



Association between heavy metals and metalloids in topsoil and mental health in the adult population of Spain



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ABSTRACT

Background and objectives: Despite the biological plausibility of the association between heavy metal exposure and mental health disorders, epidemiological evidence remains scarce. The objective was to estimate the association between heavy metals and metalloids in soil and the prevalence of mental disorders in the adult population of Spain. **Methods:** Individual data came from the Spanish National Health Survey 2011–2012, 18,073 individuals residing in 1772 census sections. Mental health was measured with the 12-item General Health Questionnaire. The concentration estimates of heavy metal and metalloid levels in topsoil (upper soil horizon) came from the Geochemical Atlas of Spain based on 13,317 soil samples. Levels of lead (Pb), arsenic (As), cadmium (Cd) and manganese (Mn) were estimated in each census section by “ordinary Kriging”. Odds ratios (OR) were calculated by multilevel logistic regression models.

Results: Compared with the lowest Pb concentration levels quartile, the OR for the second quartile was 1.29 (95%CI: 1.11–1.50), increasing progressively to 1.37 (95%CI: 1.17–1.60) and 1.51 (95%CI: 1.27–1.79) in the third and fourth quartiles, respectively. For As, the association was observed in the third and fourth quartiles: 1.21 (95%CI: 1.04–1.41) and 1.42 (95%CI: 1.21–1.65), respectively. Cd was associated also following a gradient from the second quartile: 1.34 (95%CI: 1.15–1.57) through the fourth: 1.84 (95%CI: 1.56–2.15). In contrast, Mn only showed a positive association at the second quartile. Additionally, individuals consuming vegetables > once a day the OR for the fourth quartile of Pb concentration, vs. the first, increased to 2.93 (95%CI: 1.97–4.36); similarly for As: 3.00 (95%CI: 2.08–4.31), and for Cd: 3.49 (95%CI: 2.33–5.22).

Conclusions: Living in areas with a higher concentration of heavy metals and metalloids in soil was associated with an increased probability of having a mental disorder. These relationships were strengthened in individuals reporting consuming vegetables > once a day.

1. Introduction

Mental illness is an important cause of disability and morbidity. According to the World Health Organization, 450 million people worldwide suffer from some type of mental disease, and psychiatric disorders account for the loss of one third of disability-free life-years. In Europe, mental disorders are the most common cause of disease, ahead of cardiovascular diseases and cancer (Vigo et al., 2016).

Mental disorders are characterized by their high level of heterogeneity and the variety of their causes. Close examination of these

causes has identified a complex network of factors associated not only with genetic, biological, and psychosocial characteristics of the individual, but also with environmental determinants present in the area of residence (Patel et al., 2016). Individuals' exposure to contaminated air and soil is among these environmental determinants.

In contrast with the well documented impact of air pollution on health, similar studies regarding soil pollution are scarce. The understudy of this pollution is surprising being soil the main repository of heavy metals which, unlike water or air pollutants, are persistent, bioavailable, bioaccumulable, and can be magnified in the food chain.

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In those regions with large extensions of soil contaminated by heavy metals, such as Nanning, China, the soil-to-plant transfer of metals is thought to be the main route of exposure (Cui et al., 2004). Thus, the accumulation of heavy metals in agricultural land may pose a risk to food safety (Tóth et al., 2016).

Among adults, exposure to lead (Pb) has been associated with depression, anxiety, panic disorder, reduced cognitive and response capacity, schizophrenia, Parkinson's disease, and, although not as consistently, with Alzheimer's disease (Bouchard et al. 2009; Farooqui et al., 2017; Guilarte et al., 2012; Rajan et al. 2007). Further, it has been associated with depression and phobic anxiety in women (Eum et al., 2012; Searle et al., 2014). Exposure to arsenic (As) has been associated with cognitive impairment (Liu et al., 2017), depression, anxiety, adjustment problems (Zierold et al., 2004) and Alzheimer's (Szabo et al., 2016). Whereas cadmium (Cd) has been associated with depression and schizophrenia (Berk et al. 2014), Manganese (Mn) has been linked to problems in the motor system, memory and poor cognitive performance, hyperactivity and attention deficit disorder (Rodríguez-Barranco et al., 2013; Viana et al. 2014).

