Routine contact tracing and surveillance	Surveillance, geo-tracking data from devices/software	Procurement/orders/ imports/manufacturing of equipment, records of entities, distribution of consumables (e.g. hospitals, schools)	Surveillance, other routinely collected information about use of facilities (e.g. school/ university buildings)	Routine surveillance
Tools (assigned to public health measures/intervention)		E-data collection, interviews or mixed methods data collection, sensors, biomonitoring, molecular biomarkers of exposure and effect, advanced biostatistical models				
					Crowdsourcing, community/citizen science and social media	
		Open governmental data and infrastructure databases and/or policy documents				

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Molecular epidemiology of the first wave of severe acute respiratory syndrome coronavirus 2 infection in Thailand in 2020

Jiratchaya Puenpa[1,6], Kamol Suwannakarn[2,6], Jira Chansaenroj[1], Pornjarim Nilyanimit[1], Ritthideach Yorsaeng[1], Chompoonut Auphimai[1], Rungrueng Kitphati[3], Anek Mungaomklang[3], Amornmas Kongklieng[3], Chintana Chirathaworn[4], Nasamon Wanlapakorn[1,5] & Yong Poovorawan[1]✉

The coronavirus disease 2019 pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a major global concern. Several SARS-CoV-2 gene mutations have been reported. In the current study associations between SARS-CoV-2 gene variation and exposure history during the first wave of the outbreak in Thailand between January and May 2020 were investigated. Forty samples were collected at different time points during the outbreak, and parts of the SARS-CoV-2 genome sequence were used to assess genomic variation patterns. The phylogenetics of the 40 samples were clustered into L, GH, GR, O and T types. T types were predominant in Bangkok during the first local outbreak centered at a boxing stadium and entertainment venues in March 2020. Imported cases were infected with various types, including L, GH, GR and O. In southern Thailand introductions of different genotypes were identified at different times. No clinical parameters were significantly associated with differences in genotype. The results indicated local transmission (type T, Spike protein (A829T)) and imported cases (types L, GH, GR and O) during the first wave in Thailand. Genetic and epidemiological data may contribute to national policy formulation, transmission tracking and the implementation of measures to control viral spread.

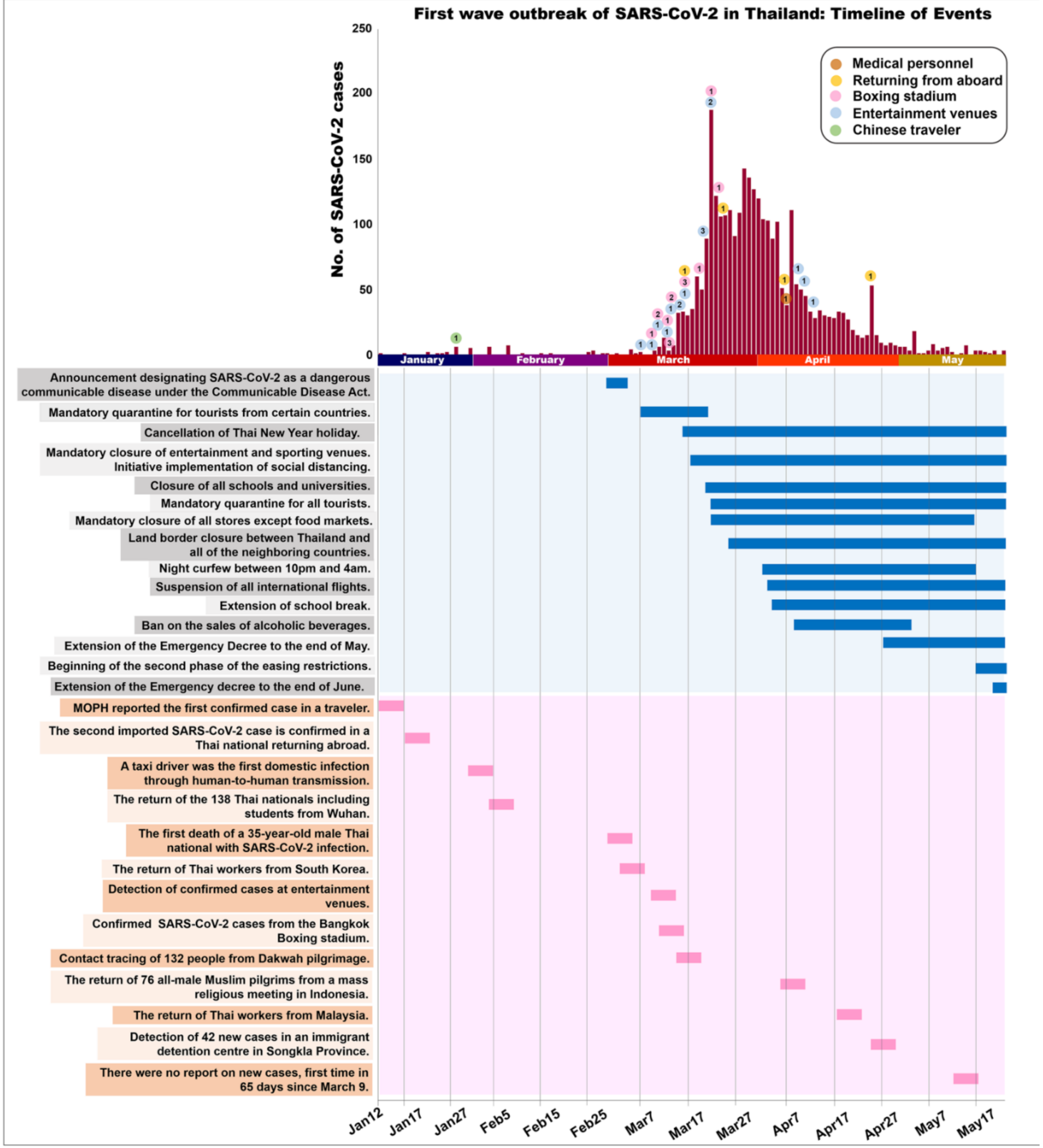
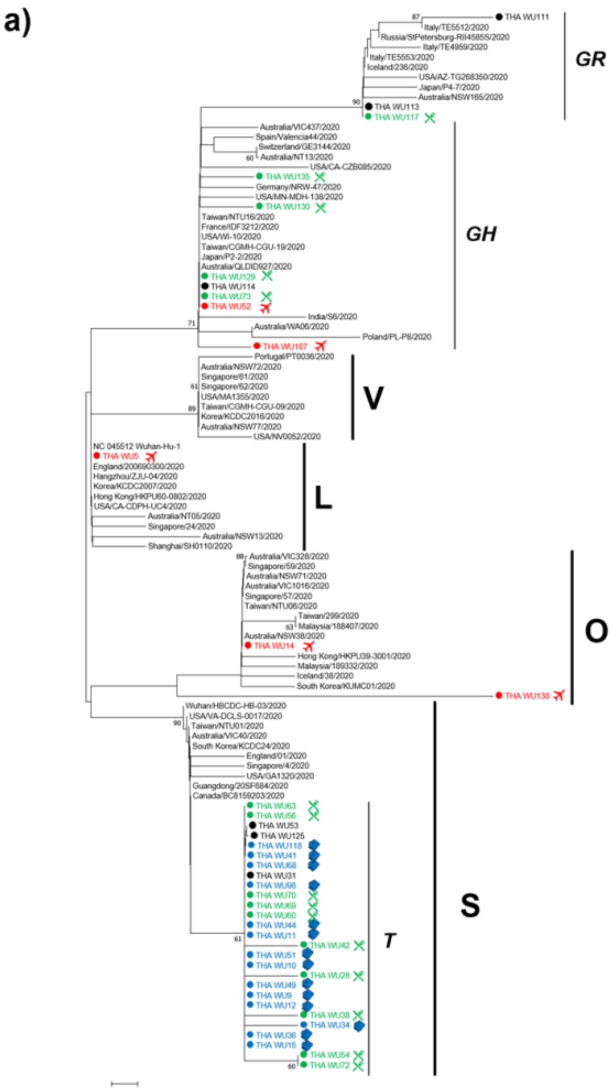


Figure 1. The first wave of SARS-CoV-2 outbreak in Thailand: Timeline of Events and the number of specimens.

a)



b)

Type	ORF1a	ORF1b			S			ORF3a	ORF8	ORF9b	ORF14
	Nucleotide positions										
	8782	13730	14408	14805	23403	23929	24047	26144	28144	28311	2881-3
L	C	C	C	C	A	C	G	G	T	C	GGG
S	T	C	C	C	A	C	G	G	C	C	GGG
GH	C	C	T	C	G	C	G	G	T	C	GGG
GR	C	C	T	C	G	C	G	G	T	C	AAC
V	C	C	C	T	A	C	G	T	T	C	GGG
T	T	C	C	C	A	C	A	G	C	C	GGG
O	C	T	C	C	A	T	G	G	T	T	GGG

Figure 2. Type of viral variations with exposure history. (**a**) Phylogenetic tree of concatenated sequences, including partial ORF1ab (nucleotide position 8,596–8,927 and 13,259–16,269), S (nucleotide position 21,320–25,541), ORF3a to E (nucleotide position 25,902–26,549), and ORF9b to ORF10 (nucleotide position 28,101–29,682). The phylogenetic tree was generated by the neighbor-joining method with 1,000 bootstrap replicates. Branch values > 60 were indicated. The blanket showed the five main types. Dots and colors precede the sequences isolated in this study with different risks of exposure. b) The pattern of nucleotide substitution change and type of SARS-CoV-2.

