COVID-19 Hasta Yönetimi?

Tanı, Tedavi ve Korunmada Ne Yapabiliyoruz?

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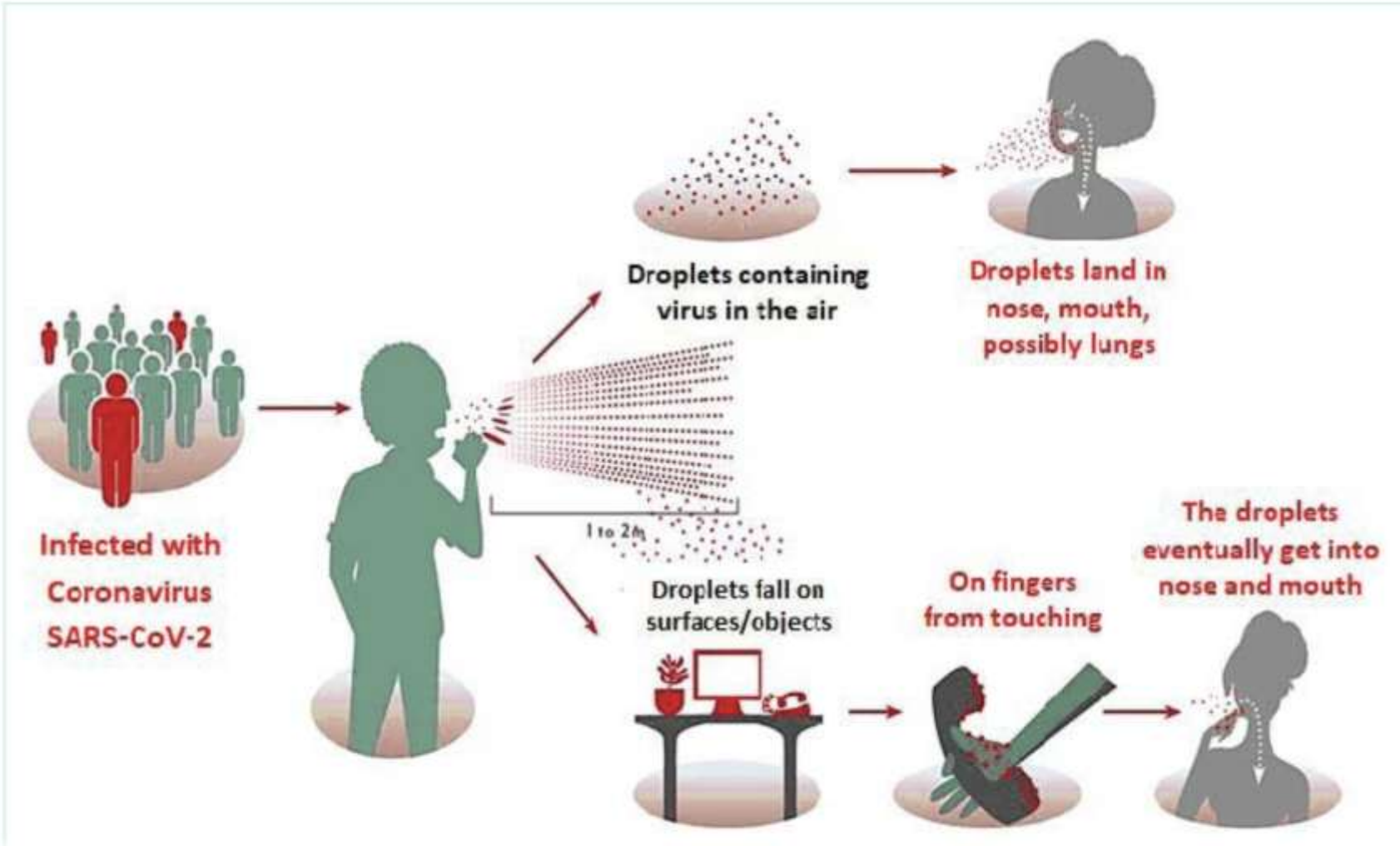
Ankara Üniversitesi Tıp Fakültesi
İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji AD

Bulaş Yolu ???



COVID-19: Transmission and infection.

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

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Scientific Brief: SARS-CoV-2 and Potential Airborne Transmission

Updated Oct. 5, 2020 Languages Print

The Coronavirus May Be Adrift in Indoor Air, C.D.C. Acknowledges

After removing guidance from its website acknowledging "airborne" transmission, the agency cited evidence that indoor air can carry virus-laden particles.

THE CORONAVIRUS CRISIS

CDC Acknowledges Coronavirus Can Spread Via Airborne Transmission

October 5, 2020 · 5:44 PM ET

MARIA GODOY

The epidemiology of SARS-CoV-2 indicates that most infections are spread through close contact, not airborne transmission

Diseases that are spread efficiently through airborne transmission tend to have high attack rates because they can quickly reach and infect many people in a short period of time. We know that a significant proportion of SARS-CoV-2 infections (estimated 40-45%) occur without symptoms and that infection can be spread by people showing no symptoms. Thus, were SARS-CoV-2 spread primarily through airborne transmission like measles, experts would expect to have observed considerably more rapid global spread of infection in early 2020 and higher percentages of prior infection measured by serosurveys. Available data indicate that SARS-CoV-2 has spread more like most other common respiratory viruses, primarily through respiratory droplet transmission within a short range (e.g., less than six feet). There is no evidence of efficient spread (i.e., routine, rapid spread) to people far away or who enter a space hours after an infectious person was there.

Airborne transmission of SARS-CoV-2 can occur under special circumstances

Pathogens that are mainly transmitted through close contact (i.e., contact transmission and droplet transmission) can sometimes also be spread via airborne transmission under special circumstances. There are several well-documented examples in which SARS-CoV-2 appears to have been transmitted over long distances or times. These transmission events appear uncommon and have typically involved the presence of an infectious person producing respiratory droplets for an extended time (>30 minutes to multiple hours) in an enclosed space. Enough virus was present in the space to cause infections in people who were more than 6 feet away or who passed through that space soon after the infectious person had left. Circumstances under which airborne transmission of SARS-CoV-2 appears to have occurred include:

- **Enclosed spaces** within which an infectious person either exposed susceptible people at the same time or to which

- **Enclosed spaces** within which an infectious person either exposed susceptible people at the same time or to which susceptible people were exposed shortly after the infectious person had left the space.
- **Prolonged exposure to respiratory particles**, often generated with expiratory exertion (e.g., shouting, singing, exercising) that increased the concentration of suspended respiratory droplets in the air space.
- **Inadequate ventilation or air handling** that allowed a build-up of suspended small respiratory droplets and particles.

Prevention of COVID-19 by airborne transmission

Existing interventions to prevent the spread of SARS-CoV-2 appear sufficient to address transmission both through close contact and under the special circumstances favorable to potential airborne transmission. Among these interventions, which include social distancing, use of masks in the community, hand hygiene, and surface cleaning and disinfection, **ventilation** and **avoidance of crowded indoor spaces** are especially relevant for enclosed spaces, where circumstances can increase the concentration of suspended small droplets and particles carrying infectious virus. At this time, there is no indication of a general community need to use special engineering controls, such as those required to protect against airborne transmission of infections, like measles or tuberculosis, in the healthcare setting.

SARS-CoV-2 is a new virus, and we are still learning about how it behaves.

There are several critical questions that need to be answered to refine guidance for prevention of COVID-19, including

- How effective are mitigation efforts to prevent SARS-CoV-2 spread, especially ventilation and masking?
- What proportion of SARS-CoV-2 infections are acquired through airborne transmission?
- What are the conditions that facilitate airborne transmission?
- What is the infectious dose for SARS-CoV-2 (how many virions are required for infection to occur)?
- Do inoculum size and route of inoculation affect risk of infection and disease severity?

Modes of transmission of virus causing COVID-19: implications for IPC precaution recommendations

Scientific brief

29 March 2020

This version updates the 27 March publication by providing definitions of droplets by particle size and adding three relevant publications.

Modes of transmission of the COVID-19 virus

Respiratory infections can be transmitted through droplets of different sizes: when the droplet particles are >5-10 µm in diameter they are referred to as respiratory droplets, and when then are <5µm in diameter, they are referred to as droplet nuclei.[1] According to current evidence, COVID-19 virus is primarily transmitted between people through respiratory droplets and contact routes.[2-7] In an analysis of 75,465 COVID-19 cases in China, airborne transmission was not reported.[8]

Droplet transmission occurs when a person is in in close contact (within 1 m) with someone who has respiratory symptoms (e.g., coughing or sneezing) and is therefore at risk of having his/her mucosae (mouth and nose) or conjunctiva (eyes) exposed to potentially infective respiratory droplets. Transmission may also occur through fomites in the immediate environment around the infected person.[8] Therefore, transmission of the COVID-19

