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Blood lead levels in indigenous peoples living close to oil extraction areas in the Peruvian Amazon

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A R T I C L E I N F O

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A B S T R A C T

Background: High blood lead levels (BLLs) have been previously reported in indigenous people living in communities in the northern Peruvian Amazon. Oil extraction activities have been conducted in the area since the 1970s and have been identified as a source of lead exposure.

Objective: Measure BLL and assess risk factors associated with BLL among indigenous populations from four river basins of the northern Peruvian Amazon.

Methods: Participants from 39 communities were selected using a two-stage stratified random selection strategy and were visited between May and June 2016. Information on risk factors was collected using structured questionnaires and blood samples were taken. Overall, complete information was available from 1047 individuals (309 $<$ 12 years old, 738 $\geq$ 12 years). BLL was determined using atomic absorption spectrophotometry in a graphite chamber. Weighted linear logistic regression models were used to study the association between socio-demographic variables, self-reported life-style factors, environmental, geographical and occupational exposures and BLLs.

Results: Geometric mean (95% CI) BLL was 4.9 (4.5, 5.4) μg/dL in participants <12 years and 5.7 (5.4, 6.0) μg/dL in older participants. There were marked differences in BLL between river basins with the highest levels observed in the Corrientes river basin [8.1 (7.2, 9.1) μg/dL <12 years and 8.8 (8.0, 9.6) μg/dL older participants]. High BLL was associated with older age, being male, living in the Pastaza, Tigre or Corrientes river basins and consumption of fish offal in children and adults. Increased Euclidean distance between residence and oil production facilities was associated with a small reduction in BLL.

Conclusion: BLLs that pose a health risk were detected in the study population of a non-industrialized and remote area of the Amazon. The highest BLLs were observed in those river basins where relative oil extraction activity and environmental levels of contaminants have been reported to be greatest.

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1. Introduction

Lead is a bioaccumulative toxicant that can affect multiple body systems and cause different health problems depending on exposure concentration and duration and age at exposure. Alterations in the nervous, immune and reproductive systems, and renal and cardiovascular problems are associated with lead exposure in both adults and children (UNEP, 2010). Children are especially vulnerable to lead exposure that can cause irreversible neurological and developmental impairment even at low levels of exposure (Canfield et al., 2003; Skerfving and Bergdahl, 2015). No blood lead level (BLL) is considered safe and adverse health effects are reported at very low levels of exposure in both children and adults (UNEP, 2010; Skerfving and Bergdahl, 2015; Menke et al., 2006; Lanphear et al., 2018).

Identifying the lead source is key to preventing human exposure. Anthropogenic sources of lead may be associated with industrialization and include release of lead impurities from raw materials such as fossil fuels and ores, and environmental discharge of lead by manufacturing, use, disposal or incineration of products that contain lead such as batteries, paint, gasoline, and ammunition (UNEP, 2010). For years, leaded gasoline was the dominant source of human exposure to lead in industrialized countries and lead-base ammunition was the main source of lead released into the soil (UNEP, 2010). However, extraction of fossil fuels has been identified as an important source of lead exposure for indigenous communities of the northern Peruvian Amazon (Cartró-Sabaté et al., 2019).

Oil extraction activities started in the northern Peruvian Amazon in the early 1970s. Two oil concessions known as Blocks 8 and 192 (formerly 1AB) overlap with the territories of the Achuar, Quechua, Kichwa, and Kukama peoples in the Corrientes, Pastaza and Tigre river basins. All are major tributaries of the Marañón River which forms the headwaters of the Amazon River. Since the 1980s, various Peruvian state agencies have reported high levels of hydrocarbons and heavy metals, including lead, related to oil extraction activities in environmental samples from the Corrientes river basin (Orta Martínez et al., 2007). In 2006, a governmental evaluation conducted in this river basin reported BBL $\geq$ 10 μg/dl in 66% of individuals younger than 18 years old (yo; n = 74) and in 79% of older individuals (n = 125) (DIGESA, 2006). Studies conducted between 2007 and 2010 also reported high BLL in the population of this basin and 25 to 43% of children participating in these studies had BLL $\geq$ 10 μg/dl (Anticona et al., 2011; Anticona et al., 2012a, Anticona et al., 2012b). These previous studies conducted in the Corrientes river included only few communities (between two and seven) which had been selected by convenience sampling. The small number of communities included and the selection strategy could have compromised the generalization of results to other communities of the Corrientes river basin. Moreover, there is no data on BLLs from the population of other three river basins also affected by the oil extraction activities conducted in Blocks 8 and 192.

The performance of this study is the result of the agreement reached between the indigenous federations of the river basins affected by the activities of blocks 8 and 192 (FEDIQUEP, ACODECOSPAT, FECONACOR and OPIKAFPE) and the Peruvian Government to respond serious concerns about potential health effects of the environmental oil-related contamination reported in the area (see Ministerial Resolution 094-2013-MINAM, Ministerial Resolution 263-2013-MINAM, and Ministerial Resolution 370-2013-MINAM and Supreme Decree 006-2014-SA (revised by Orta-Martinez el at 2018 (Orta-Martínez et al., 2018). The aims of this study were: (i) to estimate mean BLL in the indigenous population of the four river basins in the oil concessions areas of the northern Peruvian Amazon, and (ii) to identify the risk factors associated with higher BLL, including socio-demographic, environmental, geographical, occupational, and life-style factors.

2. Methods

2.1. Study population

We conducted a cross-sectional study between May and June 2016. The study was led by CENSOPAS-INS, the Centre for occupational and environmental health of the Peruvian National Institute of Health, with the participation of external researchers and the collaboration of the indigenous federations of the Marañón, Pastaza, Tigre and Corrientes river basins (OPIKAFPE, FEDIQUEP, ACODECOSPAT and FECONACOR, respectively) of Loreto department, Peru.

We selected participants using a two-stage stratified random selection strategy. We defined three strata to ensure representation of indigenous communities with different levels of exposure to oil extraction activities and therefore potentially different BLLs. Strata were based on distance to oil extraction related infrastructures and distance to contaminated sites according to data from OEFA-EM, the Environmental Assessment and Control Agency of the Peruvian Ministry for the Environment. Stratum 1 included communities located at < 50 Km, stratum 2 communities located between $\geq$ 50–200 Km and stratum 3 communities located $\geq$ 200 Km from such sites. All the indigenous communities belonging to the indigenous federations from the four river basins (n = 66) were classified across three strata. All communities from stratum 1 (n = 17) were selected to ensure representation of communities potentially exposed to the highest levels of lead. Forty-five per cent of communities from stratum 2 and 45% of stratum 3 were randomly selected (n = 10 and n = 12, respectively). Overall, 39 communities were selected (Fig. 1): eight from Marañón (four from stratum 1, four from stratum 3), 11 from Pastaza (five from stratum 1, six from stratum 3), 4 from Tigre (two from stratum 1, two from stratum 2) and 16 from Corrientes (six from stratum 1, eight from stratum 2 and two from stratum 3). We used data from the local census (revised and updated by the indigenous federations) to determine the number of families living in each community. The same proportion of families were included from all communities (between 14 and 15% of families living in the community) but ensuring that at least three families were selected from each community. Therefore, small communities were over-sampled (in six communities the number of families included ranged between 18 and 38% of all families living in the community). Traditional leaders from selected communities were contacted and dates to visit the community were agreed. All contacted communities accepted to participate in the study. During the visits, traditional leaders convened community-wide meetings during which the investigators presented the objectives of the study. Families were selected by a raffle carried out among all families participating in the meeting who had been living in a community for at least six months (random selection). Participation was offered to all members of a selected families excluding infants under six months of age.

