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Population-based seroprevalence survey: post-pandemic COVID-19 vaccination, related factors, and geographic distribution of vaccine acceptability in Chile

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Abstract

Background Prevention of infectious diseases is based on host protection, especially using vaccines. Several factors have been linked to the acceptance of vaccines in the population. Chile achieved high COVID-19 vaccination coverage early in the pandemic. The study aimed to determine the prevalence of antigens and antibodies, vaccination status, geographical distribution, and factors related to vaccine acceptability.

Methods In two Chilean cities, the fourth round of a population-based seroprevalence cross-sectional survey was conducted in May 2024. 654 participants aged seven or older were recruited. After signing consent, participants were interviewed, blood samples were taken to identify antibodies against SARS-CoV-2 using ELISA, and antigens were assessed through a nasal swab rapid test. Territorial analysis of the vaccine dose distribution was carried out.

Results All participants tested negative for antigens and positive for antibodies against SARS-CoV-2, with an overall vaccination uptake rate of 98,5%. However, their vaccination status was heterogeneous. Territorial distribution showed a slight geographical clustering of vaccine doses in both cities. 52.7% had the basic scheme and/or boosters, 32.1% had the bivalent vaccine, and 13.7% had anti-Omicron. Self-report identification with a risk group was not associated with vaccine adherence. City, age, education, and comorbidities were associated with perceived and actual risk discrepancies.

Conclusions Overall, vaccine acceptance is high. However, the acceptance of the last two doses was below expectations and showed heterogeneous geographical distribution. Adulthood is the most important predictor of vaccine uptake. Participants underestimated their level of risk. Risk communication must be improved, especially for risk groups, to help them perceive themselves as beneficiaries of vaccination. Efforts should be made to disseminate information on vaccine safety and counter misinformation to increase knowledge about vaccines.

Keywords Vaccine acceptability, COVID-19, Vaccine, SARS-CoV-2, Patient compliance, Chile

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Introduction

Vaccines are a fundamental pillar for the prevention of infectious diseases and SARS-CoV-2 virus is no exception. In the aftermath of the pandemic, in September 2023, the Strategic Advisory Group of Experts on Immunization (SAGE) of the WHO announced the publication of the COVID-19 Strategic Preparedness and Response Plan for 2023–2025 [1]. The main guidance is to focus on immunizing at-risk populations to prevent severe disease and death from COVID-19, considering specific vaccines against circulating variants of the virus [1].

Chile achieved high vaccination coverage early on, reaching 98.7% with the basic scheme (one or two doses depending on the type of vaccine), in 2021, after 12 months of a successful vaccination campaign [2]. The wide-ranging primary healthcare network favoured a broad territorial deployment, reducing the inequities determined by the country's social disparities [3, 4].

However, over time, coverage has declined in the last two years, during which a bivalent vaccine (2022) and vaccine against the Omicron variant XBB.1.5 (2023) were included in the national immunization plan [5]. In November 2023, following the WHO guidelines, Chilean Ministry of Health updated the vaccination strategy against COVID-19 which is aimed at healthy persons of 6 months of age, in addition to the administration of booster doses in the at-risk population. The risk groups include health personnel, pregnant women at any gestational stage, immunosuppressed and individuals with chronic diseases from 6 months of age, adults aged 60 and older, and other specific population groups defined by the authorities. The proposed goal was to achieve 80% coverage in the population aged 60 and older [5]. Unfortunately, bivalent vaccine coverage (year 2023) reached only 47% of the population over 60 years old and 23% of the national population [6]. Until November 2024, the coverage by target groups are as follows: individuals aged 60 and older, 31%; pregnant women, 6%; individuals aged six months to 59 years who are immunocompromised or with chronic diseases, 27%; and health workers 38% [7].

International studies indicate that vaccine coverage is influenced by systemic, social, cultural, and individual factors [8–14]. Geographical dispersion and access to health centres act as structural barriers, together with limited-service hours and reduced availability of the health workforce [8]. Likewise, the availability and proximity of vaccination centres ease of booking vaccination appointments, or the various funding/reimbursement schemes can play a role in vaccination uptake [8]. Social factors are related to the level of trust that the population has in the government, health authorities, health institutions and health personnel [9, 10]. Risk communication plays a crucial role in the messages delivered by the authorities to promote vaccination as well [11]. It has been shown that the acceptance of vaccines is higher in people who tend to be informed through traditional media and have trust in science, while those who reject vaccination believe in conspiracy theories, are more sceptical about vaccine production, and are mostly informed through social networks [9, 10, 12–14].

At the same time, various studies have shown that the level of health literacy (HL) and vaccine literacy (VL) are important individual factors related to willingness or hesitancy to be vaccinated [8, 11, 12, 15–18]. Both concepts are linked to the educational level of individuals [18]. Vaccine literacy (VL) is a concept derived from HL being defined as "the ability of people to access, process, and understand basic vaccination knowledge and vaccination services, as well as to assess the potential consequences and risks of their behaviour and make health-related decisions" [19]. VL is an integral component of HL including knowledge about vaccine safety, side effects, effectiveness, trust, information sufficiency, efficacy, vaccine mandate, and fear and anxiety [14, 17]. At the same time, VL introduces the importance of knowledge and skills to understand and appropriately judge vaccine information to motivate an appropriate vaccination decision [20]. VL may guide vaccine communication strategies to motivate groups that refuse vaccination to use vaccines by increasing their confidence [19].

Another factor that motivates health behaviour is risk awareness and risk perception of the disease [21, 22]. In turn, risk awareness has been associated with individual, demographic, geographic, and time factors [21]. For example, in the case of COVID-19, the timing was related to the type of virus variant in circulation and periods with more cases, critical bed occupancy or more deaths from the disease were reported [22]. At the same time, related to risk sensitization, being a health worker, or having chronic diseases or disabilities was associated with higher acceptance of the COVID-19 vaccine [23, 24]. Many authors identify risk communication as an important factor to be considered by authorities to address misinformation, reduce vaccine hesitancy, and improve coverage [23, 25].

Materials and methods

The objective of this study is to evaluate the prevalence of antibodies and the occurrence of the disease, while simultaneously characterizing the immunization status of a representative population sample from two Chilean cities. Furthermore, the study analyses vaccination coverage, geographical distribution, and factors influencing vaccine acceptability. This is the fourth round of serial seroprevalence assessments conducted in two Chilean cities (year 2020, 2021 and 2022). The evaluation was conducted during the month of May 2024.

Study design and setting

A population-based cross-sectional seroprevalence survey was conducted in May 2024 in two Chilean cities: the conurbation of La Serena/Coquimbo and Talca. The study was conducted in cities that correspond to the locations of the universities where the researchers are affiliated. Three previous cross-sectional studies were conducted in these two cities [2, 4, 26]. A two-stage random sample was used. Households that could not be contacted or refused to participate were replaced following a standardized procedure: A systematic jump in the same census tract was implemented. Every second house (or household) was invited to participate, moving to the right of the house that initially refused, around the block, until a household agreed to participate. If no household was available, a random selection of a new census track followed by another systematic jump was performed. All household members aged 7 years or older were invited to participate, with no exclusion criteria applied. As this is a population-based study, no exclusion is made. The sample is distributed homogeneously throughout the city, reaching all types of neighbourhoods without any discrimination.

Study size

The sample size was calculated incorporating a finite population correction factor and based on the seroprevalence of 97% that resulted in our previous round [2], with a precision of 3%, and a design effect of 2. This resulted in a minimum sample size of 249 participants for each city.

Participants

No exclusion criteria were considered. Within the selected household all members 7 years or older were invited to participate.

