Environmental Research 236 (2023) 116721

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Serum levels of PCDDs, PCDFs and dl-PCBs in general population residing far and near from an urban waste treatment plant under construction in Gipuzkoa, Basque Country (Spain)

Loreto Santa-Marina [a,b,c], Amaia Irizar [a,d], Ziortza Barroeta [a,d,*], Esteban Abad [e], Aitana Lertxundi [a,b,d], Jesús Ibarluzea [a,b,c,f], Jordi Parera [e], Nerea Urbieta [a], Elene Arruti [a], Alba Jimeno-Romero [a,d], Miren Begoña Zubero [a,d]

[a] Biodonostia Health Research Institute, Group of Environmental Epidemiology and Child Development, Paseo Doctor Begiristain s/n, 20014, San Sebastian, Spain
[b] Spanish Consortium for Research on Epidemiology and Public Health (CIBERESP), Instituto de Salud Carlos III, C/Monforte de Lemos 3-5, 28029, Madrid, Spain
[c] Department of Health of the Basque Government, Subdirectorate of Public Health of Gipuzkoa, Avenida Navarra 4, 20013, San Sebastian, Spain
[d] Department of Preventive Medicine and Public Health, University of the Basque Country (UPV/EHU), Leioa, Bizkaia, Spain
[e] Laboratory of Dioxins, IDAEA-CSIC, Jordi Girona 18, 08034, Barcelona, Spain
[f] Faculty of Psychology, University of the Basque Country (UPV/EHU), 20008, San Sebastian, Spain

ARTICLE INFO

Handling Editor: Jose L Domingo

Keywords:
Serum
Dioxins
Furans
Dioxin-like polychlorinated biphenyls
Energy recovery plant

ABSTRACT

This research focused on investigating the basal serum concentrations of polychlorinated dibenzo-*p*-dioxins, dibenzofurans (PCDD/Fs) and dioxin-like polychlorinated biphenyls (dl-PCBs) in the general population residing in two urban-industrial zones near and far from an energy recovery plant under construction in Gipuzkoa, Basque Country (Spain). The study used a cross-sectional design and included 227 participants who were randomly selected from municipal censuses in both areas. The participants were stratified based on age (ranging from 18 to 70 years) and sex. Serum samples were collected from the participants and analysed following the established protocol to measure the concentrations of PCDD/Fs and dl-PCBs. The study used multiple linear regression models to assess the impact of various sociodemographic variables, lifestyle factors, reproductive history, and diet on the variability of the measured compounds in the participants' serum. The median total toxicity equivalent (TEQ) in serum, was 10.58 pg WHO-TEQ2005 g-1 lipid. Serum PCDD levels were lower in the population residing in the "far" zone than the "near" zone. Age was positively associated with both PCDD/F and dl-PCB levels, indicating that older participants had higher concentrations of these compounds in their serum. This finding might be attributed to cumulative exposure over time. In terms of sex differences, women exhibited lower levels of dl-PCBs compared to men. Among lifestyle factors, smokers showed lower levels of dl-PCBs compared to non-smokers. Furthermore, daily alcohol consumption was significantly associated with higher serum levels of these compounds, with daily drinkers showing higher levels than non-drinkers. Consumption of local poultry was associated with significantly higher serum levels and oil consumption with low levels of PCDD/Fs.

1. Introduction

Polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), and dioxin-like polychlorinated biphenyls (dl-PCBs) are a group of highly toxic and persistent environmental pollutants. They are known to bioaccumulate in the environment and within the food chain, with a tendency to accumulate in fatty tissues of living organisms (Jeno et al., 2021). Research has shown that exposure to PCDDs, PCDFs, and dl-PCBs can lead to various health risks, including contributing to cancer development, immunological disorders, teratogenic effects (causing birth defects), reproductive issues, and neuroendocrine disorders. These adverse health effects make these compounds of significant concern to public health and environmental safety (Furue et al., 2021). While these compounds can occur naturally in processes like volcanic eruptions and forest fires, the main source of their

* Corresponding author. Biodonostia Health Research Institute, Group of Environmental Epidemiology and Child Development, Paseo Doctor Begiristain s/n, 20014, San Sebastian, Spain.
E-mail address: ziortza.barroeta@ehu.eus (Z. Barroeta).

https://doi.org/10.1016/j.envres.2023.116721
Received 20 June 2023; Received in revised form 21 July 2023; Accepted 21 July 2023
Available online 22 July 2023

Abreviations

MSWI	Municipal solid waste incineration
PCDD	Polychlorinated dibenzo-*p*-dioxins
PCDF	Polychlorinated dibenzofurans
PCDD/Fs	Sum of polychlorinated dibenzo-*p*-dioxins and polychlorinated dibenzofurans
PCB	Polychlorinated biphenyl
dl-PCB	Dioxin like PCB
HRGC	High-resolution gas chromatography
HRMS	High-resolution mass spectrometry
VOCs	Volatile organic compounds
NOx	Nitrogen oxides
IARC	Agency for Research on Cancer
LOD	Limit of determination
TEF	Toxic equivalent factor
TEQ	Toxic equivalent
ERP	Energy recovery plant
ENAC	National Accreditation Entity (In spanish Entidad Nacional de Acreditación)
WHO	World Health Organization
AhR	Aryl hydrocarbon receptor
PRTR	Pollutant release and transfer registers
FFQ	Food frequency questionnaire

formation is anthropogenic, primarily through combustion-related activities (Kaleka and Thind, 2020). Energy recovery plants (ERPs) are one such source associated to air pollutants, including PCDDs, PCDFs, and dl-PCBs. Public concern regarding ERPs stems from the emissions of these facilities, especially due to the historical lack of effective emission filtering technologies in older incineration plants (Bena et al., 2019; Zhang, 2021). PCDD/Fs are generated as by-products of industrial chemical processes and incineration (UNEP, 2009), while dl-PCBs are generated in the combustion processes of materials that contain flame-retardants. Although flame-retardants containing dl-PCBs were banned in 1986 due to their environmental persistence and toxicity, these compounds can still persist in the environment, contributing to ongoing contamination (Zhou and Liu, 2018).

PCDDs, PCDFs and dl-PCBs are structurally similar classes of halogenated aromatic hydrocarbons. There are 210 PCDD/F and 209 dl-PCB congeners, of which only seventeen 2,3,7,8 substituted PCDD/Fs and 12 dl-PCBs cause a similar spectrum of effects through a common mechanism of action (Zhang, 2021). Among the PCDD/F congeners, 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and 1,2,3,7,8-pentachlorodibenzo-p-dioxin have been extensively studied, with TCDD being the most potent and classified as a Group 1 carcinogen by the International Agency for Research on Cancer (IARC). The toxicity of these compounds is mainly mediated through their interaction with the aryl hydrocarbon receptor (AhR). When these chemicals bind to the AhR, they can trigger a variety of adverse effects in organisms, including biochemical and physiological alterations (Van den Berg et al., 2006). The concept of toxic equivalents (TEQs) is used to quantify the overall toxicity of mixtures of PCDDs, PCDFs, and dl-PCBs. TEQs represent the combined toxicity of various congeners relative to TCDD and in serum are expressed in units of picograms (pg) of TEQ per gram (g) of lipid.

The most commonly used method to assess population exposure to PCDD/Fs and PCBs involves measuring these substances and their metabolites in biological samples, such as blood, urine, or adipose tissue, taken from individuals within the population. This approach helps determine the extent of exposure in the general population, study temporal and geographical trends, and identify potential sources of exposure. Several studies have been conducted to assess the impact of municipal solid waste incineration or ERP using biomarkers of exposure (Agramunt et al., 2005; Fierens et al., 2007; Reis et al., 2007a, 2007b; Schuhmacher et al., 2002; Ferré-Huguet et al., 2009; Zubero et al., 2010, 2011, 2017; Ranzi et al., 2013). However, due to certain limitations, such as a small number of subjects investigated and the use of pooled samples, the results of some studies conducted near urban waste incinerators have been inconclusive (Albertini et al., 2006; Campo et al., 2019). To gain a comprehensive understanding of the total exposure of a population, it is essential to establish population reference values. These values consider all potential sources and routes of exposure, including air, water, and food. Only two studies were found that monitored dioxin levels in environments where an ERP was planned to be located. These studies aimed to assess the potential impact on the environment and the health of the general resident population before the plant's operation (Caserini et al., 2004; Iamiceli et al., 2021). Before the mentioned study, only one investigation had analysed the body burden of these substances in the general population of the Basque Country (Zubero et al., 2017). This study examined data from individuals residing in two areas, one located near and the other far from an ERP, which had been in operation since 2005.

The Provincial Council of Gipuzkoa in the Basque Country (Spain) initiated the construction of an Energy Recovery plant by incineration (ERP) in 2017 to address the issue of urban waste management. The study aimed to assess the exposure of the population to certain compounds before the commissioning of the Energy Recovery Plant by incineration (ERP) in February 2020. The compounds of interest in this study are polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/Fs) and dioxin-like polychlorinated biphenyls (dl-PCBs).The study involved monitoring air quality and serum levels of PCDD/Fs and dl-PCBs in the general population of the area. The first results of this study related to air quality were published by Santa-Marina et al. (2023).

The key objetives of this research are to determine the baseline serum levels of polychlorinated dibenzo-*p*-dioxins and dibenzofurans (PCDD/Fs) and dioxin-like polychlorinated biphenyls (dl-PCBs) in two selected urban-industrial areas before the ERP (Energy Recovery Plant) becomes operational. This baseline data will serve as a reference point for future comparisons after the plant starts operating. By selecting one zone near the ERP and another further away, the research aims to compare the PCDD/Fs and dl-PCBs levels between the two zones after ERP start-up. This comparison will help assess any potential impact of the ERP on the population's exposure to these pollutants. The research also aimed to identify various factors that could contribute to the variability in the levels of PCDD/Fs and dl-PCBs in the population. These factors included sociodemographic variables (such as age, gender, and socioeconomic status), lifestyle factors (such as smoking habits or occupational exposure), reproductive variables (such as pregnancy status or breastfeeding), and dietary habits. By understanding the influence of these factors, the study also provides information on the potential sources and routes of exposure to PCDD/Fs and dl-PCBs in the population.

2. Methods

2.1. Area of study

The study was conducted in two urban-industrial environments in Gipuzkoa, which is a region in the Basque Country of Spain. The two environments were located at distances of 5 km and 28 km from the ERP that was under construction. The study divided the environments into two zones: zone 1 and zone 2. Zone 1 included three municipalities, while zone 2 included two municipalities (Fig. 1). Both zones share certain characteristics that may contribute to air pollution issues. They are situated in closed valleys, which means that there is limited air dispersion in these areas. This limited air movement can lead to the accumulation of pollutants in the air, potentially worsening air quality. Additionally, heavy traffic and a significant steel industry presence

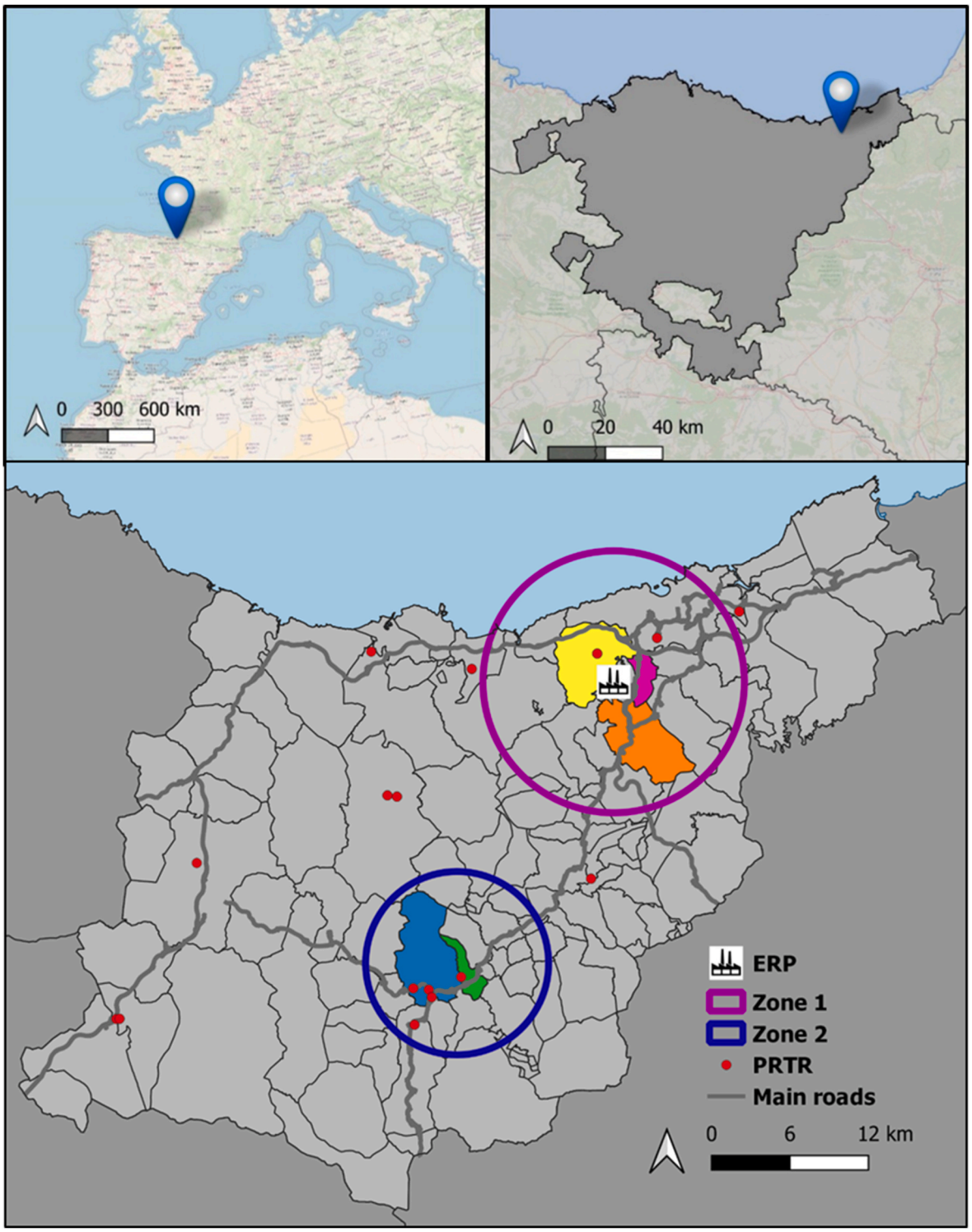

Fig. 1. Map shows the municipalities of the selected participants in both zones.

contribute to the emission of pollutants in both zones (Lertxundi et al., 2010). One noteworthy aspect is that both zones also have industries that emit PCDD/Fs according to the Spanish Registry of Pollutant Emission Sources (PRTR-Spain).

