

Factors Influencing the Acceptance of COVID-19 Vaccines in a Country With a High Vaccination Rate

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Abstract

Control of the COVID-19 pandemic largely depends on the effectiveness of the vaccination process. Understanding the factors that underlie the willingness to accept vaccination contributes pivotal information to control the pandemic. We analyzed the association between the willingness to accept the COVID-19 vaccines available and vaccine determinants amidst the Chilean vaccination process. Individual-level survey data was collected from 744 nationally representative respondents and multivariate regression models were used to estimate the association between outcome and explanatory variables. We found that trust in COVID-19 vaccines, scientists, and medical professionals increased the willingness to: accept the vaccines, booster doses, annual vaccinations, and the vaccination of children. Our results are critical to understanding the acceptance of COVID-19 vaccines in the context of a country with one of the world's highest vaccination rates. We provide information for decision-making and policy design, as well as guidelines regarding how to effectively explain vaccination programs to citizens.

Introduction

The sudden entry of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) into the human population in 2019 has had catastrophic consequences, with global deaths reaching over 4.8 million worldwide^{1,2}. In March 2020, the World Health Organization declared the coronavirus disease 2019 (COVID-19) a pandemic. In Chile, the first reported case of COVID-19 occurred in March 2020. Community transmission of the virus caused the peak of the first wave of COVID-19 cases in June 2020³. Non-pharmaceutical interventions were key to slow down the pandemic in Chile and prevent further deaths; as of October 2021, a total of 37,000 people died in Chile due to COVID-19.

Worldwide, non-pharmaceutical interventions, such as mask use, lockdowns and social distancing helped to slow down the pandemic until vaccines became available. The remarkably rapid development of vaccines against SARS-CoV-2 is turning COVID-19 into a preventable disease⁴. However, several challenges regarding the COVID-19 vaccination process remain to be addressed, including the hesitance to accept the vaccines. The first vaccine approved for emergency use in Chile was the Pfizer (BNT162b2) on December 16, 2020. The second vaccine approved by the Chilean authorities for emergency use, was the virion-inactivated CoronaVac vaccine, on January 20, 2021. CoronaVac has been the most widely used vaccine in Chile, with over 20 million doses administered, followed by Pfizer, with over 7 million doses by the end of September 2021. Studies have shown a high effectiveness of CoronaVac in preventing symptomatic COVID-19, hospitalizations and death⁵. Recently, emergency use authorization was also granted for the Oxford-AstraZeneca (ChAdOx1), Johnson & Johnson (Ad26.COV2), CanSino (Ad5-nCoV) and Sputnik V (GAM-COVIDVac) in Chile.

The success of the vaccination process strongly depends upon underlying social factors, mainly the willingness to accept the vaccination, trust in stakeholders related to the vaccination, vaccine-specific factors, communication and media, historical influences, religion, gender, socioeconomic status, politics, geographic barriers, prior experience with vaccinations, risk perception, and design of the vaccination

program⁶. Some studies have utilized surveys to explore the acceptance of COVID-19 vaccines in different countries, including the United States⁷⁻⁹, the United Kingdom⁹⁻¹¹, China^{12,13}, Indonesia¹⁴, Italy¹⁵, Ireland¹⁰ and Japan¹⁶. In addition, surveys have explored vaccine acceptance in groups of European countries¹⁷, Arab countries^{18,19} and other countries worldwide²⁰. Several of these studies have concluded that the willingness to accept a COVID-19 vaccine differs depending on the age, educational and economic level, credibility in government decisions and the perceived risk of the COVID-19 disease^{7,12,18,20-22}. In a global vaccine study carried out in 19 countries, responses were reported to have been highly heterogeneous, depending on the country surveyed²⁰; therefore, it is important to understand the acceptance of a vaccine in the context of specific countries or regions²². Vaccination against SARS-CoV-2 remains a serious challenge for most countries worldwide, especially those with poor economies. Countries with broad vaccination coverage can offer key lessons in terms of how to address the challenges regarding the COVID-19 vaccination process. In this context, the Chilean COVID-19 vaccination campaign has emerged as one of the most successful and rapid worldwide²³. By July 2021, Chile was among the first countries in the world with more doses administered per 100 people¹. However, as observed in Chile and many other countries, the vaccination rate slowed down after more than 70% of the population was fully immunized (one or two doses depending on the type of vaccine).

Understanding the determinants of vaccine acceptance is key for decision-making, establishing diverse strategies according to the characteristics and social determinations of the population, and identifying the subjectivities that underlie the decision to vaccinate. Faced with the need to obtain scientific evidence amidst the Chilean vaccination campaign, we analyzed the association between the level of willingness to accept a COVID-19 vaccine and determinants of the vaccines in Chile.

We focused on how trust in vaccines, stakeholders and people's perceptions regarding the effectiveness of prevention practices, the risk of infection, and possible side effects of vaccines were related to their willingness to accept a SARS-CoV-2 vaccine, a booster dose, an annual vaccination, and the vaccination of children. Socio-demographic variables associated with the acceptance of the vaccination process were also evaluated. Our study identified several key aspects, such as a high trust in scientists and health workers, as well as a moderate trust in the media. Our results aid in identifying the subjective dimensions related to the population's decision to be vaccinated, offering keystone evidence that could help other countries face this pandemic. The information provided by our study is also relevant to improve public health communication strategies.