Whereas most research has been focused on the effect of acute intoxications by metals, the long-term impact of low-dose exposure is understudied. Authors have argued that continuous exposure to heavy metals could give rise to a "silent pandemic" in modern society, one responsible for a subclinical and permanent decrease in the IQ, an increase in school failure, a reduction in productivity (Grandjean and Landrigan, 2006), and an increased risk of antisocial and criminal behavior (Rodríguez-Barranco et al., 2013).

Despite the biological plausibility of the association between heavy metal exposure and mental health disorders, epidemiological evidence remains scarce. Our objective was to estimate the association between cumulative exposure to heavy metals and metalloid levels found in topsoil and the prevalence of mental disorders in a representative population sample, while adjusting for relevant individual and contextual-level variables.

2. Methodology

2.1. Study design and population

To meet our objectives, we performed a cross-sectional study based on the 2011–2012 Spanish National Health Survey (Encuesta Nacional de Salud, España [ENSE]) database.

The ENSE collects information on the health status of the population as well as the main social, environmental, and lifestyle determinants of individuals residing in Spain. The ENSE is based on a multistage sample design, first selecting all the provinces and within each province selecting the municipalities, then stratifying according to the municipality's size. At this point, a sample of census tracts is chosen from each of the selected municipalities. Finally, a sample of households is selected and one individual ≥ 15 years of age is designated as potential participant. Data were collected from face-to-face interviews between July 2011 and June 2012 with a response rate of 71.1%. The original sample consisted of 20,007 individuals residing in 2000 census tracts (Spanish Ministry of Health, Consumption, and Welfare and Spanish National Institute of Statistics).

2.2. Variables

2.2.1. Mental health

Mental health was estimated based on the 12-item General Health Questionnaire (GHQ-12), developed and validated by Goldberg and colleagues (Goldberg et al., 1997). The GHQ-12 is a self-reported measure of psychological morbidity and portrays a time-efficient screening tool for the identification of people at risk of developing psychiatric disorders in community and clinical settings. Although The GHQ-12 does not provide a precise diagnosis, it is widely used in epidemiological research to monitor population mental health as well as in

clinical practice as a screening tool (Fryers et al., 2004; Gnambs and Staufenbiel, 2018). Its psychometric properties have been studied in several countries (Werneke et al., 2000) and it has been validated in Spain (Sánchez-López and Dresch, 2008).

The GHQ-12 assesses the severity of various problems in recent weeks: ability to concentrate, loss of sleep over worry, playing a useful part in life, decision-making abilities, feeling under strain, inability to overcome difficulties, ability to enjoy daily activities, ability to face problems, feelings of unhappiness and depression, loss of confidence, feeling worthless, and feeling reasonably happy. Responses are based on a 4-category Likert scale: "much less than usual" and "usual" (assigned 0 points) vs. "more than usual" and "much more than usual" (assigned 1 point). A total score of 3 or more identifies individuals with a possible mental disorder (Goldberg et al., 1998). The GHQ-12 is essentially a unidimensional index, basically reflecting general mental health rather than distinct constructs. Thus, deriving subscales for interpretations beyond its purpose is not recommended (Gnambs and Staufenbiel, 2018).

2.2.2. Heavy metals in soil

Exposure to heavy metals/metalloids was estimated based on topsoil (top 20 cm) level data from a sample of 13,505 surface soil samples distributed throughout Spain with a variable density according to the population or industrial areas of up to 1 sample/10 km² (Locutura Rupérez et al., 2012). This atlas was carried out by the Geological and Mining Institute of Spain between June 2008 and November 2010. Of all the 64 chemicals studied as part of the larger study, we selected Pb, As, Cd and Mn for these analyses due to their known relationship with mental health. The residual soil samples were analyzed by instrumental inductively coupled plasma mass spectrometry (ICP-MS). A complete description of the data collection and the analytical techniques used have been previously published (Locutura Rupérez et al., 2012; López-Abente et al., 2018; Núñez et al., 2016).

2.2.3. Covariates

When evaluating any association, all relevant individual- and contextual-level covariates available or derived from the ENSE were taken into account. Among the individual-level variables included in the dataset there were: sex, age, educational level, marital status, place of birth (Spain or abroad), sedentary leisure time (no exercise, leisure time is spent almost completely in a sedentary manner), body mass index (based on self-reported height and weight [kg/m²]), tobacco consumption (never smoker, ex-smoker, current smoker), risk drinking of any of 6 types of alcoholic beverages (self-reported regular alcohol consumption ≥ 40 g/day for men and ≥ 24 g/day for women), and binge drinking (consumption ≥ 6 alcoholic beverages in men or ≥ 5 in women, within 4–6 h in the last twelve months). Finally, we also collected dietary information from participants' self-reports on weekly consumption of the following foods: vegetables, fruit, cereal products (rice, pasta, bread, cereals) and potatoes, fish, meat, and eggs.