Data sources and measurements

A health team (nurse and trained interviewer) visited each household. The RedCap® platform was used to collect data. The survey was completed with the guidance of trained surveyors. Interviewers were trained by the investigation team to gather information consistently and minimize information bias. Nurses collected blood samples to measure IgG antibodies against SARS-CoV-2. Nasal swabs were collected to test for COVID-19 antigens and detect acute infection. Blood samples were collected and preserved under a cold chain until their daily processing in the local laboratories of each university. Serum was obtained by centrifugation of the samples at 1900*g* for 6 min, and the resulting aliquots were stored at -80 °C until their subsequent shipment to the university laboratory in Santiago, Chile, under controlled temperature conditions. IgG antibody levels were measured in serum using ELISA. For more information on laboratory methods, see reference [27].

Variables: dependent variables

Vaccination status. Classified into four categories for the entire sample population: not vaccinated, basic scheme and/or boosters, bivalent vaccine 2023, and univalent for Omicron 2024. For the population that meets the risk criteria to be vaccinated, the vaccination status was categorized as (a) not vaccinated, basic scheme and/or boosters, (b) bivalent vaccine 2023, and (c) Omicron 2024. The definition of risk groups to get the COVID-19 vaccine were defined according to the country's health authority which includes persons aged 60 years or older, persons with any of the indicated chronic non-communicable diseases [5], health workers and pregnant women.

Independent variables

City, age group (0–19, 20–29, 30–39, 40–49, 50–59, and 60 or more), sex, ethnicity (yes/no), health insurance (public/private/armed forces), education (only for participants 18 years old or more) categorized as primary or less, high school, technician, and professional or postgraduate; comorbidities (yes/no), tobacco consumption (yes/no), COVID-19 diagnosis (yes/no), number of COVID-19 episodes, self-report of belonging to a risk group for vaccination (yes/no), and body mass index categorized as underweight, normal, overweight, or obese. Self-reported belonging to a vaccination group. The belonging to a vaccination group was evaluated according to self-report by the question: Do you belong to any risk group for COVID-19? and was validated according to the characteristics recorded in the survey, presenting the condition of: people aged 60 years or older, being pregnant, being obese (self-report of weight and height), or having a chronic condition. To analyse this information, for each vaccination group a "0" was used if the person self-reported belonging to the vaccination group and had the condition and a "1" when the person did not self-report belonging to the vaccination group and had the condition.

A Directed Acyclic Graph (DAG) was designed to visualise the relationships between the factors studied and vaccination status in the study subjects. In this way, a theoretical model of the relationships is obtained, identifying possible confounding factors to be considered for statistical modelling (Fig. 1) [28]. The variables included in the theoretical model represented in the DAG were those significantly related to vaccination in the previous statistical analyses.

Statistical methods

The sample was described through proportions. In the first analysis, the vaccination coverage from the total

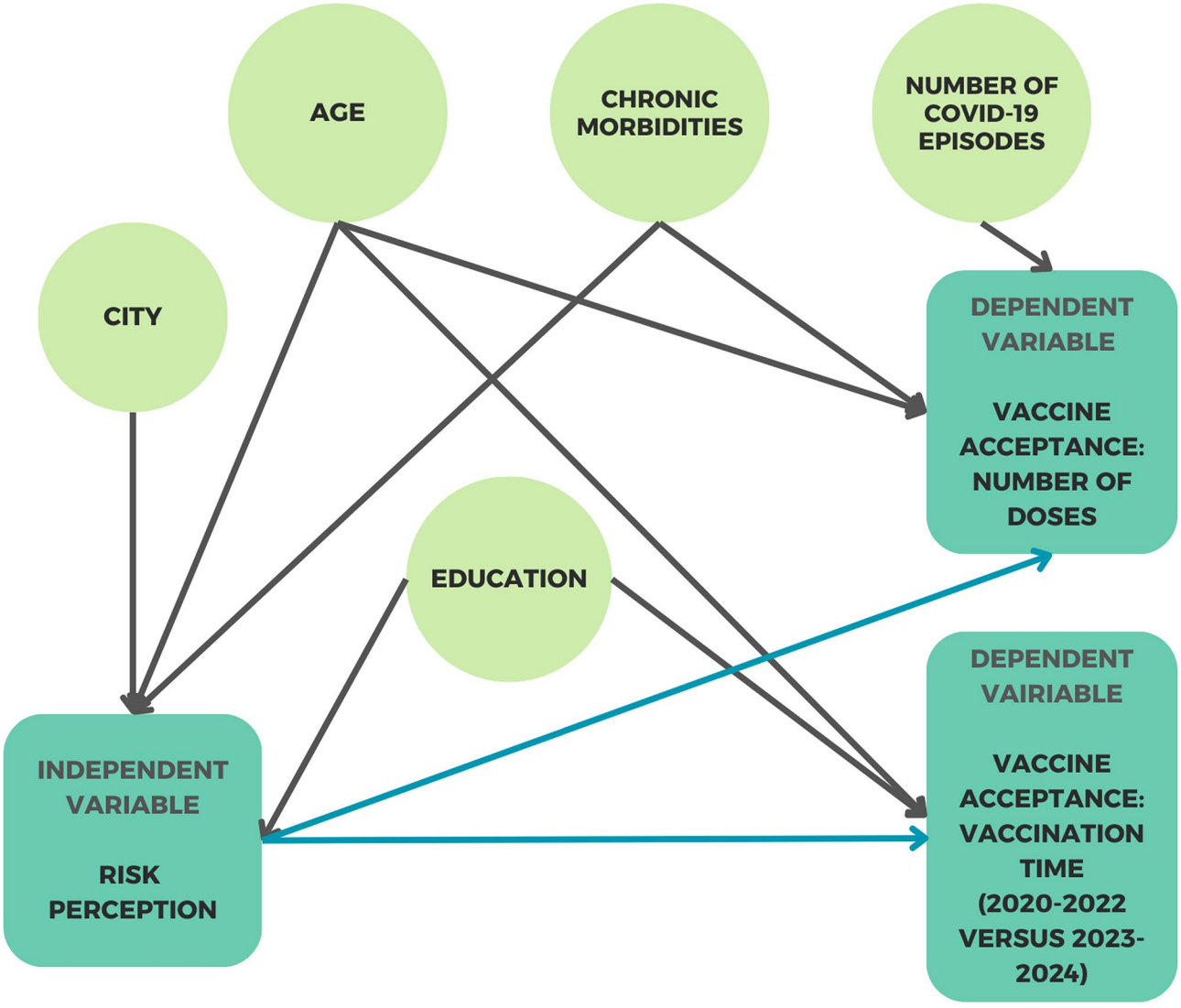

Fig. 1 DAG representing significantly associated factors with risk perception (independent variable) and two aspects of vaccination acceptability (dependent variable): the number of doses and time of vaccination. Arrows show direct relationship between variables

study sample was calculated through the proportion of unvaccinated, baseline or booster vaccination, bivalent vaccine 2023 and Omicron 2024. Expansion factors were applied to the sample results to estimate population coverage. This was done by adjusting the sample weights, using complex sample analysis. The design weights were calculated based on the probability of selecting the block dwellings within a specific census stratum. Then, the probability of selecting all members aged 7 years or older in the selected dwelling was considered. In addition, the non-response of each individual in the household was considered as the inverse of the probability determined for members aged 7 years or older who responded. The population projections for the reference year 2024 were used. These estimates were then stratified for independent variables using the chi-square test. This same analysis was repeated only for the population considered the target vaccination group as indicated by the health authority. To estimate coverage in the population considered to be at risk, we worked with the 569 individuals who present risk conditions as recorded in the survey. In other words, they are in the target group to be vaccinated, whose universe corresponds to 62,7577 people after the expansion process. For the analysis, they were separated in two vaccination groups: (1) unvaccinated and baseline or booster vaccination and (2) those who were administered bivariate vaccine 2023 and Omicron 2024. This analysis is based on the need to know the immunisation status of people at higher risk of developing a serious disease or death, which is of interest from a public health point of view.

