



## Frailty is an Independent Determinant of COVID-19 Vaccine Hesitancy in the Elderly: a Cross-sectional Study

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### ARTICLE INFO

#### Original paper

#### Article history:

Received: December 08, 2021

Accepted: April 06, 2022

Published: April 30, 2022

#### Keywords:

COVID-19 vaccine hesitancy,  
Cross-sectional study,  
Frailty

### ABSTRACT

COVID-19 vaccines have become an important hope for slowing down or stopping the pandemic. As the population ages, older adults will comprise a greater proportion of the vaccinated population. We aimed to assess influencing factors of COVID-19 vaccine hesitancy in older adults. For this aim, We conducted a cross-sectional study on a questionnaire survey of the elderly over 65 years living in the community of Haikou City from August 1st to September 30th, 2021. Univariate and multivariate Logistic regression analyses were performed to identify factors related to vaccine hesitancy. We analyzed completed questionnaires from 225 respondents (42.2% women, mean age 73.4±6.2 years). There were 99 people in the vaccine hesitation group and 126 people in the vaccine acceptance group, the incidence of vaccine hesitation in the elderly population is about 44% (99/225). The incidence of frailty in the vaccine hesitation group was much higher than that in the vaccine trust group (62.63 vs. 30.95%,  $P < 0.001$ ). The risk factors of vaccine hesitancy in the elderly aged 70-75 years and over 75 years were 2.987 times and 3.587 times higher than that in the population aged 65-70 years ( $OR = 2.987, 95\% CI: 1.424-6.265, P < 0.001$ ;  $OR = 3.587, 95\% CI: 1.804-7.131, P < 0.001$ ). Frailty is also an independent risk factor of vaccine hesitancy in the elderly population ( $OR = 2.624, 95\% CI: 1.447-4.757, P < 0.001$ ). Then the vaccination rate of the COVID-19 vaccine is far from reaching the requirements of herd immunity, and more flexible and comprehensive efforts are needed to increase the vaccination willingness of the frail elderly.

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### Introduction

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causing Coronavirus Disease 2019 (COVID-19) emerged in late 2019 and reached the level of the pandemic in March 2020. This crisis has overwhelmed health systems across the world. Judging from the progress of the new coronavirus pneumonia (corona virus disease 2019, COVID-19), to slow down or stop the epidemic of COVID-19, vaccination with the COVID-19 vaccine is considered the best choice. As the population ages, older adults will comprise a greater proportion of the vaccinated population. Therefore, it is very important to vaccinate the elderly to the greatest extent to prevent and treat COVID-19 (1).

According to the seventh national census of the National Bureau of Statistics of China, as of the end of 2020, the number of elderly people aged 60 and over in my country has reached 264.02 million, accounting for 18.7% of the total population (including 19064 million people aged 65 and over,

accounting for 13.50%), was the country with the largest elderly population in the world. The past decade has witnessed an upsurge in research on frail elderly people (2). A better understanding of frailty can help prevent it because this syndrome is an emerging global health challenge in clinical practice and public health (3). In the elderly population in China, the prevalence of frail is 4.9% - 83.4%. Analyzing the factors associated with COVID-19 vaccine hesitancy among frail older adults will have a significant impact on the group immunity of the whole elderly population.

Therefore, this cross-sectional study aims to understand the association between COVID-19 vaccine hesitancy in the prefrail community older population and identify both protective and risk factors associated with it.

### Materials and methods

#### Study design

We conducted a cross-sectional, population-based

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Cellular and Molecular Biology, 2022, 68(4): 202-207

online survey among the Hainan province population using a structured questionnaire from August 1 to September 30, 2021. It was an open online survey for all the population aged  $\geq 65$  years residing in Haikou city, Hainan province. Those willing to respond could complete the questionnaire by mobile phone. The online survey was prompted through primary social networks, including We-Chat. Participants could complete the survey questionnaire, which took approximately three minutes on average, either by mobile phone or computer. Data was collected on Wen Juan Xing.