Results

Between May 21 and June 21 of 2021, a total of 744 adults in Chile were interviewed via online surveys. The self-administered questionnaire was distributed through social networks. A summary of the socio-demographic characteristics of the respondents included in this study is shown in Supplementary Table 1. The questions were aimed at estimating four outcome variables related to the willingness to accept: (i) a SARS-CoV-2 vaccination (0=not, 1=maybe, 2=yes), (ii) a vaccine booster dose (1=yes), (iii) an annual

vaccination (1=not willing to 4=highly willing), and (iv) the vaccination of children (1=definitively no to 4=definitively yes). The questionnaire also included, as explanatory variables, a set of variables of trust and perceptions associated with the vaccination process. These questions were aimed at describing the perception of risk and trust, and responses were also recorded on a 3 or 4-point ordinal scale of agreement or disagreement. For instance, trust in the different COVID-19 vaccine stakeholders was estimated using the scale: "No trust", "Little trust", "Some trust", "High trust". The full questionnaire is shown in the Supplementary Information. In addition, Supplementary Table 2 indicates milestones that occurred during the data collection period, according to the development of the pandemic and vaccination process in Chile.

Most of the respondents (93.4% n= 695) had received at least one dose of a SARS-CoV-2 vaccine at the time of the survey (mainly CoronaVac and Pfizer), whereas 3.9% (n=29) had not yet decided if they would accept a SARS-CoV-2 vaccine and 2.7% (n=20) affirmed they would definitely not accept a SARS-CoV-2 vaccine. When asked if they would accept a hypothetical booster dose, 88.2% (n=656) of the respondents reported that they would accept and 57.8% (n=430) affirmed they would definitely accept a yearly vaccination if necessary, similar to the vaccine schedule for the influenza virus. When asked if, in the case of having children under 16 years old, they would accept that their children could be vaccinated against SARS-CoV-2, 62.5% (n=175) reported that they would "definitively accept" a SARS-CoV-2 vaccine for their children.

Multivariate regression models were used to estimate the association between the outcome and explanatory variables. An ordered logistic regression model was adjusted to analyze the outcome variables related to the willingness to accept a SARS-CoV-2 vaccine, an annual vaccination, and the vaccination of children, while a logistic regression model was used to analyze the willingness to accept a booster dose. Besides estimating the associations among the entire sample of individuals (n=744), we also analyzed if factors varied their associations when comparing samples of men (n=260) and women (n=484) as well as samples of young adults (18-29 years old, n=206) and adults (30-59, n=503). We excluded the sample of elderly people (>59 years old) only in this analysis because of the small sample (n=35). For each outcome variable, we selected the model with the best goodness of fit and parsimony using the Akaike information criterion (AIC) (Supplementary Table 3).

We computed the odds ratio for selected models, which represents the ratio of the odds that an outcome variable will occur given an explanatory variable compared to the odds of the outcome occurring in the absence of the explanatory variable. If an odds ratio is greater than 1, then an explanatory variable induces a higher level of acceptance, relative to the control of other variables used in the model. On the other hand, an odds ratio less than 1 suggests that an explanatory variable influences a lower willingness. We described only those results where the 95% confidence intervals excluded zero, which were deemed statistically credible. Although our models did not measure causal effects, log cumulative odds ratios showed how the variables related to willingness responded to variables of perception and trust or how the associations varied among genders or age groups. The access to self-reported

perceptions provided correlational evidence regarding which factors explained a greater willingness to accept the SARS-CoV-2 vaccination process.

Trust in SARS-CoV-2 vaccines increased the willingness to accept a SARS-CoV-2 vaccine, booster dose, annual vaccination and vaccination of children.

People's trust varied in relation to the vaccine in question (Kruskal-Wallis test: Chi-squared=509, d.f.=5, $p<0.001$) (Fig. 1A). While the reported trust did not differ between the CoronaVac and Pfizer vaccines (Dunn's test with Bonferroni adjustment: $z=-1.77$, $p=0.57$), the trust in the both Pfizer and CoronaVac vaccines was significantly greater than that in the other four vaccines approved by Chilean authorities (Dunn's test with Bonferroni adjustment between Pfizer vs. CanSino $z=14.1$, $p<0.001$; vs. AstraZeneca $z=14.6$, $p<0.001$; vs. Sputnik V $z=16.1$, $p<0.001$; vs. Johnson & Johnson $z=14.6$, $p<0.001$); and between CoronaVac vs. CanSino $z=12.5$, $p<0.001$; vs. AstraZeneca $z=12.9$, $p<0.001$; vs. Sputnik $z=14.5$, $p<0.001$; vs. Johnson $z=13.0$, $p<0.001$) (Fig. 1A). There were no differences in the reported trust in the AstraZeneca, CanSino, Sputnik V and Johnson & Johnson vaccines. In spite of the differences found in the trust of the aforementioned vaccines, trust in all of the vaccines was retained in one factor (Factor Analysis: Eigenvalue of Factor 1=3.6; LR test: chi-squared=2032.1, $p<0.001$), with a very high reliability coefficient (Cronbach's $\alpha=0.89$). We therefore took the average of the trust in all of the vaccines to create a variable of overall trust in vaccines against SARS-CoV-2 and used it in the multivariate regression models.

Multivariate models suggest that the increase of one unit value in trust of SARS-CoV-2 vaccines increased 4.1 times the willingness to accept SARS-CoV-2 vaccines (95%CI=2.0-8.2, $p<0.001$), 3.2 times the willingness to accept a booster dose (95%CI=1.8-5.6, $p<0.001$), twice the willingness to accept an annual vaccination (95%CI=1.6-2.8, $p<0.001$), and 1.9 times the willingness to vaccinate children (95%CI=1.4-2.6, $p<0.001$) (Table 1, row [a]). When comparing results between genders, women showed significant associations among all of the willingness variables with trust in SARS-CoV-2 vaccines (Supplementary Table 4). On the other hand, men showed a significant association between the willingness to accept the annual vaccination and trust in SARS-CoV-2 vaccines (Supplementary Table 4). Interestingly, it was observed, in both young adults and adults, that an increase of trust in SARS-CoV-2 vaccines induced a higher willingness to receive a SARS-CoV-2 vaccination, booster dose, annual vaccination and the vaccination of children (Supplementary Table 5).