The ENSE also provided the following contextual-level variables: municipal size-based strata, perceived scarcity of green areas in their area of residence (none, some, much), perceived criminality in the area of residence (none, some, much). We also included the following two variables based on 2011 Census data (Spanish National Institute of Statistics) at the section level: proportion of deficient dwellings (synthetic variable constructed by factor analysis based on the percentage of dwellings without heating, toilet, bath-shower, or water); and deprivation index (synthetic variable constructed by factor analysis based on the percentage of people without studies, casual workers, and manual workers). Finally, we estimated particulate pollution (PM₁₀), also at the census section level, based on multi-pollutant multiscale air quality models developed by the Polytechnic University of Madrid (Boldo et al., 2014, 2011).

2.3. Statistical analyses

Out of the 21,007 ENSE study participants, our sample included

18,073 individuals with valid information for all the study variables. The selected individuals were distributed across 1772 census sections. Each of these sections was assigned corresponding soil concentrations of Pb, As, Cd and Mn based on the normalized data from the Geological and Mining Institute and using the spatial interpolation method “ordinary Kriging” (Diggle and Ribeiro, 2006; Ribeiro and Diggle, 2001). Ordinary kriging had already been implemented in a previous study (Núñez et al., 2016) in which the same exact geo-chemical soil composition data were used. This method has the smallest mean-squared prediction error in the class of all linear unbiased predictors (Waller and Gotway, 2004). The concentration levels of heavy metals were categorized into quartiles.

We developed multilevel logistic regression models to evaluate the association between levels of exposure to these metals in soil and the prevalence of mental health problems, introducing the census section as a random effect. The models were fully adjusted by the variables described above: sex, age, educational level, marital status, place of birth, consumption of vegetables, fruit, cereal products, fish, meat, and eggs, sedentary leisure time, body mass index, tobacco consumption, high-risk drinking, municipal size-based strata, perceived scarcity of green areas, perceived criminality in the area of residence, proportion of deficient dwellings, deprivation index of the area of residence, and PM₁₀.

Potential interactions between heavy metals exposure and consumption of different food groups were evaluated. Given that statistically significant interactions with vegetable consumption were observed, analyses were stratified by frequency of vegetable consumption (< 1, 1, and > 1 once a day).

The general contextual effects of the multilevel logistic regression models were estimated using intraclass correlation coefficients (ICC), the percentage change in variance (PCV), and the percentage change in the area under the curve (AUC Roc), comparing the 3 following models: a) model with individual variables (model 1); b) model 1 plus random effects (census section) (model 2); c) model 2 plus the contextual variables related to area of residence, separately for each of the heavy metals (Merlo et al., 2016). Spatial interpolation analyses for the heavy metals were run with the program R and its library geoR (Ribeiro P and Diggle P, 2001). Multilevel logistic regression analyses were performed with Stata v.15 (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC).

3. Results

Based on the GHQ-12 scores, 21.9% of the Spanish adult population met the criteria for mental health problems. Tables 1 and 2 describe the

Table 1
Sample socio-demographic and lifestyle characteristics, according to the presence of mental health problems.

