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**ORIGINAL ARTICLE /** ARTIGO ORIGINAL

# Willingness to vaccinate against influenza A (H1N1)pdm09 among Brazilian civil servants: Pró-Saúde cohort study

Disposição para vacinar contra influenza A (H1N1)pdm09 entre funcionários técnico-administrativos universitários: estudo de coorte Pró-Saúde

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**ABSTRACT:** *Objective:* To investigate sociodemographic factors associated with the willingness to take the pandemic influenza vaccine. *Methods:* This is a cross-sectional study of Brazilian civil servants participating in the fourth wave (2012–2013) of the longitudinal Pró-Saúde Study. Associations were expressed as odds ratios (OR) and 95% confidence intervals (95%CI), estimated by multivariate logistic regression models. *Results:* Among 2,828 participants, 15.9% would not be willing to vaccinate in the future if the Brazilian Ministry of Health promoted a new vaccination campaign against pandemic influenza. Not willing to vaccinate in the future was strongly associated with not taking the pandemic influenza vaccine in 2010 (OR = 9.0, 95%CI 6.9 – 11.6). Among the unvaccinated, females, those aged > 60 years, and non-health care workers were less willing to vaccinate in the future. Again, in the vaccinated group, females were less willing to vaccinate. *Conclusion:* Multidisciplinary efforts should be encouraged in order to identify reasons for refusing vaccination, focusing on the individual and group perceptions of susceptibility, severity, benefits, and barriers to vaccination. Such information is needed to identify target groups for the delivery of customized interventions towards preventing emerging pandemics, such as avian influenza and COVID-19.

Keywords: Vaccination refusal. Immunization programs. Epidemiology. Influenza, human. Coronavirus infections.

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**RESUMO:** *Objetivo*: Investigar fatores sociodemográficos associados à disposição em adotar a vacina contra influenza pandêmica. *Métodos*: Estudo transversal entre servidores técnico-administrativos participantes da quarta onda (2012–2013) do estudo longitudinal Pró-Saúde. Associações foram expressas como razões de chances (RC) e intervalos de confiança de 95% (IC 95%), estimados mediante modelos de regressão logística multivariada. *Resultados*: Entre os 2.828 participantes, 15,9% não estariam dispostos a serem vacinados no futuro se o Ministério da Saúde do Brasil promovesse uma nova campanha de vacinação contra influenza pandêmica. Não estar disposto a ser vacinado no futuro foi fortemente associado a não receber a vacina contra influenza pandêmica em 2010 (RC = 9,0, IC95% 6,9 – 11,6). Entre os não vacinados, mulheres, maiores de 60 anos e profissionais de outras áreas que não a saúde estavam menos dispostos a serem vacinados no futuro. Novamente, para aqueles vacinados, as mulheres estavam menos dispostas a serem vacinadas. *Conclusão*: Abordagens multidisciplinares devem ser estimuladas para identificar as razões para recusa vacinal, com foco nas percepções individual e coletivas sobre suscetibilidade, gravidade, benefícios e barreiras à vacinação. Essas informações são necessárias para identificar grupos-alvo para a oferta de intervenções particularizadas para a prevenção de pandemias emergentes, como a de influenza aviária e de covid-19.

*Palavras-chave*: Recusa de vacinação. Programas de imunização. Epidemiologia. Influenza humana. Infecções por coronavírus.

### INTRODUCTION

Vaccines are considered the primary preventive strategy against infectious diseases, reducing the risk of infection as a result of both direct and indirect effects<sup>1</sup>. Since indirect effects depend mainly on herd immunity, high levels of vaccination coverage may be needed for interrupting transmission at the community level<sup>2</sup>.

Several demographic, social, psychological, and behavioral variables influence the decision to take or refuse vaccination and, consequently, might impact the levels of vaccine coverage<sup>3,4</sup>. Lack of confidence in vaccination leading to vaccine hesitancy has been recognized by the World Health Organization (WHO) as one of the ten major threats to public health in the world for 2019<sup>5</sup>. The problem has been alarming researchers and public health professionals in developed countries for a long time. In the United States, for instance, almost 30% of adults think that mandatory vaccine requirements are not necessary for attending public schools<sup>6</sup>, and the increase in non-medical vaccination exemptions in some metropolitan areas has been associated with a decrease in the measles, mumps, and rubella (MMR) vaccination rate<sup>7</sup>.

