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Identification of priority groups for COVID-19 vaccination in Brazil

Identificação de grupos prioritários para a vacinação contra COVID-19 no Brasil

Identificación de grupos prioritarios para la vacunación contra la COVID-19 en Brasil

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Abstract

In a context of community transmission and shortage of vaccines, COVID-19 vaccination should focus on directly reducing the morbidity and mortality caused by the disease. It was thus essential to define priority groups for vaccination by the Brazilian National Immunization Program (PNI in Portuguese), based on the risk of hospitalization and death from the disease. We calculated overrisk according to sex, age group, and comorbidities using hospitalization and death records from severe acute respiratory illness with confirmation of COVID-19 (SARI-COVID) in all of Brazil in the first 6 months of the epidemic. Higher overrisk was associated with male sex (hospitalization = 1.1 and death = 1.2), age over 45 years for hospitalization (OvRag *ranging from 1.1 to 8.5), and age over 55 year for death* (OvRag *ranging from 1.5 to 18.3). In the groups with comorbidities, chronic kidney disease, diabetes mellitus, cardiovascular disease, and chronic lung disease were associated with overrisk, while there was no such evidence for asthma. Chronic kidney disease or diabetes and age over 60 showed an even stronger association, reaching overrisk of death 14 and 10 times greater than in the general population, respectively. For all the comorbidities, there was higher overrisk at older ages, with a downward gradient in the oldest age groups. This pattern was reversed when examining overrisk in the general population, for both hospitalization and death. The current study provided evidence of overrisk of hospitalization and death from SARI-COVID, assisting the definition of priority groups for COVID-19 vaccination.*

COVID-19; Severe Acute Respiratory Syndrome; Epidemiological Monitoring; Comorbidity

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Introduction

The first case of COVID-19 in Brazil was officially confirmed on February 26, 2020, in the state of São Paulo. Shortly more than a month later, all 27 states of the country had already reported at least ten cases of the disease. Spread of the virus followed the country's air traffic flows, first reaching the most populous state capitals, connected to São Paulo and Rio de Janeiro and later the cities in the metropolitan areas and gradually reaching the countryside [1,2]. In the first six months of the pandemic in Brazil (as of August 22, 2020), according to the Coronavirus Panel (https://covid.saude.gov.br/), there were officially 5,323,630 confirmed COVID-19 cases and 155,900 deaths in the country. These records include cases (asymptomatic, mild, and severe) and deaths from SARS-CoV-2 confirmed by different laboratory tests (RT-PCR, rapid tests, serological tests), beside occasional clinical imaging diagnoses [3].

Since the beginning of the COVID-19 pandemic, there was a major movement towards provision of data and information that could assist contingency plans and mitigation strategies, among other measures. In addition, a major global movement combined efforts by various research groups, institutions, and countries in the search for vaccines against the disease [4]. As of February 23, 2021, more than 250 vaccines – 182 in preclinical development, 73 in clinical development, and of these, 16 in phase III – were being tested [5]. Of this total, five had already been approved for use in some countries [6], two vaccines were approved for emergency use in Brazil [7], and one was approved with definitive registration [8]. Even before these vaccines were released, it was known that distribution of doses according to priority groups would be necessary due to the low availability of doses for the global demand [9]. Specifically for Brazil, a continental-sized country with 210 million inhabitants, the definition of priority groups is essential for any campaign of this magnitude.

The Brazilian National Immunization Program (PNI in Portuguese), known internationally for its capacity to serve a country with continental dimensions and major socioeconomic diversity, with a broad vaccination calendar, is an important arm of the Brazilian Unified National Health System (SUS) (Brazilian Health Informatics Department. http://sipni.datasus.gov.br/si-pni-web/faces/apresentacaoSite.jsf, accessed on 16/Feb/2021) and is responsible for the National Plan for Operationalization of COVID-19 Vaccination [10]. The activities of the PNI include the annual influenza (H1N1) vaccination campaign, which is organized according to priority groups, as is COVID-19 (http://sipni.datasus.gov.br/si-pni-web/faces/apresentacaoSite.jsf).

According to the WHO, the focus for the definition of priority groups for COVID-19 vaccination in a context of community transmission should be, at the initial stage, direct to the reduction of morbidity and mortality, besides the maintenance of essential services and honoring the reciprocity principle (to protect individuals with high exposure to the virus while in service to the community) [9].

The main objective of the present study was to define risk groups for hospitalization and death from COVID-19. These analyses assisted the definition of priority groups for the National Plan for Operationalization of COVID-19 Vaccination drafted by the PNI for the campaign's first stage. A study was performed with descriptive analyses of hospitalizations and deaths from severe acute respiratory illness associated with COVID-19 (SARI-COVID) reported in the first six months of the pandemic in Brazil. The current study is an update and extension of the analyses published previously in Niquini et al. [11], especially with the use of overrisk indicators for comparison of groups.

