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Blood lead levels in a representative sample of the Spanish adult population: The BIOAMBIENT.ES project

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ABSTRACT

This paper provides the first baseline information on a national scale regarding lead exposure in the Spanish adult population. Blood lead levels were measured in a representative sample of the Spanish working population (1880 subjects aged 18–65 years) in order to help establish reference levels, follow temporal trends, identify high-exposure groups and to enable comparisons with other countries. All participants completed an epidemiological questionnaire including gender, age, occupational sector, geographic area, and dietary and lifestyle information. We found that the geometric mean of blood lead levels in the study population was 24.0 μg/L (95% CI: 23.0–25.1 μg/L), with women having significantly lower levels than men, 19.5 μg/L (18.5–20.5 μg/L) compared to 28.3 μg/L (26.7–30.0 μg/L), respectively. Mean blood lead levels were higher in elder groups in both genders. Women of a childbearing age had blood levels of 18.0 μg/L (GM). Reference values (95%) for lead in blood in the studied population was 56.80 μg/L, with −64.00 μg/L, 44.80 μg/L and 36.00 μg/L for man, women and women of childbearing age, respectively. Workers from the service sector had lower blood lead levels than those from the construction, agricultural and industry sectors. Small, although significant, geographical differences had been found.

In an European comparison, the Spanish population studied herein had lead levels similar to populations in countries such as France and Belgium, and slightly lower levels than Italian, Czech, German or UK populations.

Introduction

Human exposure to environmental lead has been extensively studied for more than 50 years, but it still remains a topic of great interest and continues to be a public health concern as new scientific evidence on the adverse effects at even very low exposure levels appears. About 90% of the total body burden of lead is present in bones and teeth. As 95% of the lead in blood is bound to the erythrocytes, this is considered to be the best indicator of individual exposure (Vahter et al., 1982). Bone stores of lead are released when there is an increased demand for calcium (pregnancy and breast-feeding) and other conditions like as pre and post-monopausal periods in women, and become the main contributor to blood lead levels (Gulson et al., 2003).

Although lead has many different commercial applications, its main uses are as an additive in paints and gasoline, and as construction material in batteries and lead pipes. Hobbies or working environments can also be a source of lead exposure, for example when stripping lead-based paint from furniture or wood work. Canned foods were once a significant source of lead as a result of the poor-quality solder joints in cans, which allowed highly acidic foods, such as tomatoes, to leach lead from the can. Contamination of drinking water with lead primarily occurs due to the use of lead solder joints or old fixtures and, of course, the use of lead pipes. Lead concentrations in the environment, and therefore atmospheric exposure by air inhalation, decreased with the ban on leaded gasoline. Afterwards, and apart from tobacco exposure, ingestion of lead became the main environmental exposure route for the general population, including soil particles and dust ingestion, drinking water from leaded pipes or ingestion of contaminated

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food (WHO, 2010). The association between decreasing blood lead levels in the general population and compliance with ban on lead in gasoline has been used as the archetypal example of how human biomonitoring (HBM) surveillance can be used as tool for environmental and health implementation policies (Hwang et al., 2004; Pino et al., 2004; Pirkle et al., 1994; Smolders et al., 2010; Stromberg et al., 2008; von Storch et al., 2003).

A large number of papers concerning lead levels in differents population groups, and their health-related effects, have been published, thereby providing information on which recommendations for limit/safety levels can be based (Den Hond et al., 2002; Schwartz et al., 1990; Schwartz, 1994; Woolf, 1990).

There is an increasing amount of evidence showing that lead can have effects on human health at much lower levels than initially suspected. The main target appears to be the developing nervous system during childhood (Ma et al., 1997), and this has increased research interests on the chronic effects of low level exposure. The doubts about 100 μg/L as safe level established by WHO in 1992 and the German Human Biomonitoring Commision (GHBMC) in 1996 (Ewers et al., 1999), prompted both the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and the GHBMC to reevaluate lead in 2010. As a result, the JECFA withdrew its provisional tolerable weekly intake guideline value (25 μg/kg) on the grounds that it was insufficient to protect against IQ loss and systolic blood pressure increase, and the GHBM commission suspended the HBM I[2] levels for children and women of childbearing age (Wilhelm et al., 2010). A new recommendation on safe blood lead values has not been established yet, as there appears to be no threshold level below which lead can be considered safe for developing human brain (ATSDR, 2005). In response to the evidences, the U.S. Centers for Disease Control and Prevention (CDC) reduced to 50 μg/L the blood lead level at which intervention is recommended in children (Betts, 2012). In addition, the International Agency for Research on Cancer (IARC) and the National Toxicology Program (NTP) consider lead and inorganic lead compounds to be probably carcinogenic to humans (group 2A) and a reasonably anticipated human carcinogen, respectively. Early symptoms of lead exposure may include: persistent fatigue, irritability, loss of appetite, stomach discomfort, reduced attention span or insomnia. In adults, lead poisoning can cause poor muscle coordination, nerve damage, increased blood pressure, hearing and vision impairment, reproductive problems and retarded foetal development even at relatively low exposure levels (Aguilera et al., 2008; Fewtrell et al., 2003; Sole et al., 1998; Zubero et al., 2010). These findings mean that the surveillance of lead levels in the population remains a high priority.

