

## 2010 A(H1N1) vaccination in pregnant women in Brazil: identifying coverage and associated factors

Vacinação contra o vírus A(H1N1) entre mulheres grávidas no Brasil em 2010: identificação da cobertura e fatores associados

Vacunación contra el virus A(H1N1) en gestantes de Brasil en 2010: cobertura y factores asociados

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### Abstract

*We studied vaccination coverage and its associated factors in the 2010 pandemic influenza vaccination of Brazilian pregnant women. A cross-sectional study of pregnant women who had given birth was performed in a municipality in southern Brazil, in 2010. Data about vaccination against A(H1N1) and sociodemographic characteristics, morbidities and prenatal care were collected. Statistical analysis was performed using a Poisson regression. Coverage was 77.4%. Most were vaccinated in the public sector (97.6%) and in the second trimester (47%). Associated factors that increased vaccination were marriage, older age, first income quartile, prenatal care and influenza before pregnancy. Education and skin color were not significantly associated with vaccination. The vaccination campaign was extensive and exhibited no inequality. Prenatal care was the factor that most affected vaccination coverage, reflecting its importance for vaccination campaign success.*

*Human Influenza; Vaccination; Pregnant Women; Prenatal Care*

### Resumo

*O objetivo foi estudar a cobertura vacinal e fatores associados na vacinação contra a gripe pandêmica de 2010 em gestantes brasileiras. Realizou-se um estudo transversal com mulheres que deram à luz em um município do sul do Brasil, em 2010. Dados sobre vacinação contra A(H1N1), características sociodemográficas, morbidades e pré-natal foram coletados. A análise estatística foi realizada utilizando-se a regressão de Poisson. A cobertura foi de 77,4%. A maioria foi vacinada no setor público (97,6%) e no segundo trimestre (47%). Fatores associados que aumentaram a vacinação foram: ser casada, maior idade, estar no primeiro quartil de renda, ter assistência pré-natal e contrair gripe antes da gravidez. Educação e cor da pele não foram associadas significativamente à vacinação. A campanha foi extensa e não apresentou desigualdade. O pré-natal foi o fator que afetou mais a cobertura vacinal, refletindo a sua importância para o futuro sucesso das campanhas de vacinação.*

*Influenza Humana; Vacinação; Gestantes; Cuidado Pré-Natal*

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## Introduction

Influenza is a highly contagious disease that has affected mankind for centuries. Although most cases are mild, the disease can cause severe clinical forms that require special medical assistance<sup>1</sup>. The last pandemic occurred in 2009 due to the A(H1N1) virus<sup>2</sup> and was responsible for numerous deaths and years of life lost<sup>3</sup>, especially in at-risk groups that are susceptible to developing the severe form of the disease. Pregnant women are one of these at-risk groups, and higher mortality in pregnant women was documented in the 1918 and 1957 pandemics<sup>1</sup> and during the 2009 outbreak<sup>4,5</sup>.

To reduce illness, vaccination campaigns were implemented during and after the 2009 pandemic<sup>6,7</sup>; however, vaccination coverage was still low in certain countries<sup>8,9</sup>. Previous data on vaccination against seasonal influenza revealed that certain populations were less likely to be vaccinated<sup>10,11,12</sup>, affecting the success of the campaigns. Factors ranged from sociodemographic characteristics to health beliefs. Studies on the last pandemic indicated that barriers continue to negatively affect vaccination in various nations<sup>12,13,14</sup>, leading to discussions of new strategies to improve coverage.

In Brazil, vaccination campaigns against the seasonal flu have been implemented since 1999, particularly among the elderly, and have been based on previous experience with the National Immunization Program for children<sup>15</sup>, which was introduced in 1973. After the A(H1N1)pdm09, following World Health Organization (WHO) recommendations, Brazilian authorities launched a major vaccination campaign before the winter of 2010. The campaign used the monovalent H1N1 vaccine (virus A/California/7/2009) and was aimed at at-risk groups. Pregnant women, regardless of their gestational age, was one of these groups, and were vaccinated between March 22 and May 21, 2010.

Given that the A(H1N1)pdm09 virus has become seasonal, and continues to circulate along with other seasonal viruses, and that there are still low vaccination rates among pregnant women, it is important to investigate the factors affecting vaccination to achieve greater coverage and to reduce morbidity and mortality in this very susceptible group<sup>16</sup>.

