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Effect of a mobile app chatbot and an interactive small-group webinar on COVID-19 vaccine intention and confidence in Japan: a randomised controlled trial

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ABSTRACT

Introduction We investigated the effect of social media-based interventions on COVID-19 vaccine intention (VI) and confidence in Japan.

Methods We conducted a three-arm randomised controlled trial between 5 November 2021 and 9 January 2022 during a low incidence (<1000/day) of COVID-19 in Japan in the midst of the second and the third waves. Japanese citizens aged ≥20 who had not received any COVID-19 vaccine and did not intend to be vaccinated were randomly assigned to one of the following three groups: (1) a control group, (2) a group using a mobile app chatbot providing information on COVID-19 vaccines and (3) a group using interactive webinars with health professionals. VI and predefined Vaccine Confidence Index (VCI) measuring confidence in the importance, safety and effectiveness were compared before and after the interventions under intention-to-treat principle. Logistic regression models were used to investigate the effect of each intervention on postintervention VI and changes of VCI compared with control.

Results Among 386 participants in each group, 359 (93.0%), 231 (59.8%) and 207 (53.6%) completed the postsurvey for the control, chatbot and webinar groups, respectively. The average duration between the intervention and the postsurvey was 32 days in chatbot group and 27 days in webinar group. VI increased from 0% to 18.5% (95% CI 14.5%, 22.5%) in control group, 15.4% (95% CI 10.8%, 20.1%) in chatbot group and 19.7% (95% CI 14.5%, 24.9%) in webinar group without significant difference (OR for improvement=0.8 (95% CI 0.5, 1.3), p=0.33 between chatbot and control, OR=1.1 (95% CI 0.7, 1.6), p=0.73 between webinar and control). VCI change tended to be larger in chatbot group compared with control group without significant difference (3.3% vs −2.5% in importance, OR for improvement=1.3 (95% CI 0.9, 2.0), p=0.18; 2.5% vs 1.9% in safety, OR=1.1 (95% CI 0.7, 1.9), p=0.62; −2.4% vs −7.6% in effectiveness, OR=1.4 (95% CI 0.9, 2.1), p=0.09). Improvement in VCI was larger in webinar group compared with control group for importance (7.8% vs −2.5%, OR=1.8 (95% CI 1.2, 2.8), p<0.01), effectiveness (6.4% vs −7.6%, OR=2.2 (95% CI 1.4, 3.4), p<0.01) and safety (6.0% vs 1.9%, OR=1.6 (95% CI 1.0, 2.6), p=0.08).

Conclusion This study demonstrated that neither the chatbot nor the webinar changed VI importantly compared with control. Interactive webinars could be an effective tool to change vaccine confidence. Further study is needed to identify risk factors associated with decreased vaccine confidence and investigate what intervention can increase VI and vaccine confidence for COVID-19 vaccines.

Trial registration number UMIN000045747.

INTRODUCTION

Regulatory approval of COVID-19 vaccines in Japan lagged behind other countries.[1] Starting in February 2021, COVID-19 vaccines were initially administered to only healthcare workers[1]; then to older adults, those with chronic disease and those working for nursing facilities (around April 2021); and, finally, to the general population. Although the COVID-19 vaccine coverage of the primary two-dose series gradually increased to ~80% in 2022, vaccine uptake was lower in Japan than it was in other high-income countries at the beginning of the vaccine rollout in 2021.[2] For instance, the coverage rate in Japan was 49% as of early August 2021, while other G7 countries, such as Canada, the UK, France and Italy, all achieved over 65% coverage rate at that time.[2]

While the delay of regulatory approval and logistical issues influenced slow rollout, it was also rooted in public vaccine hesitancy.[3] A previous study revealed that Japan was one of the least vaccine-confident countries in

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Japan is one of the least vaccine-confident countries in the world and has a long history of public uncertainties about vaccines in general.
⇒ Social media-based interventions have been implemented to increase vaccine uptake; however, there have been conflicting data available on whether social media-based interventions can increase vaccine intention and confidence.
⇒ There is a paucity of studies investigating the effect of a mobile app chatbot and interactive webinars on COVID-19 vaccine intention and confidence in Japan.

WHAT THIS STUDY ADDS

⇒ This randomised controlled trial did not find sufficient evidence that the chatbot or the webinars changed COVID-19 vaccine intention among those with high vaccine hesitancy and low acceptance in Japan in 2021 compared with control.
⇒ COVID-19 vaccine confidence for importance, safety and effectiveness increased with the webinar intervention compared with control.
⇒ Vaccine confidence in importance and effectiveness of COVID-19 vaccines decreased in the control group over time.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Interactive small-scale webinars featuring live Q&A with medical professionals may serve as an efficacious method for addressing public concerns about COVID-19 vaccines and enhancing vaccine confidence.
⇒ In light of the worsening vaccine confidence among unvaccinated individuals without any mitigation, local governments and public health organisations may necessitate conducting regular, interactive, small-group webinars, particularly in regions with low vaccine uptake or high vaccine hesitancy.
⇒ Further research is needed to investigate the strategies for recruiting and retaining participation of individuals with vaccine hesitancy in randomised controlled trials and to assess the effects of social media-based interventions on increasing vaccine intention and the vaccine confidence for COVID-19 vaccines.

the world, even before the COVID-19 pandemic.[4] Japan has a long history of public uncertainties about vaccines, such as the human papillomavirus vaccine, which led to a severe drop in coverage, from over 70% to less than 1% after the rise of public anxiety and the government's suspension of proactive recommendation of the vaccine due to public pressure about suspected vaccine adverse events.[5] A survey conducted in 15 countries in January 2021 found that intention to be vaccinated against COVID-19 was lower in Japan than in other countries: 36% of surveyed Japanese adults strongly or somewhat disagreed with being vaccinated against COVID-19.[6 7] As success of vaccine rollout ultimately depends on the public's willingness to be vaccinated,[8] increasing vaccine intention (VI) and vaccine confidence among those who are unwilling or hesitant to be vaccinated was a critical priority in 2021 to improve vaccine uptake in Japan.

During the COVID-19 pandemic, too much information and rumours, both accurate and false, have spread widely and rapidly through online platforms.[9] This 'infodemic' confused people and created uncertainty about trust in the COVID-19 vaccine. A past nationwide survey in Japan demonstrated that many study participants wanted to obtain more information on COVID-19 vaccines to make a decision about being vaccinated, including information about the compatibilities between the vaccine and their personal health conditions, the effectiveness of vaccines and medical doctors' recommendations.[7] To provide the non-health expert public with scientific evidence-based information on COVID-19 vaccines in a user-friendly manner, it is important to explore the best platform(s) to optimise public understanding of COVID-19 vaccine information and ultimately improve their VI and confidence.

Past studies indicated the potential of online interventions to increase VI and uptake by providing accurate information on vaccines and disease and by increasing public perception of vaccine benefits. For example, a randomised controlled study in 2017 demonstrated that mothers presented with accurate vaccine information on social media during their pregnancy were more likely to vaccinate their infants on time.[10] A recent cross-sectional study showed that small-group Zoom webinars helped address misconceptions surrounding COVID-19 vaccines and was associated with increased willingness to be vaccinated among 91 Asian immigrants in Canada and the USA.[11] Virtual webinars were also reported to be effective in reducing vaccine hesitancy at black church congregations.[12] On the other hand, another study suggested that social media use itself may not be directly associated with people's willingness to receive a COVID-19 vaccination.[13] There have been conflicting data available about whether and how online or virtual webinars can be used to address COVID-19 vaccine hesitancy. Furthermore, we previously published a cross-sectional study investigating the association between COVID-19 VI and the use of a chatbot in a popular messenger app in Japan.[14] Though this study indicated the potential usefulness of a social media-based chatbot to reduce vaccine hesitancy, this study was subject to multiple limitations in terms of the study design since the study was cross-sectional only among chatbot users without a comparison group. Therefore, it had both internal (eg, recall bias, interview bias) and external validity issues, and the association between chatbot use and VI could not be clearly evaluated.

To address this knowledge gap, we investigated whether social media-based interventions could increase COVID-19 VI and vaccine confidence among those with vaccine hesitancy. We used two different online interventions, a social media-based chatbot and webinars, and examined which of these were more effective at increasing COVID-19 VI and vaccine confidence. By conducting two online interventions, we examined how different online tools can be used depending on people's demands and available resources.

METHODS

Study design and setting

We conducted a three-arm randomised controlled trial to investigate the impact of a mobile app chatbot and an online interactive seminar (webinar) on COVID-19 VI and vaccine confidence among those (1) unvaccinated and unwilling or hesitant to be vaccinated; and (2) aged 20 or older in Japan from 5 November 2021 until 9 January 2022. We assessed COVID-19 VI and vaccine confidence by performing preintervention and postintervention cross-sectional surveys.

During the study period, three COVID-19 vaccines were publicly available: BNT162b2, mRNA-1273 and ChAdOx1-S/nCoV-19. The costs of vaccines were covered in full by public funds for all Japanese nationals and all eligible foreign residents. The government has strongly recommended that all people get vaccinated given the global evidence shows that the benefits of vaccination are greater than the risk of adverse event. Thanks to the government's recommendations, about 80% of Japanese people had received at least one dose of a COVID-19 vaccine when this study was conducted.[15] Third dose of COVID-19 vaccines was only available to limited healthcare workers during the present study. No new vaccines became available and no new policy was implemented during the study period of 2.5 months. The period when the postsurvey was conducted (between late December 2021 and early January 2022) covered the two key phases that influenced public perceptions on vaccines: (1) when the daily reported COVID-19 cases were relatively low with less than 1000 cases per day; and (2) when the Omicron variant emerged.

Study participants

Study participants were recruited from the panel of a Japanese internet research service company (NTTCom Online Marketing Solutions), which had approximately 120 million registered individuals as of October 2021. First, the screening survey was sent to 700 000 randomly selected persons in the panel on 20 October 2021 with the following five questions: (1) 'How old are you?'; (2) 'Have you received a COVID-19 vaccine?'; (3) 'Do you intend to be vaccinated?' (with answer options of 'Yes', 'Not sure but toward Yes', 'Not sure but toward No' and 'No'); (4) 'Do you have LINE (one of the most popular messenger apps in Japan) installed on your mobile phone? If not, are you willing to download LINE to participate in this study?'; and (5) 'Are you capable of using Zoom for webinars?' Eligibility criteria included: (1) age 20 or older; (2) had never received a COVID-19 vaccine; (3) those who selected an answer other than 'Yes' to question 3; (4) willing to use LINE; and (5) willing to use Zoom. Monetary incentives were given as follows: 1000 yen (~US$8) for those who completed the presurvey and postsurvey in the control group, 1500 yen for those who used the chatbot at least once and completed the presurvey and postsurvey and 3000 yen for those who attended at least one of 14 webinars for at least 15 min and completed presurveys and postsurveys.

Preintervention survey

Eligible persons were invited to participate in the presurvey by email on 5 November 2021. Questionnaires were placed in a secure section of a website, and persons who consented electronically received the link to the questionnaires. The presurvey ended on 10 November 2021 (a total of 5 days). The presurvey had a total of 30 questions (online supplemental text S2), including survey items used in similar studies,[16] as well as our own questions. The survey also asked for age, sex, geographic location, educational attainment, employment status, work in a healthcare setting, annual household income, presence of chronic diseases identified as risk factors for severe COVID-19 by the Japanese government,[17] history of influenza vaccine in the previous season, history of COVID-19 infection, history of any side effect from any previous vaccination and COVID-19 VI for their children, if any. Geographic locations were combined using the following categories: Hokkaido, Tohoku, Kanto (eg, Tokyo), Chubu, Kansai (eg, Osaka), Kinki, Chugoku, Shikoku, Kyushu regions and outside of Japan.[18] In addition, questions were asked about personal experience with social media involving COVID-19 vaccine information. These questions included which social network the participants use most to obtain COVID-19 vaccine information, which social media they trust most and how long they use social media per day, among others.

Intervention with LINE chatbot (chatbot group)

Persons who answered the presurvey between 5 and 10 November 2021 were randomly assigned to one of the following three groups: (1) no exposure to the LINE chatbot nor webinar (control group); (2) the mobile app chatbot users (chatbot group); and (3) online interactive seminar users (webinar group). Randomisation into three groups was conducted between 11 and 14 November 2021 by biostatisticians (EHYL and JW). Instructions for each intervention were sent on 15 November 2021 to all three groups. The chatbot was accessible on 15 November and webinars started on 16 November 2021.