The measurement of lead blood levels is the most reliable tool for establishing the degree of exposure to all sources of contamination associated with an individual's environment and lifestyle. In this respect, HBM, which is defined as the measure of a chemical, or its metabolites or reactive products, in human matrices, constitutes a powerful tool for health protection and implementation of environmental legislation (Angerer et al., 2007). Thus, HBM programs allow reference values for a given population to be established and vulnerable groups and hot-spots to be identified. Lead is one of the priority heavy metals usually included in the many HBM surveys undertaken in different worldwide countries (Berglund et al., 1991; Cerna et al., 2007; Kim and Lee, 2011; Muntner et al., 2003; Vupputuri et al., 2003). Despite this, information on background exposures and reference levels of lead for the general, non-exposed population is available for only a few European countries (Apostoli et al., 2002; Cerna et al., 2012; Falq et al., 2011; Jakubowski et al., 1996; Schroijen et al., 2008; White and Sabbioni, 1998).

In Spain, blood lead levels have been studied in different regional surveys, small-scale studies in selected population groups or in occupational studies (Aguilera et al., 2010; Sole et al., 1998; Zubero et al., 2010). A national HBM study representative of the Spanish population has never been undertaken. In 2007, following recommendations from the European Union Environment and Health Action Plan (COM(2004) 416 final), and the National Implementation Plan for the Stockholm Convention (BOE number 151, June 24, 2004), the Spanish Ministry for Food, Agriculture and the Environment funded an HBM program to enhance current understanding of the distribution of priority environmental pollutants in Spain in order to establish reference levels for some heavy metals, persistent organic pollutants (POPs) and cotinine within the Spanish population. The ministerial action was planned in two stages. The first of these (2007–2010) included the BIOAMBIENT.ES project (Esteban et al., 2012; Perez-Gomez et al., 2013). The aim of this project was to study exposure to some heavy metals, cotinine and POPs in a representative sample of the Spanish workforce by providing an estimation of the presence of these toxicants in different matrices (blood, urine and hair).

This paper presents the first data regarding blood lead levels in the Spanish population on a national scale both as a whole, as well as broken down by gender, age, economic sector, geographical region and seasonal sampling period.

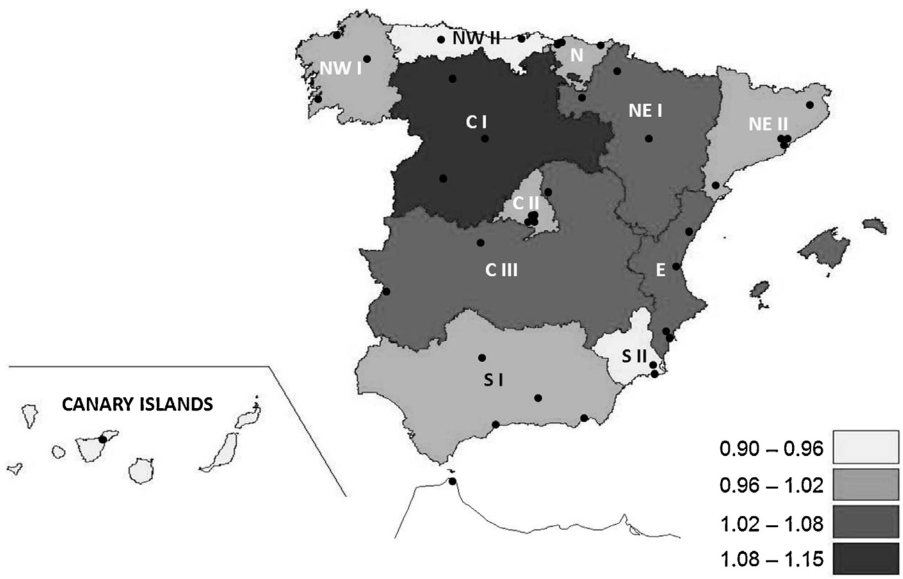
Materials and methods

Study population

Blood lead measures were one of the biomarkers included in BIOAMBIENT.ES project, a nation-wide cross-sectional epidemiological study. Participants were recruited amongst workers aged 16 years or older who had been resident in Spain for five years or more and attended the health facilities of the prevention services at *Corporacion Mutua* between March 2009 and July 2010 for their annual medical check-up. The design and field work have already been described in detail elsewhere (Esteban et al., 2012; Perez-Gomez et al., 2013).

