Environmental Research 207 (2022) 112206

Contents lists available at ScienceDirect

Environmental Research

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

Breastfeeding initiation and duration after high exposure to perfluoroalkyl substances through contaminated drinking water: A cohort study from Ronneby, Sweden

Christel Nielsen [a,*], Ying Li [b], Magdalena Lewandowski [a], Tony Fletcher [c], Kristina Jakobsson [b,d]

[a] Division of Occupational and Environmental Medicine, Department of Laboratory Medicine, Lund University, Lund, Sweden
[b] School of Public Health and Community Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Göteborg, Sweden
[c] London School of Hygiene and Tropical Medicine, London, UK
[d] Occupational and Environmental Medicine, Sahlgrenska University Hospital, Göteborg, Sweden

ARTICLE INFO

Keywords:
Perfluoroalkyl substances
Breastfeeding
Maternal exposure
Contaminated drinking water
AFFF-Foam

ABSTRACT

Background: The drinking water in parts of Ronneby was heavily contaminated with perfluoroalkyl substances (PFAS) for decades. Although PFAS has endocrine-disrupting properties and may interfere with breastfeeding, the effects in populations with a point source of high exposure are unknown.

Objectives: To investigate associations between high PFAS exposure and 1) initiation and 2) duration of breastfeeding.

Methods: We retrieved data on infant feeding practices for 2374 children born between 1999 and 2009 from Child Health Care centers in Ronneby and a reference municipality. Residential address before delivery was used as a proxy for exposure, and confounders were obtained from charts and registers. We used modified Poisson regressions to estimate the relative risks (RR) of not initiating breastfeeding, not breastfeeding exclusively after 3 months, and not breastfeeding at all at 6 months. We also estimated hazard ratios (HR) of cessation of exclusive breastfeeding before 6 months and any breastfeeding before 12 months.

Results: Mothers who had received contaminated water seemed to have a higher risk of not initiating breastfeeding (RR = 2.4; 95% CI: 0.8, 6.7). Primiparous mothers from the exposed area were at a 1.2 times increased risk (95% CI: 0.9, 1.6) of not exclusively breastfeeding at 3 months and a 1.6 times increased risk (95% CI: 1.2, 2.1) of not breastfeeding at 6 months. The results were confirmed by the Cox regressions, which further showed that the HR for cessation of any breastfeeding was time dependent and higher in early lactation, thereafter decreasing as lactation progressed. We observed no overall associations in multiparous mothers.

Discussion: Exposure to high levels of PFAS seemed to be associated with increased risks of not initiating breastfeeding and shorter breastfeeding duration in primiparous mothers. The findings imply that the ability of first-time mothers to establish breastfeeding is a sensitive outcome after high exposure to PFAS.

1. Introduction

Perfluoroalkyl substances (PFAS) are endocrine-active environmental contaminants with biological half-lives of several years (Li et al., 2018; Seals et al., 2011; Olsen et al., 2007). They have been used in a wide range of consumer products and industrial applications over time, including surface coating of textiles and paper, fire-fighting foam, and electroplating. A recent overview identified more than 200 use categories (Glüge et al., 2020).The extensive use has caused global contamination and hot spots with drinking water contamination continue to emerge worldwide (Hoppin et al., 2019; The German Federal Minist, 2020).

The physiological processes governing pregnancy and breastfeeding are highly dependent on hormonal cascades, and there is concern that endocrine disruptors may interfere with mammary gland development and lactogenesis (Fenton et al., 2012; Konkel, 2017; Criswell et al., 2020). Animal studies have confirmed that gestational exposure to perfluorooctanoic acid (PFOA) causes substantial delay in mammary gland development, resulting in morphologically underdeveloped glands that are unable to meet the nutritional requirements of the

* Corresponding author. Lund University, Occupational and Environmental Medicine, Medicon Village (402A), Scheelevägen 8, 223 81, Lund, Sweden.
E-mail address: christel.nielsen@med.lu.se (C. Nielsen).

https://doi.org/10.1016/j.envres.2021.112206
Received 18 February 2021; Received in revised form 29 September 2021; Accepted 9 October 2021
Available online 13 October 2021

offspring (White et al., 2007). Yet, the body of evidence from epidemiologic studies is insufficient to draw any conclusions about whether breastfeeding initiation might be affected by PFAS exposure in humans.

Inadequate milk supply is a leading cause of undesired early cessation of breastfeeding (Morrison et al., 2019; Odom et al., 2013; Brown et al., 2014). Epidemiological studies lend support to the observation that higher serum concentrations of perfluorooctanesulfonic acid (PFOS) and PFOA are associated with shorter breastfeeding duration (Timmermann et al., 2017; Fei et al., 2010; Romano et al., 2016). However, the existing evidence is conflicting, as no association and inverse associations have been reported (Rosen et al., 2018). The current literature is based solely on populations with background exposure and modest interindividual variation with respect to exposure levels. The lack of research from settings with a point source of high exposure from industrial plants or firefighting training sites prevents assessment of the magnitude of the effect that might be expected in such situations as the shape of the dose-response curve is unknown.

In Ronneby, Sweden, very high levels of several PFAS (sum PFAS >10,000 ng/L (Xu et al., 2021);) were unexpectedly detected in 2013 in the outgoing drinking water from one of two municipal waterworks. The contaminated waterworks supplied one-third of the population, with the remaining two-thirds receiving their water from the noncontaminated waterworks, thus resulting in a natural experiment with a population exposed to a very wide range of PFAS levels.

Sweden has one of the highest breastfeeding rates among industrialized countries (Galtry, 2003). In 2005, 98% of Swedish mothers initiated breastfeeding and 70% of children were still breastfed at 6 months of age (The National Board of Hea, 2021). Since 2002, the parental insurance scheme grants 480 days of paid parental leave per child and there is therefore no policy-related incentives for mothers to terminate breastfeeding.

Our aim was to assess the possible associations between exposure to PFAS and breastfeeding initiation and duration in the highly exposed Ronneby population, using residential history from national registers as a proxy for exposure along with routinely collected outcome data from Child Health Care (CHC) charts.

2. Methods

2.1. Setting

The municipality of Ronneby in southern Sweden has 28,000 inhabitants. Contamination by PFAS was discovered in late 2013, after which water from the noncontaminated waterworks was immediately provided to all affected households (Xu et al., 2021). The source of the contamination was the leakage of aqueous film forming firefighting (AFFF) foams from a military training range near the aquifer. It is not clear when the contamination reached the water table, but we know that AFFF foams were used at the training range starting in the mid-1980s.

