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Research Paper

Lithium in drinking water, altitude, and suicide rates in rural areas of Argentinean Andes

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A B S T R A C T

The Lithium Triangle in the Andean plateau involves high altitude (>3,000 m asl) hydrological systems having high lithium graded waters. This research was carried-out in rural areas of north westernmost Argentinean Andes and was aimed: 1) to determine concentrations of lithium in drinking waters; 2) to calculate suicide mortality rates based on available official data (2003–2013); 3) to analyze bivariate differences between lithium concentrations in drinking water, mean rates of suicide mortality, altitude of sampling sites, and water sources; 4) to analyze bivariate correlations between lithium concentrations in drinking water, mean rates of suicide mortality, and altitude; 5) to test predictive models for mean rates of suicide mortality, when considering the predictors lithium concentrations in drinking water, altitude, and water sources. Lithium determinations in drinking waters were performed by Microwave Plasma-Atomic Emission Spectrometer. Nonparametric tests were applied to analyze differences and correlations. Generalized linear models (GLM) were used to fitting models for mean rates of suicide. Drinking waters contained up to 2.98 mg L^{-1} of lithium. Mean rates of suicide mortality (per 100,000 inhabitants) were high, ranging from 19.12 (± 19.83) to 30.22 (± 16.70). Lithium but not altitude was positively correlated with suicide mortality when analyzing bivariate correlations (Li: rho = 0.76, p-value < 0.001). However, when GLM were calculated, a significant interaction effect was found between lithium and altitude (p-value < 0.001). This interaction effect would act in some way restraining the suicide mortality rates.

1. Introduction

Lithium (Li) is a widespread chemical element in the Earth's system that is distributed in minoritarian proportions through the lithosphere (lands), biosphere (living beings), and hydrosphere (waters). Consequently, at least a few Li is frequent and naturally found in drinking water and food. The ingestion of Li is known to have effects on health, due to its toxicity at certain doses.

Li has different industrial uses and applications. In psychiatry, it has been used for the treatment of mania since 1949 and, currently, it is the prototypical mood-stabilizing agent. Li reduces the recurrences of mania and bipolar depression and reduces the risk of suicide in bipolar disorder and in other mood disorders as recurrent major depression (Baldessarini et al., 2006; Guzzetta et al., 2007). However, the anti-suicidal proper-

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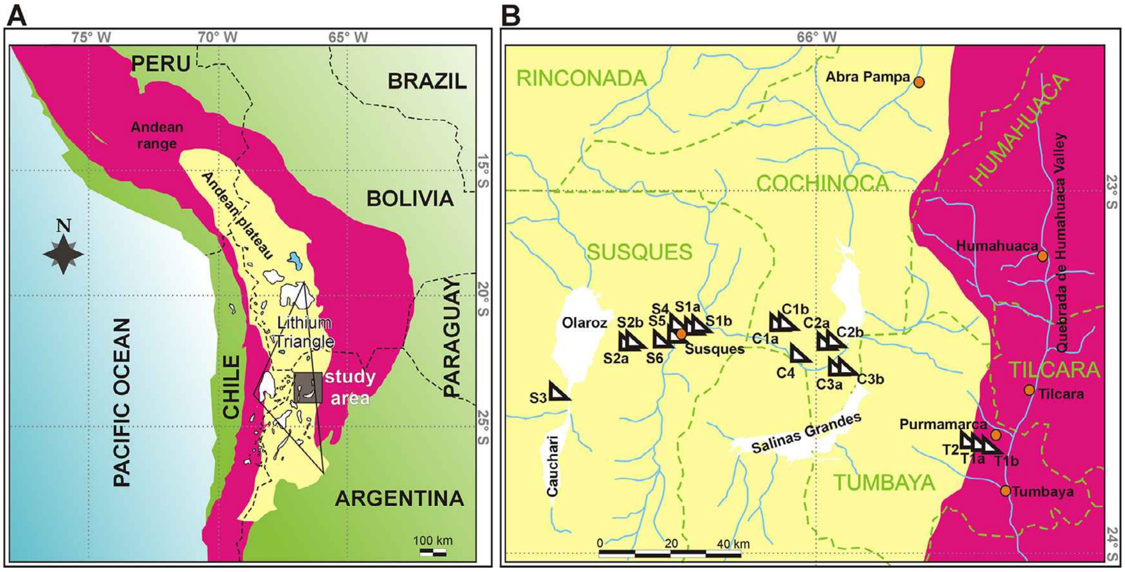

Fig. 1. A) Location map of the study area in the context of the Andean plateau and the Lithium Triangle. B) Location map of sampling sites. Legend: A) dashed black lines: international borders; continuous black line: Lithium Triangle; white areas: salt pans and salt lakes. B) Green dashed lines: border of the Administrative Departments (in capital letters); continuous light blue lines: rivers; orange dots: town heading the Administrative Departments; triangles: sampling sites. Samples: C1a, C1b: Barrancas - Abdón Castro Tolay; C2a, C2b: Rinconadillas; C3a, C3b: Santuario Tres Pozos; C4: Aguadita del Cerro Negro; S1a, S1b, S4, S5, S6: Susques; S2a, S2b: Paraje Angosto El Taire; S3: Olaroz; T1a, T1b, T2: Purmamarca. A and B) green area: extra Andean zone; pink area: Andean range; yellow area: Andean plateau.
Legend for the black and white artwork version: Fig. 1. A) dashed black lines: international borders; continuous black line: Lithium Triangle; white areas: salt pans and salt lakes. B) Gray dashed lines: border of the Administrative Departments (in capital letters); continuous black lines: rivers; white dots: town heading the Administrative Departments; triangles: sampling sites. Samples: C1a, C1b: Barrancas - Abdón Castro Tolay; C2a, C2b: Rinconadillas; C3a, C3b: Santuario Tres Pozos; C4: Aguadita del Cerro Negro; S1a, S1b, S4, S5, S6: Susques; S2a, S2b: Paraje Angosto El Taire; S3: Olaroz; T1a, T1b, T2: Purmamarca. A and B) dark gray area: extra Andean zone; middle dark gray area: Andean range; light gray area: Andean plateau.

ties of Li would be independent of its mood-stabilizing effect (Müller-Oerlinghausen, 2001). A reduction in suicide attempts was observed in high-risk patients with recurrent affective disorders both responders and non-responders to long-term Li prophylaxis, suggesting that Li might have a specific anti-suicidal effect besides its mood-stabilizing property (Ahrens and Müller-Oerlinghausen, 2001). This is important, since if Li does not prevent suicides only as a result of its mood stabilizing effect this would imply that all inhabitants exposed to Li through it chronically ingestion via drinking water may be receiving a long-term prophylaxis against suicide, although in doses lesser than clinical. Standard posology during the psychiatric treatment for adults weighing ~70 kg is from 500 to 1200 mg day^{-1} of Li salts, especially the carbonate (Li_2CO_3) and acetate ($LiCH_3COO$). This implies a daily absorption of 93 to 225 mg of Li. For instance, in bipolar disorders, the resulting therapeutic serum concentrations are expected remain between 4.16 and 6.94 mg L^{-1} of Li (Dunne, 2010). However, it is no clear what the optimum serum levels are in order to obtain an independent and protective effect for suicide (Kabacs et al., 2011).

Many studies have reported inverse associations between suicide rates and the ingestion of drinking waters containing anomalous Li concentrations (Blüml et al., 2013; Helbich et al., 2012; Kapusta et al., 2011; Ohgami et al., 2009; Schrauzer and Shrestha, 1990), although in a few research cases, such an association has not been clearly observed (Helbich et al., 2015; Kabacs et al., 2011).

