



Mothers living with contamination of perfluoroalkyl substances: an assessment of the perceived health risk and self-reported diseases

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Abstract

Widespread contamination of the superficial, drinking, and groundwater by perfluoroalkyl substances (PFASs) was discovered in the Veneto Region (northeast of Italy) in 2013. Mothers from the contaminated area were concerned about the effects of PFAS on their own and their children's health. We determined the factors that influenced the perceived risk of PFAS and the presence of self-reported diseases by conducting a study with 384 mothers of children aged 1–13 years living in the contaminated area (Red Zone, Veneto, Italy). Information on demography, the sources of exposure, and the health condition of the mothers was collected through an online survey. The serum PFAS concentration was recorded for some of the participants. We determined the factors influencing the perceived risk, risk of health outcomes, and serum PFAS levels through regression analyses. The PFAS perceived risk of the mothers increased with an increase in the trust in scientific institutions and social media, and when many friends were present, trust in politics and full-time employment had a protective effect. The PFAS perceived risk increased the occurrences of self-reported and autoimmune diseases. Longer residence (> 20 years) in the most exposed area (Red Zone A) increased the frequency of some health outcomes. Serum PFAS concentrations decreased with breastfeeding, but increased with tap water consumption, residence in Red Zone A, and residence time. The PFAS perceived risk of the mothers was associated with many factors that influenced reporting of health issues. The association between PFAS exposure and health outcomes needs further investigation.

Keywords Perfluoroalkyl substances · Cross-sectional study · Breastfeeding · Health outcomes · Risk perception

Introduction

Perfluoroalkyl substances (PFASs) are industrial compounds characterized by a fluorinated carbon chain that is attached to a functional end group. Because of their hydrophobic and lipophobic properties, they are used in various products, such as non-stick cookware and water-repellent products (Buck et al. 2011). They tend to bioaccumulate and persist in the environment and the body (Conder et al. 2008; Perez et al. 2013).

One of the first incidences of contamination was discovered in the Mid–Ohio Valley (USA), where PFAS released from a fluoropolymer-producing plant contaminated surface water and groundwater, which affected 70,000 people (Emmett et al. 2006; Frisbee et al. 2009). Similarly, in 2013, a factory, based in the Veneto Region in Italy (RIMAR-MITENI factory, Trissino, Vicenza province), active since the late 1960s, contaminated one of the largest underground aquifers in Europe (Girardi and Merler 2019; Lava et al. 2021). The residents were inadvertently exposed to PFAS

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for a long time through drinking water, which resulted in high serum PFAS levels (Domingo and Nadal 2019; Pitter et al. 2020). Besides drinking water, other factors that affected the health of individuals were gender, the duration of residence in the zone, and raising livestock (Ingelido et al. 2018; Pitter et al. 2020).

Many health problems are associated with PFAS exposure. The C8 panel, a working group that investigated the effects of PFAS contamination in the Mid–Ohio Valley, reported a “probable link” between PFAS exposure and some types of cancer, specifically, kidney and testicular cancer (Steenland and Winquist 2021), and a strong association with other health diseases, such as ulcerative colitis, pregnancy-induced hypertension, hypercholesterolemia, and liver diseases (Steenland et al. 2020). Other research groups confirmed these associations of PFAS exposure with dyslipidemia (Sunderland et al. 2019; Averina et al. 2021), kidney functionality (Blake et al. 2018), hypertension (Averina et al. 2021), and liver diseases (Girardi and Merler 2019; Costello et al. 2021). Additionally, PFAS exposure was associated with several effects during pregnancy, especially preeclampsia (Borghese et al. 2020; Bommarito et al. 2021) and glucose tolerance (Preston et al. 2020). The effects of PFAS can also occur in the unborn child because PFAS can cross the placental barrier during pregnancy. Thus, pregnant women represent an important subpopulation affected by PFAS contamination (Manzano-Salgado et al. 2015). The amount of PFAS in the blood of the pregnant mothers is negatively associated with the birth weight and/or head circumference of infants (Apelberg, et al. 2007), as well as, with a weak immune system in children (Grandjean et al. 2017) and a higher risk of birth defects (Stein et al. 2014). Furthermore, high PFAS levels in the mother’s blood were documented to interfere with the sexual development of male infants, potentially leading to infertility (Di Nisio et al. 2020). These substances pass from the mother to the child in the uterus and through breast milk. Hence, nursing by mothers with high PFAS levels is an additional and lasting source of contamination during early childhood (Fromme et al. 2010). Breastfeeding lowers maternal serum concentration of PFOA (− 3% per month of breastfeeding; 95% CI: − 5 to − 2%) and increases infant serum PFOA concentrations (6% per month of breastfeeding; 95% CI: 1–10%; Mondal et al. 2014). Therefore, prolonged breastfeeding could decrease maternal serum PFAS concentration but increase PFAS concentration in infants (Kim et al. 2020), resulting in toddlers with higher total PFAS blood concentrations than their mothers (Papadopoulou et al. 2016). Furthermore, parous women have 40% lower PFOA (95% CI: − 54 to − 23%), colostrum concentration (Jusko et al. 2016), and 70% lower PFOA plasma concentration, compared to nulliparous women (Brantsæter

et al. 2013; Tian et al. 2018); previous pregnancies probably contribute to the elimination of PFAS in lactating mothers (Manzano-Salgado et al. 2016). The effect of breastfeeding on PFAS levels in infants is particularly relevant as it is strongly recommended worldwide to breastfeed infants for the first 6 months after childbirth for their optimal growth (WHO 2002).

Although several studies have shown an association between PFAS and health risks, the information shared with the general population has been poor, which has led to confusion (Wickham and Shriver 2021). Therefore, the PFAS-exposed community, overall, ignored and/or did not fully understand the effects of such exposure, which increased the state of uncertainty regarding the impacts of the contamination on their health and socioeconomic condition (Banwell et al. 2021; Calloway et al. 2020). Uncertainty when facing potential threats increases stress and anxiety (Sapolsky et al. 2000), which can influence the perception of health problems. Among mothers, the level of perceived stress can increase due to the fear of having exposed their offspring to environmental risks, the worry of being unable to protect them, and feeling guilt for possibly being the direct source of contamination (through the placenta and breastfeeding) (Crighton et al. 2013).