In 2014-2015, all residents in the municipality were invited to free-of-charge blood samplings to have their serum concentrations measured. Approximately 13% of the population at the time participated in this biomonitoring, which showed serum concentrations of perfluorohexane sulfonic acid (PFHxS), PFOS, and PFOA 135, 35, and 5 times higher, respectively, in Ronneby relative to a nearby municipality (Karlshamn) with uncontaminated drinking water (Xu et al., 2021). Women of childbearing age (21–40 years old) had geometric mean PFHxS, PFOS, and PFOA concentrations of 60, 80, and 5 ng/mL, respectively, with 95th percentiles of PFHxS and PFOS at several hundred nanograms per milliliter. Corresponding concentrations in Karlshamn women in the same age group were 0.9, 3.2, and 1.3 ng/mL.

2.2. Participants

We retrieved CHC charts for children born between 1999 and 2009 from the three CHC centers in Ronneby ($n = 2449$; Fig. 1). According to Statistics Sweden, 2893 infants were born in the municipality during the study period: we were thus able to locate charts for ~85% of all children. We also included a reference group from Karlshamn ($n = 123$), who received uncontaminated drinking water (i.e., background levels of exposure) and were representative of the general population. Twins, children with any malformation, and children for whom there was incomplete data on feeding practices were excluded. The final study

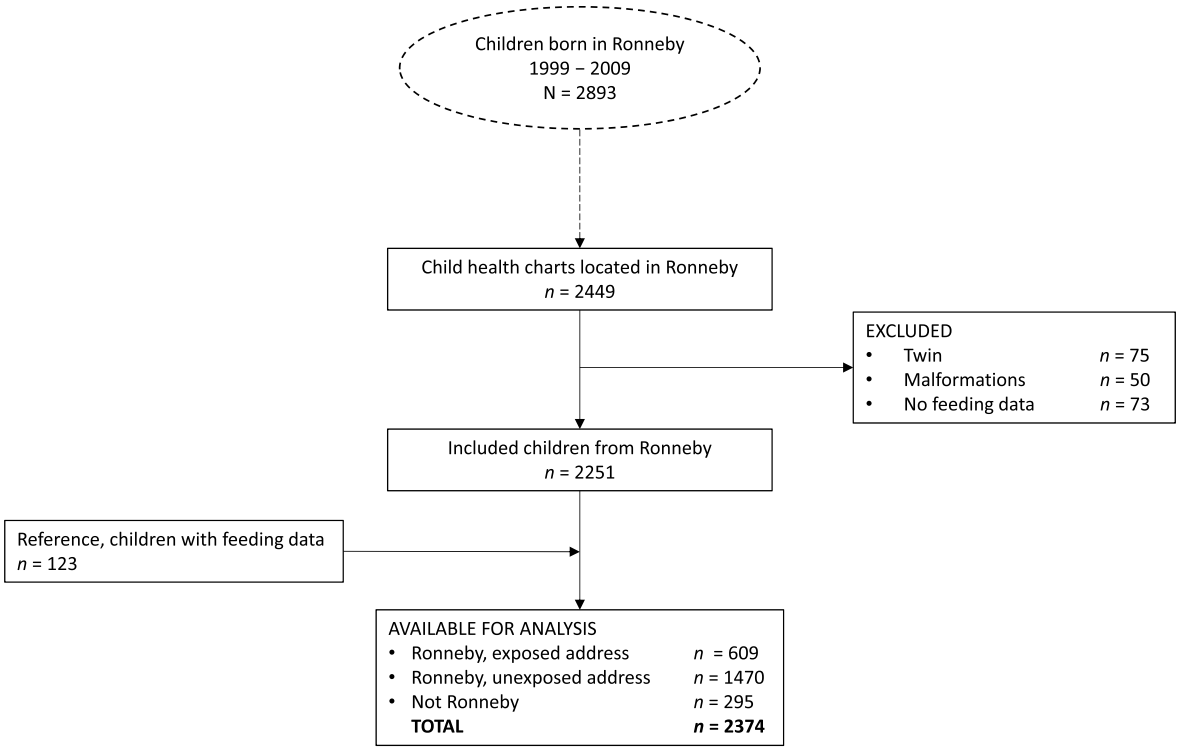

Fig. 1. Flowchart describing the inclusion of study participants.

population consisted of 2374 infants, of which 26% were from households within the area supplied with contaminated water.

The study was approved by the Regional Ethical Review Board in Lund (no. 2016/366 with amendments). Informed consent was not required, but study participants were informed of the study through advertisement in local media.

2.3. Variables and data sources

2.3.1. Outcomes: breastfeeding initiation and duration

Swedish CHC services are offered free of charge to all children, and the participation rate is close to 100% (The National Board of Hea, 2014). Nurses document infant feeding practices in the child's medical chart during each routine visit to CHC. Information on breastfeeding and formula feeding was available on a monthly basis during the first year and less frequently thereafter.

We assessed the risk of not initiating breastfeeding and, among initiators, the risks of not breastfeeding exclusively after 3 months and not breastfeeding at all at 6 months. We considered mothers who started breastfeeding when the baby was born as initiators, irrespective of breastfeeding duration and whether formula was used as supplementation. Total breastfeeding duration was defined as the latest time point when any breastfeeding occurred, regardless of supplementation from other nutritional sources. We defined exclusive breastfeeding as ongoing breastfeeding without formula supplementation taking place at or before the cutoff.

Data on occupational water supply were not available. We added information on potential confounders from the Swedish Medical Birth Register (National Board of Health and Welfare) and the Register on Participation in Education (Statistics Sweden).

2.3.2. Exposure assessment: residential address

We used the residential addresses of mothers during the 5-year window before delivery as a proxy for PFAS exposure, because we assumed that exposure levels in the time period before childbirth would have the greatest impact on breastfeeding ability. We have previously estimated biological half-lives of PFHxS and PFOS of 5.3 and 3.4 years in the Ronneby population (Li et al., 2018). Thus, a 5-year exposure window captures maternal exposure before one half-life has passed.