Methods

Data

Data on hospitalizations and deaths from SARI-COVID were obtained from SIVEP-Gripe (https://sivepgripe.saude.gov.br/sivepgripe), the official system for recording hospitalizations and deaths from severe acute respiratory illness (SARI) in the entire country. As part of the reporting protocol, every case identified as SARI has a biological sample collected for subsequent laboratory analysis. Since March 2020, testing of the samples also includes SARS-CoV-2. The study only included cases with recorded confirmation by RT-PCR, considered the gold standard laboratory diagnosis for SARS-CoV-2 infection.

We considered the records with date of first symptoms up to the 35th Epidemiological Week (EW) of 2020 (August 29, 2020) to avoid loss of information from delays in keying in and updating the laboratory diagnosis. The SIVEP-Gripe variables considered for analysis of risk factors were the following: age group (aggregated every 5 years from 0 to 4 years up to 90 years and older), sex, presence of comorbidities (diabetes mellitus, chronic kidney disease, asthma, other chronic lung diseases, and chronic cardiovascular disease – CVD). Information on systemic hypertension (SH) was obtained from searches in the open text field that lists "other comorbidities". Text searches used the strings "HAS" or "H.A.S." or "HIPERTE" based on the *stringr* wrapper (https://CRAN.R-project.org/package=stringr) available in the R environment (http://www.r-project.org). Importantly, the obesity variable was excluded from the analyses, even though it is an important risk factor for COVID-19 [12,13], due to failures in completion of this information (besides that of other comorbidities) and the difficulty in defining obesity at the time of completion in the reporting. Assessment of obesity requires body mass index (BMI). In the reporting data, not only is the obesity variable poorly completed, but many reporting forms fail entirely to fill in BMI.

Demographic data on the Brazilian population in 2020 by age group and sex were obtained from projections performed by the Brazilian Institute of Geography and Statistics (IBGE) [14].

Data on prevalence of comorbidities in the general population and stratified by age group for Brazil were obtained from the *Brazilian National Health Survey* (PNS in Portuguese) in 2013 [15,16]. The target comorbidities were diabetes mellitus, chronic kidney disease (CKD), asthma (or asthmatic bronchitis), lung diseases (pulmonary emphysema, chronic bronchitis, or chronic obstructive pulmonary disease – COPD), and CVD.

CVD, as defined by the PNS, include systemic hypertension and heart diseases (myocardial infarction, angina, heart failure, and others). To produce a consistent definition, a compound variable was created in the SIVEP-Gripe database, called CVD, which includes systemic hypertension and chronic-CVD. Age stratification for comorbidities considered three groups, 18-39 years, 40-59 years, and 60 years or older. It was not possible to calculate the prevalence in younger ages, since the PNS sample only includes individuals 18 years or older [15,16]. An estimate was made of the number of persons with each comorbidity in 2020, assuming the prevalence measured by the PNS in 2013 [15,16]. The population projection per age group is aggregated for 5-year periods as mentioned above, so that for the age group from 18-39 years, we added the projected values for the 20-24, 25-29, 30-34, and 35-39-year age groups, and for 18 and 19 years we used two-fifths of the IBGE projection for the age group from 15-19 years.

Data analysis

- **Incidence rate**

Incidence rates were calculated for hospitalizations and deaths per 1,000 inhabitants for SARI-COVID by sex, age group, comorbidity, and comorbidity by age group. Incidence rate in the period consists of the ratio between total hospitalizations (or deaths) from SARI-COVID in the target group up to the 35th EW in the entire country, divided by the group's respective projection of the population in 2020 multiplied by 1,000.

- **Calculation of overrisk**

An indicator commonly used in the comparison of risk between groups is relative risk. However, it was not possible to calculate this indicator with the available data, since the groups compared here do not consist of persons exposed versus unexposed to the target risk. We thus opted to use the term overrisk, defined here as the ratio between the risk of hospitalization or death in a specific group divided by the risk of the same event in the general population.

Formally, the overrisk (*OvR*) of a given group *i*, OvR_i, was defined as the ratio between the incidence rate of hospitalization or death in group i and the incidence rate of hospitalization or death in the general population. Let y_i be the number of hospitalizations (or deaths) in the target group *i*, and n_i the reference population for the group. Also let *Y* be the total hospitalizations (or deaths) in the general

population and *N* this population's size. The statistical model for calculation of overrisk assumes that the number of hospitalizations (or deaths) from SARI-COVID follows a binomial distribution in both the general population and the target groups. We thus have for each group *i*,

$$y_i \sim Binomial\ (n_i, \theta_i),\ i = 1, 2,...J,$$

in which θ_i is the incidence rate of hospitalizations (or deaths) in group *i*, and *J* is the total number of groups.

For the general population, we assume that

$$Y \sim Binomial\ (N, \theta_0),$$

in which θ_0 is the incidence rate of hospitalizations (or deaths) in the general population. Therefore, the overrisk of group *i* is given by

$$OvR_i = \frac{\theta_i}{\theta_0}$$

Importantly, the groups consist of partitions of the population, that is $Y = \sum_i y_i$, so the distribution defined above is an approximation. For large counts, the approximation error is small.