| | Total | Mental health problems ^a | | p-value ^b |
|---|------------|-------------------------------------|--------------|----------------------|
| | n = 18,073 | No n = 14,121 < | Yes n = 3952 | |
| Sex (%) | | | | < 0.001 |
| Men | 46.0 | 48.8 | 36.1 | |
| Women | 54.0 | 51.2 | 63.9 | |
| Age (mean) | 51.7 | 50.9 | 54.5 | < 0.001 |
| Educational level (%) | | | | < 0.001 |
| Primary or below | 26.2 | 24.9 | 30.8 | |
| Secondary, first cycle | 32.3 | 31.5 | 34.9 | |
| Secondary, second cycle | 26.2 | 27.1 | 23.1 | |
| University/College | 15.3 | 16.4 | 11.2 | |
| Marital status (%) | | | | < 0.001 |
| Single | 27.5 | 28.5 | 24.1 | |
| Married | 53.6 | 54.7 | 49.5 | |
| Widow/er | 12.8 | 11.3 | 18.4 | |
| Separated/Divorced | 6.1 | 5.6 | 6.0 | |
| Spanish Nationality (%) | | | | 0.312 |
| Yes | 91.9 | 92.0 | 91.5 | |
| No | 8.1 | 8.0 | 8.5 | |
| Vegetable consumption (times per day) | 1.02 | 0.99 | 1.14 | < 0.001 |
| Fruit consumption (times per day) | 1.70 | 1.67 | 1.79 | < 0.001 |
| Cereals consumption (times per day) | 1.55 | 1.56 | 1.52 | < 0.001 |
| Fish consumption (times per day) | 0.48 | 0.49 | 0.46 | < 0.001 |
| Meat consumption (times per day) | 0.63 | 0.64 | 0.59 | < 0.001 |
| Eggs consumption (times per day) | 0.39 | 0.39 | 0.37 | < 0.001 |
| Sedentary Leisure time (%) | | | | < 0.001 |
| No | 55.3 | 58.7 | 43.0 | |
| Yes | 44.7 | 41.3 | 57.0 | |
| Body Mass Index (%) | | | | < 0.001 |
| Underweight | 1.8 | 1.8 | 1.6 | |
| Normal weight | 39.2 | 40.1 | 35.7 | |
| Overweight | 34.4 | 34.7 | 33.5 | |
| Obesity | 16.0 | 15.3 | 18.5 | |
| Missing | 8.6 | 8.0 | 10.7 | |
| Tobacco consumption (%) | | | | 0.010 |
| Non-smoker | 54.2 | 54.5 | 53.4 | |
| Ex-smoker | 20.2 | 20.4 | 19.2 | |
| Smoker | 25.6 | 25.1 | 27.4 | |
| High-risk drinking (average consumption) (%) | | | | 0.652 |
| No | 98.5 | 98.5 | 98.6 | |
| Yes | 1.5 | 1.5 | 1.4 | |
| Binge drinking (%) | | | | < 0.001 |
| No | 87.8 | 87.0 | 90.3 | |
| yes | 12.2 | 13.0 | 9.7 | |

^a GHQ-12 (score ≥ 3).

^b Estimated using Chi-Square statistic for qualitative variables and Mann-Whitney test for quantitative variables.

Table 2
Characteristics of the residential area of the sample, according to the presence of mental health problems.

| | Total | Mental health problems ^a | | p-value ^b |
|--|------------|-------------------------------------|--------------|----------------------|
| | n = 18,074 | No n = 14,122 | Yes n = 3952 | |
| Size of municipality | | | | 0.995 |
| > 100,000 residents | 40.8 | 40.8 | 40.8 | |
| 50,000–100,000 residents | 8.8 | 8.8 | 8.7 | |
| 10,000–50,000 residents | 25.2 | 25.2 | 25.3 | |
| < 10,000 residents | 25.3 | 25.3 | 25.2 | |
| Problems due to lack of green areas (%) | | | | 0.001 |
| Many | 7.8 | 7.6 | 8.6 | |
| Some | 14.0 | 13.6 | 15.4 | |
| None | 78.2 | 78.7 | 76.0 | |
| Problems due to criminality (%) | | | | < 0.001 |
| Many | 4.4 | 3.9 | 6.0 | |
| Some | 15.9 | 15.7 | 16.8 | |
| None | 79.7 | 80.4 | 77.2 | |
| Residences with deficiencies (mean) | -0.07 | -0.07 | -0.05 | 0.165 |
| Index of Deprivation (mean) | -0.01 | -0.04 | 0.10 | < 0.001 |
| PM₁₀ | 13.9 | 13.8 | 14.0 | 0.004 |

^a GHQ-12 (score ≥ 3).

^b Estimated using Chi-Square statistic for qualitative variables and Mann-Whitney test for quantitative variables.