Related

Modes of transmission of virus caus

Access the publication

Transmission of SARS-CoV-2: implications for infection prevention precautions

Scientific brief

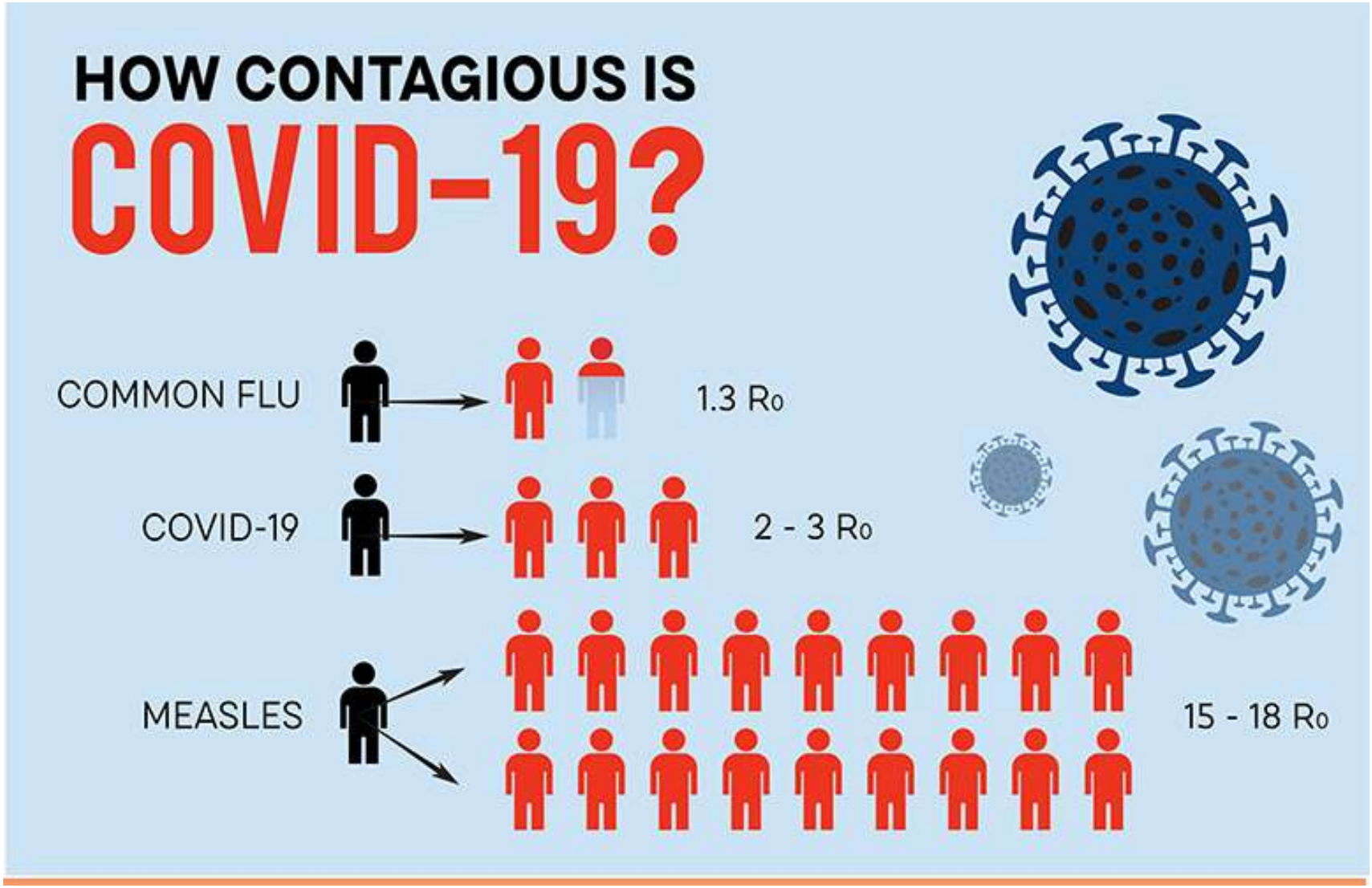
9 July 2020

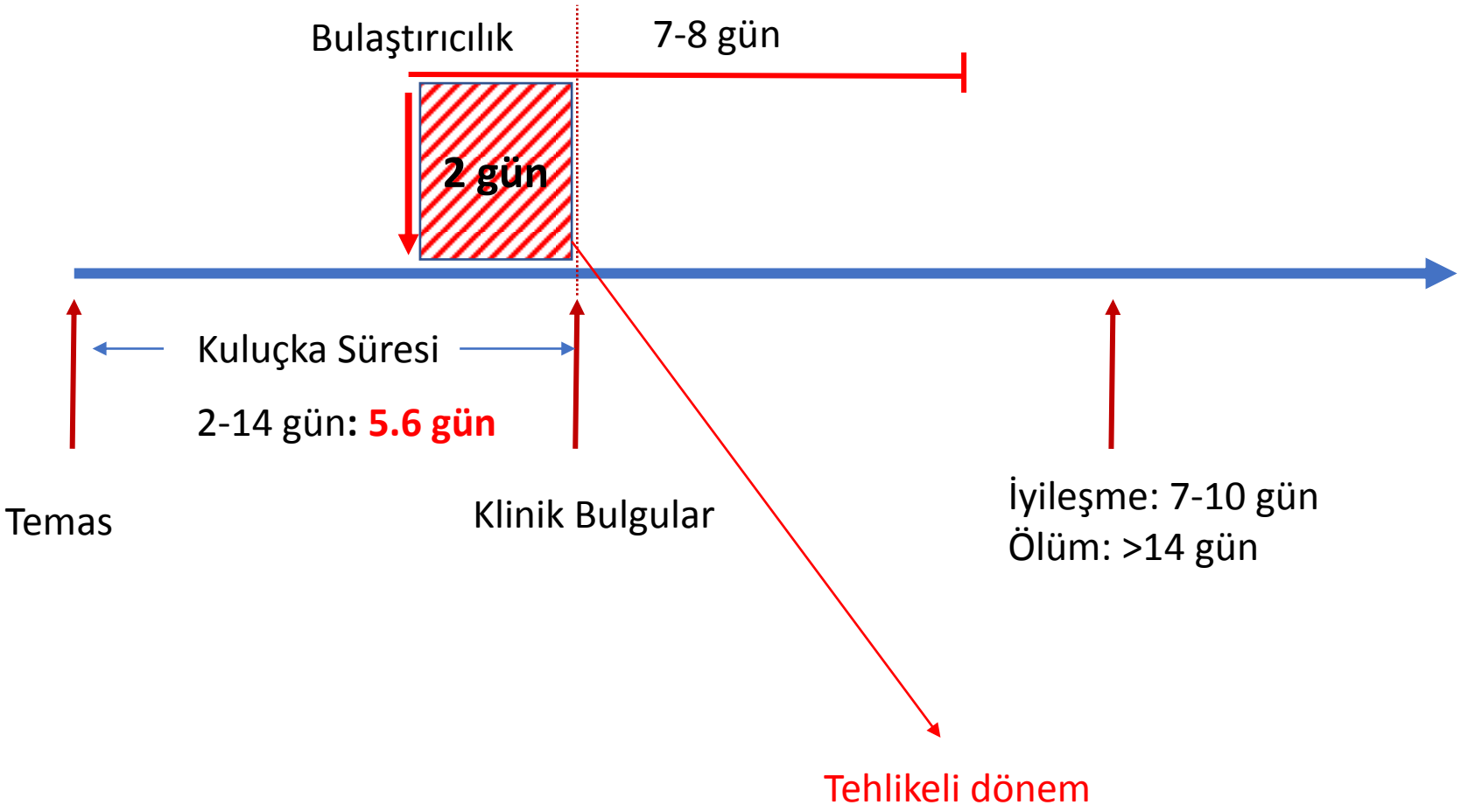
World Health Organization

Key points of the brief

Main findings

- Understanding how, when and in what types of settings SARS-CoV-2 spreads between people is critical to develop effective public health and infection prevention measures to break chains of transmission.
- Current evidence suggests that transmission of SARS-CoV-2 occurs primarily between people through direct, indirect, or close contact with infected people through infected secretions such as saliva and respiratory secretions, or through their respiratory droplets, which are expelled when an infected person coughs, sneezes, talks or sings.
- Airborne transmission of the virus can occur in health care settings where specific medical procedures, called aerosol generating procedures, generate very small droplets called aerosols. Some outbreak reports related to indoor crowded spaces have suggested the possibility of aerosol transmission, combined with droplet transmission, for example, during choir practice, in restaurants or in fitness classes.
- Respiratory droplets from infected individuals can also land on objects, creating fomites (contaminated surfaces). As environmental contamination has been documented by many reports, it is likely that people can also be infected by touching these surfaces and touching their eyes, nose or mouth before cleaning their hands.
- Based on what we currently know, transmission of COVID-19 is primarily occurring from people when they have symptoms, and can also occur just before they develop symptoms, when they are in close proximity to others for prolonged periods of time. While someone who never develops symptoms can also pass the virus to others, it is still not clear to what extent this occurs and more research is needed in this area.
- Urgent high-quality research is needed to elucidate the relative importance of different transmission routes; the role of airborne transmission in the absence of aerosol generating procedures; the dose of virus required for transmission to occur; the settings and risk factors for superspreading events; and the extent of asymptomatic and pre-symptomatic transmission.