Maternal residential address on December 31st of each year was retrieved from the Total Population register (Statistics Sweden) and linked to annual municipal lists of water supply. Thus, for each participant, we gathered information on whether she lived in Ronneby during the exposure window, and for those living in Ronneby, whether their residential water supply was from the highly contaminated waterworks, the other waterworks, or a private well. We classified Ronneby mothers as having high exposure if they had lived at least 1 year at an address with drinking water from the contaminated waterworks and as having low exposure if they had received drinking water from the other municipal waterworks or from a private well. We have applied a similar exposure assessment in previous work and compared it with measured serum concentrations (Xu et al., 2021). Thus, we know that it provides strong exposure contrasts between the categories. Any participant mother who did not live in the municipality of Ronneby for any time during the exposure window was assumed to have been exposed to background PFAS levels; these mothers constituted the reference group.

2.4. Confounders

We identified potential confounders based on established relationships according to the literature and used directed acyclic graphs to illustrate the underlying causal assumptions (Supplemental Material). Data on maternal age, parity, height, and weight during early pregnancy were retrieved from the Swedish Medical Birth Register (National Board of Health and Welfare). From Statistics Sweden, data on the mothers' highest educational attainment at the time of delivery were obtained from the Register on Participation in Education, and data on country of birth were retrieved from the Total Population Register. Data for tobacco use during pregnancy (smoking or snuff use) were obtained from the Swedish Medical Birth Register or from CHC charts when missing in the register.

2.5. Statistical methods

We assessed the risk of not initiating breastfeeding for the full dataset but restricted the analyses of the risks of not breastfeeding exclusively at 3 months and not breastfeeding at all after 6 months to mothers who had initiated breastfeeding. As these latter outcomes were not rare, a logistic regression would offer a poor approximation of risk. We therefore used a modified Poisson regression with robust error variance (Zou, 2004) to estimate adjusted relative risks (RR) among mothers with and without residential exposure to highly contaminated drinking water (high and low exposure) in relation to the reference category with background exposure.

We also estimated hazard ratios (HR) of cessation of exclusive breastfeeding before 6 months and cessation of any breastfeeding before 12 months, using Cox proportional hazard models, to evaluate the robustness of results over analytical approaches. For the latter, the proportional hazards assumption did not hold for the exposure variable and we therefore used an extension of the Cox model allowing for time-dependent variables. Data were censored at the events.

We adjusted for confounding by maternal age (<25, 25–34, or ≥ 35), country of birth (Sweden; Scandinavia, Europe, Russia, USA, Canada, and Oceania; or Africa, the Middle East, Asia, or South, Central, and Middle America), education level (compulsory school, upper secondary school, or university), body mass index (BMI) during early pregnancy (<25, 25–29, or ≥ 30), tobacco use during pregnancy (yes or no), and time period of delivery (<2005 or ≥ 2005).

Models were run on the full sample, as well as separately on data collected for primiparous and multiparous women. In models including multiparous mothers, we further adjusted for parity (1, 2, or ≥ 3) and accounted for the clustered data structure by including a within-mother grouping strategy through specification of an exchangeable correlation structure (Zou and Donner, 2013).

As we suspected *a priori* that PFAS levels in the drinking water were higher in the late period (>2005), we explored effect modification by time period through introduction of an interaction term in the analyses of not breastfeeding exclusively at 3 months and not breastfeeding at all at 6 months.

We restricted the analyses to complete cases because 1) the performance of multiple imputation in combination with modified Poisson regression remains to be validated (Zou and Donner, 2013), and 2) there were no observations with missing values pertaining to exposure or outcome and only 148 individuals with missing data on BMI. One might assume that obese mothers might be more reluctant to have their weight recorded. However, observations from participants for whom data on weight but not height were available did not suggest overrepresentation of heavy mothers, nor did maternal weight at the time of delivery. Thus, we considered missing data for BMI unrelated to the actual BMI values and the risk of introducing bias through complete-case analyses to be negligible.

We performed all statistical analyses in SAS version 9.4 (SAS Institute, Cary, NC).

3. Results

3.1. Descriptive statistics

We observed differences with respect to the distribution of confounders between exposure categories (Table 1). Mothers in the high-exposure category were younger, had lower educational attainment, and had a higher BMI than those in the low-exposure or reference

Table 1
Descriptive characteristics of the study population consisting of mothers from Ronneby with or without highly contaminated drinking water at their residential address and from a reference municipality.

	High-exposure (n = 609)		Low-exposure (n = 1470)		Reference (n = 295)	
	n (%)	Missing	n (%)	Missing	n (%)	Missing
Conception period		0		0		0
<2005	310 (51)		733 (50)		169 (57)	
≥2005	299 (49)		737 (50)		126 (43)	
Maternal age (years)		0		0		0
<25	147 (24)		224 (15)		60 (20)	
25–34	392 (64)		1028 (70)		185 (63)	
≥35	70 (11)		218 (15)		50 (17)	
Parity		0		0		0
1	259 (43)		647 (44)		150 (51)	
2	211 (35)		569 (39)		93 (32)	
≥3	139 (23)		254 (17)		52 (18)	
BMI[a]		29		92		27
<25.0	306 (53)		864 (63)		168 (63)	
25.0–29.9	166 (29)		374 (27)		72 (27)	
≥30	108 (19)		140 (10)		28 (10)	
Education level		0		2		0
Primary and lower secondary	97 (16)		138 (9)		43 (15)	
Upper secondary	378 (62)		697 (47)		125 (42)	
Post-secondary	134 (22)		633 (43)		127 (43)	
Tobacco use during pregnancy		0		0		0
Yes	127 (21)		157 (11)		41 (14)	
Maternal country of birth		0		0		0
Sweden	562 (92)		1328 (90)		246 (83)	
Scandinavia, Europe, Russia, USA, Canada, Oceania	29 (5)		88 (6)		22 (7)	
Africa, Middle East, Asia, South, Central, and Middle America	18 (3)		54 (4)		27 (9)	

[a] Body mass index at the time of enrollment in maternal health care.

groups. Furthermore, they used tobacco products during pregnancy at a higher rate and were slightly overrepresented in higher parity categories than mothers from the other categories.

3.2. Initiation of breastfeeding

The crude figures suggested a slightly lower proportion of breastfeeding initiation among mothers who had lived in the area with contaminated drinking water (Table 2). In the multivariable analyses, mothers living in Ronneby were approximately twice as likely as those not living in Ronneby to not initiate breastfeeding (Table 3). This was true irrespective of whether there was highly contaminated water at their residential address (high versus low exposure), although point estimates were higher in the high-exposure category. The estimates were associated with very wide confidence intervals because of the small numbers of noninitiators, but their upper boundaries implied substantially higher risks for noninitiation in the high- and low-exposure categories, although these estimates did not exclude negative associations.