In a third analysis, the group that self-reported having some condition to receive vaccination and had the condition (person over 60 years of age or older, pregnant, obese, chronic illness indicated by the health authority and health worker) was compared with the group that did not self-report belonging to the vaccination group and had this condition. The chi-square test and Fisher's exact test were used when the category was less than 10.

Finally, a multivariate analysis was performed through a linear regression model for complex samples, globally and separately for each city. The outcome variable was the number of doses received for participants, as a numeric continuous variable. All variables considered in the theoretical DAG model —city, age, education, COVID-episodes and comorbidities—were included in the multivariate analysis. These variables were associated with vaccine acceptance—measured by the number of doses received and the time to vaccination—in the bivariate analysis. For the statistical analyses, the STATA v15® software was used [29].

Geographical analysis

Individual data were geo-referenced according to the census track given by the address. The location was randomized at the time of mapping to ensure confidentiality. The geographical distribution of the number of vaccine doses was investigated using the ArcGis®10.7 package [30]. Spatial autocorrelation was analysed by Moran´s Index analysis of the distribution for the variables COVID-19 diagnosis during the pandemic, risk group membership and number of vaccine doses. The Moran´s Index seeks to determine the presence of systematic spatial variation in the distribution of the mapped variables [31]. Additionally, the Getis-Ord Hotspots technique [32] was used as a local spatial association analysis to determine areas of significant spatial concentration of the number of vaccine doses, in search of areas of concentration for low number of doses and high number of doses.

Ethical considerations

The study protocol was reviewed and approved by the independent Scientific Ethical Committees and by the Institutional Committees of Biosecurity of the three universities involved in the research. Adults were asked to sign informed consent. For participants under 18 years old, their parents answered the interviews, after signing their informed consent and children signed an assent form. For more details see the corresponding section at the end of the article.

Results

In May 2024, 654 participants were enrolled, and the refusal rate was 11.5%. 318 were residents of Coquimbo/La Serena, and 336 were residents of Talca (Fig. 2). The participants ranged from 7 to 95 years old (the average was 52.4 years). Population distribution of sex was 52% female. All participants tested negative for COVID-19 antigen, and had positive antibodies against SARS-CoV-2, however, their vaccination statuses were heterogeneous. Regarding population distribution of vaccination status, 52.7% had the basic scheme and/or boosters, 32.1% had the bivalent scheme and 13.7% had Omicron (Fig. 3). The overall uptake vaccination rate was 98,5%. On the other side, only 1.5% of the population (11 individuals in the sample) were not vaccinated under any scheme (Table 1).

The city of Coquimbo/La Serena exhibited a higher frequency of vaccination with the basic regimen and/or booster doses, but lower coverage rates for bivalent and Omicron-specific vaccines (Table 1). Factors significantly related to the vaccination status were age group, having comorbidities, number of COVID-19 episodes and belonging to the risk group defined by the health authorities. Younger age groups showed higher vaccination frequencies with basal and booster vaccination schedules, while older persons, people with comorbidities, those who had three times COVID-19 episodes and who belong to the risk groups showed higher vaccination frequencies during the 2023 or 2024 campaigns (Table 1).

It is noteworthy that 57.6% of the participants recognize that they belong to the risk group for receiving the vaccine, while 86.9% actually belong to the risk group as indicated by the health authority and the information recorded in the survey. In summary, one-third of the participants do not identify themselves as being at risk, even though they are.

Concerning the geographical analysis, as shown in Fig. 3, a wide extension and high vaccination coverage are observed in both cities, as there are few and spatially isolated individuals without vaccination doses. Several areas of the cities have a concentration of people with four or more doses. The autocorrelation analyses for each city (Table 2) show different situations between cities regarding COVID-19 diagnosis during the pandemic, being geographically more clustered in the La Serena-Coquimbo conurbation than in Talca. However, in both cities there is a homogeneous dispersion of risk factors and a slightly clustered pattern of the variable number of vaccine doses (Moran's Index of 0.221 for La Serena and 0.248 for Talca).

When developing the Getis-Ord Hot Spot analysis, it is observed that there are certain spatial concentration zones in both cities, as shown in Fig. 4. In the case of La Serena-Coquimbo conurbation, a significant concentration zone (95–99% confidence) of people 5–6 doses is observed in the central residential area of La Serena. At the same time, 3 significant clusters of people with 0–3 doses are observed in peripheral areas of the same city and on a sector of Coquimbo. In the case of Talca city,

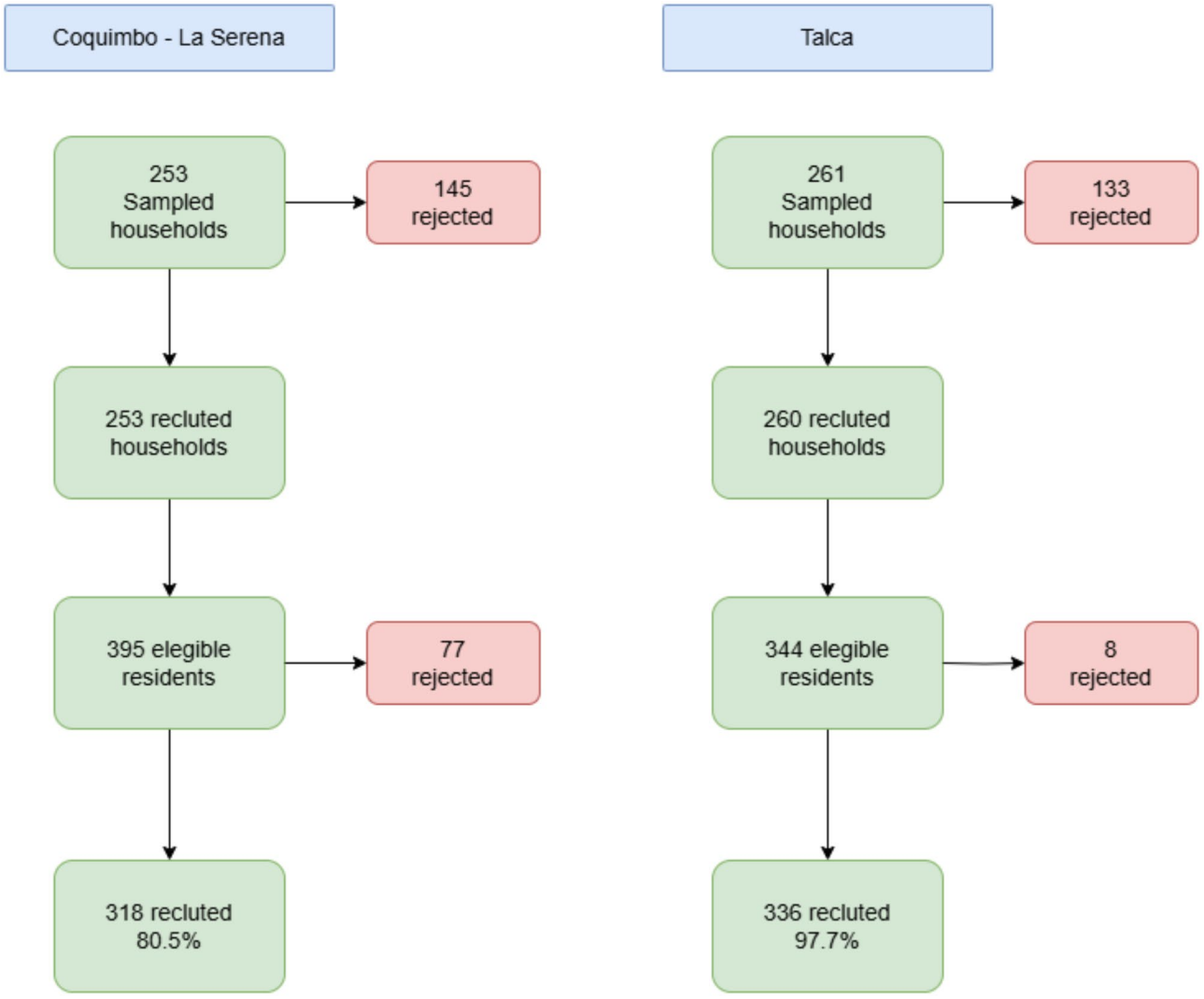

Fig. 2 Flowchart of participants in the seroprevalence study in two cities, Chile 2024

there is an important cluster (95–99% confidence) of high dose values (5–6 doses per person) in the residential centre of the city. At the same time, small sectors could be classified as clusters of low dose values, but only with 90–95% confidence.