The effects of the Li treatment on preventing suicidal behavior have been reported to be dependable upon the altitude (in terms of meters above sea level [m asl]). According to Helbich et al. (2013), Li would be negatively associated with suicide rates in low-altitude regions, whereas it would be a positive association in high-altitude regions. However, the mechanism ruling the effect of altitude on Li activity remains unknown (Helbich et al., 2013).

Li concentrations in drinking water (i.e., fresh water) use to be lower than the therapeutic dose. However, in arid and semi-arid regions of the globe, fresh water is scarce mainly due to evaporation rates typically exceed precipitation (it is important to note that fresh water availability in such a regions is also dependent on other anthropogenic factors such as high population growth and pollution, among others). Arid and semi-arid regions together represent 30% of the continental areas of Earth and involve about 20% of the global population (FAO, 2008). In South America, a vast arid region having mean precipitations of ~350 mm year^{-1} corresponds to the Andean plateau. This region, especially the part of the plateau comprised between Bolivia, Chile, and Argentina and referred to as the Lithium Triangle, contains the largest global Li resources (Kesler et al., 2012; Munk et al., 2016). Li resources in the Lithium Triangle corresponds to Li-rich brines (i.e., Li in solution, which is its ionic form Li^{+}) lying in the aquifers that underlie the salt pans. However, because Li is a very reactive and geochemical incompatible element, it is also widespread in surface waters (i.e., rivers and streams). For instance, drinking waters containing between 0.05 and 0.29 mg L^{-1} have been reported from the Bolivian plateau (González Alonso et al., 2010); grades of 1 to 3 mg L^{-1} are known in northern Chile (Figueroa et al., 2012), and concentrations up to 1 mg L^{-1} have been found in drinking waters from the Argentinean plateau (Concha et al., 2010). These Li-bearing drinking waters have been related to the anomalous serum concentrations values of up to 5.30 mg L^{-1} measured in local inhabitants of Andean regions (Figueroa et al., 2014; compare this with the therapeutic serum rage of 4.16 to 6.94 mg L^{-1} of Li mentioned above).

The widely distributed presence of Li in the very scarce available fresh waters and the high altitude (>3000 m asl) of the Andean plateau, together define an exceptional site for assessing the relationship between Li-bearing drinkable waters and altitude, and their effects on suicide rates. In this research, we focus on the north westernmost Argentinean portion of the Andean plateau (Fig. 1.A). The study area involves many rural settlements (Fig. 1.B) and includes the salt pans of Salinas Grandes, Olaroz, and Cauchari, which are relevant Li-brine type deposits of the Lithium Triangle (López Steinmetz et al., 2018). Li is also present in sources supplying the fresh water of nearby settlements (López Steinmetz, 2017a). Despite the widespread presence of Li in the hydrologic systems of the Andean plateau, little is known about the geographical distribution and Li grades in drinking water through the region. The aims of this research were: 1) to determine concentrations of Li in drinking waters of the study area; 2) to calculate suicide mortality rates based on available official data; 3) to analyze bivariate differences between Li concentrations in drinking water, mean rates of suicide mortality, altitude of sampling sites, and water sources; 4) to analyze bivariate correlations between Li concentrations in drinking water, mean rates of suicide mortality, and altitude of sampling sites; 5) to test predictive models for mean rates of suicide mortality, when considering the predictors Li concentrations in drinking water, altitude of sampling sites, and water sources.

2. Materials and methods

2.1. Study area

We consider the following localities and settlements: Barrancas - Abdón Castro Tolay (C1a and b), Rinconadillas (C2a and b), Santuario Tres Pozos (C3a and b), Aguadita del Cerro Negro (C4), Susques (Fig. 1.B), Paraje Angosto El Taire (S2a and b), Olaroz (S3), and Purmamarca (Fig. 1.B). These settlements are grouped into Administrative Departments: Cochinoca, Susques (within the plateau region), and Tumbaya (east of the plateau, in the Quebrada de Humahuaca Valley; Fig. 1.B). The study area includes the salt pans of Salinas Grandes (in the Department of Cochinoca), Olaroz, and Cauchari (in the Department of Susques). There is no Li-bearing salt pan at Purmamarca nor in the eastern Department of Tumbaya. However, this area is being included in the study due to its proximity to the hydrological frontier of the plateau (Fig. 1) and due to it constitutes an *exposure pathway* (United States Environmental Protection Agency, 1989).

Basin floor levels (i.e., salt pans) in the north westernmost Argentinean plateau are located between 3400 (Salinas Grandes) and 3900 m asl (Olaroz and Cauchari). The hydrology is ruled by extreme environmental settings: the continental climate is characterized by aridity (evaporation exceeding mean annual precipitations of ~350 mm yr^{-1}), daily temperature amplitudes often reaching 30 °C, intense solar radiation, and low oxygen diffusion in the air due to altitude. Mean annual relative humidity is 47% and atmospheric pressure 660 hPa (Pelicano et al., 2001). Rainfall in the plateau is markedly seasonal, average annual relative humidity reaches up to 47% (Pelicano et al., 2001), with ~70% of the yearly total falling during the austral summer (December-March), while the dry season spans over the rest of the year (Bianchi and Yañez, 2005). High rates of evaporation and low annual rainfall are responsible for a negative water balance. As a consequence, fluvial systems mainly consist of ephemeral streams. Despite most tributaries infiltrate before reaching the salars, some major fluvial collectors feed the systems over the year. In addition, groundwater discharges (often brackish or even saline) represent important sources of available waters (López Steinmetz and Galli, 2015).

The plateau and the Quebrada de Humahuaca Valley are low-income rural areas. The local economy largely arises from camelid, goats, and cattle breeding. Traditional and artisanal produce mainly consists of pottery, as well as textiles hand-made using llama wool (*Llama glama*). In addition, agriculture mainly includes the production of potatoes, corn, quinoa, and beans. Farming practices take place on river terrace surfaces, adjacent to floodplains and, therefore, this activity is concentrated in a restricted available surface having access to water irrigation.

The towns of Abra Pampa (3484 m asl), Susques (3675 m asl), and Tumbaya (2094 m asl) are the head settlements of the Administrative Departments of Cochinoca, Susques, and Tumbaya (Fig. 1.B). According to available data (the latest census of population having taken place in 2010), the population densities are of 1.60, 0.40, and 1.40 inhabitants km^{-2} in Cochinoca, Susques, and Tumbaya, respectively (Direction of Provincial Statistics and Census [Dirección Provincial de Estadística y Censos, DIPEC], 2012a). In the study area, the distribution of population is characterized by displaying close to roadways and rivers. These aspects determine that the typical pattern of occupation of the territory consists of scattered, rural settlements only including a few families (i.e., small population clusters) and vast unpeopled gaps separating these inhabited areas.

Concerning the supply of drinking water, 23% of homes in Cochinoca (National Institute of Statistic and Census [Instituto Nacional de Estadística y Censos, INDEC], 2010a), 24% in Susques (INDEC, 2010b), and 30% in Tumbaya (INDEC, 2010c), still do not have access to treated water and, therefore, water is directly obtained from wells, streams, rivers, or irrigation channels (INDEC, 2010a, 2010b, 2010c). In these cases, water treatment is homemade and only consists of chlorination by using sodium hypochlorite. This practice allows reducing bacterial content before human ingestion but fails in removing undesirable chemical substances present in water, such as arsenic or lead. It is important to note that even the formal water potabilization process employed in local major sanitary systems does not include the regulation of Li contents prior to human ingestion (Figueroa et al., 2012; López Steinmetz et al., 2020a). Pictures exemplifying social, infrastructural, and hydrological aspects of the study area are presented in Fig. 2.

