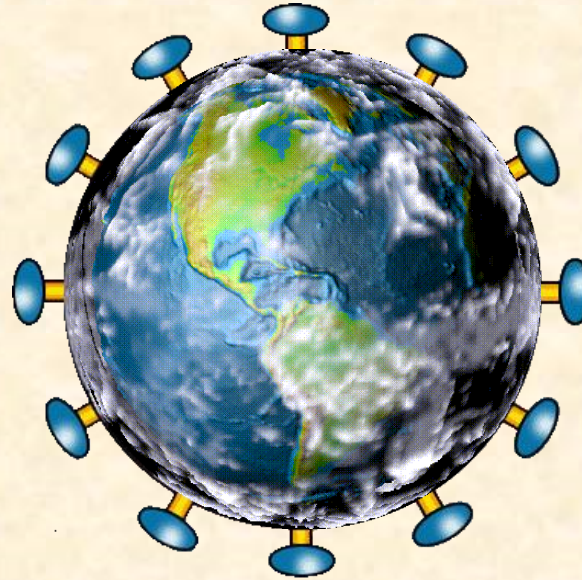




**PPGCM**

Programa de Pós-Graduação  
em Ciências Médicas  
Vice-Reitoria de Pós-Graduação



## **Abordagem clínica de pacientes com infecção pelo SARS-CoV-2 e COVID-19**

**Keny Colares**

**Março/2020**

**[kenycolares@unifor.br](mailto:kenycolares@unifor.br)**

# Epidemiologia

Coronavirus COVID-19 Global Cases by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU)

Total Confirmed  
**392.331**

Confirmed Cases by Country/Region /Sovereignty

81.588	China
63.927	Italy
46.450	US
39.673	Spain
30.150	Germany
24.811	Iran
20.149	France
9.117	Switzerland
9.037	Korea, South
6.733	United Kingdom
4.791	Austria
4.767	Netherlands
4.269	Belgium
2.647	Norway
2.088	Canada
2.060	Portugal
2.059	Sweden
2.044	Australia
1.960	Brazil
1.703	Denmark
1.656	Israel

Admin1 Admin2 Admin3

Last Updated at (M/D/YYYY)  
3/24/2020 8:41:34 AM



Cumulative Confirmed Cases Active Cases

**169**  
countries/regions

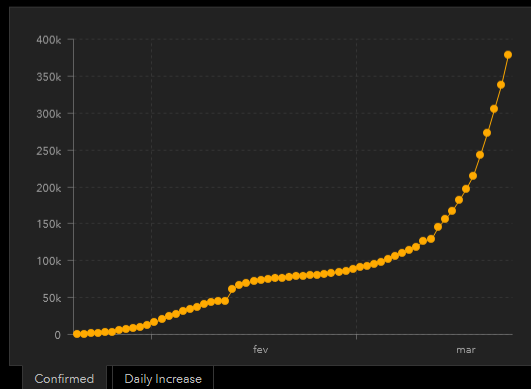
Lancet Inf Dis Article: [Here](#). Mobile Version: [Here](#). Visualization: JHU CSSE. Automation Support: [Esri Living Atlas team](#) and [JHU APL](#). Contact [US](#), [FAQ](#).  
Data sources: [WHO](#), [CDC](#), [ECDC](#), [NHC](#), [DXY](#), [1point3acres](#), [Worldometers.info](#), [BNO](#), state and national government health departments, and local media reports. Read more in this [blog](#).  
Downloadable database: [GitHub](#): [Here](#). Feature layer: [Here](#).  
Confirmed cases include presumptive positive cases.

Total Deaths  
**17.156**

6,077 deaths	Italy
3,160 deaths	Hubei China
2,696 deaths	Spain
1,934 deaths	Iran
860 deaths	France
335 deaths	United Kingdom
213 deaths	Netherlands
130 deaths	Germany
125 deaths	New York City New York US
122 deaths	Belgium
122 deaths	Switzerland

Total Recovered  
**102.972**

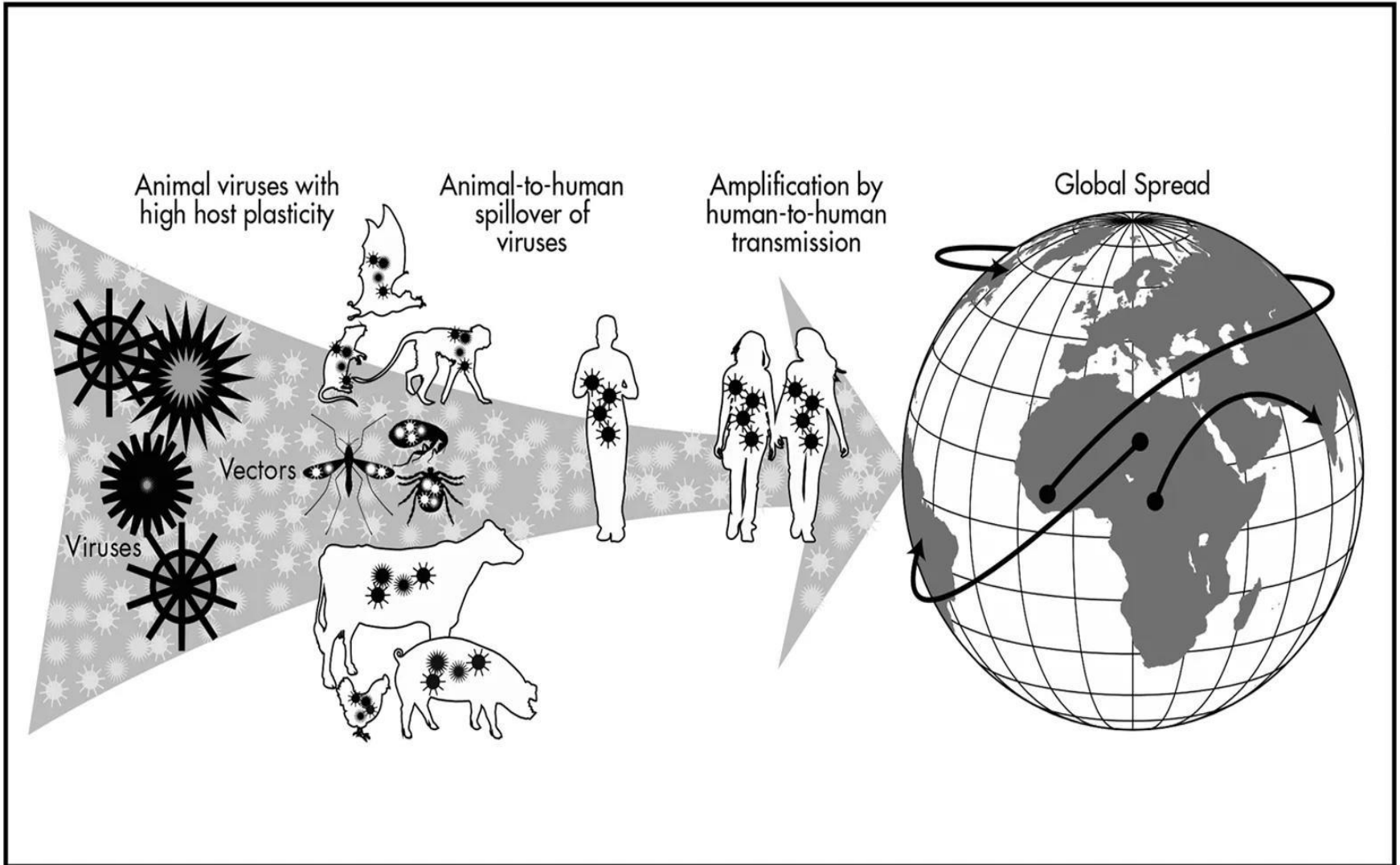
60,323 recovered	Hubei China
8,913 recovered	Iran
7,432 recovered	Italy
3,794 recovered	Spain
3,507 recovered	Korea, South
2,200 recovered	France
1,333 recovered	Guangdong China
1,250 recovered	Henan China
1,221 recovered	Zhejiang China
1,014 recovered	Hunan China
984 recovered	Anhui China



# Epidemiologia



# Doenças Emergentes



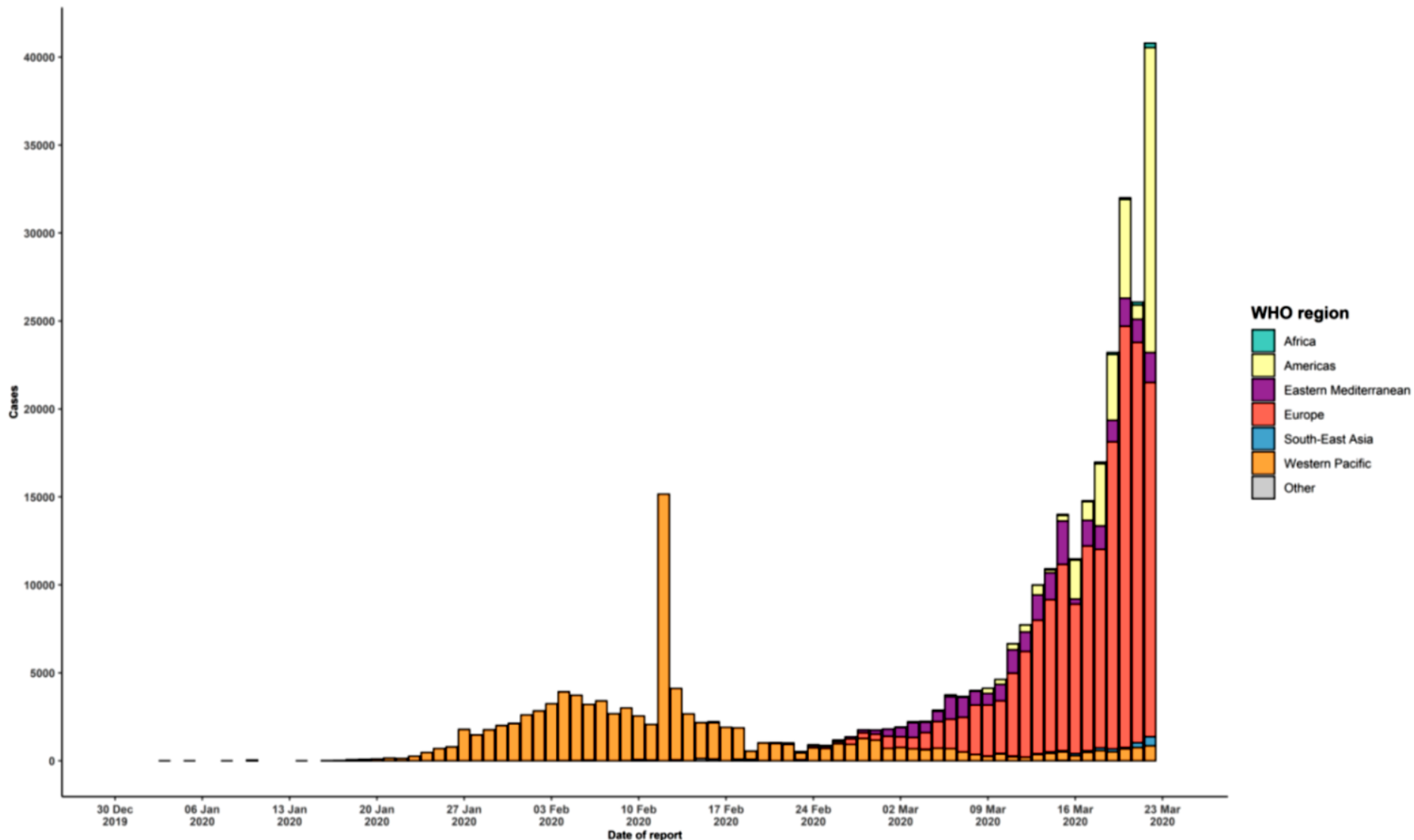
## Severe Acute Respiratory Syndrome Coronavirus as an Agent of Emerging and Reemerging Infection

Vincent C. C. Cheng, Susanna K. P. Lau, Patrick C. Y. Woo, and Kwok Yung Yuen\*

*State Key Laboratory of Emerging Infectious Diseases, Department of Microbiology, Research Centre of Infection and Immunology, The University of Hong Kong, Hong Kong Special Administrative Region, China*

The presence of a large reservoir of SARS-CoV-like viruses in horseshoe bats, together with the culture of eating exotic mammals in southern China, **is a time bomb**. The possibility of the reemergence of SARS and other novel viruses from animals or laboratories and therefore the need for preparedness should not be ignored.

# Curva epidemiológica por região

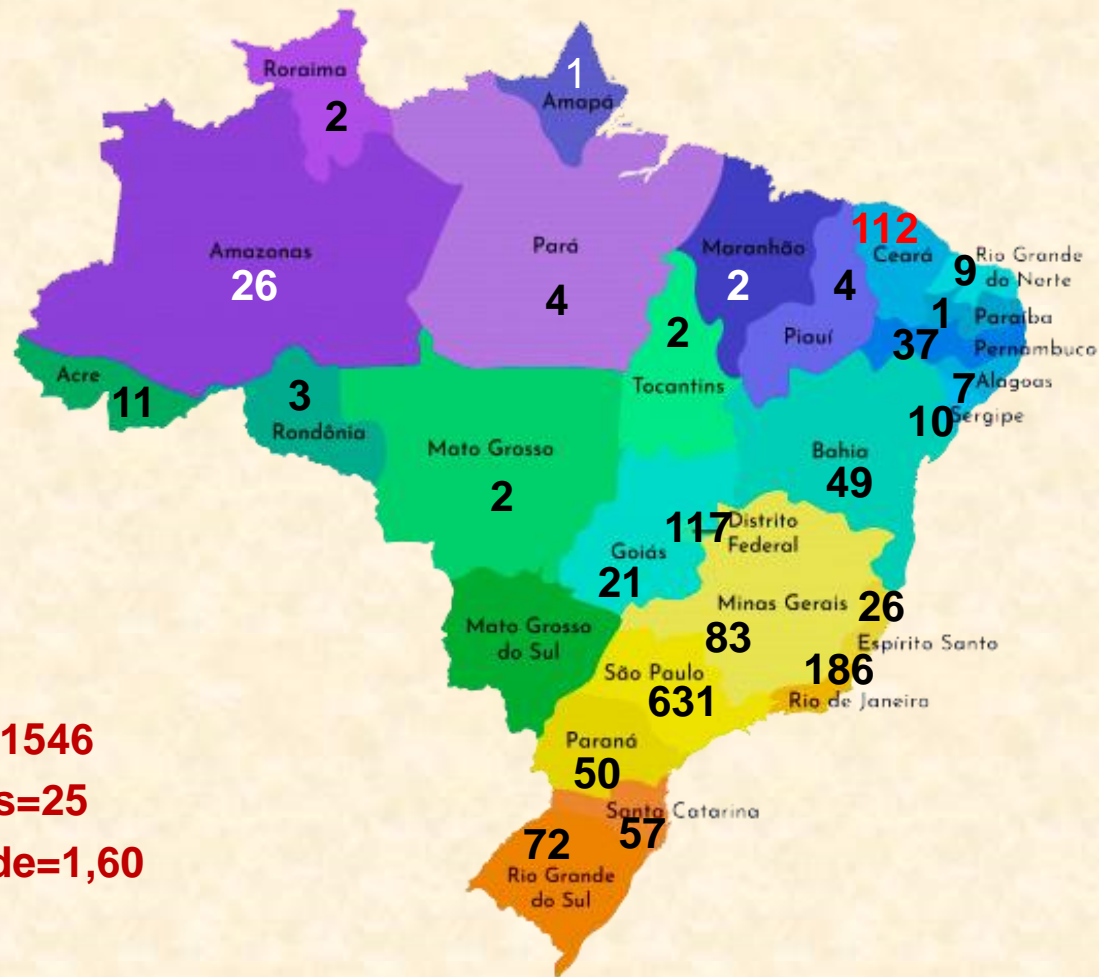


WHO - Coronavirus disease (COVID-2019) - Situation reports 63 - 23 Mar 2020

<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/>



# Brasil

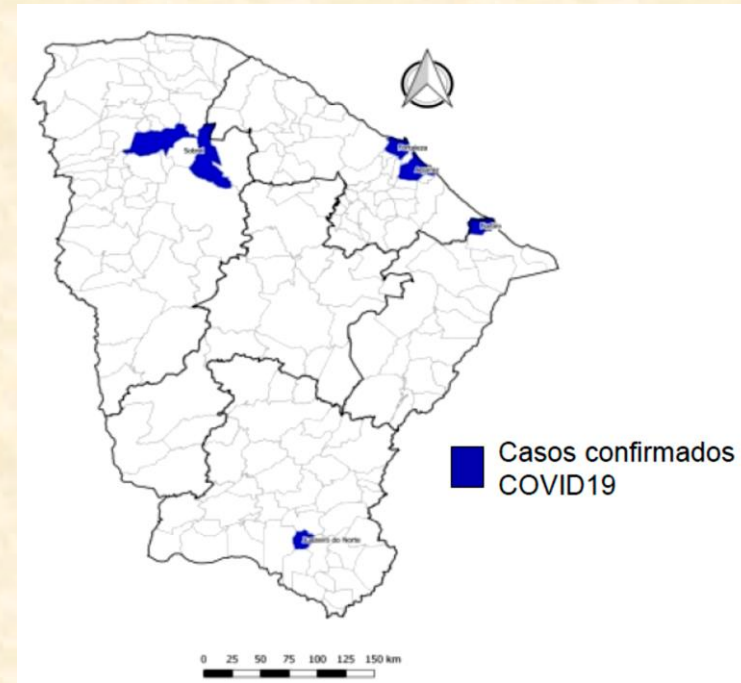


**Total=1546**  
**Óbitos=25**  
**Letalidade=1,60**



# Ceará

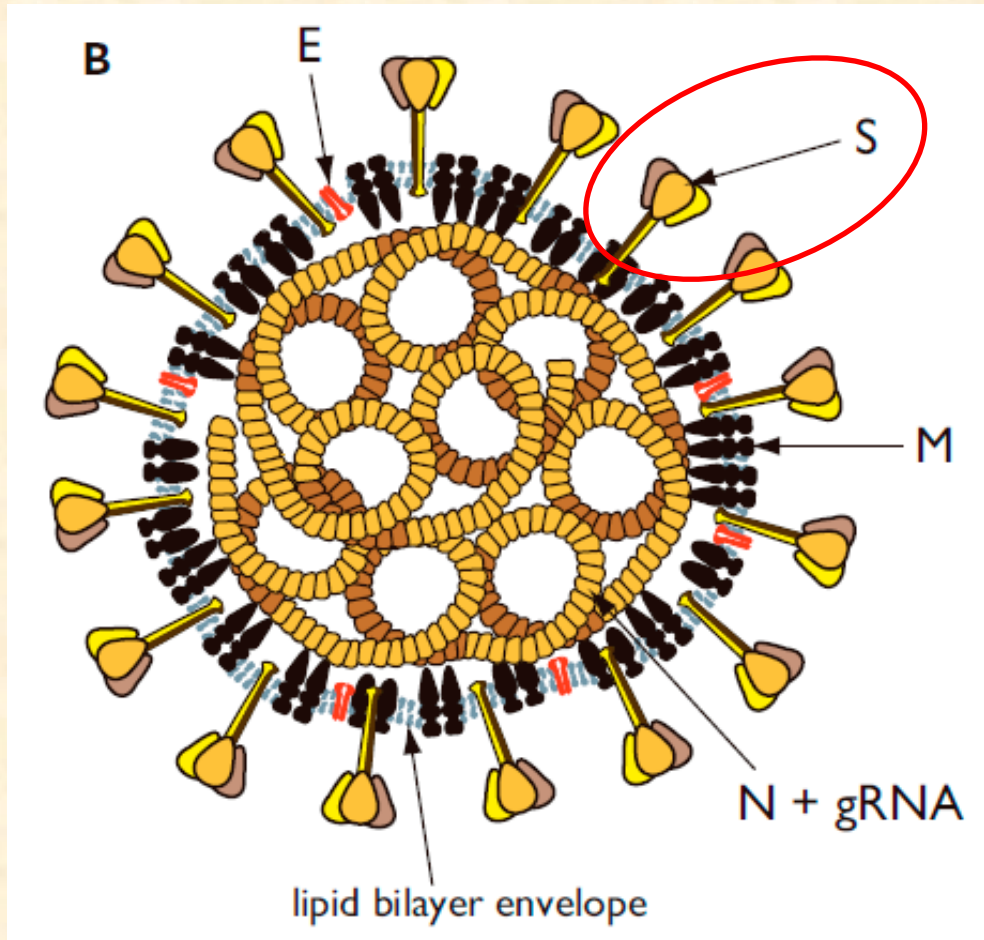
Município	Casos*	Óbitos
Aquiraz	6	0
Fortaleza	151	0
Fortim	1	0
Juazeiro do Norte	1	0
Sobral	3	0
São Paulo	1	0
Uberlândia	1	0
<b>Total</b>	<b>164</b>	<b>0</b>