Briefly, the inclusion criteria were age ≥ 16 years and having lived in Spain for five years or more. Volunteers were selected according to a stratified cluster sampling procedure that covered all geographical areas, genders and occupational sectors in order to obtain a representative sample of the Spanish workforce. In order to guarantee the nationwide representativeness of the sample, 12 geographical areas were defined by combining neighbouring regions (Map 1) to obtain the following strata: Northwest I (Galicia), Northwest II (Asturias, Cantabria), North (Basque Country), Northeast I (Navarre, La Rioja, Aragon), Northeast II (Catalonia), Central I (Castilla y León), Central II (Madrid), Central III (Castilla-La Mancha, Extremadura), East (Valencia, Balearic Islands), South I (Andalusia, Ceuta), South II (Murcia) and Canary Islands. A total of 38 Health Prevention Centers were selected from the above-mentioned geographical strata following a proportional distribution according to data from the Spanish Active Population Survey 2007 (Instituto Nacional de Estadística (INE), 2007). Sampling was undertaken in four quarterly recruitment periods (January–March, April–June, July–September, and October–December), thereby ensuring a good dispersion of the seasonal sample. In addition, in order to stratify by economical sector, two groups were defined on the basis of the National Classification of Economic Activities for 2009 (Instituto Nacional de Estadística (INE), 2009a). The first of these groups included "Service activities" and the second "Agriculture, Industry & Construction".

[2] HBM I defined as the concentration of a substance in human biological material below which no adverse health effects are expected.



Map 1. Geographical regions designed for BIOAMBIENT.ES, with sampling points indicated in black: NW I (Galicia), NW II (Asturias, Cantabria), N (Basque Country), NE I (Navarre, La Rioja, Aragon), NE II (Catalonia), C I (Castilla y León), C II (Madrid), C III (Castilla-La Mancha, Extremadura), E (Valencia, Balearic Islands), S I (Andalusia, Ceuta), S II (Murcia) and Canary Islands. The grey scale shows the ratios of the geometric mean of blood lead levels in different geographical regions versus the national geometric mean (=1).

BIOAMBIENT.ES recruited a sample of 1936 subjects aged between 18 and 65 years of both genders. 44 subject were rejected due to exclusion criteria of years of residence in Spain or lack of stratification variables in questionnaires, and 12 were discarded by insufficient volume. A total of 1880 blood samples fulfilled the criteria for inclusion in the data analysis (Esteban et al., 2012; Perez-Gomez et al., 2013).

All participants completed a self-administrated epidemiological questionnaire containing specific questions regarding risk factors related to the pollutants studied as well as basic demographic variables (diet, lifestyle and some medical determinants). A specific clinical form was also designed to be filled in by the doctors responsible for performing the health exams of the workers included, in order to gather basic clinical information for all participants in a uniform manner. In addition, participants were asked to grant access to their clinical records in order to have both the complete results of the occupational health exam as well as to obtain the data needed to assess possible occupational exposures.

Ethical approval

This study was approved by both the *Comité Etico Científico* and the legal department of IBERMUTUAMUR. Participants were asked for their written informed consent. Their collaboration was voluntary and altruistic; only a small token pen drive was given to the participants. The study was performed in accordance with legal/ethical principles and regulations concerning research involving individual information and biological samples, including organic law 15/1999 on Personal Data protection and its Regulations, Law 41/2002, on Autonomy of Patients and rights and obligations relating to health information and documentation, as well as General Health Law 14/1986. Since the study involved the collection of blood samples, the principles of the Declaration of Helsinki and those contained in the UNESCO Universal Declaration on the Human Genome and Human Rights have been observed.

An information leaflet including the individual lead results for each participant was designed in order to provide the volunteers with feedback about the research. Additionally, BIOAMBIENT.ES established a committee to study each result that could be considered as anomalous on a case-by-case in order to confirm the results and take any appropriate measures.

Blood sample collection, processing and storage

For each subject who provided consent, 5–6 mL blood samples were collected in Vacuette® tubes treated with sodium heparin for trace element analysis. Prior to sample collection, studies to determine the background contamination in the sampling material were conducted (Cañas et al., 2010). Following collection, the samples were kept in a portable isothermal bag with ice packs (at about 4–8 °C) and sent to the lab. Once in the laboratory, they were aliquoted and stored at −20 °C in polypropylene tubes previously washed with 10% HNO_3 until analysis (Esteban et al., 2012).