pathogens

MDPI

Article

Molecular Epidemiology Surveillance of SARS-CoV-2: Mutations and Genetic Diversity One Year after Emerging

Alejandro Flores-Alanis [1], Armando Cruz-Rangel [2], Flor Rodríguez-Gómez [3], James González [4], Carlos Alberto Torres-Guerrero [5], Gabriela Delgado [1], Alejandro Cravioto [1] and Rosario Morales-Espinosa [1,*]

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* Correspondence: marosari@unam.mx

Abstract: In December 2019, the first cases of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) were identified in the city of Wuhan, China. Since then, it has spread worldwide with new mutations being reported. The aim of the present study was to monitor the changes in genetic diversity and track non-synonymous substitutions (*dN*) that could be implicated in the fitness of SARS-CoV-2 and its spread in different regions between December 2019 and November 2020. We analyzed 2213 complete genomes from six geographical regions worldwide, which were downloaded from GenBank and GISAID databases. Although SARS-CoV-2 presented low genetic diversity, there has been an increase over time, with the presence of several hotspot mutations throughout its genome. We identified seven frequent mutations that resulted in *dN* substitutions. Two of them, C14408T>P323L and A23403G>D614G, located in the nsp12 and Spike protein, respectively, emerged early in the pandemic and showed a considerable increase in frequency over time. Two other mutations, A1163T>I120F in nsp2 and G22992A>S477N in the Spike protein, emerged recently and have spread in Oceania and Europe. There were associations of P323L, D614G, R203K and G204R substitutions with disease severity. Continuous molecular surveillance of SARS-CoV-2 will be necessary to detect and describe the transmission dynamics of new variants of the virus with clinical relevance. This information is important to improve programs to control the virus.

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Citation: Flores-Alanis, A.; Cruz-Rangel, A.; Rodríguez-Gómez, F.; González, J.; Torres-Guerrero, C.A.; Delgado, G.; Cravioto, A.; Morales-Espinosa, R. Molecular Epidemiology Surveillance of SARS-CoV-2: Mutations and Genetic Diversity One Year after Emerging. *Pathogens* **2021**, *10*, 184. https://doi.org/10.3390/pathogens10020184

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Received: 8 January 2021

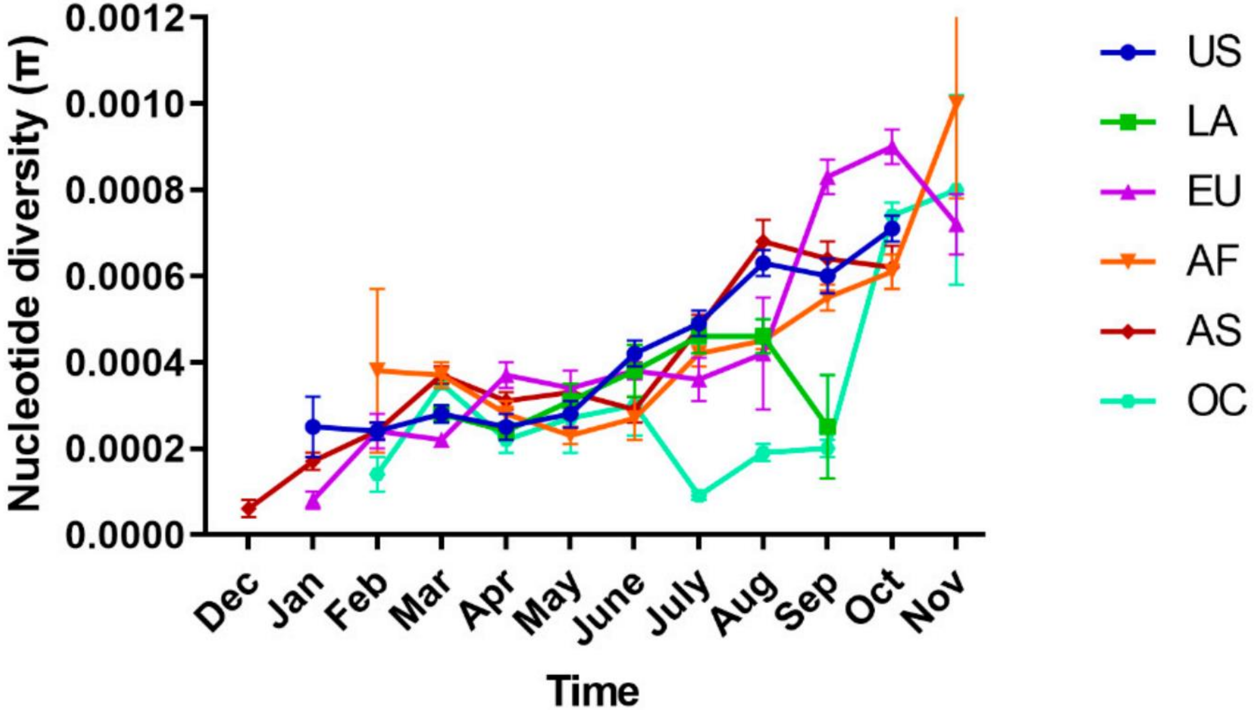

Figure 3. Temporal changes of SARS-Cov-2 nucleotide diversity (π) by region. Abbreviations: Dec, December; Jan, January, Feb, February, Mar, March; Apr, April; Aug, August; Sep, September; Oct, October; Nov, November. US, United States of America; LA, Latin America; EU, Europe; AF, Africa; AS, Asia; OC, Oceania.

Earthquake in the time of COVID-19: The story from Croatia (CroVID-20)

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Photo: During the earthquake in Zagreb on 22 March 2020, 86 patients, including 22 COVID-19 patients, were evacuated from the extensively damaged hospital buildings (authors' photo archive, used with permission).

Earthquake in the time of COVID-19: The story from Croatia (CroVID-20)

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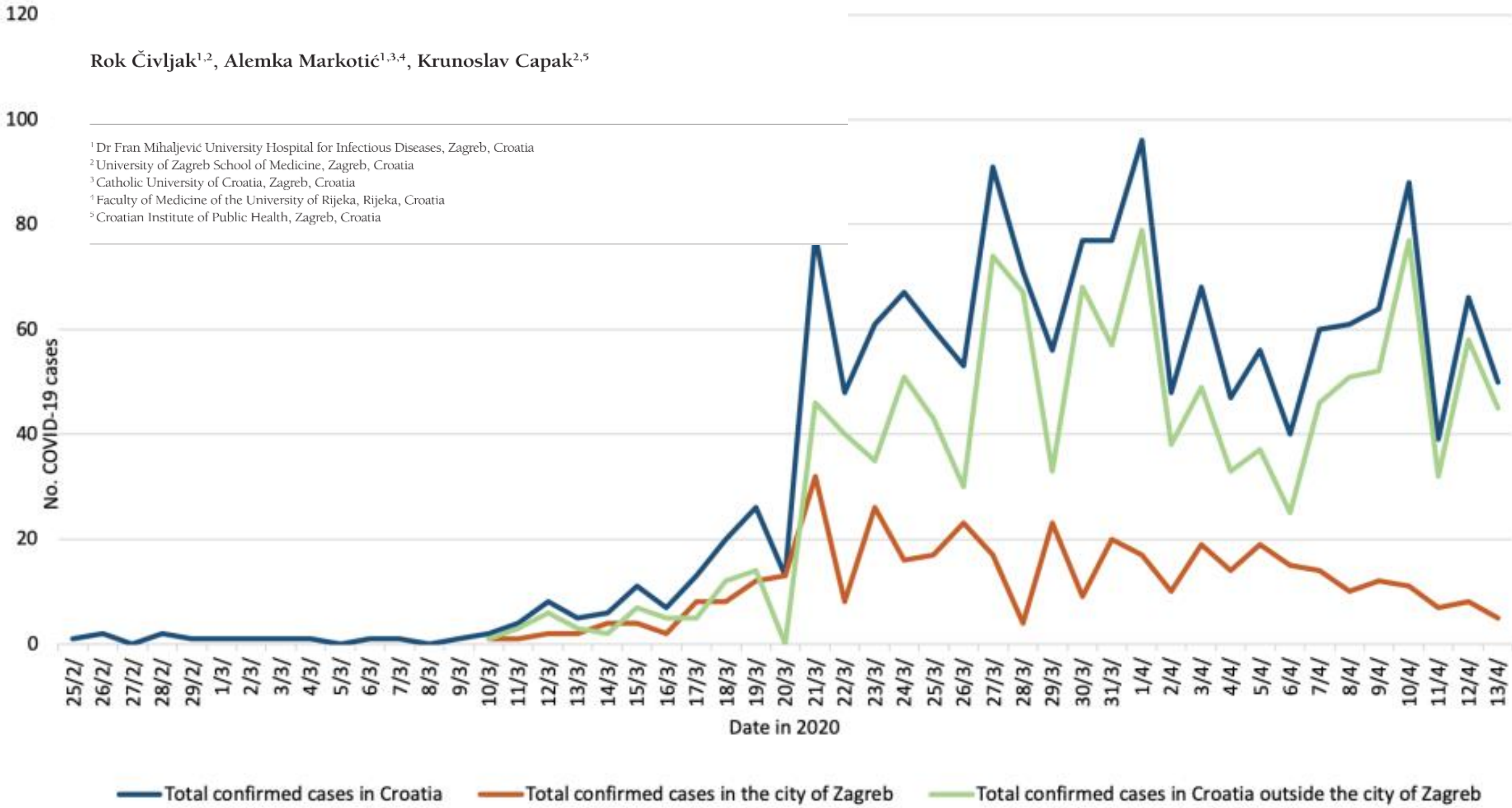

Figure 1. The number of confirmed COVID-19 cases in Croatia and the city of Zagreb six weeks since the first COVID-19 case and three weeks after the earthquake.