The study protocol was reviewed and accepted on September 24, 2015 by the Ethics and Research Committee of the National Institute of Health, Peru (code: OC-023-15, directive resolution: 732-2015-OGITT/OPE-INS). Written informed consent was obtained from traditional leaders to conduct the study in each of the communities. Also, prior to participation in the study, written informed consent was obtained from participants $\geq$ 18 yo, personal verbal consent and informed written paternal consent from participants between $\geq$ 7 and < 18 yo, and informed written paternal consent from participants < 7 yo was obtained.

2.2. Data collection and laboratory analysis

A face-to-face questionnaire was administered to the heads of households to collect information on dwelling, family characteristics and main sources of food and water in the household (supplementary material, questionnaire 1). A face-to-face questionnaire was also administered to all family members to collect information on individual

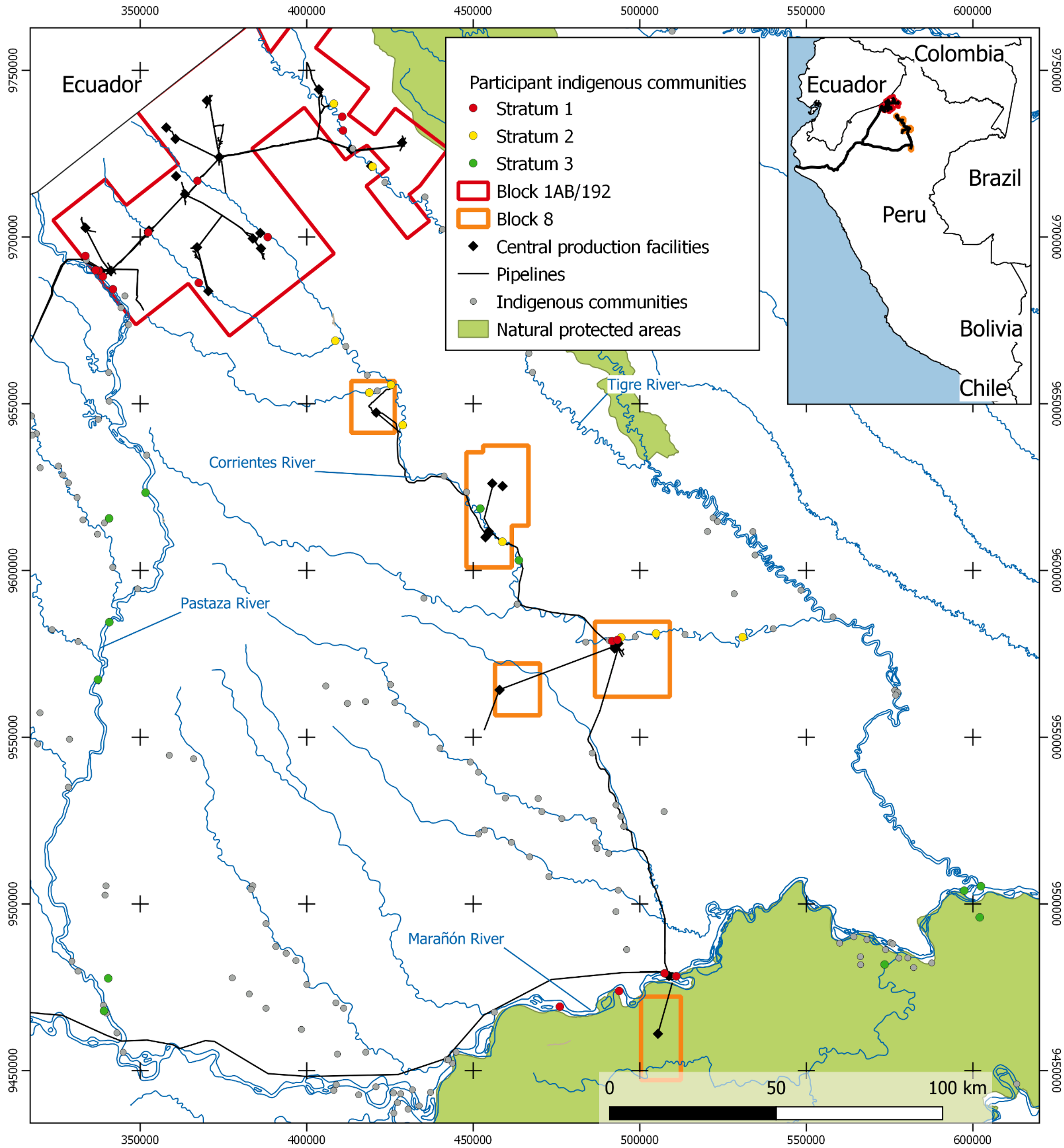

Fig. 1. Map of the study area.

risk factors, including socio-demographic, life-style and occupational characteristics (supplementary material, questionnaire 2). Information from children younger than 12 years was provided by their parents or tutors (supplementary material, questionnaire 3). Questionnaires were administered by study personnel with the support of local translators who were fluent in both Spanish and the native languages. After the interview a venous blood sample was collected in vacuum tubes with EDTA K2 (Vacuette) and preserved following standardized CENSOPAS-INS procedures (Carreón Valencia et al., 1995; Centers for Disease Control and Prevention, 2016). Samples were kept between 2 and 8 °C from extraction to reception at CENSOPAS-INS using a refrigerating chamber (Dometic TCW 2000®) with a cooling system connected to a domestic propane gas balloon. Data loggers (Trek View®) were used to monitor real time temperature to ensure maintenance of the cold chain during shipment of samples from the communities to toxicological laboratory of the National Institute of Health (INS) in Lima, Peru. Upon arrival in Lima, the samples were stored at −20 °C until they were analysed. We determined blood lead levels using atomic absorption spectrophotometry in a graphite chamber with double beam graphite furnace with Zeeman background correction and automatic sampler (Analytik Jena, ZEENIT 700P, Germany), following the protocol stablished by the National Institute of Occupational Health and Safety from Spain (Instituto Nacional de Seguridad e Higiene en el Trabajo). Blood samples were treated with a modifier solution (Triton X-100 0.1%, NH4H2PO4 0.2% and ultra-pure water) to reduce the level of interferences during the reading process, and placed in the in automatic sampler set at high temperature (1500° C) to eliminate any organic material from the samples. The limit of detection (LOD) of the method was 0.2 μg/dl. Blood lead measurement was supported by the interlaboratory comparison program organized by the Center for Toxicology of the National Institute of Public Health of Quebec, Canada with satisfactory results for 3 levels of concentration. It was also run in triplicate of internal controls of the Bio-Rad brand (Lyphochek Whole Blood Metals Control) in 3 different levels, and with coefficient of variation less than 10%.