Therefore, we conducted a study to identify which factors could facilitate or inhibit vaccination of this at-risk group during the 2010 vaccination campaign after the 2009 pandemic. We hope that this information will help health authorities to plan and implement policies to improve coverage.

## Methods

### Type of study and setting

The study was cross-sectional, and all pregnant women who delivered in one of the two hospitals from the municipality of Rio Grande, Rio Grande do Sul State, Southern Brazil, were interviewed immediately postpartum (within 24 hours of the birth), with a pre-codified questionnaire. The period of data collection was from May to October 2010. The two hospitals (Associação Caridade Santa Casa de Misericórdia, a nonprofit institution, and the hospital of the Federal University of Rio Grande) are responsible for 99% of births in the municipality. The vaccination campaign against influenza for pregnant women in 2010 began on March 22 and ended on May 21. The vaccine was provided free of charge at public health facilities and required an out-of-pocket payment at private clinics. We included all pregnant women who lived in the city and had given birth during the specified period (May-October 2010). As this study was part of another project evaluating infant health conditions and prenatal care, women who gave birth to infants of less than 500 grams and at a gestational age of less than 20 weeks were excluded. The sample size was estimated using Epi Info version 6.04d (Centers for Disease Control and Prevention, Atlanta, USA) with the following parameters: a 20% prevalence of non-vaccination, a 10% prevalence of non-vaccination among the unexposed group (considering as exposition factor, women with less than six prenatal care visits), an unexposed/exposed relationship of 05:01, a confidence level of 95% and a power of 80%. The number was increased by 10% for losses and by 25% for the analysis of confounding factors, reaching 980 individuals.

All participants read and signed an informed consent form. The project was approved by the Ethics Research Committees of the University Hospital and of the Associação de Caridade Santa Casa de Misericórdia (Protocols n. 53/2009 and 009/2009, respectively).

### Outcome and independent variables

A pretested and codified questionnaire was specifically created to collect all information from pregnant women and was administered by trained interviewers. The outcome was measured as the proportion of women who reported having been vaccinated against influenza during pregnancy among all interviewed. The place of vaccination (public or private) and the month of pregnancy when the vaccination was received

were also recorded. Independent variables were reported by the pregnant women and included age, ethnicity, level of education (incomplete primary school, completed primary school, completed high school, incomplete or completed university) family per capita income (classified in quartiles), marital status (married or cohabiting with partner), smoking during pregnancy (having smoked in any of the three trimesters of pregnancy), prenatal care (at least one prenatal care visit), number of prenatal care visits, previous ILI (influenza-like illness) within three months of the pregnancy. Among comorbidities, women were asked about having chronic obstructive pulmonary disease (COPD) or asthma, high blood pressure, diabetes mellitus (including type I, II or gestational) and anemia, before or during pregnancy.

### **Statistical analysis**

Statistical analysis included descriptions of the sample and the prevalence of vaccination within a 95% confidence interval (95%CI). A bivariate analysis was conducted to establish the crude prevalence ratio (PR) and 95%CI between the outcome and different factors. Subsequently, a multivariate analysis with an adjusted PR and 95%CI was performed. For both analytical procedures, a Poisson regression with robust variance was applied using Stata software (Stata Corp., College Station, USA). A hierarchical analysis model was used in the multivariate analysis<sup>17</sup>. All demographic and socioeconomic variables were introduced at the first level. Use of prenatal services, smoking and previous ILI were entered at the second level. Finally, related morbidities during pregnancy were included at the third level. All variables with a p-value  $\leq 0.20$  were maintained between levels. A Wald test was used to calculate the p-value of the coefficients. For ordinal variables with ordered categories, a Wald test for a linear trend was used. For variables with unordered categories, we used a test of heterogeneity. For all statistical procedures, we adopted a p-value  $\leq 0.05$  in a two-tailed test.

## **Results**

### **Descriptive analysis**

During the study period, 1,100 out of a total of 1,131 eligible pregnant women were interviewed. There was a 2.8% loss that included women who refused to be interviewed or who were not found at home after being discharged before the interview. The characteristics of the sample are

presented in Table 1. The average age of the participants was 25.9 years (SD = 6.46). One-third of the participants were aged 30 or above, 69% were white, and 83% were married or cohabited with a partner. Most of the women had not finished high school (52%). The 4<sup>th</sup> quartile had incomes that were nearly 16 times greater than the incomes of the 1<sup>st</sup> quartile. Moreover, only 5% had received no prenatal care, and 19% had completed fewer than six prenatal visits.

