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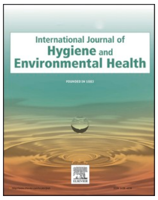

Trend analyses of persistent organic pollutants in human milk from first-time mothers in Norway between 2002 and 2021

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ABSTRACT

Introduction: Persistent organic pollutants (POPs) are stable compounds characterized by their resistance to degradation. From the 1960–70's organochlorine pesticides (OCPs), such as DDTs and polychlorinated biphenyls (PCBs) raised concerns regarding health and environmental impacts. This has led to the banning of POPs in the USA and Europe including Norway in 1980 and worldwide under the 2004 Stockholm Convention. The exposure of nursing infants to POPs has been a significant focus, prompting extensive research into the presence of these substances in human breast milk. In this study, we explored the temporal trends of POPs concentrations in breast milk sampled between 2002 and 2021 by comparing the concentration across the mother's year of birth.

Method: Two Norwegian cohorts of lactating women were utilized (the HUMIS study and the "Iodine in Early Life"-Study). Concentrations of 15 different POPs, including PCBs, OCPs, and brominated diphenyl ethers (BDEs) were measured in 513 breast milk samples that had been collected over two decades in a subset of first-time mothers.

Results: Time trend analysis indicated a steady decrease in concentration levels when adjusted for maternal age. The largest reduction was observed in β-HCH, age-adjusted (−17.1%, 95% CI -18.7, −15.4), followed by $\sum_6$BDE (−9.1%, 95% CI -10.5, −7.7), $\sum_6$PCBs (−7.1%, 95% CI -7.7, −6.5), and $\sum_2$DDTs (−7.0%, 95% CI -8.0, −6.0). In contrast, an increasing trend was noted in the median concentrations of β-HCH, $\sum_2$DDTs, and $\sum_6$BDE in the mothers born in 1990–1994 to 1995–2002.

Conclusion: Our study demonstrates a decline of most POPs in breast milk, likely attributed to international regulatory efforts like the Stockholm Convention. Notably, an increase in the 95th percentile concentrations of β-HCH, $\sum_2$DDTs, and $\sum_6$BDEs was noted in mothers born in 1990–1994 compared to those born in 1995–2002 suggests demographic shifts that may influence exposure levels. Further research is needed to explore and understand the underlying factors for the rise in median concentrations of $\sum_6$BDEs.

1. Introduction

Persistent organic pollutants (POPs) are stable compounds characterized by their resistance to biological, photolytic, and chemical degradation (L. Ritter et al., 1995). Many of these compounds have a half-life of 5–12 years in humans (Woodruff et al., 1994). Due to their hydrophobic and lipophilic properties, they accumulate in fat tissues (L. Ritter et al., 1995). These attributes not only lead to widespread environmental contamination but also pose considerable threats to human health. Specifically, POPs have been associated with adverse effects on the immunological, reproductive, and endocrine systems in humans (Omar et al., 2018). The tendency of these compounds to bioaccumulate and to biomagnify puts humans at increased risk and raises concerns particularly during critical growth and developmental phases such as

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Abbreviations: (P)BDE, (poly)brominated diphenyl ether; DDE, dichlorodiphenyldichloroethylene; DDT, dichlorodiphenyltrichloroethane; HCB, hexachlorobenzene; HCH, hexachlorocyclohexane; OCPs, organochlorine pesticides; PCB, polychlorinated biphenyls.

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infancy and early childhood (Vrijheid et al., 2016).

Infants and children's pronounced vulnerability to toxic substances is due to the developmental phases in early life and reduced chemical metabolism capabilities (Damstra, 2002). Also, due to their limited fat reserves, less tissue is available for distribution of the lipophilic toxicants. On the other hand, body growth may dilute the toxicants due to an increase in fat tissue. In utero exposure to substances like polychlorinated biphenyls (PCBs) and hexachlorobenzene (HCB), has been associated with negative birth outcomes, including smaller head circumferences and shorter gestational periods (Kezios et al., 2012; Ribas-Fitó et al., 2002; Tan et al., 2009). While the health effects of hexachlorocyclohexanes (HCHs) are unclear (Brucker-Davis et al., 2010; Eskenazi et al., 2004; Lopez-Espinosa et al., 2011; Ribas-Fitó et al., 2002), there are suggestions that exposure to HCHs and PCBs can adversely impact motor skills, language, and cognitive abilities in children by 18 months (Ruel et al., 2019; Wang et al., 2021). Furthermore, exposure to POPs early in life, both neonatally and through breastfeeding, seems linked to an increased risk of neurodevelopmental disorders such as attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) (Desalegn et al., 2023; Forns et al., 2016; Grova et al., 2019; Lenters et al., 2019).

Although there has been a global ban on the production and use of PCBs and dichlorodiphenyltrichloroethanes (DDTs) since 2004, DDTs have not been entirely prohibited as they are employed for mosquito control in malaria-infested regions (Bouwman et al., 2011; Stockholm Convention; Tren and Roberts, 2010; van den Berg et al., 2017; Wassie et al., 2012). Furthermore, β-HCH and BDEs were banned in 2009 (Convention, 2019). Despite these regulations, POPs continue to be detected in the environment and living species. Humans are mainly exposed to POPs by consumption of food (Cok et al., 2009; Rodríguez-Hernández et al., 2015). The unborn child is exposed to POPs through cord blood and placenta, and after birth by breast milk (Björvang et al., 2021; Jon Øyvind Odland et al., 2021). There are three consistent predictors of high POPs concentration in breast milk including increased maternal age, lower body mass index (BMI), and nulliparity (Orta et al., 2020). Furthermore, women who breastfeed their infants for a longer time span, tend to have lower concentrations (Hardell et al., 2010; Rylander et al., 2012), whereas a high intake of fish may be associated with higher POPs concentrations (McGraw and Waller, 2009; Pavuk et al., 2014).