In Fig. 1 Directed Acyclic Graph (DAG) is shown, representing the factors that may confuse the relation between vaccination acceptability: number of doses and time (dependent variable) and risk perception (independent variable).

Table 3 refers to people who fall within the vaccination target group according to the health authorities by the end of 2023 ($n = 569$). Vaccine coverage of the schemes of interest received, and their relationship with sociodemographic and clinical factors are shown. Sample data and population coverages are presented after the sample expansion process. Among individuals in the risk group, as defined by the health authority, nearly half (49.6%) had not received the most recent vaccination schemes. Of these, 35.1% were vaccinated with the bivalent vaccine, and 15.3% also had the univalent Omicron vaccine (data not shown). No significant differences were observed between cities.

For the latest schemes, coverage increased with age, reaching 72.0% among individuals aged 60 or older. In contrast, the number of people with incomplete schedules or unvaccinated is higher at younger ages. These differences were statistically significant. Among at-risk population, the association between educational level and vaccination schedules was only significant at the 10% level. In terms of education, no clear trend is observed, while those actually at-risk show a higher frequency of vaccination schedules in the last two years. None of the other studied variables showed any significant relation to the frequency of vaccination schedules received.

Fig. 3 Geographical distribution of the individuals according to the number of doses of vaccines registered. It shows a high and wide extension of vaccine coverage

Table 4 presents the overall and cluster linear regression models for each city, showing the factors predicting vaccination (number of vaccine doses received). It should be noted that the inclusion of this variable reduces the number of individuals included in the analysis, as there are participants who reported not having had the disease. It is observed that, globally for people at risk, the variables that influence the decision to be vaccinated more often are age over 40 years and having comorbidities. However, when each city is analysed separately, in La Serena/Coquimbo the influence of age remains significant, the influence of education emerges, and the influence of comorbidities disappears. In contrast, in Talca, age and comorbidities are maintained. In none of the models was the number of COVID-19 episodes statistically significant.

Table 5 compares the participants' self-reported information on the risk group with the information collected in the survey on risk factors defined by the health authority. Some 14% of the people are over 60 years of age, but they do not consider themselves within the risk group. This situation is significantly higher in the La Serena/Coquimbo conurbation than in Talca, and in people who have attained high school education. Likewise, the phenomenon shows a downward trend as age increases. That is, those who do not identify themselves as a risk group are closer to the lower boundary of the age group, which is 60 years.

Regarding obesity (excluding overweight), 65% do not recognize themselves as obese even though they are. None of the explored variables resulted in significance when comparing the groups. Concerning comorbidities, 60% of people report some chronic condition in the survey but are not auto reported within the risk group for vaccination. Factors associated with this situation are the city (being higher in the La Serena/Coquimbo conurbation) and age. The young adult groups (20 to 49 years of age) have the highest frequency of discordance (between 70 and 87%).

In general, around 24% of the participants had some risk condition but did not self-identify as being at risk and a priority to receive the vaccination. The situation is

Table 1 Characterization of the participants (sample) in terms of the frequencies of sociodemographic and clinical variables. Estimated vaccination coverage in the population, following population expansion process, and its relationship with sociodemographic and clinical factors. Two cities in Chile, year 2023

Variable	Category	Number and frequency of vaccinations according to the scheme received.														[a] Chi square
		Sample		Population		Vaccinated (total)		Not vaccinated		Basic scheme and/or boosters		Bivalent 2023		Omicron (until May 2024)		
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	p
Total ($n=654$)		654	100.0	722,430	100.0	711,429	98.5%	11,001	1.5	380,504	52.7	232,133	32.1	98,792	13.7	-
City	Coquimbo/La Serena	318	48.6	458,184	63.4	448,882	98.0%	9302	2.0	255,657	55.8	143,618	31.3	49,607	10.8	0.197
	Talca	336	51.4	264,246	36.6	262,546	99.4%	1700	0.6	124,847	47.2	88,515	33.5	49,185	18.6	
Age group	0–19	25	3.8	30,243	4.2	29,567	97.8%	676	2.2	28,319	93.6	634	2.1	614	2.0	0.000
	20–29	71	10.9	84,199	11.7	84,199	100.0%			66,392	78.9	12,848	15.3	4959	5.9	
	30–39	69	10.6	66,241	9.2	63,672	96.1%	2569	3.9	45,459	68.6	15,225	23.0	2988	4.5	
	40–49	102	15.6	188,008	26.0	187,323	99.6%	685	0.4	114,675	61.0	67,219	35.8	5428	2.9	
	50–59	124	19.0	132,103	18.3	129,283	97.9%	2820	2.1	67,895	51.4	43,766	33.1	17,622	13.3	
	60+	263	40.2	221,636	30.7	217,385	98.1%	4251	1.9	57,763	26.1	92,441	41.7	67,181	30.3	
Sex	Male	232	35.5	346,457	48.0	343,637	99.2%	2820	0.8	197,695	57.1	100,733	29.1	45,209	13.0	0.504
	Female	422	64.5	375,973	52.0	367,792	97.8%	8181	2.2	182,809	48.6	131,400	34.9	53,583	14.3	
Ethnicity	No	606	92.7	636,118	88.1	626,454	98.5%	9664	1.5	342,403	53.8	194,738	30.6	89,313	14.0	0.558
	Yes	48	7.3	86,312	11.9	84,975	98.5%	1337	1.5	38,101	44.1	37,395	43.3	9479	11.0	
Health Insurance ($n=634$)	Public	569	89.7	564,626	82.2	554,530	98.2%	10,096	1.8	292,701	51.8	178,947	31.7	82,882	14.7	0.624
	Private	53	8.4	111,820	16.3	111,820	100.0%	0	0.0	67,706	60.5	33,093	29.6	11,020	9.9	
	Armed forces	12	1.9	10,654	1.6	10,654	100.0%	0	0.0	729	6.8	7708	72.3	2217	20.8	
Education (age 18 and over, $n=635$)	Basic or less	97	15.3	92,337	13.0	89,509	96.9%	2828	3.1	25,026	27.1	42,855	46.4	21,628	23.4	0.120
	High school	319	50.2	399,867	56.5	394,755	98.7%	5112	1.3	228,194	57.1	121,597	30.4	44,964	11.2	
	Technician	81	12.8	91,640	12.9	90,405	98.7%	1235	1.3	39,787	43.4	36,649	40.0	13,969	15.2	
	Professional or postgraduate	138	21.7	124,278	17.6	123,128	99.1%	1149	0.9	74,500	59.9	30,398	24.5	18,231	14.7	
Comorbidities	No	294	45.0	316,797	43.9	307,206	97.0%	9592	3.0	199,968	63.1	87,755	27.7	19,482	6.1	0.006
	Yes	360	55.0	405,633	56.1	404,223	99.7%	1410	0.3	180,536	44.5	144,378	35.6	79,310	19.6	
Tobacco consumption	No	462	70.6	454,125	62.9	443,124	97.6%	11,001	2.4	220,946	48.7	146,607	32.3	75,571	16.6	0.218
	Yes	192	29.4	268,305	37.1	268,305	100.0%	0	0.0	159,558	59.5	85,526	31.9	23,221	8.7	
COVID-19 diagnosis	No	377	57.6	410,518	56.8	401,872	97.9%	8645	2.1	217,202	52.9	117,279	28.6	67,391	16.4	0.313
	Yes	277	42.4	311,912	43.2	309,556	99.2%	2356	0.8	163,302	52.4	114,854	36.8	31,400	10.1	
COVID-19 episodes ($n=277$)	Once	224	80.9	243,780	78.2	243,780	100.0%			136,982	56.2	91,119	37.4	15,679	6.4	0.001
	Twice	41	14.8	43,201	13.9	42,183	97.6%	1019	2.4	20,648	47.8	6609	15.3	14,926	34.5	
	Three times	12	4.3	24,931	8.0	23,594	94.6%	1337	5.4	5673	22.8	17,126	68.7	795	3.2	
Auto reported as at risk for vaccination	No	279	42.7	306,635	42.4	300,904	98.1%	5732	1.9	200,042	65.2	72,392	23.6	28,470	9.3	0.017
	Yes	375	57.3	415,795	57.6	410,525	98.7%	5270	1.3	180,462	43.4	159,741	38.4	70,322	16.9	
Actually, at risk for vaccination	No	85	13.0	94,853	13.1	94,177	99.3%	676	0.7	79,569	83.9	11,917	12.6	2691	2.8	0.000
	Yes	569	87.0	627,577	86.9	617,251	98.4%	10,325	1.6	300,936	48.0	220,215	35.1	96,100	15.3	