HOW CONTAGIOUS IS
COVID-19?
COMMON FLU
1.3 R0
COVID-19
2 - 3 R0
MEASLES
15 - 18 R0


Bulaştırıcılık
7-8 gün
2 gün
Kuluçka Süresi
2-14 gün: 5.6 gün
Temas
Klinik Bulgular
İyileşme: 7-10 gün
Ölüm: >14 gün
Tehlikeli dönem

KLİNİK

Sık belirtiler:

- Ateş
- Öksürük
- Bitkinlik
- Nefes Darlığı

Daha nadir:

- Burun akıntısı
- Boğaz ağrısı
- Baş ağrısı
- Kas ağrıları
- İshal
- Karın ağrısı
- Tat ve koku duyusu kaybı

Çin'deki merkezlere dayanan 72.314 hastalık raporlara göre[2]:

Hafif hastalık(%81):

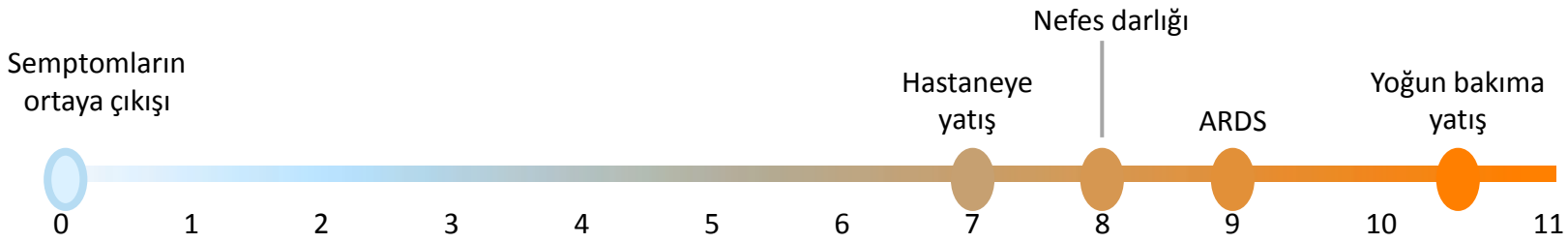
Pnömoni yok veya hafif seyirli pnömoni var

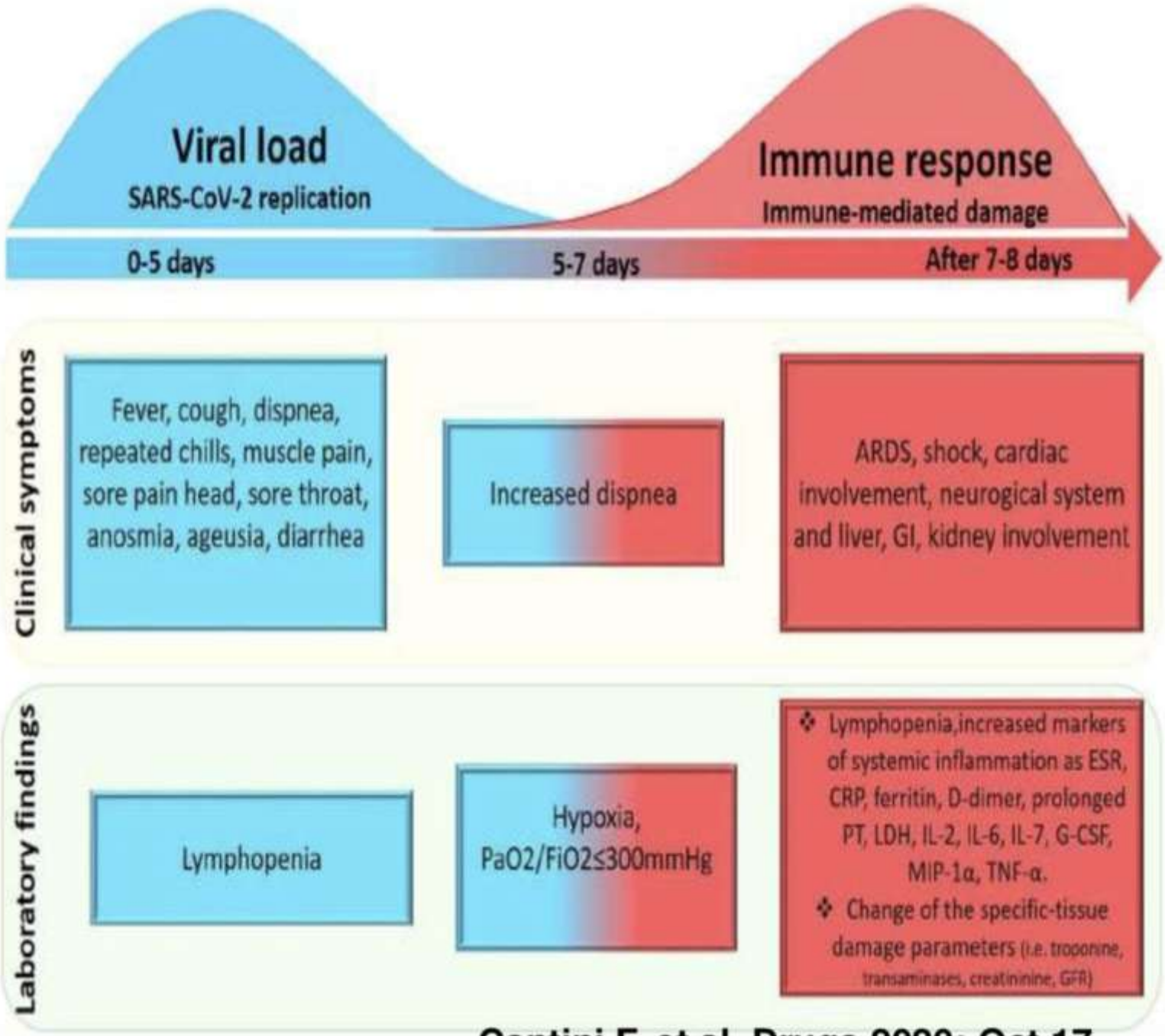
Ağır hastalık(%14):

Dispne, dakikadaki solunum sayısı ≥ 30, kan oksijen saturasyonu (SpO2) ≤ %93, PaO2/FiO2 oranı < 300 ve/veya 24-48 saat içinde AC infiltratları >%50

Kritik hastalık (%5):

Solunum yetmezliği, septik şok ve/veya çoklu organ disfonksiyonu





Cantini F, et al. Drugs 2020; Oct 17

TANI

ve

TEDAVİDE

NE YAPABİLİYORUZ?

COVID-19 TANI TESTLERİ

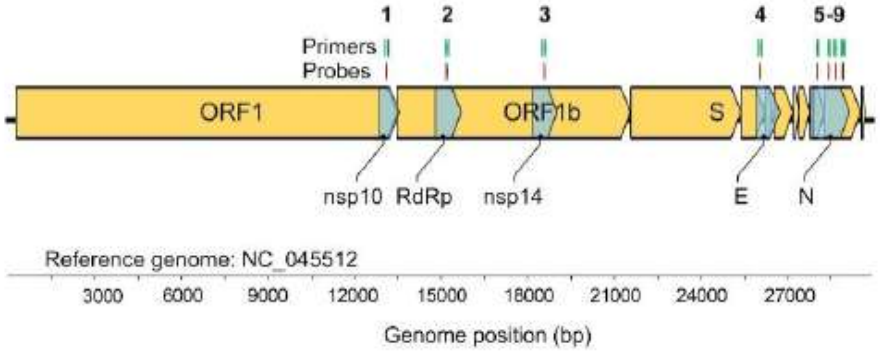
- Doğrudan tanı araçları:

- Kültür
- Antijen saptama
- Nükleik asitleri saptama (revers transkripsiyon sonrası PCR, CRISPR-CAS, LAMP, HDA)

- Dolaylı tanı araçları:

- Antikorların saptanmasına dayalı testler: IgM ve IgG yanıtları

PCR



Institute	Target	Primer/Probe	Sequence
Charité	E	E_Sarbeco_F	ACAGGTACGTTAATAGTTAATAGCGT
		E_Sarbeco_R	ATATTGCAGCAGTACGCACACA
		E_Sarbeco_P1	ACACTAGCCATCCTTACTGCGCTTCG
	RdRp	RdRp_SARSr-F	GTGA**R**ATGGTCATGTGTGGCGG
		RdRp SARSr-R	CARATGTTAAA**S**ACACTATTAGCATA
		RdRp_SARSr-P1	CCAGGTGG**W**AC**R**TCATC**M**GGTGATGC
		RdRp_SARSr-P2	CAGGTGGAACCTCATCAGGAGATGC
HKU	N	HKU-N-F	TAATCAGACAAGGAACTGATTA
		HKU-N-R	CGAAGGTGTGACTTCCATG
		HKU-N-P	GCAAATTGTGCAATTTGCGG
	nsp14	HKU-ORF1-F	TGGGG**Y**TTTACRGGTAACCT
		HKU-ORF1-R	AAC**R**CGCTTAACAAAGCACTC
		HKU-ORF1-P	TAGTTGTGATGC**W**ATCATGACTAG
China CDC	N	CCDC-N-F	GGGGAACTTCTCCTGCTAGAAT
		CCDC-N-R	CAGACATTTTGCTCTCAAGCTG
		CCDC-N-P	TTGCTGCTGCTTGACAGATT
	nsp10	CCDC-ORF1-F	CCCTGTGGGTTTTACACTTAA
		CCDC-ORF1-R	ACGATTGTGCATCAGCTGA
		CCDC-ORF1-P	CCGTCTGCGGTATGTGGAAAGGTTATGG
US CDC	N	2019-nCoV_N1-F	GACCCCAAAATCAGCGAAT
		2019-nCoV_N1-R	TCTGGTACTGCAGTTGAATCTG
		2019-nCoV N1-P	ACCCCGCATTACGTTTGGTGGACC
	N	2019-nCoV_N2-F	TTACAAACATTGGCCGCAAA
		2019-nCoV_N2-R	GCGCGACATTCCGAAGAA
		2019-nCoV_N2-P	ACAATTTGCCCCCAGCGCTTCAG
	N	2019-nCoV N3-F	GGGAGCCTTGAATACACCAAAA
		2019-nCoV_N3-R	TGTAGCACGATTGCAGCATTG
		2019-nCoV_N3-P	**AY**CACATTGGCACCCGCAATCCTG
	Human RNase P	RP-F	AGATTTGGACCTGCGAGCG
		RP-R	GAGCGGCTGTCTCCACAAGT
		RP-P	TTCTGACCTGAAGGCTCTGCGCG

