

This is the peer reviewed version of the following article:

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

Cañas AI, Cervantes-Amat M, Esteban M, Ruiz-Moraga M, Pérez-Gómez B, Mayor J, Castaño A; BIOAMBIENT.ES.

Int J Hyg Environ Health. 2014 Apr-May;217(4-5):452-9

which has been published in final form at https://doi.org/10.1016/j.ijheh.2013.09.001



| 1- 2- | BLOOD LEAD LEVELS IN A REPRESENTATIVE SAMPLE OF $\bf 1$ THE SPANISH ADULT POPULATION: THE BIOAMBIENT.ES PROJECT |
|----------|---|
| 3- | |
| 4 | Ana I. Cañasa, Marta CervantesAmatb,e, Marta Estebana, Montserrat RuizMoragac, Beatriz Perez |
| 5 | Gómez _{b,e} , Juan Mayor _d , Bioambient.es₁ and Argelia Castaño₃₂ |
| 6 | |
| 7 | aEnvironmental Toxicology, National Centre for Environmental Health (CNSA), Instituto de Salud |
| 8 | Carlos III, 28220, Madrid, Spain |
| 9 | ♭National Centre for Epidemiology, Instituto de Salud Carlos III, 28039, Madrid, Spain |
| 10 | dbermutuamur, Ramirez de Arellano 4, 28043, Madrid, Spain |
| 11 | dMutualia, Alda Recalde 24, 48009, Bilbao, Spain |
| 12 | eCIBER in Epidemiology and Public Health (CIBERESP), Spain |
| | |
| | nbient.es: Aleixandre,J.L.; Aragonés,N.; Bartolomé,M.; Calvo,E.; Cortés,M.V.; Cutanda,F.; |
| | ,O.; Jiménez,J.A.; LopezAbente,G.; LopezHerranz,A.; Méndez,C.F.; Molina,M.A.; |
| Navarr | o,C.; Pastor,R.; Pollán,M.; Román,J. and Sánchez,J. |

2 Corresponding author. To whom correspondence should be addressed

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 μ g/L (95%CI: 23.0---25.1 μ g/L), with women having significantly lower levels than men, 19.5 μ g/L (18.5---20.5 μ g/L) compared to 28.3 μ g/L (26.7---30.0 μ g/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 μ g/L. 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.

Keywords: Human biomonitoring (HBM), ICP---MS, lead exposure, blood, Spanish population.

1. 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 postmonopausal 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 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).

43

44

45

46

47

48

49

50

51

52

53

54

55

56

57

58

59

60

61

62

63

64

65

66

67

68

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

67

chronic effects of low level exposure. The doubts about 100 $\mu g/L$ as safe level established by WHO

68

in 1992 and the German Human Biomonitoring Commision (GHBMC) in 1996 (Ewers et al., 1999),

69

prompted both the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and the GHBMC

70

to reevaluate lead in 2010. As a result, the JECFA withdrew its provisional tolerable weekly intake

71

guideline value (25 $\mu g/kg)$ on the grounds that it was insufficient to protect against IQ loss and

 $72\,\mathrm{_3}\,\mathrm{systolic}$ blood pressure increase, and the GHBM commission suspended the HBM I levels for

73

children and women of childbearing age (Wilhelm et al., 2010). A new recommendation on safe

74

blood lead values has not been established yet, as there appears to be no threshold level below

75

which lead can be considered safe for developing human brain (ATSDR, 2005). In response to the

76

evidences, the U.S. Centers for Disease Control and Prevention (CDC) reduced to 50 $\mu\text{g/L}$ the

77

blood lead level at which intervention is recommended in children (Betts, 2012). In addition, the $78\,$

International Agency for Research on Cancer (IARC) and the National Toxicology Program (NTP)

79

consider lead and inorganic lead compounds to be probably carcinogenic to humans (group 2A)

80

and a reasonably anticipated human carcinogen, respectively. Early symptoms of lead exposure

81

may include: persistent fatigue, irritability, loss of appetite, stomach discomfort, reduced

82

attention span or insomnia. In adults, lead poisoning can cause poor muscle coordination, nerve

83

damage, increased blood pressure, hearing and vision impairment, reproductive problems and

84

retarded fetal development even at relatively low exposure levels (Aguilera *et al.*, 2008; Fewtrell

85

et al., 2003; Sole et al., 1998; Zubero et al., 2010). These findings mean that the surveillance of

86 lead levels in the population remains a high priority.

87

The measurement of lead blood levels is the most reliable tool for establishing the degree of

88

exposure to all sources of contamination associated with ĂŶ ŝŶĚŝ|ŝĚZĂůE environment and

89 lifestyle. In this respect, HBM, which is defined as the measure of a chemical, or its metabolites or

90

reactive products, in human matrices, constitutes a powerful tool for health protection and

91

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

93

be identified. Lead is one of the priority heavy metals usually included in the many HBM surveys

94

undertaken in different worldwide countries (Berglund $et\ al.,\ 1991;$ Cerna $et\ al.,\ 2007;$ Kim $et\ al.,\ 95$

2011; Muntner *et al.*, 2003; Vupputuri *et al.*, 2003). Despite this, information on background

³ HBM I defined as the concentration of a substance in human biological material below which no adverse health effects are expected.

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.