Dijagnostika

RESEARCH

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

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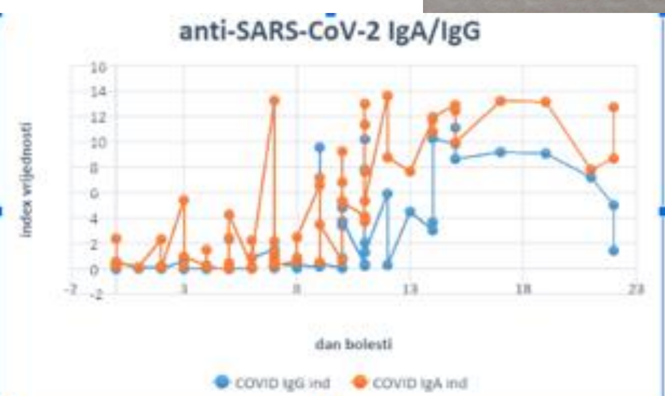
Article submitted on 21 Jan 2020 / accepted on 22 Jan 2020 / published on 23 Jan 2020


505
784
804
C
T
nCoV
360
260


anti-SARS-CoV-2 IgA/IgG
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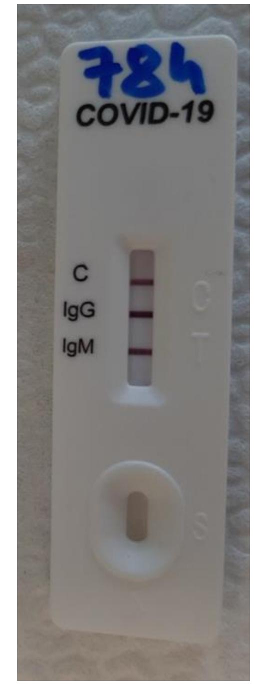
COVID IgA ind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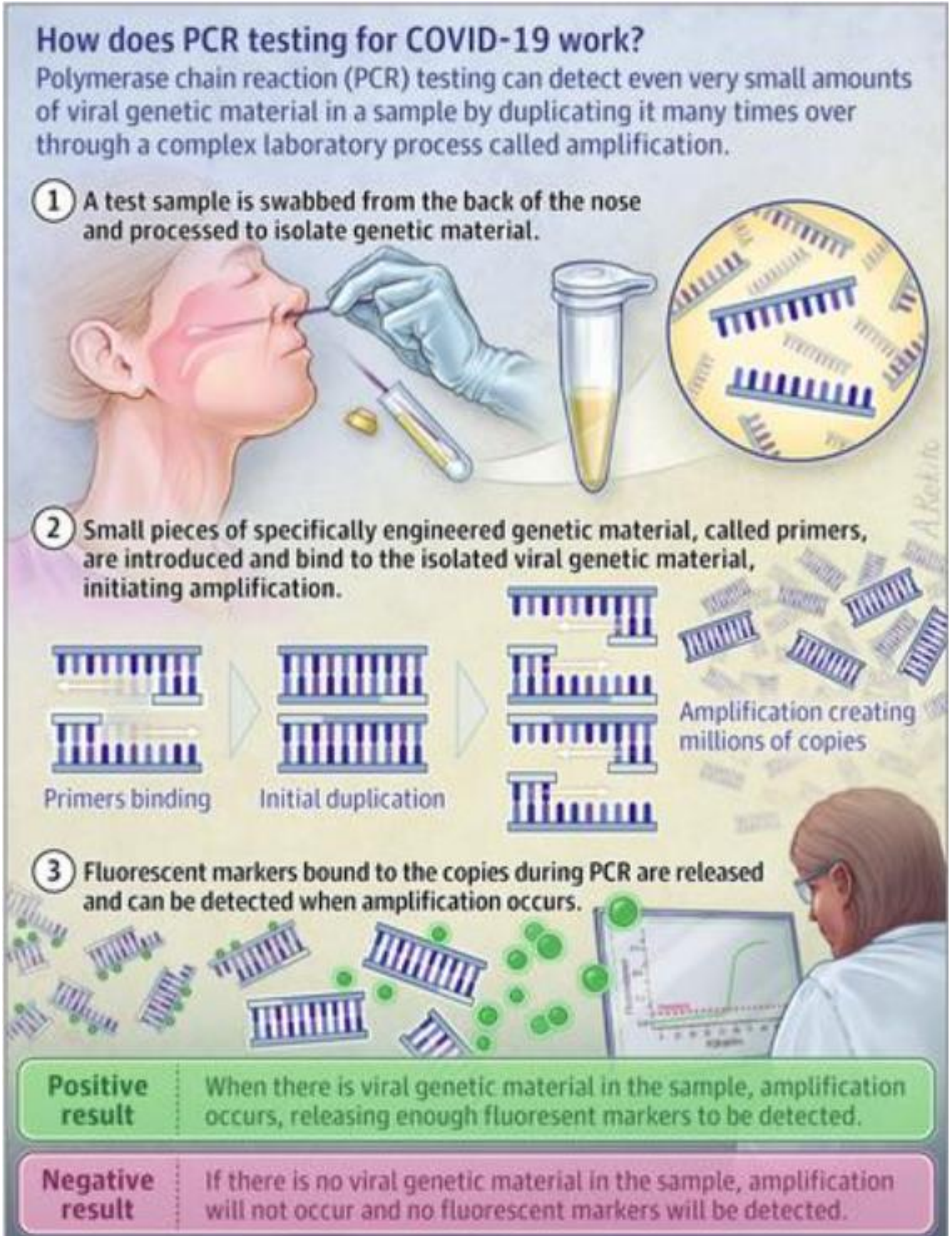
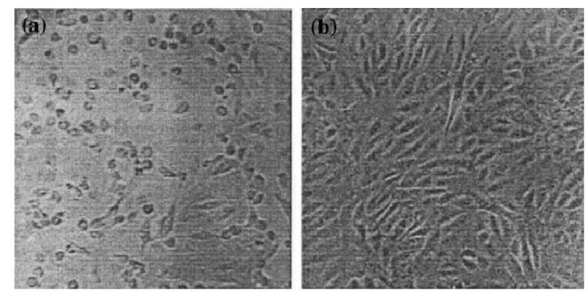

How does PCR testing for COVID-19 work?
Polymerase chain reaction (PCR) testing can detect even very small amounts of viral genetic material in a sample by duplicating it many times over through a complex laboratory process called amplification.
1 A test sample is swabbed from the back of the nose and processed to isolate genetic material.
2 Small pieces of specifically engineered genetic material, called primers, are introduced and bind to the isolated viral genetic material, initiating amplification.
Primers binding
Initial duplication
Amplification creating millions of copies
3 Fluorescent markers bound to the copies during PCR are released and can be detected when amplification occurs.
Positive result
When there is viral genetic material in the sample, amplification occurs, releasing enough fluoresent markers to be detected.
Negative result
If there is no viral genetic material in the sample, amplification will not occur and no fluorescent markers will be detected.

OVO JE ČOVJEK KOJI ĆE PRVI ZNATI JE LI KORONAVIRUS DOŠAO U HRVATSKU 'Sve možemo otkriti za najviše 8 sati'

AUTOR: Goranka Jureško OBJAVLJENO: 03.02.2020. u 16:30

Ivan Christian Kurolt

"We propagate and isolate the virus in laboratory conditions from the patient who was positive for SARS-COV-2," said a biologist at the Clinic for Infectious Diseases "Dr. Fran Mihaljevic"**dr.sc. Željka Mačak Šafranko**.



The isolated virus was sent to Germany

The isolated virus was sent to Germany at day after the earthquake that hit Zagreb. The office was completely destroyed. "To get an isolate from Croatia is very important to us because once we find that a substance can work against viruses, we have to prove that that substance doesn't just work against local viruses, but worldwide," said team leader at Helmholtz. Center for Infectious Research in Germany, **Luka Čičin-Šain.**


AJAX
Crystal Clean


3M

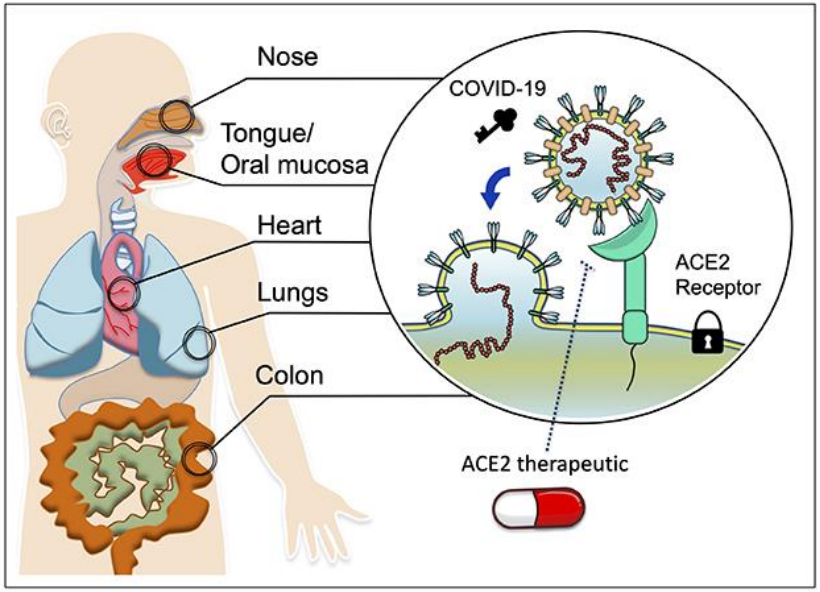
Klinička slika
Zarazna bolest s brojnim licima