Since 1978, Norway has been monitoring POPs concentrations in breast milk, both in the capacity of national studies and as an active participant in the World Health Organization (WHO) international breast milk monitoring program (Lenters et al., 2019; Polder et al., 2008, 2009; Skaare, 1981). Research conducted in Norway revealed a decreasing trend in the median levels of $\sum_{20}$PCBs in breast milk, from 1000 ng/g lipid weight (lw) in 1988 to 177 ng/g lw for $\sum_{18}$PCBs in 2000–2002 (Polder et al., 2008; Skaare et al., 1988). In the period of 2002–2006, the declining trend slowed down (Polder et al., 2009). Notably, while studies have shown that the concentration of POPs in serum has significantly declined from the late 2000s to the early 2020s (Xu et al., 2022), comprehensive data about the concentration of POPs in breast milk during this period in Norway remains limited (Helle Katrine Knutsen, 2010).

While earlier studies have focused on POPs concentrations based on the year of childbirth, the aim of this study was to analyze temporal trends in POPs concentrations in human breast milk using the mother's year of birth as the primary reference point. Specifically, this study examined trends over the period from 2002 to 2021 by analyzing POPs concentrations according to the mother's year of birth, adjusted for her age, and restricted the analysis to first-time mothers. The mothers' year of birth-based analysis reflects lifetime exposure and bioaccumulation of POPs, while the year of milk sampling-based analysis reflects more recent exposure of POPs to newborns (Quinn et al., 2011).

2. Material and methods

2.1. Recruitment and data collection

We utilized breast milk samples collected for two studies. Samples collected in 2002–2009 are from "The Norwegian Human Milk Study (HUMIS)" at the Norwegian Institute of Public Health. Whereas breast milk samples collected in 2020–2021, were part of the "Iodine project" at Innlandet Hospital Trust, Norway (Fig. 1).

2.1.1. Recruitment and data collection 2002–2009

In the population-based HUMIS birth-cohort, mother and child pairs were consecutively recruited shortly after birth by health visitors or by a medical doctor (Østfold County, Norway). Participating mothers were sent containers for milk and a questionnaire, except for Østfold County where containers and questionnaires were handed out to the mothers while in the hospital. They were asked to collect 25 ml every morning by hand on eight consecutive days, totaling 200 ml, before the child was 2 months of age, however, milk collected otherwise was also accepted and for more details we refer to earlier publications from this study (Eggesbø et al., 2011). The containers were thoroughly washed using 1 L of Extran® MA 01 (Merck) in 30 L of water, then rinsed with distilled water and dried in a 70 °C heating cabinet. The absence of toxicants in the containers' empty and washed state was checked. Containers were posted by regular mail and stored at −20 °C in a Biobank of the Norwegian Institute of Public Health upon arrival.

Information on health outcomes were obtained by questionnaires sent to all the families when the child was 1, 6, 12 and 24 months and in a subset also at 12 years of age. The recruitment started in 2002 and 2606 mother/child pairs were recruited. The recruitment took place in six counties in Norway, which represent northern, southern, western, and eastern parts of Norway including both coastal and inland areas (Rogaland, Telemark, Troms, Østfold, Oppland and Akershus).

2.1.2. Recruitment and data collection 2020–2021

In 2020–2021, breast milk samples from women with infants aged up to two years in Innlandet County, Norway, were recruited from public healthcare clinics in 30 different municipalities. The frequency of recruitment from any given municipality was based on their birth rates in 2019. Nurses were briefed on standardized recruitment protocols and supplied with the requisite instruments. A detailed description of the recruitment methodology is available in another publication (Aarsland et al., 2023).

Mothers were provided with a 50 mL polypropylene (PP) centrifuge tube (Sarstedt, Nümbrecht, Germany) for the collection of breast milk samples. Instructions were issued to store these samples in a domestic refrigerator before bringing them to the healthcare facility. Upon delivery, the samples were maintained at a refrigerated temperature of 4 °C before they were allocated into 5- and 10-mL PP centrifuge tubes (Sarstedt, Nümbrecht, Germany) and relocated for long-term storage at a temperature of −80 °C. From the 355 samples collected, 120 were randomly selected for POPs analyses. A total of 513 nullipara mothers contributed, 467 between 2002 and 2009 (HUMIS) and 46 between 2020 and 2021 (Iodine Study).

2.2. Chemical analysis of POPs in breast milk samples from HUMIS, 2002–2009

Throughout the HUMIS study, breast milk samples have been analyzed for different POPs. These analyses were performed across three specialized laboratories, each following standardized methods as described in their respective detailed publications, see below.

The Norwegian Institute of Public Health utilized solid-phase extraction and gas chromatography-mass spectrometry (GC-MS) with negative chemical ionization to determine the concentrations of organochlorine pesticides (OCPs), PCBs, and brominated flame

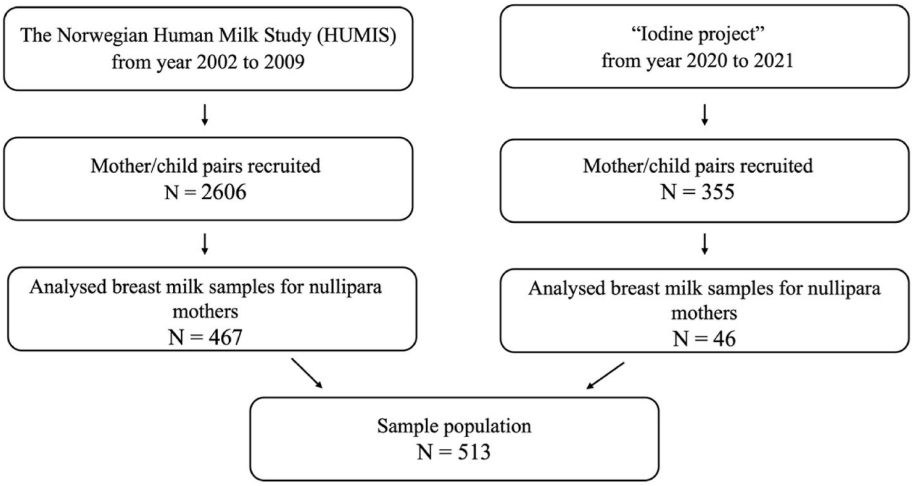

Fig. 1. An overview of the sample population. This figure provides an overview of the breast milk samples collected during the HUMIS Study (2002–2009) and the Iodine Project (2020–2021).

retardants (BFRs), following protocols detailed by Thomsen et al., 2007, 2010 and Forns et al. (2016).