Table 2
Descriptive statistics on breastfeeding duration in mothers from Ronneby with or without highly contaminated drinking water at their residential address and from a reference municipality.

	High-exposure (n = 609)		Low-exposure (n = 1470)		Reference (n = 295)	
	n (%)	Median (Q1, Q3)[a]	n (%)	Median (Q1, Q3)	n (%)	Median (Q1, Q3)
Breastfeeding initiation	579 (95)		1426 (97)		290 (98)	
Among initiators:						
Exclusive breastfeeding, 3 months	344 (59)		1028 (72)		196 (68)	
Any breastfeeding, 6 months	311 (54)		957 (67)		188 (65)	
Total breastfeeding duration, months		6 (2, 8)		7 (4, 9)		7 (4, 9)

[a] Q1, first quartile; Q3, third quartile.

Table 3
Relative risks of not initiating breastfeeding in mothers from Ronneby with or without highly contaminated drinking water at their residential address relative to mothers from a reference municipality.

Exposure category	Mothers (n)	Noninitators (n)	RR (95% CI) Crude	RR (95% CI) Adjusted
All				
High	609	30	2.52 (1.01, 6.29)	2.37 (0.84, 6.69)
Low	1470	44	1.68 (0.72, 3.90)	1.94 (0.71, 5.30)
Reference	295	5	1.00	1.00
Primiparae[a]				
High	259	8	2.32 (0.50, 10.77)	2.92 (0.34, 23.01)
Low	647	14	1.62 (0.37, 7.06)	2.73 (0.36, 20.76)
Reference	150	2	1.00	1.00
Multiparae				
High	350	22	2.80 (0.89, 8.82)	2.14 (0.68, 6.79)
Low	823	30	1.70 (0.55, 5.20)	1.64 (0.51, 5.30)
Reference	145	3	1.00	1.00

Note: All estimates are obtained by modified Poisson regression. The adjusted models accounted for time period, maternal age, parity, BMI, education level, country of birth, and tobacco use during pregnancy. RR, relative risk; CI, confidence interval.

[a] The multivariable model for primiparae did not converge when birth country was included; estimates were thus obtained from a model excluding this covariate.

3.3. Breastfeeding duration

Among initiators, the descriptive data indicated lower proportions of mothers who breastfed exclusively at 3 months and breastfed at all at 6 months in the high-exposure category. By contrast, we observed no marked differences between mothers from the low-exposure and reference categories. The median total duration for breastfeeding was 1 month shorter in the high-exposure category than in the other two

categories.

The multivariable modified Poisson regression suggested higher risks of not sustaining exclusive breastfeeding at 3 months and not breastfeeding at all after 6 months in the high-exposure category as compared with the reference category, although only reaching statistical significance for not breastfeeding at all after 6 months in primiparous mothers. There were no clear associations among low-exposure Ronneby mothers, besides a suggestion of a higher risk of not sustaining any breastfeeding at all after 6 months in primiparous mothers (Table 4). The Cox regressions provided consistent estimates with respect to exclusive breastfeeding (Table 5). The adjusted HR for cessation of any breastfeeding before 12 months in the high-exposure category was time dependent and higher in early lactation, thereafter decreasing as lactation progressed (Table 6). This seemed to be the case also for primiparous mothers in the low-exposure category.

The overall associations were clearly driven by primiparous mothers. However, when we explored the potential for interaction between exposure category and time period, we observed an ~20% higher risk after 2005 in the high-exposure category of not breastfeeding exclusively at 3 months, irrespective of parity (Table 7). Moreover, this increased risk was already detectable before 2005 in primiparous mothers who had contaminated water at their residential address. We observed a similar pattern for not breastfeeding at 6 months (Table 8), but here the results suggested a reduced risk among multiparous mothers who had given birth before 2005.

4. Discussion

4.1. Initiation

We determined that mothers who lived in the municipality of Ronneby and had highly contaminated home drinking water for at least 1 year during the 5-year period before delivery had a 2- to 3-fold higher risk of not initiating breastfeeding relative to mothers from the reference group with background levels of exposure. Notably, mothers who resided within the municipality but received drinking water from the noncontaminated waterworks (with PFAS levels well below 90 ng/L, the Swedish action level at the time) also experienced a higher risk of not initiating breastfeeding relative to the reference category. This result is suggestive of a dose-response relationship: Indeed, biomonitoring revealed that Ronneby residents who had access to noncontaminated water at their homes nevertheless showed 29, 8, and 2 times higher serum concentrations of PFHxS, PFOS, and PFOA, respectively, than those in the reference group (Xu et al., 2021). It is necessary to explore the potential interaction between exposure category and time period to determine the exposure thresholds above which an effect on breastfeeding would occur, but this was not possible due to the small number of noninitiators.

One toxicological study has investigated the effects of gestational exposure to PFOA in mice with respect to mammary gland development (White et al., 2007). The authors observed substantial delays in gland development, by as much as 10 days, relative to controls. Furthermore, this developmental delay persisted throughout lactation: Indeed, on day 20, glands from exposed dams showed little sign of involution but resembled the glands of the control group at peak lactation (weaning normally occurs at 3–4 weeks). These results indicate that the *initiation* of breastfeeding might be the most sensitive breastfeeding outcome with respect to PFAS exposure, whereas continuation of lactation, once

Table 5
Hazard ratios of cessation of exclusive breastfeeding before 6 months in mothers from Ronneby with or without highly contaminated drinking water at their residential address relative to mothers from a reference municipality.

Exposure category	Mothers (*n*)	Events (*n*)	Censored (*n*)	HR (95% CI) Crude	HR (95% CI) Adjusted
All					
High	544	321	223	1.30 (1.06, 1.59)	1.14 (0.92, 1.40)
Low	1333	572	761	0.81 (0.67, 0.98)	0.86 (0.71, 1.05)
Reference	257	132	125	1.00	1.00
Primiparae					
High	232	143	89	1.52 (1.13, 2.05)	1.30 (0.96, 1.76)
Low	588	271	317	0.98 (0.74, 1.29)	1.00 (0.76, 1.31)
Reference	130	63	67	1.00	1.00
Multiparae					
High	312	178	134	1.13 (0.86, 1.49)	0.98 (0.74, 1.31)
Low	745	301	444	0.69 (0.53, 0.89)	0.74 (0.57, 0.97)
Reference	127	69	58	1.00	1.00

Note: All estimates are obtained from Cox regression. The adjusted models accounted for time period, maternal age, parity, BMI, education level, country of birth, and tobacco use during pregnancy. HR, hazard ratio; CI, confidence interval.

