

**SENADO FEDERAL**Secretaria-Geral da Mesa
Secretaria de Comissões

Coordenação de Comissões Especiais, Temporárias e Parlamentares de Inquérito

Ofício nº 2081/2021 - CPIPANDEMIA

Brasília, 5 de agosto de 2021

A Sua Excelência o Senhor
Marcelo Queiroga
Ministro de Estado da SaúdeAssunto: **Solicitação de informações – Requerimento nº 1155/2021-CPIPANDEMIA**

Senhor Ministro,

No intuito de instruir os trabalhos da Comissão Parlamentar de Inquérito, criada pelos Requerimentos do Senado Federal nº 1371 e 1372, de 2021, para “apurar as ações e omissões do Governo Federal no enfrentamento da Pandemia da Covid-19 no Brasil; as possíveis irregularidades, bem como outras ações ou omissões cometidas por administradores públicos federais, estaduais e municipais, no trato com a coisa pública, limitado apenas quanto à fiscalização dos recursos da União repassados aos demais entes federados para as ações de prevenção e combate à Pandemia da Covid-19”, e com fulcro no art. 148 do Regimento Interno do Senado Federal, e no art. 2º da Lei nº 1.579, de 1952, encaminho a V.Ex.a o Requerimento aprovado nº 1155/2021 – CPIPANDEMIA, em anexo, para atendimento.

Solicito que a documentação seja encaminhada no prazo de 10 (dez) dias, em meio magnético, para o endereço eletrônico sec.cpipandemia@senado.leg.br. Caso haja algum problema no envio em virtude do tamanho dos arquivos, favor contatar a Secretaria da CPI no telefone do rodapé deste ofício para que seja disponibilizado *link* para envio da documentação.

Ainda, tendo em vista o princípio da publicidade da administração pública consagrado pelo art. 37 da Constituição Federal, solicito que, no caso de a documentação envolver informações resguardadas por sigilo legal, seja informado expressamente no



**SENADO FEDERAL**

Secretaria-Geral da Mesa
Secretaria de Comissões

Coordenação de Comissões Especiais, Temporárias e Parlamentares de Inquérito
encaminhamento da resposta ao presente expediente, indicando a fundamentação legal do
alegado sigilo.

Atenciosamente,

Senador Omar Aziz
Presidente da CPI Pandemia





SENADO FEDERAL
CPI DA PANDEMIA (Criada pelo RQS nº 1371/2021 e RQS nº 1372/2021)

REQUERIMENTO Nº DE - CPIPANDEMIA

Requer que sejam prestadas, pelo Senhor Ministro de Estado de Saúde, Marcelo Queiroga, informações sobre estudos realizados no começo da pandemia do coronavírus por este Ministério, no prazo máximo de 10 dias.

Senhor Presidente,

Requeiro, nos termos do art. 58, § 3º, da Constituição Federal, do art. 2º da Lei nº 1579 de 1952 e do art. 148 do Regimento Interno do Senado Federal, que sejam prestadas, pelo Senhor Ministro de Estado de Saúde, Marcelo Queiroga, informações sobre estudos realizados no começo da pandemia do coronavírus por este Ministério, no prazo máximo de 10 dias.

Nesses termos, requisita-se:

1. Projeção de número de mortos elaborada pelo então Secretário Gabbardo ao então Ministro Mandetta acerca de um cenário otimista de desenvolvimento da pandemia, bem como todo o documento apresentado;
2. Projeção de número de mortos elaborada pelo então Secretário Wanderson ao então Ministro Mandetta acerca de um cenário realista de desenvolvimento da pandemia, bem como todo o documento apresentado;
3. Projeção de número de mortos elaborada pelo infectologista Julio Croda ao então Ministro Mandetta acerca de um cenário

pessimista de desenvolvimento da pandemia, bem como todo o documento apresentado;

JUSTIFICAÇÃO

A presente Comissão Parlamentar de Inquérito, batizada como CPI DA PANDEMIA, foi criada pelos Requerimentos 1371 e 1372, ambos de 2021, com a finalidade de *apurar, no prazo de 90 dias, as ações e omissões do Governo Federal no enfrentamento da Pandemia da Covid-19 no Brasil e, em especial, no agravamento da crise sanitária no Amazonas com a ausência de oxigênio para os pacientes internados; e as possíveis irregularidades em contratos, fraudes em licitações, superfaturamentos, desvio de recursos públicos, assinatura de contratos com empresas de fachada para prestação de serviços genéricos ou fictícios, entre outros ilícitos, se valendo para isso de recursos originados da União Federal, bem como outras ações ou omissões cometidas por administradores públicos federais, estaduais e municipais, no trato com a coisa pública, durante a vigência da calamidade originada pela Pandemia do Coronavírus "SARS-CoV-2", limitado apenas quanto à fiscalização dos recursos da União repassados aos demais entes federados para as ações de prevenção e combate à Pandemia da Covid-19, e excluindo as matérias de competência constitucional atribuídas aos Estados, Distrito Federal e Municípios.*

Em audiência nesta Comissão Parlamentar de Inquérito no dia 04/05/2021, o ex Ministro Luiz Henrique Mandetta declarou que solicitou enquanto Ministro no começo da pandemia a confecção de três cenários possíveis de desenvolvimento da pandemia, em resposta ao Senador Relator Renan Calheiros:

12:24 O SR. RENAN CALHEIROS (Bloco Parlamentar Unidos pelo Brasil/MDB - AL) – Mil novecentos e cinquenta e duas, menos de duas mil.

Quais foram os fundamentos utilizados para chegar nesse número de 180 mil? Qual foi a reação do Presidente diante da sua estimativa? Que

providências ele lhe pediu que fossem tomadas para evitar que esse cenário se concretizasse? Que soluções foram apresentadas ao Presidente? Desculpe ter acumulado essas perguntas todas, mas porque, como elas têm a ver uma com as outras, se V. Sa. pudesse respondê-las de uma só vez, seria mais interessante.

O SR. LUIZ HENRIQUE MANDETTA – Os cenários não são projetos de adivinhação. Tem pessoas que acham que isso é uma coisa, é um chute; isso tem uma técnica, isso tem uma ciência para se fazer. Então, como ele tem variáveis, eu constituí três, pedi três cenários: me dê um cenário otimista, um cenário otimista imaginando que o Brasil fosse uma ilha, como a Nova Zelândia, que a gente tivesse um colchão social, que a gente tivesse condição de fechar, enfim...

Coloquei ao então Secretário Gabbardo e falei: "Me faça o cenário mais otimista de todos. Que tudo dê certo, que todo mundo faça, que nós tenhamos aquela disciplina oriental e que nós tenhamos todos os nossos passos acertados". Eles estimaram... E falei: "O cenário é até 31 de dezembro de 2020; não vamos ultrapassá-lo para 2021". Então, lá do Gabardo, veio um cenário de 30 a 40 mil óbitos.

Ao Secretário Wanderson eu disse: "Me traga o realista, com as dificuldades do Brasil, com as dificuldades de distanciamento, com as dificuldades de nosso mundo ocidental, que é a mesma que você tem na Itália, que você tem nos Estados Unidos, no mundo ocidental, esse nosso direito de ir e vir, as conquistas, o brasileiro com toda a sua característica de abraço, de beijo, de vínculo familiar, de almoço, enfim, essa nossa mistura maravilhosa, mas, assim, com a gente enfrentando, cada um fazendo a sua parte dentro do máximo das suas possibilidades". O Secretário Wanderson me trouxe um cenário que seria de 80 a 90 mil óbitos.

E ao infectologista Julio Croda: "Me dê o cenário se nós formos... Se não fizermos a testagem, não conseguirmos, não tivermos uma performance

técnica e se a nossa questão social falar mais alto e se for muito complexo, com o que vocês sabem do vírus, sem que a gente consiga interromper nada". Ele me deu, até 31 de dezembro, 180 mil óbitos.

Eu levei, expliquei; 180 mil óbitos, para quem tinha na época menos de mil, era um número muito difícil de você fazer uma assertiva dessa. Eu acho que ali ficou dúvida, porque tinha ex-secretários de saúde, Parlamentares que falavam publicamente: "Olha, essa doença não vai ter 2 mil mortos; essa doença vai durar de quatro a seis semanas". Havia uma construção também de pessoas que falavam absolutamente o contrário. E eu acho que, naquele momento, o Presidente entendeu que aquelas outras previsões poderiam ser mais apropriadas para aquele momento. E foi nesse dia mesmo que eu entreguei essa carta para ele explicando essas situações.

Um dos eixos de investigação desta CPI diz respeito à escolha do Governo Federal por uma vida de imunidade de rebanho da população para o enfrentamento da pandemia..

A aprovação do presente requerimento é fundamental ao esclarecimento dos fatos investigados por esta CPI, razão pela qual pedimos o apoio dos nobres pares.

Sala da Comissão, 29 de julho de 2021.

**Senador Humberto Costa
(PT - PE)**



Ministério da Saúde
Gabinete do Ministro
Assessoria Parlamentar

DESPACHO

ASPAR/GM/MS

Brasília, 25 de agosto de 2021.

Ao Gabinete do Ministro

Assunto: **Requerimento do Senado Federal nº 1155/2021 - CIPANDEMIA.**

1. Trata-se do **Ofício n.º 2081/2021** (0022094529), da **Comissão Parlamentar de Inquérito da Pandemia - CIPANDEMIA**, do **Senado Federal**, que encaminha o **Requerimento do Senado Federal n.º 1155/2021** (0022094711), de autoria do Senador **Humberto Costa**, por meio do qual requer que o Ministério da Saúde forneça **informações sobre estudos realizados no começo da pandemia do coronavírus.**
2. Em resposta, encaminho **por meio de endereço eletrônico de serviço de armazenamento de arquivos disponibilizado por essa Comissão,** para ciência e atendimento à solicitação do referido Requerimento, o **Despacho SVS/NUJUR/SVS/MS** (0022321235) e a **Nota Técnica n.º 1019/2021 CGPNI/DEIDT/SVS/MS** (0022276368), elaborados pela **Secretaria de Vigilância em Saúde - SVS/MS,** acompanhados dos anexos **Artigo Expected impact of COVID-19 outbreak in a major metropolitan area in Brazil** (0022257042), **Monitoring social distancing and SARS-CoV-2 transmission in Brazil using cell phone mobility data** (0022257046), **The impact of early social distancing at COVID-19 Outbreak in the largest Metropolitan Area of Brazil** (0022257054), **Nota** (0022257059), **Apresentação Análise de risco e impacto estimado no Brasil** (0022257072), **Apresentação Doença pelo Coronavírus 2019** (0022257077) e **Projeções** (0022305629).

PAULO TIAGO ALMEIDA MIRANDA

Chefe da Assessoria Parlamentar, substituto



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Referência: Processo nº 25000.119593/2021-41

SEI nº 0022399584



Ministério da Saúde
Gabinete do Ministro
Assessoria Parlamentar

OFÍCIO Nº 5839/2021/ASPAR/GM/MS

Brasília, 25 de agosto de 2021.

A Sua Excelência o Senhor

Senador **OMAR AZIZ**

Presidente da Comissão Parlamentar de Inquérito da Pandemia - CPIPANDEMIA
Senado Federal

Praça dos Três Poderes, Anexo II, Ala Alexandre Costa, sala 15 - Subsolo
CEP 70.165-900 - Brasília/DF

Assunto: **Requerimento do Senado Federal nº 1155/2021 - CPIPANDEMIA.**

Senhor Presidente,

Em resposta ao Ofício n.º **2081/2021** (0022094529), **dessa Comissão Parlamentar de Inquérito da Pandemia - CPIPANDEMIA**, de 05 de agosto de 2021, referente ao Requerimento do Senado Federal n.º 1155/2021 (0022094711), de autoria do Senador **Humberto Costa**, **encaminho por meio de endereço eletrônico de serviço de armazenamento de arquivos disponibilizado por essa Comissão**, para ciência e atendimento à solicitação do referido Requerimento, as informações prestadas pelo corpo técnico deste Ministério.

Atenciosamente,

MARCELO QUEIROGA

Ministro de Estado da Saúde



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Referência: Processo nº 25000.119593/2021-41

SEI nº 0022395910

Assessoria Parlamentar - ASPAR
Esplanada dos Ministérios, Bloco G - Bairro Zona Cívico-Administrativa, Brasília/DF, CEP 70058-900
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Ministério da Saúde
Secretaria de Vigilância em Saúde
Núcleo Jurídico da Secretaria de Vigilância em Saúde

DESPACHO

SVS/NUJUR/SVS/MS

Brasília, 20 de agosto de 2021.

À Assessoria Parlamentar (ASPAR/GM/MS)

Assunto: **CPI PANDEMIA. REQUERIMENTO Nº 1155/2021/CPIPANDEMIA**
NUP/SEI Nº 25000.119593/2021-41

1. Trata-se do Despacho ASPAR 0022094740, da Assessoria Parlamentar, que encaminha o requerimento do Senado Federal nº 1155/2021/CPIPANDEMIA (0022094711), de autoria do Senador Humberto Costa, por meio do qual requer que seja encaminhada pelo Ministério da Saúde, informações sobre estudos realizados no começo da pandemia do coronavírus por este Ministério.
2. A demanda aportou nesta Secretaria e foi redirecionada ao Departamento de Imunização e Doenças Transmissíveis (DEIDT/SVS/MS), conforme Despacho NUJUR/SVS (0022169461), de modo que aquela área técnica exarou NOTA TÉCNICA Nº 1019/2021-CGPNI/DEIDT/SVS/MS (0022276368).
3. Nesse sentido, este Gabinete/SVS ratifica as informações prestadas por sua área técnica, momento em que restitui a presente demanda à essa Assessoria para conhecimento e providências ulteriores julgadas pertinentes.
4. Colocamo-nos à disposição para quaisquer esclarecimentos adicionais.

Atenciosamente,

ARNALDO CORREIA DE MEDEIROS
Secretário de Vigilância em Saúde



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Referência: Processo nº 25000.119593/2021-41

SEI nº 0022321235



Ministério da Saúde
Secretaria de Vigilância em Saúde
Departamento de Imunização e Doenças Transmissíveis
Coordenação-Geral do Programa Nacional de Imunizações

NOTA TÉCNICA Nº 1019/2021-CGPNI/DEIDT/SVS/MS

1. ASSUNTO

1.1. CPI PANDEMIA. REQUERIMENTO Nº 1155/2021/CPIPANDEMIA.

2. ANÁLISE

2.1. Trata-se do Despacho NUJUR/SVS (0022169461), que traz o Despacho ASPAR (0022094740), da Assessoria Parlamentar, que encaminha o Ofício nº 2081/2021 - CPIPANDEMIA (0022094529), de autoria do Presidente da Comissão Parlamentar de Inquérito da Pandemia, Senador Omar Aziz, o qual faz referência ao Requerimento do Senado Federal nº 1155/2021/CPIPANDEMIA (0022094711), de autoria do Senador Humberto Costa, por meio do qual requer que seja encaminhado pelo Ministério da Saúde, informações sobre estudos realizados no começo da pandemia do coronavírus por este Ministério.

2.2. Informa-se que nos primeiros meses de 2020 o diretor do Departamento de Imunização e Doenças Transmissíveis da Secretaria de Vigilância em Saúde, Julio Croda, solicitou ao corpo técnico da Coordenação Geral do Programa Nacional de Imunizações a realização de avaliações de impacto esperado da covid-19 no território nacional bem como a avaliação da probabilidade de evolução da covid-19 para um processo pandêmico. Para responder a esta demanda, buscou-se dados da literatura médica bem como realizou-se a construção de um modelo matemático, juntamente com pesquisadores da Universidade de Brasília, para a projeção de alguns cenários plausíveis. Esse trabalho culminou com uma apresentação realizada no Centro de Operações de Emergência (COE), no âmbito da Secretaria de Vigilância em Saúde, no dia 08 de março de 2020 (0022257072), uma apresentação subsequente ao Ministro feita pelo próprio diretor Julio Croda (0022257077) e a submissão para publicação de artigos científicos (0022257042, 0022257046, 0022257054). Ainda foram realizadas estimativas por um método simplificado em um momento inicial, para projeção da necessidade de leitos e óbitos em um cenário otimista onde não ocorresse o colapso dos serviços de saúde. Os resultados dessa projeção foram encaminhados ao então Secretário de Vigilância em Saúde, Wanderson Oliveira e ao diretor, Júlio Croda e encontram-se na planilha em anexo (0022305629), juntamente com a descrição do método de cálculo, no documento em anexo (0022257059). Destaca-se que todas essas projeções possuíam elevado grau de incerteza e limitações inerentes e estavam sujeitas as limitações das informações disponíveis naquele momento.

2.3. Esses métodos de projeções foram aprimoradas pela Unidade Técnica de Vigilância, Preparação e Resposta à Emergências e Desastres da

Organização Pan-Americana da Saúde OPAS/OMS-Brasil que elaborou uma calculadora online em parceria com a Universidade de Brasília, com objetivo de projetar a pressão hospitalar de acordo com a quantidade de casos confirmados de covid-19 pelo estados e municípios do Brasil. Estas análises são disponibilizadas gratuitamente pelo link: <https://covid-calc.org/>.

3. CONCLUSÃO

3.1. As projeções do impacto esperado da pandemia no território nacional realizadas por esta coordenação nos primeiros meses da pandemia da covid-19 encontram-se referenciadas na presente nota. Destaca-se que esses modelos são simplificações da realidade e dependem fortemente de bons valores para os parâmetros baseados em dados, contendo elevada incerteza em todas as previsões, em especial aquelas realizadas a longo prazo. Ainda existem vários aspectos epidemiológicos da covid-19 que permanecem em aberto no debate científico e cientistas ainda estão tentando determinar valores mais precisos para diversos parâmetros. Dessa forma, as informações resultantes das diferentes projeções, incluindo a calculadora epidemiológica aqui citada precisam ser interpretadas com cuidado e parcimônia.

Atenciosamente,

CRISTIANNE APARECIDA COSTA HARAKI
Coordenadora Geral do Programa Nacional de Imunizações - Substituta

CÁSSIA DE FÁTIMA RANGEL FERNANDES
Diretora do Departamento de Imunização e Doenças Transmissíveis



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SEI nº 0022276368

Coordenação-Geral do Programa Nacional de Imunizações - CGPNI
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Expected impact of COVID-19 outbreak in a major metropolitan area in Brazil

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Abstract

In January 2020 China reported to the World Health Organization an outbreak of pneumonia of undetermined origin in the city of Wuhan, Hubei. In January 30, 2020, the World Health Organization declared the outbreak of COVID-19 as a Public Health Emergency of International Interest (PHEI). **Objectives:** The aim of this study is to assess the impact of a COVID-19 epidemic in the metropolitan region of São Paulo, Brazil. **Methods:** We used a generalized SEIR (Susceptibles, Exposed, Infectious, Recovered) model, with additional Hospitalized variables (SEIHR model) and age-stratified structure to analyze the expected time evolution during the onset of the epidemic in the metropolitan area of São Paulo. The model allows to determine the evolution of the number of cases, the number of patients admitted to hospitals and deaths caused by COVID-19. In order to investigate the sensibility of our results with respect to parameter estimation errors we performed Monte Carlo analysis with 100 000 simulations by sampling parameter values from an uniform distribution in the confidence interval. **Results:** We estimate 1 368 (IQR: 880, 2 407) cases, 301 (22%) in older people (≥ 60 years), 81 (50, 143) hospitalizations, and 14 (9, 26) deaths in the first 30 days, and 38 583 (IQR: 16 698, 113, 163) cases, 8 427 (21.8%) in older people (≥ 60 years), 2181 (914, 6392) hospitalizations, and 397(166, 1205) deaths in the first 60 days. **Limitations:** We supposed a constant transmission probability P_c among different age-groups, and that every severe and critic case will be hospitalized, as well as that the detection capacity in all the primary healthcare services does not change during the outbreak. **Conclusion:** Supposing the reported parameters in the literature apply in the city of São Paulo, our study shows that it is expected that the impact of a COVID-19 outbreak will be important, requiring special planning from the authorities. This is the first study for a major metropolitan center in the south hemisphere, and we believe it can provide policy makers with a prognosis of the burden of the pandemic not only in Brazil, but also in other tropical zones, allowing to estimate total cases, hospitalization and deaths, in support to the management of the public health emergence caused by COVID-19.

Introduction

In January 2020 China reported to the World Health Organization an outbreak of pneumonia of undetermined origin in the city of Wuhan, Hubei. Initially 44 cases were reported, having as common exposure contact the Wuhan seafood market. An increasing number of unrelated secondary cases have since been detected across China, and leading to the dissemination of cases into several countries [1]. The etiologic agent was identified as a new coronavirus, of the betacoronavirus family, which has since been named SARS-CoV-2, and the resulting disease COVID-19 [2]. In January 30, 2020, the World Health Organization declared the outbreak of COVID-19 as a Public Health Emergency of International Interest (ESPII) [3,4], and in March 11 declared it a Pandemic [5].

Previously to 2019, two highly pathogenic coronavirus had been described in the world. The first named SARS-CoV and described in 2003, was responsible for an epidemic of severe acute respiratory syndrome (SARS), initiated in China and with secondary cases in 26 other countries, accounting for a total of 8,096 cases and 774 deaths [case-fatality rate (CFR): 9.6%] [6, 7]. The second virus, named MERS-CoV, was identified in 2012 is a betacoronavirus responsible for the Middle East Respiratory Syndrome (MERS) [8]. Cases of MERS-CoV are reported sporadically ever since, resulting from zoonotic transmission, with a few outbreaks associated with human to human transmission, resulting in 2449 cases and 845 deaths (CFR: 34,5%), with the majority (84%) reported in Saudi Arabia [9].

SARS-CoV-2 has significant differences relative to MERS-CoV and SARS-CoV. In just over a month of the epidemic, more cases of COVID-19 were confirmed than in the entire history of SARS-CoV and MERS-CoV. Previous outbreaks of SARS-CoV and MERS-CoV have been linked to epidemic amplification phenomena, with few cases were responsible for a disproportionately high number of secondary cases, the so-called super-spreaders, with a significant number of cases resulting from nosocomial transmission. This characteristic allowed outbreaks to occur even in scenarios with an average basic reproduction number R_0 of less than one [4, 10–14]. Unlike SARS-CoV and MERS-CoV, over-dispersion events does not seem to be of a major relevance for the COVID-19 epidemic, suggesting a more homogeneous transmissibility in the population [15, 16].

Homogeneous transmissibility and the potential for transmission from asymptomatic sources [17] brings COVID-19's behavior closer to other respiratory transmission viruses, such as measles or influenza [13]. Influenza viruses, despite the differences in relation to viruses of the coronavirus family, have similar modes of transmission, and the associated clinical syndromes. Eventually new influenza viruses originating from genetic recombination in animals infect humans, and subsequently transmitted in the population, having been responsible for pandemics in the past, with the occurrence of hundreds of thousands of cases and thousands of deaths worldwide [18, 19].

Brazil has one of the largest public health care systems in the world [20], and understanding how an eventual COVID-19 epidemic in the country could affect this system is central for the preparation of a proper response. In the past, epidemiological models have been used to predict the occurrence of measles cases in order to support decision making in public health emergencies. This paper aims to present tools capable of making projections of the impact of a COVID-19 epidemic in the major metropolitan region of the country. This of particular importance not only for the size of its population, but also for being the main hub of arrival and departure from the country.

We analyze the expected time evolution during the onset of the epidemic in the metropolitan area of São Paulo, with a total estimated population of 21.5 million individuals, the fourth largest in the world. We use a generalized age-stratified SEIR model with the addition of hospitalized population variables (SEIHR model) to predict the occurrence of cases, the expected number of patients admitted to hospitals and deaths caused by COVID-19. Our approach can be adapted straightforwardly to other cities and countries, which is of great relevance in low and middle

income countries, with reduced availability of health infrastructure and preparedness to respond to an emergency.

Materials and methods

It has been shown that age-specific contact rates describes with more accuracy the dynamics of transmission of measles when using an age stratified SEIR model [21], and allows to grasp specifics of social behavior as coded in the contact matrix. Owing to different impacts of the disease across the population according to age, we consider the following age groups: 0–9, 10–39, 40–49, 50–59, 60–69, ≥ 70 years. The population in each group is obtained from the 2010 Brazilian census, corrected by the estimated population in São Paulo in 2019 (see supporting information), except for ages from 0 to 1 year, where the actual population from birth data was used [22, 23]. The variables in the model for each age class are proportions with respect to the total population at time zero: Susceptibles (S_i), Hospitalized (H_i) due to COVID-19, Exposed (E_i) (in the incubation period and not infectious), Infectious (I_i) and Recovered (R_i) individuals, $i = 1, \dots, M$, (SEIHR model), with M the number of age groups. They are such that at time zero we have $\sum_{i=1}^M n_i = 1$, with the fraction of the population in a given age group $n_i = S_i + H_i + E_i + I_i + R_i$ and M the number of age groups. The probability of hospitalizations of an infected individual of age-group i is estimated as being $\zeta_i = \mu_i^{(0)} \times 0.18 / \mu_{COV}$ with 0.18 being the proportion of severe and critical cases, μ_{COV} is the overall estimated letality of the disease and $\mu_i^{(0)}$ the proportion of fatal cases by the number of cases in age group i [24], which yields $\zeta_1 = 0$, $\zeta_2 = 0.0157$, $\zeta_3 = 0.0313$, $\zeta_4 = 0.102$, $\zeta_5 = 0.282$ and $\zeta_6 = 0.892$ for $\mu_{COV} = 2.3\%$. We assume that fatalities only occurs among hospitalized individuals. The different parameter values required are given in current published data and shown with the corresponding sources in Table 1. The aging rate from age group i to age group $i + 1$ is denoted by ν_i and is given by the inverse of the age span of the group (in the corresponding time unit). We put $\nu_0 = \nu_M = 0$ in the model equations below.

Table 1. Constant parameters in the model.

Variables	Definition	Value (CI 95%) [Ref]	Distribution
κ	Birth rate	0.01416 [25]	—
μ	Overall fatality rate from other causes	0.00608 [25]	—
ψ	Average recovery rate from hospital	1/17.5 days ⁻¹ [26]	—
P_{sc}	Proportion of severe and critical cases	18% [24]	—
μ_{COV}	Fatality rate due to the disease	0.4% – 2.9% [24]	Uniform
θ	Fatality rate in hospitalized individuals	μ_{COV} / P_{sc}	—
σ^{-1}	Inverse of incubation rate	5.0 (4.2, 6.0) days [27]	Log-Normal
γ^{-1}	Inverse of recovery rate of non-hospitalized infectious individuals	1.61 (0.35, 3.23) days ⁻¹ [28]	Not informed. Assumed Log-Norm.
ζ_i	Probability of hospitalizations for age-group i	(see text)	—
R_0	Basic reproduction number for COVID-19	2.74 (2.47, 3.03) (see supporting information)	Assumed Uniform
τ_1	Median time from illness onset to hospitalization	3.3 (2.7, 4.0) [27]	Gamma
τ_2	Average time from illness onset to death	15.0 (12.8, 17.5) [27]	Log-Normal

Constant parameters in the model with the average value, Confidence Interval (CI) of 95% if pertinent and statistical distribution of values.

We consider that hospitalized individuals are isolated and do not contribute to the force of infection, defined by

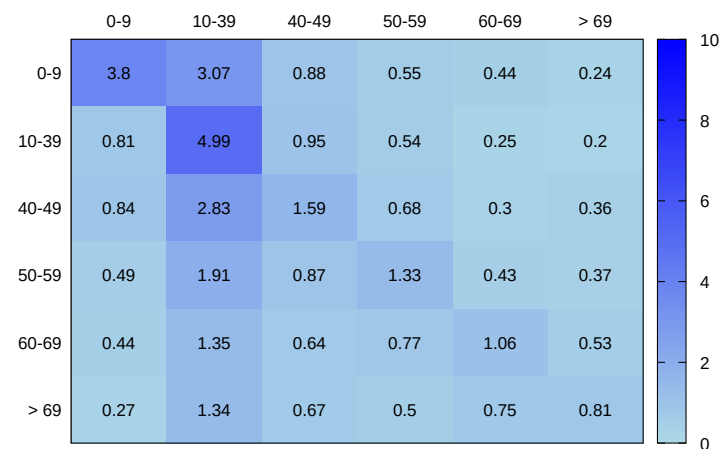
$$\lambda_i = \sum_{j=1}^M \beta_{i,j} \frac{I_j}{n_i}, \quad (1)$$

for the i -the age group, with $\beta_{i,j}$ the transmission matrix, which is estimated as follows. We first consider the contact matrix $C_{i,j}$ as given by the average number of physical contacts per time unit of and individual of age group i with any individual of group j . Since the present available information does not allow to determine a probability of contagion for each specific group, we consider the transmission probability per contact P_c being the same for all infected individuals. We thus have that $\beta_{i,j} = P_c C_{i,j}$. There are some studies determining the contact matrix for different regions in the world, but none for any Brazilian city. So we considered the study in Ref [29] where the contact matrix was determined from field studies for eight different European countries. Our working hypothesis was that these results can reasonably be transposed for the metropolitan area of São Paulo. Since contact matrices for these different countries do not vary significantly, we take their average for $C_{i,j}$, and the contact matrix resulting from this procedure is shown as a heat map in Fig 1. The transmission probability is then obtained by adjusting the value of the basic reproduction number from the relation

$$R_0 = \sum_{i,j=1}^M n_j \beta_{ij} / \gamma = \sum_{i,j=1}^M n_j P_c C_{ij} / \gamma, \quad (2)$$

We also suppose that only severe and critical cases are hospitalized.

Fig 1. Heat map for the contact matrix C_{ij} representing the number of physical contacts per day of an individual of age group i with any individual of group j .



The model schematic is given in Fig 2 and the corresponding system of differential equation is:

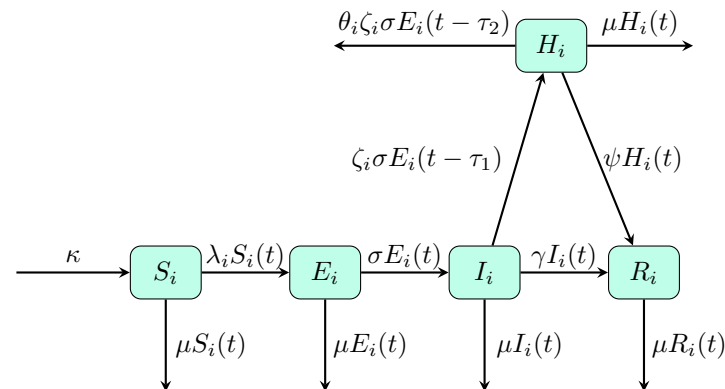
$$\begin{aligned} \frac{dS_i}{dt} &= \kappa \delta_{i,1} - \lambda_i S_i - \mu S_i - \nu_i S_i + \nu_{i-1} S_{i-1}, \\ \frac{dH_i}{dt} &= -\psi H_i + \zeta_i \lambda_i E_i(t - \tau_1) - \theta \zeta_i \lambda_i E_i(t - \tau_2) - \mu H_i, \\ \frac{dE_i}{dt} &= \lambda S_i - \sigma E_i - \zeta_i \sigma E_i - \mu E_i - \nu_i E_i + \nu_{i-1} E_{i-1}, \\ \frac{dI_i}{dt} &= \sigma E_i - \gamma I_i - \mu I_i - \nu_i I_i + \nu_{i-1} I_{i-1}, \\ \frac{dR_i}{dt} &= \gamma I_i + \psi H_i - \mu R_i - \nu_i R_i + \nu_{i-1} R_{i-1}, \end{aligned} \quad (3)$$

where all variables are taken at time t except where explicitly indicated, and δ_{ij} is the Kronecker delta (1 if $i = j$ and 0 otherwise). This system is well defined, in the sense that all variables

always remain positive and below 1 if there is no population growth. This can be verified straightforwardly simply by noticing that the gradient at the boundaries of the significance region point inward.

The solution of Eq (3) was implemented in C, and additional analysis and scripts in the symbolic language system MAPLE and are available on demand.

Fig 2. Diagram describing the model equations in Eq (3), constant parameters given in Table 1, and force of infection and transmission rate given in Eqs (2) and (1), respectively.



Results and discussion

With the onset of an outbreak in a geographically delimited region, a behavioral change is expected in the population in a relatively short time span, as well as government and health officials to intervene with drastic measures in order to reduce contacts, and thence disease propagation. Mathematically, this amounts to judiciously reduce the values of some components of the contact matrix. We consequently restrict ourselves to the first 60 days of the possible outbreak, beyond which results from simulations would not correspond any longer to a realistic setting. Nevertheless, our approach lends itself easily to model specific interventions, as for instance school closure, using the analogous of a school-term forcing in the contact matrix, commonly used to study periodic oscillations in measles [21].

The time evolution for the total number of cases, hospitalized individuals, and total fatalities, for each age group, from the average or median values for the parameters in Table 1, are shown in Figs. 3, 4 and 5, respectively. In order to investigate the sensibility of our results with respect to the estimation errors in different parameter used, we performed a Monte Carlo analysis with 100 000 simulations by sampling parameter values from an uniform distribution, in the interval defined by the corresponding confidence interval. We considered at time zero 10 cases in the age group of 10 to 39 years. In all that follows the number of cases are discounted from this initial value. Results for the medians and inter-quartile intervals for the total number of cases, fatalities and number of hospitalized individual are shown in Table 2, for 30 and 60 days of time evolution. The transmission probability P_c obtained from the Monte Carlos study is well fitted by a log-normal distribution with median of 0.148 and inter-quartile interval of (0.106, 0.247) (see supporting information).

This is a first modeling of COVID-19 dynamics using an age-stratified model, similar to approaches for other respiratory diseases epidemics having a historical and clinical relevance in a number of conditions [30,31]. This type of approach is relevant for the planning of age-dependent intervention policies, e. g. by school closing or restrictions on public gatherings.

Fig 3. Cumulative number of cases in each age group for the mean or median values for the parameters in Tab. 1, assuming a fatality rate of 2.3%.

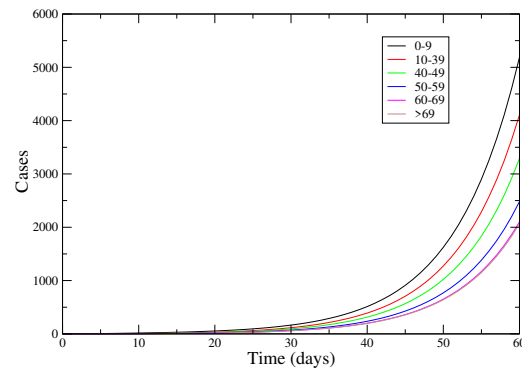


Fig 4. Number of hospitalized individual at a given moment corresponding to Fig 3.

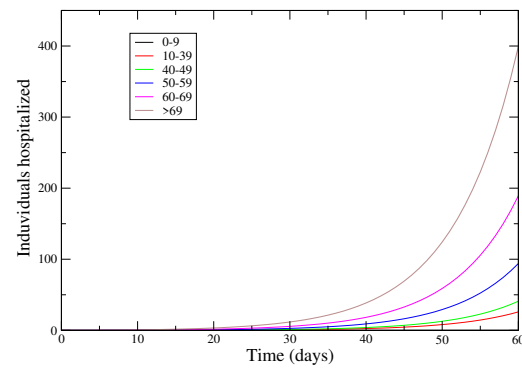
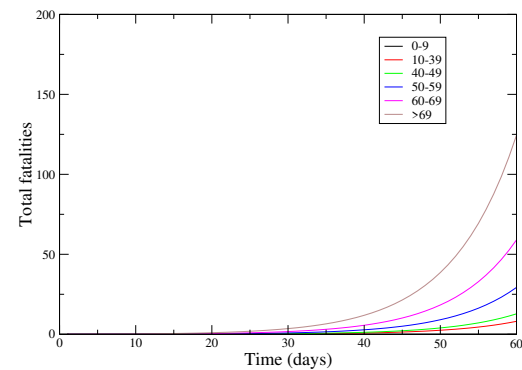


Fig 5. Cumulative number of fatalities corresponding to Fig 3.



It is also the first study of a possible epidemic of COVID-19 in a large metropolitan region in the South hemisphere.

Parameters used are described in the literature except for hospitalization probability according to age that was estimated. The contact matrix was adapted from a study of European countries, which are expected to display a similar contact structure as the major city in the southern hemisphere, and comparable in population size to the Wuhan region. Although these

Table 2. Median for the total cumulative number of cases averaged over 100,000 Monte Carlo realizations.

