


# BMJ Open Does COVID-19 have an impact on influenza vaccine knowledge, attitude and practice among medical students: a 2-year prospective cohort study

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## ABSTRACT

**Objectives** To explore the main factors affecting the knowledge, attitude and practice about influenza and influenza vaccine as well as the intention to receive influenza vaccination among the same group of medical students before (2019) and after (2021) the COVID-19 outbreak.

**Design** A population-based prospective cohort study.

**Setting** A longitudinal cohort study of a selected medical school in Chongqing, China, which ran from 2019 to 2021.

**Participants** A total of 803 medical students participated in the study in 2019 and only 484 students responded in 2021. The response rate for our survey was only 60.27% due to graduation, emails being abandoned, etc.

**Results** The influenza vaccination rate of students at this medical school was 6.7% in 2019, compared with 25.8% in 2021. The awareness rate of medical students about influenza and influenza vaccine was 82.8% in 2019 and 86% in 2021, and there was no significant statistical difference between the 2 years ( $p=0.134$ ); the number of medical students with supportive attitude towards influenza vaccine was 95.1% in 2019 and 97.1% in 2021, and there was no statistically significant difference between the 2 years ( $p=0.078$ ); the number of students who actively learnt about knowledge related to influenza vaccine rose from 183 (22.8%) in 2019 to 195 (40.3%) in 2021.

**Conclusions** The COVID-19 outbreak prompted an increase in influenza vaccination rates among medical students in Chongqing, with almost all students (96.0%) believing that the spread of COVID-19 promoted their knowledge about influenza and influenza vaccine, and the vast majority (74.8%) believing that the spread of COVID-19 promoted their willingness to receive influenza vaccine.

## BACKGROUND

Influenza, a respiratory tract infectious disease, is extremely contagious. Influenza virus antigenicity is variable and spreads rapidly. This virus can cause seasonal epidemics each year.<sup>1</sup> China's Influenza Treatment Program (2020 version) clearly states that 'annual influenza vaccination is the most effective

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Comparing knowledge attitude and practice toward influenza vaccine in the same group before and after the COVID-19 outbreak, and this condition cannot be replicated now.
- ⇒ This study will contribute to the promotion of influenza vaccination in the medical student population.
- ⇒ The data were collected online through social networking platforms. Thus, we might have failed to approach the students who were not able to access internet, resulting in a sampling bias.
- ⇒ Because our study was conducted at a medical school in Chongqing, it may limit the generalisability of the study.

means for influenza prevention, reducing the risk of influenza and serious complications in vaccinated individuals'.<sup>2</sup> During the outbreak of the COVID-19 pandemic, the Chinese Ministry of Health considers influenza vaccination for 2020–2021 to be particularly important.<sup>3</sup> Influenza vaccination has become especially important as the severe global epidemic of COVID-19 will continue this year and there may be a superimposed epidemic of COVID-19 along with influenza and other respiratory infectious diseases this winter and next spring.

As a place where students frequently gather, the relatively crowded learning and living environment of schools makes it easy for students to catch the influenza, and college students are highly mobile between campuses. Surveillance data from several provinces in recent years have shown that more than 90% of influenza each year occurs on campus. From 2004 to 2008, 90.48% of influenza outbreaks in Jiangsu Province occurred on campus. From 2006 to 2013, 97.26% of influenza outbreaks in Shanxi Province also occurred on campus.<sup>4–6</sup> Among all the students on campus, medical students

are believed to possess a higher risk of influenza illness than other students due to the specificity of their discipline. They are the future medical workers and important disseminators of health knowledge, so there is a need for vaccination for them.<sup>7</sup>

However, few has been reported regarding the current status of influenza vaccination in this group in China. From the few studies, it was found that the current vaccination rate of medical students in China was much lower than that of foreign countries. Influenza vaccination rates for medical students were 17.1% in northwest China, 25.3% in Brazil, 20.7% in Saudi Arabia, 53.8% in Australia, 76% in the UK and 43% in the USA.<sup>4 7-12</sup> To explore whether medical students' knowledge, attitude and practice about influenza and influenza vaccine have changed under the influence of today's COVID-19 epidemic, we compared the results of a survey on their knowledge and attitude about influenza and influenza vaccine among the same group of medical students before the outbreak (2019) and after the outbreak (2021) to (1) investigate the main factors affecting medical students' willingness to receive influenza vaccination; (2) provide a scientific basis for improving influenza vaccination rates among medical students and strengthening influenza prevention and control efforts in the current context.