Chemical analysis

Blood lead determinations were performed in clean-room facilities with ISO 6 air quality, differential pressures and controlled temperatures suitable for the analysis of trace element concentrations.

A PerkinElmer ELAN DRC-e ICPMS was used. The instrument was calibrated for between 0 and 250 μg/L of lead using matrix-matched calibration standards, and a calibration curve was used to obtain quantitative blood lead concentrations (m/z 208).

Blood samples were mixed gently for homogenization then diluted 1:50 in an aqueous solution containing 10 μg/L of internal rhodium standard, triton X-100 (0.05%, v/v), EDTA (0.05%, v/v), propanol (10%, v/v) and tetramethylammonium hydroxide (TMAH) 1% (v/v). Seronorm™ Trace Elements Whole Blood (Sero, Norway) was used for internal quality control (IQ) every ten blood samples. If the IQ result was not within the limits certified, the ten previous and ten subsequent samples were repeated. Participation in the three rounds per year of Quebec Multi-element External Quality Assessment Scheme (QMEQAS) was used as an external quality control. The interlaboratory blood lead results were satisfactory in all rounds.

The limit of quantification (LOQ) was 0.10 μg/L.

Statistical analysis

The complex design of the study was taken into account in all analyses. The poststratified weights were calculated taking into account occupational sector, gender and geographic region from the Spanish Active Population census of 2009 (Instituto Nacional de Estadística (INE), 2009b). Weights were applied to all estimates presented herein. For the analyses, the following socio-demographic factors have been included: gender; age group (≤29 years; 30–39 years; 40–49 years; ≥50 years and women of childbearing age: 18–45 years); geographic area and sampling period (January–March, April–June, July–September, and October–December). In addition to those already mentioned we also evaluated the possible role of educational level (primary education or less; secondary education; university or equivalent) as well as smoking status (non smoker, ex-smoker and smoker).

Blood lead levels were log-transformed and the arithmetic mean, geometric mean, confidence intervals (95%) and percentiles (10, 25, 50, 75, 90 and 95) calculated by gender, age group, geographical region, economical sector and sampling period.

In a second step, multivariate models fitted with log-transformed blood lead concentrations were used to assess the possible association between blood lead levels and the previously defined epidemiological variables. In addition possible differences in lead levels by education level and cigarette smoking were tested.

Statistical analyses were conducted using the svy commands in STATA (version.11, StataCorp, College Station, TX, USA), a software package that incorporates the sample weights and adjusts the analyses to take into account the complex sample design of the survey. $p < 0.05$ were established as the level for statistic significance.

Results

Blood lead concentrations for all study participants by socio-demographic variables are listed in Table 1.

The geometric mean (GM) for blood lead concentrations in the Spanish workforce was 24.03 μg/L (95% CI: 22.98–25.12). All samples were above the limit of quantification (0.10 μg/L) and ranged between 2.60 and 190 μg/L. Seventeen volunteers had blood lead concentrations higher than 100 μg/L (fourteen men and three women), and six exceeded 150 μg/L. The 95th percentile for blood lead concentration was 56.80 μg/L.

Men showed 38% higher blood lead levels (GM: 28.33 μg/L; 95% CI: 26.76–29.99) than women (GM: 19.47 μg/L; 95% CI: 18.55–20.45) and the geometric mean for women of childbearing age (18–45 years old) was 18.04 μg/L (95th percentile: 36.00 μg/L).

Older volunteers had higher lead levels than younger ones. Blood lead concentrations were found to gradually increase with age group, with the value for the older group (≥50 years; 33.89 μg/L; 95% CI: 31.51–36.44) being almost twice that for the youngest one (≤29 years; 19.05 μg/L; 95% CI: 17.89–20.29). Differences were also found as regards occupational sector, with volunteers from the service sector having lower blood lead concentrations than those from other sectors (agriculture, industry and construction; GM 22.49 and 28.40 μg/L, respectively). According to sampling period, those participants recruited in summer months had the lowest levels, although differences among trimesters were small.

Multivariate analysis (Table 2) confirmed that gender, age and occupational sector have a significant influence on blood lead levels. Results showed that, taking all the other factors into account, lead GM in men was a 38% higher than in women. In addition, lead GM increased a 21% by age group. Also participants

Table 1
Geometric means with 95% confidence intervals and selected percentiles (P10, P25, P50, P75, P90 and P95) of blood lead concentrations (μg/L) in BIOAMBIENT.ES participants, presented by gender, age, occupational sector, geographic area and sampling period.