Age	30 days			60 days		
	Cases	Hosp.	Fatal.	Cases	Hosp.	Fatal.
0–9	356 (227, 630)	0 (0, 0)	0 (0, 0)	10339 (4493, 30144)	0 (0, 0)	0 (0, 0)
10–39	299 (196, 519)	3 (2, 6)	1 (0, 1)	8247 (3585, 24115)	91 (37, 265)	16 (7, 47)
40–49	234 (152, 410)	5 (3, 10)	1 (1, 2)	6587 (2859, 19259)	141 (58, 410)	25 (11, 73)
50–59	178 (114, 312)	11 (7, 21)	2 (1, 3)	4986 (2156, 14633)	308 (128, 897)	55 (24, 163)
60–69	151 (96, 267)	21 (13, 38)	4 (2, 7)	4240 (1824, 12522)	570 (239, 1667)	103 (44, 312)
≥ 70	150 (96, 269)	39 (25, 69)	7 (4, 13)	4187 (1783, 12484)	1060 (447, 3121)	196 (80, 605)
Total	1368 (880, 2407)	81 (50, 143)	14 (9, 26)	38583 (16698, 113163)	2181 (914, 6392)	397 (166, 1205)

The number of cases and fatalities are cumulative. The number of hospitalized individuals represent the current number of individuals occupying a place in a hospital setting at this time. The inter-quartile interval is given by the numbers between brackets.

two cities have different climates, there is no available empirical evidence to assert its effect on the disease propagation, although clear evidence exists for H1N1 and H3N2 viruses [32]. Further research is in need to clarify this point.

Previous outbreaks of the highly pathogenic coronavirus SARS-CoV and MERS-CoV were related to epidemic amplification with a small number of super-spreader cases causing an elevated number of secondary cases, with a high impact in hospital settings. This explains outbreaks with a basic reproduction number R_0 smaller than one [4, 10–14]. The value of R_0 depends not only on the specifics of the disease, but also on a number of environmental factors, being affected by a change of social behavior in the population and by isolation of infected individuals. This was clearly observed during the recent evolution of the China outbreak, since its onset in December 2019, with a gradual decline of R_0 [33]. This is the main reason why in the present study we restricted the time span of our prognosis to 60 days, as we estimate that after a month of the onset of the outbreak, behavioral change is expected to occur, and public authorities interventions are also expected to occur during the first 60 days from the start of the outbreak.

The present study simulates the impact of COVID-19 on the local health system by a prediction of the number of hospitalized individuals, and consequently provides a tool for policy decision makers to plan the needs of healthcare services in providing people living in an area that is an international hub for the spread of COVID-19, mainly for other countries in South America. The expected number of hospitalized individuals in the first 30 days of the outbreak should be easily absorbed by the existing infrastructure in the metropolitan area of São Paulo, but increases rapidly as the outbreak unfolds, and one expects a rapid saturation of the health settings, which varies according to age. Our approach is therefore a relevant tool to provide authorities responsible for the preparations for a possible outbreak the possibility to know how much time they have at their disposal to prepare complementary health infrastructures. A more systematic and detailed analysis in this directions is the subject of ongoing research.

The determination of the value of R_0 is affected by the supposition that both the time from the start of symptoms, and confirmation, and sub-notification proportions, are roughly constant during the outbreak, resulting in a possible overestimation during the initial stage of the epidemic. The raise in the number of confirmed cases may be in great part be due to a better sensitivity of the health system surveillance and a decrease of the time lag for laboratory confirmation.

Limitations

In this section we summarize limitations of our work. We assumed that different age-group have the same transmission probability per physical contact, although no information is available to avoid this assumption. We also considered that that every severe or critic case will be in need for hospitalization and supposed, again due to a lack of more detailed data, that the probability of an infected individual from a given age group is proportional to the reported values of the death rate

in this same group. Another relevant limitation was to consider that all primary health services will have the same capacity in identifying the severity of clinical conditions, in a region with more than 20 million people living with a GINI index ranging from 0.40 to 0.69 [25], indicating, among other factors, quite different levels of access to tertiary healthcare services. Furthermore, one must consider the possibility that the health infrastructure available can be precociously collapsed. We also assume that, during the 60 days lapse from the epidemic onset, no significant behavioral changes would occur, neither strong interventions from by policy decision makers. More recently the percentage of asymptomatic cases was estimated to be as high as 34.6% [17], while all epidemic parameters previously obtained considered that all cases are symptomatic. On the other hand, the number of asymptomatic cases is expected to have a significant impact on the disease dynamics at later stages, when a substantial proportion was infected. It has nevertheless important consequences in the efficiency of isolation procedures. Although we consider here that hospitalized individuals are no longer able to infect is an oversimplification, and may contribute significantly to the number of reported cases among health professionals. The period that an infected individual transmits the virus, as given in Tab 1, is probably underestimated and was based on the only available study that explicitly cites it [28].

Conclusion

Despite having a low case fatality rate, COVID-19 has high transmissibility, with as a consequence a large number of cases when introduced in a naive population, and a large number of hospitalizations and deaths. A COVID-19 epidemic in a major urban area like São Paulo would promote a significant burden in the health care system. Measures to limit the spread of the disease will be necessary in order to slow the epidemic growth and avoid depleting the available hospitals beds and intensive care unit. Mathematical models can contribute in predicting the expected burden of disease. The approach presented here allows a detailed assessment of the impact of the onset of the epidemic in the major metropolitan area in the south hemisphere, despite major limitations in our understanding of the COVID-19 dynamics. For instance, the role of asymptomatic individuals in the progression of the epidemic is still unknown, and no data is available regarding the differences in the transmission rates between different age groups and the impact of the weather in the reproductive number.

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Author contributions

WMR, WNA and JHRC discussed and designed the initial study design. FSGS, VBG and TAHR performed the data gathering and analysis. TMRP wrote and tested all the computer code, run all simulations, and performed the main analysis of corresponding results. Some additional statistical analysis were performed by FSGS and VBG. All authors contributed equally to discussing the final design of the study and participated in the subsequent analysis, discussion and assessment of final results.

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Title: Monitoring social distancing and SARS-CoV-2 transmission in Brazil using cell phone mobility data

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Abstract: Social distancing measures have emerged as the predominant intervention for containing the spread of COVID-19, but evaluating adherence and effectiveness remains a challenge. We assessed the relationship between aggregated mobility data collected from mobile phone users and the time-dependent reproduction number $R(t)$, using severe acute respiratory illness (SARI) cases reported by São Paulo and Rio de Janeiro. We found that the proportion of individuals staying home all day (isolation index) had a strong inverse correlation with $R(t)$ ($\rho < -0.7$) and was predictive of COVID-19 transmissibility ($p < 0.0001$). Furthermore, indexes of 46.7% had the highest accuracy (93.9%) to predict $R(t)$ below one. This metric can be monitored in real time to assess adherence to social distancing measures and predict their effectiveness for controlling SARS-CoV-2 transmission.

One Sentence Summary: Mobility data to monitoring social distancing in the COVID-19 outbreak

Main Text

The coronavirus diseases 2019 (COVID-19) pandemic has caused more than 2,900,000 cases and 200,000 deaths worldwide as of April 26, 2020(1). In the absence of vaccines and effective pharmacological interventions, social distancing measures are critical to mitigate the impact on healthcare systems and allow time for a public health response around the globe(2, 3).

There is growing evidence that a significant reduction in new locally-transmitted cases have been achieved in Asia and Europe following restrictions on urban mobility and travel(2–6). To reduce the peak of transmission, starting in March of 2020, the Brazilian states of São Paulo and Rio de Janeiro in Brazil, with a population of 63 million people, implemented non-pharmacological interventions and recommended social distancing measures. This implied reductions in public gatherings; the closure of schools, universities, and businesses such as restaurants, bars and gyms; and the institution of remote or virtual work for older adults and individuals with underlying medical conditions. In light of these public health interventions only essential services (i.e., grocery stores, emergency health service) remained open. To prevent the expansion of COVID-19 epidemic, the non-pharmacological measures have to bring the time-dependent reproduction number ($R(t)$) to less than 1. This requires a 50-60% reduction of a baseline $R(t)$ between 2 and 2.5(2).

Using data from hospitalization due to severe acute respiratory illness (SARI) as a proxy for severe cases of COVID-19, we recently reported an important decline in the $R(t)$ in the metropolitan area of São Paulo after the implementation of social distancing measures(7). Although $R(t)$ is a useful tool to monitor the epidemic, it is subject to significant delays in notification. In Brazil, a time lag of 8 days exists between the date of onset of symptoms and the date of notification of a SARI case(8). Given this time, relying solely on the measurement of $R(t)$ bears a likely risk of introducing significant delays in detecting changes in the epidemic dynamics. In an epidemic with cases doubling in 5.2 days(9), a delay of 1-2 weeks in the implementation of effective social distancing would overwhelm the capacity of the healthcare system, resulting in a growing number of excess deaths(10–13). Thus, a timelier metric for COVID-19 transmission potential is required to evaluate social distancing interventions.

The wide-ranging usage of mobile phone provides an unique opportunity to monitor and control the spread of infectious diseases(14–17). Mobile phones with geolocation enablement can track movement in a timely and precise manner. To our knowledge, no study thus far has assessed the use of mobile phones for this purpose in Brazil. Monitoring human activity through mobile aggregated data can permit measurement of the effectiveness of social distancing measures in reducing transmissibility of the SARS-CoV2 virus(18). Nonetheless, the association between urban mobility and COVID-19 transmissibility has not yet been established. In this study, we assessed the relationship between social isolation measures, by using human urban movement data and the transmissibility of COVID-19.

From February 1st to April 10th, 2020 a total of 21,426 hospitalizations in 853 hospitals (58%) due to SARI were reported in the São Paulo (SP) state. A clinical diagnosis of COVID-19 was confirmed by molecular testing for 4,111 (19% of total SARI cases), 16,892 (79%) remained as suspected COVID-19 cases and 423 (2%) were confirmed for other respiratory virus diseases in

SP state. During the same period the RJ state had reported 2,540 hospitalizations in 320 hospitals (62%) due to SARI, 402 (16%) were confirmed by molecular testing for COVID-19, 2,090 (82%) remained as suspected and 48 (2%) have been confirmed for other respiratory viruses (Fig. 1A and 1D). Most SARI cases in SP and RJ have not been tested due to the shortage of SARS-CoV2 real-time polymerase cycle reaction (RT-PCR) diagnostic screening. In 2019, during the same period, 1,550 and 220 SARI cases were reported in SP and RJ, respectively. This corresponds to 1,282% and 1,054% increase in SARI cases in SP and RJ respectively between the same periods in 2019 and 2020.

Implemented social distancing Measures

Starting on March 13, 2020, two days after the World Health Organization declared COVID-19 as a pandemic, the states of São Paulo and Rio de Janeiro implemented a series of non-pharmacological interventions. These measures were implemented gradually in both states, some of these interventions are described on **Figure 1**. To investigate the impact of social distancing measures in SARS-CoV-2 transmission, we compared daily aggregated mobility data for São Paulo and Rio de Janeiro with R estimates obtained from SARI data. Here, we calculate an “isolation index” as a ratio between the number of people staying at home on a given day divided by the number of cell-phone users living in the state or city (see **Material and Methods**). First, we find that the mean isolation index from February 1st to April 10th was 40.2%, ranging from 18.5% to 69.4%. In São Paulo state, mean isolation index ranged from 13.5% to 67.9% and in the Rio de Janeiro State from 16.6% to 69.4%, with no significant difference observed between the two states (p -value = 0.210). Second, after the start of interventions we observe a sharp and significant increase in the isolation index and a corresponding decrease in the $R(t)$ (**Figs. 1B and 1E**). Overall, we find that temporal periods with $R(t) \geq 1$ had a mean isolation index below 29.3% (SD = 8.2%) while those with $R(t) < 1$ had a mean isolation index above 53.4% (SD = 3.0%) (**Figs. 1C and 1F**).

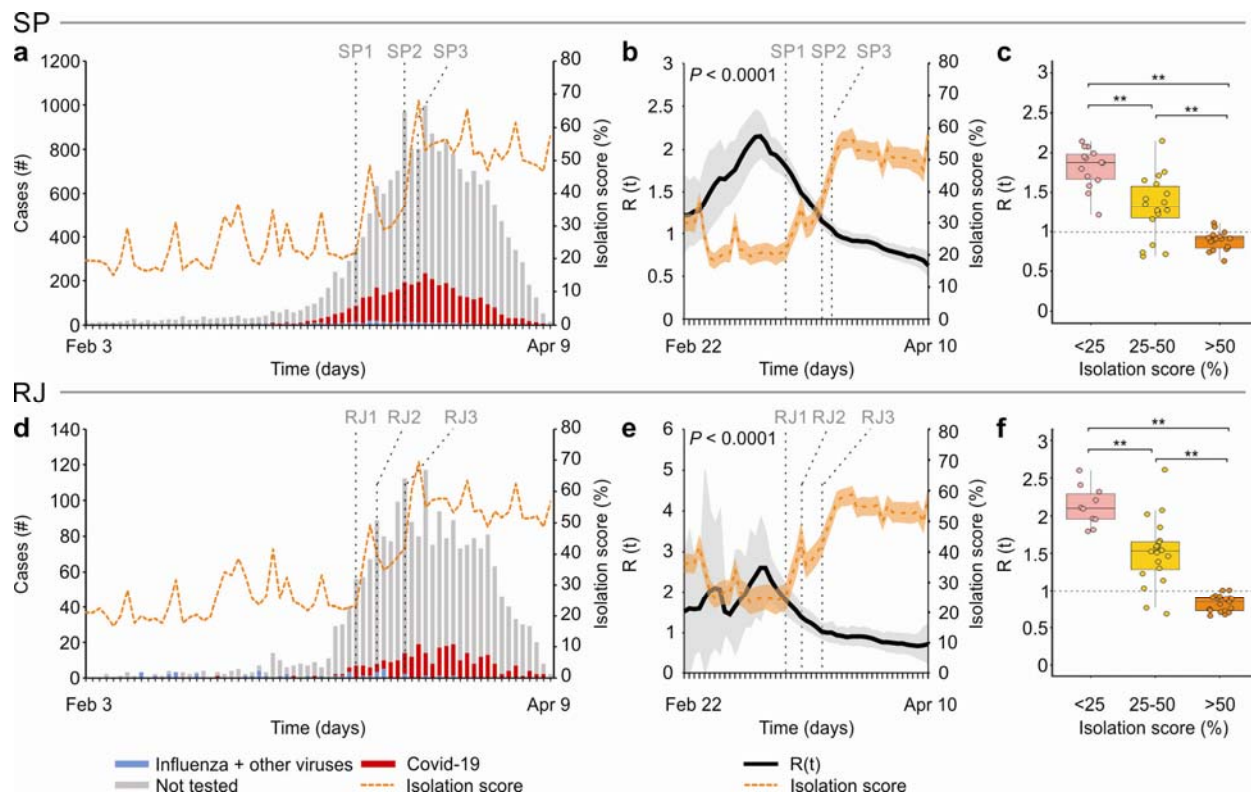


Fig. 1. Impact of interventions in the reduction of severe acute respiratory transmission in São Paulo and Rio de Janeiro states, Brazil. A and D: epidemic curve of SARI cases by date of onset of symptoms for São Paulo and Rio de Janeiro, respectively; B and E: Daily Time dependent reproductive number ($R(t)$) (grey) and isolation index (orange) (curves smoothed by Kalman Filtering method), SP and RJ respectively; C and F: boxplot showing the median, interquartile range and range of the association between of $R(t)$ and isolation index categories. SP1: March 13, 2020, SP recommended reduction in public gathering events and closure of schools; SP2: March 20, 2020, SP declares Public Calamity and prohibits religious ceremonies; SP3: March 22, 2020, SP establishes quarantine in the entire state, closure of night clubs, shopping centers, gyms, bars, restaurants and bakeries; RJ1: March 13, 2020, RJ recommended remote work, suspended public gathering events, closed schools, and entertainment establishments, prohibited the access of visitors to prisons and to COVID-19 hospitalized patients; RJ2: March 16, 2020, RJ prohibited the access to tourist places, including beaches and public pools, restricted public transport such as bus lines, airlines and cruise ships coming from states or countries with COVID-19 circulation, closed bars and restaurants, closed gyms, shopping centers and similar establishments and set restrictions on public transportation; RJ3: March 20, 2020, RJ declared Public Calamity due to the COVID-19 pandemic

Mobility data predicted the time-dependent reproduction number $R(t)$

We next conducted cross-correlation analyses with different lag days and the Granger test to investigate if the isolation index measure obtained from mobility data is able to predict $R(t)$. After the intervention began, it was also observed a gradual decrease in $R(t)$ (Fig. 1B and 1E). Furthermore, using SARI cases, cross-correlation analyses showed that isolation was highly

correlated with $R(t)$ ($\rho < -0.7$) in a lag period of up to five days in SP and RJ. Considering only COVID-19 confirmed cases, the $R(t)$ and isolation index were moderately correlated ($\rho > -0.7$) using a lag period from -2 to 0 (Fig. 2A and B).

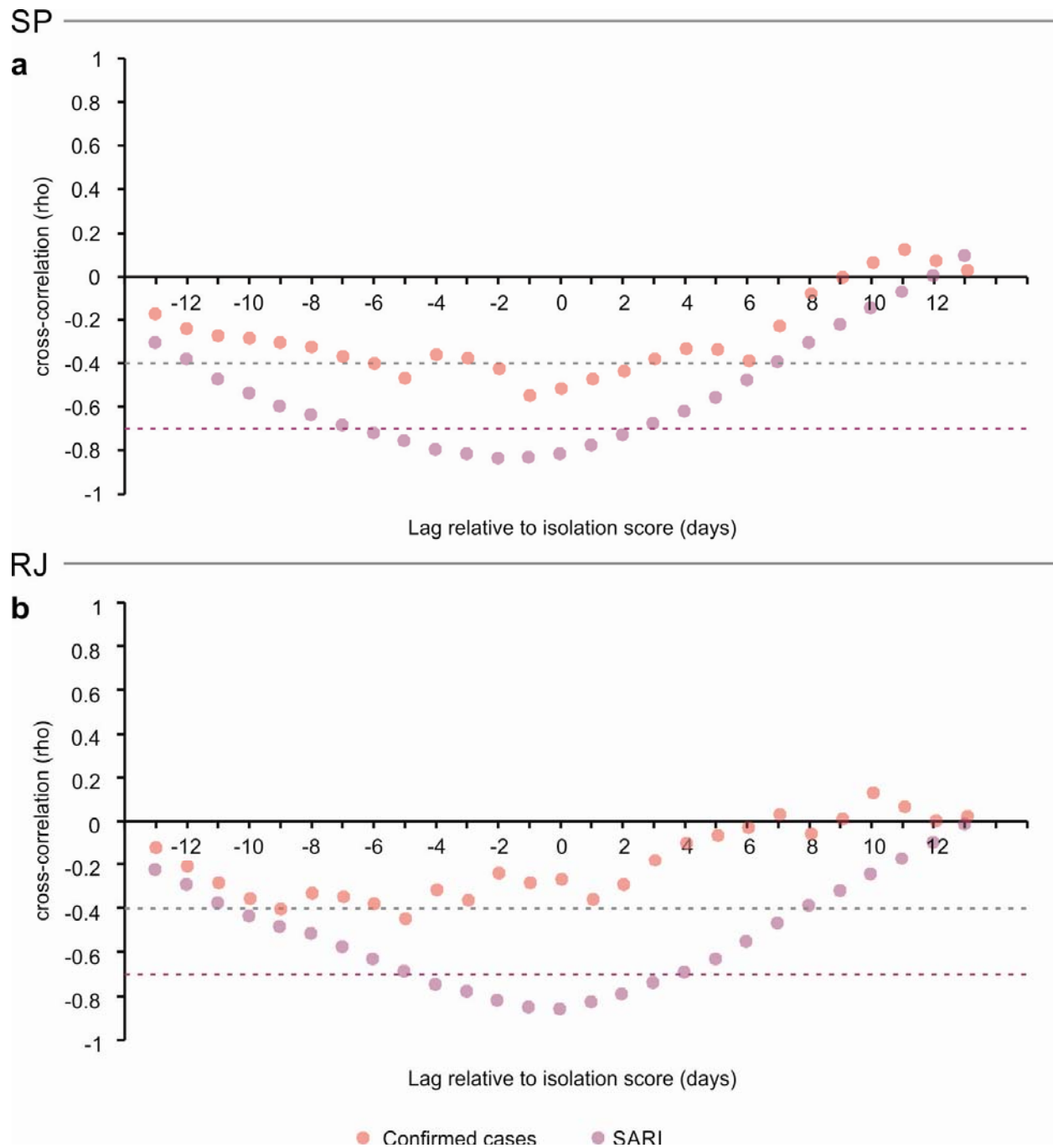


Fig. 2. Cross-correlation (ρ) between isolation index and reproductive number ($R(t)$) estimated using SARI (purple circles) and confirmed COVID-19 (red circles) cases in São Paulo (A) and Rio de Janeiro (B).

The isolation score exhibited an area under the ROC curve 93.8% (95% CI: 88% - 99.5%) to predict R values under 1.0 (**Fig. 3A**). We obtained the best accuracy with score values close to 50%. Particularly, we observed the highest accuracy (93.9%) with the cut-off of 46.7%, and cut-offs higher than 50% exhibited specificity greater than 93% (**Fig. 3B**). Furthermore, 88.9% of the areas with at least 50% isolation score had an $R < 1$. In contrast, 90.3% of the observations with an isolation score $< 50\%$ had an $R \geq 1$. The isolation scores, for both states combined, when greater than 50%, were associated with a mean R of 0.9 (ranging from 0.6 to 1.1) (**Fig. 1C and 1F**). Scores between 25-50% had a mean R of 1.4 R (ranging from 0.7 to 2.6). On the other hand, isolation scores lower than 25% exhibited a mean R of 1.9 (ranging from 1.2 to 2.6).

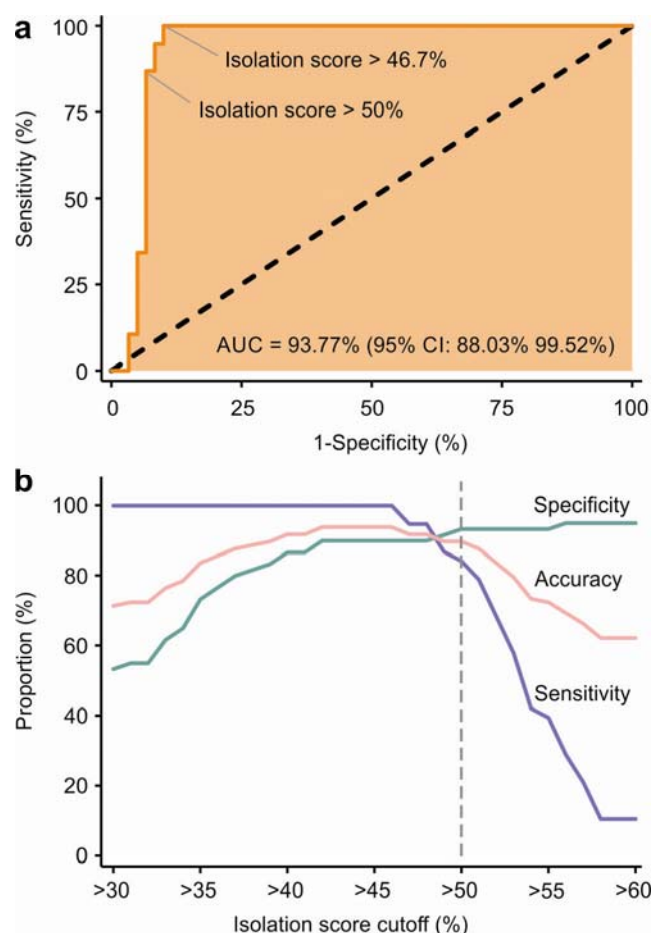


Fig. 3. A. Receiver operating characteristic curve of isolation index for prediction of $R(t) < 1$. B. Sensitivity, Specificity and Accuracy of isolation index cut-offs to predict $R(t) < 1$.

To investigate the effectiveness of interventions in areas with different human development indexes (HDI), we analyzed the isolation score time series for the 10 largest cities in the states of São Paulo and Rio de Janeiro stratified by HDI (19). We found no significant difference between the groups (**Fig. 4**). To validate the findings, we aggregated 20 cities in two groups stratified by HDI (lower and higher values). We observed the same trend and strong correlation, regardless of the group (higher and lower HDI) (**Fig. S1A**). Interestingly, we found an identical cut-off point of isolation index (50%) which was correlated with $R(t)$ values below 1 (**Fig. S1B**).

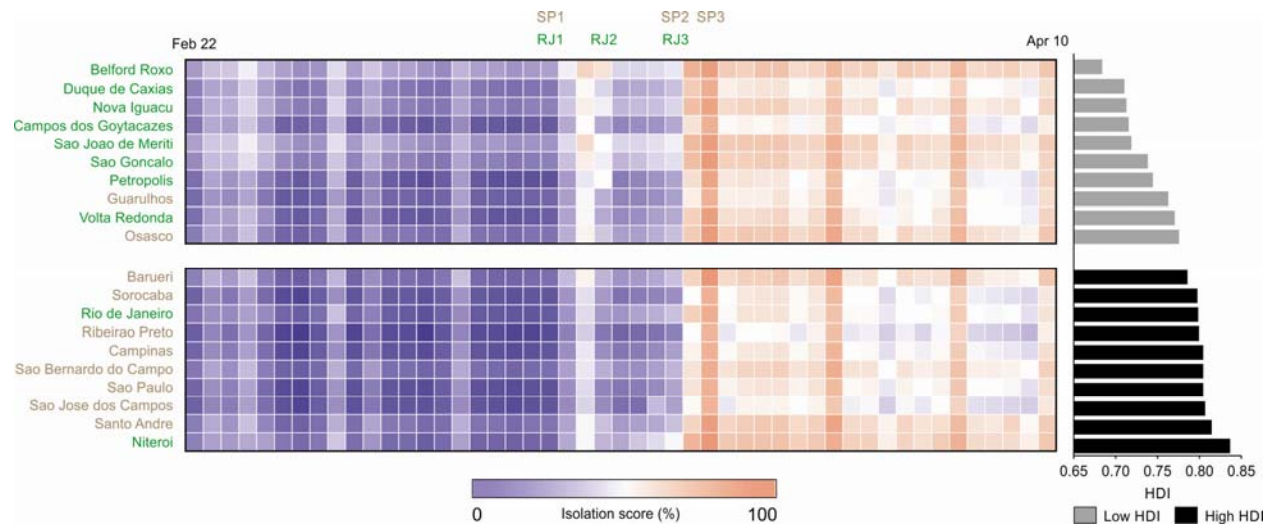


Fig. 4. Isolation index time series for the 10 largest cities in the states of São Paulo (SP) and Rio de Janeiro (RJ). SP1, SP2, SP3, RJ1, RJ2 and RJ3 correspond to intervention dates (See Fig. 1 legend)

Simulation of different interventions scenarios with isolation indexes above 50%

Assuming the $R(t)$ values associated with isolation indexes above 50% we next simulated different lengths of social distancing interventions, 30, 60 and 90 days (see **Materials and Methods**). An intervention of only 30 days was able to revert the intensive care units (ICU) demand curve only in those scenarios with the lowest values of $R(t)$, and was also associated with a quick rebound of the ICU demand curve far above the existing capacity (Figure 5). Prolonging the intervention to 60 days managed to revert the curve in most scenarios and delayed the second epidemic wave. An intervention of 90 days substantially delayed the second epidemic wave in all scenarios, although it had minimal impact on the height of both curves. According to our simulation, Rio de Janeiro state is able to stay below the ICU bed capacity threshold in the first epidemic wave in all scenarios. Conversely, São Paulo state needs to steadily increase its capacity in order to manage the first epidemic curve. Lower values of $R(t)$ were associated with smaller epidemic waves during the intervention but higher second epidemic waves (Figure 5).

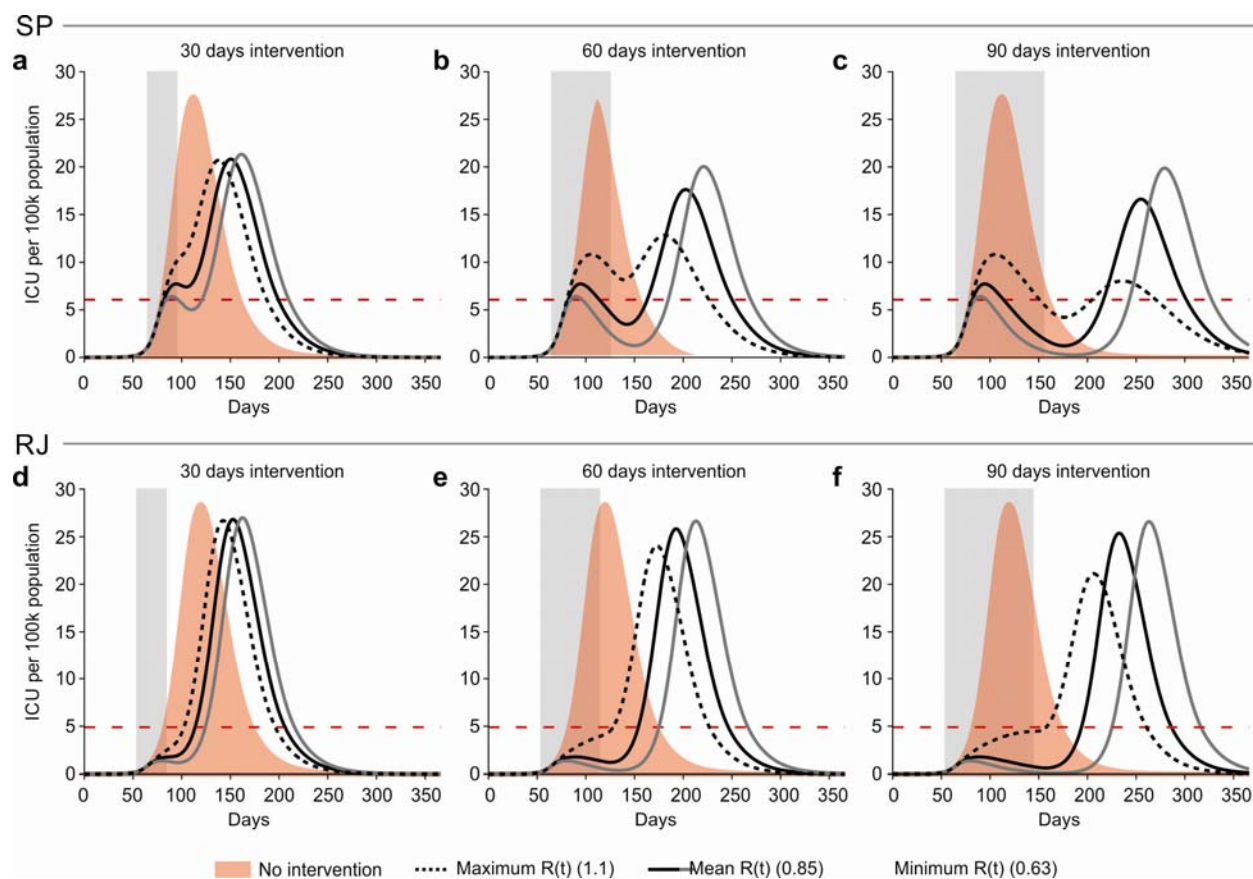


Fig. 5. Simulations of intensive care unit (ICU) demand according to different lengths of social distancing interventions for the states of São Paulo (top row) and Rio de Janeiro (bottom row). A, B and C: simulations for the São Paulo state assuming R values associated with isolation scores above 50% during 30, 60 and 90 days of intervention respectively; D, E and F: simulations for the Rio de Janeiro state assuming $R(t)$ values associated with isolation scores above 50% during 30, 60 and 90 days of intervention respectively. For each scenario we plotted the mean, minimum and maximum $R(t)$ values in the >50% isolation score category. The red horizontal line corresponds to ICU capacity for each state.

Discussion

Individual-based control efforts of COVID-19 can be challenging to implement due to the high infectiousness, relatively mild and moderate symptoms and pre symptomatic transmission^{23–25}. Consequently, social distancing measures are required to control COVID-19 in most scenarios. Here, we demonstrated that the initial social distancing measures adopted by the states of São Paulo and Rio de Janeiro successfully reduced $R(t) < 1$ by decreasing mobility across populations with lower and higher development index. We further demonstrated a strong correlation between the social isolation index and $R(t)$, and showed that isolation indexes above 50% lead to $R(t) < 1$ in most cases (89%). Our findings suggest that the isolation index can be used to monitor the effectiveness of social distancing measures and guide further interventions. By using aggregated mobility data, public health officials and policymakers can monitor in real time regional differences in social distancing intervention effectiveness and propose specific actions to reduce the transmission in specific locations(20).

Individual-based control efforts for COVID-19 can be challenging to implement due to the high infectiousness, relatively mild and moderate symptoms and pre-symptomatic transmission (21–23). Consequently, social distancing measures are required to control COVID-19 in most scenarios.

The structural impacts of social distancing should also be considered while managing its impact on disease transmission and, consequently, the healthcare systems' capacity. A previous analysis demonstrated that social distancing adopted during the Spanish flu pandemic was associated with better economic outcomes(24). However, society dynamics have changed dramatically during the past 102 years, and a continued monitorization of the COVID-19 socioeconomic impact is urgently needed. Suboptimal interventions for COVID-19 could be potentially catastrophic to public health and lead to a significant number of deaths. Thus, finding the optimal “therapeutic dosage” of such interventions is crucial, and requires a reliable and timely tool to monitor its effects.

$R(t)$ depends on the contact-rate among individuals; but the frequency of these contacts is difficult to quantify in real time through conventional approaches(25). We observed an inverse relationship between $R(t)$ and the isolation index for São Paulo and Rio de Janeiro States, the two mostly affected by the epidemic. We find that increases in the isolation index from lower than 25% to greater than 50% have lead to a reduction of $R(t)$ from approximately 2 to values less than 1, such as we observed. Highly-effective social distancing could reduce COVID-19 transmission enough to make a strategy based on contact tracing feasible, as is taking place in South Korea and Singapore(26, 27).

By using the $R(t)$ values associated with isolation indexes above 50%, we simulated social distancing interventions with varying time extensions. In most scenarios, interventions lasting between 30 to 60 days would blunt the first epidemic wave, although a shorter intervention led to a quick rebound and was not sufficient in scenarios with higher values of $R(t)$ during the intervention. Lower values of $R(t)$ resulted in a more effective control during the first wave, but with a caveat that the second epidemic wave was became significantly larger (albeit smaller than the initial peak that would have been otherwise seen in the absence of interventions). Furthermore, the delay in this peak allows the preparation of healthcare systems to mitigate health impacts by securing equipment and supplies, bolstering ICU capacity, planning for personnel needs and implementing infection control policies.

Higher values of $R(t)$ during the intervention led to more evenly distributed epidemic waves, which would make it possible to implement less stringent interventions during following waves. Although it is tempting to propose that social distancing interventions that would lead to an $R(t)$ value of 1.1, such a strategy could have potentially catastrophic consequences. The reason for this is that values of social indexes below 50% are associated with a mean $R(t)$ value of 1.4 (ranging from 0.7 to 2.6), which was not significantly different from no intervention. Aiming at achieving a $R(t)$ value of 1.1 by lowering the social isolation index could therefore lead to a scenario similar to the natural history of COVID-19. It is thus more effective and probably safer to set a goal of $R(t)$ below 1 and implement social distancing interventions that lead to social isolation indexes above 50%. This will require close monitoring after the intervention is relaxed,

since it is very likely that a second intervention will be needed to flatten a second epidemic wave.

The findings of our simulations need to be interpreted cautiously. We did not aim to precisely replicate the epidemic in both states but merely to simulate hypothetical scenarios, exploring different strategies. Also, our simulations are heavily influenced by the assumptions and parameters that were built into the model. A key assumption in our model is that infection leads to persistent immunity after recovery. Data on SARS-CoV-2 immunity is scarce, preliminary data on rhesus macaques have demonstrated immunity after an initial infection(28, 29) and plasma from recovered individuals was tested to neutralize the virus *in vitro* and *in vivo*(30–33). On the other hand antigenic drifts(34) as well as waning immunity might lead to the loss of herd immunity. If immunity is not long lasting, as has been estimated for other coronaviruses such as HCoV-OC43 and HCoV-HKU1, COVID-19 will likely enter a regular transmission cycle and become endemic(35).

Another aspect that needs to be taken in consideration is that we simulated epidemics in entire states, assuming homogeneous transmission within the state. However, it is possible that different cities will have non synchronized COVID-19 epidemics, hence interventions will need to be tailored for each city or metropolitan area individually. Moreover, our assumption that only 50% of the established ICU capacity could be used for COVID-19 might be an underestimation of the total capacity, given that during the epidemic efforts have been made to increase hospital capacity in both states, which could lead to the need of less stringent interventions.

Another potential source of bias is that we assumed that the reporting rates were stable during the epidemic. If reporting rates of SARI cases increased during the initial stages of the epidemic our initial $R(t)$ estimates would have been overestimated. Further, if the reporting rates are decreasing, it could mean that the decrease in $R(t)$ that was observed would be partially a result of a reporting bias. Although Brazil has had changes in the reporting systems for COVID-19 during the epidemic, the dataset which was used is based solely on hospitalized SARI cases which required hospitalizations. However, we used SIVEP-GRIPE data, a stable and a well-established system and recommendations for its use have not changed during the epidemic, we believe that this is the most reliable and consistent source of data for severe cases of COVID-19 in Brazil. We also accounted for potential bias related to reporting delays, which affect the end of a time series, by applying a correction factor which corresponds to the inverse of the probability of being reported up to the last date of data being collected.