To exemplify overrisk, consider a hypothetical scenario in which 100 deaths are recorded in a specific group with 100,000 persons. Suppose that in the general population there are 102,000 deaths in 210 million inhabitants. In this case, OvR_i is calculated as: (100/100,000)/(102,000/210 million), giving an OvR_i of approximately 2.1. That is, the incidence rate in group i is about twice the incidence rate in the general population.

To measure the uncertainty of the estimates of OvR_i, from the Bayesian perspective, we attributed uniform a priori distributions for θ_i and θ_0 so that the a posteriori distribution for each parameter was a beta distribution with known parameters. Samples from the a posteriori distribution of OvR_i are obtained via Monte Carlo simulation with a sampling size of 100,000 for the distribution of the *OvR* probability in each group *i*. This sample allows obtaining the 95% credibility interval (95%CI) for OvR_i, which is important for assessing whether the overrisk is significant, that is, when the lower limit of the credibility interval is greater than 1. Applying this method to the above-mentioned hypothetical example gives a 95%CI of 1.7-2.5.

Analogously, one defines stratified overrisk or *SOvR* to calculate the overrisk of a comorbidity in a specific stratum, for example, an age group. The hospitalizations (or deaths) are limited to a specific age group, and the denominator for the *SOvR* of group *i* is the incidence rate for the age group (*ag*) in question, that is,

$$OvR_i(ag) = \frac{\theta_{i,ag}}{\theta_{0,ag}}$$

in which $\theta_{i,ag}$ and $\theta_{0,ag}$ represent the incidence rates in group *i* and the general population for the target age group. The distribution of $SOvR_i(ag)$ for group *i* is derived analogously to the distribution of overrisk for group *i*.

To measure the uncertainty of the estimates of stratified overrisk, one assumes that the number of hospitalizations (or deaths) from SARI-COVID also follows a binomial distribution for age groups or groups with comorbidities.

Thus, the estimated OvR_i for comorbidity *c* and age group *ag*, called $OvR_{c,ag}$, uses the incidence rate of hospitalizations or deaths in individuals with a given comorbidity and age group as the numerator and compares them to the incidence rate in the general population (denominator). The $SOvR_{c,ag}(ag)$ uses the same numerator as $OvR_{c,ag}$, but the denominator is the incidence rate in the population of age group *ag*. Therefore, the interpretation of $SOvR_{c,ag}$ relates to the overrisk associated with a specific comorbidity in a specific age group, while $OvR_{c,ag}$ takes into account both the effect of the comorbidity and the joint effect of the age group itself.

Results

In Brazil, the total number of hospitalizations with positive RT-PCR diagnosis for SARS-CoV-2 with date of the first symptoms up to EW 35 was 292,089. During this same period, there were 102,562 deaths from SARI-COVID. These values correspond to a incidence rate of 1.4 hospitalizations and 0.5 deaths per 1,000 inhabitants during the period.

The incidence rates for hospitalizations (1.5 per 1,000 inhabitants) and deaths (0.6 per 1,000 inhabitants) were higher for males than for females. This translates as an increased overrisk of hospitalization in males of 1.115 (95%CI: 1.108; 1.122) and a decreased overrisk for females, OvR_s = 0.836 (0.831; 0.842), respectively. For deaths, the difference between the sexes is even greater, with OvR_s = 1.173 (1.161; 1.184) for males and OvR_s = 0.831 (95%CI: 0.822; 0.841) for females.

Figure 1a presents the incidence rates of hospitalizations and deaths from SARI-COVID per 1,000 inhabitants by age group. Figure 1b presents the OvR_{ag} by age group, in which the reference is the incidence rate of hospitalizations or deaths (Figure 1a) per 1,000 inhabitants in the general population. The resulting values indicate relative protection in age groups 0-4 years (OvR_{ag} = 0.150) up to 40-44 years (OvR_{ag} = 0.904), with OvR_{ag} for hospitalization reaching the minimum level between 10 and 14 years (OvR_{ag} = 0.033). Starting with the 45-49-year age group (OvR_{ag} = 1.133), there is a gradual increase in overrisk of hospitalization, reaching OvR_{ag} = 8.466 in individuals 90 years or older. In relation to deaths, there is strong relative protection in persons up to 24 years of age (OvR_{ag} < 0.050 for all the age groups), but which loses force starting at 25-29 years (OvR_{ag} = 0.144) up to 50-54 years (OvR_{ag} = 0.948). Starting at age group 55-59 years, with OvR_{ag} = 1.452, there is a gradual increase until reaching OvR_{ag} = 18.330 over 90 years of age.

Table 1 shows the prevalence and total number of persons with comorbidities by age group in Brazil, estimated by the PNS [12]. The prevalence of comorbidities, except for asthma, increases with age. CVD stand out with higher prevalence than other comorbidities in all age groups. The same table also shows the absolute number and incidence rates of hospitalizations and deaths from SARI-COVID per 1,000 inhabitants, stratified by comorbidity and age group.