The COVID-19 pandemic has brought the theme to the stage, since vaccine development has accelerated at an unprecedented pace and has been considered an utmost necessity to deal with this sanitary emergency and its immense social and economic consequences. For instance, after the March 2020 lockdown in France, 26% of adult respondents to a national survey stated that they would not take a vaccine against SARS-CoV-2 when available<sup>8</sup>. There is evidence that vaccine hesitancy is associated with political perspectives: those who had voted for radical political parties and those who abstained from voting were much more likely to state their refusal<sup>8</sup>.

This politicization was also identified in other European countries<sup>9</sup>. In the USA, compliance with vaccination plans was associated with social and institutional trust<sup>10</sup>.

In Brazil, the National Immunization Program (*Programa Nacional de Imunização* – PNI), launched in 1973, is considered one of the most well-succeeded preventive programs in the country's history<sup>11</sup>. High coverages of vaccination were commonplace since the 1980s, leading to a reduction in the incidence and mortality or elimination of many vaccine-preventable diseases, such as poliomyelitis, tetanus, pertussis, measles, and meningitis caused by *Haemophilus influenzae* type b<sup>11</sup>. Today, PNI provides 300 million free doses of vaccines each year for more than 15 diseases<sup>12</sup>. However, in recent years, the phenomenon of vaccine hesitancy has caught the Brazilian public health community's attention. Such concern followed the decrease, in some regions of the country, in the historically high levels of vaccination coverage for measles and polio, and increased after the record, in 2016, of the first measles outbreak since 2000<sup>13,14</sup>. Between 2017 and 2019, the vaccination coverage for bacillus Calmette–Guérin (BCG), hepatitis B, influenza, and rotavirus significantly decreased<sup>15</sup>. In this new scenario, better monitoring of trends in vaccine hesitancy at the population level is essential.

Knowing the characteristics of population subgroups that are more prone to refuse vaccination and their reasons for vaccine hesitancy is strategic for targeting vaccination policies<sup>13,16-19</sup>. The causes of vaccine refusal and hesitancy are multiple and complex. They may include safety concerns fueled by the dissemination of misinformation, philosophical or religious beliefs, mistrust of health practices, and a perception that the risks of acquiring certain diseases are low in the community<sup>17-19</sup>. At the same time, behaviors concerning vaccination at the population level may involve different types of individuals:

- those who vaccinate their children without safety concerns ("unquestioning acceptors");
- those who vaccinate but show some minor concerns ("cautious acceptors");
- those with significant concerns about the risks of vaccines but who still vaccinate ("hesitant individuals");
- those who choose to delay vaccination, select only some vaccines, or postpone some dose dates ("late or selective vaccinators");
- those who reject all vaccines ("non-vaccinators or refusers")<sup>17-19</sup>.

Confronting vaccine refusal and hesitancy is paramount for controlling vaccine-preventable diseases and should involve a multidisciplinary approach and intervention strategies that match the distinct parental positions regarding vaccination<sup>17,18</sup>.

In 2009, a new strain of influenza A (H1N1) virus with genetic material from different species (human, avian, and swine) was identified and soon became pandemic<sup>20</sup>. Although a vaccine was offered, vaccination rates were lower than expected, from 0.4 to 59% across 22 countries<sup>21</sup>.

In Brazil, a specific vaccination campaign against the virus started in March 2010, reaching almost 90 million people. The target groups for this vaccination campaign were children aged 6–24 months, adults aged 20–39 years, people aged 60 or more with comorbidities, pregnant women, the indigenous population, health professionals, and those with chronic diseases<sup>22</sup>. Coverage among adults between 20 to 39 years of age reached 81%, varying across Brazilian states from below 70% (Roraima – 62.7%; Rio de Janeiro – 63.5%; Bahia – 69.0%) to above 85%

(Acre – 85.5%; Distrito Federal – 86.4%; Pernambuco – 86.4%; Santa Catarina – 87.2%; Paraná – 87.4%; Goiás – 88.2%; Espírito Santo – 88.6%; São Paulo – 88.8%; Piauí – 89.5%; Amapá – 91.2%)<sup>23</sup>.