\*Confirmados



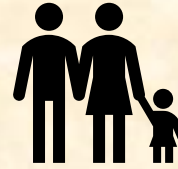
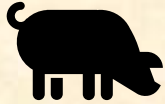
# Coronavirus



- Ordem *Nidovirales*
- Família *Coronaviridae*
- Subfam. *Coronavirinae*
- Envelope
- 80-120nm
- 26-32kb
- **RNAss ⊕**
- Não segmentado



# Coronavirus



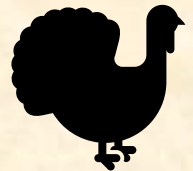
Respiratório

TGI

CNS

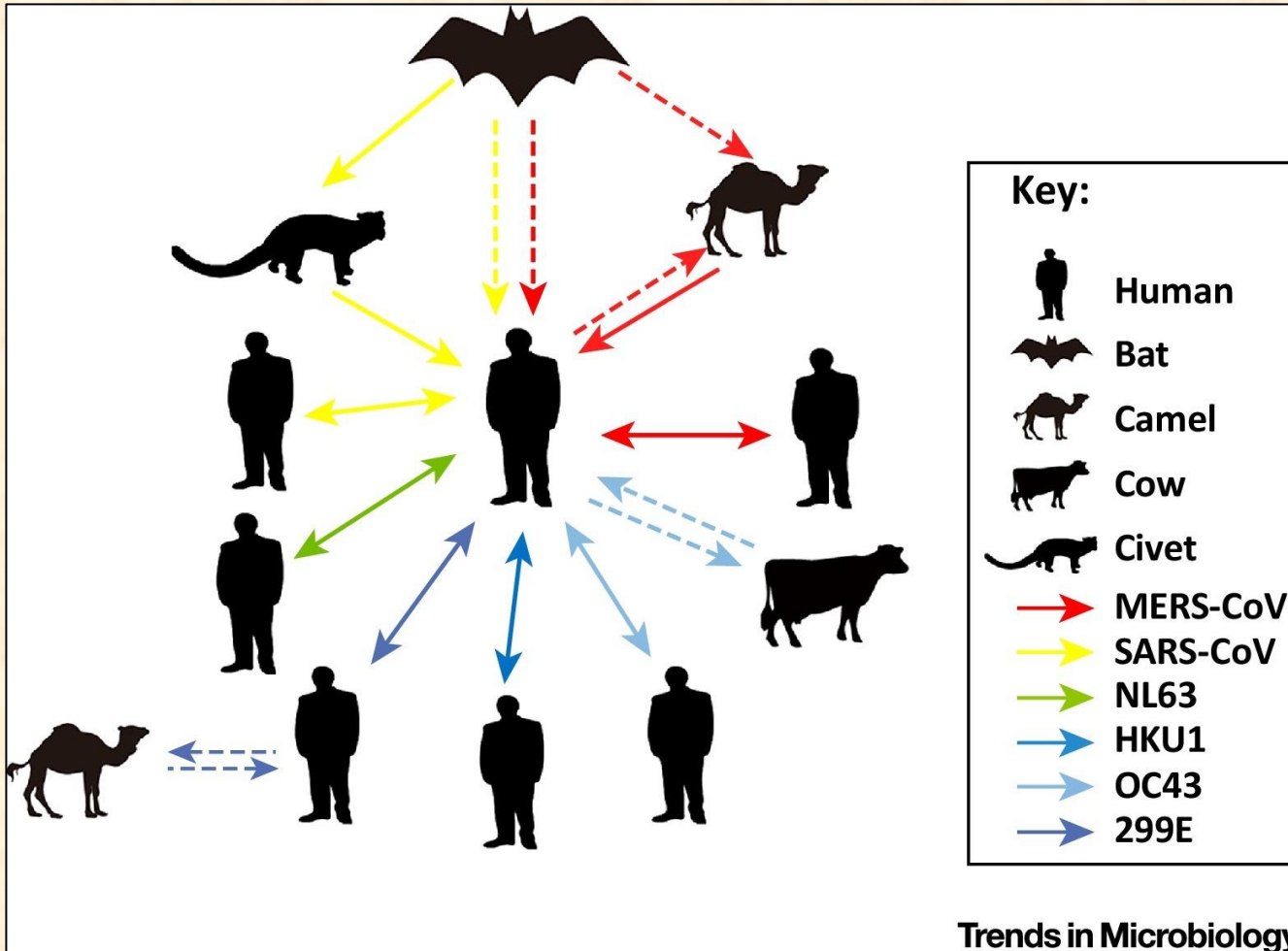
Fígado

Reprodutor





# Coronavirus



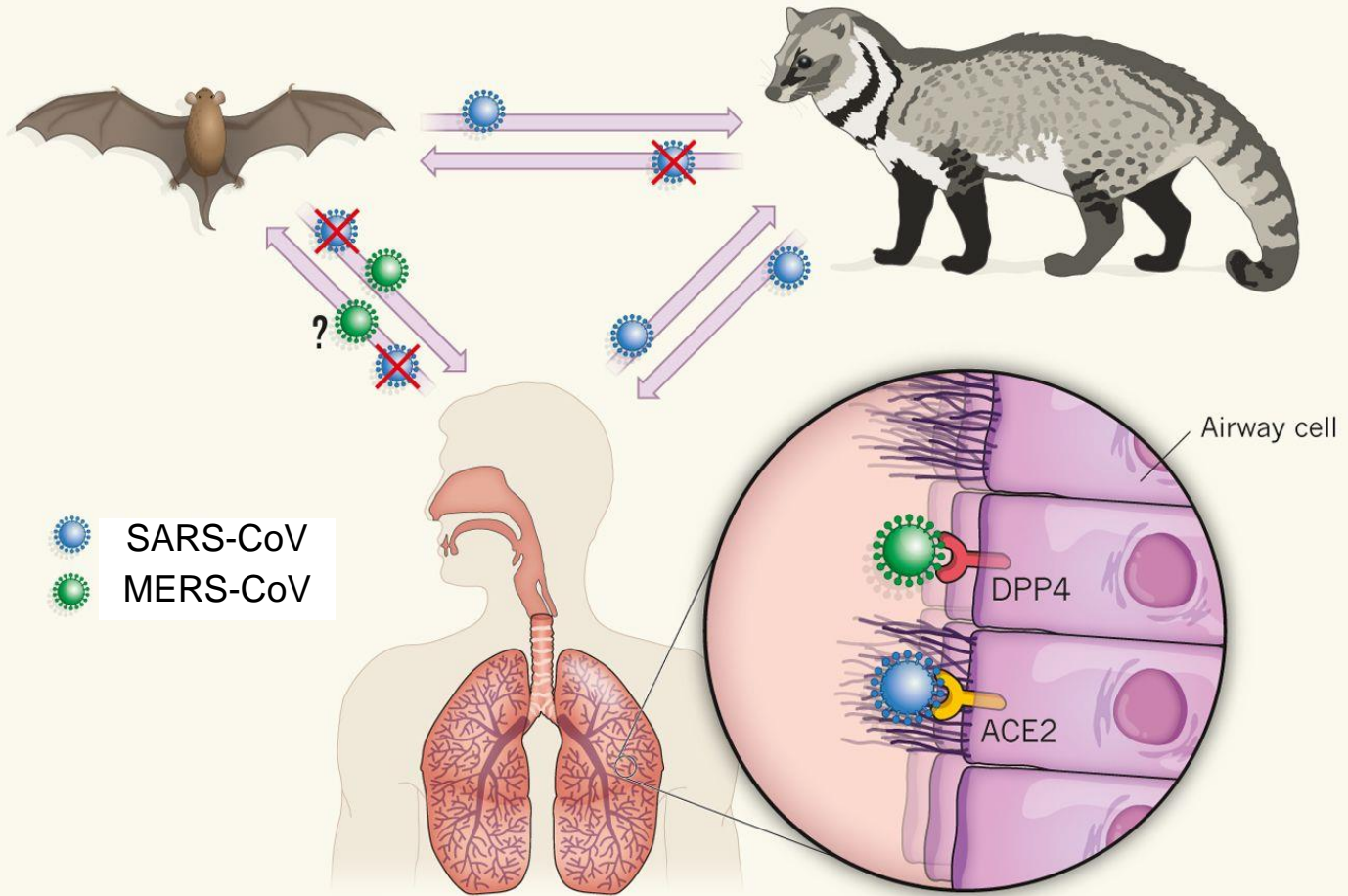


# Coronavirus

Nome	Ano	Doença	Receptor
HCoV-229E	1965	Resfriado/PN	Aminopeptidase N (APN)
HCoV-OC43	1967	Resfriado/PN	9-O-acetylated neuraminic acid
<b>SARS-CoV</b>	2003	PN/SARA	<b>Angiotensin-converting enzyme 2 (ACE-2)</b>
HCoV-NL63	2004	Resfriado/Laringite	Angiotensin-converting enzyme 2 (ACE-2)
HCoV-HKU1	2005	Resfriado/PN/TGI	?
<b>MERS-CoV</b>	2012	MERS/IRA	Dipeptidyl peptidase 4 (DPP-4)
<b>SARS-CoV-2</b>	2019	<b>COVID-19</b>	<b>Angiotensin-converting enzyme 2 (ACE-2)</b>



# Patogênese

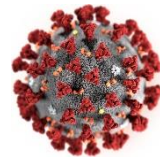




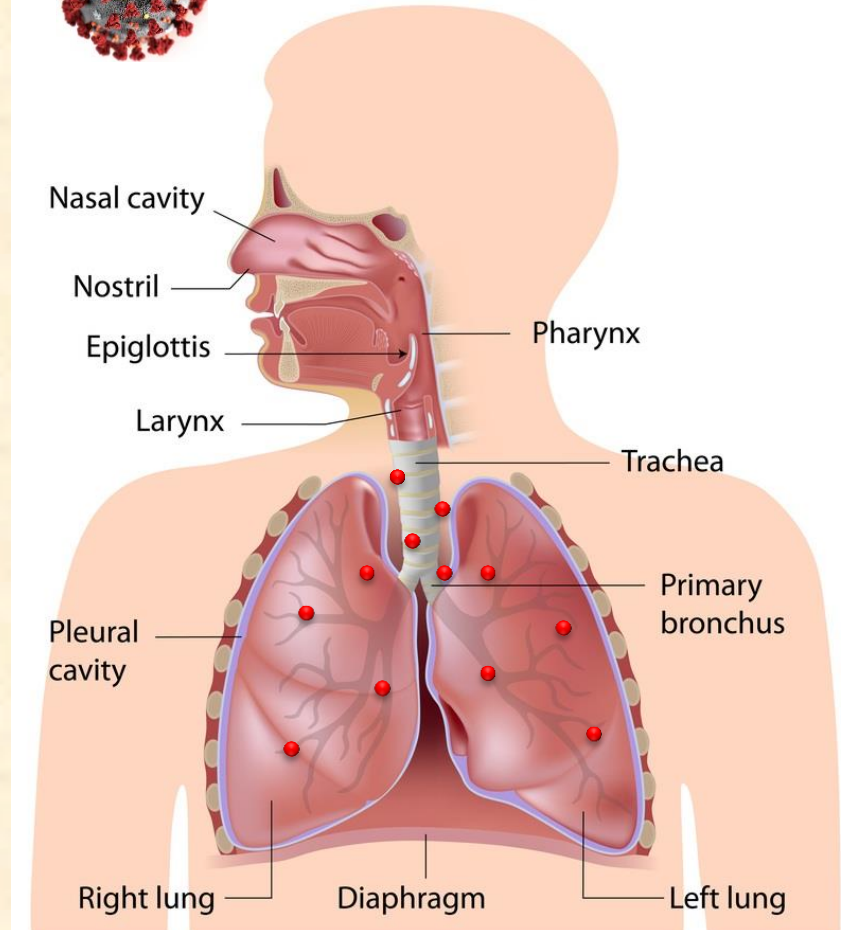
# Receptores (ectopeptidase)

**Angiotensin  
converting enzyme 2  
(ACE2)**

**Epiteliais ciliadas**  
**Pneumócitos tipo II**  
**Tecido renal**  
**Tecido cardiovascular**  
**Epitélio int. delgado**  
**Testículos**  
**Endotélio vascular**



**+ ACE2 receptors**



**Dipeptidyl peptidase 4  
(DPP4 / CD26)**

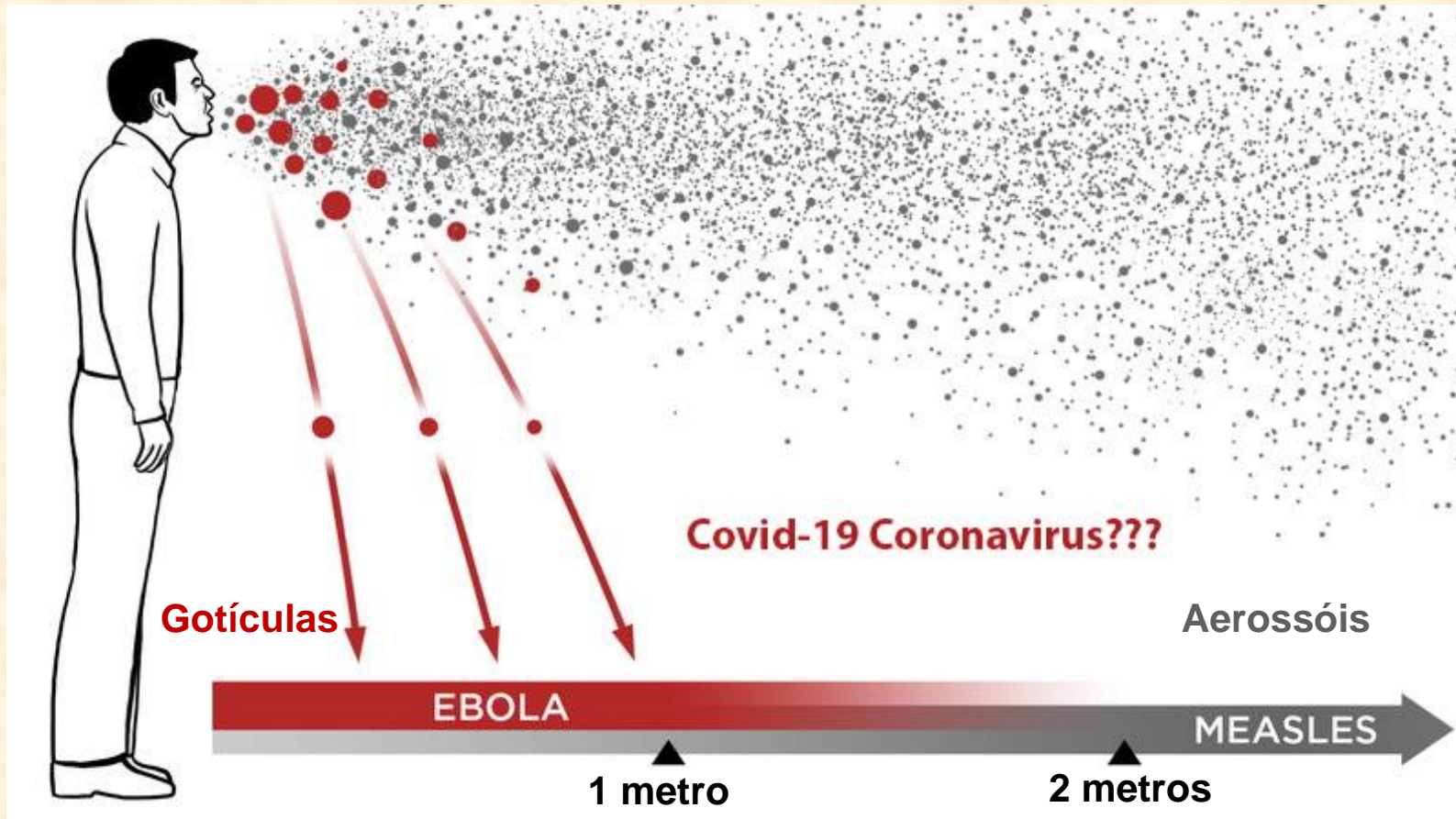
**Epitélio alveolar**  
**Epitélio bronquiolar**  
**Glândulas submucosa**  
**Macrófagos alveolares**  
**Endotélio vascular**  
**Linfócitos**  
**Céls. dendríticas**