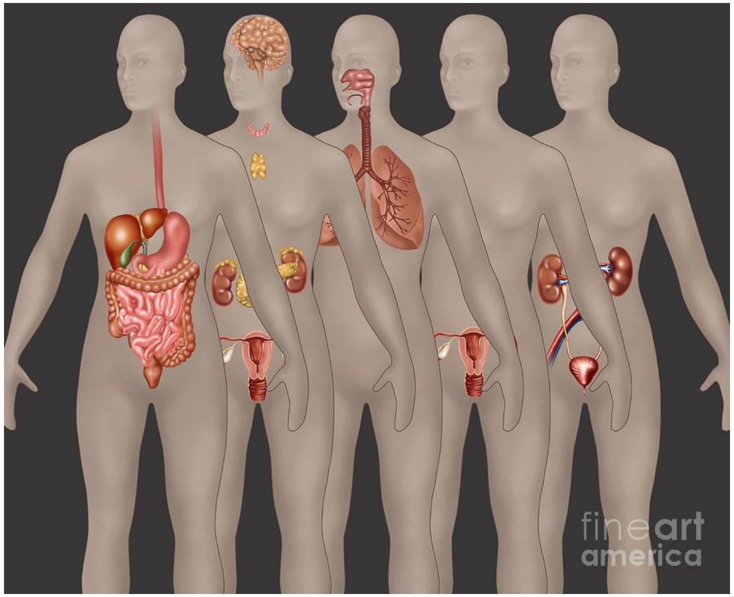
Asimptomatski

Blagi

Srednje teški

Teški





European Journal of Clinical Microbiology & Infectious Diseases
https://doi.org/10.1007/s10096-020-04019-y

ORIGINAL ARTICLE

Antibody response and the clinical presentation of patients with COVID-19 in Croatia: the importance of a two-step testing approach

Oktavija Đaković Rode [1,2] · Ivan-Christian Kurolt [1] · Ivan Puljiz [1,3] · Rok Čivljak [1,3] · Nataša Cetinić Balent [1] · Renata Laškaj [1] · Mirjana Kujundžić Tiljak [3,4] · Radojka Mikulić [1] · Alemka Markotić [1,5,6]

Received: 26 June 2020 / Accepted: 24 August 2020
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Abstract

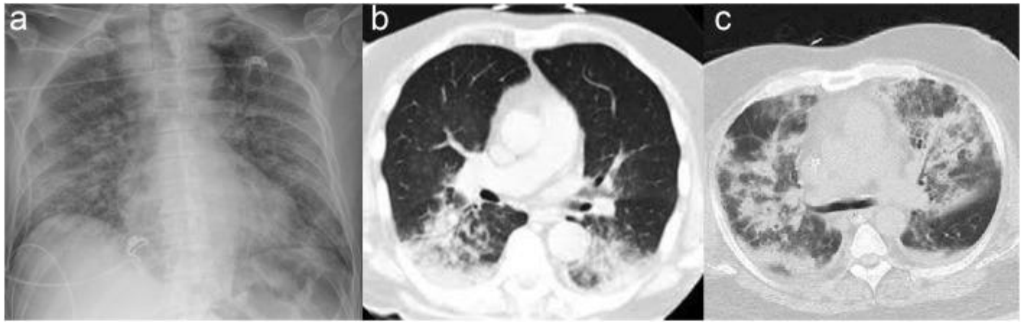
According to anti-SARS-CoV-2 seroresponse in patients with COVID-19 from Croatia, we emphasised the issue of different serological tests and need for combining diagnostic methods for COVID-19 diagnosis. Anti-SARS-CoV-2 IgA and IgG ELISA and IgM/IgG immunochromatographic assay (ICA) were used for testing 60 sera from 21 patients (6 with severe, 10 moderate, and 5 with mild disease). The main clinical, demographic, and haemato-biochemical data were analysed. The most common symptoms were cough (95.2%), fever (90.5%), and fatigue and shortness of breath (42.9%). Pulmonary opacities showed 76.2% of patients. Within the first 7 days of illness, seropositivity for ELISA IgA and IgG was 42.9% and 7.1%, and for ICA IgM and IgG 25% and 10.7%, respectively. From day 8 after onset, ELISA IgA and IgG seropositivity was 90.6% and 68.8%, and for ICA IgM and IgG 84.4% and 75%, respectively. In general, sensitivity for ELISA IgA and IgG was 68.3% and 40%, and for ICA IgM and IgG 56.7% and 45.0%, respectively. The anti-SARS-CoV-2 antibody distributions by each method were statistically different (ICA IgM vs. IgG, $p = 0.016$; ELISA IgG vs. IgA, $p < 0.001$). Antibody response in COVID-19 varies and depends on the time the serum is taken, on the severity of disease, and on the type of test used. IgM and IgA antibodies as early-stage disease markers are comparable, although they cannot replace each other. Simultaneous IgM/IgG/IgA anti-SARS-CoV-2 antibody testing followed by the confirmation of positive findings with another test in a two-tier testing is recommended.

Keywords COVID-19 diagnostics · Clinical and laboratory findings · Anti-SARS-CoV-2 antibody response · Serological methods · Two-step testing approach · Croatia

Clinical Presentation of Covid-19

Asyntomatic Infection	Absence of clinical signs and symptoms of the disease and normal chest X-ray or CT scan associated with a positive test for SARS-CoV-2
Mild Infection	Upper airway symptoms such as fever, fatigue, myalgia, cough, sore throat, runny nose and sneezing. Pulmonary clinical exam is normal. Some cases may not have fever and others may experience gastrintestinal symptoms such as nauseas, vomiting, abdominal pain, and diarrhea.
Moderate Infection	Clinical signs of pneumonia. Persistent fever, initially dry cough, which becomes productive, may have wheezing or crackles on pulmonary auscultation but shows no respiratory distress. Some individuals may not have symptoms or clinical signs, but chest CT scan reveals typical pulmonary lesions.
Severe Infection	Initial respiratory symptoms may be associated with gastrointestinal symptoms such as diarrhea. The clinical deterioration usually occurs in a week with the development of dyspnea and hypoxemia (blood oxygen saturation [SaO_2] <94%)
Critical Infection	Patients can quickly deteriorate to acute respiratory distress syndrome or respiratory failure and may present shock, encephalopathy, myocardial injury or heart failure, coagulopathy, acute kidney injury, and multiple organ dysfunction.