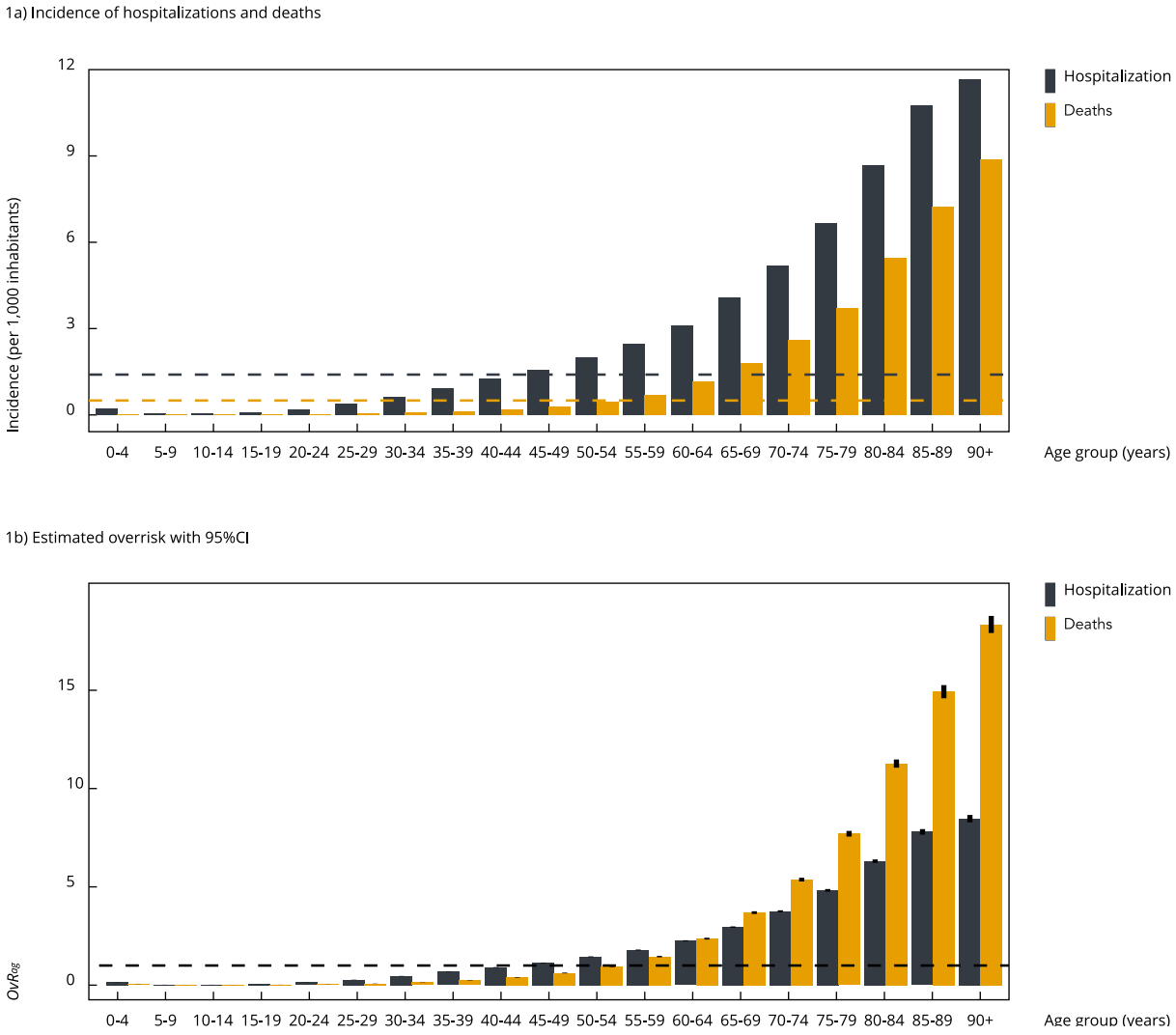
Table 2 shows the estimated overrisk of hospitalization and death stratified by comorbidity and age group. Two indicators are presented, differentiated by the denominator used. $OvR_{c,ag}$ measures the overrisk of hospitalization or death in relation to the general population. Using this indicator, the comorbidity with the highest overrisk among those studied was diabetes (Table 2). Overrisk of hospitalization is 5.39 (5.34-5.43) times higher on average for adults with diabetes compared to the overall average for the Brazilian adult population. When comparing age groups, the overrisk in persons with diabetes is heavily influenced by age, varying from 2.82 (2.72-2.93) in adults under 40 years to 6.87 (6.81-6.93) in those over 60 years (Table 2). This difference is even more drastic when comparing overrisk of death in persons with diabetes. Diabetics over 60 years of age present overrisk 10 times higher than the population average. Persons with chronic kidney disease had overrisk 4.1 times higher of hospitalization and 6.9 times higher of death compared to the general population. The effect of age on overrisk is more evident for kidney diseases than for diabetes. In young adults with chronic kidney disease, the overrisk is 1.3 times that of the population average, and in the elderly this overrisk increases 14 times. Persons with CVD showed mean overrisk 2.2 times that of the mean level in the population. Age appears again as a factor that increases overrisk, since individuals 40-59 years of age have an overrisk 1.4 times the general average, and those over 60 years have an overrisk of 3.5 times. Meanwhile, asthma only constituted overrisk when associated with age over 60 years (Table 2).