Why so many people did not get a widely available and free vaccine during a severe outbreak being broadcast in the news is intriguing. Refusal to vaccinate is an increasing global public health concern but has not been considered as such in Brazil until recent reports of measles and yellow fever outbreaks. The prospects of a vaccine against COVID-19 maximizes the relevance of increased efforts to understand past experiences with vaccine hesitancy.

We report herein our investigation among civil servants in Rio de Janeiro about their willingness to take a pandemic influenza vaccine and some associated factors if a new campaign was to be launched in the future.

#### METHODS

This is a cross-sectional study embedded in the Pró-Saúde Study, a prospective longitudinal investigation focused primarily on social and psychosocial determinants of health and health-related behaviors among Brazilian civil servants, specifically non-faculty staff actively employed at university campuses located in Rio de Janeiro State. Those relocated to another institution or who were on non-medical leave were not eligible to participate. Self-administered questionnaires were used in the four waves of data collection conducted up to now (1999, 2001–2002, 2006–2007, and 2012–2013). In the fourth wave of the study, with 2,933 participants, the questionnaire included three questions concerning the influenza A (H1N1)pdm09 vaccine. The first question assessed whether the participant had heard about influenza A (H1N1). The second asked whether they had taken the influenza A (H1N1)pdm09 vaccine. The last question concerned the subject's willingness to take a pandemic influenza vaccine in the future if a new campaign was to be launched by the Brazilian Ministry of Health.

The binary primary outcome variable was "willingness to take a pandemic influenza vaccine in the future". Since the lack of knowledge about influenza A (H1N1) is a strong determinant of vaccine uptake, data analysis was restricted to participants who answered "yes" to the question asking if they had heard about influenza A (H1N1).

Independent variables were gender (male or female), age in years at the 2010 influenza epidemic (19–39, 40–59, 60+), ethnicity (white or black/multiracial), educational level (lower than high school or high school or higher), and occupation (health-related or other). Health-related occupations included a wide range of professions but mainly nursing assistants (62%), registered nurses (12%), physicians (6%), laboratory technologists and medical laboratory technicians (6%), radiologic technologists (5%), and others (9%). Independent associations between variables were expressed as odds ratios (OR) with their respective 95% confidence intervals (95%CI) estimated by logistic regression. All variables were considered for adjustment in the multivariate analysis. Models for the outcome "willingness to vaccinate" were stratified by the history of vaccination for influenza A (H1N1)pdm09 in 2010.

This study was approved by the Research Ethics Committee of the Institute of Social Medicine at the Universidade do Estado do Rio de Janeiro on May 10, 1999 (record 224/1999) and on October 18, 2011 (CAAE 0041.0.259.000-11). All participants signed an informed consent form.

# RESULTS

Among the 2,884 participants (98.3%) with valid answers (non-missing responses), only 56 (1.9%) had not heard about influenza A (H1N1). Among those who had heard about the influenza epidemic (n = 2,828, 98.1%), 40.9% had not taken the influenza A (H1N1)pdm09 vaccine. Considering only those in the target group for vaccination (aged 20–39 or  $\geq$  60 years or health professionals), 30.7% had not taken the influenza A (H1N1)pdm09 vaccine. Around 16% of the participants would not be willing to take the vaccine in the future if the Brazilian Ministry of Health promoted a new vaccination campaign against pandemic influenza. This proportion did not significantly vary between those in the target group for vaccination (15.7%) and not in the target group (16.2%) (p = 0.699).

