MEDICINA

USP

A pandemia de doença respiratória pelo SARS-CoV-2

Objetivos

- *Sistematizar os conhecimentos sobre a doença pelo corona vírus da síndrome respiratória aguda grave 2 (SARS-CoV-2)*
  - *Origem*
  - *Distribuição e disseminação*
  - *Estrutura epidemiológica*

- *Discutir as ações de vigilância e controle da doença pelo SARS-CoV-2*

Antecedentes

- *Coronavírus emergentes:*
  - *SARS-CoV-1 – China 2002/2003 (β)*
  - *MERS-CoV – Arábia Saudita 2012 (β)*
- *Coronavírus humanos relacionados às infecções das vias aéreas superiores (IVAS):*
  - *Gênero α coronavírus:*
    - *HCoV-229E*
    - *HCoV-NL63*
  - *Gênero β coronavírus:*
    - *HCoV-OC43*
    - *HCoV-HKU1*

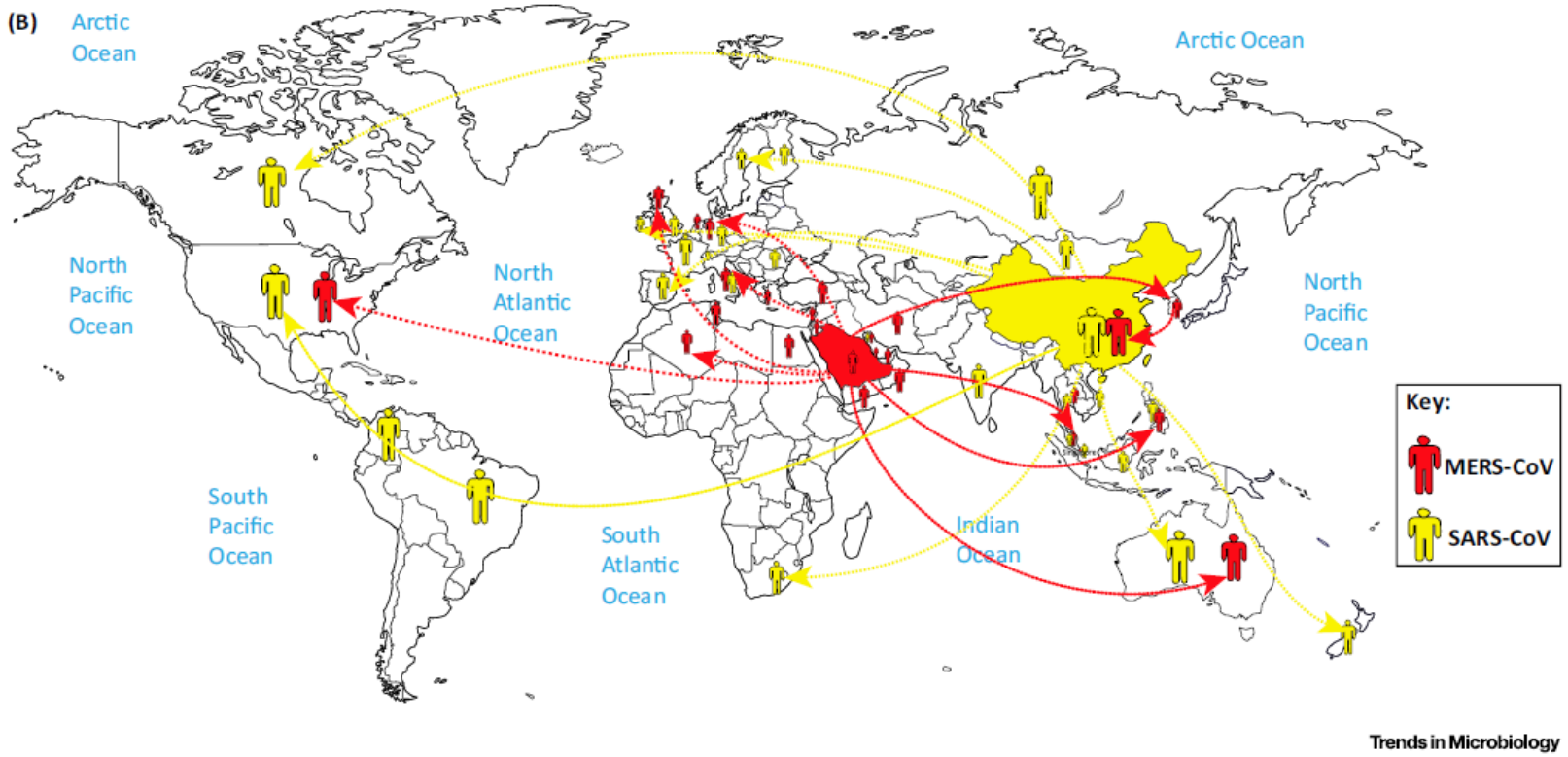


Figure 1. Global Distribution of Human Coronaviruses. (A) Green, blue, brown, and purple represent the global distribution of the NL63, HKU1, OC43, and 229E human coronaviruses, respectively. (B) Red and yellow represent the global distribution of MERS-CoV and SARS-CoV, respectively.

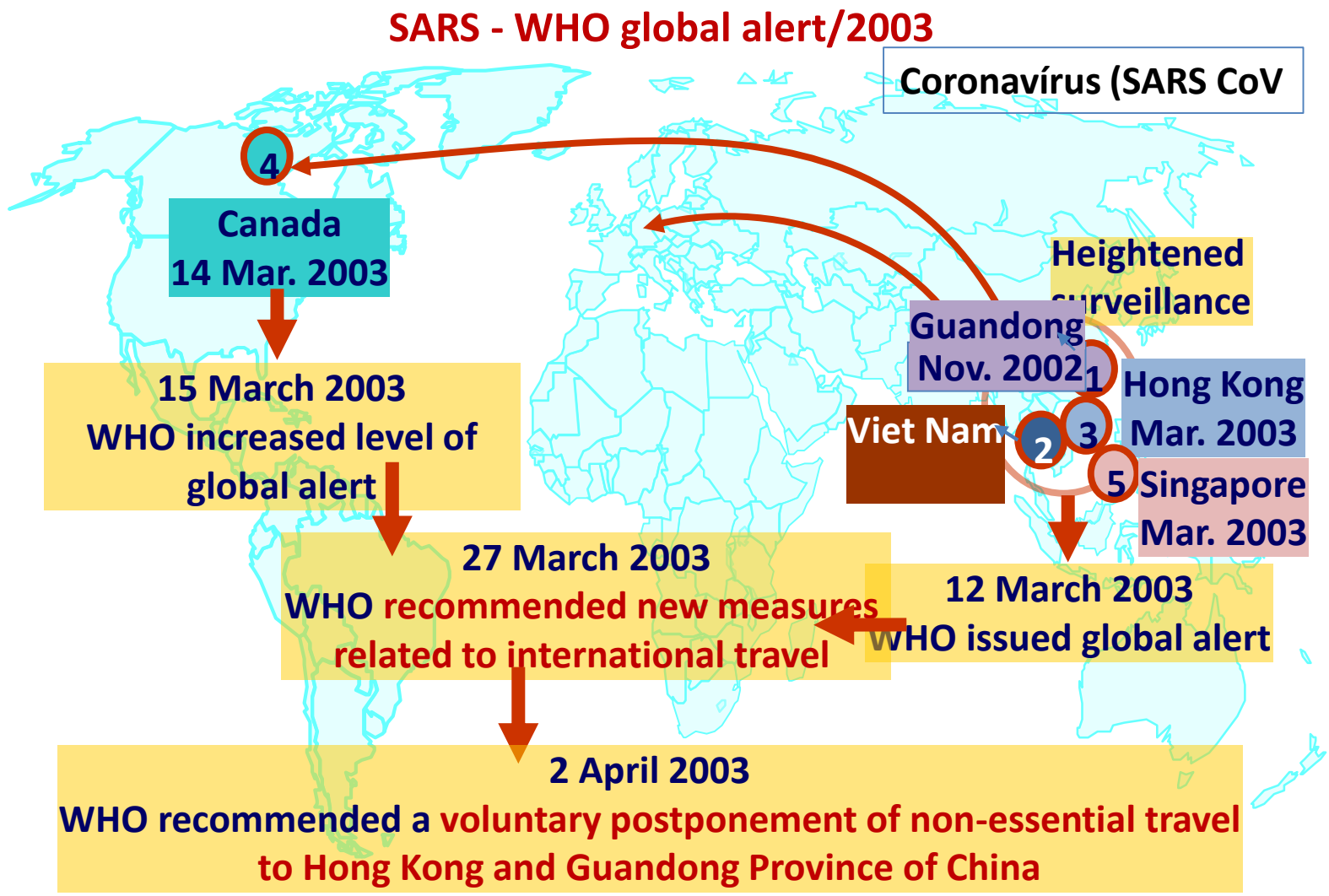
Su et al. Trends in Microbiology 2016, 24(6):490-502

NOVO RSI

Síndrome Respiratória Aguda Grave – SARS CoV
(Severe Acute Respiratory Syndrome)

Considerada a 1ª pandemia do século XXI

Coronavírus


SARS - WHO global alert/2003
Coronavírus (SARS CoV
4
Canada
14 Mar. 2003
15 March 2003
WHO increased level of
global alert
Heightened
surveillance
Guandong
Nov. 2002
1
Hong Kong
Mar. 2003
Viet Nam
2
3
5
Singapore
Mar. 2003
12 March 2003
WHO issued global alert
27 March 2003
WHO recommended new measures
related to international travel
2 April 2003
WHO recommended a voluntary postponement of non-essential travel
to Hong Kong and Guandong Province of China

Número de casos prováveis e óbitos notificados de SRAG segundo país e local de ocorrência. Revisado em 23.09.03

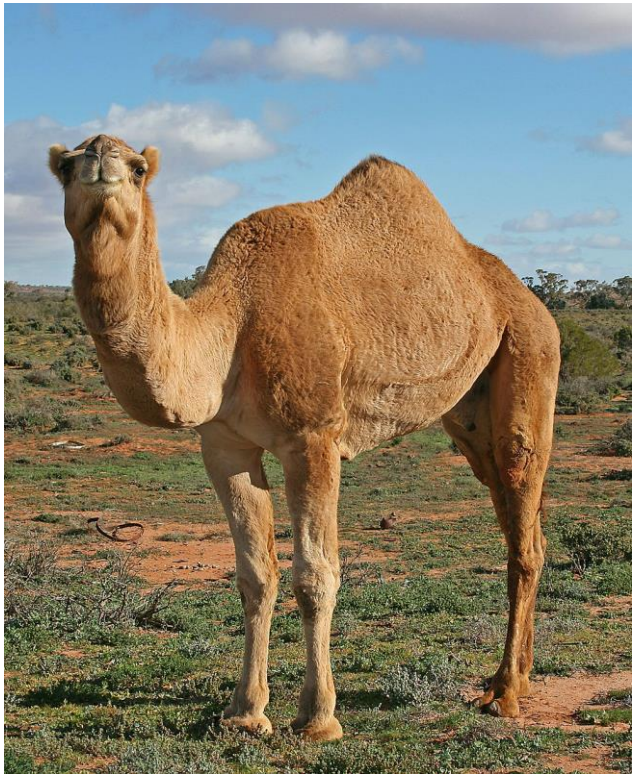
País/Local	Número de casos	Número de óbitos	Transmissão autóctone
África do Sul	1	1	Não
Alemanha	9	0	Não
Austrália	6	0	Não
Canadá	251	43	Sim
China:			
1. Hong Kong	1755	299	Sim
2. Macau	1	0	Não
3. Taiwan	346	37	Sim
Continental	5327	349	Sim
Singapura	238	33	Sim
Coréia do Sul	3	0	Não
Espanha	1	0	Não
Estados Unidos	29	0	Sim
Filipinas	14	2	Sim
França	7	1	Não
Irlanda	1	0	Não
Índia	3	0	Não
Indonésia	2	0	Não
Itália	4	0	Não
Kuwait	1	0	Não
Malásia	5	2	Não
Mongólia	9	0	Sim
Nova Zelândia	1	0	Não
Reino Unido	4	0	Não
Romênia	1	0	Não
Rússia	1	0	Não avaliado
Suécia	5	0	Não
Suíça	1	0	Não
Tailândia	9	2	Não
Vietnã	63	5	Sim
Total	8.098	774	

Fonte: Organização Mundial de Saúde

Civeta (Paguma larvata)

Síndrome Respiratória do Oriente Médio – MERS

Agente etiológico: coronavírus – MERS-CoV
Emergiu no Oriente Médio entre Abril e Junho de 2012
Até Novembro de 2019 – 2.494 casos confirmados, com 858 óbitos (letalidade de 34,4%)
A maioria dos casos ocorreu na Arábia Saudita (2.102 casos, 84%). Transmissão já confirmada em outros países do Oriente Médio (EAU, Jordânia, Qatar, Kuwait, Oman, Irã). Surto na Coréia do Sul em 2015.
Apresentação clínica: febre, tosse e dispneia. Maioria dos casos do sexo masculino, acima de 50 anos de idade.

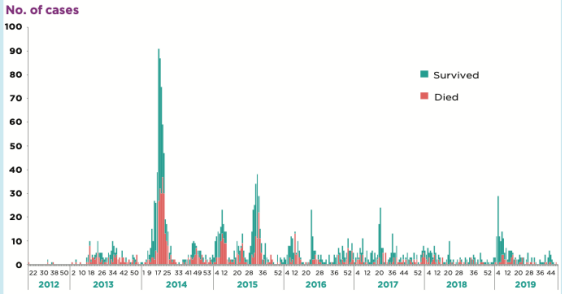


Transmissão:
Ocorre em contato próximo, domiciliar, no cuidado de pacientes com MERS.
Dromedários – reservatório do vírus
"Superdisseminadores" – o caso índice do surto da Coréia do Sul transmitiu para 18 outros casos, antes de ser diagnosticado e isolado.

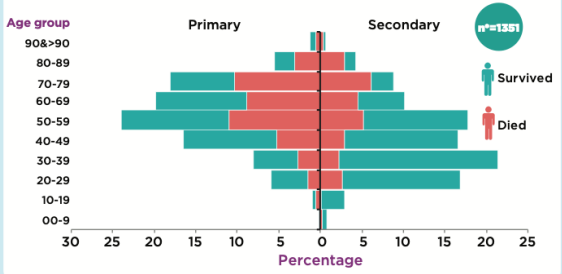
HIGHLIGHTS

- At the end of November 2019, a total of 2494 laboratory-confirmed cases of Middle East respiratory syndrome (MERS), including 858 associated deaths (case-fatality rate: 34.4%) were reported globally; the majority of these cases were reported from Saudi Arabia (2102 cases, including 780 related deaths with a case-fatality rate of 37.1%).
- Since the last update was published (October MERS situation update), a total of 12 laboratory-confirmed cases of MERS were reported globally including one healthcare worker. All of the cases were reported from Saudi Arabia with 4 associated deaths. Only one of the cases was a female. The healthcare worker was infected in October while providing care for a case. No other cluster of case was reported this month, despite 6 cases being reported from the same region. Three of the cases had their symptom onset in October.
- The demographic and epidemiological characteristics of reported cases, when compared during the same corresponding period of 2014 to 2019 (June to November), do not show any significant difference or change. The number of cases reported in this period was less than all other corresponding periods of respective years, except for 2018.
- The age group 50–59 years continues to be at the highest risk for acquiring infection of primary cases. The age group 30–39 years is most at risk for secondary cases. The number of deaths is higher in the age group 50–59 years for primary cases and 70–79 years for secondary cases.

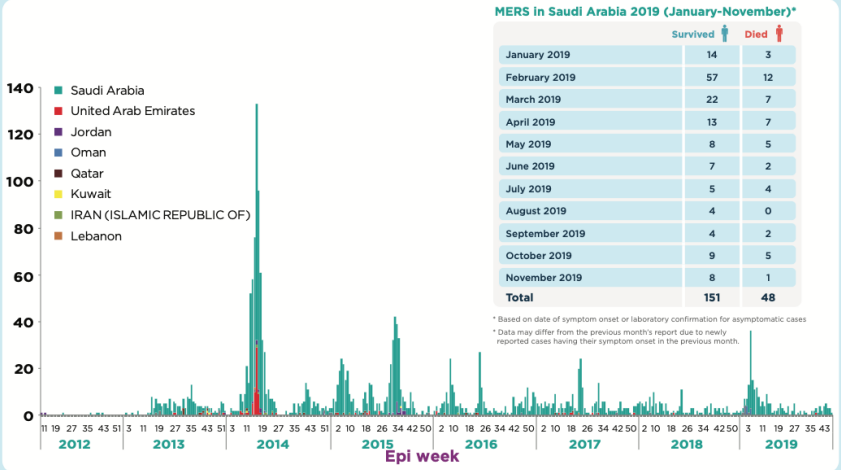
MERS cases reported from the Kingdom of Saudi Arabia by week of symptoms onset, June 2012-November 2019



Age and fatality distribution of Primary and Secondary cases of MERS reported from Saudi Arabia, 2012-November 2019



Laboratory-confirmed cases of MERS reported in Eastern Mediterranean Region, July 2012-November 2019



MERS in Saudi Arabia 2019 (January-November)*

	Survived	Died
January 2019	14	3
February 2019	57	12
March 2019	22	7
April 2019	13	7
May 2019	8	5
June 2019	7	2
July 2019	5	4
August 2019	4	0
September 2019	4	2
October 2019	9	5
November 2019	8	1
Total	151	48

* Based on date of symptom onset or laboratory confirmation for asymptomatic cases
* Data may differ from the previous month's report due to newly reported cases having their symptom onset in the previous month.

Epidemiological characteristics of MERS cases reported globally between June-November 2014 and June-November 2019

Characteristic	Jun-Nov 14	Jun-Nov 15	Jun-Nov 16	Jun-Nov 17	Jun-Nov 18	Jun-Nov 19
Number	118	407	123	139	49	52
Median age in years	52	53	52	48	56	56
Gender (% male)	77	59	67	66	87	86
% of primary cases	37	4	37	23	48	36
% of secondary cases	36	40	23	47	18	7
(%) of unknown contact history	21	1	6	0	2	19
% of HCW	16	16	17	25	0	5
% of Fatal	42	27	24	24	32	26

Characteristics of MERS cases reported from Kingdom of Saudi Arabia, June 2012-November 2019

Type of case	2012	2013	2014	2015	2016	2017	2018	2019	Grand Total
Primary	3	36	164	52	75	70	54	56	510
Secondary	2	93	264	222	60	90	35	75	841
Missing		1	15	102	103	68	52	58	399
Unknown		28	219	78	11	5	1	10	352
Total	5	158	662	454	249	233	142	199	2102

SUMMARY

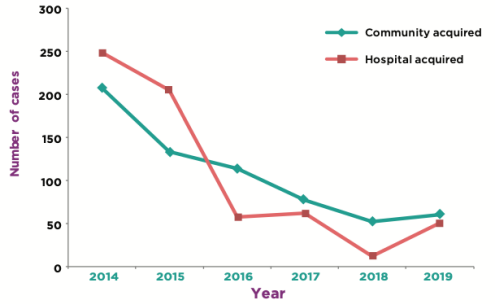
2494 Laboratory-confirmed cases reported since April 2012

858 deaths reported since April 2012

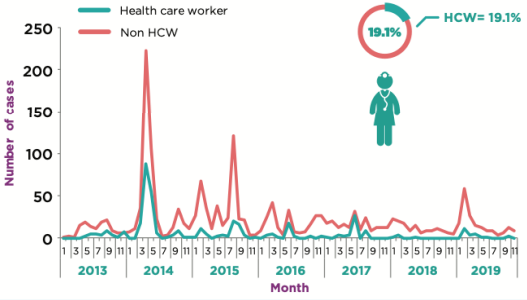
27 countries reported cases globally

12 countries reported cases since April 2012 in the Eastern Mediterranean Region

Community versus hospital acquired (symptomatic) MERS cases in Eastern Mediterranean Region, Jan 2014-Nov 2019



Cases of MERS in healthcare workers reported from Saudi Arabia Jan 2013 - Nov 2019



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Síndrome Respiratória do Oriente Médio, Relatório de Situação, OMS, novembro de 2019

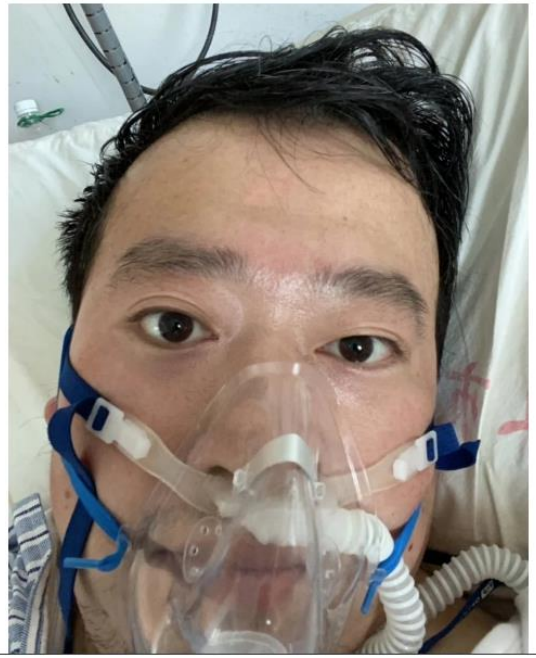
www.who.int

Coronavírus 2019

- Alerta para ocorrência de quadros de SRAG diferentes do habitual em dezembro, 2019, eu Wuhan, província de Hubei, China.
- Início de janeiro 2020, identificado o agente etiológico, um “novo” coronavirus, de provável origem zoonótica.
- Em 23/01 o governo chinês decreta o “fechamento” das fronteiras da província de Hubei. Feriado do ano novo chinês foi estendido por mais uma semana em todo o país, e até 10/03 em Hubei.
- A estratégia de barreira sanitária vem sendo recomendada pela OMS, que considera possível o controle da transmissão por meio dessa estratégia.