PCR

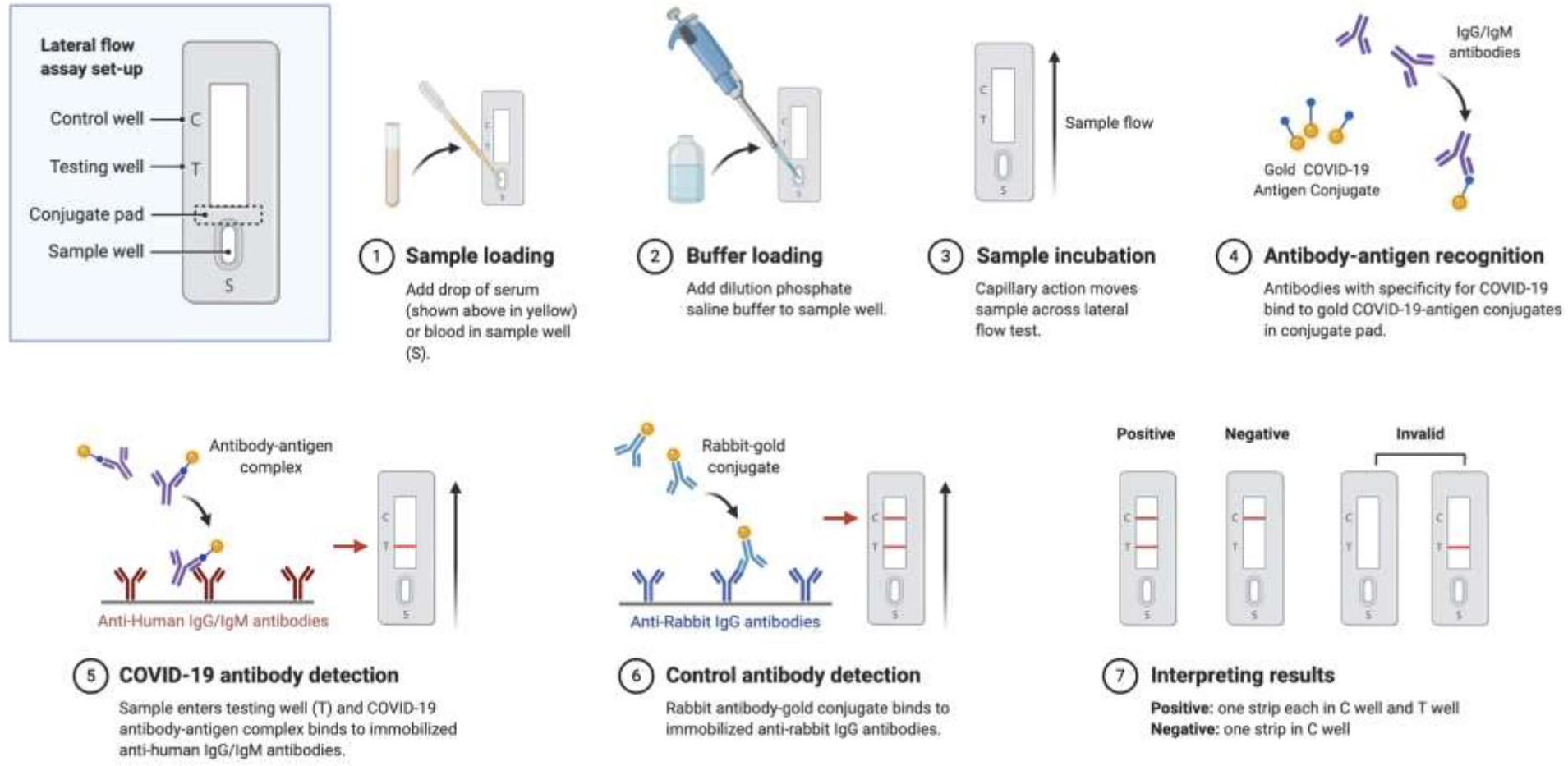
Diagnostic Test Sensitivity in the Days After Symptom Onset†

	Days after Symptom Onset		
SARS-CoV-2 Test	1–7	8–14	15–39
RNA by RT-PCR	67%	54%	45%

PCR testinde sorunlar:

1. Hastalığın evresi
2. Örnek almada
3. Örneğin lab'a ulaşmasında
4. Lab çalışmasında (in-house PCR)
5. Viral Saçılımın aralıklı olması

Hızlı Antikor Testleri:



Serolojik Testler

Türkiye'de ÜTS Kaydı Olan Anitkor Testleri ve Performansları

TEST	Üretici (teknik)	Antijen	Duyarlılık	Özgüllük	PKD**	NKD**
IgG*	Abbott (CMIA)	Nükleokapsid (N)	100	99.6	92.9	100
IgG*	Euroimmun (ELISA)	Spike (S1)	90	100	100	99
IgM+IgG*	Roche (ECLIA)	N	100	99.8	96.5	100
IgG	Dia-Pro (mikroELISA)	N+S	98	>90	-	-
IgG	Vircell (MİkroELISA)	N+S	85.0	98.0	-	-
IgG	EDI (MikroELISA)	N	100	88.7	-	-

*: FDA Onaylı Testler **: %5 Prevalansa göre

Test Öncesi Olasılığın (Prevalans) Performansa Etkisi

Prevalence (%)	IgM				IgG				IgM + IgG			
	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
20.0	89.5	99.6	98.2	98.6	94.7	99.1	96.5	98.6	100.0	98.7	95.1	100.0
7.1			94.4	99.6			89.4	99.6			85.6	100.0
4.3*			90.8	99.7			83.2	99.7			77.7	100.0
2.2			82.9	99.9			70.7	99.9			63.1	100.0
1.1			70.5	99.9			54.5	99.9			45.8	100.0
0.5			54.3	100.0			37.3	100.0			29.6	100.0
0.3			37.2	100.0			22.9	100.0			17.3	100.0

Sensitivity and specificity is shown for seropositivity for samples ≥15 days after a confirmatory PCR test.

* Estimated prevalence of SARS-CoV-2 in the high risk testing population at UC San Diego Health on April 16th, 2020

Suhandynata RT, J Appl Lab Med

Tedavi:

1462 Studies found for: **treatment | Interventional Studies | Covid-19**

Also searched for **COVID**, **SARS-CoV-2**, **Therapy** and more. See Search Details

Applied Filters: ☑ **Interventional**

Your search included: **Covid-19**

Learn more about clinical studies related to COVID-19:

- **ClinicalTrials.gov**: Federally-funded clinical studies related to COVID-19
- **WHO Trial Registry Network**: COVID-19 studies from the ICTRP database
- **NIH**: COVID-19 Treatment Guidelines
- **ClinicalTrials.gov**: Views of Listed COVID-19 Studies (Beta)

