UNIFOR | PPGCM
Programa de Pós-Graduação em Ciências Médicas
Vice-Reitoria de Pós-Graduação

HSJ
Hospital São José Doenças Infecciosas
SECRETARIA DA SAÚDE

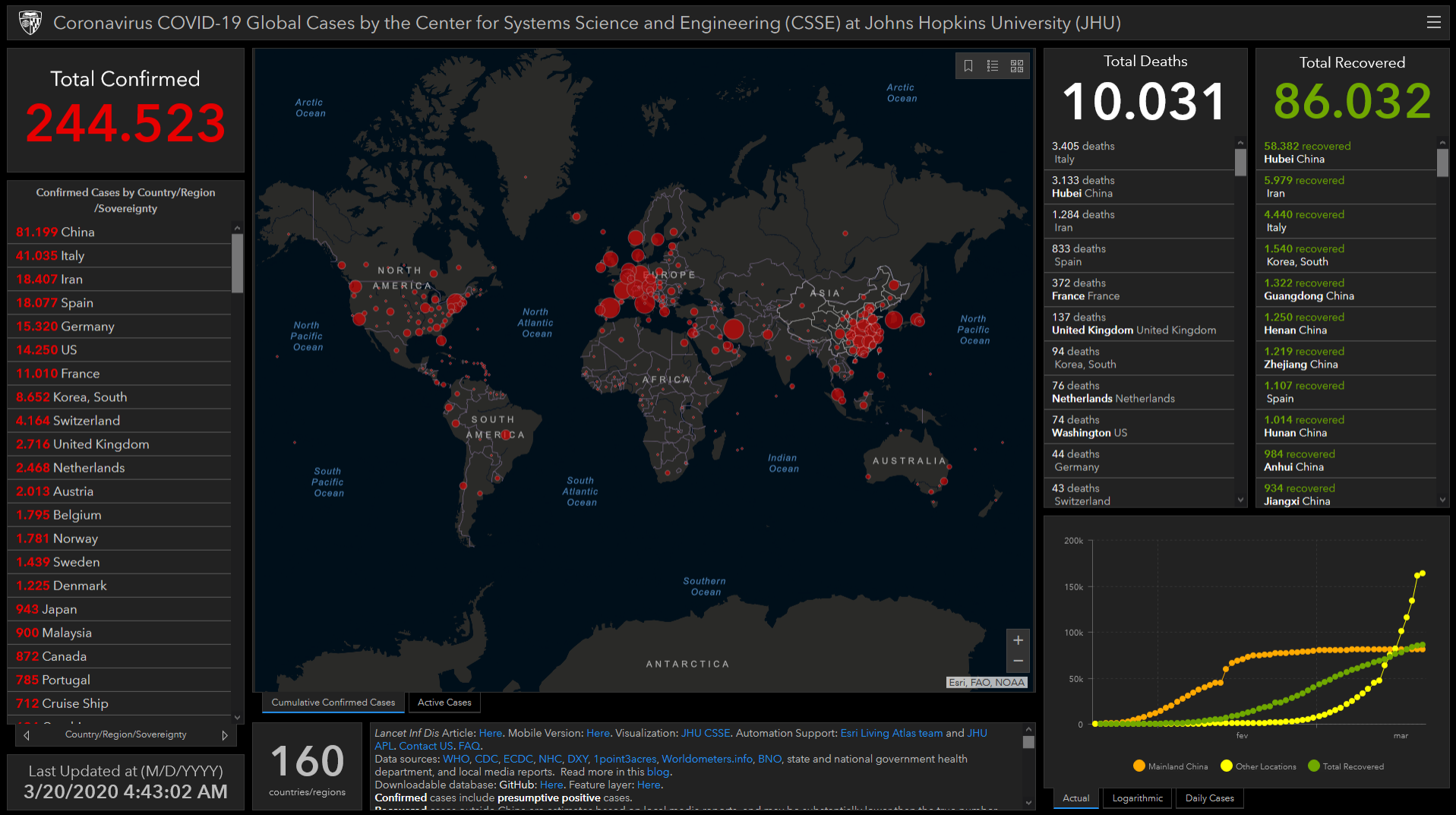
Abordagem clínica de pacientes com infecção pelo SARS-CoV-2 e COVID-19

Keny Colares

Março/2020

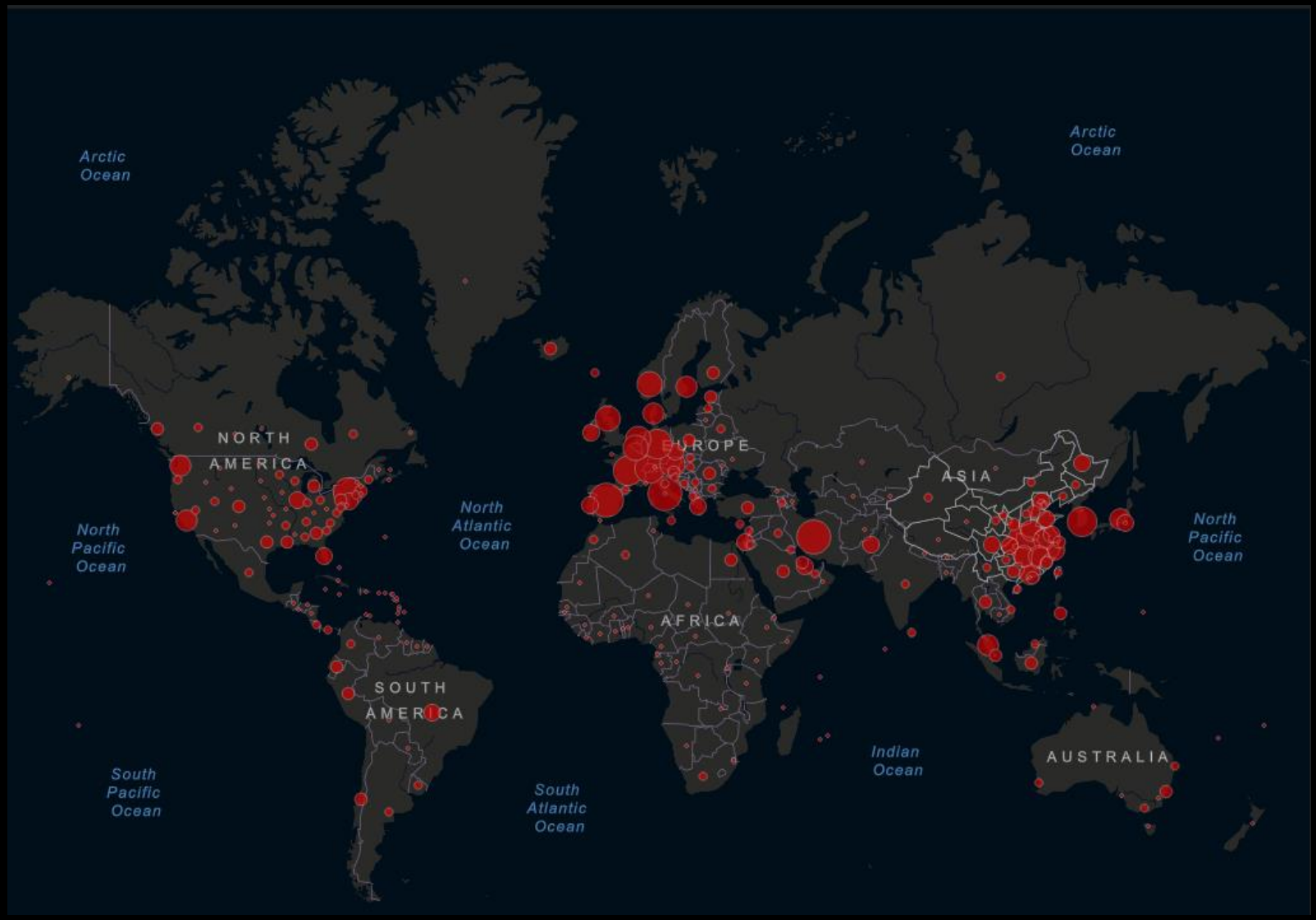
kenycolares@unifor.br

Epidemiologia



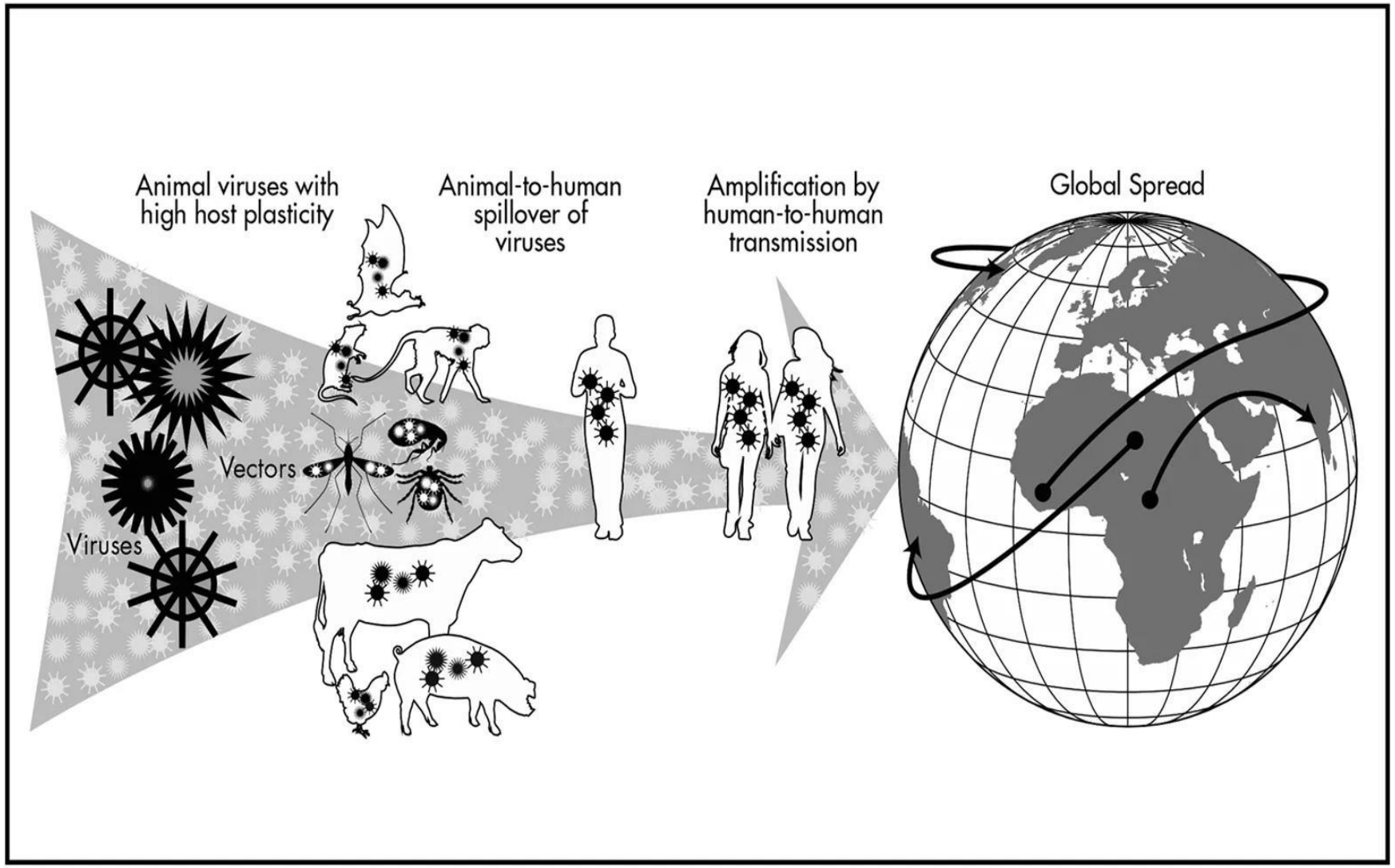
https://gisanddata.maps.arcgis.com

Epidemiologia



https://gisanddata.maps.arcgis.com

Doenças Emergentes



Kreuder Johnson C, Sci Rep 2015

CLINICAL MICROBIOLOGY REVIEWS, Oct. 2007, p. 660–694 Vol. 20, No. 4
0893-8512/07/$08.00+0 doi:10.1128/CMR.00023-07

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

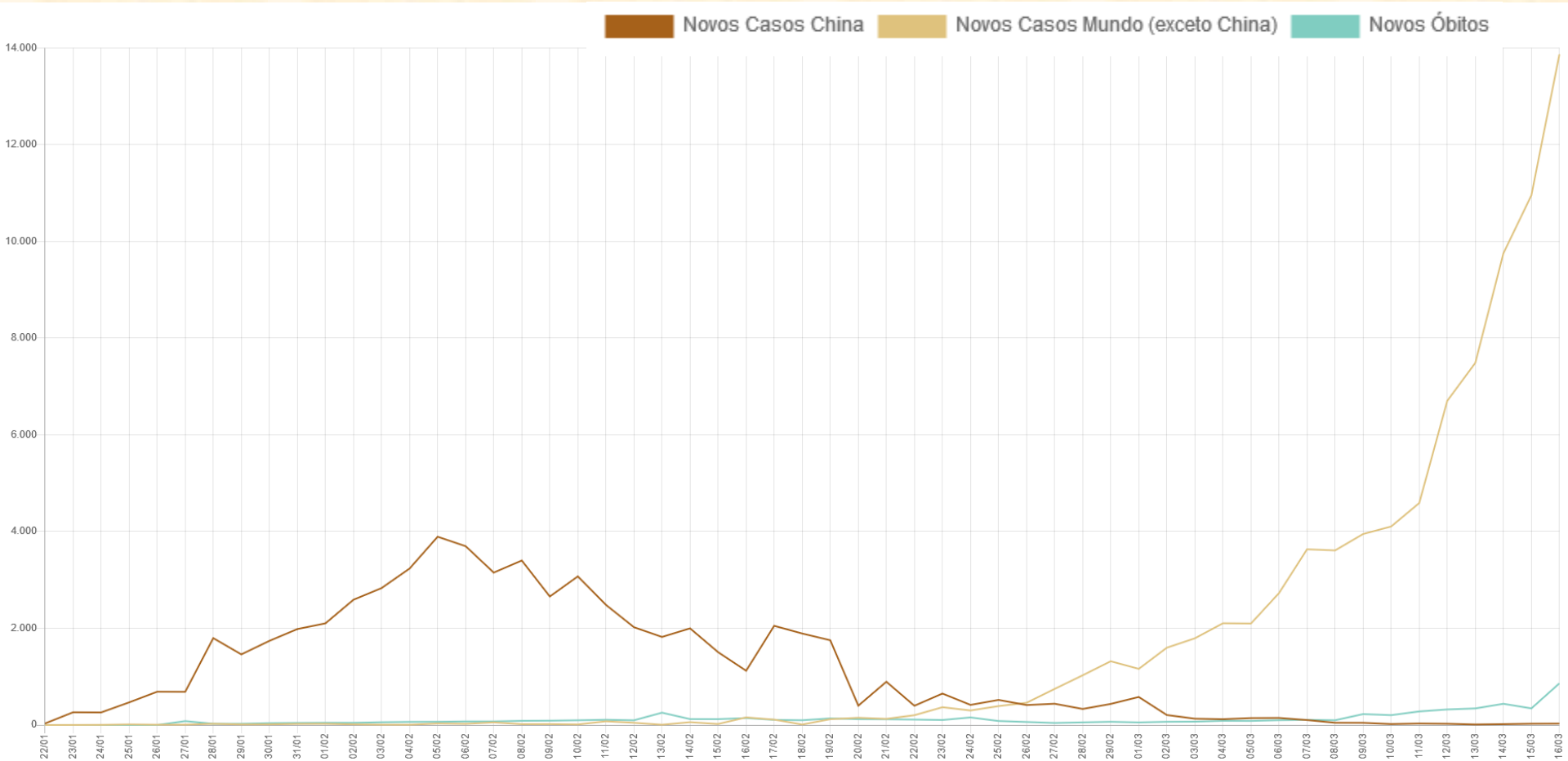
Vincent C. C. Cheng, Susanna K. P. Lau, Patrick C. Y. Woo, and Kwok Yung Yuen*

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.

Cheng VCC, Clin Microbiol Rev 2007

Novos casos (16/03/2020)



http://plataforma.saude.gov.br/novocoronavirus/

Perfil dos casos confirmados (N=550)

Idade
Média: 42 anos (+-16)

Faixa etária:

<40 anos	277 (50%)
40 - 49 anos	88 (16%)
50 - 59 anos	81 (15%)
60 - 69 anos	58 (11%)
>69 anos	31 (6%)
Não informado	12 (2%)

Sexo:
Feminino: 256 (47%)
Masculino: 279 (51%)
Não informado: 13 (2%)

Hospitalizações: 56 (10%)

UF com caso confirmado: 17

Transmissão local (212 casos):

- CE, ES, GO, PE, RS e SE **N=6**

Transmissão comunitária* (79):

- BA, DF, MG, MS, PR, RJ, SC, SP **N=8**

* Dado preliminar. Investigação de vínculo epidemiológico em andamento.