The coverage of influenza vaccination was 77.43% (95%CI: 75.0-79.9), and 98% (95%CI: 96.6-99.7) had been vaccinated at the public level. Most women had received the vaccine during the second trimester (47%). In total, 15% had ILI within three months of the pregnancy. Additionally, smoking during pregnancy was reported by 20% of the participants. The most common morbidities were anemia (40.8%), followed by high blood pressure (19.6%).

### **Multivariate analysis**

Table 2 presents the crude and adjusted PRs. At the first level and after adjustment, increased vaccination was observed among women over 20 years (20-24 years, PR = 1.16, 95%CI: 1.04-1.30; 25-29 years, PR = 1.15, 95%CI: 1.03-1.29; 30 years or more, PR = 1.10, 95%CI: 0.98-1.23; p heterogeneity test = 0.02) and participants with husbands (PR = 1.18, 95%CI: 1.06-1.31). Income was a factor that appeared to relate to the outcome but was not significant at its level. After adjusting for all levels, a significant direct effect was observed (p heterogeneity test = 0.04) with a PR = 1.04 (95%CI: 0.95-1.14) in the 2<sup>nd</sup> quartile, a PR = 0.99 (95%CI: 0.9-1.9) in the 3<sup>rd</sup> quartile and a PR = 0.92 (95%CI: 0.82-1.02) in the 4<sup>th</sup> quartile compared with the poorest individuals. At the second level of analysis, women who had received prenatal care were 63% more likely to receive the vaccine (PR = 1.63, 95%CI: 1.21-2.18). When we instead used the number of prenatal care visits, the likelihood of vaccination was 18% greater among women who had completed six or more visits (PR = 1.18, 95%CI: 1.07-1.31). Additionally, pregnant women reporting having had ILI before pregnancy had an 8% greater likelihood of having received the vaccine (PR = 1.08, 95%CI: 1.01-1.16). At the third level, no morbidities significantly affected the likelihood of vaccination.

## **Discussion**

Our study revealed that influenza vaccination coverage among pregnant women was 77.43%, which could be considered adequate but is below

Table 1

Characteristics of the pregnant women that gave birth. Rio Grande, Rio Grande do Sul State, Brazil (N = 1,100).

Variable	n	%
Age (years)	205	18.64
Less than 20	304	27.64
20-24	273	24.82
25-29	318	28.91
30 and above		
Ethnicity		
Black and other	342	31.09
White	758	68.91
Level of Education		
Incomplete Primary School	316	28.73
Completed Primary School	261	23.73
Completed High School	404	36.73
Complete or incomplete University	119	10.82
Income quartiles in USD [mean and SD] *		
1st	138.63	163.62
2nd	430.37	75.07
3rd	741.77	114.91
4th	2,204.81	3,208.69
Married or cohabiting with partner	913	83.00
Received prenatal care	1,045	95.00
Received six or more visits at prenatal care (1,030)	838	81.36
Received influenza vaccine (1,099)	851	77.43
Place of vaccination (849)		
Public	829	97.64
Private	20	2.36
Paid for the vaccine (847)	13	1.53
Trimester of vaccination (829)		
1st	164	19.79
2nd	390	47.04
3rd	275	33.17
Smoking during pregnancy (1,091)	221	20.26
Influenza like illness before pregnancy (1,053)	161	15.29
Chronic respiratory disease (1,099)	137	12.45
Anemia during pregnancy (1,085)	443	40.83
Diabetes during pregnancy (1,100)	32	2.91
High blood pressure during pregnancy (1,100)	215	19.55

SD: standard deviation.

\* USD 1.00: BRL 1.7960 (on 1 July 2010).

the 80% goal set by the central health authorities for the 2010 vaccination campaign against A(H1N1)pmd09 influenza. We identified the following factors affecting vaccination: being 20 years of age or older, being married, having received prenatal care and having ILI before pregnancy. Income was the only socioeconomic factor associated with an inverse effect on vaccination, revealing that the poorest were more likely to have been vaccinated.