Another limitation of our approach is that mobility data from mobile phones are a coarse measure of physical distancing, which does not directly capture changes in the number, duration or character of human interactions. Additionally, this approach does not account for other behavioral changes in the population (such as hand washing, respiratory etiquette and universal mask usage) that could also alter transmission patterns and lead to changes in $R(t)$.

Our findings underscore the importance of early implementation of social distancing measures to reduce SARS-CoV-2 transmission. The strong association observed here indicates that urban mobile phone-derived isolation scores are able to track temporal fluctuations in R during social distancing interventions in Brazil. If additional behavioral changes are undertaken and sustained,

the isolation score could provide a real-time metric to assess effectiveness of interventions. A major contribution of our approach is that the social isolation index data is readily available on a daily basis, in contrast with the $R(t)$ measurement, which is subject to delays (up to two weeks). Using this index will allow for a more timely assessment of the epidemic dynamics and for planning of public health mitigation strategies.

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Ethical approval: This study followed Brazilian and International legislation for conducting human research. This research project was approved by the National Research Ethics Committee

(Comissão Nacional de Ética em Pesquisa, CONEP) in Brazil, Register number (CAAE): 11946619.5.0000.5421.

Material and Methods

Mobility data

We used geolocation data collected between February 6, 2020 to April 10, 2020. Urban mobility patterns were extracted from unidentifiable personal information. We settled the likely home-residence location based on the place most often visited during non-working hours. Device location data was compiled and aggregated at both city and states level by the technology company *In Loco* (São Paulo, Brazil). As of February of 2020, Brazil totaled more than 227 million mobile phones devices in use with the states of São Paulo (66,939,000) and Rio de Janeiro (18,633,000) ranking first and third with the most devices in the country. In the same month, the technology company *In Loco* (São Paulo, Brazil) accessed geocoded information from 17,482,780 million users in the state of São Paulo (26%) and 5,390,130 (29%) in the state of Rio de Janeiro, and it reported more than 700 million monthly geolocations tracked to physical locations in these two states.

An isolation index was calculated as a ratio between the number of people staying at home on a given day divided by the number of mobile phone users living at the same state or city, expressed as a percentage. Only those mobile phones with geolocation app tracking active were considered for the index calculation.

Severe Acute Respiratory Illness and time-dependent reproduction number

Brazil has a well-established surveillance system for severe acute respiratory illness (SARI), and notification of SARI cases has become mandatory since 2009. Since then hospitalized SARI cases as well as cases of influenza like illness (ILI) reported by the sentinel surveillance sites are registered in an electronic database, SIVEP-GRIPE. Although Brazil initially established a reporting system for mild COVID-19 cases based on the REDCap platform, this was shifted on March 25, 2020 to a new reporting system, e-SUS VE. At the same time, input of SARI cases into SIVEP-GRIPE database has remained consistent. We used all hospitalized SARI cases which were reported by the states of São Paulo (SP) and Rio de Janeiro (RJ) from the same period of geolocation data collected. We included SARI cases which were confirmed for COVID-19 (positive RT-PCR for SARS-CoV-2 in any respiratory sample), as well as those suspected without any etiological diagnosis. We excluded cases with a positive PCR for other respiratory viruses and that also had not been tested for COVID-19 or that tested negative. Due to the lack of massive testing, the inclusion of SARI cases without an etiological diagnosis was carried out assuming that most SARI cases were expected to be related to COVID-19 during the epidemic. The exclusion of these cases would have led to biased results due to delays in

ascertainment of COVID-19 cases. The epidemic curve was constructed using the date of onset of symptoms.

To correct for reporting delays, we applied a daily correction factor based on the observed delays between the date of onset of symptoms and the date of data reporting. This weight corresponded to the inverse of the probability of being reported up to the last date of data being collected(18). Moreover, we restricted the analysis to patients who developed symptoms until 4 days before the last data entry. The $R(t)$ was calculated considering the epidemic curve and serial interval observed in the COVID-19 cases in Brazil, using the R0 package available in R(19). To test the temporal relationship between the isolation index and $R(t)$ time series, we used cross correlation analysis with various lag days and the Granger test (isolation index predicting $R(t)$).

We summarized the ability of the isolation index to predict a $R(t)$ lower than 1, by calculating the area under the ROC curve (AUC). Moreover, we looked for the cut-off point with the highest accuracy (proportion of observations with $R(t) < 1$ and $R(t) \geq 1$, respectively above and below the index cut-off point) and supported a recommendation by rounding up that isolation index point.

We additionally compared the $R(t)$ for the isolation index categories (under 25%, 25 - 50% and greater than 50%, based on ROC curve) using Kruskal Wallis test and post-hoc analysis was conducted through the Dunn test for multiple comparison. We also stratified the analysis by Human Development Index (HDI) in order to assess for an interaction with socioeconomic status. For this analysis, we used data from the 10 largest cities in the states of São Paulo (SP) and Rio de Janeiro (RJ) and evaluated changes in the trends of their indexes, split into two groups: high HDI (range from 0.786 to 0.837) and low HDI (range from 0.684 to 0.776) and compared the isolation indexes from February 22, 2020 to April 10, 2020 between the groups(20).

Application in intervention-effect modeling

To simulate different interventions scenarios we used an age stratified SEIR model which includes compartments for individuals requiring hospitalization and intensive care (6). We considered three different time frames of social distancing interventions (30, 60 and 90 days) and simulated the prevalence rate, ICU demand and number of deaths for COVID-19. During the intervention we used the mean, maximum and minimum reproductive numbers (R) associated with isolation indexes greater than 50% which were observed in our dataset. We used a Basic Reproductive Number (R_0) equal to 2.27 at the beginning of the epidemic, which was the peak value for the observed $R(t)$ series. After intervention we used an R value of 1.8, assuming that after ceasing the interventions residual changes in the population's behavior (such as mask usage for example) would lead to approximately a 20% reduction in transmissibility. The remaining model parameters are described in Table 1.

In all simulations, the model was seeded with a prevalence of 10^{-7} per population, which corresponds to 4.4 cases in SP and 1.65 cases in RJ, and evolved with $R_0 = 2.27$ until reaching the cumulative mortality rate which was observed at the beginning of the intervention in each

state. After reaching the established threshold, the intervention starts in our model, at that point the reproductive number gradually changes during 8 days until reaching the pre specified R value associated with the intervention. This 8 days transition period was chosen based on the observed delay between the first intervention and reaching isolation indexes above 50% in both states. With this assumption, we wanted to compare how both states would evolve and how changes in demography, capacity of the healthcare systems and the timing of the intervention would influence the ability to cope with the epidemic under otherwise similar conditions. Hospital and ICU capacities were collected from the National Registry of Health Establishment (CNES). In SP and RJ, 1481 and 523 hospitals were active in the month of February of 2020, respectively. The model assumes that 50% of the total number of ICU beds available in the public healthcare system could be allocated to COVID-19.

Table S1. Parameters used in the age stratified SEIR model to forecast the ICU beds demand, prevalence and deaths.

Parameter	Value	Source
R0	2.270	Ganem et al(6)
R(t) during intervention - min	0.628	
R(t) during intervention - mean	0.852	
R(t) during intervention - max	1.106	
R(t) after intervention	1.800	
Incubation period	3.69 days	Li et al(36)
Infectious period	3.47 days	Li et al(36)
Proportion of infected individuals hospitalized / Infection fatality ratio (IFR) by age group		Verity et al(37)
0 - 9 years	0.00% / 0.00161%	
10 - 19 years	0.0408% / 0.00695%	
20 - 29 years	1.04% / 0.0309%	
30 - 39 years	3.43% / 0.0844%	
40 - 49 years	4.25% / 0.161%	
50 - 59 years	8.16% / 0.595%	
60 - 69 years	11.8% / 1.93%	
70 - 79 years	16.6% / 4.28%	

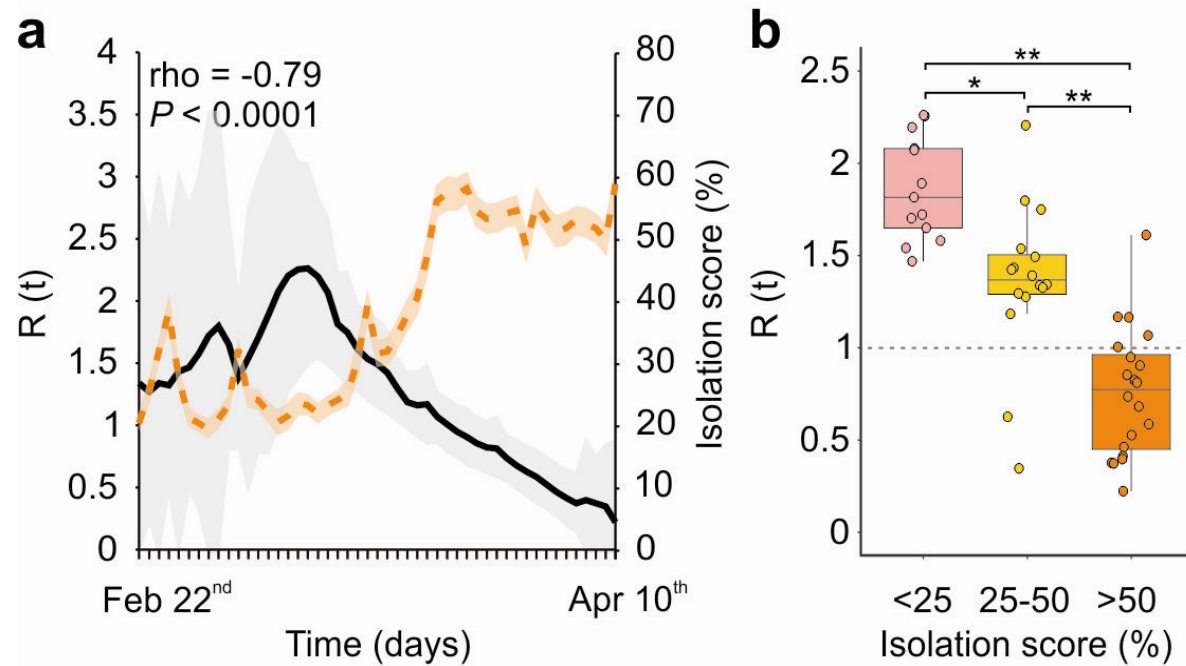
>80 years	18.4% / 7.80%	
Case fatality in individuals requiring intensive care (CFICU)	49%	Novel Coronavirus Pneumonia Emergency Response Epidemiology Team(38)
Proportion of infected individuals requiring intensive care	IFR divided by CFICU	
Length of hospital admission	10	Wang et al(39)
Length of intensive care unit stay	7.5	Assumed

Fig. S1.

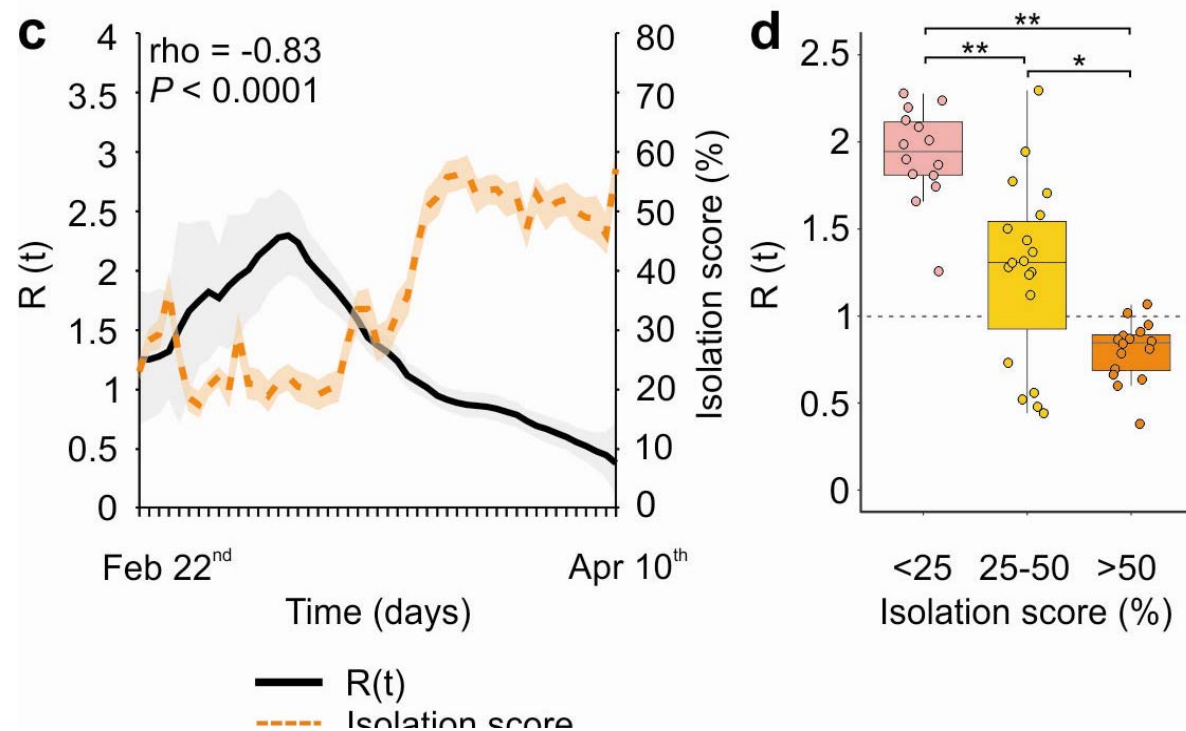
A and C: Time dependent reproductive number ($R(t)$) and isolation index per day from the cities with lower and higher HDI of Rio and São Paulo, respectively; B and D: boxplot showing the median, interquartile range and range of $R(t)$ stratified by isolation index (<25%, 25-50%, 50%) from cities with lower and higher HDI of Rio and São Paulo, respectively.

5

Low HDI



High HDI



The impact of early social distancing at COVID-19 Outbreak in the largest Metropolitan Area of Brazil.

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Running head: Impact of early social distancing at COVID-19 Outbreak

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Abstract

We calculated the impact of early social distancing on the COVID-19 transmission in the São Paulo metropolitan area and forecasted the ICU beds needed to cope the epidemic demand by using an age-stratified SEIR model. Within 60 days, these measures would avoid 89,133 deaths.

Keywords: COVID19, Social distance, Impact, hospitalization, deaths

The COVID-19 pandemic has led to the collapse of healthcare systems in several countries (1). The virus has a higher basic reproduction number (R_0) (i.e., the average number of secondary cases generated by a primary case when introduced in a fully susceptible population) and case fatality rate (CFR) when compared with Influenza (R_0 :2,5-3,2 and CFR:0,4-2,9% versus R_0 :1,2-2,3 and CFR:0,15%-0,25%, respectively) (2–5). Among the confirmed cases in China, 18.5% were considered severe and 25.3% of those required intensive care (2). To tackle the spread of disease, a range of interventions have been implemented in China, including increasing test capacity, rapid isolation of suspected and confirmed cases and their contacts, social distancing measures, as well as restricting mobility (6).

In Brazil, the first confirmed COVID-19 case was reported on February 26th in the São Paulo city and, since March 16th, the state of São Paulo has recommended several social distancing measures. These include recommending that older adults and individuals with underlying chronic medical conditions stay at home as much as possible; cancelling mass events; reducing public transportation; closing schools, universities and workplaces; and maintaining only essential services.

The São Paulo Metropolitan Area (SPMA), one of the most populous urban area in the world, has 7,300 ICU beds registered in the National Council of Health Establishments (Cadastro Nacional de Estabelecimentos de Saúde, CNES: <http://cnes.datasus.gov.br>), 2,880 of which belong to the Public Healthcare system.

As the collapse of health care systems is the major concern for most countries hit by the pandemic, non-pharmacological interventions has been recommended to flatten the epidemic curve and gain time to prepare the health system to avoid shortage of ICU beds and healthcare workers needed to treat critically ill patients (4).

The study

We evaluated the impact of early social distancing measures in the transmission of COVID-19 in the SPMA, and forecast the number of ICU beds necessary for COVID-19 patients in Brazil.

In 2009, the MoH established a mandatory notification for hospitalized cases of severe acute respiratory illness (SARI) through the National Disease Notification System (SIVEP-GRIPE). We retrieved all SARI cases reported on the SIVEP-GRIPE system between 26th February and 30th March. Those cases were included regardless of COVID19 confirmation as a proxy of COVID19 case. This proxy was used to calculate the time dependent reproductive number $R(t)$ of confirmed COVID19 cases and was chosen in order to minimize the impact of shortage of RT-PCR tests. In addition, we also calculated $R(t)$ using the daily number of COVID19 confirmed cases from the São Paulo state epidemiological records.

We calculated the $R(t)$ during one month period in the SPMA, both, for COVID19 confirmed cases, as well as for SARI cases, and estimated the expected number of SARI cases requiring an ICU bed. The reproductive number at the beginning of the epidemic (R_0) and during the epidemic (R_t) were calculated using the package R_0 R Studio (3). The expected ICU demand was calculated using an age stratified SEIR model (7), which includes compartments for individuals requiring hospitalization and intensive care. The model parameters are described in Table 1.

Considering only the confirmed cases reported by São Paulo state, the $R(t)$ was close to 2 throughout the assessed period with a large confidence interval. (Figure 1a). Underreporting and lack of confirmatory tests for COVID19 could directly affect these $R(t)$ estimations. (Figure 1a). By analyzing the number of SARI available in the Epidemiological Surveillance of Influenza System (SIVEP-GRIPE), we found that the social distancing measures reduced the $R(t)$ below to 1 with a more accurate confidence interval (Figure 1b). The R_0 was used in the SEIR model to forecast the ICU beds needed and the number of deaths in a scenario without social distancing measures. The $R(t)$ of SARI cases was used to forecast the scenario with social distancing measures.

We defined the ICU bed capacity for COVID-19 as 20% of the total number of ICU beds in the SPMA. In the absence of social distancing measures, the model

predicts that after 30 days, COVID19 patients would demand 5,384 ICU beds, which surpasses the current ICU capacity in 130%; furthermore, in the second month the ICU bed demand would be 14 times the ICU capacity. Overall, this would result in 1,783 deaths in the first month and 89,349 in the second month. While social distancing measures are maintained, the model predicts 317 deaths in the first month and a total of 1682 in the second. This scenario does not overburden the healthcare system which represents a maximum of 76% ICU beds capacity.

Using the severe cases notification systems, we identified that the social distancing measures implemented in the SPMA reduced the COVID19 $R(t)$ to less than 1. If a similar level of social distance is maintained in April and May, during influenza seasonality, no additional ICU beds for COVID-19 patients will be needed in the SPMA.

We observed that the downward trend in hospitalized cases started on 9th March, before the intervention. This could be explained by a decrease in mobility documented since the first days of March in places like national parks, dog parks, plazas, and public gardens. According to a COVID-19 Community Mobility Report informed by Google this reduction was intensified and spread to other settings since the local government declared a state of emergency(8). This report suggested that intervention was effectively applied, and it is consistent with the transmissibility reduction observed. Furthermore, our study indicated that social distancing measures impact should be monitored on daily based using hospitalized SARI cases, especially during the shortage of the COVID-19 confirmatory tests.

The baseline scenario shows that completely relaxing social distancing results in thousands of additional deaths. Figure 2 shows that the rate of fatalities per day increases dramatically when ICU capacity is overloaded. The simulation shows a swift change in the number of deaths per day in this scenario quickly spikes from 100, a week prior the system is overloaded, to a peak of 4,160 deaths per day in less than a month.

A potential limitation is that many COVID-19 patients from nearby cities usually sought for medical care in the SPMA area, which is a reference for the state of São Paulo, leading to overburden of the healthcare system even if the epidemic is controlled

in the SPMA. The last week of data has not been included to minimize the impact of delay in reporting.

Conclusions

Despite the limitations, by using SARI electronic notification systems as a proxy for severe cases of COVID19 we reported a substantial decrease on the $R(t)$ after two week of the implemented of social distance measures in the SPMA. These measures are expected to avoid 89,133 deaths within 60 days even without expanding the ICU bed capacity.

Fabiana S.G. dos Santos is a biologist and PhD candidate. Her main research interest is epidemiology of infectious diseases and mathematical modelling

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TABLES

Table 1. Parameters used in the age stratified SEIR model to forecast the ICU beds

Parameters	Values	Source
Incubation period	5.1 days	Rocha-Filho et al (8)
infectious period	1.61 day	Rocha-Filho et al (8)
Symptomatic	50%	Ferguson et al (7)
Serial interval (mean±standard deviation)	4,18±3,20	Park et al (9)
Infection Fatality Rate	0.8%	
Case Fatality Rate	1.6%	
Reproduction number	2.27	
Imported cases rate	24 cases/day	
Serial interval (mean±standard deviation)	4,18±3,20	

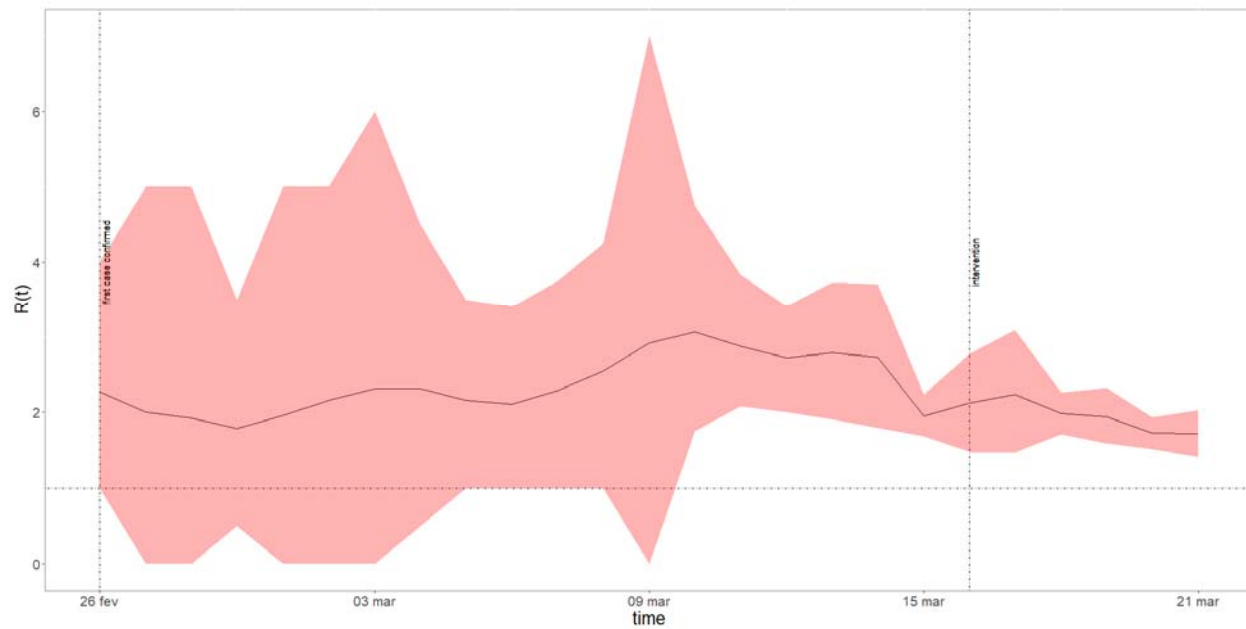
LEGENDS AND FIGURES

Figure 1. Time-dependent reproductive number $R(t)$ estimated for the confirmed COVID19 cases (a), and for the SARI cases (b). Solid line corresponds to $R(t)$, the red area of the confidence interval; the vertical dotted line represents, respectively, the date of the onset of symptoms of the first confirmed case in Brazil and date of the first social distancing measure implemented by the São Paulo state.

Figure 2. Estimation of the number of ICU patients (Black line) and fatalities (Red line). The solid line uses the time dependent reproductive number $R(t)$ measured for SPMA and the dashed line represents the scenario in which no social distancing takes place. The vertical dashed line represents the date in which the local government declared a state of emergency and the horizontal gray line represents the number of available ICU beds.

FIGURE 1.

A)



B)

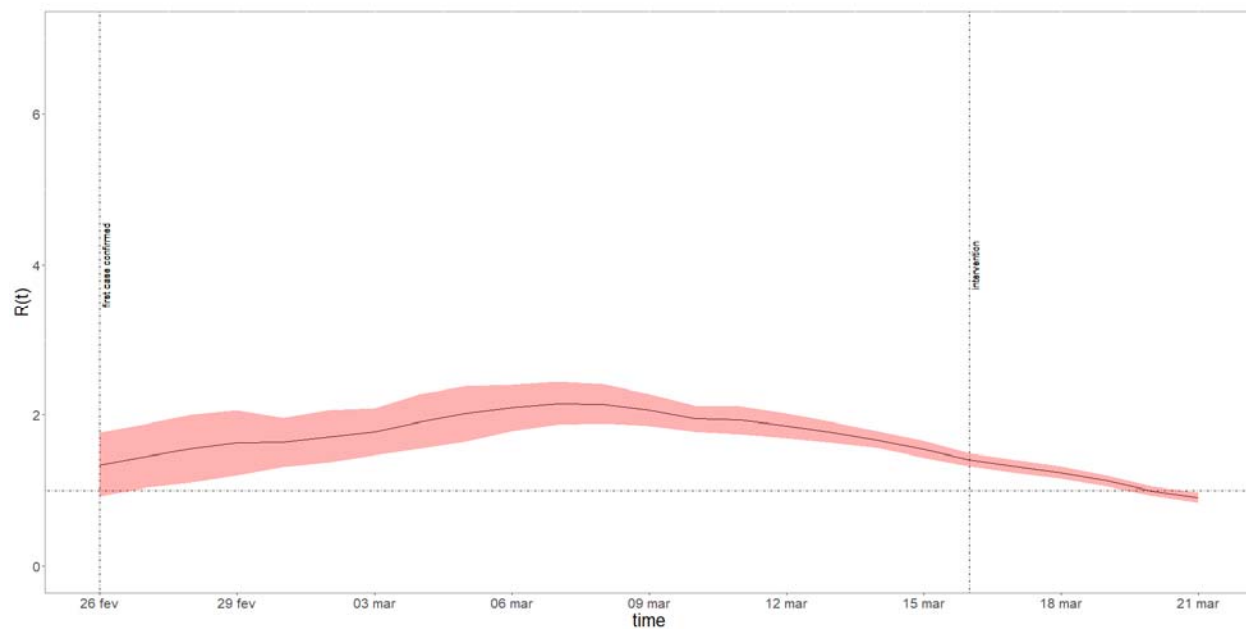
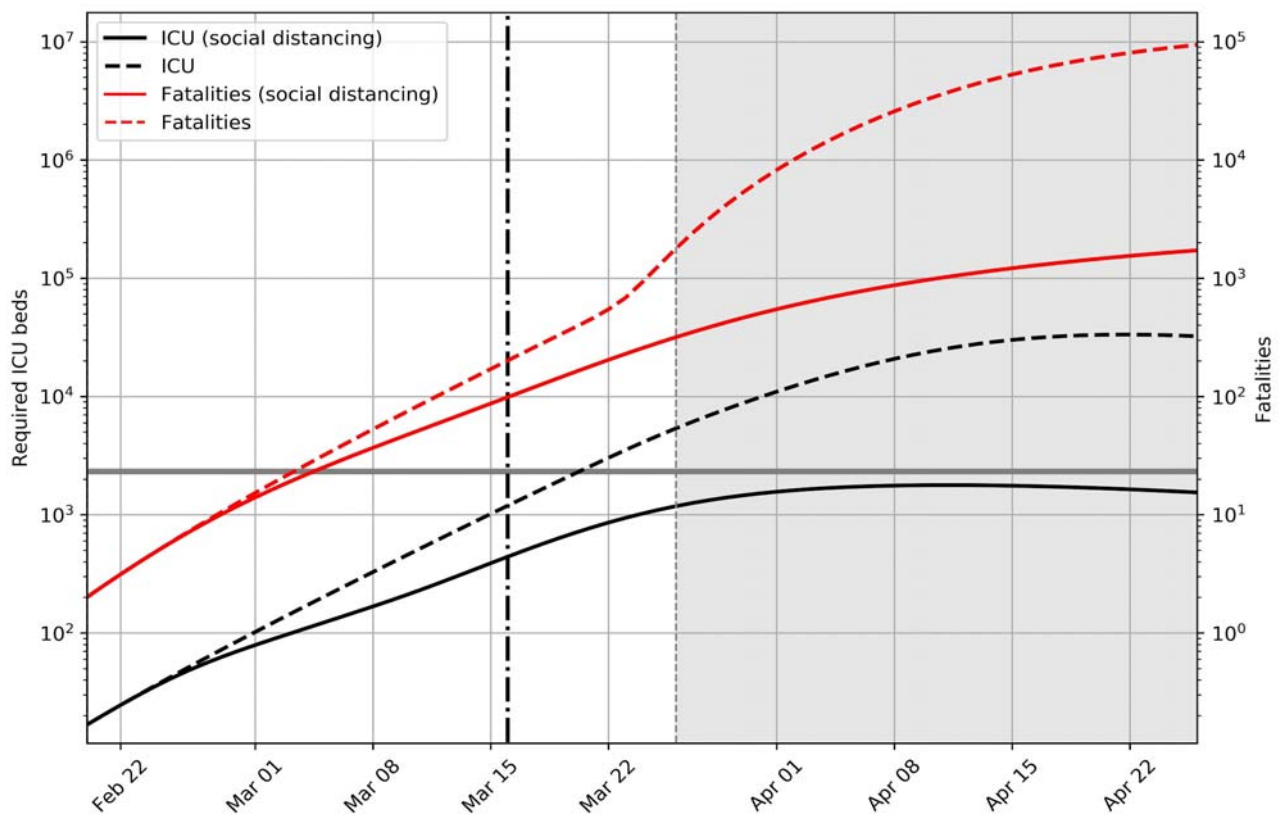


FIGURE 2.



Método de cálculo para o total de casos, internados e internados em UTI

O número básico de reprodução é o número de casos secundários gerados por um caso quando este é introduzido em uma população totalmente susceptível. O número efetivo de reprodução é o número de casos secundários gerados por um caso em uma população com um percentual de susceptíveis, e pode ser calculado com base na fórmula a seguir:

$$Re = R0 * S$$

Onde Re é o número de reprodução efetivo, R0 é o número básico de reprodução e S é o percentual da população susceptível. Considerando que quando um caso gerar menos de um caso secundário a epidemia evolui invariavelmente para a resolução, podemos fazer um cálculo aproximado de quantas pessoas precisam estar imunes para atingir a imunidade de rebanho, ou seja, o limiar a partir do qual a epidemia tende a se esgotar por esgotamento de susceptíveis. O cálculo é feito da seguinte maneira:

$$1 = R0 * S$$

Portanto:

$$1/R0 = S$$

Considerando que nesse momento não existem vacinas disponíveis para imunizar a população para o COVID-19, a única forma de ficar imune é adquirindo a doença, dessa forma a proporção de infectados (I) será:

$$I = 1-S$$

Considerando que as estimativas de casos graves, intensivos e óbitos são baseados nos dados disponíveis de casos confirmados, podemos assumir que os casos não detectados foram oligossintomáticos ou assintomáticos. Dessa forma o percentual de casos graves deve ser aplicado sobre os casos detectados, calculado conforme a equação a seguir:

$$D = I * pD$$

Sendo D = número de casos detectados e pD o percentual de casos detectados. Para calcular os hospitalizados podemos utilizar a seguinte fórmula:

$$H = D * pH$$

H seria o número de indivíduos hospitalizados, e pH o percentual de casos que tiveram doença grave. O número de pessoas que serão internadas em UTI pode ser calculada com a fórmula:

$$U = H * pU$$

Onde U = número de pessoas que serão internadas em UTI, pU é o percentual de casos hospitalizados que necessitam de tratamento intensivo. Para o número de óbitos podemos calcular com:

$$M = U * pM$$

Onde M é o número de mortos e pM o percentual de pessoas internadas em UTI que morrem.

O número total de leitos-dia necessários para abarcar toda a população de hospitalizados em enfermaria e UTI pode ser calculado com base no tempo médio de permanência em cada uma dessas unidades.

$$Ud = U * Tu$$

$$Hd = U * Th$$

Onde Hd e Ud é o número de leitos-dia necessários de enfermaria e UTI respectivamente e Tu e Th o tempo de permanência médio em UTI e enfermaria. Os dados disponíveis na literatura até o momento para cada um desses parâmetros é:

Parâmetro	Valor	Referência
R0	2,75 (IC: 1,94 – 4,41) No calculo gerado foi utilizado o valor conservador de 2	Calculado com base nos dados do artigo (Liu, Gayle, Wilder-Smith, & Rocklöv, 2020), assumindo uma distribuição log-normal das diferentes estimativas
Percentual de detecção(pD)	14% (IC: 10% - 18%)	(Li et al., 2020)
Percentual de hospitalização (pH)	18,5%	(Novel Coronavirus Pneumonia Emergency Response Epidemiology Team, 2020)
Percentual de casos críticos (pU)	25,28%	(Novel Coronavirus Pneumonia Emergency Response

		Epidemiology Team, 2020)
Percentual de óbitos (pM)	49%	(Novel Coronavirus Pneumonia Emergency Response Epidemiology Team, 2020)
Tempo de internação hospitalar (Th)	14 dias	Assumido
Tempo de internação em UTI (Tu)	14	assumido

Esses cálculos representam o que poderá ocorrer caso a epidemia progrida até o esgotamento dos susceptíveis na população, é possível estimar qual a necessidade de leitos caso a epidemia dure 6 meses, ou caso seja possível atrasar ela ao longo de 12 meses por exemplo. Nesse caso basta multiplicar o número de hospitalizados pelo tempo médio de internação e dividir pelo tempo de duração da epidemia. Esse método de cálculo no entanto não reflete o pico epidêmico. A velocidade de dispersão da epidemia irá influenciar na capacidade de atendimento, e epidemias simultâneas em cidades próximas poderão acelerar o esgotamento de recursos em cidades de referência. Por outro lado intervenções podem reduzir o número de reprodução e retardar a evolução da epidemia ou mesmo modificar o número total de casos.