Table 4
Relative risks of not achieving exclusive breastfeeding by 3 months, and any breastfeeding by 6 months, in mothers from Ronneby with or without highly contaminated drinking water at their residential address relative to mothers from a reference municipality.

Exposure category	Exclusive breastfeeding at 3 months				Any breastfeeding at 6 months		
	Mothers (*n*)	Ceased (*n*)	RR (95% CI) Crude	RR (95% CI) Adjusted	Ceased (*n*)	RR (95% CI) Crude	RR (95% CI) Adjusted
All							
High	579	235	1.23 (1.03, 1.50)	1.12 (0.92, 1.37)	268	1.26 (1.06, 1.50)	1.17 (0.97, 1.40)
Low	1426	398	0.87 (0.73, 1.04)	0.90 (0.75, 1.09)	469	0.91 (0.77, 1.08)	0.98 (0.82, 1.17)
Reference	290	94	1.00	1.00	102	1.00	1.00
Primiparae							
High	251	115	1.44 (1.10, 1.89)	1.21 (0.92, 1.61)	127	1.63 (1.24, 2.13)	1.56 (1.16, 2.11)
Low	633	205	1.02 (0.79, 1.32)	0.98 (0.75, 1.28)	218	1.11 (0.85, 1.44)	1.20 (0.90, 1.61)
Reference	148	47	1.00	1.00	46	1.00	1.00
Multiparae							
High	328	120	1.11 (0.84, 1.45)	1.05 (0.80, 1.38)	141	1.06 (0.84, 1.35)	0.92 (0.73, 1.16)
Low	793	193	0.76 (0.59, 0.98)	0.86 (0.67, 1.11)	251	0.79 (0.63, 0.99)	0.83 (0.66, 1.04)
Reference	142	47	1.00	1.00	56	1.00	1.00

Note: All estimates are obtained by modified Poisson regression. The adjusted models accounted for time period, maternal age, parity, BMI, education level, country of birth, and tobacco use during pregnancy. RR, relative risk; CI, confidence interval.

Table 6
Time-varying hazard ratios of cessation of any breastfeeding before 12 months in mothers from Ronneby with or without highly contaminated drinking water at their residential address relative to mothers from a reference municipality.

Exposure category					HR (95% CI)	
	Mothers (*n*)	Events (*n*)	Censored (*n*)	Time point (months)	Crude	Adjusted
All						
High	551	496	55	0	2.00 (1.43, 2.81)	1.58 (1.12, 2.22)
				3	1.57 (1.27, 1.94)	1.32 (1.06, 1.63)
				6	1.23 (1.05, 1.44)	1.09 (0.93, 1.29)
				10	0.89 (0.67, 1.17)	0.86 (0.65, 1.14)
Low	1338	1155	183	0	0.97 (0.71, 1.34)	1.08 (0.78, 1.49)
				3	0.97 (0.79, 1.19)	1.03 (0.84, 1.26)
				6	0.97 (0.84, 1.12)	0.99 (0.86, 1.14)
				10	0.96 (0.76, 1.22)	0.93 (0.73, 1.19)
Reference	264	230	34	0	1.00	1.00
Primiparae						
High	237	218	19	0	3.07 (1.86, 5.08)	2.49 (1.50, 4.14)
				3	2.11 (1.53, 2.90)	1.82 (1.32, 2.51)
				6	1.45 (1.15, 1.83)	1.33 (1.05, 1.69)
				10	0.88 (0.59, 1.30)	0.88 (0.59, 1.30)
Low	590	516	74	0	1.42 (0.89, 2.29)	1.53 (0.95, 2.48)
				3	1.26 (0.93, 1.71)	1.34 (0.98, 1.81)
				6	1.12 (0.91, 1.37)	1.16 (0.95, 1.43)
				10	0.95 (0.69, 1.32)	0.96 (0.69, 1.34)
Reference	134	115	19	0	1.00	1.00
Multiparae						
High	314	278	36	0	1.36 (0.86, 2.14)	1.03 (0.65, 1.64)
				3	1.20 (0.91, 1.60)	0.97 (0.73, 1.30)
				6	1.07 (0.86, 1.33)	0.92 (0.73, 1.15)
				10	0.91 (0.62, 1.35)	0.85 (0.56, 1.27)
Low	748	639	109	0	0.68 (0.44, 1.05)	0.78 (0.51, 1.20)
				3	0.76 (0.58, 1.00)	0.82 (0.62, 1.07)
				6	0.85 (0.69, 1.04)	0.86 (0.70, 1.05)
				10	0.98 (0.69, 1.39)	0.91 (0.64, 1.30)
Reference	130	115	15	0	1.00	1.00

Note: All estimates are obtained from Cox regression. The adjusted models accounted for time period, maternal age, parity, BMI, education level, country of birth, and tobacco use during pregnancy. HR, hazard ratio; CI, confidence interval.

Table 7
Relative risks of not achieving exclusive breastfeeding by 3 months in mothers from Ronneby with or without highly contaminated drinking water at their residential address relative to mothers from a reference municipality, according to the time period of delivery.

Exposure category	Early period (<2005)				Late period (≥2005)			
			RR (95% CI)	RR (95% CI)			RR (95% CI)	RR (95% CI)
	Mothers (*n*)	Ceased (*n*)	Crude	Adjusted	Mothers (*n*)	Ceased (*n*)	Crude	Adjusted
All								
High	296	103	1.10 (0.85, 1.42)	1.03 (0.78, 1.34)	283	132	1.37 (1.04, 1.81)	1.23 (0.93, 1.62)
Low	709	178	0.82 (0.65, 1.04)	0.83 (0.65, 1.07)	717	220	0.91 (0.70, 1.19)	0.98 (0.75, 1.28)
Reference	167	53	1.00	1.00	123	41	1.00	1.00
Primiparae								
High	130	47	1.36 (0.89, 2.09)	1.25 (0.79, 1.97)	121	68	1.46 (1.03, 2.06)	1.19 (0.84, 1.68)
Low	310	80	0.97 (0.65, 1.46)	0.96 (0.62, 1.49)	323	125	1.01 (0.72, 1.41)	1.00 (0.71, 1.39)
Reference	83	22	1.00	1.00	65	25	1.00	1.00
Multiparae								
High	166	56	0.90 (0.64, 1.27)	0.89 (0.64, 1.25)	162	64	1.45 (0.93, 2.26)	1.29 (0.84, 1.99)
Low	399	98	0.68 (0.50, 0.93)	0.77 (0.56, 1.05)	394	95	0.92 (0.59, 1.41)	1.01 (0.67, 1.53)
Reference	84	31	1.00	1.00	58	16	1.00	1.00

Note: All estimates are obtained from modified Poisson regression. The adjusted models accounted for maternal age, parity, BMI, education level, country of birth, and tobacco use during pregnancy. RR, relative risk; CI, confidence interval.

established (i.e. milk supply), would be of less concern.