2.2. Water sampling and chemical analysis

Water samples were collected during the dry season (August 2015), due to two main reasons: i) the lack of rainfalls results on low flows and the relative increase of Li values in water, which are then detectable during chemical analysis; and ii) during the rainy season the flow of the rivers increases, making some roads inaccessible to vehicles. The location of sampling sites is shown in Fig. 1.B. We have collected water from the following sources: streams, rivers, springs, wells, water transported by tank, and tap water. Water sourced from streams, rivers, springs, and wells are no treated waters. Water transported by tank and tap waters correspond to drinking water supplied by sanitary services and being treated using formal water potabilization processes. Seven samples were collected in Cochinoca, 8 in Susques, and 3 in Tumbaya. Samples were named with the initial letter (capitalized) of the Department where they were collected (C, S, and T) and numbered. This is followed by additional final letters (no capitalized) that are used for individualize multiple sampling in the same site. We have collected samples from all the available sampling sites in the study area.

Sampling methodology has followed the recommendations of the National Institute of Agricultural Technology of Argentina (Instituto Nacional de Tecnología Agropecuaria, 2011). We have collected 0.50 L samples using clean plastic bottles. During field surveys, samples were stored refrigerated at 4 to 8 °C. Li determinations were performed at the SUNIBROM bromatological laboratory (Superior Provincial Bromatological Unit, Ministry of Health, Jujuy Province), by employing a Microwave Plasma-Atomic Emission Spectrometer (MP-AES 4200) and following the procedure outlined

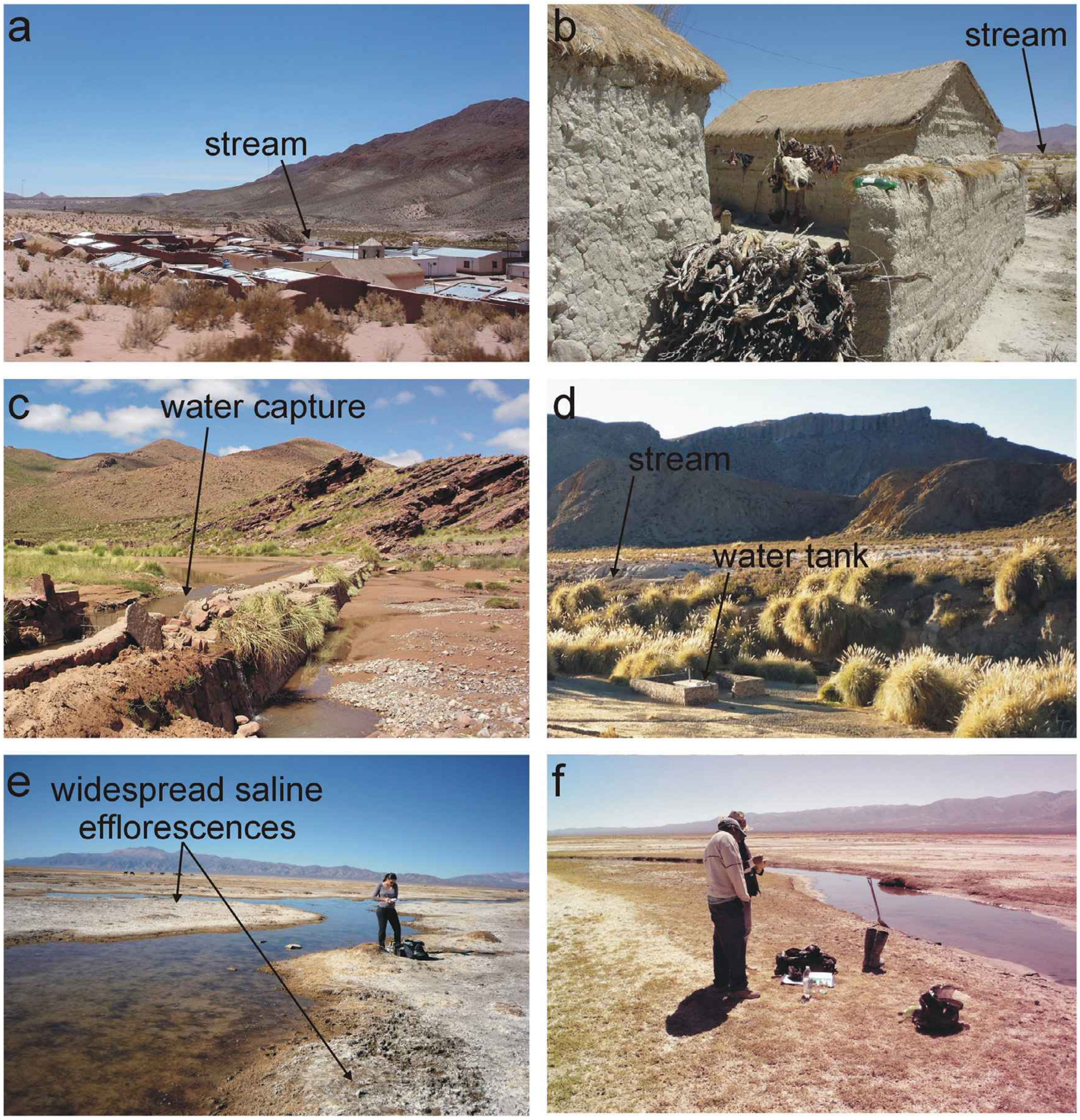

Fig. 2. Pictures showing social, infrastructural, and hydrological aspects of the study area. A) Settlement in the Susques area. B) Living conditions of inhabitants in the Andean plateau. C) Human drinking water is obtained from streams. D) Due to aridity (highly evaporative conditions) and the local seasonal rainfall regime, water availably is scarce and fluctuates through the year. Because of this, water is stored in tanks up to its consumption. E) and F) Streams mainly consist of brackish waters. The abundance of dissolved salts and the effect of evaporation are evidenced by the presence of saline efflorescence on the substrate surface.

by Clesceri et al. (1998). The lower detection limit of the analytical technique is 0.002 mg L^{-1} of Li.

2.3. Epidemiological suicide data

The computation of suicide mortality rates considered available official data on suicide deaths (DIPEC, 2012b, 2013) and population (INDEC, 2008, 2015). We have considered all the recorded cases of deaths by suicide in Cochinoca, Susques, and Tumbaya, in all age groups and in both sexes, for the period 2003–2013 (DIPEC, 2012b, 2013). Our study was constraint to considering the 2003–2013 decade due to the availability of accurate official data on suicide. It was not possible to analyze a longer period due to the lack of older and/or updated official datasets, as the unavailability of records discriminating suicide by Departments of occurrence. Suicide data include cases of death by external causes through intentional self-inflicted injuries (codes X60 to X84 of the ICD-10) (World Health Organization, 2016). Population data involve population projections according to the census of population of 2001 (INDEC, 2008), the population data reported by the census of 2010, and its projections for 2010 to 2013 (INDEC, 2015).

Crude rates of suicide mortality are reported by Administrative Department and in each year of the study period. Due to suicides are rare events, annual data is pooled over the considered decade to reduce random fluctuations of suicide cases by Administrative Department. Consequently, reported values correspond to mean rates of suicide mortality by Department for the entire study period. Suicide mortality rates are informed per 100,000 inhabitants.

2.4. Statistical analysis

Data analysis has been performed with R studio version 3.6.3 (2020–02–29). We considered p-values ≤ 0.05 as statistically significant. We reported exact p-values, except for p-values under 0.001, which are referred as < 0.001. Descriptive analyses have included median (Mdn), mean, and standard deviation (M, $\pm$ sd).

The assumptions of normality and homoscedasticity have been tested by the Shapiro-Wilk test (W), and by the Bartlett test (B), respectively. Since assumptions were not meet (Li: $W = 0.86$, p-value = 0.01 and $B = 12.19$, df = 2, p-value = 0.002; Altitude: $W = 0.75$, p-value < 0.001 and $B = \text{Inf}$, df = 2, p-value < 0.001; Annual suicide mortality rates: $W = 0.93$, p-value = 0.03 and $B = 1.58$, df = 2, p-value = 0.45), nonparametric tests were used.