Chinese Doctor, Silenced After Warning of Outbreak, Dies From Coronavirus

Dr. Li Wenliang issued a warning about a strange new virus. Then the authorities summoned him for questioning.



By Chris Buckley

Published Feb. 6, 2020 Updated Feb. 7, 2020

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WUHAN, China — He was the doctor who tried to sound a warning that a troubling cluster of viral infections in a Chinese province could grow out of control — and was then summoned for a middle-of-the-night reprimand over his candor.

On Friday, the doctor, Li Wenliang, died after contracting the very illness he had told medical school classmates about in an online chat room, the coronavirus. He joined the more than 600 other Chinese who have died in an outbreak that has now spread across the globe.

Dr. Li "had the misfortune to be infected during the fight against the novel coronavirus pneumonia epidemic, and all-out efforts to save him failed," the Wuhan City Central Hospital said on Weibo, the Chinese social media service. "We express our deep regret and condolences."

Even before his death, Dr. Li had become a hero to many Chinese after word of his treatment at the hands of the authorities emerged. In early January, he was called in by both medical officials and the police, and forced to sign a statement denouncing his warning as an unfounded and illegal rumor.

Dr. Li's death was a reminder of the risks faced by doctors, nurses and medical workers treating coronavirus patients. EPA, via Shutterstock

When Dr. Li posted his chat room warning on Dec. 30, the new coronavirus had not yet been identified. He said it resembled Severe Acute Respiratory Syndrome, or SARS, an earlier coronavirus that ravaged China nearly two decades ago.

Not long after his reprimand, Dr. Li was vindicated as thousands of Wuhan residents fell ill with fever and pneumonia symptoms. He joined their number after contracting the virus from a patient he was treating for glaucoma.

Rumores sobre o aumento da ocorrência de casos de uma síndrome respiratória aguda grave em Wuhan apareceram nas redes sociais na última semana de 2019

Defining the Epidemiology of Covid-19 — Studies Needed

Marc Lipsitch, D.Phil., David L. Swerdlow, M.D., and Lyn Finelli, Dr.P.H.

The epidemic of 2019 novel coronavirus (now called SARS-CoV-2, causing the disease Covid-19) has expanded from Wuhan throughout China and is being exported to a growing number of countries, some of which have seen onward transmission. Early efforts have focused on describing the clinical course, counting severe cases, and treating the sick. Experience with the Middle East respiratory syndrome (MERS), pandemic influenza, and other outbreaks has shown that as an epidemic evolves, we face an urgent need to expand public health activities in order to elucidate the epidemiology of the novel virus and characterize its potential impact. The impact of an epidemic depends on the number of persons infected, the infection's transmissibility, and the spectrum of clinical severity.

Thus, several questions are especially critical. First, what is the full spectrum of disease severity (which can range from asymptomatic, to symptomatic-but-mild, to severe, to requiring hospitalization, to fatal)?

Second, how transmissible is the virus?

Third, who are the infectors — how do the infected person's age, the severity of illness, and other characteristics of a case affect the risk of transmitting the infection to others? Of vital interest is the role that asymptomatic or presymptomatic infected persons play in transmission. When and for how long is the virus present in respiratory secretions?

And fourth, what are the risk factors for severe illness or death? And how can we identify groups most likely to have poor outcomes so that we can focus prevention and treatment efforts?

The table lists approaches to answering these questions, each of which has shown success in prior disease outbreaks, especially MERS and pandemic H1N1 influenza.[1]

Counting the number of cases, including mild cases, is necessary to calibrate the epidemic response. Conventional wisdom dictates that the sickest people seek care and undergo testing; early in an epidemic, case fatality and hospitalization ratios are often used to assess impact. These measures should be interpreted with caution, since it may take time for cases to become severe, or for infected persons to die, and it may not be possible to accurately estimate the denominator of infected people in order to calculate those ratios.[2] As in past epidemics, the first cases of Covid-19 to be observed in China were severe enough to come to medical attention and result in testing, but the total number of people infected has been elusive. The estimated case fatality ratio among medically attended patients thus far is approximately 2%, but the true ratio may not be known for some time.[2]

Simple counts of the number of confirmed cases can be misleading indicators of the epidemic's trajectory if these counts are limited by problems in access to care or bottlenecks in laboratory testing, or if only patients with severe cases are tested. During the 2009 influenza pandemic, an approach was described for maintaining surveillance when cases become too numerous to count. This approach, which can be adapted to Covid-19, involves using existing surveillance systems or designing surveys to ascertain each week the number of persons with a highly sensitive but nonspecific syndrome (for example, acute respiratory infection) and testing a subset of these persons for the novel coronavirus. The product of the incidence of acute respiratory infection (for example) and the percent testing positive provides an estimate of the burden of cases in a given jurisdiction.[3] Now is the time to put in place the infrastructure to accomplish such surveillance. Electronic laboratory reporting will dramatically improve the efficiency of this and other public health studies involving viral testing.

More generally, it is useful to synthesize data from simultaneous surveillance studies, epidemiologic field investigations, and case series.[1] Conducting cohort studies in well-defined settings such as schools, workplaces, or neighborhoods (community surveys) can help in describing the overall burden and the household and community attack rate; perhaps most important, it can permit rapid assessment of the severity of the epidemic by counting the number of illnesses, hospitalizations, and deaths in a well-defined population and extrapolating that rate to the larger population.[4] Understanding transmissibility remains crucial for predicting the course of the epidemic and the likelihood of sustained transmission. Several

Quatro perguntas que demandam investigação científica:

1) Quais as características clínicas da COVID19, em relação à gravidade da doença?
2) Qual a transmissibilidade do vírus?
3) Quem são os transmissores e por quanto tempo o vírus permanece nas secreções respiratórias?
4) Quais os fatores de risco para a doença grave?

Types of Evidence Needed for Controlling an Epidemic.

Evidence Needed	Study Type
No. of cases, including milder ones	Syndromic surveillance plus targeted viral testing
Risk factors and timing of transmission	Household studies
Severity and attack rate	Community studies
Severity "pyramid"	Integration of multiple sources and data types
Risk factors for infection and severe outcomes, including death	Case–control studies
Infectiousness timing and intensity	Viral shedding studies

The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL PRACTICE

Caren G. Solomon, M.D., M.P.H., *Editor*

Mild or Moderate Covid-19

Rajesh T. Gandhi, M.D., John B. Lynch, M.D., M.P.H., and Carlos del Rio, M.D.

This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the authors' clinical recommendations.

KEY CLINICAL POINTS

MILD OR MODERATE COVID-19

- Covid-19 (the illness caused by SARS-CoV-2) has a range of clinical manifestations, including cough, fever, malaise, myalgias, gastrointestinal symptoms, and anosmia.
- Diagnosis of Covid-19 is usually based on detection of SARS-CoV-2 by PCR testing of a nasopharyngeal swab or other specimen.
- Evaluation and management of Covid-19 depends on the severity of the disease; patients with mild disease typically recover at home.
- Patients with moderate or severe Covid-19 are usually hospitalized for observation and supportive care.
- There are no proven therapies for Covid-19; thus, referral of patients to clinical trials is critical.
- Infection control and prevention efforts center on personal protective equipment for health care workers, social distancing, and testing.

The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL PRACTICE

Caren G. Solomon, M.D., M.P.H., *Editor*

Severe Covid-19

David A. Berlin, M.D., Roy M. Gulick, M.D., M.P.H., and Fernando J. Martinez, M.D.

This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the authors' clinical recommendations.

KEY CLINICAL POINTS

EVALUATION AND MANAGEMENT OF SEVERE COVID-19

- Patients with severe coronavirus disease 2019 (Covid-19) may become critically ill with acute respiratory distress syndrome that typically begins approximately 1 week after the onset of symptoms.
- Deciding when a patient with severe Covid-19 should receive endotracheal intubation is an essential component of care.
- After intubation, patients should receive lung-protective ventilation with plateau pressure less than or equal to 30 cm of water and with tidal volumes based on the patient's height.
- Prone positioning is a potential treatment strategy for refractory hypoxemia.
- Thrombosis and renal failure are well-recognized complications of severe Covid-19.
- Data are needed from randomized trials to inform the benefits and risks of antiviral or immunomodulatory therapies for severe Covid-19; as of mid-May 2020, no agents had been approved by the Food and Drug Administration for treatment of these patients.
- Preliminary data from a randomized, placebo-controlled trial involving patients with severe Covid-19 suggest that the investigational antiviral remdesivir shortens time to recovery.

Fatores de risco para doença grave

- ✓ Idade > 70 anos. Sexo masculino.
- ✓ Comorbidades:
  - ✓ Hipertensão arterial, doença cardiovascular, diabetes, doença pulmonar crônica
  - ✓ Obesidade, tabagismo, neoplasias
- ✓ Para admissão a UTI: ↑ leucócitos; ↑ enzimas hepáticas (ALT e AST); ↑ DHL; ↑ procalcitonina
- ✓ Para o óbito: ↑ leucócitos; ↑ DHL

Fonte: Jordan RE et al, BMJ May 26, 2020; Zhang JY et al, Clin Infect Dis, May, 2020

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Multisystem Inflammatory Syndrome in U.S. Children and Adolescents

L.R. Feldstein, E.B. Rose, S.M. Horwitz, J.P. Collins, M.M. Newhams, M.B.F. Son, J.W. Newburger, L.C. Kleinman, S.M. Heidemann, A.A. Martin, A.R. Singh, S. Li, K.M. Tarquinio, P. Jaggi, M.E. Oster, S.P. Zackai, J. Gillen, A.J. Ratner, R.F. Walsh, J.C. Fitzgerald, M.A. Keenaghan, H. Alharash, S. Doymaz, K.N. Clouser, J.S. Giuliano, Jr., A. Gupta, R.M. Parker, A.B. Maddux, V. Havalad, S. Ramsingh, H. Bukulmez, T.T. Bradford, L.S. Smith, M.W. Tenforde, C.L. Carroll, B.J. Riggs, S.J. Gertz, A. Daube, A. Lansell, A. Coronado Munoz, C.V. Hobbs, K.L. Marohn, N.B. Halasa, M.M. Patel, and A.G. Randolph, for the Overcoming COVID-19 Investigators and the CDC COVID-19 Response Team*

ABSTRACT

BACKGROUND

Understanding the epidemiology and clinical course of multisystem inflammatory syndrome in children (MIS-C) and its temporal association with coronavirus disease 2019 (Covid-19) is important, given the clinical and public health implications of the syndrome.

METHODS

We conducted targeted surveillance for MIS-C from March 15 to May 20, 2020, in pediatric health centers across the United States. The case definition included six criteria: serious illness leading to hospitalization, an age of less than 21 years, fever that lasted for at least 24 hours, laboratory evidence of inflammation, multisystem organ involvement, and evidence of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) based on reverse-transcriptase polymerase chain reaction (RT-PCR), antibody testing, or exposure to persons with Covid-19 in the past month. Clinicians abstracted the data onto standardized forms.

RESULTS

We report on 186 patients with MIS-C in 26 states. The median age was 8.3 years, 115 patients (62%) were male, 135 (73%) had previously been healthy, 131 (70%) were positive for SARS-CoV-2 by RT-PCR or antibody testing, and 164 (88%) were hospitalized after April 16, 2020. Organ-system involvement included the gastrointestinal system in 171 patients (92%), cardiovascular in 149 (80%), hematologic in 142 (76%), mucocutaneous in 137 (74%), and respiratory in 131 (70%). The median duration of hospitalization was 7 days (interquartile range, 4 to 10); 148 patients (80%) received intensive care, 37 (20%) received mechanical ventilation, 90 (48%) received vasoactive support, and 4 (2%) died. Coronary-artery aneurysms (z scores ≥2.5) were documented in 15 patients (8%), and Kawasaki's disease–like features were documented in 74 (40%). Most patients (171 [92%]) had elevations in at least four biomarkers indicating inflammation. The use of immunomodulating therapies was common: intravenous immune globulin was used in 144 (77%), glucocorticoids in 91 (49%), and interleukin-6 or 1RA inhibitors in 38 (20%).

CONCLUSIONS

Multisystem inflammatory syndrome in children associated with SARS-CoV-2 led to serious and life-threatening illness in previously healthy children and adolescents. (Funded by the Centers for Disease Control and Prevention.)

Síndrome inflamatória com envolvimento de vários sistemas

Descrição de casuística de vários serviços pediátricos nos EUA

Período: 15/03 a 20/05/2020

Definição de caso: seis critérios:

- Doença grave que demandou hospitalização do paciente
- Idade < 21 anos
- Febre por no mínimo 24 horas
- Evidência laboratorial de inflamação
- Envolvimento de múltiplos órgãos ou sistemas
- Evidência de infecção pelo SARS-CoV-2

N = 186 pacientes

Sistemas envolvidos: gastrointestinal (92%); cardiovascular (80%); hematológico (76%); mucocutâneo (74%); respiratório (70%).

4 óbitos

Aneurisma de coronárias: 15 pacientes

Doença de Kawasaki: 74 (40%)

Doença de Kawasaki

Síndrome inflamatória vascular (vasculite)

Sintomas:

1ª fase: febre alta (>40ºC por + de 5 dias), rash cutâneo (principalmente em tronco e genitais), hiperemia de conjuntiva, edema e hiperemia da língua (língua em framboesa), linfadenopatia cervical

2ª fase: descamação da pele, dores articulares, diarreia, vômitos

3ª fase: miocardite, cardiomegalia, arritmias, aneurismas coronarianos

Estimativa da duração do período de incubação da Covid-19

- ✓ Série de 181 casos com data dos primeiros sintomas e data de exposição conhecidos.
- ✓ Pacientes fora de Wuhan
- ✓ Mediana do período de incubação: 5,1 dias (IC95%: 4,5; 5,8)
- ✓ 97,5% apresentaram sintomas em até 11 dias, e 99% em até 14 dias.
- ✓ 2,5% apresentaram sintomas em 2,2 dias ou menos.

Metanálise de 43 estudos
Período de incubação médio: 5,68 dias (IC95%: 4,78 – 6,59)

Annals of Internal Medicine ORIGINAL RESEARCH

The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application

Stephen A. Lauer, MS, PhD*; Kyra H. Grantz, BA*; Qifang Bi, MHS; Forrest K. Jones, MPH; Qulu Zheng, MHS; Hannah R. Meredith, PhD; Andrew S. Azman, PhD; Nicholas G. Reich, PhD; and Justin Lessler, PhD

Background: A novel human coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was identified in China in December 2019. There is limited support for many of its key epidemiologic features, including the incubation period for clinical disease (coronavirus disease 2019 [COVID-19]), which has important implications for surveillance and control activities.

Objective: To estimate the length of the incubation period of COVID-19 and describe its public health implications.

Design: Pooled analysis of confirmed COVID-19 cases reported between 4 January 2020 and 24 February 2020.

Setting: News reports and press releases from 50 provinces, regions, and countries outside Wuhan, Hubei province, China.

Participants: Persons with confirmed SARS-CoV-2 infection outside Hubei province, China.

Measurements: Patient demographic characteristics and dates and times of possible exposure, symptom onset, fever onset, and hospitalization.

Results: There were 181 confirmed cases with identifiable exposure and symptom onset windows to estimate the incubation period of COVID-19. The median incubation period was estimated to be 5.1 days (95% CI, 4.5 to 5.8 days), and 97.5% of those who develop symptoms will do so within 11.5 days (CI, 8.2 to 15.6 days) of infection. These estimates imply that, under conservative assumptions, 101 out of every 10 000 cases (99th percentile, 482) will develop symptoms after 14 days of active monitoring or quarantine.

Limitation: Publicly reported cases may overrepresent severe cases, the incubation period for which may differ from that of mild cases.

Conclusion: This work provides additional evidence for a median incubation period for COVID-19 of approximately 5 days, similar to SARS. Our results support current proposals for the length of quarantine or active monitoring of persons potentially exposed to SARS-CoV-2, although longer monitoring periods might be justified in extreme cases.

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For author affiliations, see end of text.
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* Dr. Lauer and Ms. Grantz share first authorship.

In December 2019, a cluster of severe pneumonia cases of unknown cause was reported in Wuhan, Hubei province, China. The initial cluster was epidemiologically linked to a seafood wholesale market in Wuhan, although many of the initial 41 cases were later reported to have no known exposure to the market (1). A novel strain of coronavirus belonging to the same family of viruses that cause severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), as well as the 4 human coronaviruses associated with the common cold, was subsequently isolated from lower respiratory tract samples of 4 cases on 7 January 2020 (2). Infection with the virus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), can be asymptomatic or can result in mild to severe symptomatic disease (coronavirus disease 2019 [COVID-19]) (3). On 30 January 2020, the World Health Organization declared that the SARS-CoV-2 outbreak constituted a Public Health Emergency of International Concern, and more than 80 000 confirmed cases had been reported worldwide as of 28 February 2020 (4, 5). On 31 January 2020, the U.S. Centers for Disease Control and Prevention announced that all citizens returning from Hubei prov-

88 confirmed cases in Chinese provinces outside Wuhan, using data on known travel to and from Wuhan to estimate the exposure interval, indicated a mean incubation period of 6.4 days (95% CI, 5.6 to 7.7 days), with a range of 2.1 to 11.1 days (7). Another analysis based on 158 confirmed cases outside Wuhan estimated a median incubation period of 5.0 days (CI, 4.4 to 5.6 days), with a range of 2 to 14 days (8). These estimates are generally consistent with estimates from 10 confirmed cases in China (mean incubation period, 5.2 days [CI, 4.1 to 7.0 days] [9]) and from clinical reports of a familial cluster of COVID-19 in which symptom onset occurred 3 to 6 days after assumed exposure in Wuhan (1). These estimates of the incubation period of SARS-CoV-2 are also in line with those of other known human coronaviruses, including SARS (mean, 5 days; range, 2 to 14 days [10]), MERS (mean, 5 to 7 days; range, 2 to 14 days [11]), and non-SARS human coronavirus (mean, 3 days; range, 2 to 5 days [12]).