LINE is a free messenger app available on electronic devices, such as smartphones, tablets and personal computers. LINE users can exchange texts, images, video and audio. LINE is the most popular messenger app in Japan: about 86 million people in Japan (roughly two-thirds of the population) use this messenger app.[19] We created a chatbot in LINE to answer COVID-19 vaccine frequently asked questions (FAQs) via text messages (online supplemental figure S1).[14] This chatbot has approximately 200 sets of questions and answers. Our chatbot works as follows: (1) users tap to select the item that they want to ask from a menu of options; the menu options are well organised with clearly labelled sections, such *as 'How do COVID-19 vaccines work?', 'What are the possible side effects of the vaccine?'* and *'What is the eligibility for vaccination?'*; (2) the chatbot automatically lists more specific questions relevant to the item that users choose in step 1; (3) users further choose a specific question that

they want to ask from the list; and (4) the chatbot automatically provides detailed information and answers to a chosen question. Users can also search questions via free text keywords and the chatbot shows potential questions that include the entered keywords. With these phased steps, users can access information that they seek very quickly without consuming a vast amount of time to find specific information from internet search engines.

The first email was sent on 15 November 2021 to study participants assigned to the chatbot group to explain how to use the chatbot and to provide them with a link through which they can access the chatbot; they also received a link to a 5 min YouTube video (https://youtu.be/nJBTHaXapQ8). One reminder was sent to participants who did not access the chatbot on 24 November 2021. The participants could access the chatbot until the end of the study period. In addition, we tracked who downloaded the chatbot and how frequently each FAQ was accessed in the chatbot during the study period to determine which participants were included for final analysis.

Intervention with interactive webinars

We conducted a total of 14 webinars via Zoom between 16 November and 7 December 2021. Each seminar was held on Tuesdays and Fridays at 10:00 and 20:00 hours to allow study participants to choose suitable dates and times. We asked participants in the webinar group to attend at least one webinar for 30 min. They were allowed to participate in more than one webinar if they preferred. They were required to choose their preferred date and time for the webinar and to register in advance through a temporary website with links to the 14 different webinar sessions. Each webinar was limited to a maximum of 40 participants to allow greater interactivity between health experts and participants. Reminder emails were sent to registrants 24 hours and 1 hour before each webinar using an automated reminder system in Zoom. We sent an email to the webinar group participants (n=386) a total of four times (initial instruction email and three reminders) to encourage them to register for at least one of the 14 seminars. Each webinar included a brief lecture about the COVID-19 vaccine (10 min) presented by physicians using PowerPoint slides, followed by Q&A sessions (additional 20–50 min). We tracked who registered and participated in each webinar. Those who stayed on a webinar less than 15 min (of 30 min) were not considered to have attended the webinar and were not included in the final analysis (n=1). The lecture included the history of vaccines, the necessity and the efficacy of the COVID-19 vaccine and the possible risks of short-term and long-term adverse events with the COVID-19 vaccine. Participants were encouraged to ask questions throughout a webinar through the Zoom Q&A chat feature, and questions from participants were collected before and during the webinar. Attendees could submit questions anonymously if they chose. Three of seven Japanese physicians (TK, YY, HT, KH, YN, KT, HM and KI) were required to attend each webinar as presenters, and the webinars were conducted in the Japanese language only. Each webinar included three physicians, one moderator and one office administrator, and all questions submitted on registrations through Zoom and during webinars were answered by physicians during the webinars.

Postintervention survey

We created three different postsurveys specific to each of the assigned groups. All three groups were asked about their history of COVID-19 vaccination since the presurvey, and their current VI and vaccine confidence for safety, importance and effectiveness. The postsurvey was sent to the chatbot and webinar groups (online supplemental text S3) between 22 December 2021 and 9 January 2022.

Sample size calculation

A previous study in France investigating the impact of an interactive web tool on patients with COVID-19 vaccine hesitancy showed that 8% of 1200 patients accepted COVID-19 vaccination after their intervention.[20] We assumed that the estimated proportion of VI in the intervention group after intervention would be 10% and that the proportion of VI in the control group would remain zero. For achieving an 80% power at 5% level of significance with equal allocation, a dropout rate of 40% and a superiority margin of 5%, the calculated sample size for each arm was 371 participants.

Outcome data and statistical analysis

The primary analysis was based on the intention-to-treat (ITT) principle. Participant characteristics were summarised using frequencies and percentages. For two-group comparisons, the χ^2 test or Fisher's exact test was used for categorical variables and the Mann-Whitney U test was used for continuous variables. For three-group comparisons, the χ^2 test was used for categorical variables.

Primary outcomes were VI and vaccine confidence. VI was measured by the proportion of those who had received a COVID-19 vaccine since the presurvey, and those who had not but who answered 'Yes, definitely' in the postsurvey to the question 'Do you intend to be vaccinated against COVID-19?'. Vaccine confidence was quantified using the Vaccine Confidence Index (VCI).[21] A previous study demonstrated that, among a multiplicity of factors influencing vaccine decisions, key drivers of public confidence in vaccines were identified as trust in the importance, safety and effectiveness of vaccines, along with compatibility of vaccination with religious beliefs.[21] A vaccine confidence survey tool was developed in 2015 and has been used in multiple different types of vaccine studies.[22] The VCI includes four vaccine confidence statements: 'Overall I think vaccines are important'; 'Overall I think vaccines are safe'; 'Overall I think vaccines are effective'; and 'Vaccines are compatible with my religious beliefs'. We decided not to use the statement about religious beliefs in our study because this statement does not fit well with Japanese customs since more than 80% of people in Japan have no religion.[23] We

present for each intervention group the proportions of participants having improvement in vaccine confidence, defined by those who responded 'do not know', 'tend to disagree' and 'strongly disagree' before intervention and responded 'strongly agree' or 'tend to agree'.

Differences in the proportion (postintervention compared with preintervention) of VI and VCI across arms were compared by fitting a logistic regression model on the postintervention VI (participants who responded 'Yes, definitely') and the postintervention VCI (participants who responded 'strongly agree' or 'tend to agree' to these specific questions on vaccine confidence). The baseline VI, VCI and intervention group were used as predictor. Missing outcomes were imputed using multivariate imputation by chained equations with 50 imputations, based on baseline characteristics including demographics, health conditions, vaccine confidence and intervention group assignment. We obtained the final estimates by pooling the estimates from 50 imputed data sets using Rubin's rules. We used R V.4.0.4 (R Development Core Team, Vienna) for statistical analysis. A p value of 0.05 was considered statistically significant.

Patient and public involvement

Patients were not involved in designing the study, determining the research questions, deciding the outcomes measured, recruiting participants or conducting the study. The burden of the intervention was not assessed; however, study participants' feedback about the chatbot and the webinars was obtained in the postsurvey. All relevant data will be shared on our website (https://corowakun-supporters.studio.site/#news). Patient advisors were not involved with this study.

RESULTS

A total of 99965 persons responded to the screening questions between 5 November and 10 November 2021. Of these, 15398 (15.4%) had not received a vaccine yet, of which 13314 (86.5%) did not intend to be vaccinated. Among 13314 eligible persons, 1158 agreed to participate in the study, completed the presurvey and were randomly assigned to one of the three different groups: control group (n=386), chatbot group (n=386) and webinar group (n=386) (figure 1). In the control group, 359/386 (93.0%) answered the postsurvey. In the chatbot group, 237/386 (61.4%) accessed the chatbot at least once, of which 231 (97.5%) answered the postsurvey. In the webinar group, 215/386 (55.7%) attended a webinar at least once, of which 207 (96.3%) answered the postsurvey. The average duration between the intervention and the postsurvey was 32 days in chatbot group and 27 days in webinar group. All 1158 participants were included for the final analysis under ITT principle. Baseline characteristics and demographics of participants were balanced across the three groups for most variables (table 1 for selected variables and online supplemental table S1 for all variables).

VI and VCI

VI was 0% for all three groups at the baseline according to inclusion and exclusion criteria. Among the control group, VI increased to 18.5% (95% CI 14.5%, 22.5%) (table 2). Vaccine confidence decreased by 2.5% (95% CI −4.3%, 9.4%) for importance of vaccines and by 7.6% (95% CI 0.7%, 14.4%) for effectiveness naturally without any intervention, while it increased by 1.9% (95% CI −2.4%, 6.2%) for safety.

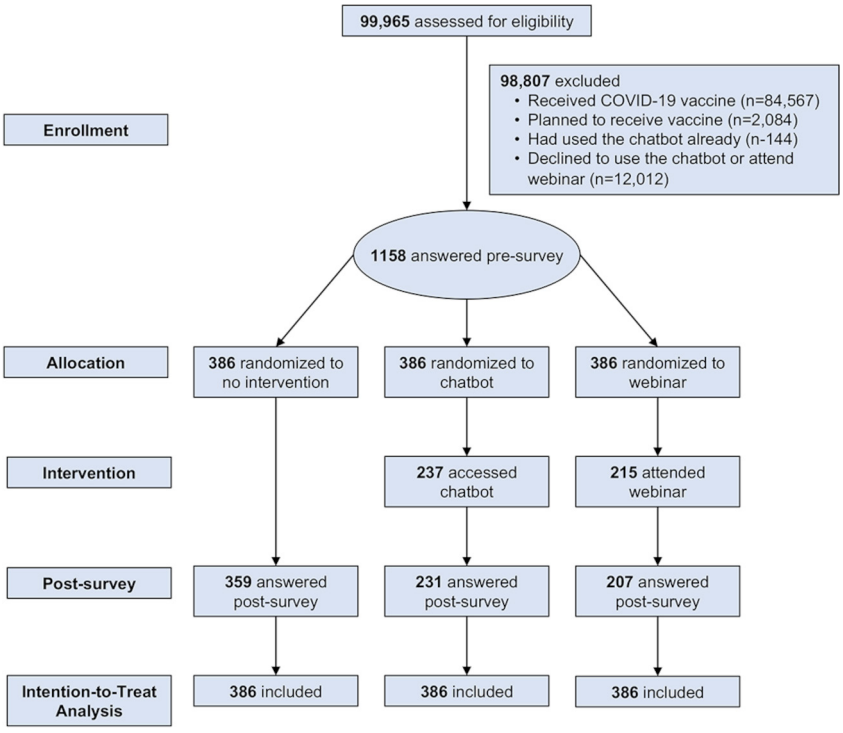

Figure 1 Study enrolment and participation.

Table 1 Baseline participant characteristics and perceptions of COVID-19 vaccines by intervention groups

All participants n=1158	Group 1 (control) n=386	Group 2 (chatbot) n=386	Group 3 (webinar) n=386
Characteristics			
Age (years), mean	44.7	45.8	46.2
Gender (%), male	53.1	54.9	55.7
Education (%)			
High school or less	28.5	26.7	32.9
Professional or vocational qualification	20.5	22.3	16.3
Bachelor's degree or above	51.0	51.0	50.8
Employment (%)			
Full time	56.2	52.6	53.1
Part-time	16.3	16.3	19.7
Unemployed	15.8	18.4	16.8
Retired	2.3	3.6	3.1
Students	0.8	1.0	0.5
Others	8.5	8.0	6.7
Healthcare worker (%)	4.7	3.1	3.1
Marital status (%)			
Married	54.1	47.2	48.7
Never married	39.6	40.7	39.4
Divorced	6.0	11.4	10.4
Widowed	0.3	0.5	1.6
Others	0.0	0.3	0.0
Income (%)			
<JPY200 million	31.6	37.6	36.5
JPY200–399 million	29.0	26.4	25.6
JPY400–599 million	21.8	19.7	23.3
JPY600–799 million	8.5	6.2	8.8
≥JPY800 million	9.1	10.1	5.7
Underlying health conditions (%)	5.4	3.6	4.7
Usually received influenza vaccine (%)	17.4	11.7	17.1
Diagnosed with COVID-19 (%)	2.6	2.3	1.3
Ever experienced a side effect or allergy after any vaccination (%)			
Yes	9.1	7.8	10.1
No	86.0	85.2	82.6
Unsure	4.9	7.0	7.3
Perception of COVID-19 vaccine			
Do you want to receive a COVID-19 vaccine in the future? (%)			
Yes, definitely (screened out)	0	0	0
Unsure, but leaning towards yes	21.8	18.9	20.7
Unsure, but leaning towards no	34.2	33.9	34.7
No, definitely not	44.0	47.2	44.6
COVID-19 vaccines are important (%)			
Strongly agree	7.3	6.0	6.7
Tend to agree	29.8	27.7	29.0

Continued

Table 1 Continued

All participants n=1158	Group 1 (control) n=386	Group 2 (chatbot) n=386	Group 3 (webinar) n=386
Do not know	31.3	36.0	32.6
Tend to disagree	15.0	16.4	16.3
Strongly disagree	16.6	14.2	15.3
COVID-19 vaccines are safe (%)			
Strongly agree	0.5	1.6	0.8
Tend to agree	8.5	8.5	9.3
Do not know	38.3	38.9	37.3
Tend to disagree	25.9	28.0	28.5
Strongly disagree	26.7	23.1	24.1
COVID-19 vaccines are effective (%)			
Strongly agree	3.9	4.7	3.9
Tend to agree	36.5	36.5	35.5
Do not know	33.7	34.5	32.1
Tend to disagree	10.6	12.2	16.3
Strongly disagree	15.3	12.2	12.2

JPY, Japanese yen.