List | By Topic | On Map | Search Details

Hide Filters

Download | Subscribe to RSS

Filters

Apply | Clear

Showing: 1-50 of **1,462** studies 50 studies per page

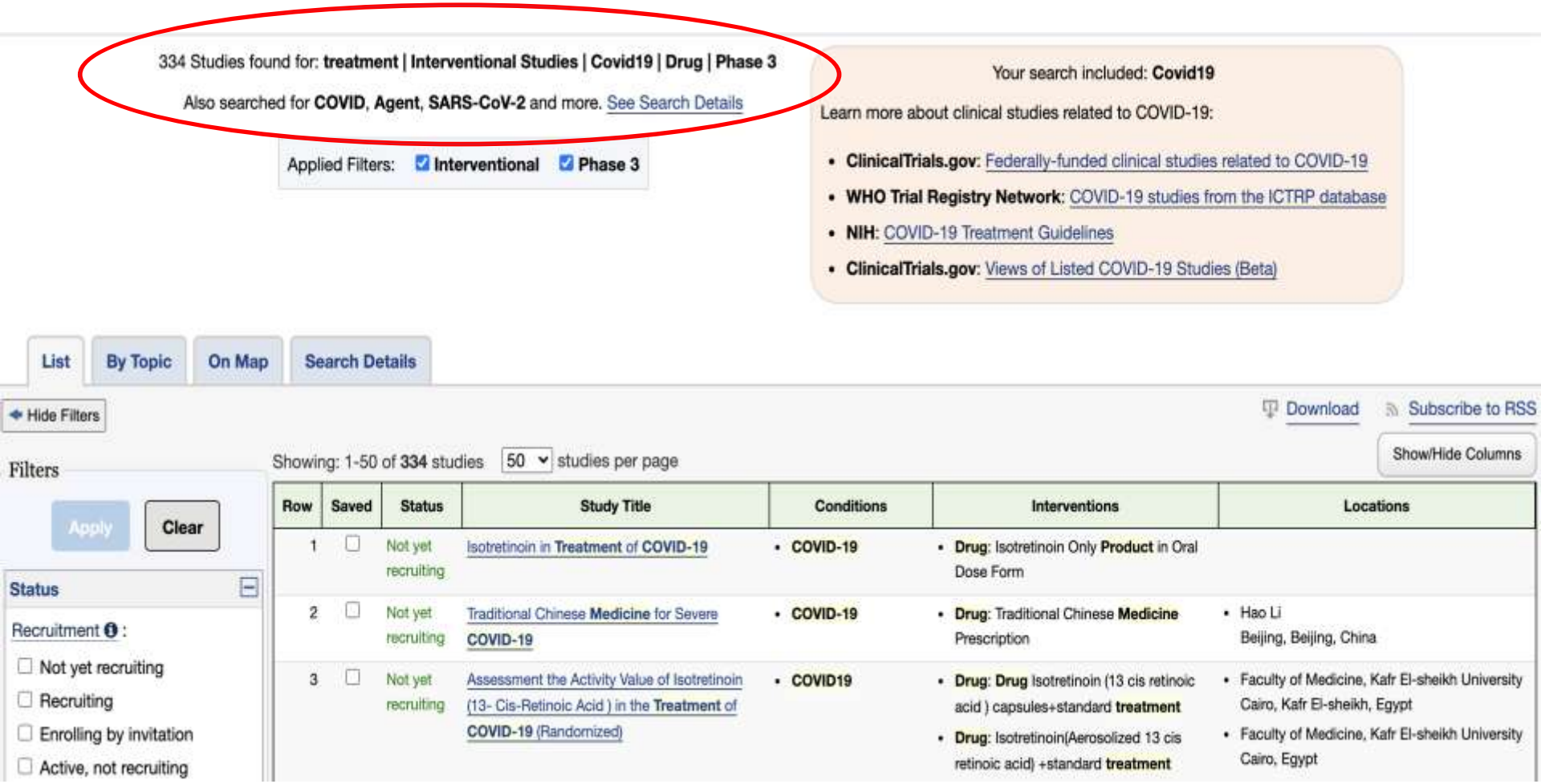
Show/Hide Columns

Status

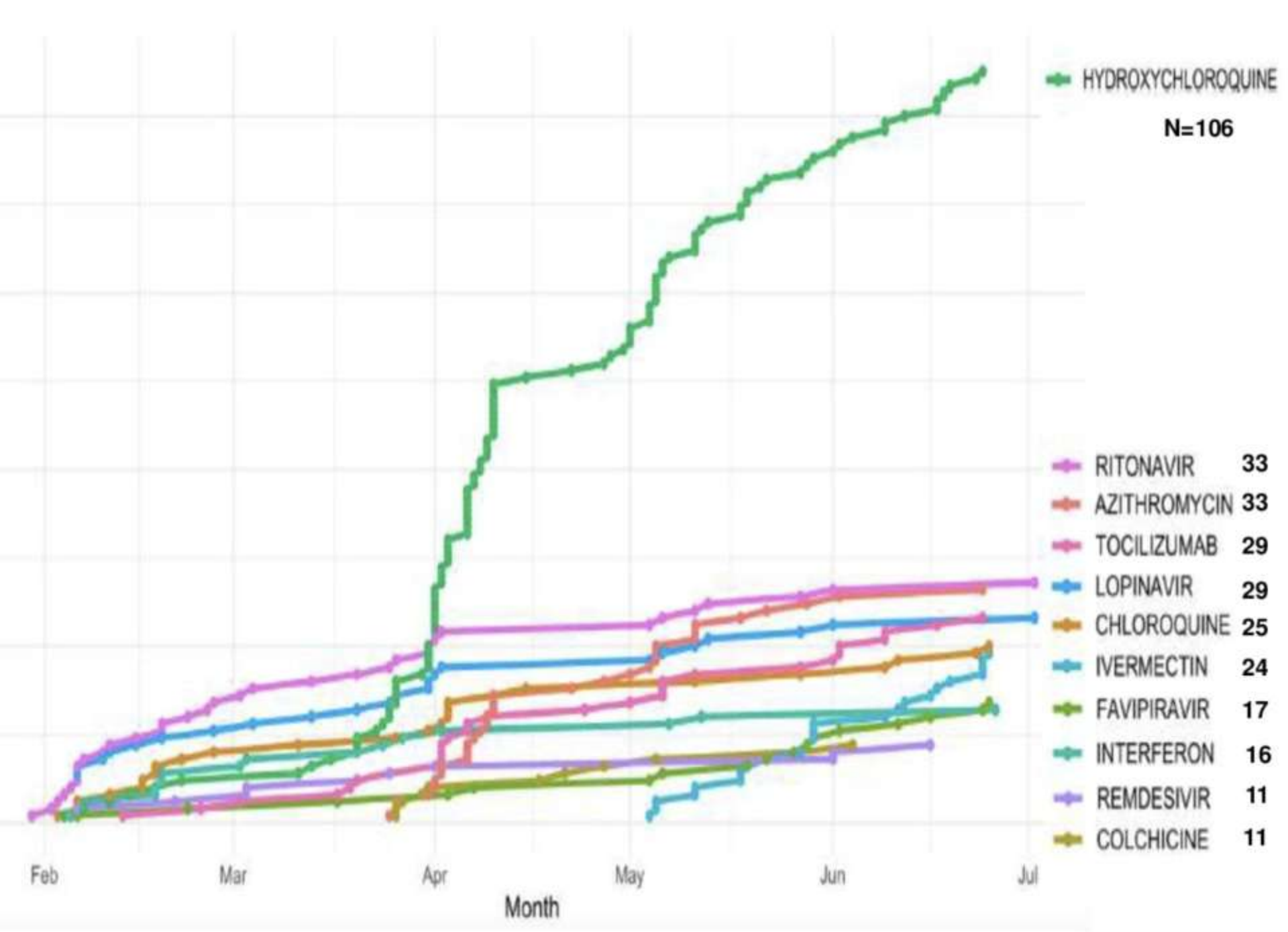
Recruitment :

- ☐ Not yet recruiting
- ☐ Recruiting
- ☐ Enrolling by invitation
- ☐ Active, not recruiting
- ☐ Suspended
- ☐ Terminated

Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	☐	Not yet recruiting	Effectiveness and Safety of Medical **Treatment** for **SARS-CoV-2** (**COVID-19**) in Colombia	• **COVID-19**	• Drug: Hydroxychloroquine • Drug: Lopinavir / Ritonavir Pill • Drug: Azithromycin • Other: Standard **treatment**	• Hospital Universitario de Neiva Neiva, Huila, Colombia • Clínica Reina Sofía Bogotá, Colombia • Fundacion Cardio Infantil Bogotá, Colombia • (and 3 more...)
2	☐	Not yet recruiting	Hyperbaric Oxygen **Therapy** (HBOT) as a **Treatment** for **COVID-19** (**COVID-19**) Infection	• **COVID-19**	• Device: Hyperbaric Oxygen **Therapy**	• Ochsner Medical Center New Orleans, Louisiana, United States
3	☐	Not yet recruiting	Photodynamic **Therapy** for the **Treatment** of **COVID-19**	• Photodynamic **Therapy**& Low	• Procedure: photobiomodulation and photodynamic **therapy**	



Hidroksiklorokin, Remdesivir, Favipiravir, Lopinavir/Ritonavir, Ribavirin, IFN, İsotretinoin, Anti-HCV, Anti-HIV, Levamizol, İvermektin, İmmünsüpresifler, İmmünmodülatörler, Dornaz alfa, DPP4 İnhibitörleri ……


HYDROXYCHLOROQUINE
N=106
RITONAVIR 33
AZITHROMYCIN 33
TOCILIZUMAB 29
LOPINAVIR 29
CHLOROQUINE 25
IVERMECTIN 24
FAVIPIRAVIR 17
INTERFERON 16
REMDESIVIR 11
COLCHICINE 11
Feb
Mar
Apr
May
Jun
Jul
Month

KLİMİK DERNEĞİ COVID-19 TEDAVİSİNDE KULLANILMAKTA OLAN ANTİVİRAL İLAÇLARLA İLGİLİ BİLİMSEL GÖRÜŞ YAYIMLADI

Hidroksiklorokin: Güncel in vitro/in vivo ve randomize kontrollü klinik çalışmalar, ayaktan veya yatan, hafif/orta/ağır seyirli COVID-19 olgularının tedavisinde hidroksiklorokinin etkili olmadığını göstermiştir. ***Hidroksiklorokin, aksini bildiren yeni randomize kontrollü klinik çalışma sonuçları olmadıkça COVID-19'un asemptomatik, hafif, orta, ağır formlarının tedavisinde veya profilaksisinde kullanılmamalıdır.*** Hidroksiklorokin, özellikle QT'yi uzatan azitromisin gibi diğer ilaçlarla birlikte kullanıldığında hayatı tehdit edebilecek kardiyotoksik istenmeyen etkilere neden olabilir.

Favipiravir

RdRp inhibitörü, Ekzonukleazlara duyarlı !?

Rusya, Çin ve Hindistan’dan 4 RKÇ (475 hasta): Olumlu sonuçlar

Japonya ve Çin’den 2 gözlemsel çalışma (2238 hasta): Olumlu sonuçlar

Devam eden 21 RKÇ var !

Favipiravir: COVID-19 tedavisinde Favipiravirin etkisini araştıran az sayıda hasta içeren üç randomize kontrollü klinik çalışmada, bu ajanın viral klirense ve/veya bazı klinik sonuçlara olumlu etkilerinin olabileceği bildirilmiştir. Bu nedenle, ***favipiravirin özellikle pnömonili ve/veya riskli COVID-19 olgularının tedavisinde kullanılabileceği düşünülmektedir.*** Ancak devam etmekte olan randomize kontrollü klinik çalışmaların sonuçları yakından izlenmeli, optimal dozunun ve tedavi süresinin belirlenebilmesi için in vitro ve ek klinik çalışmalar yapılmalıdır. Favipiravirin COVID-19 tedavisinde veya diğer indikasyonlarla kullanımı sırasında ciddi istenmeyen etkileri tanımlanmamıştır.