The incubation period can inform several important public health activities for infectious diseases, including active monitoring, surveillance, control, and modeling. Active monitoring requires potentially ex-

Epidemiology and Infection

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Review

Epidemiological characteristics of COVID-19: a systematic review and meta-analysis

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Key words:
Coronavirus; COVID-19; epidemiology; pandemic

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Abstract

Our understanding of the Coronavirus disease 2019 (COVID-19) continues to evolve and there are many unknowns about its epidemiology. This study aims to synthesise case fatality rate (CFR) among confirmed COVID-19 patients, incubation period and time from onset of COVID-19 symptoms to first medical visit, intensive care unit (ICU) admission, recovery, and death. We searched MEDLINE, Embase, Google Scholar, and bibliographies of relevant articles from 01 December 2019 to 11 March 2020 without any language restrictions. Quantitative studies that recruited people with confirmed COVID-19 diagnosis were included. Two independent reviewers extracted the data. Out of 1675 non-duplicate studies, 43 were included in the meta-analysis. The pooled mean incubation period was 5.68 (99% confidence interval [CI]: 4.78, 6.59) days. The pooled mean number of days from the onset of COVID-19 symptoms to first clinical visit was 4.92 (95% CI: 3.95, 5.90), ICU admission was 9.84 (95% CI: 8.78, 10.90), recovery was 18.55 (95% CI: 13.69, 23.41), and death was 15.93 (95% CI: 13.07, 18.79). Pooled CFR among confirmed COVID-19 patients was 0.02 (95% CI: 0.02, 0.03). We found that the incubation period and lag between the onset of symptoms and first clinical visit for COVID-19 are longer than other respiratory viral infections including Middle East respiratory syndrome and severe acute respiratory syndrome; however, the current policy of 14 days of mandatory quarantine for everyone potentially exposed to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) might be too conservative. Longer quarantine periods might be more justified for extreme cases.

nature medicine

BRIEF COMMUNICATION

https://doi.org/10.1038/s41591-020-0869-5

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Temporal dynamics in viral shedding and transmissibility of COVID-19

Xi He[1,3], Eric H. Y. Lau[2,3]✉, Peng Wu[2], Xilong Deng[1], Jian Wang[1], Xinxin Hao[2], Yiu Chung Lau[2], Jessica Y. Wong[2], Yujuan Guan[1], Xinghua Tan[1], Xiaoneng Mo[1], Yanqing Chen[1], Baolin Liao[1], Weilie Chen[1], Fengyu Hu[1], Qing Zhang[1], Mingqiu Zhong[1], Yanrong Wu[1], Lingzhai Zhao[1], Fuchun Zhang[1], Benjamin J. Cowling[2,4], Fang Li[1,4] and Gabriel M. Leung[2,4]

We report temporal patterns of viral shedding in 94 patients with laboratory-confirmed COVID-19 and modeled COVID-19 infectiousness profiles from a separate sample of 77 infector–infectee transmission pairs. We observed the highest viral load in throat swabs at the time of symptom onset, and inferred that infectiousness peaked on or before symptom onset. We estimated that 44% (95% confidence interval, 25–69%) of secondary cases were infected during the index cases' presymptomatic stage, in settings with substantial household clustering, active case finding and quarantine outside the home. Disease control measures should be adjusted to account for probable substantial presymptomatic transmission.

SARS-CoV-2, the causative agent of COVID-19, spreads efficiently, with a basic reproductive number of 2.2 to 2.5 determined in Wuhan[1,2]. The effectiveness of control measures depends on several key epidemiological parameters (Fig. 1a), including the serial interval (duration between symptom onsets of successive cases in a transmission chain) and the incubation period (time between infection and onset of symptoms). Variation between individuals and transmission chains is summarized by the incubation period distribution and the serial interval distribution, respectively. If the observed mean serial interval is shorter than the observed mean incubation period, this indicates that a significant portion of transmission may have occurred before infected persons have developed symptoms. Significant presymptomatic transmission would probably reduce the effectiveness of control measures that are initiated by symptom onset, such as isolation, contact tracing and enhanced hygiene or use of face masks for symptomatic persons.

SARS (severe acute respiratory syndrome) was notable, because infectiousness increased around 7–10 days after symptom onset[3,4]. Onward transmission can be substantially reduced by containment measures such as isolation and quarantine (Fig. 1a)[5]. In contrast, influenza is characterized by increased infectiousness shortly around or even before symptom onset[6].

In this study, we compared clinical data on virus shedding with separate epidemiologic data on incubation periods and serial intervals between cases in transmission chains, to draw inferences on infectiousness profiles.

Among 94 patients with laboratory-confirmed COVID-19 admitted to Guangzhou Eighth People's Hospital, 47/94 (50%) were male, the median age was 47 years and 61/93 (66%) were moderately ill (with fever and/or respiratory symptoms and radiographic evidence of pneumonia), but none were classified as 'severe' or 'critical' on hospital admission (Supplementary Table 1).

A total of 414 throat swabs were collected from these 94 patients, from symptom onset up to 32 days after onset. We detected high viral loads soon after symptom onset, which then gradually decreased towards the detection limit at about day 21. There was no obvious difference in viral loads across sex, age groups and disease severity (Fig. 2).

Separately, based on 77 transmission pairs obtained from publicly available sources within and outside mainland China (Fig. 1b and Supplementary Table 2), the serial interval was estimated to have a mean of 5.8 days (95% confidence interval (CI), 4.8–6.8 days) and a median of 5.2 days (95% CI, 4.1–6.4 days) based on a fitted gamma distribution, with 7.6% negative serial intervals (Fig. 1c). Assuming an incubation period distribution of mean 5.2 days from a separate study of early COVID-19 cases[1], we inferred that infectiousness started from 2.3 days (95% CI, 0.8–3.0 days) before symptom onset and peaked at 0.7 days (95% CI, −0.2–2.0 days) before symptom onset (Fig. 1c). The estimated proportion of presymptomatic transmission (area under the curve) was 44% (95% CI, 25–69%). Infectiousness was estimated to decline quickly within 7 days. Viral load data were not used in the estimation but showed a similar monotonic decreasing pattern.

In sensitivity analysis, using the same estimating procedure but holding constant the start of infectiousness from 1 to 7 days before symptom onset, infectiousness was shown to peak at 0–2 days before symptom onset, and the proportion of presymptomatic transmission ranged from 46% to 55% (Extended Data Fig. 1).

Finally, simulation showed that the proportion of short serial intervals (for example, <2 days) would be larger if infectiousness were assumed to start before symptom onset (Extended Data Fig. 2). Given the 7.6% negative serial intervals estimated from the infector–infectee paired data, start of infectiousness at least 2 days before onset and peak infectiousness at 2 days before to 1 day after onset would be most consistent with this observed proportion (Extended Data Fig. 3).

Here, we used detailed information on the timing of symptom onsets in transmission pairs to infer the infectiousness profile of COVID-19. We showed substantial transmission potential before symptom onset. Of note, most cases were isolated after symptom onset, preventing some post-symptomatic transmission.

Estimativas da dinâmica de excreção viral e transmissibilidade da Covid-19

Estimativas feitas com base na observação de uma série de 94 pacientes, com coletas de swabs desde a data do início dos sintomas até o 32º dia, e uma série de 77 pares de caso índice e caso secundário, com informação da data provável de exposição; e estimativas da carga viral pela PCR.

Período de infectividade:

Início no dia 2,3 (IC95%: 0,8; 3,0) antes do início dos sintomas.

Pico no dia 0,7 antes do início dos sintomas (IC95%: - 0,2; 2,0)

Logo, entre um e dois dias antes do início dos sintomas.

Estimativa da proporção de transmissão no período pré-sintomático: 44% (IC95%: 25%; 69%).

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Perspective

Identifying and Interrupting Superspreading Events—Implications for Control of Severe Acute Respiratory Syndrome Coronavirus 2

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Cite This Article

Abstract

It appears inevitable that severe acute respiratory syndrome coronavirus 2 will continue to spread. Although we still have limited information on the epidemiology of this virus, there have been multiple reports of superspreading events (SSEs), which are associated with both explosive growth early in an outbreak and sustained transmission in later stages. Although SSEs appear to be difficult to predict and therefore difficult to prevent, core public health actions can prevent and reduce the number and impact of SSEs. To prevent and control of SSEs, speed is essential. Prevention and mitigation of SSEs depends, first and foremost, on quickly recognizing and understanding these events, particularly within healthcare settings. Better understanding transmission dynamics associated with SSEs, identifying and mitigating high-risk settings, strict adherence to healthcare infection prevention and control measures, and timely implementation of nonpharmaceutical interventions can help prevent and control severe acute respiratory syndrome coronavirus 2, as well as future infectious disease outbreaks.

On This Page

Tables

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RIS (TXT - 2 KB)

Emerging Infectious Diseases 2020, 26(6)

Identificação de eventos e indivíduos “superdisseminadores”
Superdisseminadores, relacionados a:

- ✓ Fatores do agente etiológico:
  - ✓ Mutações que levem ao aumento da infectividade e/ou da virulência
  - ✓ Persistência no meio ambiente
  - ✓ Dose infectante
- ✓ Fatores relacionados ao hospedeiro:
  - ✓ Duração da infecção. Localização anatômica da infecção.
  - ✓ Sintomatologia e período de transmissibilidade.
  - ✓ Fatores comportamentais: etiqueta respiratória, uso de máscaras, acesso e uso de serviços de saúde, padrões culturais de contato entre as pessoas.
- ✓ Fatores ambientais:
  - ✓ Densidade populacional, fatores climáticos, adesão às medidas de higiene e distanciamento social; fatores situacionais (ambientes fechados, número de pessoas, atividade desenvolvidas), controle de infecção em serviços de saúde; oportunidade da resposta e medidas de controle.

Eventos superdisseminadores: casamento no estado do Maine, EUA

Health

Maine wedding 'superspreader' event is now linked to seven deaths. None of those people attended.

A coronavirus outbreak connected to a wedding reception held at the Big Moose Inn in Maine in early August has led to more than 175 cases of the virus and at least seven deaths. (Linda Coan O'Kresik/Bangor Daily News/AP)

The Washington Post – 16/09/2020

Casamento em 07/08/2020
65 pessoas presentes
Investigação ainda em andamento
Até 16/09, 175 casos relacionados ao casamento, com 7 óbitos.

Vigilância Epidemiológica

- ✓ No Brasil
  - ✓ Vigilância passiva de casos graves hospitalizados (no SUS).
  - ✓ Vigilância de casos moderados e leves (profissionais de saúde, rede privada).
  - ✓ Inquéritos sorológicos
- ✓ Experiências internacionais:
  - ✓ Vigilância ativa
  - ✓ Investigação de contatos e cadeias de transmissão

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'A reação do governo parecia cena de filme': como é ter covid-19 na Coreia do Sul

Rafael Barifouse
Da BBC News Brasil em São Paulo

5 maio 2020 Compartilhar

Ho Song ficou internado 19 dias em um hospital público de Seul

A vida de Ho Song, de 45 anos, virou do avesso pouco depois de chegar à Coreia do Sul no final de março.

O comerciante tinha ido ao país para visitar os pais na capital, Seul, e comprar equipamentos para seu restaurante no Brasil, onde vive desde os 12 anos.

Fonte: bbc.com/portuguese/geral-52546853

Vigilância da Covid-19 em viajantes
A experiência da Coréia do Sul

Todos os passageiros desembarcando do exterior tem obrigatoriamente de instalar o aplicativo de vigilância epidemiológica no seu celular.

Todos os dias pela manhã eles devem enviar uma mensagem informando se apresentaram sintomas compatíveis com a Covis-19. O aplicativo também registra todos os deslocamentos do indivíduo.

Quem não o fizer recebe uma ligação da VE.

No 4º dia o brasileiro apresentou sintomas, ligou informando, e marcou a coleta de secreção respiratória no mesmo dia, em um dos 630 serviços de saúde designados para essa atividade no país.

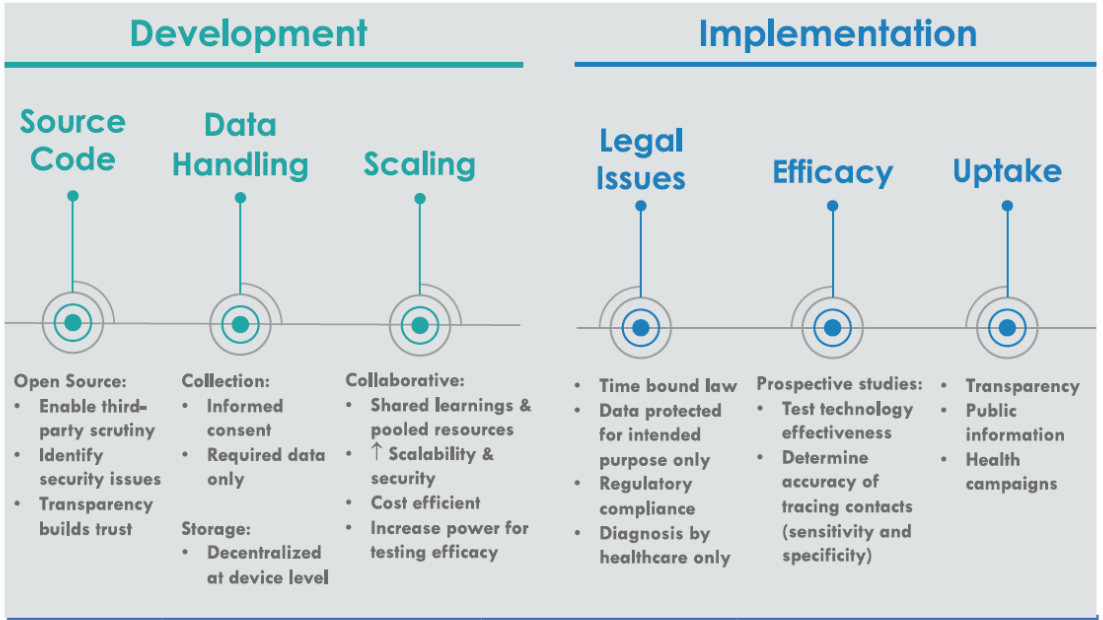
No dia seguinte ele recebeu um telefonema informando que o resultado do seu exame havia sido positivo, e que ele estivesse pronto em 30 minutos para ser levado para internação hospitalar.

No mesmo horário outra ambulância levou os seus pais para um local para colher o exame, e uma outra equipe fez a desinfecção da casa deles.

Foi feita uma entrevista, na qual ele detalhou todo o seu trajeto desde a chegada ao país. É feita a busca por imagens de câmeras de vigilância desses locais para identificar as pessoas que estiveram próximas ao caso.

Ele ficou hospitalizado por 19 dias. Durante o período fez 6 coletas de PCR e só recebeu alta depois de 2 testes negativos.

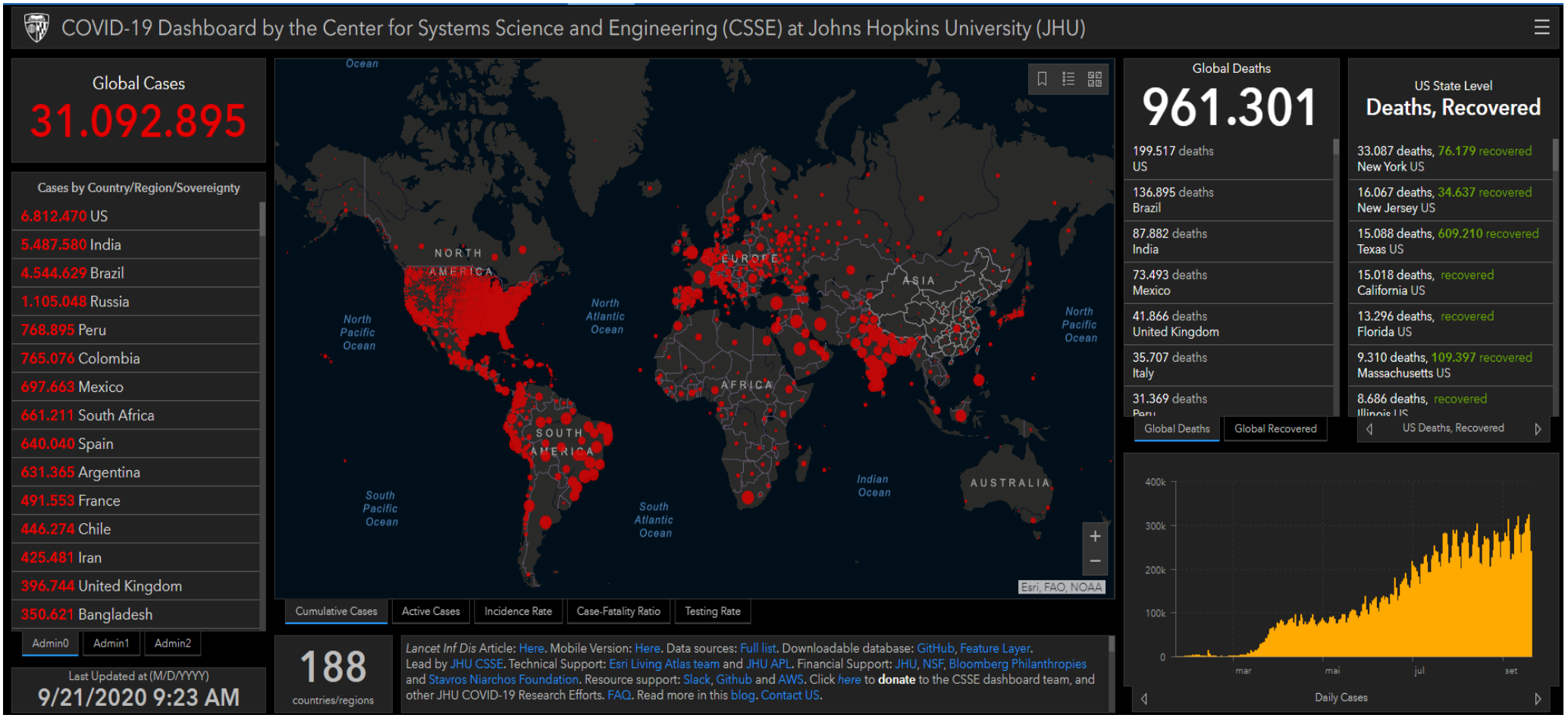
Contact Tracing and COVID-19



Type	Example	Auto-location detection	Based on Apple/Google API	Centralized Database	Notes
Self Reporting Apps	Kings College-backed 'C-19 COVID Symptom Tracker', Healthcast, ZeroBase	No	No	Yes	While they may provide useful research data and indicators if adopted widely, they are unlikely to be useful for contact tracing since they cannot automatically identify who the reporters have been in contact with or the veracity of their claims.
Custom-Built Closed-Source Location Tracking Apps and Frameworks	Norway, Russia, Vietnam, China, UK PEPP-PT (7 EU countries including France, Italy)	Yes	No	Yes	Lack of published, scrutinized source code increases risk of security flaws or hidden surveillance. Centralized database is at risk ofattack and data breaches. Not using Apple/Google API may cause battery life and other efficacy issues.
Open-Source Apps & Frameworks (not using Google/Apple API)	BlueTrace/OpenTrace (Singapore TraceTogether, Australia COVID-19 Safe). TCN Protocol, Israel	Yes	No	Yes	Published source code enhances security and trust, but centralized database may be open to attack and data breaches. Not using Apple/Google API may cause battery life and other efficacy issues.
Apps Using Google/Apple API	DP-3T (Germany, Austria, Estonia, Netherlands), California	Yes	Yes	No	Using Google/Apple API is the only way to use native operating system functionality which is lighter on battery use and better for location tracking. Lack of centralized database is good for privacy, but limits data deemed necessary by France and other countries' Governments.