AKUTNI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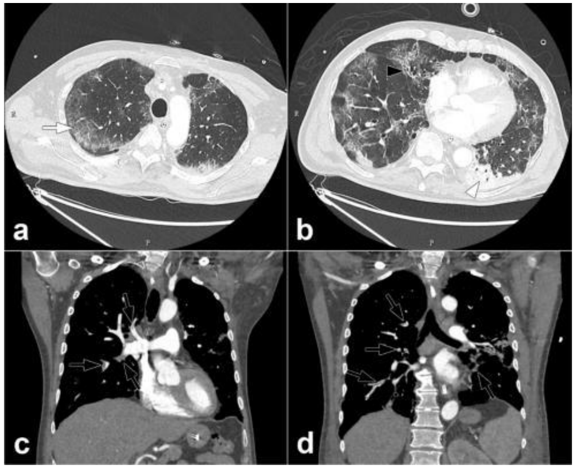
a
b
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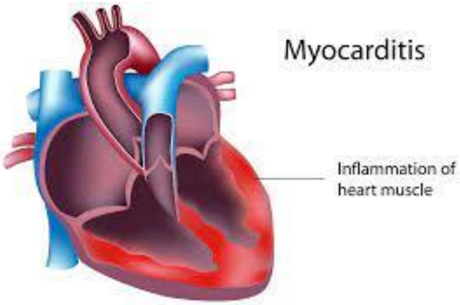
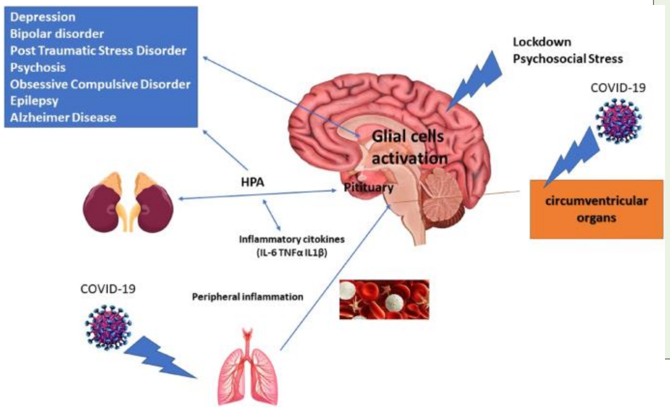
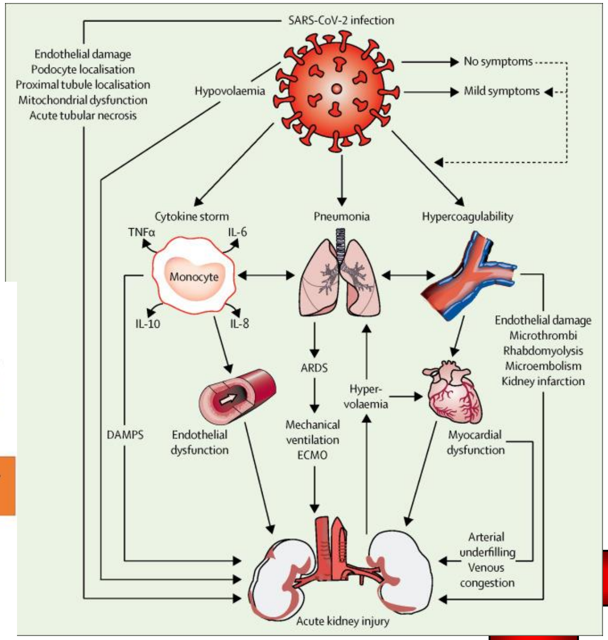
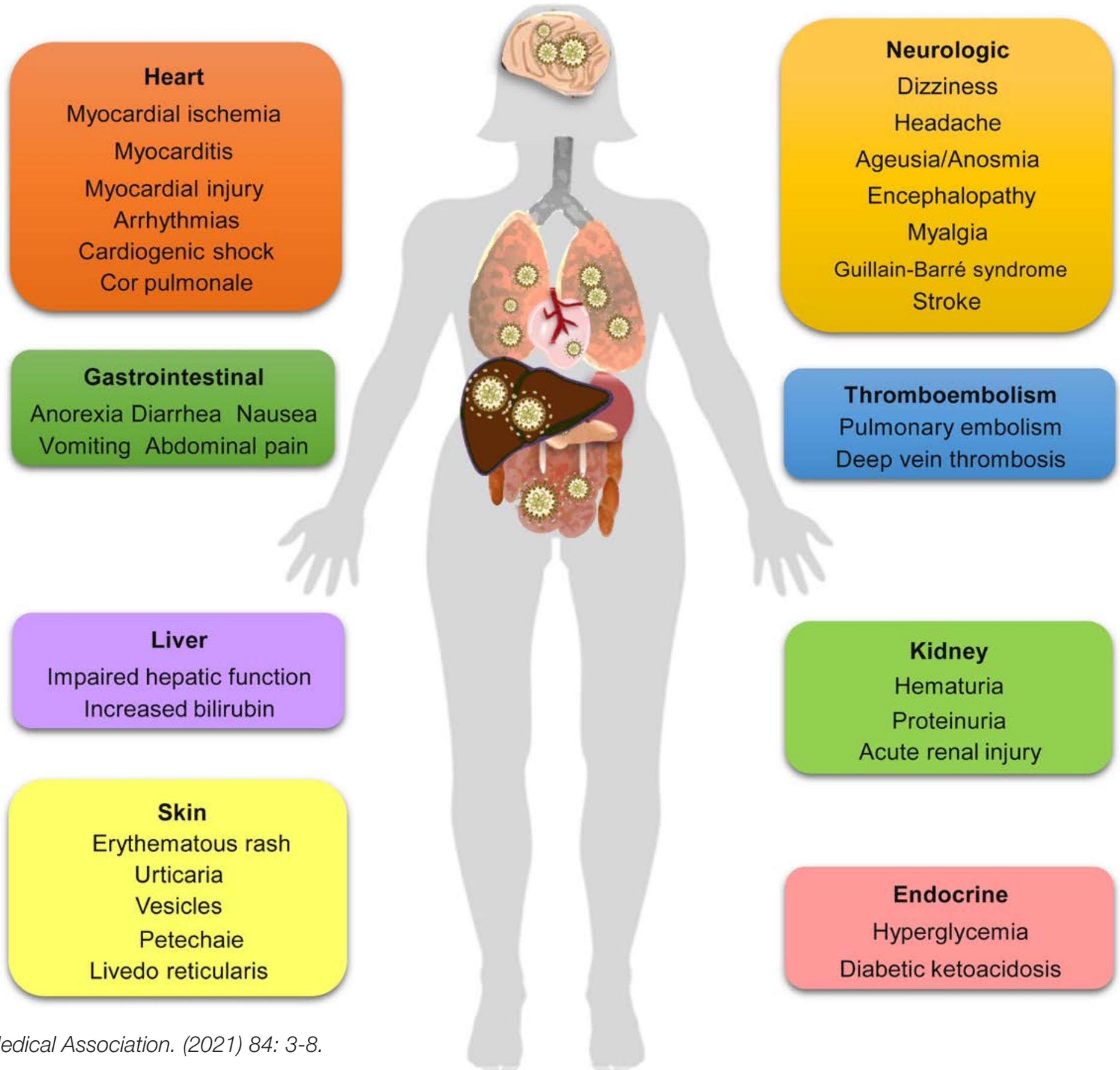
d


DERMATOLOGY SOLUTIONS
EMERGING SKIN MANIFESTATIONS OF COVID-19
• www.dermsolutionstx.com •
URTICARIA
Hives, commonly seen in viral rashes were reported in confirmed and suspected cases in Italy, France, Finland, Canada and US.
ACRAL ISCHEMIA
COVID-19 causes painful or itchy acral ischemic lesions, possibly from microthrombi, resembling perniosis.
MORBILLIFORM
Diffuse maculopapular eruption, as seen in Dengue, seen in COVID-19 patients in Italy, France and Finland
LIVEDO RETICULARIS
Transient blanching or mottling of skin from suspected ischemia of cutaneous blood vessels
VESICULAR
Chicken pox-like vesicles on erythematous base seen in COVID patients in Italy and US
PETECHIAL
Bleeding under the skin resulted in petechial eruption in COVID-19 confirmed patients in Italy and US
• Dermatologists across nations and borders are reporting skin manifestations of confirmed and suspected cases of COVID-19.
• About 20% of COVID-19 patients in north Italian hospital had skin manifestations.
• Front line workers can get free evaluation for COVID-19 related rashes. Please call, or text clinical photos to Dr Sanober Amin at HIPAA-compliant number: 214-DERM DOC.
• Updates and references available on my website www.dermsolutionstx.com/covid.
• Please submit COVID confirmed or suspected skin rashes to AAD registry at www.aad.org.


Myocarditis
Inflammation of heart muscle


Depression
Bipolar disorder
Post Traumatic Stress Disorder
Psychosis
Obsessive Compulsive Disorder
Epilepsy
Alzheimer Disease
Lockdown
Psychosocial Stress
COVID-19
Glial cells activation
Pituitary
HPA
circumventricular organs
Inflammatory citokines (IL-6 TNFα IL1β)
COVID-19
Peripheral inflammation


SARS-CoV-2 infection
Endothelial damage
Podocyte localisation
Proximal tubule localisation
Mitochondrial dysfunction
Acute tubular necrosis
Hypovolaemia
No symptoms
Mild symptoms
Cytokine storm
TNFα
IL-6
Monocyte
IL-10
IL-8
Pneumonia
Hypercoagulability
Endothelial damage
Microthrombi
Rhabdomyolysis
Microembolism
Kidney infarction
ARDS
Hyper-volaemia
DAMPS
Endothelial dysfunction
Mechanical ventilation
ECMO
Myocardial dysfunction
Arterial underfilling
Venous congestion
Acute kidney injury

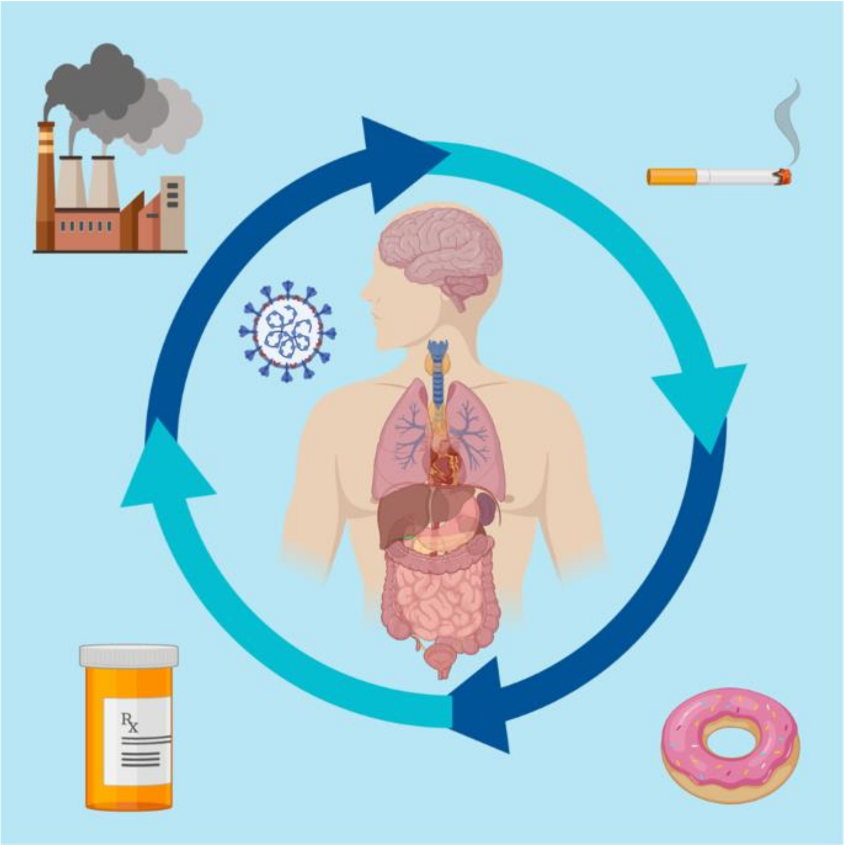


Journal of Chinese Medical Association. (2021) 84: 3-8.