Table 3
Distribution of heavy metal concentration in topsoil (mg/kg). Interpolated values at the census section level.

| | Min | P (5) | P(25) | P(50) | P(75) | P(95) | Max |
|--|-------|--------|--------|--------|--------|--------|---------|
| Interpolation for census section (n = 1772) | | | | | | | |
| Lead | 8.20 | 12.88 | 16.94 | 25.04 | 36.43 | 60.7 | 439.94 |
| Arsenic | 0.86 | 3.37 | 5.97 | 8.80 | 12.78 | 19.15 | 38.52 |
| Cadmium | 0.01 | 0.05 | 0.10 | 0.15 | 0.24 | 0.37 | 1.27 |
| Manganese | 66.64 | 171.93 | 255.73 | 336.65 | 444.35 | 626.50 | 1426.04 |

P: Percentile.

sample according to mental health status. People with mental health issues were more likely to be women, older, with lower educational levels, and widowed. Regarding lifestyle and health behaviors, individuals with mental disorders reported a higher fruit and vegetables consumption and lower cereal products, fish, meat, or eggs consumption, spent more of their leisure time in sedentary activities, were more likely to be obese and to smoke, and were less likely to report binge drinking in the last twelve months. Finally, in terms of contextual factors, mental disorders were more prevalent in people who lived in areas with higher rates of deprivation, crime's problems, air pollution (PM₁₀) and with a scarcity of green zones.

Table 3 describes the average topsoil concentration levels for the different heavy metals. Pb levels ranged (minimum and maximum range) between 8.2 mg/kg and 439.94 mg/kg; As ranged between 0.86 mg/kg and 38.52 mg/kg; Cd ranged between 0.01 mg/kg and

1.27 mg/kg; and Mn between 66.6 mg/kg and 1426 mg/kg. These values were classified by quartiles with first quartile capturing the lowest levels of exposure and the fourth quartile representing the highest level of exposure. A summary of the standard errors of the predictions in each spatial unit using the interpolation method for the log-concentration of each element analyzed is included in Supplementary Material (Table 1S).

Table 4 shows the association between these quartiles and the prevalence of mental health disorders expressed using odds ratios (ORs) and their corresponding 95% confidence intervals. Compared to Pb exposure at the lowest concentration levels (first quartile), the risk of mental health issues, for exposures classified in the second, third, and fourth quartiles were 1.29 (95%CI: 1.11–1.50), 1.37 (95%CI: 1.17–1.60), and 1.51 (95%CI: 1.27–1.79), respectively. For exposures to As, the risk did not increase until reaching the third and fourth quartiles of exposure: 1.21 (95%CI: 1.04–1.41) and 1.42 (95%CI: 1.21–1.65), respectively. Cd exposure depicted a positive association with mental health problems from the second quartile: 1.34 (95%CI: 1.15–1.57) up to 1.82 (95%CI: 1.56–2.16) for those exposed to the highest levels of concentration. Finally, Mn exposure and mental disorders showed a significant association only for the second quartile of soil concentration: 1.32 (95%CI: 1.14–1.53). The coefficients failed to reach statistical significance for the third and fourth quartile levels of Mn soil concentrations.

Next we examined whether the observed associations between heavy metal/metalloid levels in soil and mental health were modified by type of foods consumed. We found that the daily vegetable consumption did modify the magnitude of the association (Table 5). Compared to participants consuming up to once a day, the association

Table 4
Heavy metal concentration in topsoil and risks of mental health problems in the Spanish adult population.

| | Lead | | Arsenic | | Cadmium | | Manganese | |
|--|-----------------|-----------|-----------------|-----------|-----------------|-----------|-----------------|-----------|
| | OR ^a | 95%CI | OR ^a | 95%CI | OR ^a | 95%CI | OR ^a | 95%CI |
| Heavy metal exposure in quartiles | | | | | | | | |
| Quartile 1 | 1 (ref) | | 1 (ref) | | 1 (ref) | | 1 (ref) | |
| Quartile 2 | 1.29 | 1.11–1.50 | 1.03 | 0.88–1.19 | 1.34 | 1.15–1.57 | 1.32 | 1.14–1.53 |
| Quartile 3 | 1.37 | 1.17–1.60 | 1.21 | 1.04–1.41 | 1.19 | 1.02–1.39 | 1.07 | 0.92–1.24 |
| Quartile 4 | 1.51 | 1.27–1.79 | 1.42 | 1.21–1.65 | 1.82 | 1.55–2.15 | 1.04 | 0.89–1.21 |

^a Odds ratios of having mental health problems (GHQ-12, score ≥ 3), estimated using multilevel logistic models adjusted for socio-demographic, lifestyle, and residential area variables (see Tables 1 and 2).