For analyzing differences, we applied the Kruskal-Wallis test (K-W; one-way). We analyzed differences between: the Li concentrations by different water sources (public supply of treated waters by formal potabilization processes vs. other no treated water sources); the Li concentrations by altitude of the sampled sites; the Li concentrations by Administrative Departments; the departmental mean rates of suicide mortality by altitude of the sampled sites; the mean rates of suicide mortality by the Administrative Departments.

For analyzing bivariate correlations, we applied the Spearman correlation coefficient (rho). We analyzed bivariate correlations between: the Li concentrations and the departmental mean rates of suicide mortality; the Li concentrations and the altitude of sampled collection sites; the altitude of sampled collection sites and the departmental mean rates of suicide mortality.

To test predictive models for the response variable (i.e., departmental mean rates of suicide mortality), we ran multiple logistic regressions by calculating generalized linear models (GLM). Data on annual suicide mortality rates over the study period (2003–2013) were over-dispersed (Range: 0.00 to 76.63 per 100,000 inhabitants; Mean = 26.52, $\pm$ 20.83; Skewness: 0.44). For this reason, GLM were fitted by using quasi Poisson family (Zeileis et al., n.d.). We tried additive models including the predictors proposed in the fifth objective of this research (see the Introduction section). In addition, we tried an interaction model including the variables of the best-fitted additive model. To compare both the best-fitted additive model and the interaction model, we computed ANOVA and, then, the decision on which was the best-fitting model was based on the deviance statistic and the significance level of its associated chi-square statistic (Field et al., 2012). For interpreting the best-fitted model, we used the odds ratio, according to which, if the value is greater than 1, as the predictor increases, the odds of the outcome occurring increase. Conversely, a value less than 1 indicates that, as the predictor increases, the odds of the outcome occurring decrease (Field et al., 2012).

3. Results

3.1. Li grade in waters

Li has been detected in the totality of sampled waters (Table 1). Li grade ranges were 1.01 to 2.98 mg L^{-1} in Cochinoca, 0.14 to 2.43 mg L^{-1} in Susques, and 0.05 to 0.08 mg L^{-1} in Tumbaya. Li concentrations were typically the lowest in treated waters by formal potabilization processes (tap water and water transported by tanks), ranging between 0.05 and 1.02 mg L^{-1}. The highest Li concentration ranges, from 0.08 and up to 2.98 mg L^{-1}, were found in samples of no treated waters (streams, rivers, springs, and wells). These high Li-graded waters are currently being ingested by the local populations. The highest Li concentrations corresponded to samples collected at the Santuario Tres Pozos in Cochinoca (C3b ad C3a), and the head settlement of Susques (S1a and S1b). These high Li-grade waters are obtained from river and are being ingested by human after chlorination. The lowest Li concentrations corresponded to samples collected outside the plateau area, at the sample sites of Purmamarca. The mean and median concentrations of Li are presented in Table 3.

3.2. Altitude of sample collection sites

The altitude of sampling sites was comprised between 2192 m asl (sample sites T1 and T2) and 4200 m asl (sample sites S2a and b). The mean and median altitude of sample collection sites are presented in Table 3.

3.3. Suicide mortality rates

The annual suicide mortality rates of the study period are shown in Table 2. For the entire period (2003–2013), the highest mean and median rates corresponded to the Administrative Departments of Cochinoca ($M = 30.22$, $\pm$ 16.70, Mdn = 29.62) and Susques ($M = 30.21$, $\pm$ 25.01, Mdn = 26.07), whereas the lowest were found at Tumbaya ($M = 19.12$, $\pm$ 19.83, Mdn = 20.78). Suicide mean rates were characterized by high variability.

3.4. Analyses of differences

There were statistically significant differences between: i) the Li concentrations by the Administrative Departments (K-$W = 10.18$, df = 2, p-value = 0.006), ii) the mean rates of suicide mortality by the Administrative Departments (K-$W = 17$, df = 2, p-value $<$ 0.001), and iii) the departmental mean rates of suicide mortality by altitude of the sampled sites ($K = 17$, df = 7, p-value = 0.02). In contrast, no significant differences were found between the Li concentrations in treated and no treated waters (K-$W = 3.33$, df = 1, p-value = 0.07), nor between the Li concentrations by altitude of the sampled sites (K-$W = 12.45$, df = 7, p-value = 0.09).

3.5. Analyses of bivariate correlations

A statistically significant correlation, with a moderate and positive (direct) value, was found between the Li concentrations and the departmental mean rates of suicide mortality (rho = 0.76, p-value < 0.001). On the contrary, there were no significant correlations between the Li concentrations and the altitude of sampled sites (rho = 0.14, p-value = 0.58), nor between the altitude and the departmental mean rates of suicide mortality (rho = 0.15, p-value = 0.54).

3.6. Regression models

In order to test predictive models for departmental mean rates of suicide mortality (response variable), the first additive model we tried included the predictors: Li concentrations in drinking water, altitude of the sampled sites, and water sources (Table 4). In this additive model, the effect of water sources was not significant (p-value $\geq$ 0.08; Table 5). The second additive model we tried included the predictors Li concentrations in drinking water and altitude of the sampled sites (Table 4), which were both significant (Table 5). However, when comparing the latter additive model with an interaction model that included the same two predictors (Tables 4 **and** 5), the best fitted model was the interaction of Li*Altitude on suicide mortality rate (deviance statistic and significance level of its associated chi-square statistic: deviance = 0.95, df = 1, p-value = $<$ 0.001).

4. Discussion

The highest Li concentrations, from 0.08 and up to 2.98 mg L^{-1}, are found in no treated waters (streams, rivers, springs, and wells). These high Li-graded waters are currently being ingested by the

Table 1
Lithium (Li) concentrations, sources, altitude, location of collected water samples, and the Administrative Departments with its estimated population densities.

Sample[a]	Li concentration (mg L^{-1})	Water sources	Location	Altitude (m asl)	Administrative Departments and estimated population densities[b]
C1a	1.01	Stream	Barrancas. Abdón Castro Tolay	3643	Cochinoca 1.60 inhabitants km^{-2}
C1b	1.05	Stream	Barrancas. Abdón Castro Tolay	3643	
C2a	1.28	Spring	Rinconadillas	4081	
C2b	1.28	Spring	Rinconadillas	4081	
C3a	2.97	River	Santuario Tres Pozos	3541	
C3b	2.98	River	Santuario Tres Pozos	3541	
C4	1.02	Transported by tank	Aguadita del Cerro Negro	3550	
S1a	2.43	River	Susques (Capital)	3675	Susques 0.40 inhabitants km^{-2}
S1b	2.43	River	Susques (Capital)	3675	
S2a	0.6	Stream	Paraje Angosto El Taire	4200	
S2b	0.67	Stream	Paraje Angosto El Taire	4200	
S3	1.00	Well	Olaroz	4165	
S4	0.80	tap water	Susques (Capital)	3675	
S5	0.14	tap water	Susques (Capital)	3675	
S6	0.16	tap water	Susques (Capital)	3675	
T1a	0.08	River	Purmamarca	2192	Tumbaya 1.40 inhabitants km^{-2}
T1b	0.08	River	Purmamarca	2192	
T2	0.05	tap water	Purmamarca	2192	

Note: *C* = Cochinoca; *S* = Susques; *T* = Tumbaya; Li = lithium; m asl = meters above sea level.
[a] Samples are named with the initial letter (capitalized) of the Department where they were collected (C, S, and T) and numbered. This is followed by additional final letters (no capitalized) that are used for individualize multiple sampling in the same site.
[b] Based on Direction of Provincial Statistics and Census (Dirección Provincial de Estadística y Censos [DIPEC]), 2012a.