2. 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).

dŝĞĨůШłŚĞŝŶĐůZEŝŽŶĐđŝłĞdŝÅ∥ĞđĞĂŐĞшбсIJĞĂđEĂŶĚhaving 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 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 ŝŶĐůZĚĞĚ^Ğd|ŝĐĞ ĂĐłŝ|ŝłŝĞEĂŶĚłŚĞEĞĐŽŶĚAgriculture, ŶĚZEłdLJØŽŶEłdZĐłŝŽŶ 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

126

127

128

129

130

131

132

133

134

135

136

137

138

139

140

141

142

143

144

145

146

147

148

149

150

151

152

153

154

155

- 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.
- 158 Ethical approval
- 159 This study was approved by both the Comité Etico Científico and the legal department
- 160 of IBERMUTUAMUR. Participants were asked for their written informed consent. Their
- 161 collaboration was voluntary and altruistic; only a small token pen drive was given to the
- 162 participants. The study was performed in accordance with legal/ethical principles and
- 163 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
- 167 collection of blood samples, the principles of the Declaration of Helsinki and those
- 168 contained in the UNESCO Universal Declaration on the Human Genome and Human Rights
- have been observed.
- 170 An information leaflet including the individual lead results for each participant was designed
- 171 in order to provide the volunteers with feedback about the research. Additionally,
- 172 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.
- 175 Blood sample collection, processing and storage
- 176 For each subject who provided consent, 5---6 mL blood samples were collected in Vacuette®
- 177 tubes treated with sodium heparin for trace element analysis. Prior to sample collection,
- 178 studies to determine the background contamination in the sampling material were conducted
- 179 (Cañas et al., 2010). Following collection, the samples were kept in a portable isothermal bag
- 180 with ice packs (at about 4---8 °C) and sent to the lab. Once in the laboratory, they were
- 181 aliquoted and stored at ---20 °C in polypropylene tubes previously washed with 10% HNO $_3$
- until analysis (Esteban et al., 2012). Chemical analysis
- 183 Blood lead determinations were performed in clean---room facilities with ISO 6 air
- 184 quality, differential pressures and controlled temperatures suitable for the analysis of
- 185 trace element concentrations.

- 186 A PerkinElmer ELAN DRC---e ICPMS was used. The instrument was calibrated for between 0
- and 250 $\mu g/L$ of lead using matrix---matched calibration standards, and a calibration
- 188 curve was used to obtain quantitative blood lead concentrations (m/z 208).
- 189 Blood samples were mixed gently for homogenization then diluted 1:50 in an aqueous solution
- 190 containing 10 μg/L of internal rhodium standard, triton X---100 (0.05% v/v), EDTA (0.05%
- 191 v/v), propanol (10% v/v) and tetramethylammonium hydroxide (TMAH) 1% (v/v).
- 192 Seronorm[™] Trace Elements Whole Blood (Sero, Norway) was used for internal quality control
- 193 (IQ) every ten blood samples. If the IQ result was not within the limits certified, the ten
- 194 previous and ten subsequent samples were repeated. Participation in the three rounds
- 195 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.
- 198 The limit of quantification (LOQ) was 0.10 μ g/L.
- 199 Statistical analysis
- 200 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
- 202 from the Spanish Active Population census of 2009 (Instituto Nacional de Estadística (INE),
- 203 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;
- 205 40---49 years; >=50 years & women of childbearing age: 18---45 years); geographic area
- and sampling period (January' March, April'June, July'September, and October'December).
- 207 In addition to those already mentioned we also evaluated the possible role of educational
- 208 level (primary education or less; secondary education; university or equivalent) as well as
- smoking status (non smoker, ex---smoker & smoker).
- 210 Blood lead levels were log---transformed and the arithmetic mean, geometric mean,
- 211 confidence intervals (95%) and percentiles (10, 25, 50, 75, 90 and 95) calculated by
- gender, age group, geographical region, economical sector and sampling period.
- 213 In a second step, multivariate models fitted with log---transformed blood lead concentrations
- 214 were used to assess the possible association between blood lead levels and the
- 215 previously defined epidemiological variables. In addition possible differences in lead levels by
- 216 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.

221

222

3. 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 μ g/L (95% CI: 22.98---25.12). All samples were above the limit of quantification
- 227 (0.10 μg/L) and ranged between 2.60 and 190 μg/L. Seventeen volunteers had blood lead
- 228 concentrations higher than 100 μg/L (fourteen men and three women), and six exceeded 150
- μ g/L. The 95th percentile for blood lead concentration was 56.80 μ g/L.
- 230 Men showed 38% higher blood lead levels (GM: 28.33 μ g/L; 95% CI: 26.76---29.99) than
- women (GM: 19.47 μ g/L; 95% CI: 18.55---20.45) and the geometric mean for women of
- childbearing age (18---45 years old) was 18.04 μ g/L (95th percentile: 36.00 μ g/L).
- 233 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 (t50 years;
- 235 33.89 μg/L; 95% CI: 31.51---36.44) being almost twice that for tŚĞLJŽZŶŐĞEtŽŶĞ; чτε years;
- 236 19.05 μg/L; 95% CI: 17.89---20.29). Differences were also found as regards occupational sector,
- 237 with volunteers from the service sector having lower blood lead concentrations than
- 238 those from other sectors (agriculture, industry and construction; GM 22.49 and 28.40
- 239 µg/L, respectively). According to sampling period, those participants recruited in summer
- 240 months had the lowest levels, although differences among trimesters were small.
- 241 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
- 243 into account, lead GM in men was a 38% higher than in women. In addition, lead GM
- 244 increased a 21% by age group. Also participants working in agriculture, industry and
- 245 construction presented significantly higher levels that those employed in service sector.
- 246 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 μ g/L) and the highest levels for Castilla y León (GM: 27.81 μ g/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).