Table 1 shows the participants' characteristics according to the history of a recent vaccination against pandemic influenza and their willingness to take a pandemic influenza

influenza A (H1N1)pdm09 and their willingness to take a pandemic influenza vaccine, Pró-Saúde								
Study, 2012–2013.								
Variable	N	Not taken the vaccine (%)	p-value	Not willing to take the vaccine in the future* (%)	p-value			

Table 1. Participants' characteristics according to the history of a recent vaccination against

Variable	Ν	the vaccine (%)	p-value	take the vaccine in the future* (%)	p-value			
Gender								
Female	1,619	35.4		16.8				
Male	1,209	48.3	< 0.001	14.6	0.120			
Age at the influenza epidemic (years)								
19–39	345	31.0		12.2				
40–59	2,145	43.5	< 0.001	16.4	0.133			
60+	338	34.6		16.3				
Ethnicity								
White	1,333	41.9		16.1				
Black/multiracial	1,419	40.2	0.388	15.6	0.730			
Educational level								
High school or higher	2,476	40.6		16.1				
Lower than high school	330	44.2	0.210	13.6	0.247			
Occupation								
Health-related Other	1,021 1,674	28.3 49.3	< 0.001	16.7 15.5	0.403			
Vaccination against influenza A (H1N1)p	dm09							
Yes	1,671	-		4.9				
No	1,157	-		31.7	< 0.001			

\*If the Brazilian Ministry of Health promoted a new vaccination campaign against pandemic influenza.

vaccine. Participants were mostly female (57.2%), aged 40–59 years at the time of the vaccination campaign in 2010 (75.8%), with black or multiracial ethnicity (51.5%); educational level equal to or greater than high school (88.2%), and working in non-health-related occupations (62.1%) (Table 1). Lack of vaccination was significantly higher among men, those aged 40 to 59 years, and non-health-related civil servants. The proportion of subjects not willing to take the vaccine in the future did not virtually vary across strata based on gender, age, ethnicity, education, and occupation. However, the history of vaccination against pandemic influenza in 2010 was strongly associated with their willingness to take a pandemic influenza vaccine. Among those who had taken the vaccine in 2010, only 4.9% were not willing to vaccinate in the future, but among those who had not taken the vaccine, the proportion was 31.7% (OR = 9.0, 95%CI 6.9 – 11.6; data not shown in tables).

Table 2 presents the results of the multivariate analysis for willingness to take a pandemic influenza vaccine stratified by the history of a recent vaccination against pandemic influenza in 2010. Among those who had not recently taken the influenza A (H1N1)pdm09 vaccine, higher odds of not willing to vaccinate in the future were found among females

	No recent	vaccination	Recent vaccination				
Variable	Not willing to take the vaccine in the future*						
	OR	95%Cl	OR	95%CI			
Gender							
Female	1.33	1.02 – 1.76	1.84	1.05 – 3.21			
Male	1.00		1.00				
Age at the influenza epidemic (years)							
19–39	0.81	0.47 – 1.38	1.31	0.65 – 2.66			
40–59	1.00		1.00				
60+	1.56	1.02 – 2.39	0.73	0.31 – 1.74			
Ethnicity							
White	1.00		1.00				
Black/multiracial	0.97	0.74 – 1.27	1.05	0.65 – 1.71			
Educational level							
High school or higher	1.00		1.00				
Lower than high school	0.79	0.51 – 1.20	0.85	0.33 – 2.17			
Occupation							
Health-related	1.00		1.00				
Other	2.10	1.55 – 2.83	0.96	0.59 – 1.58			

Table 2. Multivariate associations between the participants' characteristics and their willingness to take a vaccine against pandemic influenza, according to the history of a recent pandemic influenza A (H1N1)pdm09 vaccination. Pró-Saúde Study, Brazil, 2012–2013.

\*If the Brazilian Ministry of Health promoted a new vaccination campaign against pandemic influenza; OR: odds ratio; 95%CI: 95% confidence interval.

(OR = 1.33, 95%CI 1.02 - 1.76), individuals aged 60 years or more (OR = 1.56, 95%CI 1.02 - 2.39), and those employed in non-health-related occupations (OR = 2.10, 95%CI 1.55 - 2.83). For those who had recently taken the influenza A (H1N1)pdm09 vaccine, unwillingness to vaccinate in the future was higher among females (OR = 1.84, 95%CI 1.05 - 3.21).