Dados atualizados em 19/03/2020 às 15:00

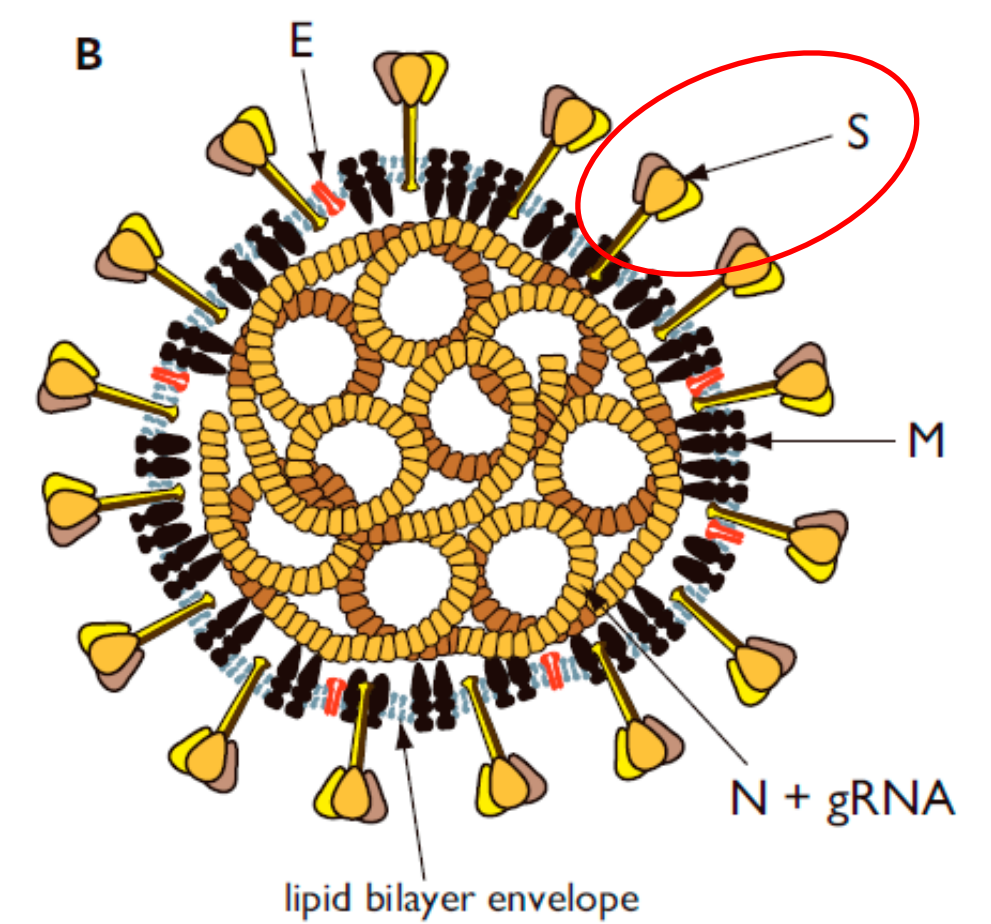
Classificação dos casos por UF de notificação - 19/03/2020 até 15:00

Norte: 8
Nordeste: 90
Sudeste: 391
Centro-Oeste: 61
Sul: 71

ID	UF	CONFIRMADOS	ÓBITOS	
		N	N	%
REGIÃO NORTE				
1	AC	3	0	0 %
2	AM	3	0	0 %
3	AP	0	0	0 %
4	PA	1	0	0 %
5	RO	0	0	0 %
6	RR	0	0	0 %
7	TO	1	0	0%
REGIÃO NORDESTE				
8	AL	4	0	0%
9	BA	30	0	0%
10	CE	20	0	0%
11	MA	0	0	0%
12	PB	1	0	0%
13	PE	28	0	0%
14	PI	0	0	0%
15	RN	1	0	0%
16	SE	6	0	0%
REGIÃO SUDESTE				
17	ES	11	0	0%
18	MG	29	0	0%
19	RJ	65	2	3,1%
20	SP	286	4	1,4%
REGIÃO CENTRO-OESTE				
21	DF	42	0	0%
22	GO	12	0	0%
23	MS	7	0	0%
24	MT	0	0	0%
REGIÃO SUL				
25	PR	23	0	0%
26	SC	20	0	0%
27	RS	28	0	0%
BRASIL		**621**	**6**	**1%**

Fonte: contato através do número CIEVS.

Coronavirus



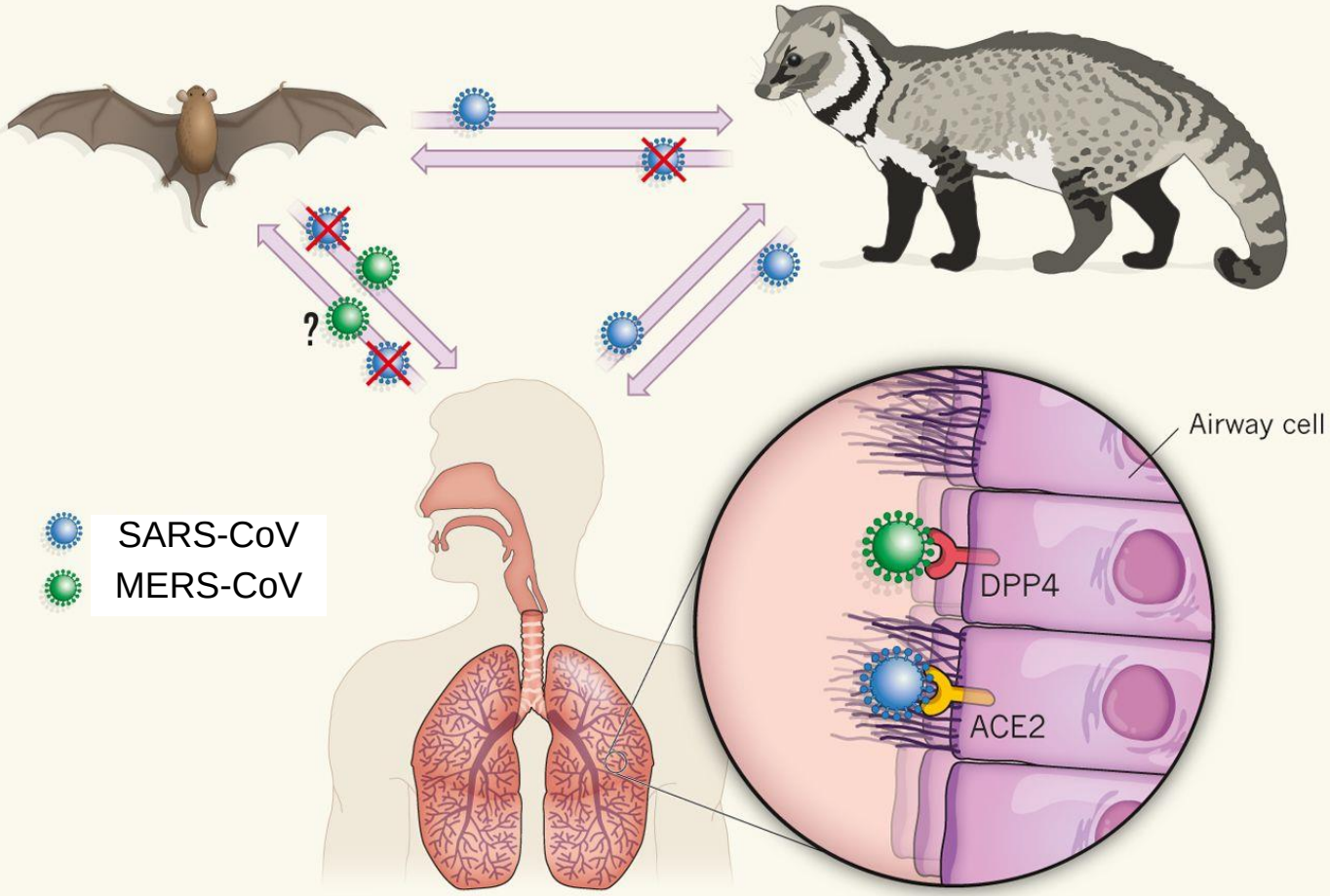
- Ordem *Nidovirales*
- Família *Coronaviridae*
- Subfam. *Coronavirinae*
- Envelope
- 80-120nm
- 26-32kb
- **RNAss ⊕**
- Não segmentado

Fields Virology, 2013

Coronavirus

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

Patogênese

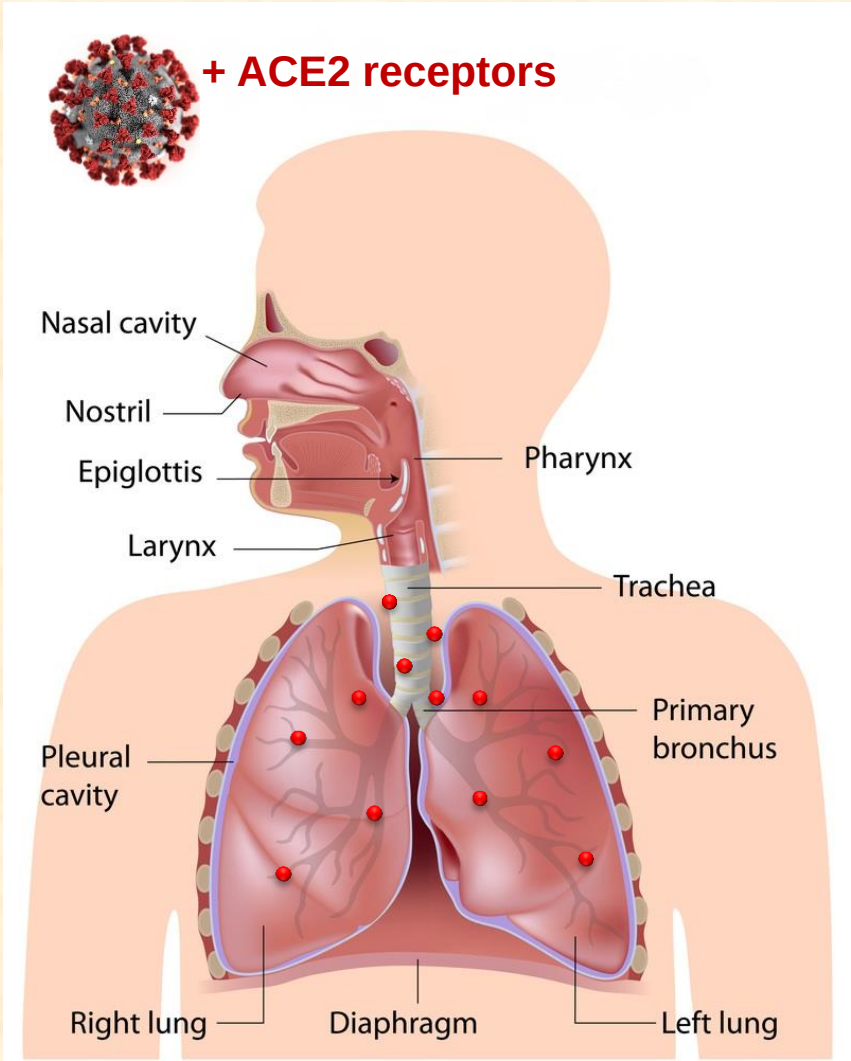


Gallagher T, Nature 2013

Receptores (ectopeptidase)

Angiotensin converting enzyme 2 (ACE2)

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

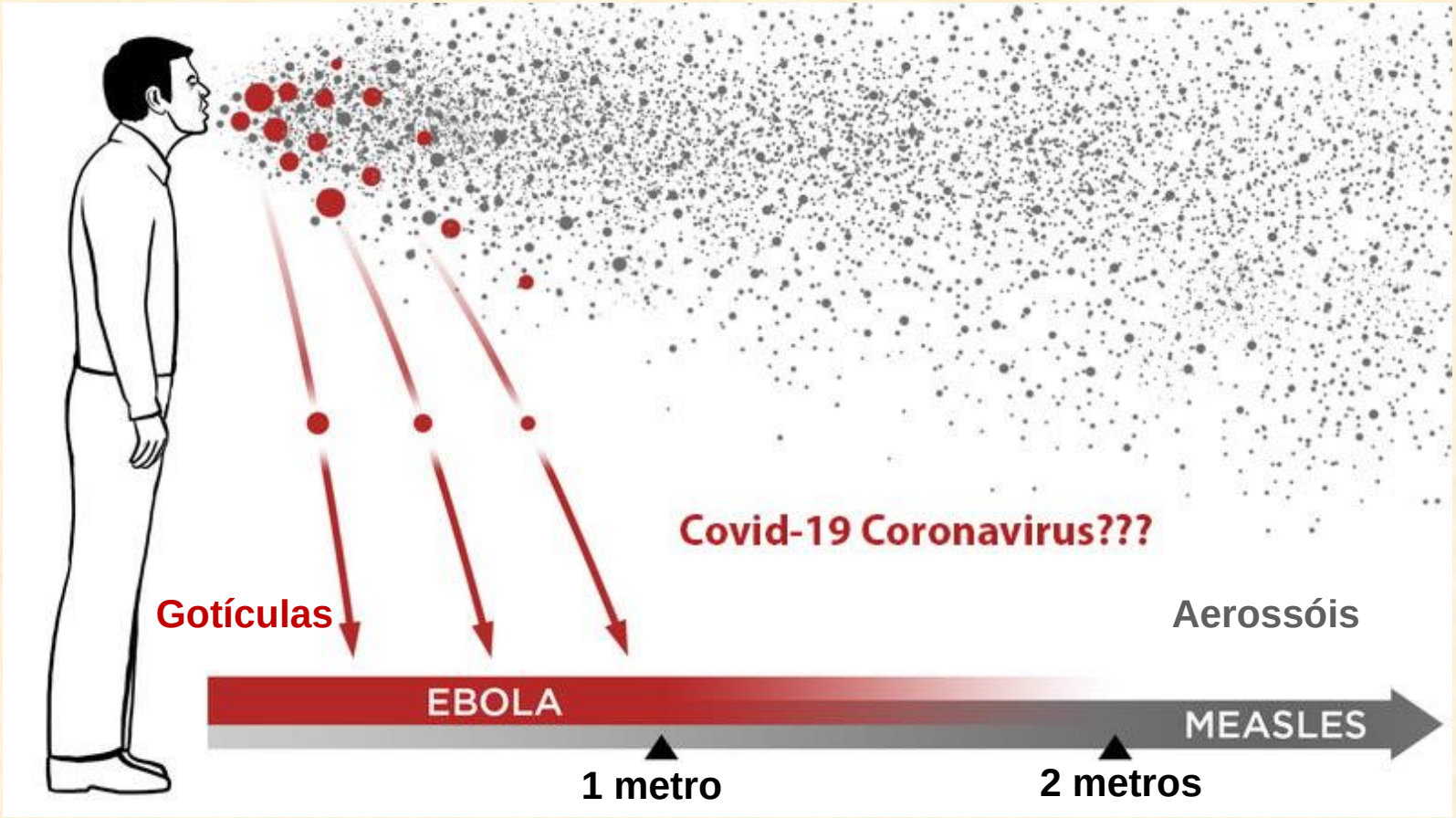


Dipeptidyl peptidase 4 (DPP4 / CD26)

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

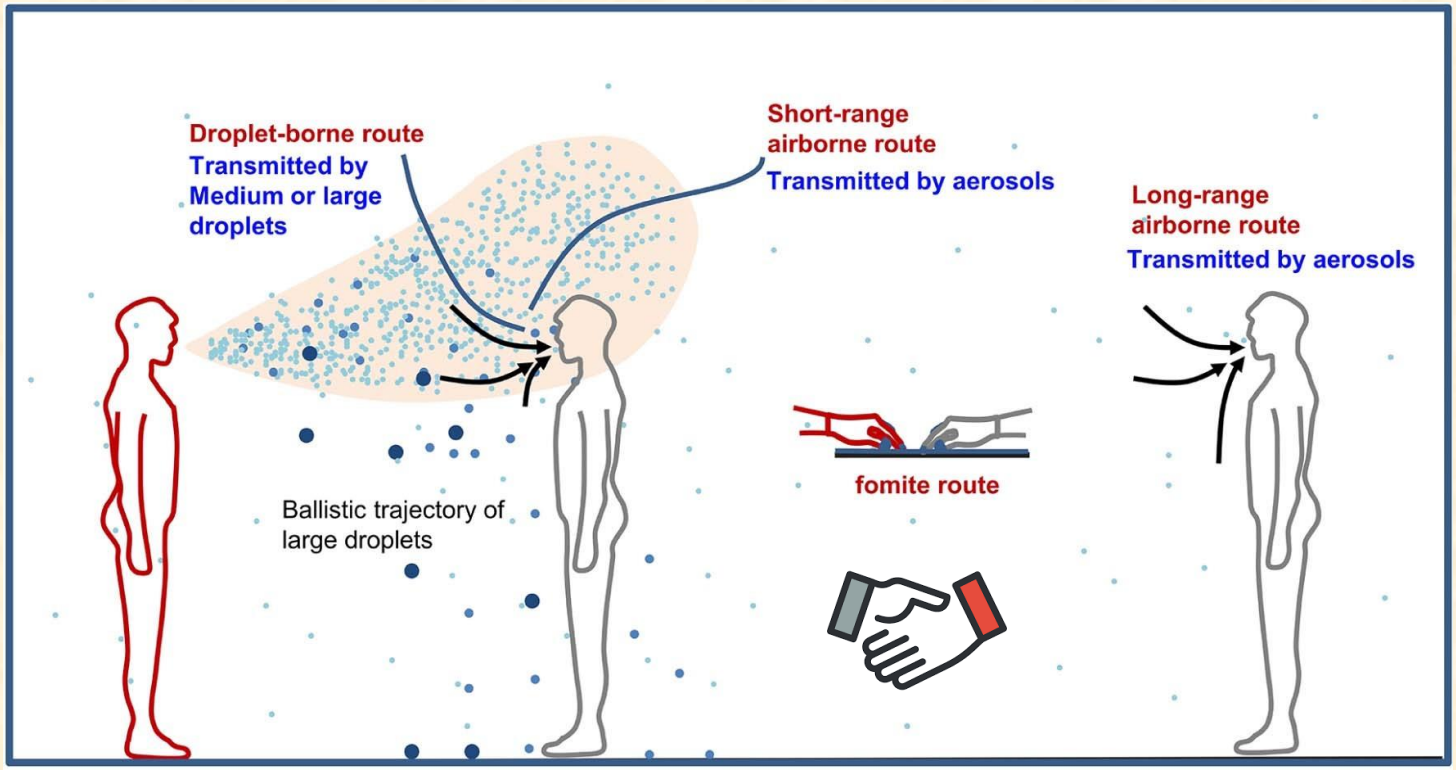
Jia HP, J Virol 2005
Singh SK, Semin Respir Crit Care Med 2016