Table 5
Heavy metal concentration in topsoil and risks of mental health problems in the Spanish adult population, according to vegetable consumption.

| Exposure level (Quartiles) | | < 1 vegetable times per day | | 1 vegetable times per day | | > 1 vegetable times per day | |
|----------------------------|------------|-----------------------------|-----------|---------------------------|-----------|-----------------------------|-----------|
| | | OR ^a | 95%CI | OR ^a | 95%CI | OR ^a | 95%CI |
| Lead | Quartile 1 | 1 (ref) | | 1 (ref) | | 1 (ref) | |
| | Quartile 2 | 1.29 | 1.06–1.58 | 1.14 | 0.94–1.39 | 1.56 | 1.07–2.26 |
| | Quartile 3 | 1.26 | 1.03–1.55 | 1.12 | 0.92–1.39 | 2.25 | 1.52–3.34 |
| | Quartile 4 | 1.18 | 0.94–1.48 | 1.37 | 1.09–1.71 | 2.93 | 1.97–4.36 |
| Arsenic | Quartile 1 | 1 (ref) | | 1 (ref) | | 1 (ref) | |
| | Quartile 2 | 1.07 | 0.88–1.32 | 0.93 | 0.77–1.13 | 1.14 | 0.80–1.63 |
| | Quartile 3 | 1.17 | 0.95–1.44 | 1.12 | 0.92–1.37 | 1.58 | 1.12–2.25 |
| | Quartile 4 | 1.18 | 0.96–1.45 | 1.01 | 0.81–1.26 | 3.00 | 2.09–4.31 |
| Cadmium | Quartile 1 | 1 (ref) | | 1 (ref) | | 1 (ref) | |
| | Quartile 2 | 1.57 | 1.29–1.91 | 1.17 | 0.95–1.45 | 1.27 | 0.86–1.87 |
| | Quartile 3 | 1.24 | 1.00–1.53 | 1.04 | 0.85–1.28 | 1.58 | 1.08–2.31 |
| | Quartile 4 | 1.68 | 1.36–2.08 | 1.47 | 1.17–1.83 | 3.49 | 2.33–5.22 |
| Manganese | Quartile 1 | 1 (ref) | | 1 (ref) | | 1 (ref) | |
| | Quartile 2 | 1.38 | 1.13–1.69 | 1.29 | 1.05–1.57 | 1.16 | 0.81–1.66 |
| | Quartile 3 | 1.02 | 0.83–1.24 | 1.35 | 1.11–1.65 | 0.83 | 0.58–1.20 |
| | Quartile 4 | 1.06 | 0.86–1.29 | 1.26 | 1.03–1.55 | 0.74 | 0.51–1.08 |

^a Odds ratios of having mental health problems (GHQ-12, score ≥ 3), estimated using multilevel logistic models adjusted for socio-demographic, lifestyle, and residential area variables (see Tables 1 and 2).

Table 6
General contextual effects of the multilevel logistic regression.

| | ICC | | Variance | | PVC | AUC Roc | | AUC Roc Change |
|--|------|-----------|----------|-------------|-------|---------|-----------|----------------|
| | % | 95%CI | 95%CI | % | | % | 95%CI | |
| Model 1 (individual variables) | – | | – | | | 65.4 | 64.5–66.3 | – |
| Model 2 (model 1 plus random effect) | 14.6 | 12.7–16.8 | 0.563 | 0.469–0.656 | – | 78.4 | 77.6–79.1 | + 19.9 |
| Model 3 (model 2 plus contextual variables including lead) | 14.1 | 12.2–16.3 | 0.540 | 0.440–0.632 | – 4.1 | 78.1 | 77.3–78.9 | + 19.4 |
| Model 3 (model 2 plus contextual variables including arsenic) | 14.0 | 12.1–16.2 | 0.538 | 0.446–0.629 | – 4.4 | 78.1 | 77.3–78.9 | + 19.4 |
| Model 3 (model 2 plus contextual variables including cadmium) | 13.7 | 11.8–15.9 | 0.522 | 0.432–0.612 | – 7.3 | 78.1 | 77.2–78.9 | + 19.4 |
| Model 3 (model 2 plus contextual variables including manganese) | 14.3 | 12.3–16.4 | 0.547 | 0.455–0.639 | – 2.8 | 78.2 | 77.4–79 | + 19.6 |

ICC: Intraclass correlation coefficient.