Table 2
Deaths by suicide, inhabitants, and suicide mortality rates (SMR) by Administrative Departments for the period 2003–2013.

Year	Suicides[a], inhabitants[b] and suicide mortality rates[c] by Administrative Departments			
		Cochinoca	Susques	Tumbaya
2003	Suicide	1	2	1
	Inhabitants	12,675	3768	4647
	SMR	7.89	53.08	21.52
2004	Suicide	4	1	2
	Inhabitants	12,878	3836	4681
	SMR	31.06	26.07	42.73
2005	Suicide	1	1	0
	Inhabitants	13,086	3903	4716
	SMR	7.64	25.62	0
2006	Suicide	3	1	1
	Inhabitants	13,295	3971	4750
	SMR	22.56	25.18	21.05
2007	Suicide	4	0	0
	Inhabitants	13,504	4041	4786
	SMR	29.62	0	0
2008	Suicide	7	0	0
	Inhabitants	13,716	4110	4821
	SMR	51.04	0	0
2009	Suicide	6	2	1
	Inhabitants	13,929	4180	4857
	SMR	43.08	47.85	20.59
2010	Suicide	6	1	0
	Inhabitants	12,656	3791	4658
	SMR	47.41	26.38	0
2011	Suicide	3	2	1
	Inhabitants	12,955	3885	4765
	SMR	23.16	51.48	20.99
2012	Suicide	7	3	3
	Inhabitants	13,036	3915	4789
	SMR	53.7	76.63	62.64
2013	Suicide	2	0	1
	Inhabitants	13,114	3943	4813
	SMR	15.25	0	20.78
2003–2013	Suicide	44	13	10
2003–2013	Suicide	67		

Note: SMR = suicide mortality rates.
[a] Number of deaths by suicide during the period 2003 to 2013 (Direction of Provincial Statistics and Census [Dirección Provincial de Estadísitca y Censo, DIPEC], 2012b, 2013).
[b] Population projections according to the census of 2001 (National Institute of Statistic and Census [Instituto Nacional de Estadística y Censos, INDEC], 2008), and population and projections according to the census of 2010 (INDEC, 2015). Population projections are estimated to July 1st of each year.
[c] Suicide mortality rates per 100,000 inhabitants.

Table 3
Mean and median of lithium concentrations in drinking water samples and of the altitude in water sampled sites from the Administrative Departments.

Administrative Departments	Lithium concentrations	
	Mean (± standard deviation)	Median
Cochinoca	1.65 mg L^{-1} (± 0.91)	1.28 mg L^{-1}
Susques	1.03 mg L^{-1} (± 0.91)	0.73 mg L^{-1}
Tumbaya	0.07 mg L^{-1} (± 0.02)	0.08 mg L^{-1}
Total of samples	1.11 mg L^{-1} (± 0.97)	1.00 mg L^{-1}
Administrative Departments	Altitude	
	Mean (± standard deviation)	Median
Susques	3867 m asl (± 266)	3675 m asl
Cochinoca	3726 m asl (± 247)	3643 m asl
Tumbaya	2192 m asl (± 0)	2192 m asl
Total of sites	3533 m asl (± 660)	3675 m asl

local populations not having access to formal treated water. As previously explained in the Materials and Methods section, this situation is affecting 23 to 24% of the Cochinoca, Susques, and Tumbaya's homes. The fact that more than 5400 people are currently daily ingesting no treated water, implicates a critic sanitary situation.

Our findings show that ingested waters in Cochinoca and Susques contain higher Li concentrations (ranging between 1.01–2.98 mg L^{-1} and 0.14–2.43 mg L^{-1}, respectively) than those of Tumbaya (0.05–0.08 mg L^{-1}). These Li grades are even higher than those that have been reported away, e.g.: 0.07–0.17 mg L^{-1} of Li in Texas, United States of America (Schrauzer and Shrestha, 1990), up to 0.06 mg L^{-1} in the Oita Prefecture, Japan (Ohgami et al., 2009), and up to 0.02 mg L^{-1} in some districts of Austria (Helbich et al., 2013). In this regard, it must be note that there is no consensus on what levels of Li in drinking water should be considered *high*. Anyhow, Li concentrations found in Cochinoca and Susques are consistent with those that have been previously reported from the southern Argentina plateau (0.01–1.00 mg L^{-1}; Concha et al., 2010) and from the Tarapaca province in northern Chile (1–3 mg L^{-1}; Figueroa et al., 2012). Taking into account all the aforementioned, in our study area, it is important to note that the ingestion of Li bearing drinkable waters is not only affecting the inhabitants residing in localities and settlements lacking of formal treated water. Indeed, treated water (tap water and water transported by tank) also contains significant Li grades (from 0.05 to 1.02 mg L^{-1}). Li levels in no treated waters (from 0.08 to 2.98 mg L^{-1}) are higher than those of formally treated drinkable water; however, the differences in the Li concentrations are not statistically significant.

On the other hand, our results show that the highest mean rates of suicide mortality are found in Cochinoca and Susques (30.22 and 30.21 per 100,000 inhabitants, respectively). Furthermore, in the three considered Administrative Departments, these suicide rates are higher than mean rates of the whole Jujuy province which has been estimated on 11.27 (per 100,000 inhabitants) in the same period (2003–2013), based on the available official data (DIPEC, 2012, 2013; INDEC, 2008, 2015).

The anti-suicidal properties of Li in therapeutic doses are well established in the literature (Baldessarini et al., 2006; Guzzetta et al., 2007). Despite that the daily ingestion of Li that would result through drinking waters is about one order of magnitude lower than the daily therapeutic doses (which are of 90 to 225 mg L^{-1} of Li, whereas the daily ingestion of about 3 L of water grading up to 3 mg L^{-1} implicates Li doses of 9 mg day^{-1}), previous researches have reported that the ingestion of Li-rich drinking waters is related with the reduction of suicide rates (Blüml et al., 2013; Helbich et al., 2012; Kapusta et al., 2011; Ohgami et al., 2009; Schrauzer and Shrestha, 1990). In order to explain the anti-suicidal effects of these low levels doses of Li, it has been postulated that the efficiency of long-term exposure to Li through the daily ingestion of drinking water would mitigate the low absolute levels of Li (Kapusta et al., 2011). However, the effects of Li through drinking water and its mechanisms of action remain unclear. This is mainly due to specific studies – which remain in fact scarce up to date – have been criticized for arising on overly simplistic statistical models and for lacking of assessment concerning additional variables such as the possible influence of space and the likely effects of interactions (Yang, 2011). Notwithstanding all these limitations, Li levels in drinking water are majorly considered as having an inverse association with suicide rates (Blüml et al., 2013; Helbich et al., 2012; Kapusta et al., 2011; Ohgami et al., 2009; Schrauzer and Shrestha, 1990).

The widely distributed presence of Li in waters and the high altitude (>3000 m asl) of the Andean plateau, together define an exceptional site for testing this postulated association. According to our dataset, when considering bivariate correlations, no protective effect may be supposed for suicide due to the Li chronic intake through drinking water. In fact and contrary to expected, our data show that the highest mean rates of suicide mortality occur in places having the higher Li concentrations in drinking water (Cochinoca and Susques). Further studies are necessary in order to better understand such an association between suicide and the chronic intake of Li-bearing drinking water, in addition to the assessment of other variables such as, but not limited to, a) socio-demography, b) the availability and accessibility to health services, c) climate, and d) geographic patterns.