The Research Centre for Toxic Compounds in the Environment at Masaryk University in the Czech Republic implemented a comprehensive analysis protocol for PCBs, and OCPs, involving freeze-drying, pressurized solvent extraction, and high-resolution GC-MS, as described by Čechová et al. (Čechová et al., 2017a; Čechová et al., 2017b).

The Norwegian University of Life Sciences conducted analyses on additional samples, employing liquid-liquid extraction, gravimetric lipid determination, and sulfuric acid clean-up, as outlined by Polder et al. (2008).

Each laboratory employed quality control measures such as procedural blanks, recovery rates, and internal standards to ensure the accuracy and reliability of their measurements. The laboratories also participated in interlaboratory comparison studies to validate their methods against consensus values, as detailed in the respective references.

2.3. *Chemical analysis of POPs in breast milk samples from the Iodine study, 2020–2021*

All chemical assays were performed at the Environmental Toxicology Laboratory of the Norwegian University of Life Sciences, situated in Ås, Norway. This facility is certified for the analytical evaluation of chemicals in biological matrices, adhering to the NS-EN ISO/IEC 17025 standard (TEST 137).

The protocol for sample preparation and chemical assessment was derived from an initial methodology outlined by Brevik et al. (Brevik, 1978), and subsequently modified by Polder et al. (2014). The laboratory utilized liquid-liquid extraction, gravimetric lipid determination, and sulfuric acid clean-up, followed by GC-MS analyses adhering to methodologies previously delineated by Mwakalapa et al. (2018) and Polder et al. (2014).

2.3.1. *Quality assurance and quality control measures*

In each batch of analyses, the inclusion of quality control samples was mandatory, comprising one unspiked sample and two spiked recovery samples using cow's milk as the matrix, a single specimen of the lab's internal reference standard derived from harp seal blubber (*Pagophilus groenlandicus*), and three procedural blanks containing internal standards and solvent only. Analyte levels detected in blank samples were averaged and subtracted from the test samples in the corresponding batch. Low blank levels were detected for PCBs −28, −118, −153, and −180, and the BDEs on the order of .01–.09 ng/mL, while PCB-138 blank levels were on the order of .10–.30 ng/mL. Both recovery and internal standard results were subjected to pre-approval prior to the analytical sequence and were continuously monitored to discern temporal trends in performance metrics. During gas chromatographic runs, a reference standard was intermittently reanalyzed at approximately every tenth sample interval to oversee any potential retention time shifts. Additionally, for each analyte subjected to mass spectrometric quantification, one qualifier ion was designated to authenticate the correct peak selection. The laboratory sustains its accreditation through annual participation in interlaboratory proficiency assessments, which include Quasimeme and Arctic Monitoring and Assessment Programme (AMAP) schemes, as well as through routine evaluation of an assortment of certified reference materials (CRMs).

Limits of detection (LOD) for individual analytes were defined as three times the noise level of each analyte, and limits of quantification (LOQ) were defined as ten times the noise level. The LODs in ng/g (wet weight, ww) for each group of analytes were as follows: β-HCH = .003, p,p'-DDE = .046, p,p'-DDT = .025, PCB-28 = .004, PCB-101 = .025, PCB-114 = .003, and the remaining PCBs = .002, BDE-28 and -154 = .006, BDE-47 = .008, BDE-99 = .021, BDE-100 and -153 = .009 and BDE-183 = .025.

2.4. *Statistical analysis*

Concentrations of the POPs were presented in ng/g lipid weight (lw) as mean, minimum, 5th, 50th, and 95th percentiles, maximum, and percentage of the LOD (Table A.2). Samples with concentrations under the LOD were assigned a value of half the lowest detected value. Quantile regressions for the 5th, 50th, and 95th percentiles with maternal year of birth and maternal age as the independent variables, and margin predictions, were performed. The margins are represented as lines with 95% confidence intervals (Graph 1a–d). Quantile regressions and margin predictions for individual substances are shown in Graph A.1a-i. The change in PCBs OCPs, BDEs, and total POPs concentration are shown graphically with the median concentration of each component stacked by maternal year of birth (Graph 2a–d). The outcome variables were logarithmically transformed before using generalized linear model regression (GLM) to explore associations between concentrations of POPs and maternal year of birth, age, change in BMI (differences between BMI at sample delivery and pre-pregnancy BMI), and fatty fish intake. Multicollinearity was assessed by estimating the variance inflation factors (VIFs) and correlation matrices, revealing no evidence of multicollinearity among the independent variables in the regression model. Results are shown as percentage (%) change in mean concentration with 95% confidence intervals for both crude and adjusted models. The data were analyzed using STATA 17.0 software (StataCorp, College Station, TX, 2023).

2.5. Outcome variables

$\sum_6$PCBs (PCB-28, -101, −118, −138, −153, and −180), β-HCH, $\sum_2$DDTs (p,p'-DDE, and p,p'-DDT), and $\sum_6$BDEs (BDE-28, -47, −99, −100, −153, and −154).