PVC: Percent variance change of model 3 vs. model 2.

AUC Roc: Area under the curve.

AUC Roc Change: Relative change (%) of the AUC Roc in models 2 and 3 vs. model 1.

between heavy metals and mental health problems of those consuming more than once a day was substantially stronger, while preserving the gradient effect according to the quartiles of exposure to Pb, As and Cd. For those consuming > once a day, the OR for the highest level of Pb exposure was 2.93 (95%CI: 1.97–4.36); for As exposure was 3.00 (95%CI: 2.09–4.31), and for Cd exposure the OR was 3.49 (95%CI: 2.33–5.22). Vegetable consumption did not modify the association between Mn exposure and mental health.

Table 6 shows the coefficients corresponding to the general contextual-level factors. The model that included the random effect (model 2) showed an ICC of 14.6%, increasing the AUC Roc by 19.9% versus model 1 which included only individual-level variables. The complete model, which included the contextual-level variables of the area of residence including heavy metals, reduced the variance with respect to model 2 from –2.8% to –7.3%. These values were not substantially modified by including the interaction between heavy metals and vegetable consumption.

4. Discussion

Our results show that residing in areas with a higher soil concentration of heavy metals and metalloids was associated with an increased risk of suffering from a mental disorder. A gradient effect was observed for Pb, As, and Cd; i.e., higher probabilities of having mental disorders as levels of exposure increase. The associations between these three soil pollutants and mental disorders were strengthened

substantially in people who consumed vegetables more than once per day.

The association detected here between exposure to topsoil metals/metalloids and mental health supports previous literature, despite broad differences in research designs and populations. Given infants' greater vulnerability to the neurotoxicity of these substances, this population has received the most research focus. For instance, pregnant mothers' exposure to heavy metals such as Pb and Cd was associated longitudinally with emotional and mental problems in their offspring (Searle et al., 2014; Sioen et al., 2013; Winter and Sampson, 2017). Exposure to Pb during childhood has been linked to problems of anxiety, impulsivity, and depression in adolescence (Winter and Sampson, 2017) as well as to anxiety and phobias in adult women (Searle et al., 2014). Cross-sectional studies based on the detection of heavy metals exposure using different types of biomarkers have concluded that even low levels of exposure to Pb (Bouchard et al. 2009; Rajan et al. 2007; Rhodes et al., 2003) and Cd (Berk et al. 2014) were associated with an increased risk of mental disorders in the adult population.

Studies linking mental health issues and exposure to heavy metals present in natural resources are almost non-existent. As far as we know, the only work of this kind was carried out in the province of Ubei, a mining area in China with high levels of Pb, Cd, and As, where residents presented with significantly higher rates of obsessive-compulsive behaviors, interpersonal sensitivity, depression, anxiety, hostility, paranoid ideation, and psychoticism, when compared to control populations in different geographical areas (Dang et al., 2008).

Our study also shows that the consumption of vegetables strengthens the association between exposure to heavy metals and mental health issues. This finding supports that, after occupational exposure, food is the main source of ingestion of toxic metals (Järup, 2003). A comparison of heavy metal levels across vegetarians, omnivores, and regular seafood consumers revealed that vegetarians were more likely to concentrate metals in blood than the other two groups (Salazar-Lugo R et al., 2013). It has also been described that food produced in agricultural or farming areas close to industrial and mining areas pose a substantial risk to the population's health (Álvarez-Ayuso et al., 2012). A recent study in four regions of India including both commercial vegetables farms and private residential vegetable gardens free of industrial contamination, showed that soil containing high metals concentrations may transfer these metals into edible parts of the leafy vegetables. Further, vegetables easily absorb and accumulate heavy metals from soil in quantities large enough to impact population health adversely, even if only evident after several years of exposure (Tasrina et al., 2015). Unfortunately due to data limitations, we were unable to adjust for other potential sources of contamination such as pesticides. Thus, there is a need for further studies to contrast this finding.