### Data collection

The structured questionnaire contained information on demographic characteristics, the status of COVID-19 vaccination, willingness to accept the COVID-19 vaccination and vaccine hesitancy.

### Vaccine hesitancy

Vaccine hesitancy was defined as hesitant, delayed, or refusal to accept the vaccine due to reasons other than vaccine availability or contraindication. It was measured among the priority population for this study since the non-priority population had no access to the COVID-19 vaccine at this stage. Vaccine-priority participants were categorized as acceptors with no hesitancy, acceptors with doubt, delayers, or refusers, and the last three categories were considered as vaccine hesitancy (4).

### Fried frailty phenotype

Primary care nurses performed a comprehensive geriatric assessment to categorize patients according to the Fried frailty phenotypes (3-5 characteristics=frail) (5).

### Statistical analysis

Categorical variables are expressed as absolute and relative frequencies in different groups, and the differences in their distribution were tested by the Chi-square test. The multivariate logistic regression model was used to explore the factors associated with vaccine hesitancy. The odds ratio (OR) and 95% confidence interval (CI) were calculated. SPSS (version 24.0, IBM, Armonk, NY, USA) was used for data cleaning and statistical analysis. The significance level was considered when the P value was  $< 0.05$ .

## Results and discussion

### Sample characteristics

A total of 257 older adults answered the questionnaire. The 32 missing or invalid questionnaires were deleted, and 225 questionnaires were finally included for analysis. The respondents worked in different departments before retirement, including administrative units (n = 20), public institutions (n = 63), farmers (n = 99) and others (n = 43). The vaccine hesitating group was 99 and the vaccine receiving group was 126. The incidence of vaccine hesitation in the elderly population is about 44% (99/225).

**Table 1.** Sample characteristics.

	vaccine trust n=126	vaccine hesitancy n=99	Statistical value t / $\chi^2$	P value
Demographics				
Age, %	72.5 $\pm$ 6.6	74.8 $\pm$ 7.1	2.565	0.011
Gender, %			0.003	0.957
Male	73(57.94)	57(57.58)		
Female	53(42.06)	42(42.42)		
Pre-retirement occupation			3.971	0.269
Administration staff	8(6.35)	12(12.12)		
public institutions staff	32(25.40)	31(31.31)		
farmer	60(47.62)	39(39.39)		
Other	26(20.63)	17(17.17)		
Place of residence			0.634	0.426
rural	55(43.65)	38(38.38)		
city	71(56.35)	61(61.62)		
Years of Education			0.001	0.983
<12 years	60(47.62)	47(47.47)		
$\geq 12$ years	66(52.38)	52(52.53)		
Living conditions			21.109	<0.001
Living with family	102(80.95)	84(84.85)		
Living alone	24(19.05)	15(15.15)		
Income situation, RMB/M			1.457	0.692
<3000	70(55.56)	60(60.61)		
3000-6000	33(26.19)	22(22.22)		
6000-10000	13(10.32)	12(12.12)		
>10000	10(7.94)	5(5.05)		
Concerned about the recent COVID-19 epidemic situation			2.043	0.564
Very concerned	53(42.06)	36(36.36)		
More attention	30(23.81)	22(22.22)		
Occasional attention	26(20.63)	21(21.21)		
No attention	17(13.49)	20(20.20)		
Fried frailty phenotype			22.483	<0.001
Frailty	39(30.95)	62(62.63)		
Non- Frailty	87(69.05)	37(37.37)		

The social demographic characteristics of 225 participants were summarized in table 1. Overall, the average age of all participants was  $73.91 \pm 6.91$  years, and the vaccine hesitating group was older (P=0.011). The proportion of participants with initial weakness

was 44 % (n=99). The differences in living conditions and Fried-frailty phenotypes between the two groups were statistically significant ( $P<0.05$ ), as shown in Table 1. The incidence of frailty in vaccine hesitant group was much higher than that in vaccine trust group (62.63% vs 30.95%,  $P<0.001$ ).