Previous epidemiologic studies have generally not addressed breastfeeding initiation, but Rosen et al. (2018) considered initiation in a sensitivity analysis. Although their results suggested no association, the authors studied a general population with very small PFAS exposure contrasts. We encourage the research community to address breastfeeding initiation specifically in future studies to validate our findings.

4.2. Duration

In addition to delayed gland development in PFOA-exposed mice, White et al. (White et al., 2009) noted reduced body weight in the offspring, indicative of insufficient nutrition. However, because of the short lactation period in rodents, animal studies have limited scope when attempting to determine whether growth impairment results only from delayed gland development or from an additional effect such as that on milk yield after lactation has been established. In this context, epidemiological studies could provide an answer.

The available literature consists of findings from general populations with background levels of exposure. Even so, this body of work points towards an increased odds ratio or RR for a shorter breastfeeding period among mothers with higher serum concentrations of PFOA and PFOS;

Table 8
Relative risks of not achieving any breastfeeding by 6 months in mothers from Ronneby with or without highly contaminated drinking water at their residential address relative to mothers from a reference municipality, according to time period of delivery.

Exposure category	Early period (<2005)				Late period (≥2005)			
			RR (95% CI)	RR (95% CI)			RR (95% CI)	RR (95% CI)
	Mothers (*n*)	Ceased (*n*)	Crude	Adjusted	Mothers (*n*)	Ceased (*n*)	Crude	Adjusted
All								
High	296	123	1.06 (0.84, 1.34)	0.97 (0.76, 1.24)	283	145	1.52 (1.17, 1.98)	1.43 (1.08, 1.88)
Low	709	230	0.86 (0.69, 1.06)	0.89 (0.71, 1.11)	717	239	0.98 (0.76, 1.28)	1.11 (0.84, 1.45)
Reference	167	62	1.00	1.00	123	40	1.00	1.00
Primipara								
High	130	55	1.46 (0.99, 2.17)	1.43 (0.92, 2.24)	121	72	1.76 (1.21, 2.55)	1.69 (1.13, 2.51)
Low	310	93	1.04 (0.71, 1.51)	1.09 (0.71, 1.68)	323	125	1.14 (0.79, 1.65)	1.31 (0.88, 1.95)
Reference	83	24	1.00	1.00	65	22	1.00	1.00
Multipara								
High	166	68	0.85 (0.63, 1.14)	0.73 (0.54, 0.98)	162	73	1.48 (0.99, 2.22)	1.25 (0.85, 1.86)
Low	399	137	0.73 (0.57, 0.95)	0.75 (0.57, 0.97)	394	114	0.94 (0.64, 1.40)	0.98 (0.67, 1.44)
Reference	84	38	1.00	1.00	58	18	1.00	1.00

Note: All estimates are obtained from modified Poisson regression. The adjusted models accounted for maternal age, parity, BMI, education level, country of birth, and tobacco use during pregnancy. RR, relative risk; CI, confidence interval.

the effect of PFHxS is less clear (Timmermann et al., 2017; Fei et al., 2010; Romano et al., 2016). A recent study further obscured any underlying pattern by showing no association or even longer breastfeeding duration with increasing PFAS serum concentrations (Rosen et al., 2018). We saw evidence for a higher risk of not breastfeeding exclusively at 3 months, and not breastfeeding at all at 6 months, among primiparous mothers who had lived in the area with highly contaminated water. Further, we also observed that primiparous mothers from the low-exposure category were at higher risk of not breastfeeding at 6 months than those in the reference category. This result suggests that extreme exposure levels are not required for an effect to occur.

There is selection with respect to breastfeeding among multiparous mothers, in that those who initiate breastfeeding often had a previous positive experience. If PFAS impairs breastfeeding, it is reasonable to speculate that multiparous mothers who were unable to establish breastfeeding in earlier pregnancies will not attempt to breastfeed at all in subsequent children, obviously resulting in smaller effect estimates when compared with primiparous mothers. Indeed, we detected no association between exposure and exclusive breastfeeding at 3 months or any breastfeeding at 6 months in the main analysis of multiparous mothers. However, we hypothesized that an effect might have become evident after 2005, when PFAS levels in the water were thought to have been the highest, and this proved to be the case.

Our results indicate that PFAS exposure affects breastfeeding duration among mothers who successfully establish lactation, suggesting that PFAS influence both mammary gland development and milk yield. A complementary study should explore the reasons for breastfeeding termination to confirm our findings. We are collecting such data within the Ronneby mother-child cohort.

4.3. Strengths and limitations

Our study is unique in that it represents the first study of breastfeeding in a population highly exposed to PFAS. Notably, because the contamination was discovered after the study population had stopped breastfeeding, maternal decisions regarding breastfeeding were not influenced by any awareness of exposure status.

A strength of our study is that information on breastfeeding was collected prospectively within the routine program of CHC. Previous studies have relied on outcome data collected through either questionnaires or interviews. However, as mothers may experience pressure to breastfeed and healthcare providers and society (Cato et al., 2020; Symon et al., 2013), there is concern that self-reported data on breastfeeding are prone to information bias. Indeed, mothers who breastfeed for a short period overestimate breastfeeding duration when data are collected retrospectively (Gillespie et al., 2006). Furthermore, socioeconomic factors are also at play, as mothers with a higher educational level or higher income overestimate breastfeeding duration more than mothers from lower socioeconomic groups, possibly because of better awareness of breastfeeding recommendations and desire to meet societal expectations (Huttly et al., 1990). In our setting, the highly exposed category differed from the others with respect to several socioeconomic indicator variables, which might have resulted in differential misclassification of the outcome as well as biased results away from the null. This risk was avoided through the use of prospectively collected outcome data.