Remdesivir

RdRp inhibitörü, Ekzonukleazlara dayanıklı

Geniş etki spektrumlu (Ebola, Marburg, Nipah, RSV, koronavirüsler)

Hepatik ekstraksiyonu yüksek (ilk geçiş etkisi): Oral kullanılamaz

Remdesivir

RdRp inhibitörü, Ekzonukleazlara dayanıklı

Geniş etki spektrumlu (Ebola, Marburg, Nipah, RSV, koronavirüsler)

Hepatik ekstraksiyonu yüksek (ilk geçiş etkisi): Oral kullanılamaz

Çin, ABD ve Çok uluslu (ABD-Avrupa-Kanada) 3 RKÇ (1884 hasta): Olumlu sonuçlar

FDA onayı: 22 Ekim 2020

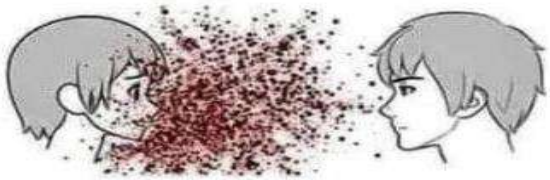
Remdesivir: SARS-CoV-2'ye karşı in vitro ve in vivo hayvan deneylerinde etkili bulunan remdesivirin 1647 COVID-19 hastasını içeren iki randomize kontrollü çalışmada klinik sonuçlara bazı olumlu etkileri olduğu gösterilmiştir. Bu nedenlerle ***remdesivirin orta/ağır seyirli COVID-19 pnömonilerinde kullanılabileceği düşünülmektedir.*** Yeni klinik çalışma sonuçlarına göre kullanım indikasyonları tekrar değerlendirilmelidir. Remdesivirin COVID-19 tedavisinde kullanımı sırasında gelişen ciddi istenmeyen etki bildirilmemiştir.

Korunma

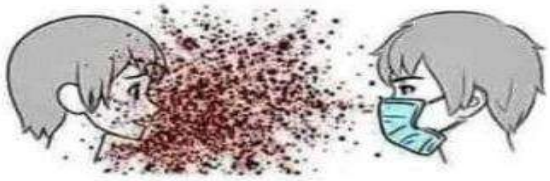
Genel Önlemler

1. Doğru Bilgi
2. Doğru ve yerinde Maske kullanımı
3. Mesafe
4. El temizliği
5. Havalandırma

Will I get Covid-19?



Definitely

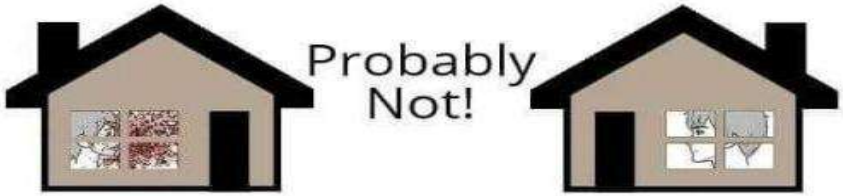


Probably

Possibly

Maybe

Maybe
Not!



Probably
Not!

Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis

*Derek K Chu, Elie A Akl, Stephanie Duda, Karla Solo, Sally Yaacoub, Holger J Schünemann, on behalf of the COVID-19 Systematic Urgent Review Group Effort (SURGE) study authors**

https://doi.org/10.1016/ S01406736(20)31142-9

COVID-19, SARS ve MERS'le ilgili 25697 hasta içeren 44 karşılaştırmalı çalışma

Maske, fizik mesafe ve gözlük/yüz koruyucunun etkisi araştırılmış

	Studies and participants	Relative effect (95% CI)
Physical distance ≥1 m *vs* <1 m	Nine adjusted studies (n=7782); 29 unadjusted studies (n=10736)	aOR 0·18 (0·09 to 0·38); unadjusted RR 0·30 (95% CI 0·20 to 0·44)
Face mask *vs* no face mask	Ten adjusted studies (n=2647); 29 unadjusted studies (n=10170)	aOR 0·15 (0·07 to 0·34); unadjusted RR 0·34 (95% CI 0·26 to 0·45)
Eye protection (faceshield, goggles) *vs* no eye protection	13 unadjusted studies (n=3713)	Unadjusted RR 0·34 (0·22 to 0·52)¶

1 metre mesafe hastalık riskini %70-82 azaltıyor

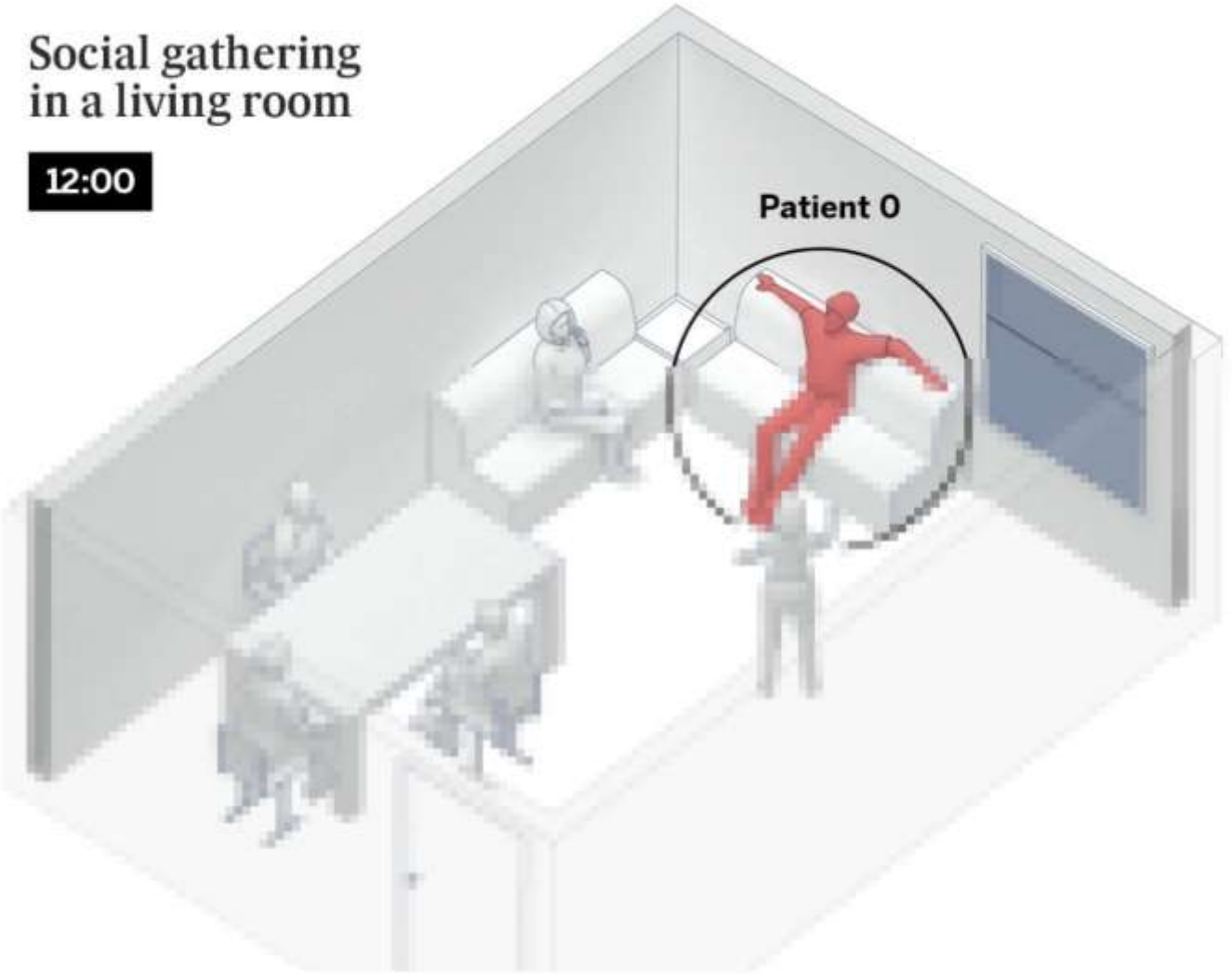
Fazladan her bir metre riski 2 kat azaltıyor