Transmissão



Thailand Medical News Feb 12, 2020

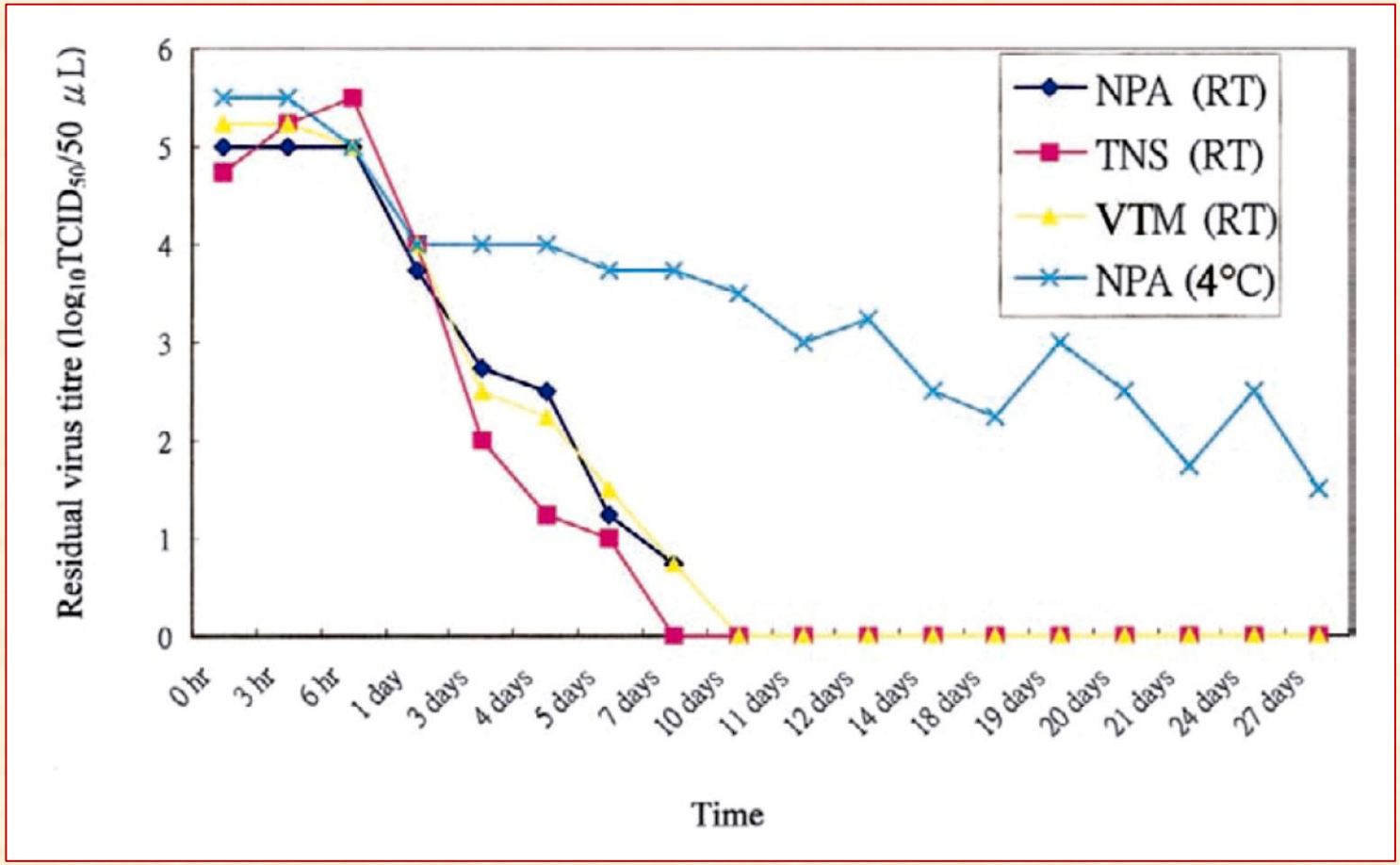
Transmissão



- Large droplets (>100 μm) : Fast deposition due to the domination of gravitational force
- Medium droplets between 5 and 100 μm
- Small droplets or droplet nuclei, or aerosols (< 5 μm): Responsible for airborne transmission

Adaptado de Wei J, Am J Infect Control 2016

Transmissão



Survival time of SARS-CoV - room temperature (RT) and at 4C.
NPA: nasopharyngeal aspirate
TNS: throat and nasal swab
VTM: viral transport medium

Lay MYY, Clin Infect Dis 2005

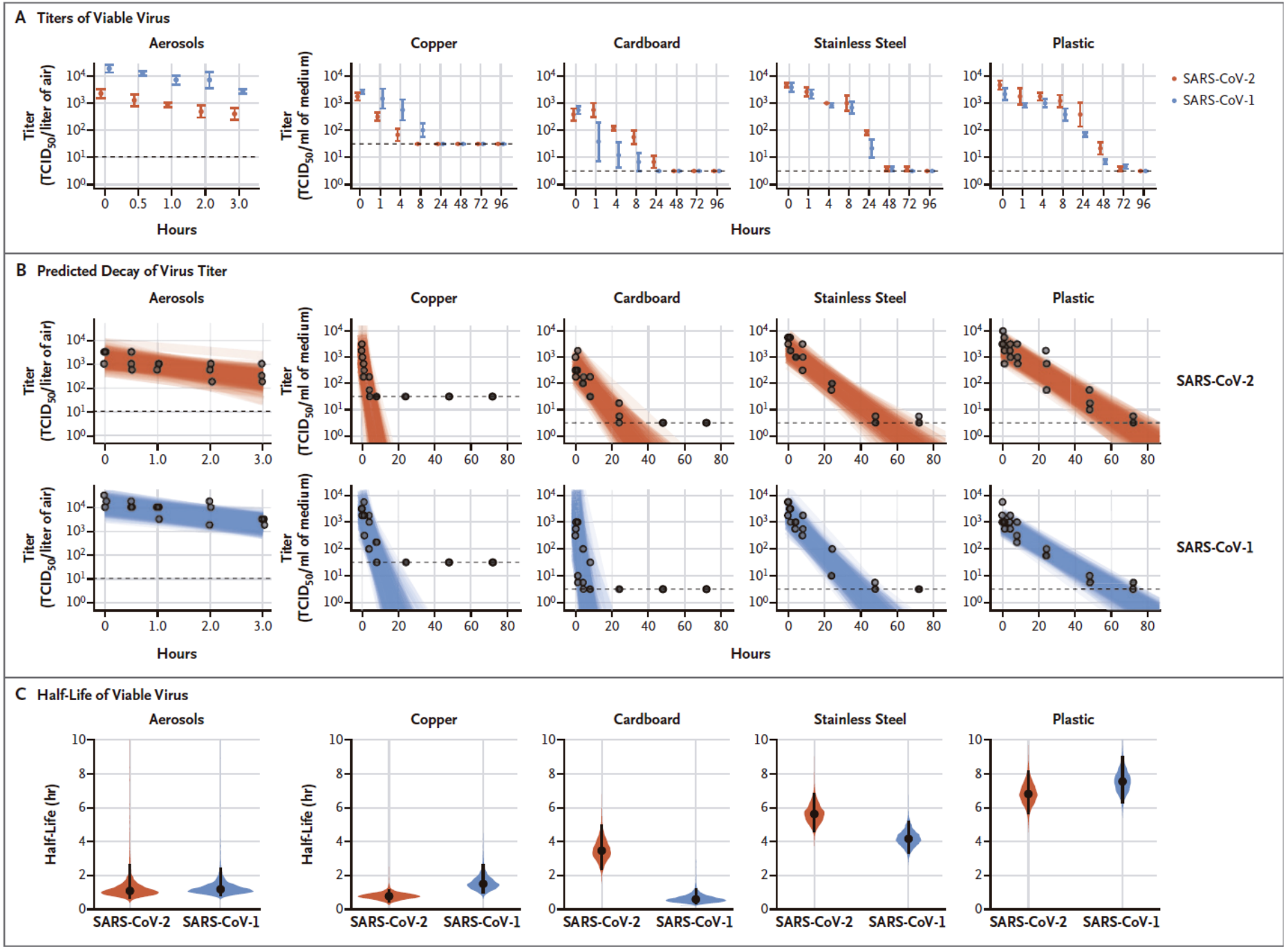
Transmissão

Inoculation, $TCID_{50}$/mL	Time taken to inactivate SARS-CoV, by surface		
	Paper	Disposable gown	Cotton gown
10^6	24 h	2 days	24 h
10^5	3 h	24 h	1 h
10^4	<5 min	1 h	5 min

Lay MYY, Clin Infect Dis 2005

Transmissão

Kampf G, J Hosp Infect – Mar 2020



van Doremalen N, New Engl J Med – 17 Mar 2020

Aerossóis

Goldberg drum

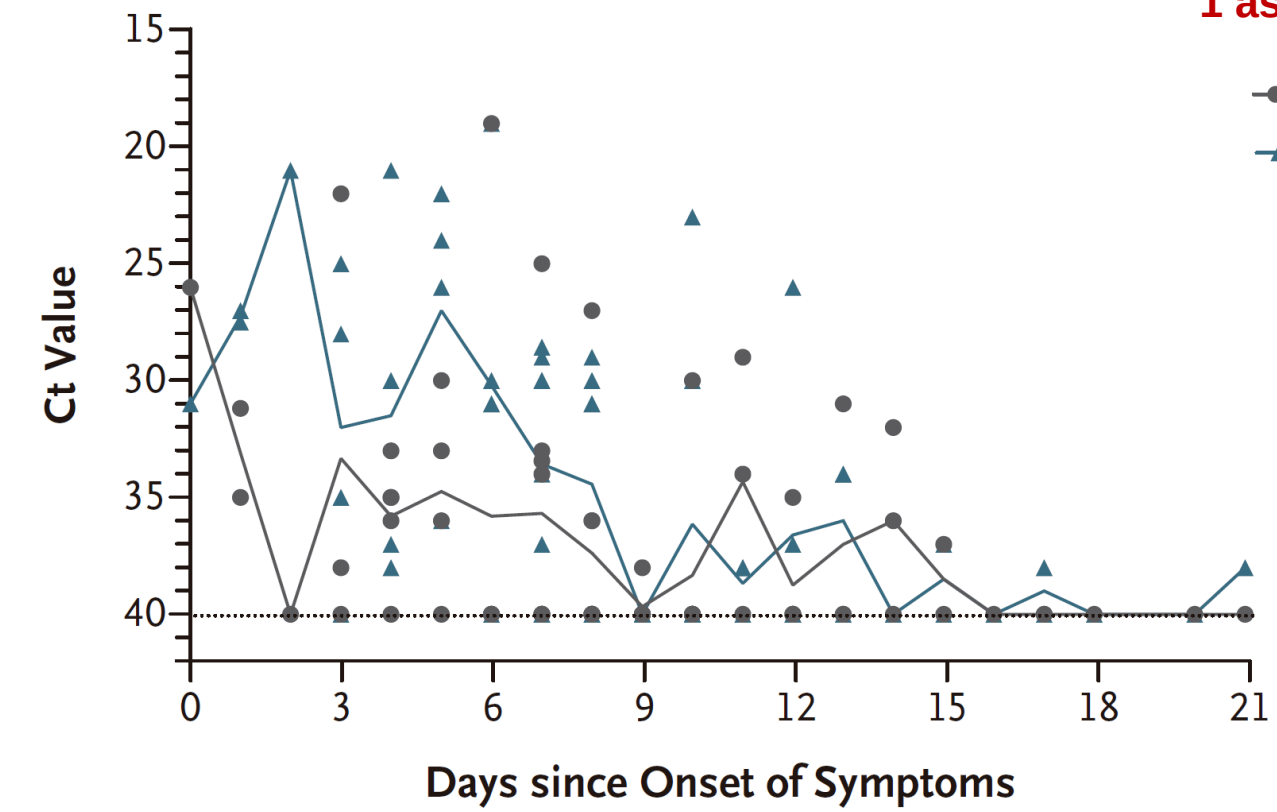
Collison nebulizer

van Doremalen N, New Engl J Med – 17 Mar 2020

Carga viral x tempo

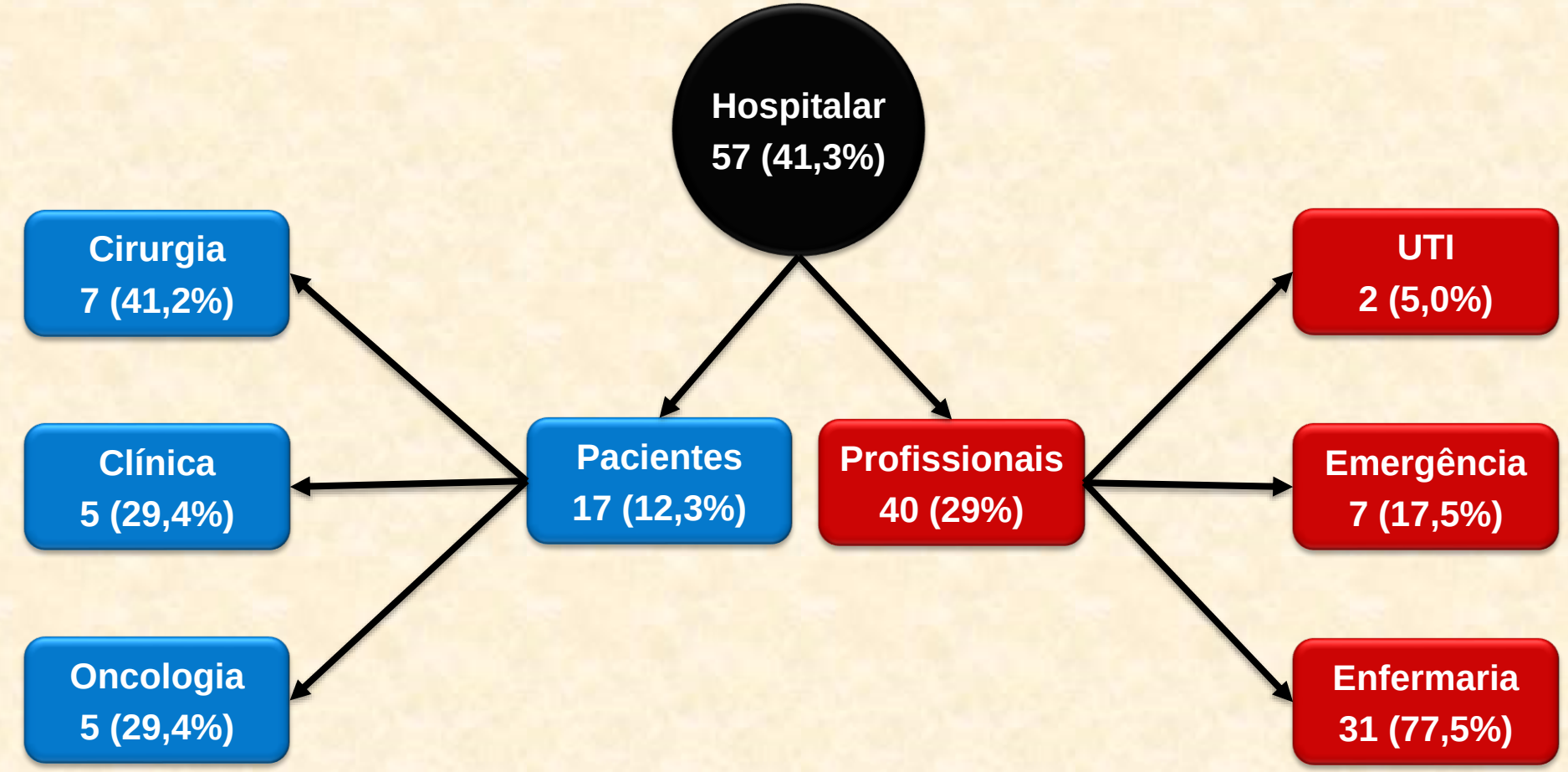
17 sintomáticos

1 assintomático



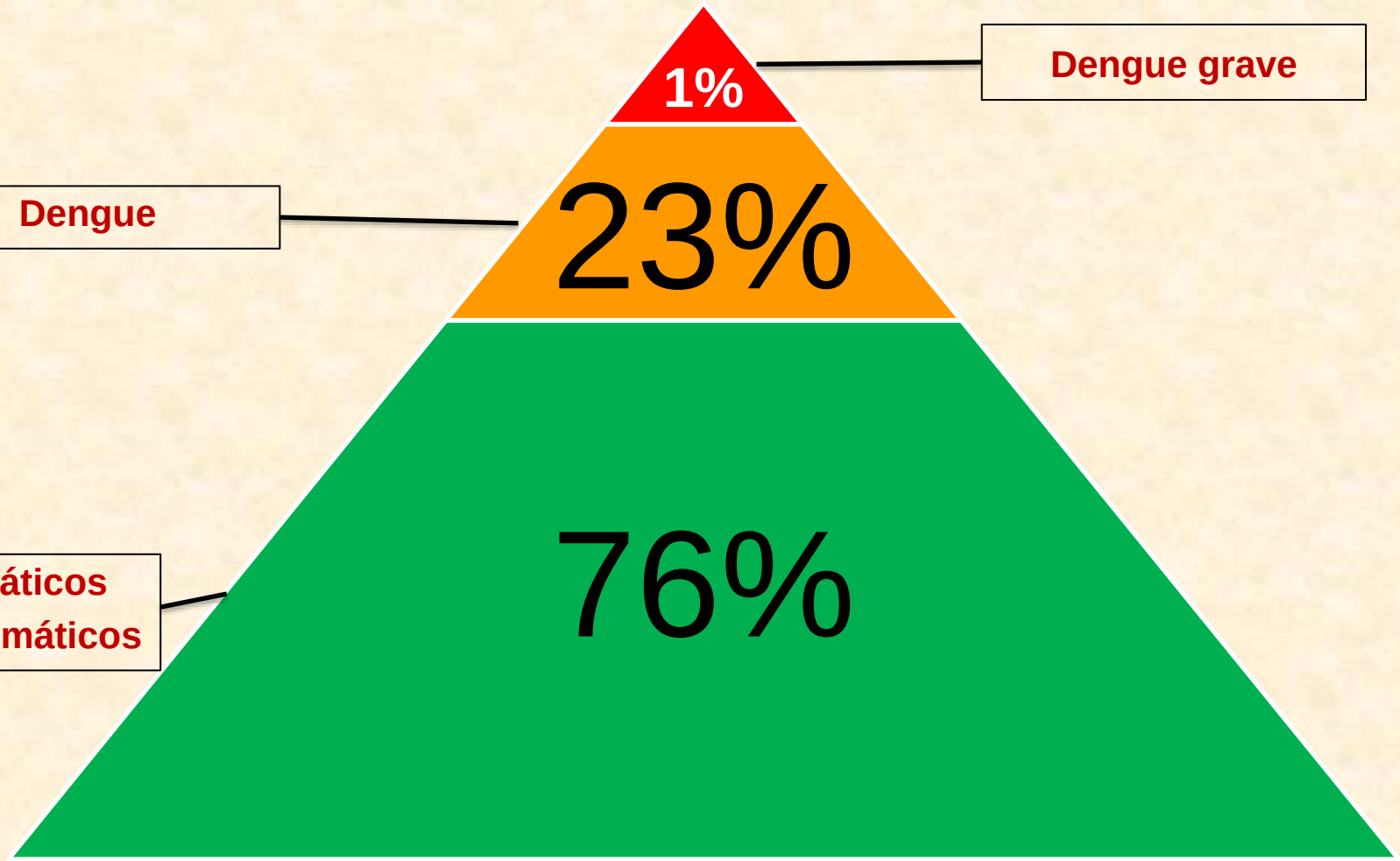
Zou L, New Engl J Med – 19 Feb 2020

Transmissão nosocomial



Wang D, JAMA 2020

Espectro clínico



Porter KR. Am J Trop Med Hyg 2005

Infecção SARS-CoV-2 / COVID-19

https://www.theladders.com/career-advice/the-iceberg-illusion-the-hidden-logic-of-success