The Euclidean distance between the residence of each participant and the closest oil processing facility (n = 22): dumping sites of produced water (the main waste product of oil-extraction operations, which accounts in average for 70% of the liquid fluids extracted from a well (Fakhru'l-Razi et al., 2009), gathering stations and pump stations and the fluvial distance between each community and the closest upstream processing facility were calculated using QGIS 3.4.13.

2.3. Statistical analysis

Participation rate was calculated by dividing the number of expected families from each community by the number of families accepting to participate from each community. Blood lead levels below LOD were replaced by LOD/2. Blood lead levels of study participants did not follow a normal distribution and were log- transformed to approach normality. We reported BLL weighted geometric mean and percent of participants with BLL above 5 μg/dL, and above 10 μg/dL according to different characteristics of the study participants, stratified by age. We used a threshold of 12 yo as to separate children from adults, because in the study context this age threshold differentiates best childhood from adulthood activities. At age 12 children are involved in the same activities than adults (hunting, fishing, working on vegetable gardens, etc.) and therefore environmental exposures are similar for children ≥ 12 than for older adults (MINSA, 2006). The Peruvian Ministry of Health also uses this threshold (RM N°400-2017-MINSA).

We used linear regression models, adjusted for age and sex to study the association between socio-demographic variables, self-reported environmental and occupational exposures and log-transformed BLL. Estimates and standard errors were calculated taking into account the multi-level study design (UCLA, 2021). Results of the regression models were back transformed and presented as Geometric Mean Ratio (GMR, 95%CI). Community within a strata and family within community were weighted to account for the sampling probability of each participant and weights were included in the models. Variables associated with BLL in the individual models for each factor adjusted for age and sex (Wald test p-value < 0.1) were considered for the multiple regression model. We checked for multicollinearity in the multiple regression models by assessing the variable inflation factors (VIF). If multicollinearity was observed (VIF > 5), we dropped one of the correlated variables included in the model. The multiple regression models was repeated separately for each river basin because of significant differences in BLLs among river basins. All analyses were made using Stata version 14 (StataCorp, College Station, TX, USA).

3. Results

3.1. Study population

Overall, 1168 participants from 370 families were enrolled in the study. Participation rate was 85%. After exclusion of participants with missing information on basic co-variables (n = 97) and those who did not provide a blood sample (n = 24), 1047 individuals were eligible for the current analysis. Of the participants, 309 (31%) were children (younger than 12 yo) and the remaining 738 (69%) were adults. Median (interquartile range, IQR) age among children was seven (4) yo and among adults 35 (24) yo. Median (IQR) Euclidean distance from communities to a processing facility was 5.5 (29.1) Km. Sixty-seven percent of communities were located downstream from a processing facility, and the median (IQR) fluvial distance of those communities to such facilities was 85.5 (130.6) Km.

3.2. Blood lead levels

The geometric mean (95% confidence interval, 95% CI) BLL for children was 4.9 (4.5, 5.4); the frequency of children with BLL ≥ 5 μg/dL and ≥ 10 μg/dL was 49 and 22%, respectively. For adults, the geometric mean (95% CI) BLL was 5.7 (5.4, 6.0); the frequency of adults with BLL ≥ 5 μg/dL and ≥ 10 μg/dL was 60 and 27%, respectively.

Geometric means according to socio-demographic characteristics and exposure to potential risk factors are presented in Table 1. There were important differences in BLLs between river basins, with the lowest values being reported in the Marañón (2.4 μg/dL in < 12 yo and and 3.1 μg/dL in ≥ 12 yo) and the highest in the Corrientes (8.0 μg/dL in < 12 yo and and 8.4 μg/dL in ≥ 12 yo) and Tigre (6.5 μg/dL in < 12 yo and and 9.2 μg/dL in ≥ 12 yo) basins. In both children and adults, BLL was higher among males, among Achuar people and among those used surface water for drinking and among those who used surface water for bathing. In adults, BLL was also higher among those who consumed fish offal, resided less than one hour walk from an abandoned petroleum infrastructure, had contact with crude oil, and had participated in remediation activities (including handling of solid waste, clean-up of environmental hazards or contaminated sites, and reforestation of contaminated sites).

3.3. Risk factors associated with blood lead levels

Table 2 shows results of the univariate models (adjusted for age and sex). In both children and adults, being male, being Achuar, living in the Corrientes or Tigre river basin, consumption of fish offal, using surface water (river, ravine or lagoon water) as the main source of drinking water (compared to public water source), and using surface water as the main bathing water (compared to using well water) were associated with higher BLL after adjusting for age and sex. Increased Euclidean distance between residence to a processing facility (produced water dumping sites, gathering stations and pumping stations) was associated with lower BLL. For participants living in communities located downstream from central production facilities, increasing fluvial distance was also associated with lower BLL, after adjusting for age and sex. In adults, living at less than one hour walking distance from old infrastructure (i.e. well and/or drainage channel), having been in contact with crude oil in the previous six months and having participated in environmental remediation activities in the previous six months, were also associated with higher BLL. Analyses conducted by river basin indicated some differences in risk factors associated with BLL depending on the river basin for both children and adults (supplementary material tables S1-S4 and S5-S8). For instance, contact with crude oil in the previous six months and participation in environmental remediation activities in the previous six months, were activities associated with higher BLL [adjusted GMR (95%CI) = 1.57 (1.10, 2.23) and 1.48 (1.13, 1.93), respectively] in the Marañón river basin but not in the other basins.

According the results from the individual models adjusted for age and sex, the following variables were selected to be included in the multiple regression models for population < 12 yo: age, sex, river basis, ethnic origin, consumption of fish offal, source of water consumption, bathing place and eucledian distance to processing facilities. And the following ones in the multiple regression models for population ≥ 12 yo age, sex, river basis, ethnic origin, consumption of fish offal, source of water consumption, bathing place, residence at least than one hour from oil extraction infrastructures and Euclidian distance to processing facilities. The final multiple regression models did not include ethnic origin as multicolinearity was detected between this variable and river basin (VIF > 5).

In the multiple regression models conducted for children, the factors that remained associated with higher BLL were older age [GMR (95%CI) = 1.08 (1.05, 1.11)], being male [GMR (95%CI) = 1.42 (1.21, 1.67)], and living in the Pastaza, Tigre or Corrientes river basin [GMR (95%CI) = 2.04 (1.57, 2.66), 2.06 (1.51, 2.80), and 3.01 (2.32, 3.90), respectively] and consumption of fish offal [GMR (95%CI) = 1.16 (0.99, 1.37)]. Increasing Euclidean distance from residence to oil processing facilities also remained associated with lower BLL [GMR (95%CI) = 0.96 (0.93, 0.98)]. There were some differences in the risk factors associated

Table 1
Characteristics of study population and blood lead levels (μg/dL) by age groups.