Table 1 (continued)

Variable	Category	Number and frequency of vaccinations according to the scheme received.														
		Sample		Population		Vaccinated (total)		Not vaccinated		Basic scheme and/or boosters		Bivalent 2023		Omicron (until May 2024)		[a] Chi square
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	p
Body mass Index (*n* = 619)	Underweight	25	4.0	29,984	4.4	28,565	95.3%	1419	4.7	8379	27.9	13,955	46.5	6230	20.8	0.334
	Normal	173	27.9	162,792	23.8	161,929	99.5%	863	0.5	106,105	65.2	40,286	24.7	15,538	9.5	
	Overweight	238	38.4	301,841	44.0	297,430	98.5%	4411	1.5	157,820	52.3	92,575	30.7	47,035	15.6	
	Obese	183	29.6	190,645	27.8	187,241	98.2%	3403	1.8	89,370	46.9	75,252	39.5	22,619	11.9	

[a] Chi-square of factors related to vaccination schedules received. Source: Designed by the authors with data from the study

significantly related to the city (lower frequency in Talca), age (higher frequency in young adults 30–39 years old), and educational level (higher frequency in the professional/postgraduate and high school groups).

Discussion

All participants had antibodies against SARS-CoV-2 in their blood, while the antigen test was 100% negative, demonstrating high immunity and the absence of acute disease in the population sample. This high seropositivity can be explained by infection during the pandemic and the high vaccination coverage achieved in the country. The overall vaccination rate reached 98.5%, although coverage in recent campaigns 2023–2024 was lower, reaching 50% by May 2024. The geographical distribution of vaccine doses showed clustering in both cities, indicating that social determinants related to territoriality might influence adherence to the COVID-19 vaccine. Factors related to vaccination status were age, having comorbidities, history of COVID-19 disease, and self-perception of being at risk. Almost a quarter of the participants did not identify themselves as being at risk, even though they were. Nearly half of those at risk of severe COVID-19 had not received the most recent vaccination schemes.

None of the individuals tested positive for antigens, indicating an undetectable level of SARS-CoV-2 viral circulation at the time of evaluation. Given this result, we hypothesized that SARS-CoV-2 is likely to be established as a prevalent infection in the spring-summer season, as has been observed in the northern hemisphere, and with a very low presence during autumn-winter [33]. This can be explained by the dominance of other respiratory viruses occupying ecological niches, which in autumn-winter is given by traditional respiratory viruses such as influenza, respiratory syncytial virus, rhinovirus, and others. Data from the Ministry of Health indicate that the incidence of COVID-19 began to increase in September, as well as deaths in October, reaching 62 cases per week and 12 deaths per week during the epidemiological week 42 (October 13-19th, 2024) [34].

The overall acceptance rate found in the study was 84,8% including basal schemes (2020–2021), boosters (2022), and the bivalent vaccine 2023, which is higher than reported in other studies. An umbrella review of COVID-19 vaccine acceptance that included studies published after 2022 found a global acceptance rate of 60.23% (95%CI: 58.27, 62.18), ranging from 48.93 (95% CI: 48.40, 49.46) to 73.31 (95% CI: 72.84, 73.87) [35]. A survey of COVID-19 vaccine acceptance across 23 countries in 2022 described a global acceptance rate of 79.1% ranging from 47.9% in South Africa to 98.3% in India [36]. Additionally, the acceptance for COVID-19 boosters was 87.9% globally, ranging from 72.9% in South Korea to 98.9 in China. They also reported an increase in acceptance

Table 2 Territorial analysis with Moran index for COVID-19 diagnosis during the pandemic, risk group status, and number of vaccine doses

City	Variable	Moran's Index	Expected index	Z score	*p* Value	Conclusion
La Serena - Coquimbo	COVID-19 diagnosis	0.396	-0.003	5,227	0.000	Clustered
	Be at risk	0.104	-0.003	1,415	0.157	Dispersed or random distribution
	Number of vaccine doses	0.221	-0.003	2,958	0.003	Slightly clustered
Talca	COVID-19 diagnosis	0.111	-0.002	1,583	0.113	Dispersed or random distribution
	Be at risk	-0.115	-0.002	-1,157	0.116	Dispersed or random distribution
	Number of vaccine doses	0.248	-0.002	3,505	0.000	Slightly clustered