In the chatbot group, VI increased to 15.4% (95% CI 10.8%, 20.1%). Vaccine confidence increased by 3.3% (95% CI −4.0%, 10.7%) for importance and 2.5% (95% CI −2.3%, 7.4%) for safety, and it decreased by 2.4% (95% CI −5.2%, 9.9%) for effectiveness. There was no statistically significant difference in VI in the postsurvey between the chatbot and control groups (15.4% in the chatbot group and 18.5% in the control group, OR of improvement=0.8 (95% CI 0.5, 1.3), p=0.330, table 2). Vaccine confidence tended to be higher in the chatbot compared with the control group but there was no significant difference in importance (3.3% vs −2.5%, OR of =1.3 (95% CI 0.9, 2.0), p=0.177), safety (2.5% vs 1.9%, OR=1.1 (95% CI 0.7, 1.9), p=0.622) or effectiveness (−2.4% vs −7.6%, OR=1.4 (95% CI 0.9, 2.1), p=0.093).

In the webinar group, VI increased to 19.7% (95% CI 14.5%, 24.9%). Vaccine confidence increased by 7.8% (95% CI 0.3%, 15.4%) for importance, 6.0% (95% CI 0.6%, 11.4%) for safety and 6.4% (95% CI −1.4%, 14.3%) for effectiveness. VI in the postsurvey was similar between the control group and webinar group (19.7% in the webinar group and 18.5% in the control group, OR=1.1

Table 2 Vaccine intention and confidence after interventions under an intention-to-treat analysis

All participants (n=1158)	Group 1 (control) n=386 % (95% CI)	Group 2 (chatbot) n=386 % (95% CI)	Group 3 (webinar) n=386 % (95% CI)	Group 2 versus group 1		Group 3 versus group 1	
				OR (95% CI)	P value*	OR (95% CI)	P value*
Willing to be vaccinated†	18.5 (14.5, 22.5)	15.4 (10.8, 20.1)	19.7 (14.5, 24.9)	0.8 (0.5, 1.3)	0.330	1.1 (0.7, 1.6)	0.730
Change in vaccine confidence‡							
COVID-19 vaccines are important.	−2.5 (−9.4, 4.3)	3.3 (−4.0, 10.7)	7.8 (0.3, 15.4)	1.3 (0.9, 2.0)	0.177	1.8 (1.2, 2.8)	0.004
COVID-19 vaccines are safe.	1.9 (−2.4, 6.2)	2.5 (−2.3, 7.4)	6.0 (0.6, 11.4)	1.1 (0.7, 1.9)	0.622	1.6 (1.0, 2.6)	0.077
COVID-19 vaccines are effective.	−7.6 (−14.4, −0.7)	−2.4 (−9.9, 5.2)	6.4 (−1.4, 14.3)	1.4 (0.9, 2.1)	0.093	2.2 (1.4, 3.4)	<0.001

Missing outcomes were imputed using multiple imputation method.
*Assessed by logistic regression models (full results in online supplemental table S2).
†Including those who have received a COVID-19 vaccine or have not received a COVID-19 vaccine but are willing.
‡Difference in % (postintervention vs preintervention) of those who responded 'strongly agree' or 'tend to agree'. (Other responses were 'do not know', 'tend to disagree' and 'strongly disagree'.)

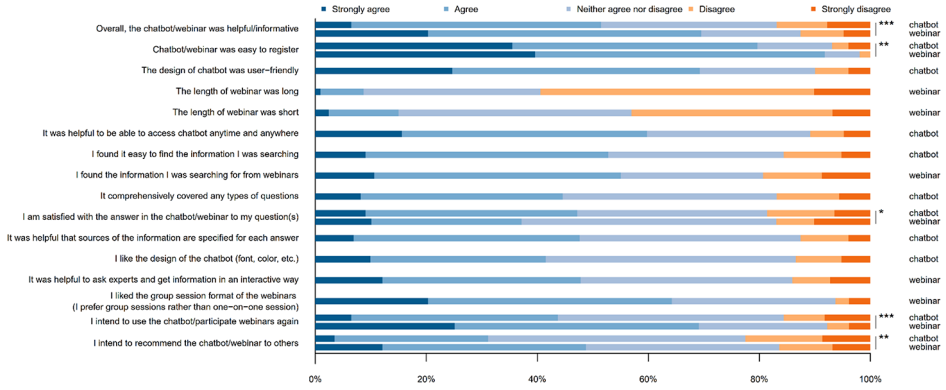

Figure 2 Feedback on chatbot and webinar interventions. Statistically significant differences indicated by *p<0.05, **p<0.01 and ***p<0.001, respectively.

(95% CI 0.7, 1.6), p=0.730, table 2). Vaccine confidence for importance and effectiveness significantly increased in the webinar group compared with the control group (7.8% vs −2.5%, OR=1.8 (95% CI 1.2, 2.8), p=0.004 and 6.4% vs −7.6%, OR=2.2 (95% CI 1.4, 3.4), p<0.001). Vaccine confidence for safety increased in the webinar group; however, the difference was not statistically significant (6.0% vs 1.9%, OR=1.6 (95% CI 1.0, 2.6), p=0.077). The full logistic model results were shown in online supplemental table S2.

Feedback for the chatbot and the webinar

Figure 2 presents feedback obtained from the postsurvey for the chatbot and webinar groups. Overall, a favourable response was more frequently seen in the webinar group compared with the chatbot group for most questions. The proportion of those who strongly agreed that the intervention was informative was 6.5% in the chatbot group and 20.3% in the webinar group (p<0.001). The proportion of those who strongly agreed that they intend to recommend the intervention to others was 3.5% in the chatbot group and 12.1% in the webinar group (p=0.001). The proportion of those who strongly agreed to use the intervention again was 6.5% in the chatbot group and 25.1% in the webinar group (p<0.001).

Comparison within the chatbot group

The association between the number of chatbot accesses and VI and VCI is summarised in online supplemental table S3. The median number of chatbot accesses was 15 in those willing to be vaccinated in the postsurvey compared with 9 in those who remained vaccine hesitant (p<0.001). The number of chatbot accesses was not associated with vaccine confidence.

Comparison within the webinar group

The association between webinar attendance and VI and VCI within the webinar group is summarised in online supplemental table S4. The duration of webinar attendance in minutes was not associated with either VI or VCI. The number of attended webinar sessions was not associated with either VI or vaccine confidence.

DISCUSSION

We did not find sufficient evidence that the chatbot or the webinar changed COVID-19 VI among those with vaccine hesitancy in Japan in 2021 compared with control. However, vaccine confidence for importance, safety and effectiveness increased with the webinar intervention compared with control. A small-group interactive webinar might be an effective tool for changing vaccine hesitancy. However, given there was no increase in VI despite improved confidence in importance and effectiveness, confidence index alone might not correlate well with COVID-19 VI in Japan. Further research is needed to investigate how to recruit and retain those with vaccine hesitancy in randomised controlled trials and whether social media-based interventions can increase VI and VCI for COVID-19 vaccines.

In this study, 15%–20% of participants with vaccine hesitancy, in either the control or intervention group, changed their minds and were accepting of the COVID-19 vaccine by the end of the study period. Social norms and awareness of COVID-19 vaccine status of persons close to those with vaccine hesitancy are important factors in Japan,[24 25] and the already high vaccine uptake at the beginning of the study period (at ~80%) might have helped change vaccine hesitancy over time regardless of whether VCI decreased or increased. Additionally, according to a global systematic review on the determinants of vaccine hesitancy, perceived vaccine safety was one of the most frequently cited factors in past studies.[26] Previous nationwide surveys in Japan also suggested that concerns about side effects and the safety of COVID-19 vaccines could be influential reasons for vaccine unwillingness or hesitancy.[7 27] Therefore, we speculate one potential reason why VI did not significantly increase with the webinar intervention despite the increase in vaccine confidence might be due to the lack of significant change in confidence for safety compared with control.

We calculated the proportion of those willing to be vaccinated after intervention, stratified by groups with and without improvement in the three dimensions of vaccine confidence and intervention arms (online supplemental table S5) to see the association between

VI and vaccine confidence after interventions. However, we observed different patterns of VI across three arms, which indicates that interventions may have modified the relationship between VI and confidence. The Working Group on Vaccine Hesitancy established by the Strategic Advisory Group of Experts of WHO indicated that vaccine hesitancy is the behaviour that reflects a constellation of factors that may influence the vaccination decision-making.[28] This group highlighted 3Cs including complacency, convenience and confidence as a model of vaccine hesitancy. The fact that our intervention might have affected the factors above differently and we only focused on confidence factor in the postsurvey may explain why we observed a different pattern in the association between COVID-19 VI and confidence across three arms. We need to explore how different social media-based interventions change various factors (ie, 3Cs) that affect VI, so we can understand the most appropriate intervention for each factor.

Our previous cross-sectional study indicated that a free chatbot had the possibility to decrease vaccine hesitancy[14]; however, this randomised controlled trial demonstrated that the chatbot did not change VI nor vaccine confidence. We hypothesise that the chatbot might have been more effective early in the pandemic when accurate, specific and sought-after information was not readily and widely available to the public. This may be because vaccine hesitancy is due to lack of scientific information and is about underlying emotions behind vaccine decision-making.[29] Changing people's perceptions of vaccines requires more interaction between the public and the medical community to understand the emotions involved in vaccine hesitancy and confidence.[30]

Thus, the webinar offered a platform where a health expert addressed an individual's vaccine concerns and negative emotions by talking with them directly. In fact, our interactive webinar significantly increased vaccine confidence for importance and effectiveness. Feedback from participants showed a significantly favourable response in the webinar group compared with the chatbot group. Live questions asked by webinar participants covered topics like the safety of COVID-19 vaccines, vaccine effectiveness of the three available vaccines, the influence of new variants and common myths, among others. Nevertheless, there have been conflicting data available on whether educational interventions reduce vaccine hesitancy.[31–33] Our study limited the number of participants in webinars to 40, and questions were asked anonymously. Providing a small, interactive and possibly anonymous webinar where individuals can discuss their concerns directly with professionals might be an effective strategy for increasing vaccine confidence, which could in turn decrease vaccine hesitancy.

Confidence in the importance and effectiveness of COVID-19 vaccines decreased in the control group over time. This means that those who remain vaccine hesitant may be even more hesitant about COVID-19 vaccines than before. The period when the postsurvey was conducted covered two key phases that possibly influenced the participants' perceptions on vaccines. During the first phase, the daily reported COVID-19 cases in Japan were relatively low, which might have affected 'importance' in vaccine confidence. The second phase was the emergence of the Omicron variant in other countries despite available vaccines, which might have affected 'effectiveness' in vaccine confidence. Also, the fact that individuals, including those who are vaccinated, are still at risk for COVID-19 infection even in the third year of the pandemic might have caused tiredness, frustration and anxiety, possibly contributing to this worsening VCI in the control group.