Trust in scientists and medical professionals increased the acceptance of a SARS-CoV-2 vaccination, booster dose, annual vaccination, and the vaccination of children, while trust in religious leaders reduced the willingness to accept an annual vaccination and the vaccination of children.

People's trust in stakeholders varied significantly (Kruskal-Wallis test: 2285.9, d.f.=8, $p<0.001$) (Fig. 1B). Scientists received the highest score of trust among all of the stakeholders included in the study (Dunn's test with a Bonferroni adjustment: $z>6.7$ and $p<0.001$ in all comparisons), followed by medical professionals, the Chilean Public Health Institute (ISP), and WHO professionals (Fig. 1B). The lowest scores of trusts were reported for politicians and religious leaders. For instance, 63% ($n=472$) and 28% ($n=207$) of individuals reported a "high trust" and "some trust", respectively, in scientists, and more than

70% reported a “high trust” (43%, n=323) or “some trust” (36%, n=267) in medical professionals. On the contrary, 64% (n=479) and 45% (n=334) of the surveyed individuals reported not trusting religious leaders and politicians (Fig. 1B). Factor analysis suggests that the variability of trust in stakeholders included in the study can be explained by four groups: (a) the scientific and medical professional group, including, WHO, and ISP professionals (Retained Factor 1: Eigenvalue=2.3, LR test Chi-square=1407, $p<0.001$, Cronbach’s alpha=0.85); (b) the politicians group, including the authorities of the Ministry of Health (Retained Factor 1, Eigenvalue=0.8; LR test Chi-square=247.3, $p<0.001$; Cronbach’s alpha=0.7); (c) the relative group, including family and friends (Retained Factor 1=0.8, LR test Chi-Square=289.9, $p<0.001$; Cronbach’s alpha=0.7), and (d) a fourth group with religious leaders only. To incorporate trust in stakeholder groups into the multivariate regression models, we averaged the reported trust scores for all of the stakeholders included in each group.

Table 1

Associations regarding the willingness to accept a SARS-CoV-2 vaccination, third dose, annual vaccination, and to vaccinate children, with variables of trust and perception among in Chile (n=744). Columns [1], [3], and [4] show the results of the ordered logit multivariate models. Column [2] shows logit model results. For all columns, cells show odd ratio coefficients and, in parenthesis, confidence intervals at 95%. For each outcome variable, Table 1 shows the model with best goodness of fit and parsimony compared with other candidate models, which was selected using Akaike Information Criterion (see Supplementary Table 3). * and ** refer to significant levels at 5% and 1%.

Outcome variables					
Explanatory variables		Willingness to receive a SARS-CoV-2 vaccination	Willingness to receive a third dose vaccination	Willingness to receive an annual vaccination	Willingness to vaccinate children
		[1]	[2]	[3]	[4]
Trust in vaccines	[a]	4.1** (2.0 - 8.2)	3.2** (1.8 - 5.6)	2.1** (1.6 - 2.8)	1.9** (1.4 - 2.6)
Trust in scientists and medical professionals	[b]	2.4* (1.2 - 5.0)	2.8** (1.5 - 5.0)	2.2** (1.6 - 3.1)	2.6** (1.8 - 3.6)
Trust in politicians	[c]	2.5* (1.1 - 5.6)	1.5 (0.8 - 2.6)	1.2 (0.9 - 1.6)	1.3 (0.9 - 1.7)
Trust in religious leaders	[d]	0.9 (0.5 - 1.8)	0.7 (0.4 - 1.0)	0.7* (0.6 - 1.0)	0.7** (0.5 - 0.9)
Trust in relatives	[e]	1.7 (0.9 - 3.3)	1.3 (0.8 - 2.1)	1.1 (0.8 - 1.4)	1.2 (0.9 - 1.6)
Trust in social media	[f]	0.9 (0.4 - 1.9)	0.4** (0.2 - 0.7)	1.0 (0.7 - 1.3)	0.7* (0.5 - 1.0)
Trust in press	[g]	0.8 (0.3 - 1.7)	1.4 (0.8 - 2.6)	1.1 (0.8 - 1.5)	1.1 (0.8 - 1.6)
Perceived effectiveness of prevention practices	[h]	2.1* (1.0 - 4.5)	2.4** (1.3 - 4.5)	2.4** (1.6 - 3.4)	2.4** (1.6 - 3.5)
Perceived risk of infection	[i]	2.0* (1.1 - 3.7)	1.5 (0.9 - 2.3)	1.4* (1.1 - 1.8)	1.2 (0.9 - 1.5)