## MATERIAL AND METHODS

### Study design and settings

In this prospective cohort study, a survey study focusing on influenza and influenza vaccine awareness and willingness to vaccinate was first conducted among freshman-year to senior-year medical students in a medical school in Chongqing, China from September 2019 to October 2019, and the questionnaire applied was named Q1. A new survey on influenza and influenza vaccine knowledge, attitude and practice to vaccinate with some slight modifications due to the COVID-19 was sent by email to volunteers who had previously received the questionnaire (Q1) in November 2021, and the new questionnaire was named Q2. The questionnaire data were compiled and collected in January 2022. The final return rate of the questionnaire was only 60.27% due to graduation, email discontinuation, etc. All participants in 2019 were randomly selected and volunteered to participate in this experiment and were not involved in the conduct of the study.

### Patient and public involvement

This research was done without patient involvement. Patients were not invited to comment on the study design and were not consulted to develop patient-relevant outcomes or interpret the results. Patients were not invited to contribute to the writing or editing of this document for readability or accuracy.

### Questionnaire

Both questionnaires (Q1 and Q2) were pilot tested on a sample of 30 participants, and their feedback was used to

further modify the items. The finalised instrument was administered electronically. The questionnaires used the precautionary measures promoted by the National Health Commission of the People's Republic of China on its official website as questions to determine the level of knowledge about influenza prevention. The survey consisted of two parts. The first part collected demographic information on profession and gender, while the second part asked about respondents' knowledge about influenza and the influenza vaccine, as well as attitude towards influenza vaccine—a set of questions with a Cronbach's  $\alpha$  coefficient greater than 0.7.

### Survey

We collated questions on influenza-related knowledge and influenza vaccine attitude from both Q1 and Q2 and analysed them after excluding redundant and repetitive questions. Influenza-related knowledge was scored 1 point for a correct answer and 0 point for a wrong answer. The full score was 18 points and a score  $\geq 11$  would be judged as knowing. Influenza vaccine knowledge rate (%) = number of correct answers/total number of respondents  $\times 100\%$ . For influenza vaccine attitude, a score was assigned according to the attitude towards influenza vaccine (5=very positive, 4=positive, 3=fair, 2=negative, 1=very negative). The full score was 25, any scores  $\geq 15$  would be considered as having a positive attitude towards influenza vaccine. Vaccine vaccination rate (%) = number of influenzas vaccinated/total number of surveyed  $\times 100\%$ . Influenza vaccination willingness rate (%) = number of people willing to receive influenza vaccination/total number of people surveyed  $\times 100\%$ .

### Data analysis

Epidata V.3.0 software was used for double data entry, and SPSS V.24.0 software was used for statistical analysis. The differences between rates were analysed by  $X^2$  test, and unconditional logistic stepwise regression analysis was used for influencing factors of influenza vaccination intention. The level of statistical significance was chosen to be 0.05 ( $\alpha=0.05$ ).

## RESULTS

### Demographics

A total of 803 medical students participated in the study between September and October 2019. Only 484 medical students answered the questionnaire during the return visit in November 2021. We define freshmen, sophomores and juniors as lower division students, and seniors and fifth-year students as the senior group. In the comparison between 2021 and 2019, there are statistically significant differences in gross monthly income (GMI), age and grade level, and the specific information can be seen in [table 1](#).

### Knowledge

The knowledge rate of medical students about influenza and influenza vaccine was 82.8% in 2019 and 86% in

**Table 1** Demographic characteristics of the study participants in Chongqing

Demographic information	2019 n (%)	2021 n (%)	Total	P value
Gender				
Male	294 (36.6)	179 (37.0)	473	0.894
Female	509 (63.4)	305 (63.0)	814	
GMI				
<¥4000	507 (63.1)	275 (56.8)	782	0.025
≥¥4000	296 (36.9)	209 (43.2)	505	
Age				
18–20 years old	350 (43.6)	177 (36.6)	527	0.013
21–23 years old	453 (56.4)	307 (63.4)	760	
Grade level				
Lower division	167 (20.8)	39 (8.1)	206	<0.001
Senior group	636 (79.2)	445 (91.9)	1081	
GMI, gross monthly income.				

