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RESEARCH PAPER

Knowledge, attitudes, and practices regarding hantavirus disease and acceptance of a vaccine trial in rural communities of southern Chile

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ABSTRACT

Andes hantavirus cardiopulmonary syndrome, transmitted by *Oligoryzomys longicaudatus*, has no approved treatment, a case fatality rate of 35%, and documented person-to-person transmission. An Andes vaccine, highly needed for prevention, is in development. We aimed to evaluate knowledge, attitudes and practices (KAP) regarding hantavirus disease and willingness to participate in a future Andes vaccine trials through a cross sectional face-to-face oral survey of a randomly selected adult sample from 2 rural communes in southern Chile. Human subjects approval was obtained from our institutional IRBs, and participants signed informed consent. We enrolled 319 subjects from Corral and 321 from Curarrehue; 98% had heard about hantavirus disease and its reservoir but only half knew about transmission, symptoms and prevention. Participants fear the disease but are only partially aware of their own risk. One third of participants reported presence of rodents inside their homes. Despite moderate confidence in their health system, most subjects perceived vaccines as beneficial, and 93% would accept an approved hantavirus vaccine. Half would agree to participate in a vaccine trial and 29% would allow their children to participate. Motivations to participate were mainly altruistic, while risk perception was the main reason for declining. Knowledge about hantavirus disease and prevention practices require reinforcement, and a vaccine trial seems feasible in these populations.

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Introduction

Hantavirus cardiopulmonary syndrome (HCPS) occurs throughout the Americas, with variable incidence and mortality.[1-4] Andes virus (ANDV) has a case fatality rate of 34% and is the only known etiologic agent of HCPS in Chile.[5] At present there is no specific treatment or vaccine for this disease. The main reservoir of ANDV is the wild sigmodontine rodent, *Oligoryzomys longicaudatus*, which is distributed through central and southern Chile and southern Argentina. Rodents become infected for life by horizontal transmission, whereas the principal route of infection in humans is through inhalation of rodent excreta. However, ANDV is the only hantavirus in which person-to-person transmission, primarily in small clusters among sex partners and other close household contacts, also occurs.[6-8]

The annual incidence of HCPS in Chile ranges from 0.2–0.5/100.000 inhabitants. Seventy percent of cases occur in men, and the median age is 32 with a range of 6 weeks to 80 y.[9] Despite active public health educational efforts focused on avoiding exposure to rodents and their excretions, the incidence of disease has remained stable.

Immune responses to hantaviruses are only partially understood, but it has been suggested that innate and cellular immune responses contribute to pathogenesis of the disease. Nevertheless, passive transfer of neutralizing antibodies (NAbs) to Gn and Gc envelope glycoproteins provides protection from infection in different animal models and can also protect against disease in the Syrian hamster model.[10-12] In humans, high titers of NAbs against SNV at hospital admission are associated with reduced mortality.[13] An open study in Chile of treatment of HCPS by passive transfusion of anti-ANDV immune serum was promising, but the open study design prevented analysis of efficacy.[14] Most vaccine efforts are directed to developing of NAbs to the glycoproteins Gn and Gc, coded in the hantavirus M segment.[10]

An effective hantavirus vaccine targeted against ANDV or multiple, pathogenic New World hantaviruses is needed in order to decrease the significant morbidity and mortality from HCPS. In Chile and Argentina, a candidate vaccine should target high risk groups such as rural inhabitants, agriculture and forestry workers, soldiers and adventure travelers. It might also be used after natural disasters, as we observed an increased incidence of HCPS in the affected region following a major earthquake in 2010. Hantaviruses have also been recognized as a potential bioterrorist threat and are classified as a NIAID category A priority pathogen.[15]

A candidate ANDV vaccine is likely to be available for use in human trials in the near future.[16-19] A Hantaan virus (HTNV)

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inactivated vaccine has been in use in China since 1990. DNA vaccines carrying plasmids with M segments from pathogenic New and Old World hantaviruses are in development. A phase I clinical trial of a DNA HTNV and/or Puumala (PUUV) vaccine showed that they were safe and immunogenic,[20] and a DNA vaccine for HCPS, including Sin Nombre virus (SNV) and ANDV M segments, was immunogenic in non-human primates and produced human IgG NAbs following vaccination of transchromosomal bovines.[12,21]