The second indicator in Table 2, $SOvR_{c,ag}(ag)$, compares overrisk for those with comorbidity and a specific age group in relation to the total population of that age group. This allows isolating the effect of comorbidity from the known effect of age. Among young adults, the presence of comorbidity greatly increases the overrisk, especially for diabetes [$SOvR_{c,ag}$ (18-39 years) = 7.8], chronic kidney disease [$SOvR_{c,ag}$ (18-39 years) = 3.55], and CVD [$SOvR_{c,ag}$ (18-39 years) = 1.75]. Asthma alone did not appear as an overrisk factor for young adults. From 40 to 59 years, diabetes is associated with overrisk of 3.0 compared to the mean risk for the population in this group, and chronic kidney disease has an overrisk of 1.96. Asthma did not appear as a risk factor in this age group.

The OvR_{ag} for the age groups used in Table 2 are 0.360, 1.278, and 3.680 for hospitalization in the age groups 18-39, 40-59, and 60 years or older and 0.120, 0.807, and 5.431 for death, respectively.

Figure 1

Distribution of incidence of hospitalizations and deaths per 1,000 inhabitants, and estimated overrisk with 95% credibility interval (95%CI) for hospitalization and death from SARI-COVID by age group.



Notes: the dashed lines in 1a represent the incidence in the total population for hospitalization (1.4) and death (0.5); The dashed line in 1b represents OvR = 1, that is, absence of overrisk.

Table 1

Prevalence of comorbidities in the adult population in Brazil according to the *National Health Survey* (PNS, 2013), total estimated cases by comorbidity and age group in the population in 2020, absolute numbers and incidence rate per 1,000 inhabitants of hospitalizations and deaths from severe acute respiratory illness from COVID-19 (SARI-COVID) up to the 35th Epidemiological Week of 2020.

Age group (years)	Estimates for Brazil (PNS)		SARI-COVID			
	Prevalence (IC95%)	Total cases	Hospitalizations	Hospitalizations per 1,000	Deaths	Deaths per 1,000
Diabetes mellitus						
18-39	1.0 (0.8-1.2)	752,295	2,922	3.9	688	0.9
40-59	7.3 (6.6-7.9)	3,879,034	20,591	5.3	6,364	1.6
60+	18.1 (16.9-19.3)	5,301,610	50,142	9.5	26,323	5.0
Total adults	-	9,932,938	73,655	7.4	33,375	3.4
Cardiovascular diseases						
18-39	7.2 (6.3-8.1)	5,416,521	4,715	0.9	891	0.2
40-59	31.9 (29.6-34.2)	16,950,846	32,858	1.9	8,667	0.5
60+	62.0 (58.5-65.5)	18,160,210	86,312	4.8	44,539	2.5
Total adults	-	40,527,577	123,885	3.1	54,097	1.3
Chronic kidney disease						
18-39	0.6 (0.5-0.8)	451,377	796	1.8	249	0.6
40-59	1.8 (1.5-2.1)	956,474	3,304	3.5	1,500	1.6
60+	2.8 (2.2-3.3)	820,139	8,595	10.5	5,673	6.9
Total adults	-	2,227,989	12,695	5.7	7,422	3.3
Asthma						
18-39	4.6 (4.2-5.1)	3,460,555	1,497	0.4	172	0.0
40-59	3.9 (3.5-4.3)	2,072,361	2,760	1.3	588	0.3
60+	4.8 (4.1-5.5)	1,405,952	3,298	2.3	1,521	1.1
Total adults	-	6,938,867	7,555	1.1	2,281	0.3
Other chronic lung disease						
Total adults	1.8 (1.6-2.0)	2,837,836	11,015	3.9	6,129	2.2

95%CI: 95% credibility interval.

Discussion

In this article we identify risk groups for COVID-19 in the first six months of the pandemic in Brazil to assist the definition of priority groups for the National Plan for Operationalization of COVID-19 Vaccination prepared by the PNI. Factors such as male sex, older age groups, and comorbidities are associated with overrisk of hospitalization and death from SARI-COVID, as found in other studies [12,13,17,18].

Male sex showed 33% and 41% overrisk of hospitalization and death compared to female sex, respectively. Although the proportions of cases did not differ significantly between the sexes, men showed higher odds of developing serious cases and evolving to death, due to biological differences such as immune response mechanisms and behavioral and sociocultural factors related to alcohol and tobacco consumption, work/occupation, and adherence to protective measures [19,20].

Age is a strong and well-established risk factor for hospitalization and death from COVID-19 [12,21,22]. Younger age groups (up to 40-44 years) were associated with relative protection from hospitalization or death during the first months of the pandemic, compared to the mean risk in the general population. Starting at 45-49 years there is an overrisk, reaching eight-fold in the age group 90 years and older (OvR_{ag} = 8.466). In relation to overrisk of death, younger age groups present strong rela-

Table 2

$OvR_{c,ag}$ and $SOvR_{c,ag}(ag)$ for hospitalization and death from SARI-COVID and 95% credibility interval (95%CI).