Espectro clínico

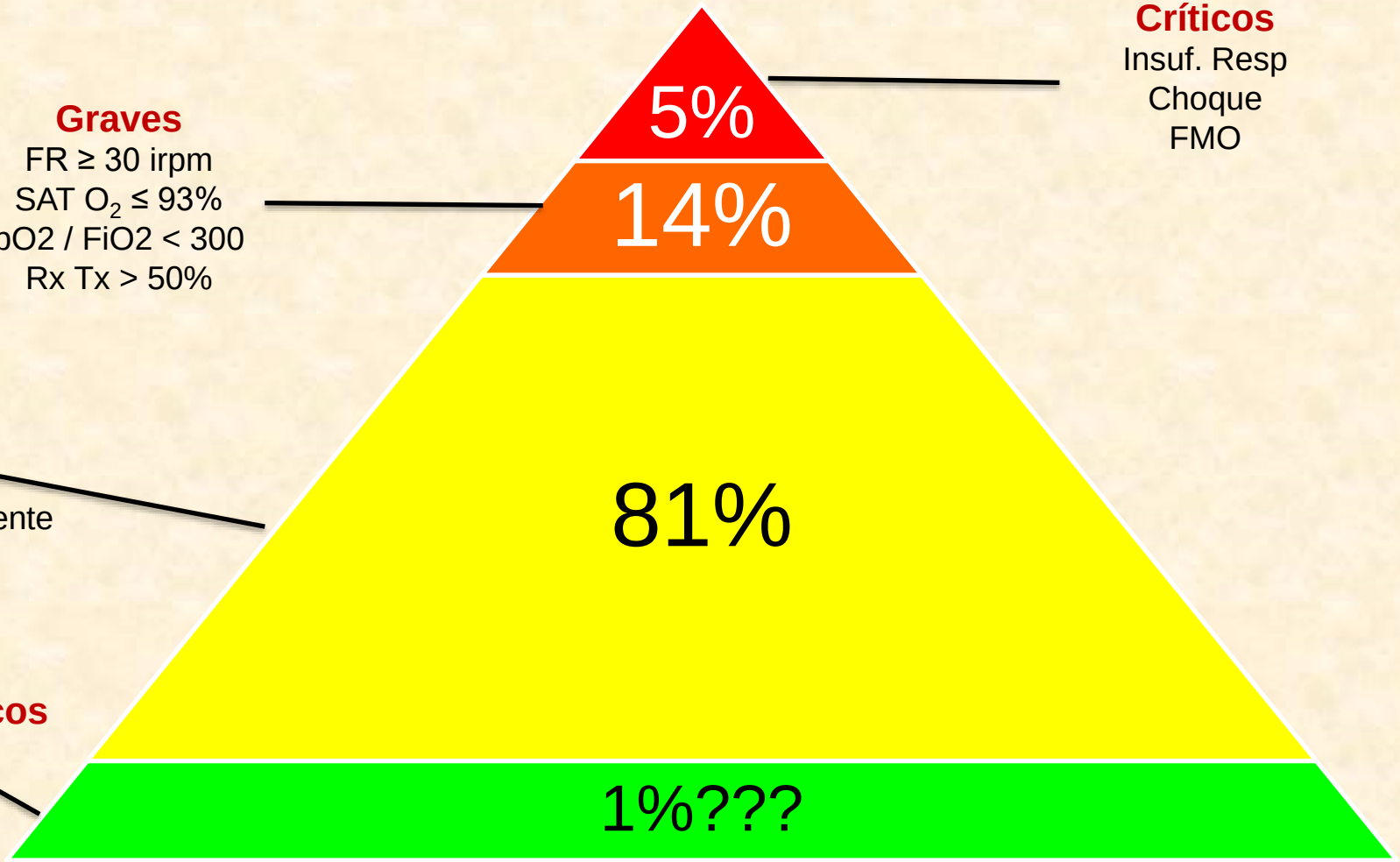
- Casos: 72.314*
- Confirmados: 44.672 (62%)
- Masc / Fem: 51,4 / 48,6% (CFR=2,8/1,7%)
- Letalidade: 2,3%
- Profissionais saúde: 3,8%
  - ✓Grave+críticos (14,8%)
  - ✓Óbitos: 5

*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

Wu Z, JAMA – 24 Feb 2020

Assintomáticos

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

Ruiyun Li[1]*, Sen Pei[2]*†, Bin Chen[3]*, Yimeng Song[4], Tao Zhang[5], Wan Yang[6], Jeffrey Shaman[2]†

[1]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. [2]Department of Environmental Health Sciences, Mailman School of Public Health, Columbia University, New York, NY 10032, USA. [3]Department of Land, Air and Water Resources, University of California, Davis, Davis, CA 95616, USA. [4]Department of Urban Planning and Design, The University of Hong Kong, Hong Kong. [5]Ministry of Education Key Laboratory for Earth System Modeling, Department of Earth System Science, Tsinghua University, Beijing 10084, P. R. China. [6]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%)