Extrapulmonary involvements in patients with coronavirus disease 2019 (COVID-19).

ACE2 se lako distribuira kroz brojne organe, kao i nosnu sluznicu i može se modulirati farmakološkim, toksikološkim i prehrambenim čimbenicima.

Izloženost toksinima iz okoliša, kao i izbor načina života mogu utjecati na ekspresiju ACE2 i mogu povećati ozbiljnost infekcije.



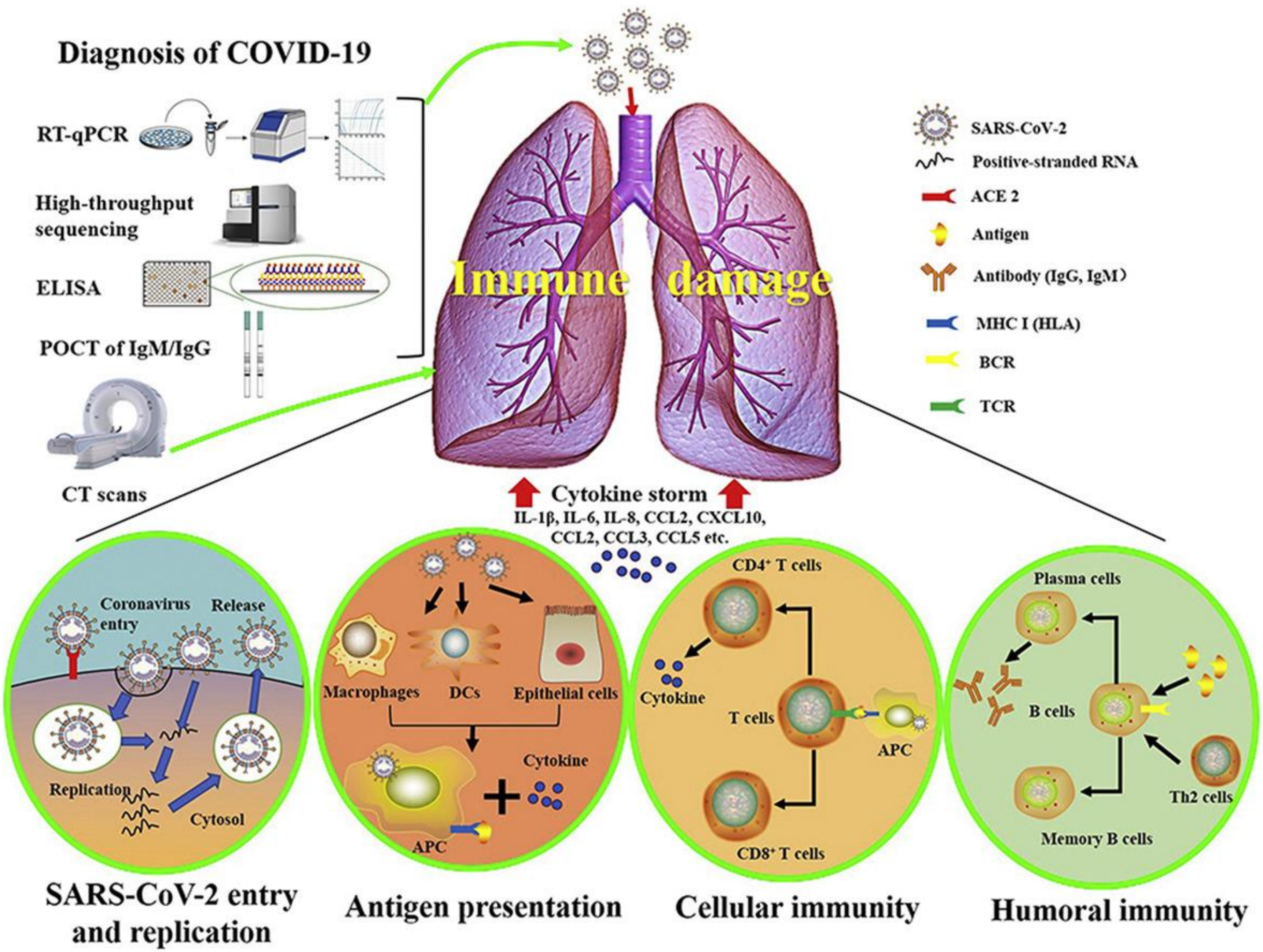
Nikotin smanjuje ekspresiju ACE2 u neuronima i gliji. Dok bi oštećenje plućnog tkiva uzrokovano pušenjem vjerojatno pogoršalo patologiju COVID-19, konzumacija nikotina drugim metodama (npr. oralnim pastilama ili transdermalnim flasterom) mogla bi potencijalno dati određenu otpornost na neurološke komplikacije.

Naughton, S.X., Raval, U., Harary, J.M. *et al.* The role of the exposome in promoting resilience or susceptibility after SARS-CoV-2 infection. *J Expo Sci Environ Epidemiol* **30,** 776–777 (2020). https://doi.org/10.1038/s41370-020-0232-4

Utvrđeno je da ACE inhibitori i blokatori receptora angiotenzina II tipa-I (ABR) losartan i olmesartan značajno povećavaju ekspresiju ACE2 kod ljudi i životinjskih modela. Ibuprofen, često primjenjivani nesteroidni protuupalni lijek (NSAID), također je pokazao da povećava ACE2.

Ranije se pokazalo da dijeta s visokim udjelom masti povećava ekspresiju ACE2 mRNA u masnom tkivu, kao i u bubrezima i jetri.

Imunopatogeneza



Xiaowei Li, Manman Geng, Yizhao Peng, Liesu Meng, Shemin Lu. Molecular immune pathogenesis and diagnosis of COVID-19. Journal of Pharmaceutical Analysis, Volume 10, Issue 2, 2020: 102-108, ISSN 2095-1779, https://doi.org/10.1016/j.jpha.2020.03.001.

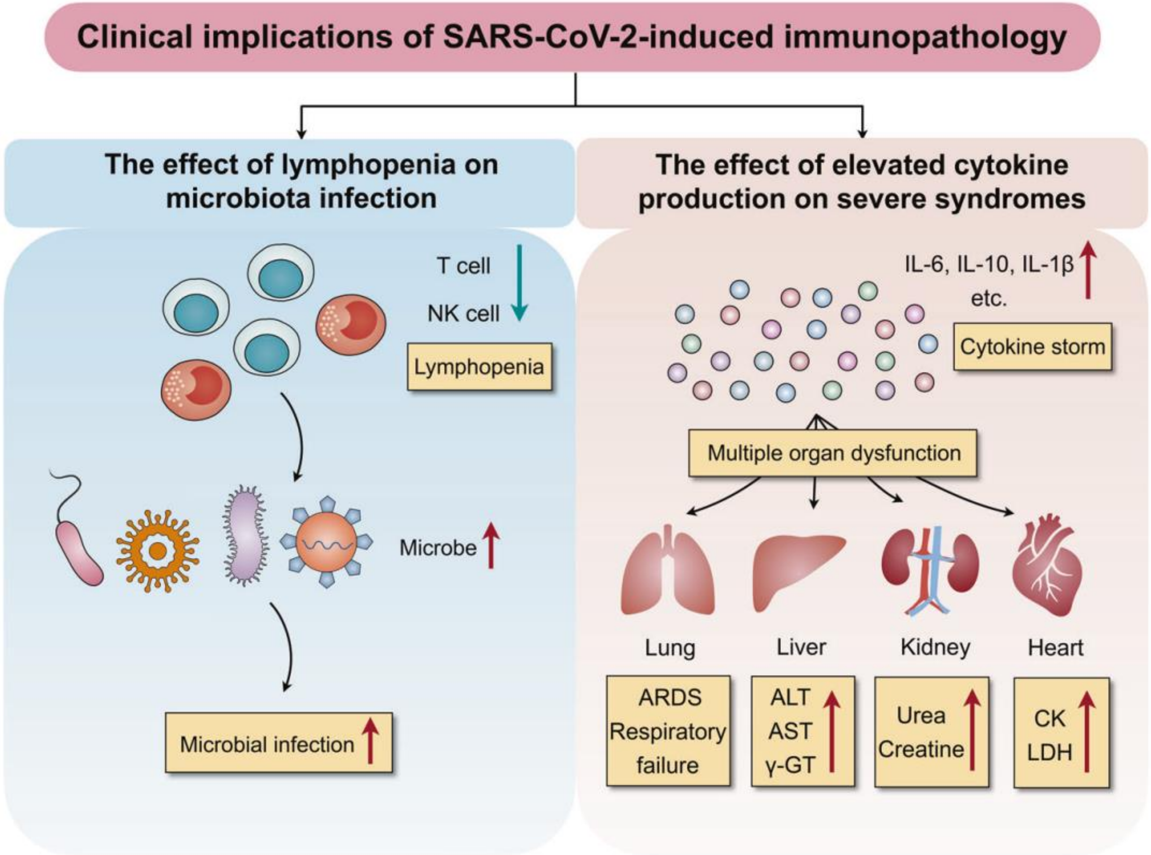
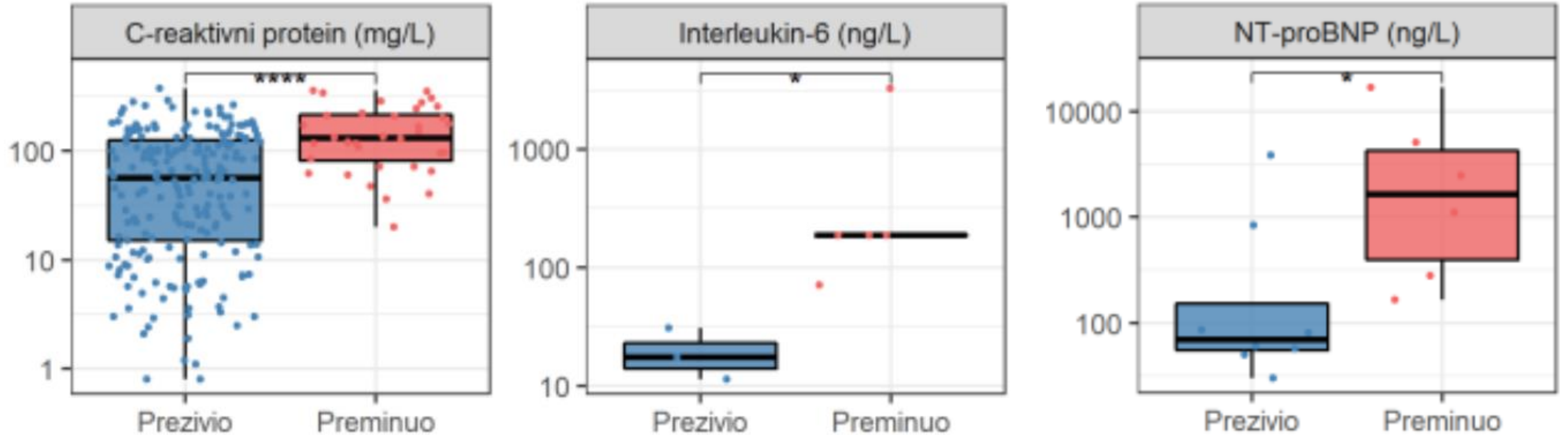