Referências

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- Liu, Y., Gayle, A. A., Wilder-Smith, A., & Rocklöv, J. (2020). The reproductive number of COVID-19 is higher compared to SARS coronavirus. *Journal of Travel Medicine*, (February), 1–6. <https://doi.org/10.1093/jtm/taaa021>
- Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. (2020). [The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China]. *China CDC Weekly*, 2(x), 1–10. <https://doi.org/10.3760/cma.j.issn.0254-6450.2020.02.003>

COVID-19, análise de risco e impacto estimado no Brasil

COE ampliado, 08/03/2020



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Tópicos

Breve atualização epidemiológica do COVID-19

Análise comparativa com o comportamento do H1N1 na pandemia de 2009 e com a gripe espanhola

Modelo de projeção de casos em São Paulo

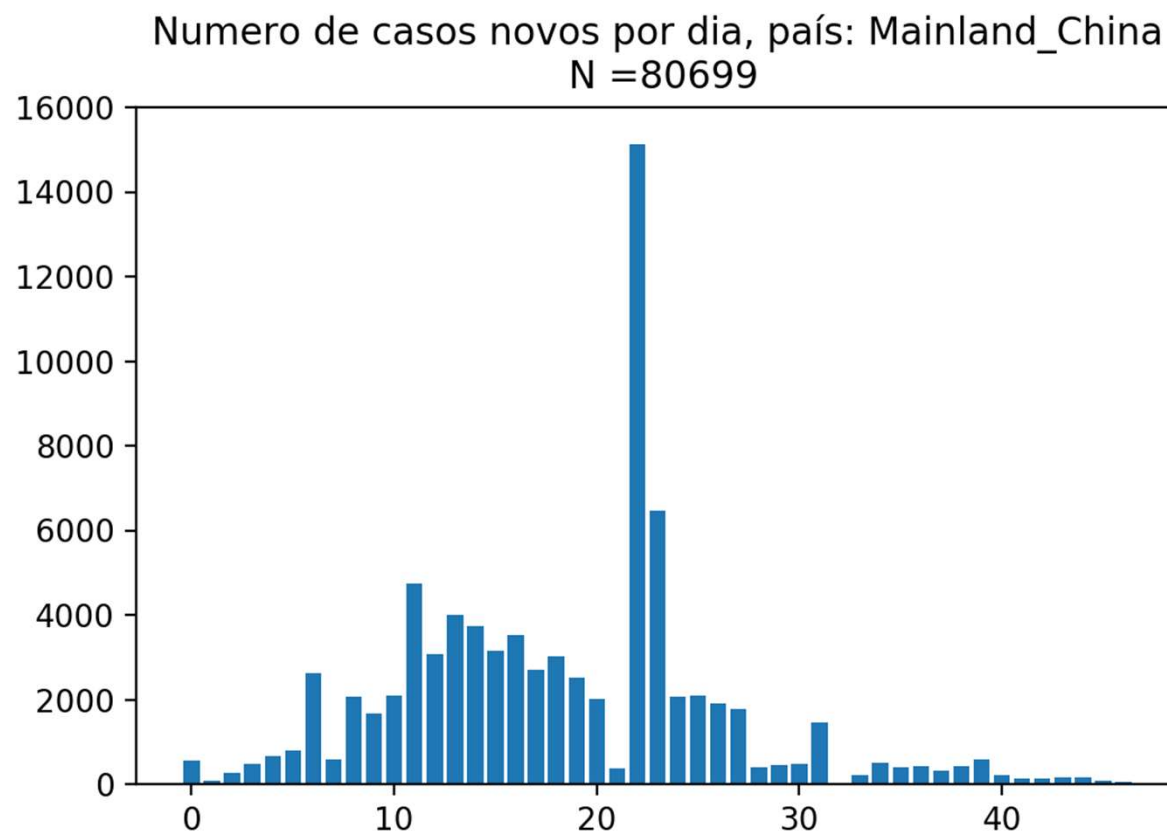
Avaliação da disponibilidade de leitos no SUS (OPAS)



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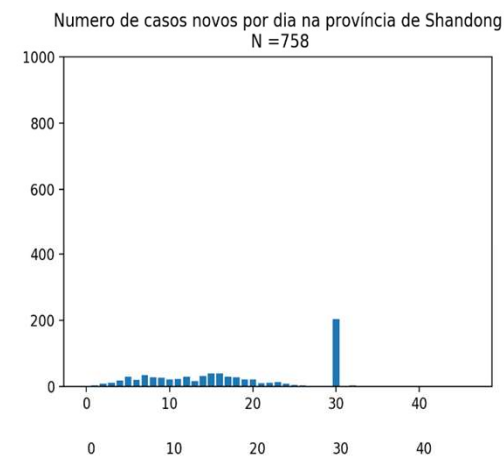
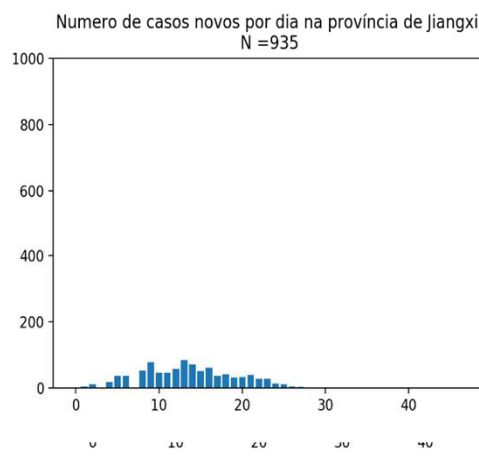
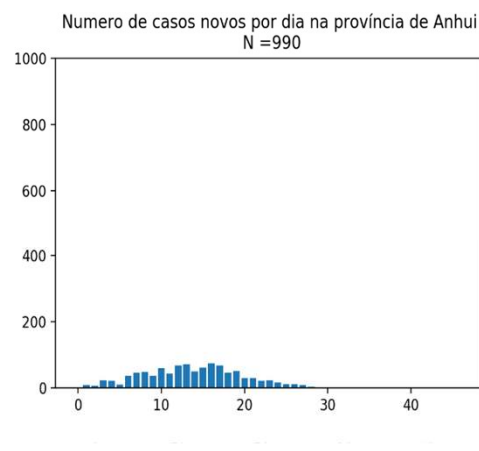
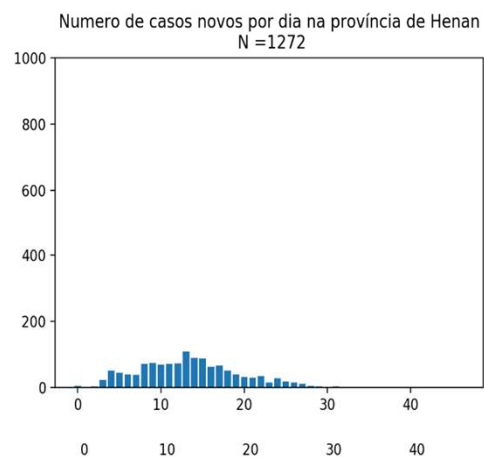
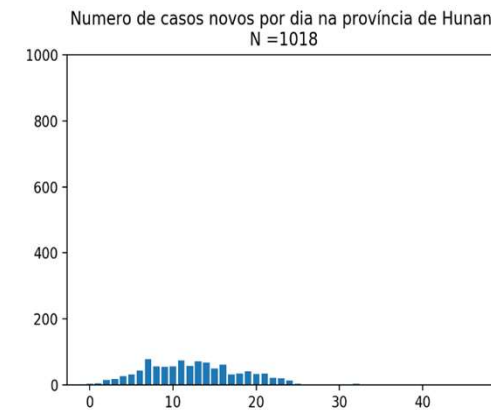
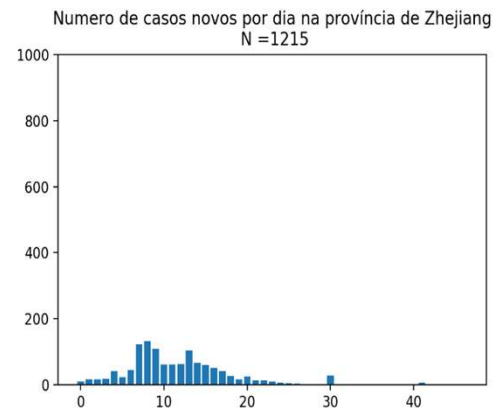
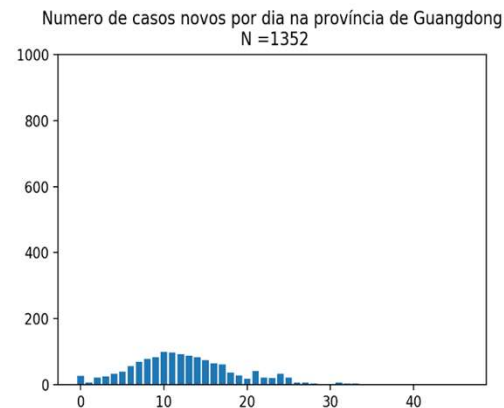
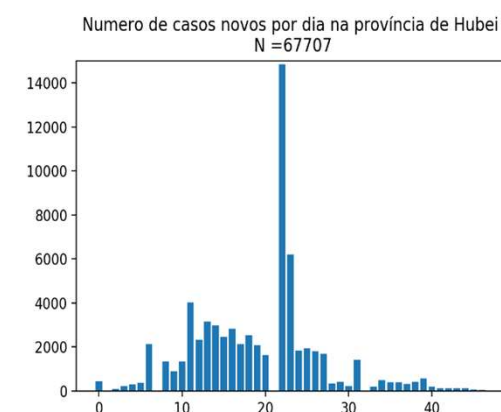


Curva epidêmica do COVID-19 na China, casos novos por dia a partir do dia 22/01/2020



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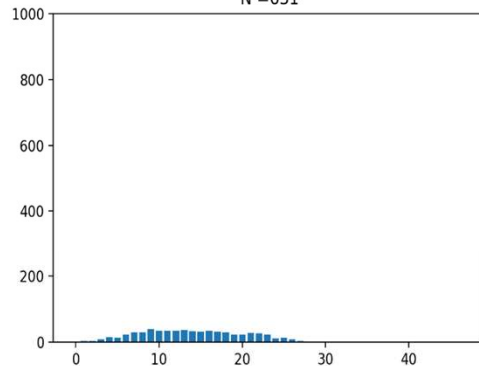
Curvas epidêmicas do COVID-19 por província da China, casos novos por dia a partir do dia 22/01/2020



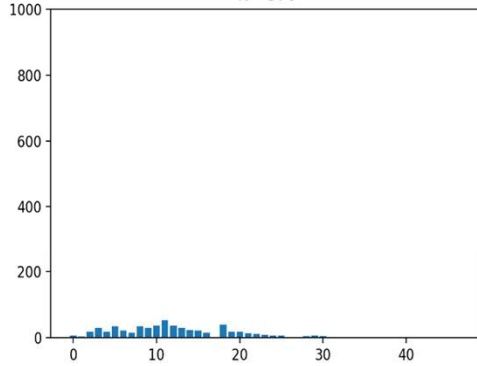
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Curvas epidêmicas do COVID-19 por província da China, casos novos por dia a partir do dia 22/01/2020

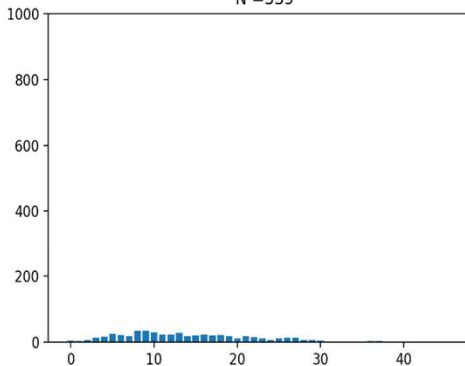
Numero de casos novos por dia na província de Jiangsu
N = 631



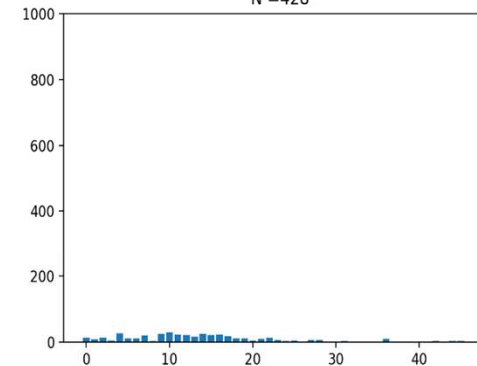
Numero de casos novos por dia na província de Chongqing
N = 576



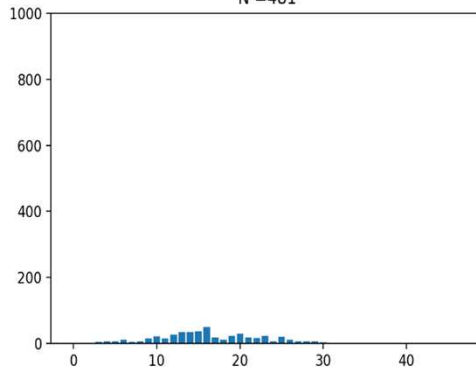
Numero de casos novos por dia na província de Sichuan
N = 539



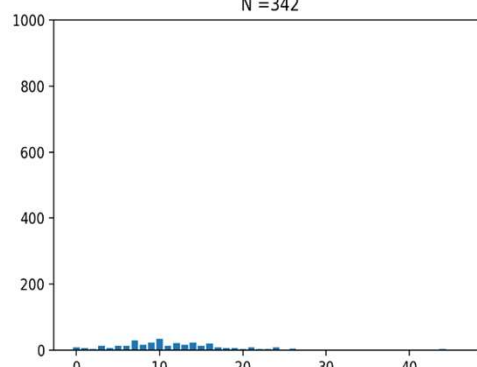
Numero de casos novos por dia na província de Beijing
N = 428



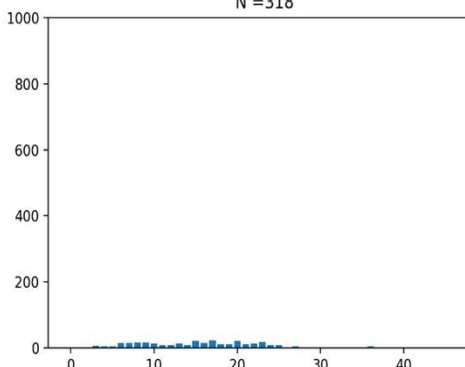
Numero de casos novos por dia na província de Heilongjiang
N = 481



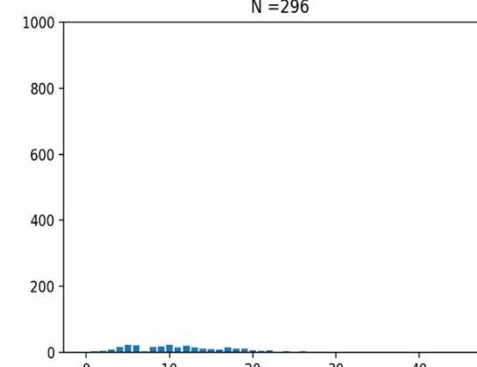
Numero de casos novos por dia na província de Shanghai
N = 342



Numero de casos novos por dia na província de Hebei
N = 318

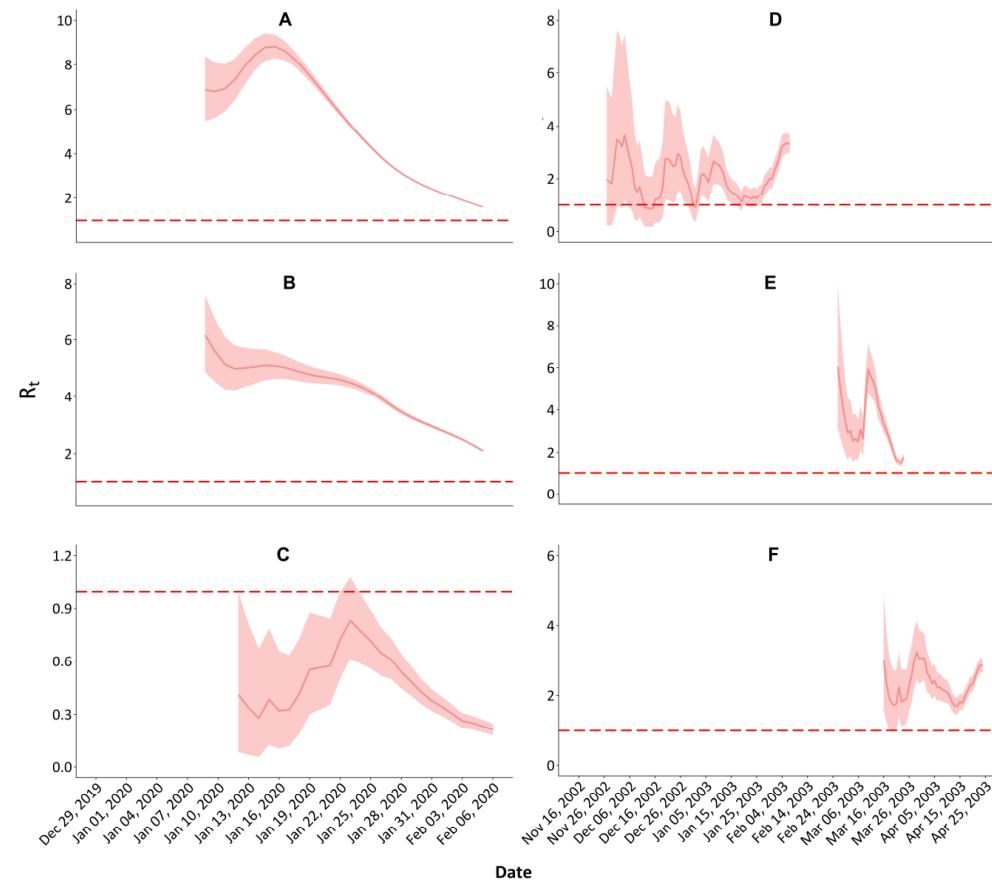


Numero de casos novos por dia na província de Fujian
N = 296



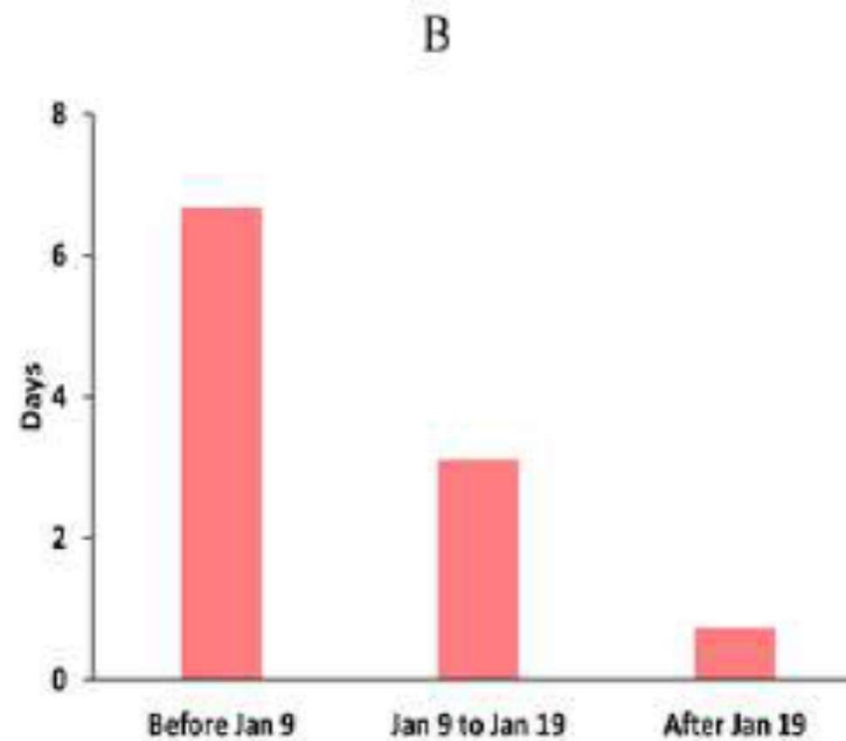
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Evolução do número de reprodução do COVID-19 comparando com SARS. China, Wuhan e Guangdong



Liu, T. *et al.* (2020a) 'Time-varying transmission dynamics of Novel Coronavirus Pneumonia in China', *bioRxiv*, p. 2020.01.25.919787. doi: 10.1101/2020.01.25.919787.

Evolução do tempo médio entre o início dos sintomas e o isolamento, Guangdong



Liu, T. *et al.* (2020) 'Transmission dynamics of 2019 novel coronavirus (2019-nCoV)', *The Lancet*, pre print.

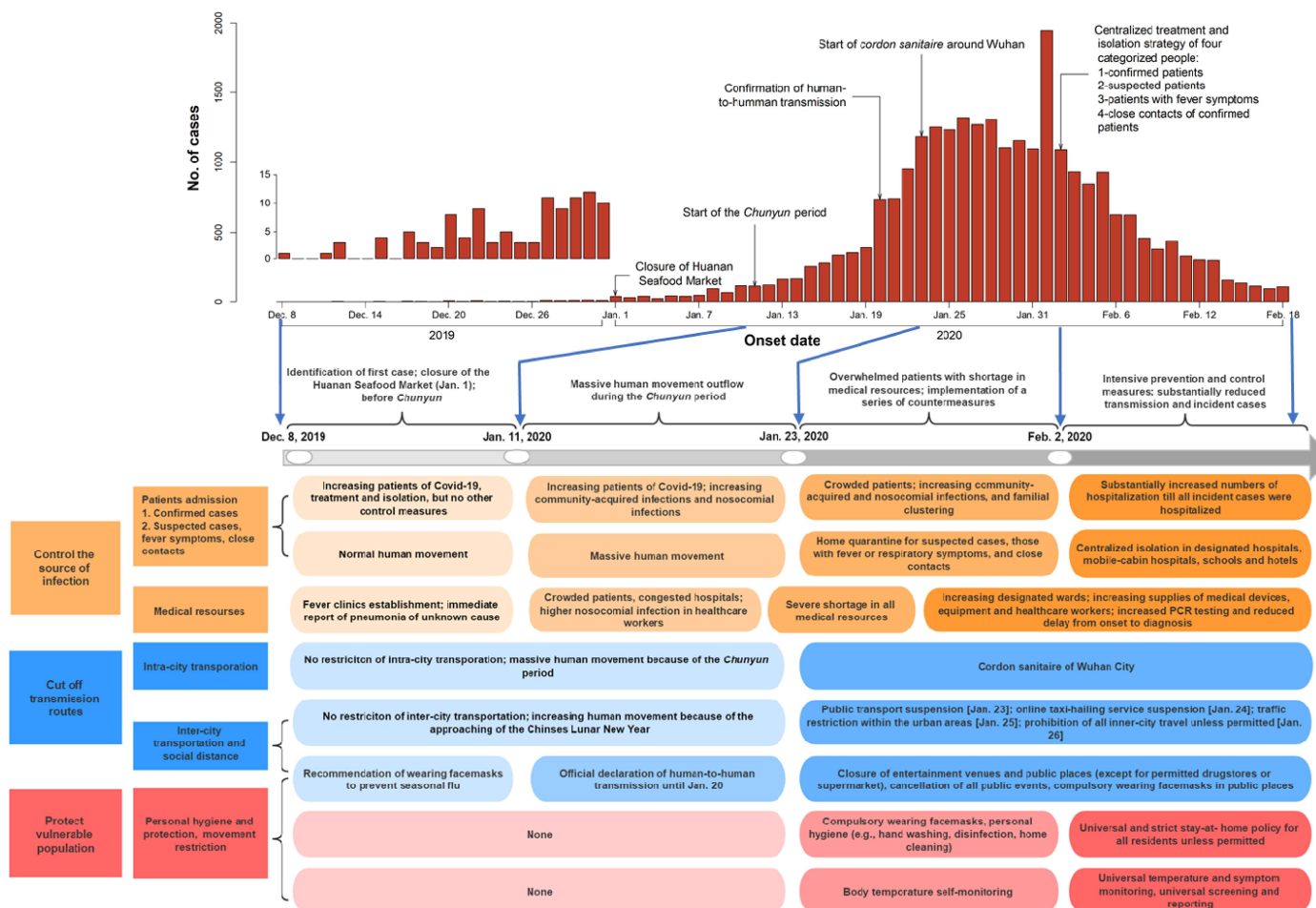


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Evolução da epidemia e das intervenções na China

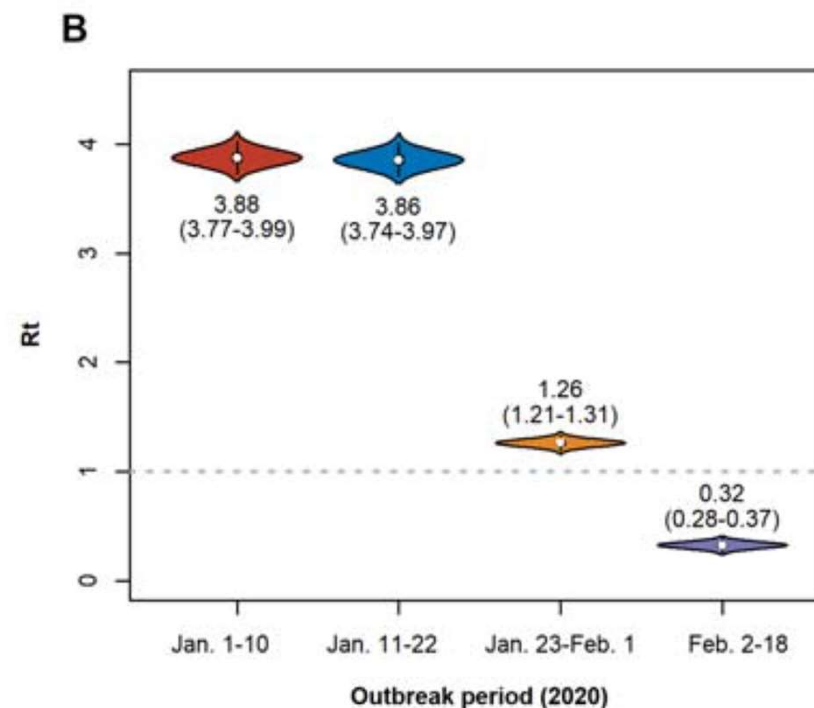
Figure 1. The daily Covid-19 onset and the control measures across different periods



Wang, C. *et al.* (2020) 'Evolving Epidemiology and Impact of Non-pharmaceutical Interventions on the Outbreak of Coronavirus Disease 2019 in Wuhan, China', *medRxiv*

Medidas de intervenção em Wuhan a partir do dia 23 de Janeiro

- Cordão sanitário na cidade de Wuhan
- Suspensão dos transportes públicos e taxi por aplicativos
- Restrição do tráfego nas áreas urbanas
- Proibição de viagens na região interna da cidade
- Fechamento de espaços públicos, cancelamento de eventos, uso obrigatório de máscaras cirúrgicas em público
- Quarentena domiciliar para toda população

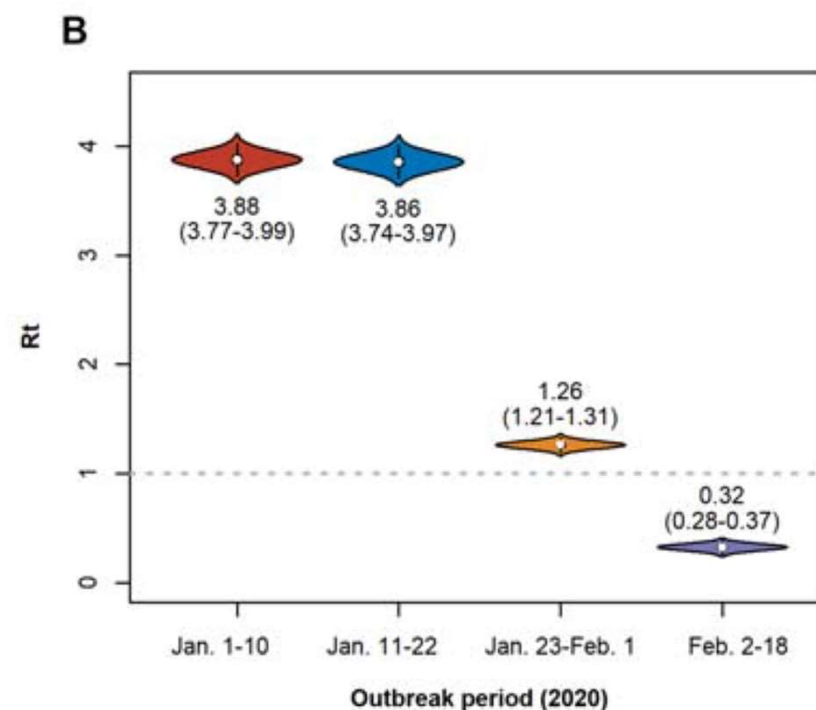


Wang, C. *et al.* (2020) 'Evolving Epidemiology and Impact of Non-pharmaceutical Interventions on the Outbreak of Coronavirus Disease 2019 in Wuhan, China', *medRxiv*

Medidas de intervenção em Wuhan a partir do dia 23 de Janeiro

Os autores estimam que as intervenções evitaram até 94.5% dos casos!!!

IC: (93.7 a 95.2%)



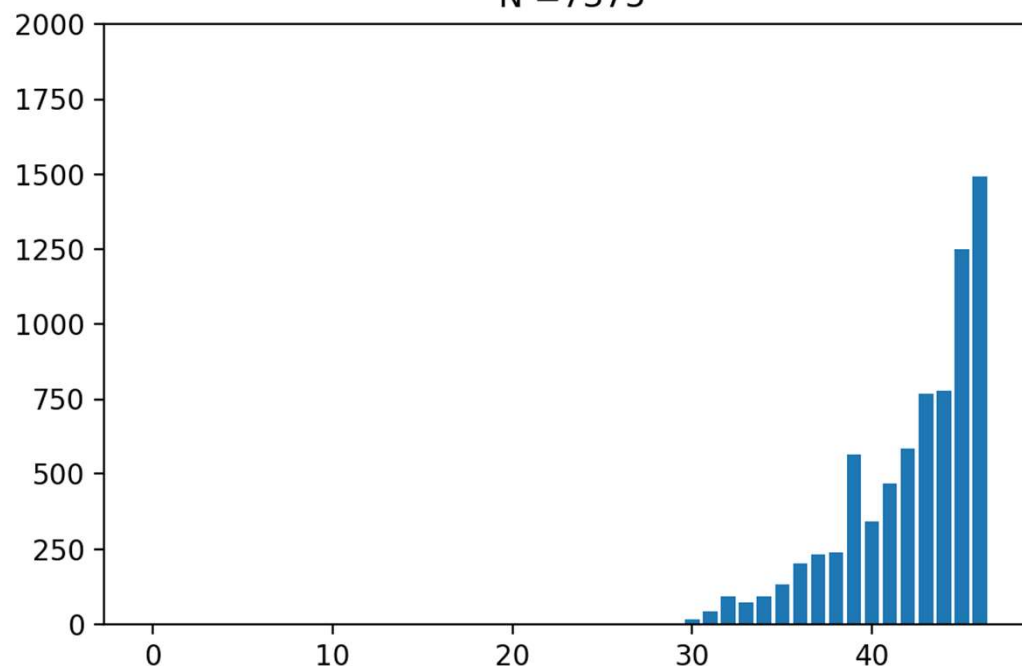
Wang, C. *et al.* (2020) 'Evolving Epidemiology and Impact of Non-pharmaceutical Interventions on the Outbreak of Coronavirus Disease 2019 in Wuhan, China', *medRxiv*



Curvas epidêmicas do COVID-19, casos novos por dia a partir do dia 22/01/2020

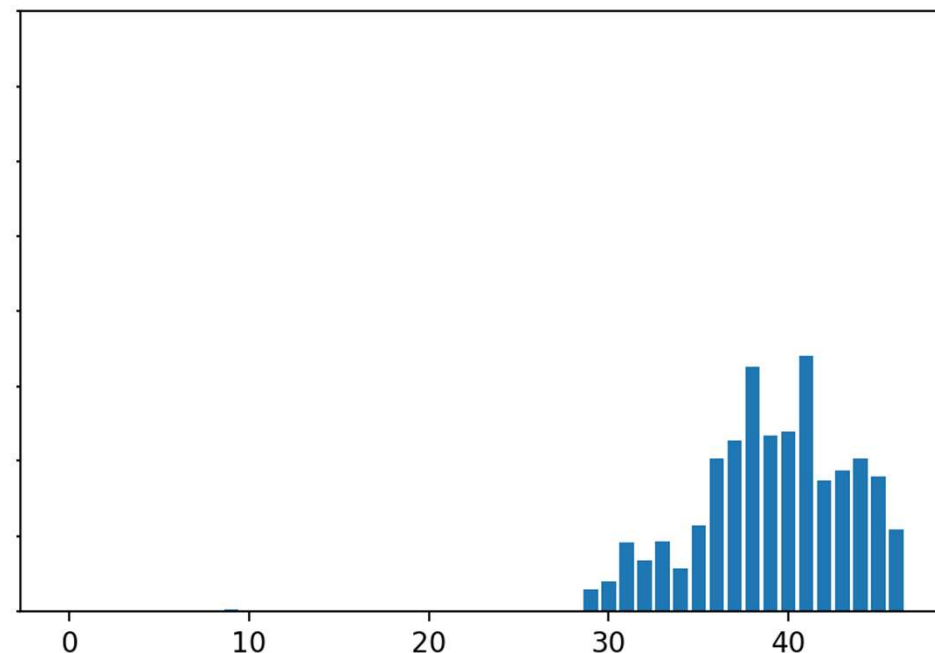
Italia

Numero de casos novos por dia, país: Italy
N = 7375



Coréia do Sul

Numero de casos novos por dia, país: South_Korea
N = 7314

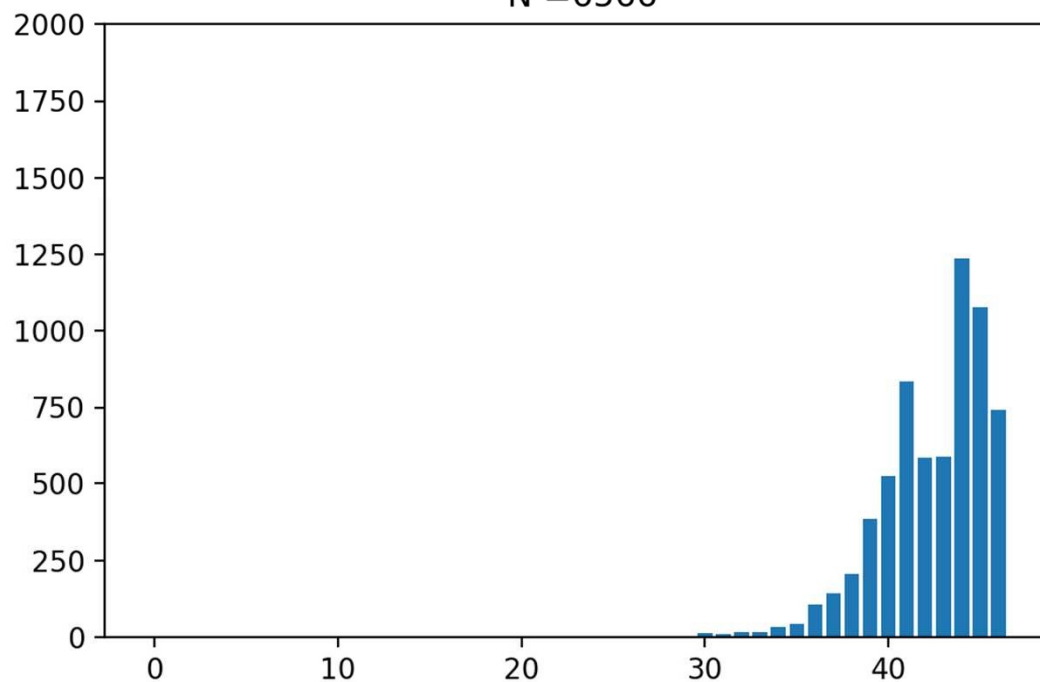


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Curvas epidêmicas do COVID-19, casos novos por dia a partir do dia 22/01/2020