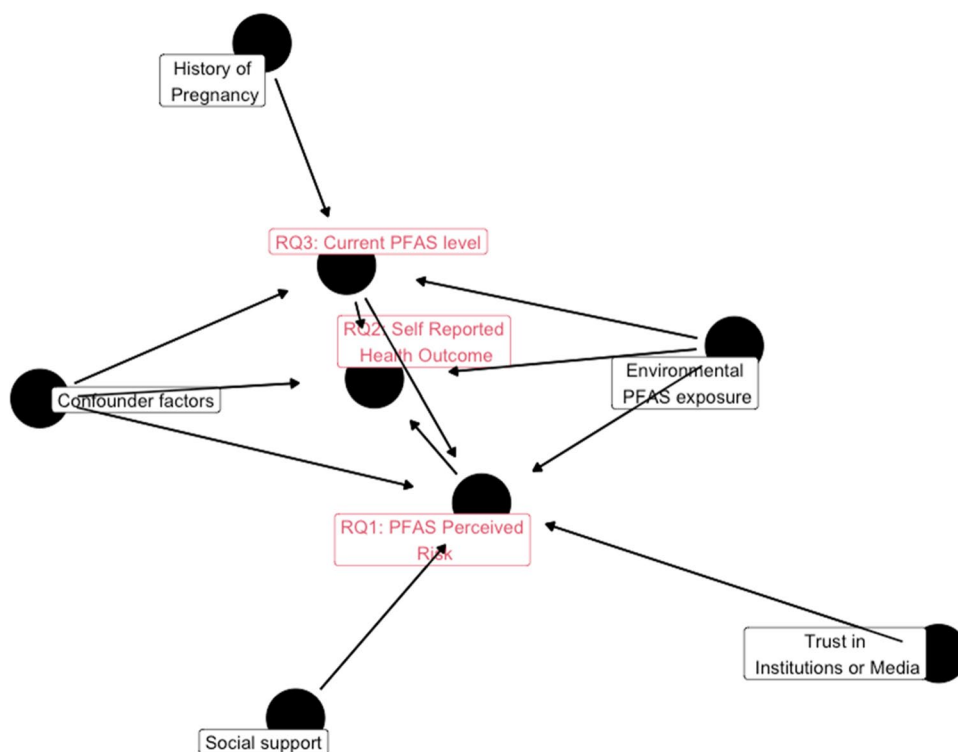
In this study, we assessed mothers living in a Region of Italy with high PFAS contamination. The data were derived from a pilot study known as the TEDDY-Child (Tracing the Environmental Determinants of the Development of Your Child) study that investigated the potential effects of PFAS exposure on multiple domains related to the development of children.

The perceived risk of the mothers due to PFAS exposure, the self-reported health outcomes, and the real determinants of high serum blood PFAS levels were jointly analyzed along with three separate but related research questions (RQs):

- RQ1: What environmental and subjective factors influence the risk perception of mothers regarding PFAS contamination?
- RQ2: Do environmental factors that are linked to PFAS exposure and risk perception influence the occurrences of self-reported diseases?
- RQ3: What environmental and individual factors are the best predictors of serum blood PFAS levels?

The theoretical-simplified network of relationships between and within the RQs and influencing variables is represented in Fig. 1 by means of a directed acyclic graph (DAG). The aim of this study was to explore each research question among a subpopulation of mothers of young children living in a territory affected by a severe PFAS contamination.

Fig. 1 Directed acyclic graph among study variables. In red, the dependent variables investigated in each research question



Methods

Study population

The sample was derived from the TEDDY-Child study (Tracing the Environmental Determinants of the Development of Your Child) that was conducted by the University of Padua to investigate the effects of PFAS on the development of children in the Veneto Region (Italy). From March to June 2021, 384 participants (mothers) were recruited from families that lived in contaminated areas in Veneto, called the “Red Zone” (Pitter et al. 2020). This is a territory comprising the province of Padua, Vicenza, and Verona formed by 30 municipalities. The population here was exposed to PFAS via contaminated drinking water for several decades. The regional Health Service subdivided the 30 municipalities into two areas based on the different intensities of PFAS contamination, namely, Red Zone A and Red Zone B, depending on whether the municipality was located above the contaminated region of the underground aquifer (Pitter et al. 2020). The recruitment was voluntary, and all participants provided informed consent. The study was approved by the ethical committee of the researchers’ university (Protocol number 4051). Data used in this analysis were derived from two subsequent ad hoc questionnaires provided to the participants to determine the sociodemographic characteristics and lifestyle of the mothers and their children; detailed information of the children 1–13 years old (born after 2008) was collected.

Blood PFAS measures

A health surveillance program was launched in January 2017 as a free population-based screening program offered by the regional Health Service for the residents of the Red Zone. PFASs were quantified using high-performance liquid chromatography-tandem mass spectrometry (HPLC–MS/MS) [Prominence UFLC XR 20 (Shimadzu) coupled to an API 4000TM LC–MS/MS System (Sciex)] that included perfluorooctanesulfonate (PFOS), perfluorooctanoic acid (PFOA), perfluorohexanesulfonic acid (PFHxS), perfluorononanoic acid (PFNA), perfluoroheptanoic acid (PFHpA), perfluorobutanesulfonic acid (PFBS), perfluorohexanoic acid (PFHxA), perfluorobutanoic acid (PFBA), perfluoropentanoic acid (PFPeA), perfluorodecanoic acid (PFDeA), perfluoroundecanoic acid (PFUnA), and perfluorododecanoic acid (PFDoA). Additional information on the analytical method is published in another study (Pitter et al. 2020). Out of the 384 participants, 148 reported their serum concentrations for 12 types of PFAS. The analysis was performed for 2017–2020 (82.8% in 2018). Three types of PFAS, including PFOA, PFOS, and PFHxS, were considered for the subsequent analysis. Out of 148 measurements, three measurements of PFHxS and two of PFOS were missing, while the remaining measurements were higher than the limit of quantification (LOQ) equal to 0.5 ng/mL.

Self-reported health outcome

The participants were asked to report the presence of pathologies or diseases. The question was in an open-text format, and the response was decoded by extracting the presence of autoimmune diseases (thyroid problems, celiac disease, lower immune functioning, Crohn's disease, type 1 and type 2 diabetes, lupus, rheumatoid arthritis, and psoriasis), cardiovascular diseases (high cholesterol, high blood pressure, stroke, cardiomyopathy, left atrial myxoma, high triglycerides, atrial fibrillation, ventricular tachycardia, and heart palpitations), liver diseases (increased liver enzymes, altered liver functioning, and cholecystitis), cancer (any benign or malignant tumor), and complications during pregnancy (preeclampsia, gestational diabetes, and preterm delivery).

Descriptive statistical analysis

The variables were summarized in tables and figures (frequency for categorical variables, median and interquartile range (IQR) for continuous variables). Wilcoxon test was performed to compare the distribution of continuous variables between the two Red Zones (A and B) and by binary categorization of blood PFOA concentrations according to the median value (17 ng/mL). The relationship between categorical variables was tested using chi-squared tests. The differences among and between groups were considered to be statistically significant at $p < 0.05$.

Missing data imputation

To fill the missing values for the records of some participants, we used the multivariate imputation by chained equations (MICE) algorithm (Van Buuren 2011), under the missing at random (MAR) assumption. From the 384 participants, only some data were missing; the variables with the relative percentage of missing data were tap water usage (0.52%), meat consumption (0.26%), vegetable consumption (0.26%), number of children (0.26%), body mass index (0.52%), education level (0.52%), employment (0.26%), type of house (0.52%), perceived risk of PFAS (0.52%), health outcomes (3.90%), trust in scientific institutions (0.26%), trust in political institutions (2.08%), trust in social media (1.82%), and Multidimensional Scale of Perceived Social Support (MSPSS; Zimet et al. 1988) by friends (0.78%). The imputation process was performed by predictive mean matching for the continuous distribution of the variables, except for dichotomous variables where a binary logistic regression was performed. The imputation algorithm was iterated 30 times and the convergence was graphically evaluated to inspect the variability of the imputed values.

RQ1: cumulative logistic model — factors influencing risk perception

We evaluated the PFAS perceived health risk on a 10-point Likert scale and asked the respondents, “To what extent do you think PFAS can affect your health and physical well-being?” We used a cumulative logistic model to evaluate which factors influenced the level of the perceived risk of PFAS. We included variables for the trust in scientific institutions (10-point Likert), political institutions (10-point Likert), and social media (10-point Likert). Additionally, individual predictors, such as the mother's age (≤ 38 , 38–44, > 44 years), the education level (middle school, high school, degree, or higher), residence time (≤ 20 years or > 20 years), the employment status of the mother (housewife/unemployed, part-time, and full-time), PFAS measurement (absent, present-PFOA [≤ 17 ng/mL], present-PFOA [> 17 ng/mL]), residence in the Red Zone (A or B), tap water consumption (10-point Likert scale), and the number of children, were considered. Only those variables were selected that minimized the Akaike information criterion (AIC) in a backward approach. Since low values of risk perception were infrequent, we merged the values of the response variables from 1 to 3 in a unique category (≤ 3 , $n = 10$, 2.6%). The results were reported as odds ratios (ORs) through exponentiation of the regression coefficients and relative 95% Confidence Interval (95% CI). The analysis was performed using the ordinal package in the R software (R-Core Team 2021).