For instance, soil concentrations of Pb and As as well as Pb concentrations in wheat exceeded the maximum allowed levels for agricultural land and products in the area close to the Clara mine in Zamora (Spain). Further, the conditions of the soil translated into a substantial risk of mobilization of these metals (Álvarez-Ayuso et al., 2012). In a mining area in China, rice and vegetable consumption were identified as the main sources of exposure to Cd, Cu, Pb, and As (Cai et al., 2015). Further, in the city of Ningbo, one of China's most industrialized cities, the presence of heavy metals was analyzed in soil samples, irrigation water, vegetables, and biomarkers in students. High correlations were found for Pb and/or Cd between soil samples and irrigation water with levels detected in vegetables. Additionally, a high bioaccumulation of Pb and other metals related to the consumption of vegetables and rice was observed (Li et al., 2018).

Whereas the associations between exposure to Pb, Cd, or As and the risk of mental health problems presented as a gradient effects, the likelihood of mental disorders did not increase with higher Mn concentration in soil; further, no interaction with vegetable consumption was observed. Of the elements examined here, Mn is the only essential one for the organism as a cofactor of numerous cellular enzymes in key physiological processes. However, high exposures are toxic, causing neurological damage, memory impairment, and mental confusion. It is possible that, due to the small particle size, the main source of exposure may be through atmospheric emission and deposition on topsoil (Ferri et al., 2012; Viana et al. 2014). However, Mn seems to neither bind to the soil nor to bioaccumulate as much as the other heavy metals. This is supported by two findings in the Ningbo study: no correlation between Mn topsoil and irrigation water levels with Mn levels in vegetables; and Mn having the lowest bioaccumulation of all the metals studied (Li et al., 2018).

From the perspective of general contextual effects of multilevel logistic regression models, accounting for the area of residence moderately increased the model's discriminant capacity, i.e., its ability to identify groups at risk of poor mental health. In contrast, the model's contextual variables, including heavy metals, failed to explain the variability observed in the area of residence significantly when estimating small reductions in variance.

Our results should be interpreted within the context of its limitations. Among these, the main ones are: first, its cross-sectional design prevents the establishment of causal associations. Second, heavy metal estimates were based on spatial modeling from 13,505 objective soil samples. Third, the mental health variable is based on self-reported information from the GHQ-12 questionnaire rather than on a medical diagnosis. Nevertheless, the GHQ-12 is one of the most widely used instruments to identify mental health problems in the field of public

health, in addition to screening tests in the clinical setting, and it has been validated in Spain (Sánchez-López and Dresch, 2008). Similarly, the variables extracted from the ENSE are self-reported. Finally, the food questionnaire included in the Spanish National Health Survey is a brief questionnaire collecting data on the frequency of intake of 15 food groups. From these data is not possible to differentiate among different types of vegetables or the specific composition of other food groups.

The study also has several strengths. First, our findings are based on a large representative sample of all the different regions in Spain. Second, the richness of the data allows associations to be adjusted for numerous individual and contextual potential confounders, especially smoking and exposure to particulate contamination. Tobacco smoke is both a potent source of exposure to the metals under consideration here (Richter et al., 2009) and far more prevalent in individuals with mental illness than in the general population (Prochaska et al., 2017). Finally, exposure to particles not only increases with levels of contamination by heavy metals but has also been associated with the incidence and severity of mental health problems, especially anxiety and depression (Buoli et al., 2018).

5. Conclusions

In sum, our results show a statistical association between the trace contents of heavy metals and metalloids in topsoil and the probability of having a mental disorder, observing dose-response relationships for Pb, As, and Cd, specifically. These associations were strengthened among those individuals reporting the consumption of vegetables more than once per day.

These findings strongly suggest that the presence of potentially toxic elements in trace concentrations in topsoil may be one more factor in the etiology of mental illnesses; further, it is highly possible that exposure to these elements materializes through food intake. Although these relationships need to be confirmed in future longitudinal studies, public health initiatives should be called to monitor topsoil concentrations of these elements with the aim of limiting the commercialization of products grown in agricultural areas with high concentrations of heavy metals and metalloids (Liu et al., 2013; Tóth et al., 2016).

Author statement

I.G. and A.A. conceptualization. I.M., A.B., G.L., P.F. and I.G. acquired data. A.A., O.N., P.F. and I.G. performed the statistical analyses. A.A. and I.G. drafted the manuscript. All authors revised and approved the final manuscript.

Ethics committee approval

Ethical approval was not required for secondary analysis of anonymous data in this study.

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Declaration of competing interest

The authors declared no potential conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envres.2019.108784>.

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