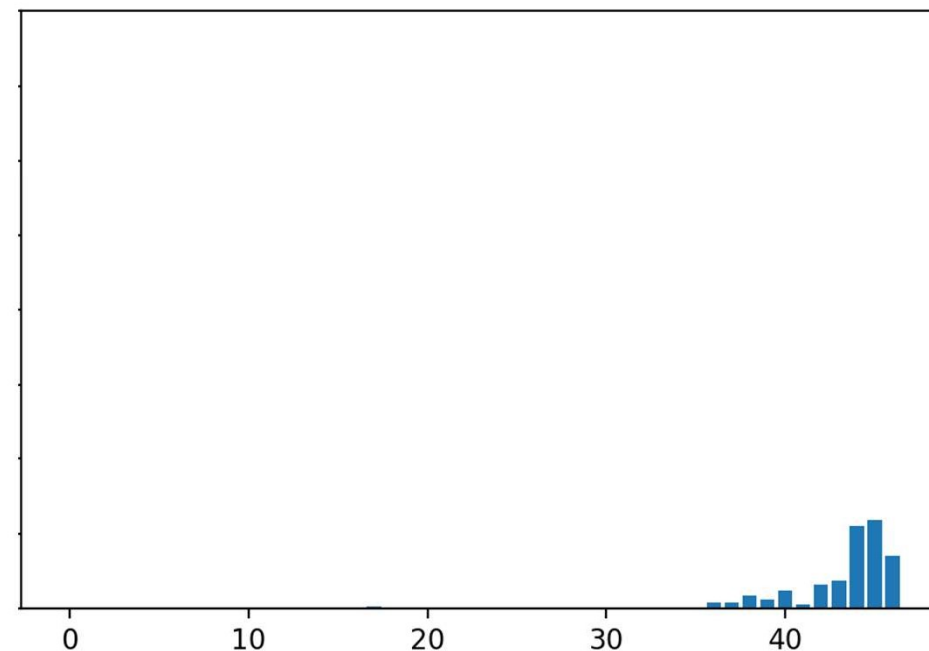
Irã

Numero de casos novos por dia, país: Iran
N = 6566

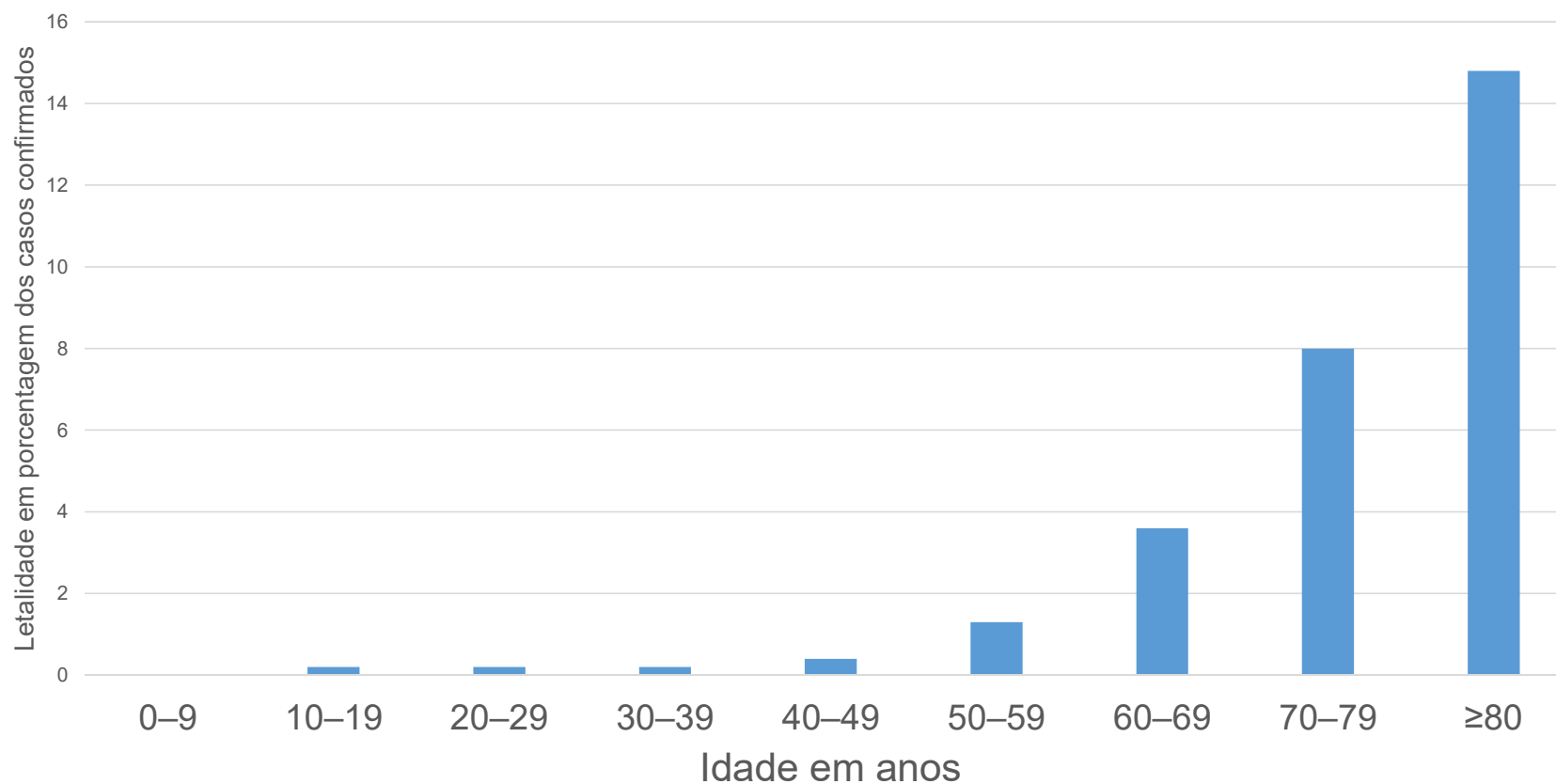


França

Numero de casos novos por dia, país: France
N = 1126



Letalidade do Covid – 19 por faixa etária, China



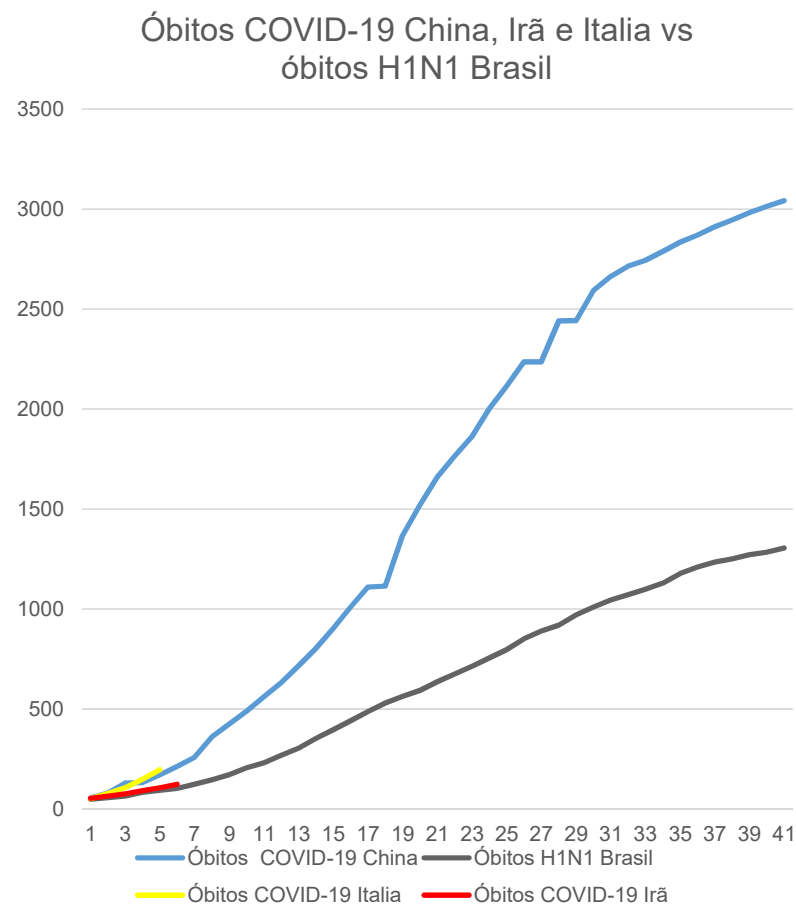
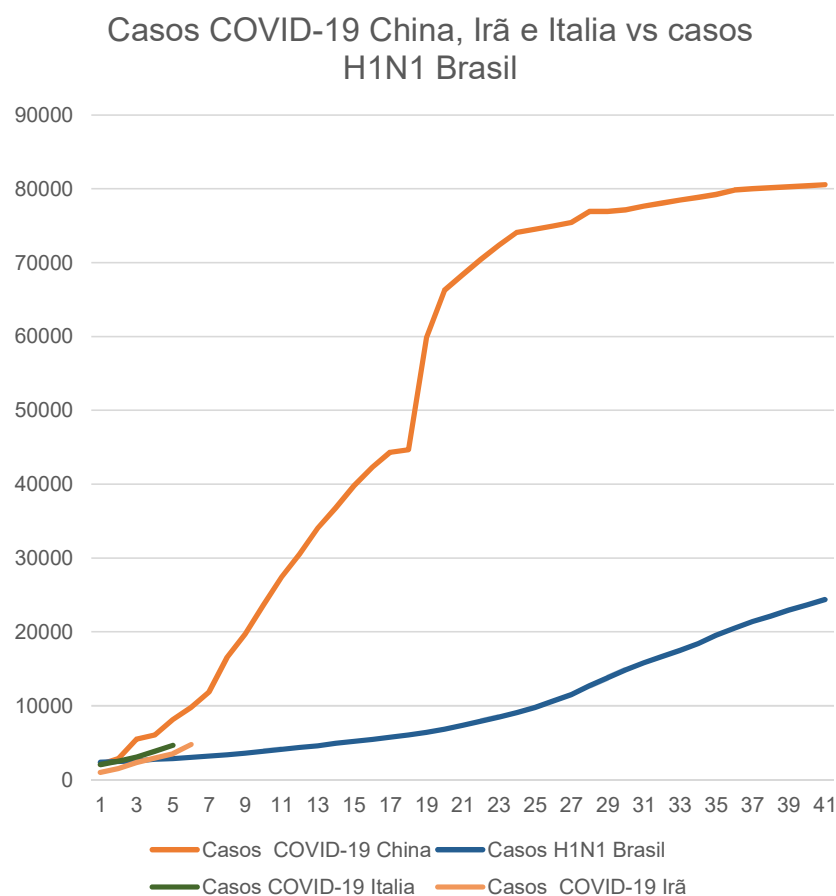
Novel Coronavirus Pneumonia Emergency Response Epidemiology Team (2020), *China CDC Weekly*, 2(x), pp. 1–10. doi: 10.3760/cma.j.issn.0254-6450.2020.02.003.



Comparativo do COVID-19 e o virus influenza H1N1 na pandemia de 2009

	COVID-19	H1N1 pandemia 2009
R0	2,74 (2,47 – 3,23)	1,5 (1,2 – 2,3) 1,525 (1,45 – 1,60) - China
Letalidade	0,4% - 2,9%	0,15% - 0,25% - Mundo 0,08% - WHO 1,2% - México, casos confirmados
Tempo de duplicação da epidemia	2,4 – 3,6	6,3 (dp = 2,6) 5,7 (dp= 1,5)

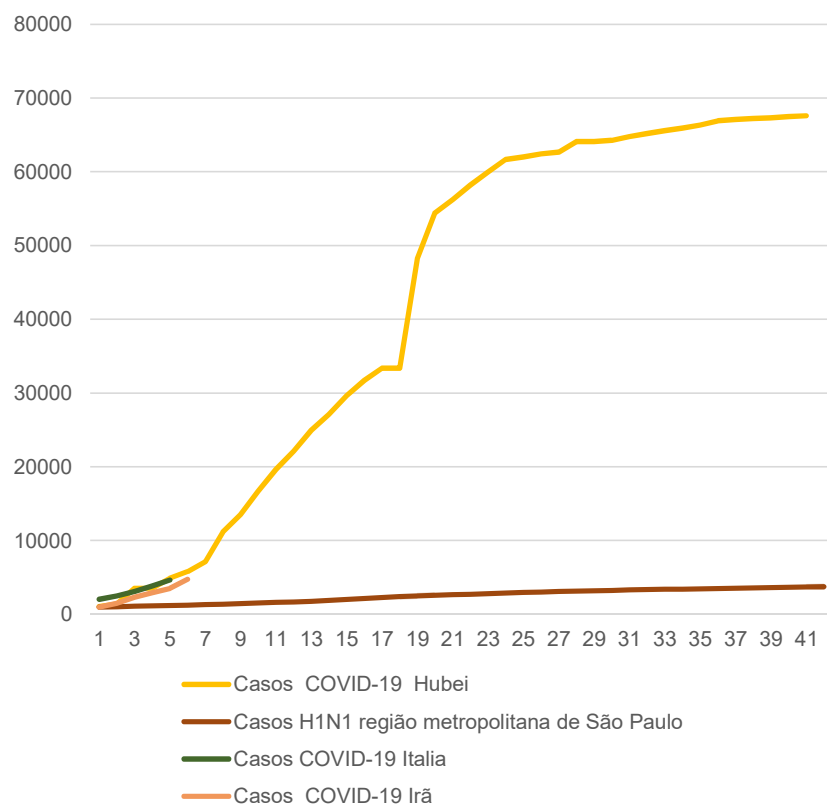
Gráfico comparativo do número total de casos e óbitos de COVID-19 em diferentes regiões e do H1N1 durante a pandemia de 2009 no Brasil, a partir do momento em que se confirmou óbito de número 50



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Gráfico comparativo do número total de casos e óbitos de COVID-19 em diferentes regiões e do H1N1 durante a pandemia de 2009 no Brasil, a partir do momento em que se confirmou óbito de número 50

Casos COVID-19 Hubei, Irã e Italia vs casos H1N1 região metropolitana de São Paulo



Óbitos COVID-19 Hubei, Irã e Italia vs óbitos H1N1 região metropolitana de São Paulo

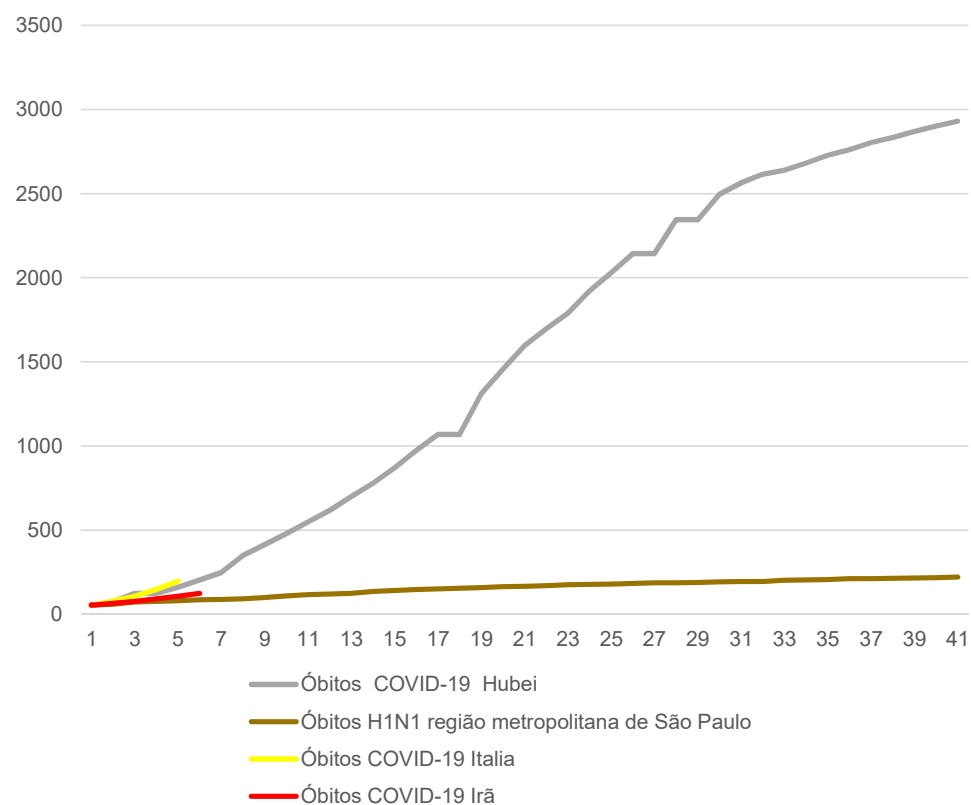
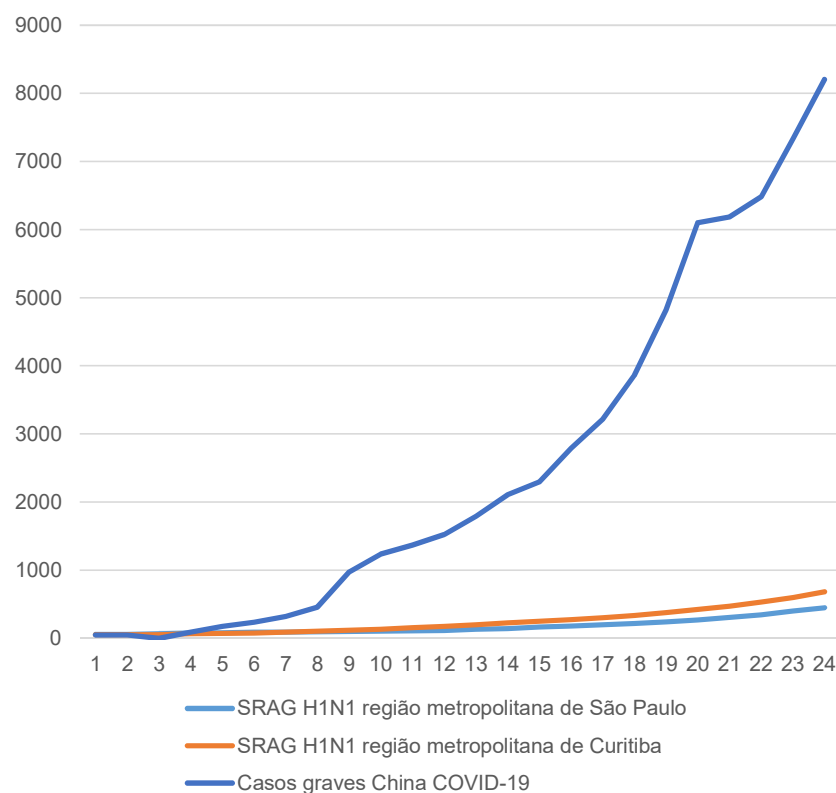
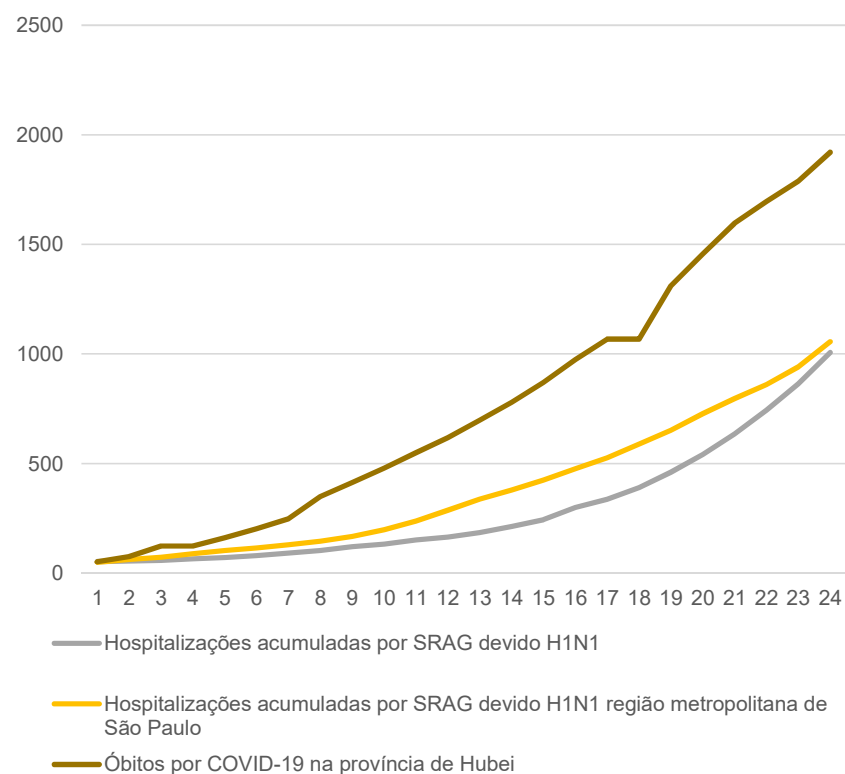


Gráfico comparativo do número total de casos graves, óbitos e internações de COVID-19 em diferentes regiões e do H1N1 durante a pandemia de 2009 no Brasil, a partir dos primeiros 50 casos graves, hospitalizações ou óbitos, a depender da curva

Casos graves de COVID-19 comparados com SRAG por H1N1 Brasil 2009



Hospitalizações por H1N1 no Brasil 2009 vs óbitos por COVID-19 em Hubei



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Características populacionais das diferentes cidades

Região urbana (cidades conurbadas)	População	Área em Km2	População por Km2
São Paulo	20.935.000	3.043	6.900
Wuhan	8.470.000	1.619	5.200

Wendel Cox Consultancy. (2019). Demographia World Urban Areas: 15 th Annual Addition. In *Demographia* (Vol. 15). Retrieved from <http://www.demographia.com/db-worldua.pdf>



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Comparativo do COVID-19 e o virus influenza H1N1 na pandemia de 1918 (gripe espanhola)

	COVID-19	H1N1 pandemia 1918 (gripe espanhola)
R0	2,74 (2,47 – 3,23)	2 (1,7 – 2,3)
Letalidade	0,4% - 2,9%	0,7% - 3,25% Reino Unido 0,8% - 3,1% EUA 4,2% - Genebra 0,3% - 6% Mundo 2,8% - Islândia (valor máximo)
Tempo de duplicação da epidemia	2,4 – 3,6	3



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Comparação do número de reprodução do COVID-19 e o influenza A H1N1 em 1918 (gripe espanhola)

H1N1 1918

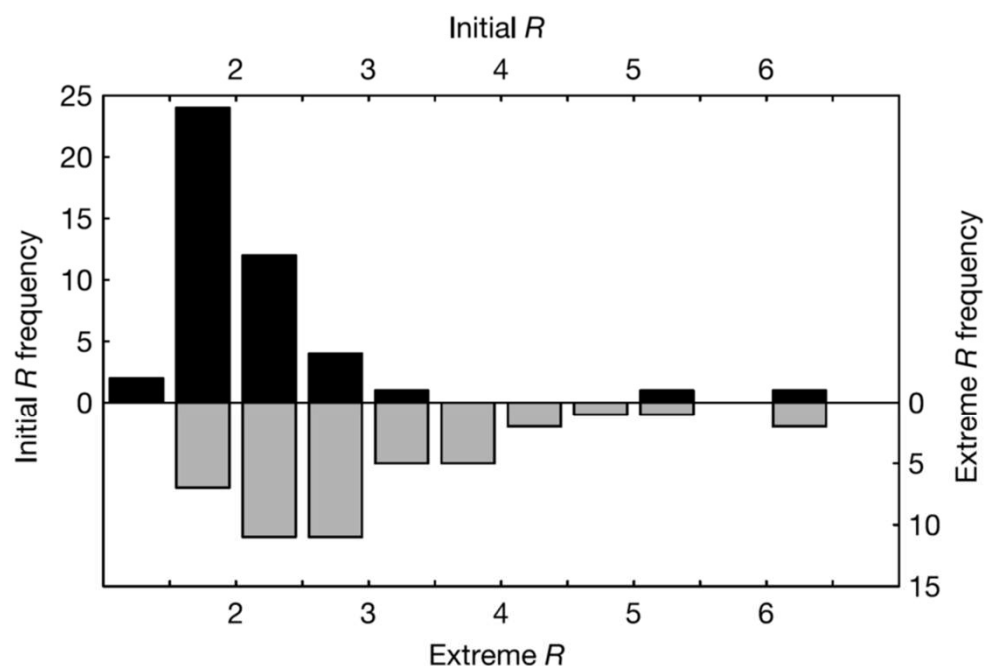
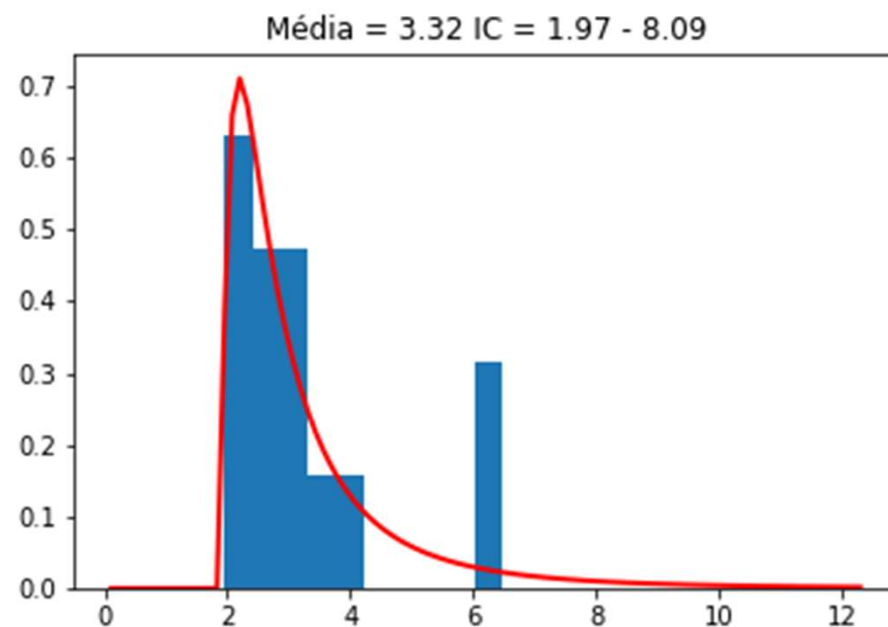


Figure 2 Histogram of initial and extreme estimated R values for 45 cities during the 1918 influenza pandemic. Dark bars show initial R estimates, grey bars show extreme R estimates.

Mills, C. E (2004), *Nature*, 432(7019), pp. 904–906. doi: 10.1038/nature03063

COVID-19



Histograma das estimativas iniciais do R_0 do COVID-19 na China e curva normalizada assumindo uma distribuição log-normal

Liu, Y. *et al.* (2020), *Journal of travel medicine*, (February), pp. 1–6. doi: 10.1093/jtm/taaa021

Comparação do número de reprodução do COVID-19 e o influenza A H1N1 em 1918

H1N1 1918

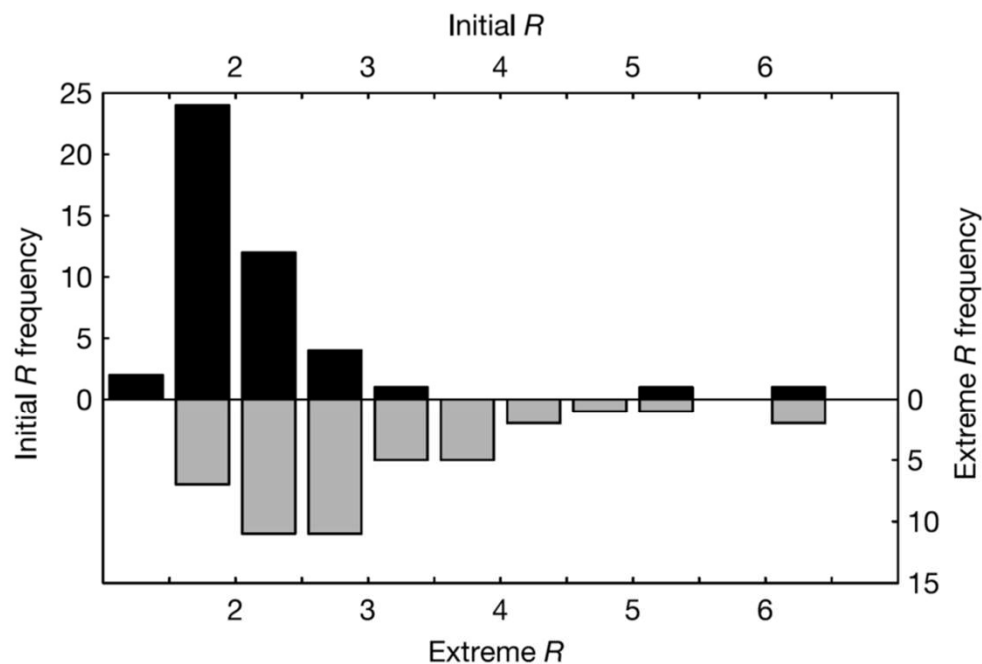
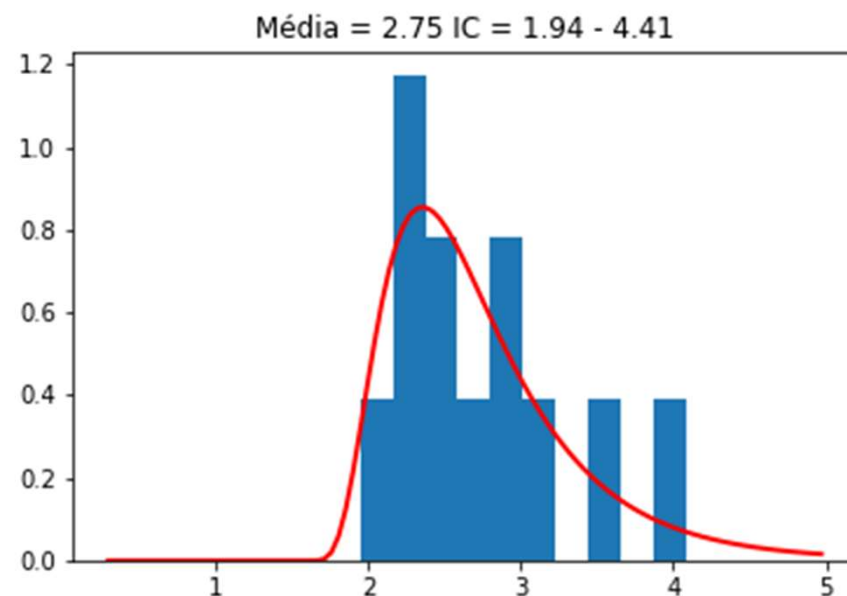


Figure 2 Histogram of initial and extreme estimated R values for 45 cities during the 1918 influenza pandemic. Dark bars show initial R estimates, grey bars show extreme R estimates.

Mills, C. E (2004), *Nature*, 432(7019), pp. 904–906. doi: 10.1038/nature03063

COVID-19



Histograma das estimativas iniciais do R_0 do COVID-19 na China e curva normalizada assumindo uma distribuição log-normal, excluindo-se os valores extremos

Liu, Y. *et al.* (2020), *Journal of travel medicine*, (February), pp. 1–6. doi: 10.1093/jtm/taaa021

Laboratório de Modelagem de Dinâmica de Doenças

Dr. Tarcísio M. Rocha Filho – CIFMC-IF/UnB

Me. Victor Bertollo Gomes Porto – MS

Me. Carlos César – IF/UnB

Me. Fabiana Ganem – MS

Dr. Thiago Rocha - OPAS

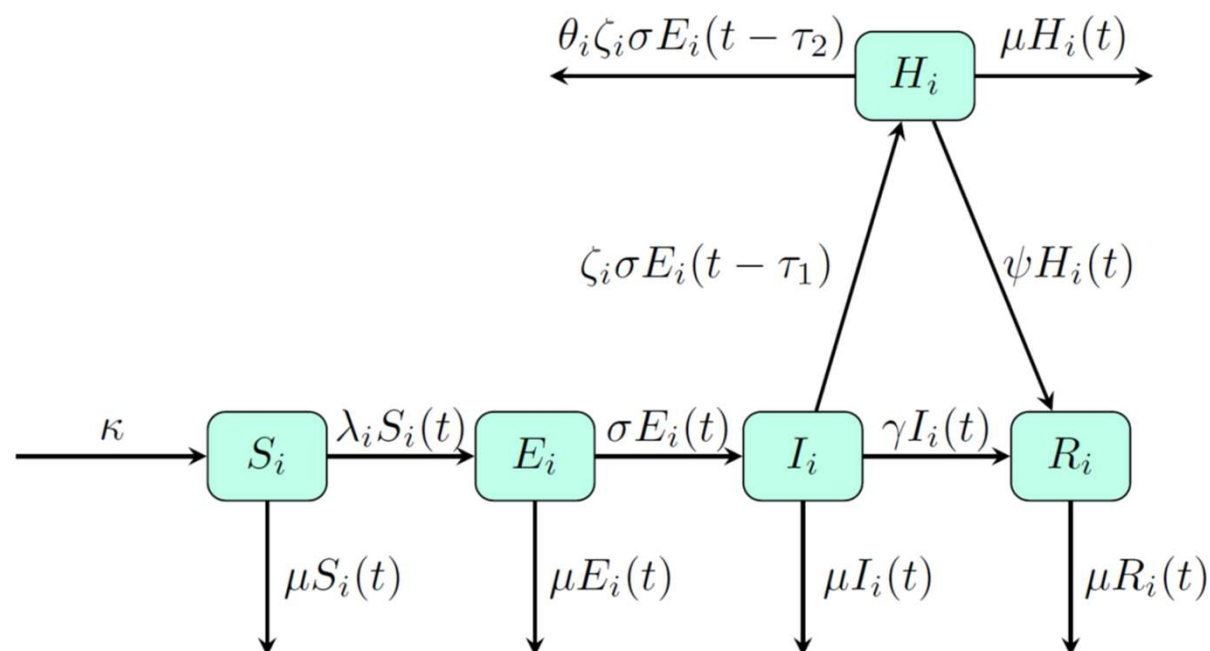
Dr. Walter Ramalho – FCE/UnB,

Dr. Wildo Araújo – NMT/UnB.



Foi construído um modelo do tipo SEIR, determinístico, com estratificação por faixa etária, incluindo um campo para hospitalizações (SHEIR)

Fig 2. Diagram describing the model equations in Eq (3), constant parameters given in Table 1, and force of infection and transmission rate given in Eqs (2) and (1), respectively.



A progressão entre os diferentes estágios é definida por equações diferenciais

$$\begin{aligned}\frac{dS_i}{dt} &= \kappa\delta_{i,1} - \lambda S_i - \mu S_i - \nu_i S_i + \nu_{i-1} S_{i-1}, \\ \frac{dH_i}{dt} &= -\psi H_i + \zeta_i \lambda_i E_i(t - \tau_1) - \theta \zeta_i \lambda_i E_i(t - \tau_2) - \mu H_i, \\ \frac{dE_i}{dt} &= \lambda S_i - \sigma E_i - \zeta_i \sigma E_i - \mu E_i - \nu_i E_i + \nu_{i-1} E_{i-1}, \\ \frac{dI_i}{dt} &= \sigma E_i - \gamma I_i - \mu I_i - \nu_i I_i + \nu_{i-1} I_{i-1}, \\ \frac{dR_i}{dt} &= \gamma I_i + \psi H_i - \mu R_i - \nu_i R_i + \nu_{i-1} R_{i-1},\end{aligned}$$



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Os parâmetros do modelo foram extraídos da literatura

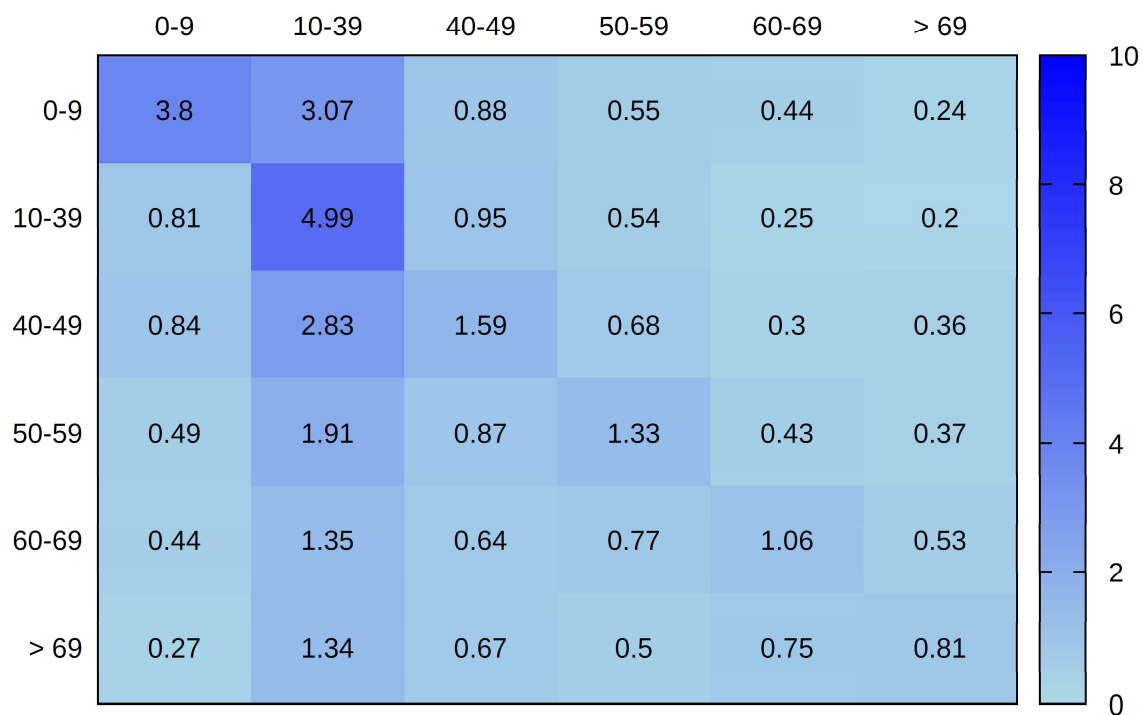
Table 1. Constant parameters in the model.

Variables	Definition	Value (CI 95%) [Ref]	Distribution
κ	Birth rate	0.01416 [28]	–
μ	Overall fatality rate from other causes	0.00608 [28]	–
ψ	Average recovery rate from hospital	1/17.5 days ⁻¹ [29]	–
P_{sc}	Proportion of severe and critical cases	18% [27]	–
μ_{COV}	Mortality proportion due to the disease	0.4% – 2.9% [27]	Uniform
θ	Morbidity proportion in hospitalized individuals	μ_{COV} / P_{sc}	–
σ^{-1}	Inverse of incubation rate	5.0(4.2; 6.0) days [30]	Log-Normal
γ^{-1}	Inverse of recovery rate of non-hospitalized infectious individuals	1.61(0.35; 3.23) days ⁻¹ [31]	Not informed. Assumed Log-Norm.
ζ_i	Probability of hospitalizations for age-group i	(see text)	–
R_0	Basic reproduction number for COVID-19	2.74(2.47; 3.03) (see complementary material)	Assumed Uniform
τ_1	Median time from illness onset to hospitalization	3.3(2.7; 4.0) [30]	Gamma
τ_2	Average time from illness onset to death	15.0(12.8; 17.5) [30]	Log-Normal

Constant parameters in the model with the average value, Confidence Interval (CI) of 95% if pertinent and statistical distribution of values.

A matriz de contato foi construída com base nos dados da literatura, o R0 foi extraído da literatura e incorporado nas diferentes faixas etárias

Fig 1. Heat map for the contact matrix C_{ij} representing the number of physical contacts per day of an individual of age group i with any individual of group j .

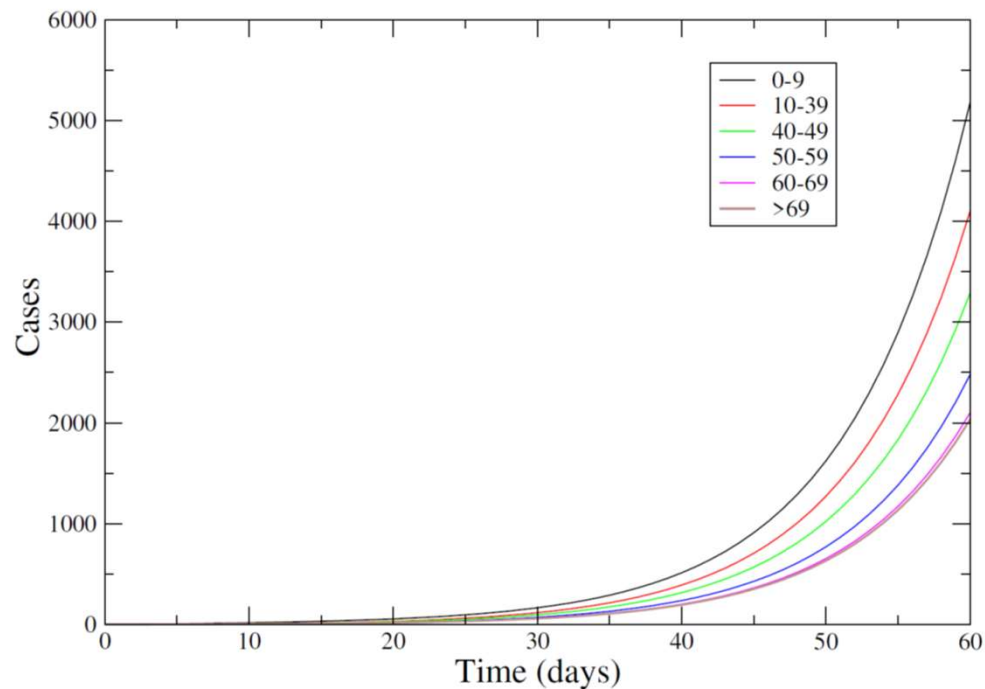


$$R_0 = \sum_{i,j=1}^M n_j \beta_{ij} / \gamma = \sum_{i,j=1}^M n_j P_c C_{ij} / \gamma,$$

Mossong, Joël, et al. *PLoS medicine* 5.3 (2008): e74.