4. 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: 25.7µg/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 et al., 1998) (see Table 4). Probably due to the fact that the 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 contributedted 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 et al., 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: $13.8 \,\mu g/L$) (CDC Centers for Disease Control and Prevention, 2012), Canada (GM: $15.0 \,\mu g/L$) (Wong S.L. *et al.*, 2008) or Korea (GM: $19.1 \,\mu g/L$; 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 gasoline came into force in Spain in 2001. A comparison of our data with those provided by NHANES for the period 1999---2000 (GM: $17.5 \,\mu g/L$) 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 μ g/L) than in women (19.5 μ g/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; Vahter *et al.*, 2002).

Our value for the 95th total population percentile (56.8 μ g/L) is far below the initial maximum recommended blood lead value and EPA action level (100 μ g/L). Seventeen volunteers (less

than 1% of population) had blood lead levels above 100 μ g/L. The 95th percentiles for men (64.0 μ g/L) and women (44.8 μ g/L) are also lower than 95th percentiles for the German population (90 μ g/L for men and 70 μ g/L for women) (Schulz *et al.*, 2012).

313

314

315

316

317

318

319

320

321

322

323

324

325

326

327

328

329

330

331

332

333

334

335

336

337

338

339

340

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 (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 *et al.*, 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 et al., 2006). As there is no apparent safe threshold below which adverse effects do not US---CDC recommends follow--occur, the ZĐĂĐŀŝ|ŝŀŝĞEĂŀďůŽŽĔůĞĂĚůĞ|Ğů£шоб 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.

343

344

345

346

347

348

349

350

351

352

353

354

355

356

357

358

359

360

361

362

363

364

365

366

367

368

369

370

371

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 Pg/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 (>30mg/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.

Acknowledgments

This work was funded by the Spanish Ministry of Agriculture, Food and Environment (MAGRAMA) and The Institute of Health Carlos III (ISCIII) agreement, SEG 1251/07. The

- $402\,$ authors would like to thank nurses and doctors from Corporacion Mutua, $\,$ BIOAMBIENT.ES $\,$
- 403 volunteers and M.
- 404 Rodríguez, S. González, M. Rosado and S. Gómez for their collaboration.

Reference List

408

- 409 Aguilera, I., Daponte, A., Gil, F., Hernandez, A.F., Godoy, P., Pla, A., Ramos, J.L., 2008.
- Biomonitoring of urinary metals in a population living in the vicinity of industrial sources:
- 411 A comparison with the general population of Andalusia, Spain. Sci. Total Environ. 407 (1),
- 412 669--678.
- 413 Aguilera, I., Daponte, A., Gil, F., Hernandez, A.F., Godoy, P., Pla, A., Ramos, J.L., 2010. Urinary
- levels of arsenic and heavy metals in children and adolescents living in the industrialised
- area of Ria of Huelva (SW Spain). Environ. Int. 36 (6), 563---569.
- 416 Angerer, J., Ewers, U., Wilhelm, M., 2007. Human biomonitoring: State of the art. Int.
- 417 J. Hyg. Environ. Health 210 (3---4), 201---228.
- 418 Apostoli, P., Baj, A., Bavazzano, P., Ganzi, A., Neri, G., Ronchi, A., Soleo, L., Di Lorenzo, L.,
- Spinelli, P., Valente, T., Minoia, C., 2002. Blood lead reference values: the results of
- an Italian polycentric study. Sci. Total Environ. 287 (1---2), 1---11.
- 421 Apostolou, A., Garcia---Esquinas, E., Fadrowski, J.J., McLain, P., Weaver, V.M., Navas---
- 422 Acien, A.,
- 423 2012. Secondhand Tobacco Smoke: A Source of Lead Exposure in US Children and
- 424 Adolescents. Am. J. Public Health 102 (4), 714---722.
- 425 ATSDR, 2005. Draft toxicological profile for lead. http://www.atsdr.cdc.gov/toxprofiles/tp13.pdf.
- 426 Batariova, A., Spevackova, V., Benes, B., Cejchanova, M., Smid, J., Cerna, M., 2006. Blood
- 427 and urine levels of Pb, Cd and Hg in the general population of the Czech Republic and
- 428 proposed reference values. Int. J. Hyg. Environ. Health 209 (4), 359---366.
- 429 Becker, K., Kaus, S., Krause, C., Lepom, P., Schulz, C., Seiwert, M., Seifert, B., 2002.
- 430 German Environmental Survey 1998 (GerES III): environmental pollutants in blood of
- the German population. Int. J. Hyg. Environ. Health 205 (4), 297---308.
- 432 Berglund, M., Vahter, M., Slorach, S., 1991. Determination of Human Exposure to Lead
- 433 and Cadmium --- A Who/Unep Pilot---Study. Chemical Speciation and Bioavailability, Vol 3,
- Nos 3---4, December 1991: Proceedings of the Symposium on the Bioavailability and Dietary
- 435 Exposure of
- 436 Lead 69---72.
- 437 ĞHE<^†f6f†hÐĚĂŀĞE'ZŝĚĞůŝŶĞEĨŽđŚŝůĚđĞŶE>ĞĂĚdžĐŽEZđĞEnviron. Health Persp. 120
- 438 (7), a268.
- 439 Bierkens, J., Holderbeke, M., Cornelis, C., Torfs, R. 2011a. Exposure Through Soil and
- Dust Ingestion Dealing with Contaminated Sites. (ed. F. A. Swartjes), pp. 261---286:
- 441 Springer Netherlands.