Main exposure – Maternal year of birth.

Covariates: Information on maternal age (in years), BMI (kg/m^2): difference in BMI is one unit change in BMI at sample delivery from pre-pregnancy BMI, and fatty fish intake (number of meals/week) was derived from maternal reports. Smoking status was planned as a covariant. However, BMI and smoking status are not independent of each other. The difference in BMI and fatty fish intake was originally included in quantile regressions and margin prediction. However, these variables had lots of missing observations and were not associated with the outcome. General demographic characteristics are summarized in Table 1. The Norwegian education system mandates 10 years of compulsory education. However, most youths complete an additional 2–3 years of complimentary education before electing to pursue higher education.

2.6. Ethical consideration

This study adheres to the guidelines set out in the Declaration of Helsinki. The HUMIS study was approved by the Norwegian Data Inspectorate (ref. 2002/1398), and Regional Ethics Committee for Medical Research (ref. S-02122). Human milk samples from 2020 to 2021 have received approval from the Norwegian Regional Committees for Medical and Health Research Ethics (REC South-East C) with reference number 26762.

Table 1
General demographic characteristics of participating mothers and infants. N = 513.

	n	n (%)
Maternal age (years)	513	27.6 (4.4)
16–24		136 (25.2)
25–29		259 (48.0)
30–34		107 (19.8)
34–42		38 (7.0)
Nullipara	513	513 (100)
Maternal year of birth	509	
>1970		33 (6.5)
1970–1974		106 (20.8)
1975–1979		198 (38.9)
1980–1984		108 (21.2)
1985–1989		22 (4.3)
1990–1994		29 (5.7)
1995–2002		13 (2.6)
Maternal BMI at sample time (kg/m^2)	513	
<18.5 (underweight)		10 (1.9)
18.5–24.9 (normal weight)		207 (40.4)
25–29.9 (overweight)		127 (24.8)
>30 (obese)		169 (32.9)
Prepregnancy BMI (kg/m^2)	513	
<18.5 (underweight)		26 (5.1)
18.5–24.9 (normal weight)		303 (59.1)
25–29.9 (overweight)		122 (23.8)
>30 (obese)		62 (12.1)
Smoking status, No smoking		320 (62.5)
Maternal education level	512	
<12 years		36 (7.0)
12 years		62 (12.1)
>12 years		414 (80.9)
Child's sex, male		297 (58.1)
Child's age when sample was collected	429	
<3 weeks		43 (10.0)
>3–6 weeks		232 (54.1)
>6–9 weeks		91 (21.2)
>9 weeks–3 months		32 (7.5)
>3 months		31 (7.2)

BMI: Body mass index.

3. Results

In total, 513 mothers were included in this analysis. The average maternal age at birth was 27.6 years (Table 1), with the lowest average age being 21.9 years for mothers born between 1990 and 1994, and the highest average age of 36.7 years for mothers born before 1970 (Table A.1). More than 60% of the mothers reported never smoking, with the highest percentage (96.6%) observed among mothers born between 1990 and 1994, and the lowest (45.5%) among mothers born before 1970 and between 1985 and 1989. Breast milk samples were collected within 0–1 year after birth, with most samples collected between 3 and 6 weeks postpartum.

In the cohort of 513 participants (Table 1), 100% exhibited detectable levels of $\sum_6$PCBs. This was followed by 99.6% with detectable levels of $\sum_2$DDTs, and 97.5% and 96.3% having detectable levels of β-HCH and $\sum_6$BDEs, respectively (Table A.1). The highest median concentration was observed for $\sum_6$PCBs at 74.8 ng/g lipid weight (lw), with the 5th and 95th percentiles being 24.2 ng/g lw and 160.5 ng/g lw, respectively. However, $\sum_2$DDTs displayed the greatest variation, with the 5th to 95th percentiles ranging from 15.7 ng/g lw to 162.7 ng/g lw, and a maximum concentration measured at 1295.6 ng/g lw. Concentrations for each category of maternal year of birth are shown in Tables A.3a–g.

Temporal trend analyses revealed a consistent reduction in concentrations depending on the year of birth and adjusted for maternal age (Graphs 2a–d). The highest decrease was for β-HCH adjusted for maternal age (−17.1%, 95% CI -18.7%, −15.4%), indicating a reduction in the mean concentration by 17.1% for each year increase in the maternal year of birth. For $\sum_6$BDEs, the GLM reveals a 9.1% decrease in the mean concentration for each increase in year of birth (−9.1%, 95% CI -10.5%, −7.7%), while $\sum_6$PCBs and $\sum_2$DDTs show mean reductions of 7.1% (95% CI -7.7%, −6.5%) and 7.0% (95% CI -8.0%, −6.0%), respectively for each increase in year of birth.

An upward trend in the predicted 95th percentile was observed for the mothers born in 1990–1994 compared to the mothers born in 1995–2002 for $\sum_6$PCBs, $\sum_2$DDTs, and $\sum_6$BDEs (Fig. 2a–c). Similarly, the unadjusted median concentrations for β-HCH, $\sum_2$DDTs (Fig. 3a and b), and $\sum_6$BDEs (Fig. 3c) also showed an increase from the mothers born in 1990–1994 to those born in 1995–2002 (Tables A.3a–f) (see Fig. 3d).

The regression analyses revealed significant associations between maternal characteristics and concentrations of POPs in our study (Table 2). Specifically, the maternal year of birth was inversely related to POP concentrations across all categories. For each additional year in maternal year of birth, there was a notable reduction in the concentrations of $\sum_6$PCBs, β-HCH, $\sum_2$DDTs, and $\sum_6$BDEs. The adjusted regression models showed a decrease in the concentration of $\sum_6$PCBs by 7.3% (95% CI: -8.1% to -6.5%) and by 7.2% (95% CI: -8.5% to -5.8%) for $\sum_2$DDTs. Similarly, concentrations of β-HCH and $\sum_6$BDEs decreased by 15.0% (95% CI: -17.0% to -13.0%) and 8.6% (95% CI: -10.3% to -6.8%), respectively. Maternal year of birth also has the highest beta coefficient (beta: .59–.86), indicating the strongest influence on the change in concentration in the adjusted models.