Source: Designed by the authors with data from the study

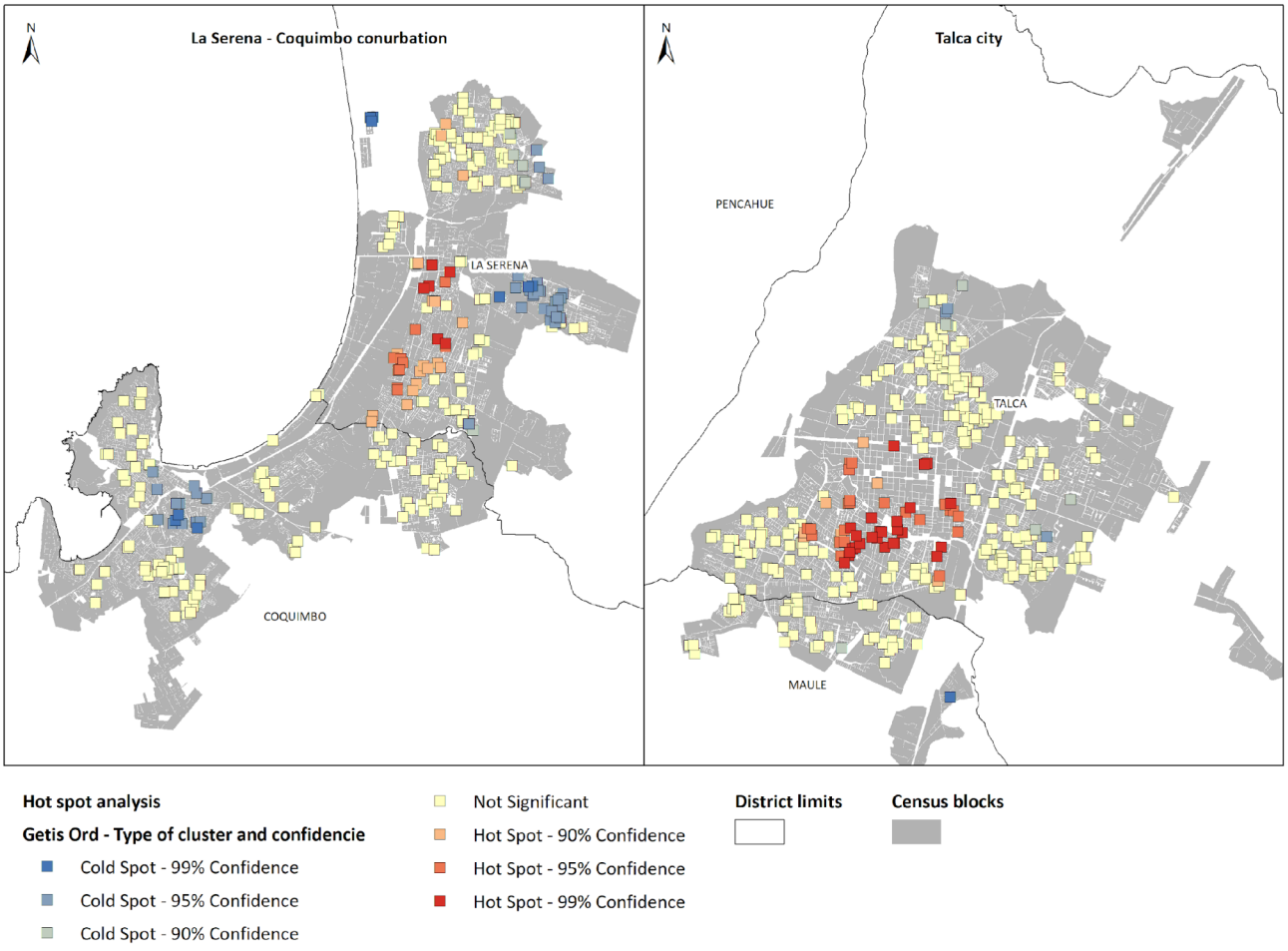

Fig. 4 Getis-Ord Hot spot analysis for the vaccine doses geographical distribution. It is observed that there are certain areas of spatial concentration in both cities, of both high and low numbers of vaccine doses

from 2020 to 2021 and from 2021 to 2022 in most countries [36]. In a previous study carried out in Chile by the same research team in 2022, a 99.9% acceptance for the basal scheme and booster is described [2].

The National Immunization Survey–Adult COVID Module (NIS-ACM) conducted between October 30 and December 31, 2022, in the USA found a 27.1% (95% CI: 26.4–27.7) acceptance rate to bivalent booster in the adult population [37]. This rate is lower than what we found in Chile in May 2023 (32.1%). This discrepancy could be explained in part by the difference in the date of both studies, sociodemographic differences, VL [25], and differences in the health system (Chile has a primary health network in charge of deploying the national immunization program). Both countries recommended bivalent vaccine boosters for adolescents aged 12–17 years and adults aged ≥ 18 years, on September 1, 2022, in the USA and September 30, 2022, in Chile [5].

No monovalent Omicron vaccine acceptance rates are reported in the scientific literature at this moment. In this

Table 3 Characterization of the participants who meet the risk criteria to be vaccinated (sample) regarding the frequencies of sociodemographic and clinical variables. Vaccination coverage in the target population*, according to the schemes of interest received, after the expansion process and its relationship with sociodemographic and clinical factors. Two cities in Chile, 2023

Variable	Category	Sample		Population		Vaccination coverage in at risk population, according to scheme received				
						Not vaccinated, basic scheme and/or boosters		Bivalent 2023 + Omicron (until May 2024)		[a] Chi square
		n	%	*n*	%	*n*	%	*n*	%	*p*
Target population (*n* = 569)	Frequency	569	1.0	627,577	1.0	311,261	49.6	316,316	50.4	-
City	Coquimbo/La Serena	270	47.5	389,090	62.0	205,671	52.9	183,420	47.1	0.3340
	Talca	299	52.5	238,486	38.0	105,590	44.3	132,896	55.7	
Age group	0–19	9	1.6	6882	1.1	6268	91.1	614	8.9	0.0030
	20–29	55	9.7	65,362	10.4	53,151	81.3	12,211	18.7	
	30–39	53	9.3	54,372	8.7	38,805	71.4	15,567	28.6	
	40–49	85	14.9	172,177	27.4	104,612	60.8	67,565	39.2	
	50–59	104	18.3	107,148	17.1	46,410	43.3	60,737	56.7	
	60+	263	46.2	221,636	35.3	62,014	28.0	159,622	72.0	
Sex	Male	199	35.0	303,554	48.4	159,059	52.4	144,495	47.6	0.5810
	Female	370	65.0	324,023	51.6	152,202	47.0	171,821	53.0	
Ethnicity	No	527	92.6	549,023	87.5	279,035	50.8	269,988	49.2	0.4480
	Yes	42	7.4	78,554	12.5	32,226	41.0	46,328	59.0	
Health Insurance (*n* = 555)	Public	499	89.9	493,952	81.2	244,458	49.5	249,494	50.5	0.4320
	Private	44	7.9	103,808	17.1	61,164	58.9	42,643	41.1	
	Armed forces	12	2.2	10,654	1.8	729	6.8	9925	93.2	
Education (age 18 and over, *n* = 562)	Primary or less	93	16.5	90,540	14.6	26,057	28.8	64,483	71.2	0.0760
	Highschool	281	50.0	338,359	54.4	181,875	53.8	156,485	46.2	
	Technician	70	12.5	82,075	13.2	32,837	40.0	49,238	60.0	
	Professional or postgraduate	118	21.0	110,759	17.8	64,649	58.4	46,110	41.6	
Comorbidities	No	214	37.6	225,669	36.0	132,615	58.8	93,054	41.2	0.1350
	Yes	355	62.4	401,908	64.0	178,645	44.4	223,262	55.6	
Tobacco consumption	No	404	71.0	400,512	63.8	190,895	47.7	209,617	52.3	0.6620
	Yes	165	29.0	227,065	36.2	120,366	53.0	106,699	47.0	
COVID-19 diagnosis	No	325	57.1	340,905	54.3	167,068	49.0	173,837	51.0	0.8960
	Yes	244	42.9	286,672	45.7	144,193	50.3	142,479	49.7	
COVID-19 episodes (*n* = 244)	Once	193	79.1	219,314	76.5	115,657	52.7	103,657	47.3	0.4660
	Twice	39	16.0	42,427	14.8	21,526	50.7	20,901	49.3	
	Three times	12	4.9	24,931	8.7	7010	28.1	17,921	71.9	
Auto reported risk for vaccination	No	198	34.8	214,614	34.2	127,728	59.5	86,887	40.5	0.0970
	Yes	371	65.2	412,963	65.8	183,533	44.4	229,429	55.6	
Body mass Index (*n* = 544)	Underweight	23	4.2	27,317	4.5	7131	26.1	20,186	73.9	0.4830
	Normal	100	18.4	84,233	13.9	37,577	44.6	46,656	55.4	
	Overweight	238	43.8	301,841	50.0	162,231	53.7	139,610	46.3	
	Obese	183	33.6	190,645	31.6	92,773	48.7	97,872	51.3	

*Target population for vaccination includes: 60 years and over, obesity and overweight, pregnant women, chronic condition/immunocompromised, health personnel. [a] Chi-square of factors related to vaccination schedules received. Source: Designed by the authors with data from the study

study, 30.3% of older adults in the two cities received the 2024 COVID-19 vaccine which was monovalent for Omicron variants. It is not possible to comment on coverage about this specific vaccine since it has been restricted to risk groups, because the measurement was carried out only two months after the campaign was initiated, and because the recommendation was to administer it one year after the bivalent vaccine was administered [5].