- Bierkens, J., Smolders, R., Van Holderbeke, M., Cornelis, C., 2011b. Predicting blood lead
- levels from current and past environmental data in Europe. Sci. Total Environ. 409 (23),
- 444 5101---5110. Bono, R., Pignata, C., Scursatone, E., Rovere, R., Natale, P., Gilli, G.,
- 445 1995. Updating about reductions of air and blood lead concentrations in Turin, Italy,
- following reductions in the lead content of gasoline. Environ. Res. 70 (1), 30---34.
- 447 Bowers, T.S., Beck, B.D., 2006. What is the meaning of non---linear dose---response
- relationships between blood lead concentrations and IQ? Neurotoxicology 27 (4), 520---
- 449 524.
- 450 Cañas, A., Castaño, A., Esteban, M., Navarro, C., Jimenez---Guerrero, J.A., 2010. Selection
- of sampling material for the analysis of heavy metals in blood for human biomonitoring
- 452 studies. Toxicol. Lett. 196S (S44).
- 453 CDC Centers for Disease Control and Prevention, 2012. Fourth National Report on
- 454 Human Exposure to Environmental Chemicals, Updated Tables, September 2012.
- 455 http://www.cdc.gov/exposurereport/.
- 456 Cerna, M., Krskova, A., Cejchanova, M., Spevackova, V., 2012. Human biomonitoring in the
- 457 Czech Republic: An overview. Int. J. Hyg. Environ. Health 215 (2), 109---119.
- 458 Cerna, M., Spevackova, V., Batariova, A., Smid, J., Cejchanova, M., Ocadlikova, D., Bavorova,
- 459 H., Benes, B., Kubinova, R., 2007. Human biomonitoring system in the Czech Republic. Int.
- 460 J. Hyg. Environ. Health 210 (3---4), 495---499.
- 461 Christensen, J.M., 1995. Human Exposure to Toxic Metals --- Factors Influencing Interpretation
- of Biomonitoring Results. Sci. Total Environ. 166 (1---3), 89---135.
- Clark, N.A., Teschke, K., Rideout, K., Copes, R., 2007. Trace element levels in adults from the
- west coast of Canada and associations with age, gender, diet, activities, and levels of
- other trace elements. Chemosphere 70 (1), 155---164.
- 466 Den Hond, E., Nawrot, T., Staessen, J.A., 2002. The relationship between blood pressure
- and blood lead in NHANES III. J. Hum. Hypertens. 16 (8), 563---568.
- 468 Esteban, M., Ruiz---Moraga, M., Perez---Gomez, B. and Castaño, A. 2012. Aspectos prácticos
- de la fase preanalítica del estudio de biovigilancia BIOAMBIENT.ES. Gac. Sanit. 27 (1), 77-
- 470 --80.
- 471 Ettinger, A.S. et al., 2010. Guidelines for the identification and manegement of lead exposure
- in pregnant and lactating women. www.cdc.gov/nceh/lead.
- 473 Ewers, U., Krause, C., Schulz, C., Wilhelm, M., 1999. Reference values and human
- 474 biological monitoring values for environmental toxins --- Report on the work and
- 475 recommendations of the
- 476 Commission on Human Biological Monitoring of the German Federal Environmental Agency.
- 477 Int. Arch. Occ. Env. Health 72 (4), 255---260.

- 478 Falq, G., Zeghnoun, A., Pascal, M., Vernay, M., Le Strat, Y., Garnier, R., Olichon, D., Bretin,
- 479 P.,
- 480 Castetbon, K., Frery, N., 2011. Blood lead levels in the adult population living in France
- the French Nutrition and Health Survey (ENNS 2006---2007). Environ. Int. 37 (3), 565---
- 482 571.
- 483 Fewtrell, L., Kaus, S., Pruss---Ustun, A., 2003. Lead. Assessing the environmental burden of
- desease at national and local levels. Geneva: World Health Organization FOREGS, 2012.
- Geochemical Baseline Mapping. http://weppi.gtk.fi/publ/foregsatlas/index.php.
- 486 Goldman, R.H., White, R., Kales, S.N., Hu, H., 1994. Lead---Poisoning from Mobilization
- of Bone Stores During Thyrotoxicosis. Am. J. Ind. Med. 25 (3), 417---424.
- 488 Guan, H., Piao, F.Y., Li, X.W., Li, Q.J., Xu, L., Yokoyama, K., 2010. Maternal and Fetal Exposure
- to Four Carcinogenic Environmental Metals. Biomed. Environ. Sci. 23 (6), 458---465.
- 490 Gulson, B.L., Mizon, K.J., Korsch, M.J., Palmer, J.M., Donnelly, J.B., 2003. Mobilization of lead
- from human bone tissue during pregnancy and lactation --- a summary of long---term
- 492 research. Sci. Total Environ. 303 (1---2), 79---104.
- 493 Hwang, Y.H., Ko, Y., Chiang, C.D., Hsu, S.P., Lee, Y.H., Yu, C.H., Chiou, C.H., Wang, J.D.,
- 494 Chuang, H.Y., 2004. Transition of cord blood lead level, 1985---2002, in the Taipei
- area and its determinants after the cease of leaded gasoline use. Environ. Res. 96 (3),
- 496 274---282.
- 497 Instituto Nacional de Estadística (INE), 2007. Spanish Active Population Survey 2007.
- 498 www.ine.es.
- 499 Instituto Nacional de Estadística (INE), 2009a. Clasificación Nacional de Actividades Económicas
- 500 2009 (CNAE---2009). www.ine.es.
- 501 Instituto Nacional de Estadística (INE), 2009b. Spanish Active Population Survey 2009.
- www.ine.es.
- Jakubowski, M., TrzcinkaOchocka, M., Razniewska, G., Christensen, J.M., Starek, A., 1996.
- Blood lead in the general population in Poland. Int. Arch. Occ. Env. Health 68 (3), 193---
- 505 198.
- 506 Kim, N.S., Lee, B.K., 2011. National estimates of blood lead, cadmium, and mercury levels in
- the Korean general adult population. Int. Arch. Occ. Env. Health 84 (1), 53---63.
- Kristiansen, J., Christensen, J.M., Iversen, B.S., Sabbioni, E., 1997. Toxic trace element reference
- levels in blood and urine: influence of gender and lifestyle factors. Sci. Total Environ. 204
- 510 (2),
- 511 147---160.
- Landrigan, P., Nordberg, M., Lucchin, R., Nordberg, G., Grandjean, P., Lregren, A., Alessio, L.,
- 513 2007. The declaration of Brescia on prevention of the neurotoxicity of metals. Am. J. Ind.
- 514 Med. 50