Jia HP, J Virol 2005

Singh SK, Semin Respir Crit Care Med 2016

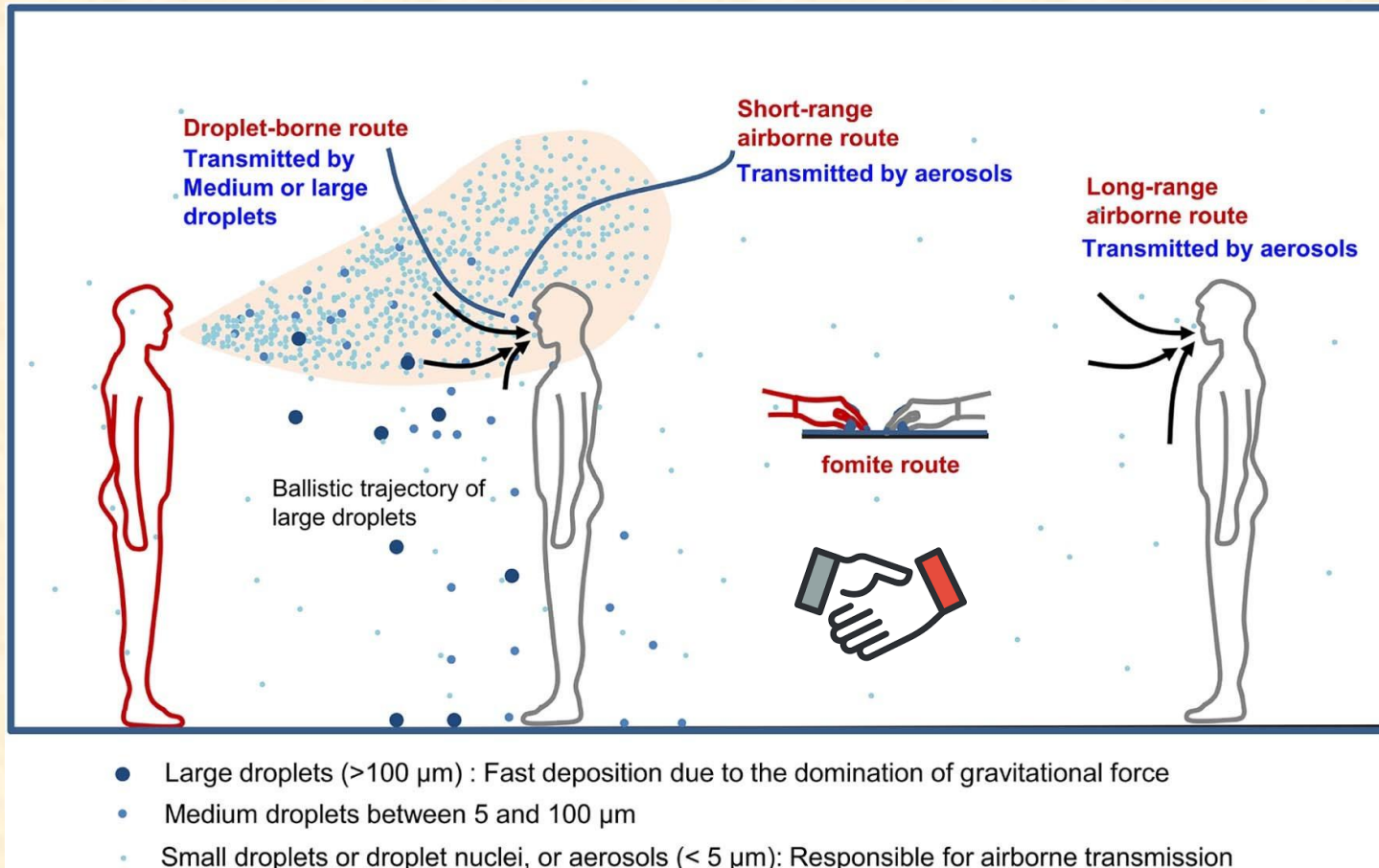


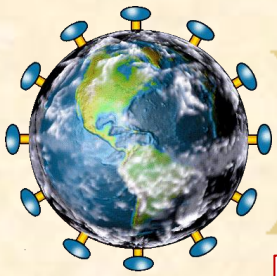
# Transmissão



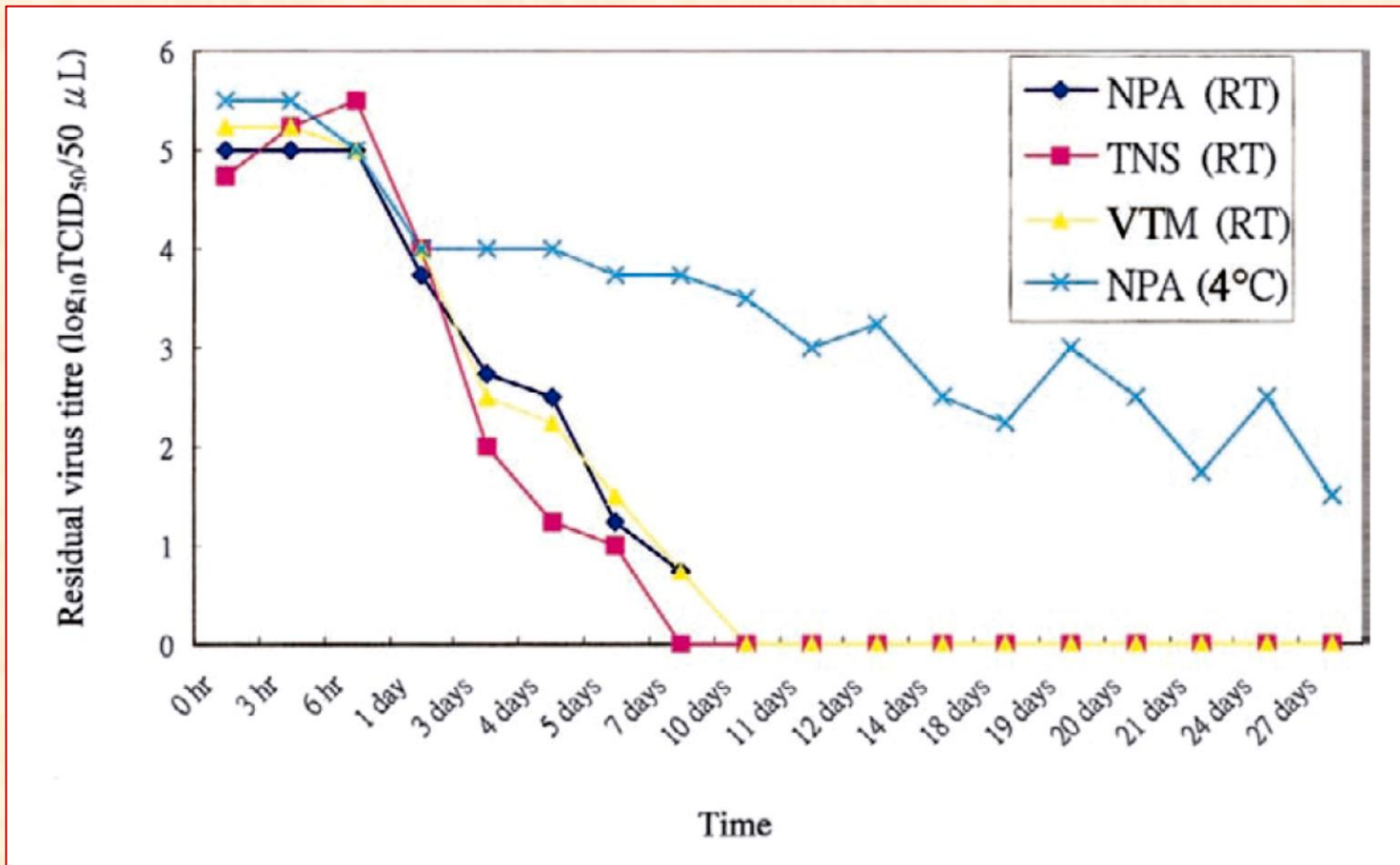


# Transmissão





# Transmissão



**Survival time of SARS-CoV** - room temperature (RT) and at 4C.

NPA: nasopharyngeal aspirate

TNS: throat and nasal swab

VTM: viral transport medium



# Transmissão

Inoculation, TCID <sub>50</sub> /mL	Time taken to inactivate SARS-CoV, by surface		
	Paper	Disposable gown	Cotton gown
10 <sup>6</sup>	24 h	2 days	24 h
10 <sup>5</sup>	3 h	24 h	1 h
10 <sup>4</sup>	<5 min	1 h	5 min



# Transmissão



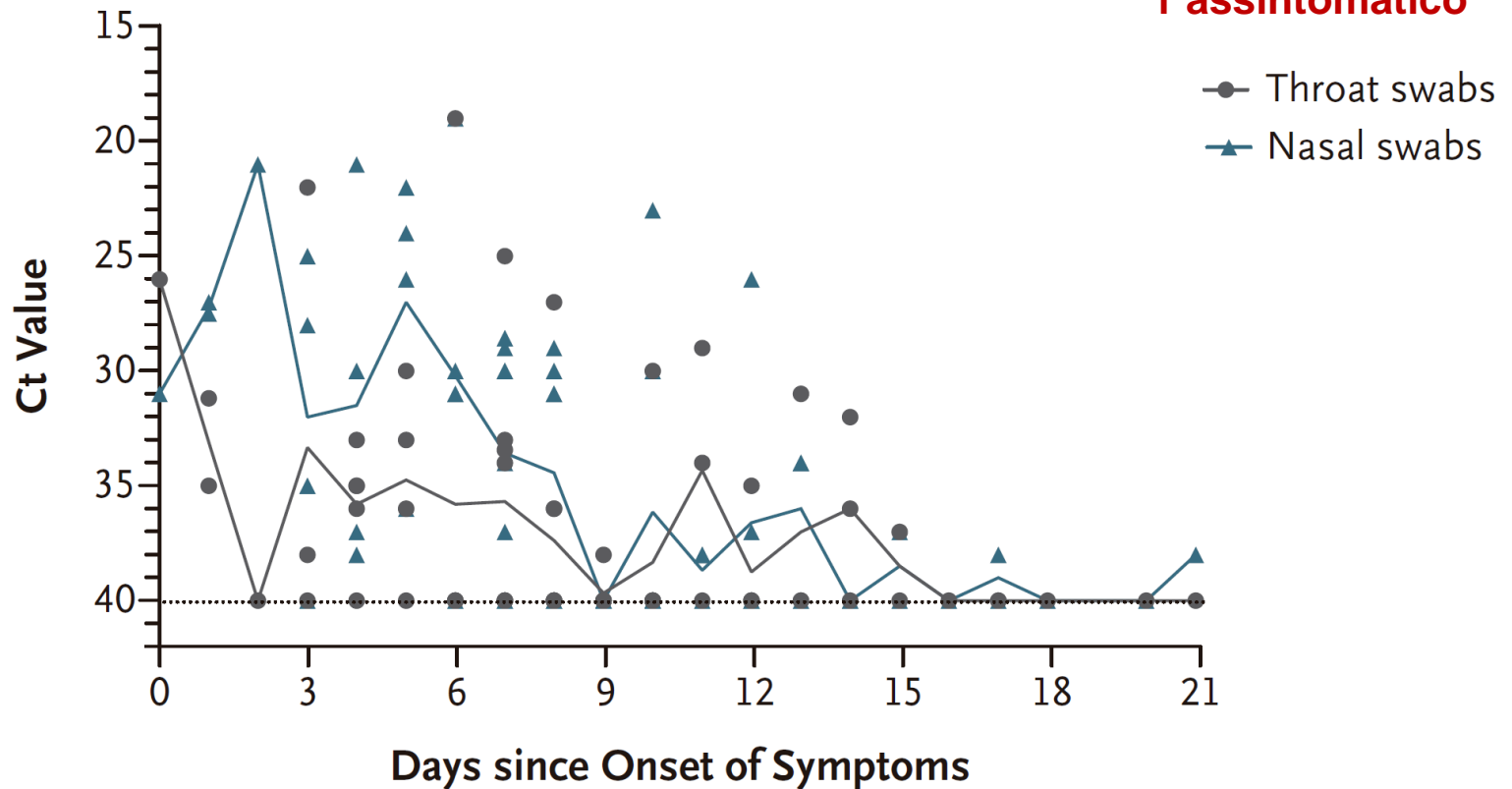


# Carga viral x tempo

**C** Aggregated Ct Values

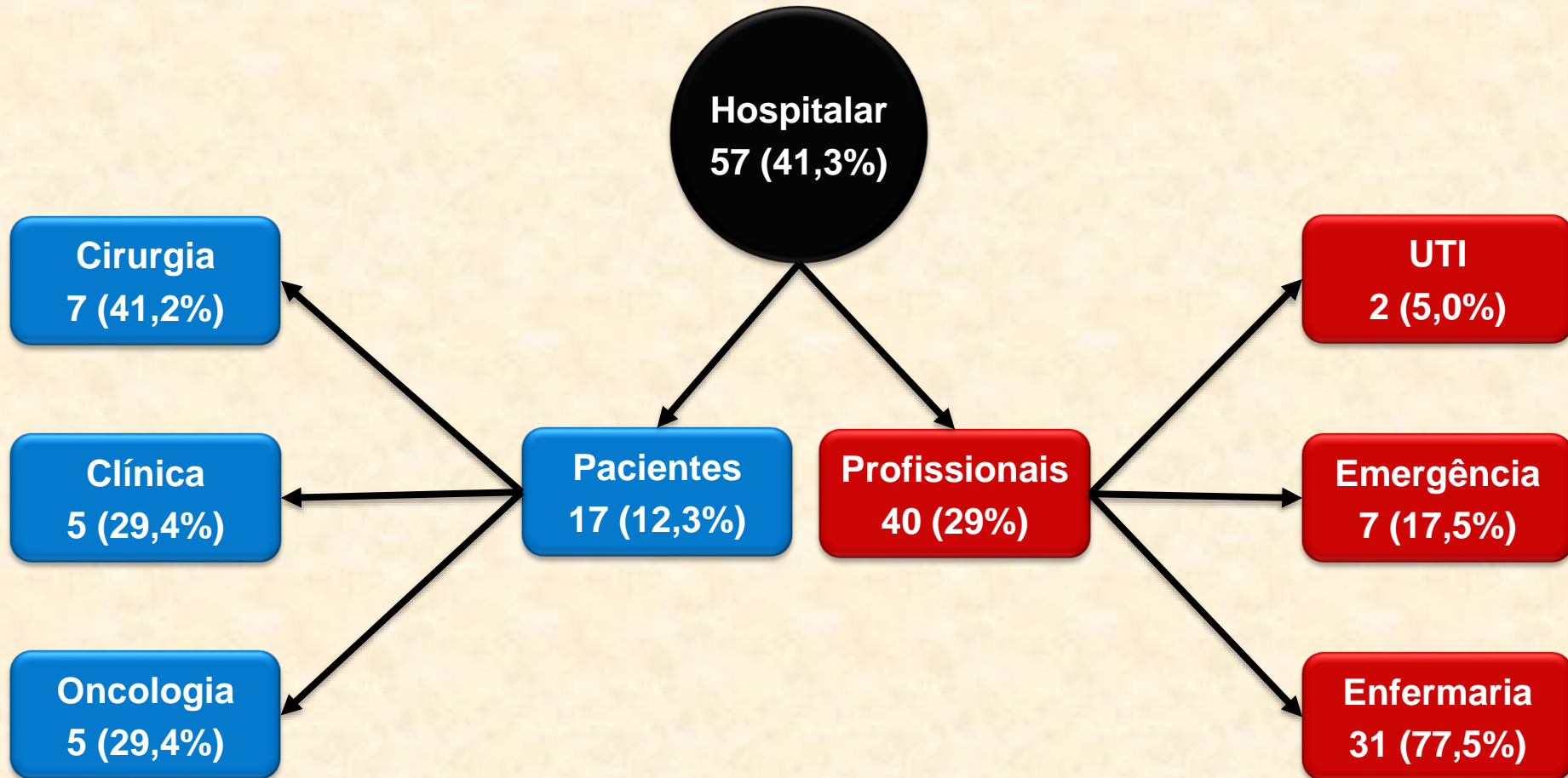
**17 sintomáticos**

**1 assintomático**



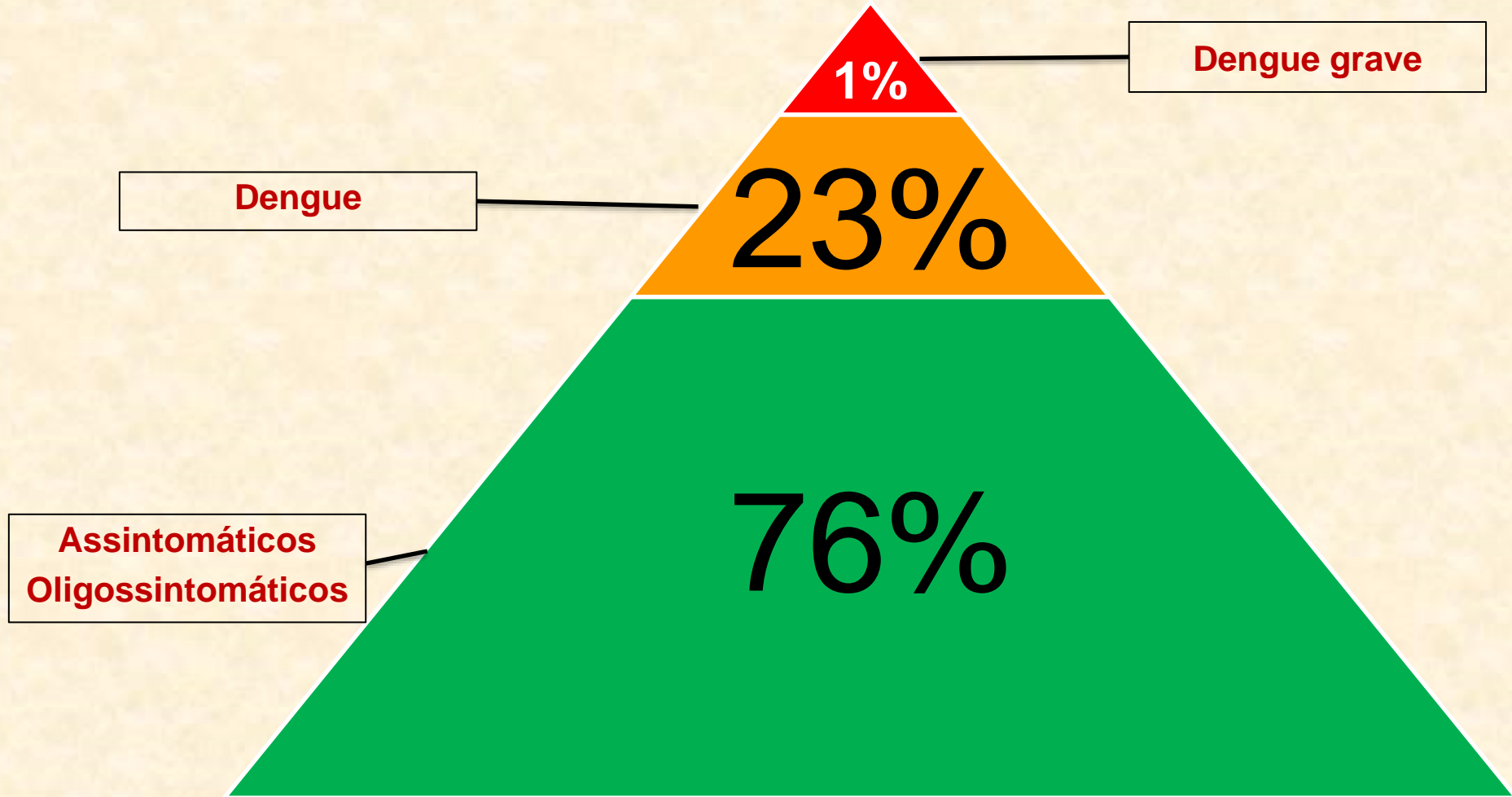


# Transmissão nosocomial



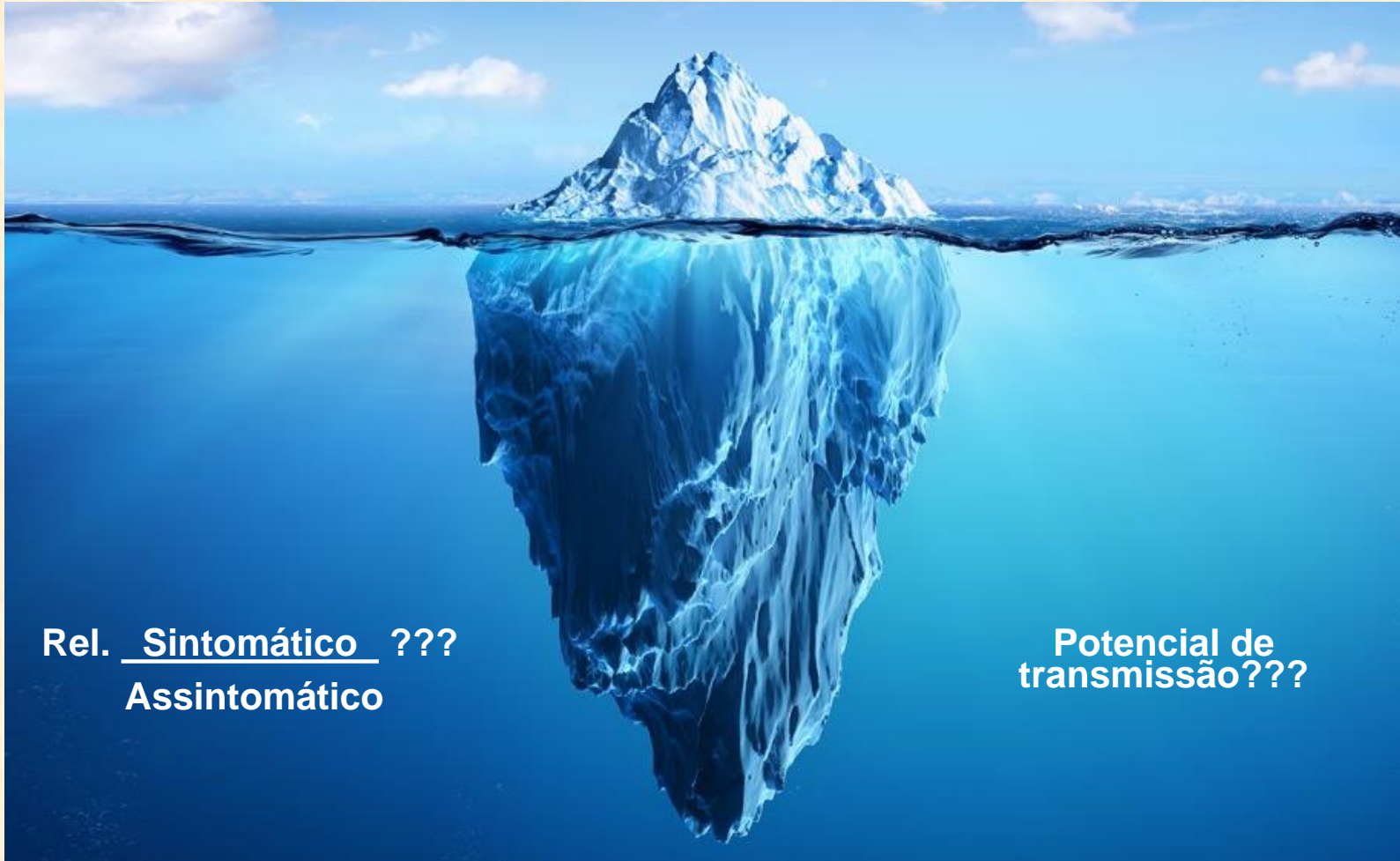


# Espectro clínico





# Infecção SARS-CoV-2 / COVID-19



Rel. Sintomático ???  
Assintomático

Potencial de  
transmissão???