Outcome variables					
Preoccupation regarding side effects of vaccines	[j]	0.6**	0.9	0.9	0.8*
		(0.4 - 0.9)	(0.6 - 1.2)	(0.8 - 1.1)	(0.7 - 1.0)
Perceived comprehension of vaccines	[k]	0.7	0.6	1.1	1.1
		(0.4 - 1.2)	(0.4 - 1.0)	(0.8 - 1.4)	(0.8 - 1.4)
Perceived prevention of severity due to vaccines	[l]	1.3	1.0	1.0	0.8**
		(0.9 - 1.9)	(0.7 - 1.3)	(0.8 - 1.1)	(0.7 - 0.9)
Perceived relaxation of prevention practices thanks to vaccination	[m]	1.4	0.7	0.7**	1.0
		(0.8 - 2.3)	(0.5 - 1.1)	(0.6 - 0.9)	(0.8 - 1.3)
Perceived pandemic stopping thanks to vaccination	[n]	1.3	1.4*	1.4**	1.3**
		(0.9 - 2.0)	(1.0 - 1.9)	(1.2 - 1.7)	(1.1 - 1.5)
Perceived impact on quality of life	[o]	0.6*	1.0	0.9	0.8
		(0.3 - 1.0)	(0.6 - 1.6)	(0.7 - 1.1)	(0.6 - 1.1)
COVID-19 infection in family	[p]	0.7	0.9	1.0	0.8
		(0.3 - 1.7)	(0.5 - 1.7)	(0.7 - 1.4)	(0.5 - 1.1)
Age	[q]	1.1*	1.0	1.0	1.0**
		(1.0 - 1.1)	(1.0 - 1.0)	(1.0 - 1.0)	(1.0 - 1.1)
Gender (Women=1)	[r]	1.3	0.9	1.1	1.3
		(0.5 - 3.2)	(0.4 - 1.7)	(0.8 - 1.6)	(0.9 - 1.9)
Schooling	[s]	0.9	1.0	0.9	0.9
		(0.7 - 1.2)	(0.8 - 1.2)	(0.8 - 1.0)	(0.8 - 1.0)
Multivariate model		Ordered logit	Logit	Ordered logit	Ordered logit

We found evidence that individuals with higher trust in scientists and medical professionals significantly increased (by 2.4 times) their acceptance of SARS-CoV-2 vaccinations (95% CI=1.2-5.0, $p=0.01$), as well as their willingness to accept a booster dose (by 2.8 times) (95% CI=1.5-5.0, $p=0.001$) (Table 1, row [b] of the columns [1]-[2]). Similarly, an increase of trust in scientists and medical professionals also increased 2.2-fold the willingness to accept an annual vaccination (95% CI=1.6-3.1, $p<0.001$) and 2.6 times the vaccination of children (95% CI=1.8-3.6, $p<0.001$) (Table 1, row [b] of the columns [3]-[4]). Interestingly, some groups responded differently in relation to their trust in scientists and medical professionals and thus showed comparatively different associations with the willingness variables. For instance, women did not vary their willingness to accept a SARS-CoV-2 vaccine and booster dose when they reported a higher or lower level of trust in scientists and medical professionals. In contrast, men showed that a higher trust in scientists and medical professionals increased 46.1 and 4.2 times their willingness to accept a SARS-CoV-2 vaccine (95% CI=2.5-862.1, $p=0.01$) and booster dose (95% CI=1.3-13.1, $p=0.02$), respectively (Supplementary Table 4). In the case of the willingness to accept an annual vaccination and the vaccination of children, both women and men showed a similar positive impact of trust in scientists and medical professionals (Supplementary Table 4). We found evidence that young people and adults differed in terms of how their trust in scientists and medical professionals impacted the variables of willingness. For instance, young people did not vary their willingness to accept a SARS-CoV-2 vaccine, booster dose, annual vaccination, and the vaccination of children as their levels of trust in scientists and medical professionals increased (Supplementary Table 5). On the contrary, adults showed that a higher level of trust increased their willingness to receive a SARS-CoV-2 vaccine, booster dose, annual vaccination, and the vaccination of children by around three-fold (Supplementary Table 5). In contrast, our results showed that willingness to accept both an annual vaccination (95%CI=0.6-0.9, $p=0.02$) and the vaccination of children (95%CI=0.6-0.9, $p=0.004$) decreased by 30% with a one unit increase of trust in religious leaders (Table 1, row [d] of the columns [3]-[4]). However, when comparing between genders, the trust in religious leaders decreased the willingness to accept the booster dose only among men. Both women and men decreased their willingness to vaccinate children as their trust in religious leaders increased (Supplementary Table 4). Trust in religious leaders impacted the willingness scores differently between age groups. For instance, only adults showed a decrease in their willingness to accept a booster dose as trust in religious leaders increased, while only young individuals with greater trust in religious leaders decreased their willingness to accept an annual vaccination and the vaccination of children. Lastly, people's trust varied between social media (Fig. 1C). Multivariate analyses showed that an increase of trust in social media was associated with a lower willingness to accept a booster dose (OR=0.4, 95%CI=0.2-0.7, $p=0.001$) and the vaccination of children (OR=0.7, 95%CI=0.7-1.0, $p=0.03$) (Table 1, row [f] of the columns [2] and [4]).

A higher perceived risk of infection and effectiveness of prevention practices as well as less concern regarding side effects of vaccines increased the willingness to accept a SARS-CoV-2 vaccine.

People's perceptions of the effectiveness of prevention practices varied according to the practice (Kruskal-Wallis test: Chi-squared=591.1, d.f.=7, $p<0.001$) (Fig. 1D). For instance, the vaccination was perceived as

more effective compared to lockdown (Dunn's test with Bonferroni adjustment: $z=10.2$, $p<0.001$), but less effective than the use of a mask ($z=-6.22$, $p<0.001$), hand-washing ($z=-10.1$, $p<0.001$), physical distance ($z=-9.3$, $p<0.001$), avoid social gatherings ($z=-7.1$, $p<0.001$), and quarantine ($z=-3.9$, $p=0.001$). Also, the use of a mask was perceived as less effective than hand-washing ($z=-4.8$, $p<0.001$) and physical distance ($z=-3.3$, $p=0.011$). The lockdown was perceived as the least effective practice to prevent the infection of SARS-CoV-2 among all of the practices included in the study (Fig. 1D). Notwithstanding the different perceptions of effectiveness across practices, results suggest that the variability of perceptions can be retained in one factor (factor analysis: eigenvalue of factor 1=3.0; LR test: chi-squared=1292.1, $p<0.001$), with the set of variables showing a high internal consistency (Cronbach's alpha=0.81). We calculated the overall perceived effectiveness of the prevention practices for each individual as the average value of perceived effectiveness among all practices, and used this new variable in the multivariate analysis.