This study has several limitations. First, since the study was conducted entirely online, actual vaccine uptake after the intervention could not be investigated. Second, we could not evaluate the effect of in-person seminars. Although some people prefer online seminars with anonymous participation—especially in Japanese culture contexts—in-person seminars may have more potential, including more direct, open and honest communication than occurs online. In addition, in-person seminars can provide COVID-19 vaccines on-site immediately following the seminars for those who become agreeable. Third, even with a monetary incentive, the participation rate was not as high as we expected. To reduce attrition bias, we used multivariate imputation to predict outcome variables of non-respondents. The ITT and per-protocol analyses gave broadly similar outcomes (table 2 and online supplemental table S6), and all numbers were within the 95% CIs indicating statistically insignificant differences. Additionally, we compared the participants' characteristic between those who completed assigned interventions and those who did not (online supplemental table S7). However, we could not identify a clear difference between the two groups. Fourth, though our study confirmed that an interactive webinar might have a role in increasing vaccine confidence, our research cannot determine the most effective method to recruit those who have not received and do not intend to receive a COVID-19 vaccine in a real-world setting without any incentive. Fifth, those who did not have internet access were unable to participate in our study. Given that digital technologies are now considered a new determinant of health, we need to discuss the best way to recruit those with vaccine hesitancy who do not have internet access.[34] Sixth, racial differences were not evaluated because all participants were Japanese. Seventh, this study used three professionals, one moderator and one administrative person for each webinar, and scheduling webinars with medical professionals and administrative persons on a regular basis might not be feasible without providing incentives to presenters, likely requiring support from local communities or external funding.

In conclusion, neither the chatbot nor the webinar improved VI among those with vaccine unwillingness and hesitancy in Japan in 2021 compared with control. Small interactive webinars that include live Q&A sessions with

medical experts have the potential to effectively address public concerns regarding COVID-19 vaccines and to improve vaccine confidence. Future research needs to focus on the relationship between vaccine confidence and COVID-19 VI in Japan. Given the worsening vaccine confidence among those unvaccinated without intervention, local government and public health agencies may need to organise regular, small interactive webinars, especially in areas with low vaccine uptake or high vaccine hesitancy. More prospective studies are needed to evaluate the effect of on-site interactive seminars with the capability of administering vaccines during or after the seminar to those who change their COVID-19 VI.

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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.

Patient consent for publication Obtained.

Ethics approval This study involves human participants and was approved by the Institutional Review Board at Kanto Central Hospital, Tokyo, Japan. Participants gave informed consent to participate in the study before taking part. This study was registered with UMIN Clinical Trials Registry (UMIN000045747) (online supplemental text S1). All participants signed an electronic consent form.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All the data used and/or analyzed is available from the corresponding author upon reasonable request.

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Supplemental material

Kobayashi T, *et al. BMJ Global Health* 2023; 8:e010370. doi: 10.1136/bmjgh-2022-010370

Text S1: Study Protocol (page 2-11)

Registration number: UMIN Clinical Trial Registry (identifier UMIN000045747)

Ethical application status: Approved from Kanto Central Hospital

Type of registration: Prospectively registered

Project title

Effect of a Mobile App Chatbot and an Interactive Small Group Webinar on COVID-19 Vaccine Intention and Confidence in Japan: A Randomized Clinical Trial

Background

A survey conducted in fifteen countries in January 2021 found that intent to take a COVID-19 vaccine was lower in Japan than in other countries: 36% of Japanese adults strongly or somewhat disagreed about getting a COVID-19 vaccine.[1] However, prior to the COVID-19 pandemic, Japan already had one of the world's highest vaccine hesitancy rates.[2] Japan also has a long history of public uncertainty regarding vaccines. For example, the Human Papillomavirus (HPV) vaccination rate among adolescent girls fell from over 70% to less than 1% following public concerns about possible vaccine adverse events.[3]

Our research aims to understand how a chatbot and online webinars could be used to address vaccine hesitancy among those ages 20 (the legal age) and older in Japan. Our research targets Japan because public concerns about COVID-19 vaccines could exacerbate the general mistrust of vaccines in Japan. Furthermore, research on COVID-19 vaccine hesitancy has focused on the United States and Europe, and thus geographic gaps in evidence exist regarding the effect of social media on COVID-19 vaccine intention. The current effort to address COVID-19 vaccine hesitancy in Japan primarily provides scientific information via government websites. However, there are limitations to this approach because information presented this way is typically too formal, not user-friendly, and not individualized. Therefore, addressing COVID-19 vaccine hesitancy requires more innovative solutions.

Vaccine hesitancy could be associated with a lack of scientific information or with the emotions underlying vaccine decision-making.[4] We will provide tailored information based on

individuals' concerns and feelings. We will not simply spread general information to the public because we believe that addressing individuals' concerns reduces negative sentiments about vaccines. This is why we developed a free chatbot to provide COVID-19 vaccines information via text messages.[5] The chatbot is a user-friendly platform for people to access vaccine information that they would like to know. People can select a question to ask from menu options in the chatbot, and they can get tailored information based on their concerns and interests. We previously published a cross-sectional study investigating the association between the use of this chatbot in a popular messenger app and vaccine intention for COVID-19 in Japan.[5] Though this study demonstrated the potential usefulness of a social media-based chatbot to reduce vaccine hesitancy, this study was subject to multiple design limitations because the study was cross-sectional without a comparison group. Therefore, it had both internal (i.e., recall bias, interview bias) and external validity issues, and the association between chatbot use and vaccine intention could not be evaluated clearly.

We also need to create more opportunities for interactions between the public and the medical community to better understand people's emotions. The webinar will offer a platform where a health expert can promptly address an individual's concerns about COVID-19 vaccines. It will also provide a forum for an expert to listen to and understand what people are really concerned about, enabling a dialogue to address and manage people's negative emotions about COVID-19 vaccines.

Previous studies indicated the potential of online interventions to increase vaccine intention by providing accurate information about vaccines and diseases and by improving public perception of vaccines' benefits. For example, a randomized controlled study published by Glanz et al. in 2017 demonstrated that mothers presented with vaccine information on social media during their pregnancy were more likely to vaccinate their infants on time.[6] However, a recent study published by Othman et al. in 2022 showed that just using social media was not directly associated with willingness to receive a COVID-19 vaccination.[7] How online or social media-based interventions can be utilized to increase vaccine intention in Japan is not well-known, especially for COVID-19.

Aims

We aim to investigate whether a social media-based chatbot and webinars affect COVID-19 vaccine intention and vaccine confidence among those who are hesitant to be vaccinated against COVID-19 and to examine which online interventions (a chatbot or webinars) are more effective at increasing COVID-19 vaccine intention and vaccine confidence.

Study design

This will be a three-arm randomized controlled trial:

a) The control group
b) The chatbot group
c) The webinar group

Study participants

Study participants will be recruited from the panel of a Japanese Internet research service company (NTTCom Online Marketing Solutions Corporation), which has approximately 120 million registered individuals as of October 2021. The company will send a screening survey to randomly selected persons depending on the sample size calculation (see details below). The screening survey will include the following five questions: (1) “How old are you?”; (2) “Have you received a COVID-19 vaccine?”; (3) “Do you intend to be vaccinated?” (with answer options of “Yes”, “Not sure but leaning towards Yes”, “Not sure but leaning towards No”, and “No”); (4) “Do you have LINE (one of the most popular messenger apps in Japan) installed on your mobile phone? If not, are you willing to download LINE to participate in this study?”; and, (5) “Are you capable of using Zoom (a videoconferencing app) for webinars?”. Eligibility criteria are: (1’) those ages 20 and older, (2’) those who have never received a COVID-19 vaccine, (3’) those who select an answer other than “Yes” to question #3, (4’) those who are willing to use LINE, and (5’) those who are willing to use Zoom. The questionnaires will be placed in a secured section of a website, and persons who consent electronically receive the link to the questionnaires. Monetary incentives will be given as follows: $10 for those in the control group who complete the pre- and post-survey, $15 for those who use the chatbot at least once and complete the pre- and post-survey, and $30 for those who attend at least one of 14 webinars (at least more than 15 minutes) and complete pre- and post-survey.

Interventions

Intervention with LINE chatbot (the chatbot group)

LINE is a free messenger app available on electronic devices, such as smartphones, tablets, and personal computers. LINE users can exchange texts, images, videos, and audio. LINE is the most popular messenger app in Japan; about 86 million people in Japan (roughly two-thirds of the population) use this messenger app. [8] We created a chatbot in LINE to answer COVID-19 vaccine frequently asked questions (FAQs) via text messages. To generate the

chatbot, we first searched for COVID-19 vaccine FAQs using Japanese government websites and the United States Centers for Disease Control and Prevention website. [9] [10] Approximately two hundred questions that we thought were important were selected. We then composed our corresponding answers to these two hundred questions and included them in the chatbot. The two hundred questions were then classified into seven categories: (1) what we should know before vaccination; (2) what we should know on the day of vaccination; (3) what we should know after vaccination; (4) eligibility; (5) effectiveness; (6) adverse effects; and, (7) questions related to age, comorbidities, allergies, medications, pregnancy, or breastfeeding. We also prepared two additional categories: (8) link to the Japanese government's website; and, (9) link to inquiry. Our chatbot works as follows: (1) users select one of the seven categories that they would like to know the answer to; (2) the chatbot responds with more specific questions in the selected category; (3) users choose the specific items that they would like to know more about; (4) the chatbot provides detailed information; (5) users may also search questions by typing in keywords; and (6) the chatbot shows potential questions that include the keywords. Study participants assigned to the chatbot group first receive an email that explains how to download LINE and the chatbot, provides a direct link for these downloads, and covers how to use the chatbot with a five-minute YouTube video (https://youtu.be/nJBTHaXapQ8). This YouTube video explains in detail the steps to download and use it. In addition, we plan to track who downloads the chatbot and how frequently each FAQ is accessed in the chatbot during the study period to determine which participants we should include for the final analysis.

Intervention with interactive webinars

We plan to conduct a total of 14 webinars via the Zoom videoconferencing application between November 16 and December 7, 2021. Each seminar will be held on Tuesdays and Fridays at 10 a.m. and 8 p.m. so that the study participants can choose suitable dates and times according to their availability. We will ask them to attend at least one webinar for at least 15 minutes. Participants can participate in more than one webinar if they are interested. They are required to choose their preferred date and time for the webinar and to register in advance on the website (this temporary website that we create will host 14 different links to the webinar registrations). Each webinar will be limited to a maximum of 40 participants. For those who have registered, reminder emails will be sent to them 24 hours and 1 hour before the webinar using an automated reminder system in Zoom. We will send an email to the webinar group participants four times (the initial instructions email and three reminders) to encourage them to register for at least one of 14 webinars. Each webinar will include a brief lecture about COVID

vaccines presented by physicians (10 minutes) using PowerPoint slides, followed by Q&A sessions (additional 20 minutes at least and up to 50 minutes for those who stay and ask more questions). The lecture will include the history of vaccines, the necessity and the efficacy of the COVID vaccine, and the short- and long-term adverse events. Participants will be engaged to ask questions throughout a webinar through the Q&A chat in Zoom, and questions from participants will be collected before and during the webinar as well. Attendees will be able to submit questions using their names or anonymously. Three of seven Japanese physicians (T.K, Y.Y, H.T, K.H, Y.N, K.T, and K.I) are required to attend each webinar as presenters, and the webinars will be conducted in the Japanese language only. Each webinar will include three physicians, one moderator, and one office administrator. Physicians will answer all questions submitted upon registration through Zoom and during webinars. We will track who registered and participated in each webinar. Those who stay on a webinar for less than 15 minutes (out of 30 minutes) will not be counted as attending a webinar and will not be included in the final analysis.