Comorbidity/Age bracket (years)	Hospitalization		Death	
	$OvR_{c,ag}$ (95%CI)	$SOvR_{c,ag}(ag)$ (95%CI)	$OvR_{c,ag}$ (95%CI)	$SOvR_{c,ag}(ag)$ (95%CI)
Diabetes mellitus				
18-39	2.823 (2.727-2.930)	7.824 (7.545-8.139)	1.896 (1.752-2.040)	15.790 (14.561-17.016)
40-59	3.853 (3.796-3.907)	3.014 (2.969-3.058)	3.392 (3.309-3.483)	4.202 (4.085-4.312)
60+	6.868 (6.809-6.932)	1.866 (1.847-1.886)	10.265 (10.129-10.410)	1.890 (1.864-1.915)
Total adults *	5.385 (5.342-5.429)	4.185 (4.152- 4.219)	6.949 (6.864-7.038)	5.190 (5.129-5.255)
Cardiovascular diseases				
18-39	0.632 (0.615-0.650)	1.754 (1.702-1.806)	0.340 (0.319-0.360)	2.837 (2.624-3.044)
40-59	1.408 (1.393-1.423)	1.101 (1.087-1.115)	1.057 (1.036-1.081)	1.310 (1.276-1.343)
60+	3.450 (3.424-3.476)	0.938 (0.930-0.945)	5.071 (5.014-5.127)	0.934 (0.923-0.944)
Total adults *	2.220 (2.206-2.236)	1.725 (1.714-1.737)	2.760 (2.732-2.789)	2.062(2.042-2.083)
Chronic kidney disease				
18-39	1.280 (1.194-1.369)	3.555 (3.318-3.800)	1.144 (1.005-1.288)	9.530 (8.369-10.746)
40-59	2.510 (2.425-2.596)	1.964 (1.897-2.034)	3.246 (3.081-3.406)	4.024 (3.805-4.237)
60+	7.609 (7.449-7.762)	2.066 (2.020-2.109)	14.295 (13.942-14.687)	2.634 (2.569-2.702)
Total adults *	4.138 (4.068-4.205)	3.216 (3.159-3.277)	6.891 (6.741-7.052)	5.149 (5.027-5.270)
Asthma				
18-39	0.315 (0.299-0.330)	0.871 (0.827-0.915)	0.104 (0.089-0.119)	0.861 (0.739-1.004)
40-59	0.967 (0.931-1.007)	0.757 (0.729-0.785)	0.588 (0.538-0.635)	0.729 (0.671-0.789)
60+	1.703 (1.648-1.766)	0.463 (0.447-0.478)	2.237 (2.130-2.351)	0.412 (0.391-0.433)
Total adults *	0.790 (0.773-0.808)	0.615 (0.601-0.628)	0.680 (0.651-0.708)	0.508 (0.487-0.529)
Other chronic lung disease				
Total adults *	2.818 (2.764-2.868)	2.190 (2.150-2.230)	4.465 (4.356-4.576)	3.338 (3.259-3.421)

95%CI: 95% credibility interval; $OvR_{c,ag}$: takes into account both the effect of the comorbidity and the joint effect of the age group itself; $SOvR_{c,ag}$: relates to the overrisk associated with a specific comorbidity in a specific age group.

* In the lines for total adults, the $OvR_{c,ag}$ uses as the reference the incidence rate in the general population, while the $SOvR_{c,ag}(ag)$ uses as the reference the incidence rate in the adult population.

tive protection up to 24 years, with OvR_{ag} close to zero. Starting at 55-59 years there is increased overrisk, reaching nearly 18 times in the age group 90 years and older. Importantly, the increase is not exponential in terms of the absolute numbers and proportions of cases, since there is a concentration in the age groups from 15-69 years. This may be related to the greater exposure of these age groups, since they represent the active workforce and are subject to greater flexibilization of social distancing measures [21].

Ranzani et al. [22] showed that a large proportion (84%) of patients hospitalized with COVID-19 in Brazil presented at least one comorbidity, but the authors did not report specific information on the comorbidities. Among the comorbidities assessed in the current study, chronic kidney disease, diabetes, other lung diseases, and CVD showed higher risk of hospitalization and death. Presence of chronic kidney disease or diabetes and age over 60 appeared as an even stronger risk factor, reaching 10 to 14 times greater overrisk of death than in the general population. Other studies show these diseases as important risk factors for infection [18], hospitalization [13], and death from COVID-19 [23].

In general, all the comorbidities are associated with higher specific overrisk by age group in younger ages, with a downward gradient in older age groups, a pattern that is inverted when considering the overrisk in relation to the general population, both for hospitalization and death. This phenomenon occurs because when we compare to the general population, the overrisk is combined with the age group's specific risk, which naturally has a large and preponderant impact. For example,

for CVD there is no evidence of overrisk in the young population, 18-39 years of age, compared to the general population. However, there is overrisk of hospitalization in young persons with CVD, 1.7 times greater than in persons in the same age group. The overrisk of death is 2.8 times.