Fonte: Sinha P & Paterson AE. Contact tracing: can "big tech" come to rescue, and if so, at what cost? E Clin Med June, 15, 2020

Distribuição de casos e óbitos por COVID-19 segundo país, em 21/09/2020



Fonte: www.coronavirus.jhu.edu

Inquérito nacional de soroprevalência na Espanha
Realizado entre 27/04 e 11/05
Seleção aleatória de 35.883 domicílios e 61.075 participantes

	Point-of-care test		Immunoassay	
	Number of participants	Seroprevalence (95% CI)	Number of participants	Seroprevalence (95% CI)
Overall	61 075	5·0% (4·7–5·4)	51 958	4·6% (4·3–5·0)
Sex				
Female	31 726	5·0% (4·7–5·5)	27 141	4·6% (4·2–5·0)
Male	29 349	5·0% (4·6–5·4)	24 817	4·6% (4·2–5·0)
Age, years				
0–19	11 422	3·4% (2·9–3·9)	6527	3·8% (3·2–4·6)
20–34	8469	4·4% (3·7–5·1)	7569	5·0% (4·3–5·8)
35–49	14 532	5·3% (4·7–5·9)	13 354	4·9% (4·3–5·5)
50–64	15 094	5·8% (5·3–6·5)	13 906	4·7% (4·1–5·3)
≥65	11 558	6·0% (5·4–6·8)	10 602	4·5% (3·8–5·3)
Nationality				
Spanish	57 858	5·0% (4·7–5·4)	49 520	4·6% (4·2–4·9)
Other	2643	5·6% (4·3–7·3)	2178	5·7% (4·3–7·5)
Occupation*				
Active worker	25 759	5·8% (5·3–6·3)	23 763	5·3% (4·9–5·9)
Unemployed	4459	3·3% (2·6–4·1)	3981	3·5% (2·7–4·6)
Student	3550	4·6% (3·6–5·8)	3060	4·8% (3·8–6·1)
Retired	11 895	6·0% (5·4–6·8)	10 932	4·5% (3·8–5·3)
Permanent or temporary disability	1476	4·1% (2·9–5·9)	1342	3·6% (2·4–5·5)
House person	3369	4·3% (3·5–5·4)	3033	3·3% (2·5–4·3)
Unpaid social work	49	3·1% (0·7–11·4)	42	4·5% (1·4–13·6)
Other	965	4·2% (2·8–6·2)	839	3·3% (2·1–5·2)
Occupation sector†				
Telecommuting	11 899	6·4% (5·7–7·0)	10 947	5·9% (5·3–6·6)
Retail	1640	4·7% (3·4–6·6)	1515	4·5% (3·1–6·5)
Transport	800	5·9% (3·9–8·7)	731	5·8% (3·6–9·2)
Police, firefighters, or public safety	643	6·2% (4·1–9·2)	589	6·3% (4·0–9·9)
Cleaning	804	4·1% (2·6–6·4)	748	4·5% (2·9–7·1)
Health care	1109	10·2% (7·9–13·0)	1048	10·0% (7·7–12·9)
Nursing home or other social work	1016	7·7% (5·6–10·5)	947	7·9% (5·9–10·6)
Home caregiver	403	6·4% (3·1–12·1)	372	3·7% (1·6–8·3)
Other	7444	4·3% (3·6–5·0)	6865	3·4% (2·8–4·0)
Household size, residents				
1	4863	5·1% (4·3–6·0)	4456	4·0% (3·3–5·0)
2	14 042	5·7% (5·1–6·5)	12 894	5·1% (4·4–5·8)
3–5	38 964	4·8% (4·5–5·3)	32 140	4·6% (4·2–5·1)
≥6	3206	3·8% (2·7–5·3)	2468	3·2% (2·1–4·8)

(Table 1 continues on next page)

(Continued from previous page)

	Point-of-care test		Immunoassay	
	Number of participants	Seroprevalence (95% CI)	Number of participants	Seroprevalence (95% CI)
Census tract income‡				
<5th percentile	2865	5·1% (3·4–7·5)	2382	4·6% (3·1–6·7)
5th to <25th percentile	13 278	5·0% (4·2–5·9)	11 229	4·7% (3·8–5·8)
25th to <50th percentile	15 356	5·0% (4·3–6·0)	13 096	4·6% (3·9–5·6)
50th to <75th percentile	14 074	4·8% (4·1–5·6)	11 804	4·3% (3·6–5·1)
75th to <95th percentile	12 183	5·0% (4·2–5·9)	10 583	4·6% (3·7–5·7)
≥95th percentile	3319	6·2% (4·7–8·0)	2864	5·4% (4·0–7·4)
Municipality size, inhabitants				
≥100 000	18 530	6·4% (5·8–7·1)	15 974	6·0% (5·4–6·7)
20 000–99 999	18 547	4·2% (3·7–4·7)	15 553	3·8% (3·3–4·3)
5000–19 999	12 940	3·7% (3·2–4·4)	10 727	3·2% (2·7–3·9)
<5000	11 058	4·2% (3·5–5·1)	9704	3·8% (3·0–4·9)

SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. *Among participants aged 17 years or older. Active workers are defined as anyone who is working, regardless of whether they had to leave the house to do so. †Among active workers during lockdown. One worker did not provide the sector. ‡Categories based on percentiles from province-specific distributions of census tract average income in 2017.

Table 1: **Seroprevalence of SARS-CoV-2 by general characteristics**

Fonte: Pollán M et al. Prevalence of SARS-CoV-2 in Spain. Lancet 06/07/2020

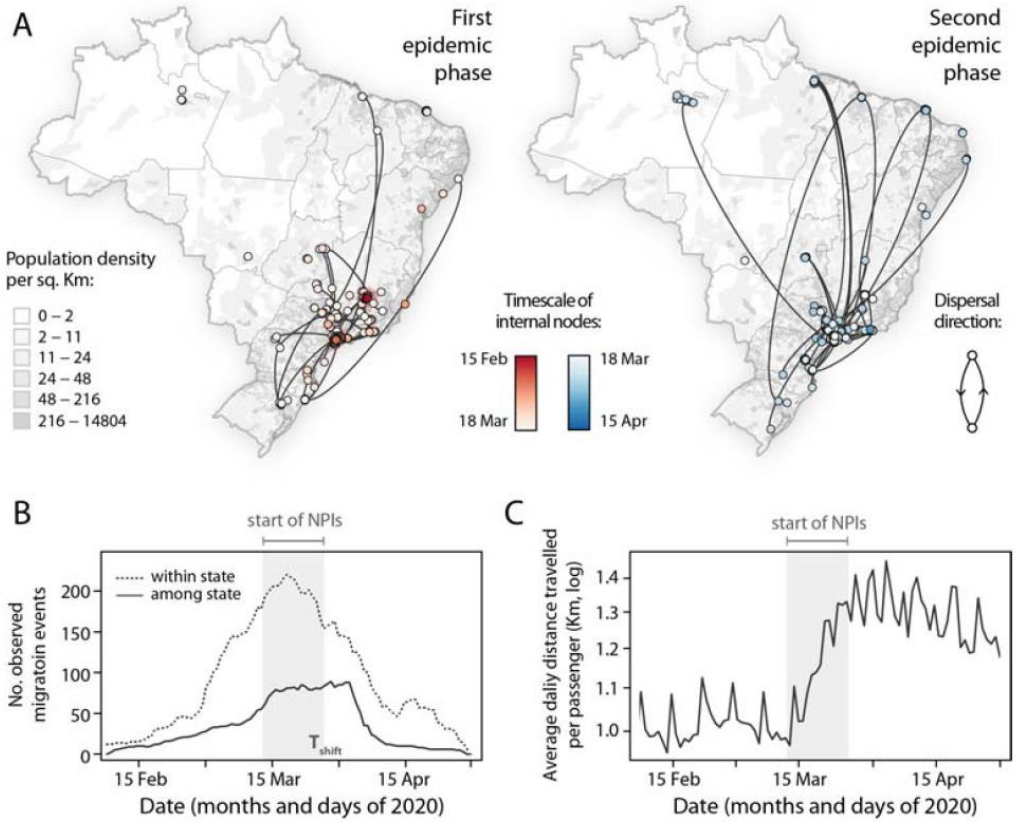


Fig. 4. Spread of SARS-CoV-2 in Brazil. (**A**) Spatiotemporal reconstruction of the spread of Brazilian SARS-CoV-2 clusters containing 3 or more sequences during the first phase (left) and the second epidemic phase (right). Circles represent nodes of the MCC phylogeny and are coloured according to their inferred time of occurrence. Shaded areas represent the 80% high posterior density (HPD) interval and depict the uncertainty of the phylogeographic estimates for each node. Solid curved lines denote the links between sequences and the directionality of movement. Sequences belonging to clusters with less than 3 sequences were also plotted in the map with no lines connecting them. Background population density in 2020 for each municipality was obtained from the Brazilian Institute of Geography (https://www.ibge.gov.br/). **Fig. S14** shows a zoomed version of virus spread in the Southeast region. (**B**) Estimated number of within state and between state virus migrations over time. (**C**) Average distance travelled by an air passenger per day in Brazil calculated using openly available data from the National Civil Aviation Agency of Brazil (www.anac.gov.br/en). Light grey boxes indicate starting dates of NPIs across Brazil.

Candido DS et al. Evolution and epidemic spread of SARS-CoV-2 in Brazil. medRxiv
DOI: 10.1101/2020.06.11.20128249

CORONAVÍRUS
COVID-19

DEFINIÇÕES OPERACIONAIS[14]

CASOS SUSPEITOS

DEFINIÇÃO 1: SÍNDROME GRIPAL (SG)

Indivíduo com quadro respiratório agudo, caracterizado por pelo menos dois (2) dos seguintes sinais e sintomas: febre (mesmo que referida), calafrios, dor de garganta, dor de cabeça, tosse, coriza, distúrbios olfativos ou distúrbios gustativos.

OBSERVAÇÕES:

- **Em crianças**: além dos itens anteriores considera-se também obstrução nasal, na ausência de outro diagnóstico específico.
- **Em idosos**: deve-se considerar também critérios específicos de agravamento como sincope, confusão mental, sonolência excessiva, irritabilidade e inapetência.
- Na suspeita de COVID-19, a febre pode estar ausente e sintomas gastrointestinais (diarreia) podem estar presentes.

DEFINIÇÃO 2: SÍNDROME RESPIRATÓRIA AGUDA GRAVE (SRAG)

Indivíduo com SG que apresente: dispneia/desconforto respiratório OU pressão ou dor persistente no tórax OU saturação de O2 menor que 95% em ar ambiente OU coloração azulada (cianose) dos lábios ou rosto.

OBSERVAÇÕES:

- **Em crianças**: além dos itens anteriores, observar os batimentos de asa de nariz, cianose, tiragem intercostal, desidratação e inapetência;
- Para efeito de notificação no Sivep-Gripe, devem ser considerados os casos de SRAG hospitalizados ou os óbitos por SRAG independente de hospitalização.

CASOS CONFIRMADOS DE COVID-19

POR CRITÉRIO CLÍNICO

Caso de **SG** ou **SRAG** associado a anosmia (disfunção olfativa) OU ageusia (disfunção gustatória) aguda sem outra causa pregressa.

POR CRITÉRIO CLÍNICO-EPIDEMIOLÓGICO

Caso de **SG** ou **SRAG** com histórico de contato próximo ou domiciliar, nos 14 dias anteriores ao aparecimento dos sinais e sintomas com caso confirmado para COVID-19.

POR CRITÉRIO CLÍNICO-IMAGEM

Caso de **SG** ou **SRAG** ou óbito por **SRAG** que não foi possível confirmar por critério laboratorial E que apresente pelo menos uma (1) das seguintes alterações tomográficas:

- **OPACIDADE EM VIDRO FOSCO** periférico, bilateral, com ou sem consolidação ou linhas intralobulares visíveis ("pavimentação"), **OU**
- **OPACIDADE EM VIDRO FOSCO** multifocal de morfologia arredondada com ou sem consolidação ou linhas intralobulares visíveis ("pavimentação"), **OU**
- **SINAL DE HALO REVERSO** ou outros achados de pneumonia em organização (observados posteriormente na doença).

OBSERVAÇÃO: segundo o Colégio Brasileiro de Radiologia, quando houver indicação de tomografia, o protocolo é de uma Tomografia Computadorizada de Alta Resolução (TCAR), se possível com protocolo de baixa dose. O uso de meio de contraste endovenoso, em geral, não está indicado, sendo reservado para situações específicas a serem determinadas pelo radiologista.[15]

POR CRITÉRIO LABORATORIAL

Caso de **SG** ou **SRAG** com teste de:

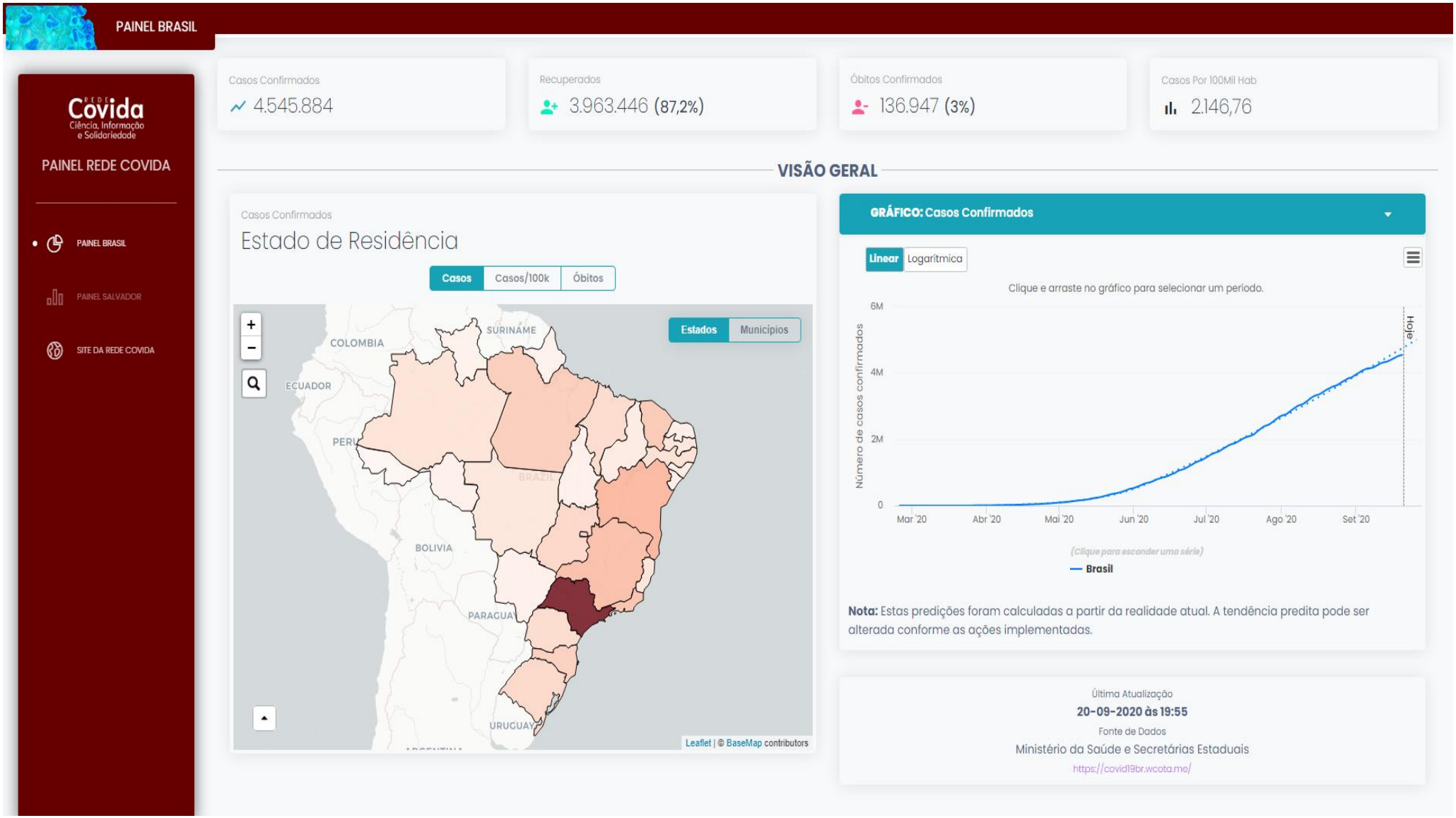
- **BIOLOGIA MOLECULAR:** resultado **DETECTÁVEL** para SARS-CoV-2 realizado pelo método RT-qPCR em tempo real.
- **IMUNOLÓGICO:** resultado **REAGENTE** para IgM, IgA e/ou IgG* realizado pelos seguintes métodos:
  - Ensaio imunoenzimático (*Enzyme-Linked Immunosorbent Assay* - ELISA);
  - Imunocromatografia (teste rápido) para detecção de anticorpos;
  - Imunoensaio por Eletroquimioluminescência (ECLIA).
- **PESQUISA DE ANTÍGENO**: resultado **REAGENTE** para SARS-CoV-2 pelo método de Imunocromatografia para detecção de antígeno.

OBSERVAÇÃO: *Considerar o resultado IgG reagente como critério laboratorial confirmatório somente em indivíduos sem diagnóstico laboratorial anterior para COVID-19.

POR CRITÉRIO LABORATORIAL EM INDIVÍDUO ASSINTOMÁTICO

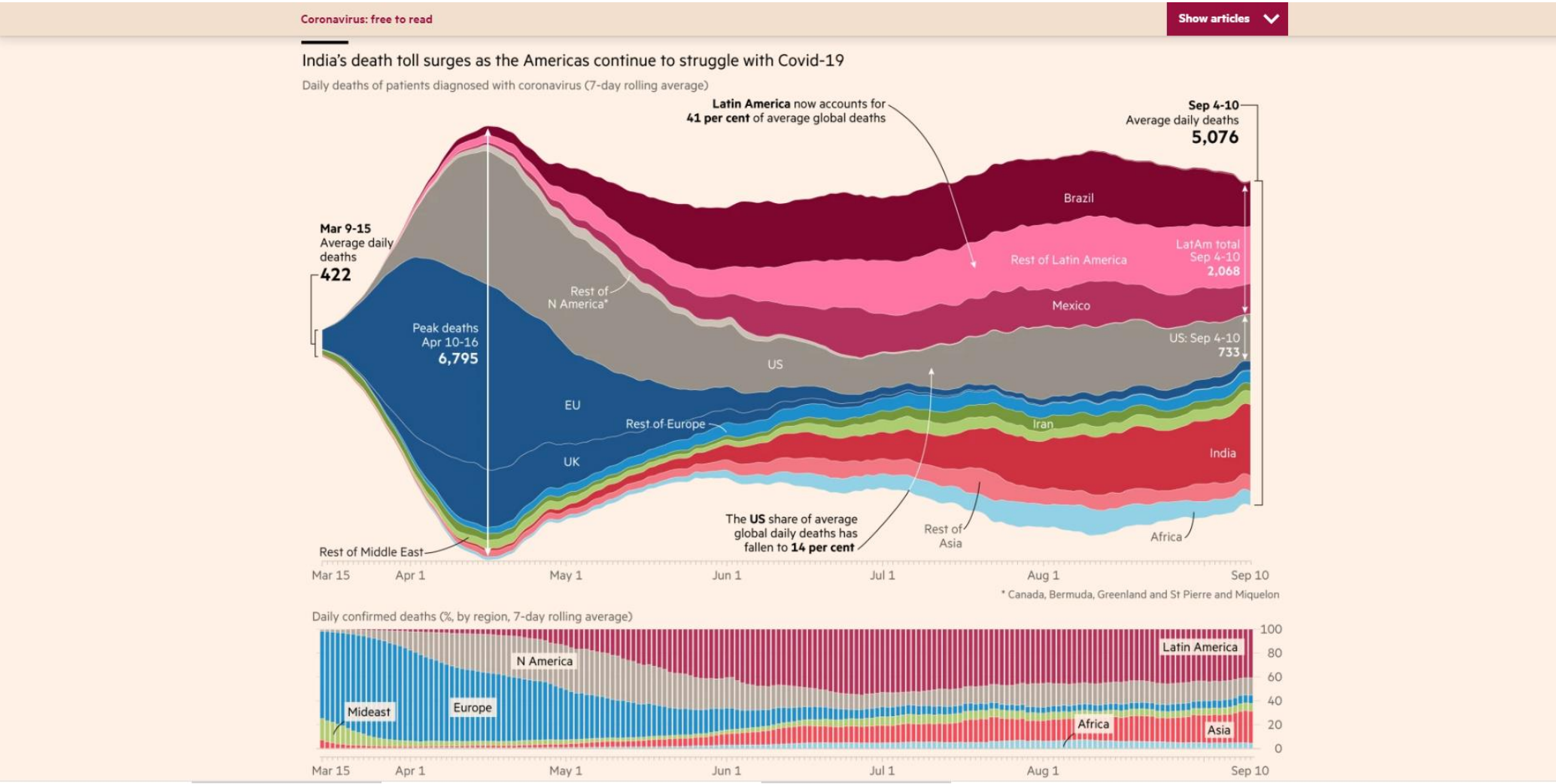
Indivíduo **ASSINTOMÁTICO** com resultado de exame:

- **BIOLOGIA MOLECULAR:** resultado **DETECTÁVEL** para SARS-CoV-2 realizado pelo método RT-qPCR em tempo real.
- **PESQUISA DE ANTÍGENO**: resultado **REAGENTE** para SARS-CoV-2 pelo método de Imunocromatografia para detecção de antígeno.



Fonte: www.painel.covid19br.org

COVID-19: distribuição temporal dos óbitos em países selecionados



Fonte: Financial Times, em 21/09/2020, www.ft.com

COVID-19 NO BRASIL

Dados até 20/09/2020

CORONAVÍRUS COVID-19 | MINISTÉRIO DA SAÚDE | PÁTRIA AMADA BRASIL GOVERNO FEDERAL

Região | UF | Município | Reg.Metropolitana/Interi...