- 515 (10), 709---711.
- 516 Lee, J.W., Lee, C.K., Moon, C.S., Choi, I.J., Lee, K.J., Yi, S.M., Jang, B.K., Yoon, B.j., Kim, D.S.,
- 517 Peak,
- 518 D., Sul, D., Oh, E., Im, H., Kang, H.S., Kim, J., Lee, J.T., Kim, K., Park, K.L., Ahn, R., Park,
- 519 S.H., Kim, S.C., Park, C.H., Lee, J.H., 2012. Korea National Survey for Environmental
- 520 Pollutants in the
- Human Body 2008: Heavy metals in the blood or urine of the Korean population. Int. J.
- 522 Hyg. Environ. Health 215 (4), 449---457.
- 523 Llop, S., Porta, M., Martinez, M.D., Aguinagalde, X., Fernández, M., Fernández---Somoano,
- A., Casas, M., Vrijheid, M., Ayerdi, M., Tardón, A., Ballester, F., 2013. Estudio de la
- evolución de la exposición a plomo en la población infantil española en los últimos 20
- años. ¿Un ejemplo no reconocido de "salud en todas las políticas"?. Gac. Sanit. 27 (2),149-
- 527 --155. Ma, Y., Ye, G., Tang, S., 1997. Influence of prenatal exposure to low levels of lead
- on the neuro--behavioral development of neonates. Zhonghua yi xue za zhi 77 (10), 774-
- 529 --775.
- Muntner, P., He, J., Vupputuri, S., Coresh, J., Batuman, V., 2003. Blood lead and chronic
- kidney disease in the general United States population: Results from NHANES III. Kidney
- 532 Int. 63 (3), 1044---1050.
- Navas---Acien, A., Selvin, E., Sharrett, A.R., Calderon---Aranda, E., Silbergeld, E., Guallar,
- 534 E., 2004. Lead, cadmium, smoking, and increased risk of peripheral arterial disease.
- 535 Circulation 109 (25), 3196---3201.
- 536 Osterloh, J.D., Clark, O.H., 1993. Effects of Hyperparathyroidism on Blood Lead Concentrations
- 537 in Man. Environ. Res. 62 (1), 1---6.
- Perez---Gomez, B., Pastor---Barriuso, R., Cervantes---Amat, M., Esteban, M., Ruiz---Moraga,
- 539 M., Aragones, N., Pollan, M., Navarro, C., Calvo, E., Roman, J., Lopez---Abente, G., Castano,
- A., 2013. BIOAMBIENT.ES study protocol: rationale and design of a cross---sectional human
- biomonitoring survey in Spain. Environ. Sci. Pollut. Res. 20 (2), 1193---1202.
- 542 Pino, P., Walter, T., Oyarzun, M.J., Burden, M.J., Lozoff, B., 2004. Rapid drop in infant blood
- lead levels during the transition to unleaded gasoline use in Santiago, Chile. Arch. Environ.
- 544 Health
- 545 59 (4), 182---187.
- 546 Pirkle J.L., Brody D.J., Gunter E.W., Kramer R.A., Paschal D.C., Flegal K.M., Matte T.D., 1994.
- The decline in blood lead levels in the United States. The National Health and
- Nutrition Examination Surveys (NHANES). J. Am. Med. Assoc. 272 (4), 284---291.
- 549 Rudge, C.V., Rollin, H.B., Nogueira, C.M., Thomassen, Y., Rudge, M.C., Odland, J.O.,
- 550 2009. The placenta as a barrier for toxic and essential elements in paired maternal
- and cord blood samples of South African delivering women. J. Environ. Monit. 11 (7),
- 552 1322---1330.