RQ2: logistic regression model — assessment of health outcomes

To determine the factors that might influence the presence of self-reported health issues (any outcomes, including autoimmune diseases, liver diseases, cardiovascular diseases, and pregnancy complications), five different logistic regression models were estimated. The selected regressors included PFAS measurements (absent, present-PFOA [≤ 17 ng/mL], present-PFOA [> 17 ng/mL]), residence in the Red Zone (A or B), the perceived health risk of PFAS (10-point Likert scale), tap water consumption (10-point Likert scale), and the number of children. The models were also adjusted for the following confounding factors: the mother's age (≤ 38 , 38–44, > 44 years), the education level (middle school, high school, university degree, or higher), residence time (≤ 20 , > 20 years), and the mother's employment status (housewife/unemployed, part-time, or full-time). The results were reported using ORs with the relative 95% CI. To avoid excessive reliance on statistical significance, we emphasized the strength of associations between parameters by reporting the 95% CI only (Amrhein et al. 2019).

RQ3: linear regression model — determinants of blood serum PFAS

Several linear regression models were computed to determine the characteristics that influence the level of each type of PFAS (PFOA, PFOS, and PFHxS). Three separate linear regression models were estimated by type of PFAS, considering the log-transformed PFAS values as dependent variables and the following maternal and pregnancy-related characteristics: age (in years), the education level (middle school or lower, high school, university degree, or higher), the mother's employment status (housewife/unemployed, part-time, or full-time), the number of children before and after 2008, and the number of abortions. Limited to the time window between 2008 and 2021 in the model, we included as covariates the following determinants: breastfeeding duration of the first children (no or no yet breastfed, 1–6 months, 6–12 months, 12–24 months, and > 24 months), breastfeeding duration of the second children (no or no second child, 1–6 months, 6–12 months, 12–24 months, and > 24 months), breastfeeding of the third child had (no or no third child, yes), time since last pregnancy (categorized into 0 or before blood analysis, 0–7 years, > 7 years). Furthermore, we considered the following maternal lifestyle and characteristics: tap water consumption (10-point Likert scale), meat consumption (local meat, supermarket, butcher's shop, or no consumption), vegetable consumption (local market, own garden, supermarket, or neighboring farms), living in a detached house (no or yes), residence time (≤ 20 years or > 20 years), and the area of residence at the time of blood collection (Red Zone A or B). All the time-related variables were rescaled to the date of blood analysis. We performed backward stepwise regression that started with a full model and, at each step, gradually removed variables from the regression model based on the AIC index after testing the presence of interactions between included variables through an F statistic test. The results were reported using the estimated coefficients and the relative 95% confidence intervals. We used a Leave-One-Out Cross-Validation (LOOCV) procedure to obtain the Leave-One-Out coefficient of determination (Q^2) that could be compared to the one from the original linear regression model (R^2). The regression residual was analyzed to check the overall goodness of the model and for the presence of outliers or influential points.

Results

The participants were between 24 and 56 years (median: 43 years) with a high education level (40% of the participants had a university degree or higher educational qualification, and only 7.6% of the participants had a middle school degree) (Table 1). Regarding job employment, mothers were

mainly full-time workers (60%) with lower percentages of homemakers or unemployed individuals (14%) and part-time employees (26%). The respondents mainly lived in the Red Zone A (56%), and 37% of them were long-term residents (≥ 20 years). The consumption of tap water was low-to-medium (median: 3). Most participants had not undergone PFAS measurements (61%). The number of children ranged between 1 and 6 (median: 2). The perceived risk of PFAS was high (median: 8, *IQR*: 7–10). The participants reported high trust in scientific institutions (median: 8, *IQR*: 7–10) and low confidence in political institutions and social media (both median: 3, *IQR*: 1–5). Some of the participants (44%) reported the presence of at least one serious disease and a decreasing frequency of autoimmune diseases (17%), cardiovascular diseases (5.5%), liver diseases (3.4%), and cancer (5.7%). Many of the participants (23%) had at least one pregnancy-related complication. With respect to the Red Zone B, the participants who lived in Red Zone A reported significantly higher tap water consumption ($P = 0.031$), number of PFAS measurements ($P < 0.001$), and of children ($P = 0.010$). Figure 2 shows the extension of the Red Zone in the Veneto Region and the number of mothers participating from each municipality.

Perceived health risk due to PFAS

The result of the cumulative logistic regression is reported in Table 2. The participants who reported a higher perceived health risk due to PFAS also reported high trust in scientific institutions (1-point increase *OR*: 1.15; 95% *CI*: 1.05–1.26) and social media (1-point increase *OR*: 1.11; 95% *CI*: 1.01–1.22), whereas, trust in political institutions had a protective effect (1-point increase *OR*: 0.83; 95% *CI*: 0.76–0.92). Participants with full-time employment were less worried about the health risk due to PFAS exposure than a housewife or an unemployed individual (*OR*: 0.54; 95% *CI*: 0.31–0.93). The social support of friends was associated with a higher perceived risk of PFAS (1-point increase *OR*: 1.13; 95% *CI*: 1.03–1.25).

Health outcomes

Mothers living in the Red Zone for a long time did not report an increase in the frequency of diseases, except for cancer (> 20 years: *OR*: 2.15, 95% *CI*: 0.80–5.92). Mothers living in Red Zone A reported risk effects of cardiovascular and liver diseases with respect to those in the Red Zone B (*OR*: 1.63; 95% *CI*: 0.60–9.81, and *OR*: 2.28; 95% *CI*: 0.61–9.81, respectively). One point increase in the consumption of tap water was associated with a relative increase in the probability to report an increase of 7% in any self-reported disease (95% *CI*: 1–14%), 21% cancer (95% *CI*: 6–40%), 6%

Table 1 The main characteristics of the participants, overall and by zone of residence