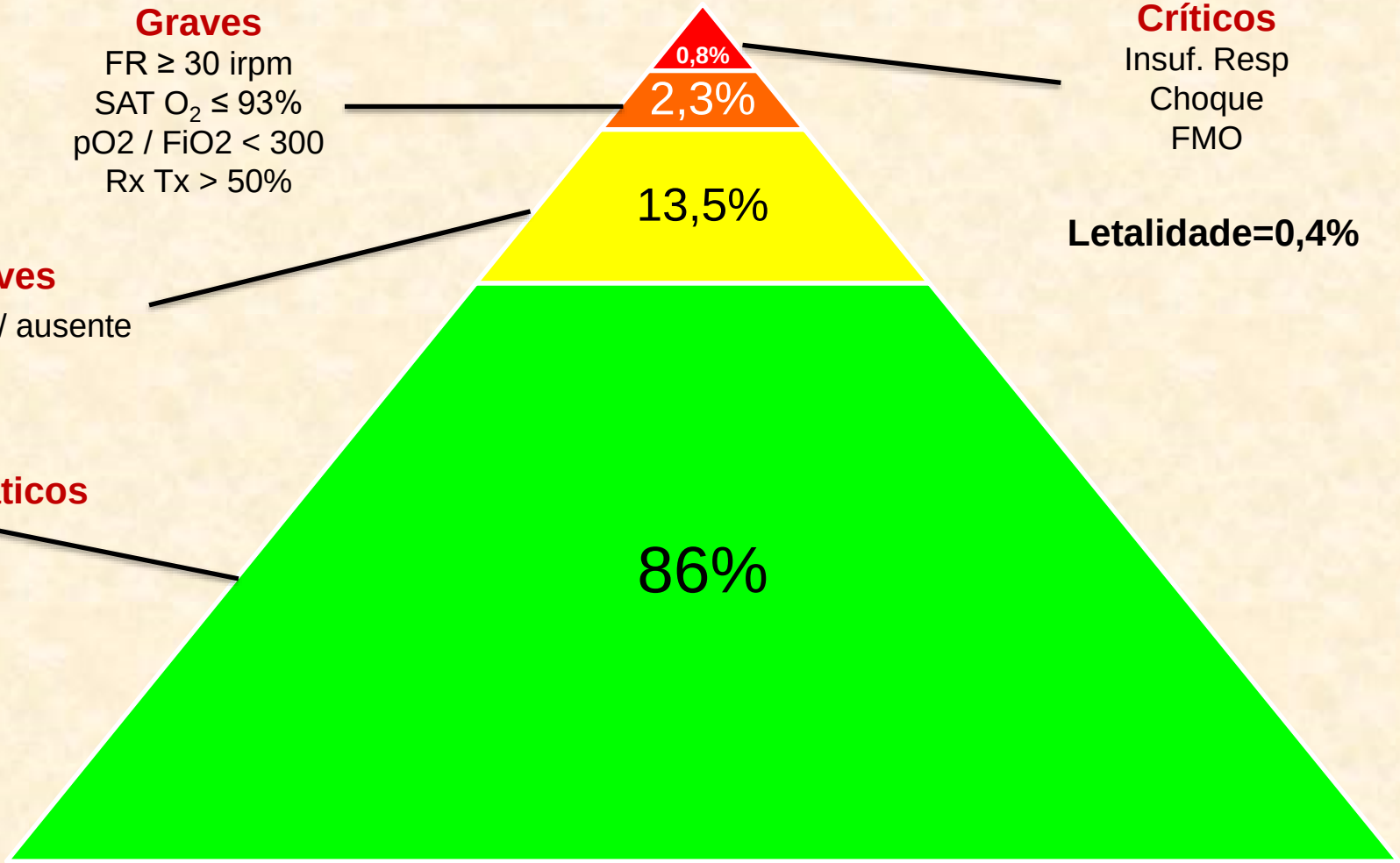
Fonte da infecção (ND) = 79%

Li R, Science – 16 Mar 2020

Espectro clínico

Graves
FR ≥ 30 irpm
SAT O_2 ≤ 93%
pO2 / FiO2 < 300
Rx Tx > 50%

Críticos
Insuf. Resp
Choque
FMO



Letalidade=0,4%

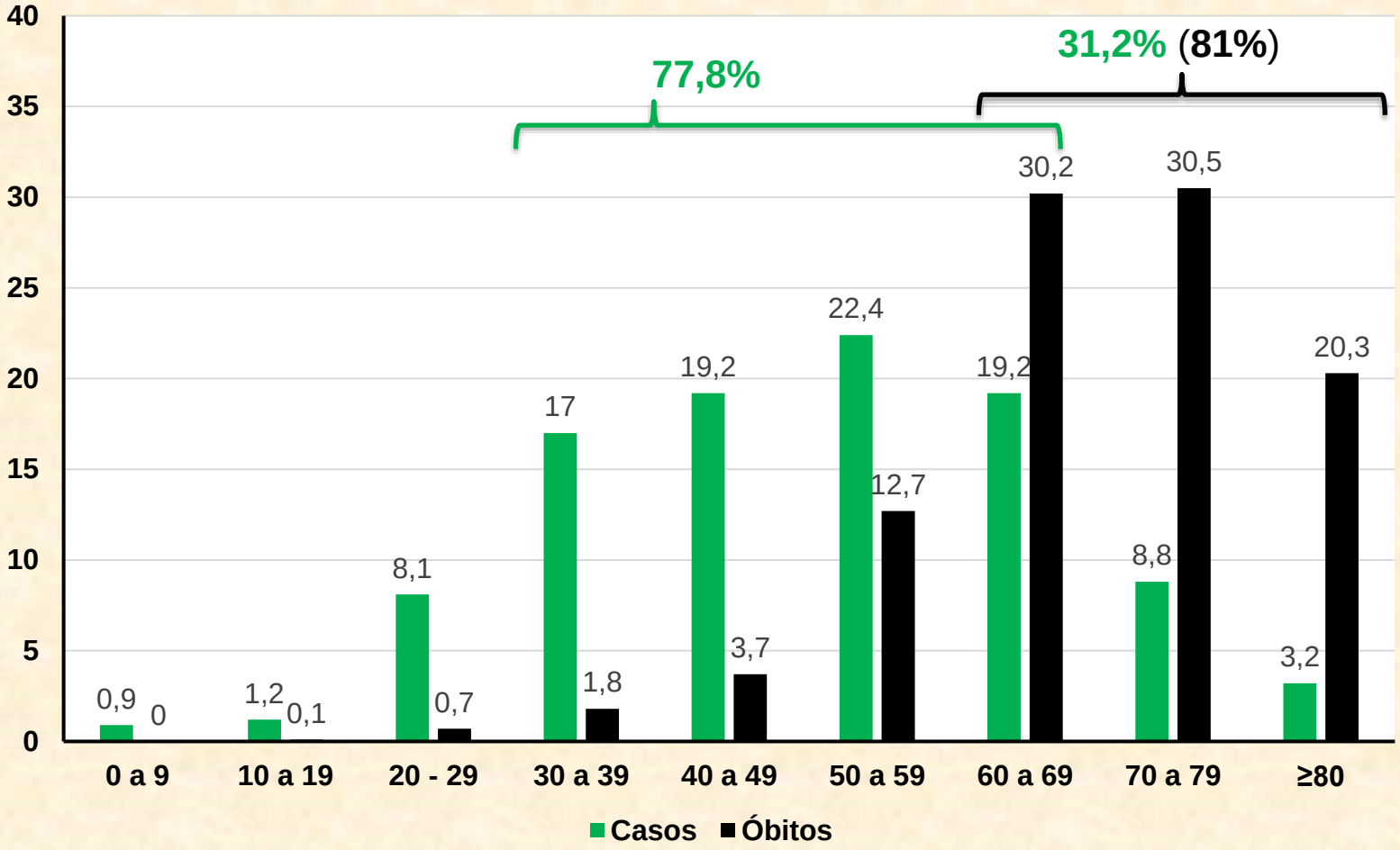
Leves
PN leve / ausente

Assintomáticos

N = 44.415

Wu Z, JAMA – 24 Feb 2020

Faixa etária - Casos x óbitos (%)*



N=44.672

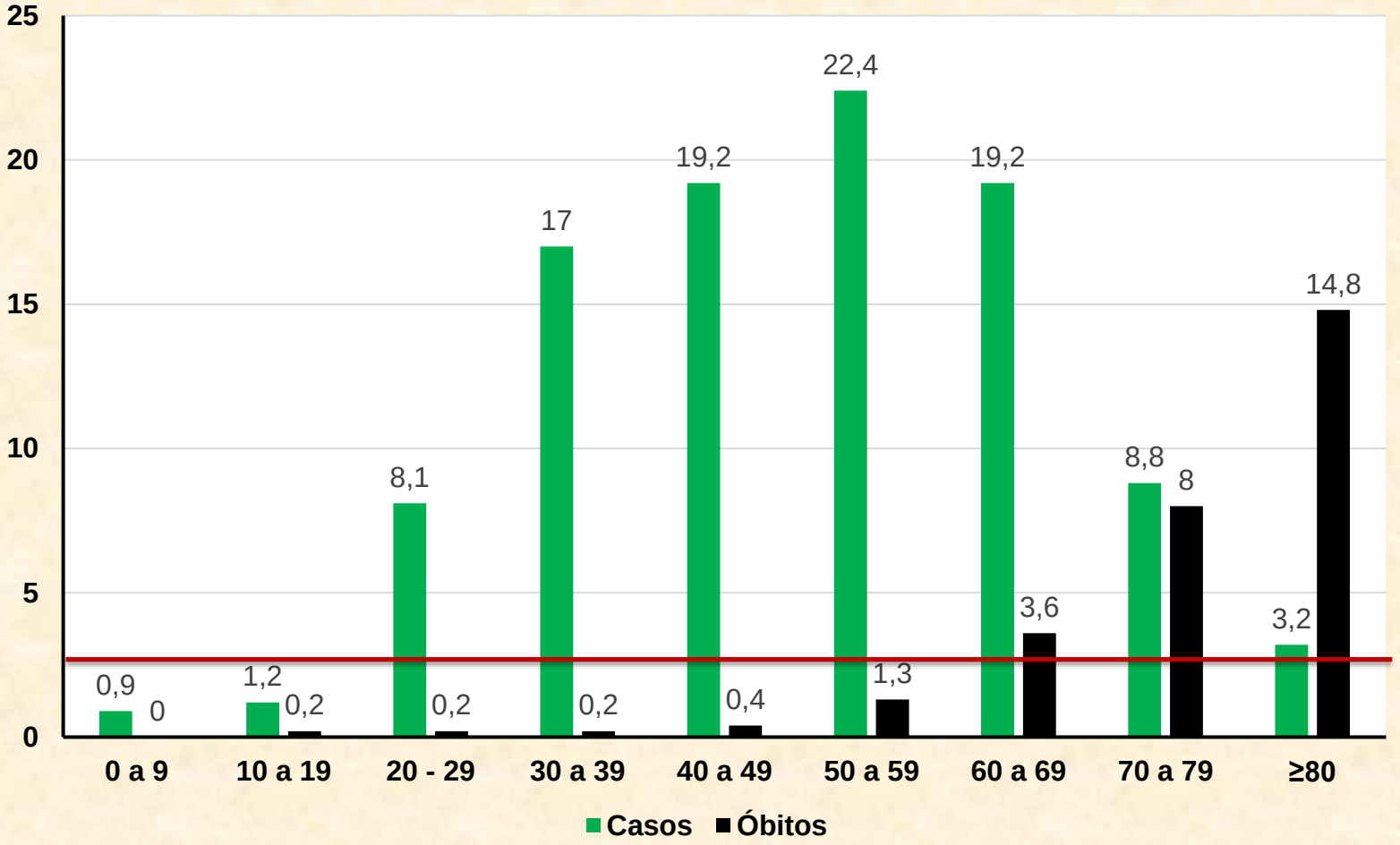
Óbitos=1.023

*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

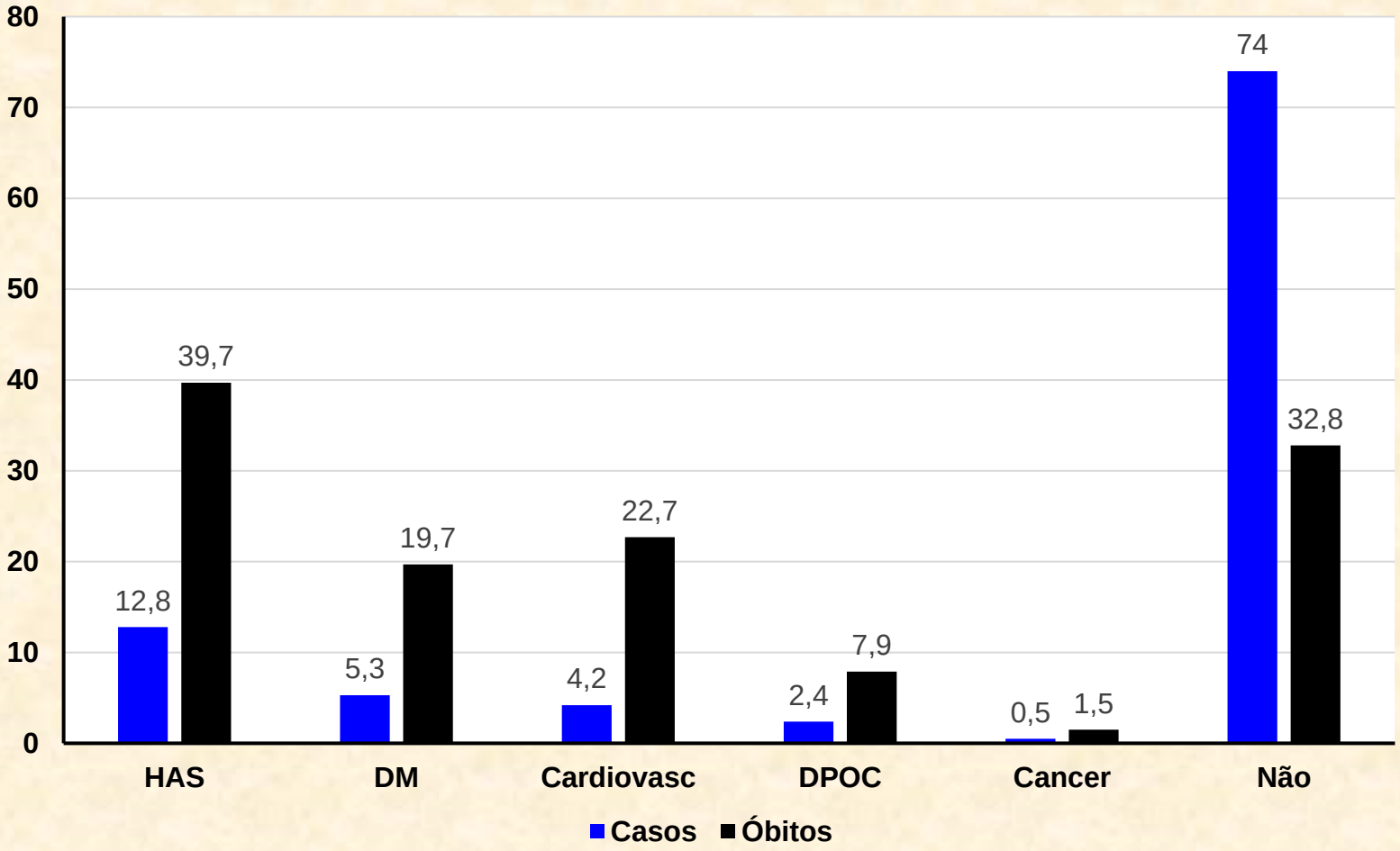
CFR=2,3

*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

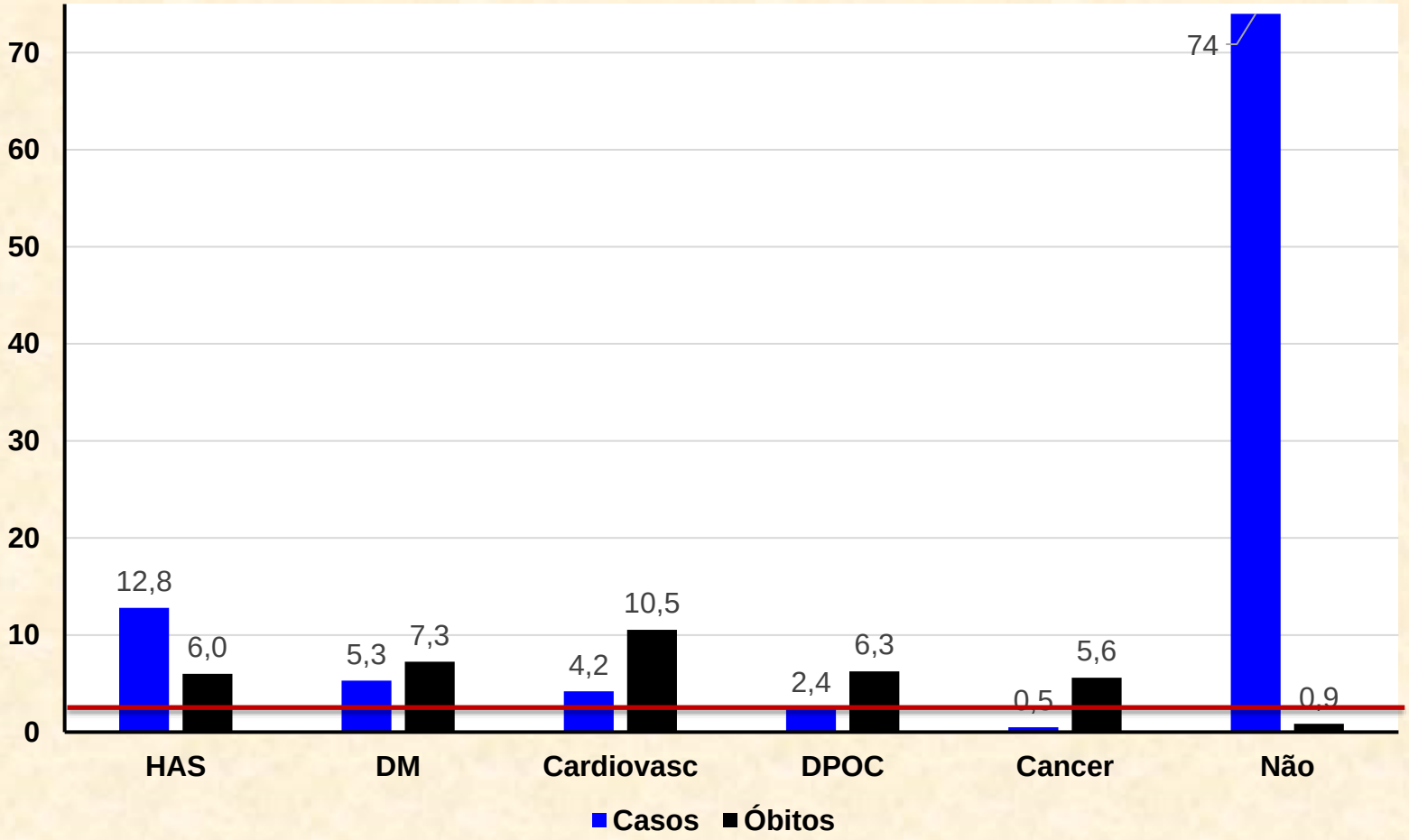
Óbitos=504

*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%

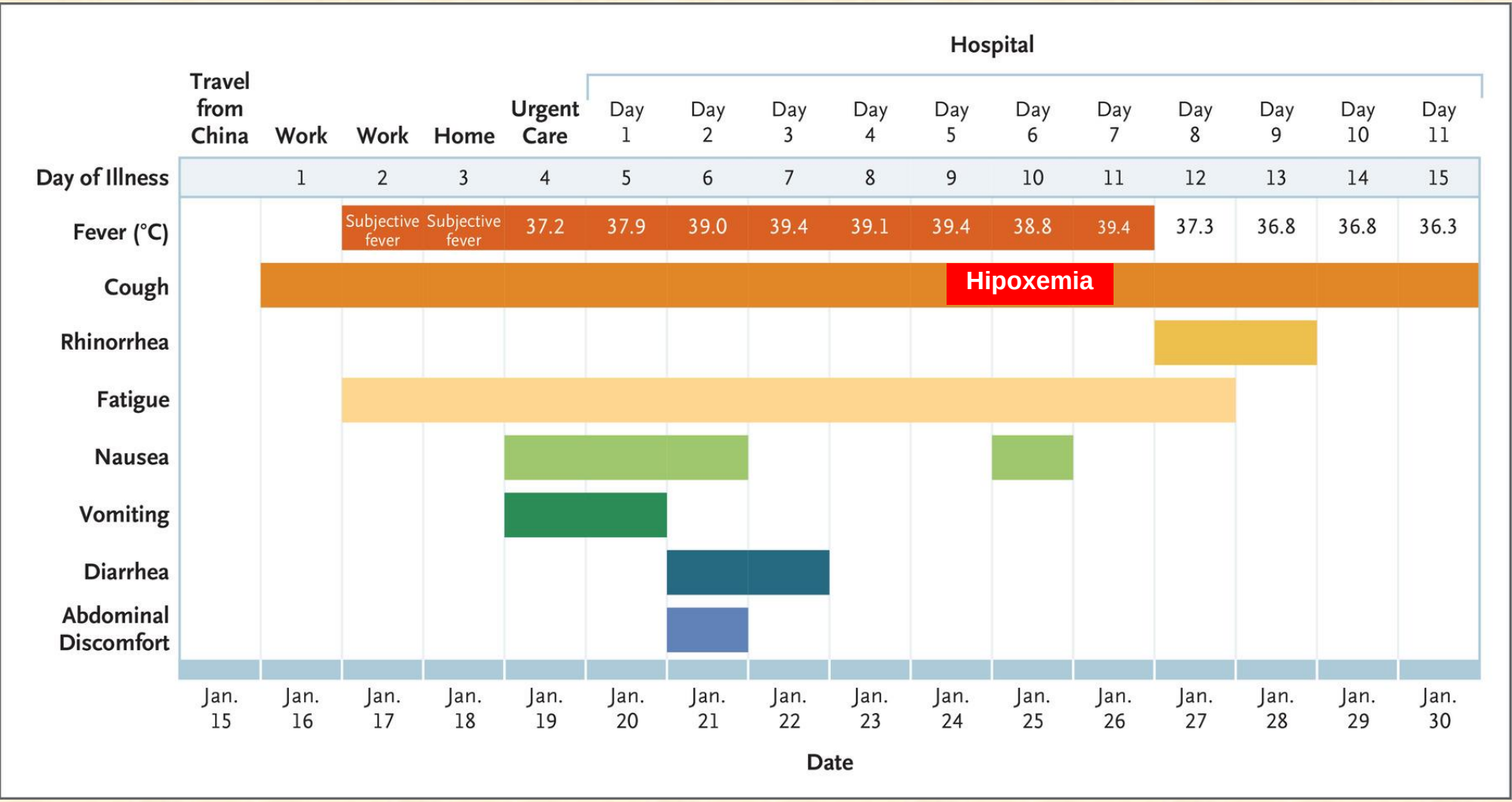
*Até 11 Feb 2020

Home

China CDC Weekly, 21 Feb 2020

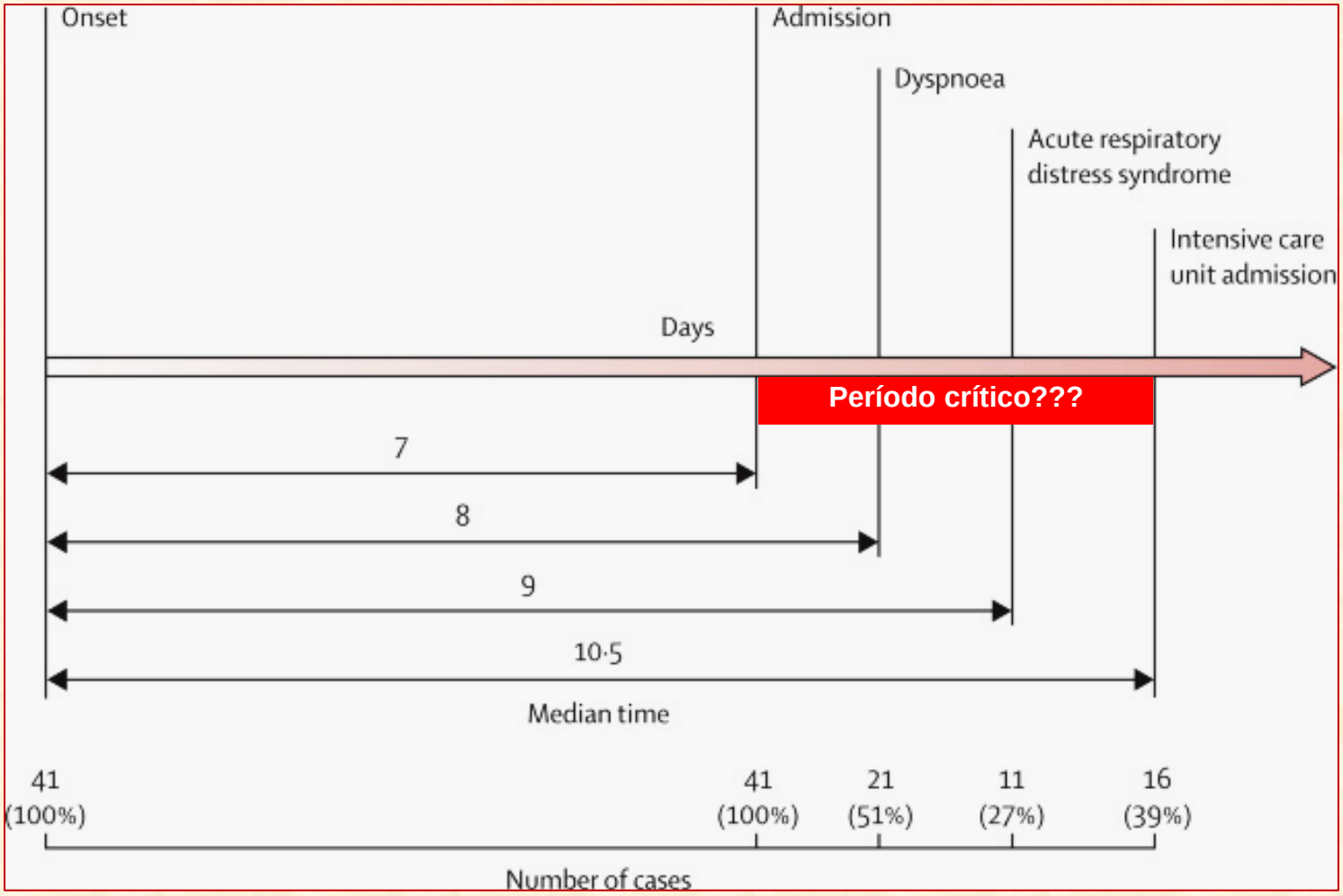
http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51

História natural



Adaptado de Holshue ML, New Engl J Med 2020

História natural (N=41)



Huang C, Lancet 2020

Características

	N=41 (%)[1]	N=99 (%)[2]	N=138 (%)[3]
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).

Adaptado: [1]Huang C, Lancet - 24 Jan 2020 [2]Chen N, Lancet – 15 Feb 2020 [3]Wang D, JAMA 07 Feb 2020

Sintomatologia

Sintomas, N (%)	N=41[1]	N=99[2]	N=138[3]	N=140[4]	N=1099[5]
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: [1]Huang C, Lancet - 24 Jan 2020 [2]Chen N, Lancet – 15 Feb 2020 [3]Wang D, JAMA 07 Feb 2020
[4]Zhang JJ, Allergy - 19 Feb 2020 [5]Guan WJ, New Engl J Med 28 Feb 2020

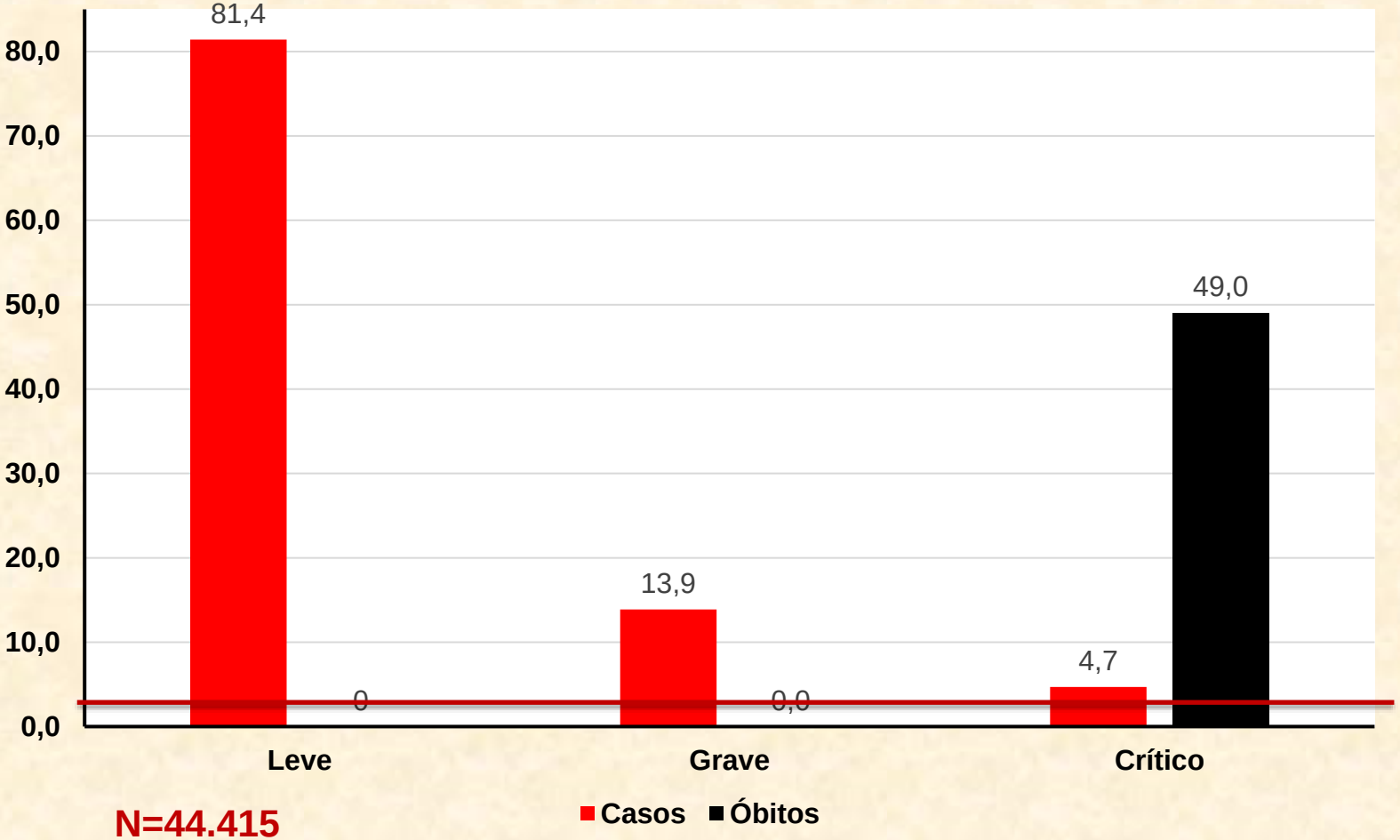
Complicações

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

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

Adaptado: [1]Huang C, Lancet - 24 Jan 2020 [2]Chen N, Lancet – 15 Feb 2020 [3]Wang D, JAMA 07 Feb 2020