There is no evidence of overrisk for asthma, although it presents an overrisk of hospitalization and death when compared to the general population at older ages. This overrisk is only attributed to age, since the overrisk of hospitalization (and death) in persons over 60 years with asthma is 1.7 (2.2) times greater than the general population, while the overrisk of hospitalization (and death) in persons over 60 years is 3.7 (5.4) times greater. The relative protective effect of asthma has been reported in other studies, and some hypotheses have been raised, such as prompt adoption of protective measures [24]; aspects related to type-2 immune response that cause the accumulation of eosinophils [24,25,26,27]; treatment commonly indicated for asthma [28,29,30]; and poor description of comorbidities for COVID-19 [24]. However, more in-depth studies are still needed to establish the causes of this apparent protective effect of asthma in COVID-19.

The current analysis used available data from the SIVEP-Gripe notification system (https://sivepgripe.saude.gov.br/sivepgripe), thus taking advantage of the existing infrastructure and data flows in the surveillance of respiratory syndromes in the country. The importance of SIVEP-Gripe during the pandemic was clearly demonstrated by the follow-up done with the system for monitoring SARI cases, InfoGripe (http://info.gripe.fiocruz.br), which proved capable of identifying the impact of the novel coronavirus on the hospital network even before laboratory confirmation of the first cases [31].

This study has some limitations that are inherent to data collected for surveillance purposes. First, there is a potential bias in the completion and keying-in of the reporting forms without direct case-by-case follow-up in the hospital network, as would occur in a clinical trial. This is exemplified by failure to complete fields in the five comorbidities analyzed in this article, varying from 8.8% in CVD to 25.9% in asthma, where these are limited to the comorbidities listed explicitly as individual variables in the SIVEP-Gripe database. In the way the forms are constructed, the fields for comorbidities that are not filled out probably indicate their absence, but there may also be cases of persons with comorbidities but without adequate recording, which would mean an underestimation of the calculated overrisk. Besides, these fields are completed with information provided by the patient or accompanying person, potentially leading to under-notification. Still, this is the same procedure used in the PNS, thereby favoring the data's comparability. An important difference that may minimize failures in the PNS is that data completion is performed after standardization and training of the study's interviewers on the questions and/or data collection.

Although we assume that the definitions of diseases in the PNS and SIVEP-Gripe are equivalent, it is possible that they are not. For example, the PNS uses the term chronic kidney failure, while SIVEP-Gripe uses chronic kidney disease. As informed in the *Methods* section, CVD was created from chronic CVD and information from the open field on hypertension, but this may not be sufficient for perfect mutual consistency of the variables, although we do not believe that eventual differences are sufficient to invalidate the comparisons.

Another important limitation is the underestimation of uncertainty calculated for overrisk, since the populations are estimates from projections by the IBGE or estimates by the PNS, and these uncertainties were ignored when calculating the distribution of overrisk. Another potential bias is related to the PNS data used in the analyses. These data refer to the year 2013 and thus may be outdated for representing the profile of diseases in the general population in 2020.

The current study makes a key contribution to the elaboration of the national vaccination plan, but it should not be considered in isolation since there are other risk factors that were not considered, because they are absent from at least one of the available databases used in the analyses. Examples include liver cirrhosis [32], sickle cell disease [33], Down syndrome [34], and cancer [35,36]. There is also evidence of greater morbidity and mortality from diseases with airborne transmission in populations such as indigenous peoples [37] the prison population [38]. Further quantitative or qualitative studies are necessary to complement the definition of risk groups. Other elements besides individual risk should orient the definition of priority groups. COVID-19 vaccine is a common good, and its use should be guided by equity and health promotion values. Its distribution, especially in a context of limited doses, should consider principles of maximization of human welfare (reduction of mortality and suffering), reci-

procity with those most dedicated to frontline care and cure (healthcare workers), equity (access by the most vulnerable), and legitimacy [9]. These objectives can only be met through negotiation with society.

In addition, the COVID-19 epidemic has direct and indirect effects on population groups with comorbidities. The direct effect is increased risk of hospitalization and death from SARI-COVID in the presence of comorbidities, already well-documented. The indirect effect is reduction of care and treatment of these conditions due to reduced mobility and access to healthcare services, which may have resulted in the lack of control of these conditions. It is thus necessary to emphasize the impact of COVID-19 on noncommunicable diseases. The resumption of public health promotion policies for NCDs, including in response to the pandemic and to complement vaccination, must be included as an urgent and essential component to minimize serious cases and deaths from the association of COVID-19 with the underlying condition [39]. Throughout the world, human and financial resources have been shifted to deal with the pandemic, which has also impacted the follow-up of these diseases [39] by the family health teams in SUS.

In early 2020, when the COVID-19 pandemic was declared, the following question was raised: are we prepared to deal with this pandemic in Brazil? [40]. The underfinancing and dismantlement of the SUS have caused a huge reduction in human resources and infrastructure, directly impacting the data's quality and certainly the success of the PNI in reaching the necessary vaccination coverage.