The baseline survey and post-intervention survey

Pre-intervention survey:

The pre-survey includes a total of 30 questions. To quantify attitudes and beliefs regarding COVID-19 vaccines, we will use Vaccine Confidence Index (VCI). A previous study demonstrated, among multiple factors influencing vaccine decisions, key drivers of public confidence in vaccines were trust in the importance, safety, and effectiveness of vaccines, and compatibility of vaccination with religious beliefs.[11] The VCI survey tool was developed in 2015 and has been utilized in multiple vaccine studies.[12] VCI includes the four vaccine confidence statements: “Vaccines are important for children to have”; “Overall, I think vaccines are safe”; “Overall, I think vaccines are effective”; and, “Vaccines are compatible with my religious beliefs”. We will not use the last statement about religious beliefs for our study because this statement does not fit customs in Japan where more than 80% of people practice no religion or Buddhism. We will also include survey items used in similar studies and will add our own questions.[13] Our other survey items ask for age, sex, geographic location, educational attainment, employment status, marital status, whether they work in a healthcare setting, annual household income, presence of chronic diseases identified as risk factors for severe COVID-19 by the Japanese government [9], history of receiving the influenza vaccine in the previous season, history of COVID-19 infection, history of any side effects from any previous vaccination, and COVID-19 vaccine intention for their children if they have a child. Geographic locations will be combined

using the following categories: Hokkaido, Tohoku, Kanto (e.g., Tokyo), Chubu, Kansai (e.g., Osaka), Kinki, Chugoku, Shikoku, Kyushu regions, and outside of Japan.[14] In addition, we will ask questions about personal experiences with social media and COVID-19 vaccine information. These questions include which social network the participants use most to obtain COVID-19 vaccine information, which social media they trust most, how long they use social media per day, etc. (see details in appendix S2)

Persons who answer the pre-survey will be randomly assigned to one of the following three groups: (i) a group with no exposure to the LINE chatbot nor a webinar (i.e., the control group), (ii) a group with exposure to the mobile app chatbot (i.e., the chatbot group), and (iii) a group with exposure to online interactive seminars (i.e., the webinar group). Instructions for each intervention will be sent to the three groups on November 15, 2021.

We created five different post-surveys the vary based on the assigned group and whether the study participants actually used the chatbot or attended the webinar. All three groups will be asked about (1) whether they received a COVID-19 vaccine since completing the pre-survey, (2) vaccine intention, and (3) VCI for the safety, importance, and effectiveness. We will also ask for feedback on the interventions for the chatbot group and the webinar group. The post-survey will be conducted from December 2021 through January 2022.

Sample size calculation

A previous study in France investigating the impact of an interactive web tool on patients with COVID-19 vaccine hesitancy showed that 8% of 1200 patients accepted COVID-19 vaccination after their intervention.[15] We assumed that the estimated proportion of Vaccine Intention (VI) in the intervention group after the intervention will be 10% and that the proportion of VI in the control group will remain zero. For achieving an 80% power at a 5% level of significance with equal allocation, a dropout rate at 40%, and a superiority margin of 5%, the calculated sample size for each arm is 371.

Statistical analysis

Participant characteristics will be summarized using frequencies and percentages. For two group comparisons, the Chi-squared test or Fisher's exact test will be used for categorical variables, and the U-Mann Whitney test will be used for continuous variables. For three group comparisons, the Chi-squared test will be used for categorical variables.

Primary outcomes are Vaccine Intention (VI) and VCI. VI is measured by the proportion of those who received the COVID-19 vaccine since the pre-survey, and those who have not

received the COVID-19 vaccine but answered “Yes” in the post-survey to the question “Do you intend to be vaccinated against COVID-19?” The difference in the proportion (post-intervention – pre-intervention) of vaccine intention will be assessed by Chi-square test. Vaccine confidence is quantified using Vaccine Confidence Index.[11] Changes in vaccine confidence across arms will be compared using a mixed effects logistic regression model by comparing proportions of participants who responded “strongly agree” or “tend to agree” to these specific questions on vaccine confidence. We will use R version 4.0.4 (R Development Core Team, Vienna) for statistical analysis. A p-value of 0.05 will be considered statistically significant.

Ethical approval

IRB was obtained in October 2021 from Kanto Central Hospital. Consent will be electronically obtained from all study participants.

Recruitment

September 2021: We contacted a Japanese Internet research service company (NTTCom Online Marketing Solutions Corporation).

October 2021: The screening survey was sent to 700,000 randomly selected persons in the panel on October 20, 2021 with the following five questions: (1) “How old are you?”; (2) “Have you received a COVID-19 vaccine?”; (3) “Do you intend to be vaccinated?” (with answer options of “Yes”, “Not sure but leaning towards Yes”, “Not sure but leaning towards No”, and “No”); (4) “Do you have LINE (one of the most popular messenger apps in Japan) installed on your mobile phone? If not, are you willing to download LINE to participate in this study?”; and, (5) “Are you capable of using Zoom (a videoconferencing app) for webinars?”.

November 5, 2021 - November 10, 2021: The study details and the consent form were sent through NTTCom to the possibly eligible research panel of NTTCom. Once the consent form was obtained electronically, they were sent the link to the questionnaires placed in a secured section of a website. A total of 99,965 persons responded to the screening questions between November 5 to November 10, 2021. Of them, 15,398 (15.4%) persons had not received the vaccine yet, of which 13,314 (86.5%) did not intend to be vaccinated. Among 13,314 eligible persons, 1,158 agreed to participate in the study, completed the pre-survey, and were randomly assigned to 3 different groups: 386 in the control group, 386 in the chatbot, and 386 in the webinar group.

Project summary

COVID-19 vaccination started in February 2021 in Japan, and the coverage is 26.4% of all populations in Japan as of 27 July 2021 (https://ourworldindata.org/covid-vaccinations). While the reasons behind the slow rollout might be mostly logistical issues, they are also likely rooted in public vaccine hesitancy.

To better understand how social media could be used to address vaccine hesitancy in Japan, we will conduct a randomized controlled trial (RCT) using social media interventions to increase the intention to receive COVID-19 vaccines (vaccine intention) and confidence in COVID-19 vaccines (vaccine confidence), targeting those ages 20 and older in Japan. Persons who meet the eligibility criteria will be randomized into the following groups: (i) a control group (with no exposure to the chatbot nor a webinar, (ii) a group with a free LINE chatbot providing information on COVID-19 vaccines; (iii) a group with free webinars where a health professional interactively provides participants with information on COVID-19 vaccines. Groups (ii) and (iii) will be provided with the assigned interventions over 5-6 weeks. All three groups will complete a pre- and post-survey online to investigate vaccine intention and confidence.

We will analyze how the LINE chatbot and webinars affect vaccine intention and vaccine confidence after these interventions. We will also compare the effectiveness of the LINE chatbot with that of a webinar to see which format (unidirectional vs. bidirectional) addresses vaccine hesitancy in Japan more effectively.

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Text S2: Pre-survey

1. What is your sex?
   a. Male
   b. Female
   c. Others (please state) _____
   d. Prefer not to say

2. How old are you?

Select a number (20-120)

3. What is your highest level of education?
   a. Elementary school or secondary school
   b. High school
   c. Professional or vocational qualification
   d. Bachelor's degree
   e. Master's degree
   f. Doctoral degree

4. Where do you live?

< Japan-specific answer options>

Select from 47 prefectures in Japan + Others (please state) _____

5. Are you employed currently?
   a. Full-time
   b. Part-time
   c. Unemployed
   d. Retired
   e. Student
   f. Others (please state) _____

6. Do you work in a healthcare setting currently?
   a. Yes, I work in a healthcare setting as a medical doctor

b. Yes, I work in a healthcare setting as a health professional other than a medical doctor

c. No. I do NOT work in a healthcare setting.

7. Do you have any of the following illnesses/diseases? (Select all that apply)

a. Chronic respiratory disease
b. Chronic heart disease (including hypertension)
c. Chronic kidney disease
d. Chronic liver disease (except for fatty liver or chronic hepatitis)
e. Diabetes treated with insulin or other oral medication, or diabetes with any complication
f. Blood disease (except for anemia)
g. Disease with immune suppression (including neoplasms, regardless of treatment)
h. Receiving treatment that may suppress the immune system (e.g. steroids)
i. Neurological or neuromuscular disease due to immune deficiency
j. Physical decline associated with a neurological disease or a neuromuscular disease (such as a respiratory disease)
k. Chromosomal abnormality
l. Severe psychosomatic disorder (overlapping severe physical disability and severe intellectual disability)
m. Depression/anxiety disorder
n. Sleep Apnea syndrome
o. Obesity (BMI over 30, which would typically be a person of 170cm height weighing 87kg, or 160cm height weighing 77kg)
p. No underlying health conditions
q. Others (please state) _____

8. Are you married?

a. Married
b. Never married
c. Divorced
d. Widowed
e. Others (please state) _____

9. What is your income?
a. Less than JPY 2 million
b. JPY 200 million < JPY 400 million
c. JPY 400 million < JPY 600 million
d. JPY 600 million < JPY 800 million
e. JPY 800 million or higher

10. Do you receive the influenza vaccine annually?
a. Yes
b. No
c. Unsure

11. Have you ever been diagnosed (tested positive or diagnosed by doctor) with COVID-19?
a. Yes
b. No
c. Unsure

12. Have you ever experienced a side effect or allergy after any vaccination?
a. Yes
b. No
c. Unsure

13. To what degree do you agree with the following statement?
"Overall, I think COVID-19 vaccines are important."
a. Strongly agree
b. Tend to agree
c. Do not know
d. Tend to disagree
e. Strongly disagree

14. To what degree do you agree with the following statement?
"Overall, I think COVID-19 vaccines are safe."
a. Strongly agree

b. Tend to agree
c. Do not know
d. Tend to disagree
e. Strongly disagree

15. To what degree do you agree with the following statement?
"Overall, I think COVID-19 vaccines are effective."

a. Strongly agree
b. Tend to agree
c. Do not know
d. Tend to disagree
e. Strongly disagree

16. How many children do you have in each of the following age ranges? If you do not have any children, please enter "0" for each range.

a. Age 0-5: 0-20 (dropdown list to select the number of children)
b. Age 6-11: 0-20
c. Age 12-18: 0-20
d. Age 19 or above: 0-20

17. (If you have at least one child) Do you want to have your child/children vaccinated against COVID-19, if it is indicated and available for them?

a. Yes, definitely.
b. Unsure, but leaning towards yes.
c. Unsure, but leaning towards no.
d. No, definitely not.
e. No, I do not have any children.

18. Which of the following, if any, might convince you to receive a COVID-19 vaccine? (can choose multiple)

a. Recommendation from a friend
b. Recommendation from a family member
c. Recommendation from a politician I like
d. Recommendation from a celebrity I like

e. Recommendation from the Government
f. Recommendation from a doctor or other healthcare worker
g. Others (please state) _____
h. Do not know

19. Have you encouraged any of the following to get a COVID-19 vaccine? (can choose multiple)

a. Spouse
b. Parent
c. Sibling
d. Son or daughter
e. Friend
f. Colleague
g. Others (please state) _____
h. I have not encouraged anyone to get a COVID-19 vaccine

20. Which of the following emotions have you experienced in the past two weeks? (can choose multiple)

a. Fear
b. Joy
c. Anger
d. Hope
e. Anxiety
f. Empathy
g. Grief
h. Trust
i. Others_____ [Free response]

21. To what degree do you agree with the following statements? Please place a checkmark in the box that applies to you.

Statement	Strongly Agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
I may get a COVID-19 infection within the next 6 months					
COVID-19 is a serious disease					
I believe that getting a COVID-19 vaccine will ease my anxiety					
I do not need to get a COVID-19 vaccine because I wash my hands frequently with soap or sanitizer, which can help prevent the spread of COVID-19					
I do not need to get a COVID-19 vaccine because I practice social distancing, which can help prevent the spread of COVID-19					
I believe that vaccines can help					

control the spread of COVID-19					
It is easy to find relevant information on COVID-19 vaccines					

22. To what degree do you agree with the following statement? Please place a checkmark in the box that applies to you.

Statement	Strongly Agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
I will get a COVID-19 vaccine if many others have received it.					
I will get a COVID-19 vaccine if a COVID-19 vaccine certificate or passport is required for work or school.					
I will get a COVID-19 vaccine if a COVID-19 vaccine certificate					

or passport is required for travel, social events, or dine-in.					
COVID-19 vaccination should be compulsory for all citizens in Japan					

23. In the past month, on average, how much time per day do you spend actively using social media?

a. None
b. Less than 10 minutes per day
c. More than 10–less than 30 minutes per day
d. More than 30–less than 60 minutes per day
e. More than 1 hour–less than 2 hours per day
f. More than 2 hours–less than 3 hours per day
g. More than 3 hours per day

24. In the past month, which social media platforms have you used? (Please choose all that apply.)

a. Facebook
b. Twitter
c. YouTube
d. WhatsApp
e. LINE
f. Facebook Messenger
g. Instagram
h. TikTok
i. LinkedIn
j. Others (please state) _____

25. In the past month, from which of these social media platforms did you receive information regarding COVID-19 vaccines? (Please choose all that apply.)

a. Facebook
b. Twitter
c. YouTube
d. WhatsApp
e. LINE
f. Facebook Messenger
g. Instagram
h. TikTok
i. LinkedIn
j. Others (please state) _____

26. Please rank your TOP THREE sources of information for learning about COVID-19 vaccines in order of trust (Please only select and rank the top three information sources, with 1 being the most trusted).