Regarding socio-demographic variables, as previously explained, neither the main socio-demographic variables nor the suicide mortality rates by sex and age were available in official data. However, given that suicide attempts are known as the main precursors of completed suicide, some assumptions regarding socio-demographic features may be proposed based on previous local researches. On this basis, it may be expected that age (younger) rather than sex would likely rules the suicide rates of the local population (López Steinmetz, 2017b). Furthermore, additional socio-demographic variables, such as marital status (López Stein-

Table 4
Results of multiple linear regressions by using generalized linear models (GLM; family: quasi Poisson) for the response variable mean rates of suicide mortality in the Administrative Departments for the period 2003–2013.

Models	Predictors	Dev. Res.		Null dev. (df)	Res. dev. (df)	Dispersion par.
		Min	**Max**			
1 Additive	SMR ~ Li + Alt + Water	−0.37	0.30	11.99 (17)	0.53 (10)	0.05
2 Additive	SMR ~ Li + Alt	−0.34	0.42	11.99 (17)	1.39 (15)	0.09
3 Interaction	SMR ~ Li * Alt	−0.35	0.16	11.99 (17)	0.44 (14)	0.03

Note: Dev. Res. = Deviance Residuals; Min = Minimum; Max = Maximum; Null dev. (df) = Null deviance on degrees of freedom; Res. dev. (df) = Residual deviance on degrees of freedom; Dispersion par. = Dispersion parameter for quasi Poisson family; SMR = Mean rates of suicide mortality; Li = Lithium concentrations in drinking waters; Alt = Altitude of the sampled sites; Water = Water sources.

Table 5
Results of multiple linear regressions by using generalized linear models (GLM; family: quasi Poisson) for the response variable mean rates of suicide mortality in the Administrative Departments for the period 2003–2013.

Model 1 (additive model)						
Predictors	Estimate	Std. error	t value	p-value[a]	95% CI	
					2.5%	97.5%
Intercept	2.43	0.08	30.31	< 0.001	2.28	2.59
Li	0.06	0.02	2.69	0.02	0.02	0.10
Alt	0.0002	0.00003	7.28	< 0.001	0.0002	0.0003
Water: spring	−0.03	0.05	−0.56	0.59	−0.13	0.07
Water: stream	0.03	0.05	0.60	0.56	−0.07	0.13
Water: tap water	0.10	0.05	1.95	0.08	−0.001	0.19
Water: transported by tank	0.11	0.05	1.96	0.08	−0.001	0.21
Water: well	−0.03	0.06	−0.50	0.63	−0.16	0.10
Model 2 (additive model)						
Predictors	**Estimate**	**Std. error**	**t value**	**p-value**[a]	**95% CI**	
					2.5%	**97.5%**
Intercept	2.517e+00	8.633e-02	29.16	< 0.001	2.35	2.68
Li	3.464e-02	1.488e-02	2.33	0.03	0.005	0.06
Alt	2.203e-04	2.42e-05	9.08	< 0.001	0.0002	0.0003
Model 3 (interaction model; best model)						
Predictors	**Estimate**	**Std. error**	**t value**	**p-value**[a]	**95% CI**	
					2.5%	**97.5%**
Intercept	2.284e+00	6.621e-02	34.50	< 0.001	2.15	2.41
Li	8.675e-01	1.519e-01	5.71	< 0.001	0.57	1.17
Alt	3.007e-04	2.039e-05	14.75	< 0.001	0.0003	0.0003
Li*Alt	−2.365e-04	4.306e-05	−5.49	< 0.001	−0.0003	−0.0002

Note: Std. error = Standard error; 95% CI = 95% Confidence interval; Li = Lithium concentrations in drinking waters; Alt = Altitude of the sampled sites; Water = Water sources (Spring, Stream, Tap water, Transported by tank, Well, River).
[a] Exact p-values are informed, except for p-values under 0.001, which are informed as < 0.001.

metz, 2017c) and employment (López Steinmetz et al., 2020b), may be expected as reflecting common local features of the general population rather than the specific features of the people attempting or completing suicide.

As for the availability of health services, this may be an additional important constraining variable. In the three considered Administrative Departments there are public health institutions offering free of charge, accessible health assistance for all inhabitants. Therefore, health care would be considered as independent from socioeconomic status. However, health services in the study area do not include mental health services, which might be related to the high suicide rates. Nevertheless, it is important to note that diagnosed mental disorders have a relatively low prevalence in local cases of suicide attempt compared to foreign populations (López Steinmetz, 2017d).

As for climatic conditions in the plateau and the Quebrada de Humahuaca Valley, these are characterized by seasonal rainfalls and, thus, river water flows fluctuates over the year (Pelicano et al., 2001). This determines the availability of water and the Li grade in the hydrological systems. Aridity, together with geological factors, determines that the concentrations of Li in water highly shift through time and space. This shifting pattern on the Li concentrations could be related to the high mean rates of suicide mortality found here and their regional variability, as a consequence of exposing inhabitants to changing Li doses through drinking water over the year. Hydrologic variations directly rule the hydrochemistry of rivers and springs, and thus ionic content is the highest during the dry season (Casares, 2013). Since waters sampling were carried out during the dry season, lower Li concentrations would be expected to be found during the rainy season. The effects of such natural variations in Li concentrations could be mimicking one of the most important effects of the discontinuation of pharmacological treatment with Li that has been reported in the literature as driving an increase in suicidal behaviors (Kallner et al., 2000; Müller-Oerlinghausen, 2001).

Regarding to altitude, this is an additional geographic variable that has been reported as being related to suicide rates. In high altitude regions, metabolic stress plus mild hypoxia would enhance the symptoms of mood disorders and, thus, increase suicide rates (Kim et al., 2011). However, this mechanism has been object of ongoing debate based on it fails to control potential confounding factors, such as socio-demographic variables and mental health services availability, which could be considered as more likely explanations of higher suicide rates in high-altitude – and, thus, isolated – regions (Betz et al., 2011). Based on our data, we found no significant bivariate correlation between altitude and suicide mortality rates.

On the other hand, previous studies have shown that altitude influences the pharmacokinetics of Li in healthy humans, that these changes could be clinically significant (Arancibia et al., 2003), and that Li is negatively associated with suicide rates in low-altitude regions, whereas this association is positive in high-altitude regions (Helbich et al., 2013). Taking into consideration these antecedents along with the paradoxical result we found here when analyzing bivariate correlations (i.e., a positive correlation between Li and suicide rates), we have tried multiple regressions in order to explain the variability of departmental mean rates of suicide mortality. We noted that referred previous studies fail to define a unified criterion on what is considered *high altitude*. For example, Helbich et al. (2013) have considered locations up to 1217 m asl, whereas Arancibia et al. (2003) inspected areas that are settled up to 4360 m asl. Wherever the “high altitude” begins, all of our sampling sites might be considered in absolute terms as being placed at *high-altitude*, as they are between 3541 and 4081 m asl in Cochinoca, between 3675 and 4200 m asl in Susques, and at 2192 m asl in Tumbaya. Both Li and altitude of sampling sites revealed as significant predictors of mean rates of suicide mortality. Despite that only Li (and not altitude) was positive correlated with suicide mortality when analyzing bivariate correlations, a significant interaction effect between Li and altitude was found through running multiple regressions. This interaction effect would act in some way restraining the suicide mortality rates. However, these findings must be interpreted with caution and considered within the context of several limitations. First, the relatively small number of suicides during the study period (i.e., 67 suicides during 2003–2013 on a total population of about 21,870 inhabitants) and the great variability of the departmental mean rates of suicide mortality. In this regard, further studies would be necessary together with other epidemiological methods better able to assess datasets from small populations, e.g., community-based mixed methods (Korngiebel et al., 2015; Monasta et al., 2008). Likewise, conclusions emerged from the statistical analyses applied on our dataset would be not stronger enough due to the small size of samples. Secondly, although we have controlled for some variables thought to be linked with suicidal risk, there are a number of additional factors that may significantly affect suicidal risk, which includes, but are not limited to, history of mood disorders, history of substance-related disorders, previous suicide attempts, and cognitive functions, among others. Thus, further researches should include some of these factors. Thirdly, samples were collected during the dry season, but due to hydrologic variations ruling the hydrochemistry of rivers and springs in this Andean region, lower Li concentrations would be expected to be found during the rainy season. Therefore, a replication study revealed as necessary to be conducted during the dry period. Similarly, a temporal analysis contrasting suicide rates in the dry versus the rainy seasons would be necessary (if this official data become available in the future). Despite these limitations, this is the first time that a such study is conducted in the forgotten populations of the remote Andean plateau. Our findings revealed major traits of the local phenomena, and represent a valuable shed light for further research on mental health, suicide, and its relation to the Lithium Triangle.