Possible limitations of this research include the study design, which might have been inappropriate for establishing causal relationships. Additionally, recall bias could have occurred because the data were obtained from interviews with mothers after birth and not from medical records.

The strengths of this study included that all women who gave birth in the city were approached for interview (because the study was con-

Table 2

Crude and adjusted prevalence ratios (PR) and 95% confidence interval (95%CI) for vaccination during pregnancy and associate factors. Rio Grande, Rio Grande do Sul State, Brazil (n = 1,099) \*.

Variable	Prevalence (n)	Crude PR (95%CI)	p-value	Adjusted PR (95%CI)	p-value
Age (years) **,***					
Less than 20	69.12 (141)	1.00	0.02 #	1.00	0.02 #
20-24	81.25 (247)	1.18 (1.06-1.31)		1.16 (1.04-1.30)	
25-29	80.59 (220)	1.17 (1.05-1.30)		1.15 (1.03-1.29)	
30 and above	76.42 (243)	1.11 (0.99-1.23)		1.10 (0.98-1.23)	
Ethnicity **					
Black and other	78.01 (266)	1.00		1.00	
White	77.18 (585)	0.99 (0.92-1.06)	0.8	0.98 (0.92-1.05)	0.6
Level of education **					
Incomplete Primary School	75.32 (238)	1.00	0.4 #	1.00	0.3 #
Complete Primary School	79.62 (207)	1.06 (0.97-1.15)		1.07 (0.98-1.17)	
Complete High School	78.96 (319)	1.05 (0.97-1.14)		1.05 (0.96-1.14)	
Complete or incomplete University	73.11 (87)	0.97 (0.86-1.10)		0.98 (0.85-1.12)	
Income quartiles in USD [mean and SD] **,***					
1st	77.02 (181)	1.00	0.2 #	1.00	0.04 #
2nd	81.16 (224)	1.05 (0.96-1.15)		1.04 (0.95-1.14)	
3rd	77.82 (221)	1.01 (0.92-1.11)		0.99 (0.90-1.09)	
4th	74.01 (225)	0.96 (0.87-1.06)		0.92 (0.82-1.02)	
Married or cohabiting with partner **,***					
No	66.84 (125)	1.00		1.00	
Yes	79.61 (726)	1.19 (1.07-1.32)	0.001	1.18 (1.06-1.31)	0.002
Smoking during pregnancy ##					
No	78.83 (685)	1.00	0.2	1.00	0.4
Yes	74.21 (164)	0.94 (0.86-1.02)		0.97 (0.89-1.05)	
Received prenatal care ***,##					
No	47.27 (26)	1.00		1.00	
Yes	79.02 (825)	1.67 (1.26-2.21)	0.001	1.63 (1.21-2.18)	0.001
Six or more prenatal care visits ***,##					
No	70.31 (135)	1.00		1.00	
Yes	81.00 (678)	1.15 (1.04-1.27)	0.004	1.18 (1.07-1.31)	0.001
Influenza like illness before pregnancy ***,##					
No	76.21 (679)	1.00		1.00	
Yes	82.61 (133)	1.08 (1.01-1.17)	0.04	1.08 (1.01-1.16)	0.04
Chronic respiratory disease ###					
No	78.17 (752)	1.00		1.00	
Yes	72.26 (99)	0.92 (0.83-1.03)	0.2	0.93 (0.83-1.04)	0.2
Diabetes during pregnancy ###					
No	77.51 (827)	1.00		1.00	
Yes	75.00 (24)	0.97 (0.79-1.19)	0.2	0.97 (0.80-1.18)	0.8
High blood pressure during pregnancy ###					
No	77.04 (681)	1.00		1.00	
Yes	79.07 (170)	1.02 (0.95-1.11)	0.5	1.01 (0.93-1.10)	0.8
Anemia during pregnancy ###					
No	75.98 (487)	1.00		1.00	
Yes	80.81 (358)	1.06 (1.00-1.13)	0.05	1.06 (0.99-1.13)	0.08

SD: standard deviation.

\* One missing value;

\*\* First level of model;

\*\*\* Final model;

# Heterogeneity test;

## Second level of model;

### Third level of model.

ducted in the only two hospitals in the city), and that there was only a 2.8% loss. Moreover, we only included women who had given birth during the end of the vaccination campaign (May 2010) and seven months after (October 2010), minimizing the probability of including mothers who were not vaccinated during the campaign.