Additionally, maternal age showed a complex relationship with POP concentrations. Crude regression analyses suggested that older maternal age was associated with higher concentrations of $\sum_6$PCBs and β-HCH. However, after adjusting for other variables, the analyses revealed the opposite trend. Specifically, a decrease in the concentration of $\sum_6$PCBs (-2.8%, 95% CI: -4.0% to -1.6%), β-HCH (-10.1%, 95% CI: -13.1% to -7.0%), and $\sum_6$BDEs (-7.3%, 95% CI: -9.8% to -4.7%) with each year increase of maternal age.

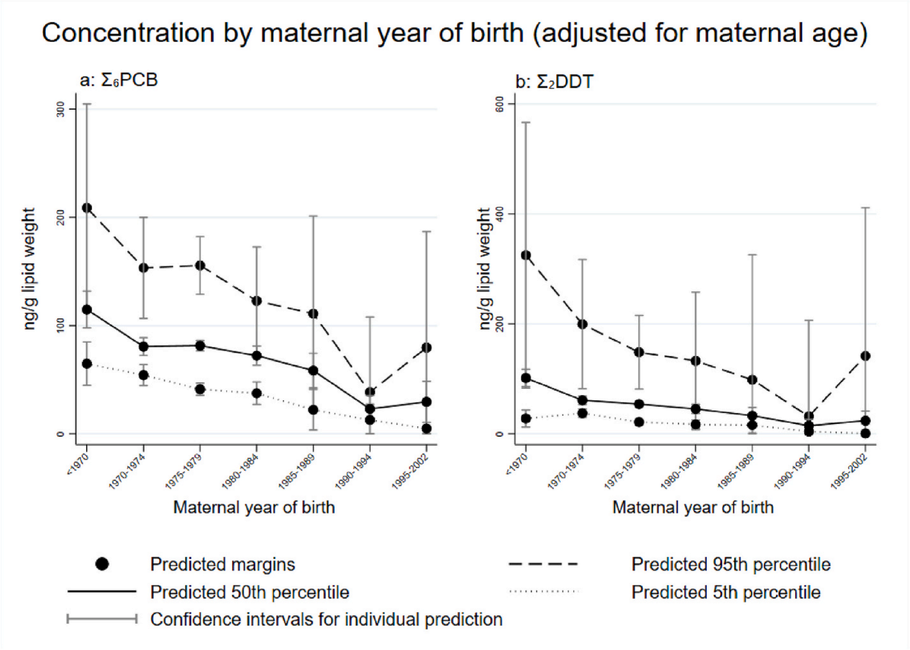

Fig. 2a. Concentration of PCBs and DDTs in human milk among 513 first-time mothers. Estimated margins for 5th- (Dotted line), 50th- (Straight line) and 95th- (Dashed line) percentile of a) $\sum_6$PCBs (polychlorinated biphenyls; PCB-28, -101, −118, −138, −153) concentration in ng/g lipid weight (lw); and b) $\sum_2$DDTs (*p,p'- dichlorodiphenyldichloroethylen* and *p,p'- dichlorodiphenyltrichloroethane*) concentration in ng/g lw.

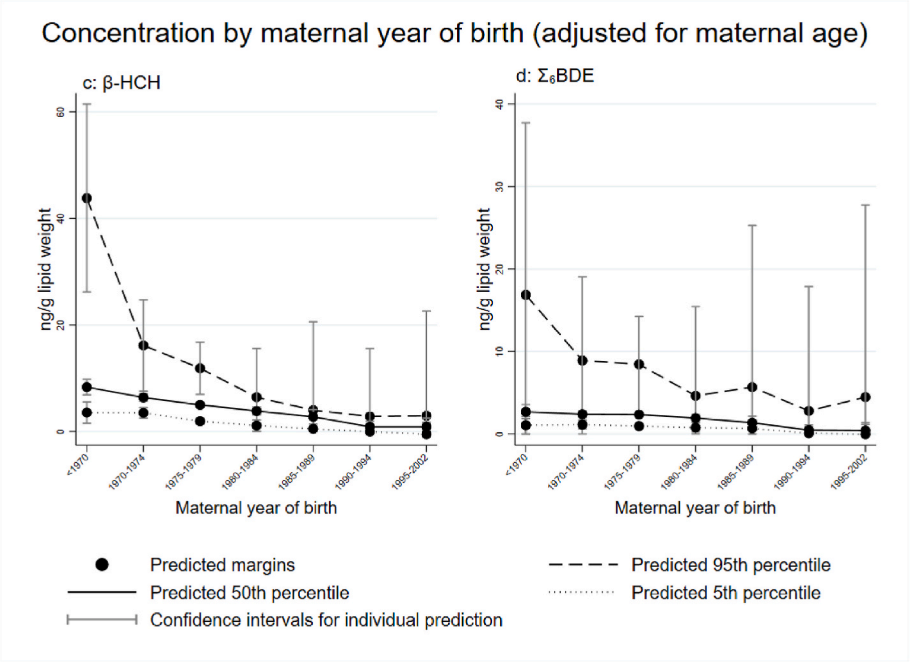

Fig. 2b. Concentration of PCBs and DDTs in human milk among 513 first-time mothers. Estimated margins for 5th- (Dotted line), 50th- (Straight line), and 95th- (Dashed line) percentile of c) β-HCH (hexachlorocyclohexane) concentration in ng/g lipid weight (lw), and d) $\sum_6$BDE (brominated diphenyl ether; BDE-28, -47, −99, −100, −153, and −154) concentration in ng/g lw.