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Declaration of Competing Interest

None.

References

Arancibia, A., Paulos, C., Chávez, J., Ritschel, W.A., 2003. Pharmacokinetics of lithium in healthy volunteers after exposure to high altitude. Int. J. Clin. Pharmacol. Ther. 41 (5), 200–206. doi:10.5414/cpp41200.

Ahrens, B., Müller-Oerlinghausen, B., 2001. Does lithium exert an independent antisuicidal effect? Pharmacopsychiatry 34 (4), 132–136. doi:10.1055/s-2001-15878.

Baldessarini, R.J., Tondo, L., Davis, P., Pompili, M., Goodwin, F.K., Hennen, J., 2006. Decreased risk of suicides and attempts during long-term lithium treatment: a meta-analytic review. Bipolar Disord. 8 (5p2), 625–639. doi:10.1111/j.1399-5618.2006.00344.x.

Betz, M., Valley, M.A., Lowenstein, S.R., Hedegaard, H., Thomas, D., Stallones, L., Honigman, B., 2011. Elevated suicide rates at high altitude: sociodemographic and health issues may be to blame. Suicide Life Threat. Behav. 41 (5), 562–573. doi:10.1111/j.1943-278x.2011.00054.x.

Bianchi, A.R., Yañez, C.E., 2005. Base de Datos Mensuales de Precipitaciones del Noroeste Argentino. Instituto Nacional de Tecnología Agropecuaria, Estación Experimental Regional Agropecuaria Salta, Salta.

Blüml, V., Regier, M.D., Hlavin, G., Rockett, I.R.H., König, F., Vyssoki, B., Bschor, T., Kapusta, N.D., 2013. Lithium in the public water supply and suicide mortality in Texas. J. Psychiatr. Res. 47 (3), 407–411. doi:10.1016/j.jpsychires.2012.12.002.

Casares, M.V., 2013. Biodisponibilidad y toxicidad de metales pesados en aguas naturales con características físico-químicas extremas. Bases para su monitoreo y remediación. Acta Toxicol. Argentina 21 (1), 56–57.

Clesceri, L.S., Greenberg, A.E., Eaton, A.D., 1998. Standard Methods for the Examination of Water and Wastewater, 20th Ed. American Public Health Association, USA.

Concha, G., Broberg, K., Grandér, M., Cardozo, A., Palm, B., Vahter, M., 2010. High-level exposure to lithium, rubidium, cesium, boron and arsenic via drinking water in the Andes of northern Argentina. Environ. Sci. Technol. 44 (17), 6875–6880. doi:10.1021/es1010384.

Cuadro 2.2.5. Superficie y densidad poblacional, según departamento. Provincia de Jujuy. Censos 1991-2010. In: Anuario Estadístico Provincia de Ju- juy, Año 2012, DIPEC, Jujuy: DIPEC, 2012a. p. 39.

Cuadro 3.55. Tendencia defunciones por suicidio. Provincia de Jujuy. Años 2003-2012. In: Anuario Estadístico Provincia de Jujuy, Año 2012, DIPEC, Jujuy: DIPEC, 2012b. p. 139.

Cuadro 3.60. Defunciones por suicidio según residencia por grupo etario y sexo. Provincia de Jujuy. Año 2013. In: Anuario Estadístico Provincia de Jujuy, Año 2013, DIPEC, Jujuy: DIPEC, 2013. p. 188.

Cuadro 10. Población total estimada al 30 de junio de cada año calendario, por departamento. Provincia de Jujuy. Periodo 2001-2010. In: Estimaciones de población total por departamento y año calendario periodo 2001-2010, N° 34, INDEC, Buenos Aires: INDEC, 2008. p. 17.

Cuadro 1.10. Población estimada al 1° de julio de cada año calendario por sexo, según departamento. Provincia de Jujuy. Años 2010-2025. In: Estimaciones de Población por Sexo, Departamento y Año Calendario 2010-2025, N°38, IN- DEC, Buenos Aires: INDEC, 2015. p. 62.

Dunne, F.J., 2010. Lithium toxicity: the importance of clinical signs. Br. J. Hosp. Med. 71 (4), 206–210. doi:10.12968/hmed.2010.71.4.47513.

FAO (2008). Chapter 1: drylands, people and land use, in waters and cereals. In: Drylands. Available: http://www.fao.org/docrep/012/i0372e/i0372e01.pdf [Accessed 10 November 2019].

Field, A., Miles, J., Field, Z., 2012. Discovering Statistics Using R. SAGE Publications Inc, London.

Figueroa, L., Barton, S., Schull, W., Razmilic, B., Zumaeta, O., Young, A., Kamiya, Y., Hoskins, J., Ilgren, E., 2012. Environmental lithium exposure in the North of Chile-I. Nat. Water Sources. Biol. Trace Element Res. 149 (2), 280–290. doi:10.1007/s12011-012-9417-6.

Figueroa, L.T., Barton, S.A., Schull, W.J., Young, A.H., Kamiya, Y.M., Hoskins, J.A., Ilgren, E.B., 2014. Environmental lithium exposure in the North of Chile – tissue exposure indices. Epidemiol. Biostat. Public Health 11 (1) e8847-1–e8847-15.

González Alonso, S., Esteban-Hernández, J., Valcárcel-Rivera, Y., Hernández-Barrera, V., Gil de Miguel, Á., 2010. Contaminación del agua en fuentes cercanas a campos petrolíferos de Bolivia. Rev. Panam. Salud Pública 28 (4), 235–243. doi:10.1590/s1020-49892010001000001.

Guzzetta, F., Tondo, L., Centorrino, F., Baldessarini, R.J., 2007. Lithium treatment reduces suicide risk in recurrent major depressive disorder. J. Clin. Psychiatry 68 (3), 380–383. doi:10.4088/jcp.v68n0304.

Helbich, M., Blüml, V., Leitner, M., Kapusta, N.D., 2013. Does altitude moderate the impact of lithium on suicide? A spatial analysis of Austria. Geospat. Health 7 (2), 209–218. doi:10.4081/gh.2013.81.

Helbich, M., Leitner, M., Kapusta, N.D., 2012. Geospatial examination of lithium in drinking water and suicide mortality. Int. J. Health Geogr 11 (1), 19. doi:10.1186/1476-072x-11-19.

Helbich, M., Leitner, M., Kapusta, N.D., 2015. Lithium in drinking water and suicide mortality: interplay with lithium prescriptions. Br. J. Psychiatry 207 (1), 64–71. doi:10.1192/bjp.bp.114.152991.

Instituto Nacional de Estadística y Censos, 2010a. Cuadro H2-D. Provincia de Jujuy, Departamento Cochinoca. Hogares por Tipo de Desagüe del Inodoro, Según Provisión y Procedencia del Agua. Año 2010. Buenos Aires: INDEC Available: http://www.dipec.jujuy.gov.ar/idx_censo2010/hogares/departamentos/cochinoca/H2-D_38_7.xls .