## Espectro clínico

- Casos: 72.314\*
- Confirmados: 44.672 (62%)
- Masc / Fem: 51,4 / 48,6%  
(CFR=2,8/1,7%)
- Letalidade: 2,3%
- Profissionais saúde: 3,8%
  - ✓ Grave+críticos (14,8%)
  - ✓ Óbitos: 5

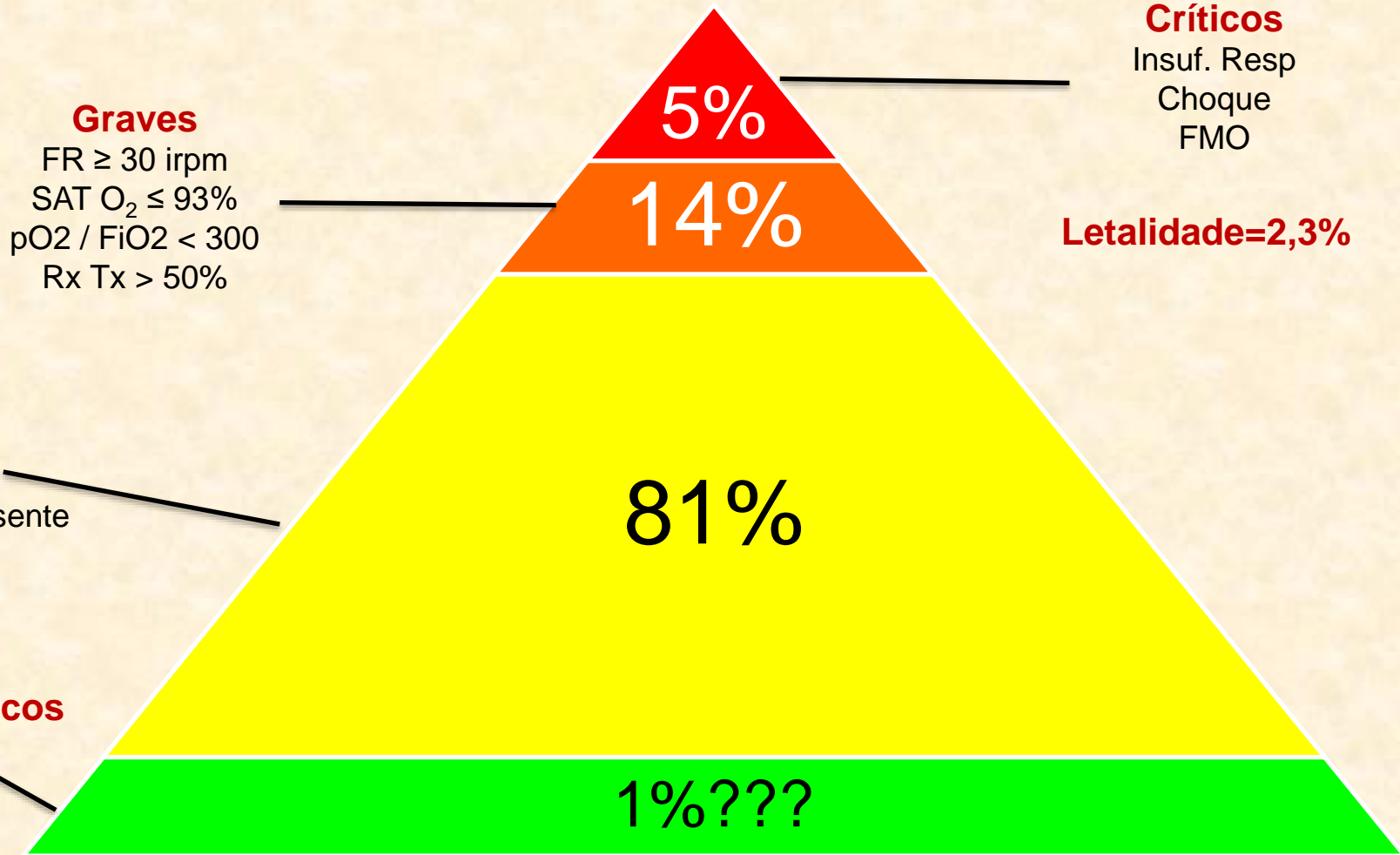
\*Até 11 Feb 2020

CDC China <http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51>

Wu Z, JAMA – 24 Feb 2020



# Espectro clínico



**N = 44.415**

**CDC China** <http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51>

**Wu Z, JAMA – 24 Feb 2020**



# Assintomáticos

## Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV2)

Ruiyun Li<sup>1\*</sup>, Sen Pei<sup>2\*†</sup>, Bin Chen<sup>3\*</sup>, Yimeng Song<sup>4</sup>, Tao Zhang<sup>5</sup>, Wan Yang<sup>6</sup>, Jeffrey Shaman<sup>2†</sup>

<sup>1</sup>MRC Centre for Global Infectious Disease Analysis, Department of Infectious Disease Epidemiology, School of Public Health, Faculty of Medicine, Imperial College London, London W2 1PG, UK. <sup>2</sup>Department of Environmental Health Sciences, Mailman School of Public Health, Columbia University, New York, NY 10032, USA. <sup>3</sup>Department of Land, Air and Water Resources, University of California, Davis, Davis, CA 95616, USA. <sup>4</sup>Department of Urban Planning and Design, The University of Hong Kong, Hong Kong. <sup>5</sup>Ministry of Education Key Laboratory for Earth System Modeling, Department of Earth System Science, Tsinghua University, Beijing 10084, P. R. China. <sup>6</sup>Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY 10032, USA.

\*These authors contributed equally to this work.

†Corresponding author. Email: sp3449@cumc.columbia.edu (S.P.); jls106@cumc.columbia.edu (J.S.)

Estimation of the prevalence and contagiousness of undocumented novel coronavirus (SARS-CoV2) infections is critical for understanding the overall prevalence and pandemic potential of this disease. Here we use observations of reported infection within China, in conjunction with mobility data, a networked dynamic metapopulation model and Bayesian inference, to infer critical epidemiological characteristics associated with SARS-CoV2, including the fraction of undocumented infections and their contagiousness. We estimate 86% of all infections were undocumented (95% CI: [82%–90%]) prior to 23 January 2020 travel restrictions. Per person, the transmission rate of undocumented infections was 55% of documented infections ([46%–62%]), yet, due to their greater numbers, undocumented infections were the infection source for 79% of documented cases. These findings explain the rapid geographic spread of SARS-CoV2 and indicate containment of this virus will be particularly challenging.

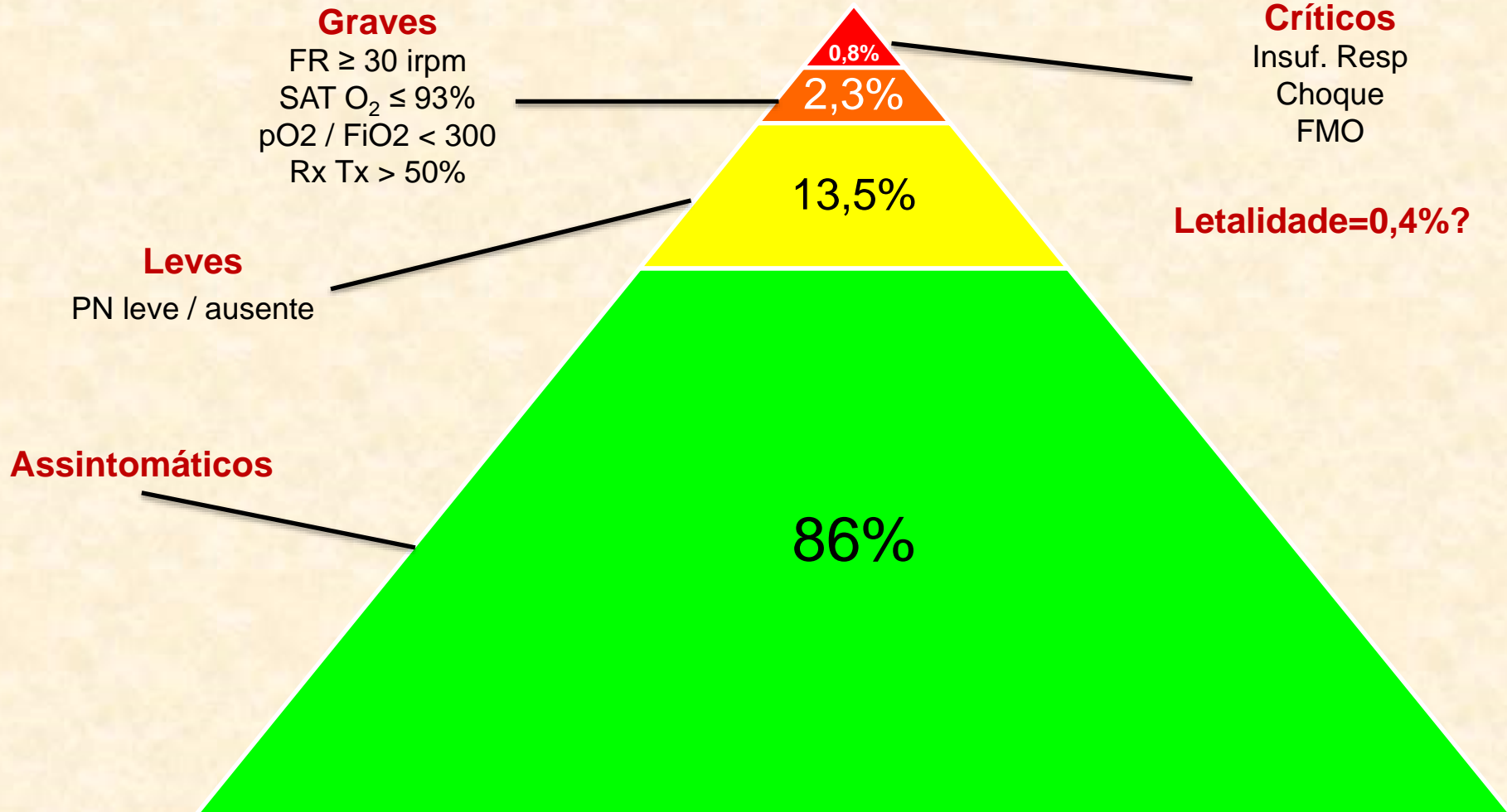
**Infecção não documentada (ND) = 86% (6:1) (IC 95%; 82-90%)**