## DISCUSSION

The study results revealed that during the Brazilian pandemic influenza vaccination campaign, which widely and freely provided the influenza A (H1N1)pdm09 vaccine, lack of vaccination was as high as 40% in the investigated population. Considering only the campaign target group (people aged 20–39 years and  $\geq$  60 years or health professionals), lack of vaccination reached 30%. We found associations between sociodemographic characteristics and attitudes towards vaccination against influenza A (H1N1)pdm09 that are relevant for the control of the current COVID-19 and other future pandemics.

The lower vaccination coverage among those aged 40–59 years and employed in nonhealth-related occupations was probably associated with the fact that the campaign targeted specific subgroups (health professionals, those aged 20–39 years, and those with comorbidities, who tend to be older). Concerning gender, the lower coverage among men is in line with the evidence that men are less likely to use health services than women<sup>24</sup>. These results are similar to those of other studies that found lower pandemic influenza vaccine coverage in males and non-health care workers<sup>25,26</sup>.

A key finding was that willingness to vaccinate is strongly associated with previous experience of getting the influenza A (H1N1)pdm09 vaccine, corroborating previous results<sup>25,27,28</sup>. Therefore, communication efforts oriented towards young people might be strategic for breaking the chain of vaccine hesitancy in the future, with potential effects not only on the individual's willingness to be vaccinated in older ages but also regarding their children.

It is somewhat intriguing that women had higher vaccination coverage while, at the same time, declaring to be less willing to vaccinate in the future compared to males, regardless of being previously vaccinated or not. This female behavior towards vaccine hesitancy might be related to personal experiences and feelings concerning the severity of adverse effects of vaccines, including the possibility (dismissed by science) that some of them may cause autism<sup>28</sup>.

Among those who had not been vaccinated, individuals aged 60+ years and employed in non-health-related occupations were less likely to vaccinate in the future. With respect to age, studies on pandemic influenza hesitancy have produced inconsistent results, some indicating that older age is a barrier to vaccine uptake and some reporting the opposite<sup>29</sup>, suggesting that the role of age might be mediated by other factors, such as comorbidities, fear of adverse effects, and different perceptions of the benefits of vaccination. The finding that people working in non-healthcare-related occupations are less likely to take the pandemic influenza vaccine is in line with other studies<sup>27,29,30</sup> and might reflect both the facts that health care workers were a target group for vaccination and that they usually have better knowledge regarding the risks of not being vaccinated. Although plausible, the results of our study should be interpreted with caution due to some limitations. Despite the pandemic being a landmark event, information bias may have occurred because the individuals might not remember taking the pandemic vaccine, either because of the time elapsed or because they actually took the seasonal influenza vaccine in previous years. Probably, such errors most affected the participants who reported receiving the vaccine, particularly those who were not targeted by the campaign. Thus, figures about vaccination coverage in this population may be overestimated, as well as the measures of association for age and health professions. Concerning the question about vaccination, the fact that someone had heard of the vaccine does not mean the same as receiving medical advice to vaccinate, especially for the age groups that were not part of the target population of subsequent campaigns. Therefore, the actual knowledge about the importance of vaccination varied among those who had heard about the vaccine. Considering this result, we may infer that the willingness to vaccinate among study participants could have been higher if we had included those who had heard about the vaccine and also received specific advice to vaccinate.

Our study focused only on the pandemic influenza vaccine, but the recent outbreaks of measles and yellow fever associated with low vaccination coverages suggest that this problem might be broader in Brazil, affecting the general population's perception of the importance of vaccination. Further studies should be conducted to monitor the trends in vaccine coverage in Brazil at a sub-national level and to identify factors associated with vaccine hesitancy, concentrating on individual perceptions of susceptibility, severity, benefits, and barriers to vaccination<sup>4,31</sup>.

Taking into account that a vaccine against COVID-19 is likely to be available in 2021, such data might be used to identify target groups for the delivery of customized interventions after segmentation techniques are employed to detect subgroups on the vaccine hesitancy continuum that may represent vaccine refusal clusters, geographically and in social networks.

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