BRASIL

27/03/2020 a 20/09/2020

População	Recuperados (Brasil)	Em acompanhamento (Brasil)
210.147.125	3.851.227	556.507

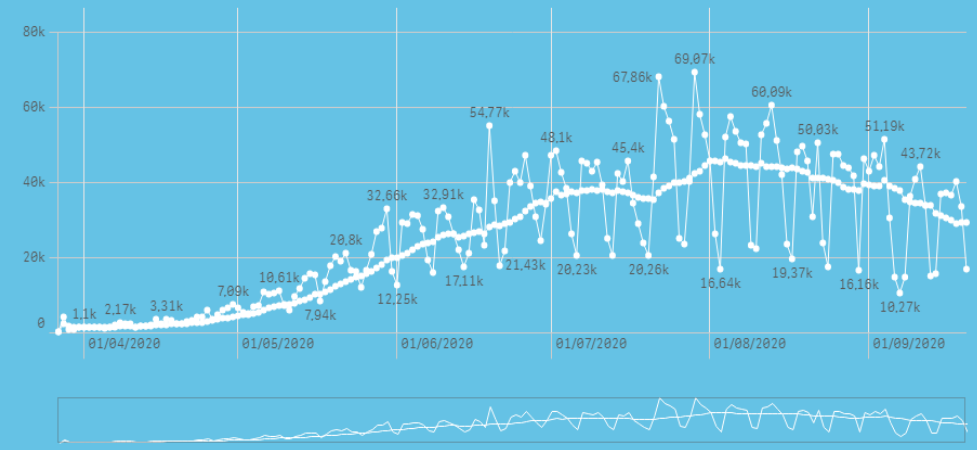
CASOS

Casos Novos	Casos Acumulados	Casos Acumulados 100mi
16.389	4.544.629	2.163

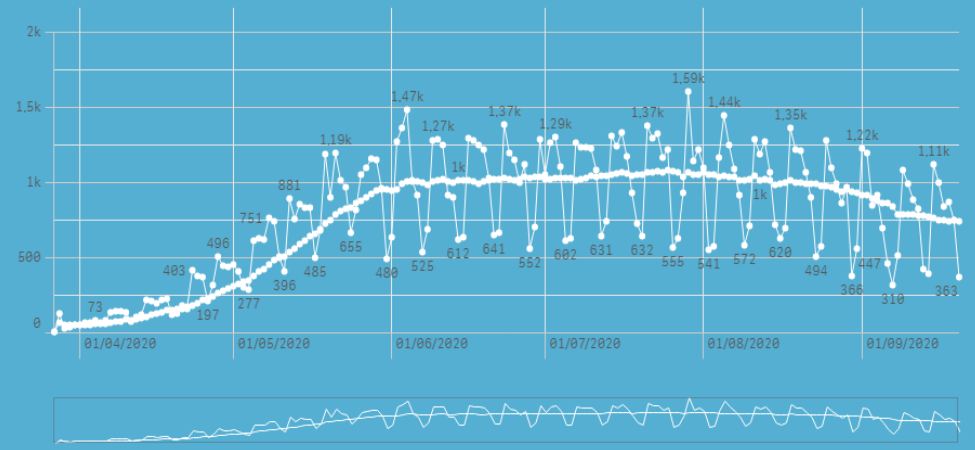
ÓBITOS

Óbitos Novos	Óbitos Acumulados	Óbitos Acumumulados 100mi
363	136.895	65

Casos novos por dia de notificação com Média Móvel de 14 dias



Óbitos novos por dia de notificação com Média Móvel de 14 dias



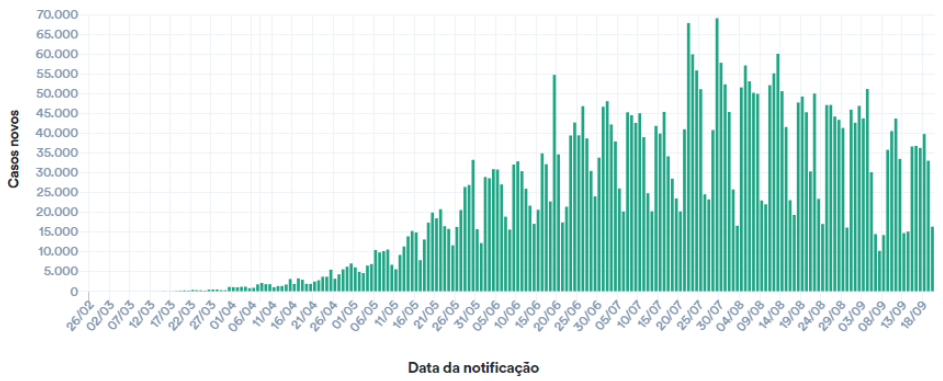
Detalhar por

Região | Estado | Município | Região Metropolitana | Todos

Região	População	Casos Novos	Casos Acumulados	Casos Acumulados 100mi	Óbitos Novos	Óbitos Acumulados	Óbitos Acumumulados 100mi
Totais	**210.134.852**	**16.389**	**4.544.629**	**2.163**	**363**	**136.895**	**65**
Sudeste	88.371.433	6.890	1.581.553	1.790	140	61.765	70
Nordeste	57.071.654	3.447	1.272.966	2.230	115	37.842	66
Centro-Oeste	16.297.074	2.359	544.019	3.338	58	11.617	71
Sul	29.963.711	2.416	545.285	1.820	34	11.133	37
Norte	18.430.980	1.277	600.806	3.260	16	14.538	79

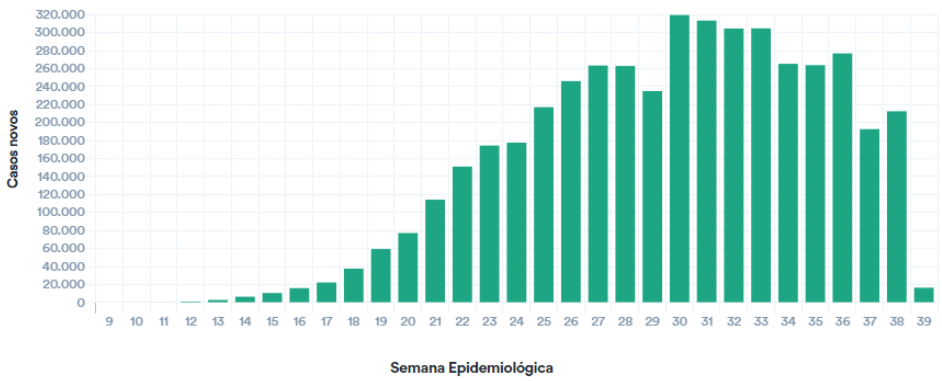
Casos Confirmados

Casos novos de COVID-19 por data de notificação



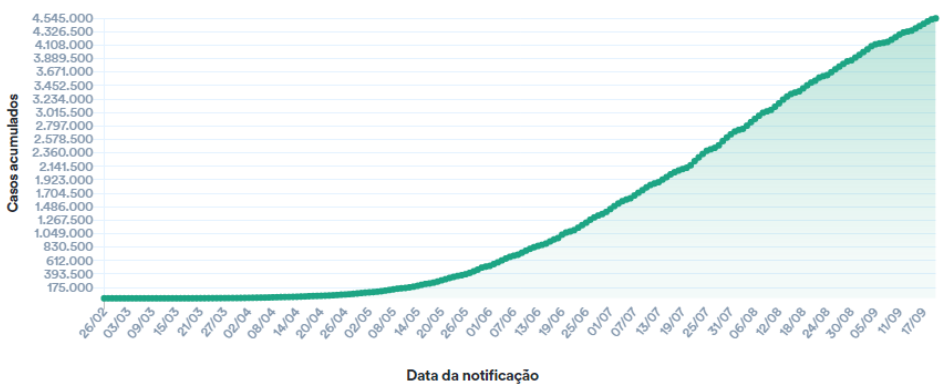
Fonte: Secretarias Estaduais de Saúde. Brasil, 2020

Casos novos de COVID-19 por Semana Epidemiológica de notificação



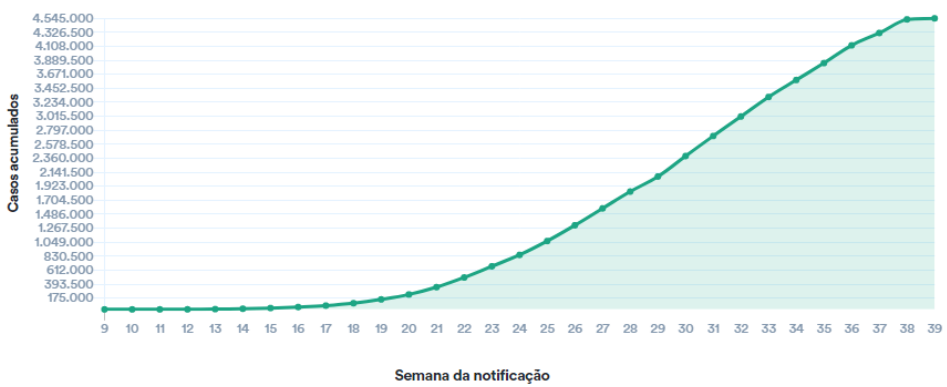
Fonte: Secretarias Estaduais de Saúde. Brasil, 2020

Casos acumulados de COVID-19 por data de notificação



Fonte: Secretarias Estaduais de Saúde. Brasil, 2020

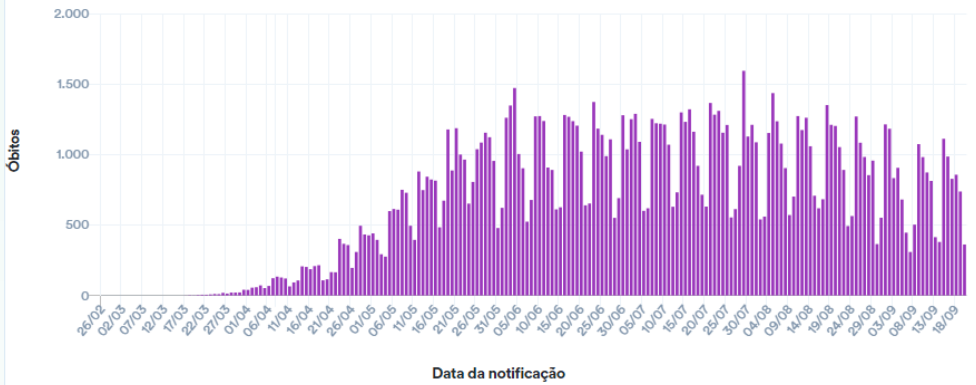
Casos acumulados de COVID-19 por Semana Epidemiológica de notificação



Fonte: Secretarias Estaduais de Saúde. Brasil, 2020

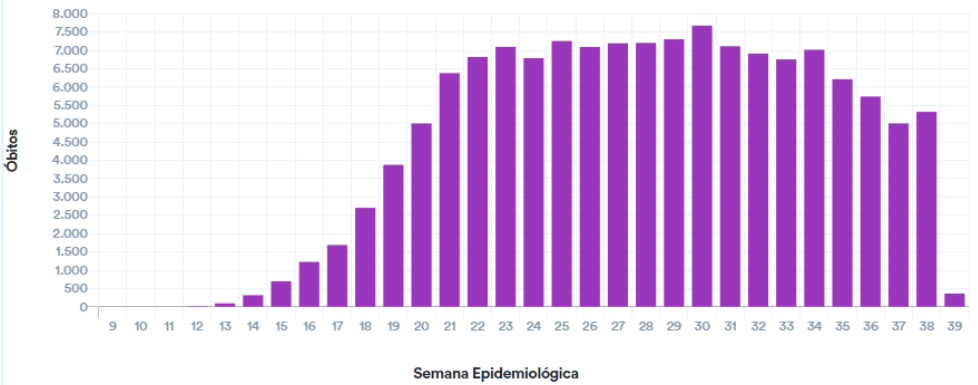
Óbitos Confirmados

Óbitos de COVID-19 por data de notificação



Fonte: Secretarias Estaduais de Saúde. Brasil, 2020

Óbitos de COVID-19 por Semana Epidemiológica de notificação



Fonte: Secretarias Estaduais de Saúde. Brasil, 2020

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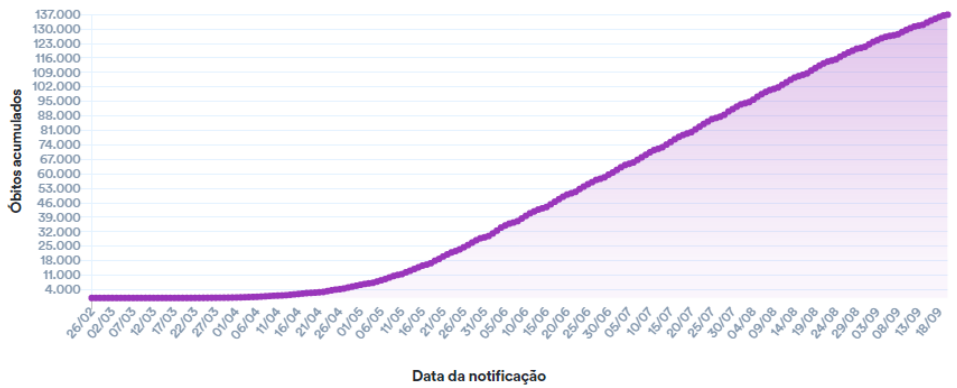
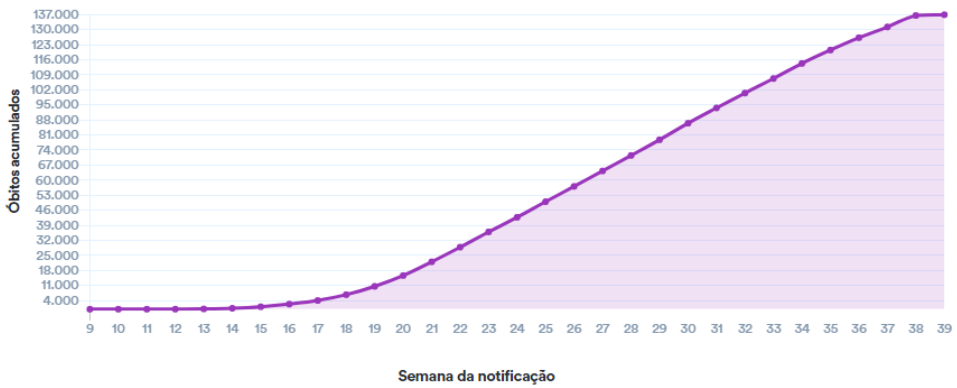
Óbitos acumulados de COVID-19 por data de notificação



Fonte: Secretarias Estaduais de Saúde. Brasil, 2020

Óbitos acumulados de COVID-19 por Semana Epidemiológica de notificação



Fonte: Secretarias Estaduais de Saúde. Brasil, 2020

Situação epidemiológica da COVID-19, Estado de São Paulo, em 21/09/2020

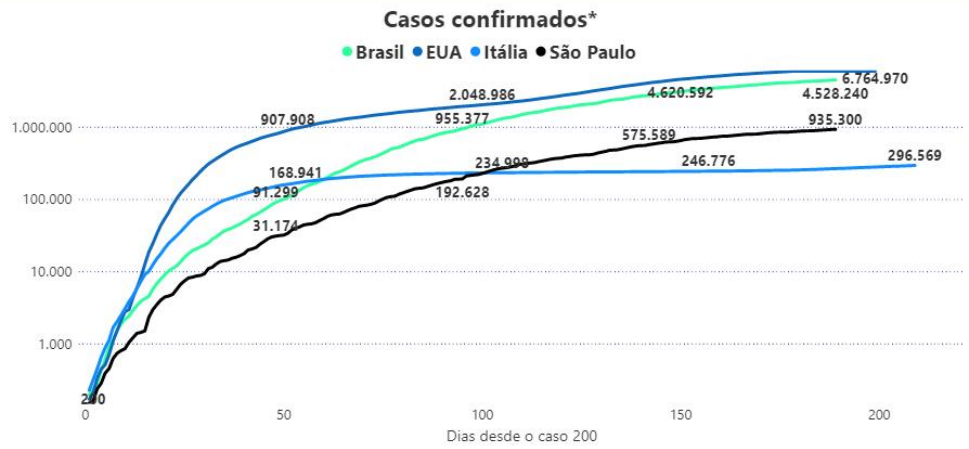
saopaulo.sp.gov.br

Cidadão SP /governosp

SP CONTRA O NOVO CORONAVÍRUS

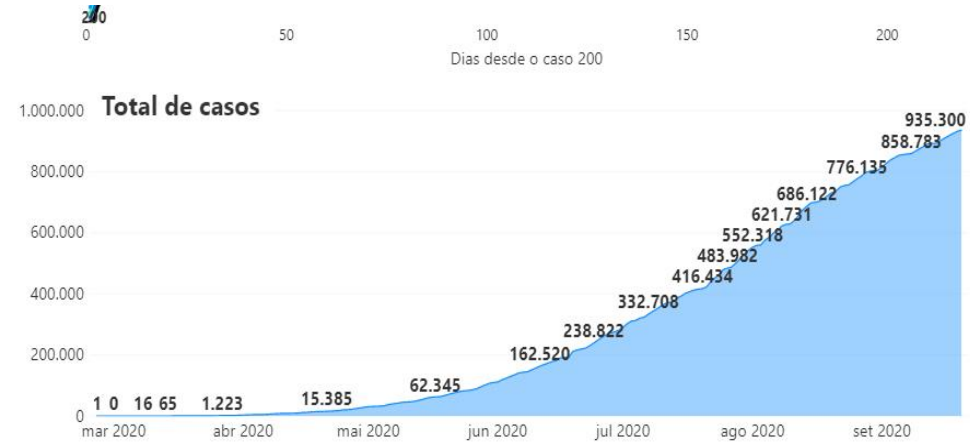
BOLETIM COMPLETO

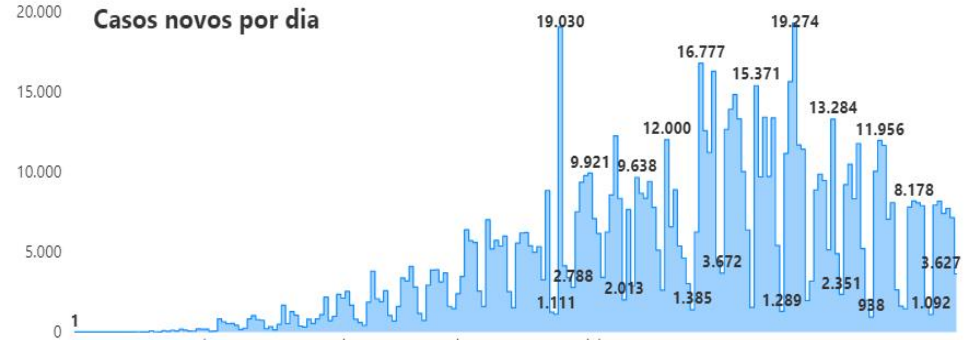
Estado SP, Brasil, outros países | Dep. Regional Saúde e municípios | Casos e óbitos | SIMI | Situação Epidemiológica

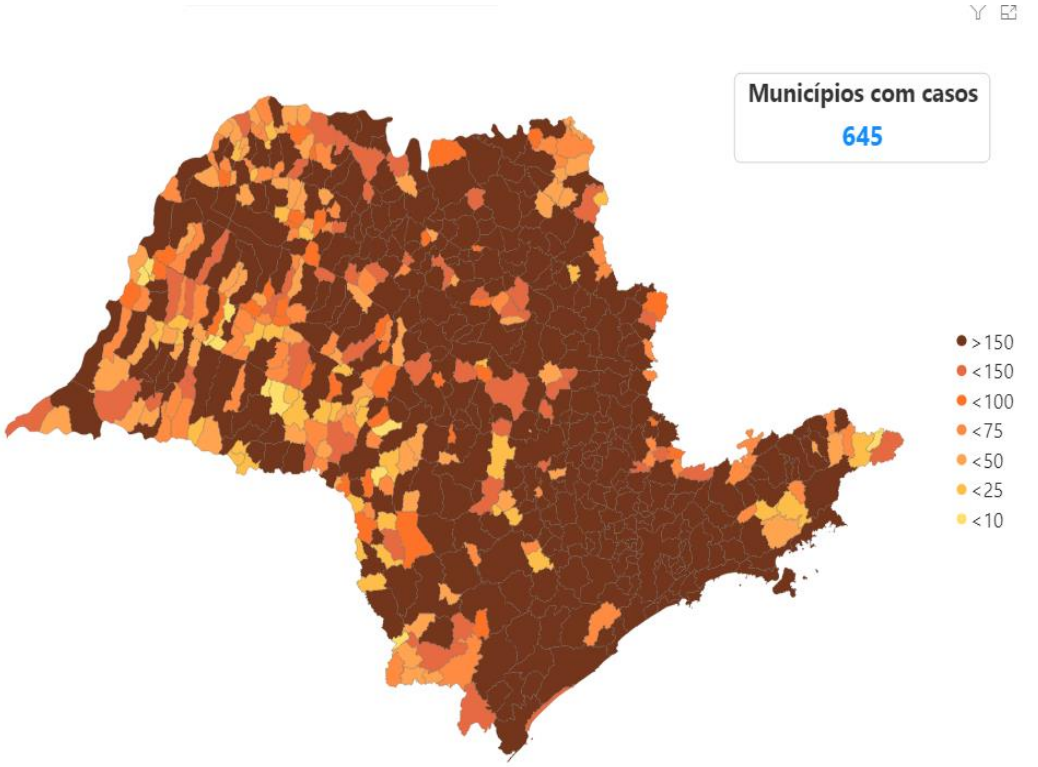


	Casos	Variação diária	Óbitos	Variação diária	Letalidade
São Paulo	935.300	0%	33.952	0%	3,6%
Brasil**	4.528.240	1%	136.240	0%	3,0%
Mundo**	30.685.001	1%	955.843	1%	3,1%