The sporadic presentation of the disease and low incidence suggest that it is exceedingly unlikely that vaccine efficacy studies would be feasible in humans. Strategies for future licensing of an ANDV vaccine in Chile will probably require an approach in which immunogenicity and safety are demonstrated in population at risk of the disease, and efficacy is demonstrated through studies proving passive protective immunity by sera from vaccinated subjects in an animal model using the framework of the "animal rule" of the US Food and Drug Administration.[22]

People at highest risk of acquiring the disease are rural inhabitants, who frequently have socioeconomic and educational disadvantages that make them vulnerable. As such, before implementing any clinical trials of investigational vaccines in this population, we felt that it was important to assess the baseline knowledge, attitudes and practices (KAP) regarding hantavirus disease, willingness to participate in a future ANDV vaccine trial and the motivations for their acceptance/rejection to this participation in 2 rural communities in southern Chile. The KAP study method provides information regarding what is known, believed and done by a particular population related to a specific topic. It provides information regarding reasons and motivations for people's conduct in a determinate area. The three levels of understanding obtained allow for better design of strategies or programs taking into account the community's perceptions and needs.[23,24,25,26] We hypothesized that knowledge of the disease and risk perception, together with confidence in health system would be associated with willingness to participate in a vaccine trial.

Results

We enrolled 319 subjects from Corral and 321 from Curarrehue. Demographic characteristics are shown in Table 1. A higher proportion of women were enrolled than men, but gender distribution was similar at the 2 sites. Participants from Corral where slightly older, whereas there was a higher proportion of indigenous Mapuche and rural subjects in Curarrehue. Consistent with socioeconomic characteristics of the commune, the educational level was lower and inadequate housing higher in Curarrehue.

Knowledge about hantavirus disease

Most of the participants had heard about hantavirus disease and about the rodent reservoir known as "ratón colilargo," but when shown a picture of an *O. longicaudatus*, only 18% had seen the rodent, with higher frequency in Curarrehue and in men. With regard to the disease, 58% reported knowing its symptoms. When asked to describe the symptoms, fever was correctly mentioned by 46%, followed by vomiting and headache. With respect to the mode of transmission, 61% declared that they knew the mode of transmission, but only 46% mentioned that it is transmitted by rodents or their droppings. Sixty-three percent of participants reported that they knew how to prevent the disease, with a higher proportion in Corral. Correct measures, like keeping the home and surroundings clean and ventilating before entering closed dwellings, were also mentioned with higher frequency in Corral, but rodent control was mentioned with low frequency in both communes. The main information source regarding hantavirus disease in both communes was television. The radio was the second most common information source, with higher impact in Curarrehue. Posters and flyers, school and newspapers were mentioned more frequently in Corral. See Table 2.

Table 1. Sample socio-demographic characteristics from the 2 study sites[(a)].

	Curarrehue (n = 321)	%	Corral (n = 319)	%	Total (n = 600)	%	*p* value[(b)]
Age (mean, years)	48.2		51.5		49.9		0.019
Sex							
Female	197	61	198	62	395	62	0.46
Ethnicity							
Mapuche	219	68	82	26	301	47	0.000
Other indigenous	0	0	2	0	2	0	
Not indigenous	102	32	233	74	335	53	0.000
Rural inhabitants	224	70	109	35	333	53	0.000
Years of formal studies (mean, years)	7		7.9		7.5		0.004
Housing							
Concrete	1	0.3	28	9	29	5	0.000
Other	315	99.7	284	91	599	95	
House Floor							
Cemented floor	64	20	33	11	97	15	0.000
Wood floor	254	80	280	89	534	85	0.002
Dirt floor	0	0	1	0	1	0	
Latrine	159	71	57	16	216	34	0.000

[(a)]Comparison of the socio-demographic characteristics of the randomly selected subjects who agreed to answer the study survey from the communes of Curarrehue and Corral in southern Chile.
[(b)]Differences in proportion of affirmative answers between study sites (Curarrehue and Corral) using chi-square test (χ^2).