Characteristics	Overall, <i>N</i> = 384 ¹	Red Zone		<i>P</i> -value ²
		A, <i>N</i> = 217 ¹	B, <i>N</i> = 167 ¹	
Mother's age (years)				0.87
[24,38]	136 (35%)	79 (36%)	57 (34%)	
(38,44]	124 (32%)	70 (32%)	54 (32%)	
(44,56]	124 (32%)	68 (31%)	56 (34%)	
Educational level				0.42
Middle school	29 (7.6%)	13 (6.0%)	16 (9.6%)	
High school	201 (52%)	116 (53%)	85 (51%)	
Degree or higher	154 (40%)	88 (41%)	66 (40%)	
Residential time				0.078
≤ 20 years	242 (60%)	128 (59%)	114 (60%)	
> 20 years	142 (37%)	89 (41%)	53 (32%)	
Employment				0.38
Housewife/unemployed	52 (14%)	25 (12%)	27 (16%)	
Part-time	99 (26%)	59 (27%)	40 (24%)	
Full-time	233 (61%)	133 (61%)	100 (60%)	
PFAS measurement				< 0.001
Absent	236 (61%)	119 (55%)	117 (70%)	
Present – [PFOA ≤ 17 ng/mL]	74 (19%)	37 (17%)	37 (22%)	
Present – [PFOA > 17 ng/mL]	74 (19%)	61 (28%)	13 (7.8%)	
Tap water habit	3 (1, 8)	4 (1, 9)	3 (1, 6)	0.031
PFAS perceived health risk	8 (7, 10)	8 (7, 9)	8 (7, 10)	0.94
MSPSS friends score	4.25 (2.75, 6)	4.5 (3, 6)	4 (2.5, 6)	0.27
Total N. of children	2 (1, 2)	2 (2, 3)	2 (1, 2)	0.010
Trust in scientific institutions	8 (7, 10)	8 (7, 10)	8 (6, 9.5)	0.42
Trust in political institutions	3 (1, 5)	3 (1, 5)	3 (1, 5)	0.54
Trust in social media	3 (1, 5)	3 (1, 5)	2 (1, 5)	0.28
Self-reported disease	168 (44%)	93 (43%)	75 (45%)	0.69
Autoimmune disorders	66 (17%)	39 (18%)	27 (16%)	0.58
Cardiovascular disorders	22 (5.7%)	14 (6.5%)	8 (4.8%)	0.58
Liver diseases	14 (3.6%)	10 (4.6%)	4 (2.4%)	0.25
Cancer	22 (5.7%)	12 (5.5%)	10 (6.0%)	0.85
Pregnancy complications	88 (23%)	50 (23%)	38 (23%)	0.95

¹Median (IQR) or frequency (%). ²Wilcoxon rank sum test; Pearson's chi-squared test

pregnancy complication (95% *CI*: – 1–14%), and 5% autoimmune disorders (95% *CI*: – 3–13%).

When PFOA was present, the reporting of any self-reported disease was higher (*OR*: 1.73, 95% *CI*: 1.01–3.00 and *OR*: 1.40, 95% *CI*: 0.78–2.52 for PFOA levels below and above 17 ng/mL, respectively). Additionally, the PFAS perceived risk was associated with an increase in the occurrence of self-reported diseases (+ 14% for each 1-point increase; 95% *CI*: 2–28%) and autoimmune diseases (+ 19% for each 1-point increase; 95% *CI*: 2–40%). The number of children was not associated with any of the considered outcomes (Table 3).

PFAS concentration in the blood

The maternal PFAS concentrations for PFOA, PFOS, and PFHxS showed a median concentration of 17 ng/mL (*IQR*: 8–35), 3.10 ng/mL (*IQR*: 2.30–4.20), and 2.20 ng/mL (*IQR*: 1.40–3.40), respectively. When the blood was analyzed, participants from Red Zone A reported a higher concentration of all types of PFAS relative to those from Red Zone B (Table S1). The concentrations of PFAS showed significant pairwise positive correlations, particularly between PFOA and PFHxS (Pearson's correlation: 0.821, *P* < 0.001) (Fig. 3).

Fig. 2 **a** Red Zone in the Veneto Region (Italy), **b** subdivision of the Red Zone to Zone A and Zone B, **c** and **d** the number of participants and those with PFAS measurement for each municipality, respectively

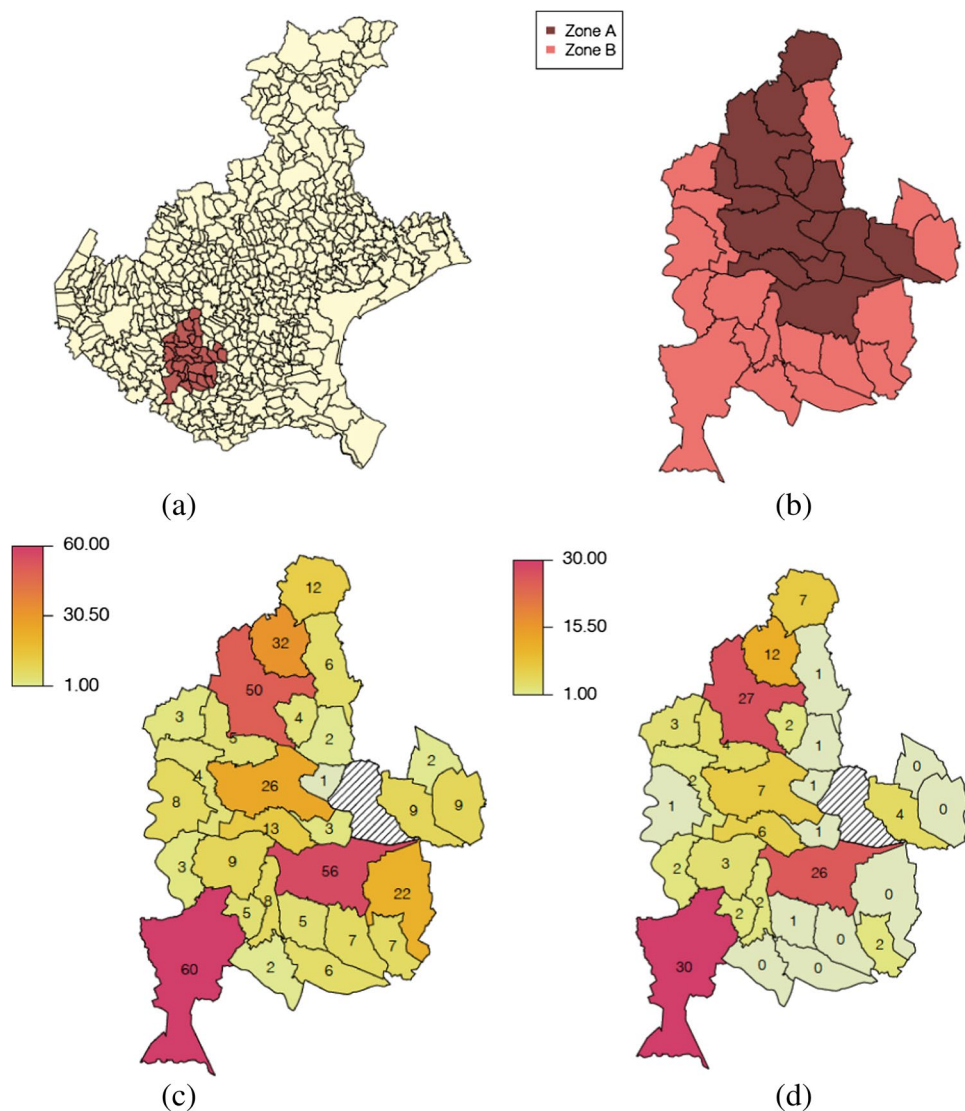


Table 2 The Odds Ratios* (ORs) and the 95% CI estimated by a cumulative logistic regression model with the perceived health risk of PFAS as the dependent variable

Predictors	OR	95% CI	P-values
Trust in scientific institutions [+ 1 pt.]	1.15	1.05–1.26	0.004
Trust in political institutions [+ 1 pt.]	0.83	0.76–0.92	<0.001
Trust in social media [+ 1 pt.]	1.11	1.01–1.22	0.037
Housewife/unemployed (reference)	1.00	-	-
Part-time	0.70	0.38–1.29	0.253
Full-time	0.54	0.31–0.93	0.028
MSPSS friends score [+ 1 pt.]	1.13	1.03–1.25	0.011

*Bold values denote statistical significance at the $p < 0.05$ level

The most important characteristics of the mothers concerning the concentration of PFOA, based on the median PFOA level, were the residence time ($P < 0.001$), residence in the Red Zone A or B ($P < 0.001$), number of children

before 2008 ($P < 0.001$), breastfeeding duration of the first child ($P < 0.001$), and the consumption of tap water ($P = 0.021$) (Table 4).