Ranked first:
Ranked second:
Ranked third:

a. National television (e.g. NHK)
b. Radio
c. International television (e.g. CNN, BBC)
d. Newspapers or magazines
e. Social media
f. National public health authorities (e.g. Ministry of Health, Labour and Welfare)
g. Healthcare workers
h. Religious leaders
i. International health authorities (e.g. World Health Organization)
j. Community organizations
k. Scientists
l. Government websites
m. The internet or search engines
n. Family and friends

o. Work, school, or college/university
p. Do not know
q. Others (please state) _____

27. Have you ever seen or heard any COVID-19-associated information on social media that might have persuaded you not to immunize yourself/your child/children against COVID-19?

a. Yes (please give us an example [free response])
b. No
c. Do not know

28. Decide whether *you think the following statement is true or false*.

	True	Unsure	False
Genetic recombination technology is used in a COVID-19 vaccine to cause changes in genes (chromosomes) through vaccination			
Many people have died after getting the COVID-19 vaccines			
COVID-19 vaccination is associated with infertility and/or miscarriage			
COVID-19 vaccination causes COVID-19 infection to those who receive the vaccines and the people around them			
COVID-19 vaccines were approved without completing the normal clinical trials approval process			
The safety of COVID-19 vaccines has not been confirmed yet because the clinical trials are not completed yet			
In animal experiments, many animals died after getting the COVID-19 vaccines			

29. Please tell us briefly why you responded “Unsure, but leaning towards yes”, “Unsure, but leaning towards no”, or “No, definitely not” for the screening question* that “Do you want to receive a COVID-19 vaccine in the future”?

_____ [Free response]

*(For your reference, the screening question was the following):
Do you want to receive a COVID-19 vaccine in the future?
a. Yes, definitely.
b. Unsure, but leaning towards yes.
c. Unsure, but leaning towards no.
d. No, definitely not.

30. Please tell us briefly what would change your mind about a COVID-19 vaccine so that you get vaccinated?

_____ [Free response]

Text S3: Post-survey

1. Have you received a COVID-19 vaccine?
   a. Yes
   b. No

   2. (For those who chose “a” for #1)
      Please tell us briefly what influenced your decision about a COVID-19 vaccine and the reason why you got vaccinated against COVID-19?
      _____ [Free response]

   3. (For those who chose “b” for #1)
      Do you want to receive a COVID-19 vaccine in the future?
      a. Yes, definitely.
      b. Unsure, but leaning towards yes.
      c. Unsure, but leaning towards no.
      d. No, definitely not.

      4. (For those who chose “a” for #3)
         Please tell us briefly what influenced your decision about a COVID-19 vaccine and the reason why you want to receive a COVID-19 vaccine?
         _____ [Free response]

      5. (For those who chose “b”, “c”, ”d” for #3)
         Please tell us briefly why you chose “the answer (b, c or d)” for #3?
         _____ [Free response]

6. Would you choose to receive an annual booster against COVID-19 if it is recommended?
   a. Yes, definitely.

b. Unsure, but leaning towards yes.
f. Unsure, but leaning towards no.
g. No, definitely not.

7. How many children do you have in each of the following age ranges? If you do not have any children, please enter "0" for each range.
   a. Age 0-5: 0-20 (dropdown list to select the number of children)
   b. Age 6-11: 0-20
   c. Age 12-18: 0-20
   d. Age 19 or above: 0-20

8. (if you have at least one child) Do you want to have your child/children vaccinated against COVID-19 if it is indicated and available for them?
   a. Yes, definitely.
   b. Unsure, but leaning towards yes.
   c. Unsure, but leaning towards no.
   d. No, definitely not.

9. (if you have at least one child) Please tell us briefly why you chose “the answer for #8”?
   _____ [Free response]

10. To what degree do you agree with the following statement?
    “Overall, I think COVID-19 vaccines are important”
    a. Strongly agree
    b. Tend to agree
    c. Do not know
    d. Tend to disagree
    e. Strongly disagree

11. To what degree do you agree with the following statement?
    “Overall, I think COVID-19 vaccines are safe.”

a. Strongly agree
b. Tend to agree
c. Do not know
d. Tend to disagree
e. Strongly disagree

12. To what degree do you agree with the following statement?
"Overall, I think COVID-19 vaccines are effective."
a. Strongly agree
b. Tend to agree
c. Do not know
d. Tend to disagree
e. Strongly disagree

13. Which of the following emotions have you experienced in the past two weeks? (can choose multiple)

a. Fear
b. Joy
c. Anger
d. Hope
e. Anxiety
f. Empathy
g. Grief
h. Trust
i. Others_____ [Free response]

14. To what degree do you agree with the following statement? Please place a check mark in the box that applies to you.

	Strongly Agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree

I may get a COVID-19 infection within the next 6 months					
COVID-19 is a serious disease					
I believe that getting a COVID-19 vaccine will ease my anxiety					
I do not need to get a COVID-19 vaccine because I wash hands frequently with soap or sanitizer, which can help prevent the spread of COVID-19					
I do not need to get a COVID-19 vaccine because I practice social distancing,					
I believe a vaccine can help control the spread of COVID-19					
It is easy to find relevant information on COVID-19 vaccines					

15. To what degree do you agree with the following statement? Please place a check mark in the box that applies to you.

	Strongly Agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
I will get a COVID-19 vaccine if many others have received it.					

I will get a COVID-19 vaccine if a COVID-19 vaccine certificate or passport is required for work or school.					
I will get a COVID-19 vaccine if a COVID-19 vaccine certificate or passport is required for travel, social events or dine-in.					
COVID-19 vaccination should be compulsory for all citizens in Japan					

16. Please rank your TOP THREE sources of information for learning about COVID-19 vaccines in order of trust (Please only select and rank the top three information sources, with 1 being the most trusted).

Ranked first:

Ranked second:

Ranked third:

a. National television (e.g. NHK)
b. Radio
c. International television (e.g. CNN, BBC)
d. Newspapers or magazines
e. Social media
f. Ministry of Health, Labour and Welfare
g. Healthcare workers
h. Religious leaders
i. International health authorities (e.g. World Health Organization)
j. Community organizations (e.g. local governments)
k. Scientists
l. Government websites
m. The internet or search engines
n. Family and friends
o. Work, school, or college/university

p. Others (please state) _____

17. Decide whether *you think the following statement is true or false*. Please place a check mark in a box that applies to you.

	True	Unsure	False
Genetic recombination technology is used in a COVID-19 vaccine to cause changes in genes (chromosomes) through vaccination			
Many people have died after getting the COVID-19 vaccines			
COVID-19 vaccination is associated with infertility and/or miscarriage			
COVID-19 vaccination causes COVID-19 infection to those who receive the vaccines and people around them			
COVID-19 vaccines were approved without completing the normal clinical trials approval process			
The safety of COVID-19 vaccines has not been confirmed yet because the clinical trials are not completed yet			
In animal experiments, many animals died after getting the COVID-19 vaccines			

Questions 18-22 are only applicable to those who are assigned to either chatbot or webinar.

18. (For chatbot group) On which platform would this chatbot be most helpful?(Select all that apply)
    a. Ministry of Health, Labour and Welfare website
    b. Health-related website operated by non-government
    c. SMS on your mobile phone

d. LINE
e. WhatsApp
f. Facebook Messenger
g. Skype message
h. Google Hangout
i. Other _____ [free response]

(For webinar group) On which platform would this webinar be most helpful? (Select all that apply)

a. Zoom
b. YouTube
c. Skype
d. Google Meet
e. Teams
f. Clubhouse
g. Face-to-face settings
h. Other_____ [free response]

19. What information were you seeking? (Check all that apply)

1. COVID-19 vaccine safety/side effects
2. COVID-19 vaccine effectiveness
3. How to receive a COVID-19 vaccine (e.g. whether you can choose the type of the vaccines, the length between first and second doses, etc.)
4. What life is like after you receive a COVID-19 vaccine (e.g. wearing masks after vaccination, taking a bath or driving on the day when you receive a vaccine, etc.)
5. Eligibility for COVID-19 vaccines
6. COVID-19 vaccine boosters
7. COVID-19 vaccines and pregnancy
8. COVID-19 new variants
9. Other ____ [free response]

20. To what degree do you agree with the following statement? Please place a check mark in the box that applies to you.

For chatbot-group

Statement	Strongly Agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
Overall, the chatbot was helpful/informative					
It was easy to register for the chatbot					
The design of the chatbot was user-friendly					
It was helpful to be able to access the chatbot anytime and anywhere					
It was easy to find the information I was searching for in the chatbot					
The chatbot comprehensively covered many types of questions					
I am satisfied with the chatbot's answer(s) to my question(s)					

It was helpful that the sources of the information are specified for each answer					
I like the design of the chatbot (font, color, etc.)					
I intend to use the chatbot again					
I intend to recommend the chatbot to others					

For webinar-group

Statement	Strongly Agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
Overall, the webinar was helpful/informative					
It was easy to register for the webinar					
The length of the webinar was long					
The length of the webinar was short					

I found the information I was searching for from the webinars					
I am satisfied with the webinars' answer(s) to my question(s)					
It was helpful to ask experts and get information in an interactive way					
I liked the group session format of the webinars (I prefer group sessions rather than one-on-one sessions)					
I intend to participate in the webinars again					
I intend to recommend the webinars to others					

21. What was most useful in the chatbot/webinar?
_____ Free response

22. Do you have suggestions to improve the chatbot/webinar?
_____ Free response

Figure S1. Corowa-kun's Consultation Room: a free messenger app chatbot, Japan

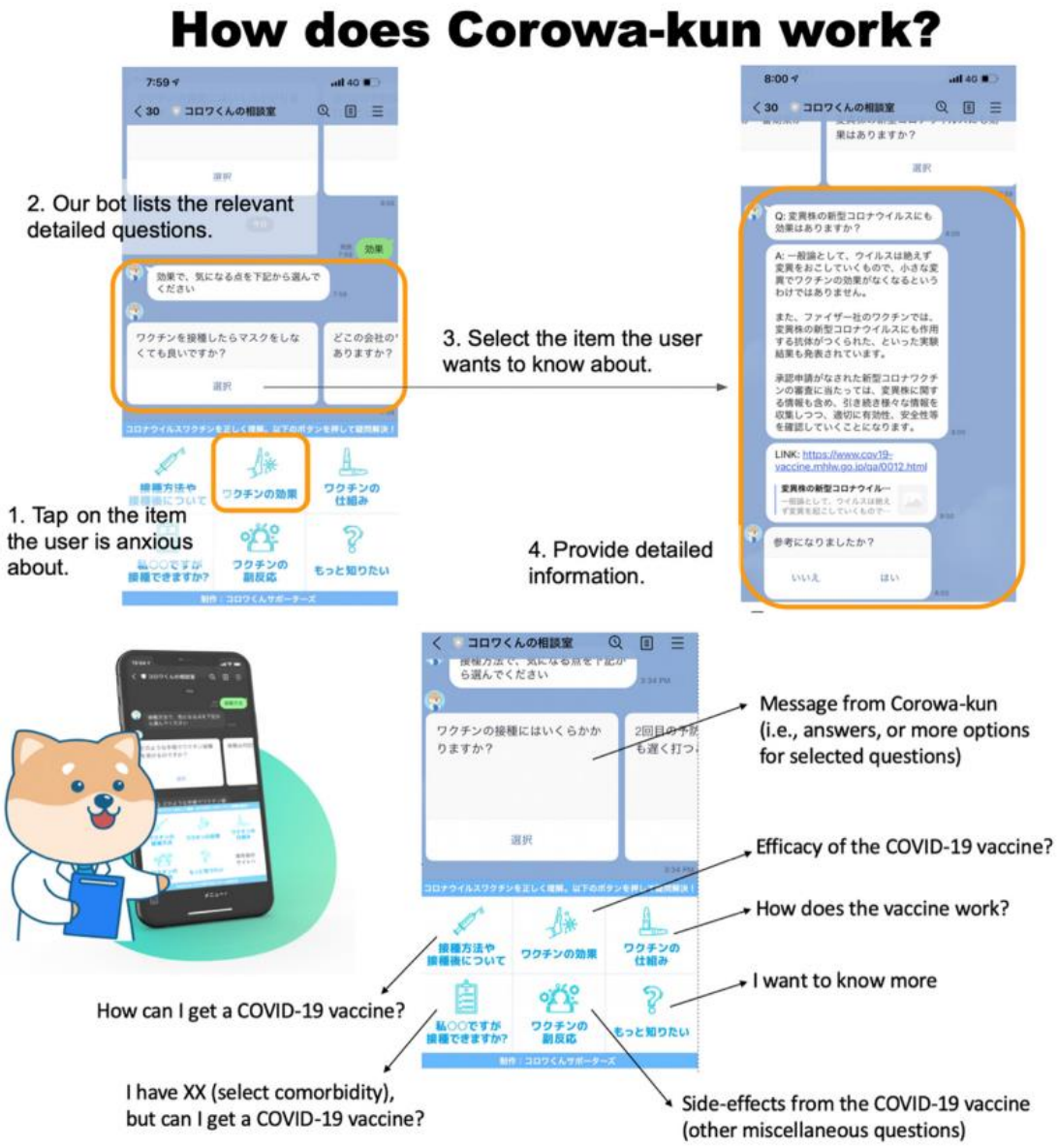

Table S1. Baseline participant characteristics and perceptions of COVID-19 vaccines by intervention groups.