Most people perceived that the probability of becoming infected with COVID-19 was "little probable" ($n=423$, 56.8%) or "some probable" ($n=239$, 32.1%) (Fig. 1E). Only 49 of the surveyed individuals (6.6%) reported that getting COVID-19 was "highly probable". In turn, people reported being "little worried" ($n=306$, 41%) or "not worried" ($n=190$, 25.5%) about the side effects of vaccines. A total of only 79 individuals of the sample reported being "highly worried" about the side effects of vaccines ($n=79$, 10.6%) (Fig. 1E). In turn, people's trust varied between types of press media (Fig. 1F).

When the perceived effectiveness of infection prevention practices was a score unit higher, the willingness to accept a SARS-CoV-2 vaccine increased by 2-fold (95%CI=1.0-4.5, $p=0.05$), the booster dose by 2.4 times (95%CI=1.3-4.5, $p=0.005$), an annual vaccination by 2.4 times (95%CI=1.6-3.4, $p<0.001$), and the vaccination of children by 2.4-fold (95%CI=1.6-3.5, $p<0.001$) (Table 1, row [h]). Moreover, when the perception of infection risk increased by one unit value, the willingness to accept a SARS-CoV-2 vaccine doubled (95%CI= 1.1-3.7; $p=0.02$) and the willingness to accept an annual vaccination increased by 1.4 times (95%CI=1.1-1.8; $p=0.01$) (Table 1, row [i] of the columns [1] and [3]). In contrast, when preoccupation regarding the side effects of SARS-CoV-2 vaccines increased by one unit value, the willingness to accept a SARS-CoV-2 vaccine decreased by 40% (95% CI=0.4-0.9; $p=0.01$) and the willingness to vaccinate children decreased by 20% (95% CI=0.7-1.0; $p=0.02$) (Table 1, row [j] of the columns [1] and [4]).

Moreover, we found that associations of willingness variables with the perceived effectiveness of prevention practices, perceived infection risk and preoccupation regarding side effects, varied among genders and cohorts. For instance, when comparing results between genders, women showed significant associations among all willingness variables with the perceived effectiveness of prevention practices (Supplementary Table 4). On the other hand, men showed a significant association between the willingness to accept the annual vaccination and the perceived effectiveness of prevention practices (Supplementary Table 4). Analyses across age groups suggest that only adults increased their willingness to accept a booster dose as their perceived effectiveness of prevention practices increased. Both adults and young people with a higher perceived effectiveness of prevention practices showed a greater willingness to accept an annual vaccination and the vaccination of children (Supplementary

Table 5). Also, perception of infection risk was positively and significantly associated with the willingness to accept a SARS-CoV-2 vaccine (OR=2.4; 95%CI=1.1-5.1; p=0.02) and booster dose (OR=1.7; 95%CI=0.9-3.1; p=0.08) among women, but not among men (Supplementary Table 4). Preoccupation regarding the side effects of vaccines decreased the willingness to accept SARS-CoV-2 vaccines in both women (OR=0.5; 95% CI=0.3-0.8, p=0.008) and men (OR=0.2; 95%CI=0.0-0.9; p=0.03), but only men decreased their willingness to vaccinate children as their preoccupation regarding side effects increased (OR=0.7; 95%CI=0.5-0.9; p=0.02) (Supplementary Table 4). Similarly, increased worry about side effects decreased the willingness to accept a SARS-CoV-2 vaccine (OR=0.3, 95%CI=0.1-0.6, p=0.002) and booster dose (OR=0.3, 95%CI=0.1-0.8, p=0.01) only among young people. Instead, adults showed that a higher preoccupation regarding side effects decreased their willingness to vaccinate children (OR=0.7, 95%CI=0.6-0.9, p=0.01) (Supplementary Table 5).

Interestingly, when individuals perceived that vaccines reduce the severity of COVID-19, their willingness to vaccinate their children also increased by 20% (OR=0.8, 95%CI=0.7-0.9, p=0.002) (Table 1, row [l] of the column [4]). When respondents showed an increased perception that prevention practices could be relaxed thanks to vaccination, a reduction in the willingness to accept an annual vaccination was observed (OR=0.7, 95%CI=0.6-0.9, p=0.001) (Table 1, row [m] of the columns [3]). Individuals who reported a higher agreement that vaccination would stop the pandemic showed a higher willingness to accept a booster dose (OR=1.4, 95%CI=1.0-1.9, p=0.03), annual vaccination (OR=1.4, 95%CI=1.2-1.7, p<0.001), and the vaccination of children (OR=1.3, 95%CI=1.1-1.5, p=0.001) (Table 1, row [n] of the columns [2]-[4]). Lastly, individuals who reported that the pandemic positively impacted their subjective well-being showed less willingness to accept a SARS-CoV-2 vaccine (OR=0.6, 95%CI=0.3-1.0, p=0.04), but did not vary their willingness to accept a booster dose, annual vaccination, and the vaccination of children (Table 1, row [o]).

Discussion

We contribute to the existing literature focusing on whether the willingness to accept a vaccination is affected by trust and perceptions of diverse issues related to the COVID-19 pandemic, in the context of a country with one of the world's highest vaccination rates. Our findings provide relevant information for decision-making processes, particularly for the design and communication of vaccination implementation programs in countries where COVID-19 vaccination remains low.