Número cumulativo de casos por faixa etária para os primeiros 60 dias na região metropolitana de São Paulo

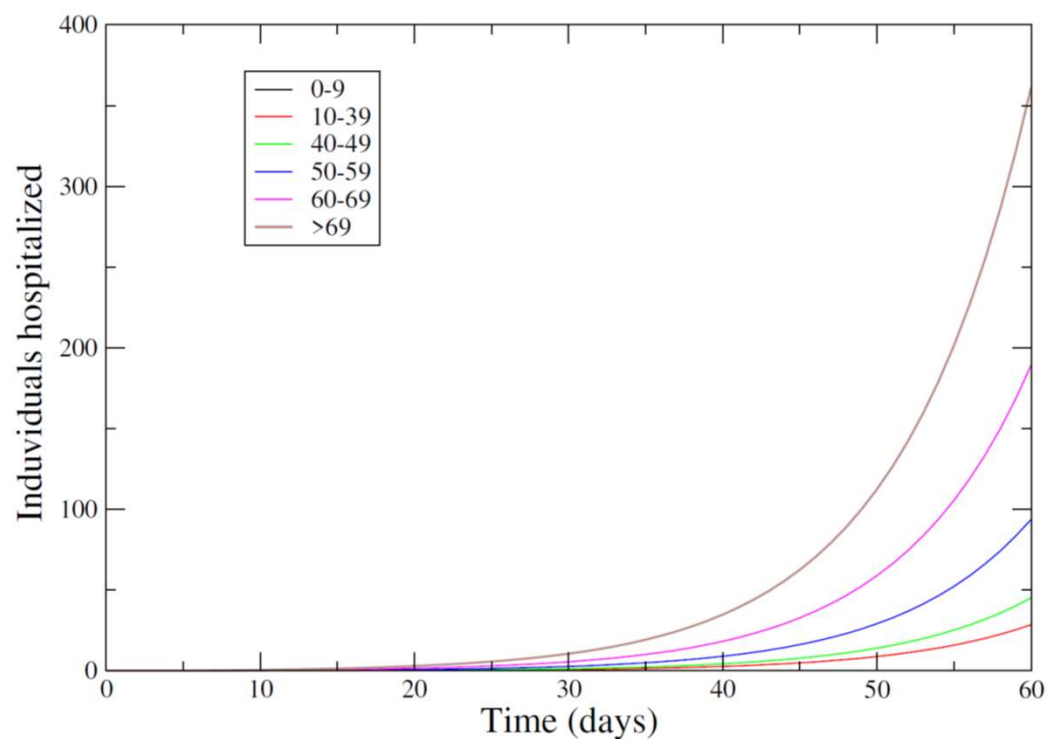
Fig 3. Cumulative number of cases in each age group for the mean or median values for the parameters in Tab. 1, assuming a fatality rate of 2.3%.



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Número de indivíduos hospitalizados por faixa etária para os primeiros 60 dias na região metropolitana de São Paulo

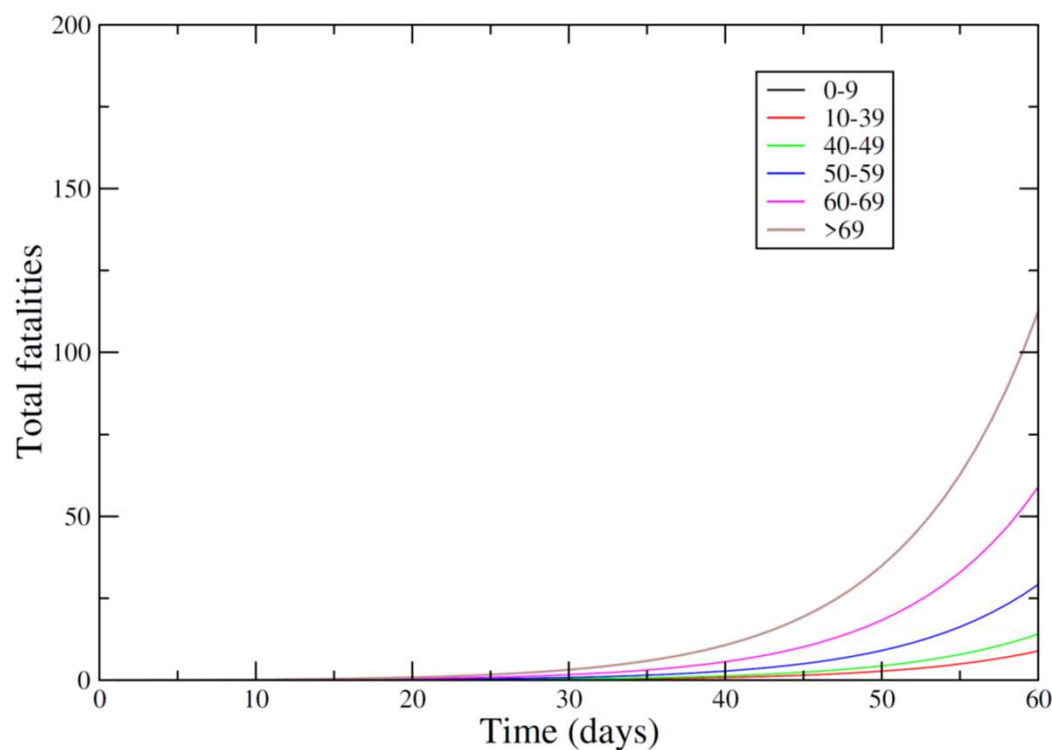
Fig 4. Number of hospitalized individual at a given moment corresponding to Fig 3.



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Número cumulativo de óbitos por faixa etária para os primeiros 60 dias na região metropolitana de São Paulo

Fig 5. Cumulative number of fatalities corresponding to Fig 3.



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Número cumulativo de casos, óbitos e número máximo de pessoas internadas num determinado dia para a região metropolitana de São Paulo, 30 e 60 dias após o início do surto

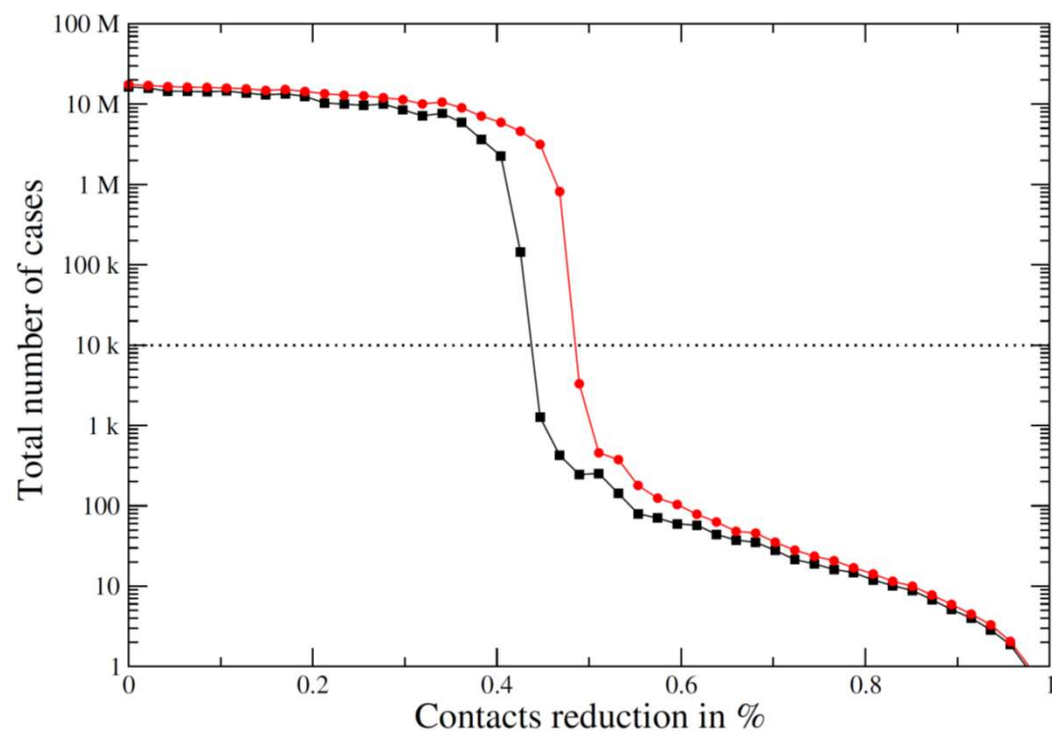
Table 2. Median for the total cumulative number of cases averaged over 100, 000 Monte Carlo realizations.

Age	30 days			60 days		
	Cases	Hosp.	Fatal.	Cases	Hosp.	Fatal.
0–9	354(226;628)	0(0;0)	0(0;0)	10259(4458;29888)	0(0;0)	0(0;0)
10–39	299(195;517)	4(2;7)	1(0;1)	8181(3559;23911)	99(41;288)	18(8;51)
40–49	234(151;410)	6(3;11)	1(1;2)	6543(2842;19136)	154(63;447)	27(12;80)
50–59	177(114;311)	11(7;21)	2(1;3)	4946(2142;14519)	305(127;888)	55(23;162)
60–69	150(96;267)	21(13;37)	4(2;7)	4212(1814;12429)	566(238;1653)	103(43;310)
≥ 70	148(94;264)	36(23;64)	7(4;12)	4096(1750;12198)	970(409;2853)	179(73;551)
Total	1362(877;2396)	79(48;139)	14(9;25)	38233(16564;112109)	2103(883;6154)	383(160;1158)

The number of cases and fatalities are cumulative. The number of hospitalized individuals represent the maximal population attained at any particular time. The inter-quartile interval is given by the numbers between brackets.

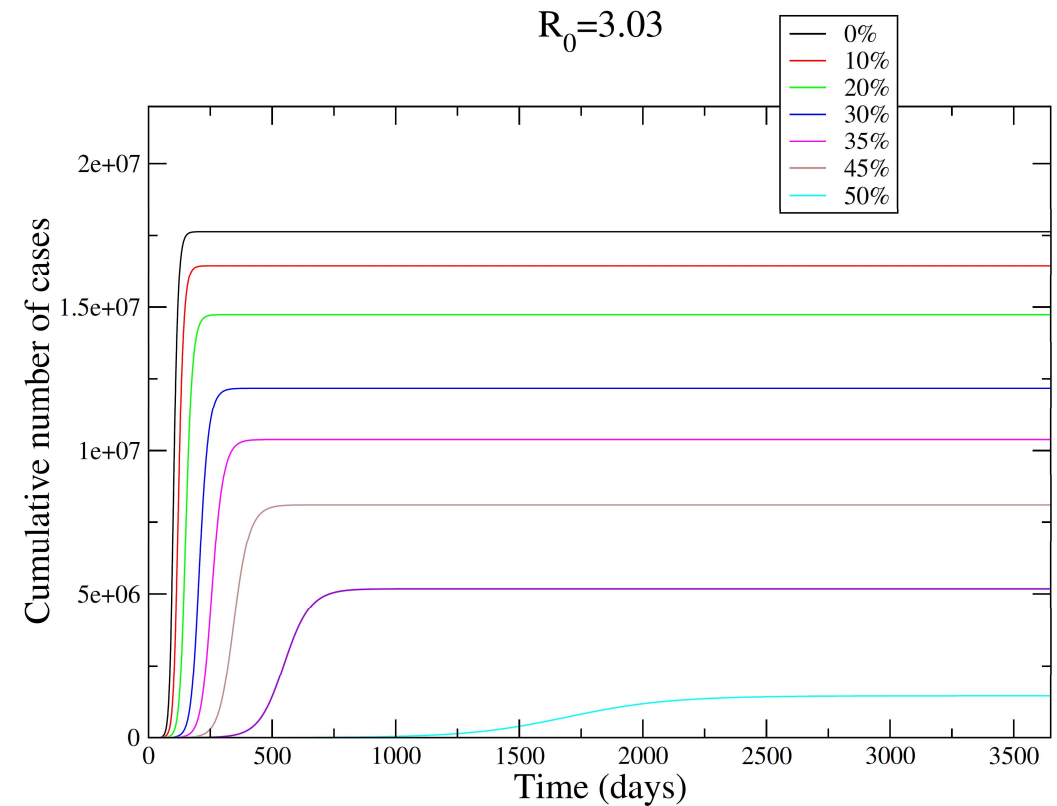
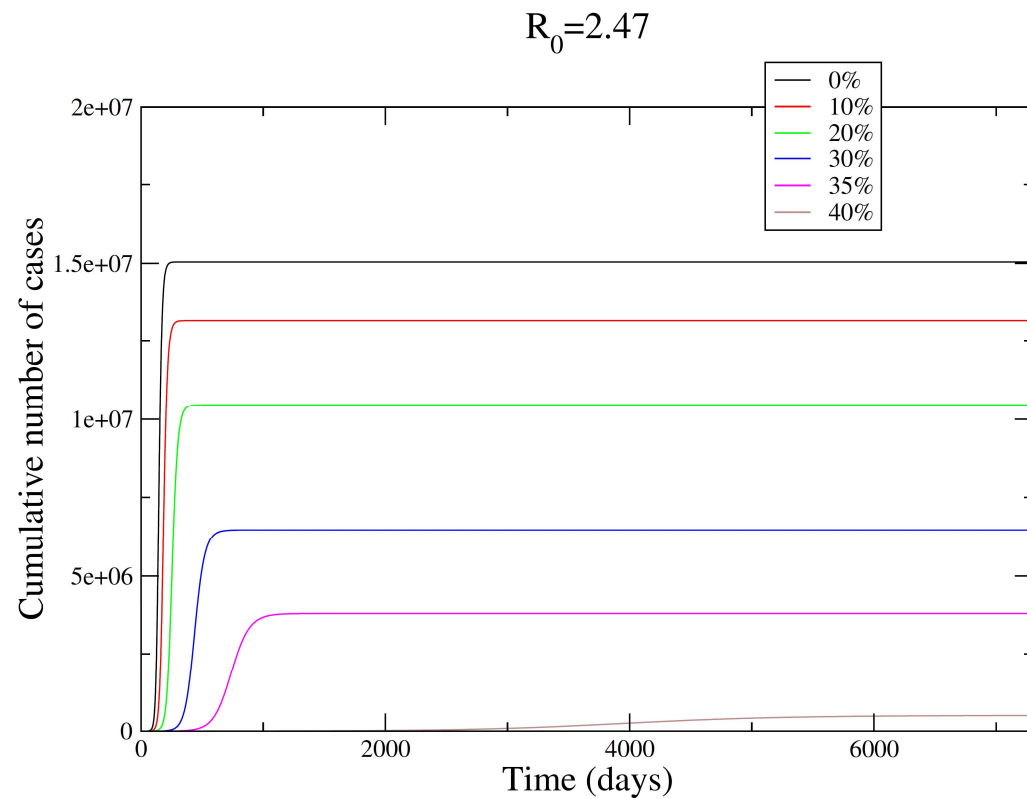
Impacto da redução do número de contatos por dia no número total de casos

Fig 2. Number of total cases from a Monte Carlo analysis with 1000 realizations from the parameter in Table 2 in the main text, except in the sharp transition region with 10 000 realizations.



16
ANOS

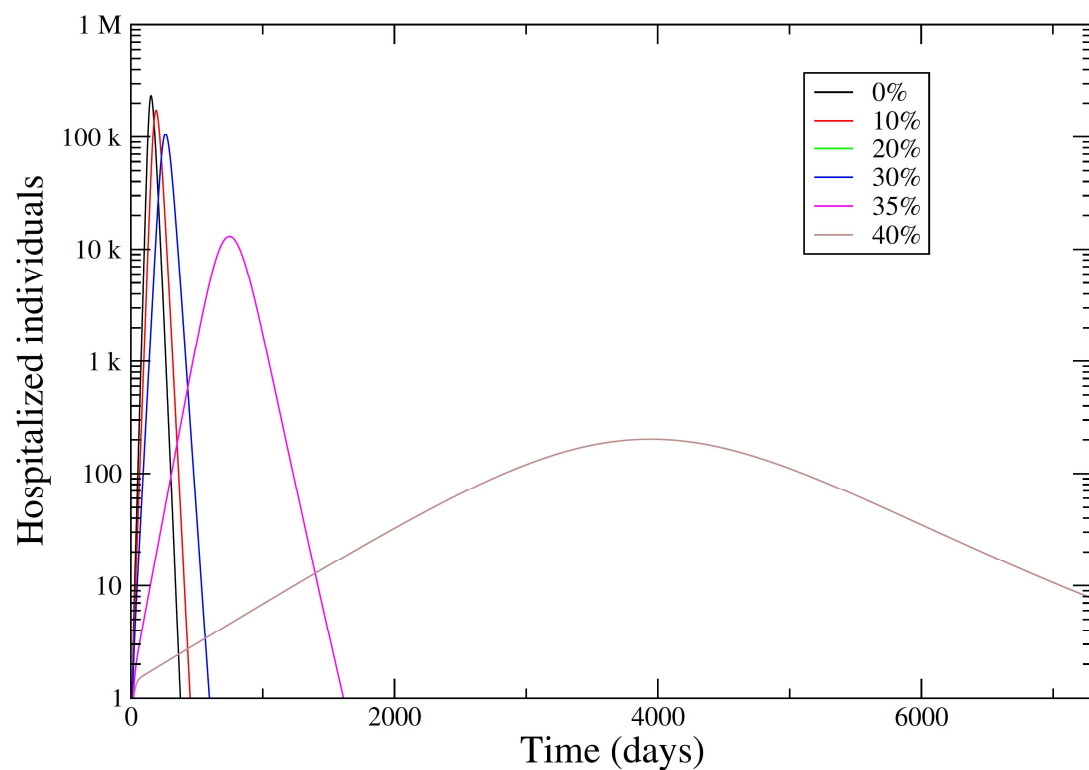
Número cumulativo de casos para diferentes valores de R_0 e taxas de redução no número de contatos dias na população



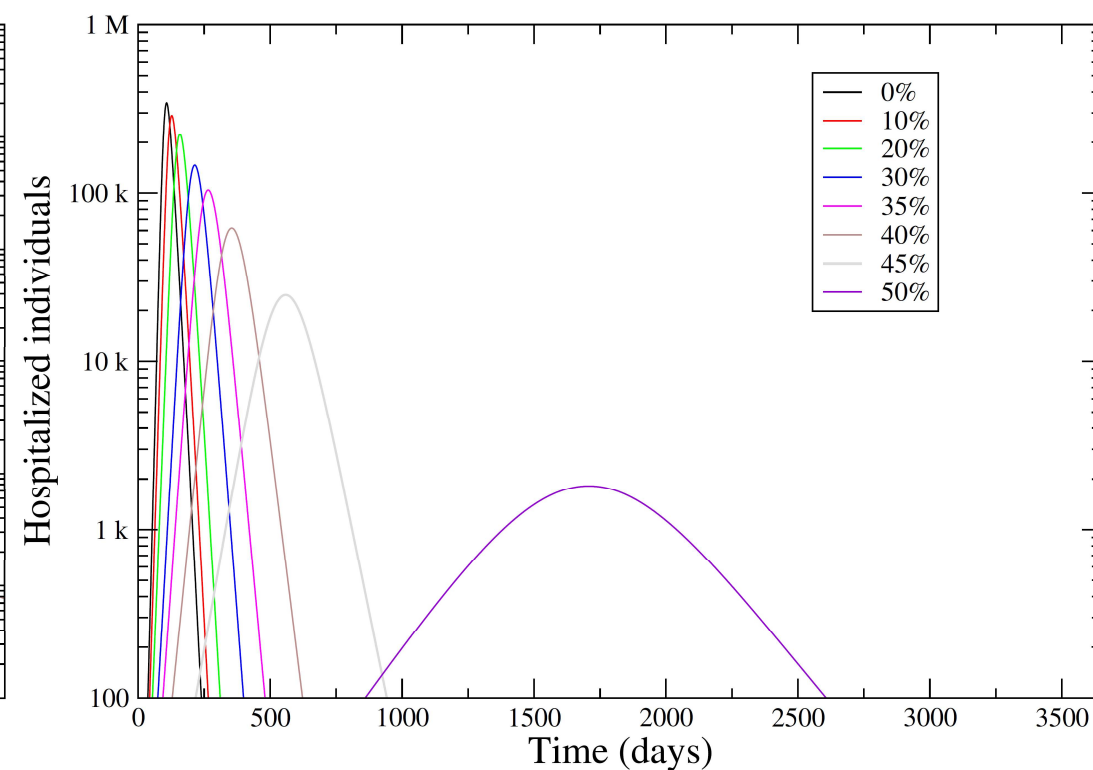
16 ANOS

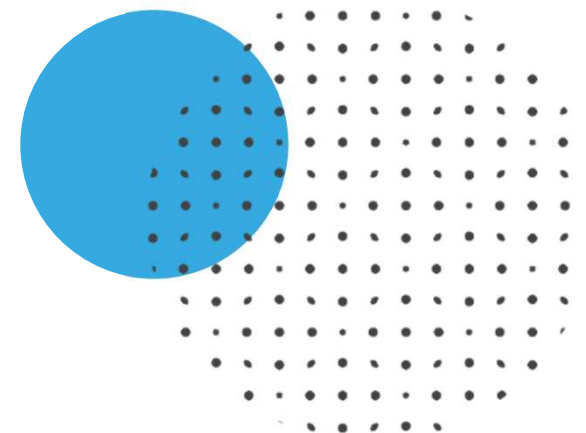
Número de pacientes internados num dado momento para diferentes valores de R_0 e taxas de redução no número de contatos dias na população

$R_0=2.47$



$R_0=3.03$





Secretaria de Vigilância em Saúde

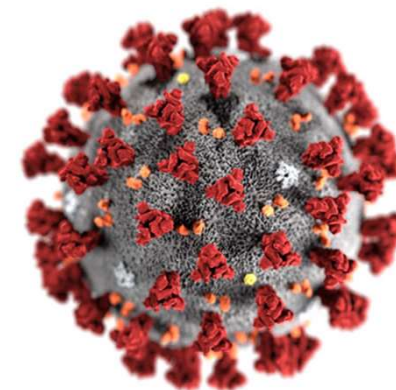


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Doença pelo Coronavírus 2019

COVID-19



Emergência de Saúde Pública de Importância Nacional e Internacional (ESPIN/ESPII)

Modelagem e intervenções não farmacológicas

Julio Croda | Diretor de Imunizações e Doenças transmissíveis



17 de março de 2020

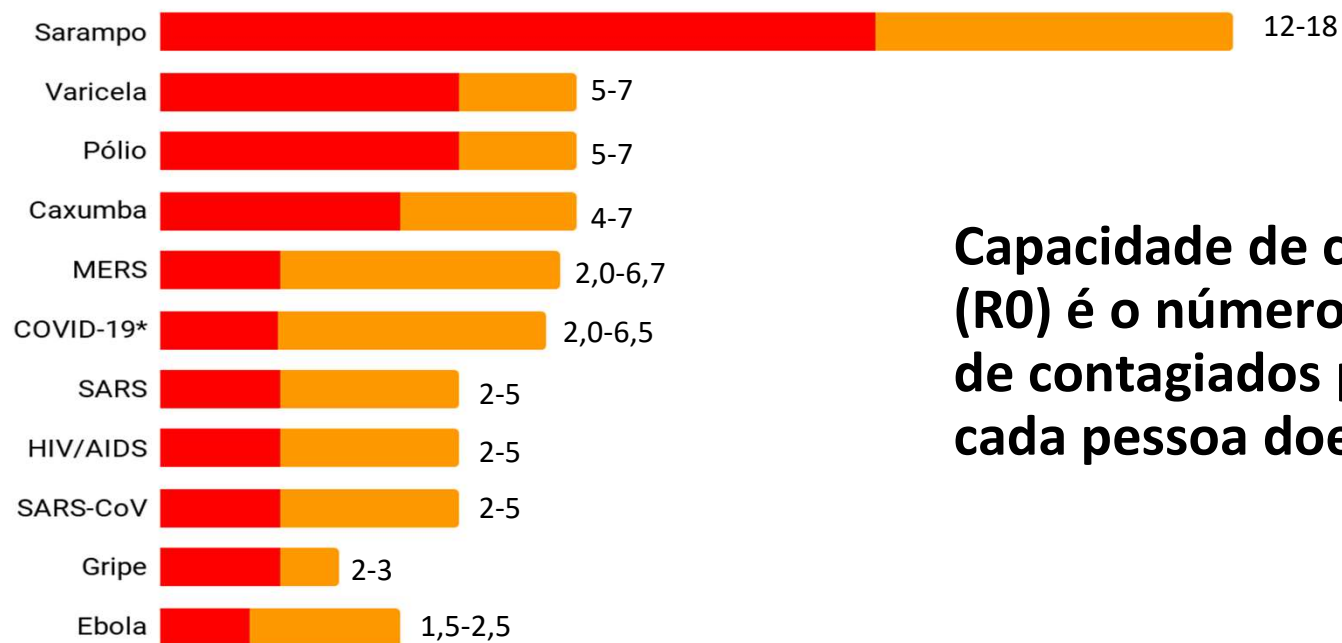


Conceitos básicos

(a) mitigação, concentra-se em desacelerar, mas não necessariamente em impedir a disseminação da epidemia - reduzindo a demanda de cuidados de saúde e protegendo aqueles com maior risco de doenças graves contra infecções;

(b) supressão, reverter o crescimento da epidemia, reduzindo brutalmente o número de casos rapidamente e indefinidamente.

Estimativa da Capacidade de Contágio (R0) comparativo com outras doenças virais de importância de Saúde Pública



Capacidade de contágio (R0) é o número médio de contagiados por cada pessoa doente.

*baseado em estimativas de Du et al, Medrxiv; Tang et al, Clin Med

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PÁTRIA AMADA
BRASIL

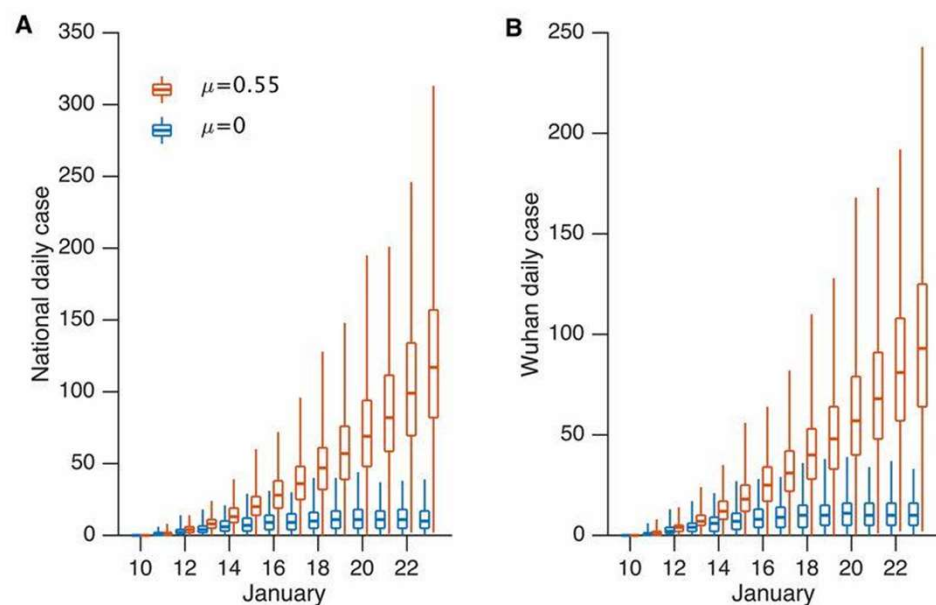
Cite as: R. Li *et al.*, *Science*
10.1126/science.abb3221 (2020).

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

Ruiyun Li^{1*}, Sen Pei^{2**†}, Bin Chen^{3*}, Yimeng Song⁴, Tao Zhang⁵, Wan Yang⁶, Jeffrey Shaman^{2†}

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

*These authors contributed equally to this work.



- 86% de todas as infecções não foram notificadas
- A taxa de transmissão de infecções não documentadas foi de 55%
- As infecções não documentadas foram a fonte de infecção para 79% dos casos notificados
- Essas descobertas explicam a rápida disseminação geográfica do SARS-CoV2 e a contenção desse vírus será particularmente desafiadora
- Novas recomendações da OMS de ampliar testagem

Comparativo do COVID-19 e o vírus influenza H1N1 na pandemia de 2009 e 1918

	COVID-19	H1N1 pandemia 2009	H1N1 pandemia 1918 (gripe espanhola)
R0	2,74 (2,47 – 3,23)	1,5 (1,2 – 2,3) 1,525 (1,45 – 1,60) - China	2 (1,7 – 2,3)
Letalidade	0,4% - 2,9%	0,15% - 0,25% - Mundo 0,08% - WHO 1,2% - México, casos confirmados	0,7% - 3,25% Reino Unido 0,8% - 3,1% EUA 4,2% - Genebra 0,3% - 6% Mundo 2,8% - Islândia (valor máximo)
Tempo de duplicação da epidemia	2,4 – 3,6	6,3 (dp = 2,6) 5,7 (dp= 1,5)	3

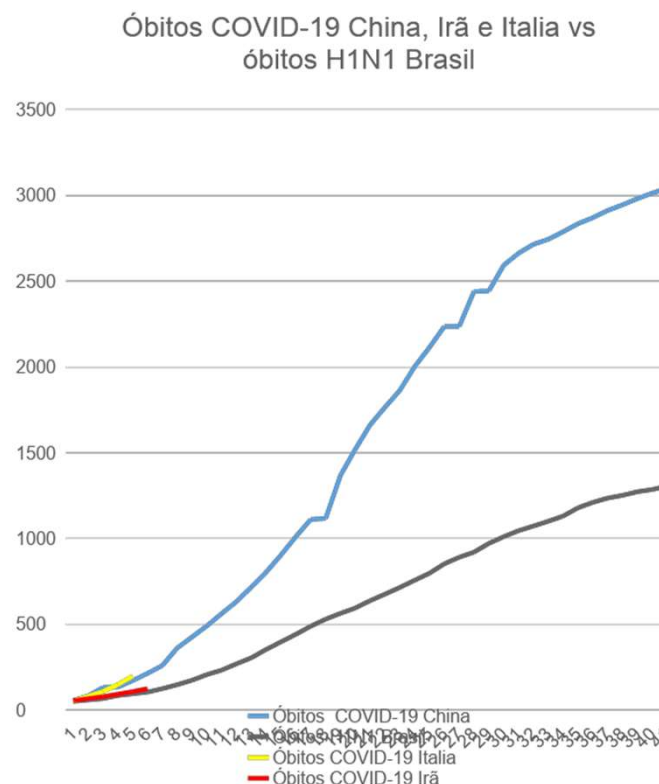
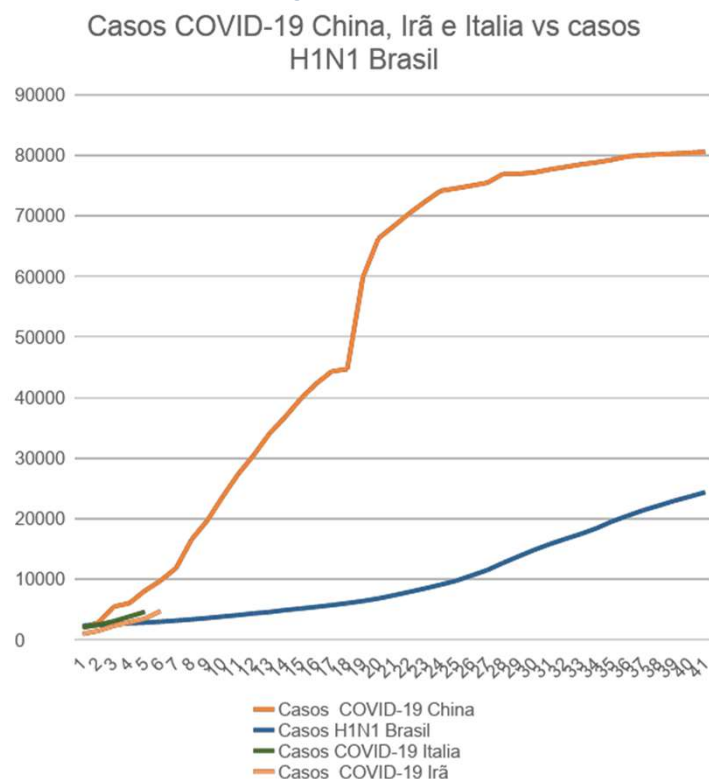
Características populacionais das diferentes cidades

Região urbana (cidades conurbadas)	População	Área em Km2	População por Km2
São Paulo	20.935.000	3.043	6.900
Wuhan	8.470.000	1.619	5.200

Wendel Cox Consultancy. (2019). Demographia World Urban Areas: 15 th Annual Addition. In *Demographia* (Vol. 15). Retrieved from <http://www.demographia.com/db-worldua.pdf>



Gráfico comparativo do número total de casos e óbitos de COVID-19 em diferentes regiões e do H1N1 durante a pandemia de 2009 no Brasil, a partir do momento em que se confirmou óbito de número 50