Attitudes

Almost all of the enrollees classified hantavirus as a severe/very severe disease that can cause death. Sixty-six percent in Corral and 24% in Curarrehue ($p < 0.000$) reported that they knew someone who had hantavirus disease. Farm workers were perceived as the group with highest risk of disease, followed by forestry workers and rural inhabitants. Of note, participants from Curarrehue, the commune with more farming and forestry workers, mentioned these risk factors less frequently.

Risk perception

39% of participants considered themselves at high/very high risk of acquiring hantavirus disease, compared with a perceived risk of 31% for their families and 49% for members of their communities. The reasons mentioned for being at risk were

Table 2. Knowledge about hantavirus disease by study site[a].

	Curarrehue	%	Corral	%	Total	%	*p* value[b]
Have you heard about "hanta" disease? (Yes)	309	96	315	99	624	98	0.038
Have you heard about "raton colilargo"? (Yes)	304	95	315	99	619	97	0.005
Have you seen the rodent (picture of *O. longicaudatus*)? (Yes)	68	21	47	15	115	18	0.022
Do you know the symptoms of "hanta" disease? (Yes)	180	56	189	59	369	58	0.232
Could you tell me them? (open answer):							
Fever	136	42	159	50	295	46	0.035
Flu like	14	4	17	5	31	5	0.350
Headache	63	20	39	12	102	16	0.007
Gastrointestinal symptoms	78	24	107	34	185	29	0.006
Myalgia	37	12	28	9	65	10	0.154
Do you know how "hanta" is transmitted? (Yes)	175	55	212	66	387	61	0.001
Could you tell me how? (open answer):							
Through rodent/rodent droppings	127	40	167	52	294	46	0.001
Do you know how to prevent "hanta" disease? (Yes)	166	52	234	73	400	63	0.000
Could you tell me how? (open answer):							
House cleanliness	89	28	143	45	232	37	0.000
Clean surroundings	73	23	76	24	149	23	0.409
Rodent control	9	3	13	4	22	3	0.253
Ventilating closed rooms	52	16	78	25	130	20	0.006
How did you mainly learn about this disease?							
Through TV	204	64	185	58	389	61	0.087
Radio	46	14	86	27	132	21	0.000
Health facilities	31	10	42	13	73	11	0.102
Relatives, friends, neighbors	25	8	27	9	52	8	0.433
Posters, flyers	18	6	94	30	112	18	0.000
School	10	3	27	9	37	6	0.003
Newspapers	3	1	11	3	14	2	0.027
Magazines	1	0	6	2	7	1	0.060

[a]Answers of participants to a structured KAP questionnaire to assess their knowledge regarding hantavirus disease symptoms, mode of transmission, prevention, and the sources of information.
[b]Differences in proportion of affirmative answers between study sites (Curarrehue and Corral) using chi-square test (χ^2).

Table 3. Attitudes toward hantavirus disease in the study sites[a].

	Curarrehue	%	Corral	%	Total	%	*p* value[b]
How severe do you think is "hanta" disease?							
Severe or very severe	308	96	309	97	617	97	0.334
Do you believe that someone can die from hantavirus? Yes	312	98	311	99	623	98	0.199
Do you know someone who has had "hanta" disease? Yes	78	24	211	66	289	45	0.000
Which people do you think have higher risk of getting "hanta" disease?							
Farm workers	176	55	230	72	406	63	0.000
Forestry workers	130	41	74	23	204	32	0.000
Rural inhabitants	104	32	89	28	193	30	0.124
What do you think is your own risk of acquiring hantavirus disease?							
Low/very low	91	28	95	30	186	29	0.368
Moderate	81	25	95	30	176	28	0.110
High/very high	131	41	115	36	246	39	0.130
What do you think is the risk of a member of your family of acquiring Hantavirus disease?							
Low/very low	80	25	113	36	193	30	0.003
Moderate	74	23	95	30	169	27	0.038
High/very high	109	34	90	28	199	31	0.059
What do you is the risk of people in your community for acquiring hantavirus disease?							
Low/very low	32	10	40	13	72	11	0.191
Moderate	74	23	95	30	169	27	0.036
High/very high	160	51	153	48	313	49	0.317
Have you ever thought you have "hanta" disease?							
Yes	22	7	14	4	36	6	0.117
Did you seek for health attention at that time?	11	50	6	60	17	53	0.445
In general, how do you feel about your health service capacity to solve your health problems?							
Unsatisfied/very unsatisfied	126	39	144	45	270	42	0.071
Indifferent	20	6	23	7	43	7	0.364
Satisfied/very satisfied	160	50	138	44	298	47	0.06
How is your trust in your health personnel?							
Low/very low	75	24	94	30	169	27	0.088
Moderate	74	24	110	35	184	29	0.003
High/very high	145	47	103	32	248	40	0.000