Our results indicate that higher acceptance of SARS-CoV-2 vaccines, a booster dose, annual vaccination and vaccination of children correlates with a high level of trust in experts in the field (scientists and medical professionals). These significant and positive associations emphasize the pivotal role that trust in experts plays in the vaccination process against COVID-19. In contrast, trust in political or religious leaders proved to be extremely low and, on the contrary, when it was high, the refusal to vaccinate was also higher. Our results are consistent with other studies, where a high trust in health workers has been associated with high acceptance of vaccination^{24,25}. This is also consistent with the lack of trust in vaccine experts, which has been associated with support towards political stances against vaccines²⁶

Our findings also emphasize how crucial trusted information sources are, suggesting that confidence in health authorities significantly affects vaccine acceptance²⁷.

Trust in the government has also been associated with vaccine acceptance²⁰. In the Chilean context, trust in national and health authorities is lower²⁸ than in other countries²⁹. Trust in the Chilean government could have diminished when COVID-19 infections continued to increase despite the success of the vaccination campaign (first doses). This could be related to the initial message of the vaccination campaign provided by Chilean authorities, which presented the vaccine as the only possibility to control the virus²⁸. In the Chilean case, all of the communes in Santiago, the capital of Chile, entered an obligatory quarantine during the data collection period due to the increase in COVID-19 cases. The low trust in the Chilean authorities and its negative impact on the willingness to accept a vaccination could be the result of generalized criticisms to the authorities due to the management of social inequalities related to how the COVID-19 pandemic impacted socioeconomic groups differently³⁰. Our results show the need to further investigate this aspect in future studies, as well as considering the emergence of "new actors" within society in which trust could be deposited, as our findings show: in the scientific world and medical professionals.

Our study identified that adults had a higher acceptance of the vaccination process. Higher acceptance of a vaccine in the adult population could be associated with the perception of the risk of infection of SARS-CoV-2. It has been described that the willingness to be vaccinated is more related to age than to gender, indicating that those who perceive a greater susceptibility to the effects of the virus are more open to accept vaccination and even willing to take a booster dose²⁹.

In concordance with previous studies, trust in vaccines aids in explaining the acceptance of vaccination uptake³¹. In the current SARS-CoV-2 pandemic, the development of new vaccination platforms has been achieved. Those surveyed in our study reported a high trust in all vaccines, albeit the CoronaVac and Pfizer vaccines proved to be the most trusted. While CoronaVac has reported lower efficacies and effectiveness than Moderna and AstraZeneca,^{5,32} it has received more trust among residents of Chile. The high trust in the Pfizer and CoronaVac vaccines coincides with them being the most administered in the country. Governments must proactively provide information on selected vaccine manufacturers and new platforms to break down potential knowledge barriers that may affect trust in vaccines. Consistent with other studies,^{14,24} our results strengthen the idea that high trust in vaccines and a high perceived effectiveness of prevention practices increase the willingness of people to accept vaccination for themselves and their children, as well as to accept a booster dose and annual vaccination programs.

Our results emphasize that the preoccupation regarding side effects of vaccines decreased the acceptance of SARS-CoV-2 vaccines^{24,33,34}. One of our novel findings in the existing literature is that the preoccupation regarding the side effects of vaccines also decreased the willingness to vaccinate children, while it did not affect the willingness to accept a booster dose and annual vaccination programs. We also evidence that determinants of willingness to accept vaccination vary among genders and cohorts. For

instance, trust in scientists and medical professionals influenced the willingness to accept SARS-CoV-2 vaccines and a booster dose only among men and adults, but not among women or young individuals. The reasons for this gender difference are not clear. They could be explained by trust; however, this is not enough to explain the willingness to be vaccinated by women, which should be further explored in future research.

Our findings must be considered in light of some limitations. First, we captured different degrees of confidence through an ordinal scale with 4 values, while the variability of confidence may be higher. Second, although we included different socio-demographic characteristics, additional aspects should be included, such as cultural, ethnic, rurality and income, among others. Third, provided the context of physical distance, the application of the online survey might exclude people with lower accessibility or knowledge about the internet and technology. Although these limitations, the present study is consistent and extremely relevant, clearly identifying the underlying factors affecting the willingness to accept a SARS-CoV-2 vaccine, an annual vaccination, booster doses and the vaccination of children.

In conclusion, our study reports that people show a high intention to receive a booster dose of the COVID-19 vaccine, annual vaccination and vaccination in children under 16 years of age. Vaccine acceptance is associated with trust in scientists, medical professionals and in different media, such as television and radio. The perceived risk of becoming ill with COVID-19 is a factor that determined the acceptance of vaccination, childhood vaccination and booster doses in adults.

This study provides fundamental information regarding aspects such as trust and confidence towards key factors and stakeholders involved in the COVID-19 vaccination process. Other aspects, such as communication strategies, social media, information needs, or interlocutors must be deepened in future qualitative studies, in which it could be relevant to differentiate the perception of risk in relation to COVID-19 and knowledge of this virus. The successful acceptance of the vaccination process against COVID-19 may be useful to establish future strategies, information pathways and vaccination processes that increase the acceptance of future vaccines in the population in Chile and worldwide.

Methods

Ethical approval for this study was obtained from the Universidad Autónoma de Chile ethics committee on April 19th, 2021 with reference to CEC 10-21. The study utilized a cross-sectional online survey design of adults living in Chile. A structured questionnaire was designed, validated by three experts, and then applied at the national level in order to ensure the representativeness of the diverse social realities in Chile. A three-step questionnaire validation process was carried out: (a) content validity evaluation by experts (immunology, public health, design and preparation of health questionnaires); (b) construct validity, through a factor analysis of the different items included in the questionnaire; and (c) reliability, including internal consistency -assessed with Cronbach's Alpha coefficient. After this process, the questions were adjusted.