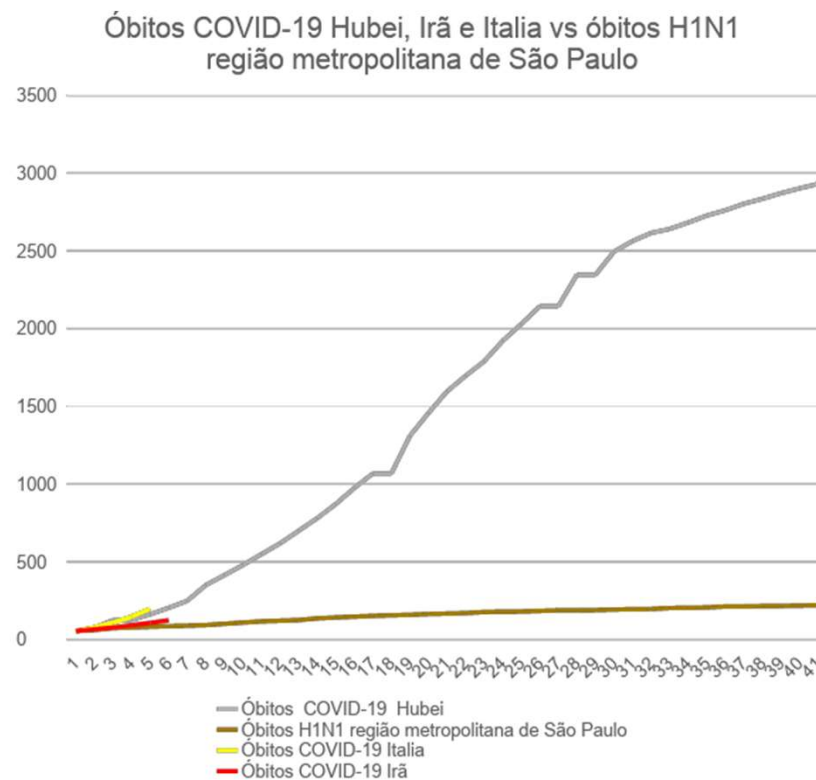
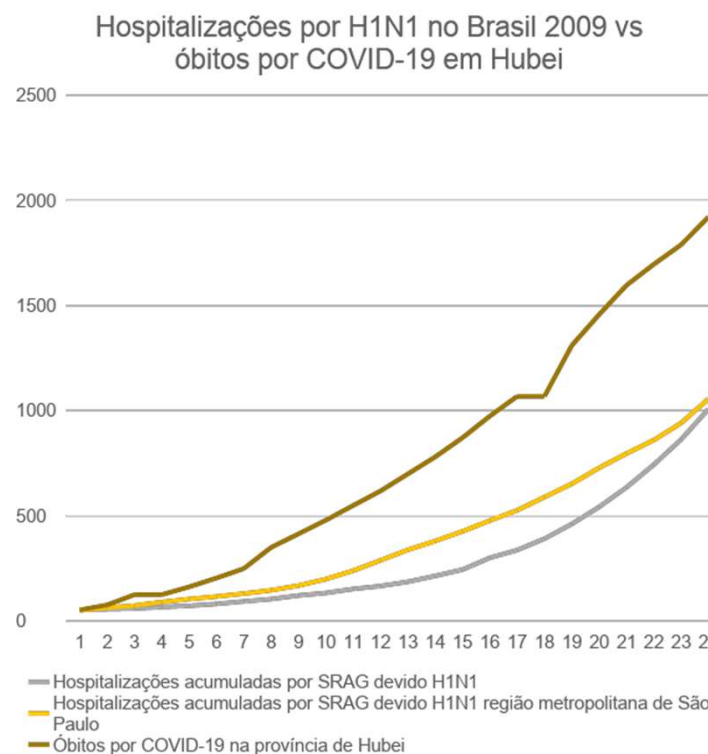
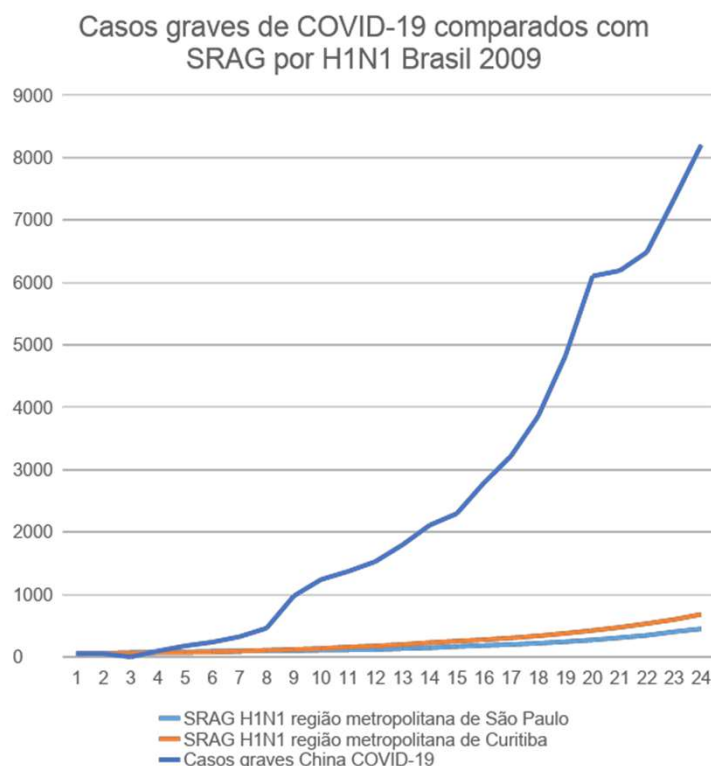
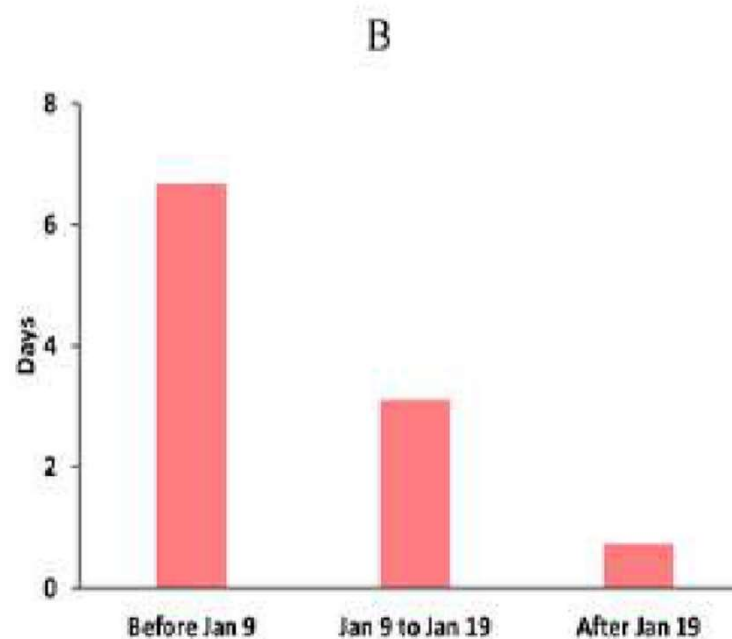


Gráfico comparativo do número total de casos graves, óbitos e internações de COVID-19 em diferentes regiões e do H1N1 durante a pandemia de 2009 no Brasil, a partir dos primeiros 50 casos graves, hospitalizações ou óbitos, a depender da curva

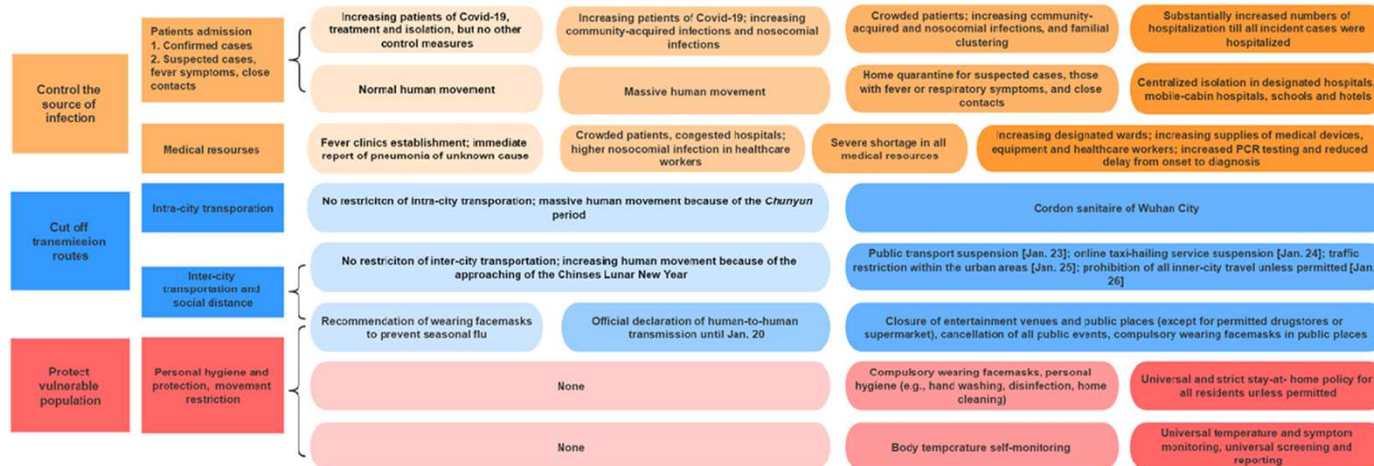
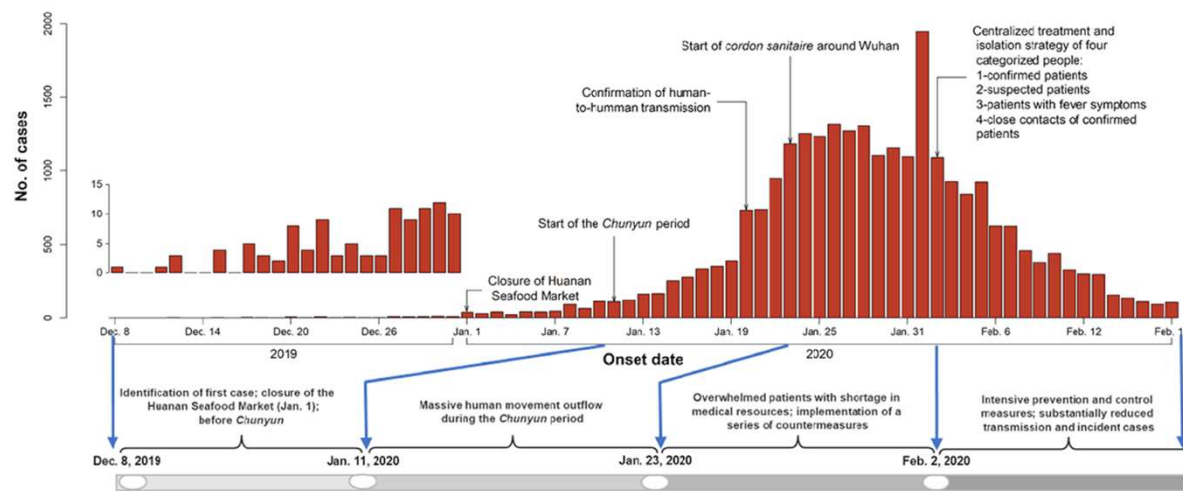


Evolução do tempo médio entre o início dos sintomas e o isolamento, Guangdong



Liu, T. *et al.* (2020) 'Transmission dynamics of 2019 novel coronavirus (2019-nCoV)', *The Lancet*, pre print.

Evolução da epidemia e das intervenções na China



Wang, C. *et al.* (2020)
'Evolving Epidemiology and Impact of Non-pharmaceutical Interventions on the Outbreak of Coronavirus Disease 2019 in Wuhan, China', *medRxiv*

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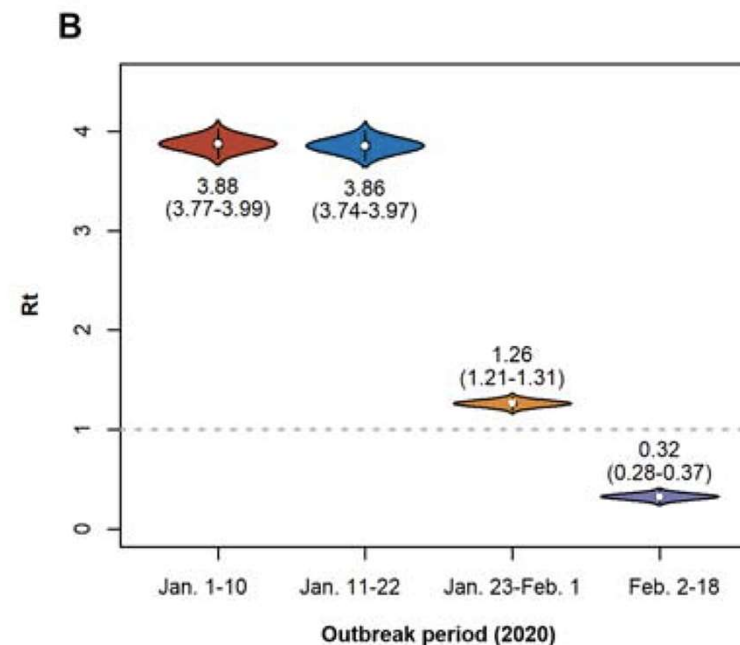
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Medidas de intervenção em Wuhan a partir do dia 23 de Janeiro

- Cordão sanitário na cidade de Wuhan
- Suspensão dos transportes públicos e taxi por aplicativos
- Restrição do tráfego nas áreas urbanas
- Proibição de viagens na região interna da cidade
- Fechamento de espaços públicos, cancelamento de eventos, uso obrigatório de máscaras cirúrgicas em público
- Quarentena domiciliar para toda população

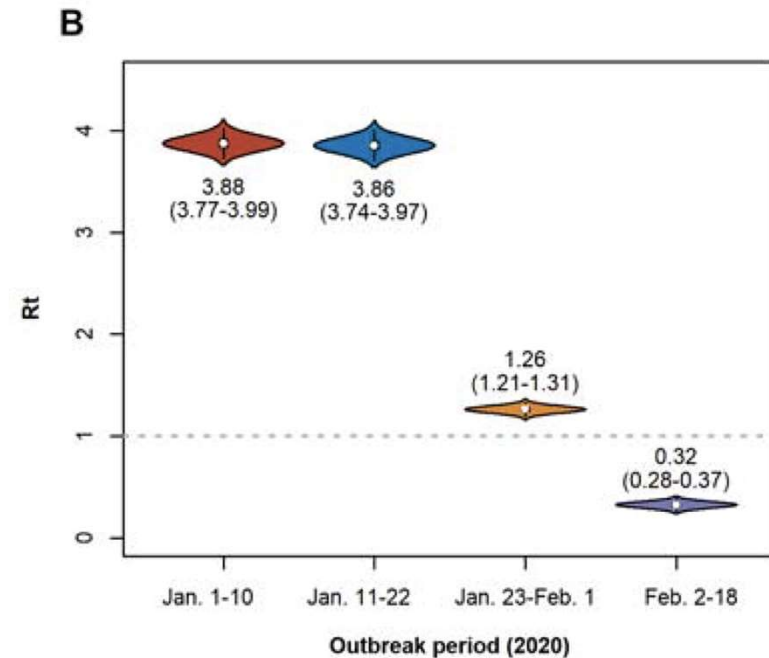


Wang, C. *et al.* (2020) 'Evolving Epidemiology and Impact of Non-pharmaceutical Interventions on the Outbreak of Coronavirus Disease 2019 in Wuhan, China', *medRxiv*

Medidas de intervenção em Wuhan a partir do dia 23 de Janeiro

Os autores estimam que as intervenções evitaram até 94.5% dos casos!!!

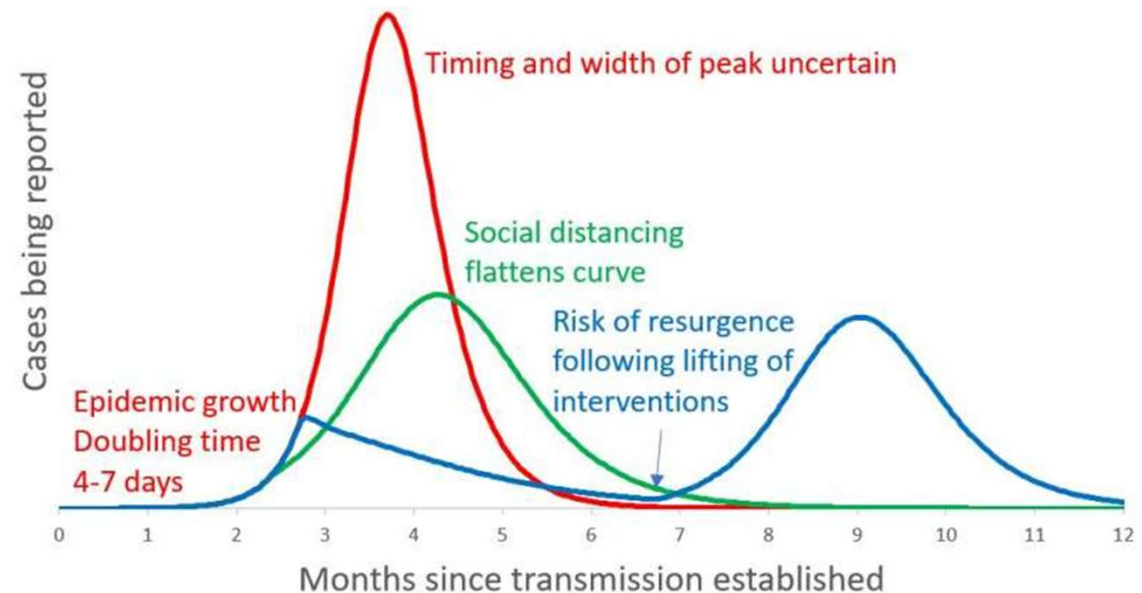
IC: (93.7 a 95.2%)



Wang, C. *et al.* (2020) 'Evolving Epidemiology and Impact of Non-pharmaceutical Interventions on the Outbreak of Coronavirus Disease 2019 in Wuhan, China', *medRxiv*

Controle do COVID-19

- 1) Reduzir o R_0 por meio de Intervenções não farmacológica (NIPs) como a redução da taxa de contato entre pessoas pela contenção de movimento e ações de isolamento e quarentena.
- 2) Manter o nível de infecção suficientemente baixo para evitar demandas logísticas exponenciais, como a superlotação de hospitais, que causariam o colapso do sistema de saúde
- 3) permitir que a economia e a funcionalidade da sociedade sejam preservadas.



Laboratório de Modelagem de Dinâmica de Doenças

Dr. Tarcísio M. Rocha Filho – CIFMC-IF/UnB

Me. Victor Bertollo Gomes Porto – MS

Me. Carlos César – IF/UnB

Me. Fabiana Ganem – MS

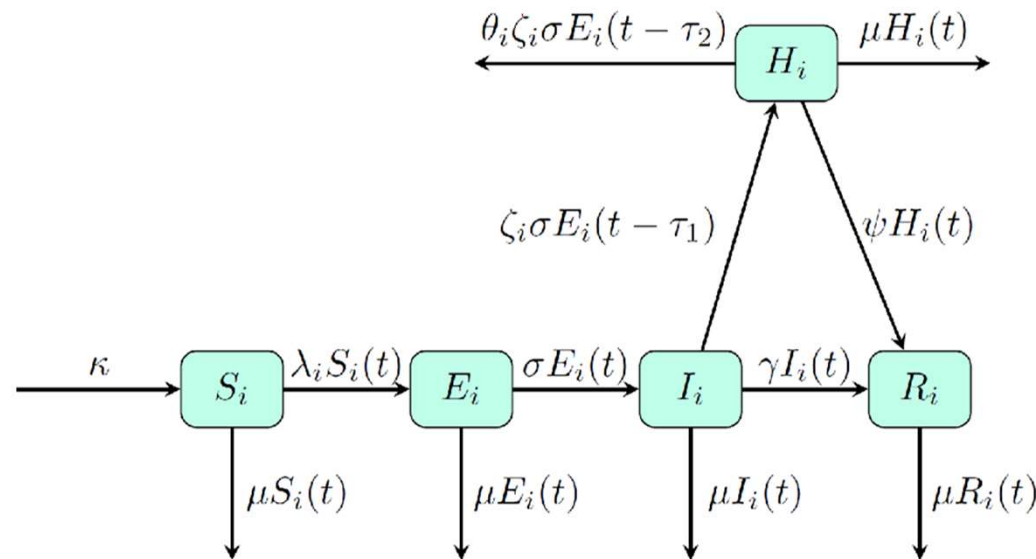
Dr. Thiago Rocha - OPAS

Dr. Walter Ramalho – FCE/UnB,

Dr. Wildo Araújo – NMT/UnB.



Foi construído um modelo do tipo SEIR, determinístico, com estratificação por faixa etária, incluindo um campo para hospitalizações (SHEIR)



A progressão entre os diferentes estágios é definida por equações diferenciais

$$\frac{dS_i}{dt} = \kappa\delta_{i,1} - \lambda S_i - \mu S_i - \nu_i S_i + \nu_{i-1} S_{i-1},$$

$$\frac{dH_i}{dt} = -\psi H_i + \zeta_i \lambda_i E_i(t - \tau_1) - \theta \zeta_i \lambda_i E_i(t - \tau_2) - \mu H_i,$$

$$\frac{dE_i}{dt} = \lambda S_i - \sigma E_i - \zeta_i \sigma E_i - \mu E_i - \nu_i E_i + \nu_{i-1} E_{i-1},$$

$$\frac{dI_i}{dt} = \sigma E_i - \gamma I_i - \mu I_i - \nu_i I_i + \nu_{i-1} I_{i-1},$$

$$\frac{dR_i}{dt} = \gamma I_i + \psi H_i - \mu R_i - \nu_i R_i + \nu_{i-1} R_{i-1},$$

Os parâmetros do modelo foram extraídos da literatura

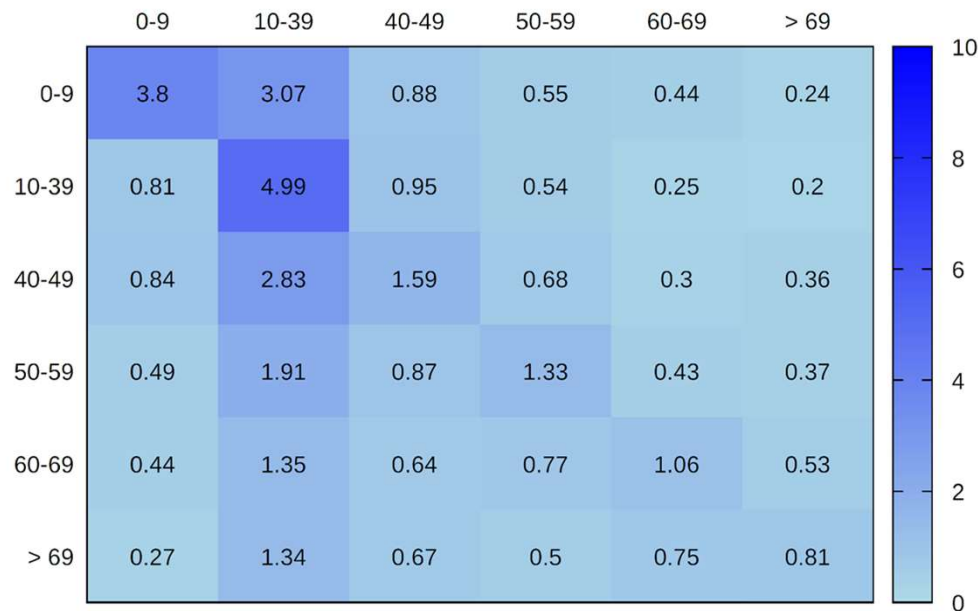
Table 1. Constant parameters in the model.

Variables	Definition	Value (CI 95%) [Ref]	Distribution
κ	Birth rate	0.01416 [28]	–
μ	Overall fatality rate from other causes	0.00608 [28]	–
ψ	Average recovery rate from hospital	$1/17.5 \text{ days}^{-1}$ [29]	–
P_{sc}	Proportion of severe and critical cases	18% [27]	–
μ_{COV}	Mortality proportion due to the disease	0.4% – 2.9% [27]	Uniform
θ	Morbidity proportion in hospitalized individuals	μ_{COV}/P_{sc}	–
σ^{-1}	Inverse of incubation rate	5.0(4.2; 6.0) days [30]	Log-Normal
γ^{-1}	Inverse of recovery rate of non-hospitalized infectious individuals	1.61(0.35; 3.23) days^{-1} [31]	Not informed. Assumed Log-Norm.
ζ_i	Probability of hospitalizations for age-group i	(see text)	–
R_0	Basic reproduction number for COVID-19	2.74(2.47; 3.03) (see complementary material)	Assumed Uniform
τ_1	Median time from illness onset to hospitalization	3.3(2.7; 4.0) [30]	Gamma
τ_2	Average time from illness onset to death	15.0(12.8; 17.5) [30]	Log-Normal

Constant parameters in the model with the average value, Confidence Interval (CI) of 95% if pertinent and statistical distribution of values.

A matriz de contato foi construída com base nos dados da literatura, o R0 foi extraído da literatura e incorporado nas diferentes faixas etárias

Fig 1. Heat map for the contact matrix C_{ij} representing the number of physical contacts per day of an individual of age group i with any individual of group j .

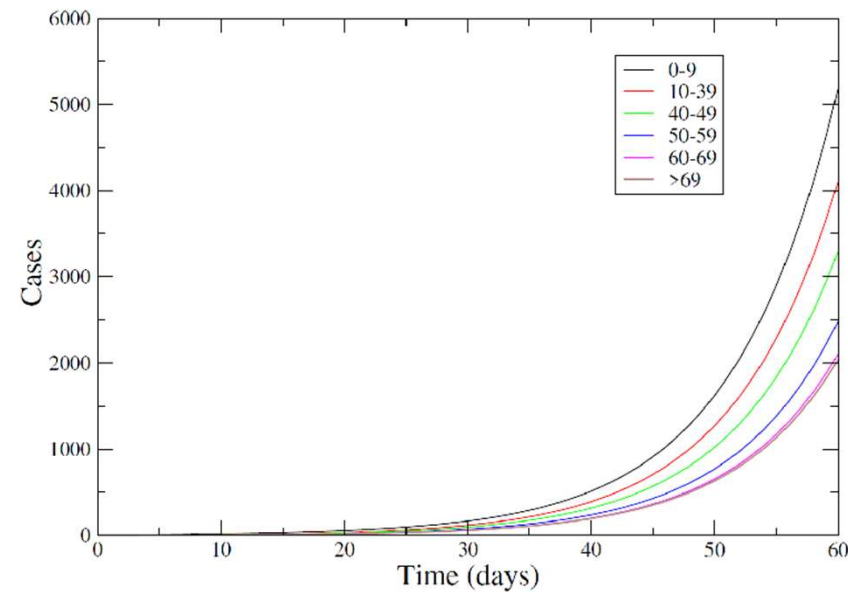


$$R_0 = \sum_{i,j=1}^M n_j \beta_{ij} / \gamma = \sum_{i,j=1}^M n_j P_c C_{ij} / \gamma,$$

Mossong, Joël, et al. *PLoS medicine* 5.3 (2008): e74.

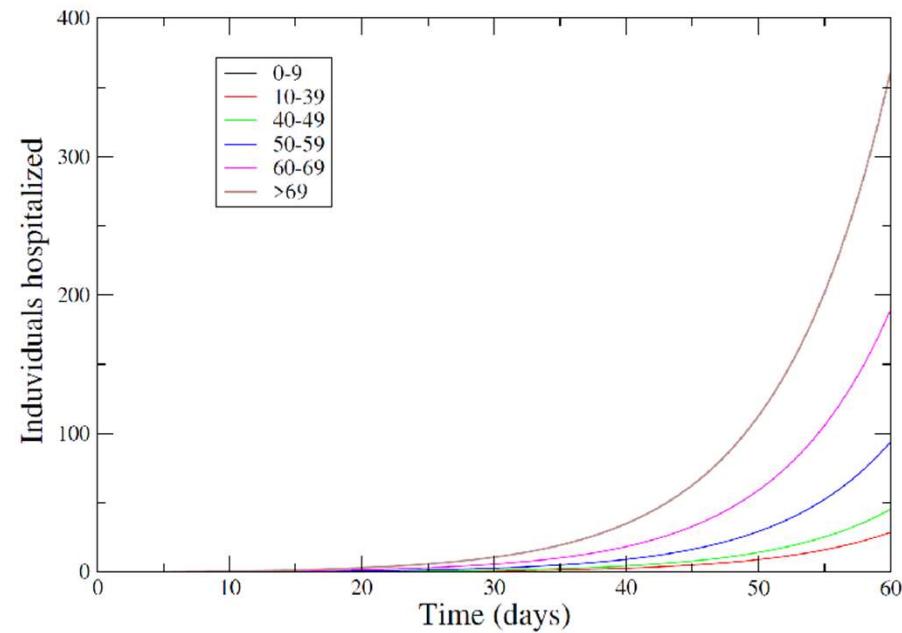
Número cumulativo de casos por faixa etária para os primeiros 60 dias na região metropolitana de São Paulo

Fig 3. Cumulative number of cases in each age group for the mean or median values for the parameters in Tab. 1, assuming a fatality rate of 2.3%.



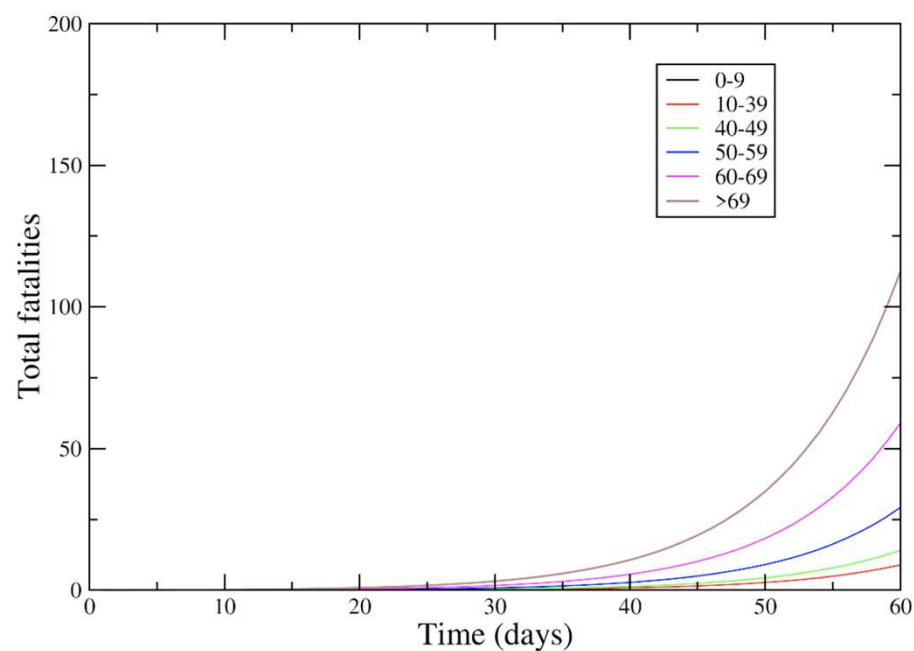
Número de indivíduos hospitalizados por faixa etária para os primeiros 60 dias na região metropolitana de São Paulo

Fig 4. Number of hospitalized individual at a given moment corresponding to Fig 3.



Número cumulativo de óbitos por faixa etária para os primeiros 60 dias na região metropolitana de São Paulo

Fig 5. Cumulative number of fatalities corresponding to Fig 3.



Número cumulativo de casos, óbitos e número máximo de pessoas internadas num determinado dia para a região metropolitana de São Paulo, 30 e 60 dias após o início do surto

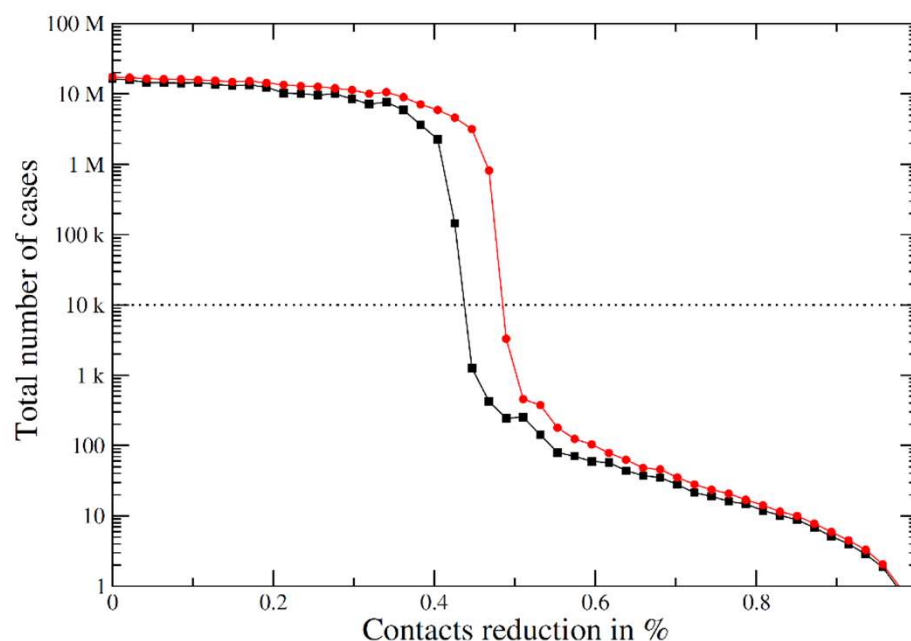
Table 2. Median for the total cumulative number of cases averaged over 100, 000 Monte Carlo realizations.

Age	30 days			60 days		
	Cases	Hosp.	Fatal.	Cases	Hosp.	Fatal.
0–9	354(226;628)	0(0;0)	0(0;0)	10259(4458;29888)	0(0;0)	0(0;0)
10–39	299(195;517)	4(2;7)	1(0;1)	8181(3559;23911)	99(41;288)	18(8;51)
40–49	234(151;410)	6(3;11)	1(1;2)	6543(2842;19136)	154(63;447)	27(12;80)
50–59	177(114;311)	11(7;21)	2(1;3)	4946(2142;14519)	305(127;888)	55(23;162)
60–69	150(96;267)	21(13;37)	4(2;7)	4212(1814;12429)	566(238;1653)	103(43;310)
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The number of cases and fatalities are cumulative. The number of hospitalized individuals represent the maximal population attained at any particular time. The inter-quartile interval is given by the numbers between brackets.

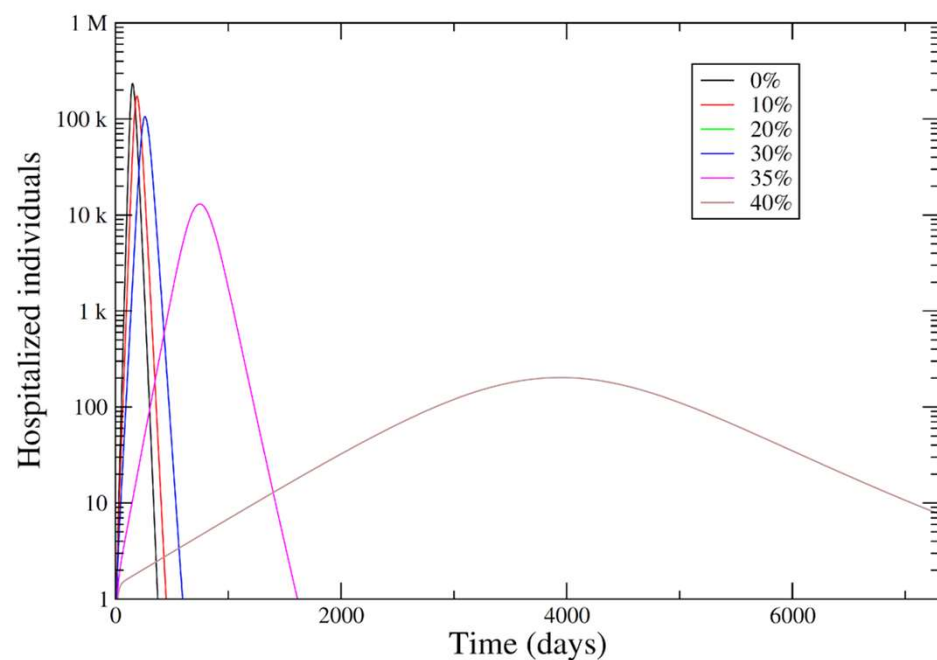
Impacto da redução do número de contatos por dia no número total de casos

Fig 2. Number of total cases from a Monte Carlo analysis with 1000 realizations from the parameter in Table 2 in the main text, except in the sharp transition region with 10 000 realizations.