[a]Answers of participants to a structured KAP questionnaire to assess their attitudes and feelings regarding the severity of hantavirus disease, risk perception, and satisfaction with health services
[b]Differences in proportion of affirmative answers between study sites (Curarrehue and Corral) using chi-square test (χ^2)

living or working in a high risk place, presence of rodents in the environment and picking up wood or wild fruits. Six percent of the people reported that they had thought at some point that they had hantavirus disease, and 67% reported that they would feel fear if they were diagnosed with hantavirus disease.

Satisfaction with the health system and health personnel

Forty-seven percent of the subjects reported that they feel satisfied/very satisfied with their hospital or local health center capacity to attend their health problems. The proportion was lower in Corral, in women and among younger subjects. In Curarrehue, 47% reported high trust in health personnel versus only 32% in Corral. See Table 3.

Practices

Almost one third of the participants in both sites reported presence of rodents inside their homes during the past year. Forty percent reported holes through which rodents can enter. Thirty-six percent stored wood inside or near the house and 16% stored crops inside the house, more frequently in Curarrehue. Presence of rodents in storehouses was also higher in Curarrehue than in Corral.

With respect to cleaning practices of places with rodent droppings, 63% answered spontaneously that they cleaned with chlorine or disinfectant, and 82% answered "always" when asked if they cleaned with chlorine or detergent. Ninety percent

Table 4. Practices regarding hantavirus disease[a].

	Curarrehue	%	Corral	%	Total	%	*p* value[b]
Have you had rodents inside your home this year? (yes)	100	31	97	31	197	31	0.314
Does your home have holes where mice can enter? (yes)	138	43	102	32	240	38	0.003
Have you had rodents in your storerooms this year? (yes)	172	54	89	28	261	41	0.020
Do you ventilate at least 30 minutes before entering a closed dwelling? Always	275	86	242	77	517	81	0.352
Do you trap rodents? (yes)	245	77	235	74	480	75	0.268
When you clean closed dwellings, do you avoid raising dust? (yes)	263	86	216	80	479	83	0.045
Do you clean places with rodent droppings with chlorine/detergent?	203	63	202	63	405	63	0.524
Do you clean with detergent or bleach areas with signs of rodents? (always)	256	80	272	85	528	83	0.150
Do you store wood inside or near your home (less than 30m)? (yes)	131	41	102	32	233	36	0.012
Do you store crops inside your home? (yes)	62	19	40	13	102	16	0.024
Do you hunt or kill rodent predators (owls, foxes, snakes)?							
Never	294	92	292	92	586	92	0.519
Always	18	6	5	2	23	4	0.010

[a]Answers of participants to a structured KAP questionnaire to assess their exposure to rodents and behaviors that can increase/decrease exposure to rodents or their droppings.
[b]Differences in proportion of affirmative answers between study sites (Curarrehue and Corral) using chi-square test (χ^2)

reported that they ventilated closed buildings before entering. Half of the people reported that they cut weeds around the house monthly, and 90% that they keep the garbage can with a closed lid. Only 5.7% in Curarrehue and 1.6% in Corral declared that they hunted owls, foxes, snakes or wildcats, the natural predators of the reservoir. See Table 4.