2021, and there was no statistically significant difference between the two comparisons ( $p=0.134$ ). The following six questions: (1) ‘wearing a mask can prevent the spread of the influenza to some extent’; (2) ‘incubation period of influenza’; (3) ‘influenza can be spread through

close contact with patient’; (4) ‘influenza vaccination for immunity is less costly and more cost-effective than developing immunity from influenza infection’; (5) ‘the best time to get an influenza vaccination’; and (6) ‘How often should you get an influenza vaccination?’ are significantly more known to the students in 2021 than in 2019. Meanwhile, these three questions: (1) ‘patients with influenza can spread the infection before symptoms appear’; (2) ‘influenza vaccination does not give you the influenza although it carries live virus’; and (3) ‘What do you think the purpose of influenza vaccination is?’ are less known to the students in 2021 than in 2019 ([table 2](#)).

### Attitudes

The percentage of medical students who were supportive of influenza vaccine was 95.1% in 2019 and 97.1% in 2021, with no statistically significant difference between the two comparisons ( $p=0.078$ ). As compared with the students’ responses from 2019, a higher percentage of medical students in 2021 believe that the influenza vaccine is safe (91.5%>65.1%); the influenza vaccination is necessary (83.9%>67.0%); the seasonal influenza vaccine is effective in preventing seasonal influenza (86.8%>73.2%); vaccination is important. However, we also observed a higher percentage of students in 2021 worried about the

**Table 2** Comparison of influenza vaccine knowledge in 2019 and 2021

Knowledge	Knowledge awareness level		P value
	2019 awareness rate n (n/N×100%)	2021 awareness rate n (n/N×100%)	
Wearing a mask helps to prevent the spread of the influenza	699 (87.0)	472 (97.5)	<0.001
Influenza is mainly spread by respiratory (coughing, sneezing) droplets	785 (97.8)	475 (98.1)	0.640
Incubation period of influenza	193 (24.0)	156 (32.2)	0.001
Influenza carriers (without symptoms) can spread the infection	706 (87.9)	391 (80.8)	0.001
Patients are contagious	525 (65.4)	439 (90.7)	<0.001
The influenza shot that contains live viruses cannot cause people to get influenza	690 (85.9)	272 (56.2)	<0.001
Influenza vaccination for immunity is less costly and more cost-effective than developing immunity from influenza infection	373 (46.5)	420 (86.8)	<0.001
The best time to get vaccinated	412 (51.3)	310 (64.0)	<0.001
Frequency of vaccination	297 (37.0)	213 (44.0)	0.013
Perception of the aim of influenza vaccination	733 (91.3)	422 (87.2)	0.020
Side effects of influenza vaccination			
Fever	540 (67.2)	364 (75.2)	0.002
Pain and swelling at the injection site	672 (83.7)	419 (86.6)	0.160
Headaches	448 (55.8)	318 (65.7)	<0.001
Influenza vaccination priority groups			
People over 60 years old	577 (71.9)	351 (72.5)	0.797
Patients with chronic illnesses and infirmity	705 (87.8)	400 (82.6)	0.011
Health facility staff, especially front-line staff	715 (89.0)	415 (85.7)	0.082
Pupils and kindergarten children	714 (88.9)	420 (86.8)	0.253
Pregnant women over the first trimester of pregnancy	360 (44.8)	192 (39.7)	0.069