The results of the regression model based on the log-PFAS concentration are summarized in Table 5. In each model, all the variables related to pregnancy and to residence time explained a discrete level of variance (Table S2). For variables not related to pregnancy, consumption of tap water was associated with an increase in both the log-PFOA and log-PFHxS levels. The interaction between tap water consumption and the residence time (Table 4, Fig. 4) showed a higher increase in the log-PFOA and log-PFHxS levels for those who were long-time residents (> 20 years) than in the short-time residents.

Living in Red Zone B was associated with a lower PFAS concentration ($P < 0.001$ for the three models). For the interaction with tap water consumption, the log-PFOA model indicated a differential effect of drinking tap water with

Table 3 Adjusted* Odds Ratios** (ORs) and 95% CI estimated by logistic regression models with dependent variables as self-reported diseases, autoimmune disorders, cardiovascular diseases, liver diseases, cancer, and pregnancy-related complications with respect to the reference category***

	Self-reported disease		Autoimmune disorders		Cardiovascular diseases		Liver diseases		Cancer		Pregnancy complications	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Environmental factors												
Residential time [> 20 years]	0.97	0.62–1.53	0.98	0.53–1.78	1.15	0.42–3.00	0.88	0.24–3.08	2.15	0.80–5.92	0.87	0.50–1.47
Red Zone [area A]	0.87	0.56–1.37	1.15	0.64–2.07	1.63	0.60–4.73	2.28	0.61–9.81	0.69	0.25–1.93	1.12	0.67–1.89
Tap water habit [+ 1 pt.]	1.07	1.01–1.14	1.05	0.97–1.13	0.96	0.83–1.10	0.88	0.71–1.06	1.21	1.06–1.40	1.06	0.99–1.14
Individual factors												
PFAS meas. [present, PFOA ≤ 17 ng/mL]	1.73	1.01–3.00	1.35	0.67–2.66	0.77	0.17–2.60	1.08	0.20–4.49	1.06	0.26–3.55	1.24	0.66–2.27
PFAS meas. [present, PFOA > 17 ng/mL]	1.40	0.78–2.52	0.80	0.36–1.71	1.22	0.37–3.67	1.02	0.18–4.73	1.32	0.39–4.29	0.69	0.33–1.39
PFAS perceived risk [+ 1 pt.]	1.14	1.02–1.28	1.19	1.02–1.40	1.04	0.82–1.35	1.06	0.78–1.52	1.05	0.81–1.40	1.12	0.98–1.29
Number of children [+ 1]	0.92	0.69–1.21	0.77	0.52–1.12	1.04	0.57–1.79	0.97	0.44–1.90	1.24	0.70–2.10	0.86	0.62–1.19
Observations		384		384		384		384		384		384
R ² Tjur		0.069		0.028		0.036		0.056		0.134		0.035

*Adjusted also for mother's age in continuous form, education level, and employment. **Bold values denote statistical significance at the $p < 0.05$ level. ***Education level [high school], Red Zone [A], residential time [≤ 20 years]; PFAS measurement [absent]

the residence zone ($P = 0.042$, Fig. 4). Food consumption explained a limited level of variance (Table S2); specifically, local meat consumption and the lack of meat consumption increased log-PFOA and log-PFHxS levels, compared to the levels for those who consumed meat from the supermarket. The consumption of vegetables grown in the garden of the participants was associated with higher log-PFOS values relative to the values for those participants who bought vegetables from the supermarket. Living in a detached house was also associated with reduced log-PFOA and log-PFHxS levels ($P = 0.002$ and $P = 0.075$, respectively) relative to the levels in those living in other types of houses. Overall, the variance explained by the pregnancy-related predictors was high, specifically for the log-PFOA concentration (Table S2; 36% PFOA, 17% PFOS, and 17% PFHxS).

The number of children conceived before 2008 was negatively associated with the log-PFOA and log-PFHxS concentrations. The number of abortions was negatively associated with the log-PFOS levels ($P = 0.001$), particularly, in mothers living in Red Zone A (Fig. 4). Conversely, the concentrations of PFOA and PFOS were positively associated with time since the last pregnancy. A progressive reduction in the log-PFOA concentrations was associated with longer breastfeeding of the first, second, and third child. This reduction was also significant for PFOS levels, but only for the first two pregnancies between 2008 and 2018, while for PFHxS, the association was limited to the breastfeeding of the first child only (Table 5).

The total variance explained by the models for log-PFOA, PFOS, and PFHxS was 54.0%, 29.4%, and 35.2%, respectively (R^2 adjusted). However, only the model that estimated the log-PFOA concentration showed a good predictive power ($Q^2 = 45.8\%$).

Discussion

This study assessed mothers (of young children) living in a severely PFAS-contaminated region. These mothers were exposed to elevated levels of PFOA through drinking water till 2017. The data was used to determine the environmental and individual factors that might influence the perception of health risks due to exposure to PFAS. Additionally, we investigated whether perceived risk, along with environmental factors linked to PFAS exposure, was associated with self-reported diseases in the mothers. From some of the participants, we also evaluated the real environmental and individual influencing factors that might be associated with the serum PFAS levels in the mothers.

The perceived risk of being exposed to PFAS was strongly associated with the trust in scientific and political institutions and information from social media. We found that the risk perception of the participants was associated