Vaccine perception

Over 90% of participants had received vaccines, and most knew the benefits of vaccines or perceived them as good. Less than 1% perceived vaccines as bad or had fear of vaccines. Most would get themselves vaccinated if there was an approved hantavirus vaccine, without differences for commune, sex or age, but only 80% would vaccinate their children. (Table 5).

Willingness to participate in a vaccine trial

Half of the participants declared that they would agree to participate in a vaccine study for hantavirus, with no significant difference between sites. In those who agreed to participate, more than half would do so because it is a benefit for society

Table 5. Attitudes toward vaccines[a].

	Curarrehue	%	Corral	%	Total	%	*p* value[b]
Have you ever been vaccinated? (Yes)	301	94	312	98	613	96	0.013
In your opinion, what is your perception about vaccines? (open answer):							
Vaccines protect against diseases	292	91	302	95	594	93	0.048
Vaccines are good	300	94	307	96	607	95	0.079
Vaccines are bad/cause fear	3	1	1	0	4	1	0.314
Would you agree to receive a licensed hantavirus vaccine? (yes)	301	94	291	91	592	93	0.067
For people who would not agree to receive a licensed hantavirus vaccine: What is the main reason for not accepting a licensed hantavirus vaccine? (open answer) Fear/ mistrust	11	3	7	2	18	3	0.220
Would you allow your children to receive a licensed hantavirus vaccine? (yes)	242	78	260	82	502	80	0.122
For people who would not agree to receive a licensed hantavirus vaccine: What is the main reason for not accepting a licensed hantavirus vaccine? (open answer) Fear/ mistrust	4	1	5	2	9	1	0.319
Would you agree to participate in a hantavirus vaccine evaluation study? (yes)	165	52	161	51	326	51	0.074
What is/are the main reasons for agreeing to participate? (open answer)							
It is the only way to know if vaccine is good	11	3	18	6	29	5	0.108
To learn about hantavirus	7	2	20	6	27	4	0.006
To prevent hantavirus	48	15	33	10	81	13	0.048
It is a benefit for society, to help others	95	30	80	25	175	27	0.094
What is/are the main reasons for refusing to participate(open answer)							
Fear/dislike vaccines	16	5	21	7	37	12	0.112
Because they are old/ vulnerable	21	7	25	8	46	14	0.145
They don't want to be a subject in an investigation/be like guinea pigs	8	2	7	2	15	5	0.586
Don't have time/not interested	5	2	4	1	9	3	0.595
A new vaccine is risky	91	28	65	20	156	49	0.055
Would you agree to allow your children to participate in a hantavirus vaccine evaluation study? (yes)	84	26	101	32	185	29	0.076

(*Continued on next page*)

Table 5. (*Continued*)

	Curarrehue	%	Corral	%	Total	%	*p* value[(b)]
What is/are the main reasons for agreeing to allow their children to participate?(open answer):							
It is the only way to know if vaccine is good	4	1	8	2	12	4	0.288
To learn about hantavirus	6	2	45	14	21	7	0.077
To prevent hantavirus	43	13	34	11	77	24	0.012
It is a benefit for society and science, to help others	28	9	32	10	60	19	0.467
What is/are the main reason(s) for refusing to allow their children to participate (open answer):							
Because they are vulnerable and minor	25	8	4	1	29	9	0.000
You should not experiment with children	11	3	5	2	16	5	0.104
A new vaccine is risky	86	27	94	29	180	56	0.139
For people who refused to allow both themselves and their children to participate in hantavirus vaccine study: In which conditions would you agree to participate?							
when vaccine has been proven and is safe	21	12	34	21	55	16	0.021
If paid	0	0	6	4	6	2	0.012
Under no circumstance	137	79	66	41	203	60	0.000

[(a)] Answers of participants to a structured KAP questionnaire to assess their acceptance of a licensed hantavirus vaccine and willingness to participate in a hantavirus vaccine trial

[(b)] Differences in proportion of affirmative answers between study sites (Curarrehue and Corral) using chi-square test (χ^2)

and 25% to prevent the disease. Among those who did not want to participate, 57% considered it a risk because it was a new vaccine. They reported the decision not to participate would not change even if they were paid. In contrast only 29% would allow their children to participate in a vaccine study for hantavirus. The main reason for not accepting was risk of a new and unknown vaccine. (Table 5).