**Table 3** Comparison of influenza vaccine attitudes in 2019 vs 2021

Attitude	2019		2021		P value
	n	% (n/N)	n	% (n/N)	
Influenza vaccine is safe					
Agree	523	65.1	443	91.5	<0.001
Disagree	280	34.9	41	8.5	
Influenza vaccination is necessary					
Agree	538	67.0	406	83.9	<0.001
Disagree	265	33.0	78	16.1	
You are not worried about the side effects of the influenza vaccine					
Agree	205	25.5	271	56.0	<0.001
Disagree	598	74.5	213	44.0	
The seasonal influenza vaccine is more effective in preventing seasonal influenza					
Agree	588	73.2	420	86.8	<0.001
Disagree	215	26.8	64	13.2	
Annual influenza vaccination is important for you					
Agree	346	43.1	287	59.3	<0.001
Disagree	457	56.9	197	40.7	
You are planning to get an influenza vaccination this autumn/winter					
Agree	268	33.4	187	38.6	0.056
Disagree	535	66.6	297	61.4	

side impacts of influenza vaccine relative to those in 2019 (56.0%>25.5%) (table 3).

### Practices

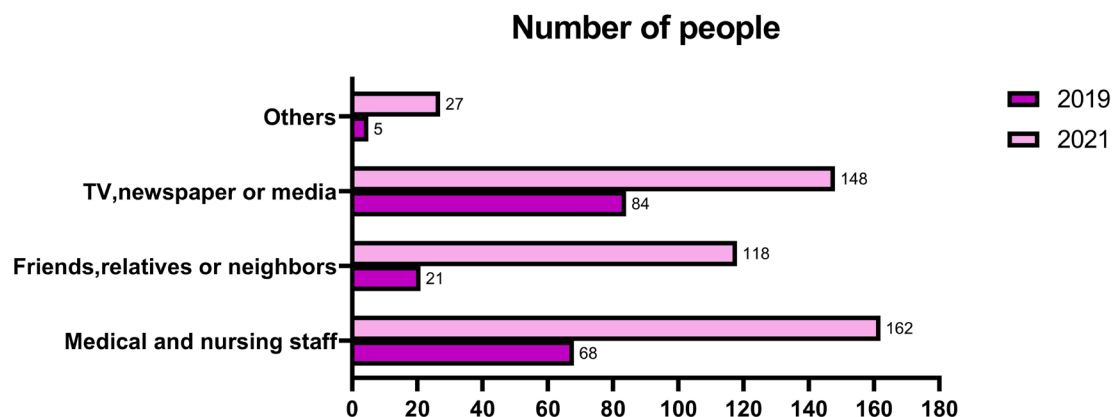
The main source of influenza vaccine information in 2019 was television, newspapers and the media (48.6%), while the main source in 2021 was healthcare professionals (35.6%) (figure 1).

The number of people actively seeking information about influenza vaccine rose from 183 (22.8%) in 2019 to 195 (40.3%) in 2021. The number of people who received influenza vaccination in 2021 was much higher than in 2019 (25.8%>6.7%), and the most significant increase in adverse reactions to vaccination was seen in the phenomenon of temporary mild pain, redness and swelling at the injection site (39.2%>18.5%). Among the reasons

for receiving influenza vaccination, both 'to enhance resistance and prevent influenza' (88.8%>75.9%) and 'recommended by government and health authorities' (72.0>44.4%) were selected by a higher percentage of students in 2021 relative to 2019 (table 4).

The three main reasons for not getting vaccinated in 2019 were 'did not think it was necessary to get vaccinated' (53.8%), 'did not know about the influenza vaccine' (46.1%) and 'did not have time' (41.1%). The three main reasons for not getting vaccinated in 2021 were: 'didn't have time to get vaccinated' (43.5%), 'didn't think it was necessary to get vaccinated' (43.2%) and 'didn't know about the influenza vaccine' (35.9%) (figure 2).