The maternal change in BMI from pre-pregnancy to after birth (difference in BMI), and fatty fish intake (an increase of one fatty fish meal per week), were examined in relation to POP concentrations. In the adjusted model, we found that low weight loss after birth, was associated with a decrease in all POP categories, ranging from -2.6% to -3.5%. However, only $\sum_6$PCBs demonstrated a statistically significant reduction (-3.5%, 95% CI: -5.8 to -1.3). Furthermore, each additional fatty fish meal consumed per week was associated with increased concentrations of $\sum_6$PCBs, β-HCH, and $\sum_2$DDTs in the adjusted model. Although only the association with $\sum_6$PCBs (13.4%, 95% CI: 6.0% to 21.4%) reached significance. In contrast, both the adjusted and crude models indicated a significant reduction in $\sum_6$BDEs for each additional fatty fish meal consumed per week.

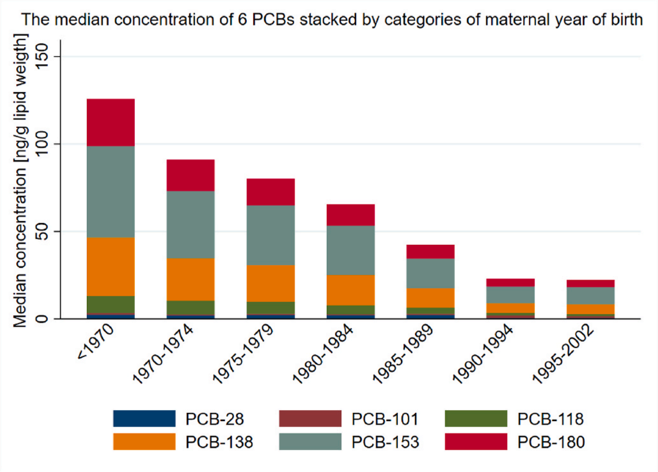

Fig. 3a. Median concentration (ng/g lipid weight) of 6 PCBs (polychlorinated biphenyls; PCB-28, -101, −118, −138, −153) stacked by maternal year of birth category.

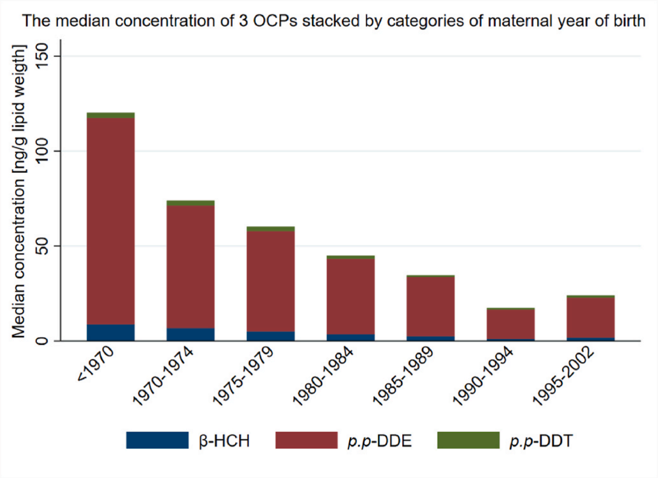

Fig. 3b. Median concentration (ng/g lipid weight) of 3 OCPs (Organochlorine pesticides): β-HCH (hexachlorocyclohexane), *p.p*-DDE (*p,p'*- dichlorodiphenyldichloroethylen) and *p.p*-DDT (*p,p'*- dichlorodiphenyltrichloroethane) stacked by maternal year of birth category.

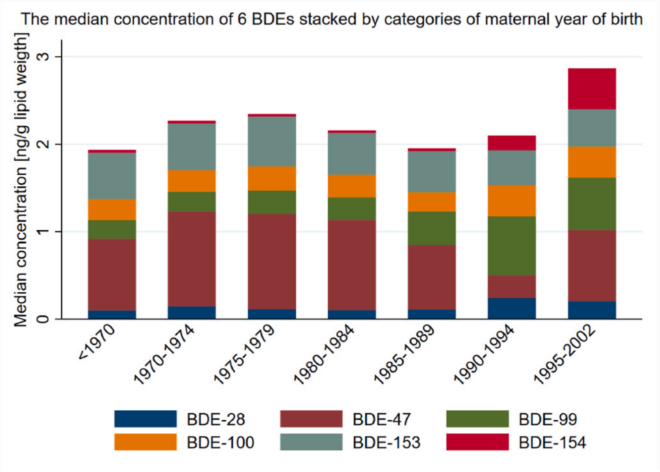

Fig. 3c. Median concentration (ng/g lipid weight) of 6 BDEs (brominated diphenyl ether; BDE-28, -47, −99, −100, −153 and −154) stacked by maternal year of birth category.

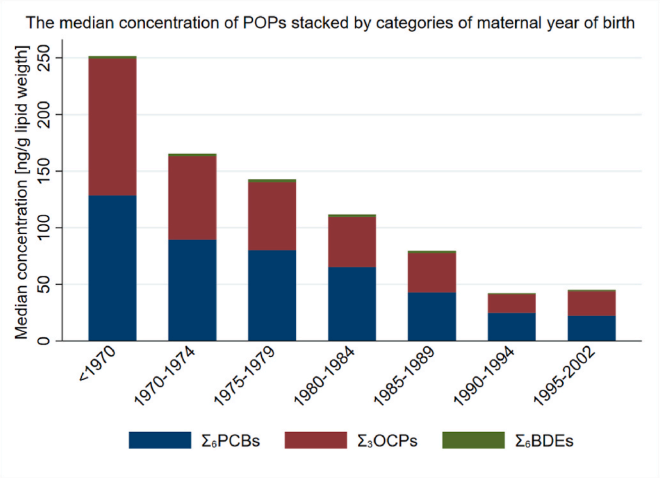

Fig. 3d. Median concentration (ng/g lipid weight) of all investigated POP (Persistent organic pollution; 6 PCBs (polychlorinated biphenyls; PCB-28, -101, −118, −138, −153), 3 OCPs (Organochlorine pesticides): β-HCH (hexachlorocyclohexane), *p.p*-DDE (*p,p'*- dichlorodiphenyldichloroethylen) and *p.p*-DDT (*p,p'*- dichlorodiphenyltrichloroethane), and 6 BDEs (brominated diphenyl ether; BDE-28, -47, −99, −100, −153 and −154) stacked by maternal year of birth category.