Variable	Category	< 12 years old, n = 309		≥ 12 years old, n = 738	
		n (%)	GM (95% CI)	n (%)	GM (95% CI)
Age (years), median (IQR)		7 (4)	–	35 (24)	–
Sex	Male	152 (49%)	6.2 (5.4, 7.1)	347 (47%)	7.8 (7.2, 8.4)
	Female	157 (51%)	4.0 (3.5, 4.5) **	391 (53%)	4.3 (4.0, 4.7) **
Ethnic origin	Achuar	120 (39%)	8.1 (7.2, 9.1)	242 (33%)	8.8 (8.0, 9.6)
	Quechua and Kichwa	111 (36%)	4.3 (3.8, 5.0)	300 (41%)	5.8 (5.3, 6.4)
	Mestizo, Kukama and other peoples	78 (25%)	2.8 (2.3, 3.4) **	196 (27%)	3.2 (2.9, 3.6) **
River basin	Marañón	70 (23%)	2.4 (2.0, 3.0)	167 (23%)	3.1 (2.7, 3.4)
	Pastaza	95 (31%)	4.2 (3.6, 4.9)	262 (36%)	5.2 (4.8, 5.7)
	Tigre	21 (7%)	6.5 (5.1, 8.2)	60 (8%)	9.2 (8.1, 10.4)
	Corrientes	123 (40%)	8.0 (7.1, 9.0) **	249 (34%)	8.4 (7.6, 9.2) **
Fish offal consumption	No	111 (36%)	4.4 (3.7, 5.3)	182 (25%)	5.07 (4.4, 5.8)
	Yes	198 (64%)	5.3 (4.7, 5.9)	556 (75%)	5.91 (5.5, 6.3) *
Alcohol consumption (only ≥ 12 years old)	No			608 (82%)	5.47 (5.1, 5.9)
	Yes			130 (18%)	6.83 (6.0, 7.8)
Smoking (only ≥ 12 years old)	No			656 (89%)	5.6 (5.2, 5.9)
	Yes			82 (11%)	6.9 (5.9, 8.1)
Burning of household waste	No	168 (54%)	5.1 (4.5, 5.9)	415 (56%)	6.00 (5.5, 6.5)
	Yes	141 (46%)	4.7 (4.1, 5.4)	323 (44%)	5.4 (4.9, 5.9)
Main source of water for consumption	Public water source	157 (51%)	4.5 (3.9, 5.2)	338 (46%)	5.8 (5.3, 6.4)
	Well or spring water	72 (23%)	5.1 (4.3, 6.2)	202 (27%)	5.6 (5.0, 6.2)
	Rain	30 (10%)	4.4 (3.3, 5.9)	79 (11%)	4.3 (3.5, 5.2)
	Surface water (river, ravine, lagoon)	50 (16%)	6.7 (5.4, 8.3) *	119 (16%)	6.7 (5.7, 7.7) **
Main bathing place		211 (68%)		501 (68%)	
	Surface water (river, ravine, lagoon)		5.4 (4.8, 6.0)		6.2 (5.8, 6.7)
	Well	57 (18%)	4.0 (3.2, 5.0)	141 (19%)	5.0 (4.4, 5.7)
	Others	41 (13%)	4.4 (3.5, 5.4) *	96 (13%)	4.4 (3.7, 5.2) **
Residence at less than one hour walk	None of this places	103 (33%)	4.8 (4.1, 5.7)	207 (28%)	5.6 (5.00, 6.3)
	Active infrastructures	47 (15%)	4.3 (3.4, 5.3)	140 (19%)	5.6 (4.9, 6.3)
	Oil spill, environmental remediation spot	135 (44%)	5.2 (4.4, 6.1)	351 (48%)	5.6 (5.1, 6.1)
	Old infrastructures (not in use)	24 (8%)	5.6 (4.4, 7.2)	40 (5%)	8.1 (6.3, 10.5) *
Vegetable garden at less than one hour walk	None of this places	143 (46%)	5.0 (4.3, 5.7)	326 (44%)	5.36 (4.9, 5.9)
	Active infrastructures	41 (13%)	5.2 (4.1, 6.6)	104 (14%)	6.4 (5.6, 7.4)
	Oil spill, environmetal remediation spot	119 (39%)	4.8 (4.1, 5.7)	291 (39%)	5.8 (5.2, 6.3)
	Old infrastructures (not in use)	6 (2%)	5.0 (2.6, 9.6)	17 (2%)	6.9 (4.5, 10.6)
Use of crude oil to keep insects away from the house	No	189 (61%)	4.9 (4.3, 5.5)	463 (63%)	5.9 (5.4, 6.2)
	Yes	120 (39%)	5.1 (4.4, 5.9)	275 (37%)	5.5 (5.0, 6.1)
Contact with crude oil in the last 6 months (only ≥ 12 years old)	No			646 (88%)	5.5 (5.1, 5.8)
	Yes			92 (12%)	7.4 (6.3 8.70) **
Participation in environmental remediation activities in the last 6 months (only ≥ 12 years old)[a]	No			566 (77%)	5.1 (4.8, 5.5)
	Yes			172 (23%)	7.9 (7.1, 8.8) **

GM: Geometric mean; 95% CI: 95% confidence interval; [a] Environmental remediation activities include handling of solid waste, cleaning of environmental liabilities or contaminated sites and reforestation of contaminated areas; * p-value for ANOVA < 0.05; ** p-value for ANOVA < 0.001.

with BLL depending on the river basin (Fig. 2). Remarkably, increasing Euclidean distance from residence to oil processing facilities was associated with a small decrease in BLL in the Pastaza river basin [GMR (95% CI) = 0.96 (0.93, 0.99)] and the Marañón river basin [GMR (95%CI) = 0.93 (0.87, 1.01)] but it was associated with increased BLL in the Corrientes river basin [GMR (95%CI) = 1.33 (1.03, 1.73)].

In the multivariate models conducted for adults, being male [GMR (95%CI) = 1.70 (1.52, 1.90)], living in the Pastaza, Tigre or Corrientes river basin [GMR (95%CI) = 1.85 (1.58, 2.17), 2.85 (2.43, 3.33) and 2.88 (2.45, 3.37), respectively] and consumption of fish offal [GMR

Table 2
Associations between sociodemographic, life-style, environmental and occupational characteristics and blood lead levels (μg/dL) by age group.