All participants n=1158	Group 1 (control) n=386	Group 2 (chatbot) n=386	Group 3 (webinar) n=386
Characteristics			
Age (y), mean	44.7	45.8	46.2
Gender, % male	53.1	54.9	55.7
Education, %			
High school or less	28.5	26.7	32.9
Professional or vocational qualification	20.5	22.3	16.3
Bachelor's degree or above	51.0	51.0	50.8
Residential location, %			
Hokkaido	4.1	3.1	4.7
Tohoku	3.1	5.2	3.9
Kanto	44.3	47.4	44
Chubu	15.8	11.7	9.8
Kinki	18.9	18.7	24.1
Chugoku	5.7	3.4	4.7
Shikoku	0.8	1	2.1
Kyusyu	7.3	9.6	6.7
Employment, %			
Full-time	56.2	52.6	53.1
Part-time	16.3	16.3	19.7
Unemployed	15.8	18.4	16.8
Retired	2.3	3.6	3.1
Students	0.8	1.0	0.5
Others	8.5	8.0	6.7
Healthcare worker, %	4.7	3.1	3.1
Marital status, %			
Married	54.1	47.2	48.7

Never married	39.6	40.7	39.4
Divorced	6.0	11.4	10.4
Widowed	0.3	0.5	1.6
Others	0.0	0.3	0.0
Income, %			
< JPY 200 mil	31.6	37.6	36.5
JPY 200-399 mil	29.0	26.4	25.6
JPY 400-599 mil	21.8	19.7	23.3
JPY 600-799 mil	8.5	6.2	8.8
≥ JPY 800 mil	9.1	10.1	5.7
Underlying health conditions, %[b]	5.4	3.6	4.7
Usually received flu vaccine, %	17.4	11.7	17.1
Diagnosed with COVID-19, %	2.6	2.3	1.3
Ever experienced a side effect or allergy after any vaccination, %			
Yes	9.1	7.8	10.1
No	86.0	85.2	82.6
Unsure	4.9	7.0	7.3
How many children of the following age range? (mean)			
0-5y	0.12	0.15	0.16
6-11y	0.13	0.13	0.13
12-18y	0.19	0.17	0.12
≥19y	0.34	0.41	0.40
Which might convince you to take a COVID-19 vaccine? (%)			
Recommendation from a friend	7.8	6.5	4.7
Recommendation from a family member	15.3	14.0	14.2
Recommendation from a politician that I like	0.8	0.5	0.0

Recommendation from a celebrity that I like	1.8	1.6	1.8
Recommendation from the Government	4.4	2.3	2.8
Recommendation from a doctor or other healthcare worker	28.2	22.5	21.2
Have you personally encouraged any of the following to take a COVID-19 vaccine? (%)			
Spouse	5.4	2.6	3.6
Parent	6.0	4.1	3.1
Sibling	0.0	0.3	1.3
Son or daughter	1.0	0.8	1.6
Friend	2.3	0.5	0.0
Colleague	1.6	0.3	0.3
I have not personally encouraged anyone to take a COVID-19 vaccine	87.3	92.5	92.5
Which of the following emotions have you experienced in the past two weeks? (%)			
Fear	16.3	15.8	15.8
Joy	49.7	51.3	48.4
Anger	42.2	42.2	38.1
Hope	27.7	28.0	25.4
Anxiety	65.0	64.0	63.7
Empathy	28.2	33.2	33.4
Grief	27.5	29.5	30.3
Trust	21.5	19.9	19.4
I may get COVID-19 infection within the next 6 months, %			
Strongly agree	1.8	1.0	2.1
Agree	6.7	6.7	5.7
Neither agree nor disagree	42.5	44.6	40.2
Disagree	25.9	24.9	26.4
Strongly disagree	23.1	22.8	25.6

COVID-19 is a serious disease, %			
Strongly agree	14.0	17.1	16.8
Agree	29.5	28.0	31.1
Neither agree nor disagree	31.3	30.3	25.4
Disagree	14.5	13.0	14.8
Strongly disagree	10.6	11.7	11.9
I believe that getting a COVID-19 vaccine will ease my anxiety, %			
Strongly agree	0.8	1.3	1.3
Agree	7.5	7.0	7.8
Neither agree nor disagree	34.5	32.9	29.8
Disagree	23.6	26.2	25.6
Strongly disagree	33.7	32.6	35.5
I do not need to take a COVID-19 vaccine because I wash hands frequently with soap or sanitizer, which can help prevent the spread of COVID-19, %			
Strongly agree	8.0	5.7	7.0
Agree	14.2	16.6	12.2
Neither agree nor disagree	50.8	51	48.7
Disagree	19.7	18.7	20.2
Strongly disagree	7.3	8.0	11.9
I do not need to take a COVID-19 vaccine because I practice social distancing, which can help prevent the spread of COVID-19, %			
Strongly agree	7.3	3.9	6.5
Agree	12.4	16.1	13.0
Neither agree nor disagree	54.9	53.4	47.2
Disagree	18.4	18.9	21.8
Strongly disagree	7.0	7.8	11.7

I believe a vaccine can help control the spread of COVID-19, %			
Strongly agree	5.4	5.4	3.4
Agree	30.8	29.0	35.8
Neither agree nor disagree	39.6	41.5	36
Disagree	11.7	9.8	12.4
Strongly disagree	12.4	14.2	12.4
It is easy to find relevant information on COVID-19 vaccines, %			
Strongly agree	4.1	5.4	3.9
Agree	19.2	19.4	21.8
Neither agree nor disagree	48.4	48.2	42.7
Disagree	19.2	19.7	22.0
Strongly disagree	9.1	7.3	9.6
I will take a COVID-19 vaccine if many others have taken it, %			
Strongly agree	1.3	0.8	1.6
Agree	12.7	10.6	13.7
Neither agree nor disagree	30.8	33.4	23.6
Disagree	24.9	24.9	28.8
Strongly disagree	30.3	30.3	32.4
I will take a COVID-19 vaccine if a COVID-19 vaccine certificate or passport were required for work or school, %			
Strongly agree	6.7	6.7	5.4
Agree	29.0	26.2	30.8
Neither agree nor disagree	29.5	33.9	28.8
Disagree	14.8	12.7	13.5
Strongly disagree	19.9	20.5	21.5
I will take a COVID-19 vaccine if a COVID-19 vaccine certificate or passport were required for travel, social events or dine-in, %			

Strongly agree	6.0	4.7	6.2
Agree	23.3	22.3	25.6
Neither agree nor disagree	30.1	33.2	25.1
Disagree	17.4	16.8	18.4
Strongly disagree	23.3	23.1	24.6
COVID-19 vaccination should be compulsory for all citizens in Japan, %			
Strongly agree	1.0	0.8	1.3
Agree	2.8	2.1	2.3
Neither agree nor disagree	23.1	19.4	18.4
Disagree	18.7	23.6	19.9
Strongly disagree	54.4	54.1	58.0
In the past month, on average, how much time per day have you spent actively using social media? (%)			
None	9.3	9.3	9.1
Less than 10 min	19.4	23.1	22.0
More than 10 min–less than 30 min	20.5	26.2	23.3
More than 30 min–less than 60 min	18.9	14.5	18.7
More than 1 hour–less than 2 hours	16.3	13.2	11.7
More than 2 hours–less than 3 hours	6.2	5.4	3.4
More than 3 hours per day	9.3	8.3	11.9
In the past month, what social media platforms have you usually used? (%)			
Facebook	34.5	35.8	36.8
Twitter	54.4	57.5	57.8
YouTube	73.3	77.7	75.1
WhatsApp	2.1	0.8	0.8
LINE	81.9	86.5	83.9
Facebook Messenger	10.9	11.7	12.7
Instagram	47.2	43.8	43.5
TikTok	9.3	10.4	7.5

LinkedIn	1.8	1.6	1.3
Don't use social media	2.6	2.8	3.6
In the past month, from which of these social media platforms have you received information regarding COVID-19 vaccine from? (%)			
Facebook	8.0	7.5	10.1
Twitter	23.2	19.2	25.1
YouTube	22.0	21.2	23.3
WhatsApp	0.0	0.3	0.0
LINE	15.8	13.0	16.1
Facebook Messenger	0.8	0.5	2.1
Instagram	7.5	6.7	7.3
TikTok	1.8	1.6	2.6
LinkedIn	0.5	0.3	0.0
Not received information from social media	57.0	59.6	52.6
Have you ever seen or heard any COVID-19 associated information on social media that might have persuaded you not to immunize yourself/your child/children against COVID-19? (%)			
Yes	34.2	37.8	40.4
No	44.6	39.9	38.3
Don't know	21.2	22.3	21.2
Genetic recombination technology is used in COVID-19 vaccine to cause changes in genes (chromosomes) through vaccination, %			
True	16.3	19.4	12.4
Unsure	59.8	56.2	64.0
False	23.8	24.4	23.6

Many people have died after getting the COVID-19 vaccines, %			
True	46.1	43.5	42.5
Unsure	37.3	38.1	40.2
False	16.6	18.4	17.4
COVID-19 vaccination is associated with infertility and/or miscarriage, %			
True	14.2	17.4	11.9
Unsure	62.7	60.4	63.7
False	23.1	22.3	24.4
COVID-19 vaccination causes COVID-19 infection to those who receive the vaccines and people around them, %			
True	11.1	12.7	13.5
Unsure	44.3	41.2	41.7
False	44.6	46.1	44.8
COVID-19 vaccines were approved without completing the normal process of the clinical trial, %			
True	40.2	46.1	42.7
Unsure	41.7	36.3	35.8
False	18.1	17.6	21.5
The safety of COVID-19 vaccines has not been confirmed yet because the clinical trial is not completed yet, %			
True	49.7	52.6	48.2
Unsure	38.3	32.9	37.0
False	11.9	14.5	14.8
In animal experiments, many animals died after getting the COVID-19 vaccines, %			
True	19.4	16.3	18.9
Unsure	61.4	67.9	58.5
False	19.2	15.8	22.5

Perception of COVID-19 vaccine			
Do you want to receive a COVID-19 vaccine in the future? (%)			
Yes, definitely (Screened out)	0	0	0
Unsure, but leaning towards yes	21.8	18.9	20.7
Unsure, but leaning towards no	34.2	33.9	34.7
No, definitely not.	44.0	47.2	44.6
COVID-19 vaccines are important, %			
Strongly agree	7.3	6.0	6.7
Tend to agree	29.8	27.7	29.0
Do not know	31.3	36.0	32.6
Tend to disagree	15.0	16.4	16.3
Strongly disagree	16.6	14.2	15.3
COVID-19 vaccines are safe, %			
Strongly agree	0.5	1.6	0.8
Tend to agree	8.5	8.5	9.3
Do not know	38.3	38.9	37.3
Tend to disagree	25.9	28.0	28.5
Strongly disagree	26.7	23.1	24.1
COVID-19 vaccines are effective, %			
Strongly agree	3.9	4.7	3.9
Tend to agree	36.5	36.5	35.5
Do not know	33.7	34.5	32.1
Tend to disagree	10.6	12.2	16.3
Strongly disagree	15.3	12.2	12.2

[a] Chi-square or Fisher's exact test

[b] According to the response "No underlying health conditions" only. Some participants reported both "Chronic respiratory disease / Chronic heart disease" and "No underlying health conditions

Table S2. Full logistic model results for between-arms comparison of vaccine intention and confidence after interventions under an intention-to-treat analysis. Missing outcomes were imputed using multiple imputation method.