Gravidade x letalidade (%)*



N=44.415

Óbitos=1,023

CFR=2,3%

*Até 11 Feb 2020

China CDC Weekly, 21 Feb 2020

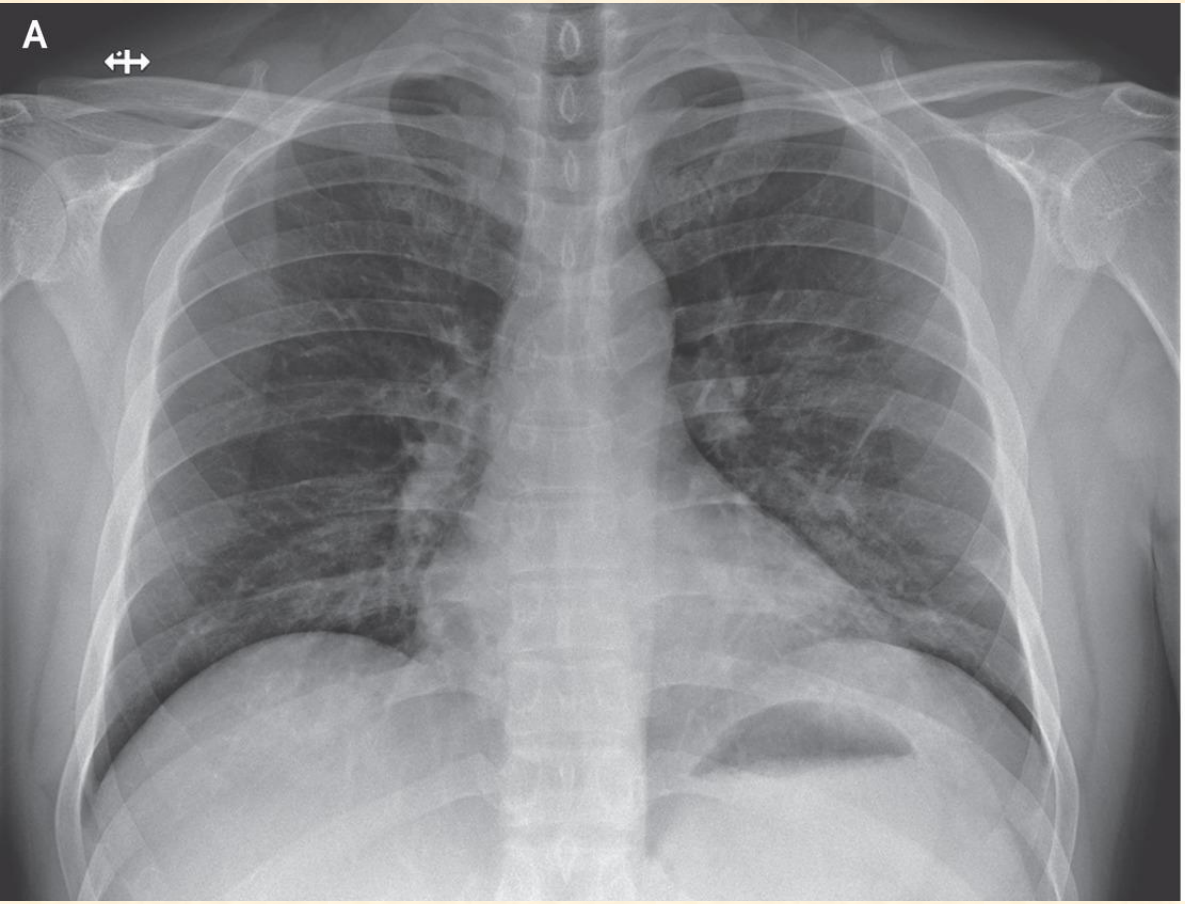
http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51

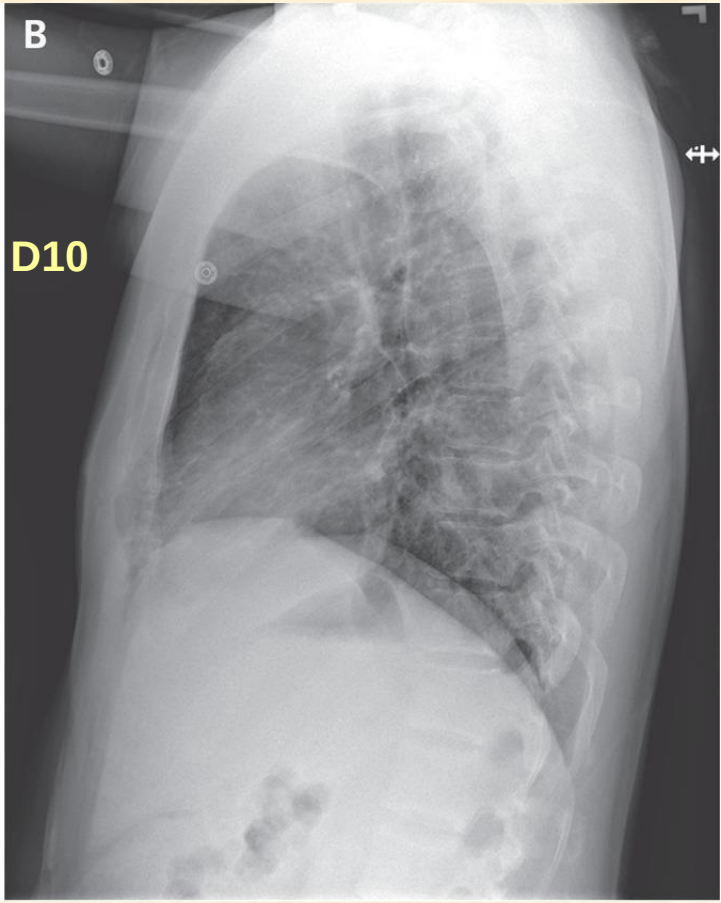
Radiologia (Rx e TC)

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

Adaptado de Chen N, Lancet 2020

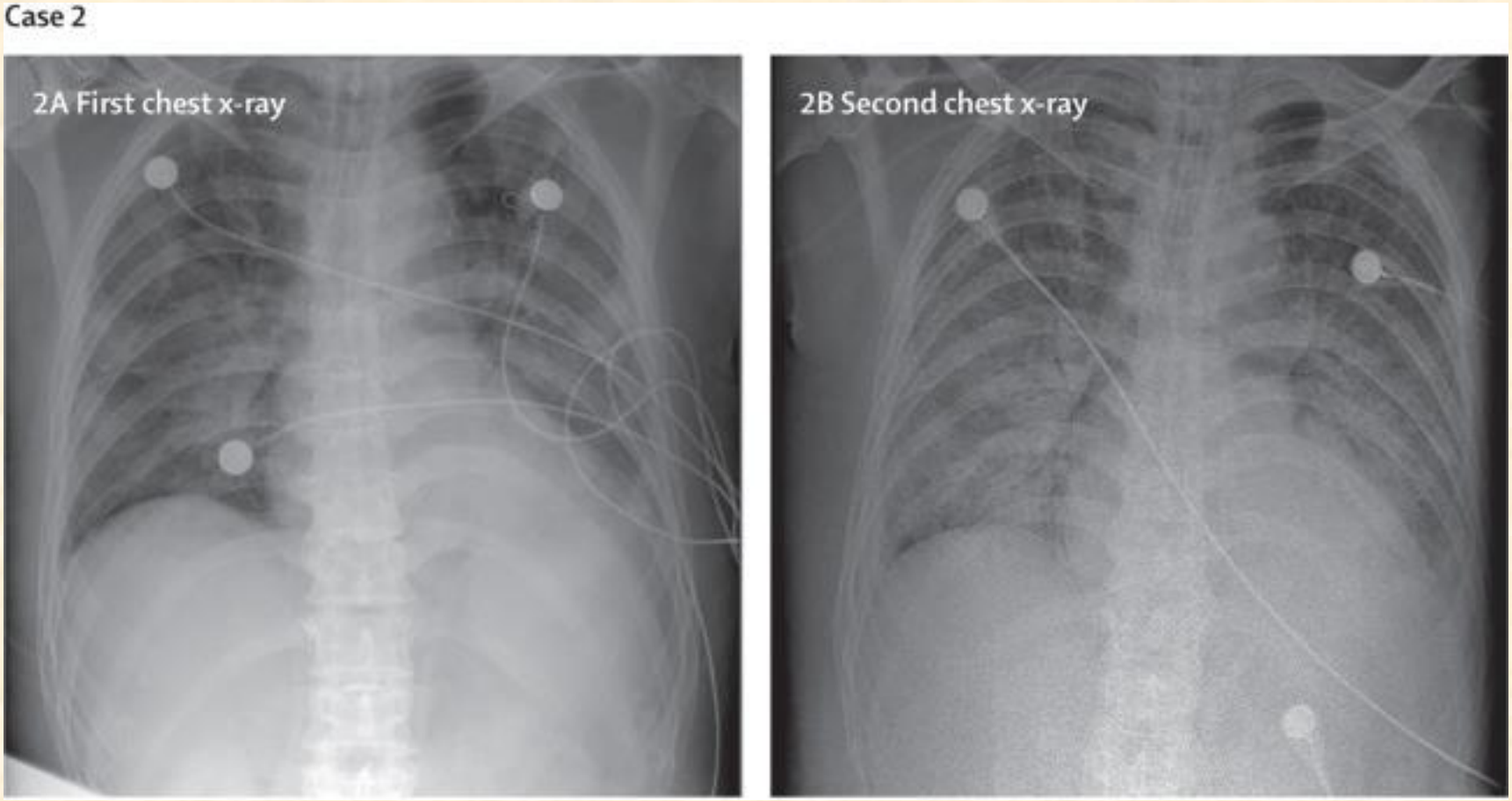
Radiologia





Holshue ML, New Engl J Med 2020

Radiologia

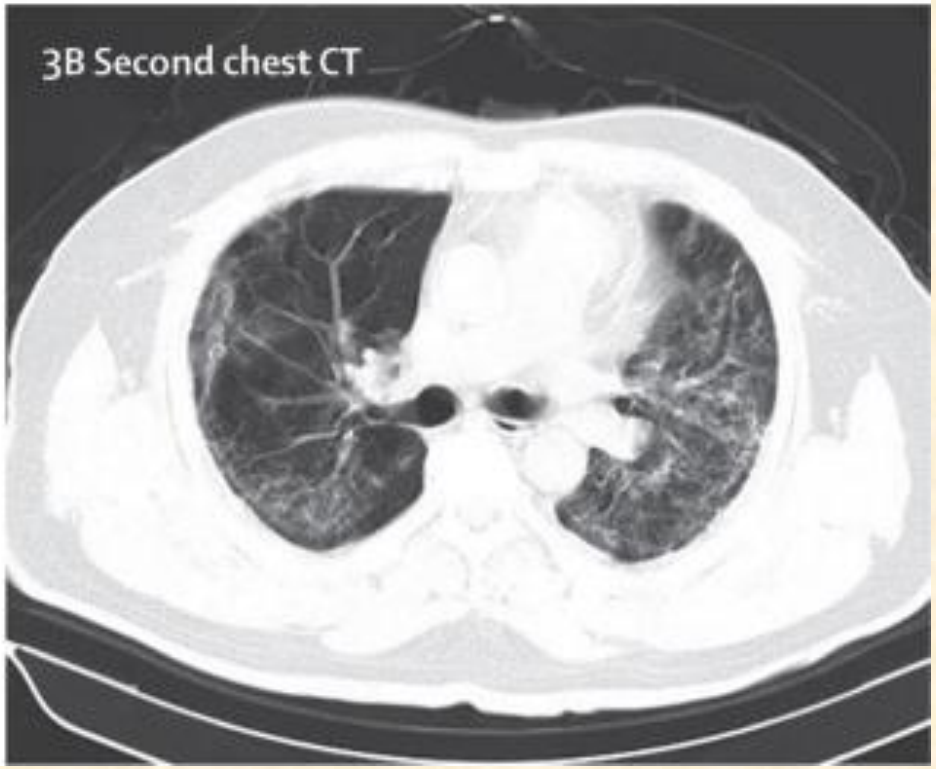


06/Jan/2020 **10/Jan/2020**

Chen N, Lancet 2020

Radiologia

Case 3



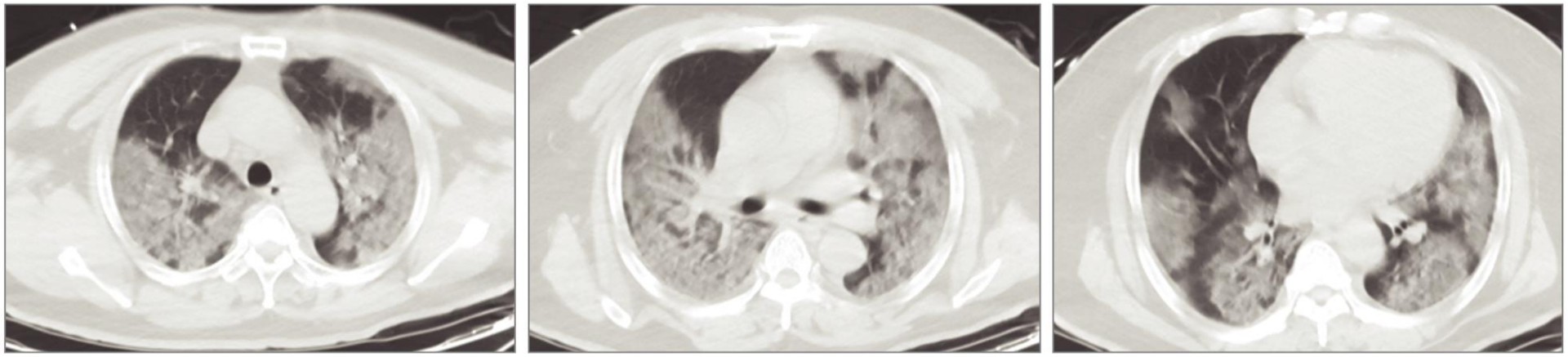
01/Jan/2020

15/Jan/2020

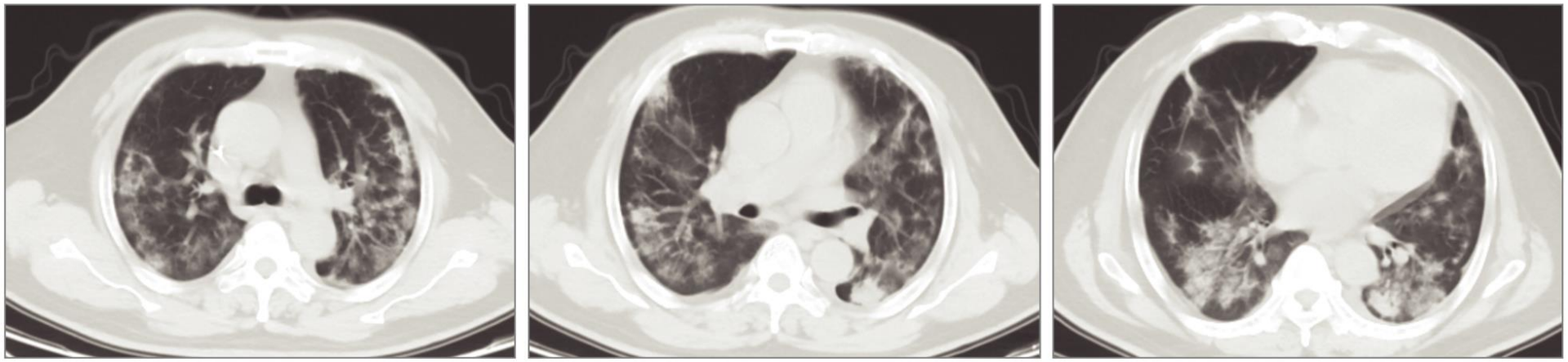
Chen N, Lancet 2020

Evolução radiológica

A Computed tomography images on day 5 after symptom onset **D5**

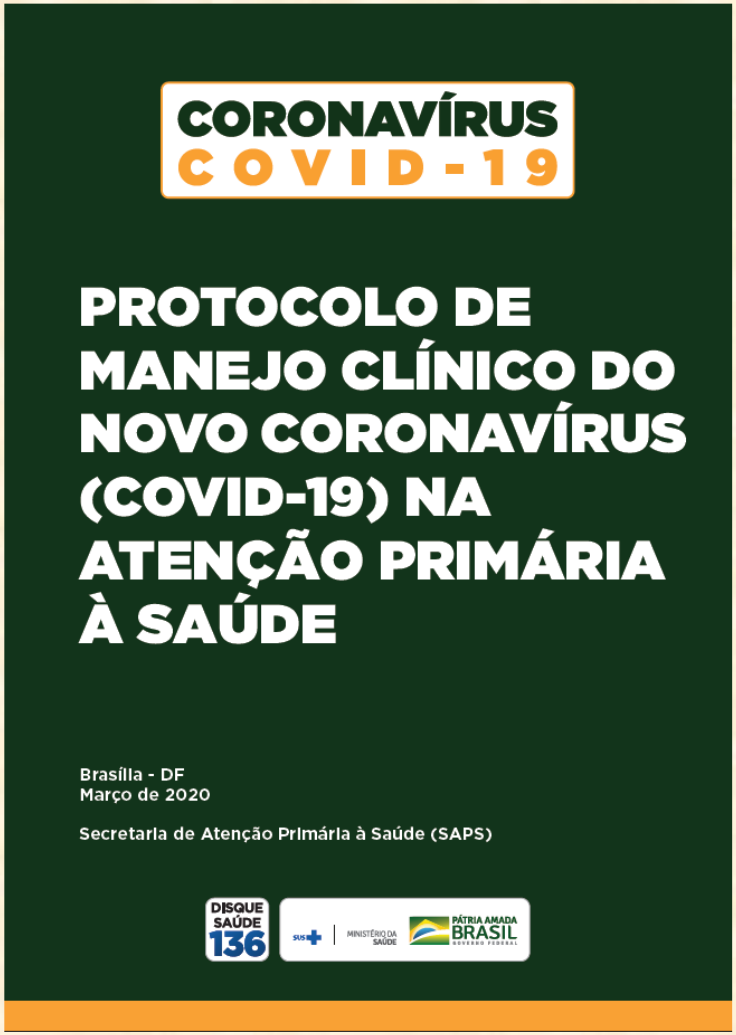


B Computed tomography images after treatment on day 19 after symptom onset **D19**