Statistical analysis

Bivariate analysis showed that willingness to participate in a hantavirus vaccine trial was significantly higher in men, in people who reported having seen the "colilargo" rodent, those who received information on hantavirus disease mainly through the health system, and those that recognized vomiting and abdominal pain as a hantavirus disease symptom. Subjects who perceived farm and forestry workers, older people and rural inhabitants as high risk groups were also more willing to participate in a vaccine trial. Those who perceived themselves or their communities at high risk and those who had high confidence in the health personnel were also more willing to participate.

Practices associated with willingness to participate included being careful not to raise dust when cleaning, storing crops and wood away from the house and trapping rodents. Having a latrine and presence of rodents in their storerooms were also associated to willingness to participate. People who would accept a licensed vaccine were more willing to participate in a vaccine trial.

In the multivariate analysis the only significant variables for willingness to participate in a vaccine trial were reporting vomiting as part hantavirus disease, storing crops near the house and perceiving forestry workers as high risk people.

Discussion

The present study enabled the assessment of baseline understanding of hantavirus disease, risk perception and practices regarding disease prevention in 2 rural communities in southern Chile. We also assessed attitudes toward vaccines and willingness to voluntarily participate in a hantavirus vaccine study. We found that the great majority of participants in this survey had some knowledge about hantavirus disease and had heard about its rodent reservoir, but less than half were aware that the disease is transmitted by rodents and their droppings. Most subjects reported not to have seen the specific reservoir, *O. longicaudatus*, and fever as the main symptom of the disease was mentioned by less than half of the participants. Television had the highest communicational impact.

People in these communes were aware that hantavirus disease can be very severe and cause death. They perceived themselves, their families and communities at risk of acquiring this disease because of the place they live in and their occupations. Most fear the disease, probably as a result of living in small communities where cases and deaths have occurred. A widely reported outbreak of 5 hantavirus cases with 2 deaths and documented person-to-person and nosocomial transmission occurred in Corral in 2011, probably accounting for higher reporting of knowing someone who had hantavirus disease in this locality.[27]

Although correct preventive practices like ventilating closed dwellings, using bleach or detergent and not raising dust when cleaning places with rodent droppings were frequently mentioned, 30 and 40% reported presence of rodents inside their homes and storerooms, respectively. Muñoz-Zanzi found an even higher presence of rodents in rural and slum households.[28] Storing wood and crops inside the homes was also reported. Of note, rodent control was mentioned by only 3% of the subjects as a preventive measure for hantavirus. Education probably needs to be reinforced in this respect, but control of rodent infestation of homes will probably require an improvement in housing standards to avoid indoor contact with rodents.

In Chile public authorities, local governments, health and educational services and media have widely disseminated information about this disease and its mode of transmission. Mc Connell reported higher knowledge and prevention of hantavirus disease in southern Chile than in Panama and New Mexico and attributed this to more effective public health messages.[29] Nevertheless, our results highlight an insufficient knowledge of hantavirus disease and its prevention and frequent contact with rodents inside homes constituting an important risk for acquiring this severe disease. Specific

preventive practices at work should also be explored in future studies.

Although confidence in health services and health personnel was moderate, there was a positive perception toward vaccines, and most people were willing to get vaccinated with a licensed vaccine for hantavirus. Half would also agree to participate in a new vaccine study, mainly for altruistic reasons. However, acceptance diminished in the case of their children, fearing an unknown risk.

Our results demonstrate the need for improving knowledge and preventive practices of hantavirus disease in these rural populations. Higher knowledge of the disease, risk perception, confidence in health system and better preventive practices may influence the decision to participate in a future vaccine trial. Adequate planning of future ANDV vaccine trials in these communities seems feasible provided previous interventions to ensure adequate understanding of the risks and benefits of participating in a vaccine trial.