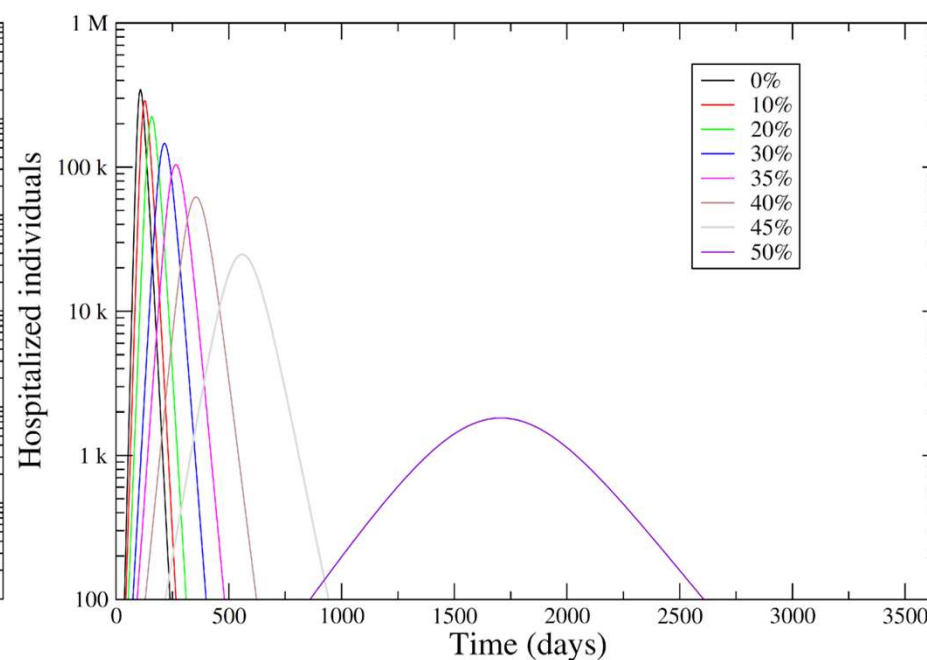


Número de pacientes internados num dado momento para diferentes valores de R_0 e taxas de redução no número de contatos dias na população

$$R_0=2.47$$



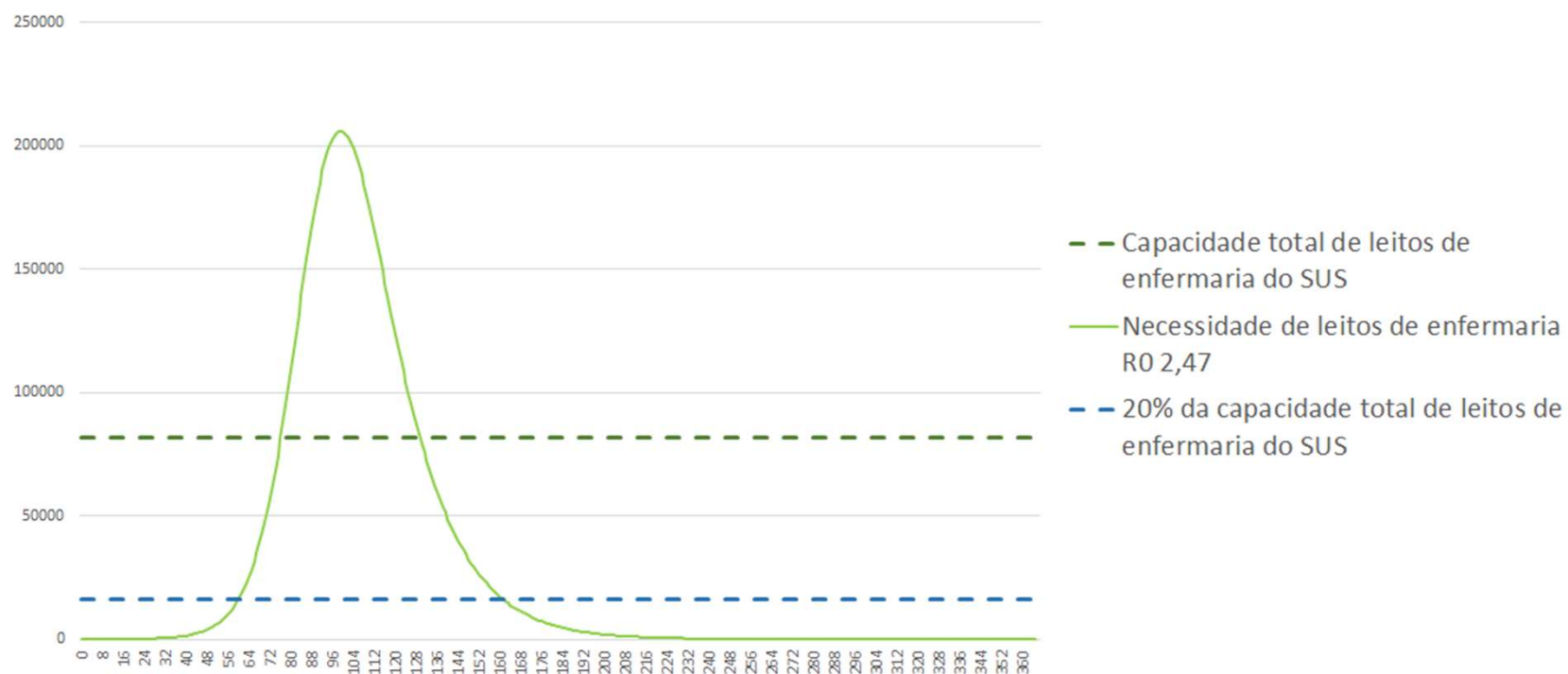
$$R_0=3.03$$



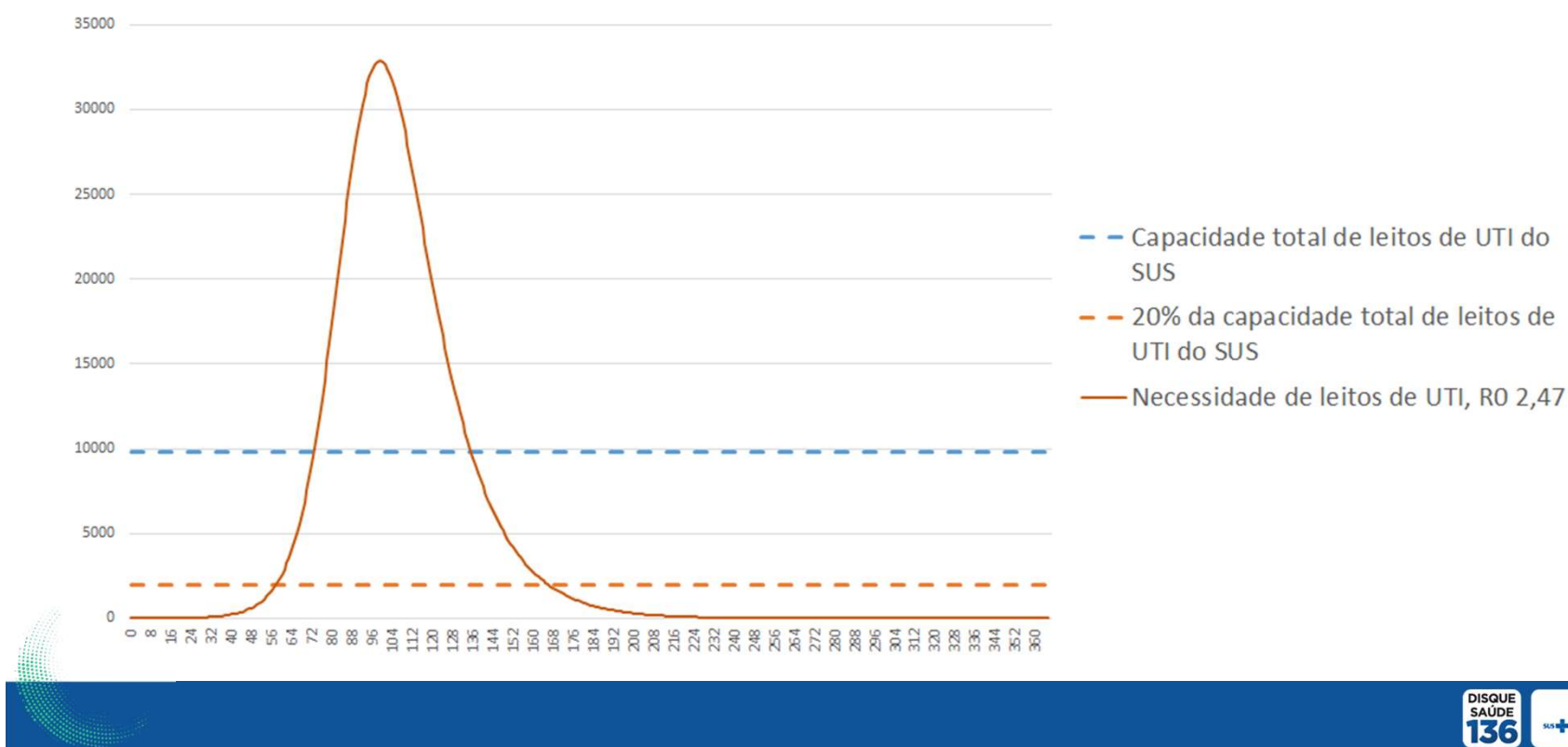
Estimadas em "papel de padaria" para a Grande São Paulo

- $R_0=2$
- Para se ter imunidade de rebanho: 50%
- 10 milhões de infectados na Grande São Paulo
- 1,4 milhões de notificações (86% das infecções)
- 280 mil internações (20% irão necessitar internação)
- 35 mil internações em UTI (12,5% das internações em UTI)
- 245 mil dias/UTI (Média de 7 dias na UTI)
- **671 leitos de UTI na Grande São em 1 ano apenas para o COVID-19**
(245mil/365 dias)
- **17.500 Óbitos**

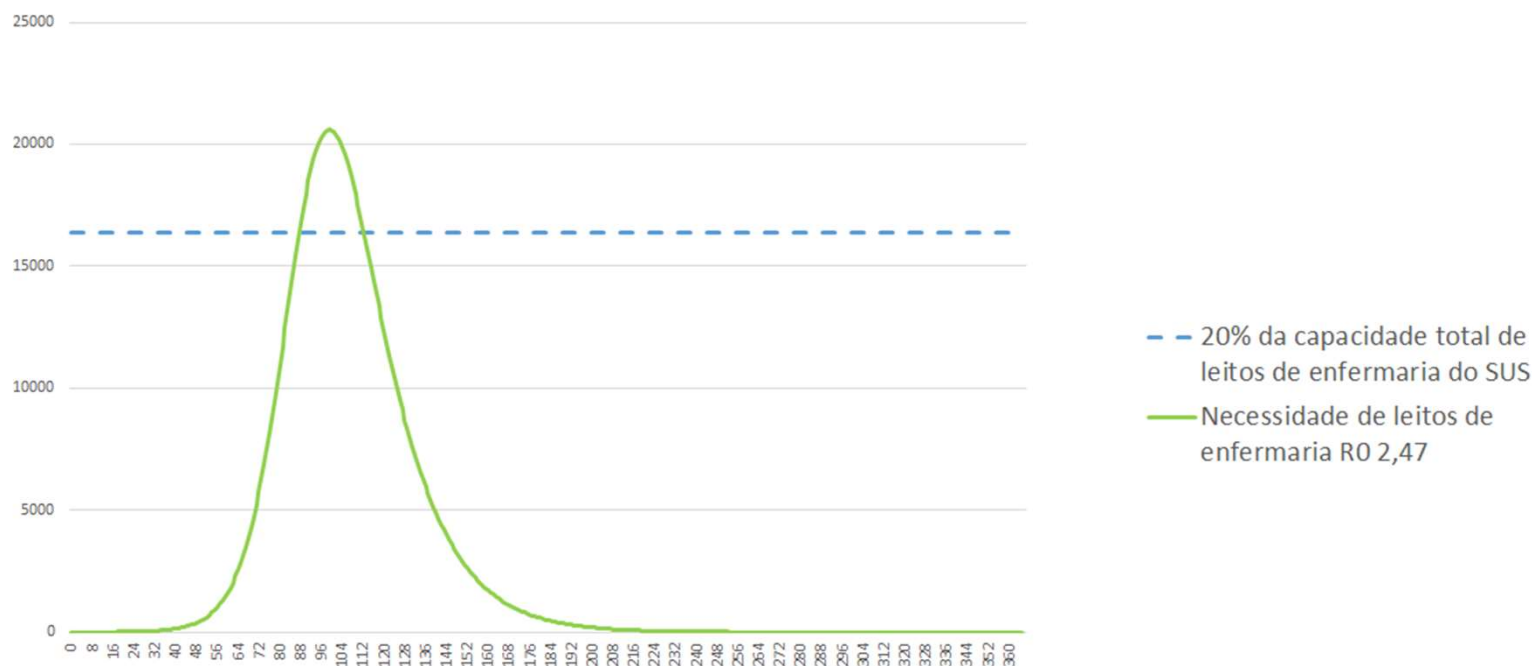
Necessidade de leitos de internação em enfermaria nas capitais Brasileiras: cenário pessimista, $R_0 = 2.47$.



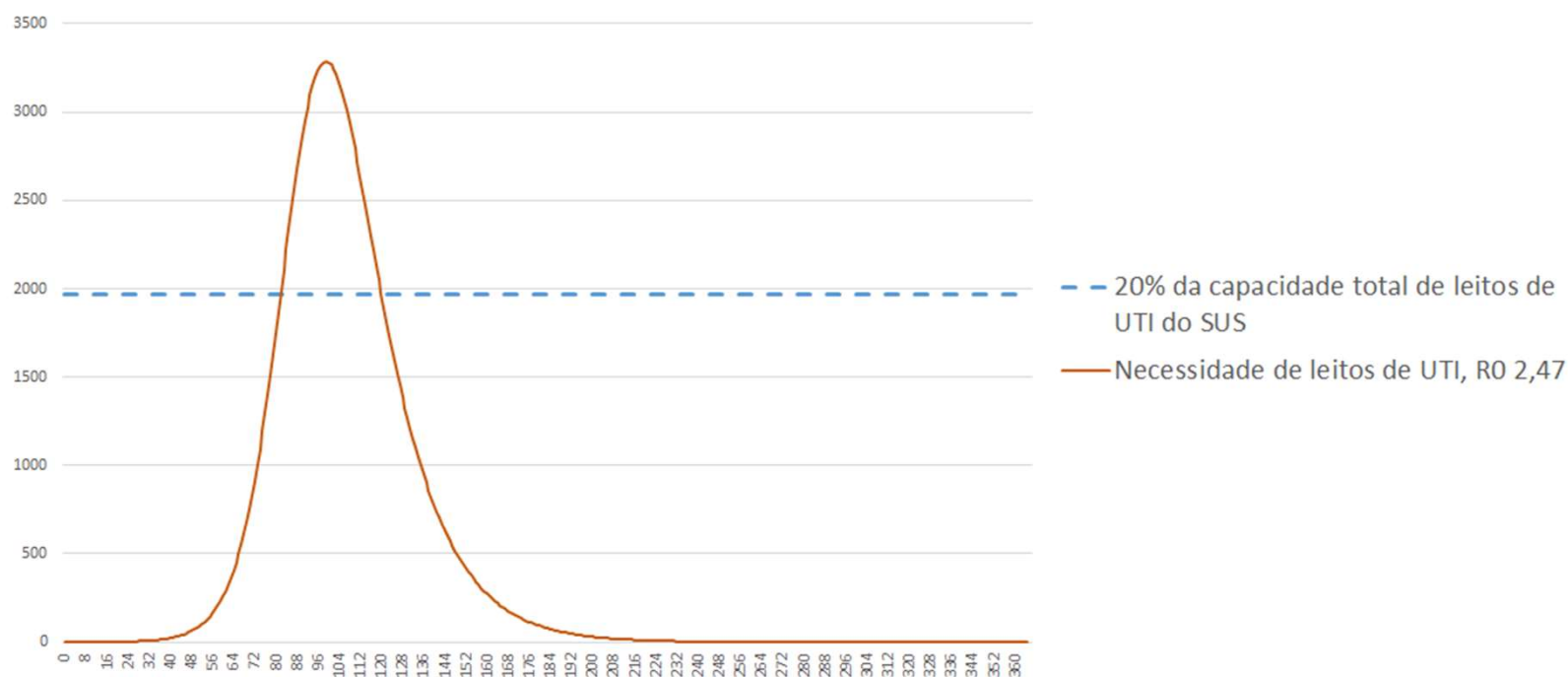
Necessidade de leitos de internação em UTI nas capitais Brasileiras: cenário pessimista, $R_0 = 2.47$.



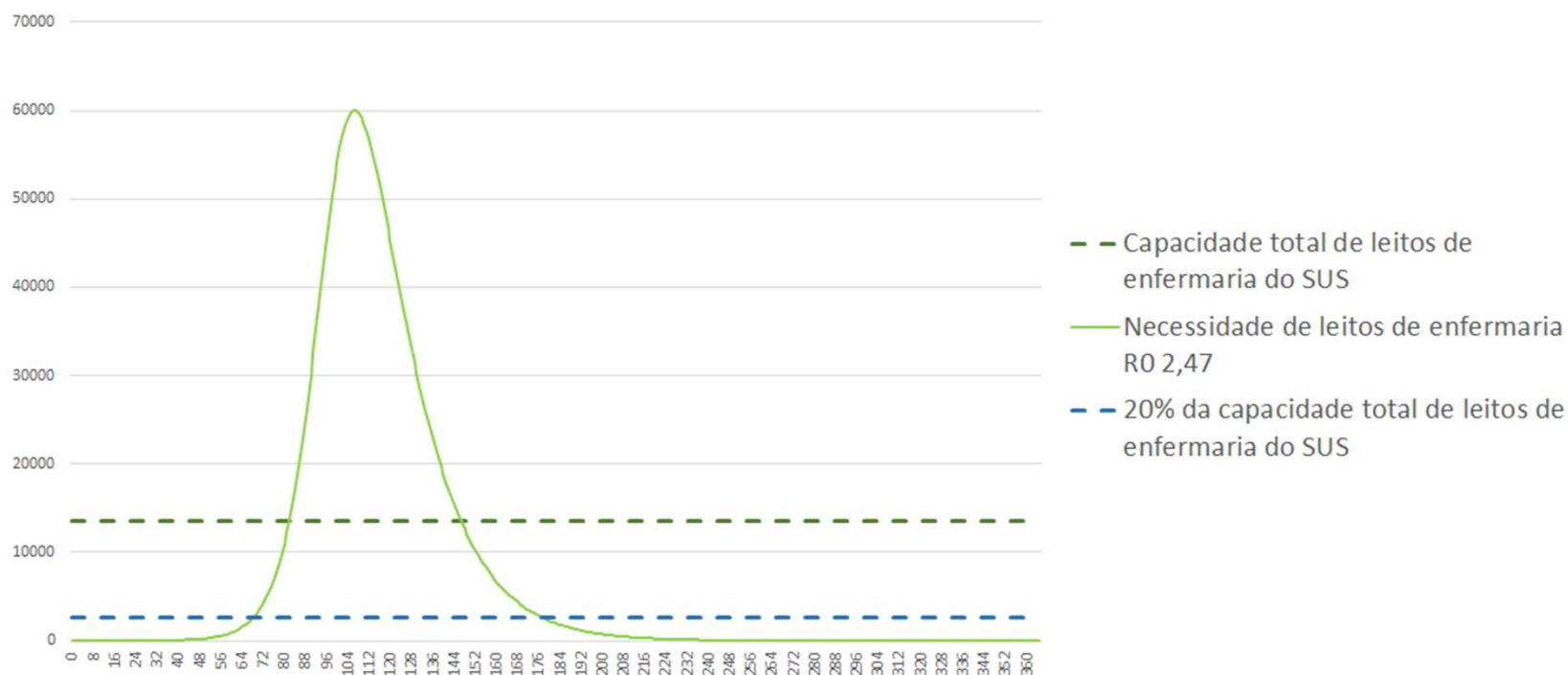
Necessidade de leitos de internação em enfermaria nas capitais Brasileiras: cenário otimista, $R_0 = 2.47$ mas assumindo que apenas 10% dos casos são detectados pelos sistemas



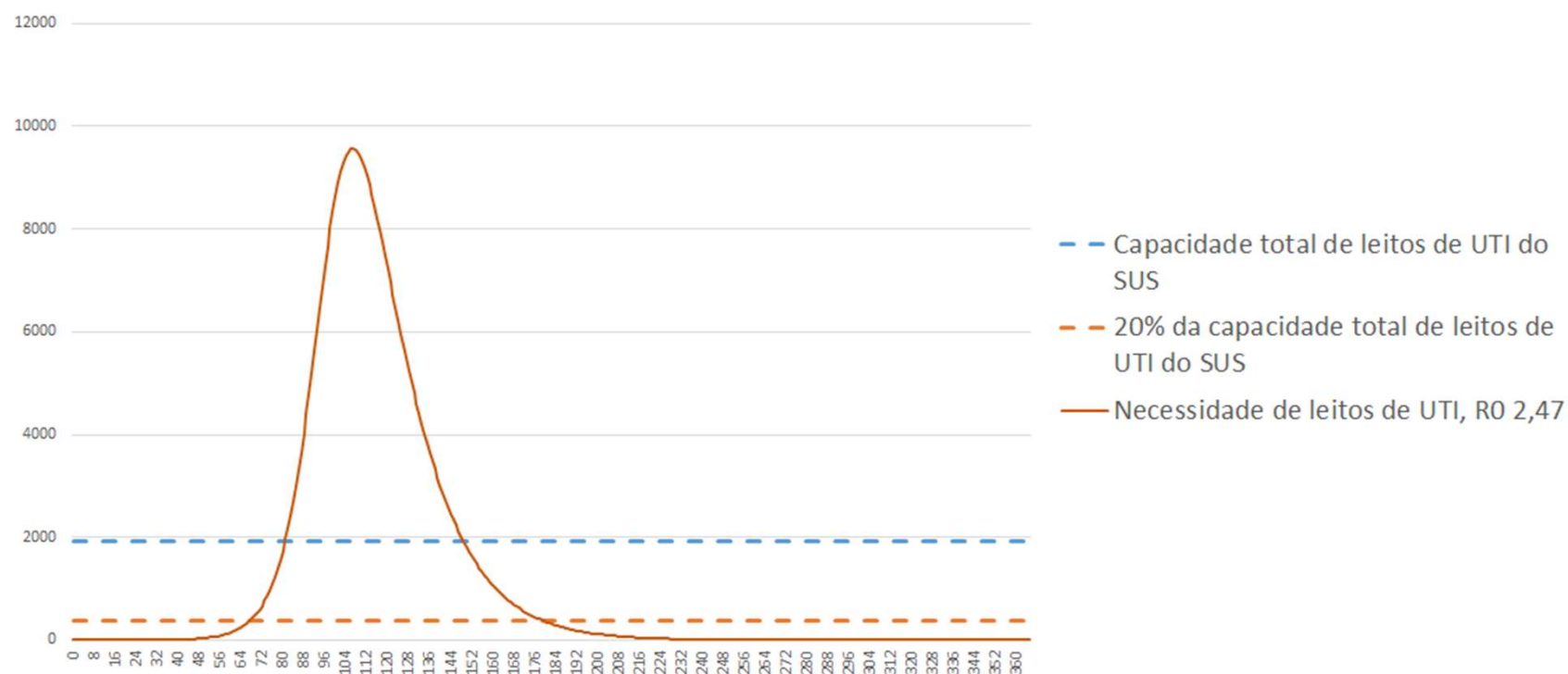
Necessidade de leitos de internação em UTI nas capitais Brasileiras: cenário otimista, $R_0 = 2.47$ mas assumindo que apenas 10% dos casos são detectados pelos sistemas



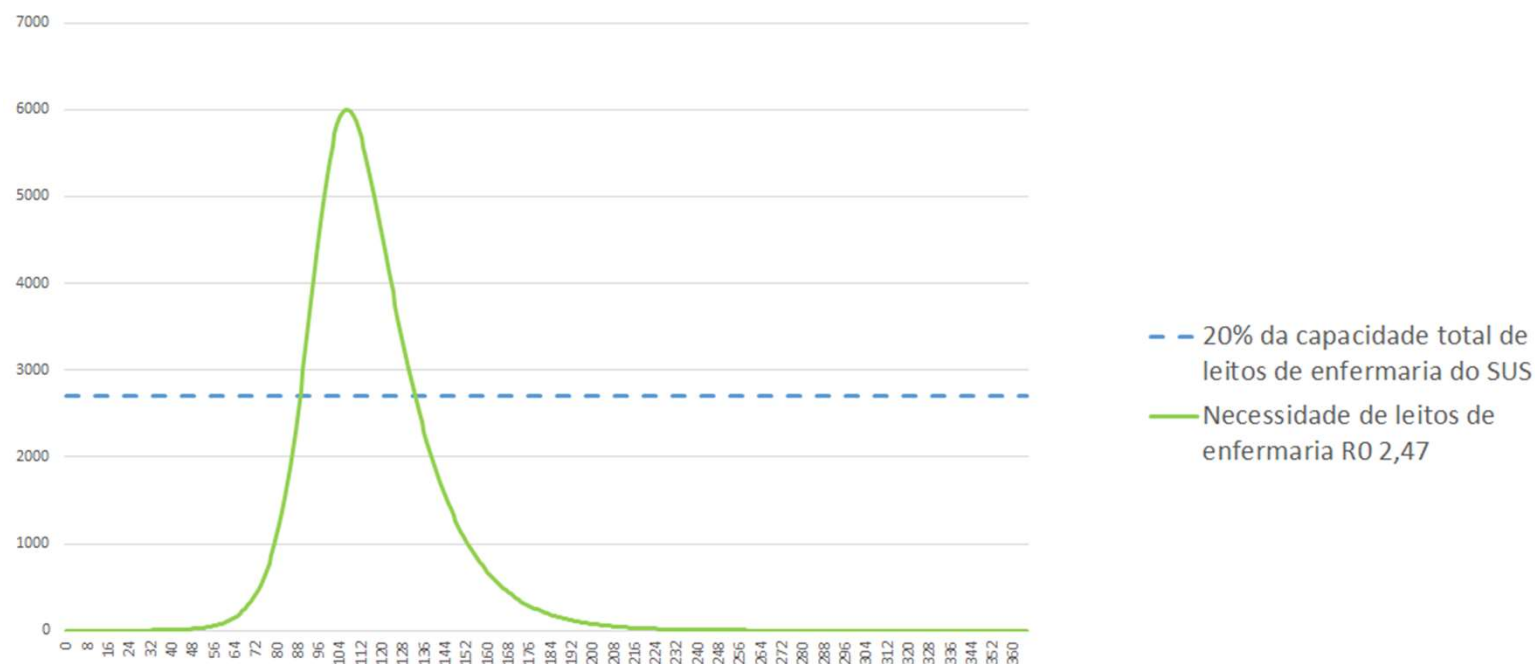
Necessidade de leitos de internação em enfermaria na cidade de São Paulo: cenário pessimista, $R_0 = 2.47$.



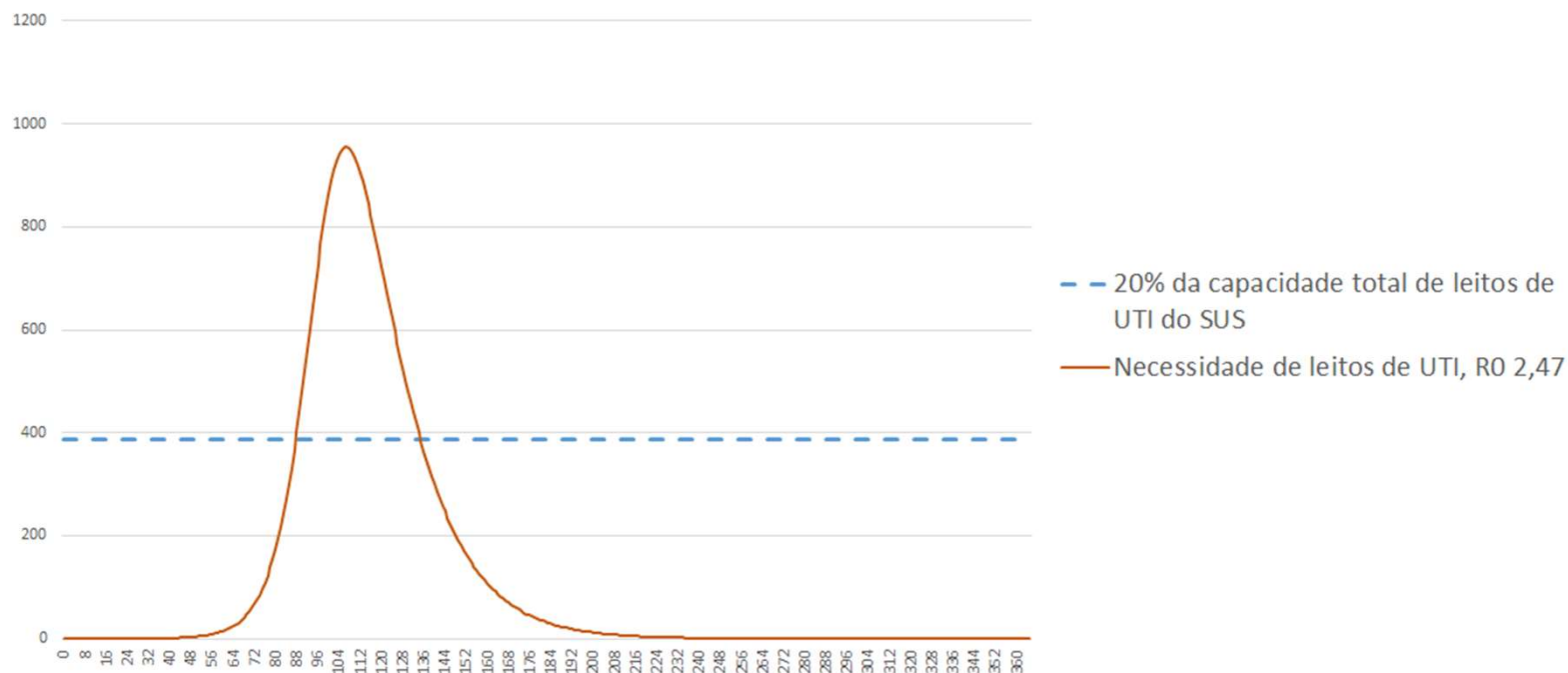
Necessidade de leitos de internação em UTI na cidade de São Paulo: cenário pessimista, $R_0 = 2.47$.



Necessidade de leitos de internação em enfermaria na cidade de São Paulo: cenário otimista, $R_0 = 2.47$ mas assumindo que apenas 10% dos casos são detectados pelos sistemas



Necessidade de leitos de internação em UTI na cidade de São Paulo: cenário otimista, $R_0 = 2.47$ mas assumindo que apenas 10% dos casos são detectados pelos sistemas



Modelagem da intervenções não farmacológicas Imperial Collage, UK

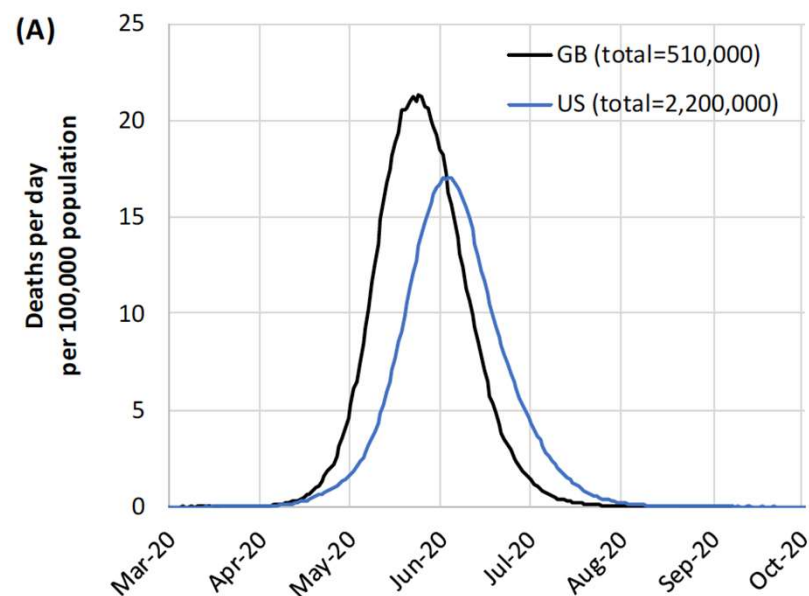
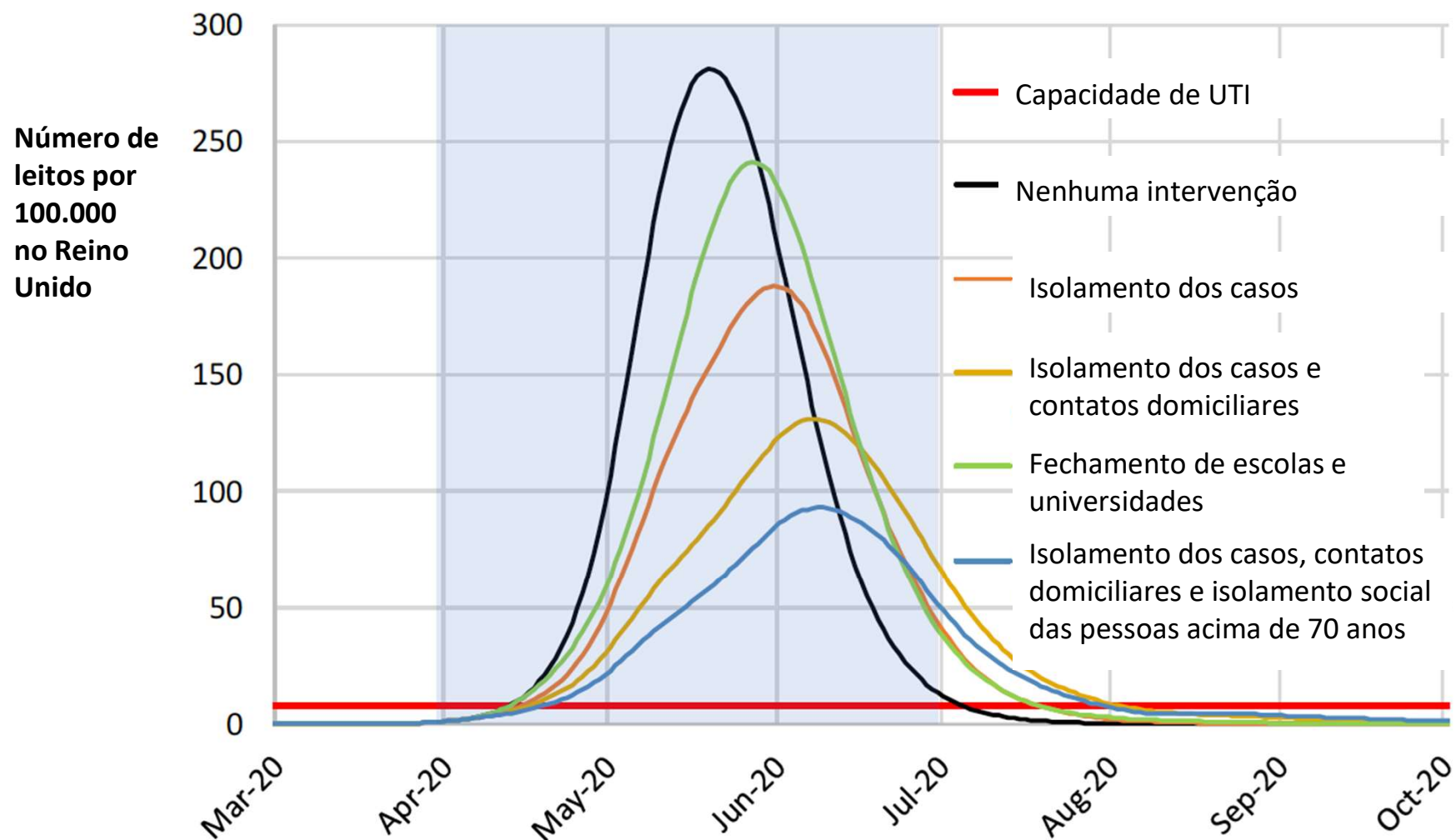


Table 2: Summary of NPI interventions considered.

Label	Policy	Description
CI	Case isolation in the home	Symptomatic cases stay at home for 7 days, reducing non-household contacts by 75% for this period. Household contacts remain unchanged. Assume 70% of household comply with the policy.
HQ	Voluntary quarantine home	Following identification of a symptomatic case in the household, all household members remain at home for 14 days. Household contact rates double during this quarantine period, contacts in the community reduce by 75%. Assume 50% of household comply with the policy.
SDO	Social distancing of those over 70 years of age	Reduce contacts by 50% in workplaces, increase household contacts by 25% and reduce other contacts by 75%. Assume 75% compliance with policy.
SD	Social distancing of entire population	All households reduce contact outside household, school or workplace by 75%. School contact rates unchanged, workplace contact rates reduced by 25%. Household contact rates assumed to increase by 25%.
PC	Closure of schools and universities	Closure of all schools, 25% of universities remain open. Household contact rates for student families increase by 50% during closure. Contacts in the community increase by 25% during closure.



Modelo "Ideal"

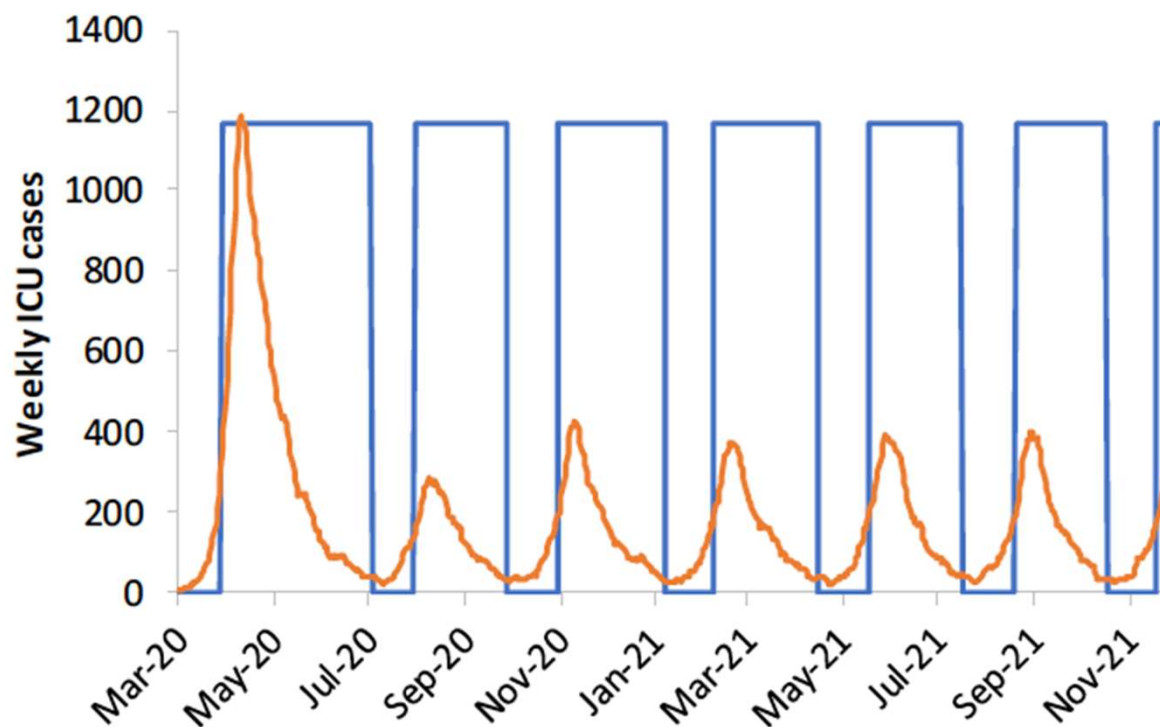


Ilustração do desencadeamento adaptativo das estratégias de supressão no Reino Unido, para $R_0 = 2,2$, um gatilho "on" quando atingir 100 casos internados em UTI em uma semana e um gatilho "off" quando atingir 50 casos de UTI.