2.2. Study population

The participants were selected using a random sampling technique. The researchers obtained data from municipal censuses from five municipalities within the study area. This sampling method ensures that the participants represent the larger population. The random sampling was stratified by sex and limited to the age range of 18–70 years. A letter was sent to the selected individuals' homes, informing them about the study's objective and requesting their participation. This initial contact introduced them to the study and provided an opportunity for the individuals to decide whether they wanted to participate. After the initial contact, a follow-up telephone call was made to confirm whether the selected individuals met the inclusion criteria. The inclusion criteria

involved specific requirements such as residency in the municipality for the last five years, not working in industries associated with certain chemicals (PCDD/Fs and PCBs), not being pregnant, and not having any significant diseases. These criteria aimed to eliminate potential confounding factors that could affect the study's results. The study received approval from the Clinical Research Ethics Committee of Euskadi. Before participating in the study, each participant provided written informed consent. This consent indicated that they understood the study's purpose, procedures, potential risks, and voluntarily agreed to take part. The study recruited a total of 227 participants between 2017 and 2018. Among them, 122 resided in zone 1, and 105 resided in zone 2.

2.3. Blood sample collection

Blood samples were collected in 2018 from participants in the healthcare centers of the municipalities. Each participant had a 60 mL blood sample drawn by healthcare professionals. The blood extractions were conducted using vacutainers without anticoagulant. After extraction, the samples were transported to the Basque Biobank (https://www.biobancovasco.org) within 90 min. At the Biobank, the serum was aliquoted and stored at −80 °C. The entire process followed a protocol established by the reference laboratory according to Patterson et al. (1991).

2.4. Questionnaires and covariates

Data on the characteristics of the participants, including sociodemographic variables (gender, age, social class and educational level), lifestyle (tobacco and alcohol consumption), reproductive history (number of children, breastfeeding, and menopause) and frequency of locally produced products consumption (milk, cheese, meat and poultry, and vegetables), were collected through a questionnaire administered by an interviewer in face-to-face interviews in the healthcare centers. The participants' social class was determined using the Spanish adaptation of the British Registrar-General's Social Class classification. It was categorized into five levels: I, II, III, IV, and V (Domingo-Salvany et al., 2000). To increase statistical power, these five levels were grouped into two broader categories: manual (IV–V) and non-manual (I-III).

The educational level was based on the number of years of schooling completed, and grouped into two categories [primary and secondary school (15 years) and university or postgraduate (16 years)]. The body mass index (BMI) (underweight: <18.5 kg m^{-2}, normal weight: 18.5–24.9 kg m^{-2}, overweight: 25.0–29.9 kg m^{-2} and obese: 30.0 kg m^{-2}) and the weight change in the last 5 years (Put on weight, lost weight and no change) were recorded.

Dietary intake was assessed using a semi-quantitative food frequency questionnaire (FFQ) administered at the time of blood and urine sampling. The FFQ used in the study consisted of 39 food items and was adapted from Willett's questionnaire (Willett et al., 1985), which was originally developed in 1985. The adapted version of the questionnaire was specifically validated for use in adults living in Spain (Vioque, 2006). Each food item in the FFQ had specified standard units or serving sizes. Participants were asked to indicate their frequency of consumption for each of the 39 food items. The response options included five possible answers, ranging from "never or less than once a month" to "six or more times a day". The questionnaire assessed the consumption frequencies of various food groups in categories, including dairy products, meat, cereals, pasta, fruits and vegetables, canned foods, oils, as well as the intake of blue and white fish. For the purpose of the analysis, the frequencies of food consumption were categorized into three groups: "never or less than three times a month," "weekly," and "daily". To facilitate the analysis of food and nutrient intake patterns, the frequency categories were transformed into grams of daily consumption. This conversion likely involved assigning standard portion sizes and units to each food item and then calculating the approximate daily intake based on the reported frequencies. The transformed values of daily consumption were further categorized into two groups based on the median values. Participants whose intake was above the median were placed in one group, and those below the median were placed in the other group.

2.5. Laboratory analysis

In this study, 7 polychlorinated dibenzo-*p*-dioxins (PCDDs), 10 polychlorinated dibenzo-furans (PCDFs) and twelve dioxins-like polychlorinated biphenyls (dl-PCBs) were analysed at the Laboratory of Dioxins of the Institute of Environmental Assessment and Water Research of the Spanish National Research Council (IDAEA-CSIC) of Barcelona (Spain), accredited by the ENAC (National Accreditation Entity https://www.enac.es/web/enac/courses-campus-enac) according to criteria included in the UNE-EN ISO/IEC 17025 standards.

Briefly, serum samples (~20g) were spiked with known amounts of ^{13}C labelled dioxins and dl-PCBs standards (EPA-1613LCS and WP-LCS respectively from Wellington Laboratories Inc., Guelph, Canada). Afterwards, solid-phase extraction (SPE) approach using C_{18} cartridges (SPE Cartridges – C_{18}; Strata® Giga Tube C_{18}, Phenomenex, CA, USA) was carried out to quantitatively isolate target compounds from the matrix. Elution was accomplished with n-hexane (Honeywell, North Carolina, US). In order to remove organic components, fat content and other interfering substances, n-hexane extracts were purified using silica gel (Supelco, Bellefonte, PA, USA) modified with sulphuric acid (44%) (JTBaker, NJ, USA). Further, additional sample clean-up was carried out by solid-liquid adsorption chromatography, using multilayer silica, basic alumina and carbon columns. Purified extracts were rotary concentrated, transferred into vials and concentrated to dryness by a gentle stream of nitrogen prior to the mass spectrometry analysis. To evaluate the recovery rates, final extracts were reconstructed in a known amount of a mixture of labelled $^{13}C_{12}$-PCDD/Fs (EPA-1613ISS, Wellington Laboratories Inc, Guelph, Canada) and $^{13}C_{12}$-dl-PCBs (WP-ISS, Wellington Laboratories Inc, Guelph, Canada).

Instrumental analysis was based on the use of gas chromatography coupled to high resolution mass spectrometry (GC-HRMS). Analyses were performed on an Agilent gas chromatograph (Agilent Technologies, Palo Alto, CA, USA) coupled to an AutoSpec Premier high resolution mass spectrometer (Waters, Manchester, UK) at 10,000 resolving power (10% valley definition). Gas chromatographic separation was performed on a DB-5MS fused silica column (60 m × 0.25 mm i.d. x 0.25 μm film thickness, Agilent J&W, CA, USA). Quantification was carried out by the isotopic dilution method. Relative response factors were measured for each individual compound by the analysis of six different calibration solutions for PCDD/Fs and dl-PCBs. Finally, the results were expressed on a fat basis (pg/g lipid) and TEQ (toxic equivalent) values using WHO-TEQ_{2005} (Van den Berg et al., 2006). WHO-TEQ_{2005} values were calculated in 'upperbound', assuming the limit of detection (LOD) for those non-detected or below the LOD congeners. More detailed information on instrumental analysis is reported elsewhere (Zubero et al., 2011). The lipid content in the sample was measured by enzymatic methods (Patterson et al., 1991). The requirements for ensuring quality data include the application of quality assessment and quality control (QA/QC) measures. A survey of laboratory cross-contamination was demonstrated by the analysis of a control blanks every 20 serum samples. In addition, the analysis of a quality control sample every 20 serum samples is also part of the current analytical quality control practices.

2.6. Data treatment and statistical analysis

The study initially described various variables related to sociodemographics, reproductive factors, lifestyle, and food consumption using absolute frequencies and percentages for categorical variables and mean and standard deviation for quantitative variables.

For contaminants with concentrations below the limit of detection (LOD), a value equal to half the LOD was assigned. The study used the

Spearman rank correlation to examine the relationship between PCDD/F and dl-PCB congeners. A statistical descriptive analysis was conducted, which involved calculating the geometric means (GM), 95% confidence intervals (95%CI), and percentiles (25th, 50th, and 75th) of the lipid-corrected data for each group of pollutants.

The TEQ values (pg g^{-1}) of the 17 PCDD/F and 12 dl-PCB congeners were calculated based on their Toxic Equivalency Factors (TEFs) derived from the 2005 World Health Organization (WHO) system (Van den Berg et al., 2006). The geometric mean and 95% confidence intervals of each group of pollutants (PCDD/Fs, dl-PCBs and PCDD/Fs + dl-PCB) concentrations were calculated in relation to sociodemographic, lifestyle, reproductive and food consumption variables. Independent samples t-tests and ANOVA tests were used for comparisons. Prior to the statistical tests, log-transformation was applied to all biomarkers of exposure due to their asymmetry, as determined by the Shapiro-Wilk test ($p < 0.05$). Variables with a p-value <0.1 were included in subsequent multiple linear regression analyses, which employed a backward stepwise approach.

The variables study area, age, and gender were retained as study design variables in the multiple linear regression models. Food intakes in grams per day (g/day) were categorized based on their median values. The concentrations of dioxins, furans, and dl-PCBs were expressed in picograms of compound per gram of lipid (pg g-1 lipid) and in WHO-TEQ2005. Statistical analyses were conducted using the R Studio software (4.2.1).

3. Results

Table 1 shows the characteristics of the samples. The total number of participants in the study was 227. The 53.7% of the participants lived in zone 1, and slightly more than half of the participants were women (52.9%). The average age was 45.8 (standard deviation 12.7) years, 33.5% were under 40 years of age, 35.2% were between 41 and 53 years old, and 31.3% were older than 54 years. Regarding weight, 44.9% of the participants had a normal weight, 54.2% had overweight or were obese. Among the sample, 57.7% of the participants reported weight change in the previous 5 years, 35.7% having put on weight and 22% having lost weight. In terms of education level, 34.4% had a university degree, 43.2% had secondary studies and 22.5% had completed primary education. In relation to social habits, 17.2% smoked daily and 9.7% consumed alcohol daily. Among the female participants, 38.3% had menopause, 70.8% had children and 62.5% had breastfed. Regarding food consumption, 92% of the participants reported consuming locally sourced food, garden products the most consumed group (79.7%), followed by cheese (64.3%), poultry (59.5%) and milk (22.5%). Median food consumption (g/day) was 168.40 for vegetables, followed by fruits (136.17), fish (175.23), meat (160.68), cereals and pasta (134.40), dairy (87.07), canned (36.0) and oil (16.50).

Table 2 presents the geometric means (GM) (95% CI), minimum and maximum values and medians with the 25th and 75th percentiles of the PCDD/F and dl-PCB values of each congener, as well as the WHO-TEQ_{2005} values and sums. The total geometric mean WHO-TEQ_{2005} value for compounds with dioxin activity was 10.58 pg WHO-TEQ_{2005} g^{-1}, being 7.0 pg WHO-TEQ_{2005} $g^{-1}$and 3.35 pg WHO-TEQ_{2005} g^{-1} the values for dioxin-furans and total PCBs, respectively. The samples with furan levels under the limit of quantification (LOD) ranged between 0% and 93.8%, and, in the case of dioxins, between 0% and 15.8%. On the other hand, the majority of mono-ortho PCBs were above the LOD and the *non-ortho* percentage under the LOD ranged between 0% and 69.2%. We observed high concentrations of *mono-ortho* PCBs, but since they have a low toxicity, their contribution to the WHO-TEQ_{2005} is small.

Regarding the contributions of each congener to total PCDD, PCDF and PCDD/F, OCDD contributed the most to the total PCDD (71%); 2,3,4,7,8-PeCDF to the total PCDF (22%), and OCDD to the sum PCDD/F (56%) (Fig. 2). PCB-118 had the highest contribution among dl-PCBs (36%). No significant differences were observed between zones in the

Table 1
Characteristics of the samples (N = 227). Anthropometric, socioeconomic and habit variables.