Materials and methods

Human subjects approval was obtained from our institutional IRBs. The study was conducted in accordance with the Declaration of Helsinki. We performed a descriptive cross-sectional face-to-face survey of representative adult populations older than 18 y. We chose 2 rural locations in high risk areas in southern Chile with occurrence of cases in the last 5 years: the Andean location of Curarrehue with a population of 7,715 inhabitants, and the coastal location of Corral with 4,909 inhabitants in 2012.[30] Both locations are defined as communes corresponding to the smallest administrative unit according to the political-geographic division of Chile. See Table 6.

We developed a structured KAP questionnaire to assess knowledge, attitudes and practices regarding hantavirus disease and vaccines and willingness to participate in a future hantavirus vaccine trial.[24] The questionnaire had 77 open and closed questions covering 1) demographics; 2) knowledge of hantavirus disease, mode of transmission and symptoms; 3) attitude toward hantavirus disease and risk perception; 4) prevention practices; 5) attitude toward health providers and vaccines; 6) acceptability of a licensed vaccine for hantavirus; and 7) acceptability of participating in a hantavirus vaccine trial. We validated the questionnaire and method for the survey with 12 subjects from a rural location in Region Metropolitana. These were not included in the final analysis. We selected a representative sample of the adult population in both communes, considering a proportion sample with a 35% of acceptability to participate in a vaccine trial, an α error of 5% and a confidence interval of 95%.

Sample selection was performed in 3 steps: A) Selection of blocks or geographic units through simple random sampling, using a geospatial method and identifying rural and urban households according to the 2002 national census; B) Selection of homes within each block or geographic unit. The number of households in each geographic unit was determined using the ArcGIS 9.3 software. For household selection in urban areas, we scanned a block of homes from the southeast corner in counterclockwise direction and through "systematic jumps" of 2 homes, until a positive contact was done (home with at least one adult). In scattered rural areas, the homes were addressed in north-to-south direction, also through "systematic jumps" and then in the opposite direction. C) Selection of a subject older than 18 from the selected home to answer the survey. If more than one adult lived in the home, subject selection was done randomly through a Kish table.

Table 6. Characteristics of the study sites, the Andean commune of Curarrehue (39°21′S 71°35′ W) and the coastal commune of Corral (39°52′ S 73°26′ W), in southern Chile.

	Curarrehue	Corral
Ecological region	Andean	coastal
Surface (km^2)[31,32]	1170	767
Altitude (average, meters above sea level)	406	61
Rural population[27]	5555	1610
Urban population[27]	2160	3299
Total population[27]	7715	4909
Indigenous people[27]	4932	532
Rural households[31,32]	1463	764
Urban households[31,32]	584	1190
Total households[31,32]	2047	1954
Population density (inhabitants/km2)[31,32]	5.8	7.1
Poverty (%)[33]	23	19
Illiteracy (%)[34]	12	10
Households with sanitation deficit (%)[34]	41	31
Cases of HCPS 1995–2012[35]	5	12

We contacted community authorities and explained the study objectives and procedures. For the performance of the survey, we sought written informed consent from the selected subjects. Individuals that consented to participate were orally interviewed by trained personnel who read the questions to the participants and wrote down the answers. The completion of the questionnaire took approximately 30 minutes and was performed at participants' homes. We used pictures of *Oligoryzomys longicaudatus* and scales of agreement to aid in the answers. Answered questionnaires were transferred into a database for analysis.

We performed descriptive analysis of each of the variables by commune, using chi-square test to establish statistical difference between them. For categorical variables we used absolute and relative frequencies, and for quantitative variables we used measures of central tendency, like mean or median. We performed bivariate analysis between the dependent variable "willingness to participate in a hantavirus vaccine trial" and each of the independent variables through Pearson chi-squared test or univariate logistic regression. We also explored explanatory models of acceptability to participate in a vaccine trial through a multivariate logistic regression model incorporating those variables that were significant in the bivariate model. A p value < 0.05 (OR, IC 95%) was considered as significant. For statistical analysis we used SPSS version 19.0 software.

Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

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