The vaccination status was related to age; people over 60 years presented higher frequencies of vaccine uptake, especially in the last two campaigns. At the same time, people with comorbidities showed higher vaccination

Table 4 Predictive multiple linear regression model for number of vaccine doses in at-risk population. The model is presented globally and separately for La Serena/Coquimbo and Talca cities

Variable	Category	Global	La Serena/ Coquimbo	Talca
City		0.160		
Age	0–19			
	20–29	0.787	0.858	
	30–39	0.671	0.572	0.0631
	40–49	1.251**	1.464*	0.423*
	50–59	1.152*	1.178*	0.577*
	60+	1.294**	1.261*	0.886**
Co morbidities		0.365*	0.420	0.346*
Education	Basic or less			
	Highschool	-0.484	-0.806*	0.133
	Technician	-0.131	-0.304	0.187
	Professional or postgraduate	-0.293	-0.243	-0.0316
COVID-19 episodes	Once			
	Twice	0.153	0.129	0.281
	Three times	-0.204	-0.365	0.0548
N	244	106	138	

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

rates at all moments. During the pandemic, media reports stated that people with obesity and chronic illnesses, as well as older adults, had higher mortality and ICU hospitalization rates [22]. Awareness of risk conditions was widespread, especially during the first year of the pandemic (2020), when vaccine availability was still limited, but continued to be of interest afterward [21, 24, 38, 39].

As observed in this study, previous history of COVID-19 infections (AOR = 3.41; 95% CI:1.77, 5.06) and comorbidities (AOR = 1.54; 95% CI:1.18, 1.90) have been reported associated with COVID-19 vaccine acceptance [35]. Persons with previous episodes of the disease could be more willing to get vaccinated to avoid a new episode and its complications, and those with comorbidities could be more aware of the complications and seriousness of the disease. Another factor that has been mentioned as a motivation for vaccine uptake is that patients with chronic health problems receive vaccine recommendations during their medical check-ups [24]. However, when all variables are evaluated in a predictive model for vaccination, age is the most important factor. In addition, the presence of comorbidities and educational level are shown to be influential, depending on the city. Contrary to expectations, in the La Serena/Coquimbo conurbation, a negative relationship was observed between secondary education and the number of vaccine doses. That is, people with less education were more likely to have received vaccinations. It is possible that factors beyond those included in the model - age, comorbidity - may be influencing the vaccination decision of people with that level of education.

Regarding vaccination for at-risk populations, about half of the population considered at risk of severe COVID-19 do not have the recommended vaccination schedules (years 2023–2024) and the geographical distribution of the number of doses showed hot-spots of both high and low number of doses in both cities. This fact raises questions about the reasons behind what has been observed. Is there a difficulty in risk communication? Is there a low perception of risk? Or are there other factors behind the low coverage of recent schemes? Could social determinants explain the geographical concentrations of areas with different vaccination coverage? Clearly, the door is open for further research in this area.

Having raised these questions, some answers can be found in a deeper analysis of the variables explored in this study.

Risk perception is a factor of interest for motivation to take preventive measures, including vaccination, and was studied in this way during the COVID-19 pandemic [21]. When asking participants to self-report belonging to a risk group for COVID-19 vaccination it was noted that approximately a quarter of them did not self-report as a risk group for receiving the COVID-19 vaccine despite being at risk, according to personal characteristics recorded in the survey.

As far as age is concerned, it is observed that a large proportion of the population at risk due to age did not receive the vaccine during 2024, probably because the campaign began in Chile on March 26, 2024 [5]. A study that examined 192 countries with reported data found that for persons with 60 or more years, 44.3% (13·5–69·7) completed the basic scheme plus two boosters, and for 2023-24 vaccination 23·6% (6·6–52·4) with heterogeneity

Table 5 Comparison between self-reported at-risk persons belonging to the COVID-19 vaccination group and information collected in the survey on personal characteristics of study participants in two cities in Chile in 2023

Variable		[a] Elderly person					[b] Obesity					[c] Chronic condition					[d] Belongs to a risk group for vaccination				
	Category	Are elderly (60 + years) and self-report being in the vaccination group		Are elderly and do not report being in the vaccination group		*p* value	Belongs to BMI obesity category and self-report obesity		Body mass index obesity category and do not self-report having obesity		*p* value	Has chronic disease (including obesity) and self-reports have been in the vaccination group		Has chronic disease (including obesity) and self-reports not been in the vaccination group		*p* value	Has any risk condition and self-reports been in the vaccination group		Has any risk condition and does not self-report being in the vaccination group		*p* value
		n	%	*n*	%		*n*	%	*n*	%		*n*	%	*n*	%		*n*	%	*n*	%	
Total		226	85.9	37	14.1		64	34.9	119	65.0		158	39.7	240	60.3		364	76.2	114	23.8	
City	La Serena/Coquimbo	93	80.1	23	19.8	0.020	29	35.8	52	64.2	0.877	61	32.8	125	67.2	0.008	157	70.09	67	29.92	0.003
	Talca	133	90.4	14	9.5		35	34.3	67	65.7		97	45.75	115	54.25		207	81.5	47	18.5	
Age	Under 10 years						0	0	0	0	0.672	0	0	0	0	0.0001	0	0	0	0	0.0001
	10–19						0	0	1	100		0	0	3	100		0	0	3	100	
	20–29						9	42.9	12	57.1		9	28.1	23	71.9		25	67.6	12	32.4	
	30–39						8	33.3	16	66.7		4	12.9	27	87.1		17	48.6	18	9	
	40–49						18	40.9	26	59.1		17	29.8	40	70.2		36	57.1	27	42.9	
	50–59						10	25.6	29	74.4		31	42.5	42	57.5		44	57.1	33	42.9	
	60 +						19	35.2	35	64.8		97	48.0	105	52.0		242	92.0	21	8.0	
	60–64	64	78.1	18	22.0	0.019															
	65–69	43	84.3	8	15.7																
	70–74	51	86.4	8	13.6																
	75–79	39	92.9	3	7.1																
	80 +	29	100	0	0																
Sex	Male	77	89.5	9	10.5	0.241	20	34.5	38	65.5	0.925	47	35.1	87	64.9	0.179	120	73.6	43	26.4	0.350
	Female	149	84.2	28	15.8		44	35.2	81	64.8		111	42.1	153	57.9		244	77.5	71	22.5	
Education	Basic or less	68	94.4	4	5.6	0.031	15	45.5	18	54.5	0.482	37	48.7	39	51.3	0.128	84	92.3	7	7.7	0.0001
	Highschool	107	80.5	26	19.6		29	31.5	63	68.5		82	40.2	122	59.8		173	72.7	65	27.3	
	Technician	21	84.0	4	16		7	30.4	16	69.6		17	41.5	24	58.5		42	77.8	12	22.2	
	Professional or postgraduate	30	90.9	3	9.1		13	38.2	21	61.8		22	29.7	52	70.3		65	70.6	27	29.4	
Health insurance	Public	197	84.9	35	15.1	0.214	60	36.4	105	63.6	0.314	144	40.7	210	59.3	0.405	325	77.2	96	22.8	0.308
	Private	17	100	0			2	16.7	10	83.3		8	27.6	21	72.4		24	66.7	12	33.3	
	Armed forces	8	88.9	1	11.1		1	50	1	50		3	42.9	4	57.1		9	81.8	2	18.2	
Ethnicity	No	214	85.9	35	14.0	0.613	59	35.12	109	64.9	0.566	150	40.43	221	59.57	0.313	342	77.03	102	22.97	0.104

Table 5 (continued)