### Factors associated with COVID-19 vaccine hesitancy in the elderly

By univariate analysis (Table 2), assignment: 65-70 years: 0, 71-75 years: 1,  $\geq 75$  years: 2; Living with family: 0, Living alone: 1; Frailty: 1, Non-Frailty: 0; COVID-19 vaccine hesitancy (assignment: Yes = 1, no = 0), the following factors were significantly associated with the COVID-19 vaccine hesitancy: age, Living alone, frailty. By multivariate analysis, age is an independent risk factor for vaccine hesitancy in the elderly ( $P < 0.001$ ). The risk factors of vaccine hesitancy in the elderly aged 70-75 were 2.987 times higher than that in the population aged 65-70 (OR=2.987, 95% CI: 1.424-6.265,  $P < 0.001$ ); The risk of vaccine hesitancy in people over 75 years old was 3.587 times higher than that in people aged 65-70 years (OR=3.587, 95% CI: 1.804-7.131,  $P < 0.001$ ), Table 3. Frailty is also an independent risk factor of vaccine hesitancy in the elderly population (OR=2.624, 95% CI: 1.447-4.757,  $P < 0.001$ ), Table 3.

**Table 2.** Univariate Logistic analysis of covid-19 vaccine hesitancy in the elderly.

	B	SE	Wald	P	OR	95%CI
65-70years	-	-	25.870	<0.001	-	-
71-75years	1.277	0.366	12.168	<0.001	3.587	1.750-7.354
$\geq 75$ years	1.605	0.332	23.347	<0.001	4.980	2.597-9.551
Living alone	0.564	0.558	1.024	0.312	1.758	0.589-5.245
Frailty	1.319	0.283	21.654	<0.001	3.738	2.145-6.514

**Table 3.** Multivariate Logistic analysis of covid-19 vaccine hesitancy in the elderly.

	B	SE	Wald	P	OR	95%CI
65-70years	-	-	15.416	<0.001	-	-
71-75years	1.094	0.378	8.382	0.004	2.987	1.424-6.265
$\geq 75$ years	1.277	0.351	13.277	<0.001	3.587	1.804-7.131
Frailty	0.965	0.304	10.100	0.001	2.624	1.447-4.757
constant	-1.370	0.255	28.890	<0.001	0.254	

### Differences in frail components in older adults with vaccine hesitancy and vaccine trust

Comparison of frail components between vaccine trust and vaccine hesitancy group, diet for most or all

of the past 4 weeks, a distance of one block without assistance (100m), suffering from more than 5 chronic diseases, weight loss of more than 5% within 1 year had significant statistical differences ( $P<0.05$ ).

Differences in frail components in older adults with vaccine hesitancy and vaccine trust have been shown in Table 4.

**Table 4.** Differences in frail components in older adults with vaccine hesitancy and vaccine trust.

Frail components	Trust n = 126	Hesitancy n = 99	$\chi^2$	P value
Fatigue for most or all of the past 4 weeks	58(46.03)	60(60.61)	4.722	0.030
It is difficult to go up the stairs without assistance	60(47.62)	55(55.56)	1.398	0.237
Distance of one block without assistance (100m)	38(30.16)	55(55.56)	14.747	<0.001
Suffering from more than 5 chronic diseases	32(25.40)	42(42.42)	7.282	0.007
Weight loss of more than 5% within 1 year	38(30.16)	44(44.44)	4.885	0.027

In the present study, age and frailty are independent and important predictors of COVID-19 vaccine hesitancy in the elderly. This illustrates the importance of assessing the frailty of the population to be vaccinated with covid-19, which can predict vaccine hesitancy regardless of other factors. The World Health Organization (WHO) defined vaccine hesitancy as a behavior influenced by a number of factors, including issues of confidence (do not trust the vaccine or provider), complacency (do not perceive a need for a vaccine, do not value the vaccine), and convenience (access) (4). Vaccine-hesitant individuals are a heterogeneous group who hold varying degrees of indecision about specific vaccines or vaccination. In general vaccine-hesitant individuals may accept all vaccines but remain concerned about vaccines. Some may refuse or delay some vaccines but accept others; some individuals may refuse all vaccines (4).