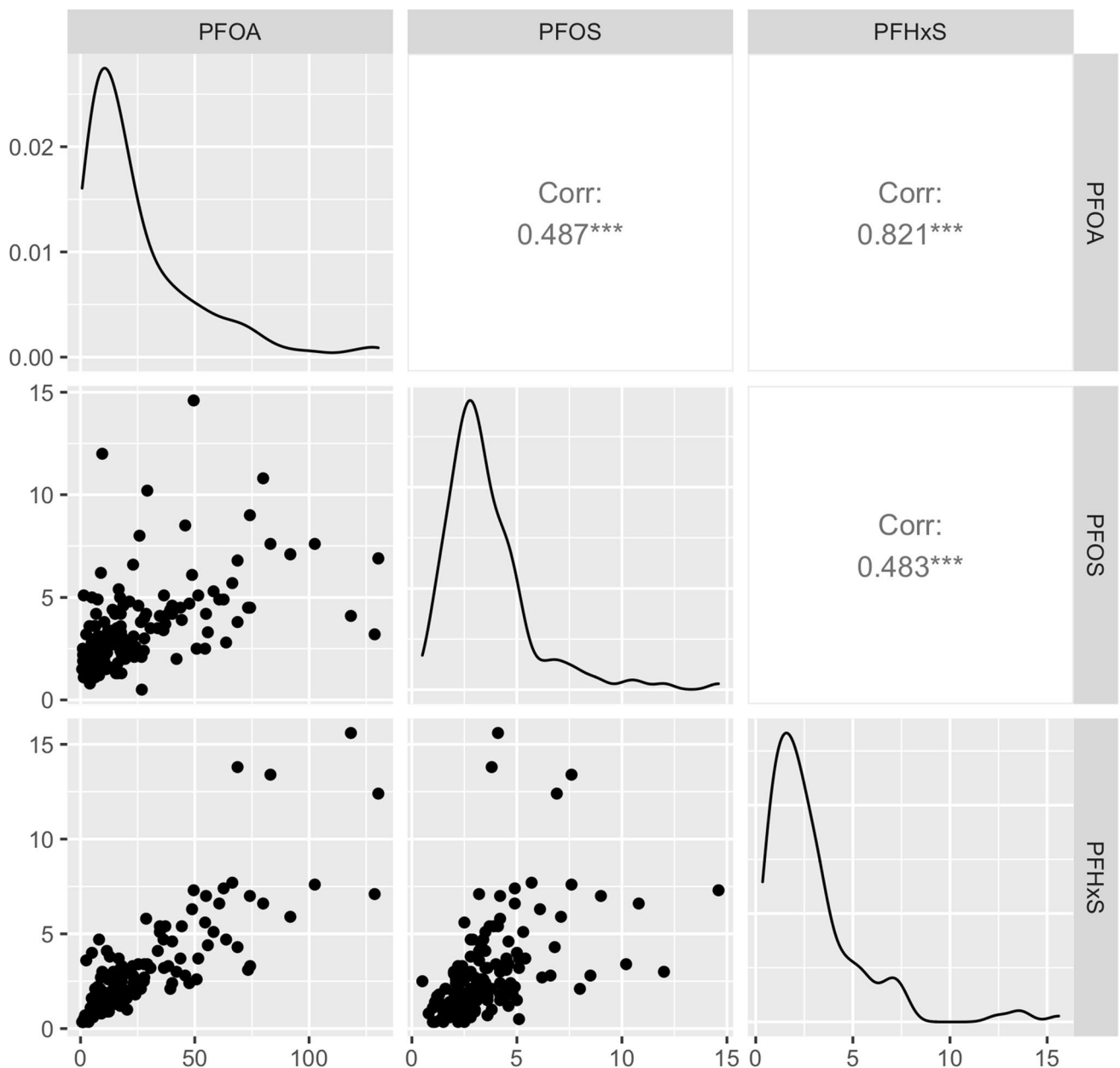


Fig. 3 Pairwise Pearson's correlation among PFOA, PFOS, and PFHxS concentrations

with the information provided to the public by institutions and the media (Goldstein 2017). PFAS contamination is often “invisible,” i.e., individuals are unable to detect such substances in the water or food. Moreover, the effects are uncertain, and there is a long gap between the first exposure and the detection of contamination and possible consequences in individuals (Goldstein 2017). Interestingly, the trust in scientific institutions was positively associated with perceived risk; thus, indicating that those who had greater trust in scientific information perceived stronger detrimental effects of PFAS (Steenland et al. 2020). The effect of trust in political institutions was strongly associated with

the reduction in perceived risk. After the detection of PFAS contamination, the local authority equipped water treatment plants with granular activated carbon filters, while a surveillance program of the exposed population was conducted (Pitter et al. 2020). In general, the trust in these mitigation and health measures reduced the perception of risk (Viklund 2003). Previous studies have reported several common concerns of the members of the community who faced PFAS contamination: health issues due to unhygienic living conditions, loss of confidence in governmental institutions, feeling insecure, frustration, and lack of control/agency over the situation; all these issues can be resolved by a renewed trust in

Table 4 The characteristics of the mothers with PFAS measurements, overall and by PFOA concentration according to the median value (17 ng/mL)

	N	Overall, N= 148 ¹		PFOA concentration (ng/mL)		P-value ²
		≤17], N= 74 ¹	> 17], N= 74 ¹	≤17], N= 74 ¹	> 17], N= 74 ¹	
Age (years)	148	43.0 (38, 47)	42.0 (37.2, 45)	44 (39, 47)	0.070	
Educational level	148				0.46	
High school		81 (55%)	39 (53%)	42 (57%)		
Degree or higher		56 (38%)	31 (42%)	25 (34%)		
Middle school		11 (7.4%)	4 (5.4%)	7 (9.5%)		
Mother employment	148				0.49	
Housewife/unemployed		17 (11%)	8 (11%)	9 (12%)		
Part-time		44 (30%)	19 (26%)	25 (34%)		
Full-time		87 (59%)	47 (64%)	40 (54%)		
Residential time [>20 years]	148	86 (58%)	20 (27%)	42 (57%)	<0.001	
Residence	148				<0.001	
Red Zone – area A		98 (66%)	37 (50%)	61 (82%)		
Red Zone – area B		50 (34%)	37 (50%)	13 (18%)		
Detached house	148	67 (45%)	39 (53%)	28 (38%)	0.069	
BMI (kg/m ²)		22.7 (20.8, 25.5)	22.6 (20.9, 25.3)	22.8 (20.6, 25.9)	0.97	
N. of children before 2008	148	1 (1, 2)	1 (1, 2)	1 (1, 1.75)	<0.001	
N. of children after 2008	148	0 (0, 1)	0 (0, 1)	0 (0, 1)	0.15	
Number of abortions	148	0 (0, 1)	0 (0, 1)	0 (0, 1)	0.33	
Breastfeeding duration 1st child	148				<0.001	
No or no yet breastfed		30 (20%)	3 (4.1%)	27 (36%)		
1–6 months		40 (27%)	18 (24%)	22 (30%)		
6–12 months		37 (25%)	23 (31%)	14 (19%)		
12–24 months		32 (22%)	21 (28%)	11 (15%)		
> 24 months		9 (6.1%)	9 (12%)	0 (0%)		
Breastfeeding duration 2nd child	66				0.056	
No or no child		10 (15%)	3 (7.1%)	7 (29%)		
1–6 months		7 (11%)	5 (12%)	2 (8.3%)		
6–12 months		19 (29%)	11 (26%)	8 (33%)		
12–24 months		23 (35%)	19 (45%)	4 (17%)		
> 24 months		7 (11%)	4 (9.5%)	3 (12%)		

Table 4 (Continued)

	N	Overall, N= 148 ¹	PFOA concentration (ng/mL)		P-value ²
			[> 17], N = 74 ¹		
			≤ 17], N = 74 ¹	> 17], N = 74 ¹	
Breastfeeding duration 3rd child	9				0.22
No or no child		0 (0%)	0 (0%)	0 (0%)	
1–6 months		1 (11%)	0 (0%)	1 (100%)	
6–12 months		1 (11%)	1 (12%)	0 (0%)	
12–24 months		5 (56%)	5 (62%)	0 (0%)	
> 24 months		2 (22%)	2 (25%)	0 (0%)	
Times since last pregnancy	148				0.068
No or before blood analysis		22 (15%)	9 (12%)	13 (18%)	
(0,7] years		82 (55%)	48 (65%)	34 (46%)	
> 7 years		44 (30%)	17 (23%)	27 (36%)	
Tap water habit	148	4 (1, 9)	3 (1, 8)	5 (2, 9)	0.021
Meat consumption	148				0.44
Local farmer		12 (8.1%)	4 (5.4%)	8 (11%)	
Supermarket		66 (45%)	37 (50%)	29 (39%)	
Butcher's shop		65 (44%)	31 (42%)	34 (46%)	
No consumption		5 (3.4%)	2 (2.7%)	3 (4.1%)	
Vegetable consumption	148				0.15
Local market		17 (11%)	12 (16%)	5 (6.8%)	
Own garden		44 (30%)	19 (26%)	25 (34%)	
Supermarket		66 (45%)	30 (41%)	36 (49%)	
Neighboring farmers		21 (14%)	13 (18%)	8 (11%)	

¹Median (IQR) or frequency (%). ²Wilcoxon rank sum test; Pearson's chi-squared test; Fisher's exact test

Table 5 The coefficients estimated* by regression models for the log-PFAS concentration with respect to the reference category**