Fig. 3 Clinical implications of SARS-CoV-2-induced immunopathology. Patients with COVID-19 and presenting with lymphopenia are more prone to infections with the microbe, which leads to disease progression and increased severity. In addition, cytokine storms can initiate inflammatory-induced multiple organ dysfunction, including lung injury that can lead to ARDS, respiratory failure, liver injury with alanine aminotransferase (ALT), aspartate aminotransferase (AST), and γ-glutamine transferase (γ-GT) upregulation, kidney injury with increased urea and creatine levels, and heart injury with increased creatine kinase (CK) and lactate dehydrogenase (LDH) levels

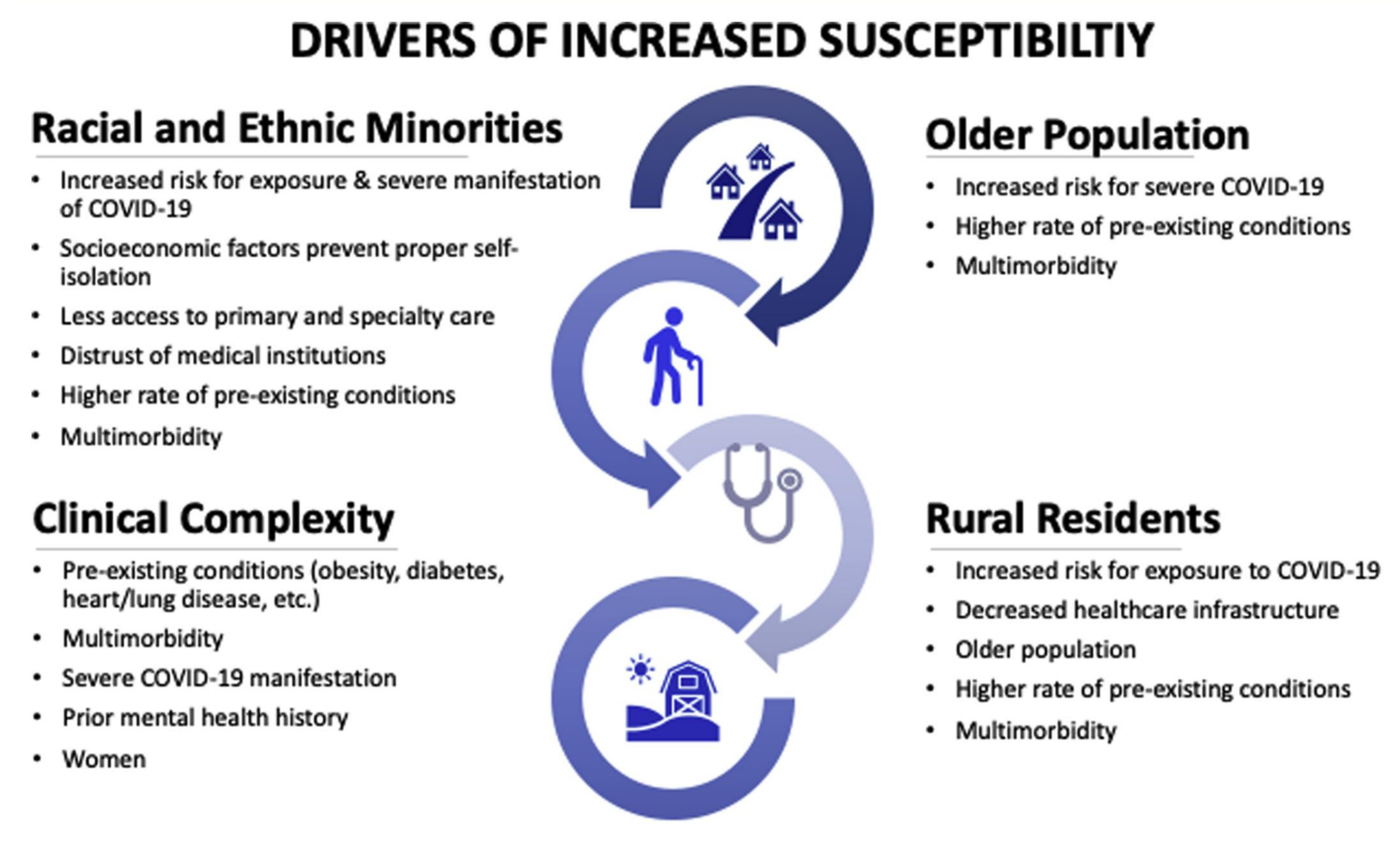
Yang, L., Liu, S., Liu, J. *et al.* COVID-19: immunopathogenesis and Immunotherapeutics. *Sig Transduct Target Ther* **5,** 128 (2020). https://doi.org/10.1038/s41392-020-00243-2



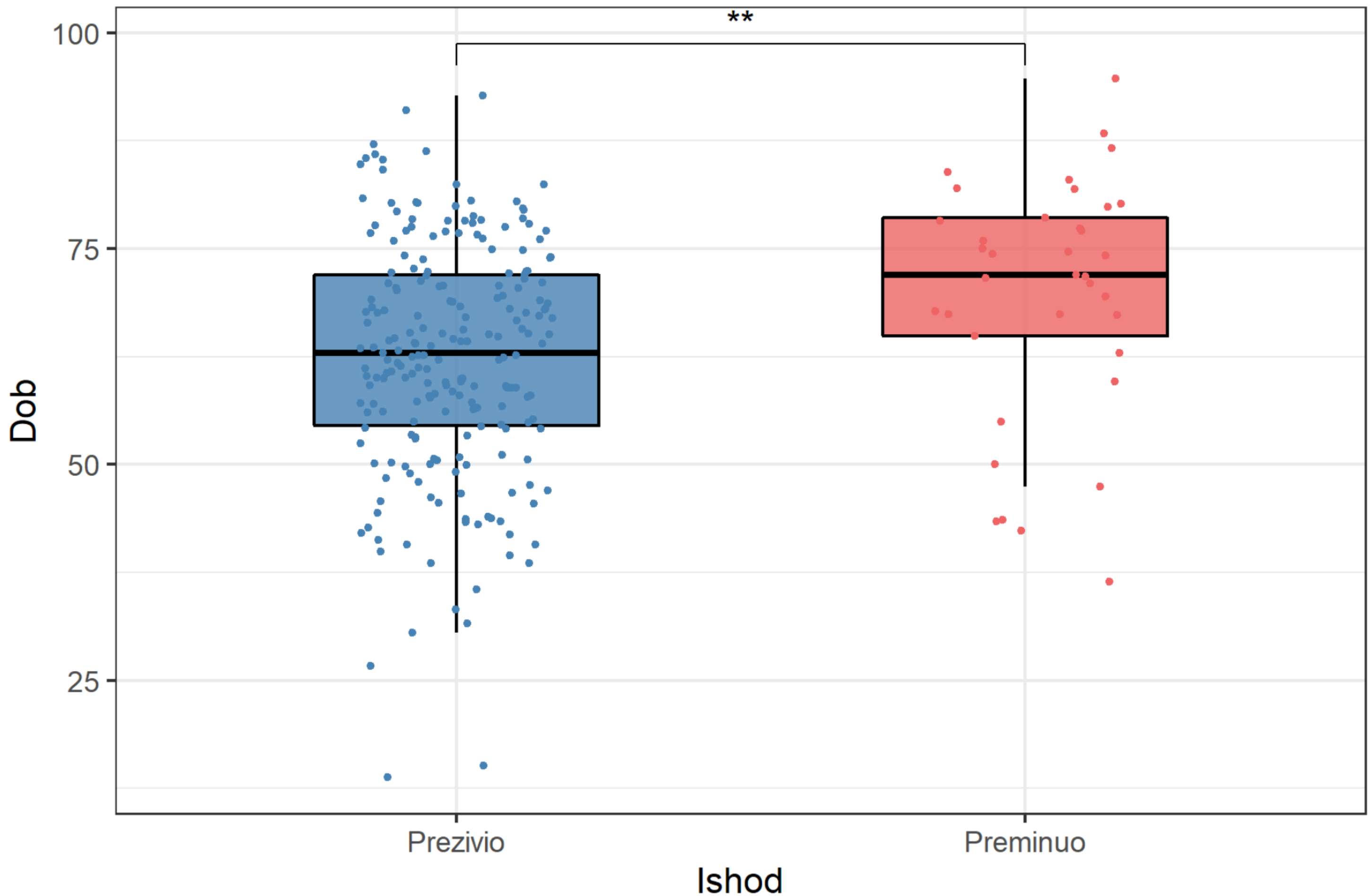
Slika 4. Raspodjele laboratorijskih parametara COVID-19 pacijenata s obzirom na ishod. U obzir su uzeti nalazi napravljeni pri primitku pacijenata. Y-os je logaritamski skalirana radi bolje razlučivosti. Razine laboratorijskih parametara su uspoređene Mann-Whitney U testom (ns = nije značajno, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$).