Variable		N (%) Mean (SD)[a]	Missing
Zone	Zone 1	122 (53.7%)	0 (0%)
	Zone 2	105 (46.3%)	
Age (years)		45.8 (12.7)[a]	0 (0%)
Age (tertiles)	≤40	76 (33.5%)	0 (0%)
	41 a 53	80 (35.2%)	
	≥54	71 (31.3%)	
Gender	Male	107 (47.1%)	0 (0%)
	Female	120 (52.9%)	
BMI(kg/m^2)			
<18.5 kg m^{-2}	Under weight	2 (0.8%)	0 (0%)
18.5–24.9 kg m^{-2}	Normal weight	102 (44.9%)	
25.0–29.9 kg m^{-2}	Overweight	76 (33.5%)	
≥30.3 kg m^{-2}	Obesity	47 (20.7%)	
BMI(kg m^{-2})		26.3 (4.3%)	
Weight change last 5 years	Put on weight	81 (35.7%)	11
	Lost weight	50 (22.0%)	(4.8%)
	No change	85 (37.4%)	
Educational level	Primary school	51 (22.5%)	0 (0%)
	Secondary school	98 (43.2%)	
	University	78 (34.4%)	
Social class	Manual	127 (55.9%)	0 (0%)
	Non- manual	100 (44.1%)	
Tobacco consumption	Non- smoker	99 (43.6%)	
	Ex- smoker	70 (30.8%)	
	Occasional smoker	18 (7.93%)	
	Smoker	39 (17.2%)	
Alcohol consumption	Non-drinker	28 (12.3%)	1 (0.4%)
	Occasional drinker	111 (48.9%)	
	Weekends drinker	65 (28.6%)	
	Daily consumption	22 (9.7%)	
Locally produced food consumption	Yes	209 (92.1%)	2 (0.8%)
	No	16 (7.1%)	
Local milk	Yes	51 (22.5%)	4 (1.7%)
	No	172 (75.8%)	
Local cheese	Yes	146 (64.3%)	9 (3.9%)
	No	72 (31.7%)	
Local vegetable products	Yes	181 (79.7%)	4 (1.7%)
	No	42 (18.5%)	
Local poultry	Yes	135 (59.5%)	3 (1.3%)
	No	89 (39.2%)	
Menopause[b]	Yes	46 (38.3%)	1 (0.8%)
	No	73 (60.8%)	
Parity[b]	Yes	85 (70.8%)	1 (0.8%)
	No	34 (28.3%)	
Breastfed[b]	Yes	75 (62.5%)	1 (0.8%)
	No	44 (36.7%)	
Dietary Variables	Median (g/day)	N (%)	Missing
Vegetables	≤168.40	164 (72.2%)	1 (0.4%)
	>168.40	62 (27.3%)	
Meat	≤160.68	115 (50.7%)	1 (0.4%)
	>160.68	111 (48.9%)	
Fish	≤175.23	153 (67.4)	1 (0.4%)
	>175.23	73 (32.2%)	

(*continued on next page*)

Table 1 (*continued*)

Dietary Variables	Median (g/day)	N (%)	Missing
Dairy	≤87.07	151 (66.5%)	2 (0.8%)
	>87.17	74 (32.6%)	
Canned	≤36.00	156 (68.7%)	1 (0.4%)
	>36.00	70 (30.8%)	
Fruit	≤136.17	114 (50.2%)	2 (0.8%)
	>136.17	111 (48.9%)	
Cereals and pasta	≤134.40	131 (57.7%)	3 (1.3%)
	>134.40	93 (41.0%)	
Oil	≤16.50	176 (77.5%)	2 (0.8%)
	>16.50	49 (21.6%)	

*SD: Standard deviation.
[a] SD: Standard deviation.
[b] Only for women.

contribution of congeners. Regarding the correlations (Fig. 3), the congeners 1,2,3,6,7,8-HxCDD and 2,3,4,7,8-PeCDF showed high positive correlations with all congeners. However, the most abundant congener (OCDD) had a low correlation with other congeners. The dl-PCBs exhibited high levels of correlation among themselves.

Table 3 shows the geometric mean (GM) and 95% CIs for each pollutant in relation to socio-demographic, reproductive, lifestyle and food consumption variables. There were no statistically significant differences observed between study zones for any pollutant. Men had higher levels of dl-PCBs compared to women ($p = 0.003$). However, no significant differences were found for PCDD/Fs. Older participants had higher levels of both PCDD/Fs ($p < 0.001$) and dl-PCBs ($p < 0.001$) compared to younger participants. Similarly, participants with higher BMI had higher levels of PCDD/Fs ($p = 0.020$) and dl-PCB levels ($p = 0.022$) compared to those with normal weight. A significant inverse relationship was found between the level of education and pollutant levels. Higher education levels were associated with lower levels of all pollutants, with statistically significant differences observed for all of the pollutants. Menopausal women had higher levels of PCDD/Fs and dl-PCBs, and women with children had higher levels of PCDD/Fs ($p = 0.049$) and total dioxin-like ($p = 0.035$) compounds, with dl-PCBs, levels approaching statistical significance ($p = 0.069$). Concerning to smoking

Table 2
Levels of PCDD/Fs and dl-PCBs (pg g^{-1} lipid) in serum, Toxic Equivalent Factor (WHO TEF), WHO-TEQ_{2005} (pg g^{-1} lipid) values.

	N < LOD	%< LOD	GM [CI95%]	Median [P25, P75]	Min	Max	WHO TEF 2005	WHO-TEQ_{2005}
DIOXINS								
2,3,7,8-TCDD	10	4.4	0.82 [0.76, 0.88]	0.83 [0.56, 1.19]	0.06	3.10	1	0.82
1,2,3,7,8-PeCDD	4	1.7	2.36 [2.19, 2.55]	2.49 [1.66, 3.52]	0.39	9.26	1	2.36
1,2,3,4,7,8-HxCDD	36	15.8	1.34 [1.25, 1.44]	1.36 [0.92, 2.05]	0.14	4.26	0.1	0.13
1,2,3,6,7,8-HxCDD	0	0	8.42 [7.59, 9.33]	8.63 [4.56, 15.73]	0.93	44.82	0.1	0.84
1,2,3,7,8,9-HxCDD	34	14.9	1.94 [1.80, 2.08]	2.01 [1.30, 2.93]	0.40	6.26	0.1	0.19
1,2,3,4,6,7,8-HpCDD	2	0.8	8.37 [7.79, 9.00]	8.41 [5.72, 11.40]	2.66	50.75	0.01	0.08
D_OCDD	0	0	65.19 [60.73, 69.98]	62.87 [45.72, 88.28]	20.42	256.23	0.0003	0.02
TOTAL DIOXINS								**4.68**
FURANS								
2,3,7,8-TCDF	14	6.2	0.50 [0.45, 0.55]	0.50 [0.29, 0.76]	0.05	18.48	0.1	0.05
1,2,3,7,8-PeCDF	11	4.8	1.03 [0.96, 1.11]	1.00 [0.74, 1.52]	0.13	3.95	0.03	0.03
2,3,4,7,8-PeCDF	0	0	4.69 [4.38, 5.02]	4.71 [3.31, 7.04]	0.77	16.14	0.3	1.41
1,2,3,4,7,8-HxCDF	6	2.6	1.91 [1.80, 2.03]	1.96 [1.42, 2.56]	0.19	4.91	0.1	0.19
1,2,3,6,7,8-HxCDF	4	1.7	2.25 [2.12, 2.39]	2.23 [1.65, 3.19]	0.30	6.35	0.1	0.22
2,3,4,6,7,8-HxCDF	68	28.9	0.94 [0.86, 1.03]	1.04 [0.70, 1.45]	0.03	3.95	0.1	0.09
1,2,3,7,8,9-HxCDF	58	25.5	1.27 [1.19, 1.37]	1.32 [0.96, 1.77]	0.11	4.88	0.1	0.13
1,2,3,4,6,7,8-HpCDF	24	10.5	2.57 [2.39, 2.75]	2.41 [1.90, 3.35]	0.67	90.52	0.01	0.03
1,2,3,4,7,8,9-HpCDF	213	93.8	1.71 [1.61, 1.82]	1.81 [1.30, 2.29]	0.49	3.35	0.01	0.02
F_OCDF	108	47.5	4.11 [3.83, 4.42]	4.05 [2.94, 5.49]	0.79	24.24	0.0003	0.00
TOTAL FURANS								**2.27**
TOTAL DIOXIN + FURANS								**7.00**
NON-ORTHO PCB								
PCB-77	0	0	21.35 [19.75, 23.08]	19.65 [14.80, 25.22]	6.52	200.00	0.0001	0.00
PCB-81	157	69.2	2.03 [1.85, 2.21]	2.09 [1.38, 3.15]	0.19	8.65	0.0003	0.00
PCB-126	2	0.8	19.03 [17.40, 20.81]	19.21 [11.77, 29.67]	2.64	197.25	0.1	1.9
PCB-169	4	1.7	30.46 [27.65, 33.54]	33.95 [17.87, 54.38]	2.84	135.50	0.03	0.91
TOTAL NON-ORTHO PCB								**2.92**
MONO-ORTHO PCB								
PCB-105		0	0	963.54 [889.06, 1044.26]	924.31 [634.01, 1432.64]	188.74	6997.07	0.00003
PCB-114		0	0	303.90 [274.02, 337.04]	303.43 [170.28, 567.72]	35.12	2158.31	0.00003
PCB-118		0	0	4829.71 [4427.03, 5269.01]	4648.82 [3151.61, 7520.78]	737.47	47815.63	0.00003
PCB-123		5	2.3	55.82 [51.10, 60.97]	53.24 [35.83, 81.42]	10.26	675.41	0.00003
PCB-156		0	0	3999.72 [3554.02, 4501.31]	4639.62 [1986.00, 8180.91]	246.13	22283.74	0.00003
PCB-157		0	0	828.66 [739.91, 928.04]	913.98 [444.68, 1577.93]	58.78	5236.63	0.00003
PCB-167		0	0	1371.39 [1229.18, 1530.06]	1365.71 [784.89, 2440.71]	114.88	13535.82	0.00003
PCB-189		0	0	805.10 [709.29, 913.85]	1071.41 [403.68, 1654.17]	32.14	3826.88	0.00003
TOTAL MONO-ORTHO PCB								
TOTAL dl-PCB								
TOTAL								

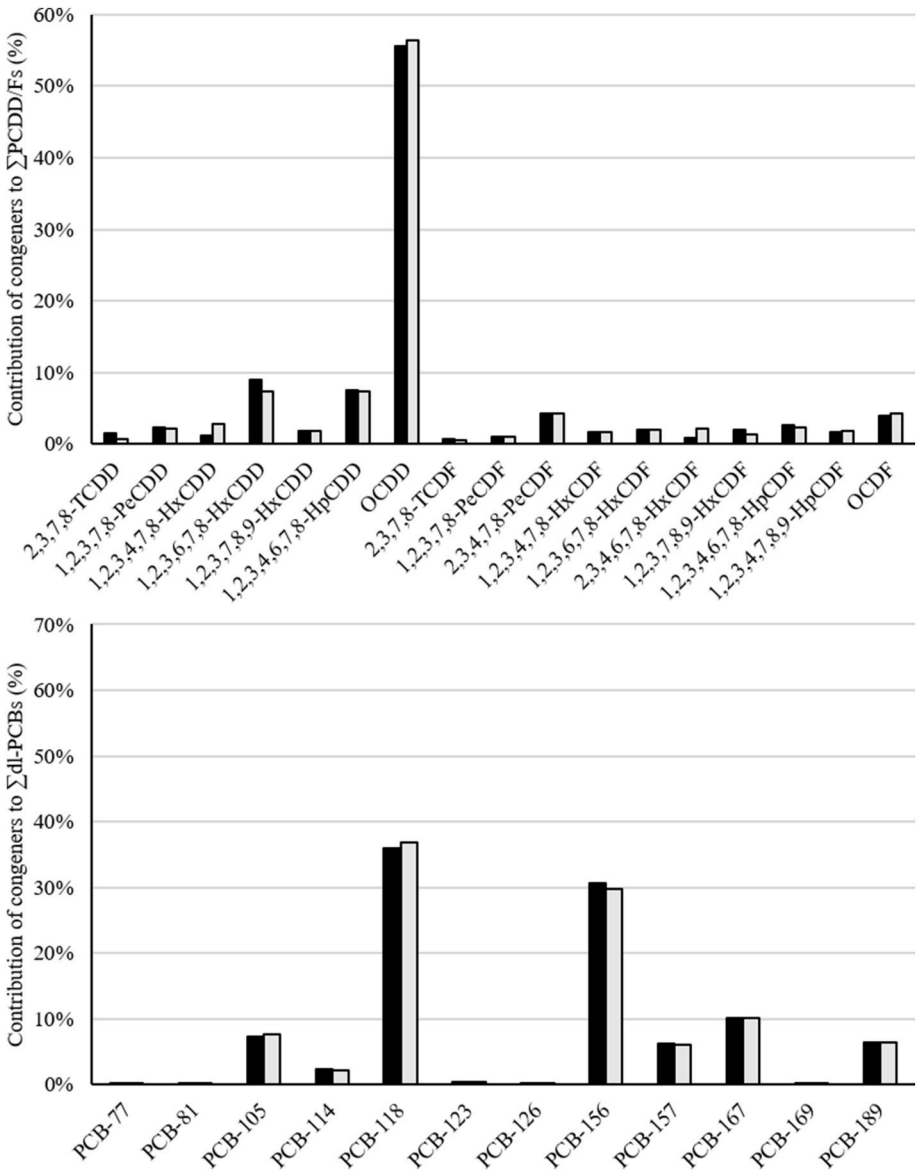

Fig. 2. Composition profiles based on the relative contribution (%) of each PCDD/Fs congener to ∑PCDD/Fs and dl-PCB congeners to ∑dl-PCBs in terms of concentrations for different zones (Zone 1 and 2).

consumption, smokers had lower levels of dl-PCBs compared to non-smokers ($p = 0.002$). Participants who consumed alcohol had higher levels of dl-PCBs compare to non-consumers ($p < 0.001$). Participants who did not consume local milk had higher levels of dl-PCBs, but no differences were found in other products. Subjects who reported higher consumption of oils, cereals, and pasta had significantly lower levels of PCDD/Fs and the sum of PCDD/Fs and dl-PCBs.