Variable	Category	<12 years old, n = 309		≥ 12 years old, n = 738	
		GMR (95% CI) [a]	p-value [b]	GMR (95% CI) [a]	p-value [b]
Age (years) [c]		1.06 (1.03, 1.10)	<0.001	1.00 (1.00, 1.00)	0.916
Sex [d]	Female	1.00 (1.00, 1.00)		1.00 (1.00, 1.00)	
	Male	1.59 (1.36, 1.87)	<0.001	1.80 (1.62, 2.00)	<0.001
Ethnic origin	Achuar	1.00 (1.00, 1.00)		1.00 (1.00, 1.00)	
	Quechua and Kichwa	0.59 (0.48, 0.72)		0.68 (0.59, 0.78)	
	Mestizo, Kukama and other peoples	0.37 (0.28, 0.49)	<0.001	0.36 (0.31, 0.41)	<0.001
River basin	Marañón	1.00 (1.00, 1.00)		1.00 (1.00, 1.00)	
	Pastaza	1.74 (1.32, 2.31)		1.78 (1.55, 2.06)	
	Tigre	2.46 (1.77, 3.43)		2.92 (2.50, 3.41)	
	Corrientes	3.02 (2.33, 3.92)	<0.001	2.78 (2.41, 3.20)	<0.001
Fish offal consumption	No	1.00 (1.00, 1.00)		1.00 (1.00, 1.00)	
	Yes	1.20 (0.94, 1.53)	0.138	1.22 (1.05, 1.42)	0.011
Alcohol consumption (only ≥ 12 years old)	No			1.00 (1.00, 1.00)	
	Yes			0.95 (0.81, 1.12)	0.516
Smoking (only ≥ 12 years old)	No			1.00 (1.00, 1.00)	
	Yes			0.91 (0.75, 1.11)	0.332
Burning of household waste	No	1.00 (1.00, 1.00)		1.00 (1.00, 1.00)	
	Yes	0.97 (0.76, 1.23)	0.768	0.96 (0.82, 1.12)	0.576
Main source of water for consumption	Public water source	1.00 (1.00, 1.00)		1.00 (1.00, 1.00)	
	Well or spring water	0.99 (0.75, 1.32)		1.00 (0.85, 1.18)	
	Rain	0.92 (0.61, 1.38)		0.82 (0.67, 1.02)	
	Surface water (river, ravine, lagoon)	1.40 (1.04, 1.89)	0.100	1.22 (1.00, 1.48)	0.042
Main bathing place	Surface water (river, ravine, lagoon)	1.00 (1.00, 1.00)		1.00 (1.00, 1.00)	
	Well	0.71 (0.52, 0.97)		0.85 (0.71, 1.01)	
	Others	0.82 (0.66, 1.02)	0.066	0.76 (0.60, 0.95)	0.022
Residence at less than one hour walk	None of these places	1.00 (1.00, 1.00)		1.00 (1.00, 1.00)	
	Active infrastructures	0.81 (0.57, 1.15)		0.91 (0.74, 1.12)	
	Oil spill, environmental remediation spot	1.02 (0.77, 1.35)		0.96 (0.80, 1.15)	
	Old infrastructures (not in use)	0.96 (0.68, 1.36)	0.593	1.35 (1.01, 1.80)	0.086
Vegetable garden at less than one hour walk	None of these places	1.00 (1.00, 1.00)		1.00 (1.00, 1.00)	
	Active infrastructures	1.02 (0.76, 1.38)		1.18 (0.98, 1.42)	
	Oil spill, environmental remediation spot	0.99 (0.74, 1.32)		1.10 (0.92, 1.31)	
	Old infrastructures (not in use)	1.03 (0.64, 1.67)	0.996	1.32 (0.80, 2.18)	0.300
Use of crude oil to keep insects away from the house	No	1.00 (1.00, 1.00)		1.00 (1.00, 1.00)	
	Yes	1.06 (0.83, 1.36)	0.629	0.99 (0.84, 1.17)	0.923
Contact with crude oil in the last 6 months (only ≥ 12 years old)	No			1.00 (1.00, 1.00)	
	Yes			1.24 (1.03, 1.50)	0.025
Participation in environmental remediation activities in the last 6 months (only ≥ 12 years old) [e]	No			1.00 (1.00, 1.00)	
	Yes			1.20 (1.03, 1.39)	0.019
Euclidean distance to closest processing facility (10 km)		0.94 (0.92, 0.96)	<0.001	0.96 (0.95, 0.97)	<0.001
Minimum upstream fluvial distance processing facility (10 km) [f]		1.00 (1.00, 1.00)	0.328	1.00 (1.00, 1.00)	0.013

GMR: Geometric mean ratio; 95% CI: 95% confidence interval [a] Individual models adjusted for age and sex; [b] P-values based on Wald test; [c] Individual model adjusted for sex; [d] Individual model adjusted for age; [e] Environmental remediation activities include handling of solid waste, cleaning of environmental liabilities or contaminated sites and reforestation of contaminated areas; [f] Only among those living downstream from central production facilities (<12 years old, n = 217; ≥ 12 years old, n = 489).