During the COVID-19 epidemic in 2021, most students believed that the epidemic promoted awareness of

**Figure 1** Sources of influenza vaccine information for 2019 vs 2021.

**Table 4** Comparison of influenza vaccination behaviour in 2019 vs 2021

Behaviour	2019		2021		P value
	n	% (n/N)	n	% (n/N)	
Do you take the initiative to learn about the influenza vaccine?					
Yes	183	22.8	195	40.3	<0.001
No	620	77.2	289	59.7	
Did you get an influenza vaccination last year?					
Yes	54	6.7	125	25.8	<0.001
No	749	93.3	359	74.2	
Did you have any of the following adverse reactions in your last influenza vaccination?					
Severe allergic reactions	7	13.0	23	18.4	0.362
Dizziness	9	16.7	26	20.8	0.483
Low fever	7	13.0	23	18.4	0.337
Transient mild pain, redness and swelling at the injection site	10	18.5	49	39.2	0.004
No adverse reactions	36	66.7	67	53.6	0.136
What are your reasons for getting the influenza vaccine?					
Build up your resistance and prevent influenza	41	75.9	111	88.8	0.033
Recommendation from government and health authorities	24	44.4	90	72.0	<0.001
Recommended by family and friends	17	31.5	58	46.4	0.061
Other	3	5.6	1	0.8	0.061
Have you had an influenza-like illness within 1 year of vaccination?					
Yes	8	14.8	17	13.6	<0.001
No	25	46.3	96	76.8	
Don't remember	21	38.9	12	9.6	

influenza and influenza vaccine (96%) and willingness to receive influenza vaccination (74.8%) (table 5).

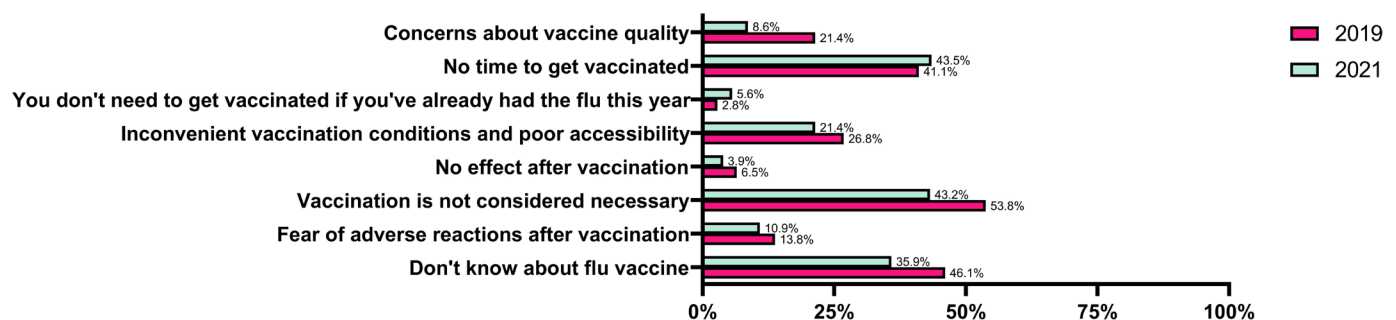
#### Analysis of single factors affecting medical students' vaccination intentions in 2021

The vaccination rate of medical students who actively learnt about influenza vaccine was significantly higher than that of medical students who did not actively learn about it (47.2%>11.4%), and the vaccination rate of medical students who actively learnt about respiratory viral infectious diseases during COVID-19 was also higher than that of medical students who did not actively learn about it (29.5%>8.3%) (table 6).

#### DISCUSSION

This study showed that the influenza vaccination rate of medical students in the studied medical school was only 6.7% in the 2019 influenza season, which is lower than the vaccination levels of medical students in other cities such as Urumqi, China (9.2% in 2010).<sup>9</sup> In 2021, the vaccination rate of medical students against influenza rose to 25.8%, which was not as high as the vaccination level of medical students in developed countries such as the USA and the UK, but it is also a significant improvement as compared with 2019. This finding indicates that the COVID-19 outbreak has significantly boosted the

#### Proportion


**Figure 2** Main reasons for not getting an influenza vaccination in 2019 vs 2021.

**Table 5** Analysis of COVID-19-related behaviours in 2021 (frequency statistics)

COVID-19-related acts	Number of people	Percentage
The COVID-19 outbreak promotes your learning about respiratory infectious diseases		
Yes	400	82.6
No	84	17.4
The COVID-19 outbreak raised your awareness of influenza and influenza vaccine		
Yes	384	96.0
No	16	4.0
The COVID-19 outbreak boosts your intention to get influenza vaccinated		
Yes	362	74.8
No	122	25.2

influenza vaccination rate of the medical students that we studied. Similar results were obtained in a teaching and research hospital in Milan, during the COVID-19 pandemic, and influenza vaccination rates for physicians and administrative staff rise significantly.<sup>13</sup> This may be

due to the fact that there are numerous studies showing a significant reduction in the possibility of contracting COVID-19 after receiving the influenza vaccine, therefore, the willingness to receive the influenza vaccine has increased.<sup>14 15</sup>