Multiple lineal regression analysis (Table 4) showed a positive association between PCDD levels and Zone 1. The analysis suggests that samples from Zone 1 had higher levels of PCDD compared to samples from Zone 2. The results indicate that as age increases, the levels of all three contaminants also tend to increase. It implies that older individuals may have accumulated higher levels of contaminants over time. The analysis revealed that the levels of dl-PCBs were lower in women compared to men. The study found that individuals who consumed local poultry had significantly higher levels of contaminants compared to non-consumers. In relation to the diet, higher oil consumption was associated with lower levels of contaminants. This implies that individuals who reported consuming more oil had relatively lower levels of contaminants. Regarding lifestyles, smokers had lower dl-PCB levels compared to non-smokers, indicating that smoking may interfere with dl-PCB metabolism and elimination. Additionally, the analysis showed that drinkers had higher levels of contaminants compared to non-drinkers, suggesting that alcohol consumption may be associated with increased contaminant exposure. Similar results were obtained when conducted separate analyses for each gender (Tables S1 and S2).

4. Discussion

The study found that the TEQ values for PCDD/Fs and dl-PCBs in the population (10.58 pg WHO-TEQ2005 g-1) were found to be similar to those reported in previous studies analysing baseline levels in general populations (Table 5), such as in the studies by Harden et al. (2007) and Rawn et al. (2012), and were lower than those reported in general population studies conducted in France (Frery et al., 2007), Japan (Uemura et al., 2009; Arisawa et al., 2011), Taiwan (Hsu et al., 2009) and the USA (Lakind et al., 2009).

Additionally, the levels of PCDD/Fs and dl-PCBs observed in the Gipuzkoa population were comparable to those reported in a study conducted in the Basque Country in 2013 by Zubero et al. (2017), which

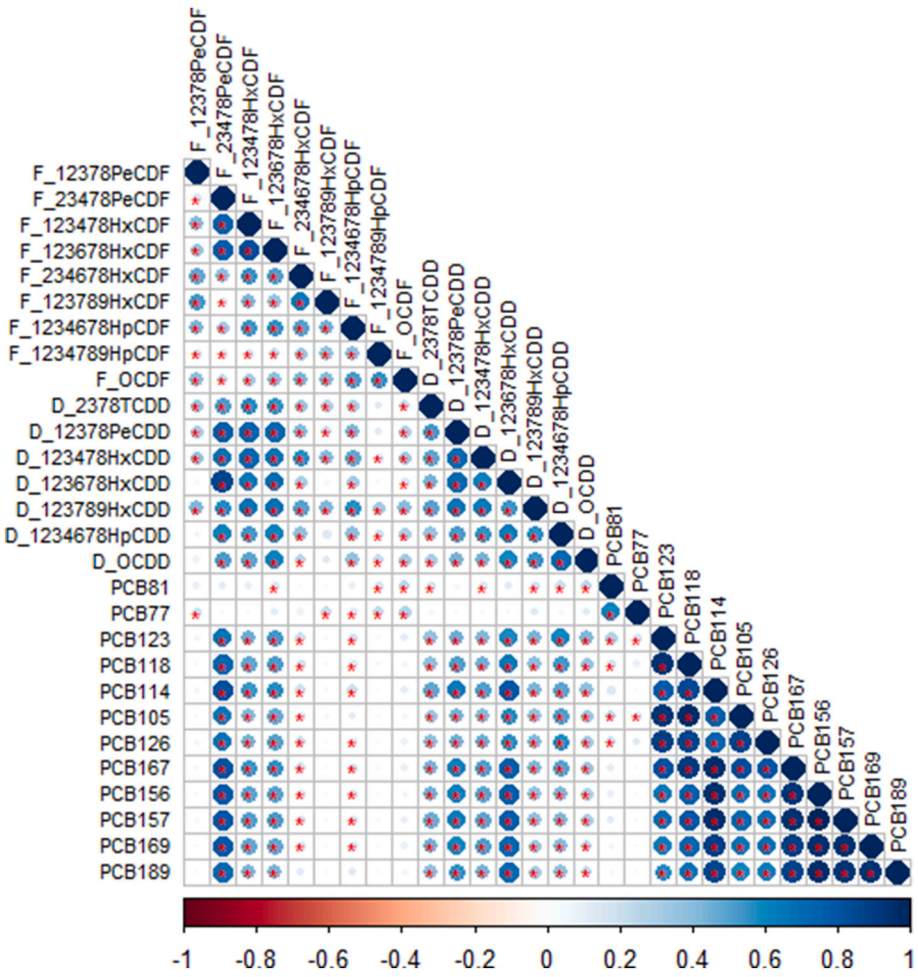

Fig. 3. PCDD/F and dl-PCB congeners Spearman rank correlation analysis results.* indicate the ones statistically significant.

is geographically and temporally close to the present study. The percentage of the contributions of the congeners of PCDD/Fs and dl-PCBs found in serum samples in this study were similar to those observed in studies conducted on general populations, such as the studies by Arisawa et al. (2011), Fromme et al. (2015), and Gao et al. (2019). The contribution of the congeners were also similar to those found in studies examining PCDD/Fs and dl-PCBs in food samples, such as studies by Marin et al. (2011), Llobet et al. (2003), Bocio and Domingo (2005), a nd Bordajandi et al. (2004). However, Santa-Marina et al., (2023) noted that the contribution of PCDD/Fs and dl-PCBs congeners found in air samples within the same study area were different from those observed in serum samples. This difference indicates that the primary exposure to these compounds in the population is through dietary intake rather than inhalation. In this study, one of the key factors considered is the variable "zone". The study was designed to establish the levels of dioxins-furans and PCBs in serum samples in the general population residing near and far from an ERP under construction. Taking this into consideration, the comparison of contaminant levels in the population residing in both zones will allow to evaluate the potential impact of the ERP. Regarding the variables associated with PCDD/Fs and dl-PCB levels in population, the study area was not associated with the levels of contaminants measured in serum in the bivariate analysis. However, after adjusting for other variables, the difference in PCDD levels between residents of zone 1 and zone 2 became evident. This finding is consistent with the higher levels of PCDDs found in the air of zone 1, as reported in the study by Santa-Marina et al. (2023).

The study found significantly higher PCDD/F and dl-PCB levels in older people, which is consistent with expectations because these compounds are persistent and tend to accumulate in the body over time. Previous studies (Chovancová et al., 2012; Mrema et al., 2014; Whong et al., 2015; Raffetti et al., 2017; Lin et al., 2018; Coakley et al., 2018; Muzembo et al., 2019) have also reported a positive relationship between higher PCDD/F and dl-PCB levels and age. Gender was identified as a determining factor in the body burdens of PCDD/Fs and dl-PCBs. Some studies have reported higher levels of PCDD/Fs in women, which has been attributed to their higher intake of fatty products through the diet (Reis et al., 2007a; Knutsen et al., 2011). However, other studies have found no difference in levels between genders (Harden et al., 2007; Coakley et al., 2018). On the other hand, the study observed higher levels of dl-PCBs in men compared to women, but no significant differences were found for PCDD/Fs. These results align with a study by Zubero et al. (2017) conducted in the Basque Country. The stratified analysis by sex revealed that women who had breastfed had lower levels of these compounds, with significant differences found for dl-PCBs. This finding is consistent with previous studies (Humblet et al., 2011; Mrema et al., 2014; Zubero et al., 2017).Overall, these results provide valuable insights into the age and gender-related differences in the accumulation of these persistent organic pollutants in the human body. It also suggests that breastfeeding may have a protective effect against the accumulation of dl-PCBs.

This study found lower levels of dl-PCBs in smokers, which is consistent with the results reported by Chen et al. (2005) and Zani et al. (2019) who also found higher dl-PCB levels in non-smokers compared to smokers. On the other hand, studies by Chang et al. (2020), Helou et al. (2021), and Lan et al. (2021) did not find any association between dl-PCB levels and smoking. Jain and Wang (2011) reported an

Table 3
Geometric mean and 95% confidence intervals (95% CI) for levels of PCDD/Fs, dl-PCBs and PCDD/F + dl-PCB (pg WHO-TEQ_{2005} g^{-1} lipid) as a function of socio-economic characteristics and p-values for independent comparison means in ln scale (*t*-test and ANOVA).

		PCDD/F	dl-PCB	PCDD/F + dl-PCB
		GM [95% CI]	GM [95% CI]	GM [95% CI]
TOTAL		7.00 [6.59, 7.44]	3.35 [3.08, 3.64]	10.58 [9.93, 11.28]
Zone	Zone 1	7.39 [6.81, 8.01]	3.49 [3.12, 3.91]	11.11 [10.21, 12.09]
	Zone 2	6.58 [6.00, 7.22]	3.20 [2.82, 3.63]	10.01 [9.09, 11.02]
	p-value	*0.063*	*0.312*	*0.108*
Age, years	≤40	5.26 [4.67, 5.93]	2.05 [1.79, 2.35]	7.49 [6.69, 8.38]
	41–53	6.79 [6.29, 7.33]	3.27 [2.96, 3.62]	10.26 [9.53, 11.04]
	>54	9.57 [8.79, 10.42]	5.52 [4.88, 6.24]	15.33 [13.99, 16.81]
	p-value	***<0.001***	***<0.001***	***<0.001***
Age, years (continuous)	p-value	***<0.001***	***<0.001***	***<0.001***
Gender	Men	7.18 [6.61, 7.81]	3.82 [3.40, 4.29]	1.25 [10.33, 12.26]
	Female	6.85 [6.26, 7.49]	2.98 [2.65, 3.36]	10.03 [9.13, 11.00]
	p-value	0.44	**0.003**	0.073
Body mass index (kg/m$^{2)}$	Under weight	12.22 [0.0, 44478.24]	3.92 [0.0, 53256.46]	16.15 [0.00, 80976.83]
	Normal weight	6.43 [5.82, 7.10]	2.94 [2.59, 3.34]	9.59 [8.68, 10.61]
	Overweight	7.92 [6.99, 8.96]	4.12 [3.41, 4.98]	12.24 [10.65, 14.08]
	Obesity	7.18 [6.56, 7.86]	3.50 [3.05, 4.02]	10.92 [9.91, 12.03]
	p-value	***0.020***	***0.022***	***0.016***
Body mass index (kg m^{-2}) (continuous)	p-value	*0.079*	***0.013***	***0.034***
Weight change last 5 years	No changes	6.91 [6.23, 7.67]	3.45 [3.02, 3.94]	10.61 [9.56, 11.78]
	Put on weight	7.94 [7.03, 8.98]	3.63 [3.05, 4.32]	11.79 [10.37, 13.41]
	Lost weight	6.70 [6.05, 7.43]	3.21 [2.76, 3.73]	10.14 [9.07, 11.34]
	p-value	*0.113*	*0.544*	*0.221*
Education level	Primary	7.98 [7.01, 9.09]	4.04 [3.35, 4.87]	12.23 [10.60, 14.11]
	Secondary	7.21 [6.57, 7.91]	3.31 [2.90, 3.77]	10.78 [9.79, 11.87]
	University	6.20 [5.60, 6.86]	3.02 [2.64, 3.44]	9.41 [8.49, 10.44]
	p-value	***0.007***	***0.04***	***0.01***
Social class	Manual	7.04 [6.49, 7.64]	3.22 [2.87, 3.62]	10.51 [9.64, 11.46]
	Non- manual	6.95 [6.33, 7.63]	3.52 [3.12, 3.98]	10.68 [9.71, 11.76]
	p-value	*0.832*	*0.294*	*0.798*
Tobacco consumption	Non smoker	6.86 [6.21, 7.56]	3.37 [2.95, 3.85]	10.47 [9.45, 11.61]
	Ex-smoker	7.53 [6.78, 8.38]	4.02 [3.50, 4.62]	11.76 [10.55, 13.11]
	Occasionally	6.38 [5.20, 7.82]	3.11 [2.36, 4.10]	9.66 [7.86, 11.88]
	Regular smoker	6.76 [5.82, 7.86]	2.48 [2.03, 3.03]	9.40 [8.05, 10.97]
	p-value	*0.415*	***0.002***	*0.1*
Alcohol consumption	Non drinker	7.06 [5.66, 8.82]	2.95 [2.24, 3.89]	10.21 [8.14, 12.81]
	Occasionally	6.78 [6.23, 7.39]	3.01 [2.68, 3.38]	10 [9.16, 10.9]
	Weekends	6.83 [6.11, 7.63]	3.51 [3.03, 4.06]	10.56 [9.43, 11.82]
	Daily drinker	8.83 [7.40, 10.54]	5.94 [4.56, 7.74]	15.02 [12.24, 18.42]
	p-value	*0.103*	***<0.001***	***0.004***
Locally produced food consumption	Yes	7.07 [6.64, 7.52]	3.37 [3.10, 3.67]	10.67 [10.00, 11.38]
	No	6.12 [4.45, 8.43]	2.89 [1.84, 4.53]	9.26 [6.61, 12.98]
	p-value	*0.362*	*0.485*	*0.395*
Local milk	Yes	6.66 [5.84, 7.59]	2.81 [2.34, 3.36]	9.71 [8.50, 11.1]
	No	7.11 [6.62, 7.63]	3.52 [3.20, 3.87]	10.84 [10.07, 11.68]
	p-value	*0.384*	***0.029***	*0.152*
Local cheese	Yes	7.14 [6.65, 7.67]	3.37 [3.05, 3.71]	10.74 [9.98, 11.55]
	No	6.87 [6.08, 7.76]	3.42 [2.91, 4.03]	10.52 [9.27, 11.94]
	p-value	*0.587*	*0.862*	*0.782*
Local vegetables	Yes	7.13 [6.68, 7.62]	3.42 [3.13, 3.74]	10.78 [10.08, 11.53]
	No	6.46 [5.44, 7.67]	3.03 [2.36, 3.87]	9.73 [8.07, 11.72]
	p-value	*0.282*	*0.349*	*0.3*
Local poultry	Yes	7.28 [6.72, 7.88]	3.54 [3.17, 3.95]	11.09 [10.21, 12.04]
	No	6.59 [5.97, 7.28]	3.04 [2.67, 3.46]	9.80 [8.85, 10.86]
	p-value	*0.125*	*0.078*	*0.064*
Menopause[a]	Yes	8.94 [8.02, 9.96]	4.35 [3.68, 5.15]	13.54 [12.01, 15.26]
	No	5.80 [5.16, 6.51]	2.35 [2.04, 2.70]	8.31 [7.40, 9.32]
	p-value	***<0.001***	***<0.001***	***<0.001***
Parity[a]	Yes	7.24 [6.51, 8.07]	3.18 [2.74, 3.69]	10.67 [9.54, 11.94]
	No	5.97 [5.07, 7.02]	2.53 [2.08, 3.09]	8.60 [7.27, 10.18]
	p-value	***0.049***	*0.069*	***0.035***
Breastfed[a]	Yes	7.12 [6.34, 7.99]	3.08 [2.63, 3.60]	10.45 [9.28, 11.78]
	No	6.43 [5.55, 7.44]	2.82 [2.33, 3.42]	9.36 [8.00, 10.94]
	p-value	*0.273*	*0.486*	*0.262*