Predictors	Log-PFOA model			Log-PFOS model			Log-PFHxS model		
	Est	95% CI	P-value	Est	95% CI	P-value	Est	95% CI	P-value
(Intercept)	3.48	2.94–4.02	<0.001	1.64	1.02–2.26	<0.001	1.59	1.13–2.06	<0.001
Tap water habit [+1 pt.]	0.09	0.03–0.16	0.004				0.09	0.04–0.14	0.001
Residential time [>20 years]	–0.08	–0.36–0.51	0.725	0.47	–0.67 to –0.27	<0.001	0.56	–0.79 to –0.33	<0.001
Tap water * residential time [>20 years]	0.10	–0.18 to –0.03	0.006				0.07	–0.14 to –0.01	0.022
Red Zone [B]	–1.09	–1.54 to –0.65	<0.001	–0.33	–0.50 to –0.16	<0.001	–0.53	–0.77 to –0.30	<0.001
Tap water * Red Zone [B]	0.08	0.00–0.16	0.042						
Meat [local meat]	0.33	–0.16–0.82	0.189				0.26	–0.19–0.71	0.262
Meat [Butcher's shop]	0.10	–0.17–0.36	0.465				–0.01	–0.23–0.24	0.946
Meat [no-consumption]	0.76	0.04–1.48	0.040				0.71	0.09–1.32	0.025
Vegetables [local market]				–0.23	–0.50–0.03	0.085			
Vegetables [own garden]				0.27	0.08–0.47	0.006			
Vegetables [neighboring farmers]				–0.09	–0.33–0.15	0.470			
BMI (+1 kg/m ²)				–0.02	–0.04–0.00	0.090			
Detached house [yes]	–0.40	–0.65 to –0.15	0.002				–0.19	–0.41–0.02	0.075
N. children before 2008 [+1]	–0.24	–0.43 to –0.05	0.013	0.24	–0.01–0.48	0.058	–0.29	–0.47 to –0.11	0.002
N. children after 2008 [+1]							–0.14	–0.30–0.01	0.076
N. of abortions [+1]				–0.22	–0.35 to –0.09	0.001			
N. of abortions [+1]* Red Zone [B]				0.24	0.06–0.42	0.009			
Time since last preg- nancy [0–7 years]	0.13	–0.27–0.53	0.525	0.14	–0.11–0.38	0.272			
Time since last preg- nancy [>7 years]	0.48	0.02–0.95	0.041	0.39	0.11–0.67	0.007			
Breastfeeding 1st child [1–6 months]	–0.30	–0.68–0.08	0.121	–0.19	–0.43–0.05	0.124	–0.34	–0.65 to –0.03	0.034
Breastfeeding 1st child [6–12 months]	–0.62	–1.02 to –0.21	0.003	–0.38	–0.64 to –0.12	0.005	–0.36	–0.69 to –0.04	0.029
Breastfeeding 1st child [12–24 months]	–0.71	–1.13 to –0.29	0.001	–0.14	–0.42–0.13	0.306	–0.33	–0.66–0.00	0.051
Breastfeeding 1st child [>24 months]	–1.29	–1.92 to –0.65	<0.001	–0.23	–0.62–0.17	0.253	–0.82	–1.33 to –0.31	0.002
Breastfeeding 2nd child [1–6 months]	–0.49	–1.08–0.11	0.109	–0.40	–0.83–0.03	0.066			
Breastfeeding 2nd child [6–12 months]	–0.32	–0.73–0.09	0.123	–0.35	–0.72–0.01	0.059			
Breastfeeding 2nd child [12–24 months]	–0.45	–0.87 to –0.04	0.032	–0.12	–0.48–0.25	0.531			
Breastfeeding 2nd child [>24 months]	–0.69	–1.32 to –0.05	0.034	–0.64	–1.11 to –0.17	0.008			
Breastfeeding 3rd child [yes]	–0.75	–1.31 to –0.19	0.009						
Observations/predictors	148/10			146/9				145/7	
R ² /R ² adjusted/Q ²	0.606/0.540/0.458			0.386/0.294/0.219				0.401/0.352/0.299	

*Bold values denote statistical significance at the $p < 0.05$ level. **Residence [≤ 20 years], Red Zone [A], meat [supermarket], vegetables [supermarket], breastfeeding 1st child [no], breastfeeding 2nd child [no], breastfeeding 3rd child [no], detached house [no], time since last pregnancy [no or before blood analysis]

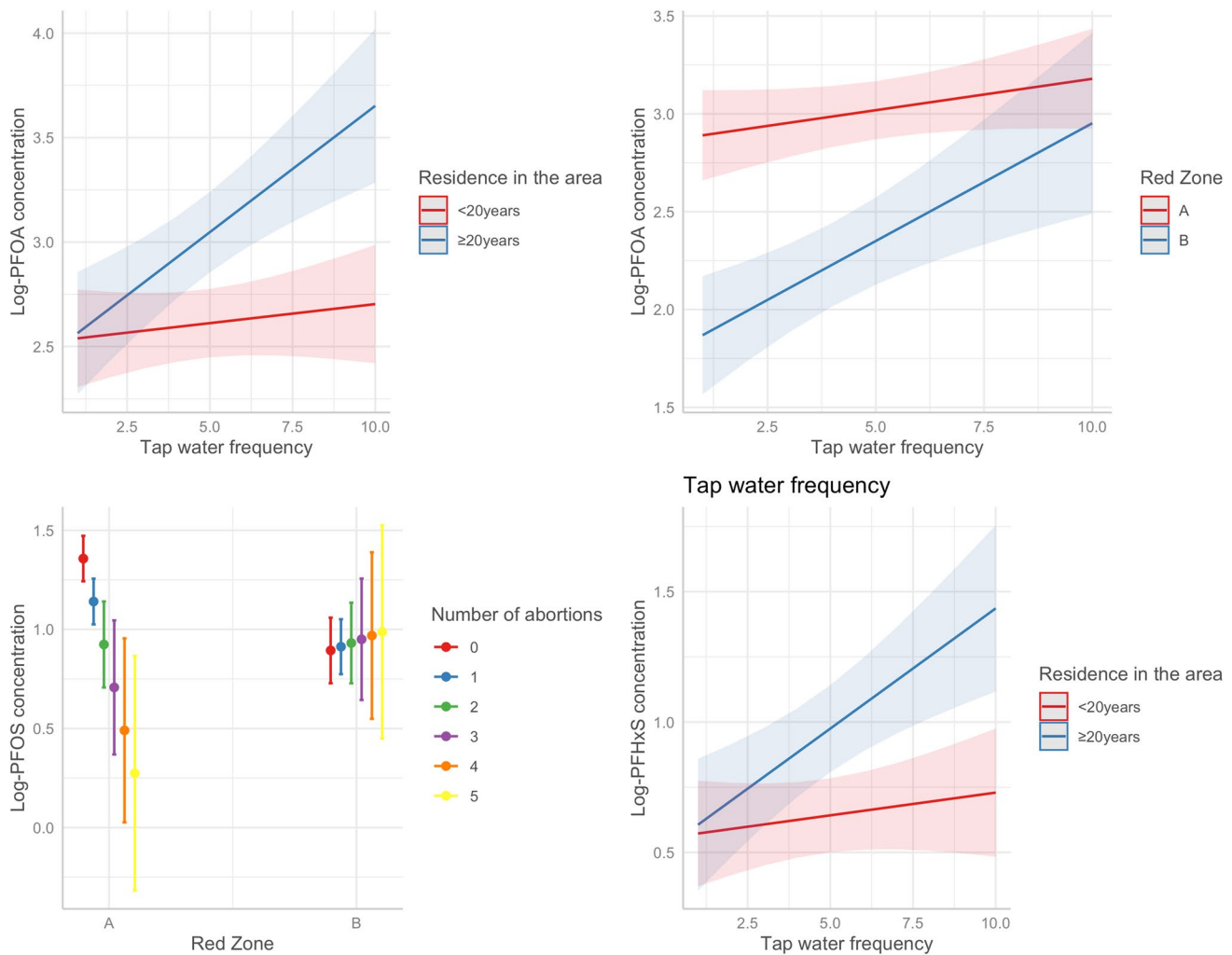


Fig. 4 The predicted log-PFAS values, based on the interactions between variables in the log-PFAS linear regression models