Variable		[a] Elderly person					[b] Obesity					[c] Chronic condition					[d] Belongs to a risk group for vaccination				
	Category	Are elderly (60 + years) and self-report being in the vaccination group		Are elderly and do not report being in the vaccination group		*p* value	Belongs to BMI obesity category and self-report obesity		Body mass index obesity category and do not self-report having obesity		*p* value	Has chronic disease (including obesity) and self-reports have been in the vaccination group		Has chronic disease (including obesity) and self-reports not been in the vaccination group		*p* value	Has any risk condition and self-reports been in the vaccination group		Has any risk condition and does not self-report being in the vaccination group		*p* value
		n	%	*n*	%		*n*	%	*n*	%		*n*	%	*n*	%		*n*	%	*n*	%	
	Yes	12	85.7	2	14.3		5	33.33	10	66.7		8	29.63	19	70.37		22	64.71	12	35.29	
Comorbidities	No	46	83.6	9	16.4	0.663	23	31.5	50	68.5	0.261	1	1.37	72	98.6	0.0001	92	66.2	47	33.8	0.0001
	Yes	180	86.5	28	13.5		41	37.3	69	62.7		157	48.3	168	51.7		272	80.2	67	19.8	

[a] Health Insurance: $n = 258$; [b] Education: 1 participant under 18 years of age; [b] Health insurance: $n = 179$; [c] Education: 3 participants under 18 years of age

[d] Education: 3 participants under 18 years of age; [d] Health insurance: 10 people without information. [d] Risk group for vaccination include: 60 years and over, obesity (no overweight), pregnant women, chronic condition/immunocompromised, and health personnel. *Chi-square

by region [40]. Age is an objective variable. Each person knows his or her age and may or may not recognize him or herself as belonging to a risk group. In Chile, the health authority defines risk group according to age, being over 60 years old. However, 22% of people aged 60–64 and 16% of people aged 65–69 did not consider themselves to be at risk. There was a decreasing trend in the frequency of discrepancies with increasing age. So, it seems that the threshold over which someone meets the criteria of being at risk is not sufficiently clear for the population. One explanation may be that the retirement age in Chile is 60 for women and 65 for men. Other social benefits of food and solidarity old-age pension are provided for all people over 65 years of age. This may lead to confusion among the elderly. Educational level was found to be significantly associated with the discrepancy between actual age and self-perception of being at risk. Another possibility is that the risk communication strategies or messages failed to reach the target population.

Concerning obesity, 65% of obese participants, according to the body mass index calculated with the weight and height records of the survey, do not recognize themselves as obese. The misclassification found in our study is higher than is described by other authors. A study conducted in the USA reported that misclassification on their nutritional status was about 30% [41], while a Peruvian study reported that 54% of people underestimate their BMI category [42]. Another study carried out in Chile [43] on the perception of obesity showed a low concordance (43.3% v/s 53.7 discordance) between self-perception of obesity and the actual state of the condition, being lower in women, people with less education, and in rural areas, indicating a denial of the condition and, therefore, underestimation of the risk that obesity entails. In this study, none of the variables assessed were associated with this discrepancy. International studies report that sex, ethnicity, rurality, and income are factors related to discrepancies in self-perception of body image [41, 44–47]. The discrepancy between self-perceived body image and actual nutritional status can also be explained by social patterns and is a situation that merits further study in behavioural psychology. Certainly, the self-perception of an underestimated overweight and obese condition leads to a low perception of risk, not only for COVID-19 infection but also for other types of health consequences, related to cancer, cardiovascular and metabolic diseases.

As for the presence of chronic pathologies defined as being at risk, i.e. diabetes, arterial hypertension, chronic kidney disease, chronic respiratory pathologies, immunosuppression, or cancer, about 60% of the participants who had this condition did not recognize themselves as being in the risk group. The discrepancy was only associated with age, with the frequency of misclassification being higher in young adults (30–49 years).

Overall, people who have any risk condition and do not self-report be in the vaccination group were about one-quarter of the participants. That was associated with age and educational level. People aged between 40 and 60 years had higher frequencies of mismatches between self-reported and corrected risk conditions according to survey records. Surprisingly, people with the highest level of education also showed higher discrepancies.

As discussed, the discrepancy between the perception of being at risk and actually having characteristics defined as being at risk can be explained by individual factors of people (age, sex, education, HL, VL, health condition, work), although it could also be related to messages received through the media, social networks or other sources of information. Risk communication has been studied as an influential factor in the acceptance of vaccination [17, 46]. Over time, pandemic control strategies progressively reduced incidence and mortality, and it was no longer a topic of interest in the media. The absence of public messages may have influenced risk perception, therefore a decline in the vaccine acceptance rate was observed. However, some people, mostly elderly and chronic patients, maintain the self-perception of being at risk and adhere to vaccines.

One limitation of this study is that even though all participants tested positive for antibodies against SARS-CoV-2, we do not know their neutralizing capacity, which is under investigation. The sample size provides statistical power to make comparisons between two groups for variables with two categories. However, we cannot ensure the power holds when variables have more than two strata. Then the variables found to be statistically significant are actual, but given the sample size, we cannot say the same for variables that were not significantly associated. The main strength of the study is that it has a community-based, randomized, and representative sample of two Chilean cities, allowing the results to be extrapolated to these populations.

Conclusions

In both cities, immunization against SARS-CoV-2 reaches most of the population. However, the distribution of vaccine doses differs according to territorial factors, age, education, and the population's perception of risk. The variable that best predicts vaccination status in at-risk population is age. The presence of comorbidities and educational level also play a role, although in different ways in each city.

Risk communication must be improved, especially for risk groups, to help them perceive themselves as beneficiaries of vaccination for COVID-19. Regarding the perceived increased risk of COVID-19 severity, healthcare

professionals and government authorities have been identified as pivotal factors influencing vaccine acceptance [25]. Additionally, disseminating information about the safety of the vaccine and counteracting misinformation should be implemented to increase vaccine literacy.

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Author contributions
Conceptualization, L.N-F. and M.R-S.; Methodology, M.R-S., P.R. and M.A.; Software, P.R., M.A., J.C. and L.C.; Validation, P.R., M.A., X.M. and L.C.; Formal Analysis, P.R., M.A., J.C. and L.C.; Investigation, L.N-F., M.R-S., K.O., M.S., X.M and L.J.C.; Resources, L.N-F., M.S., K.O., L.J.C. and M.R-S; Data Curation, P.R., M.A. and L.C; Writing – Original Draft Prepa-ration, L.N-F. and M.R-S.; Writing – Review & Editing M.R-S., L.N-F., P.R., J.C., L.J.C. and M.A.; Visualization, L.N-F., M.R-S.; Supervision, L.N-F. and M.R-S.; Project Administration, L.N-F. and M.R-S.; Funding Acquisition, L.N-F. and M.R-S.

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Data availability
Data is provided within the manuscript or supplementary information files. Data could be sent upon written request to the corresponding author while maintaining the confidentiality of the participants.

Declarations

Ethics approval
The study was conducted in accordance with the Declaration of Helsinki, and the study protocol was reviewed and approved by three independent Scientific Ethical Committees: (1) Scientific ethical committee from the Faculty of Medicine, Universidad Católica del Norte, Resolution number 63/2023, dated October 16th, 2023. (2) Scientific ethical committee from the Faculty of Medicine, Universidad del Desarrollo, dated December 13th, 2023, and (3) Scientific ethical committee from Universidad de Talca, Folio 30-2023-E, dated April 17th, 2024. Additionally, it was approved by the Institutional Committee of Biosecurity of Universidad Católica del Norte 07/2023 dated October 2023, Universidad del Desarrollo, CIB-FORM-01B, dated 14 November 2023, and Universidad de Talca 20-CBS-2023 dated November 9th, 2023.

Informed consent
Any research article describing a study involving humans should contain this statement. Informed consent was obtained from all subjects involved in the study, including assent to minors (7 to 17 years).

Consent for publication
All authors reviewed and approved the final version of the manuscript for publication.

Competing interests
The authors declare no competing interests.

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