Situação epidemiológica da COVID-19, Estado de São Paulo, em 21/09/2020







Situação epidemiológica da COVID-19, Estado de São Paulo, em 21/09/2020

Dep. Regional de Saúde

Todos

Municípios

Todos

CASOS 935.300

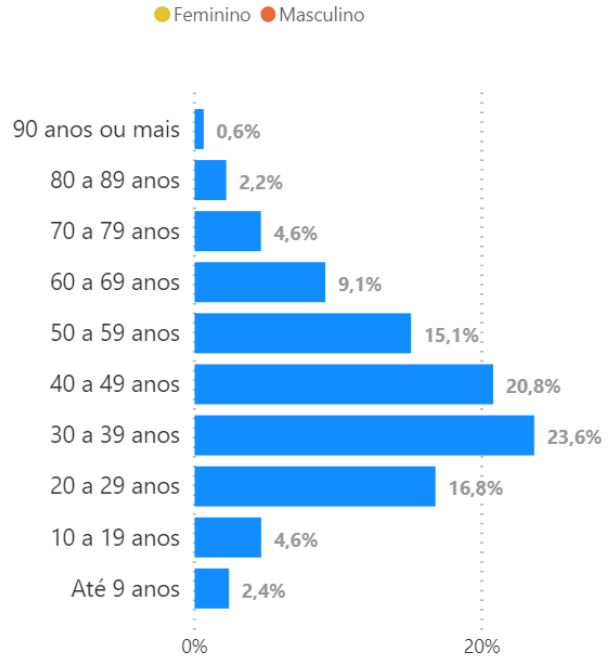
SEXO

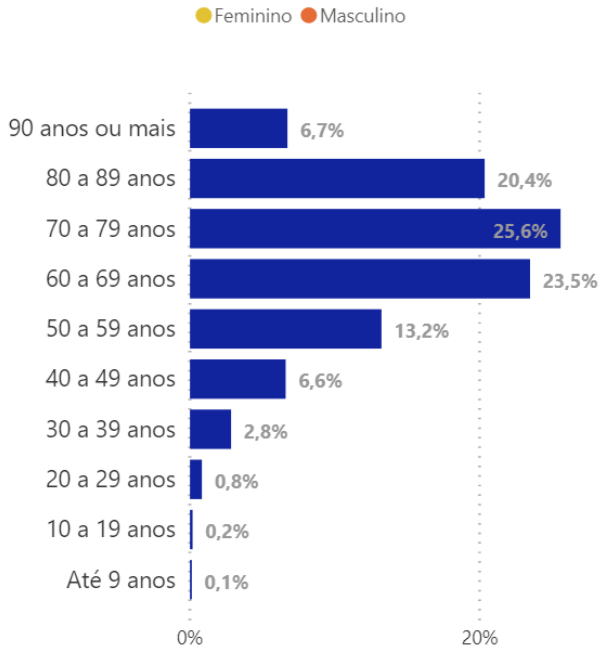
ÓBITOS 33.952

LETALIDADE

Feminina	Masculina
2,9%	4,5%

FAIXA ETÁRIA

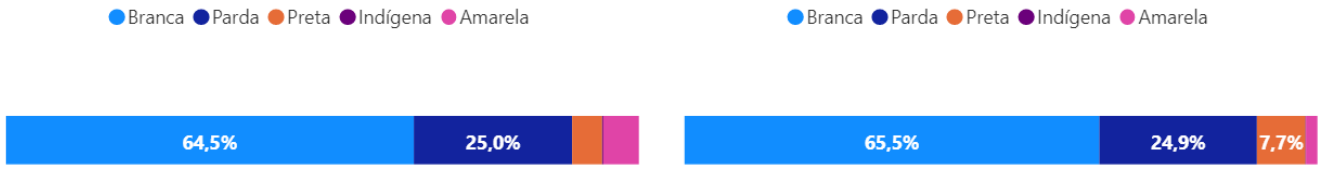




Faixa etária	Letalidade
90 anos ou mais	37,8%
80 a 89 anos	33,3%
70 a 79 anos	20,1%
60 a 69 anos	9,4%
50 a 59 anos	3,2%
40 a 49 anos	1,2%
30 a 39 anos	0,4%
20 a 29 anos	0,2%
10 a 19 anos	0,1%
Até 9 anos	0,2%
Total	**3,6%**

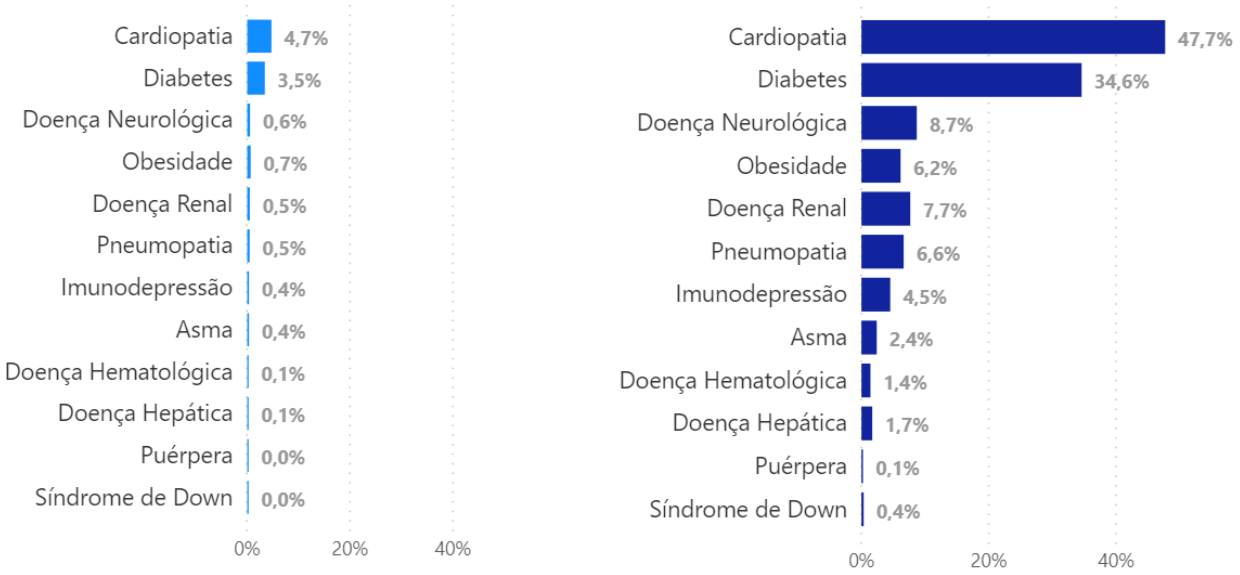
Situação epidemiológica da COVID-19, Estado de São Paulo, em 21/09/2020

RAÇA/COR*



Raça/Cor	Letalidade
Branca	3,4%
Parda	3,4%
Preta	5,5%
Indígena	1,3%
Amarela	1,1%
Total	**3,4%**

DOENÇAS PREEXISTENTES**



Doença preexistente	Letalidade
Cardiopatia	36,5%
Diabetes	36,3%
Doença Neurológica	53,2%
Obesidade	31,6%
Doença Renal	50,7%
Pneumopatia	47,2%
Imunodepressão	43,1%
Asma	22,9%
Doença Hematológica	41,7%
Doença Hepática	50,9%
Puérpera	13,7%
Síndrome de Down	36,3%
Total	**38,1%**

Dados atualizados em 20/09/2020. Horário: 13h30

Casos Confirmados, Suspeitos e Óbitos Confirmados

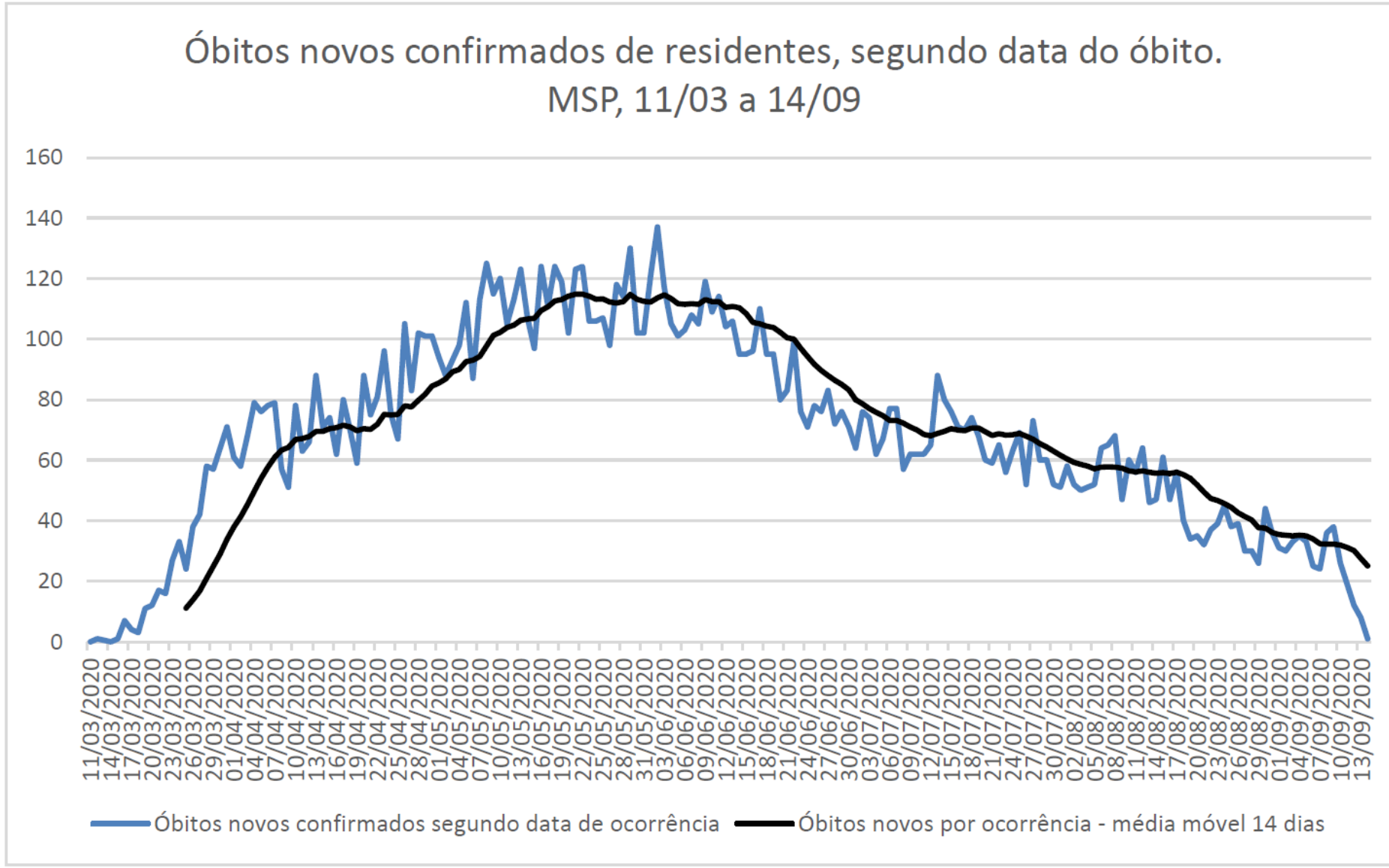
	SUSPEITOS (MONITORADOS)	CONFIRMADOS		ÓBITOS	
		Casos Confirmados	Variação dia anterior %	Óbitos Confirmados	Variação dia anterior%
Mundo	...	30.685.001	2%	955.843	1%
Brasil	...	4.528.240	1%	136.240	0%
Estado de São Paulo	...	953.300	2%	33.952	0%
Município de São Paulo	**387.275**	**320.961**	**0%**	**12.366**	**0%**

Fontes: Mundo e Brasil: Johns Hopkins, 20/09/2020. Estado SP: CVE-SES-SP, 20/09/2020. Município SP: SIVEP Gripe e E-SUS VE, 20/09/2020.

Óbitos acumulados por datas de notificação e ocorrência – (SIM/PMSP)

Data	CONFIRMADOS				SUSPEITOS (data do óbito)	TOTAL
	NOTIFICAÇÃO (publicado 1ª vez)	Variação por notificação	OCORRÊNCIA (data do óbito)	Variação por ocorrência		
29/08	12.053	44	12.681	29	5.506	18.187
30/08	12.060	7	12.731	50	5.526	18.257
31/08	12.143	83	12.768	37	5.551	18.319
01/09	12.276	133	12.800	32	5.568	18.368
02/09	12.396	120	12.831	31	5.589	18.420
03/09	12.523	127	12.865	34	5.595	18.460
04/09	12.585	62	12.900	35	5.608	18.508
05/09	12.594	9	12.936	36	5.615	18.551
06/09	12.595	1	12.962	26	5.629	18.591
07/09	12.595	0	12.988	26	5.639	18.627
08/09	12.662	67	13.028	40	5.650	18.678
09/09	12.767	105	13.068	40	5.666	18.734
10/09	12.803	36	13.098	30	5.686	18.784
11/09	12.817	14	13.133	35	5.701	18.834
12/09	12.850	33	13.171	38	5.717	18.888
13/09	12.862	12	13.207	36	5.739	18.946
14/09	12.930	68	13.235	28	5.750	18.985
15/09	13.111	181	13.258	23	5.765	19.023
16/09	13.166	55	13.269	11	5.766	19.035
17/09	13.244	78	13.277	8	5.767	19.044
18/09	13.279	35	13.322	45	5.767	19.046
19/09	13.322	43	13.322	0	5.743	19.065

https://www.prefeitura.sp.gov.br/cidade/secretarias/saude/vigilancia_em_saude/doencas_e_agravos/coronavirus/index.php?p=295572


Óbitos novos confirmados de residentes, segundo data do óbito.
MSP, 11/03 a 14/09
160
140
120
100
80
60
40
20
0
11/03/2020
14/03/2020
17/03/2020
20/03/2020
23/03/2020
26/03/2020
29/03/2020
01/04/2020
04/04/2020
07/04/2020
10/04/2020
13/04/2020
16/04/2020
19/04/2020
22/04/2020
25/04/2020
28/04/2020
01/05/2020
04/05/2020
07/05/2020
10/05/2020
13/05/2020
16/05/2020
19/05/2020
22/05/2020
25/05/2020
28/05/2020
31/05/2020
03/06/2020
06/06/2020
09/06/2020
12/06/2020
15/06/2020
18/06/2020
21/06/2020
24/06/2020
27/06/2020
30/06/2020
03/07/2020
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09/07/2020
12/07/2020
15/07/2020
18/07/2020
21/07/2020
24/07/2020
27/07/2020
30/07/2020
02/08/2020
05/08/2020
08/08/2020
11/08/2020
14/08/2020
17/08/2020
20/08/2020
23/08/2020
26/08/2020
29/08/2020
01/09/2020
04/09/2020
07/09/2020
10/09/2020
13/09/2020
Óbitos novos confirmados segundo data de ocorrência
Óbitos novos por ocorrência - média móvel 14 dias

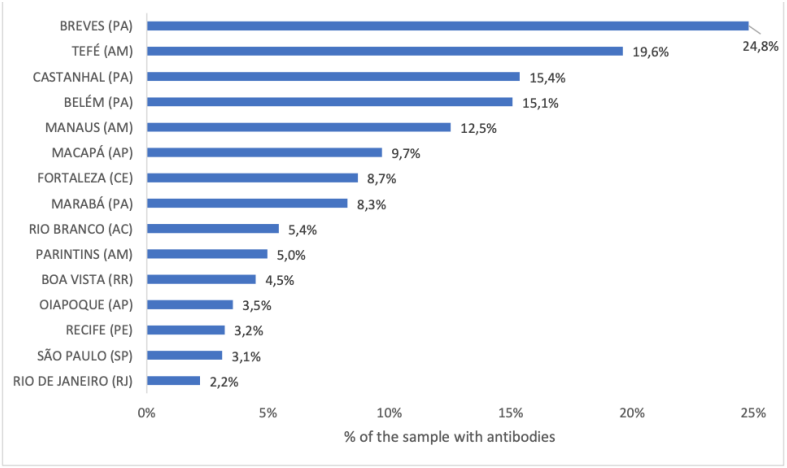
SMS – Inquérito sorológico municipal SARS-CoV-2

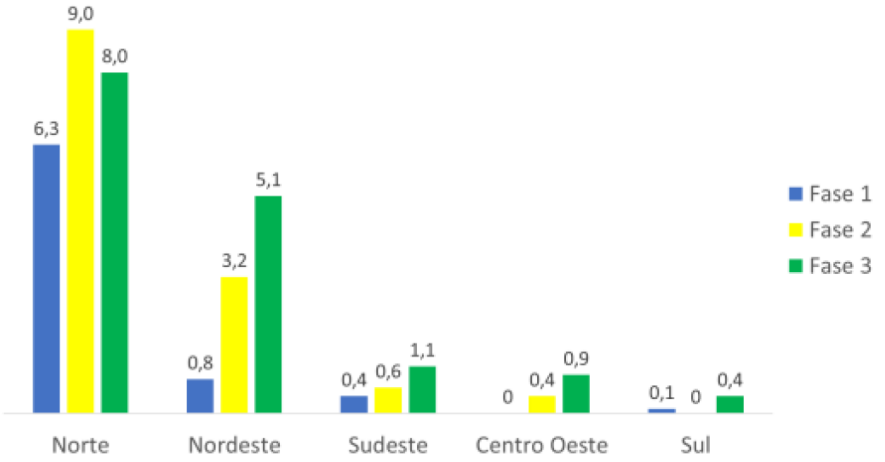
FASES	Data de Coleta	Prevalência Resultado (%)	Estimativa de pessoas infectadas por SARS-CoV-2
0	21/06	9,5	1.163.942
1	06/07	9,8	1.200.698
2	13/07	11,1	1.359.975
3	06/08	10,9	1.335.471
4	17/08	11,0	1.347.723
5	27/08	13,9	1.703.031

National serosurvey for SARS-C0V-2 antibodies – EPICOVID-19-BR

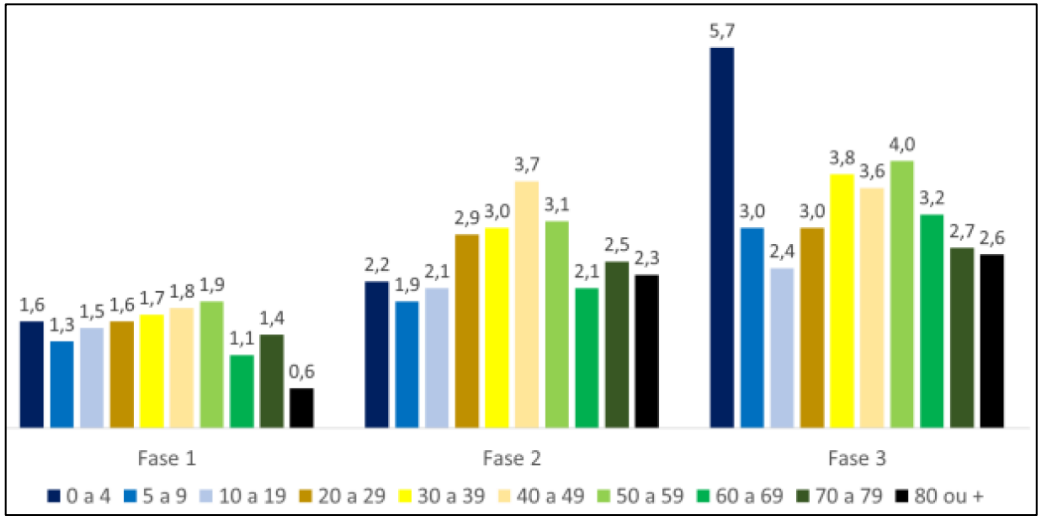
Sample of 133 municipalities with a population above 100,000. Total population 68.6 million (32.7% of Brazil)
1st survey – May 14 – 21. n = 25,025 Seroprevalence: 1.9% (95% CI: 1.7 – 2.1)
2nd survey – June 4 – 7. n = 31,165 Seroprevalence: 3.1% (95% CI: 2.8 – 3.4)
3rd survey – June 21 – 24. n = 33,207 Seroprevalence: 3.8% (95%CI: 3.5 – 4.2)
4th survey – August 27 – 30. n = 33,250. Seroprevalence: 1.4% (95% C.I.: 1.2 – 1.6)

1st survey – 9 of the 10 municipalities with the highest prevalence located in the Amazon Region.
2nd survey – 7 of the 10 municipalities with the highest prevalence located in the Amazon Region.
3rd survey – 5 of the 10 municipalities with the highest prevalence located in the Amazon Region.