We used a proxy measure of exposure (i.e. residential address) rather than measured serum concentrations. Proxy variables can lower the risk of bias arising from confounding by maternal factors related to physiology or behavior and may be less susceptible to reverse causation (Weisskopf and Webster, 2017). The latter are issues that have been highlighted as a concern among multiparous mothers in previous breastfeeding studies (Fei et al., 2010; Rosen et al., 2018), because the correlation between previous experiences and subsequent breastfeeding duration is high (Huang et al., 2019) and PFAS are excreted into breast milk (Haug et al., 2011; Kärrman et al., 2007). Previous breastfeeding experiences are unrelated to residential address and our study does therefore not suffer from these biases.

On the other hand, proxy measures are associated with larger measurement error and a potential risk of exposure misclassification. However, we validated the exposure assessment based on residential address in previous work based on a subset of the population (n = 3310), for which we also had measured serum concentrations, and found strong contrasts between the exposure categories (Xu et al., 2021). Further, the exposure was still ongoing when the mothers gave birth. The uptake of PFAS from the extremely contaminated water was certainly much greater than the elimination that occurred during previous pregnancies and breastfeeding episodes in multiparous mothers. Finally, the consumption of bottled water in Sweden is very low in comparison with other countries and amounted to merely 0.06 L/day in the early 2000s (Westrell et al., 2006). Taken together, we consider the risk of bias from exposure misclassification of minor concern in the present study.

Breastfeeding rates among Ronneby mothers who had not received the highly contaminated drinking water at their residential address and mothers from the reference municipality matched very well with the overall rate measured in the county of Blekinge, of which Ronneby is a municipality, at the time (). Thus, we consider the study sample to be representative of the underlying population.

4.4. Practical relevance

Our results indicate that mothers who have high exposure to PFAS, particularly primiparous mothers, might benefit from intensified support from the healthcare system when establishing breastfeeding. In this context, we stress that there might because for concern regarding breastfeeding in highly exposed populations. Breast milk is an important exposure route for infants (Papadopoulou et al., 2016; Kingsley et al., 2018; Mogensen et al., 2015), and breastfeeding must therefore be considered in a cost-benefit framework . However, to date there have been no studies assessing the extent to which PFAS pass from maternal serum into breast milk at high exposure levels and a scientific basis for evaluation of the potential need for restrictive recommendations in situations with a point source of exposure is therefore lacking. Without evidence to the contrary, mothers from the studied municipality are advised to breastfeed as intended, with the assumption that the health benefits of breastfeeding outweigh potential harmful effects. There is an urgent need to investigate PFAS transfer through breast milk at high levels of exposure and to assess the impact of breastfeeding duration on serum PFAS concentrations in infants. We are currently undertaking such studies.

5. Conclusions

Mothers who were exposed to highly contaminated drinking water at their residential address seemed to have substantially higher risk of not being able to initiate breastfeeding. This result was present also among mothers who lived in Ronneby but had received noncontaminated drinking water. Primiparous mothers from the highly exposed area who initiated breastfeeding were at increased risk of not sustaining exclusive breastfeeding at 3 months as well as of not breastfeeding at all at 6 months. The associations were strongest in early lactation and decreased as lactation progressed. We observed no overall associations in multiparous mothers besides a possible increased risk of shorter breastfeeding duration among multiparous mothers who gave birth towards the end of the study period. The findings imply that the ability of first-time mothers to establish breastfeeding is a sensitive outcome after high exposure to PFAS.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

This work was funded by the Swedish Research Council for Health, Working Life and Welfare, Forte (no. 2015-00166) and the Swedish Research Council for the Environment, Agricultural Sciences and Spatial Planning, Formas (no. 2017-00896). The funding sources were not involved in the design or execution of the research.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2021.112206.