	N	Geometric Mean (CI 95%)	P10	P25	P50	P75	P90	P95
Total								
	1880	24.03 (22.98–25.12)	13.00	16.80	22.90	33.90	47.40	56.80
Gender*								
Male	962	28.33 (26.76–29.99)	15.60	19.60	27.30	39.30	52.60	64.00
Female	918	19.47 (18.55–20.45)	11.20	14.30	18.70	25.00	35.30	44.80
Females of childbearing age (18–45 years)	700	18.04 (17.18–18.94)	11.10	13.70	17.60	22.70	31.90	36.00
Age (years)*								
≤29	372	19.05 (17.89–20.29)	11.20	14.30	18.40	24.90	34.80	46.30
30–39	764	21.92 (20.87–23.03)	12.70	16.20	21.10	28.70	40.10	47.90
40–49	466	27.32 (25.72–29.01)	14.80	19.10	25.90	38.40	52.80	59.10
≥50	278	33.89 (31.51–36.44)	18.20	24.10	33.60	47.90	58.60	72.10
Occupational sector*								
Services	1225	22.49 (21.41–23.63)	12.20	16.10	21.60	31.40	43.30	52.60
Other sectors	655	28.40 (26.39–30.57)	15.00	19.20	27.30	40.50	55.40	68.70
Geographic area								
Galicia	147	24.10 (21.90–26.52)	12.90	16.50	22.50	33.70	45.50	54.70
Asturias, Cantabria	99	22.35 (18.18–27.47)	11.20	15.90	22.50	30.00	44.90	53.00
Basque country	149	23.55 (17.70–31.32)	12.00	15.70	22.60	34.20	55.60	57.10
Navarre, La Rioja, Aragón	145	25.27 (22.96–27.81)	13.10	17.10	25.45	37.60	49.70	58.00
Catalonia	247	23.85 (22.68–25.08)	13.70	17.30	23.10	34.10	44.90	54.20
Castilla y León	153	27.81 (24.39–31.72)	15.90	19.50	27.10	38.00	52.40	59.20
Madrid	199	23.77 (21.81–25.91)	12.40	16.80	22.90	34.40	47.00	52.80
Castilla-La Mancha, Extremadura	150	24.73 (20.68–29.58)	13.70	17.40	22.20	34.90	54.30	64.40
Valencia, Balearic Islands	205	24.91 (21.17–29.32)	12.80	17.70	23.90	35.50	50.40	63.00
Andalusia, Ceuta	239	23.31 (19.61–27.48)	13.10	16.00	21.80	31.50	44.80	72.80
Murcia	97	21.17 (19.81–22.63)	11.90	14.90	20.00	28.90	41.40	50.90
Canary Islands	50	22.93 (18.58–28.31)	12.50	15.50	21.70	27.40	48.70	83.30
Sampling period								
January–March	349	25.07 (22.56–27.86)	13.70	17.50	23.90	36.80	47.70	55.00
April–June	562	23.22 (21.21–25.41)	12.70	16.60	22.20	32.30	43.50	55.00
July–August	373	22.34 (20.53–24.30)	11.80	15.60	22.30	32.15	47.10	55.60
September–December	561	25.28 (23.31–27.43)	13.80	17.70	23.80	34.90	47.70	58.10

* $p < 0.05$; CI: confidence interval.

Table 2
BIOAMBIENT.ES participants: Association between lead levels and socio-demographic variables and sampling trimester. Multivariate lineal regression models. Statistically significant differences $p < 0.05$.

	Exp(b)[**]	(CI 95%)		p-Value
Gender	1.38	1.31	1.45	0.000
Age[a]	1.21	1.18	1.24	0.000
Occupational sector	1.12	1.05	1.20	0.001
Geographical region[a]				
Galicia	1.04	0.98	1.10	0.170
Asturias, Cantabria	0.91	0.84	0.99	0.024
Basque country	1.03	0.81	1.31	0.794
Navarre, La Rioja, Aragón	1.04	0.97	1.12	0.228
Catalonia	1.02	0.94	1.11	0.617
Castilla y León	1.15	0.97	1.38	0.106
Madrid	0.97	0.92	1.03	0.265
Castilla-La Mancha, Extremadura	1.00	0.92	1.08	0.922
Valencia, Balearic Islands	1.04	0.90	1.21	0.593
Andalusia, Ceuta	0.98	0.88	1.10	0.714
Murcia	0.94	0.89	1.00	0.052
Canary Islands	0.90	0.67	1.21	0.459
Sampling period[a]				
January–March	1.05	0.98	1.14	0.175
April–June	0.96	0.91	1.02	0.185
July–August	0.95	0.88	1.01	0.108
September–December	1.04	0.99	1.11	0.137

[a] Reference: geometric mean for all Bioambient participants.
[**] Adjusted by sex, age, economic sector, geographical area and sampling trimester.
Gender: reference category "female".
Occupational sector: reference category "service sector".

working in agriculture, industry and construction presented significantly higher levels that those employed in service sector. Differences by sampling period were not statistically significant.