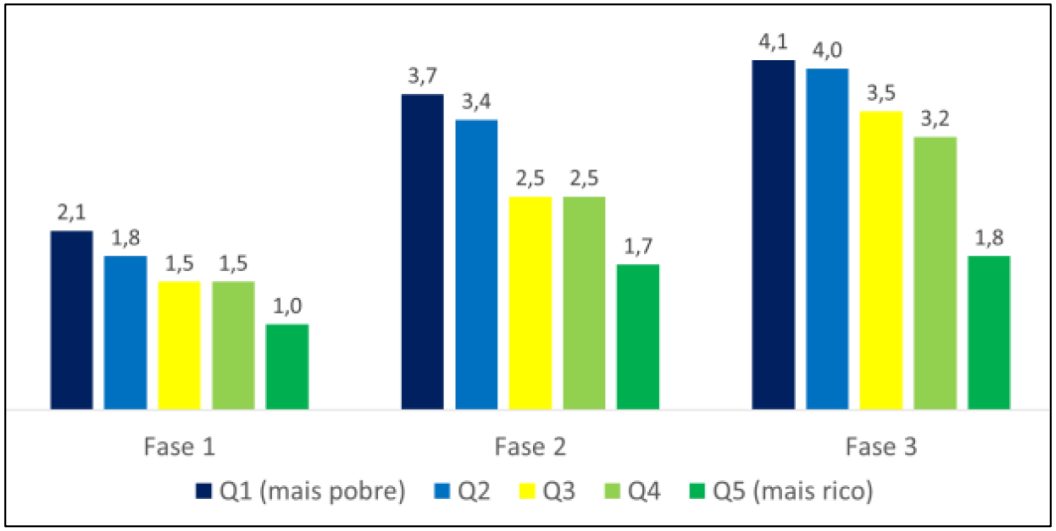




http://epidemio-ufpel.org.br/uploads/downloads/19c528cc30e4e5a90d9f71e56f8808ec.pdf .



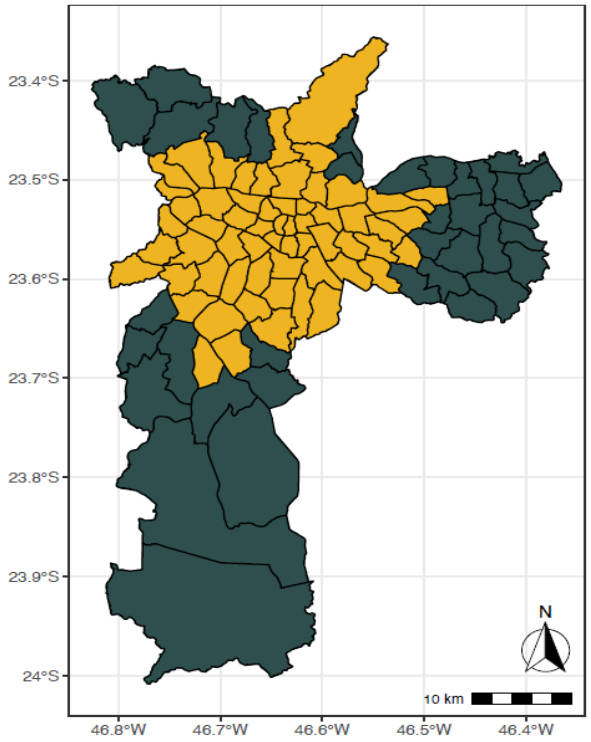
Inquérito Nacional de Soroprevalência de anticorpos anti SARS-CoV-19 – 3º inquérito
Distribuição da amostra segundo faixa etária, faixas de renda, e raça/cor



Cor da pele	Testados	Positivos
Branca	32.383	372 (1,1%)
Parda	40.088	1237 (3,1%)
Preta	11.304	282 (2,5%)
Amarela	2.446	52 (2,1%)
Indígena *	1.219	66 (5,4%)

http://epidemio-ufpel.org.br/uploads/downloads/19c528cc30e4e5a90d9f71e56f8808ec.pdf

Inquérito domiciliar para estimar a soroprevalência da infecção por SARS-CoV-2 no município de SP.
Autores: B Tess, MC Alves, F Reinach, C Granato, MC Pintão, E Rizzatti



A soroprevalência da infecção pelo vírus SARS-CoV-2 foi medida na população de todo o município, nos distritos com maior renda e metade da população, e nos distritos com menor renda e metade da população.

Soroprevalência

Estratos	n=1183 %	Prevalência %	IC 95%	Valor de p
Total	100.0	**11.4**	9.2 - 13.6	
Distritos mais ricos	48.3	6.5	4.4 - 8.5	<0.0001
Distritos mais pobres	51.7	16.0	12.2 - 19.8	

*teste quiquadro com ajuste de Rao-Scott

A soroprevalência medida é 2,5 vezes maior nos distritos com a metade mais pobre da população (16% versus 6,5%)

Métodos:

- Entrevista e coleta de sangue venoso para sorologia. Amostra aleatória de 12 domicílios localizados em 115 setores censitários. Todos os moradores . 18 nãos foram convidados a participar. N = 1.183 participantes.
- **Sorologia: kit comercial MAGLUMI-IgM 2019 nCoV (CLIA) e MAGLUMI-IgG 2019 nCoV (CLIA). Sensibilidade: 99,5%**

Nos 35 dias que separam a Fase 2 da Fase 3, não foi possível identificar mudanças estatisticamente significantes da soroprevalência no Município de São Paulo. Se houve mudança, ela se encontra dentro do intervalo de confiança da medida

Distritos

FASE 2 (15 a 24 de junho)

Estratos	n=1183 %	Prevalência %	IC 95%	Valor de p
Total	100	**11,4**	9,2 - 13,6	
Distritos mais ricos	48	6,5	4,4 - 8,5	<0.0001
Distritos mais pobres	52	16,0	12,2 - 19,8	

*teste quiquadro com ajuste de Rao-Scott

FASE 3 (20 a 29 de julho)

Estratos	n=1470 %	Prevalência %	IC 95%	Valor de p
Total	100	**11,5**	9,1 - 13,9	
Distritos mais ricos	48	10,7	8,1 - 13,4	0,5195
Distritos mais pobres	52	12,3	8,4 - 16.2	

*teste quiquadro com ajuste de Rao-Scott

Setores

FASE 2 (15 a 24 de junho)*

Estratos	Renda do estrato	n=1183 %	Prevalência %	IC 95%	Valor p
Total		100	**11,4**	9,2 - 13,6	
Setores de maior renda	R$ 6.740 e mais	27	6,2	3,0 - 9,4	0,0014
Setores de renda intermediária	R$ 2.797 a R$ 6.739	32	9,9	6,3 - 13,4	
Setores de menor renda	até R$ 2.796	41	16,1	11,9 - 20,2	

*teste quiquadro com ajuste de Rao-Scott

FASE 3 (20 a 29 de julho)*

Estratos	Renda do estrato	n=1470 %	Prevalência %	IC 95%	Valor p
Total		100	**11,5**	9,1 - 13,9	
Setores de maior renda	R$ 5.541 e mais	22	6,3	3,4 - 9,1	0,0014
Setores de renda intermediária	R$ 3.350 a R$ 5.540	37	12,4	8,3 - 16,5	
Setores de menor renda	até R$ 3.349	42	13,4	9,3 - 17,5	

*teste quiquadro com ajuste de Rao-Scott

*Pós estratificação por renda média do setor censitário com entrevistas: setores censitários foram ordenados pela renda média do setor do maior para o menor e um terço dos setores foi alocado a cada estrato.

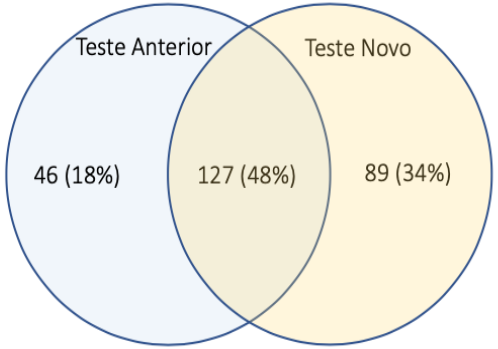
Na Fase 3 introduzimos um novo teste sorológico capaz de detectar anticorpos para outros epítopos do SARS-CoV-2. Com isso, considerando a combinação dos dois testes, a soroprevalência aumentou de 11,5% para 17,9%, ou seja, 56% em relação à medida usando somente o teste anterior

FASE 3 (20 a 29 de julho)

Estrato	n=1470 %	Teste Anterior Prevalência	Teste Anterior IC 95%	Teste Novo Prevalência	Teste Novo IC 95%	Combinação dos Testes Prevalência	Combinação dos Testes IC 95%
Total	100	**11,5**	9,1 – 13,9	**14,8**	12,1 – 17,6	**17,9**	15,0 – 20,9
Setores de maior renda	22	6,3	3,4 - 9,1	6,8	3,4 - 10,2	9,4	6,0- 12,8
Setores de renda intermediária	37	12,4	8,3 - 16,5	15,2	10,4 - 19,9	18,4	13,3 - 23,4
Setores de menor renda	42	13,4	9,3 - 17,5	18,7	14,3 - 23,0	22,0	17,2 - 26,7

Teste Anterior: Maglumi IgM e IgG
Fabricante: Snibe
Método: Quimioluminescência
Detecta IgG e IgM separadamente
Antigeno: Spike Protein e Nucleo Capsid Protein

Teste Novo: Elecsys SARS-CoV-2
Fabricante: Roche
Método: Eletroquimioluminescência
Detecta anticorpos totais
Antigeno: Nucleo Capsid Protein



n = 1470 (100%)
Total Negativo: 1208 (82%)
Total Positivo: 262 (18%)
Positvo Somente Anterior: 46 (18%)
Positivo Somente Novo: 89 (34%)
Positivo em Ambos: 127 (48%)

Obs: resultados não ponderados

O diagrama acima demonstra que apesar de ambos testes identificarem 127 dos indivíduos soropositivos, o teste anterior identificou 46 indivíduos que não foram identificados pelo teste novo e o teste novo identificou 89 indivíduos que não foram identificados pelo teste anterior.

Medidas de Prevenção e Controle

- ✓ Medidas não farmacológicas
  - ✓ Reforço a higiene, medidas de desinfecção
  - ✓ Medidas de distanciamento social
- ✓ Medidas Farmacológicas
  - ✓ Terapêuticas
    - ✓ Reposicionamento de fármacos já utilizados para outras indicações
  - ✓ Preventivas
    - ✓ Vacinas

CORRESPONDENCE

Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1

TO THE EDITOR: A novel human coronavirus that is now named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (formerly called HCoV-19) emerged in Wuhan, China, in late 2019 and is now causing a pandemic.[1] We analyzed the aerosol and surface stability of SARS-CoV-2 and compared it with SARS-CoV-1, the most closely related human coronavirus.[2]

We evaluated the stability of SARS-CoV-2 and SARS-CoV-1 in aerosols and on various surfaces and estimated their decay rates using a Bayesian regression model (see the Methods section in the Supplementary Appendix, available with the full text of this letter at NEJM.org). SARS-CoV-2 nCoV-WA1-2020 (MN985325.1) and SARS-CoV-1 Tor2 (AY274119.3) were the strains used. Aerosols (<5 μm) containing SARS-CoV-2 ($10^{5.25}$ 50% tissue-culture infectious dose [$TCID_{50}$] per milliliter) or SARS-CoV-1 ($10^{6.75-7.00}$ $TCID_{50}$ per milliliter) were generated with the use of a three-jet Collison nebulizer and fed into a Goldberg drum to create an aerosolized environment. The inoculum resulted in cycle-threshold values between 20 and 22, similar to those observed in samples obtained from the upper and lower respiratory tract in humans.

Our data consisted of 10 experimental conditions involving two viruses (SARS-CoV-2 and SARS-CoV-1) in five environmental conditions (aerosols, plastic, stainless steel, copper, and cardboard). All experimental measurements are reported as means across three replicates.

SARS-CoV-2 remained viable in aerosols throughout the duration of our experiment (3 hours), with a reduction in infectious titer from $10^{3.5}$ to $10^{2.7}$ $TCID_{50}$ per liter of air. This reduction was similar to that observed with SARS-CoV-1, from $10^{4.3}$ to $10^{3.5}$ $TCID_{50}$ per milliliter (Fig. 1A).

SARS-CoV-2 was more stable on plastic and stainless steel than on copper and cardboard, and viable virus was detected up to 72 hours after application to these surfaces (Fig. 1A), although the virus titer was greatly reduced (from $10^{3.7}$ to $10^{0.6}$ $TCID_{50}$ per milliliter of medium after 72 hours on plastic and from $10^{3.7}$ to $10^{0.6}$ $TCID_{50}$ per milliliter after 48 hours on stainless steel). The stability kinetics of SARS-CoV-1 were similar (from $10^{3.4}$ to $10^{0.7}$ $TCID_{50}$ per milliliter after 72 hours on plastic and from $10^{3.6}$ to $10^{0.6}$ $TCID_{50}$ per milliliter after 48 hours on stainless steel). On copper, no viable SARS-CoV-2 was measured after 4 hours and no viable SARS-CoV-1 was measured after 8 hours. On cardboard, no viable SARS-CoV-2 was measured after 24 hours and no viable SARS-CoV-1 was measured after 8 hours (Fig. 1A).

Both viruses had an exponential decay in virus titer across all experimental conditions, as indicated by a linear decrease in the $\log_{10}TCID_{50}$ per liter of air or milliliter of medium over time (Fig. 1B). The half-lives of SARS-CoV-2 and SARS-CoV-1 were similar in aerosols, with median estimates of approximately 1.1 to 1.2 hours and 95% credible intervals of 0.64 to 2.64 for SARS-CoV-2 and 0.78 to 2.43 for SARS-CoV-1 (Fig. 1C, and Table S1 in the Supplementary Appendix). The half-lives of the two viruses were also similar on copper. On cardboard, the half-life of SARS-CoV-2 was longer than that of SARS-CoV-1. The longest viability of both viruses was on stainless steel and plastic; the estimated median half-life of SARS-CoV-2 was approximately 5.6 hours on stainless steel and 6.8 hours on plastic (Fig. 1C). Estimated differences in the half-lives of the two viruses were small except for those on cardboard (Fig. 1C). Individual replicate data were noticeably "noisier" (i.e., there was more variation in the experiment, resulting in a larger standard error) for cardboard than for other surfaces (Fig. S1 through S5), so we advise caution in interpreting this result.

We found that the stability of SARS-CoV-2 was similar to that of SARS-CoV-1 under the experimental circumstances tested. This indicates that differences in the epidemiologic characteristics of these viruses probably arise from other factors, including high viral loads in the upper

Estabilidade do SARS-CoV-19 em aerossóis e superfícies

- ✓ Permanece viável em aerossóis por 3 horas.
- ✓ Foi mais estável em superfícies de plástico e aço inoxidável, do que em cobre ou papelão.
- ✓ Permaneceu viável em superfícies de plástico até 72 horas, e até 48 horas em aço inoxidável, porém os títulos de vírus caíram muito nesse período.
- ✓ Cobre – não encontrados vírus viáveis após 4 horas.
- ✓ Papelão – não encontrados vírus viáveis após 24 horas.
- ✓ Meia-vida média:
  - ✓ 5,6 horas em superfícies de aço inoxidável.
  - ✓ 6,8 horas em superfícies de plástico.
  - ✓ Entre 1,1 e 1,2 horas em aerossóis.

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**

Summary

Background Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes COVID-19 and is spread person-to-person through close contact. We aimed to investigate the effects of physical distance, face masks, and eye protection on virus transmission in health-care and non-health-care (eg, community) settings.

Methods We did a systematic review and meta-analysis to investigate the optimum distance for avoiding person-to-person virus transmission and to assess the use of face masks and eye protection to prevent transmission of viruses. We obtained data for SARS-CoV-2 and the betacoronaviruses that cause severe acute respiratory syndrome, and Middle East respiratory syndrome from 21 standard WHO-specific and COVID-19-specific sources. We searched these data sources from database inception to May 3, 2020, with no restriction by language, for comparative studies and for contextual factors of acceptability, feasibility, resource use, and equity. We screened records, extracted data, and assessed risk of bias in duplicate. We did frequentist and Bayesian meta-analyses and random-effects meta-regressions. We rated the certainty of evidence according to Cochrane methods and the GRADE approach. This study is registered with PROSPERO, CRD42020177047.

Findings Our search identified 172 observational studies across 16 countries and six continents, with no randomised controlled trials and 44 relevant comparative studies in health-care and non-health-care settings (n=25 697 patients). Transmission of viruses was lower with physical distancing of 1 m or more, compared with a distance of less than 1 m (n=10 736, pooled adjusted odds ratio [aOR] 0·18, 95% CI 0·09 to 0·38; risk difference [RD] −10·2%, 95% CI −11·5 to −7·5; moderate certainty); protection was increased as distance was lengthened (change in relative risk [RR] 2·02 per m; $p_{interaction}$=0·041; moderate certainty). Face mask use could result in a large reduction in risk of infection (n=2647; aOR 0·15, 95% CI 0·07 to 0·34, RD −14·3%, −15·9 to −10·7; low certainty), with stronger associations with N95 or similar respirators compared with disposable surgical masks or similar (eg, reusable 12–16-layer cotton masks; $p_{interaction}$=0·090; posterior probability >95%, low certainty). Eye protection also was associated with less infection (n=3713; aOR 0·22, 95% CI 0·12 to 0·39, RD −10·6%, 95% CI −12·5 to −7·7; low certainty). Unadjusted studies and subgroup and sensitivity analyses showed similar findings.

Interpretation The findings of this systematic review and meta-analysis support physical distancing of 1 m or more and provide quantitative estimates for models and contact tracing to inform policy. Optimum use of face masks, respirators, and eye protection in public and health-care settings should be informed by these findings and contextual factors. Robust randomised trials are needed to better inform the evidence for these interventions, but this systematic appraisal of currently best available evidence might inform interim guidance.

Funding World Health Organization.