4. Discussion

The temporal trend analyses revealed consistent reductions in concentrations by maternal year of birth, adjusted for maternal age, with β-HCH demonstrating the most pronounced decrease, followed closely by $\sum_6$BDEs, $\sum_6$PCBs and $\sum_2$DDTs. However, an upward trend in the predicted 95th percentile was observed for mothers born in 1990–1994 to those born in 1995–2002.

The findings from our study corroborate the downward trends observed in other regions and countries (van den Berg et al., 2017). This global decrease can be largely attributed to the concerted efforts of national and international regulations, notably the Stockholm Convention, which has significantly limited the production, use, and release of POPs (Stockholm Convention). In Sweden, the ongoing biomonitoring programs have similarly documented reductions in dietary intakes of various POPs between 1996 and 2017 (Gyllenhammar et al., 2021). In the Swedish study, when adjusted for maternal age, BMI difference, and education, the greatest annual decrease in Swedish breast milk was observed for β-HCH (−10%), followed by $\sum_4$BDEs (BDE-47, -99, −100 and −153) and $\sum_8$PCBs (PCB-28, -105, −118, −138, −153,- 165, −167 and −180), which decreased by 7.4% and 6%, respectively. Notably, the decrease in $\sum_2$DDTs (*p,p'*-DDT and *p,p'*-DDE), recorded at 8.7%, was more pronounced than the decline observed in our findings. Furthermore, they found an average increase in BDE-209 concentrations by 4.7% each year, which contrasts with the decreasing trend observed in other studies. Studies from Canada and Croatia align with the global decrease pattern, demonstrating the decline of POPs in human breast milk, indicative of successful regulatory interventions (Krauthacker et al., 2009; Rawn et al., 2017). In the Croatian study, they found that the concentrations of β-HCH and *p,p'*-DDE in breast milk decreased by 60% or more (β-HCH: 280–40 ng/g lw and *p,p'*-DDE: 1900–620 ng/g lw) between 1981 and 1989. While the decrease between 1989 and 2003 was lower (β-HCH: 40–20 ng/g lw and *p,p'*-DDE: 400–257 ng/g lw). This slowdown in the reduction rates was attributed to the already low levels, where only some samples had median concentrations above the determination limit.

The observed increase of POPs in the 95th percentile of mothers born

Table 2

Impact of maternal factors on concentrations of persistent organic pollutant (POP) in breast milk. Crude and adjusted estimates are presented as % change in mean concentration with 95% confidence intervals. N = 513.

$\sum_6$PCBs			
	Crude % (95% CI)	Adjusted % (95% CI)	Beta
Maternal year of birth	−6.0 (−6.5, −5.5)	−7.3 (−8.1, −6.5)	.86
Maternal age (years)	4.7 (3.7, 5.8)	−2.8 (−4.0, −1.6)	.23
Fatty fish intake (1/week)	15.9 (6.9, 25.7)	13.4 (6.0, 21.4)	.13
Difference in BMI*	−1.4 (−4.7, 1.9)	−3.5 (−5.8, −1.3)	.11
$\sum_2$DDTs			
	Crude % (95% CI)	Adjusted % (95% CI)	Beta
Maternal year of birth	−6.5 (−7.2, −5.7)	−7.2 (−8.5, −5.8)	.61
Maternal age (years)	6.0 (4.6, 7.4)	−1.0 (−3.0, 1.1)	.06
Fatty fish intake (1/week)	10.6 (−1.3, 24.0)	6.8 (−4.6, 19.5)	.05
Difference in BMI*	−.7 (−5.0, 3.8)	−2.6 (−6.3, 1.2)	.06
β-HCH			
	Crude % (95% CI)	Adjusted % (95% CI)	Beta
Maternal year of birth	−12.3 (−13.6, −10.9)	−15.0 (−17.0, −13.0)	.79
Maternal age (years)	6.4 (3.5, 9.3)	−10.1 (−13.1, −7)	.36
Fatty fish intake (1/week)	12.7 (−6.2, 35.4)	14.7 (−4.7, 38.2)	.06
Difference in BMI*	1.4 (−7.4, 11.1)	−3.5 (−9.4, 2.9)	.05
$\sum_6$BDEs			
	Crude % (95% CI)	Adjusted % (95% CI)	Beta
Maternal year of birth	−4.8 (−5.9, −3.6)	−8.6 (−10.3, −6.8)	.59
Maternal age (years)	−.8 (−2.6, 1.1)	−7.3 (−9.8, −4.7)	.35
Fatty fish intake (1/week)	−15.6 (−26.9, −2.5)	−16.4 (−28.3, −2.7)	.11
Difference in BMI*	.8 (−4.7, 6.7)	−3.4 (−8.3, 1.9)	.06

BMI = Body mass index; $\sum_6$PCBs (polychlorinated biphenyls) = PCB-28, -101, −118, −138, and −180; $\sum_2$DDTs = sum concentration off *p.p*'-DDE and *p.p*'-DDT; β-HCH = beta-hexachlorocyclohexane; $\sum_6$BDEs (brominated diphenyl ether) = BDE-28, -47, −99, −100, −153 and −154; CI = confidence interval. * Per one unit change in BMI at sample delivery from pre-pregnancy BMI; Beta are standardized regression coefficients that denote the relative influence of the independent variables on the dependent variables in the adjusted models.