**Taxa de transmissão (ND) = 55% (IC 95%; 46-62%)**

**Fonte da infecção (ND) = 79%**



# Espectro clínico



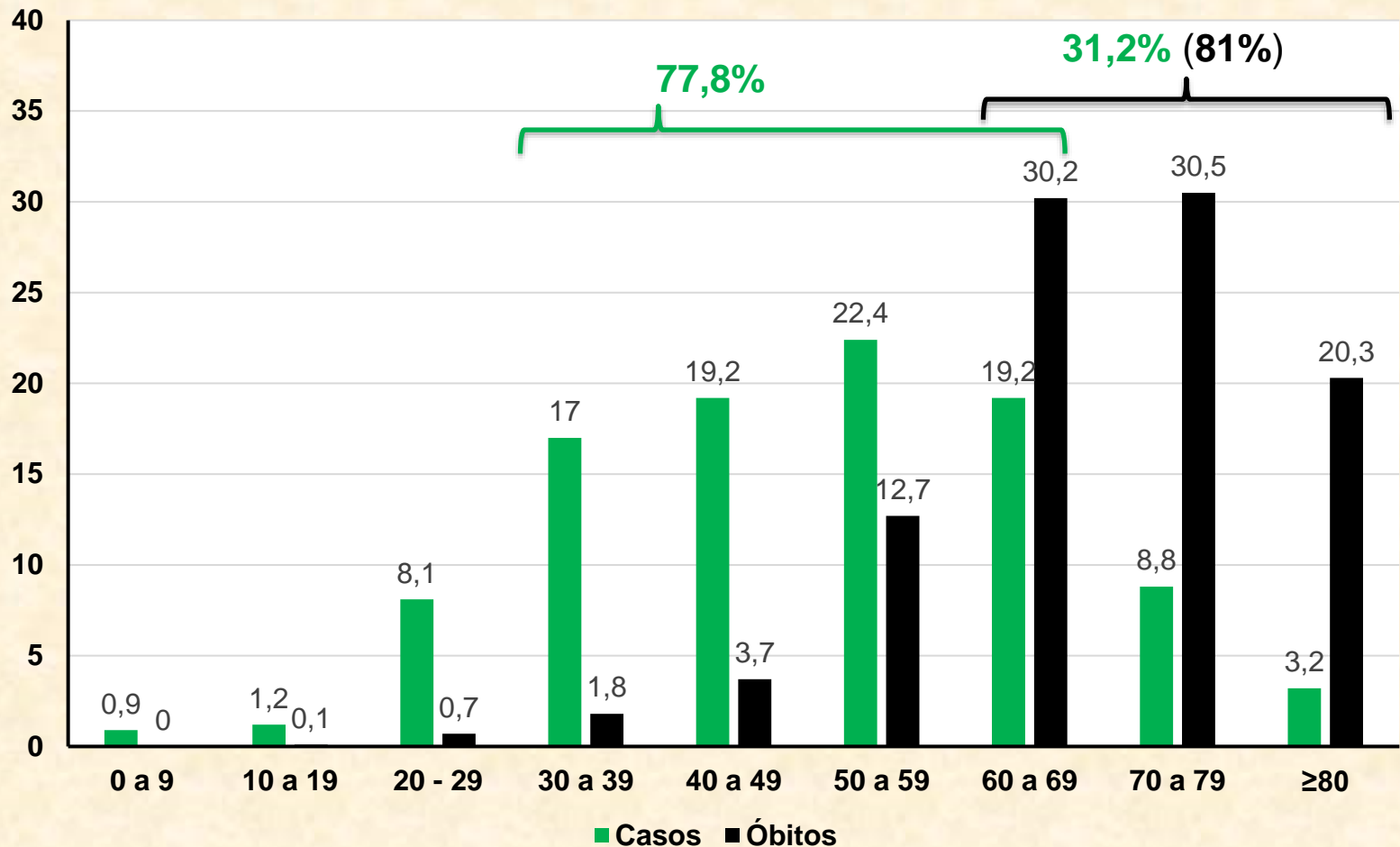
**N = 44.415**

CDC China <http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51>

Adaptado de Wu Z, JAMA – 24 Feb 2020



# Faixa etária - Casos x óbitos (%)\*



**N=44.672**

**Óbitos=1.023**

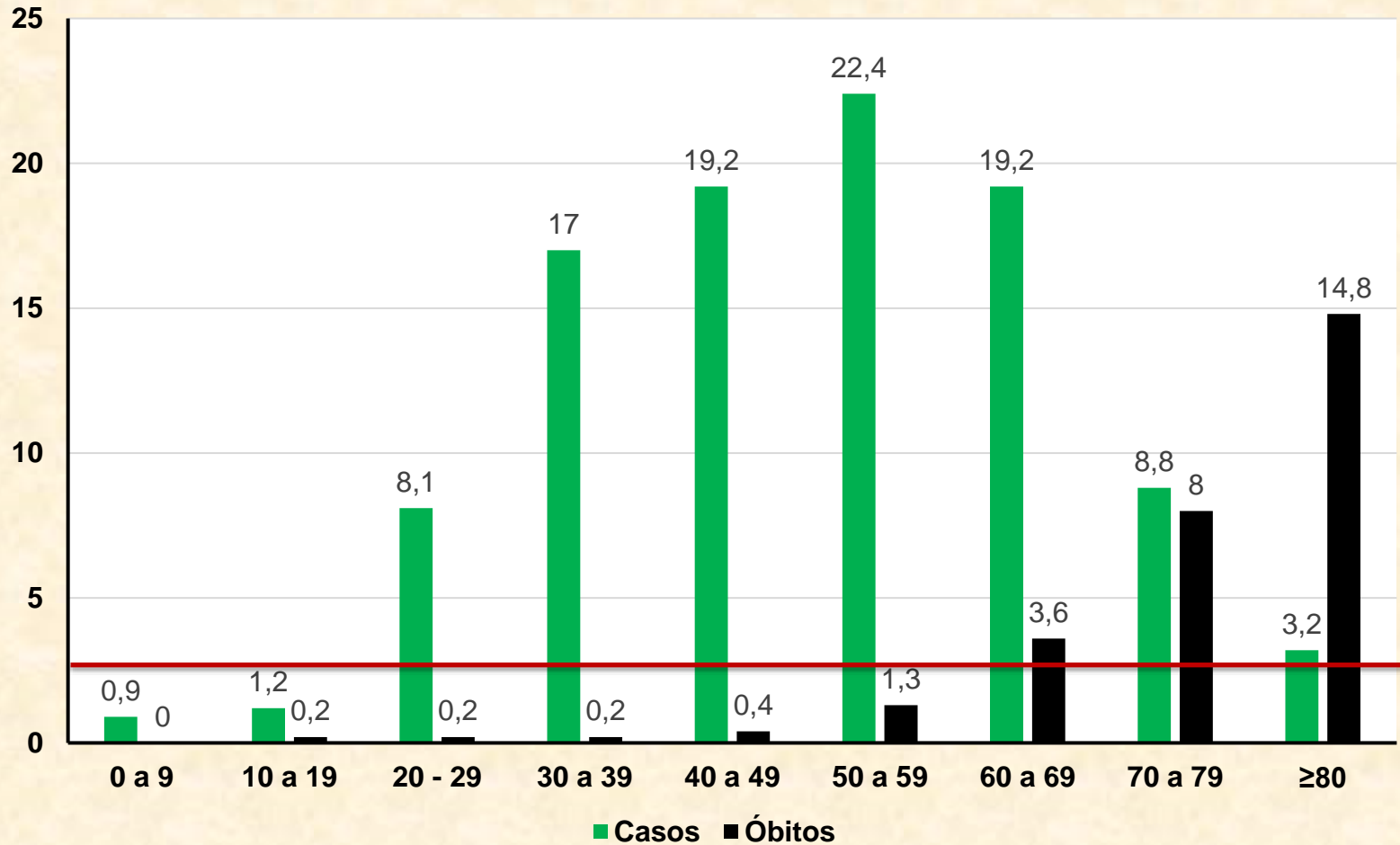
\*Até 11 Feb 2020

China CDC Weekly, 21 Feb 2020

<http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51>



# Faixa etária x letalidade (%)\*



**N=44.672**

**CFR=2,3**

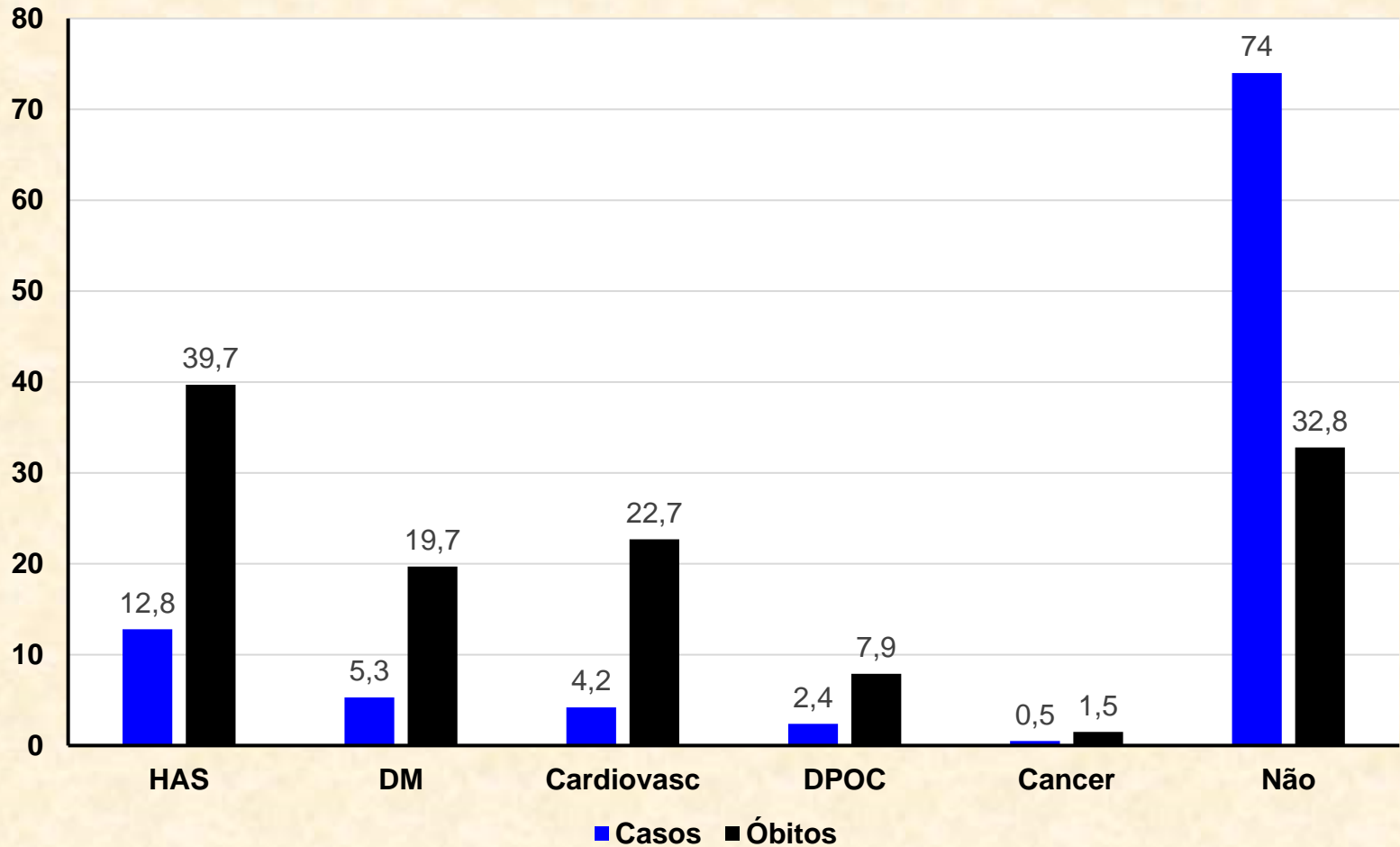
\*Até 11 Feb 2020

China CDC Weekly, 21 Feb 2020

<http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51>



# Comorbidade x óbitos (%)\*



**N=20.812**

**Óbitos=504**

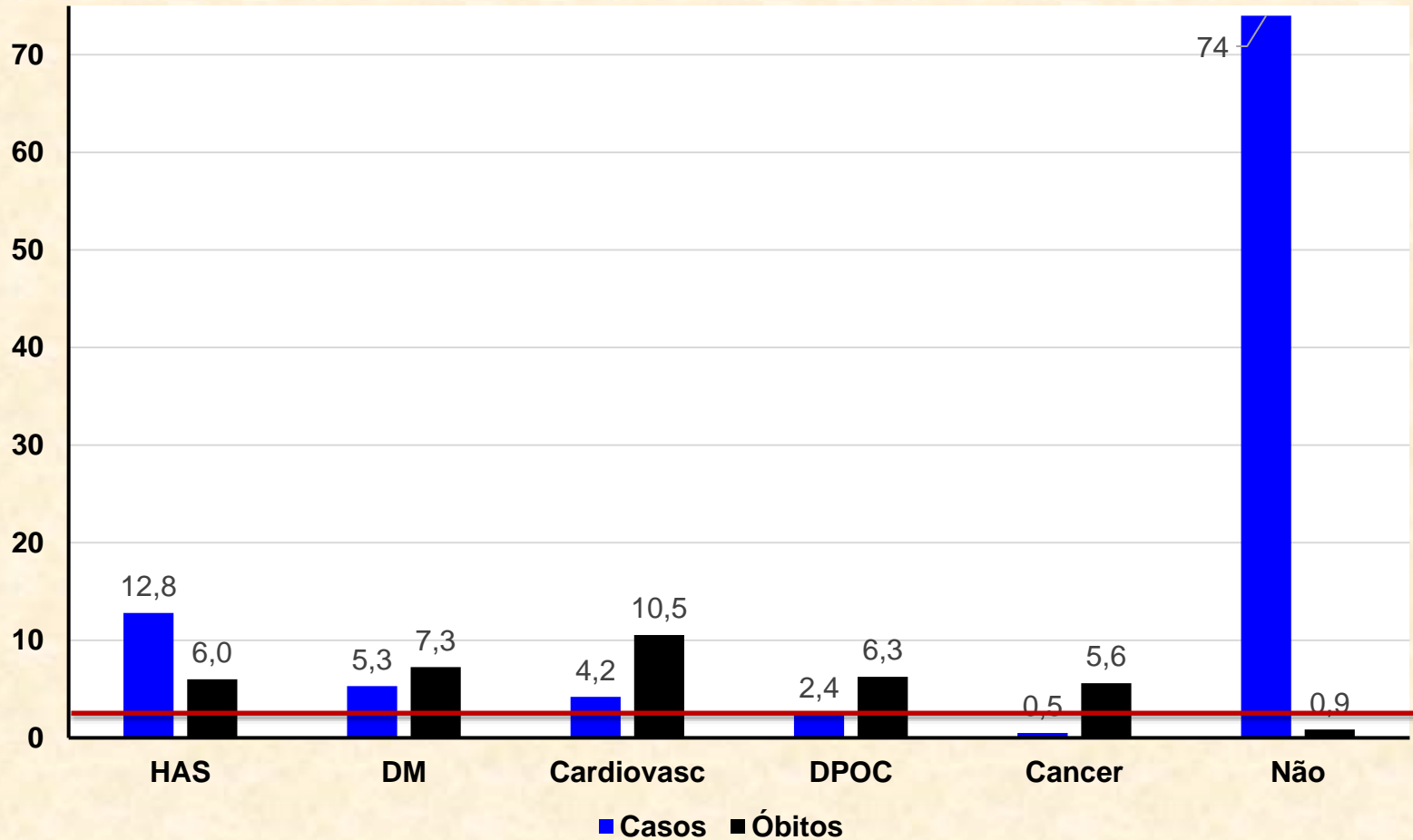
\*Até 11 Feb 2020

China CDC Weekly, 21 Feb 2020

<http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51>



# Comorbidade x letalidade (%)\*



**N=20.812**

**CFR=2,4%**

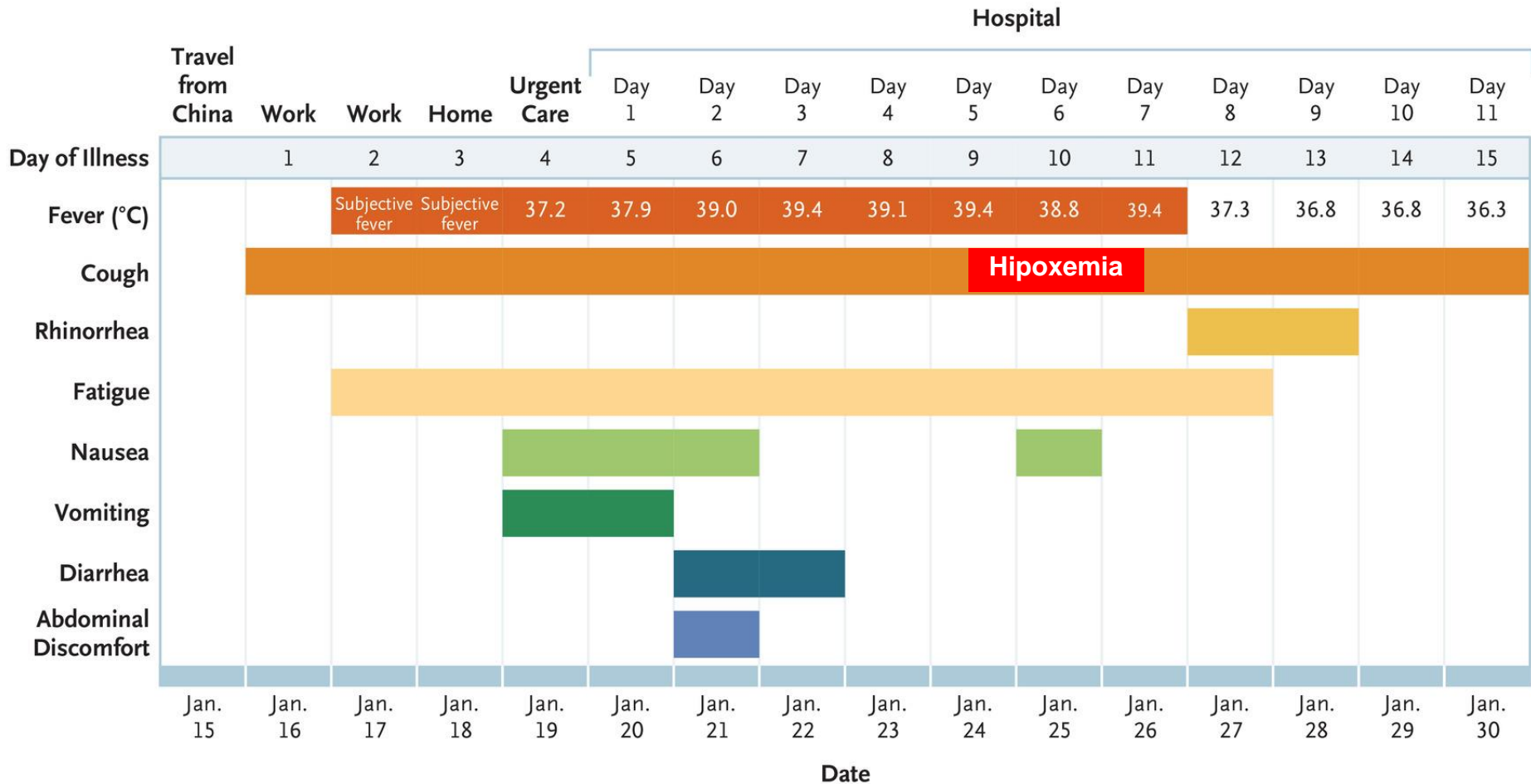
\*Até 11 Feb 2020

Home  
China CDC Weekly, 21 Feb 2020

<http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51>

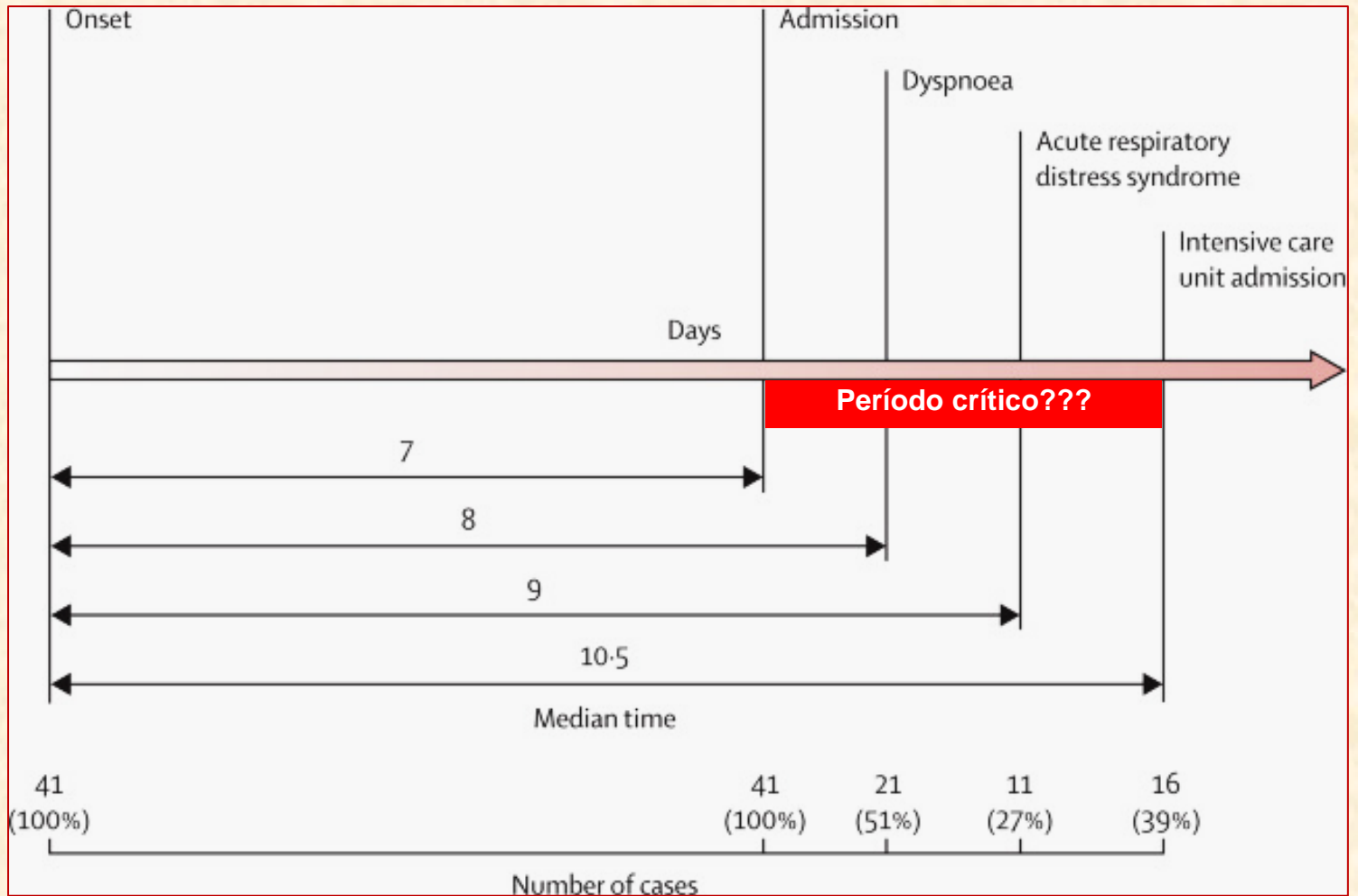


# História natural





# História natural (N=41)

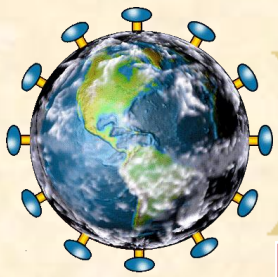




# Características

	<b>N=41 (%)<sup>1</sup></b>	<b>N=99 (%)<sup>2</sup></b>	<b>N=138 (%)<sup>3</sup></b>
Idade	49 (41-58)	55,5 (13,1)	56 (42-68)
≥ 65	6 (14,6)	NA	NA
Masculino	30 (73,2)	67 (67,7)	75 (54,3)
Nosocomial	NA	NA	57 (41,3)
Prof. Saúde	NA	NA	40 (29)
Comorbidade	13 (31,7)	50 (51)	64 (46,4)
T. Dispneia (IQR)	8 (5-13)	NA	5 (1-10)
T. Admissão (IQR)	7 (4-8)	NA	7 (4-8)
T. SARA (IQR)	9 (8-14)	NA	8 (6-12)

n (%), n/N (%), média (DP) e mediana (IQR).