A. Markotić i sur. – neobjavljeni rezultati

FIGURE 1 Patients at Highest Risk for PASC



Whereas data on risk factors for postacute sequelae of severe acute respiratory syndrome coronavirus 2 infection (PASC) are scarce, early published reports suggests several clinical and sociodemographic risk factors. COVID-19 = coronavirus disease 2019.



Slika 7. Raspodjela dobi pacijenata po ishodu. Utvrđena je statistički značajna razlika dobi preživjelih i preminulih pacijenata (**t-test, p = 0.0051**).

A. Markotić i sur. – neobjavljeni rezultati

Table 1. Risk Factors for Severe Diseases.

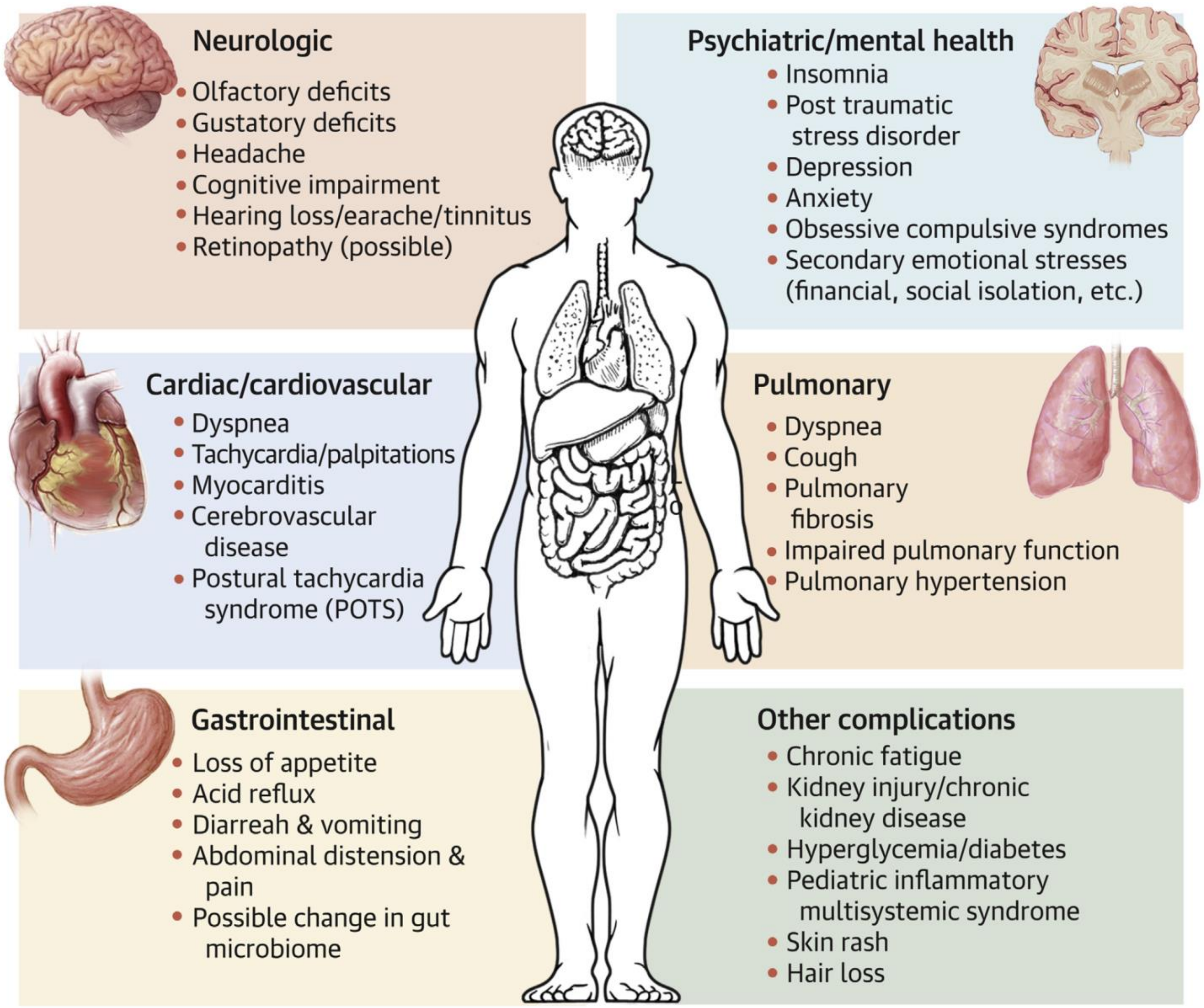
Risk factors for serious illness	Factors that have not yet been fully evaluated
Elderly people over 65 years old [9]	
Patients with cancer [10]	
Chronic obstructive pulmonary disease [11]	
Chronic kidney disease [12]	
Type 2 diabetes [13]	Asthma [18]
Hypertension [14]	Use of steroids [19] or biologics [20] HIV infection (especially CD4 < 200/μL) [21]
Dyslipidemia [9]	Pregnancy [22], [23]
Cardiovascular disease [15]	
Obesity (BMI over 30) [16]	
Smoking [14]	
Immunodeficiency after solid organ transplantation [17]	

TABLE 1 Factors involved in age-related differences of SARS-CoV-2 pathogenesis

Factors involved in age-related differences of SARS-CoV-2 pathogenesis	Adults	Children	References
Expression of ACE2 receptor and TMPRSS2	↑	↓	96, 98, 136
Comorbidities and medications	↑	↓	99, 100, 101, 102
Innate immune responses	↓	↑	103
Adaptive immune responses	↑	↓	72, 109
Pre-existing antibodies to other HCoVs	↑	↓	104, 109
Trained immune responses	↓	↑	125, 126
ADE and macrophage hyperactivation	↑	↓	106, 117, 119
Cytokine storm	usually ↑	usually ↓(except for MIS-C)	80, 121, 122
Vitamin D and other micronutrients	↓	↑	127, 130

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; ACE2, angiotensin-converting enzyme 2; TMPRSS2, transmembrane protease serine 2; HCoVs, human coronaviruses; ADE, antibody-dependent enhancement; MIS-C, multisystem inflammatory syndrome in children.

CENTRAL ILLUSTRATION Multi-System Manifestation of PASC



Jiang, D.H. et al. J Am Coll Cardiol Basic Trans Science. 2021;■(■):■-■.

Postacute sequelae of severe acute respiratory syndrome coronavirus 2 infection (PASC) is an emerging multisystemic condition that manifests subsequent to an acute infection of severe acute respiratory syndrome coronavirus 2. Conditions and symptoms characterized in the published reports and developing or persisting beyond 28 days of the initial coronavirus disease 2019 are summarized in this figure by body systems. POTS = postural tachycardia syndrome.


COVID-19
VACCINE
Pfizer
Johnson&Johnson
COVID-19
VACCINE
for injection only
10 ml


EU STRATEGY ON
COVID-19 THERAPEUTICS
European Commission
Commission européenne
Commission européenne
European Commission

Members of the COVID-19 therapeutics subgroup

Experts	
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Krzysztof PYRC*	Head at the Laboratory of Virology Małopolska Centre of Biotechnology Jagiellonian University in Kraków
Jesús RODRÍGUEZ BAÑO*	Head of the Infectious Diseases division at Hospital Universitario Virgen Macarena
Timo WOLF*	Head of the Isolation Unit for Highly Pathogenic Infections, University Hospital Frankfurt
Nick CAMMACK	Covid-19 Therapeutics Lead, Wellcome Trust
Francesca CECCHERINI SILBERSTEIN	Chair of Virology University of Rome Tor Vergata
Lennie DERDE	EU Coordinating Investigator, Intensivist, UMC Utrecht
Mirjana HUIC	Specialist in clinical pharmacology and toxicology, HTA/EBM Expert, HTA/EBM Centre, Croatia
Ulrike PROTZER	Director, Institute of Virology Technische Universität München
Claudia WILD	Chief Executive Officer (CEO) HTA Austria - Austrian Institute for Health Technology Assessment GmbH

Antiviral monoclonal antibodies	Oral antivirals	Immunomodulators
casirivimab/imdevimab (Ronapreve)	molnupiravir	tocilizumab (Actemra)
sotrovimab (Xevudy)	PF-07321332	anakinra (Kineret)
AZD7442	AT-527	baricitinib (Olumiant)
		lenzimulab

Hvala na pozornosti !