Instituto Nacional de Estadística y Censos, 2010b. Cuadro H2-D. Provincia de Jujuy, Departamento Susques. Hogares por Tipo de Desagüe del Inodoro, Según Provisión y Procedencia del Agua. Año 2010. Buenos Aires: INDEC Available: http://www.dipec.jujuy.gov.ar/idx_censo2010/hogares/departamentos/susques/H2-D_38_84.xls .

Instituto Nacional de Estadística y Censos, 2010c. Cuadro H2-D. Provincia de Jujuy, Departamento Tumbaya. Hogares por Tipo de Desagüe del Inodoro, Según Provisión y Procedencia del Agua. Año 2010. Buenos Aires: INDEC Available: http://www.dipec.jujuy.gov.ar/idx_censo2010/hogares/departamentos/tumbaya/H2-D_38_98.xls .

Instituto Nacional de Tecnología Agropecuaria, 2011. Protocolo de Muestreo, Transporte y Conservación de Muestras de Agua con Fines Múltiples (Consumo Humano, Abrevado Animal y Riego). Buenos Aires: INTA Available: https://inta.gob.ar/sites/default/files/script-tmp-protocolo_de_muestreo_de_aguas_inta.pdf .

Kabacs, N., Memon, A., Obinwa, T., Stochl, J., Perez, J., 2011. Lithium in drinking water and suicide rates across the East of England. Br. J. Psychiatry 198 (5), 406–407. doi:10.1192/bjp.bp.110.088617.

Kallner, G., Lindelius, R., Petterson, U., Stockman, O., Tham, A., 2000. Mortality in 497 patients with affective disorders attending a lithium clinic or after having left it. Pharmacopsychiatry 33 (1), 8–13. doi:10.1055/s-2000-7965.

Kapusta, N.D., Mossaheb, N., Etzersdorfer, E., Hlavin, G., Thau, K., Willeit, M., Praschak Rieder, N., Sonneck, G., Leithner Dziubas, K., 2011. Lithium in drinking water and suicide mortality. Br. J. Psychiatry 198 (5), 346–350. doi:10.1192/bjp.bp.110.091041.

Kesler, S.E., Gruber, P.W., Medina, P.A., Keoleian, G.A., Everson, M.P., Wallington, T.J., 2012. Global lithium resources: relative importance of pegmatites, brine and other deposits. Ore Geol. Rev. 48. doi:10.1016/j.oregeorev.2012.05.006, 55–69.

Kim, K., Mickelson, J.B., Brenner, B.E., Haws, C.A., Yurgelun Todd, D.A., Renshaw, P.F., 2011. Altitude, gun ownership, rural areas, and suicide. Am. J. Psychiatry 168 (1), 49–54. doi:10.1176/appi.ajp.2010.10020289.

Korngiebel, D.M., Taualii, M., Forquera, R., Harris, R., Buchwald, D., 2015. Addressing the challenges of research with small populations. Am. J. Public Health 105 (9), 1744–1747 10.2105%2FAJPH.2015.302783.

López Steinmetz, R.L., 2017a. Lithium- and boron-bearing brines in the Central Andes: exploring hydrofacies on the eastern Puna plateau between 23° and 23°30'S. Miner. Deposita 52 (1), 35–50. doi:10.1007/s00126-016-0656-x.

López Steinmetz, L.C., 2017b. Caracterización de riesgo diferencial-demográfico en urgencias psicológicas: intento de suicidio y otros motivos de consulta. Rev. Argent Cienc. Comport. 9 (1), 44–53.

López Steinmetz, L.C., 2017c. Análisis de soledad objetiva y subjetiva en intentos de suicidio. Premio Fac. Psicol. Univ. Buenos Aires 2017, 103–129.

López Steinmetz, L.C., 2017d. Factores psicopatológicos de riesgo en intentos de suicidio. Cienc. Psicol. 11 (2), 89–100. doi:10.22235/cp.v11i2.1350.

López Steinmetz, R.L., Galli, C.I., 2015. Hydrological change during the Pleistocene-Holocene transition associated to the Last Glacial Maximum-Altithermal in the eastern border of Northern Puna. Andean Geol. 42 (1), 1–19. doi:10.5027/andgeoV42n1-a01.

López Steinmetz, R.L., Fong, S.B., Boyer, E., López Steinmetz, L.C., Tejerina, N.E., Meuric, V., 2020a. Lithium and boron in calcified tissues of vicuna and its relation to the chronic exposure by water ingestion in the Andean lithium triangle. Environ. Toxicol. Chem. 39 (1), 200–209. doi:10.1002/etc.4608.

López Steinmetz, L.C., López Steinmetz, R.L., Godoy, J.C., 2020b. Is unemployment less important than expected for suicide attempted in developing regions? Occupational profile of suicide attempts in Jujuy, north westernmost Argentina. Int. J. Soc. Psychiatry 66 (1), 67–75. doi:10.1177/0020764019882728.

López Steinmetz, R.L., Salvi, S., García, M.G., Béziat, D., Franco, G., Constantini, O., Córdoba, F.E., Caffe, P.J., 2018. Northern Puna plateau-scale survey of Li brine-type deposits in the Andes of NW Argentina. J. Geochem. Explor. 190. doi:10.1016/j.gexplo.2018.02.013, 26—38.

Monasta, L., Andersson, N., Ledogar, R.J., Cockcroft, A., 2008. Minority health and small numbers epidemiology: a case study of living conditions and the health of children in 5 foreign Romá camps in Italy. Am. J. Public Health 11 (98), 2035–2041 10.2105%2FAJPH.2007.129734.

Müller-Oerlinghausen, B., 2001. Arguments for the specificity of the antisuicidal effect of lithium. Eur. Arch. Psychiatry Clin. Neurosci. 251 (S2), 1172–1175. doi:10.1007/bf03035132.

Munk, L.A., Hynek, S.A., Bradley, D., Boutt, D., Labay, K., Jochens, H., 2016. Lithium brines: a global perspective. In: P. L. Verplanck, and M. W. Hitzman, Reviews in Economic Geology, 18. Society of Economic Geologists, Alaska, pp. 339–365.

Ohgami, H., Terao, T., Shiotsuki, I., Ishii, N., Iwata, N., 2009. Lithium levels in drinking water and risk of suicide. Br. J. Psychiatry 194 (5), 464–465. doi:10.1192/bjp.bp.108.055798.

Pelicano, G., Combetto, A., Benedetti, A., de la Cuetara, O., March 2001. Energías renovables, una opción para el abastecimiento de un recurso escaso: el agua en la Puna jujeña. VIII Encuentro de Geógrafos de América Latina. Universidad de Chile, Santiago de Chile, Chile.

Schrauzer, G.N., Shrestha, K.P., 1990. Lithium in drinking water and the incidences of crimes, suicides and arrests related to drug addictions. Biol. Trace Elem. Res. 25 (2), 105–113. doi:10.1007/bf02990271.

United States Environmental Protection Agency, 1989. EPA/540/1-89/002. Risk assessment: guidance for superfund, volume I, human health evaluation manual (part A). Washington D.C.: USEPA.

World Health Organization, 2016. International Classification of Diseases and Related Health Problems, 10th ed. WHO, Geneva (ICD-10).

Yang, M., 2011. Lithium concentrations in drinking water. Br. J. Psychiatry 198 (6), 493–494. doi:10.1192/bjp.198.6.493a.

Zeileis A., Kleiber C., Jackman S. 2020 (n.d.). Regression models for count data in R. Available: https://cran.r-project.org/web/packages/pscl/vignettes/countreg.pdf [Accessed 09 April 2020].