# Sintomatologia

Sintomas, N (%)	N=41 <sup>1</sup>	N=99 <sup>2</sup>	N=138 <sup>3</sup>	N=140 <sup>4</sup>	N=1099 <sup>5</sup>
Febre	98	83	98,6	91,7	43,8 / 88,7
Fadiga / Mialgia	44	11	69,6 / 34,8	75 / -	38,1 / 14,9
Confusão	-	9	-	-	-
Cefaleia	8	8	6,5	-	13,6
Tonturas	-	-	9,4	-	-
Tosse / Expect.	76 / 28	82 / -	59,4 / 26,8	75 / -	67,8 / 33,7
Dispneia / Desc. Tx	55 / -	31 / 2	31,2 / -	36,7	18,7 / -
Dor garganta	-	5	17,4	-	13,9
Hemoptise	5	-	-	-	0,9
Rinorreia	-	4	-	-	-
Cong. nasal / conj.	-	-	-	-	4,8 / 0,8
Anorexia / TGI	-	-	39,9 / -	12,2 / 39,6	-
Diarreia	3	2	10,1	12,9	3,8
Náuseas/vômitos	-	1	10,1 / 3,6	17,3 / 5	5
Dor abd.	-	-	2	5,8	-

Adaptado: <sup>1</sup>Huang C, Lancet - 24 Jan 2020  
<sup>4</sup>Zhang JJ, Allergy - 19 Feb 2020

<sup>2</sup>Chen N, Lancet – 15 Feb 2020  
<sup>5</sup>Guan WJ, New Engl J Med 28 Feb 2020

<sup>3</sup>Wang D, JAMA 07 Feb 2020



# Laboratório (admissão)

Variável	Total (N=138)	UTI (N=36)	Não-UTI (N=102)	<i>p</i>
Leucócitos (10 <sup>9</sup> /L)	4,5 (3,3-6,2)	6,6 (3,6-9,8)	4,3 (3,3-5,4)	<b>0,003</b>
Neutrófilos (10 <sup>9</sup> /L)	3,0 (2,0-4,9)	4,6 (2,6-7,9)	2,7 (1,9-3,9)	<b>&lt;0,001</b>
Linfócitos (10 <sup>9</sup> /L)	0,8 (0,6-1,1)	0,8 (0,5-0,9)	0,9 (0,6-1,2)	<b>0,03</b>
Monócitos (10 <sup>9</sup> /L)	0,4 (0,3-0,5)	0,4 (0,3-0,5)	0,4 (0,3-0,5)	0,96
Plaquetas (10 <sup>9</sup> /L)	163 (123-191)	142 (119-202)	165 (125-188)	0,78
T. Protrombina (s)	13,0 (12,3-13,7)	13,2 (12,3-14,5)	12,9 (12,3-13,4)	0,37
TPTA (s)	31,4 (29,4-33,5)	30,4 (28,0-33,5)	31,7 (29,6-33,5)	0,09
D-dímero (mg/L)	203 (121-403)	414 (191-1324)	166 (101-285)	<b>&lt;0,001</b>
Procalcit. (≥0,5)*	49 (35,5)	27 (75,0)	22 (21,6)	<b>&lt;0,001</b>

\* N (%)



# Laboratório (admissão)

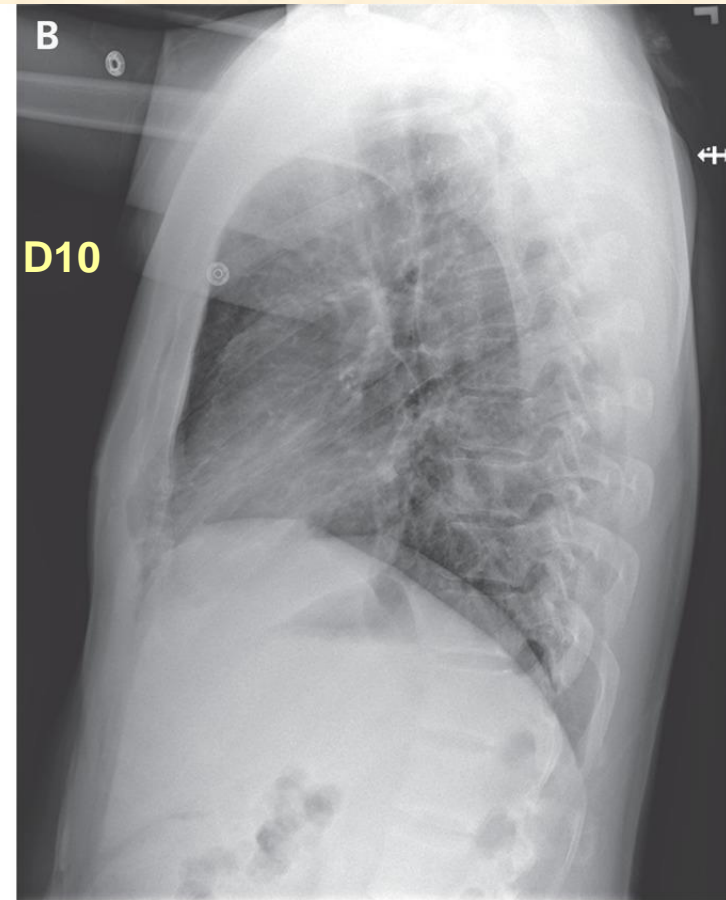
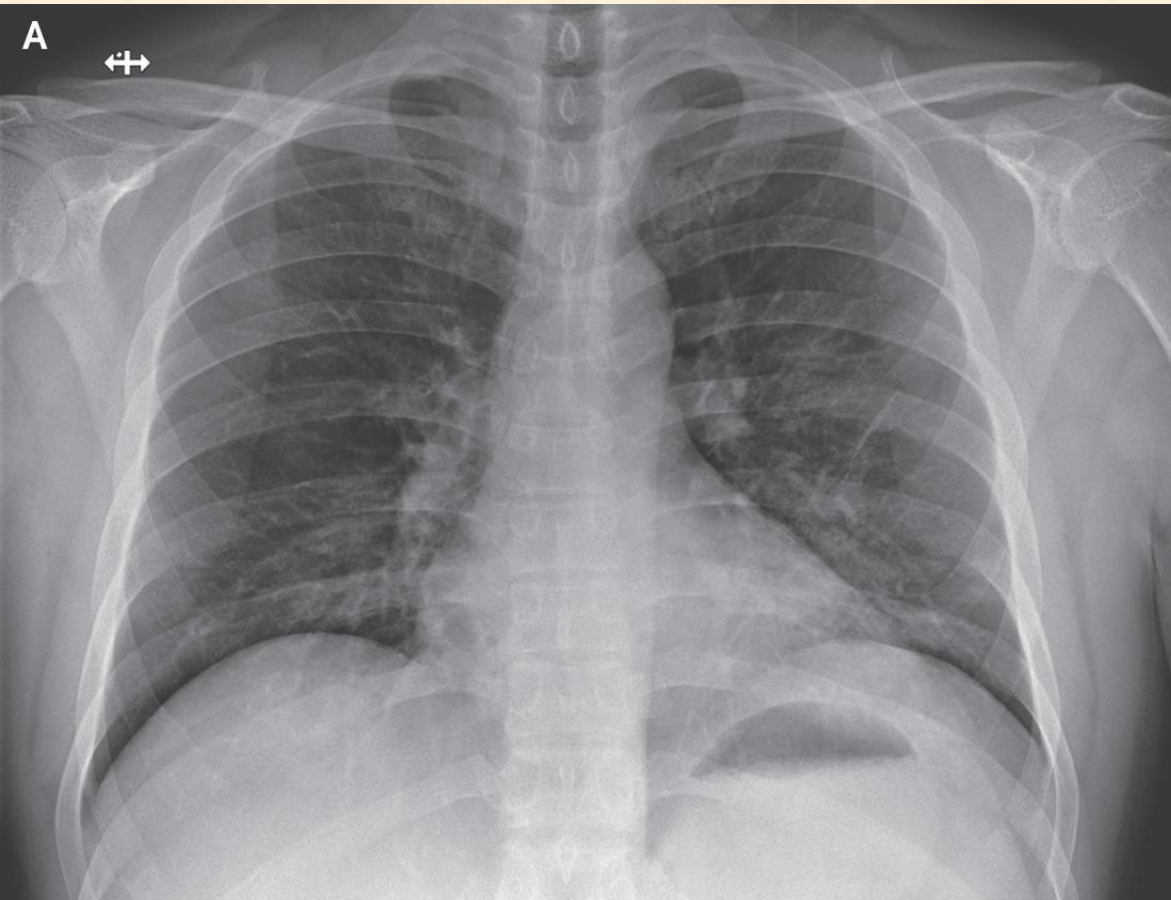
Variável	Total (N=138)	UTI (N=36)	Não-UTI (N=102)	p
CPK (U/L)	92 (56-130)	102 (62-252)	87 (54-121)	0,08
CK-MB (U/L)	14 (10-18)	18 (12-35)	13 (10-14)	<0,001
Troponina I (pg/mL)	6,4 (2,8-18,5)	11,0 (5,6-26,4)	5,1 (2,1-9,8)	0,004
LDH (U/L)	261 (182-403)	435 (302-596)	212 (171-291)	<0,001
ALT/TGP (U/L)	24 (16-40)	35 (19-57)	23 (15-36)	0,007
AST/TGO (U/L)	31 (24-51)	52 (30-70)	29 (21-38)	<0,001
Bilirrubina (mmol/L)	9,8 (8,4-14,1)	11,5 (9,6-18,6)	9,3 (8,2-12,8)	0,02
Ureia (mmol/L)	4,4 (3,4-5,8)	5,9 (4,3-9,6)	4,0 (3,1-5,1)	<0,001
Creatinina (mmol/L)	72 (60-87)	80 (66-106)	71 (58-84)	0,04
Tórax*	138 (100)	36 (100)	102 (100)	>0,99

\* N (%)

opacidades irregulares  
ou vidro fosco



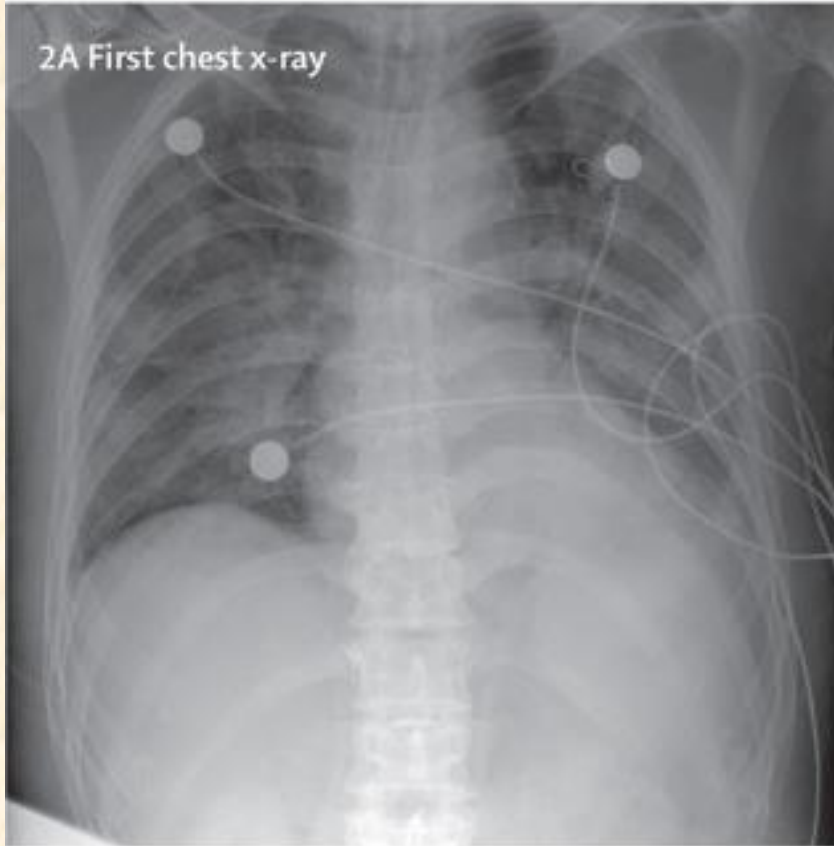
# Radiologia



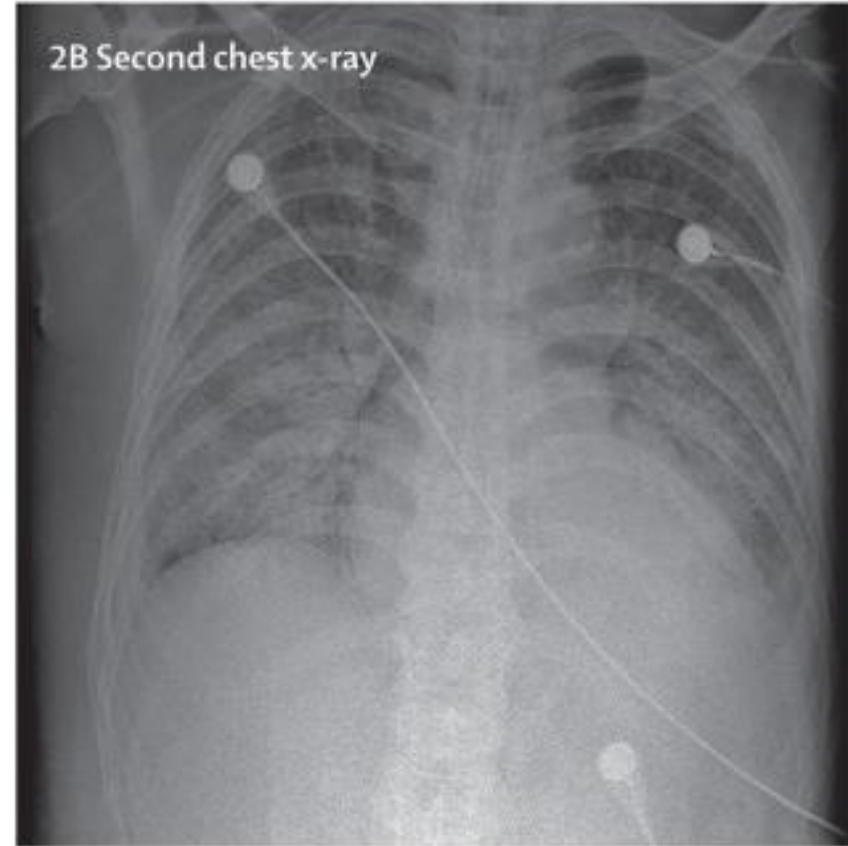


# Radiologia

Case 2



06/Jan/2020



10/Jan/2020



# Radiologia

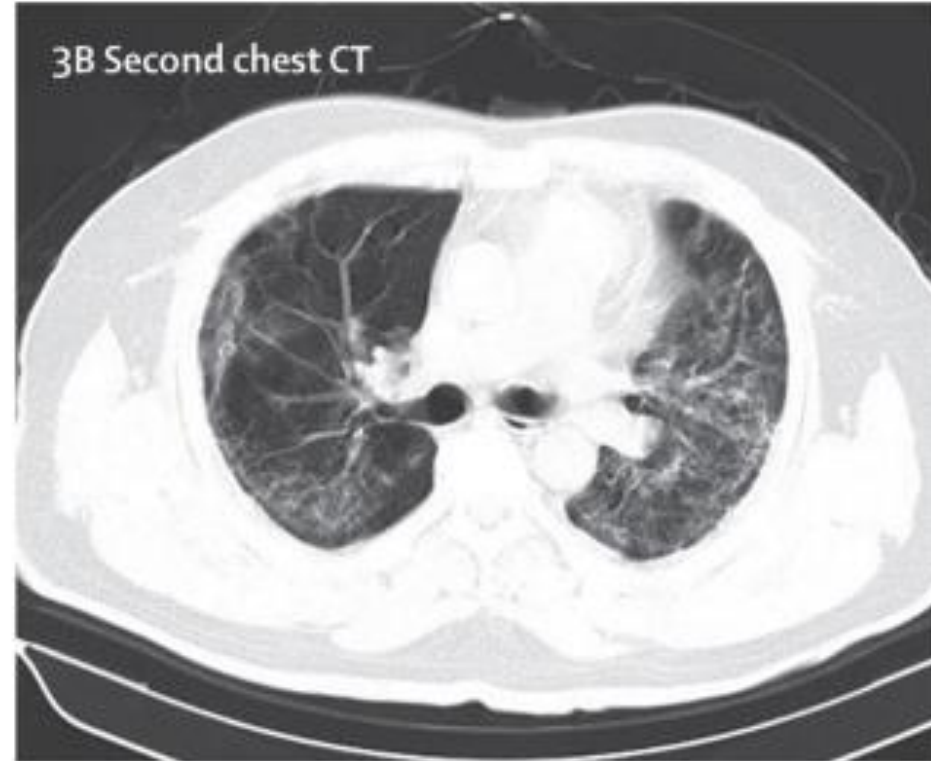
## Case 3

3A First chest CT



01/Jan/2020

3B Second chest CT



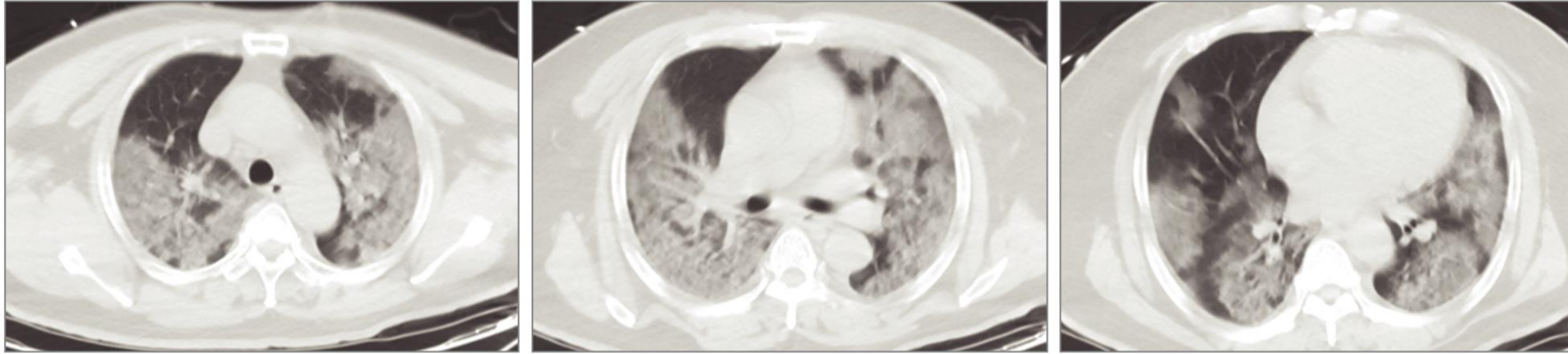
15/Jan/2020



# Evolução radiológica

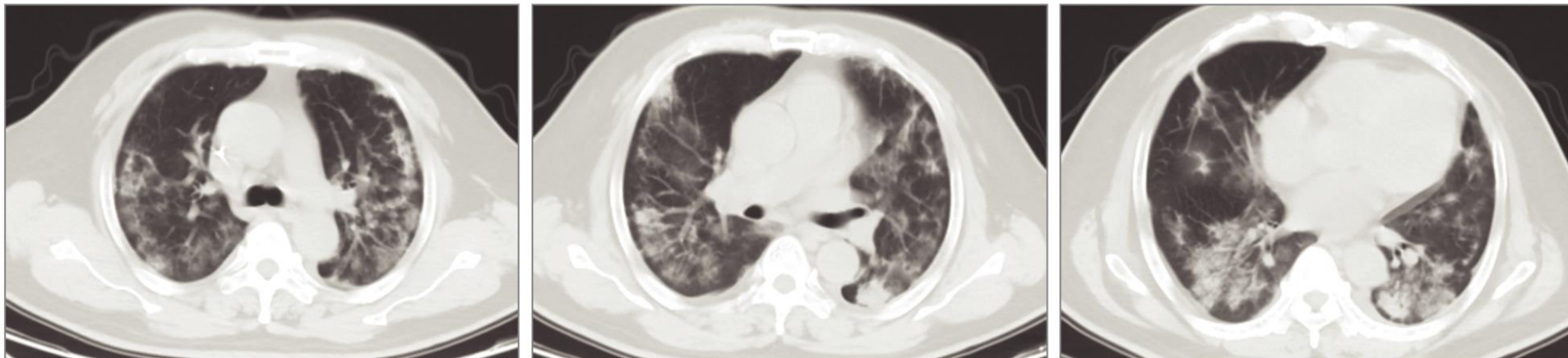
**A** Computed tomography images on day 5 after symptom onset

**D5**



**B** Computed tomography images after treatment on day 19 after symptom onset

**D19**





# Complicações

	<b>N=41 (%)<sup>1</sup></b>	<b>N=99 (%)<sup>2</sup></b>	<b>N=138 (%)<sup>3</sup></b>
<b>SARA</b>	12 (29.3)	17 (17.2)	27 (19.6)
<b>Disfunção renal</b>	3 (7.3)	3 (3.0)	5 (3.6)
<b>Lesão cardíaca</b>	5 (12.2)	NA	10 (7.2)
<b>Infecção</b>	4 (9.8)	5 (5.1)	NA
<b>Choque</b>	3 (7.3)	4 (4.0)	12 (8.7)
<b>Admissão UTI</b>	13 (31.7)	23 (23.2)	36 (26.1)
<b>Mortalidade</b>	6 (14.6)	11 (11.1)	6 (3.4)

n (%), n/N (%), média (DP) e mediana (IQR).