Studies in other countries reported that influenza A(H1N1) vaccination coverage in the general population and in specific groups varies between 4.8% and 92%, depending on the country and the group studied<sup>14</sup>, with participation being consistently lower among pregnant women<sup>8,18,19</sup>. The 77% vaccination coverage observed in our study is higher than in other countries and is reliable based on official national figures<sup>20</sup>. Comparing to the results obtained in Brazil, the few studies performed in non-developed countries showed a very low coverage for H1N1 vaccination in pregnant women: 12.8% in India<sup>21</sup>, 8.9% in Turkey<sup>18</sup> and 6.2% in Hong Kong<sup>22</sup>. On the other hand, studies performed in developed countries showed better results than the former countries but still below the values reached in Brazil. In France, Blondel et al.<sup>19</sup> found 29.3%, in the USA, Centers for Disease Control and Prevention (CDC)<sup>23</sup> found a rate of 40.4%, in the Netherlands<sup>24</sup> 63% and in Canada<sup>25</sup> 76.4%.

This increased coverage in Brazil may be attributed to the strategy of the influenza A(H1N1) virus vaccination campaign<sup>26</sup>. Although the vaccinations were restricted to a certain number of weeks prior to the seasonal influenza peak (winter in southern Brazil), all public health facilities, and mainly primary care facilities, offered the vaccine at no cost to pregnant women, regardless of whether they were receiving prenatal care. Moreover, in the private sector, certain clinics offered the vaccine in exchange for out-of-pocket payments. The involvement of scientific societies, professional associations and health service managers helped to support and fortify this vaccination strategy. Additionally, social mobilization and communications campaigns were developed by considering the specificities of each target group and using all possible media sources<sup>26</sup>. It appears that the implementation models of campaigns in specific countries influence their results and affect local adherence, and higher vaccination coverage partially relies on the type of policy adopted by public authorities and on access to the vaccine<sup>27</sup>.

Safety issues were a major obstacle in convincing pregnant women to be vaccinated in some countries. Studies that examined the reasons why pregnant women refuse vaccination indicated health behavior issues, including the safety of the vaccine for the women and their babies,

as major barriers to receiving the vaccine<sup>13,25,28</sup>. In contrast to what occurred in countries in the northern hemisphere during the first wave of vaccination in October 2009, when safety issues prevented many people from receiving the vaccine, the Brazilian campaign was launched after the northern hemisphere vaccinations (March and May 2010), when knowledge about the A(H1N1) vaccine was more widespread; this timing likely improved coverage.

Moreover, the attitudes of health care providers and physicians toward the effectiveness and safety of the vaccine seemed to be fundamental<sup>29</sup>. In the 2010 Brazilian A(H1N1) vaccination campaign, which was planned as a national program, the vaccine was mandatory in all public health facilities, and particularly in those facilities offering prenatal care. The campaign was implemented within the primary health care network and other health centers, and the positive attitudes of health facilities toward the vaccine were critical to the strategy. The high vaccination rates among pregnant Brazilian women in the public sector (97% of those vaccinated used these facilities) are in agreement with the results of other studies, which indicated that the role of the provider in recommending vaccination was important in increasing vaccinations among pregnant women<sup>30</sup>. Moreover, the Brazilian population has been accustomed to receiving vaccinations in the public sector since the National Immunization Program for Children was established in 1973.

In addition to health behaviors, considering reasons that might inhibit people from receiving vaccines, studies have shown that demographic and socioeconomic factors can reduce coverage among pregnant women<sup>13,14,19,30,31</sup>. In line with previous studies, we found that younger pregnant women were less likely to have been vaccinated<sup>13,19,32</sup>. This phenomenon occurred not only in pregnant women but also in other groups, such as hospital workers and the general population<sup>14</sup>. This finding may be related to the very strong belief among older women that the vaccine is safe<sup>13</sup>, but also to parity, once those older pregnant women had previous contact with health services and are used to receive health care, including vaccines. It also may be explained by a higher perception of risk about influenza infection. Another demographic factor that we examined was the influence of marital status on vaccination. Even when adjusted for age, marriage continued to be related to the outcome, indicating that social support from partners could positively affect vaccination rates.