- 553 Schroijen, C., Baeyens, W., Schoeters, G., Den Hond, E., Koppen, G., Bruckers, L., Nelen, V.,
- De Mieroop, E.V., Bilau, M., Covaci, A., Keune, H., Loots, I., Kleinjans, J., Dhooge,
- W., Van Larebeke, N., 2008. Internal exposure to pollutants measured in blood and urine
- of Flemish adolescents in function of area of residence. Chemosphere 71 (7), 1317---1325.
- 557 Schuhmacher, M., Belles, M., Rico, A., Domingo, J.L., Corbella, J., 1996a. Impact of reduction
- of lead in gasoline on the blood and hair lead levels in the population of Tarragona
- Province, Spain, 1990---1995. Sci. Total Environ. 184 (3), 203---209.
- 560 Schuhmacher, M., Hernandez, M., Domingo, J.L., FernandezBallart, J.D., Llobet, J.M., Corbella,
- J., 1996b. A longitudinal study of lead mobilization during pregnancy: Concentrations in
- maternal and umbilical cord blood. Trace Elem. Electroly. 13 (4), 177---181.
- 563 Schulz, C., Wilhelm, M., Heudorf, U., Kolossa---Gehring, M., 2012. Reprint of Update of
- the reference and HBM values derived by the German Human Biomonitoring Commission.
- 565 Int. J. Hyg. Environ. Health 215 (2), 150---158.
- Schwartz, J., 1994. Low---Level Lead---Exposure and Childrens Iq --- A Metaanalysis and Search
- 567 for A
- 568 Threshold. Environ. Res. 65 (1), 42---55.
- 569 Schwartz, J., Landrigan, P.J., Baker, E.L., Orenstein, W.A., Vonlindern, I.H., 1990. Lead---
- Induced Anemia --- Dose---Response Relationships and Evidence for A Threshold. Am. J.
- 571 Public Health 80
- 572 (2), 165---168.
- 573 Silbergeld, E.K., Schwartz, J., Mahaffey, K., 1988. Lead and osteoporosis: Mobilization of lead
- from bone in postmenopausal women. Environ. Res. 47 (1), 79---94.
- 575 Skerfving, S., Nilsson, U., Schutz, A., Gerhardsson, L., 1993. Biological Monitoring of
- 576 Inorganic Lead. Scand. J. Work Env. Health 19 (59---64).
- 577 Smith, D.R., Osterloh, J.D., Flegal, A.R., 1996. Use of endogenous, stable lead isotopes
- to determine release of lead from the skeleton. Environ. Health Persp. 104 (1), 60---66.
- 579 Smolders, R., Alimonti, A., Cerna, M., Den Hond, E., Kristiansen, J., Palkovicova, L.,
- Ranft, U., Selden, A.I., Telisman, S., Schoeters, G., 2010. Availability and comparability
- of human biomonitoring data across Europe: A case---study on blood---lead levels. Sci.
- 582 Total Environ. 408 (6), 1437---1445.
- 583 Sole, E., Ballabriga, A., Dominguez, C., 1998. Lead exposure in the general population
- of the Metropolitan Area of Barcelona: Blood levels and related factors. Sci. Total Environ.
- 585 224 (1---3), 19---27.
- 586 Stromberg, U., Lundh, T., Skerfving, S., 2008. Yearly measurements of blood lead in
- 587 Swedish children since 1978: The declining trend continues in the petrol---lead---free period
- 588 1995---2007. Environ. Res. 107 (3), 332---335.

- Vahter, M., Akesson, A., Liden, C., Ceccatelli, S., Berglund, M., 2007. Gender differences in the disposition and toxicity of metals. Environ. Res. 104 (1), 85---95.
- Vahter, M., Berglund, M., Akesson, A., Liden, C., 2002. Metals and women's health. Environ.
- 592 Res. 88 (3), 145---155.
- Vahter, M., Friberg, L., Lind, B., 1982. Assessment of Exposure to Lead and Cadmium Through
- Biological Monitoring. J. Am. Coll. Toxicol. 1 (3), 117---117.
- 595 von Storch, H., Costa---Cabral, M., Hagner, C., Feser, F., Pacyna, J., Pacyna, E., Kolb, S., 2003.
- Four decades of gasoline lead emissions and control policies in Europe: a retrospective
- 597 assessment. Sci. Total Environ. 311 (1---3), 151---176.
- 598 von Storch, H., Hagner, C., 2004. Controlling lead concentrations in human blood by regulating
- the use of lead in gasoline. Ambio 33 (3), 126---132.
- Vupputuri, S., He, J., Muntner, P., Bazzano, L.A., Whelton, P.K., Batuman, V., 2003. Blood
- lead level is associated with elevated blood pressure in blacks. Hypertension 41 (3), 463-
- 602 --468.
- 603 White, M.A., Sabbioni, E., 1998. Trace element reference values in tissues from inhabitants
- of the European Union. X. A study of 13 elements in blood and urine of a United Kingdom
- 605 population. Sci. Total Environ. 216 (3), 253---270.
- 606 WHO, World Health Organization, 2010. Exposure to lead: a major public health concern.
- 607 Copenhague: World Health Organization.
- 608 Wilhelm, M., Heinzow, B., Angerer, J., Schulz, C., 2010. Reassessment of critical lead effects
- by the German Human Biomonitoring Commission results in suspension of the human
- 610 biomonitoring values (HBM I and HBM II) for lead in blood of children and adults. Int. J.
- 611 Hyg. Environ. Health 213 (4), 265---269.
- 612 Wittmers, L.E., Wallgren, J., Alich, A., Aufderheide, A.C., Rapp, G., 1988. Lead in Bone
- 613 .4.
- Distribution of Lead in the Human Skeleton. Arch. Environ. Health 43 (6), 381---391.
- 615 Wong S.L., Lye E.J.D., 2008. Lead, mercury and cadmium levels in Canadians. Health Rep. 19
- 616 (4).
- Woolf, D.A., 1990. Etiology of Acute Lead Encephalopathy in Omani Infants. J. Trop. Pediatrics
- 618 36
- 619 (6), 328---330.
- Zubero, M.B., Aurrekoetxea, J.J., Ibarluzea, J.M., Arenaza, M.J., Rodriguez, C., Saenz, J.R., 2010.
- Heavy metal levels (Pb, Cd, Cr and Hg) in the adult general population near an urban
- solid waste incinerator. Sci. Total Environ. 408 (20), 4468---4474.