Wang D, JAMA 2020

Manejo COVID-19

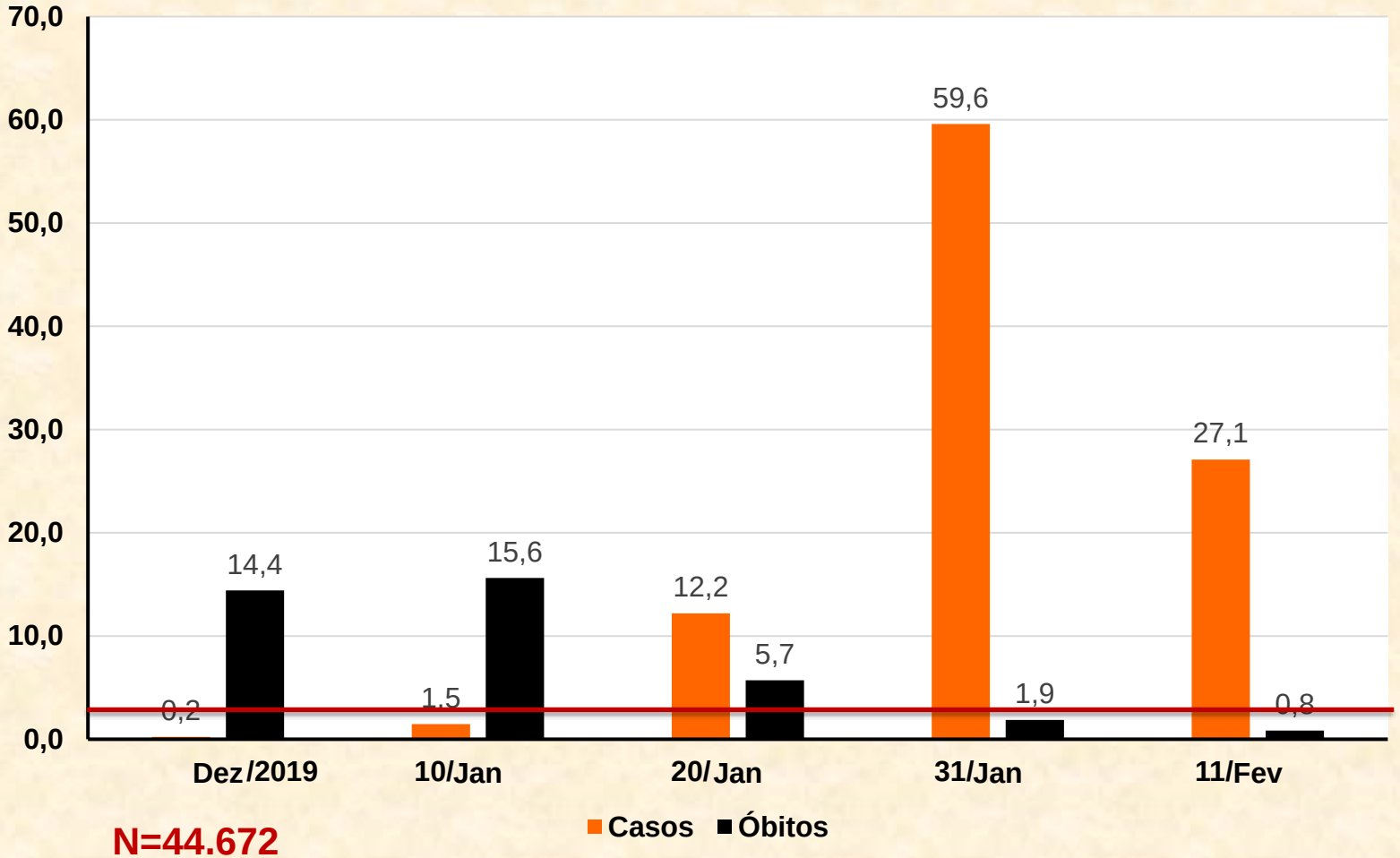


Brasil, Protocolo de manejo clínico da COVID-19 na APS – 18 Mar 2020

Fases da resposta

FASES DE RESPOSTA	MODELO DE VIGILÂNCIA	AÇÕES POR TIPO DE TRANSMISSÃO	
		Local	Comunitária
CONTENÇÃO limitar a transmissão do vírus	Identificação de casos relacionados a viagem ou contato próximo e domiciliar	Notificar FORMSUS2 e Coletar para RT-PCR	NA
	Identificação de casos na comunidade	SG (Casos negativos) e SRAG (todos) para RT-PCR	NA
MITIGAÇÃO evitar casos graves e óbitos	Vigilância Sentinela de Síndrome Gripal	NA	Notificar SIVEP-GRIPE e Coletar
	Vigilância Universal de Síndrome Respiratória Grave	NA	Notificar SIVEP-GRIPE e Coletar

Início COVID-19 x letalidade (%)*



N=44.672

Óbitos=1,023

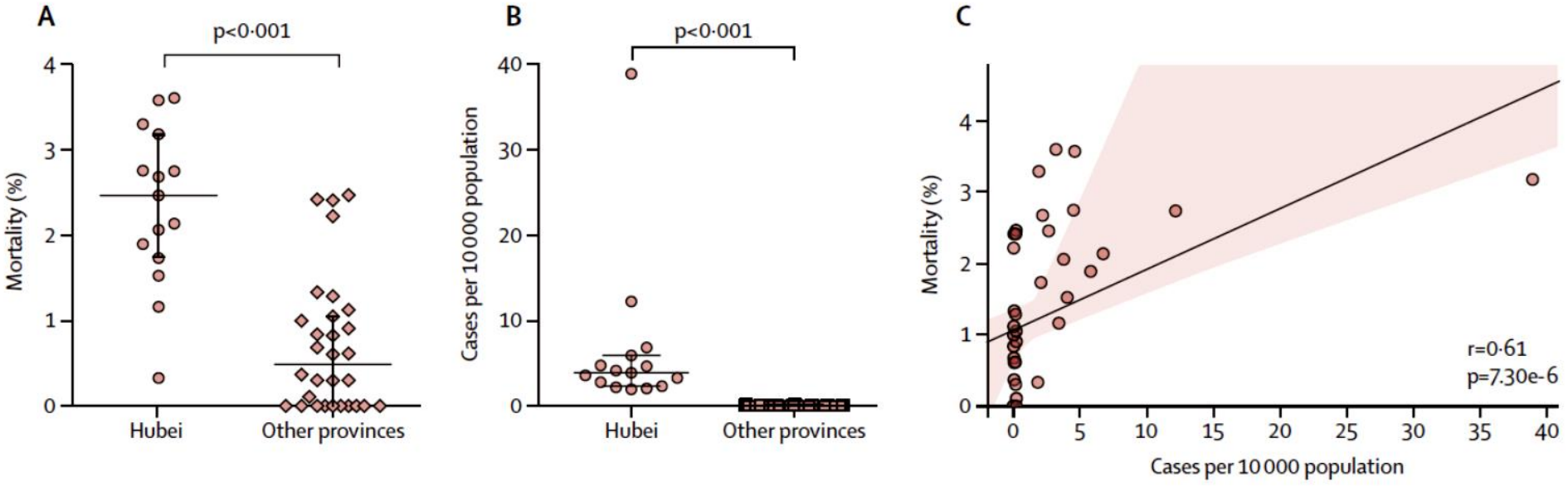
CFR=2,3%

*Até 11 Feb 2020

China CDC Weekly, 21 Feb 2020

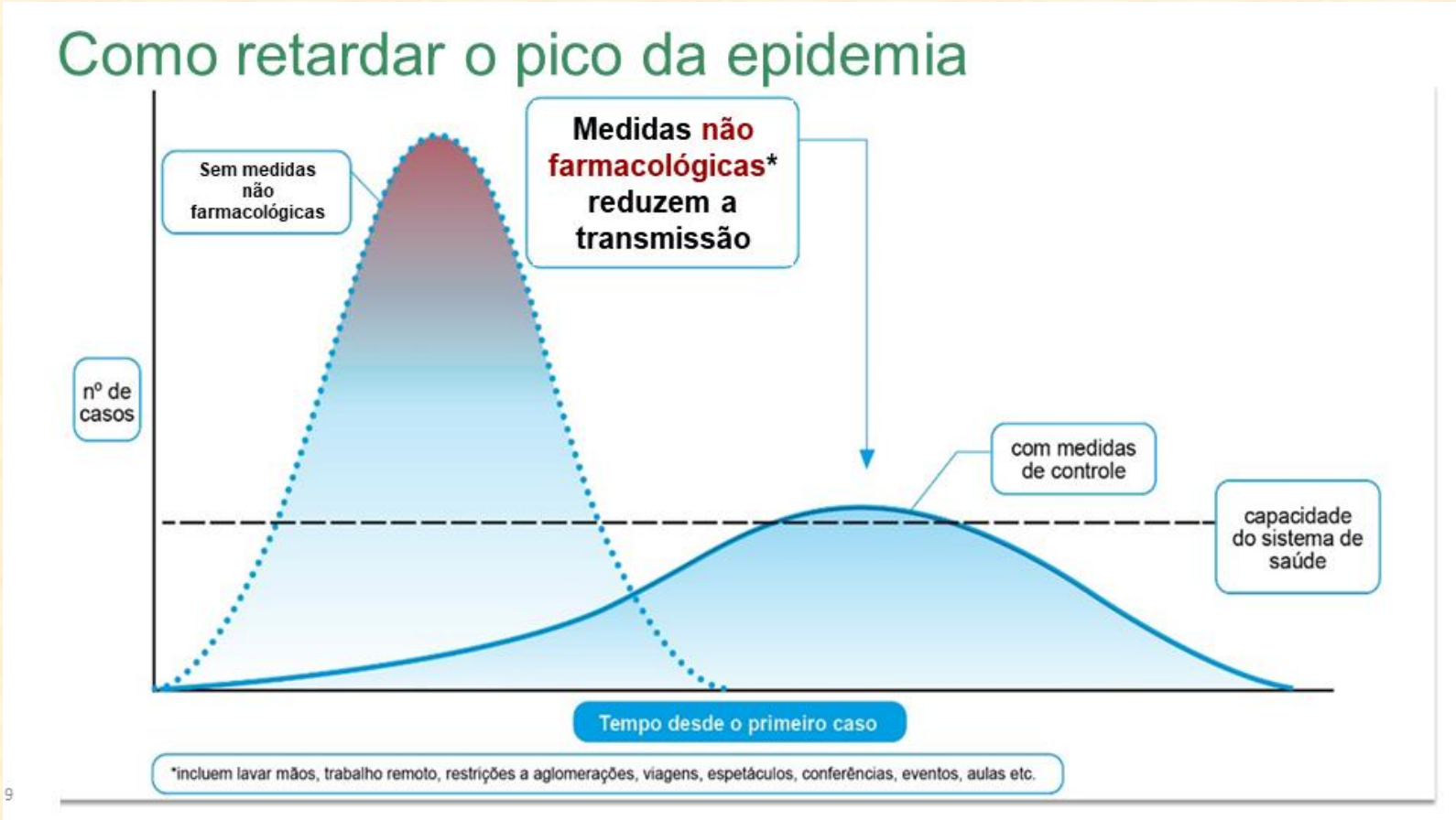
http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51

Recursos saúde x letalidade



Ji Y, Lancet Glob Health – 25 Feb 2020

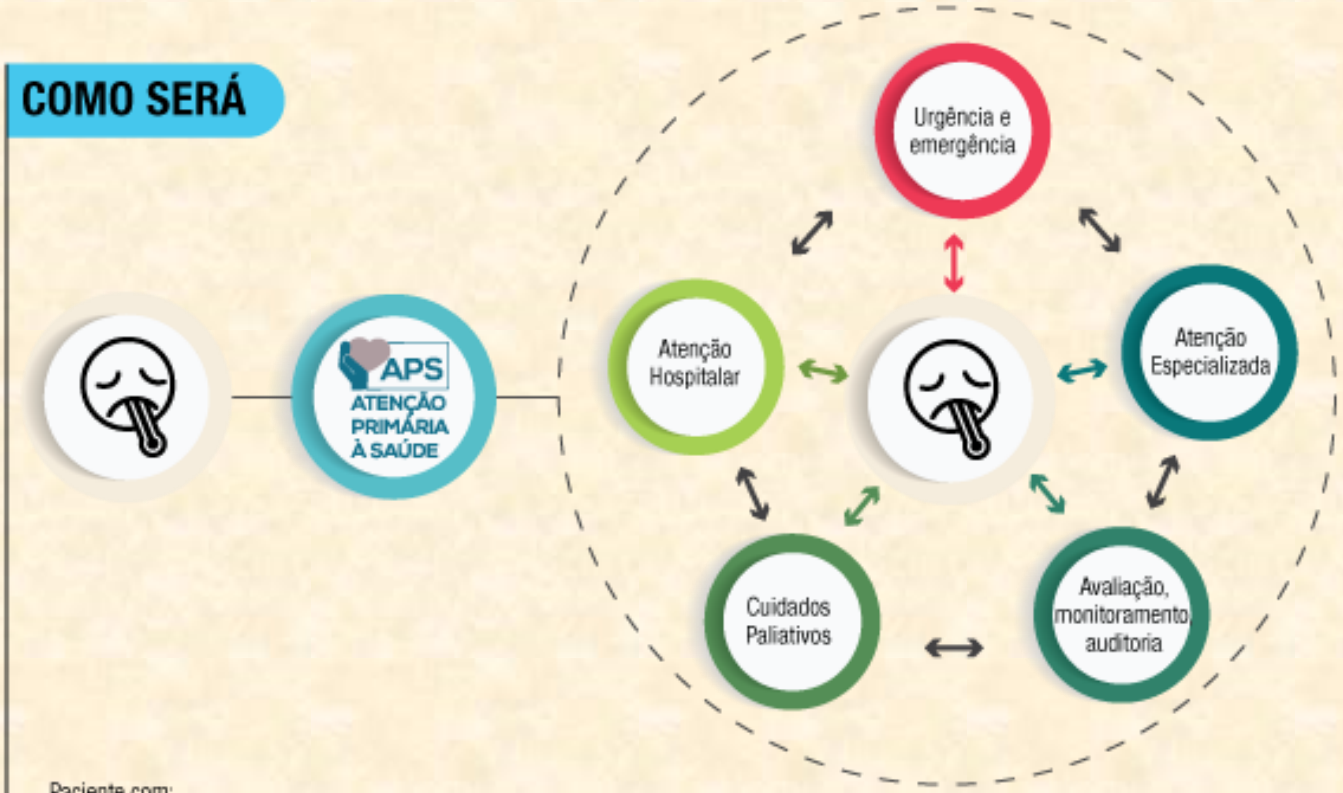
Mitigação


Como retardar o pico da epidemia
Sem medidas não farmacológicas
Medidas não farmacológicas* reduzem a transmissão
nº de casos
com medidas de controle
capacidade do sistema de saúde
Tempo desde o primeiro caso
*incluem lavar mãos, trabalho remoto, restrições a aglomerações, viagens, espetáculos, conferências, eventos, aulas etc.

Mitigação

- Medidas de educação
  - ✓Isolamento de sintomáticos
  - ✓Etiqueta respiratória
  - ✓Medidas de higiene
- Medidas não-farmacológicas
  - ✓Distanciamento social
  - ✓Redução mobilidade

Papel dos serviços de APS/ESF



http://www.ans.gov.br/aans/noticias-ans/qualidade-da-saude/4422-ans-lanca-projeto-para-estimular-atencao-primaria-em-saude

Abordagem sindrômica

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

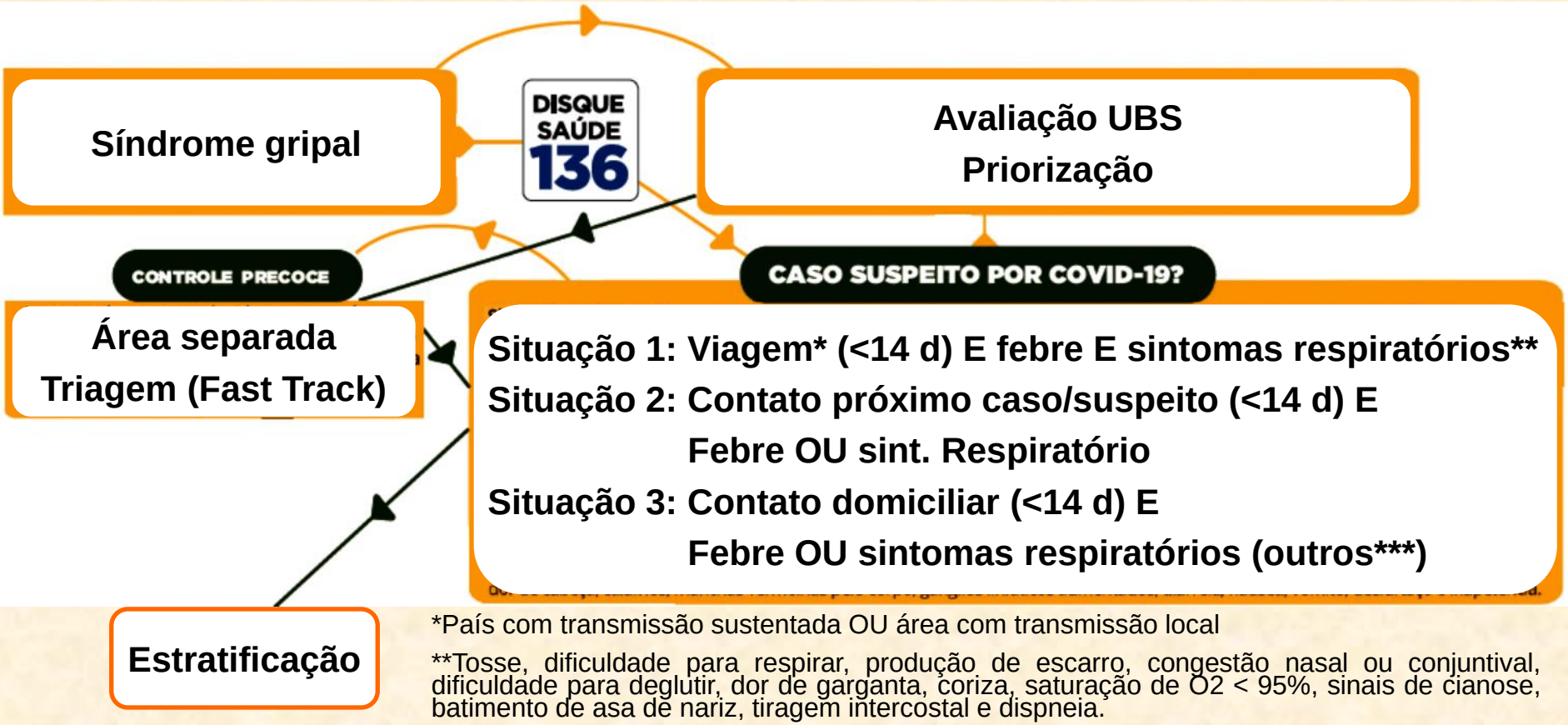
Adaptado de CDC, Cold Versus Flu (acesso 19 Mar 2020)
https://www.cdc.gov/flu/symptoms/coldflu.htm

Manejo APS

- Caso suspeito
- Precaução e controle de infecção
- Classificação e estratificação
  - ✓Leves: manejo e isolamento domiciliar
  - ✓Graves: estabilização/encaminhamento
- Notificação
- Monitoramento clínico
- Prevenção comunitária/vigilância ativa

Brasil, Protocolo de manejo clínico da COVID-19 na APS – 18 Mar 2020

Caso suspeito



*País com transmissão sustentada OU área com transmissão local

**Tosse, dificuldade para respirar, produção de escarro, congestão nasal ou conjuntival, dificuldade para deglutir, dor de garganta, coriza, saturação de O2 < 95%, sinais de cianose, batimento de asa de nariz, tiragem intercostal e dispneia.