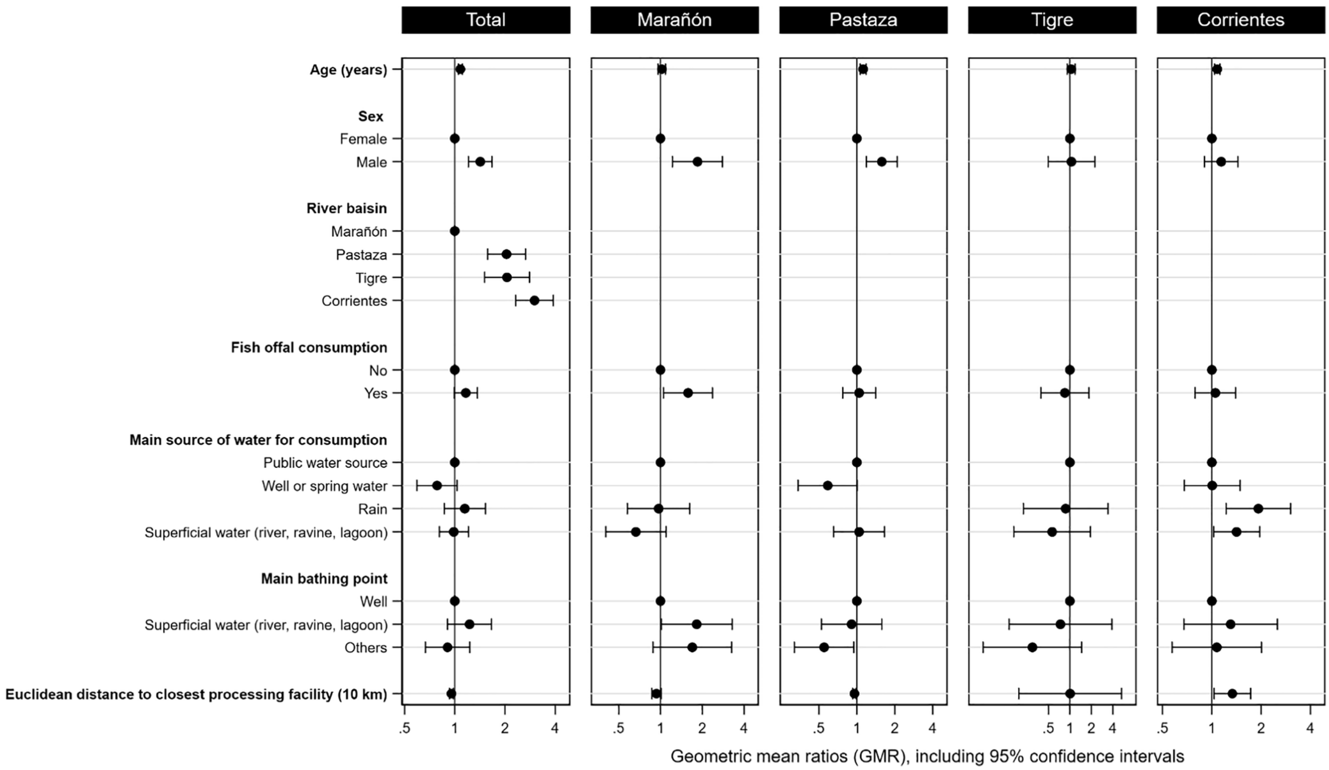

Fig. 2. Multiple regression analysis of sociodemographic, life-style, environmental, occupational and geographical characteristics associated with BLL among participants < 12 by river basin.

(95%CI) = 1.24 (1.09, 1.40)] were associated with increased BLL. Using subterranean water (well or spring water) as the main source of drinking water and using sources of water other than surface water or well water for bathing were associated with lower BLL [GMR (95%CI) = 0.80 (0.68, 0.93) and 0.79 (0.64, 0.99)]. There were some differences in the risk factors associated with BLL depending on the river basin (Fig. 3). Similar

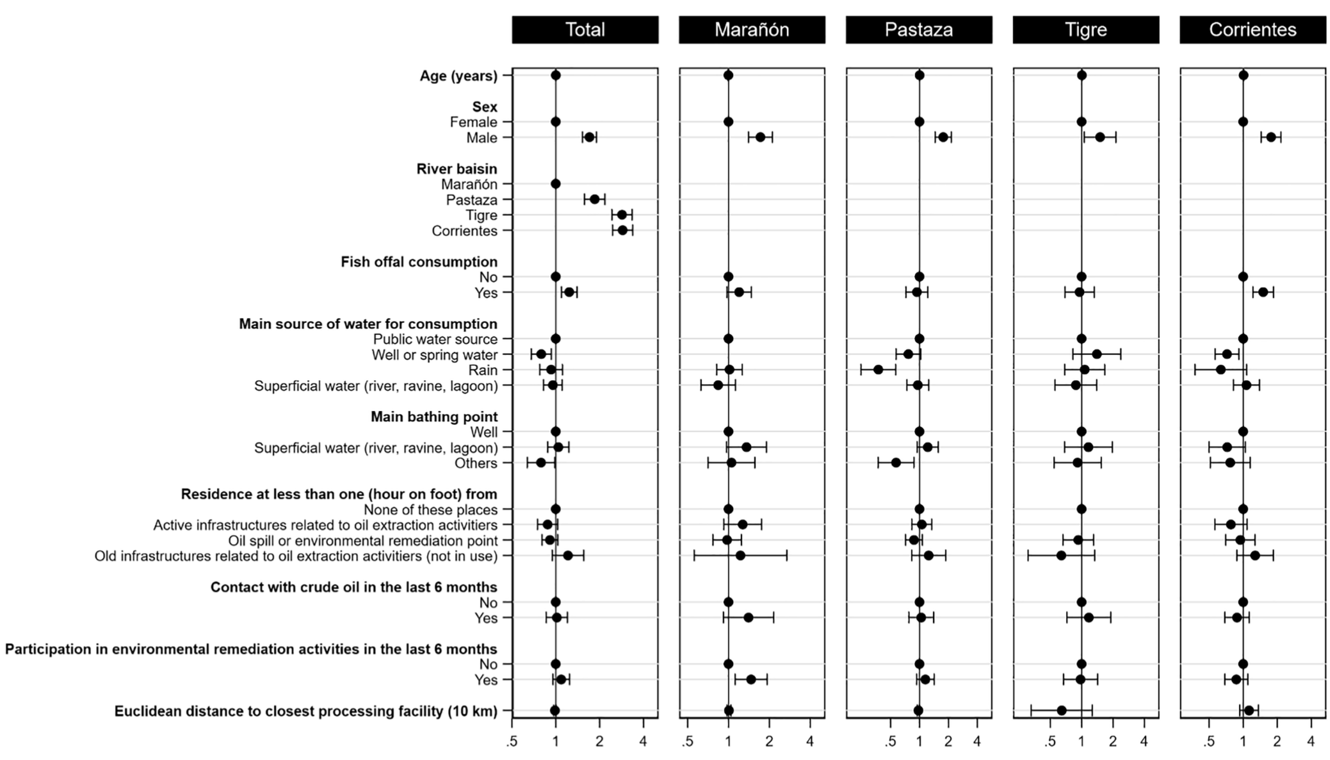

Fig. 3. Multiple regression analysis of sociodemographic, life-style, environmental, occupational and geographical characteristics associated with BLL among participants ≥ 12 by river basin.

to previously observed for children, increasing Euclidean distance from residence to oil processing facilities was associated with a small decrease in BLL in the Pastaza river basin [GMR (95%CI) = 0.97 (0.953, 1.00)].

4. Discussion

We report high BLLs among indigenous people living in the largest onshore oil extracting area of Peru. The highest levels were found among participants from the Corrientes river basin, where most of the oil extraction activities were concentrated and the highest amount of produced water had been released.

In both children and adults, being male, living in the Pastaza, Tigre and Corrientes river basins and, consumption of fish offal were associated with higher BLL. Increasing Euclidean distance between residence and a central production facility was associated with a small reduction in BLL. Older age was associated with higher BLL among population < 12 yo. There were some differences in risk factors for BLLs between river basins.

Being male was an important risk factor for higher BLL in both children and adults. Higher BLL among males have been consistently reported in previous studies in different population (Delage et al., 2015; Hense et al., 1992; Leroyer et al., 2001). Differences in BLL by sex have been generally explained by lower occupational exposures among females. In our study population, daily activities are clearly different between males and females from an early age (MINSA, 2006). Higher BLL at older age have been also consistently reported in the literature. Higher BLL at older ages could indicate a cumulative effect of exposure among older individuals as lead accumulates in the bone with a half-life of up to 25 years. Higher BLL at older ages could be explained by the release of lead from bone to circulation (Silbergeld et al.).