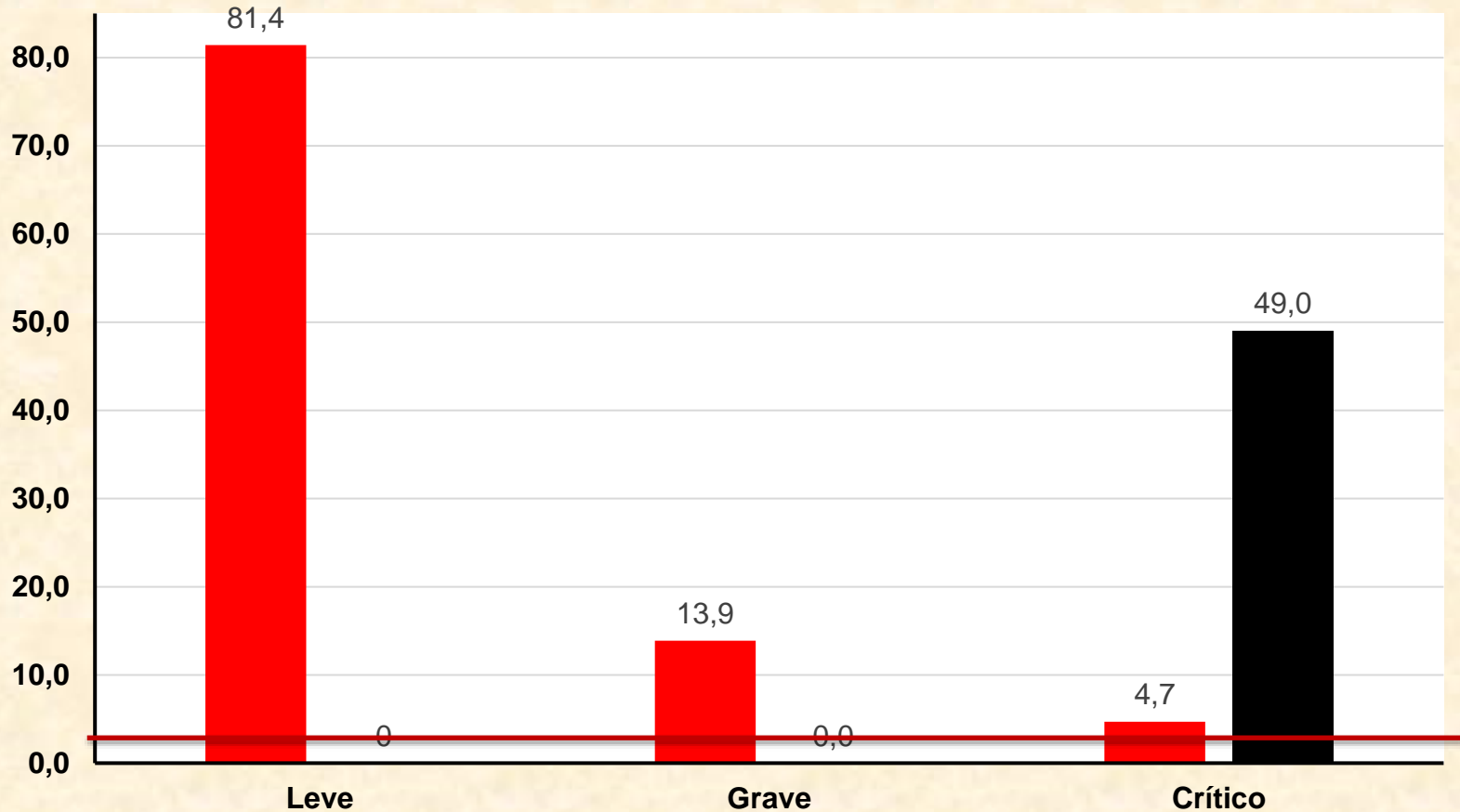


# Complicações

Variável	Total (N=138)	UTI (N=36)	Não-UTI (N=102)	<i>p</i>
	N (%)	N (%)	N (%)	
<b>Choque</b>	12 (8,7)	11 (30,6)	1 (1,0)	<0,001
<b>Lesão cardíaca</b>	10 (7,2)	8 (22,2)	2 (2,0)	<0,001
<b>Arritmias</b>	23 (16,7)	16 (44,4)	7 (6,9)	<0,001
<b>SARA</b>	27 (19,6)	22 (61,1)	5 (4,9)	<0,001
<b>IRA</b>	5 (3,6)	3 (8,3)	2 (2,0)	0,11



# Gravidade x letalidade (%)\*



**N=44.415**

**Óbitos=1,023**

**CFR=2,3%**

■ Casos ■ Óbitos

\*Até 11 Feb 2020

China CDC Weekly, 21 Feb 2020

<http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51>

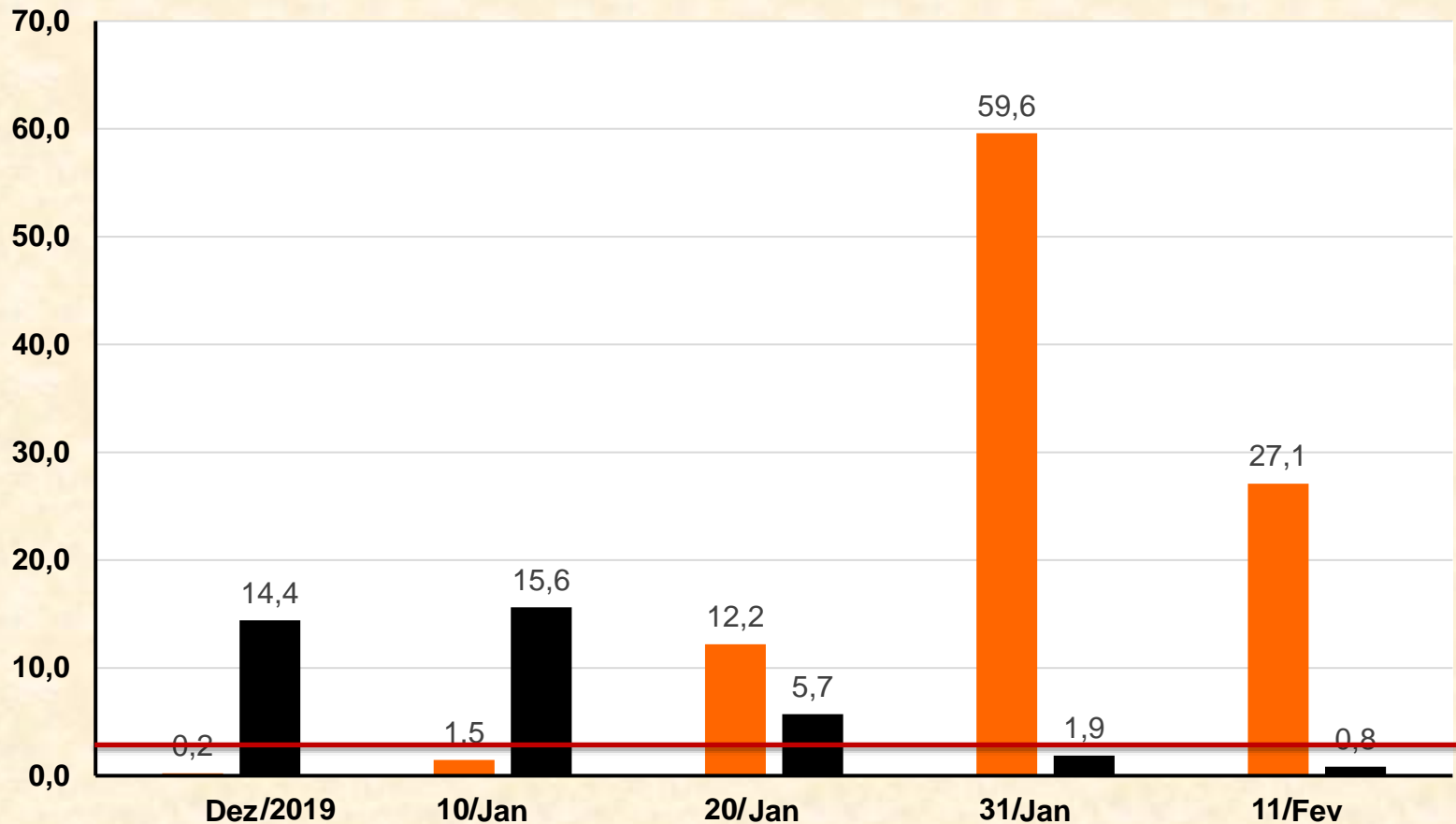


# Radiologia (Rx e TC)

Achados	N (%)
Pneumonia unilateral	25 (25)
Pneumonia bilateral	74 (75)
Velamentos múltiplos / em vidro fosco	14 (14)
Pneumotórax	1 (1)



# Início COVID-19 x letalidade (%)\*



**N=44.672**

**Óbitos=1,023**

**CFR=2,3%**

■ Casos ■ Óbitos

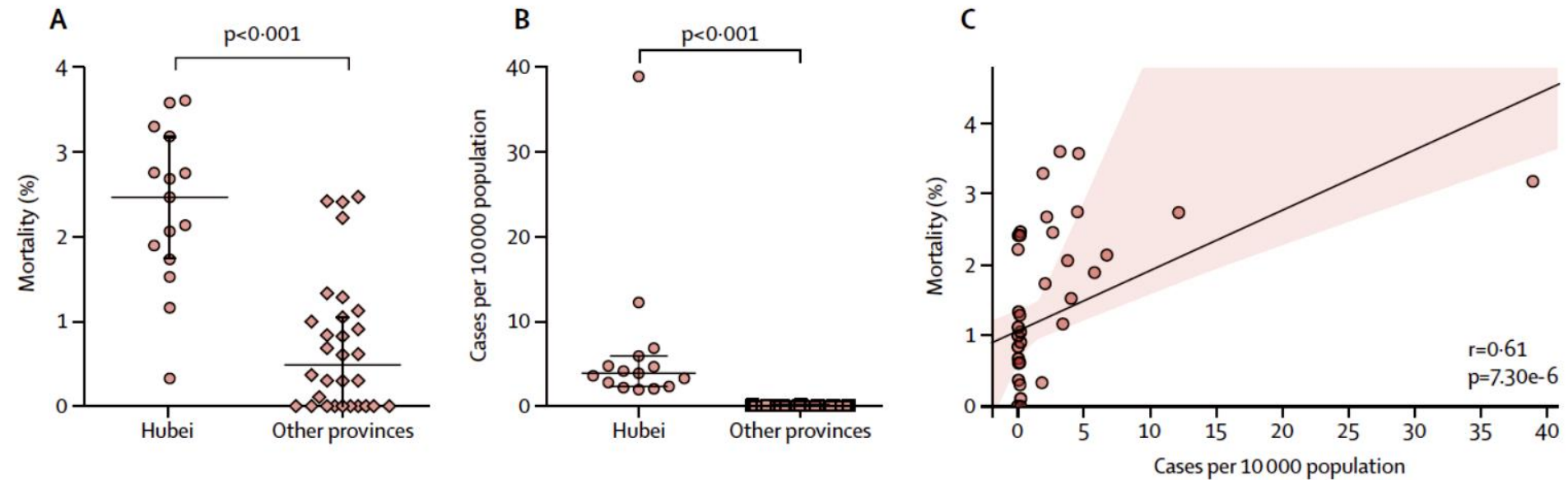
\*Até 11 Feb 2020

China CDC Weekly, 21 Feb 2020

<http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51>



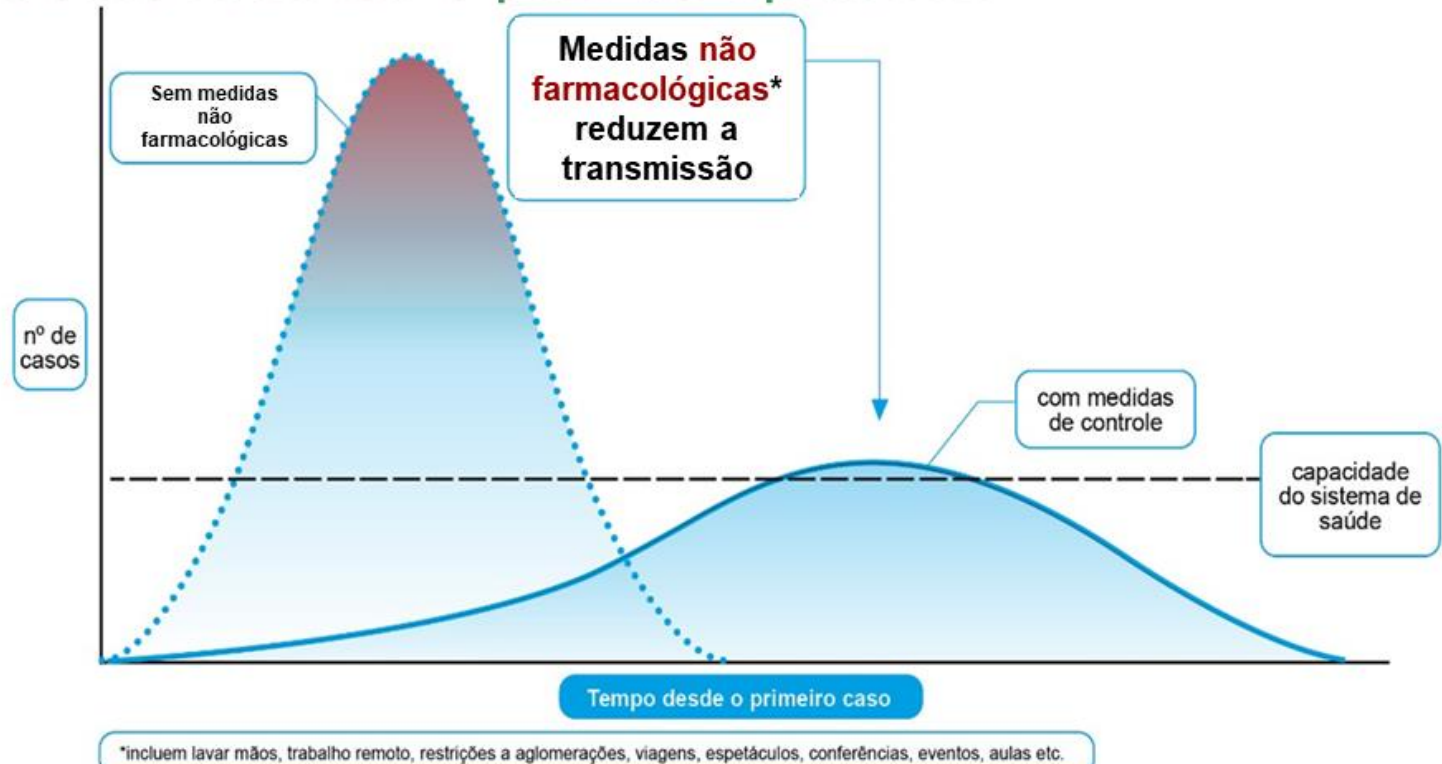
# Recursos saúde x letalidade





# Mitigação

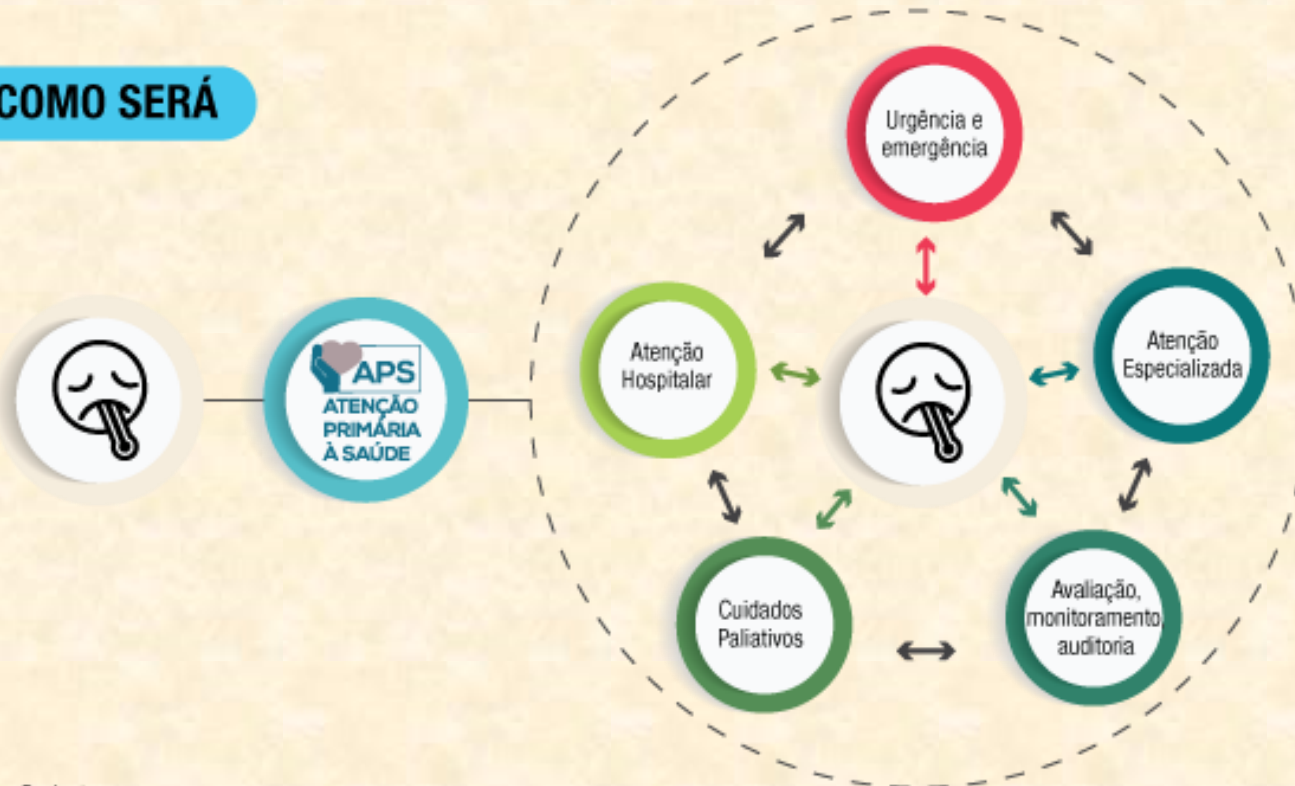
## Como retardar o pico da epidemia





# Papel dos serviços de APS/ESF

## COMO SERÁ



Paciente com:  
Doenças cardiovasculares, diabetes, doenças respiratórias, câncer,  
doenças e condições ligadas ao ciclo de vida, à maternidade e ao  
período perinatal, depressão, demência e doenças bucais.



# Abordagem sindrômica

Sintomas/sinais	Resfriado	Sd. Gripal
<b>Início</b>	Gradual	Abrupto
<b>Febre</b>	Rara	Usual
<b>Arrepios</b>	Incomum	Muito comum
<b>Cefaleia</b>	Raro	Comum
<b>Mialgia</b>	Leve	Importante
<b>Fadiga/fraqueza</b>	Às vezes	Comum
<b>Espirros</b>	Comum	Às vezes
<b>Congestão nasal</b>	Comum	Às vezes
<b>Dor de garganta</b>	Comum	Às vezes
<b>Tosse/Desc. Tórax</b>	Leve-moderado	Importante



# Estratificação

Síndrome	Características
<b>Doença não complicada</b>	Quadro VA sup S/ dispneia, desidratação, choque
<b>Pneumonia não complicada</b>	FR < 30 (adulto)
<b>Pneumonia severa</b>	FR > 30 Sat O <sub>2</sub> < 90 Insuf. Respiratória
<b>SARA</b>	Velamento bilateral ↓ PaO <sub>2</sub> /FiO <sub>2</sub> < 300 (PEEP>5)
<b>Sepsis</b>	Disfunção de órgãos
<b>Choque séptico</b>	Hipotensão persistente Vasopressores



## Diagnóstico

- Síndrome gripal (SG)
  - ✓ Critério clínico-epidemiológico
- Sd. Respiratória Aguda Grave (SRAG)
  - ✓ RT-PCR



# Diagnóstico



**Aspirado  
nasofaríngeo**

Fonte: BRASIL,2014



**Swab nasal**

Fonte: BRASIL,2014.