The structured questionnaire was applied through an online platform between May 21 and June 21. With a confidence level of 95% and a confidence interval of 5%, it was estimated that a minimum of 500 people more than 18 years old constitute a representative sample at the national level. A total of 744 volunteers completed the questionnaire, with 58% distributed throughout the Metropolitan region (which concentrates 40% of the national population) and 42% throughout the rest of the country.

The questionnaire captured variables regarding the willing to accept vaccines, variables of trust, variables of perceptions and socio-demographic variables. (a) Outcome variables, four in total, were related to the willingness to accept vaccines : (i) The willingness to accept SARS-CoV-2 vaccines was estimated in three values (3=yes, 2=maybe, and 1=no); (ii) The willingness to accept a vaccine booster shot after having a complete vaccination scheme was included as a dichotomous variables (yes=1); (iii) The willingness to accept an annual vaccination was assessed on a 4-value ordinal scale (from 1=not willing to 4=highly willing) and (iv) the willingness to accept the vaccination of children, was assessed on a 4-value ordinal scale (from 1=definitively no to 4=definitively yes).

(b) Explanatory variables, also four in total, focused on trust in (i) vaccines, (ii) stakeholders, (iii) social media, and (iv) press. To reflect the trust in vaccines, our aim was to prompt people to report their trust in each of the vaccines approved in Chile: CoronaVac, Pfizer (BNT162b2), CanSino (Ad5-nCoV), Oxford-AstraZeneca (ChAdOx1), Sputnik V Gam-COVID-Vac), and Johnson& Johnson (Ad26.COV2). We also assessed the trust in different stakeholders, including scientists, medical professionals, ISP professionals, WHO professionals, Ministry of Health, family, friends, politicians, and religious leaders. Similarly, we included questions to assess trust in social media as sources of information, which might influence the willingness to accept vaccines and treatments. Among social media, we asked for people to express their trust in general websites, Twitter, WhatsApp, Facebook, Instagram, and Tik Tok. Lastly, trust in the press was also included in the questionnaire as formal information sources that might influence individuals, such as national and international newscasts, national and international newspapers, and radio broadcasts. For all of these questions, we used a 4-value ordinal scale, from 1=no trust to 4=high trust.

We prompted people to assess their perceptions about a set of factors that might explain their level of willingness to accept the vaccination process against COVID-19. First, individuals' perception of the effectiveness of COVID-19 prevention practices was captured through a 4-value ordinal scale, from 1=not effective to 4=highly effective. We included the most frequent Chilean prevention practices, such as vaccination, use of mask, hand-washing, social distancing, avoiding social gatherings, quarantine, and "sanitary clinics", which refer to free Chilean establishments that meet the quality and safety conditions of both the person who must comply with the quarantine or isolation measure and the staff in charge of their care, available to people positive with COVID-19 or those that must undergo a quarantine due to close contact with an infected individual. Second, we also captured the perceived risk of infection on an ordinal scale with four values (from 1=not probable to 4=highly probable). Third, the preoccupation regarding side effects of the vaccines was assessed by a self-reported level of concern using a scale from not worried (=1) to highly worried (=4). Fourth, we also assessed the perceived comprehension of

the CoronaVac, Pfizer, CanSino, Oxford-AstraZeneca, Sputnik V, and Johnson& Johnson vaccines, where individuals reported the level of information they considered having about each vaccine. The individual self-report was assessed using a 4-value ordinal scale (from 1=no information to 4=a lot of information). Fifth, the idea that prevention practices could be relaxed due to vaccination was proxied with the claim “the vaccination” (i) can stop using a mask, (ii) can relax the measures to prevent physical interactions with other people, (iii) will prevent me from contracting COVID-19, (iv) will prevent me from getting severely ill, and (v) will stop the COVID-19 pandemic. The answer to each practice was captured on a 5-value ordinal scale (from 1=highly disagree to 5=highly agree). Sixth, we evaluated the perceived impact of the COVID-19 pandemic on quality of life. We proxied the concept of quality of life with the impact on the job, education, health, familial coexistence, and general well-being of the household members. We assessed the impact of the pandemic on a 5-value ordinal scale, from 1=very negative to 5=very positive.

Control variables:

Lastly, the structured questionnaire included a set of questions to capture control variables that might be associated to the outcome or explanatory variables. We asked whether the respondent or any family member had been infected with COVID-19, and whether the illness was acute. We also collected information on age, gender, administrative region of residence, schooling and nationality.

Statistical analysis:

Factor analyses following Cronbach’s Alpha were carried out to analyze the retained factors and the degree of internal consistency and reliability among variables of trust and perception. We took the average of each factor to create the variables of trust included in the multivariate regression analyses.

We were interested in estimating the association between outcome variables of willingness to accept vaccination and explanatory variables of trust and perceptions, while controlling for age, gender, and schooling. We used the following general equation (1):

$$WTA = \alpha \text{ Trust} + \beta \text{ Perception} + \gamma \text{ Control} \quad (1)$$

Where WTA represents one of the four outcome variables of willingness to accept. Trust includes the explanatory variables of trust, while Perception stands for variables of perceptions. Lastly, Control captures the control variables including (a) age, (b) gender, (c) schooling, (d) having contracted COVID-19, (e) sub-national region of residence, and (f) nationality. α , β , and γ represents the odds ratio as a measure of association among variables.

When the outcome variables were willingness to accept a SARS-CoV-2 vaccine, annual vaccines, and vaccination of children, we used ordered logistic multivariate models. In turn, logistic multivariate models were used for when the outcome variable was a COVID-19 vaccine booster shot. In all of the models, we used the same explanatory and control variables. For each outcome variable, we adjusted a set of

different models omitting one or more explanatory and control variables. We used the Akaike information criterion (AIC) to perform model comparisons and select the model with the best goodness of fit and parsimony. We ranked the AIC values and defined that the lower AIC value represents the best fitted model (Supplementary Table 3).