			PCDD/F	dl-PCB	PCDD/F + dl-PCB
			GM [95% CI]	GM [95% CI]	GM [95% CI]
Vegetables	≤168.40		7.12 [6.62, 7.65]	3.34 [3.02, 3.70]	10.68 [9.89, 11.53]
	>168.40		6.72 [5.98, 7.56]	3.39 [2.90, 3.95]	10.36 [9.21, 11.66]
	p-value		*0.410*	*0.878*	*0.671*
Meat	≤160.68		7.15 [6.53, 7.84]	3.41 [3.01, 3.85]	10.79 [9.80, 11.87]
	>160.68		6.86 [6.32, 7.45]	3.30 [2.93, 3.71]	10.4 [9.54, 11.33]

(*continued on next page*)

Table 3 (*continued*)

		PCDD/F	dl-PCB	PCDD/F + dl-PCB
		GM [95% CI]	GM [95% CI]	GM [95% CI]
	p-value	*0.499*	*0.698*	*0.569*
Fish	≤175.23	6.99 [6.48, 7.54]	3.47 [3.14, 3.83]	10.65 [9.84, 11.53]
	>175.23	7.04 [6.33, 7.83]	3.12 [2.66, 3.66]	10.47 [9.36, 11.7]
	p-value	*0.912*	*0.265*	*0.796*
Dairy	≤87.07	7.18 [6.64, 7.77]	3.54 [3.18, 3.94]	10.98 [10.11, 11.92]
	>87.17	6.68 [6.05, 7.36]	3.03 [2.65, 3.47]	9.89 [8.95, 10.94]
	p-value	*0.247*	*0.074*	*0.112*
Fruit	≤136.17	7.2 [6.63, 7.81]	3.17 [2.84, 3.55]	10.56 [9.69, 11.50]
	>136.17	6.8 [6.20, 7.46]	3.51 [3.09, 3.98]	10.56 [9.59, 11.63]
	p-value	*0.365*	*0.241*	*0.994*
Canned	≤36.00	7.15 [6.65, 7.69]	3.34 [3.02, 3.68]	10.71 [9.94, 11.54]
	>36.00	6.69 [5.96, 7.51]	3.39 [2.87, 4.01]	10.34 [9.12, 11.72]
	p-value	*0.331*	*0.873*	*0.631*
Cereals and pasta	≤134.40	7.57 [7.00, 8.2]	3.56 [3.18, 3.97]	11.37 [10.46, 12.36]
	>134.40	6.27 [5.70, 6.90]	3.07 [2.70, 3.50]	9.55 [8.65, 10.54]
	p-value	***0.003***	*0.091*	***0.008***
Oil	≤16.50	7.29 [6.79, 7.82]	3.46 [3.15, 3.81]	10.99 [10.22, 11.82]
	>16.50	6.04 [5.37, 6.80]	2.91 [2.41, 3.50]	9.14 [8.04, 10.40]
	p-value	***0.008***	*0.095*	***0.015***

[a] Only for women.

interaction between caffeine consumption and smoking, with smokers who consumed caffeine having lower levels of PCBs compared to non-smokers. Unfortunately, in our case was unable to analyse this relationship as the caffeine intake variable was not included. When stratifying by gender, our study found significantly lower levels of dl-PCBs in male smokers and in female ex-smokers. In contrast, Fierens et al. (2007) observed lower levels in women smokers compared to men. The authors suggested that these differences could be attributed to a higher metabolism rate in female smokers. It is known that smoking can induce the cytochrome CYP1A enzyme (Buchthal et al., 1995), so further research is needed to examine the specific effect of smoking on the metabolization of PCBs. Regarding alcohol consumption, our study found that daily consumers had the highest levels of PCBs. Similar findings have been reported in studies conducted in Japan by Arisawa et al. (2011) and in Lebanon by Harmouche-Karaki et al. (2019). However, Lan et al. (2021) did not find any associations between alcohol drinking and PCB levels in serum in their study. In conclusion, the relationship between smoking, caffeine consumption, alcohol drinking, and dl-PCB levels is complex and not yet fully understood. Further research is necessary to clarify the mechanisms behind these associations and to account for potential confounding factors.

We also found significantly higher levels for all the compounds analysed in people that reported consuming local poultry. Studies that have analysed the levels of PCDDs, PCDFs and PCBs in eggs and poultry, indicate that locally produced foods have been found to contain higher levels of these contaminants (EFSA CONTAM Panel, 2018; Weber et al., 2015; Rusin et al., 2019). This suggests that the source of contamination is likely related to the local environment. Soil is identified as the primary source of contamination, especially in areas with industrialization and high traffic density. This finding suggests that industrial activities and traffic contribute to the environmental presence of PCDDs, PCDFs, and PCBs in the study area, potentially leading to their accumulation in the

Table 4
Linear regression models for levels of PCDD/Fs, dl-PCBs and total (PCDD/Fs + dl-PCBs) in WHO-TEQ$_{2005}$ (pg g^{-1} lipid) in ln scale.

TOTAL	ln_PCDD	ln_PCDF	ln_PCDD/F	ln_dl-PCB	ln PCDD/F + dl-PCB
Zone					
Zone 1	0 (Ref.)	0 (Ref.)	0 (Ref.)	0 (Ref.)	0 (Ref.)
Zone 2	**−0.121 (-0.242, -0.0002)**	−0.054 (−0.158, 0.05)	−0.1 (−0.21, 0.011)	−0.105 (−0.232, 0.022)	−0.103 (−0.208, 0.003)
Age, years	**0.019 (0.014, 0.024)**	**0.015 (0.01, 0.019)**	**0.017 (0.013, 0.022)**	**0.031 (0.025, 0.036)**	**0.022 (0.017, 0.026)**
Gender					
Male	0 (Ref.)	0 (Ref.)	0 (Ref.)	0 (Ref.)	0 (Ref.)
Female	−0.044 (−0.166, 0.078)	−0.052 (−0.157, 0.053)	−0.049 (−0.161, 0.063)	**−0.225 (-0.354, -0.097)**	−0.106 (−0.213, 4.38e^{-05})
Tobacco consumption					
Non smoker	0 (Ref.)	0 (Ref.)	0 (Ref.)	0 (Ref.)	0 (Ref.)
Ex-smoker	−0.109 (−0.256, 0.038)	−0.122 (−0.248, 0.004)	−0.11 (−0.244, 0.024)	**−0.182 (-0.336, -0.028)**	**−0.135 (-0.263, -0.008)**
Smoker	−0.125 (−0.274, 0.024)	−0.126 (−0.254, 0.001)	−0.126 (−0.262, 0.01)	**−0.354 (-0.51, -0.198)**	**−0.201 (-0.33, -0.072)**
Alcohol consumption					
Non drinker	0 (Ref.)	0 (Ref.)	0 (Ref.)	0 (Ref.)	0 (Ref.)
Occasionally	0.02 (−0.169, 0.209)	0.048 (−0.114, 0.21)	0.028 (−0.145, 0.2)	0.108 (−0.09, 0.307)	0.052 (−0.112, 0.216)
Weekends	−0.035 (−0.24, 0.171)	−0.019 (−0.195, 0.157)	−0.031 (−0.218, 0.157)	0.129 (−0.087, 0.344)	0.019 (−0.159, 0.197)
Daily drinker	0.065 (−0.201, 0.33)	0.141 (−0.088, 0.369)	0.087 (−0.156, 0.33)	**0.361 (0.082, 0.64)**	0.183 (−0.048, 0.414)
Local poultry					
No	0 (Ref.)	0 (Ref.)	0 (Ref.)	0 (Ref.)	0 (Ref.)
Yes	**0.145 (0.023, 0.268)**	**0.182 (0.077, 0.287)**	**0.156 (0.045, 0.268)**	**0.209 (0.08, 0.337)**	**0.181 (0.074, 0.287)**
Cereals and pasta					
≤134.40	0 (Ref.)	0 (Ref.)	0 (Ref.)	0 (Ref.)	0 (Ref.)
>134.40	−0.103 (−0.23, 0.025)	−0.042 (−0.151, 0.067)	−0.084 (−0.20, 0.032)	0.044 (−0.09, 0.178)	−0.044 (−0.155, 0.067)
Oil					
≤16.50	0 (Ref.)	0 (Ref.)	0 (Ref.)	0 (Ref.)	0 (Ref.)
>16.50	−0.149 (−0.299, 0.0002)	**−0.133 (-0.262, -0.005)**	**−0.141 (-0.278, -0.004)**	**−0.189 (-0.346, -0.032)**	**−0.158 (-0.288, -0.028)**
R^2	0.303	0.273	0.304	0.503	0.417

Table 5
Arithmetic mean concentrations (pg TEQ g^{-1} lipid) of PCDD/Fs, dl-PCB and PCDD/Fs + dl-PCB in serum blood from general population obtained in this study and other studies worldwide with data from 2000 to 2022. Note that the used TEF equivalences for each reference are different.

Country	Study period	N	Subjects	PCDD/F	dl-PCB	PCDD/F + dl-PCB	TEQ	Notes	Reference
Spain	Feb–Apr 2018	227	General population. Age 18-70	7.00 (6.59–7.44)	3.35 (3.08–3.64)	10.58 (10.70–12.18)	WHO-TEQ_{2005}	Geometric mean and confidence interval values	Present study
Spain	2006	322	Residents in a district of Bilbao, living far/near a MSWI	23.5	15.6		WHO-TEQ_{1998}		Zubero et al. (2009)
Spain	2008	326	Residents in a district of Bilbao, living far/near a MSWI	23.6	23.6		WHO-TEQ_{1998}		Zubero et al. (2011)
Spain	2013	127	Residents in a district of Bilbao, living far/near a MSWI	6.1	10.7	16.8	WHO-TEQ_{2005}		Zubero et al., 2013
Spain	1995–2012	Exposed 68 Control 180	Residents of Mataró, living far/near a MSWI	14.4 (exposed) 15.3 (control)					Parera et al. (2013)
Spain	1999	20	Residents closed to HWI of Tarragona. Age 28-62	27.0 (14.8–48.9)			I-TEQ	Mean and range values	Schuhmacher et al., 1999
Spain	2018	20	Residents closed to HWI of Tarragona. Age 19-69	27.0			I-TEQ	Measured in plasma	Nadal et al. (2019)
Spain	2018	37	Residents closed to HWI of Tarragona. Age 19-69	6.8			I-TEQ	Temporal trends were observed since 1998. Measured in plasma	Nadal et al. (2019)
Portugal	Jan–Jun 2001	46	General population. Age 21-70	21.7			WHO-TEQ_{1998}		Calheiros et al. (2002)
Portugal	1999 and 2002	138	Residents living far/near a MSWI. Age 18-65	15.8 (Near) 15.3 (Far)			WHO-TEQ_{1998}		Reis et al. (2007a)
France	Mar–Jul 2005	1030	General population. Age 30-65	13.7		27.7	WHO-TEQ_{1998}	No differences in dioxin levels between inhabitants residing near an incinerator and those living in referent areas.	Frery et al. (2007)
Italy	2004	94	General population	22.0		54.0	WHO-TEQ_{1998}	Controls of subjects exposed to PCBSs	Turrio-Baldassarri et al. (2008)
Italy	May 2005	30	General population. Age 59-84	21.7		46.5	WHO-TEQ_{1998}	Residents in >2 km from a petrochemical plant, controls of residents <2 km	Consonni (2006)
Italy	May 2005–Dec 2006	74	Residents living far/near two MSWI. Age 27–67.	9.3 (Near) 9.1 (Far) 8.6 (Near) 8.0 (Far)			WHO-TEQ_{1998}	Volunteers resident in 2 cities >5 km from 2 MSWIs, controls of 4 groups of nearby residents	De Felip et al. (2008)
Italy	2013	85	Residents living near a WtE incinerator and farmers working and/or living in farms near the WtE			14.3	WHO-TEQ_{2005}	Basal levels, before the start-up of the WtE	Iamiceli et al., (2021)
Italy	2016	85	Residents living near a WtE incinerator and farmers working and/or living in farms near the WtE			11.3	WHO-TEQ_{2005}		Iamiceli et al., (2021)
Greece	Nov 2002–Feb 2004	10	Blood donors. Age 27-66	6.8			WHO-TEQ_{1998}		Costopoulou et al. (2006)

(*continued on next page*)

Table 5 (*continued*)