However, the level of influenza vaccination among medical students in Chongqing is still low and needs to be further improved, and it is recommended that medical students be included in the key recommended vaccination targets for influenza vaccination.

Looking at the demographic characteristics of the students, the GMI in 2021 is higher than that in 2019, which our speculation may be due to inflation. Over time, the age and grade level in 2021 are higher than in 2019, which is also in line with the objective rule and our speculation.

In terms of knowledge, there was no significant difference between the comparison of 2021 and 2019 ( $p=0.134$ ). However, on average, only a quarter of the students knew the incubation period time of influenza, and one similar study found that university education has a positive impact on influenza knowledge,<sup>16</sup> indicating that students at this university do not pay much

**Table 6** Analysis of factors influencing medical students' willingness to receive vaccinations in 2021

Variables	Number of people vaccinated (%)	Number of unvaccinated persons (%)	OR value (95% CI)	P value
Gender				
Male	49 (27.4)	130 (72.6)	1.136 (0.747 to 1.726)	0.551
Female	76 (24.9)	229 (75.1)	Reference	
Age				
18–20	48 (27.1)	129 (72.9)	1.111 (0.7300 to 1.692)	0.622
21–23	77 (25.1)	230 (74.9)	Reference	
Grade level				
Lower school	14 (35.9)	25 (64.1)	1.685 (0.846 to 3.355)	0.137
Upper school	111 (24.9)	334 (75.1)	Reference	
GMI				
<¥4000	65 (23.6)	210 (76.4)	0.769 (0.511 to 1.157)	0.207
≥¥4000	60 (28.7)	149 (71.3)	Reference	
Attitudes towards the influenza vaccine				
Negative	1 (7.1)	13 (92.9)	Reference	0.140
Active	124 (26.4)	346 (73.6)	4.659 (0.603 to 35.984)	
Level of knowledge				
Understanding	112 (26.9)	304 (84.7)	1.559 (0.820 to 2.962)	0.443
Don't understand	13 (19.1)	55 (80.9)	Reference	
Proactive about information about influenza vaccines				
Yes	92 (47.2)	103 (52.8)	6.929 (4.380 to 10.963)	<0.001
No	33 (11.4)	256 (88.6)	Reference	
Learning about respiratory infectious diseases during the COVID-19 outbreak				
Yes	118 (29.5)	282 (70.5)	4.603 (2.062 to 10.275)	<0.001
No	7 (8.3)	77 (91.7)	Reference	

GMI, gross monthly income.

attention to influenza-related courses. The questions 'wearing a mask can prevent the spread of influenza to some extent,' 'influenza can be spread through close contact with patients' and 'compared with developing immunity from influenza infection, getting immunity from influenza vaccination has better cost-effectiveness' are answered significantly more correctly in 2021 than in 2019. This is because of the emergence of COVID-19, which is more widely known due to state and government campaigns and changes in daily lifestyle (eg, the need to wear a mask when using public transportation). The question 'side impacts of influenza vaccination: fever, headache' was also better answered in 2021, probably due to the reactions that occurred during the vaccination with COVID-19 or the possible side impacts told by doctors or teachers before the vaccination.<sup>17 18</sup> As for the question 'chronically ill and frail people are the priority recommended population for influenza vaccination', the answer was reversely better in 2019 than in 2021 (87.8%>82.6%), which we speculate that this may be due to the fact that the COVID-19 vaccine is prohibited for patients with acute exacerbation of chronic disease or severe uncontrolled chronic disease in the Chinese New Crown Vaccination Technical Guidelines (V.1), so some participants misunderstood that influenza vaccine is also contraindicated for patients with chronic disease, thus leading to a poor response to this question.<sup>19-22</sup>

Regarding the comparison of attitudes towards influenza vaccine, although there was no significant difference between 2021 and 2019 ( $p=0.078$ ), students in 2021 were more likely to believe that influenza vaccine is safe and important, that vaccination against influenza is necessary and that they are not concerned about the side impacts of influenza vaccine. There are good reasons to attribute this to the COVID-19 epidemic.