Maske kullanımı hastalık riskini %66-85 azaltıyor

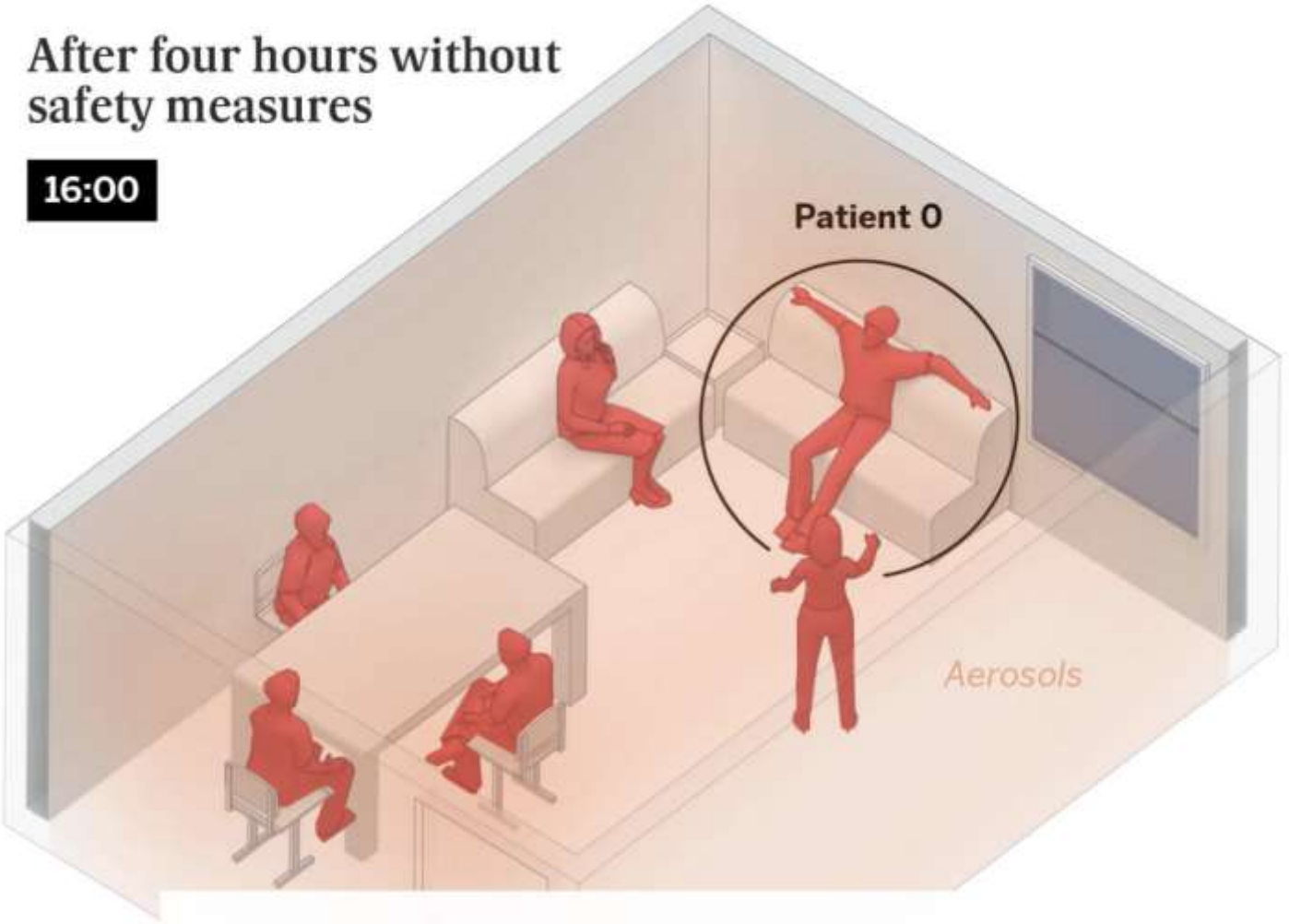
Gözlük/yüz koruyucu hastalık riskini %48-78 azaltıyor

Social gathering in a living room

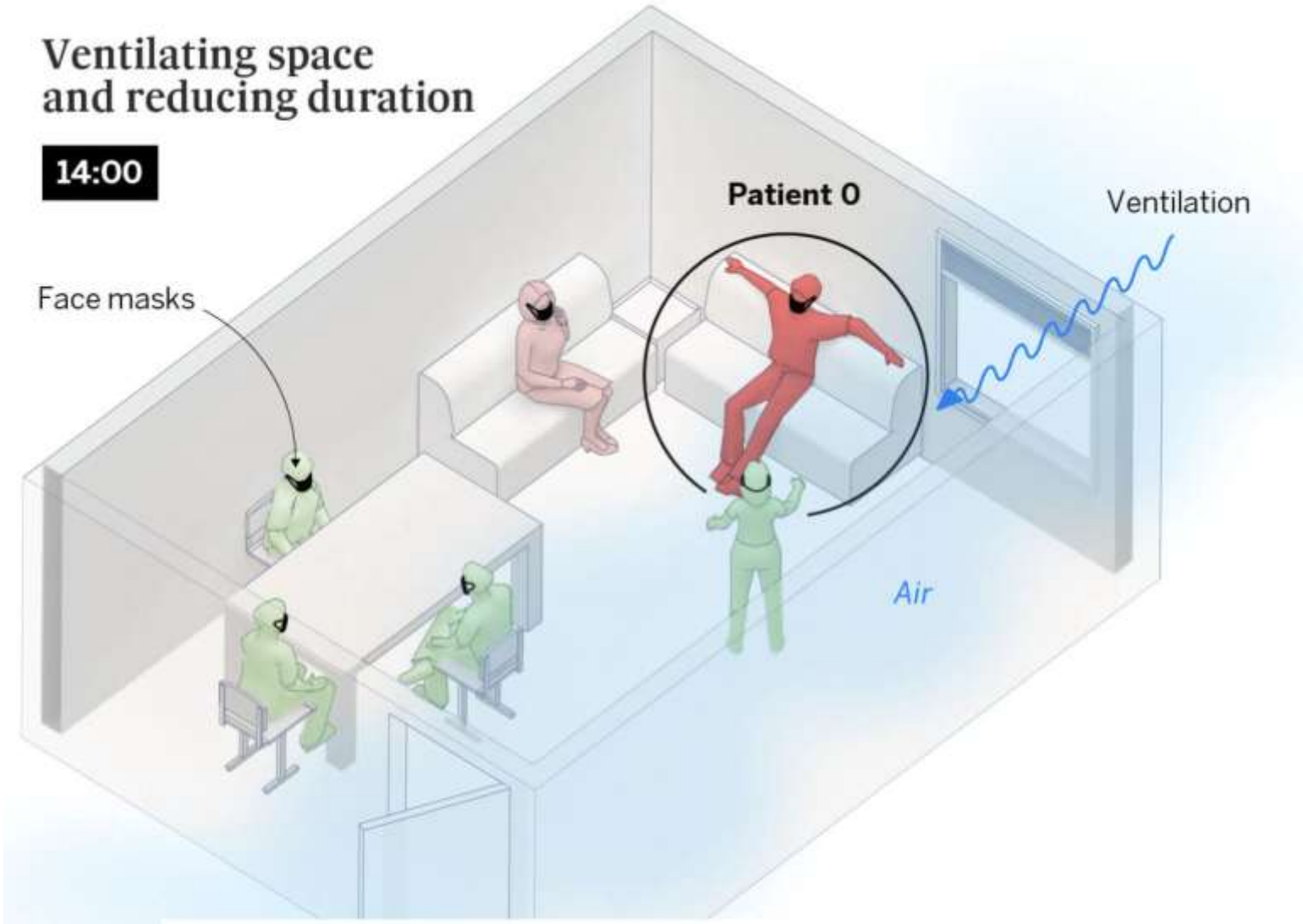
12:00



Six people get together in a private home, one of whom is infected. **Some 31% of coronavirus outbreaks recorded in Spain** are caused by this kind of gathering, mainly between family and friends.



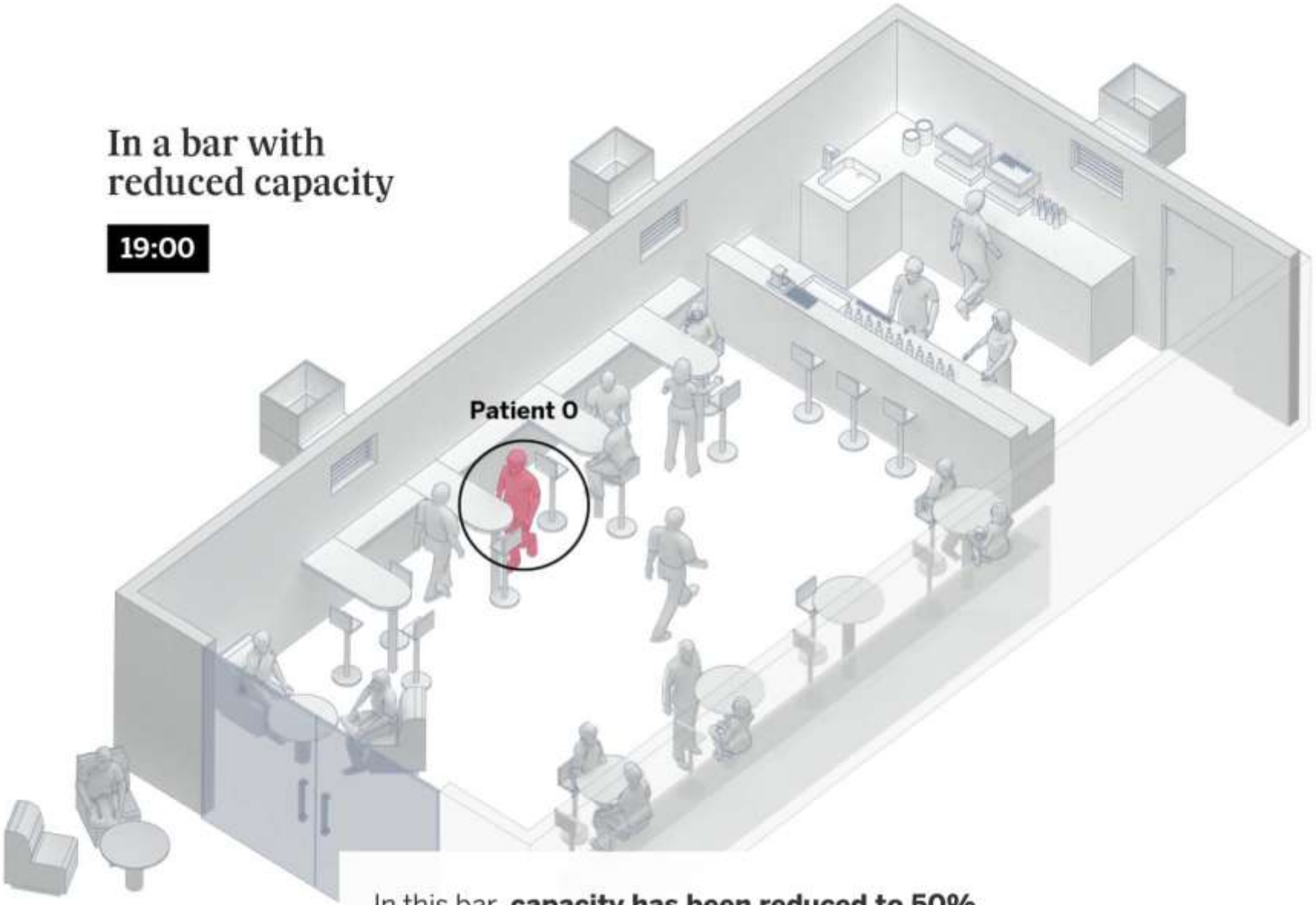
Irrespective of whether safe distances are maintained, if the six people spend four hours together talking loudly, without wearing a face mask in a room with no ventilation, **five will become infected,** according to the scientific model explained in the methodology.