All participants (n=1158)	Group 2 (chatbot) vs. Group 1 (control) OR (95% CI)	Group 3 (webinar) vs. Group 1 (control) OR (95% CI)
Willing to be vaccinated [a]		
Constant	0.2 (0.2, 0.3)	0.2 (0.2, 0.3)
Group difference	0.8 (0.5, 1.3)	1.1 (0.7, 1.6)
Improvement in vaccine confidence [b]		
COVID-19 vaccines are important		
Constant	0.2 (0.1, 0.2)	0.2 (0.1, 0.2)
Baseline confidence in vaccine importance	13.2 (8.9, 19.6)	13.8 (9.2, 20.5)
Group difference	1.3 (0.9, 2.0)	1.8 (1.2, 2.8)
COVID-19 vaccines are safe		
Constant	0.1 (0.1, 0.1)	0.1 (0.1, 0.1)
Baseline confidence in vaccine safety	14.1 (7.8, 25.4)	11.0 (6.1, 19.7)
Group difference	1.1 (0.7, 1.9)	1.6 (1.0, 2.6)
COVID-19 vaccines are effective		
Constant	0.1 (0.1, 0.2)	0.1 (0.1, 0.2)
Baseline confidence in vaccine effectiveness	11.8 (8.0, 17.4)	11.0 (7.5, 16.2)
Group difference	1.4 (0.9, 2.1)	2.2 (1.4, 3.4)

[a] Including those who have received a COVID-19 vaccine or not received a COVID-19 vaccine but are willing

[b] Difference in % (post-intervention vs. pre-intervention) of those who responded “strongly agree” or “tend to agree.” (Other responses were “do not know,” “tend to disagree,” “strongly disagree”)

Table S3. Association between chatbot access and vaccine intention and confidence.

	No. of chatbot accesses, median (IQR)		p-value[a]
Group 2 (chatbot) (n=231)	Yes	No	
Willing to be vaccinated[b]	15 (9-29)	9 (6-13)	<0.001
Vaccine confidence index after chatbot use			
COVID-19 vaccines are important	10 (7-15)	10 (7-15)	0.158
COVID-19 vaccines are safe	12 (10-14)	9 (6-15)	0.510
COVID-19 vaccines are effective	10 (7-17)	9 (6-14)	0.208
Perceptions of COVID-19 or vaccination after chatbot use			
Willing to vaccinate their child/children against COVID-19	12 (9-16)	10 (7-14)	0.046
I may get COVID-19 infection within the next 6 months	11 (7-15)	10 (6-15)	0.151
COVID-19 is a serious disease	11 (7-16)	9 (6-13)	0.632
I believe that getting a COVID-19 vaccine will ease my anxiety	13 (10-18)	9 (6-14)	0.837
I do not need to take a COVID-19 vaccine because I wash hands frequently with soap or sanitizer, which can help prevent the spread of COVID-19	9 (7-13)	10 (6-15)	0.538
I do not need to take a COVID-19 vaccine because I practice social distancing, which can help prevent the spread of COVID-19	9 (7-13)	10 (6-15)	0.749
I believe a vaccine can help control the spread of COVID-19	11 (7-16)	9 (6-15)	0.573
It is easy to find relevant information on COVID-19 vaccines	12 (7-18)	9 (6-14)	0.397

I will take a COVID-19 vaccine if many others have taken it.	12 (9-15)	10 (6-15)	0.050
I will take a COVID-19 vaccine if a COVID-19 vaccine certificate or passport were required for work or school.	12 (8-16)	9 (5-14)	0.456
I will take a COVID-19 vaccine if a COVID-19 vaccine certificate or passport were required for travel, social events or dine-in	10 (7-15)	10 (6-15)	0.088
COVID-19 vaccination should be compulsory for all citizens in Japan	10 (9-12)	10 (6-15)	0.476

[a] Difference in willingness to be vaccinated was assessed by logistic regression model; changes in VCI and perception of COVID-19 or vaccination were assessed by mixed effects logistic regression model. Both models used logarithm of the number of chatbot access due to the skewness of the access distribution.

[b] Including those who have received a COVID-19 vaccine or not received a COVID-19 vaccine but are willing.

Table S4. Association between webinar attendance and vaccine intention and confidence.

	Duration of webinar attendance (minutes), median (IQR)		p-value[a]	No. who attended webinar sessions, median (IQR)		p-value[a]
Group 3 (webinar) (n=207)	Yes	No		Yes	No	
Willing to be vaccinated [b]	52 (41-65)	61 (44-70)	0.211	1 (1-1)	1 (1-1)	0.373
Vaccine confidence index after webinar use						
COVID-19 vaccines are important	60 (44-67)	58 (43-70)	0.798	1 (1-1)	1 (1-1)	0.959
COVID-19 vaccines are safe	61 (43-71)	59 (44-70)	0.096	1 (1-1)	1 (1-1)	0.154
COVID-19 vaccines are effective	60 (45-67)	58 (42-70)	0.378	1 (1-1)	1 (1-1)	0.457

[a] Difference in willingness to be vaccinated was assessed by logistic regression model; changes in vaccine confidence index and perception to COVID-19 or vaccination were assessed by mixed effects logistic regression model. Both models used logarithm of the number of webinar attendance access due to the skewness of the access distribution.

[b] Including those who have received COVID-19 vaccine or not taken COVID-19 vaccine but willing to received.

Table S5: Vaccine intention among participants with and without improvement in vaccine confidence after intervention under an intention-to-treat analysis. Missing outcomes were imputed using multiple imputation method.

	Willing to be vaccinated[a]		
All participants (n=1158)	Group 1 (control) n=386 (%)	Group 2 (chatbot) n=386 (%)	Group3 (webinar) n=386 (%)
Improvement in vaccine confidence [b]			
COVID-19 vaccines are important			
Improved	9.6	14.9	25.2
Did not improve	19.4	15.5	18.7
COVID-19 vaccines are safe			
Improved	50.8	37.8	36.4
Did not improve	16.3	13.7	17.8
COVID-19 vaccines are effective			
Improved	27.8	23.7	25.9
Did not improve	17.8	14.5	18.6

[a] Including those who have received a COVID-19 vaccine or not received a COVID-19 vaccine but are willing
[b] Improvement in vaccine confidence refers to those who responded “do not know,” “tend to disagree,” “strongly disagree” pre-intervention and responded “strongly agree” or “tend to agree.” post-intervention.

Table S6. Vaccine intention and confidence after interventions under a per-protocol analysis.

All participants (n=797)	Group 1 (control) n=359 (%, 95% CI)	Group 2 (chatbot) n=231 (%, 95% CI)	Group3 (webinar) n=207 (%, 95% CI)	Group 2 vs. Group 1		Group 3 vs. Group 1	
				OR (95% CI)	p-value[a]	OR (95% CI)	p-value[a]
Willing to be vaccinated[b]	18.7 (14.6, 22.7)	14.7 (10.1, 19.3)	18.8 (13.5, 24.2)	0.8 (0.5, 1.2)	0.215	1.0 (0.7, 1.6)	0.958
Change in vaccine confidence[c]							
COVID-19 vaccines are important	-2.2 (-9.2, 4.8)	-0.8 (-9.7, 7.9)	8.7 (-0.7, 18.1)	1.1 (0.7, 1.7)	0.659	2.0 (1.3, 3.1)	0.002
COVID-19 vaccines are safe	1.9 (-2.5, 6.4)	1.7 (-4.1, 7.6)	4.8 (-1.4, 11.1)	1.1 (0.6, 1.9)	0.797	1.4 (0.8, 2.4)	0.241
COVID-19 vaccines are effective	-8.1 (-15.1, -1.0)	-3.5 (-12.5, 5.5)	5.3 (-4.3, 14.9)	1.4 (0.9, 2.2)	0.086	2.3 (1.5, 3.5)	<0.001

[a] Assessed by logistic regression model.
[b] Including those who have received a COVID-19 vaccine or not received a COVID-19 vaccine but are willing.
[c] Difference in % (post-intervention vs. pre-intervention) of those who responded “strongly agree” or “tend to agree.” (Other responses were “do not know,” “tend to disagree,” “strongly disagree”)

Table S7. Baseline participant characteristics and perceptions of COVID-19 vaccines by chatbot and webinar groups and completion of intervention.

	Group 2 (chatbot) n=386		Group 3 (webinar) n=386	
Participants in the chatbot and webinar groups n=772	Intervention completed, n=231	Non-compliant, n=155	Intervention completed, n=207	Non-compliant, n=179
Characteristics				
Age (y), mean	45.0	46.9	44.6	48.0
Gender, % male	51.5	60.0	50.1	61.5
Education, %				
High school or less	24.7	29.7	32.9	33.0
Professional or vocational qualification	22.5	21.9	14.5	18.2
Bachelor's degree or above	52.8	48.4	52.7	48.6
Employment, %				
Full-time	48.9	58.1	53.1	53.1
Part-time	16.0	16.8	18.0	20.7
Unemployed	20.8	14.8	17.9	15.6
Retired	3.9	3.2	2.4	3.9
Students	0.9	1.3	0.5	0.6
Others	9.5	5.8	7.2	6.1
Healthcare worker, %	2.6	3.9	1.9	4.5
Marital status, %				
Married	48.9	44.5	50.2	46.9
Never married	43.3	36.8	38.6	40.2
Divorced	6.5	18.7	10.6	10.1
Widowed	0.9	0.0	0.5	2.8
Others	0.4	0.0	0.0	0.0
Income, %				
< JPY 200 mil	35.1	41.3	40.1	32.4
JPY 200-399 mil	28.6	23.2	19.3	33.0
JPY 400-599 mil	19.9	19.4	23.2	23.5

JPY 600-799 mil	6.9	5.2	11.1	6.1
≥ JPY 800 mil	9.5	11.0	6.3	5.0
Underlying health conditions, %	2.6	3.9	1.9	4.5
Usually received flu vaccine, %	13.4	9.0	16.9	17.3
Diagnosed with COVID-19, %	3.0	1.3	1.9	0.6
Ever experienced a side effect or allergy after any vaccination, %				
Yes	10.0	4.5	11.6	8.4
No	85.3	85.2	80.7	84.9
Unsure	4.8	10.3	7.7	6.7
Perception of COVID-19 vaccine				
Do you want to receive a COVID-19 vaccine in the future? (%)				
Yes, definitely (Screened out)	0	0	0	0
Unsure, but leaning towards yes	18.2	20.0	20.8	20.7
Unsure, but leaning towards no	36.4	30.3	33.3	36.3
No, definitely not.	45.5	49.7	45.9	43.0
COVID-19 vaccines are important, %				
Strongly agree	8.2	2.6	5.3	8.4
Tend to agree	29.0	25.8	31.4	26.3
Do not know	35.1	37.4	32.9	32.4
Tend to disagree	13.4	20.0	15.0	17.9
Strongly disagree	14.3	14.2	15.5	15.1
COVID-19 vaccines are safe, %				
Strongly agree	0.9	2.6	0.5	1.1
Tend to agree	10.0	6.5	9.2	9.5
Do not know	39.4	38.1	36.2	38.5
Tend to disagree	26.8	29.7	30.9	25.7
Strongly disagree	22.9	23.2	23.2	25.1
COVID-19 vaccines are effective, %				
Strongly agree	5.6	3.2	2.4	5.6
Tend to agree	38.1	34.2	40.1	30.2
Do not know	33.8	35.5	30.4	34.1

Tend to disagree	10.0	15.5	15.0	17.9
Strongly disagree	12.6	11.6	12.1	12.3