BLLs were high in the study population. Although no BLL is considered safe, a 5 μg/dL threshold has been used by the National Institute for Occupational Safety and Health (NIOSH), USA, since 2015 to define elevated BLL, based on evidence for adverse health outcomes among adults (Alarcon et al., 2016). Mean (geometric mean) BLL in the study population was higher than 5 μg/dL, and 49% of children and 60% of adults had BLL above this threshold. Values observed in the present study are similar to those reported for children < 12 yo almost 20 years ago in Lima metropolitan area (Peru), when the use of leaded gasoline was still allowed (Espinoza et al., 2003). Among younger children (≤5 yo), BLLs were about two times higher than values reported among ≤ 5 yo in studies from Europe conducted between 1999 and 2007 (5.6 μg/dL in the study population and 2.6 μg/dL in a joint evaluation of European studies (Bierkens et al., 2011), which also included the period when leaded gasoline was still used in Europe (until 2005 in some countries). Values were also much higher (6.5 times higher) than values reported among young children from the United States between 2013 and 2014, after banning leaded gasoline (0.84 μg/dL (Tsoi et al., 2016). Similarly, BLLs in adults (≥18 yo) were almost 5 times higher than values reported in the USA between 2009 and 2010 (5.8 μg/dL versus 1.2 μg/dL) (Centers for Disease Control and Prevention, 2019).

There were important differences in BLL among river basins. The highest mean BLL was detected in the Corrientes river basin and the lowest in the Marañón river basin. The differences in BLLs observed among river basins may be explained by geographic variation in environmental release of produced water to surface waters. Produced water may contain high concentrations of hydrocarbons and heavy metals (including lead (0.002–8.8 mg/L)) although the relative concentrations of these contaminants can vary in large part depending on the characteristics of the geologic formation (Fakhru'l-Razi et al., 2009). Lead has been reported in produced water from the study area (Yusta-García et al., 2017). In the study area (blocks 1AB and 8), produced water was released on soils and rivers between the beginning of oil extraction and 2009, when re-injection of produced water back to the oil reservoir was completely implemented in the area (Orta-Martínez et al., 2018). In 2008, nearly 940,000 barrels of produced water were daily discharged in the study area (oil blocks 192 and 8) (Cartró-Sabaté et al., 2019), so approximately 5.14 tons of lead were discharged during that year (Yusta-García et al., 2017). However, the amount of lead dumped into each of the four river basins under study varied markedly. The Corrientes and Tigre river basins were, by far, where the largest volumes of produced water and by extension, lead, were dumped. This explains the higher levels of lead reported in sediments and soils in these river basins, compared levels reported in the Pastaza and Marañón basins (Yusta-García et al., 2017; Ministerio de Energía y Minas del Perú, 2005). This may explain the higher BLLs detected in the Corrientes and Tigre river basins compared to BLLs in the other river basins. As shown in Fig. 4, BLLs were higher in those river basins where the amount of produced water dumped had been higher.

Blood lead levels of children in the Corrientes river basin are similar to levels reported in studies conducted in the same area between 2009 and 2010 (Anticona et al., 2011; Anticona et al., 2012a, Anticona et al., 2012b) but are lower than results from previous studies conducted in 2006 (average BLL in a convenient sample of 59 children from five communities: 10.14 μg/dL [12]; percentage of children and adults with BLL ≥ 10 μg/dL in a convenient sample of 75 children and 124 adults from seven communities: 66% and 79% respectively (DIGESA, 2006). The reduction of BLL in the Corrientes river basin in the last years may be explained by temporal variation in environmental release of produced water to surface waters. Complete reinjection of produced water into wells (instead of dumping to streams) in the Corrientes river basin began in December 2007 (Orta-Martínez et al., 2018; Comisión de Pueblos Andinos Amazónicos y Afroperuanos, Ambiente y Ecología, 2013), which may explain the reduction in BLL detected in the population of this river basin from studies conducted before (DIGESA, 2006) and after that year (Anticona et al., 2011; Anticona et al., 2012a, Anticona et al., 2012b). Similarly, a sharp decrease of other contaminants have been detected in the rivers of the region after 2009 (Moquet et al., 2014). No previous data on BLL are available for the other river basins.

In the Corrientes, Tigre, Pastaza and Marañón river basins, levels of environmental contaminants (lead, cadmium, barium, hexavalent chromium, and petrogenic hydrocarbons among others) have been reported in surface waters, soils and sediments above the Peruvian and international standards. They have been associated with dumping of produced water (as explained above) and frequent oil spills of varying magnitude, including recurrent leaks from poorly maintained infrastructure (DIGESA, 2006; Ministerio de Energía y Minas, 1999; Oficina de Evaluación y Fiscalización Ambiental, 2012; Autoridad Nacional del Agua, 2012); reviewed by Orta-Martinez et al (Orta Martínez et al., 2007) and Yusta-García (Yusta-García, 2019). Moreover, there is evidence that Pb may have entered the food chain and that diet may currently be an important route of exposure for the local populations. At least ten wildlife species, including the four species most frequently consumed in indigenous people's diets (i.e. Tapirus terrestri, Cuniculus paca, Mazama americana and Peccary tajacu) (Bodmer and Lozano, 2001) have been reported to feed on petroleum-contaminated soils in the study area (Orta-Martínez et al., 2018; Cartró-sabaté and Amazo'n'oil, 2018). High lead levels have been detected in livers from those four species and other 14 species (including other mammals, birds and replies) also commonly consumed by the local population in the study area (Cartró-Sabaté et al., 2019). Lead's entry into the food chain is consistent with the observation that 50% of fish collected in the area during the study period had Pb levels above levels considered safe for human consumption by the European Union the European Union (EUC Regulation 1881/2006; personal communication) and with the identification of consumption of fish offal as a risk factor for higher BLL in our study. Other anthropogenic activities such as hunting with lead-based ammunition and fishing using lead weights have been suggested as sources of higher BLL in the area (Anticona et al., 2011; Anticona et al., 2012a, Anticona et al., 2012b). However, Cartro et al. 2019, based on lead isotopic fingerprinting analysis in wildlife hunted for human consumption in the Pastaza and Corrientes river basins, indicated that,

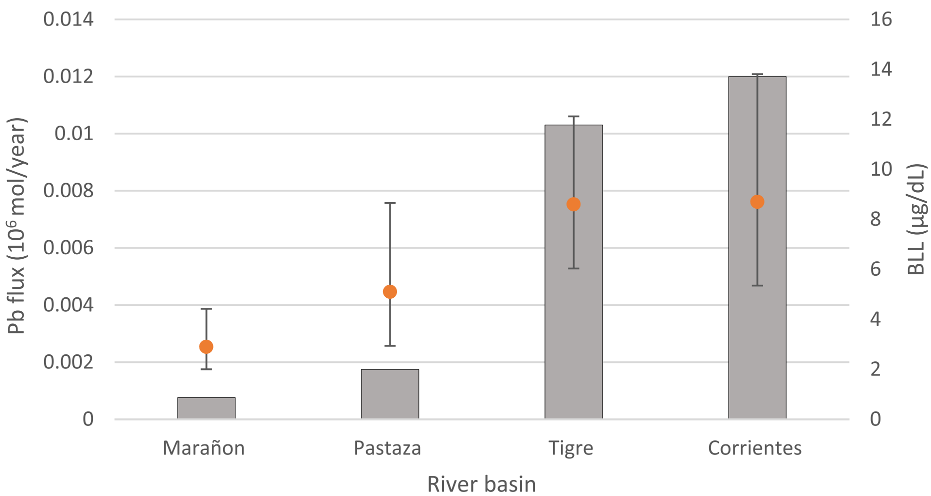

Fig. 4. Estimated average lead flux (10^6 mol/year) from dumping of produced water in 2008 in the Marañón, Pastaza, Tigre and Corrientes river basins (extracted from Yusta-García et al (Yusta-García et al., 2017); Table 3) and BLL (μg/dL) detected in the current study in the same river basins Grey bars: average lead flux (10^6 mol/year) from dumping of produced water; orange circles: geometric mean BLL and lower and upper quartiles (p25 and p75). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