The regional variation in human blood lead levels was small. Although the lowest blood lead levels were found for the Murcia region (GM: 21.17 μg/L) and the highest levels for Castilla y León (GM: 27.81 μg/L). Multivariate analysis showed that only in Asturias-Cantabria (in the North coast of Spain) lead GM was significantly lower than the national (BIOAMBIENT.ES) geometric mean. The ratios between the geometric means for different geographical regions and the national mean are shown in Map 1. Again, Castilla y León presents the highest ratio, Murcia and Asturias-Cantabria the lowest. In addition to those already mentioned we also evaluated the possible role of educational level as well as smoking status. No differences were found in lead levels by educational level or smoking status (data not shown).

Discussion

The aim of our study was to present blood lead levels for an important segment of the Spanish general population on a national scale for the first time. This baseline information will contribute to setting Spanish reference values for adults up to 65 years of age. The study design omitted the assessment of adults not actively included in the labour market (unemployed). At the time of the study the unemployment rate was 7.95% (Instituto Nacional de Estadística (INE), 2009b). Since we opted for efficiency, we assumed the limitation that this part of the population would be out of our scope.

The Spanish population studied herein exhibits similar blood lead levels (GM: 24.0 μg/L) to the adult populations in other neighbouring countries such as France (GM: 25.7 μg/L) (Falq et al., 2011), with the comparison by age group being very similar (see Table 3), and Belgium (adult group between 50 and 65 years old; Table 4) (Schroijen et al., 2008). However, the Spanish values are slightly lower than those reported for Italian (Apostoli et al., 2002), Czech (Batariova et al., 2006; Cerna et al., 2012), Poland (Jakubowski et al., 1996), German (Becker et al., 2002) or UK populations (White and Sabbioni, 1998) (see Table 4). Probably due to the fact that the

Table 3
Blood lead levels (μg/L) in different age groups in Spain and France (Falq et al., 2011).

Age group	Geometric mean (CI 95%)	
	Spain	France
19–39	20.9 (19.9–22.0)	18.7 (17.8–19.6)
40–59	29.3 (28.0–30.7)	29.3 (28.2–30.5)
>60	34.7 (27.7–43.3)	39.3 (37.7–41.1)

sampling date of these latter studies is prior to ours. The decreasing use of leaded gasoline and, to a lesser extent, the control of industrial emissions in industrialized countries over the last few decades have contributed to a widespread decrease in blood lead concentrations in the general population (Bono et al., 1995; Hwang et al., 2004; Pino et al., 2004; von Storch et al., 2003; von Storch and Hagner, 2004). Unfortunately, as this is the first study performed at a national level, we cannot demonstrate a reduction in blood lead levels in the Spanish population on a country basis. However, a comparison of the current Spanish values with the data published in 1998 from a population in the metropolitan area of Barcelona (45.8 μg/L) shows the expected decrease (Sole et al., 1998). In a similar study, Schuhmacher et al. corroborated the impact of a reduction in lead levels in gasoline on blood levels in the Spanish region of Tarragona between 1990 and 1995 (Schuhmacher et al., 1996a), and Llop et al. verified the reduction of lead in Spanish children during the last 20 years in several Spanish regions (Llop et al., 2013).

Spanish blood lead levels are higher than those for adults in the USA (GM: 13.8 μg/L) (CDC Centers for Disease Control and Prevention, 2012), Canada (GM: 15.0 μg/L) (Wong and Lye, 2008) or Korea (GM: 19.1 μg/L; see Table 4) (Lee et al., 2012). However, although the samples in these latter three countries were collected during the same time as the samples in our study (2007–2009), the use of leaded gasoline in the USA and Canada had been decreasing since the 1980s. In this respect, the EPA reported that blood lead levels declined by 37% between 1976 and 1980 due to a 50% decrease in the use of leaded gasoline over that period. The initial phase-out of lead from gasoline was completed by 1986, and leaded gasoline was unavailable for the whole country from 1991. The ban on leaded

Table 4
Blood lead levels obtained in HBM programs in different countries. Geometric means, 95th percentile (μg/L), age of study population, sampling years and references are presented.