624

Table 1

| | N | Geometric Mean (CI 95%) | P10 | P25 | P50 | P75 | P90 | P95 |
|--|------|----------------------------|-------|-------|-------|-------|-------|-------|
| Total | | | | | | | | |
| | 1880 | 1880 24.03 (22.9825.12) 1 | | 16.80 | 22.90 | 33.90 | 47.40 | 56.80 |
| Gender * | | | | | | | | |
| Male | 962 | 28.33 (26.7629.99) | 15.60 | 19.60 | 27.30 | 39.30 | 52.60 | 64.00 |
| Female | 918 | 19.47 (18.5520.45) | 11.20 | 14.30 | 18.70 | 25.00 | 35.30 | 44.80 |
| Females of childbearing age (1845 years) | | | | | | | | |
| | 700 | 18.04 (17.1818.94) | 11.10 | 13.70 | 17.60 | 22.70 | 31.90 | 36.00 |
| Age (years) * | | | | | | | | |
| чтє | 372 | 19.05 (17.8920.29) | 11.20 | 14.30 | 18.40 | 24.90 | 34.80 | 46.30 |
| 3039 | 764 | 21.92 (20.8723.03) | 12.70 | 16.20 | 21.10 | 28.70 | 40.10 | 47.90 |
| 4049 | 466 | 27.32 (25.7229.01) | 14.80 | 19.10 | 25.90 | 38.40 | 52.80 | 59.10 |
| шбе | 278 | 33.89 (31.5136.44) | 18.20 | 24.10 | 33.60 | 47.90 | 58.60 | 72.10 |
| Occupational sector * | | | | | | | | |
| Services | 1225 | 22.49 (21.4123.63) | 12.20 | 16.10 | 21.60 | 31.40 | 43.30 | 52.60 |
| Other sectors | 655 | 28.40 (26.3930.57) | 15.00 | 19.20 | 27.30 | 40.50 | 55.40 | 68.70 |
| Geographic area | | | | | | | | |
| Galicia | 147 | 24.10 (21.9026.52) | 12.90 | 16.50 | 22.50 | 33.70 | 45.50 | 54.70 |
| Asturias, Cantabria | 99 | 22.35 (18.1827.47) | 11.20 | 15.90 | 22.50 | 30.00 | 44.90 | 53.00 |
| Basque Country | 149 | 23.55 (17.7031.32) | 12.00 | 15.70 | 22.60 | 34.20 | 55.60 | 57.10 |
| Navarre, La Rioja, Aragón | 145 | 25.27 (22.9627.81) | 13.10 | 17.10 | 25.45 | 37.60 | 49.70 | 58.00 |
| Catalonia | 247 | 23.85 (22.6825.08) | 13.70 | 17.30 | 23.10 | 34.10 | 44.90 | 54.20 |
| Castilla y León | 153 | 27.81 (24.3931.72) | 15.90 | 19.50 | 27.10 | 38.00 | 52.40 | 59.20 |
| Madrid | 199 | 23.77 (21.8125.91) | 12.40 | 16.80 | 22.90 | 34.40 | 47.00 | 52.80 |
| CastillaLa Mancha, Extremadura | 150 | 24.73 (20.6829.58) | 13.70 | 17.40 | 22.20 | 34.90 | 54.30 | 64.40 |
| Valencia, Balearic Islands | 205 | 24.91 (21.1729.32) | 12.80 | 17.70 | 23.90 | 35.50 | 50.40 | 63.00 |

Table 2.docx

| Andalusia, Ceuta | 239 | 23.31 (19.6127.48) 13.1 | 16.00 | 21.80 | 31.50 | 44.80 | 72.80 |
|-------------------|-----|-------------------------|-------|-------|-------|-------|-------|
| Murcia | 97 | 21.17 (19.8122.63) 11.9 | 14.90 | 20.00 | 28.90 | 41.40 | 50.90 |
| Canary Islands | 50 | 22.93 (18.5828.31) 12.5 | 15.50 | 21.70 | 27.40 | 48.70 | 83.30 |
| Sampling period | | | | | | | |
| JanuaryMarch | 349 | 25.07 (22.5627.86) 13.7 | 17.50 | 23.90 | 36.80 | 47.70 | 55.00 |
| AprilJune | 562 | 23.22 (21.2125.41) 12.7 | 16.60 | 22.20 | 32.30 | 43.50 | 55.00 |
| JulyAugust | 373 | 22.34 (20.5324.30) 11.8 | 15.60 | 22.30 | 32.15 | 47.10 | 55.60 |
| SeptemberDecember | 561 | 25.28 (23.3127.43) 13.8 | 17.70 | 23.80 | 34.90 | 47.70 | 58.10 |

^{*} p < 0.05; CI: confidence interval

| | exp(b)** | (CI 95%) | | Pvalue |
|---|----------|----------|------|--------|
| 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 |
| CastillaLa 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 |
| AprilJune | 0,96 | 0,91 | 1,02 | 0,185 |
| JulyAugust | 0,95 | 0,88 | 1,01 | 0,108 |

 September---December
 1,04
 0,99
 1,11
 0,137

GenderdőiĞdőŶÐĞĐĂŀĞŐŽdLJīĞŵĂůĞ_

Occupational sector: reference category service sector

^a Reference: geometric mean for all Bioambient participants

| | Age group Geometric Mean (C | | | | | |
|------|-----------------------------|-----------------|--|--|--|--|
| | Spain | France | | | | |
| | | | | | | |
| 1939 | 20.9 (19.922.0) | 18.7 (17.819.6) | | | | |
| 4059 | 29.3 (28.030.7) | 29.3 (28.230.5) | | | | |
| > 60 | 34.7 (27.743.3) | 39.3 (37.741.1) | | | | |
| | | | | | | |

 $[\]ensuremath{^{**}}$ Adjusted by sex, age, economic sector, geographical area and sampling trimester.