Country	Study period	N	Subjects	PCDD/F	dl-PCB	PCDD/F + dl-PCB	TEQ	Notes	Reference
Germany	Apr–Oct 2005	48	General population. Age 14-60	7.7		14.3	WHO-TEQ_{2005}	Residents in Munich or nearby	Fromme et al. (2009)
Germany	Feb–Mar 2013	70	General population. Age 4-76	6.3	4.4	10.7	WHO-TEQ_{2005}	Population near a factory for recycling of cables and electronic waste	Fromme et al. (2015)
Belgium	Oct–Dec 2000	232	Blood donors. Age 22-66	23.1			WHO-TEQ_{1998}	Samples taken after the 1999 incident of animal food contamination with PCDD/Fs and PCBs	Debacker et al. (2007)
Belgium	2000–2001	142	Residents living far/near a MSWI. Age 33-72	37.9 (Near) 24.1 (Near) 23.9 (Far)			WHO-TEQ_{1998}		Fierens et al. (2007)
Czech Republic	2003	20	Blood donors	8.9		24	WHO-TEQ_{1998}	Subject living 80 km from a chemical plant	Černá et al. (2007)
Slovakia	Aug 2001–Feb 2002	320	General population, adults.	15.0			WHO-TEQ_{1998}		Kocan et al. (2004)
Slovakia	Sep 2006–Mar 2007	126	General population. Age 24-76	14.5 (Exposed) 9.4 (Control)	22.6 (Exposed) 13.8 (Control)	38.4(Exposed) 22.9(Control)	WHO-TEQ_{1998}	81 subjects from areas close to MWI and metallurgical industries (Exposed) and 45 from non-dioxin exposed areas (Control)	Chovancová et al. (2012)
Norway	2003	High consumers 111 Control 73	Representative consumers, controls of subjects with high fish/game consumption in the Norwegian Fish and Game study			35.1 (High consumers) 28.7 (Control)	WHO-TEQ_{2005}		Kvalem et al. (2009)
Sweden	2006	Exposed 7 Control 8	Exposed and control residents near a saw-mill	39.2 (Exposed) 20.3 (Control)			WHO-TEQ_{2005}		Åberg et al. (2010)
USA	1999–2000		General population	15.4			WHO-TEQ_{2005}		Lakind et al., 2009
USA	2001–2002		General population	18.1			WHO-TEQ_{2005}		Lakind et al., 2009
USA	2003–2004		General population	13.9			WHO-TEQ_{2005}		Lakind et al., 2009
USA	May 2002	113	General population	20.2			WHO-TEQ_{1998}		Wong et al. (2008)
USA	2003	200	General population	34.0			WHO-TEQ_{1998}		Dahlgren et al. (2007)
USA	2004–2005	251	General population	15.1		18.5	WHO-TEQ_{2005}		Hedgeman et al. (2009)
Canada	2007–2009	4583	General population. Age 6-79			11.0	WHO-TEQ_{2005}	Samples from Candaian Health Measures Survey (CHMS)	Rawn et al. (2012)
Australia	Nov 2002–Apr 2003	9090	Random population. Age 16-60	6.9		10.9	WHO-TEQ_{1998}	Subjects from 5 different regions	Harden et al. (2004) Harden et al. (2007)
Japan	2002	259	General population	14.0		23.0	WHO-TEQ_{1998}	Based on Ministry of the Environment reports 2003	Arisawa et al. (2011)
Japan	2002	38	General population of rural area and urban area	16.5		25.8	WHO-TEQ_{2005}	Based on Ministry of the Environment reports 2007 and 2008	Furuya et al. (2010)
Japan	2004	38	General population of rural area and urban area	15.5		23.6	WHO-TEQ_{2005}	Based on Ministry of the Environment reports 2007 and 2008	Furuya et al. (2010)

(*continued on next page*)

Table 5 (*continued*)

Country	Study period	N	Subjects	PCDD/F	dl-PCB	PCDD/F + dl-PCB	TEQ	Notes	Reference
Japan	2002–2006	1374	General population. Age 15-73	12.0		20.0	WHO-TEQ_{1998}		Uemura et al. (2009)
Japan	2005	38	General population of rural area and urban area	16.0		23.6	WHO-TEQ_{2005}	Based on Ministry of the Environment reports 2007 and 2008	Furuya et al. (2010)
Japan	2006	39	General population of rural area and urban area	14.0		23.3	WHO-TEQ_{2005}	Based on Ministry of the Environment reports 2007 and 2008	Furuya et al. (2010)
Japan	2002–2007	1656	General population of rural. Age 15-73	10.3	5.7	16	WHO-TEQ_{2005}	Based on Ministry of the Environment reports 2007 and 2008	Arisawa et al. (2011)
Korea	2001–2002	103	General population living near a MSWI (N = 75)	6.6 ± 3.47			I-TEQ		Moon et al., (2005)
Korea	2000–2002	7	General population. Age 21-57	4.1		6.6	WHO-TEQ_{2005}	Residents >10 km from IWI/MSWI facilities	Park et al. (2009)
Korea	2003	20	Age >20	11.0			I-TEQ	Residents living >12 km away from an incinerator	Park et al. (2004)
Korea	2005	20	General population	11.2			I-TEQ	Residents living 20 km away from an incinerator	Leem et al. (2006)
Korea	2006	11	General population. Age 21-57	4.1		6.6	WHO-TEQ_{2005}	Residents >10 km from IWI/MSWI facilities	Park et al. (2009)
Korea	2006	49	Residents living near a MSWI	11.9			WHO-TEQ_{2005}		Park et al., (2013)
Korea	2001–2011	954 PCDD/F 539 dl-PCB	Residents living near/far a MSWI	9.4 (Near) 9.1 (Far)	5.4 (Near) 4.7 (Far)		WHO-TEQ_{2005}	Blood samples collected yearly	Park et al., (2014)
China	Nov-2012	305	General population. Age 24-50		2.0		WHO-TEQ_{2005}		Gao et al. (2019)
Taiwan	1999–2003	84	Residents living far/near a MSWI. Age 18-65	18.7 (Near A) 19.4 (Near B) 20.8 (Near C) 19.0 (Far)			I-TEQ	They were zones A, B and C, considered as affected emission exposure zones from the incinerator, and zone D as the background	Huang et al. (2007)
Taiwan	2003	19	Residents <5 km from an MWI. Age 18-65	13.6			I-TEQ		Chen et al. (2005)
Taiwan	2001–2006	251	General population. Age 18-59	11.5		18.0	WHO-TEQ_{1998}		Hsu et al. (2009)
South Africa Tswana	2010	693	General population. Age 37-84	4.5 ± 1.9	2.4 ± 2.4		WHO-TEQ_{2005}		Pieters and Focant (2014)

food chain. Similar results have been reported by other studies, such as Zubero et al. (2011) in the Basque Country and Iamiceli et al. (2021) in Turin, Italy. Both studies also found higher concentrations of PCBs in locally grown food products, reinforcing the notion that locally produced foods can act as a significant route of exposure to these contaminants.

Over the last few years, many studies have observed a decrease in the level of these compounds over time (Zubero et al., 2017; Raffetti et al., 2017; Muzembo et al., 2019; Nadal et al., 2019), reaching to levels similar to the ones found in this study. Zubero et al. (2017) found that between the years 2006 and 2013, the levels of PCDD/Fs decreased from 23.45 pg WHO-TEQ2005 g-1 to 4.67 pg WHO-TEQ2005 g-1, and the levels of dl-PCBs decreased from 15.56 pg WHO-TEQ2005 g-1 to 3.13 pg WHO-TEQ2005 g-1, in a population living near and far from a ERP in Bizkaia (Spain). It is important to note that in the 2006 and 2008 analyses, pools of samples grouped by age and sex were used, whereas in 2013, individual samples were analysed. This change in analysis methodology may have contributed to more accurate and precise measurements in the later study.

The study by Nadal et al. (2019) investigated the mean concentration of polychlorinated dibenzo-*p*-dioxins and polychlorinated dibenzofurans (PCDD/Fs) in plasma of a population living near a hazardous waste incinerator in Tarragona, Spain. They found that the mean concentration in 2018 was 6.79 pg I-TEQ g-1, which was significantly lower than the baseline concentration in 1998 (27.0 pg I-TEQ g-1). The authors attributed this reduction to a decreasing trend in the daily dietary intake of PCDD/Fs, which decreased from 210.1 pg I-TEQ in 1998 to 8.54 pg WHO-TEQ2005 in 2018.

Likewise, Raffetti et al. (2017) evaluated the temporal trends in serum levels of PCDD/Fs and dl-PCBs in the same participants. They

observed a decrease in total PCB serum levels over time for each age group: −3.9% for subjects aged ≤55 years, −4.0% for subjects aged 56–65 years, and −3.4% for subjects aged ≥66 years. Likewise, in the last decades, the Japanese Ministry of the Environment has been biomonitoring dioxins in the general Japanese population and, in response to public concerns, has taken measures to reduce dioxin exposure. Muzembo et al. (2019) compared dioxin data from 2011 to 2016 with data from previous surveys conducted between 2002 and 2010. They found that the median blood dioxin level in the 2011–2016 survey had decreased by 41.3% compared to the 2002–2010 surveys. These findings suggest that regulatory measures implemented by the Japanese government have been effective in reducing dioxin exposure. Nevertheless, the study of Lakind et al. (2009) focused on the levels of PCDD/Fs in serum of the general population in the United States. They found that levels increased from the 1999–2000 period to the 2001–2002 period but subsequently decreased in the 2003–2004 period.

The exposure to PCDD/Fs and dl-PCBs from ERPs has been, and is still, a matter of concern to a large part of the population. According to a recent study conducted in the same study area, the resident population near the ERP under construction declared a low level of acceptance. However, the acceptance of ERPs improved when they were located further away from the residents' area of residence (Subiza-Pérez et al., 2020). The perception of high risk associated with ERPs has been observed not only in the study area but also in other countries, such as Taiwan (Lin et al., 2018) and China (Hou et al., 2019), as mentioned in studies conducted in those regions. Studies that assessed biomarkers in populations residing in areas exposed to emissions from new ERPs did not report higher levels of PCDD/Fs and dl-PCBs in individuals living close to these plants when compared to those residing further away (Reis et al., 2007a; Fierens et al., 2007; De Felip et al., 2008; Zubero et al., 2011; Park et al., 2014; Nadal et al., 2019). However, it is important to note that some of the key limitations of these biomarker studies were the lack of data on PCDD/Fs and dl-PCBs levels from the period before the establishment of the incineration plants. This limitation could have potentially hindered their ability to capture changes in exposure levels over time, particularly related to the setup and operation of the ERPs.

The purpose of the present study is to overcome this limitation by characterizing the population exposure to PCDD/Fs and dl-PCBs before the implementation of the ERP in order to establish baseline levels of these pollutants in the population residing near and far from the area of the plant before its start-upThis will enable to compare the spatial and temporal evolution of PCDD/Fs and dl-PCBs after the ERP is implemented and operations start.

The study possesses several strengths that contribute to its overall reliability and significance. Firstly, the study include its focus on the general population, which enhances its relevance to public health concerns. The recruitment process using random sampling techniques further strengthens the study's validity, as it minimizes bias in participant selection. Additionally, the individual-based analysis of samples rather than pooling them together provides a more accurate assessment of exposure levels for each participant. It provides a detailed understanding of the distribution and variations of these contaminants among the study participants, leading to more precise conclusions. However, the study has certain weaknesses. The restricted sample size may limit the statistical power and generalizability of the findings. A larger sample size would have yielded more robust results. Moreover, self-reported data for tobacco and alcohol consumption collected through a questionnaire could be subject to social desirability bias, potentially affecting the accuracy of the data.

Nonetheless, despite these limitations, the study serves as an important foundation for future research. It establishes baseline levels of PCDD/Fs and dl-PCBs in the general population and provides a framework for assessing trends in these pollutants over time. Furthermore, it paves the way for exploring potential associations between exposure to these contaminants and the development of health risks.

5. Conclusions

The study conducted in Gipuzkoa, Basque Country (Spain) aimed to determine the baseline levels of PCDD/Fs and dl-PCBs in the general population. The study also aimed to identify the factors that influenced the concentrations of these pollutants. The findings of the study indicated that the levels of PCDD/Fs and dl-PCBs in the general population of Gipuzkoa were comparable to, and in some cases even lower than, levels reported in other national and international studies conducted in urban-industrial areas. This suggests that the pollution levels in Gipuzkoa were not significantly higher than those found in other similar regions. The study identified several factors that were found to be significant determinants of the concentrations of these pollutants. These factors included the area of residence, age, smoking and drinking habits, as well as the consumption of oil and locally produced poultry. Understanding the determinants of pollutant concentrations is important for implementing effective strategies to reduce exposure and mitigate potential health risks. By identifying the factors that influence PCDD/F and dl-PCB levels, health and environmental administrations can establish policies and regulations to minimize population exposure and mitigate potential health risks associated with these pollutants.

Author contribution

L. Santa Marina: Conceptualization, Methodology, Investigation, Writing – original draft preparation, Formal analysis, Funding acquisition; **A. Irizar:** Conceptualization, Methodology, Reviewing and Editing, Funding acquisition; **Z. Barroeta:** Writing – original draft preparation **E. Abad:** Formal analysis; **A. Lertxundi:** Conceptualization, Methodology, Reviewing and Editing, Funding acquisition, Supervision; **J. Ibarluzea:** Conceptualization, Methodology, Reviewing and Editing, Funding acquisition; **J. Parera:** Formal analysis, Reviewing and Editing; **N. Urbieta:** Investigation; Data curation; **E. Arruti:** Data analysis; **A. Jimeno:** Investigation; Data curation; **M.B. Zubero:** Methodology, Reviewing and Editing, Supervision.