Country		N	Blood lead geometric mean (μg/L)			P95	Sampling year	Age population
			Total	Male	Female			
Spain								
		1880	24.0	28.3	19.5	56.3	2009	18–65
France								
	(Falq et al., 2011)	1949	25.7	30.0	22.1	73.0	2006–2007	18–74
Italy								
	(Apostoli et al., 2002)	1164	MA:38.5[a]	MA:45.1[a]	MA:30.6[a]	86.0	2000	18–64
Germany								
	GerES II (Schulz et al., 2007)	3966	45.5	55.0	37.7	105.0	1990–1992	25–69
	GerES III (Becker et al., 2002)	4646	30.7	35.8	26.3	71.0	1998	18–69
Czech Republic								
	(Batariova et al., 2006)	1188	33.0	37.0	26.0	72.0	2001–2003	18–58
	(Cerna et al., 2012)	3245	–	Median:40[b]	Median:28[b]	–	2001–2003	18–58
	(Cerna et al., 2012)	1227	–	Median:23[b]	Median:14[b]	–	2005–2009	18–58
Poland								
	(Jakubowski et al., 1996)	567	–	42.5–76.8	23.8–48.3		1992–1994	Adults
United Kingdom								
	(White and Sabbioni, 1998)	214	39.4	–	–	–		Adults
Belgium								
	(Schroijen et al., 2008)	1679	21.7	–	–	47.0[c]	2002–2006	14–15
	(Schroijen et al., 2008)	1586	39.6	–	–	–	2002–2006	50–65
Korea								
	KorSEPI (Kim and Lee, 2011)	1997	26.1	29.8	22.9	56.1	2005	≥20
	KorSEPIII (Lee et al., 2012)	5087	19.1	22.7	16.1	42.3	2008	≥20
United States								
	CDC 2012	4207	17.5	20.1	13.7	52.0	1999–2000	≥20
	CDC 2012	4525	15.2	16.9	12.2	43.0	2003–2004	≥20
	CDC 2012	5364	13.8	14.7	11.1	39.0	2007–2008	≥20
Canada								
	(Wong and Lye, 2008)	3464	15.0	–	–	41.1	2007–2009	20–79

[a] MA: Arithmetic mean.
[b] Median.
[c] 90 percentile.

gasoline came into force in Spain in 2001. A comparison of our data with those provided by NHANES for the period 1999–2000 (GM: 17.5 μg/L) shows that the differences are smaller, thus confirming that the main contribution to lead exposure in the general population comes from leaded gasoline. Leaded paint is also an important source of lead in the population. Sale of paints containing lead was banned in USA in 1978 and in Spain in 1992.

The geometric mean of the blood lead levels in our study was higher in men (28.3 μg/L) than in women (19.5 μg/L) in agreement to findings of other authors and also in the same range of 20–30% higher (Christensen, 1995; Clark et al., 2007; Kristiansen et al., 1997; Skerfving et al., 1993). Two factors are considered to explain such gender-related differences: higher lead exposure due to male lifestyles, occupation, smoking and alcohol consumption (Navas-Acien et al., 2004; Vahter et al., 2007) and the higher blood haematocrit levels in men (given that lead is bound to erythrocytes) (Vahter et al., 1982, 2002).

Our value for the 95th total population percentile (56.8 μg/L) is far below the initial maximum recommended blood lead value and EPA action level (100 μg/L). Seventeen volunteers (less than 1% of population) had blood lead levels above 100 μg/L. The 95th percentiles for men (64.0 μg/L) and women (44.8 μg/L) are also lower than 95th percentiles for the German population (90 μg/L for men and 70 μg/L for women) (Schulz et al., 2012).

In agreement with previous studies (Apostoli et al., 2002; Batariova et al., 2006; Clark et al., 2007), blood lead levels were found to be positively correlated with age, thereby once again demonstrating the cumulative nature of lead exposure and the importance of reducing environmental exposure as much as possible. Wittmers et al. (1988) reported that bone lead levels increased linearly with age but declined after an age of 40–55 years, especially in women, due to higher calcium demand and concomitant higher rates of accumulated lead release (Wittmers et al., 1988). The skeleton contributes between 40% and 70% of the lead in blood (Smith et al., 1996), and different studies have provided evidence of significant bone release of lead during periods of accelerated bone turnover and mineral loss, such as osteoporosis, thyroid and parathyroid hormone imbalances or menopause (Goldman et al., 1994; Gulson et al., 2003; Osterloh and Clark, 1993; Silbergeld et al., 1988). As a result, the similarity between age groups is considered to be a key factor when comparing values from different HBM programs.