Socioeconomic factors (income and education) have been reported to be barriers to vaccination<sup>14,19,30,31,33,34</sup>. In contrast, our study

showed that the poorest quartile had higher vaccination rates than did the richest quartile and that ethnicity and education, in contrast to what happened in other countries<sup>19,33</sup>, did not influence vaccination coverage. These results highlight the advantage of having universal coverage and an extensive primary health care network, in which most pregnant women and other risk groups had received the vaccination<sup>26</sup>. This phenomenon, where the poor have better coverage than the rich, had been observed previously for vaccination of children<sup>35,36</sup>. It may reflect a rejection of vaccination by pregnant rich women for reasons related to health behavior and the perception of service quality<sup>35,36,37</sup>. This situation introduces new and complex elements in understanding and analyzing the formula for equity in health and in adopting measures towards better coverage.

Additionally, prenatal care affected the vaccination campaign. Pregnant women who had received prenatal care (95% of the sample) or who had completed six or more visits were more likely to be vaccinated. Prenatal care was one of the most important predictors in our study and was considered to be a major factor influencing vaccination among pregnant women in a study in France<sup>19</sup> and in Sydney, Australia<sup>38</sup>. Previous vaccination for seasonal influenza is also related to receiving the new vaccine<sup>30</sup>. We did not explore this relationship because vaccination for seasonal influenza during pregnancy was not recommended before the 2009 pandemic.

However, we found that a previous ILI was associated with a higher probability of receiving the vaccination.

None of the morbidities that commonly occur during pregnancy and that can increase the risk of undesired outcomes in influenza patients (such as diabetes, high blood pressure or chronic respiratory disease) were significantly associated with vaccination. Similar results were found in the French study that was cited previously<sup>19</sup>.

In conclusion, we performed a study to verify A(H1N1)pmd09 vaccination coverage after the 2009 pandemic in a municipality of Brazil and investigated which factors were associated with vaccination. The most important factor predicting vaccination was receiving prenatal care. However, because upcoming coverage aims to reach 100% of the target population, it is necessary to develop strategies that reach and convince groups under better socioeconomic conditions, including those individuals who question vaccine safety and women not receiving prenatal care. Moreover, new investigations should further examine the reasons why certain pregnant women refuse vaccination. The development of future policies confronting new pandemics, whatever the agent, should consider a pre-established and appropriate plan for vaccines to be offered in a timely manner and with easy access. This plan includes strengthening primary health care services and convincing all social strata of the target population to adhere.

## Resumen

*El objetivo fue estudiar la cobertura de vacunación y los factores relacionados a ella durante la pandemia de 2010, en mujeres brasileñas embarazadas. Se realizó estudio transversal con las mujeres que dieron a luz en un municipio del sur del Brasil en 2010. Datos sobre la vacunación contra A(H1N1), las características sociodemográficas, comorbilidad y prenatal fueron recogidas. El análisis estadístico se realizó mediante la regresión de Poisson. La cobertura fue de un 77,4%. La mayoría fueron vacunados en el sector público (97,6%) y durante el segundo trimestre (47%). Los factores relacionados con el aumento de la vacunación fueron: tener marido, mayor edad, pertenecer al primer cuartil de ingresos, haber recibido cuidado prenatal y haber tenido gripe antes del embarazo. Educación y color de la piel no se asociaron significativamente con la vacunación. La campaña fue extensa y no mostró la desigualdad. El cuidado prenatal fue el factor que más afectó la cobertura de inmunización, lo que refleja su importancia para éxito de las futuras campañas de vacunación.*

*Gripe Humana; Vacunación; Mujeres Embarazadas; Atención Prenatal*

## Contributors

R. A. Mendoza-Sassi carried out the statistical analysis, interpretation of findings, drafting and reviewing the manuscript, and read the final version of the manuscript. J. A. Cesar assisted with the study design, interpretation of findings, helped reviewing and drafting the manuscript and read the final version of the manuscript. J. M. Cagol, I. A. Duarte, L. M. Friedrich and V. K. Santos assisted with the data analysis, helped to review the manuscript and read the final version of the manuscript. L. Zhang assisted with the study design, interpretation of findings, reviewing and drafting the manuscript and read the final version of the manuscript.

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