political institutions (Calloway et al. 2020). Conversely, trust in information on social media reshapes public risk perception by increasing self-reported knowledge (Liu et al. 2021). Within the population of child-bearing women, those who were full-time employees perceived a lower PFAS health risk than housewives or unemployed individuals, suggesting that maternity (probably linked to the status of housewife or unemployment) might make them more worried about their children's future (Signorino 2012). Previous studies (Jetten et al. 2012) suggested that having a strong network of friends imparts psychological benefits, but in this context, it might contribute to amplifying the perceived risk. Specifically, within the population of the mothers living in the "red zone" (highly contaminated), mothers with a wider social network were more connected to the community and were frequently reminded of the possible risks of environmental contamination.

The analysis of the self-reported diseases showed that mothers with higher risk perception related to PFAS exposure reported more health issues and autoimmune disorders. Similarly, participants in the surveillance program with known PFAS levels showed higher occurrences of self-reported diseases. High-risk perception is associated with a change in the lifestyle and adoption of health-protective measures (Gerber and Neeley 2005; Coi et al. 2016). Exposure to chronic environmental pollution was associated with an increase in the general distress among contaminated communities because these individuals face uncertainty, worries related to health risks (cancer clusters, unexplained deaths, worsening health conditions, and the future health of children) (Calloway et al. 2020; Banwell et al. 2021), and the potential of further being exposed to the contaminants every day (e.g., water sources and usage) (Calloway et al. 2020). A continuous and high-stress response can cause immune

dysregulation, which might lead to autoimmune disease by altering or amplifying cytokine production (Stojanovich 2010).

Among environmental factors, consumption of tap water was associated with more reports on health issues, particularly of cancer, as well as a longer residence time. The residents of Red Zone A had two times higher risk of liver diseases than those of Red Zone B. Drinking contaminated water is a well-known source of PFAS exposure (Domingo and Nadal 2019). This could be a reason for the long-term residents of Red Zone A to report a higher PFAS concentration (Pitter et al. 2020). Several studies found an association between PFAS exposure and markers of liver diseases (Armstrong and Guo 2019; Bassler et al. 2019), while the association between PFAS exposure and common types of cancer in young mothers (e.g., breast cancer) showed mixed results (Bonefeld-Jørgensen et al. 2014; Hurley et al. 2018; Tsai et al. 2020). Additionally, a higher risk of cardiovascular diseases was reported in residents of Red Zone A compared to those living in Red Zone B. Despite researches reported mixed findings (Winquist and Steenland 2014), this result was in line with previous studies that showed an association between serum blood PFAS concentration and the risk of cardiovascular diseases (Shankar et al. 2012; Huang et al. 2018), where a platelet-centered mechanism might be the biological link (De Toni et al. 2020; Meneguzzi et al. 2021).

Factors derived from environmental contamination, such as the contamination of food, may or may not be associated with real exposure (Dettori et al. 2020), and this discrepancy can be modulated by a combination of objective (e.g., exposure levels) and subjective factors (e.g., socioeconomic conditions and cultural values). In this study, we evaluated which factors influenced PFAS levels among mothers of young children. Pregnancy-related variables (breastfeeding, number of abortions, number of children, and time since last pregnancy) were the major determinants of PFAS levels in the mother's blood. Breastfeeding significantly influenced all log-PFAS models, especially the log-PFOA model, which estimated a large effect up to the birth of the third child. This result confirmed that mothers who breastfed exhibited lower PFAS concentrations than those who did not breastfeed. A significant quantity of PFAS can be removed from the body through breast milk (Mondal et al. 2014). Conversely, PFAS can be passed through breastfeeding from the mother to nursed infants and accumulate with the PFAS from prenatal placental transfer and postnatal exposure to contaminants (e.g., through environmental exposure, diet, or tap water consumption) (Kim et al. 2020), posing some questions about the potential effect of that PFAS exposure to the child health and development (Harris et al. 2021).

We found that the area of residence was another significant predictor of PFAS concentration in the mother's blood (Pitter et al. 2020). Based on our analysis, individuals living

in the municipalities of the Red Zone located above the site of groundwater contamination (Red Zone A) showed a higher blood PFAS level than those residing outside (Red Zone B). Additionally, participants from municipalities outside Red Zone A showed lower PFAS concentrations, especially when they consumed tap water less often. The association between PFAS levels and other variables, such as the source of meat or vegetables, was lower in our study than that reported for the general population (Brantsaeter et al. 2013; Berg et al. 2014).

Most of the questionnaires were completed by the participants. From some of the participants, we also obtained a measure of the serum blood PFAS concentration. The variables recorded allowed us to conduct three types of analyses to address specific research questions. This was the first study to simultaneously analyze the perceived risk, health outcomes, and PFAS determinants in the same population. Some results, especially those regarding the determinants of PFAS concentration, are very important (Mondal et al. 2014). This study had a small sample size, which might affect the generalizability of our results. Moreover, the participants were mothers who volunteered to participate in an online survey that was mainly spread through word-of-mouth. The online modality implied a certain selection bias since certain types of participants were under-represented, for example, those with a low education level. Basically, the cross-sectional nature of the study and self-reporting of diseases limited the causal attribution of the results. To overcome this latter point, we introduced some confounding variables in the analysis (e.g., age, education level, and employment status) to keep into account the non-probability sampling and to perform an adjustment of the risk estimates. In terms of health outcomes, we grouped and analyzed several diseases into a single comprehensive category, which limited our ability to derive strong associations between the PFAS measures and a specific disease.

Conclusions

This study was the first to be conducted from a highly PFAS-contaminated area in Italy that examined perceived risk and factors influencing the PFAS concentration in mothers with young children. This study pointed out the importance of the circulation periodicity and the reliability of the information disclosed to residents to control the perceived risk. However, comprehensive large-scale epidemiological studies are required to determine the association between the occurrences of some diseases and the historical PFAS exposure. In addition, preventive health measures can promote the screening of PFAS serum levels in future mothers, while intervention programs can support mothers who breastfeed their children with intervention programs promoting

parenting practices for a positive mother-infant relationship. Furthermore, research programs should concentrate on assessing the influence of PFAS on the health and development of children.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s11356-022-20085-5>.

Author contribution Conceptualization: PG, AL, and SS; methodology and formal analysis: PG; validation: PG, AL, and SS; investigation: PG, LM, and SS; funding acquisition: PG, AL, and SS; data curation: SL and LM; writing—original draft preparation: PG, AL, and SS; writing—review and editing: PG, AL, LM, and SS; supervision: PG and SS. All authors have read and agreed to the published version of the manuscript.

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Data availability The dataset generated during and/or analyzed during the current study is available from the corresponding author upon reasonable request.

Declarations

Ethics approval The study was approved by the ethical committee of the researchers' university (protocol number 4051).

Informed consent Informed consent was obtained from all the participants involved in the study.

Conflict of interest The authors declare no competing interests.

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