although hunting ammunition is indeed an important source of lead contamination, oil-related contamination is also a major source of lead exposure for wild animals (Cartró-Sabaté et al., 2019). No lead isotope data is available for fish, but past high lead levels in water streams might have contributed to lead levels in fish, as already reported in older studies (Marco, 1993). However, we observed differences in the association between fish offal consumption and BLL between river basins and between children and adults that require more careful evaluation.

Participation in environmental remediation activities and contact with crude oil have been associated with higher BLL in other settings (Pérez-Cadahía et al., 2008). We observed a positive association between participation in environmental remediation activities, and contact with crude, and higher BLL in the individual models, but in the multiple regression models this association was not observed. This observation reinforces the hypothesis exposed above, that diet might be the main route of lead exposure for the local population. However, in the Marañón river basin, participation in environmental remediation activities and higher BLL remained associated in the multivariate analysis. In the Marañón and Pastaza river basins, dumping of Pb along with produced water has been 8.9 times lower than in the other two river basins (Yusta-García et al., 2017; Ministerio de Energía y Minas del Perú, 2005), moreover the flow rate in the Marañón river basin is much higher than in the other basins leading to a higher dilution of contaminants. The main source of oil related contamination reported in communities from this basin has been through discrete oil spills of the North Peruvian oil pipeline, such as two major oil spills that occurred 24 and 18 months before the conduct of this study, involving environmental remediation activities in the area (Expediente Resolución Directoral No. 844-2015-OEFA/DFSAI Expediente No. 1306-2014-OEFA/DFSAI/PAS.2015; UTM WGS84 N9474535, E467992; (Goldenberg, 2014). Therefore, it seems plausible that in the Marañón river basin, the primary exposure route for lead may be occupational activities and not through contamination of the trophic chain, as suggested for the Corrientes, Tigre, and Pastaza river basins. Nevertheless, these results could be also explained by response bias, since information on risk factors, including occupation and environmental exposures were self-reported. Given the concern of the local population about the potential health effects of exposure to contamination related to oil extraction activities, it is likely that participants over-reported certain exposures, such contact with crude oil, participation in remediation activities and residential distance to a contaminated site. However, participants could not have known their BLL at the time of participation and over-reporting cannot have been conditioned on measured BLL, so differential misclassification is unlikely. If over-reporting of contact with crude oil, participation in remediation activities or errors in reporting of residential distance to a contaminated site did occur, this would have caused non-differential bias, leading to a dilution of the association between self-reported risk factors and BLL. Response bias is more likely to have occurred in the Corrientes basin. The population from this basin is especially aware and concern about the potential health problems related to exposure to oil extraction related contamination after the governmental measurement of blood lead and cadmium levels conducted in the basin in 2006 (DIGESA, 2005). Response bias might had been less of a problem in the less polluted areas, like the Marañón and Pastaza basins.

This study has two other potential limitations. First, not all families from the community participated in the initial meeting and therefore, they could not participate in the raffle that was conducted to select participating families. This could have biased our results if families attending and do not attending the meeting were different in their exposure to the studied risk factors or their BLL. However, participation in the meetings was very high for most of the communities. It is relevant to keep in mind that the study arouse from the claims of the local population to the government and therefore, the willingness to participate was high. It is also important to take into account the convening power that indigenous leaders have when they have to bring their community together in a meeting. Second, collection of data through interviews is always prone to interviewer's bias. Both interviewers and interpreters were trained to minimize this risk. Interpreters were educated indigenous peoples fluent in Spanish and they got familiarized with all the items included in the questionnaire before the interviews. Still, if interviewer bias had occurred, it would have caused non-differential bias (it was not possible to know BLL at the moment of the interview), leading to a dilution of the association between risk factors and BLL.

The main strengths of the study are the use of a large sample size of participants from the four river basins overlapping with oil blocks 8 and 192 (formerly 1AB) and from all the ethnic groups that inhabit the area. This is the largest study conducted to date on a general population exposed to oil-related contamination. In the study region, BLLs have been previously estimated only in the Corrientes river basin, where the highest levels of environmental contamination had been previously reported. The inclusion of the four river basins increased variation in exposure to levels of Pb and to different risk factors, helping in their identification and allowing a more complete picture of the situation in the whole oil extraction area. We used standardized and validated protocols of CENSOPAS-INS to assess exposure and collect biological samples in remote areas of the Peruvian Amazon.

In conclusion, we detected BLLs that pose a risk for health among inhabitants of a non-industrialized and remote area of the Amazon. The highest BLLs were observed in areas where levels of produced water dumping were reported to be high in past studies, which supports that oil extraction activities have contributed to BLLs observed among the population. In river basins with more intense extraction activity, both our data and existing data suggest that diet is a likely route of lead exposure. In the river basin with less intense extraction activity, occupational exposures seem the main route of exposure. However, we acknowledge that these hypotheses have to be validated using studies that include detailed evaluation of food frequency consumption, objective measurements of occupational exposures and isotopic analysis of food, environmental and blood samples to identify the sources and routes of lead exposure in the population. Findings presented here alert about the health risks that affect the indigenous peoples of the Amazon, but are relevant for millions of people from low an middle income countries (LMICs) that inhabit rural areas close to conventional oil reservoirs (O'Callaghan-Gordo et al., 2016) and are at risk of similar environmental and occupational exposures.

CRediT authorship contribution statement

Cristina O'Callaghan-Gordo: Conceptualization, Data curation, Formal analysis, Investigation, Supervision, Writing - original draft. **Jaime Rosales:** Methodology, Formal analysis, Investigation, Writing - review & editing. **Pilar Lizárraga:** Project administration, Data curation, Investigation, Writing - review & editing. **Frederica Barclay:** Conceptualization, Investigation, Writing - review & editing. **Tami Okamoto:** Conceptualization, Investigation, Writing - review & editing. **Diana M. Papoulias:** Conceptualization, Investigation, Writing - review & editing. **Ana Espinosa:** Data curation, Methodology, Formal analysis. **Martí Orta-Martinez:** Methodology, Investigation, Writing - review & editing. **Manolis Kogevinas:** Conceptualization, Investigation, Writing - review & editing. **John Astete:** Conceptualization, Resources, Investigation, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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