Declarations

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Author contributions

LFF obtained ethical approval for the study via the Universidad Autónoma de Chile ethics committee. LFF, FZR, NCM and DTA conceptualized and designed the study and FZR, AA, CPM, GC and LFF designed and performed the statistical analyses. All of the authors contributed to the questionnaire design. CPM and GC created all of the tables and figures for publication. LFF, NCM, DTA, AA and FZR wrote the final manuscript. All of the authors reviewed the results and approved the final version of the manuscript.

Additional Information

The authors declare no competing interests.

Data availability

The datasets generated and analyzed during the current study are not publicly available due to the restrictions applied by the Universidad Autónoma de Chile ethics committee as requested in the Informed Consent. The protocol was approved to use the data for the current study only, but they are available from the corresponding author on reasonable request.

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Figures

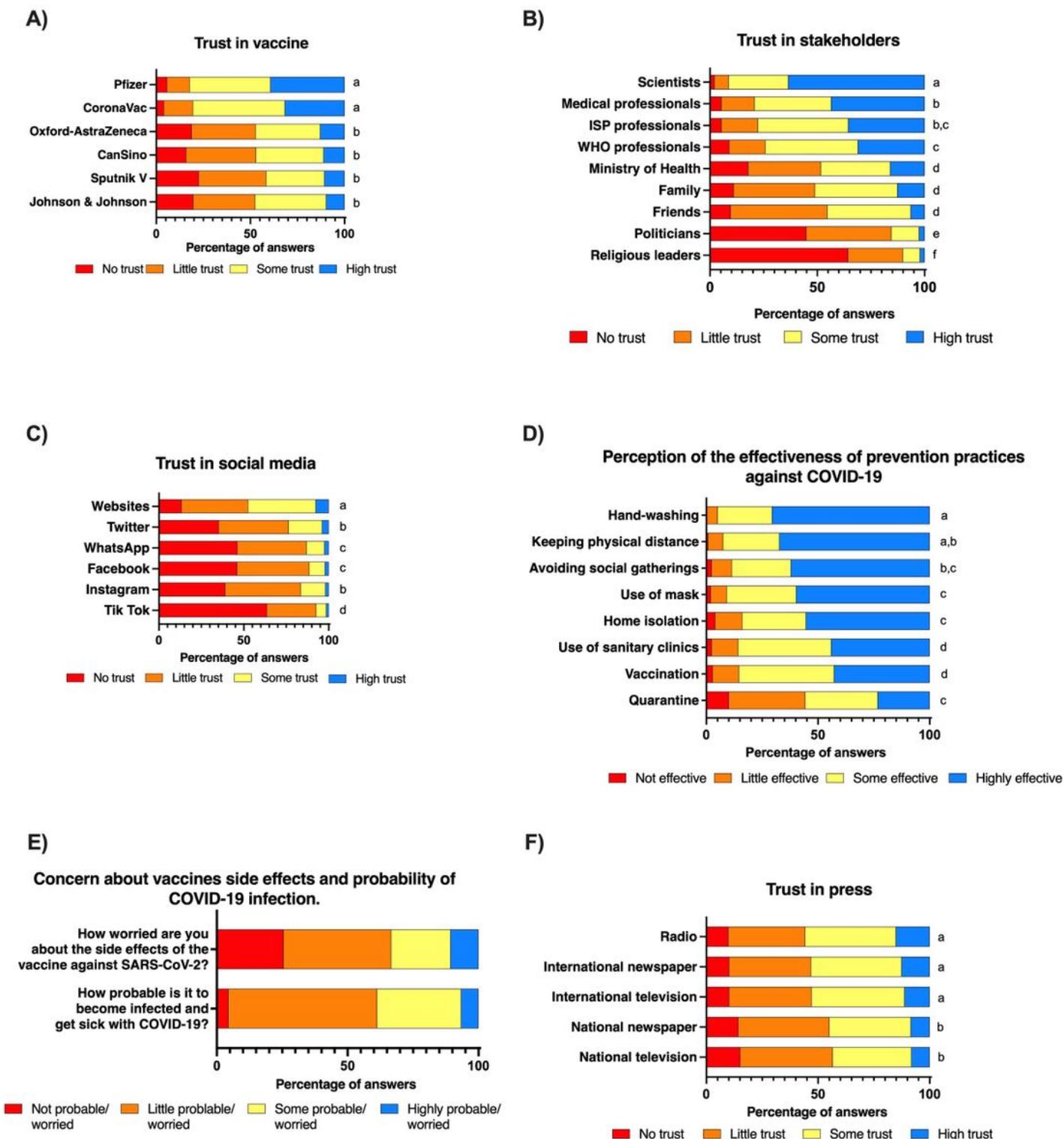


Figure 1

Respondents' perceptions of vaccine side effects, getting sick from COVID-19, effectiveness of COVID-19 control practices, and trust in vaccines, stakeholders, social media, and the press (n=744). The bars indicate the breakdown of the percentage of respondents providing an answer given to each question asked. The full questionnaire is shown in the Supplementary Information. ISP (Instituto de Salud Pública), WHO (World Health Organization). (A) Trust in vaccine. (B) Trust in stakeholders. (C) Trust in social media. (D) Perception of the effectiveness of prevention practices against COVID-19. (E) Concern about vaccines side effects and probability of COVID-19 infection. (F) Trust in press. For all figures, different letters indicate a significant difference of trust or perception (Dunn's test with Bonferroni adjustment, $p < 0.01$).

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