**Swab oral**



# Tratamento

- Suporte
  - ✓ Ventilatório
  - ✓ Circulatório
  - ✓ Extracorpórea
- Balanço de Líquidos
- Corticoides?
- Anti-inflamatórios?
- Antivirais?

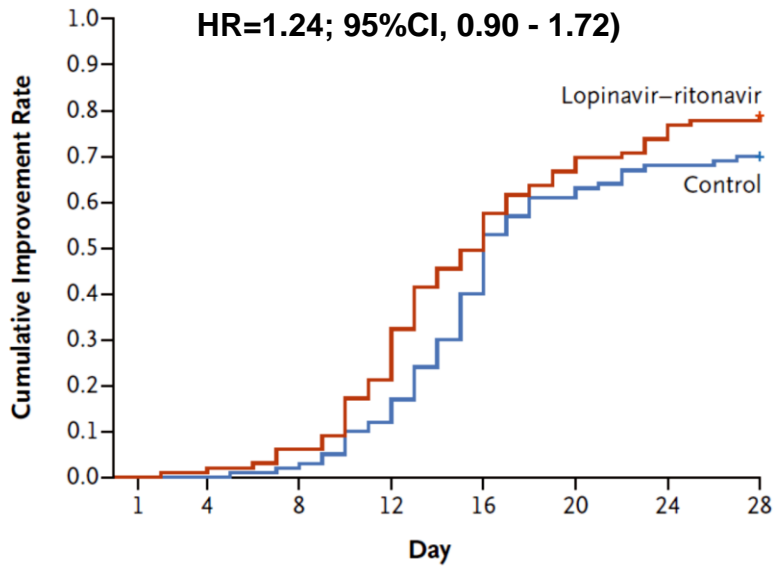


# Tratamento

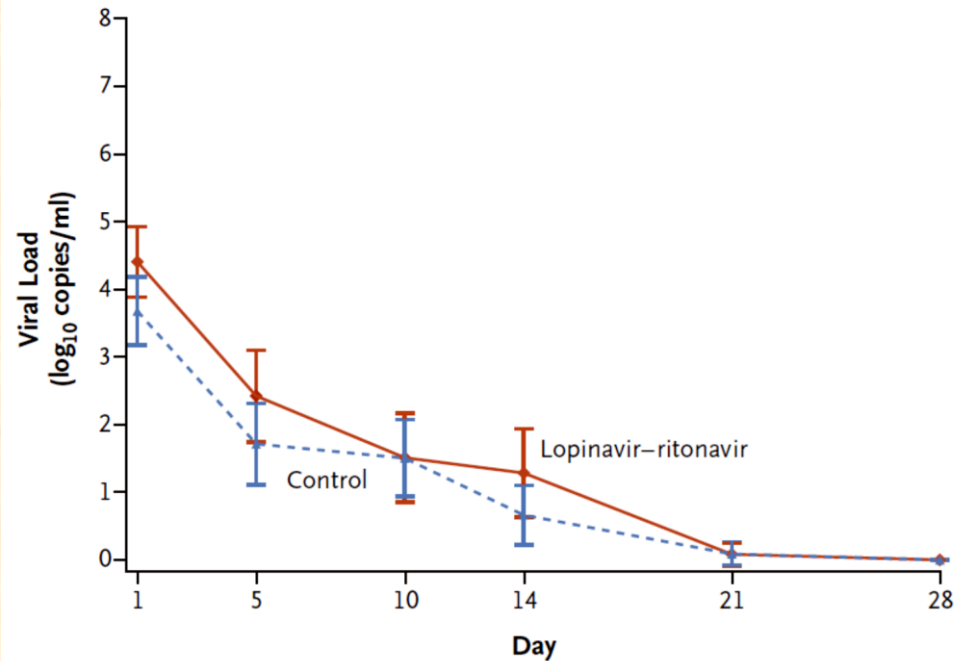
	<b>N=41 (%)<sup>1</sup></b>	<b>N=99 (%)<sup>2</sup></b>	<b>N=138 (%)<sup>3</sup></b>
<b>Antiviral</b>	38 (92,7)	75 (75,8)	124 (89,9)
<b>Antibióticos</b>	41 (100)	70 (70,7)	138 (100)
<b>Antifúngicos</b>	NA	15 (15,2)	NA
<b>Corticoides</b>	9 (22,0)	19 (19,2)	62 (44,9)
<b>Diálise contínua</b>	3 (7,3)	9 (9,1)	2 (1,4)
<b>Imunoglobulina</b>	NA	27 (27,3)	NA
<b>Vent. Mecânica</b>	2 (4,9)	4 (4,0)	17 (12,3)
<b>Extracorpórea</b>	2 (4,9)	3 (3,0)	4 (2,9)



# Lopinavir-r x SOC



No. at Risk	1	4	8	12	16	20	24	28
Lopinavir-ritonavir	99	98	93	78	50	33	26	22
Control	100	100	98	88	60	39	32	30



## Mortalidade (D28)

**Lopinavir/r = 99**

**19,2%**

**SOC = 100**

**25%**

## Diferença

**- 5.8 % (95% CI, -17.3 to 5.7)**



# Cloroquina

- Malária (>70 anos)
- Inibição SARS-CoV-2 (in vitro)
- Teste COVID-19
  - ✓ > 100 pacientes
  - ✓ ↓ alterações radiológicas
  - ✓ Pesquisa negativa RNA
  - ✓ ↓ tempo de doença



# Remdesivir e cloroquina

Cell Research

[www.nature.com/cr](http://www.nature.com/cr)  
[www.cell-research.com](http://www.cell-research.com)



LETTER TO THE EDITOR **OPEN**

## Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro

*Cell Research* (2020) 0:1–3; <https://doi.org/10.1038/s41422-020-0282-0>

### Dear Editor,

In December 2019, a novel pneumonia caused by a previously unknown pathogen emerged in Wuhan, a city of 11 million people in central China. The initial cases were linked to exposures in a seafood market in Wuhan.<sup>1</sup> As of January 27, 2020, the Chinese authorities reported 2835 confirmed cases in mainland China, including 81 deaths. Additionally, 19 confirmed cases were identified in Hong Kong, Macao and Taiwan, and 39 imported cases were identified in Thailand, Japan, South Korea, United States, Vietnam, Singapore, Nepal, France, Australia and Canada. The pathogen was soon identified as a novel coronavirus (2019-nCoV), which is closely related to severe acute respiratory syndrome CoV (SARS-CoV).<sup>2</sup> Currently, there is no specific treatment against the new virus. Therefore, identifying effective antiviral agents to combat the disease is urgently needed.

to be 100% effective in protecting mice against Ebola virus challenge, although its  $EC_{50}$  value in Vero E6 cells was as high as  $67 \mu\text{M}$ ,<sup>4</sup> suggesting further in vivo studies are recommended to evaluate this antiviral nucleoside. Nafamostat, a potent inhibitor of MERS-CoV, which prevents membrane fusion, was inhibitive against the 2019-nCoV infection ( $EC_{50} = 22.50 \mu\text{M}$ ,  $CC_{50} > 100 \mu\text{M}$ ,  $SI > 4.44$ ). Nitazoxanide, a commercial antiprotozoal agent with an antiviral potential against a broad range of viruses including human and animal coronaviruses, inhibited the 2019-nCoV at a low-micromolar concentration ( $EC_{50} = 2.12 \mu\text{M}$ ;  $CC_{50} > 35.53 \mu\text{M}$ ;  $SI > 16.76$ ). Further in vivo evaluation of this drug against 2019-nCoV infection is recommended. Notably, two compounds remdesivir ( $EC_{50} = 0.77 \mu\text{M}$ ;  $CC_{50} > 100 \mu\text{M}$ ;  $SI > 129.87$ ) and chloroquine ( $EC_{50} = 1.13 \mu\text{M}$ ;  $CC_{50} > 100 \mu\text{M}$ ,  $SI > 88.50$ ) potentially blocked virus infection at low-micromolar concentration and showed high SI

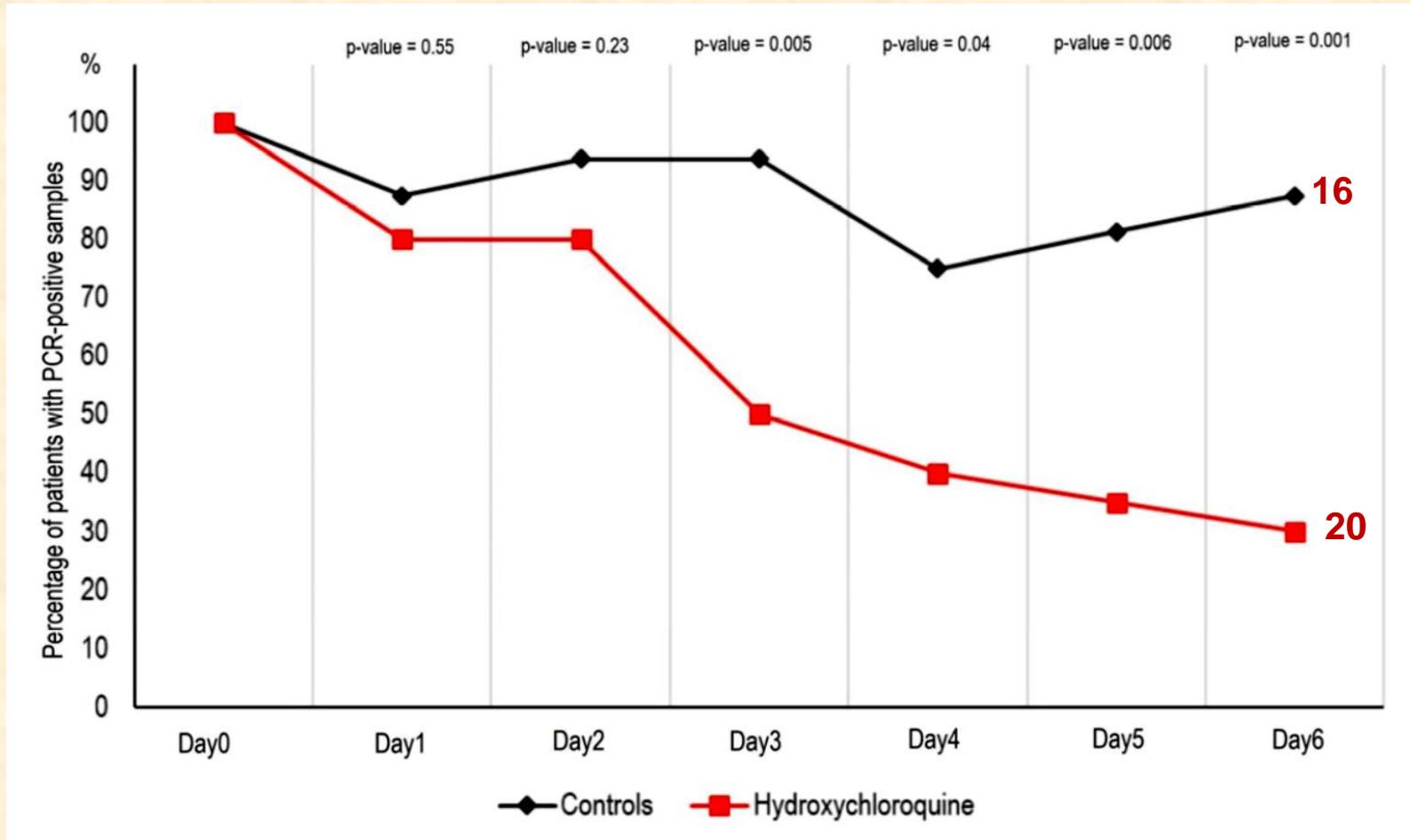


# Hidroxiclороquina e Azitromicina

	<b>HCQ</b>	<b>Controle</b>	<b>Total</b>	<b><i>p</i></b>
<b>N</b>	20	16	36	-
<b>Azitromicina</b>	6	-	6	-
<b>Idade (anos)</b>	51.2 ± 18.7	37.3 ± 24.0	45.1 ± 22.0	0.06
<b>Masc (%)</b>	9 (45.0)	6 (37.5)	15 (41.7)	0.65
<b>T. Início</b>	4.1 ± 2.6	3.9 ± 2.8	4.0 ± 2.6	0.88
<b>Clínico</b>				<b>0.30</b>
<b>Assintomático</b>	2 (10,0)	4 (25.0)	6 (16.7)	-
<b>TR alto</b>	12 (60.0)	10 (62.5)	22 (61.1)	-
<b>TR baixo</b>	6 (30.0)	2 (12.5)	8 (22.2)	-

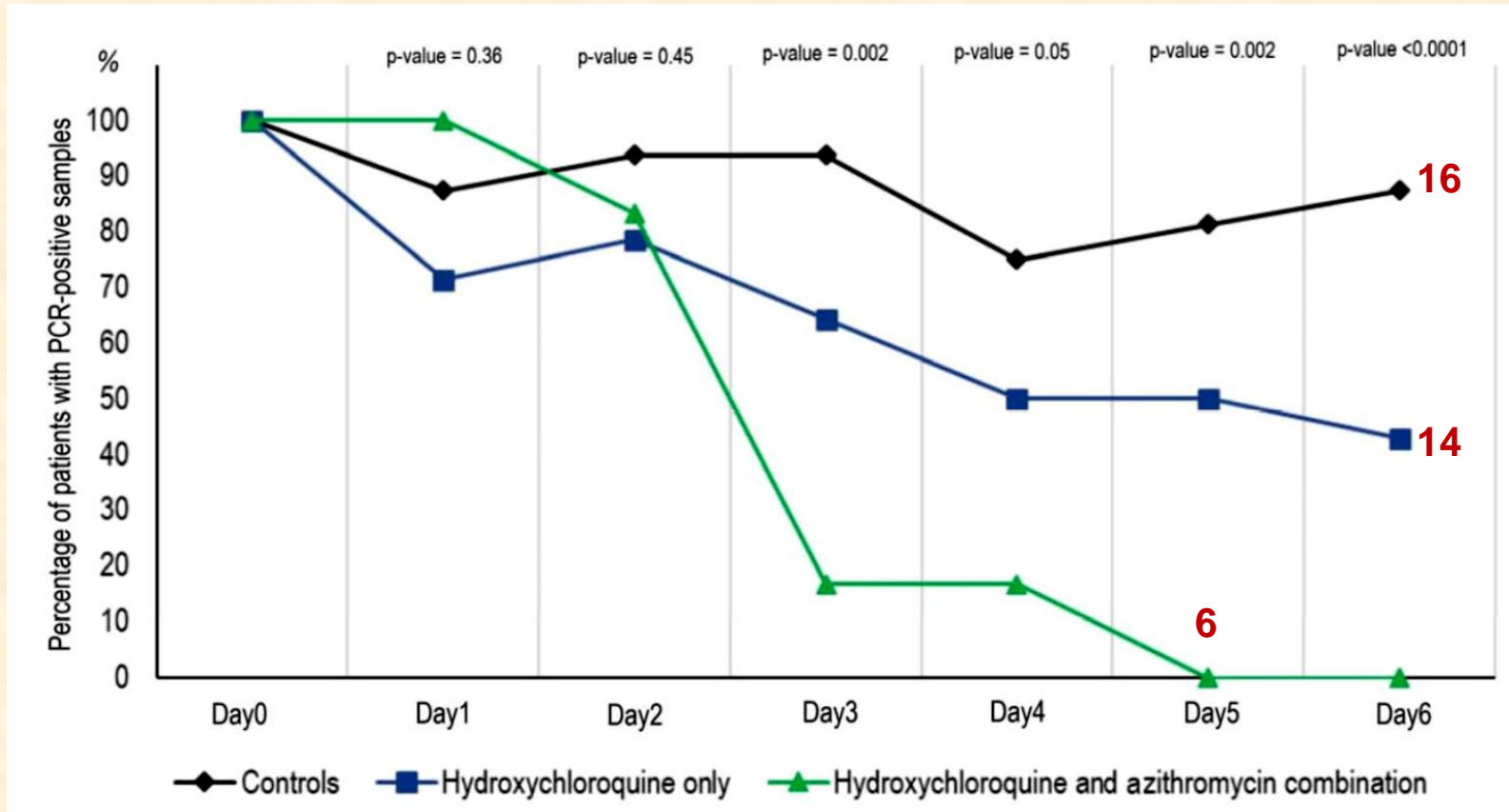


# Hidroxicloroquina





# Hidroxicloroquina





# Toxicidade

BATE-PAPO UOL HOST CURSOS PAGSEGURO UOL BUSCA EMAIL CONTA UOL SAC

PRODUTOS CORONAVÍRUS NOTÍCIAS CARROS ECONOMIA FOLHA ESPORTE ENTRETÉ TV E FAMOSOS UNIVERSA VIVABEM TILT NOSSA START + CANAIS

## CORONAVÍRUS

### Coronavírus: homem nos EUA morre após se automedicar com cloroquina



Homem estava na faixa dos 60 anos  
Imagem: iStock/Getty Images

**Do UOL, em São Paulo**  
24/03/2020 08h17

Um homem na faixa dos 60 anos no estado do Arizona, nos Estados Unidos, morreu após usar sem orientação médica a [cloroquina](#), usada para o tratamento de malária, [lúpus](#) e artrite, em uma aparente tentativa de se tratar da covid-19, doença respiratória causada pelo novo [coronavírus](#).



# Corticosteroides

## Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury

	Outcomes of corticosteroid therapy*	Comment
MERS-CoV	Delayed clearance of viral RNA from respiratory tract <sup>2</sup>	Adjusted hazard ratio 0.4 (95% CI 0.2-0.7)
SARS-CoV	Delayed clearance of viral RNA from blood <sup>5</sup>	Significant difference but effect size not quantified
SARS-CoV	Complication: psychosis <sup>6</sup>	Associated with higher cumulative dose, 10 975 mg vs 6780 mg hydrocortisone equivalent
SARS-CoV	Complication: diabetes <sup>7</sup>	33 (35%) of 95 patients treated with corticosteroid developed corticosteroid-induced diabetes
SARS-CoV	Complication: avascular necrosis in survivors <sup>8</sup>	Among 40 patients who survived after corticosteroid treatment, 12 (30%) had avascular necrosis and 30 (75%) had osteoporosis
Influenza	Increased mortality <sup>9</sup>	Risk ratio for mortality 1.75 (95% CI 1.3-2.4) in a meta-analysis of 6548 patients from ten studies
RSV	No clinical benefit in children <sup>10,11</sup>	No effect in largest randomised controlled trial of 600 children, of whom 305 (51%) had been treated with corticosteroids

CoV=coronavirus. MERS=Middle East respiratory syndrome. RSV=respiratory syncytial virus. SARS=severe acute respiratory syndrome. \*Hydrocortisone, methylprednisolone, dexamethasone, and prednisolone.

Table: Summary of clinical evidence to date



# Precauções e Controle de Infecção

Situação	Recomendações
<b>Caso suspeito e acompanhantes</b>	Máscara cirúrgica Etiqueta respiratória Higiene das mãos
<b>Profissionais de saúde</b> <b>Profissionais de apoio</b>	Máscara cirúrgica Higiene das mãos Gorro Avental Proteção olhos (óculos ou facial) Luvas de procedimento
<b>Procedimentos (aerossóis)*</b>	Máscara N95 / FFP2

\*Intubação ou aspiração traqueal, ventilação não invasiva, ressuscitação cardiopulmonar, ventilação manual antes da intubação, indução de escarro, coletas de amostras nasotráqueais e broncoscopias

“A pandemic is more than a disease. It tests a society’s health systems, its government and politicians, and its economy”

The Economist, 29/02/2020

“Uma pandemia é mais que uma doença. Ela testa o sistema de saúde de uma sociedade, seus governantes e políticos e a sua economia”

The Economist, 29/02/2020