The most important reason for influenza vaccination among medical students in both 2021 and 2019 was 'to increase resistance and prevent influenza', which is consistent with other studies,<sup>23-25</sup> indicating that concerns for one's health are the driving factor for influenza vaccination in this group. The reason 'recommended by the government and health authorities' increased from 44.4% in 2019 to 72% in 2021, this is likely because of the government's strong call for people to get COVID-19 vaccine in the past year, which led to the group's increased interest in influenza vaccination.

Among students who reported not receiving the influenza vaccine, the reasons for not receiving the vaccine in 2021 and 2019 are not very different, with a significant percentage of students not considering it necessary, suggesting that the influenza vaccine is not being taken seriously by this group. Among those who have not received the influenza vaccine, the percentage of students who have 'never heard of the influenza vaccine' reached 46.1% in 2019 and 35.9% in 2021. It is recommended that health education on influenza and influenza vaccine should be strengthened, such as holding a competition on influenza and influenza vaccine knowledge and

providing specific training on influenza vaccination in degree programmes. Vaccine safety was the least influential factor impeding vaccination, indicating solid expertise among study participants. The results of the present study suggest that providing more information about increasing influenza vaccine awareness and basic knowledge of influenza vaccines among study participants may help improve vaccine coverage.

This study found that students with more knowledge about influenza vaccine were more inclined to receive influenza vaccine, which is consistent with previous studies.<sup>26</sup> Students who took the initiative to learn about respiratory viral infectious diseases during COVID-19 transmission were also more likely to get the influenza vaccine, suggesting that the promotion and dissemination of knowledge about COVID-19 also helped people to understand more about influenza and influenza vaccine. This shows that in the current environment, we should attach knowledge about influenza to the promotion of COVID-19-related knowledge and prevention methods, so that people can receive COVID-19 vaccination and also pay attention to influenza vaccination, thereby increasing the influenza vaccination rate.

### Limitations

This study has certain limitations. First, the data were collected via self-reported questionnaires, which can be a potential cause of reporting bias. Second, since our data were collected from medical students only, there is a possibility that they might have answered the questions positively on the basis of their medical knowledge as they had already perceived what would be expected from them. Third, the data were collected online through social networking platforms. Thus, we might have failed to approach the students who were not able to access internet, resulting in a sampling bias. Last, because our study was conducted at a medical school in Chongqing, China, it may limit the generalisability of the findings from this study. We will subsequently expand the sample source in hope of obtaining better results.

### Conclusion

The COVID-19 outbreak prompted an increase in influenza vaccination rates among medical students in Chongqing (6.7% in 2019 to 25.8% in 2021), with almost all students (96.0%) believing that the spread of COVID-19 promoted their knowledge of influenza and influenza vaccine, and the vast majority (74.8%) believing that the spread of COVID-19 promoted their willingness to receive influenza vaccine. We could disseminate information about influenza vaccine along with information about COVID-19 vaccine to help increase influenza vaccination rates.

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**Contributors** YW and XT drafted the manuscript. GW and XT designed the questionnaire. YW and FZ collected the data. GW, LG, QL, YJ and FZ participated in

data analysis and data extraction. YW and XW finalised the manuscript. All authors read and approved the final manuscript. XT is the guarantor of our article.

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**Competing interests** None declared.

**Patient and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

**Patient consent for publication** Not required.

**Ethics approval** This 2-year prospective cohort study was approved by the Ethics Committee of Chongqing Medical University. Participation in this study was voluntary, and informed consent was gained. Our data collection procedures complied with the institutional and national ethical guidelines and followed the Declaration of Helsinki. The anonymity and confidentiality of data were maintained. Written informed consent was obtained from the investigators for this experiment.

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**Data availability statement** Data are available upon reasonable request.

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