***Fadiga, mialgia/artralgia, dor de cabeça, calafrios, manchas vermelhas pelo corpo, gânglios linfáticos aumentados, diarreia, náusea, vômito, desidratação e inapetência.

Brasil, Protocolo de manejo clínico da COVID-19 na APS – 18 Mar 2020

Contato próximo

- Contato direto (físico)
- Contato secreções
- Contato frontal (<2m / >15min)
- Ambiente fechado (<2m / >15min)
- Cuidado de saúde sem EPI
- Passageiro aeronave (2 assentos)

Contato domiciliar

- Residir mesma casa/ambiente.
- Colegas de dormitório
- Creche
- Alojamento

Estratificação

Estratificação da Gravidade e Manejo Clínico

APS/ESF

SG

Sem comorbidade descomp.

Centro Ref. / Atenção especializada

SG + Dispneia ou

- Sat. O2 < 95%
- Desconforto/taquipneia
- Descompensação doença de base
- Hipotensão
- Insuficiência respiratória aguda

ou

Comorbidade descompensada

- Cardiopatia
- Pneumopatia crônica
- Doença renal crônica
- Imunossuprimidos
- Doenças genéticas
- Gestantes

NOTIFICAÇÃO IMEDIATA

Via formulário pelo Formsus2.saude.gov.br/ http://bit.ly/2019-ncov

Manejo APS

SRAG

Brasil, Protocolo de manejo clínico da COVID-19 na APS – 18 Mar 2020

Manejo

SÍNDROME GRIPAL - INDICAÇÃO DE ISOLAMENTO DOMICILIAR

Manejo clínico APS

Monitoramento: visita ou telefone

Farmacológicas

Oseltamivir (SG+risco)

Situação vacinal

Clínicas

Revisão (48h)

Alimentação/hidratação

Isolamento

Cuidados domésticos

- **Acompanhamento equipe de saúde**
- **Medidas de isolamento**

Atestado médico (família)

Monitoramento por telefone a cada 48 horas até o fim do período de isolamento domiciliar

DESFECHO

Diagnóstico

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

Diagnóstico

Aspirado nasofaríngeo

Fonte: BRASIL,2014

Swab nasal

Swab oral

Fonte: BRASIL,2014.

Tratamento

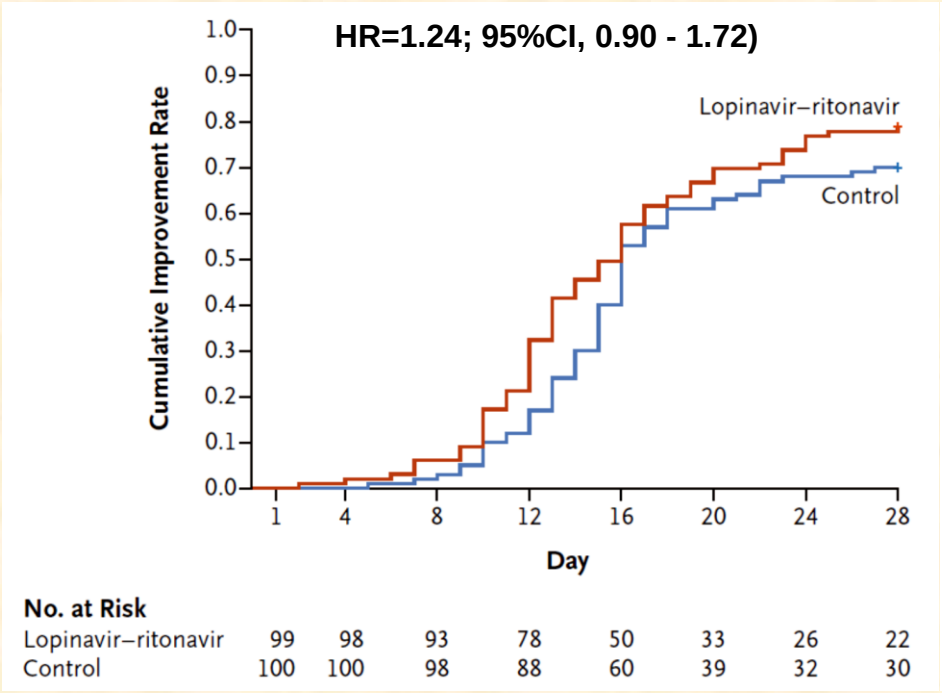
- Suporte
  - ✓Ventilatório
  - ✓Circulatório
  - ✓Extracorpórea
- Balanço de líquidos
- Corticoides?
- Anti-inflamatórios?
- Antivirais?

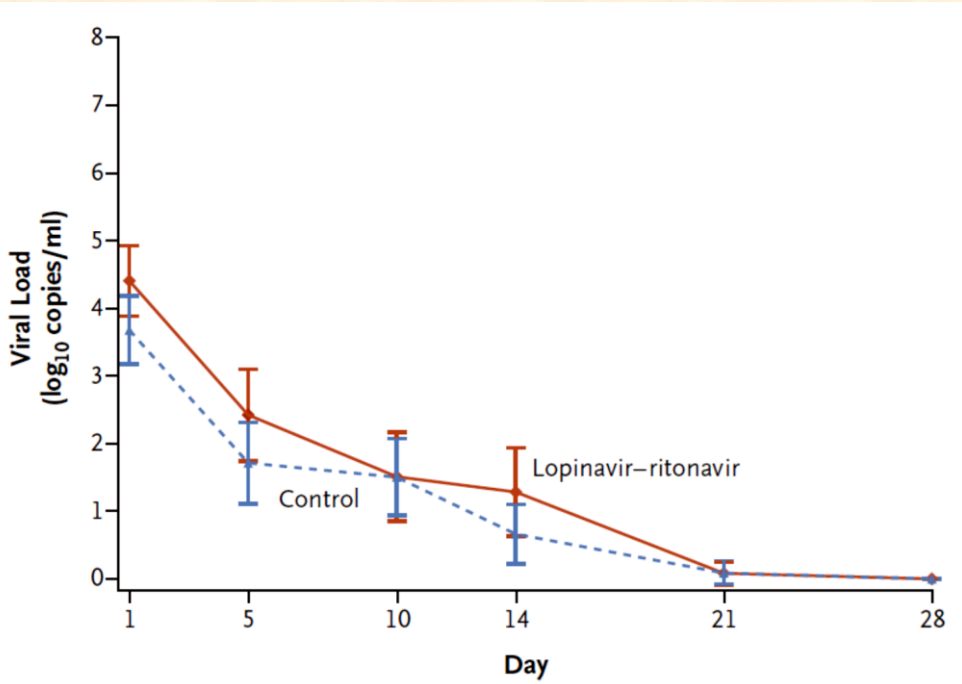
Tratamento

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

Adaptado: [1]Huang C, Lancet - 24 Jan 2020 [2]Chen N, Lancet – 15 Feb 2020 [3]Wang D, JAMA 07 Feb 2020

Lopinavir-r x SOC





	Mortalidade (D28)	Diferença
Lopinavir/r = 99	19,2%	- 5.8 % (95% CI, −17.3 to 5.7)
SOC = 100	25%	

Cao B, New Eng J Med – 18 Mar 2020

Cloroquina

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

Gao J, Biosci Trends – 19 Feb 2020

Remdesivir e cloroquina

Cell Research

www.nature.com/cr
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.[1] 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 sever acute respiratory syndrome CoV (SARS-CoV).[2] 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 μM,[4] 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 ($EC_{50} = 22.50$ μM, $CC_{50} > 100$ μM, $SI > 4.44$). 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 ($EC_{50} = 2.12$ μM; $CC_{50} > 35.53$ μM; $SI > 16.76$). Further in vivo evaluation of this drug against 2019-nCoV infection is recommended. Notably, two compounds remdesivir ($EC_{50} = 0.77$ μM; $CC_{50} > 100$ μM; $SI > 129.87$) and chloroquine ($EC_{50} = 1.13$ μM; $CC_{50} > 100$ μM, $SI > 88.50$) potently blocked virus infection at low-micromolar concentration and showed high SI

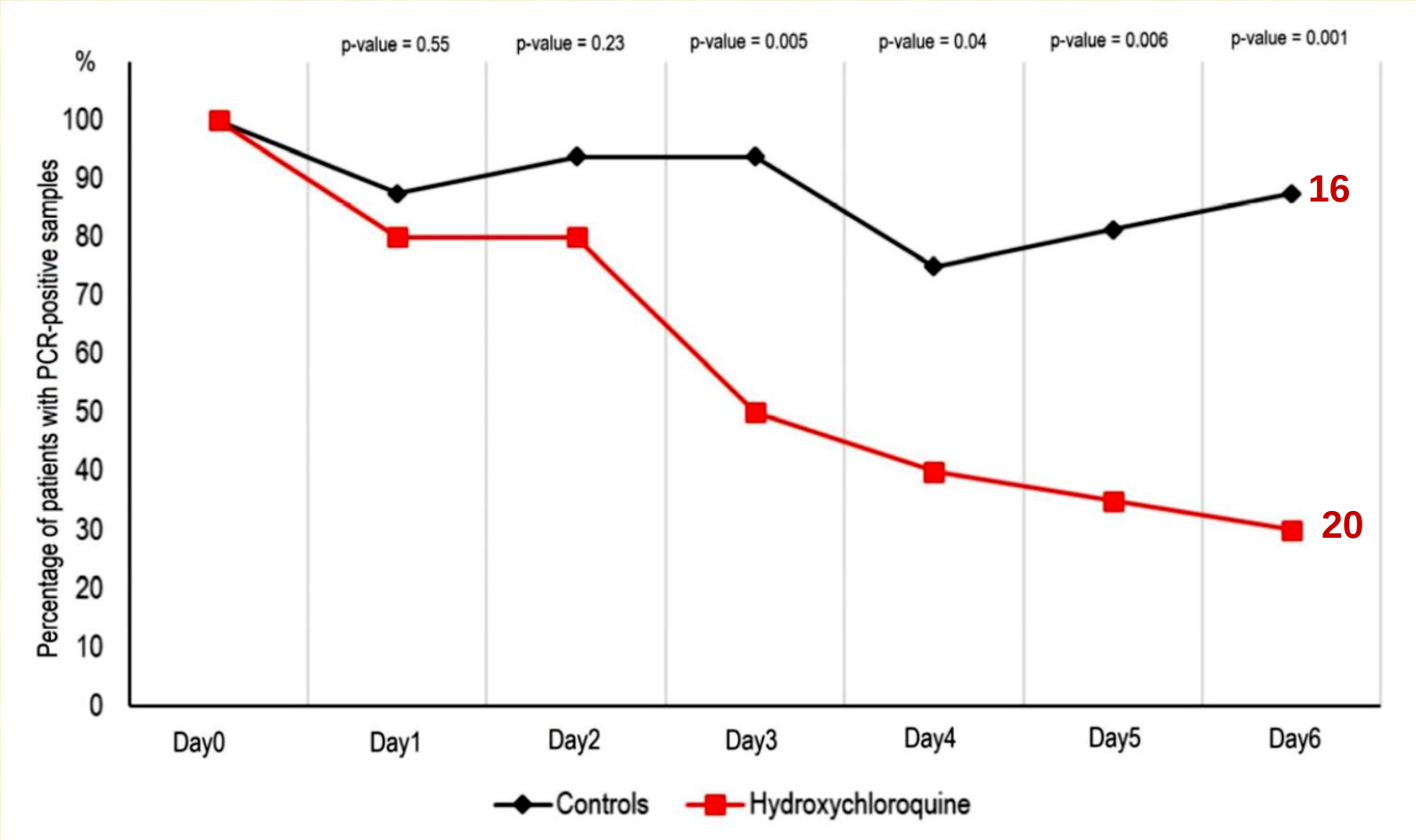
Wang M, Cell Res – 4 Feb 2020

Hidroxicloroquina e Azitromicina

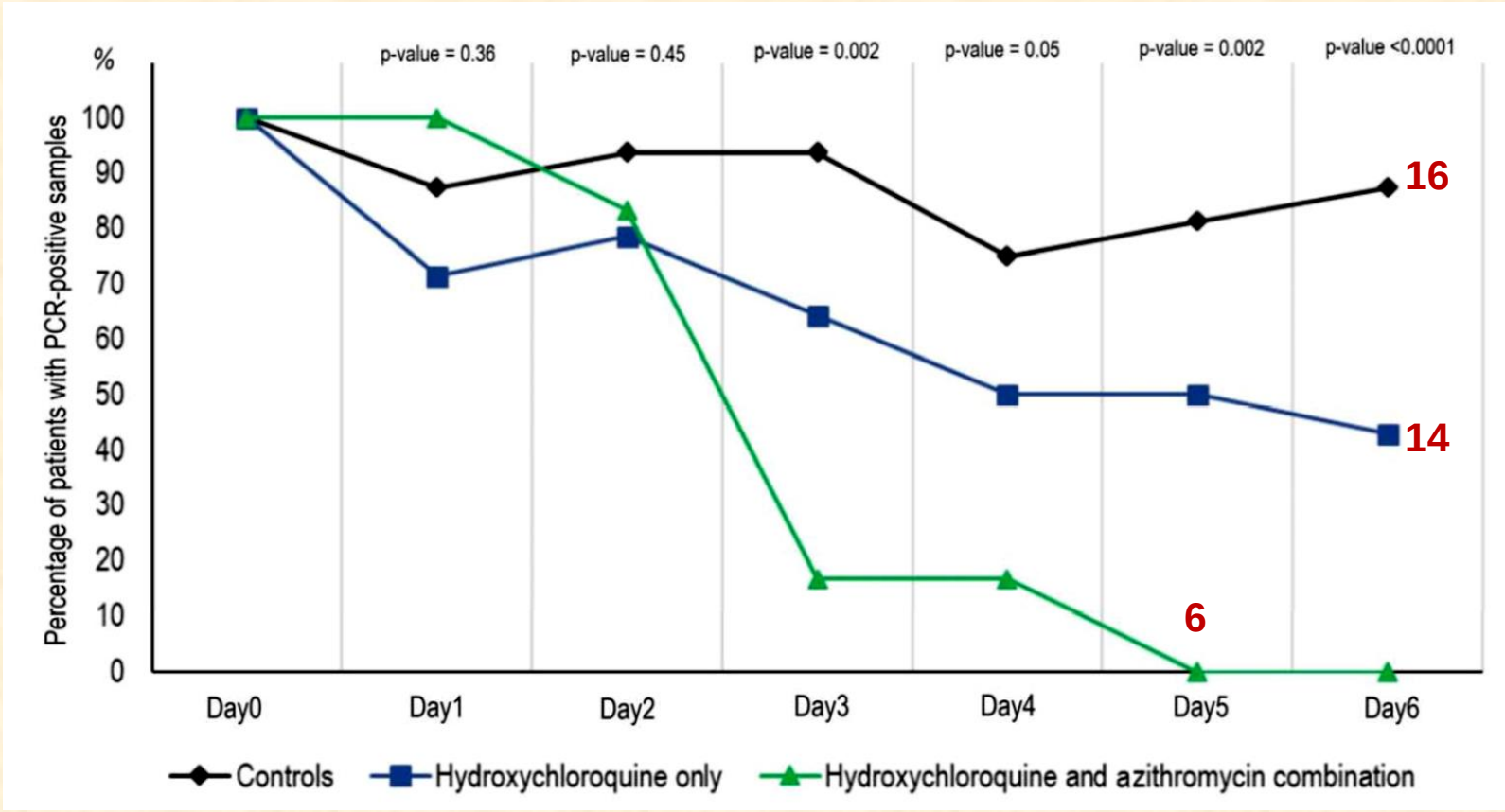
	HCQ	Controle	Total	*p*
N	20	16	36	-
Azitromicina	6	-	6	-
Idade (anos)	51.2 ± 18.7	37.3 ± 24.0	45.1 ± 22.0	0.06
Masc (%)	9 (45.0)	6 (37.5)	15 (41.7)	0.65
T. Início	4.1 ± 2.6	3.9 ± 2.8	4.0 ± 2.6	0.88
Clínico				0.30
Assintomático	2 (10,0)	4 (25.0)	6 (16.7)	-
TR alto	12 (60.0)	10 (62.5)	22 (61.1)	-
TR baixo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

Adaptado de Gautret P, Int J Antimicrob Agents – 17 Mar 2020

Hidroxicloroquina



Hidroxicloroquina



Gautret P, Int J Antimicrob Agents – 17 Mar 2020

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[7]	Adjusted hazard ratio 0·4 (95% CI 0·2–0·7)
SARS-CoV	Delayed clearance of viral RNA from blood[5]	Significant difference but effect size not quantified
SARS-CoV	Complication: psychosis[6]	Associated with higher cumulative dose, 10 975 mg *vs* 6780 mg hydrocortisone equivalent
SARS-CoV	Complication: diabetes[7]	33 (35%) of 95 patients treated with corticosteroid developed corticosteroid-induced diabetes
SARS-CoV	Complication: avascular necrosis in survivors[8]	Among 40 patients who survived after corticosteroid treatment, 12 (30%) had avascular necrosis and 30 (75%) had osteoporosis
Influenza	Increased mortality[9]	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[10,11]	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**

Russel CD, Lancet – 15 Feb 2020

“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