As children and foetuses are the most vulnerable to lead exposure, the most important population group from a public-health point of view is women of a reproductive age (18–45 years old). There is good evidence that maternal lead exposure during pregnancy can result in foetal lead exposure since lead is able to cross the placental barrier, with maternal blood lead levels correlating with umbilical cord blood levels (Guan et al., 2010; Rudge et al., 2009; Schuhmacher et al., 1996b). Such exposure can adversely affect child health, increasing the risk of developmental disorders, reducing IQ and producing behavioural problems (Bowers and Beck, 2006). As there is no apparent safe threshold below which adverse effects do not occur, the US-CDC recommends follow-up activities at blood lead levels ≥50 μg/L in pregnant women (Ettinger et al., 2010). The geometric mean for 18 to 45-year-old Spanish women (18.0 μg/L) and her 95th percentile (36 μg/L) was far below the recommended CDC action level, and only ten women of childbearing age had lead levels above 50 μg/L. The fact that no threshold can be established for lead exposure means that the aim of decreasing lead exposure as much as possible remains an important public health objective. Maternal biomonitoring of toxic metal levels may help to reduce prenatal exposure and therefore the potential for future adverse developmental effects.

In BIOAMBIENT.ES blood lead levels in agricultural, construction or industry sector workers are significantly higher than those from the services sector. The most plausible explanation is the longer periods spent outdoors by workers in the former sectors, which would increase their exposure to lead in the air or soil compared to that of service sector workers. Indeed, the relationship between lead in air and blood is well known (Bierkens et al., 2011b; Smolders et al., 2010; Stromberg et al., 2008). Other factor to consider could be the use of devices or working materials using in agricultural, construction or industry sector that might contain traces of lead.

Bioambient participants were mainly born in Spain (94.36%), and only 163 (8.7% of the total) reported having resided in their present address for less than 5 years. These data suggest that our population residence is quite stable and that our data may reflect fairly well environmental exposure on the areas of recruitment. No differences were found as regards blood lead concentration and sampling period, thus indicating no seasonal variation of exposure in the studied population. In contrast, some differences were found depending on the geographical region in which the volunteers lived. Thus, the maximum difference in the crude data was 7 μg/L between the geometric mean blood lead levels of inhabitants from the Murcia region (south-east) and those living in Castilla y León (central-north). Water lead concentrations are known to be the lowest in the south-eastern region of Spain (<0.015 μg/L) as these areas have low levels in the subsoil and alkaline groundwaters, in which the solubility of lead is low (FOREGS, 2012). This could contribute to the low blood lead levels found in participants from the Murcia region. However, after correcting for influencing factors in the multivariate analyses, only volunteers from the Asturias-Cantabria region showed statistically significantly lower levels than the national geographic mean. The highest lead concentrations in both top and subsoil are found in north-western Spain (>30 mg/kg), although lead in stream water is not correlated to those in soil (FOREGS, 2012). Lead in soil can contribute to lead in air, with settled dust and vegetation due to atmospheric deposition also being possible exposure sources. Indeed, exposure to settled house dust has been identified as an important contributor to lead exposure (Bierkens et al., 2011a). Since lead emission sources have largely been reduced in the last years, there is a need to survey levels of lead in the soil, diet and drinking water as these causal exposure sources have a longer lead half-life than air. In light of this, an extended environmental surveillance system is recommended in order to identify, quantify and further reduce remaining sources of lead exposure.

Although exposure to lead has decreased, lead remains a public health problem as several sectors of the general population are still at risk. In light of recent scientific data regarding lead neurotoxicity at low concentrations, and taking into account its possible carcinogenicity, the health-related limits for all population groups are currently being suspended (Wilhelm et al., 2010). In 2007, the Scientific Committee on Neurotoxicology and Psychophysiology and the Scientific Committee on the Toxicology of Metals of the International Commission on Occupational Health convened the Declaration of Brescia on prevention of this metal's neurotoxicity and recommended that the blood lead action level for children and females of a childbearing age should be reduced to 50 μg/L (Landrigan et al., 2007). Increasing scientific evidence has since shown the association between lead exposure and adverse health outcomes for different population groups (Apostolou et al., 2012). As a result, further preventive measures to reduce lead exposure, especially for the most vulnerable populations such as women of a childbearing age and young children, are required due to the impact of lead on the developing brain and transfer of lead from the mother to the foetus.

As HBM surveys can help to maintain a strict control of exposure of the population to hazardous chemicals, lead should remain on the list of chemicals to be monitored in order to support public health policies.

In summary, this paper presents the first values for blood lead levels in the adult Spanish working population at a national level. Of special interest in terms of public health are blood lead levels in women of a childbearing age presented here. Future studies in this respect should therefore target the subgroups not included in this survey in order to gain a more complete overview of population lead exposure.

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