Table 4.docx

| Country | | N | Blood lead | | | | Sampling year | Age population |
|---------------|----------------------------------|------|------------|----------------|----------------|------------|------------------|----------------|
| | Geometric Mean (μg/L) | | | | yeui | population | | |
| | | | Total | Male | Female | | | |
| Spain | | | | | | | | |
| | | 1880 | 24.0 | 28.3 | 19.5 | 56.3 | 2009 | 1865 |
| France | | | | | | | | |
| | (Falq et al., 2011) | 1949 | 25.7 | 30.0 | 22.1 | 73.0 | 20062007 | 1874 |
| Italy | | | | | | | | |
| | (Apostoli et al., 2002) | 1164 | a | a | a | 86.0 | 2000 | 1864 |
| | | | MA:38.5 | MA:45.1 | MA:30.6 | | | |
| Germany | | | | | | | | |
| | GerES II (Schulz et al, 2007) | 3966 | 45.5 | 55.0 | 37.7 | 105.0 | 19901992 | 2569 |
| | GerES III(Becker et al., 2002) | 4646 | 30.7 | 35.8 | 26.3 | 71.0 | 1998 | 1869 |
| Czech Repu | ublic | | | | | | | |
| | (Batariova et al., 2006) | 1188 | 33.0 | 37.0 | 26.0 | 72.0 | 20012003 | 1858 |
| | (Cerna et al, 2012) | 3245 | | b | b | | 20012003 | 1858 |
| | | | | Median:40 | Median:28 | | | |
| | (Cerna <i>et al.,</i> 2012) | 1227 | | b Median:23 | b Median:14 | | 20052009 | 1858 |
| Poland | | | | | | | | |
| | (Jakubowski <i>et al,</i> 1996) | 567 | | 42.576.8 | 23.848.3 | | 19921994 | adults |
| United King | gdom | | | | | | | |
| | (White & Sabbioni, 1998) | 214 | 39.4 | | | | | adults |
| Belgium | | | | | | | | |
| | (Schroijen et al., 2008) | 1679 | 21.7 | | | с | 20022006 | 1415 |
| | | | | | | 47 | | |
| | (Schroijen <i>et al.</i> , 2008) | 1586 | 39.6 | | | | 20022006 | 5065 |
| Korea | | | | | | | | |
| | KorSEPI (Kim & 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 | 19992000 | >=20 |
| | CDC 2012 | 4525 | 15.2 | 16.9 | 12.2 | 43.0 | 20032004 | >=20 |

Table 5.docx

| | CDC 2012 | 5364 | 13.8 | 14.7 | 11.1 | 39.0 | 20072008 | >=20 |
|--------|--------------------|------|------|------|------|------|----------|------|
| Canada | | | | | | | | |
| | (Wong et al, 2008) | 3464 | 15.0 | | | 41.1 | 20072009 | 2079 |

a

MA: Arithmetic mean

b

Median

c 90 Percentile

Map 1.jpg

Click here to download high resolution image

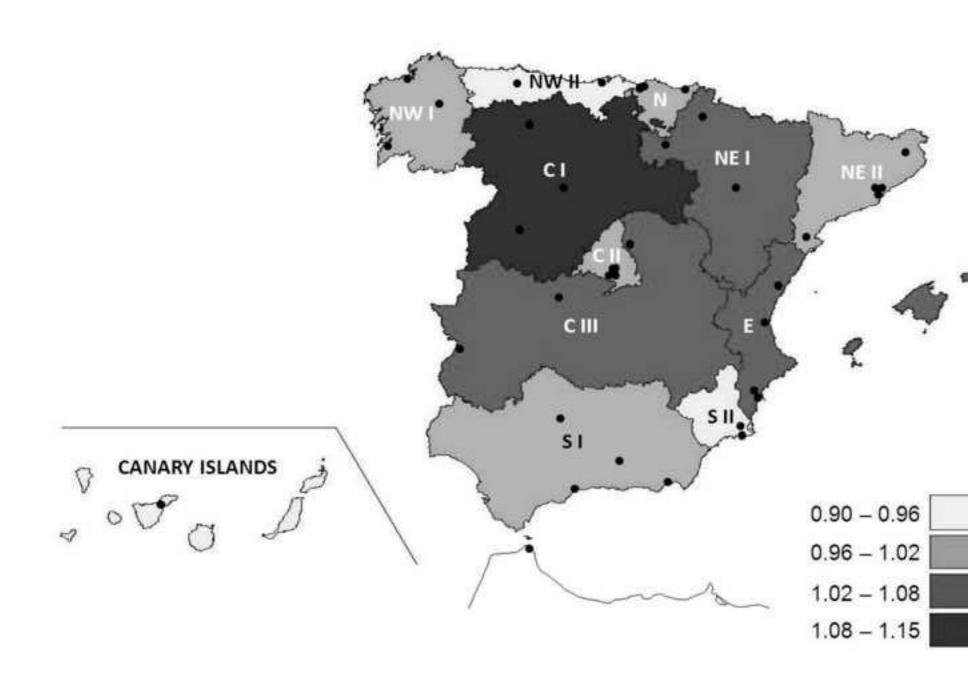




Table and figures legends

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).

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

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.

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

Table 4. Blood lead levels obtained in HBM programs in different countries. Geometric means,

95th percentile ($\mu g/L$), age of study population, sampling years and references are presented.