Funding

This research, conducted between 2017 and 2019 before the operation of the Energy Recovery plant, was funded through a public tender (017/11-HH-ZE) by the Gipuzkoa Provincial Council. However, the funding source did not play any part in the study's design, data collection and analysis, or the interpretation and writing of the manuscript.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Jesus Ibarluzea reports financial support was provided by Gipuzkoa Provincial Council.

Data availability

Data will be made available on request.

Acknowledgements

The authors express their gratitude to all the participants who selflessly donated their blood and to the personal healthcare centers of the municipalities where the blood samples were taken. This study would not have been possible without their support.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2023.116721.

References

Åberg, A., Tysklind, M., Nilsson, T., MacLeod, M., Hanberg, A., Andersson, R., Bergek, S., Lindberg, R., Wiberg, K., 2010. Exposure assessment at a PCDD/F contaminated site in Sweden—field measurements of exposure media and blood serum analysis. Environ. Sci. Pollut. Control Ser. 17, 26–39.

Agramunt, M.C., Schuhmacher, M., Hernandez, J.M., Domingo, J.L., 2005. Levels of dioxins and furans in plasma of nonoccupationally exposed subjects living near a hazardous waste incinerator. J. Expo. Anal. Environ. Epidemiol. 15, 29–34.

Albertini, R., Bird, M., Doerrer, N., Needham, L., Robison, S., Sheldon, L., Zenick, H., 2006. The use of biomonitoring data in exposure and human health risk assessments. Environ. Health Perspect. 114, 1755–1762.

Arisawa, K., Uemura, H., Hiyoshi, M., Kitayama, A., Takami, H., Sawachika, F., Nishioka, Y., Hasegawa, M., Tanto, M., Satoh, H., Shima, M., Sumiyoshi, Y., Morinaga, K., Kodama, K., Suzuki, T.I., Nagai, M., 2011. Dietary patterns and blood levels of PCDDs, PCDFs, and dioxin-like PCBs in 1656 Japanese individuals. Chemosphere 82 (5), 656–662.

Bena, A., Gandini, M., Cadum, E., Procopio, E., Salamina, G., Orengia, M., Farina, E., 2019. Risk perception in the population living near the Turin municipal solid waste incineration plant: survey results before start-up and communication strategies. BMC Publ. Health 19 (1), 1–9.

Buchthal, J., Grund, K.E., Buchmann, A., Schrenk, D., Beaune, P., Bock, K.W., 1995. Induction of cytochrome P4501A by smoking or omeprazole in comparison with UDP-glucuronosyltransferase in biopsies of human duodenal mucosa. Eur. J. Clin. Pharmacol. 47, 431–435.

Calheiros, J.M., Coutinho, M., Borrego, C., Santos, R., Päpke, O., 2002. PCDD/PCDF levels in human blood and breast milk in the region of Oporto, Portugal. Organohalogen Compd. 55, 279–282.

Campo, L., Bechtold, P., Borsari, L., Fustinoni, S., 2019. A systematic review on biomonitoring of individuals living near or working at solid waste incinerator plants. Crit. Rev. Toxicol. 49 (6), 479–519.

Caserini, S., Cernuschi, S., Giugliano, M., Grosso, M., Lonati, G., Mattaini, P., 2004. Air and soil dioxin levels at three sites in Italy in proximity to MSW incineration plants. Chemosphere 54 (9), 1279–1287.

Černá, M., Kratěnová, J., Žejglicová, K., Brabec, M., Malý, M., Šmíd, J., 2007. Levels of PCDDs, PCDFs, and PCBs in the blood of the non-occupationally exposed residents living in the vicinity of a chemical plant in the Czech Republic. Chemosphere 67, S238–S246.

Chang, C.J., Terrell, M.L., Marcus, M., Marder, M.E., Panuwet, P., Ryan, P.B., Pearson, M., Barton, H., Barr, D.B., 2020. Serum concentrations of polybrominated biphenyls (PBBs), polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs) in the Michigan PBB Registry 40 years after the PBB contamination incident. Environ. Int. 137, 105526.

Chen, H.L., Liao, P.C., Su, H.J., Guo, Y.L., Chen, C.H., Lee, C.C., 2005. Profile of PCDD/F levels in serum of general Taiwanese between different gender, age and smoking status. Sci. Total Environ. 337 (1–3), 31–43.

Chovancová, J., Conka, K.A., Stachová Sejáková, Z.S., Dömötörová, M., Drobná, B., Wimmerová, S., 2012. PCDD/PCDF, dl-PCB and PBDE serum levels of Slovak general population. Chemosphere 88 (11), 1383–1389.

Coakley, J., Bridgen, P., Bates, M.N., 2018. Chlorinated persistent organic pollutants in serum of New Zealand adults, 2011-2013 Sci. Total Environ. 615 (1–3), 624–631.

Consonni, D., 2006. Mortality of the population exposed to dioxin after the seveso accident. Epidemiology 17 (6), S83–S84.

Costopoulou, D., Vassiliadou, I., Papadopoulos, A., Makropoulos, V., Leondiadis, L., 2006. Levels of dioxins, furans and PCBs in human serum and milk of people living in Greece. Chemosphere 65 (9), 1462–1469.

Dahlgren, J., Takhar, H., Schecter, A., Schmidt, R., Horsak, R., Paepke, O., Warshaw, R., Lee, A., Anderson-Mahoney, P., 2007. Residential and biological exposure assessment of chemicals from a wood treatment plant. Chemosphere 67 (9), S279–S285.

De Felip, E., Abballe, A., Casalino, F., di Domenico, A., Domenici, P., Iacovella, N., Ingelido, A.M., Pretolani, E., Spagnesi, M., 2008. Serum levels of PCDDs, PCDFs and PCBs in non-occupationally exposed population groups living near two incineration plants in Tuscany, Italy. Chemosphere. 72 (1), 25–33.

Debacker, N., Sasse, A., van Wouwe, N., Goeyens, L., Sartor, F., van Oyen, H., 2007. PCDD/F levels in plasma of a belgian population before and after the 1999 belgian PCB/DIOXIN incident. Chemosphere 67 (9), S217–S223.

Domingo-Salvany, A., Regidor, E., Alonso, J., Alvarez-Dardet, C., 2000. Una propuesta de medida de la clase social Grupo de Trabajo de la Sociedad Española de Epidemiologia y de la Sociedad Española de Medicina de Familia y Comunitaria. Atención Primaria 25, 350–363.

EFSA CONTAM Panel (EFSA Panel on Contaminants in the Food Chain), 2018. Scientific Opinion on the risk for animal and human health related to the presence of dioxins and dioxin-like PCBs in feed and food, 5333 EFSA J. 16 (11), 331. https://doi.org/10.2903/j.efsa.2018.5333. pp.

Ferré-Huguet, N., Nadal, M., Schumacher, M., Domingo, J.L., 2009. Monitoring metals in blood and hair of the population living near a hazardous waste incinerator: temporal trend. Biol. Trace Elem. Res. 128, 191–199.

Fierens, S., Mairesse, H., Heilier, J.F., Focant, J.F., Eppe, G., De Pauw, E., Bernard, A., 2007. Impact of iron and steel industry and waste incinerators on human exposure to dioxins, PCBs, and heavy metals: results of a cross-sectional study in Belgium. J. Toxicol. Environ. Health, Part A 70, 222–226.

Frery, N., Zeghnoun, A., Sarter, H., Volatier, J.L., Falq, G., Pascal, M., Grange, D., Schmitt, M., Bérat, B., Fabre, P., Guillois-Becel, Y., Noury, U., Pouey, J., Mathieu, A., Heymann, C., Lucas, N., Thébault, A., Eppe, G., Focant, J.F., Le Strat, Y., Pelletier, B., Salines, G., 2007. Exposure factors influencing serum dioxin concentrations in the French dioxin and incinerators study. Organohalogen Compd. 69, 1013–1016.

Fromme, H., Albrecht, M., Boehmer, S., Büchner, K., Mayer, R., Liebl, B., Wittsiepe, J., Bolte, G., 2009. Intake and body burden of dioxin-like compounds in Germany: the INES study. Chemosphere 76 (11), 1457–1463.

Fromme, H., Albrecht, M., Appel, M., Hilger, B., Völkel, W., Liebl, B., Roscher, E., 2015. PCBs, PCDD/Fs, and PBDEs in blood samples of a rural population in South Germany. Int. J. Hyg Environ. Health 218 (1), 41–46.

Furue, M., Ishii, Y., Tsukimori, K., Tsuji, G., 2021. Aryl hydrocarbon receptor and dioxin-related health hazards—lessons from Yusho. Int. J. Mol. Sci. 22 (2), 708.

Furuya, H., Kayama, F., Hasegawa, M., Nagai, M., Suzuki, T., 2010. A longitudinal study of trends in blood dioxins and dioxin-like compounds levels in residents from two locations in Japan during 2002–2006. Arch. Environ. Contam. Toxicol. 58, 892–900.

Gao, Q., Ben, Y., Dong, Z., Hu, J., 2019. Age-dependent human elimination half-lives of dioxin-like polychlorinated biphenyls derived from biomonitoring data in the general population. Chemosphere 222, 541–548.

Harden, F., Müller, J., Toms, L., Gaus, C., Moore, M., Päpke, O., 2004. Dioxins in the Australian population: levels in blood. National dioxins program technical report 9, 1–119. Australia.

Harden, F.A., Toms, L.M.L., Paepke, O., Ryan, J.J., Müller, J.F., 2007. Evaluation of age, gender and regional concentration differences for dioxin-like chemicals in the Australian population. Chemosphere 69 (9), 318–324.

Harmouche-Karaki, M., Mahfouz, Y., Salameh, P., Matta, J., Helou, K., Narbonne, J.F., 2019. Patterns of PCBs and OCPs exposure in a sample of Lebanese adults: the role of diet and physical activity. Environ. Res. 179, 108789.

Hedgeman, E., Chen, Q., Hong, B., Chang, C.W., Olson, K., LaDronka, K., Ward, B., Adriaens, P., Demond, A., Gillespie, B.W., Lepkowski, J., Franzblau, A., Garabrant, D.H., 2009. The University of Michigan Dioxin Exposure Study: population survey results and serum concentrations for polychlorinated dioxins, furans, and biphenyls. Environ. Health Perspect. 117 (5), 811–817.

Helou, K., Matta, J., Harmouche-Karaki, M., Sayegh, N., Younes, H., Mahfouz, Y., Mahfouz, M., Karake, S., Finan, R., Abi-Tayeh, G., Narbonne, J.F., 2021. Maternal and cord serum levels of polychlorinated biphenyls (PCBs) and organochlorine pesticides (OCPs) among Lebanese pregnant women and predictors of exposure. Chemosphere 266, 129211.

Hou, G., Chen, T., Ma, K., Liao, Z., Xia, H., Yao, T., 2019. Improving social acceptance of waste-to-energy incinerators in China: role of place attachment, trust, and fairness. Sustainability 11, 1727.

Hsu, J.F., Lee, C.C., Su, H.J., Chen, H.L., Yang, S.Y., Liao, P.C., 2009. Evaluation of background persistent organic pollutant levels in human from Taiwan: polychlorinated dibenzo-*p*-dioxins, dibenzofurans, and biphenyls. Environ. Int. 35 (1), 33–42.

Huang, H.Y., Jeng, T.Y., Lin, Y.C., Ma, Y.C., Kuo, C.P., Sung, F.C., 2007. Serum dioxin levels in residents living in the vicinity of municipal waste incinerators in Taiwan. Inhal. Toxicol. 19 (5), 399–403.

Humblet, O., Sergeyev, O., Altshul, L., Korricks, A., Williams, P.L., Emond, C., Birnbaum, L.S., Burns, J.S., Lee, M.M., Revich, B., Shelepchikov, A., Feshin, D., Hauser, R., 2011. Temporal trends in serum concentrations of polychlorinated dioxins, furans, and PCBs among adult women living in Chapaevsk, Russia: a longitudinal study from 2000 to 2009. Environ. Health 10, 62.

Iamiceli, A.L., Abate, V., Abballe, A., Bena, A., De Filippis, S.P., Dellatte, E., De Luca, S., Fulgenzi, A.R., Iacovella, N., Ingelido, A.M., Ivaldi, C., Marra, V., Miniero, R., Valentini, S., Farina, E., Gandini, M., Orengia, M., Procopio, E., Salamina, G., De Felip, E., 2021. Biomonitoring of the adult population living near the waste incinerator of Turin: serum concentrations of PCDDs, PCDFs, and PCBs after three years from the plant start-up. Chemosphere 272, 129882.

IARC. Complete List of Agents evaluated and their classification. https://monographs.iarc.fr/list-of-classifications. Available at:

Jain, R.B., Wang, R.Y., 2011. Association of caffeine consumption and smoking status with the serum concentrations of polychlorinated biphenyls, dioxins, and furans in the general U.S. population: NHANES 2003-2004. J. Toxicol. Environ. Health, Part A 74 (18), 1225–1239.

Jeno, J.G.A., Rathna, R., Nakkeeran, E., 2021. Biological implications of dioxins/furans bioaccumulation in ecosystems. Environmental Pollution and Remediation 395–420.

Kaleka, A.S., Thind, S.K., 2020. Dioxins and dioxin-like compounds (DLCs). In: Sharma, A., Kumar, M. (Eds.), Pollutants and Protectants: Evaluation and Assessment Techniques. I K International Publishing House Pvt. Ltd, pp. 75–97.