in 1990–1994 and those born in 1995–2002 indicate a deviation from the overall declining trend reported in our and other studies. This warrants a closer examination of underlying factors that could contribute to this deviating pattern. A possible explanation may be that immigration can introduce significant variability in POP exposure and accumulation as immigrants may come from regions with different environmental regulations, industrial practices, and usage histories of POPs (Skaare et al., 1988). This hypothesis would correspond with previous studies reporting significant disparities in POPs concentrations between ethnic Norwegian and non-Norwegian women (Lenters et al., 2019). For example, countries that have continued to use DDT for malaria control may have populations with higher baseline exposures to this compound (Bouwman et al., 2011; Tren and Roberts, 2010; van den Berg et al., 2017; Wassie et al., 2012). If non-Norwegian women form a substantial proportion of the study cohort, their inclusion could skew the higher percentile concentrations upwards. Unfortunately, maternal country of origin was not fully collected in the current study and was therefore not adjusted for.

Even though we found a decrease in the mean concentration of $\sum_6$BDEs for each successive year of maternal birth, the increase in median concentrations in milk samples from those born in 1990–1994 to those born in 1995–2002 suggested an increasing trend (Fig. 2b). Dietary sources, particularly fatty fish, have been identified as the primary contributors also to BDEs intake due to their high lipid content (Chain, 2011). However, in contrast to the findings for the other POPs, both adjusted and crude models indicated a significant reduction in $\sum_6$BDEs for each fatty fish meal consumed per week. Historical data reveal high levels of BDEs in fish from Lake Mjøsa, likely due to industrial emissions near Lillehammer (Berg et al., 2013). The BDE concentrations reported by Berg et al. are among the highest recorded in biological samples. Furthermore, a study from 2008 showed that the concentration of $\sum_4$BDEs (BDE-28, -47, −99, and −100) in passive air samples from the area around Mjøsa, was more than 3 times higher compared to the air sample from Oslo (Mariussen et al., 2008). Thus, industrial emissions may indirectly influence the increase in BDE levels that we observed as 83% of the mothers born in 1990–1994 and 85% of those born in 1995–2002 were living in this region.

The regression analysis in the current study reveals that the maternal year of birth variable (with the highest beta coefficient (beta: .59–.86)) has the greatest impact on POPs concentrations in breast milk, more so than any of the other variables. While our study found that maternal year of birth was a significant predictor of POP concentrations, our literature search did not reveal other studies with the same focus, as the prevailing research tends to concentrate more on the year of sample collection. In line with current literature, we found that a higher BMI difference (indicating less weight loss after pregnancy) is associated with lower concentrations (2.5–3.5% decrease) of all POPs in breast milk (Gyllenhammar et al., 2017). Furthermore, each additional fatty fish meal consumed per week was associated with increased concentrations of $\sum_6$PCBs, β-HCH, and $\sum_2$DDTs, with only the association with $\sum_6$PCBs reaching statistical significance (McGraw and Waller, 2009; Pavuk et al., 2014). Conversely, the concentration of BDEs appears to decrease with additional fatty fish intake.

The strengths of our study are the robust design and comprehensive temporal span, which covers nearly two decades of data on POP concentrations in breast milk. The large sample size of 513 mothers enhances the statistical power and generalizability of our findings within the Norwegian population. Moreover, the chemical analysis conducted across specialized laboratories, adhering to quality control measures, ensures the reliability of our data.

Our study also has some limitations that warrant consideration. The samples were collected at different infant ages and did not follow a set protocol. This may have introduced measurement error, however, as this is a random error we expect that this has biased our estimates towards zero. The increase in the 95th percentile concentrations of POPs between the mother born in 1990–1994 and those born in 1995–2002 might be influenced by demographic changes, including immigration, that were not fully accounted for in our analysis. Additionally, while we have accounted for several confounding variables, there may be other unmeasured factors influencing concentrations of POPs. Further, the reliance on self-reported data for certain variables, such as fish intake, is susceptible to reporting biases. Lastly, despite rigorous quality assurance procedures, variations in analytical methods over time and between laboratories could contribute to inconsistencies in the measurement of POP concentrations.

5. Conclusion

Our study underscores a consistent decline in concentrations of POPs in breast milk, aligning with global trends observed in other regions and countries. This decline is largely attributed to national and international regulations. However, our analysis revealed an upward trend in the 95th percentile concentrations of POPs from mothers born in 1990–1994 to mothers born in 1995–2002. Moreover, while regression analysis suggests a decreasing trend in the mean concentration of $\sum_6$BDEs, the observed median concentrations for the youngest included mothers indicate a contrasting increase. Further investigation into potential exposure sources, such as dietary habits and environmental factors, is necessary to understand these trends fully.

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CRediT authorship contribution statement

Kristina R. Nermo: Writing – review & editing, Writing – original draft, Visualization, Validation, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Kjersti S. Bakken:** Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation. **Jan L. Lyche:** Writing – review & editing, Writing – original draft, Resources, Methodology, Investigation, Conceptualization. **Anuschka Polder:** Writing – review & editing, Writing – original draft, Validation, Methodology. **Aina Jansen:** Writing – review & editing, Writing – original draft, Supervision. **Siri Kaldenbach:** Writing – original draft, Resources, Investigation, Data curation, Conceptualization. **Gabrielle Haddad-Weiser:** Validation, Resources, Methodology, Investigation, Conceptualization. **Tor A. Strand:** Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Merete Å. Eggesbø:** Writing – review & editing, Writing – original draft, Validation, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

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.

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Appendix A. Supplementary data

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