The risk of infection drops to below one when the group **uses face masks, shortens the length of the gathering by half and ventilates the space used.**

In a bar with reduced capacity

19:00

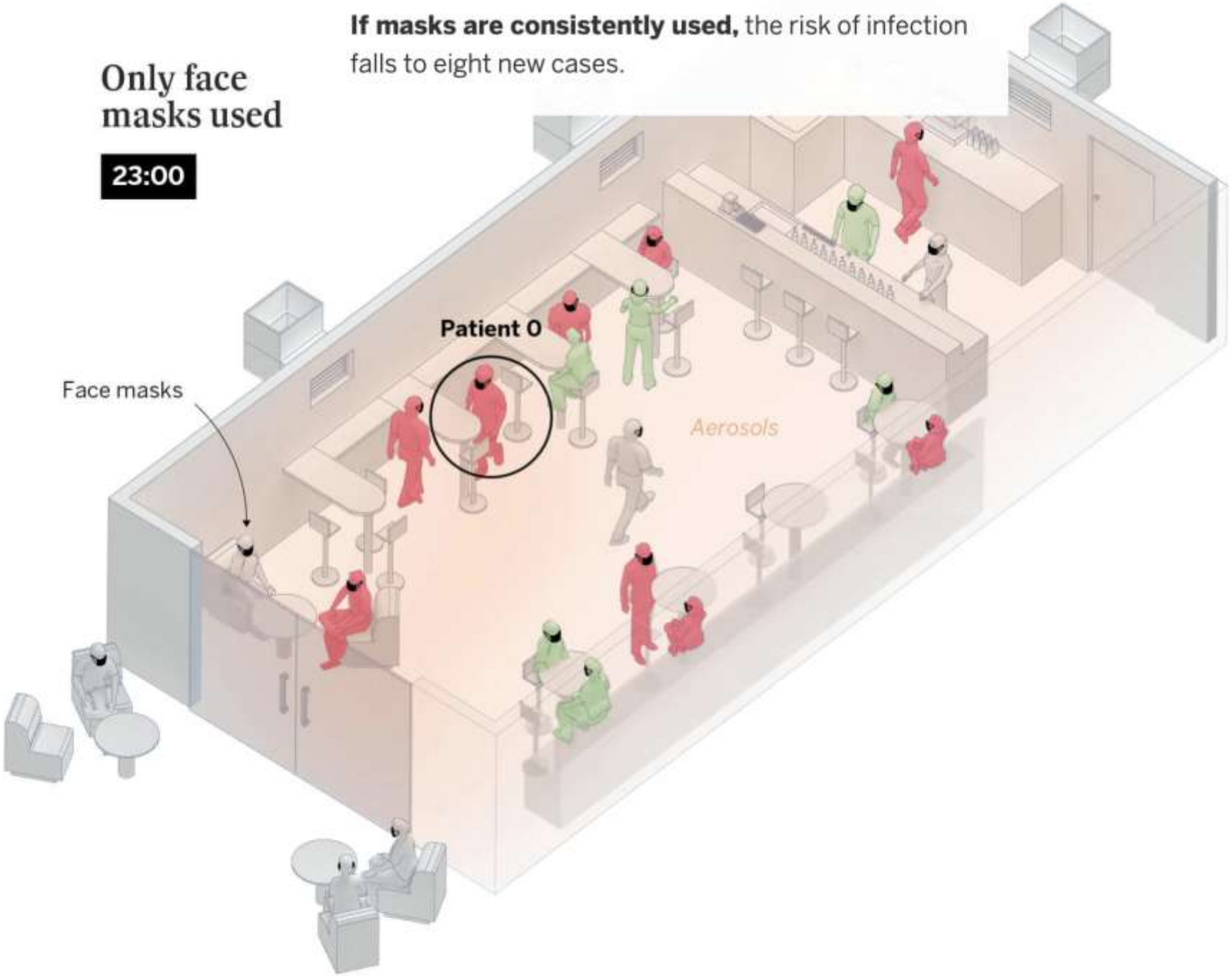


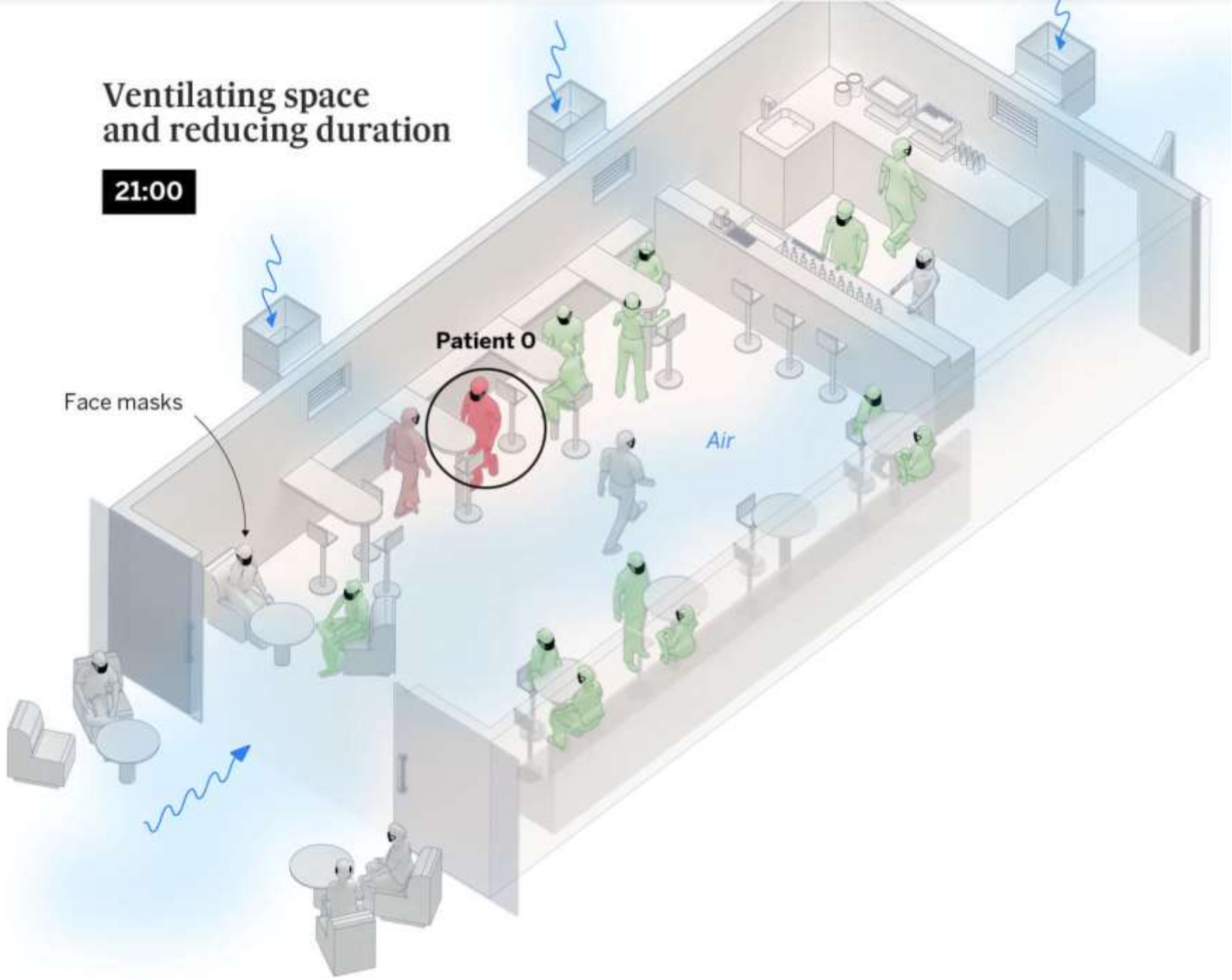
In this bar, **capacity has been reduced to 50%.** There are 15 patrons and three members of staff. The windows are closed and there is no mechanical ventilation.

If masks are consistently used, the risk of infection falls to eight new cases.

Only face masks used

23:00




Ventilating space
and reducing duration
21:00
Patient 0
Face masks
Air

KLİMİK TÜRK KLİNİK MİKROBİYOLOJİ VE İNFEKSİYON HASTALIKLARI DERNEĞİ

Bilimle Sağlıkla 34 .Yıl

Teşekkürler…