Knutsen, H.K., Kvalem, H.E., Haugen, M., Meltzer, H.M., Brantsaeter, A.L., Alexander, J., Apke, O.P., Liane, V.H., Becher, G., Thomsen, C., 2011. Sex, BMI and age in addition to dietary intakes influence blood concentrations and congener profiles of dioxins and PCBs. Mol. Nutr. Food Res. 55, 772–782.

Kocan, A., Drobna, B., Petrik, J., Jursa, S., Chovancova, J., Conka, K., Balla, B., Sovcikova, E., Trnovec, T., 2004. Human exposure to PCBs and some other presistent organochlorines in eastern Slovakia as a consequence of former PCB production. Organohalogen Compd. 66, 3539–3546.

Kvalem, H.E., Knutsen, H.K., Thomsen, C., Haugen, M., Stigum, H., Brantsæter, A.L., Frøshaug, M., Lohmann, N., Päpke, O., Becher, G., Alexander, J., Meltzer, H.M., 2009. Role of dietary patterns for dioxin and PCB exposure. Mol. Nutr. Food Res. 53 (11), 1438–1451.

Lakind, J.S., Hays, S.M., Aylward, L.L., Naiman, D.Q., 2009. Perspective on serum dioxin levels in the United States: an evaluation of the NHANES data. J. Expo. Sci. Environ. Epidemiol. 19 (4), 435–441.

Lan, T., Liu, B., Bao, W., Thorne, P.S., 2021. BMI modifies the association between dietary intake and serum levels of PCBs. Environ. Int. 156, 106626.

Leem, J.H., Lee, D.S., Kim, J., 2006. Risk factors affecting blood PCDDs and PCDFs in residents living near an industrial incinerator in Korea. Arch. Environ. Contam. Toxicol. 51, 478–484.
Lertxundi, A., Martínez, M.D., Ayerdi, M., Alvarez, J., Ibarluzea, J.M., 2010. Air quality assessment in urban areas of Gipuzkoa (Spain). Gac. Sanit. 24 (3), 187–192.
Lin, M., Ma, Y., Yuan, H., Luo, X., Wang, Q., Liu, A., Wang, Y., Jin, J., 2018. Temporal trends in dioxin-like polychlorinated biphenyl concentrations in serum from the general population of Shandong province, China: a longitudinal study from 2011 to 2017. Environ. Pollut. 243, 59–65.
Llobet, J.M., Domingo, J.L., Bocio, A., Casas, C., Teixidó, A., Müller, L., 2003. Human exposure to dioxins through the diet in Catalonia, Spain: carcinogenic and non-carcinogenic risk. Chemosphere 50 (9), 1193–1200.
Marin, S., Villalba, P., Diaz-Ferrero, J., Font, G., Yusà, V., 2011. Congener profile, occurrence and estimated dietary intake of dioxins and dioxin-like PCBs in foods marketed in the Region of Valencia (Spain). Chemosphere 82 (9), 1253–1261.
Moon, C.S., Chang, Y.S., Kim, B.H., Shin, D., Ikeda, M., 2005. Evaluation of serum dioxin congeners among residents near continuously burning municipal solid waste incinerators in Korea. Int. Arch. Occup. Environ. Health 78, 205–210.
Mrema, E.J., Rubino, F.M., Mandic-Rajcevic, S., Sturchio, E., Turci, R., Osculati, A., Brambilla, G., Minoia, C., Colosio, C., 2014. Exposure to priority organochlorine contaminants in the Italian general population. Part 2: fifteen priority polychlorinated biphenyl congeners in blood serum. Hum. Exp. Toxicol. 33, 170–184.
Muzembo, B.A., Iwai-Shimada, M., Isobe, I., Arisawa, K., Shima, M., Fukushima, T., Nakayama, S.F., 2019. Dioxins levels in human blood after implementation of measures against dioxin exposure in Japan. Environ. Health Prev. Med. 24, 6.
Nadal, M., Mari, M., Schumacher, M., Domingo, J.L., 2019. Monitoring dioxins and furans in plasma of individuals living near a hazardous waste incinerator: temporal trend after 20 years. Environ. Res. 173, 207–211.
Parera, J., Serra-Prat, M., Palomera, E., Mattioli, L., Abalos, M., Rivera, J., Abad, E., 2013. Biological monitoring of PCDD/Fs and PCBs in the City of Mataró. A population-based cohort study (1995–2012). Sci. Total Environ. 461, 612–617.
Park, S., Kim, S.J., Kim, K.S., Lee, D.S., Kim, J.G., 2004. Influence of an industrial waste incinerator as assessed by the levels and congener patterns of polychlorinated dibenzo-*p*-dioxins and polychlorinated dibenzofurans. Environ. Sci. Technol. 38 (14), 3820–3826.
Park, H., Ikonomou, M.G., Kim, H.S., Choi, J.W., Chang, Y.S., 2009. Dioxin and dioxin-like PCB profiles in the serum of industrial and municipal waste incinerator workers in Korea. Environ. Int. 35 (3), 580–587.
Park, H., Kim, J., Chang, Y.S., 2013. Prevalence of low chlorinated dibenzo-*p*-dioxin/dibenzofurans in human serum. Chemosphere 90 (5), 1658–1663.
Park, H., Park, E., Chang, Y.S., 2014. Ten year time trend of dioxins in human serum obtained from metropolitan populations in Seoul, Korea. Sci. Total Environ. 470, 1338–1345.
Patterson, D.G., Isaacs, S.G., Alexander, L.R., Turner, W.E., Hampton, L., Bernert, J.T., Needham, L.L., 1991. Method 6, Determination of Specific Polychlorinated Dibenzo-*P*-Dioxins and Dibenzofurans in Blood and Adipose Tissue by Isotope Dilution-High-Resolution Mass Spectrometry, vol. 108. IARC Scientific Publications, pp. 299–342.
Pieters, R., Focant, J.F., 2014. Dioxin, furan and PCB serum levels in a South African Tswana population: comparing the polluting effects of using different cooking and heating fuels. Environ. Int. 66, 71–78.
PRTR-Spain. Spanish Register of Pollutant Emissions Sources. https://www.prtr-es.es.
Raffetti, E., Speziani, F., Donato, F., Leonardi, L., Orizio, G., Scarcella, C., Apostoli, P., Magoni, M., 2017. Temporal trends of polychlorinated biphenyls serum levels in subjects living in a highly polluted area from 2003 to 2015: a follow-up study. Int. J. Hyg Environ. Health 220, 461–467.
Ranzi, A., Fustinoni, S., Erspamer, L., Campo, L., Gatti, M.G., Bechtold, P., Bonassi, S., Trenti, T., Goldoni, C.A., Bertazzi, P.A., 2013. Biomonitoring of the general population living near a modern solid waste incinerator: a pilot study in Modena, Italy. Environ. Int. 61, 88–97.
Rawn, D.F., Ryan, J.J., Sadler, A.R., Sun, W.F., Haines, D., Macey, K., Van Oostdam, J., 2012. PCDD/F and PCB concentrations in sera from the Canadian health measures survey (CHMS) from 2007 to 2009. Environ. Int. 47, 48–55.
Reis, M.F., Miguel, J.P., Sampaio, C., Aguiar, P., Melim, J.M., Papke, O., 2007a. Determinants of dioxins and furans in blood of non-occupationally exposed populations living near Portuguese solid waste incinerators. Chemosphere 67, S224–S230.
Reis, M.F., Sampaio, C., Brantes, A., Aniceto, P., Melim, M., Cardoso, L., Gabriel, C., Simao, F., Miguel, J.P., 2007b. Human exposure to heavy metals in the vicinity of Portuguese solid waste incinerators Part 1: biomonitoring of Pb, Cd and Hg in blood of the general population. Int. J. Hyg Environ. Health 210, 439–446.
Rusin, M., Dziubanek, G., Marchwińska-Wyrwał, E., Ćwieląg-Drabek, M., Razzaghi, M., Piekut, A., 2019. PCDDs, PCDFs and PCBs in locally produced foods as health risk factors in Silesia Province, Poland. Ecotoxicol. Environ. Saf. 172, 128–135.
Santa-Marina, L., Barroeta, Z., Irizar, A., Alvarez, J.I., Abad, E., Muñoz-Arnanz, J., Jimenez, B., Ibarluzea, J., Urbieta, N., Jimeno-Romero, A., Zubero, M.B., Lertxundi, A., 2023. Characterization of PCDD/F and dl-PCB levels in air in Gipuzkoa (Basque Country, Spain). Environ. Res. 228, 115901.
Schuhmacher, M., Domingo, J.L., Llobet, J.M., Lindström, G., Wingfors, H., 1999. Dioxin and dibenzofuran concentrations in blood of a general population from Tarragona, Spain. Chemosphere 38 (5), 1123–1133.
Schuhmacher, M., Domingo, J.L., Agramunt, M.C., Bocio, A., Muller, L., 2002. Biological monitoring of metals and organic substances in hazardous-waste incineration workers. Int. Arch. Occup. Environ. Health 75, 500–506.
Subiza-Pérez, M., Santa Marina, L., Irizar, A., Gallastegi, M., Anabitarte, A., Urbieta, N., Babarro, I., Molinuevo, A., Vozmediano, L., Ibarluzea, J., 2020. Explaining social acceptance of a municipal waste incineration plant through sociodemographic and psycho-environmental variables. Environ. Pollut. 263, 114504.
Turrio-Baldassarri, L., Abate, V., Battistelli, C.L., Carasi, S., Casella, M., Iacovella, N., 2008. PCDD/F and PCB in human serum of differently exposed population groups of an Italian city. Chemosphere 73, S228–S234.
Uemura, H., Arisawa, K., Hiyoshi, M., Kitayama, A., Takami, H., Sawachika, F., Dakeshita, S., Nii, K., Satoh, H., Sumiyoshi, Y., Morinaga, K., Kodama, K., Suzuki, T. I., Suzuki, T., 2009. Prevalence of metabolic syndrome associated with body burden levels of dioxin and related compounds among Japan's general population. Environ. Health Perspect. 117 (4), 568–573.
UNEP (United Nations Environmental Programme), 2009. Stockholm convention. Reports and Decisions. Available at: http://chm.pops.int/TheConvention/POPsReviewCommittee/ReportsandDecisions/tabid/3309/Default.aspx.
Van den Berg, M., Birnbaum, L.S., Denison, M., De Vito, M., Farland, W., Feeley, M., et al., 2006. The 2005 World Health Organization reevaluation of human and mammalian toxic equivalency factors for dioxins and dioxin-like compounds. Toxicol. Sci. 93 (2), 223–241.
Vioque, L., 2006. Validez de la evaluación de la ingesta dietética. In: Serra Majem, L., Aranceta Bartina, J. (Eds.), Nutrición Y Salud Publica Métodos Bases Científicas Y Aplicaciones. Masson-elsevier, Barcelona, pp. 199–210.
Weber, R., Watson, A., Petrlik, J., Winski, A., Schwedler, O., Baitinger, C., Behnisch, P., 2015. High levels of PCDD/F, PBDD/F and PCB in eggs around pollution sources demonstrates the need to review soil standards. Organohalogen Compd. 77, 615–618.
Whong, L.Y., Uddin, M.S., Turner, W., Ragin, A.D., Dearwent, S., 2015. Serum PCB concentrations in residents of Calcasieu and Lafayette Parishes, Louisiana with comparison to the U.S. population. Chemosphere 118, 156–162.
Willett, W.C., Sampson, L., Stampfer, M.J., Rosner, B., Bain, C., Witschi, J., Charles, H., Speizer, F.E., 1985. Reproducibility and validity of a semiquantitative food frequency questionnaire. Am. J. Epidemiol. 122 (1), 51–65.
Wong, L.E., Millette, M.D., Uddin, M.S., Needham, L.L., Patterson, D.G., Turner, W., Henderson, A., 2008. Serum dioxin levels in residents of Calcasieu and Lafayette parishes, Louisiana with comparison to the US population. J. Expo. Sci. Environ. Epidemiol. 18 (3), 252–261.
Zani, C., Magoni, M., Speziani, F., Leonardi, L., Orizio, G., Scarcella, C., Gaia, A., Donato, F., 2019. Polychlorinated biphenyl serum levels, thyroid hormones and endocrine and metabolic diseases in people living in a highly polluted area in North Italy: a population-based study. Heliyon 5 (6), e01870.
Zhang, X., 2021. Conflicts and order: controversies over municipal solid waste incineration in China. PhD Thesis.
Zhou, Y., Liu, J., 2018. Emissions, environmental levels, sources, formation pathways, and analysis of polybrominated dibenzo-*p*-dioxins and dibenzofurans: a review. Environ. Sci. Pollut. Control Ser. 25 (33), 33082–33102.
Zubero, M.B., Ibarluzea, J.M., Aurrekoetxea, J.J., Rivera, J., Parera, J., Abad, E., Goñi, F., López, F., Etxeandia, A., Rodríguez, C., Sáenz, J.R., 2009. Serum levels of polychlorinated dibenzodioxins and dibenzofurans and PCBs in the general population living near an urban waste treatment plant in Biscay, Basque Country. Chemosphere 76 (6), 784–791.
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, 4468–4474.
Zubero, M.B., Aurrekoetxea, J.J., Ibarluzea, J.M., Rivera, J., Parera, J., Abad, E., Rodríguez, C., Sáenz, J.R., 2011. Evolution of PCDD/Fs and dioxin-like PCBs in the general adult population living close to a MSW incinerator. Sci. Total Environ. 410–411, 241–247.
Zubero, M.B., Eguiraun, E., Aurrekoetxea, J.J., Lertxundi, A., Abad, E., Parera, J., Goñi-Irigoyen, F., Ibarluzea, J., 2017. Changes in serum dioxin and PCB levels in residents around a municipal waste incinerator in Bilbao, Spain. Environ. Res. 156, 738–746.