In addition, the overall incidence of vaccine hesitancy in the elderly population was (44%), which was higher than the national cross-sectional survey data of covid-19 vaccine hesitancy in China (35.5%) (6), which may be due to the fact that most of the study population in the latter was under the age of 50, and the proportion of people over the age of 50 was only 13.2%, while the age in our study was over 65 years old. Fisher et al (7) conducted a survey of 991

American adults on vaccine attitudes from April 16 to 20, 2020. 30% of the elderly over the age of 60 were included. The results found that 31.6% are uncertain about vaccination, 10.8% do not plan to get the vaccination, and vaccination hesitates. The proportion reached 42.4%. This suggests that the elderly population has a higher rate of vaccine hesitancy, which will affect the hesitancy rate of the entire population. With the aging of society, it is crucial to guide the safe vaccination of the elderly. The middle age group had a reduced willingness to be vaccinated compared with 18-34 years old people and over 60 years old people (8).

In addition, this study also found that the crude prevalence of frailty in the elderly covid-19 vaccine hesitant population was 62.63% (62/99), which was much higher than 31.0% (36/126) in the vaccine trust group. At present, the relationship between frailty and vaccine hesitancy in the elderly population has not been fully discussed. One of the most important aspects of this study is frailty is an independent risk factor influencing vaccine hesitancy in the elderly by multivariate Logistic regression. Frailty is a state of the reduced physiological reserve, which exceeds the expectation of normal aging (9). It is considered to be the result of the cumulative effect of multiple physiological changes over time. The prevalence of frailty in community-dwelling elders increases with age: 4% in 65 to 69-year-olds, 7% in 70 to 74-year-olds, 9% in 75 to 79 year-olds, 16% in 80 to 84 year-olds, and 26% in 85-year-olds and older (10). Frailty is not only an independent predictor of complications after elective orthopaedic surgery (11), poor prognosis of elderly patients with myocardial infarction (12) and burns mortality after hospitalization (13), but also an independent predictor of Alzheimer's disease (14) and colorectal cancer (15). To the best of our knowledge, this is the first time we have studied the relationship between frailty and vaccine hesitancy in the elderly population. Due to low immunity, the elderly adults are not only the susceptible population to COVID-19 but also the population with high post-infection critical illness and mortality. Therefore, in order to vaccinate the elderly population as much as possible, we must solve the obstacle of receiving the vaccine for this population.

Our study has some limitations. First, the online questionnaire leads to a biased selection, which may

be due to the lack of representation of the target population. Second, although we have carried out quality control, there may be errors in the information because the online questionnaire cannot be modified after filling in; However, these errors are unlikely to change our results. Third, this study is a cross-sectional survey, which can not show the dynamic trend. Fourth, the incidence of vaccine hesitancy may also be affected by other factors. Therefore, we may overestimate or underestimate the coverage. In relation to Covid-19, many studies have been conducted on its cause, prevention, diagnosis, prevalence, and other issues that need attention (16-23).

### Conclusions

This research provides information about the COVID-19 vaccination campaign for the elderly. It is best for the elderly to be screened for frailty before being vaccinated. The frail elderly population has a higher incidence of vaccine hesitation. Interventions can be carried out from psychological, physical, and family aspects to increase the vaccination rate of the elderly population.

### Acknowledgments

Not applicable.

### Interest conflict

The authors declare that they have no conflict of interest.

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