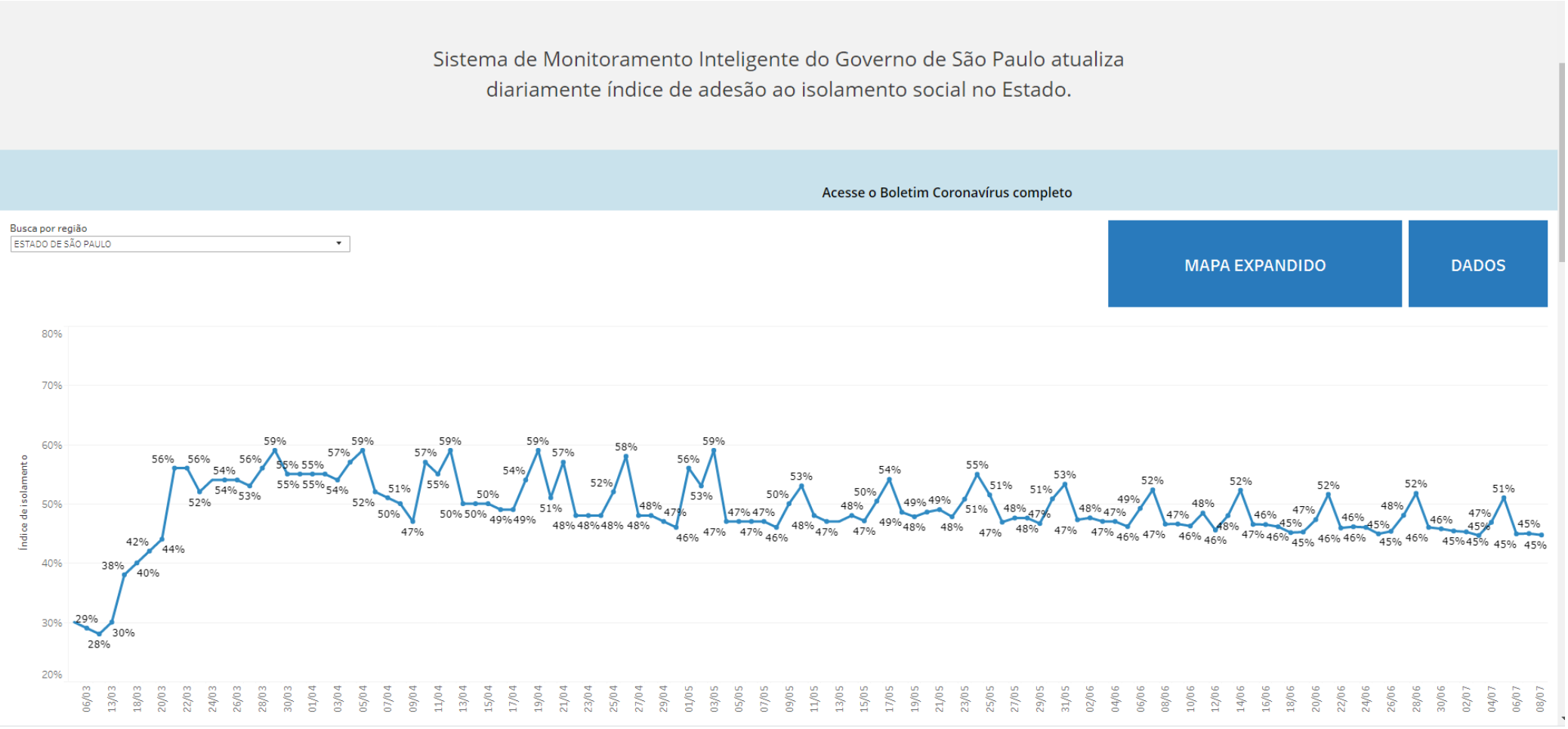
Revisão sistemática e metanálise

Máscaras, distanciamento físico e proteção ocular na prevenção da transmissão do SARS-CoV-2

- ✓ Transmissão foi menor com 1 metro de distância ou mais: aOR 0,18 (IC95%: 0,09 – 0,38).
- ✓ Transmissão reduzida com o uso de máscaras: aOR 0,15 (IC95%: 0,07 – 0,34), com associação mais forte no uso de máscaras N95 ou similares.
- ✓ Uso de proteção ocular também associou-se à menor transmissão: aOR 0,22 (IC95%: 0,12 – 0,39)

Fonte: Chu et al. Lancet 2020, 395: 1973-87

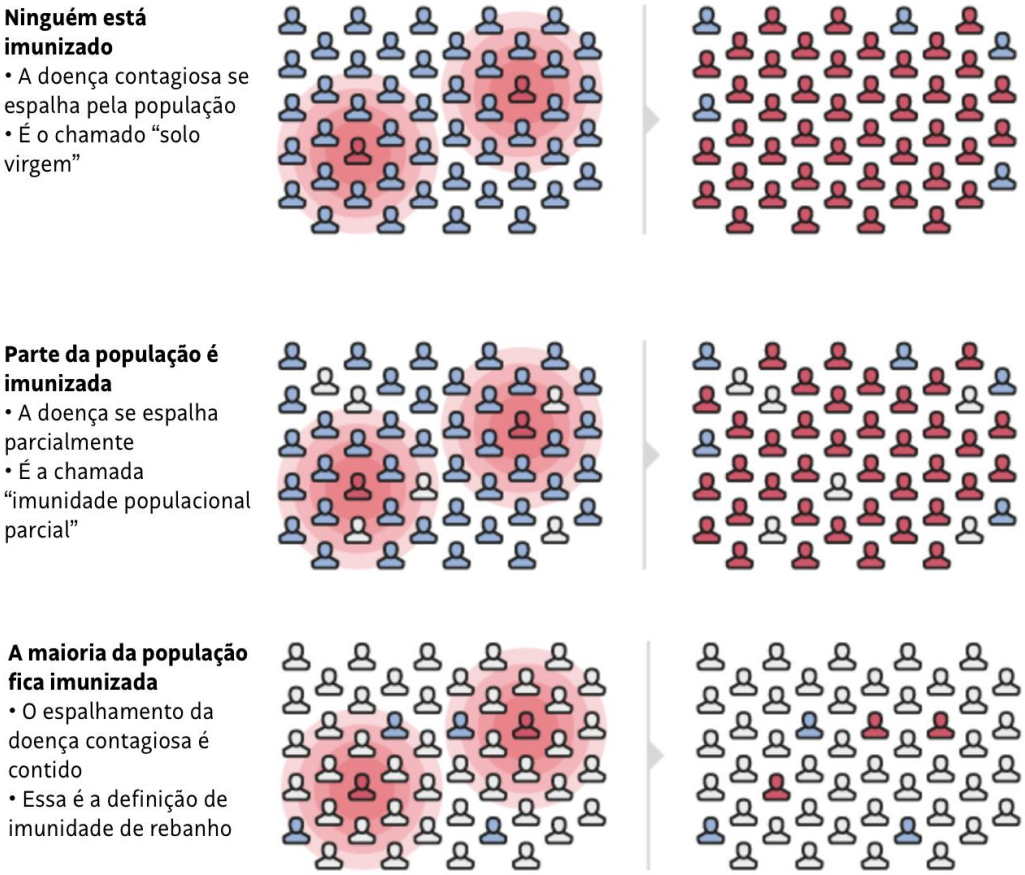
Índice de isolamento social, Estado de São Paulo, Brazil, Maio – Julho, 2020



https://www.saopaulo.sp.gov.br/coronavirus/isolamento/

Como funciona a imunidade de rebanho

Não imunizado e saudável
Imunizado e saudável
Não imunizado, doente e contagioso



Fonte: Kallás E. Folha de São Paulo, 26/05/2020

A imunidade coletiva ("de rebanho")

Proporção da população a partir da qual a transmissão do agente infeccioso cairia a valores de $R_0 < 1$
Para algumas doenças preveníveis por vacinação foi calculada:
Sarampo: 92% a 95%
Influenza: 33% a 34%
Não se sabe em relação à Covid-19
Questões:
Acurácia dos testes de anticorpos
Pacientes que tiveram quadros leves, apresentam títulos de anticorpos muito baixos.
Não se sabe a duração da imunidade conferida pela infecção.

Pandemia de influenza, 2009/2010

- Artigo de metanálise.
- van Kerkhove M et al. Estimating age-specific cummulative incidence for the 2009 influenza pandemic. *[Influenza and Other Respiratory Viruses 2013. DOI: 10.1111/irv.1274]*
- Incluiu 27 estudos, de 19 países.
- Soroprevalência pré-pandêmica: **5%** (IC95%: 3% - 7%).
- Incidência acumulada: **24%** (IC95%: 20% - 27%). Maior em 5-19 anos: 46% (IC95%: 36% - 56%). Mais baixa: > 65 anos: 11% (IC95%: 5% - 18%). Excluindo países onde poderia haver a inclusão de vacinados: **21%** (IC95%: 18% - 25%).
- Soroprevalência pós-pandemia: **32%** (IC95%: 26% - 39%).
- O vírus pandêmico original [A/California/7/2009/(H1N1)pdm09] permaneceu na composição das vacinas anuais até 2016-17 (Hemisfério Norte) e 2016 (Hemisfério Sul), sendo substituído pela cepa A/Michigan/45/2015(H1N1)pdm09

Pandemia de febre Zika, 2007 – 2016

- Soroprevalência pós-pandemia:
- Yap. Estados Federados da Micronésia. Soroprevalência: **78%** *[Duffy MR et al. Zika virus outbreak on Yap island, Federated States of Micronesia. New Engl J Med 2009, 360:2536-43].*
- *Polinésia Francesa.* Inquérito em escolares no Taiti. Realizado entre maio e junho de 2014. n = 476. Soroprevalência: **66%**, dos quais 29% assintomáticos. *[Aubry M et al. Emerg Infect Dis 2017, 23(4)]*
- Salvador. Amostra de conveniência (pacientes com HIV, TB, pré-natal), n = 633. Soroprevalência: **63,3%** (IC95%: 59,5% - 66,8%), usando ELISA. *[Martins-Netto E et al. mBio, 2017]*
- Santos, SP, 2016 – 2017. Coorte de parturientes e recém-nascidos. Durante e pós epidemia. Soroprevalência: **15,3%** (IC95%: 13,3% - 17,4%), usando ELISA e **7,2%** (IC95%: 5,5% - 9,2%), usando neutralização em citometria de fluxo.

Imunidade coletiva à COVID-19

- Proporção de suscetíveis na população
- Número básico de reprodução. Número de reprodução no momento.
- Taxa de contatos
- Duração da imunidade.
- Imunidade cruzada a outros coronavirus humanos.

Science

REPORTS

Cite as: Kissler *et al.*, *Science* 10.1126/science.abb5793 (2020).

Projecting the transmission dynamics of SARS-CoV-2 through the postpandemic period

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It is urgent to understand the future of severe acute respiratory syndrome–coronavirus 2 (SARS-CoV-2) transmission. We used estimates of seasonality, immunity, and cross-immunity for betacoronaviruses OC43 and HKU1 from time series data from the USA to inform a model of SARS-CoV-2 transmission. We projected that recurrent wintertime outbreaks of SARS-CoV-2 will probably occur after the initial, most severe pandemic wave. Absent other interventions, a key metric for the success of social distancing is whether critical care capacities are exceeded. To avoid this, prolonged or intermittent social distancing may be necessary into 2022. Additional interventions, including expanded critical care capacity and an effective therapeutic, would improve the success of intermittent distancing and hasten the acquisition of herd immunity. Longitudinal serological studies are urgently needed to determine the extent and duration of immunity to SARS-CoV-2. Even in the event of apparent elimination, SARS-CoV-2 surveillance should be maintained since a resurgence in contagion could be possible as late as 2024.

Se a imunidade induzida pela infecção pelo SARS-CoV-2 for duradoura, deve demorar pelo menos 5 anos até um próximo surto, porém se for de curta duração poderá haver surtos anuais ou bi-anuais.

Projetando a dinâmica de transmissão do SARS-CoV-2 no período pós-pandêmico

Modelagem que considera a sazonalidade, imunidade, e imunidade cruzada para os outros beta coronavírus humanos, agentes etiológicos de resfriado, OC43 e HKU1, e o SARS-CoV-1

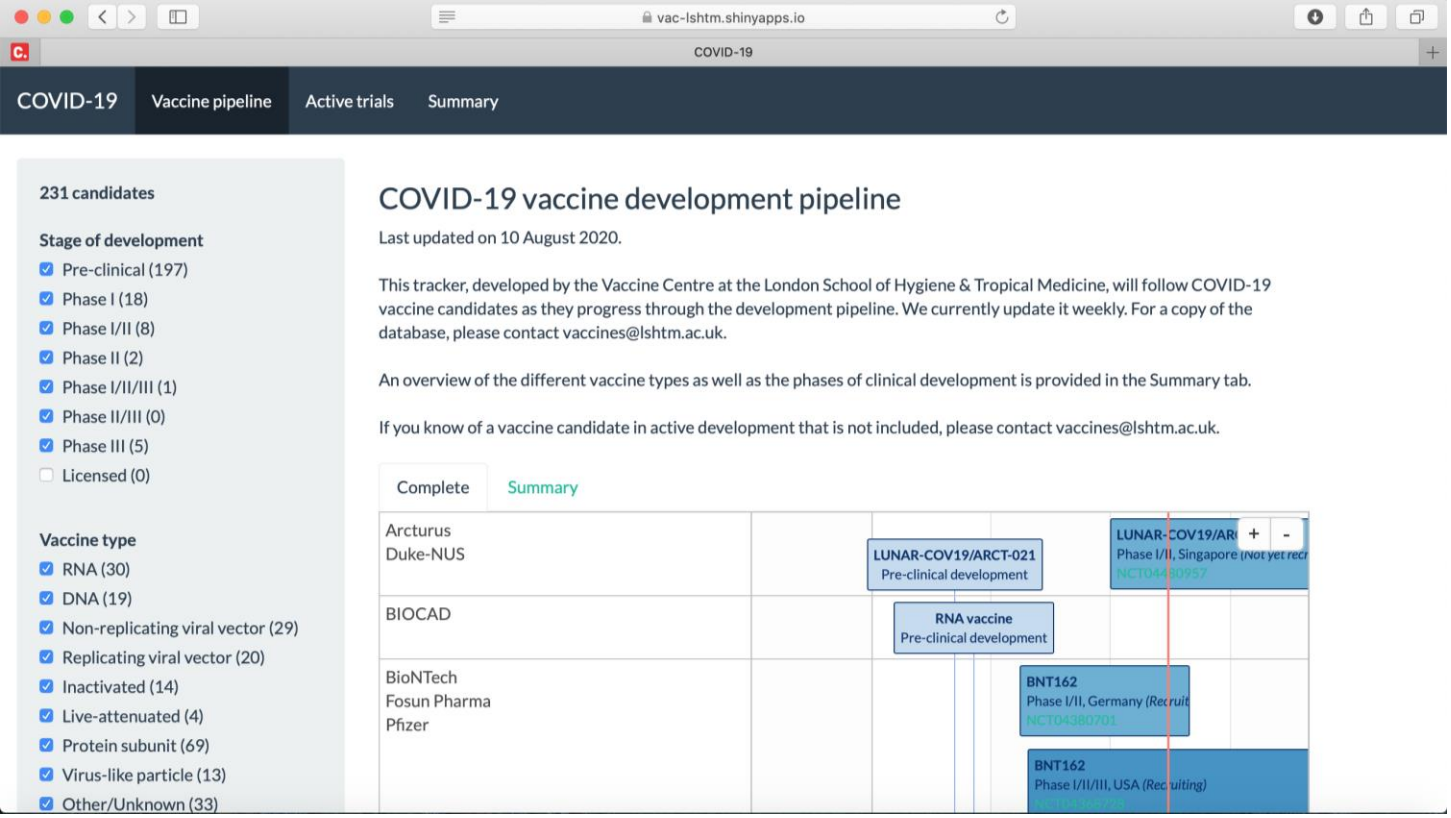
O HCoV-OC43 e o HCoV-HKU1 induzem imunidade de curta duração (estimada em 45 semanas), enquanto que o SARS-CoV-1 induz imunidade mais duradoura. Há imunidade cruzada entre o HCoV-OC43 e o SARS-CoV1, e entre o HCoV-OC43 e o HCoV-HKU1

A dinâmica de transmissão pós-pandêmica vai depender da duração da imunidade conferida pela infecção, e da existência ou não de imunidade cruzada com os outros coronavírus humanos.

Se a duração da imunidade induzida pelo SARS-CoV-2 não for permanente, haverá epidemias anuais, bi-anuais ou esporádicas (dependendo da duração da imunidade).

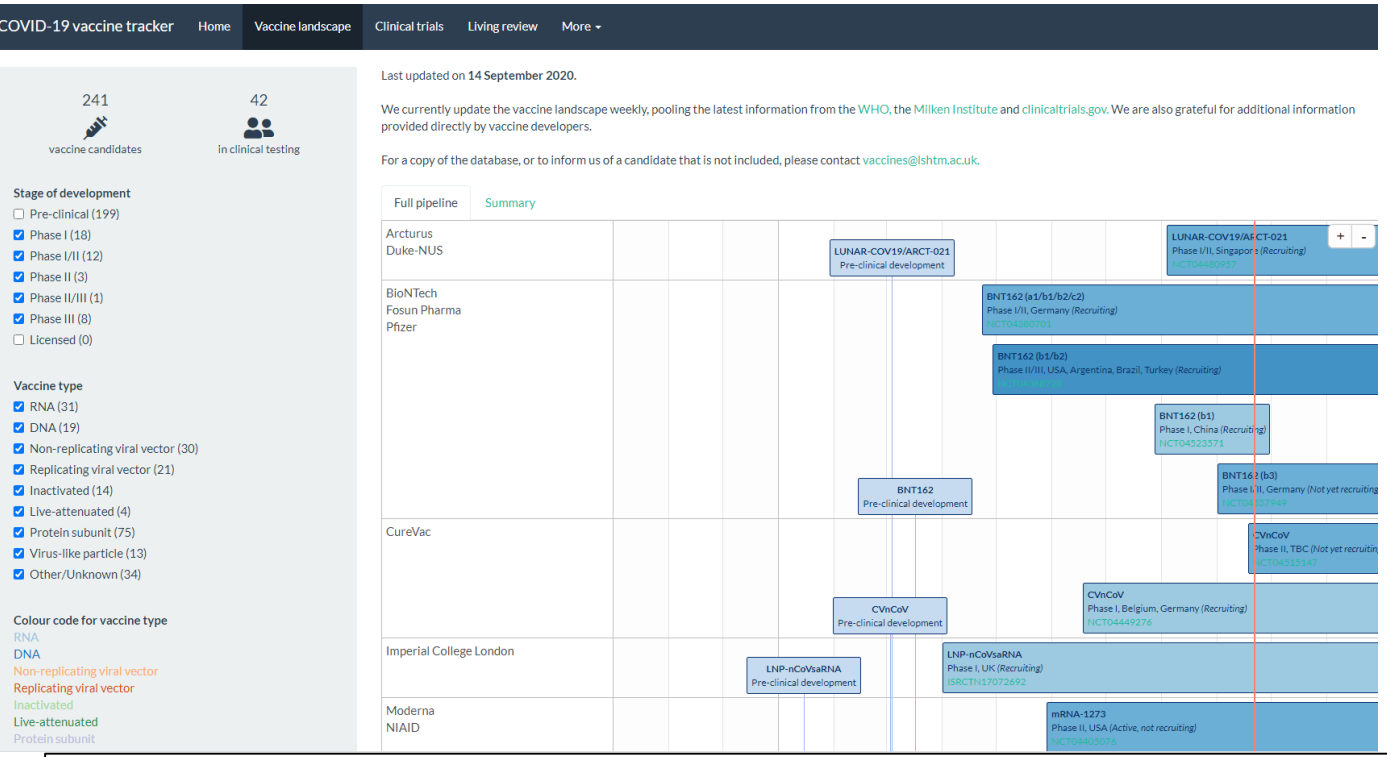
Se a duração da imunidade induzida pelo SARS-CoV-2 for permanente, pode haver um intervalo de 5 anos ou mais até a próxima grande epidemia.

Se houver um baixo nível de imunidade cruzada induzida pelos outros beta coronavírus (30%), a transmissão do SERS-CoV-2 pode ser interrompida por até 3 anos.



Vacinas contra COVID-19
Informação em 13/08/2020

- ✓ 197 projetos de pesquisa em execução
- ✓ 34 projetos em fase clínica de avaliação
- ✓ 6 projetos em ensaio clínico em fase 3
  - ✓ BioNTech/Fosun Pharma/Pfizer – vacina RNA
  - ✓ Moderna/NIAID – vacina mRNA
  - ✓ Univ. Oxford/Astra-Zeneca – vacina com vetor adenovírus
  - ✓ Sinovac/Butantan – vacina inativada
  - ✓ Sinopharm/ Beijing Institute of Biological Products – vacina inativada
  - ✓ Sinopharm/ Wuhan Institute of Biological Products – vacina inativada



Vacinas contra COVID-19
Informação em 21/09/2020

- ✓ 241 projetos de pesquisa em execução
- ✓ 42 projetos em fase clínica de avaliação
- ✓ 8 projetos em ensaio clínico em fase 3
  - ✓ BioNTech/Fosun Pharma/Pfizer – vacina RNA
  - ✓ Moderna/NIAID – vacina mRNA
  - ✓ Univ. Oxford/Astra-Zeneca – vacina com vetor adenovírus
  - ✓ Sinovac/Butantan – vacina inativada
  - ✓ Sinopharm/ Beijing Institute of Biological Products – vacina inativada
  - ✓ Sinopharm/ Wuhan Institute of Biological Products – vacina inativada
  - ✓ Jensen – vacina com vetor adenovírus
  - ✓ Gamaleya – vacina com vetor adenovírus

Considerações finais

- Em 9 meses a Covid-19 chegou a quase todos os países e territórios do mundo (apenas 3 países e 6 territórios sem registro de casos em 20/09/2020).
- Esforço sem precedentes da comunidade científica mundial
- Conhecimento e tecnologia em desenvolvimento, em processo contínuo de reformulação e reavaliação em tempo real.
- Medidas de controle com foco nas medidas de barreira, vigilância epidemiológica, rastreamento de contatos, isolamento, quarentena e medidas de proteção individual.

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