References

Brown, C.R., Dodds, L., Legge, A., Bryanton, J., Semenic, S., 2014. Factors influencing the reasons why mothers stop breastfeeding. Can. J. Public Health 105 (3), e179–e185.
Cato, K., Sylvén, S.M., Henriksson, H.W., Rubertsson, C., 2020. Breastfeeding as a balancing act – pregnant Swedish women's voices on breastfeeding. Int. Breastfeed. J. 15 (1), 16.
Criswell, R., Crawford, K.A., Bucinca, H., Romano, M.E., 2020. Endocrine-disrupting chemicals and breastfeeding duration: a review. Curr. Opin. Endocrinol. Diabetes Obes. 27 (6), 388–395.
Fei, C., McLaughlin, J.K., Lipworth, L., Olsen, J., 2010. Maternal concentrations of perfluorooctanesulfonate (PFOS) and perfluorooctanoate (PFOA) and duration of breastfeeding. Scand. J. Work. Environ. Health 36 (5), 413–421.
Fenton, S.E., Reed, C., Newbold, R.R., 2012. Perinatal environmental exposures affect mammary development, function, and cancer risk in adulthood. Annu. Rev. Pharmacol. Toxicol. 52 (1), 455–479.
Galtry, J., 2003. The impact on breastfeeding of labour market policy and practice in Ireland, Sweden, and the USA. Soc. Sci. Med. 57 (1), 167–177.
Gillespie, B., d'Arcy, H., Schwartz, K., Bobo, J.K., Foxman, B., 2006. Recall of age of weaning and other breastfeeding variables. Int. Breastfeed. J. 1 (1), 4.
Glüge, J., Scheringer, M., Cousins, I.T., DeWitt, J.C., Goldenman, G., Herzke, D., 2020. An overview of the uses of per- and polyfluoroalkyl substances (PFAS). Environ. Sci. Proc. Impacts 22 (12), 2345–2373.
Haug, L.S., Huber, S., Becher, G., Thomsen, C., 2011. Characterisation of human exposure pathways to perfluorinated compounds-comparing exposure estimates with biomarkers of exposure. Environ. Int. 37 (4), 687–693.
Hoppin, J., Kotlarz, N., de Kort, T., Ng-A-Tham, J., Starling, A., Adgate, J., et al., 2019. An Overview of Emerging PFAS in Drinking Water Worldwide. The International Society for Environmental Epidemiology, Utrecht, the Netherlands (Environmental Epidemiology).
Huang, Y., Ouyang, Y.Q., Redding, S.R., 2019. Previous breastfeeding experience and its influence on breastfeeding outcomes in subsequent births: a systematic review. Women Birth 32 (4), 303–309.
Huttly, S.R., Barros, F.C., Victora, C.G., Ju, Beria, Vaughan, J.P., 1990. Do mothers overestimate breast feeding duration? An example of recall bias from a study in southern Brazil. Am. J. Epidemiol. 132 (3), 572–575.
Kärrman, A., Ericson, I., van Bavel, B., Darnerud, P.O., Aune, M., Glynn, A., et al., 2007. Exposure of perfluorinated chemicals through lactation: levels of matched human milk and serum and a temporal trend, 1996-2004, in Sweden. Environ. Health Perspect. 115 (2), 226–230.
Kingsley, S.L., Eliot, M.N., Kelsey, K.T., Calafat, A.M., Ehrlich, S., Lanphear, B.P., et al., 2018. Variability and predictors of serum perfluoroalkyl substance concentrations during pregnancy and early childhood. Environ. Res. 165, 247–257.
Konkel, L., 2017. Mother's milk and the environment: might chemical exposures impair lactation? Environ. Health Perspect. 125 (1), A17–A23.
Li, Y., Fletcher, T., Mucs, D., Scott, K., Lindh, C.H., Tallving, P., et al., 2018. Half-lives of PFOS, PFHxS and PFOA after end of exposure to contaminated drinking water. Occup. Environ. Med. 75 (1), 46–51.
Mogensen, U.B., Grandjean, P., Nielsen, F., Weihe, P., Budtz-Jorgensen, E., 2015. Breastfeeding as an exposure pathway for perfluorinated alkylates. Environ. Sci. Technol. 49 (17), 10466–10473.
Morrison, A.H., Gentry, R., Anderson, J., 2019. Mothers' reasons for early breastfeeding cessation. MCN Am. J. Matern./Child Nurs. 44 (6), 325–330.
Odom, E.C., Li, R., Scanlon, K.S., Perrine, C.G., Grummer-Strawn, L., 2013. Reasons for earlier than desired cessation of breastfeeding. Pediatrics 131 (3), e726–e732.
Olsen, G.W., Burris, J.M., Ehresman, D.J., Froehlich, J.W., Seacat, A.M., Butenhoff, J.L., et al., 2007. Half-life of serum elimination of perfluorooctanesulfonate, perfluorohexanesulfonate, and perfluorooctanoate in retired fluorochemical production workers. Environ. Health Perspect. 115 (9), 1298–1305.
Papadopoulou, E., Sabaredzovic, A., Namork, E., Nygaard, U.C., Granum, B., Haug, L.S., 2016. Exposure of Norwegian toddlers to perfluoroalkyl substances (PFAS): the association with breastfeeding and maternal PFAS concentrations. Environ. Int. 94, 687–694.
Romano, M.E., Xu, Y., Calafat, A.M., Yolton, K., Chen, A., Webster, G.M., et al., 2016. Maternal serum perfluoroalkyl substances during pregnancy and duration of breastfeeding. Environ. Res. 149, 239–246.
Rosen, E.M., Brantsæter, A.L., Carroll, R., Haug, L., Singer, A.B., Zhao, S., et al., 2018. Maternal plasma concentrations of per- and polyfluoroalkyl substances and breastfeeding duration in the Norwegian mother and child cohort. Environ. Epidemiol. 2 (3).
Seals, R., Bartell, S.M., Steenland, K., 2011. Accumulation and clearance of perfluorooctanoic acid (PFOA) in current and former residents of an exposed community. Environ. Health Perspect. 119 (1), 119–124.
Symon, A.G., Whitford, H., Dalzell, J., 2013. Infant feeding in eastern scotland: a longitudinal mixed methods evaluation of antenatal intentions and postnatal satisfaction—the feeding your baby study. Midwifery 29 (7), e49–e56.
The German Federal Ministry for the Environment, the German Federal Environment Agency, 2020. International Conference: PFAS – Dealing with Contaminants of Emerging Concern. Online (Germany). https://www.bmu.de/fileadmin/Daten_BMU/Download_PDF/Bodenschutz/pfas_konferenzbericht_long_en_bf.pdf. (Accessed 8 September 2021). Accessed.
The National Board of Health and Welfare. Vägledning för barnhälsovården (in Swedish). https://www.socialstyrelsen.se/globalassets/sharepoint-dokument/artikelkatalog/vagledning/2014-4-5.pdf. Accessed September 8, 2021.
The National Board of Health and Welfare. Statistik om amning (in Swedish). https://www.socialstyrelsen.se/statistik-och-data/statistik/statistikamnen/amning/. Accessed September 8, 2021.
Timmermann, C.A., Budtz-Jorgensen, E., Petersen, M.S., Weihe, P., Steuerwald, U., Nielsen, F., et al., 2017. Shorter duration of breastfeeding at elevated exposures to perfluoroalkyl substances. Reprod. Toxicol. 68, 164–170.
Weisskopf, M.G., Webster, T.F., 2017. Trade-offs of personal versus more proxy exposure measures in environmental epidemiology. Epidemiology 28 (5), 635–643.

Westrell, T., Andersson, Y., Stenström, T.A., 2006. Drinking water consumption patterns in Sweden. J. Water Health 4 (4), 511–522.
White, S.S., Calafat, A.M., Kuklenyik, Z., Villanueva, L., Zehr, R.D., Helfant, L., et al., 2007. Gestational PFOA exposure of mice is associated with altered mammary gland development in dams and female offspring. Toxicol. Sci. 96 (1), 133–144.
White, S.S., Kato, K., Jia, L.T., Basden, B.J., Calafat, A.M., Hines, E.P., et al., 2009. Effects of perfluorooctanoic acid on mouse mammary gland development and differentiation resulting from cross-foster and restricted gestational exposures. Reprod. Toxicol. 27 (3–4), 289–298.
Xu, Y., Nielsen, C., Li, Y., Hammarstrand, S., Andersson, E.M., Li, H., et al., 2021. Serum perfluoroalkyl substances in residients following long-term drinking water contamination from firefighting foam in Ronneby, Sweden. Environ. Int. 147.
Zou, G., 2004. A modified Poisson regression approach to prospective studies with binary data. Am. J. Epidemiol. 159 (7), 702–706.
Zou, G.Y., Donner, A., 2013. Extension of the modified Poisson regression model to prospective studies with correlated binary data. Stat. Methods Med. Res. 22 (6), 661–670.