Despite the limitations discussed above, the current study provided support for the National Plan for Operationalization of COVID-19 Vaccination under the PNI through identification of population groups with overrisk of hospitalization and death from the disease. We used data that were collected routinely in the healthcare establishments, emphasizing the importance of the availability of quality data. The pandemic clearly revealed Brazil's prevailing reality, which has been identified for years by researchers and healthcare workers: the need for a notification system that is well operated and completed by properly trained workers and the urgency of guaranteeing financing for the SUS [40].

Contributors

R. M. Lana contributed to the study design, data processing, analysis, writing and critical revision of the text. L. P. Freitas, C. T. Codeço and A. G. Pacheco contributed to data interpretation, writing and critical revision of the text. L. M. F. Carvalho contributed to the analysis, data interpretation and critical revision of the text. D. A. M. Villela, F. C. Coelho, V. B. G. Porto and C. Gava contributed to the interpretation of the data and critical revision of the text. O. G. Cruz contributed to the interpretation of the data. R. P. Niquini contributed to the study's conception and interpretation of the data. M. F. C. Gomes contributed to the study design, data collection and processing, writing and critical review of the text. L. S. Bastos contributed to the study design, data collection and processing, analysis, writing and critical review of the text. All authors reviewed and approved the final version for publication.

Additional informations

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Resumo

Em um contexto de transmissão comunitária e escassez de vacinas, a vacinação contra a COVID-19 deve focar na redução direta da morbidade e da mortalidade causadas pela doença. Portanto, é fundamental a definição de grupos prioritários para a vacinação pelo Programa Nacional de Imunizações (PNI), baseada no risco de hospitalização e óbito pela doença. Para tal, calculamos o sobrerrisco por sexo, faixa etária e comorbidades por meio dos registros de hospitalização e óbito por síndrome respiratória aguda grave com confirmação de COVID-19 (SRAG-COVID) em todo o Brasil nos primeiros seis meses de epidemia. Apresentaram maior sobrerrisco pessoas do sexo masculino (hospitalização = 1,1 e óbito = 1,2), pessoas acima de 45 anos para hospitalização (SR_{fe} *variando de 1,1 a 8,5) e pessoas acima de 55 anos para óbitos* (SR_{fe} *variando de 1,5 a 18,3). Nos grupos de comorbidades, doença renal crônica, diabetes mellitus, doença cardiovascular e pneumopatia crônica conferiram sobrerrisco, enquanto para asma não houve evidência. Ter doença renal crônica ou diabetes mellitus e 60 anos ou mais mostrou-se um fator ainda mais forte, alcançando sobrerrisco de óbito 14 e 10 vezes maior do que na população geral, respectivamente. Para todas as comorbidades, houve um sobrerrisco mais alto em idades maiores, com um gradiente de diminuição em faixas mais altas. Esse padrão se inverteu quando consideramos o sobrerrisco em relação à população geral, tanto para hospitalização quanto para óbito. O presente estudo forneceu evidências a respeito do sobrerrisco de hospitalização e óbito por SRAG-COVID, auxiliando na definição de grupos prioritários para a vacinação contra a COVID-19.*

COVID-19; Síndrome Respiratória Aguda Grave; Monitoramento Epidemiológico; Comorbidade

Resumen

En un contexto de transmisión comunitaria y escasez de vacunas, la vacunación contra la COVID-19 debe enfocarse en la reducción directa de la morbilidad y de la mortalidad causadas por la enfermedad. Por lo tanto, es fundamental la definición de grupos prioritarios para la vacunación por el Programa Nacional de Inmunizaciones (PNI), basada en el riesgo de hospitalización y óbito por la enfermedad. Para tal fin, calculamos el sobrerriesgo por sexo, franja de edad y comorbilidades mediante los registros de hospitalización y óbito por síndrome respiratorio agudo grave con confirmación de COVID-19 (SRAG-COVID) en todo Brasil, durante los primeros seis meses de epidemia. Presentaron mayor sobrerriesgo personas del sexo masculino (hospitalización = 1,1 y óbito = 1,2), personas por encima de 45 años para hospitalización (SR_{fe} *variando de 1,1 a 8,5) y personas por encima de 55 años para óbitos* (SR_{fe} *variando de 1,5 a 18,3). En los grupos de comorbilidades, enfermedad renal crónica, diabetes mellitus, enfermedad cardiovascular y neumopatía crónica ofrecieron sobrerriesgo, mientras que para el asma no hubo evidencia. Sufrir una enfermedad renal crónica o diabetes mellitus y tener 60 años o más mostró un factor todavía más fuerte, alcanzando sobrerriesgo de enfermedad 14 y 10 veces mayor que en la población general, respectivamente. Para todas las comorbilidades, hubo un sobrerriesgo más alto en edades mayores, con un gradiente de disminución en franjas más altas. Este patrón se invirtió cuando consideramos el sobrerriesgo en relación con la población general, tanto para hospitalización como para óbito. El presente estudio proporcionó evidencias respecto al sobrerriesgo de hospitalización y óbito por SRAG-COVID, ayudando en la definición de grupos prioritarios para la vacunación contra la COVID-19.*

COVID-19; Síndrome Respiratorio Agudo Grave; Monitoreo Epidemiológico; Comorbilidad

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